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*本誌掲載の講演要旨のCOIについてはプログラム委員会ならびにコンプライアンス委員会の承認を得ている

会長講演 (Presidential Lecture)

産婦人科の未来に向けて～私の子宮体がん発生機構解明への挑戦～

For the future of Obstetrics and Gynecology

～My challenge to an elucidation of the endometrial cancer development～

九州大学 加藤 聖子

Kyushu University

KATO Kiyoko

産婦人科学はヒトの発生から老年期までを対象とした学問である。専門分野として周産期・生殖内分泌・婦人科腫瘍・女性ヘルスケアがあり、それぞれに様々な疾患があり、病態がある。生命倫理やリプロダクティブヘルス・ライツなどの社会医学も重要である。各分野の専門家が力を合わせて創り上げ躍進する「共創と飛翔」の学問であると考え。

時代の流れとともに概念、治療法も変化してきている。これらの変化に対応するためには継続的な研鑽と研究が必要である。私は医師になりたての頃、患者さんを診ていく中で、治療により救われる命とともに、失う命に伴う悲しみを知った。その経験から専門分野として婦人科腫瘍を選び、がん発生機構の解明の研究を始めた。

【1) RAS 遺伝子との出会い】

私が医師になった1980年代、がんは遺伝子の病気であるという概念が定着し、がん遺伝子・がん抑制遺伝子の研究が盛んになってきていた。幸運なことに主人に帯同して渡米し働き始めたのは、がん遺伝子RASをテーマとした研究室であった。そこで、一から分子生物学の手法を習い、KRAS蛋白の翻訳後修飾の研究を行い論文博士の学位が取得できた(Kato K et al. Proc Natl Proc Sci 1992)。自分の研究が将来、癌治療に役立つかもしれないという期待を感じ、研究の楽しさを知った。

【2) 子宮体癌の研究の開始】

帰国後も癌の基礎研究を続けたいと思い、別府

市の生体防御医学研究所に赴任した。何を研究テーマにするかを考える中で着目したのは子宮体癌である。生活様式の欧米化とともに子宮体癌の増加が報告されていた。子宮体癌は約8割がエストロゲン依存性であり、2～3割にKRAS遺伝子の変異が同定されている。まずはKRASシグナル経路とエストロゲン経路のクロストークの研究を行い、KRASはエストロゲンレセプター(ER)の発現と機能を亢進し、その経路にAP-1を介したMDM2の発現亢進・p53機能抑制が関与していることを明らかにした(Kato K et al. Oncogene 1997, J Bio Chem 2002)。本経路の阻害剤は子宮体癌の分子標的薬の候補になると考えられる。

【3) がん幹細胞研究】

子宮体がんにおいて高分化型早期の症例の予後は良いが、悪性度の高い組織型、進行期の症例は難治性となる。治療抵抗性のがんの克服ががん治療研究の課題である。治療抵抗性の要因として、がん組織に存在するがん幹細胞の存在が考えられている。幹細胞は自己複製能と多分化能を持つ細胞と定義されるが、最近、がん幹細胞には可塑性や多様性があること、周囲のがん微小環境と相互作用を持つことが報告され、多角的な治療戦略が必要である。私はこの癌幹細胞に着目し、Side-population(SP)細胞を分離する方法を用いて子宮体がん幹細胞の解析を始めた。子宮体がんのSP細胞は、自己複製能・長期増殖能の他に、間質細胞への分化や運動能の亢進を示すことを報告し、この性質が再発や転移に関与すると考えている

(Kato K et al. Am J Pathol 2010, Kusunoki S et al. Gynecol Oncol 2013). さらにマイクロアレイによる網羅的解析を行い SP 細胞は非 SP 細胞に比べ、炎症性サイトカインや増殖因子、間質形成に関与する遺伝子群の発現が増加し、TGF β を介した上皮間葉移行 (EMT) の経路や間質リモデリングの経路が亢進していることを明らかにした (Yusuf N et al. Gynecol Oncol 2014, Yoshida S et al. BMC Cancer 2021). これまでの結果より、がん幹細胞の重要な特徴は自己複製能と上皮間葉移行 (EMT) であり、EMT に関与する分子の中でも fibronectin, SPARC の発現の亢進が、がん幹細胞の運動能や浸潤能、周囲のがん関連線維芽細胞に関与していると考えている。SP 細胞は幹細胞研究の有効なツールではあるが、その割合は 1% 以下と少数であり継代培養や解析が難しい。この分画を増やすためいくつかの遺伝子導入を試みてきたが、がんや胚細胞のみに発現が報告されている YBX2 を子宮体癌細胞株に導入したところ (IK-YBX2 細胞株)、SP 細胞の分画が約 10 倍に増加することを明らかにした。この IK-YBX2 細胞株を用いてマイクロアレイ解析を行い YBX2 強制発現細胞に発現が亢進している遺伝子として cancer testis antigen の一つである CT45A5 を同定し、がん幹細胞形質や予後に関連することを報告した (Suzuki I et al. Sci Rep 2021)。ES 細胞では stemness に関与する遺伝子は脱メチル化され発現が亢進していることが報告されている。また、我々は網羅的なメチル化解析を行い、脱メチル化により発現が増加している遺伝子を網羅的に解析し、ERK の脱リン酸化酵素である DUSP6 を同定した。子宮体癌細胞における DUSP6 の機能を解析したところ、自己複製能に関与し、活性化型 RAS の下流のシグナルバランスを増殖優位の MAPK から細胞生存優位の AKT へ変化させていた。また予後不良因子であった (Kato M et al. Int J Cancer 2020)。これらの結果より、がん幹細胞の自己複製能は再発、EMT 誘導による運動能・浸潤能の亢進は転移に関与し予後不良の原因になることが考えられる。

【4】難治性がんに対する新規治療法開発の試み

癌細胞の周囲微小環境は多様性を持ち、がんの浸潤や治療抵抗性に関与することが報告されている。我々は、子宮体癌の SP 細胞は SPARC を高発現していること、SPARC 過剰発現子宮体癌細胞は、遊走能亢進や fibronectin の発現増加、マウスに間質に富んだ腫瘍を形成すること、臨床検体の解析では予後不良の組織型 (漿液性癌、明細胞癌) に発現が亢進していることを報告した (Yusuf N et al 2014)。更に SPARC は細胞外に分泌されること、癌細胞だけではなく周囲の正常線維芽細胞を CAF 様に変化させることを明らかにした (Yoshida S et al. BMC Cancer 2021)。SPARC はアルブミンと結合する性質を持つことを利用し、通常の抗がん剤は SPARC 高発現子宮体癌細胞の増殖を抑制しないが、アルブミン結合抗がん剤は細胞増殖を抑制し、マウスの腫瘍形成能も抑制することを明らかにした。予後不良の組織型 (漿液性癌、明細胞癌) の治療法に応用できると考えられる。

【5】産婦人科の未来に向けて

長年、がん研究に取り組んできたが、私の子宮体癌発生機構の解明への挑戦はまだ道半ばである。がん細胞の持つ多様性が大きな壁である。遺伝子変異をシークエンスにより同定し、遺伝子を細胞に導入し、その性質を解析するという実験を繰り返してきたが、今は次世代シークエンス、3次元培養、単一細胞解析など新しい技術が次々に登場し多くの知見が得られる時代になった。今後とも次々と研究手法は進歩していくであろう。最初は私一人で始めた子宮体癌の研究であったが、その後は九州大学や順天堂大学の大学院生が取り組んでくれた。これまでご指導いただいた先生、一緒に研究してくれた仲間達に感謝する。今後、新しい発見により少しでもがん発生機構の解明に近づき、患者さんの予後を改善する治療法の開発が進むことを願う。

There are the four fields in Obstetrics and Gynecology, which are perinatal medicine, gynecologic oncology, reproductive endocrinology and women' healthcare. These are each deeply related and we treat and support the women during the whole life-stage. Since 1989, I have continued to basic research to an elucidation of the endometrial cancer development as well as clinical works. In this lecture, I would like to introduce my studies. I started my research in USA in 1989. I studied the post-translational modification of RAS protein. This experience was the very exciting for me and I would like to continue the basic research. After coming back to Japan, I investigated the crosstalk between RAS signal pathway and Estrogen receptor (ER) signal pathway.

We demonstrated that activated RAS protein enhanced the expression and functions of ER via MDM2/P53 pathway. Next, I performed the research of Cancer Stem-like Cells (CSCs) of endometrial cancer using side population cells (SP cells). We demonstrated that SP cells of endometrial cancer cells had a self-renewal and a long-term proliferation activity and a differentiation potential to both tumor cells and stromal cells and showed EMT. We have identified several important genes in regulating endometrial CSC phenotypes, which are DUSP6, YBX2, CT45 A5 and SPARC. These genes might be the candidates of the CSCs' markers and the therapeutic targets in the future.

特別講演

近未来の〈子づくり〉を考える—不妊治療から生殖技術へ

東京都立墨東病院 久 具 宏 司

特別講演

2020年の日本の出生児数は840,832人であった。2010年の1,071,305人から、10年間で21.5%減少したことになる。合計特殊出生率は2005年に1.26と最低水準を記録した後は2015年に1.45と持ち直したが再び下降に転じ、2020年には1.34と、前年から0.02ポイント下がった。1970年代から1980年代にかけての出生児数の急激な減少による産む世代の女性の人口減少に起因する、2005年以降の出生率の見せかけの上昇が終わり、今後の出生児数は加速度的に減少していくと予測される。男女ともに進む晩婚化と非婚化、さらに結婚した後も子をもうけるまでの期間が年々長期化しており、その結果晩産化がますます進行している。日本女性の第1子出産平均年齢は、2020年には30.7歳であり、2010年から0.8歳上昇した。これらの晩産化、その結果としての少子化は、先進国共通の課題となっている。

このような社会情勢の中、「生殖医療」に寄せられる期待は大きい。2020年12月、民法に特例が定められ、提供配偶子を用いた妊娠で生まれた子どもの親子関係が明確になった。日本でも今後卵子提供妊娠が増加するかもしれない。しかしながら、この特例は第三者から配偶子が提供された場合の法的親子関係を定立させたに過ぎず、特例法の施行をもって配偶子提供の実施が自由に行えるようになったということではない。精子提供にせよ卵子提供にせよ、生まれた子どもの遺伝上の親を知る権利の保証とその実行についての議論がまだまだ不十分である。卵子提供の場合は、提供を受ける女性をどのように診断するかも大きな課題である。

しかしそもそも、年齢が上昇した後に否応なく選択する卵子提供よりも、より若年の女性を対象とした卵子凍結保存こそが晩産化社会における最善の解決策として、あらゆる方面から大きな期待が寄せられることになるであろう。今後ますます女性の活躍が期待される社会を迎え、女性本人の若い時期の卵子の凍結保存は、女性個人と女性活躍の場となる組織の両者にとって、ウィンウィン関係を形作る手段と言えるであろう。しかし、これはもはや従来産婦人科医が手掛けてきた不妊カップルに対する「不妊治療」とは、趣旨が異なる。一見、現代の行き詰った社会と追い詰められた女性にとって、風穴を開ける技術のように見えるが、どこかに陥穽(落とし穴)がないだろうか。妊娠して子どもをつくる女性個人についてみると、卵子凍結保存の駆使により希望どおりの人生設計への道が開かれることになり、同時に女性を雇用する組織も効率的な人事運用が可能となる。しかし、社会全体を俯瞰した場合に、晩産化が進行することを前提にした対応策の構築でよいのか、より広い視野に立って考えてみる必要がある。さらに、凍結保存された配偶子はどのように守られるべきなのか、また、その保存される期限はどのように設定されるのか、このような議論は未だ緒に就いてすらいない。

本講演では、卵子凍結保存が広く普及した時に社会にもたらされる変容を予想するとともに、卵子提供、卵子凍結保存が医療として内包する問題点を提起し、「生殖医療」の在り方を考察する。際限なく広がる生殖補助技術を前に、ふと足を止めて客観視するアンチテーゼである。

Special Lecture

Child-making in the near future - From infertility treatment to reproductive technology

KUGU Koji

Tokyo Metropolitan Bokutoh Hospital

The number of live birth in Japan has been continuously decreasing through decades. Total fertility rate in Japan in 2020 is 1.34, which is one of the lowest levels in all countries. The marriage age is getting higher in both men and women. The rate of men or women who have not married is also increasing. Moreover, the period from marriage to first child-bearing is getting longer year by year. Together with these trends, the average age of women's child-bearing is getting higher and higher through decades reaching to 30.7 years of age in 2020. These tendencies are common among many advanced countries. Under the situation of increasing age of child-bearing, reproductive technology is expected to play an important role in giving babies to women of advanced age. The two principal measures of the technology are oocyte donation and cryopreservation of oocyte. Oocyte cryopreservation particularly keeps the focus of the women's attention since women can use their own oocyte through this method. Oocyte cryopreservation is a feasible method for not only women themselves but also companies employing women. Women can work continuously and develop their careers in such companies without interruption caused by pregnancy, nursing their kids or receiving education. Moreover, such companies can not only make the most of women's activity

but also impress the public by the company's principle of allowing women to continue their careers. Consequently oocyte cryopreservation is likely to be accepted to present society. However, cryopreservation of one's own oocyte may accelerate the increase of child-bearing age, which is a serious pitfall. Progressive increase of the age of child-bearing may induce serious decline of population and hollowing of working-age population, both of which may induce economic shrinkage. We should give a serious consideration about the promotion of oocyte cryopreservation. As for oocyte donation, there are several issues to be considered and solved before introduction to clinical practice. The propriety and method of informing the hereditary origin to the offspring are the principal issue. Besides, there are two more subjects to be thoroughly addressed. One is the recruitment of ovum donors, which should be discussed in association with commercialism and eugenics. The other is the determination of candidacy of recipient, which is related to the diagnosis of ovarian reserve. Preparation of working environment which enables women to develop their careers consistent with child-bearing, nursing and receiving education may be the only one goal the society should aim at. Construction of social system for making the goal come true is expected.

招請講演 1

どこまできたのか 女性研究者の活躍促進

国立研究開発法人科学技術振興機構科学技術プログラム推進部 山村 康子

2006年当時、日本の研究者の女性割合は緩やかに増加しつつありましたが、多くの諸外国でその割合が20%を超える中、11.9%と低い水準に留まっています。また、女性研究者が増加しない要因として、ライフイベント（出産、子育て、介護等）中の研究継続が難しいこと、指導的立場の上位職に就きにくいことなどが指摘されていました。そこで、2006年3月28日に閣議決定された「第3期科学技術基本計画」においては、人材の育成、確保、活躍の促進の一環として、女性研究者の活躍促進に関する方向性（環境整備、意識改革、採用、昇進・昇格、裾野拡大）が盛り込まれました。特に女性研究者割合が低い自然科学系分野については、女性研究者の新規採用割合に関する目標値<自然科学系全体としては25%（理学系20%、工学系15%、農学系30%、保健系30%）>が初めて具体的に設定されました。

文部科学省は、2006年から15年間、第3期～第5期科学技術基本計画、第6期科学技術・イノベーション基本計画に基づき、女性研究者がその能力を最大限発揮し活躍できるよう、「女性研究者研究活動支援事業（科学技術振興調整費女性研究者支援モデル育成）」、「女性研究者養成システム改革加速事業（科学技術振興調整費女性研究者養成システム改革加速）」、「ダイバーシティ研究環境実現イニシアティブ」,「特別研究員-RPD」,「女子中高生の理系進路選択支援プログラム」等の事業を展開し、女性研究者の科学技術・学術分野への参画拡大に取り組んできました。具体的には、①研究とライフイベント（出産・育児・介護等）との両立や多様な価値観や働き方を受容する研究環境の整備、②男女共同参画意識の醸成、③ライフイベントによる研究中断からの復帰・復職支援、④女性研究者の次世代育成、⑤女性研究者の研究力

強化や上位職・マネジメント層への積極的な登用を図ってきました。当該事業を実施した機関においては、女性研究者の2大ニーズである、ライフイベント中の研究支援者の配置、病児・病後児保育支援を含め様々な研究環境整備の取組が推進された結果、任期を付さないテニュアポストに就く女性研究者の離職が10年間で約85%減少しました。さらに、研究者の女性優先公募や女性限定公募、特に優秀な女性研究者を対象とした昇任制度等の実施により、女性研究者の研究業績等に見合った積極的な採用、上位職（教授、准教授）や機関の意志決定に関わるマネジメント層への登用が進められました。大学においては女性教授不在の部局が減少しつつあり、また、副学長や理事等への女性の登用が促進されています。

大学の上位職教員の女性割合は分野により差があり、自然科学系分野では低いことが知られています。医学部医学科では、学部生の女性割合、大学院医学系研究科博士後期課程学生の女性割合は、それぞれ34.4%、29.1%（2020年）と比較的高いにもかかわらず、テニュアポストに就く教授、准教授の女性割合は、それぞれ9.9%、15.2%（2020年）と未だ低く、女性の医学部長や附属病院長に至っては極端に少ない状況となっています。女性研究者が学位を取得した後の育成における課題が指摘されています。主な課題は、①教育・研究・臨床とライフイベントとの両立（研究時間の確保の難しさ）、②女性研究者の登用に対する機関構成員の無意識のバイアス（ライフイベントを抱えている、あるいは将来抱えるだろう女性研究者を上位職やマネジメント層へ登用することへの躊躇）、③女性研究者自身の無意識のバイアス（上位職やマネジメント層を目指すことへの躊躇）です。現在文部科学省が進めている「ダイバーシティ研究

環境実現イニシアティブ」では、上位職（教授、准教授）に就く女性研究リーダー、機関の意志決定に関わる女性マネジメント層のさらなる育成を目指しています。①教育・研究・臨床とライフイベントとの両立に係る課題は、研究支援員の配置や保育支援（一般保育、夜間保育、病児・病後児保育等）を行うことにより、一定程度は解消されつつあります。しかし一方、②、③の課題とされる無意識のバイアスは心の中のブラインド・スポットに潜んでおり、その排除は容易ではありません。無意識のバイアスを軽減し、排除する最初のステップは、個人が有する無意識のバイアスを認識することであり、次のステップは無意識の

バイアスから解放されたポジティブな経験をすることです。そしてさらなるステップとして、無意識のバイアスを介在させない採用や登用等の仕組みを構築することが不可欠です。

上述「女性研究者研究活動支援事業（科学技術振興調整費女性研究者支援モデル育成）」、「女性研究者養成システム改革加速事業（科学技術振興調整費女性研究者養成システム改革加速）」、「ダイバーシティ研究環境実現イニシアティブ」の3事業の実施機関がこれら課題の解決に向け、どのように対応し、女性研究者の支援、育成を進め、活躍促進を図ってきたかその概要をご紹介します。

招請講演 2

九州を元気に！～JR九州のこれまでの変遷～（予定）

九州旅客鉄道株式会社 青柳俊彦

□はじめに

JR九州は、会社として、3つのおこないを約束している。

それは、「誠実」、「成長と進化」、そして「地域を元気に」である。

これは、当社がお客さまの元気に支えられている企業であることから、地域を元気にすることは当社にとって、非常に大切な使命であると考えている。

□コロナ禍

2020年2月頃からの日本でコロナウィルスの猛威により、大きく社会が変わってしまった。

「STAY HOME」、「人流の抑制」、「移動制限」など、動くことや外食することが制限されることとなった。

これにより、観光業界、飲食業界は大きな痛手を食うこととなった。

□九州を元気に。

このコロナ禍において、当社も大打撃を受けることとなった。

人流に頼っていた事業展開をしていたため、非常に厳しい環境となった。

この苦しい時に、我々は何をすべきなのか？

我々が約束している地域を元気にする取組みは、何があるのか？

【その日まで、ともにがんばろうプロジェクト】

それを考えて始まった取組みが「その日まで、ともにがんばろうプロジェクト」である。

ホテルや観光地の方々が、コロナ禍があけるまで、頑張っている姿を一つの動画にまとめ、「わたしたちは、負けない姿」、「わたしたちは、みんなで頑張る姿」を誓い合った。

また、各駅でも、周辺で苦しんでいる方々をポスターにまとめ、みんなで「その日まで、ともに

がんばろう」と誓い合った。

勿論、当社も一緒にがんばりたいという思いを込めて。

【HKT48 とのプロジェクト】

我々の九州を元気にしたい取組と一緒に活動したいとHKT48の皆さんが参画してくれた。

HKT48のメンバーが九州の観光地に向かい、観光地の魅力を、自分たちで伝える動画を作ってくれた。

第一弾から第三弾まで、2年弱の間、一緒に活動することとなった。

【九州新幹線全線開業 10周年～流れ星新幹線～】

皆さんに支えられた九州新幹線。

東日本大震災の翌日に開業し、その時に流した「祝！九州」の動画は、皆さんから大きな反響を得ることが出来た。

あれから10年、本当に皆さんに支えて頂いた。

その感謝とコロナ禍からの脱却、そして皆さんの夢や願いを叶えられるように一夜限りの「流れ星新幹線」を運転した。

これは、世界で初めて、新幹線から光線を放ち、まるで新幹線が流れ星になったかのような演出をするものであった。

皆さんの願いをラッピングした新幹線、そして皆さんの願いを一つの本にして、太宰府天満宮に奉納した。

【西九州新幹線開業】

2022年秋の西九州新幹線の開業に向けた取組みについて。

□まとめ

当社では、ななつ星をはじめとした沢山のD&S列車（観光列車）がある。これらのコンセプトは列車のデザインと、その土地ならではのストーリーである。

そのストーリーは、運転する沿線や地元でのストーリーを列車に見立てている。勿論、列車内で販売しているものは、その土地ならではのものがある。

このD&S列車が走ることで、お客さまを観光地にお運びすることは勿論、その土地の良いもの

をご提供することで地域を元気にできると信じている。

これからも、地域を元気にすることが当社のミッションと考えている。

そのために、知恵を絞り、これからも走っていききたい。

シンポジウム 1 **P** 新たな診断・治療開発に向けた婦人科がん分子機構の解明

1) がん幹細胞モデルを基盤としたがんの不均一性を考慮した個別化医療への展開

新潟大学 石 黒 竜 也

【目的】

がん組織内に含まれるがん細胞は不均一な性質を有する細胞集団で構成される。がん幹細胞 (Cancer stem cells, CSCs) は腫瘍形成能・自己複製能・分化能などを有し、がんの増殖や転移などがん全体の挙動を司る一部のがん細胞である。また、化学療法や放射線療法に対する治療抵抗性を示す。この CSCs 理論に基づく、がんの機能的な不均一性を標的とした治療戦略は、新たな治療アプローチとして期待されている。また CSCs 研究において、臨床の性質を保持した細胞を用いた解析は、臨床に即した治療への展開を可能にする。そこで本研究では、婦人科腫瘍臨床検体より CSCs の安定的な *in vitro* 培養系を確立し、CSCs の生化学的特徴を明らかにすることで、新規治療への発展の礎とすることを目的とした。

【方法】

新潟大学医歯学総合病院産科婦人科および国立がん研究センター中央病院婦人腫瘍科で精査加療された患者様より同意取得後、手術・処置時に摘出した腫瘍および腹水検体の一部を使用した。検体は酵素処理後に、無血清培地・低接着プレートを用いた浮遊培養下に 3 次元培養を行った。培養樹立した細胞は、免疫不全マウスへの皮下投与により腫瘍形成能を検証した。同 *in vitro*, *in vivo* 実験系を軸に各種機能解析を施行した。なお両機関の倫理審査委員会の承認の下に研究を遂行し、情報は匿名化して管理した。

【成績】

1. 悪性腫瘍臨床検体由来のがん幹細胞の安定的培養

卵巣がんおよび子宮体がん臨床検体より安定的

な 3 次元細胞 (スフェロイド細胞) の培養に成功した。スフェロイドの形成能は、CSCs 性質のひとつである自己複製能を反映する実験系として広く用いられているが、我々の樹立したスフェロイド細胞は、免疫不全マウスにおける腫瘍形成能や分化能などの他の CSCs 性質を有していた。

ターゲットシーケンス解析より、スフェロイド細胞とその由来となった臨床腫瘍組織では、多くの遺伝子変異が共通しており、また免疫不全マウス内でスフェロイド細胞から形成された移植片腫瘍は元のスフェロイド細胞と共通した遺伝子変異を有していた。

2. CSCs の特異的制御機構の解明と CSCs を標的とした新規治療法の考案

(1) 卵巣がん CSCs : 卵巣がんスフェロイド細胞中の、特にアルデヒド脱水素酵素 (ALDH) 高活性を有する細胞が、腫瘍形成能やスフェロイド形成能などの CSCs 性質を有していた。卵巣がんスフェロイド細胞の安定培養に必要な Rho キナーゼ阻害剤は ALDH 活性を誘導した。また同 ALDH 高活性卵巣がん CSCs は、SOX2, Nanog などの幹細胞の多能性維持に寄与する因子を高発現していた。

ALDH 活性阻害剤ジスルフィラムまたは RNA 干渉による ALDH 発現抑制を介した ALDH 活性の抑制は、SOX2 発現を抑制し、卵巣がん CSCs の増殖を抑制した。また RNA 干渉による SOX2 発現の抑制も、同様に卵巣がん CSCs の増殖を抑制した。しかし、SOX2 過剰発現は ALDH 活性を抑制し、卵巣がん CSCs の増殖を抑制した。すなわち、卵巣がん CSCs において、ALDH 活性と SOX2 の間には、互いをコントロールする特異的な制

御メカニズムが存在していることが明らかになった。

(2) 子宮体がん CSCs：子宮体がんスフェロイド細胞においても、卵巣がん同様に ALDH 高活性細胞は、腫瘍形成能やスフェロイド形成能が高く、また Oct-4 や c-Myc などの多能性因子を高発現し、ALDH 低活性細胞への分化能を有している CSCs であった。また ALDH 活性が子宮体がん CSCs の維持に重要であり、ALDH 阻害剤または RNA 干渉による ALDH 発現抑制を介した ALDH 活性の抑制は子宮体がんの増殖を抑制した。一方、ALDH 低活性細胞に比し ALDH 高活性 CSCs のパクリタキセルに対する感受性は低かったが、パクリタキセルと ALDH 活性阻害剤の併用は、協調的に子宮体がんの増殖を抑制した。

マイクロアレイ解析より、ALDH 高活性 CSCs は解糖系関連因子の発現が亢進していた。また細胞外フラックスアナライザーを用いた解析より、ALDH 高活性 CSCs は解糖系が亢進していた。ALDH 高活性 CSCs は糖の取り込みが亢進しており、とりわけ糖輸送体 GLUT1 の発現が子宮体がん CSCs の解糖系において中心的な役割を有していた。RNA 干渉または GLUT1 阻害剤 (BAY 876) による GLUT1 抑制により、子宮体がん CSCs の増殖は抑制された。さらに、パクリタキセルと GLUT1 阻害剤の併用は、in vitro および in vivo 実験系において子宮体がんの増殖を協調的に抑制した。

3. 卵巣がん・子宮体がんにおける ALDH 発現の臨床的意義

卵巣がん 113 例・子宮体がん 258 例の原発腫瘍組織の免疫染色による解析で、両がん種ともに進行例で優位に ALDH が高発現していた。また卵巣がん・子宮体がんともに ALDH 高発現群は予後不良であり、ALDH 発現が独立した予後因子として抽出された。とりわけ子宮体がんにおいては、ALDH と GLUT1 の高発現群の予後が不良であった。

【結論】

本研究で、卵巣がん、子宮体がん臨床検体由来の CSCs 性質を有するスフェロイド細胞の安定的な培養法を確立した。加えて、由来臨床検体の性質を保持した同細胞を用い、卵巣がん・子宮体がんともに ALDH が機能的な意義と臨床指標の意義を有する因子であることを明らかにした。さらに、卵巣がん・子宮体がん CSCs の特異的な制御メカニズムを基に、ALDH 阻害剤・GLUT1 阻害剤のがん増殖抑制効果を示した。これら阻害剤の卵巣がん・子宮体がん臨床治療への新規展開が期待される。一方、より効果的な治療の展開に向け、症例ごとに治療の有効性を評価し、治療法を選定する個別化医療への発展が求められる。今後は、がん幹細胞スフェロイド細胞モデルを ex vivo 治療効果予測モデルへ応用展開することで、将来的な実臨床治療の開発促進へ寄与することができると考えられる。

Symposium 1 **P** Molecular mechanisms of development and progression of gynecologic cancer, leading to novel diagnostics and therapeutics

1) Personalized medicine targeting cancer heterogeneity based on a cancer stem cell model

ISHIGURO Tatsuya

Niigata University

[Objective] Cancerous tissues comprise heterogeneous malignant cells. Cancer stem cells (CSCs), a subpopulation of cells with tumorigenic, self-renewal, and differentiation potential, are instrumental in cancer propagation and proliferation. *in vitro* culture systems derived from human clinical specimens may be a useful platform to develop new therapeutic strategies for refractory cancer. In this study, we introduced a stable cultivation method for gynecological CSCs. Furthermore, we investigated the biochemical characteristics of CSCs to develop an innovative treatment approach targeting CSCs.

[Methods] Tumor or ascites samples were obtained from patients treated at the Niigata University Medical & Dental Hospital or National Cancer Center Hospital. Following enzymatic dissociation of cancerous tissues, cells were cultured in ultra-low attachment dishes in a serum-free medium. A xenograft model was established after transplantation of stable growing cells. Our study protocol was approved by the Ethics Committee, and all patients provided informed consent.

[Results] 1. *in vitro* human gynecological CSCs cultivation: We successfully established an *in vitro* three-dimensional culture system using ovarian and uterine endometrial cancer specimens. Our three-dimensional cells (tumor-derived spheroids) showed characteristics of CSCs, including *in vivo* tumorigenic and differ-

entiation potential. Spheroid cells and the original cancer shared similar mutation profiles.

2. Investigation of a specific regulatory mechanism underlying CSCs proliferation and a novel treatment approach targeting CSCs: (1) Ovarian CSCs: Spheroid cells with high expression of aldehyde dehydrogenase (ALDH) activity (ALDH-high cells) showed various CSCs characteristics. Functional analyses using gene knock-down and a chemical inhibitor revealed that ALDH and SOX2 are essential for ovarian CSCs proliferation, whereas SOX2 overexpression inhibits ALDH1A1 and suppresses ovarian CSCs, which suggests feedback regulation of CSCs proliferation; SOX2 and ALDH1A1 form a negative feedback loop. (2) Uterine endometrial CSCs: ALDH-high endometrial cancer spheroid cells also showed CSCs potential. ALDH activity inhibition reduces endometrial CSCs propagation. Compared with ALDH-low cells, ALDH-high cells showed greater resistance to paclitaxel, and paclitaxel + ALDH inhibitor combination therapy synergistically inhibited endometrial cancer cell progression. Further analysis showed that high ALDH levels correlated with glycolytic pathway activation and elevated glucose transporter 1 (GLUT1). GLUT1 blockade inhibited characteristics of CSCs, and GLUT1 inhibition synergized with paclitaxel to block endometrial cancer proliferation.

[Conclusion] We established a stable cultivation

method for ovarian and endometrial CSCs and observed that ALDH is essential for CSCs propagation in both cancers. ALDH or GLUT1 inhibitors suppress cancer propagation based on the specific regulatory mechanism underlying ovarian and endometrial CSCs. ALDH or GLUT1 inhibitors may be useful as novel treatment agents

for gynecologic cancers. Our cultivation method may enable screening of patients with high ALDH levels, who tend to respond to anti-ALDH or GLUT treatment. Therefore, this novel approach may be useful to identify patients who are likely to benefit from ALDH or GLUT inhibitor therapy.

シンポジウム 1 P 新たな診断・治療開発に向けた婦人科がん分子機構の解明

2) 卵巣癌オルガノイドバンクの構築と統合オミクス解析による新規治療開発

慶應義塾大学 千代田 達 幸

【目的】

卵巣癌診療には *BRCA1/2* もしくは homologous recombination deficiency をバイオマーカーとする poly (ADP-ribose) polymerase (PARP) 阻害薬が導入されたが、卵巣悪性腫瘍 88 例を対象とした我々のがん遺伝子パネル解析では druggable 遺伝子変化が認められたのは 40.9% のみであり、依然として新たなバイオマーカーに基づく治療開発が必要である。これまで多くの卵巣癌治療が研究開発されてきたにも関わらず、臨床で効果が確認された薬剤はごく少数にとどまる。その一因として、卵巣癌研究に頻用される SKOV3, HeyA8 等の卵巣癌細胞株はゲノム上卵巣癌とは考えにくいこと、研究で通常用いられる 2 次元培養での薬剤感受性試験は 3 次元培養 (3D) と結果が大きく異なり、3D での薬剤感受性がより臨床と合致すること、が挙げられる。これらの欠点を克服するのがオルガノイドである。組織を疑似した 3D 構造体であるオルガノイドは 2009 年に小腸での作成が報告されて以来、急速に研究が進んでいる。オルガノイドは生体組織に近い生物学的機能を保持しており、個々の卵巣癌患者からオルガノイドを作成できればより臨床に即した治療開発ができる。従来薬剤スクリーニングに用いられてきた細胞株の 2 次元培養は生体内の腫瘍を再現しているとは言い難いが、オルガノイド培養により卵巣癌を生体に近い状態で 3D 培養しスクリーニングを行うことで、難治性卵巣癌に対する革新的な創薬が可能となる。卵巣癌オルガノイドはアバターとして患者に薬剤を投与する前に治療効果の検証に用いることもでき、卵巣癌オルガノイドを短期間で効率的に作成できれば癌治療を変革できる。本

研究では 1. 卵巣癌と生物学的に類似した卵巣癌オルガノイドの効率的な作成法を確立し、2. 卵巣癌オルガノイドバンクを用いて high-throughput drug screening (HTDS) を行い、オミクスデータと階層的に統合解析することにより新しいバイオマーカーに基づく新規治療法を開発すること、を目的とした。

【方法】

1. 卵巣癌オルガノイド培養法の確立と元の卵巣癌組織とのゲノム・病理学的類似性の検討、薬剤感受性試験の妥当性解析

同意を得た卵巣癌手術検体を用いて、小腸オルガノイドの培養液組成をベースとして効率的に卵巣癌オルガノイドを作成できるニッチ因子の組み合わせを検討した。培養法の確立後、7 例 (漿液性癌 3 例、明細胞癌 1 例、類内膜癌 3 例) を用いてオルガノイドと元の腫瘍組織との類似性を HE 染色、免疫組織化学染色、1,053 個関連遺伝子の targeted exome sequencing により比較した。卵巣癌治療薬の薬剤感受性試験を行い、薬剤感受性試験の結果と臨床経過との相関について解析を行った。

2. 卵巣癌オルガノイドバンクを用いた HTDS とオミクスの統合解析による明細胞癌新規治療法の開発

卵巣明細胞癌オルガノイド 6 例を対象に 364 化合物 (文部科学省分子プロファイル支援) の標準阻害剤ライブラリーで HTDS を行い、また明細胞癌オルガノイド 2 例を対象に 4650 化合物の低分子化合物ライブラリー (Selleck) を用いた HTDS を行った。そして 2 つの HTDS で共通する薬剤を抽出し、候補薬剤を用いた薬剤感受性試験を行っ

た。また whole transcriptome sequencing (WTS) のデータと薬剤感受性データを統合解析し、新規バイオマーカー候補を抽出した。

【成績】

1. 卵巣癌オルガノイド培養法の確立と元の卵巣癌組織とのゲノム・病理学的類似性の検討、薬剤感受性試験の妥当性解析

FGF-2, IGF-1, noggin, Wnt3A, R-spondin 等を含む卵巣癌オルガノイド培養液の組成を確立した。異なる組織型を含むオルガノイド作成の成功率は80%であり、作成したオルガノイドは形態学的に元の腫瘍の特徴を有していた。7例を用いたゲノム解析では59.5%の遺伝子変異は元の腫瘍と共通しており、癌に関わる主要な遺伝子変異は保持されていた。variant allele frequency, copy number variation もオルガノイドと元の腫瘍は類似していた。薬剤感受性試験においてパクリタキセル、カルボプラチンの感受性が低いオルガノイドの症例は同じ進行期であっても早期に再発し、また *BRCA1* に病的変異を有するオルガノイドはオラパリブの感受性が有意に高く、オルガノイドの薬剤感受性は臨床を反映していると考えられた。卵巣癌オルガノイドは元の腫瘍の形態学的、ゲノム、薬剤感受性の特徴を保持した *ex vivo* モデルと考えられた。

2. 卵巣癌オルガノイドバンクを用いた HTDS とオミクスの統合解析による明細胞癌新規治療法の

開発

上記薬剤感受性試験において明細胞癌オルガノイドはパクリタキセル、カルボプラチンに抵抗性であり、明細胞癌の抗がん剤抵抗性を支持する結果であった。364 標準阻害剤、4650 低分子化合物を用いた HTDS を行い、明細胞癌の候補薬剤として9つの化合物を抽出した。候補薬剤を用いた薬剤感受性試験をオルガノイド10例に対して行い、それぞれのオルガノイドの WTS のデータと統合解析し、バイオマーカー候補を抽出した。同定したバイオマーカー候補が関わるシグナル伝達経路について、既存のデータセットを用いた解析により明細胞癌において活性化していることが確認された。

【結論】

2021年8月までに卵巣癌オルガノイド54例を樹立し、卵巣癌オルガノイドバンクを構築した。我々が確立した培養法は成功率が80%と高く、1か月以内に作成可能でありオルガノイドの卵巣癌精密医療への導入に大きく寄与することができる。また、明細胞癌オルガノイドを用いて HTDS により卵巣明細胞癌の新規治療薬候補を抽出した。複数のオルガノイドを用いた薬剤感受性試験および WTS の統合解析によりバイオマーカー候補を抽出することが可能であった。現在ゲノムの変異情報とも階層的に解析を行っている。これらの成果をもとに臨床に還元していきたい。

Symposium 1 **P** Molecular mechanisms of development and progression of gynecologic cancer, leading to novel diagnostics and therapeutics

2) Establishment of ovarian cancer organoid biobank and development of novel therapeutics by integrated omics analysis

CHIYODA Tatsuyuki

Keio University

[Objective]

Culturing ovarian cancer cells in three-dimension by organoid culture and screening using those will enable innovative drug discovery for ovarian cancer. In this study, we aimed to establish an efficient method for the development of ovarian cancer organoids that are biologically similar to ovarian cancer, and to develop novel biomarker-based therapeutics by high-throughput drug screening (HTDS) using organoids with integrative analysis of omics data.

[Methods]

1. Establishment of an ovarian cancer organoid culture method, examination of genomic and pathological similarities with the original ovarian cancer tissue, and validity analysis of drug sensitivity tests

We investigated the combination of niche factors that can efficiently create ovarian cancer organoids. After that, the similarities between organoids and the original tumor tissues were compared by HE staining and targeted exome sequencing of 1,053 genes using seven cases. A drug sensitivity test of ovarian cancer drugs was performed, and the correlation between drug sensitivity testing results and the clinical course was examined.

2. Development of novel therapeutics for clear cell carcinoma by integrated analysis of HTDS

HTDS was performed with a standard inhibitor library of 364 compounds in 6 ovarian clear

cell carcinoma organoids, and HTDS with a library of 4650 small molecule compounds (Selleck) was performed in 2 clear cell carcinoma organoids. Drugs common in the two tests of HTDS were extracted and used for drug susceptibility tests. We also performed an integrative analysis of whole transcriptome sequencing (WTS) data and drug sensitivity data to extract novel candidate biomarkers.

[Results]

1. The composition of ovarian cancer organoid cultures was established. The success rate of organoid creation was 80%, and the organoids had the pathological features of the original tumor. Genomic analysis using seven cases showed that 59.5% of gene mutations were common to the original tumor. In drug sensitivity studies, organoids with low sensitivity to paclitaxel and carboplatin relapsed early even in the same advanced stage, and organoids with pathological mutations in *BRCA1* showed significantly higher sensitivity to olaparib.

2. HTDS using 364 standard inhibitors and 4650 small molecule compounds was performed, and nine compounds were extracted as candidate drugs. A drug sensitivity test with candidate drugs was performed on 10 organoids, and integrated analysis with data from the WTS of each organoid was performed to extract biomarker candidates. Signaling pathways involving the identified biomarker candidates were confirmed

to be activated in clear cell carcinoma using existing datasets.

[Conclusion]

We established 54 ovarian cancer organoids until August 2021. We extracted novel drug can-

didates for ovarian clear cell carcinoma by HTDS using organoids. Also, it was possible to extract the biomarker candidate by drug sensitivity test using organoids and integrated analysis of WTS.

シンポジウム 1 **P** 新たな診断・治療開発に向けた婦人科がん分子機構の解明

3) 三量体 G タンパクの機能解析に基づいた新たな婦人科がん治療の開発

九州大学 八木裕史

【目的】

G タンパク共役受容体 (GPCR) を介したシグナル伝達経路は癌の進展に深く関与している。ヒト癌組織を用いた網羅的遺伝子解析の結果、GPCR やそのリガンドだけでなく、細胞内で coupling する三量体 G タンパク、エフェクター分子、低分子量 G タンパクなど、シグナルの制御に関わる様々な遺伝子の異常が明らかとなった。三量体 G タンパクの一つである $G\alpha_{13}$ は、様々な癌種において高発現していること、その高発現が臨床的予後と相関することが報告されている。また、内在性のリガンドが同定されていない orphan GPCR の多くが $G\alpha_{13}$ と coupling することが報告されており、これらの orphan GPCR が癌の進展に関与していることが示唆されている。しかし、 $G\alpha_{13}$ が制御するシグナル伝達経路や癌の発生や進展における役割については十分明らかになっていない。その理由として、多くの GPCR が $G\alpha_{13}$ を含む複数種の三量体 G タンパクと coupling すること、 $G\alpha_{13}$ のみと特異的に coupling する GPCR がこれまでに同定されていないことなどから、 $G\alpha_{13}$ シグナルのみの解析が困難であることが挙げられる。以上のような背景から、本研究の目的は、純粋な $G\alpha_{13}$ シグナルを細胞内に再構築する実験系を確立し、 $G\alpha_{13}$ の制御するシグナル伝達経路、 $G\alpha_{13}$ の活性化により誘導される遺伝子、タンパクの発現や表現型の変化を解析することにより、婦人科がん（卵巣癌、子宮頸癌、子宮体癌）の発生および悪性形質獲得における $G\alpha_{13}$ シグナルの役割を明らかにすること、新たな治療標的を同定することである。

【方法】

IRB の承認と患者の同意を得たヒト卵巣癌、子宮頸癌、子宮体癌組織における $G\alpha_{13}$ のタンパク

発現について、免疫組織化学染色法を用いて解析した。ヒト卵巣癌、子宮体癌細胞株を用いて、 $G\alpha_{13}$ の機能解析を行った。細胞内に純粋な $G\alpha_{13}$ シグナルを再構築するために、ムスカリン受容体 M4 の遺伝子変異体 ($G\alpha_i$ receptors activated solely by synthetic ligands), $G\alpha_{13}$ と $G\alpha_i$ のキメラタンパクである $G\alpha_{13S}$ を作成し、これらを安定的に発現した細胞株を樹立した。また、 $G\alpha_{13}$ 野生型、 $G\alpha_{13}$ 恒常的活性化型遺伝子変異体 ($G\alpha_{13QL}$) を過剰発現した細胞株を樹立した。これらを用いて、 $G\alpha_{13}$ の活性化が制御する一次的なシグナル伝達経路、それに伴う遺伝子およびタンパク発現の変化、最終的に誘導される表現型について、経時的かつ網羅的な解析を行った。ウエスタンブロット法、細胞免疫染色法、time-lapse imaging, migration assay, spheroid assay を用いて、細胞内シグナル、細胞形態、運動能、浸潤能、増殖能の評価を行った。造腫瘍能については、ヌードマウスを用いた ectopic tumor xenograft model を用いて解析を行った。GPCR と三量体 G タンパクとの間の coupling specificity については、bioluminescence resonance energy transfer (BRET) assay を用いて解析した。

【成績】

① ヒト婦人科癌組織における $G\alpha_{13}$ の発現

ヒト卵巣癌、子宮頸癌、子宮体癌において組織型に関わらず $G\alpha_{13}$ の発現が亢進していることが明らかとなった。

② $G\alpha_{13}$ およびそのシグナル関連分子の発現レベルや遺伝子変異が GPCR シグナルに及ぼす影響

BRET assay により GPCR と三量体 G タンパクとの間のタンパク質間相互作用を解析した結果、 $G\alpha_{13}$ の高発現に伴い GPCR の coupling specificity が変化し、 $G\alpha_{13}$ が制御するシグナル伝達経

路が dominant になることが明らかとなった。 $G\alpha_{13}$ は、guanine nucleotide exchange factor (GEF) および GTPase activating protein (GAP) を介して低分子量 G タンパク (Rho, Rac) の活性化を制御している。ARHGAP35 は Rho の活性化を負に制御する RhoGAP のひとつで、子宮体癌の約 20% に遺伝子変異を認める。子宮体癌細胞株を用いた解析の結果、ARHGAP35 の機能欠失型の遺伝子変異や発現レベルの低下が、 $G\alpha_{13}$ -Rho シグナルの増強に関与していることが明らかとなった。これらの結果から、 $G\alpha_{13}$ の高発現に伴う GPCR の coupling specificity の変化、低分子量 G タンパク (Rho, Rac) シグナル関連分子の遺伝子変異などによる機能の変化が $G\alpha_{13}$ シグナルの増強、それに伴う癌の悪性形質獲得に関与していることが示唆された。

③ $G\alpha_{13}$ シグナルの活性化により誘導される遺伝子およびタンパク発現、表現型の変化

卵巣癌、子宮体癌細胞を用いたマイクロアレイ解析の結果、 $G\alpha_{13}$ の一時的な活性化により誘導される遺伝子群と、 $G\alpha_{13}$ や $G\alpha_{13}QL$ の過剰発現により誘導される遺伝子群は大きく異なることが示された。これらの解析から、 $G\alpha_{13}$ による癌の悪性形質獲得には、Hippo シグナル経路の制御、転写因子の Activator protein-1 (AP-1) の誘導が重要な役割を果たしていることが明らかとなった。

④ $G\alpha_{13}$ の活性化は Hippo シグナル経路を介して卵巣癌細胞の進展を制御する

Hippo シグナル経路は臓器のサイズを制御するシグナルとして知られており、癌の発生や進展にも関与している。 $G\alpha_{13}$ の活性化が、Hippo シグナル経路の中心的な分子である LATS1 のリン酸化、それに引き続くプロテアソーム依存性のタン

パク分解を誘導することにより、YAP の核内移行、転写の亢進、上皮間葉転換 (epithelial-mesenchymal transition) が生じることが明らかとなった。また、YAP の活性を阻害することにより卵巣癌細胞の造腫瘍能、浸潤能が抑制されることが示された。

⑤ $G\alpha_{13}$ は転写因子 AP-1 を介して増殖能、造腫瘍能を制御する

AP-1 は JUN, FOS, ATF, MAF ファミリーの分子から構成されるヘテロ二量体の転写因子で、細胞外からの刺激に対して直ちに誘導される Immediate early genes のひとつとして知られている。 $G\alpha_{13}$ の活性化により誘導される遺伝子群には AP-1 に関連したものが多く含まれることが明らかとなった。AP-1 の機能を阻害することにより卵巣癌細胞、子宮体癌細胞の増殖能、造腫瘍能が抑制されることが示された。

【結論】

現在の治療薬の約 35% は GPCR を標的としているが、それらの治療薬が標的としているのは、GPCR 全体の約 15% に過ぎない。また、ヒト癌組織で発現を認める GPCR のうち 140 種以上についてはリガンド分子やその機能が不明であり、興味深いことにそれらの多くは、 $G\alpha_{13}$ と coupling することが報告されている。シグナル選択的な GPCR アンタゴニストや、GPCR シグナルを間接的に阻害するアロステリックタンパクなど、新たなコンセプトに基づく治療薬が開発されつつある現状を考慮すると、本経路の阻害剤は婦人科癌治療薬の有力な候補となりうる。 $G\alpha_{13}$ の機能解析に基づく治療標的の同定は、癌に対する新たな治療法の開発につながると期待でき、社会的意義は大きいものと考えられる。

Symposium 1 **P** Molecular mechanisms of development and progression of gynecologic cancer, leading to novel diagnostics and therapeutics

3) The role of G-protein coupled receptor signaling in gynecologic cancer

YAGI Hiroshi

Kyushu University

[Objective]

G protein-coupled receptors (GPCRs) are seven transmembrane receptors that represent the largest family of cell surface receptors. GPCR signaling regulates diverse biological functions, including cell proliferation, migration and angiogenesis. Cancer cells can co-opt the activity of GPCR signaling to proliferate autonomously and metastasize to other organs. Dysregulation of GPCR signaling contributes to the progression of various human cancers. Here, we evaluated the role of $G\alpha_{13}$, among heterotrimeric G proteins, in the progression of gynecologic malignancy and the potential benefits of targeting $G\alpha_{13}$ -regulated signaling circuits in cancer treatment.

[Methods]

All human tumor samples were obtained with patients' consent and relevant IRB approval. The expression of Gal3 in human cancer tissues was examined by immunostaining. To examine the effect of $G\alpha_{13}$ activation on human cancer cells, we employed a synthetic biology approach using a mutant GPCR and chimeric G protein, and constitutively active mutant of $G\alpha_{13}$ ($G\alpha_{13}^{QL}$). Changes in cell shapes, motility, proliferation, tumor forming capacity, gene or protein expression profiles and intracellular signaling pathways induced by $G\alpha_{13}$ activation were analyzed.

[Results]

1. $G\alpha_{13}$ is highly expressed in human gynecologic cancer tissues

Human cervical, endometrial and ovarian cancer tissues were subjected to immunohistochem-

istry to determine protein levels of $G\alpha_{13}$. $G\alpha_{13}$ was overexpressed in cancer tissues, but not in normal control tissues.

2. $G\alpha_{13}$ -regulated signalling is enhanced by $G\alpha_{13}$ overexpression and loss-of-function mutations of ARHGAP35

The bioluminescence resonance energy transfer assay revealed change in coupling specificity of GPCR in accordance with the intracellular expression level of $G\alpha_{13}$. Recent genome-wide analysis revealed that approximately 20% of endometrial cancers harbor mutations in ARHGAP35, GTPase activating proteins which inactivates Rho by catalyzing the hydrolysis of GTP back into GDP. Rho pull-down assay revealed that Rho GAP activity was impaired in most of tumor-derived mutant of ARHGAP35. These data suggested that overexpression of $G\alpha_{13}$, along with loss-of-function mutations in ARHGAP35, contribute to aggressive phenotype of human endometrial cancer.

3. Downstream target of $G\alpha_{13}$ activation involved in the progression of gynecologic cancers

Microarray analysis revealed that $G\alpha_{13}$ activation upregulates genes related to AP-1 transcription factor, which is composed of FOS, JUN, ATF and MAF protein families, and hippo signaling pathway. *In vitro* experiments using human ovarian and endometrial cancer cells demonstrated that $G\alpha_{13}$ activation induces dysregulation of AP1 activity and hippo signalling pathway, leading to aggressive cancer phenotypes, thereby identifying a potential target for pre-

venting cancer progression.

[Conclusion]

Although GPCRs are associated with cancer progression and represent one of the most drug-gable molecules, there are relatively few cancer

treatments targeting these receptors. Therefore, by better understanding the molecular mechanisms underlying GPCR function in cancer, we can identify novel strategies for cancer diagnosis, prevention and treatment.

シンポジウム 1 P 新たな診断・治療開発に向けた婦人科がん分子機構の解明

4) 卵巣がん細胞由来核酸搭載エクソソームの機能解析と臨床応用

名古屋大学 横井 暁

【背景/目的】

卵巣がん細胞は極めて容易に腹腔内へ転移を起し、診断時多くの患者はすでに腹膜転移を伴った進行期の状態という、婦人科がんの中でも極めて予後の悪いがんである。卵巣がんの予後を悪くする大きな要因として①早期発見が困難、②治療困難な腹膜播種性転移を高頻度で来す、③化学療法に対し次第に耐性を示すという点が挙げられ、これら問題に対する解決の糸口となりえる候補として、細胞外小胞、エクソソームに着目した。エクソソームはあらゆる細胞が放出する 100nm 前後の微細な膜小胞でタンパク質や核酸などといった生理活性を持つ分子を内包する。がんなどの疾患ではそのプロファイルが変化することが分かっていたが、卵巣がん悪性化メカニズムにどのように寄与するか、またその臨床的応用性についてはほとんど明らかにされていなかった。我々は、卵巣がん細胞由来エクソソーム、および卵巣がん患者体液中エクソソームを対象として、内包される核酸、とりわけ、マイクロ RNA (miRNA)、メッセンジャー RNA (mRNA)、DNA に着目し、その機能および臨床的意義を明らかにすることを目的とした。

【方法】

解析対象とするエクソソームは、患者腹水および血液から、また種々の卵巣がん細胞株および卵巣上皮細胞株の培養上清から、主に超遠心法にて抽出した。ヒト由来試料に関しては各研究施設での施設倫理審査委員会の認証の下、個別同意を得た上で使用した。エクソソームの性状はウエスタンブロッティングによるエクソソームマーカーのチェック、Nano particle tracking assay による粒子計測、凍結電子顕微鏡検査による画像解析によって評価した。細胞間コミュニケーションツ

ルとしてのエクソソームの機能解析を行うため、ヒト腹膜中皮細胞も使用した。マウスモデルは腹腔内にごん細胞を投与する腹膜播種モデルと、がん細胞を卵巣節に移植する同所移植モデルを用いた。エクソソームの解析方法として、定量 PCR や、次世代シーケンサー、イメージングフローサイトメトリー解析などを併用した。遺伝子の発現解析は遺伝子発現マイクロアレイ解析を行った。診断精度モデル作成には Dynacom 社の機械学習スクリプトも活用した。

【成績】

卵巣がんエクソソーム中の核酸である ① mRNA ② miRNA ③ DNA、それぞれについてその成績・成果を解説する。① 培養細胞よりエクソソームを抽出し、その機能について検討した。卵巣上皮細胞由来のエクソソームに比べ、卵巣がん細胞由来のエクソソームが卵巣がん細胞同所移植による腹膜播種モデルマウスにおいて転移を促進することを発見した。その機構に卵巣がん細胞と中皮細胞のエクソソームを介した関わりがあることを明らかにし、さらに、卵巣がん細胞由来エクソソームが MMP1 mRNA を搭載し、受け手の中皮細胞においてアポトーシスを誘導することにより腹膜播種を促進させるメカニズムが存在することを証明した (Yokoi A, Kajiyama H, Ochiya T, et al., *Nature Communications*. 2017.)。また卵巣がん患者腹水中にも MMP1 mRNA を多く含有するエクソソームが存在することを同定し、同エクソソームが同様に腹膜中皮細胞のアポトーシスを誘導することを証明した。② 遺伝子発現を抑制的に制御することにより、がん悪性化に関わるとしてエビデンスが蓄積していた miRNA は、エクソソームに内包され、細胞外へ放出され安定的に存在し、体液中を循環することが分かっていた。我々

はエクソソームに内包されて血中を循環する miRNA を対象とし、卵巣がん早期診断バイオマーカー探索を行った。13種の卵巣がん細胞株と3種の正常卵巣上皮細胞株から抽出したエクソソームの miRNA プロファイルを取得、さらに、卵巣がん患者血清中の miRNA を Deep Sequence によって解析し、定量 PCR にて検証した結果、早期診断バイオマーカーとして利用できる診断アルゴリズムを作成した (Yokoi A, Kajiyama H, Ochiya T, et al., *Oncotarget*. 2017)。また、これらの経験を活かし、国立がん研究センターが主導した体液 miRNA プロジェクト (2014-2019) のメンバーとして参加し、卵巣がん患者約 400 例、健常や他がん患者 4000 例を超える大規模血清サンプルから、全 miRNA プロファイルをマイクロアレイ解析にて取得し、機械学習により、血清中 miRNA の診断バイオマーカーとしての極めて高い可能性を国際学会誌に論文報告した (Yokoi A, Yoshioka Y, Ochiya T, et al., *Nature Communications*. 2018)。③エクソソームに DNA が含まれる可能性について、その存在はわかっていたものの、どのように DNA が搭載されるか、また卵巣がんにおいてどのような DNA がエクソソームに搭載されて分泌されるのかなど不明な点が多かった。卵巣がんはゲノム不安定性の強いがんであることを確認したのち、卵巣がん細胞が放出する DNA 搭載エクソソームの生合成機構の解明に取り組んだ。施設内のフローサイトメトリー部門と協力し、

イメージング FACS 装置を用いて、エクソソームの中の 5-10% を成す DNA を搭載する部分集団を一粒子レベルで特異的に解析する手法を確立した。その手法を用いて、卵巣がんが放出する DNA 搭載エクソソームの解析を進め、がん細胞が DNA をエクソソームへ輸送するメカニズムを明らかにした (Yokoi A, Prados AV, Sood AK, et al., *Science Advances*. 2019)。現在は、エクソソーム中の DNA や、次世代シーケンサーによる miRNA 網羅解析を軸とした、バイオマーカー探索、および疾患機構解明を継続し解析しており、本シンポジウムにおいて、最新の知見につき紹介する。

【独創点】

我々はこれまで、卵巣がん細胞が放出するエクソソームの様々な生物学的意義を明らかにしてきたが、それぞれの研究がクリニカルクエストンに基づく仮説に立脚したものであり、結果としてエクソソーム内の mRNA, miRNA, DNA と、あらゆる細胞外核酸を標的とすることになった。それぞれの成果は、過去に報告のない新しい知見であった。エクソソームを取り巻く研究情勢はその注目度の高さから、日々拡大かつ変化している。常にアップデートしつつも、その中で難治性婦人科疾患、特に卵巣がんに関わる未知かつ重要な機能を、基礎からトランスレーショナルに関わる部分まで、今後も広く追求し、あらゆる婦人科悪性疾患の予後改善に貢献するため、常に新しい観点から診断・治療開発の確立を目指す。

Symposium 1 **P** Molecular mechanisms of development and progression of gynecologic cancer, leading to novel diagnostics and therapeutics

4) Investigation of exosomes carrying nucleic acids in ovarian cancer

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Ovarian cancer is the most lethal reproductive system cancer and a leading cause of women's cancer-related death. It is critical to understand the underlying molecular mechanisms, which may ultimately improve patient outcomes. Recently, it has been recognized that small membranous extracellular vesicles (EVs) including exosomes secreted from all living cells that play an essential role in cell-to-cell communication. Recent evidence has demonstrated that cancer cells positively secrete EVs to both proximal surrounding cells and distal sites, thereby enabling the development of a cancer microenvironment

that in turn promotes cancer invasion and metastasis. We have intensively investigated the role of ovarian cancer-derived EVs carrying nucleic acids. The EVs carrying MMP1 mRNAs promote peritoneal dissemination and the EVs carrying miRNAs can be the biomarkers for early detection. Ovarian cancer cells secrete DNAs in EVs via micronuclei and those EVs can be the novel targets for biomarkers and therapeutics. Our works have contributed to providing its clinical relevance which could lead to benefitting patients with ovarian cancer.

シンポジウム 2 P 予後と関連づけた胎児・胎盤機能の基礎的・臨床的病態解明と治療戦略

1) 超音波を用いた新たな胎児発育評価

慶應義塾大学 池ノ上 学

【背景】

出生体重は周産期予後の重要な予測因子であるだけでなく、児の長期予後とも関連する。低出生体重児では成人期の心血管疾患や生活習慣病の頻度が高く、また妊娠糖尿病（Gestational diabetes mellitus：GDM）の母体から出生した Heavy for date 児では、小児期のメタボリックシンドローム（肥満、高血圧、高脂血症、耐糖能異常）の発症リスクが上昇する（Developmental Origins of Health and Disease：DOHaD）。従って、胎児期における発育の評価は極めて重要である。これまで超音波断層法を用いた胎児推定体重がそのゴールドスタンダードとして用いられてきたが、±10%程度の測定誤差がある。これは推定体重が、主に児頭大横径や大腿骨長などの骨成分を主体に算出され、脂肪や骨格筋などの軟部組織量が考慮されていないことが一因である。さらに出生時の体脂肪率は小児期の体脂肪率と相関し、蓄積された脂肪組織から分泌されるアディポカインは、インスリン抵抗性を根幹とするメタボリックシンドロームを惹起する。そのため、脂肪量も含めて胎児発育を詳細に評価し適切な周産期管理を行うことは、新生児予後のみならず小児期・成人期も含めた長期予後の改善を目指す上で重要である。そこで本研究では、これまで注目されてこなかった胎児期における脂肪量に着眼し、新たな超音波パラメーターを用いて新生児体脂肪率の予測因子や胎児脂肪量の規定因子を探索することとした。

【目的】

ヒト新生児は他の哺乳類と比較して体脂肪率が高く、脂肪量の個体差は出生体重にも大きな影響を与える。新生児期における脂肪量の計測法はすでに確立されているが、これまでヒト胎児における脂肪量を計測した報告は少ない。そこでまず、

(i) 超音波を用いて妊娠中期・後期にヒト胎児脂肪量の計測を行い、新生児体脂肪率の予測能について検討した。

次に、胎児脂肪量の規定因子について検討を行った。胎盤から臍帯静脈を介して胎児へ流入した血液は、一部が静脈管を介して心臓・脳へ運ばれ、残りは炭水化物や脂質などの栄養基質の合成・分解の場である肝臓へ流入する。ヒツジを用いた動物実験では、胎児肝血流量の増加により、肝細胞におけるインスリン様成長因子などの糖代謝・脂質代謝関連ホルモンの分泌が促進されることが示されている。一方で、これまでヒト胎児における肝血流量と脂肪量の関連についての報告は少ないことから、(ii) ヒト胎児における胎児肝血流量が新生児体脂肪率へ与える影響について検討を行った。

また、母体糖代謝異常例では、胎児膵β細胞の刺激による高インスリン血症が誘因となり、妊娠後期における胎児の体幹・上肢の脂肪量の増加や、新生児体脂肪率の上昇をきたす。近年、脂肪を含む胎児軟部組織量のパラメーターとして胎児四肢容積が注目され、出生体重の予測にも用いられているが、これまで母体糖代謝異常が胎児四肢容積に与える影響について検討した報告はない。そこで、(iii) GDM群における胎児四肢容積の発育の特徴を、正常耐糖能（Normal glucose tolerance：NGT）群と比較検討することとした。

【方法】

(i) 胎児脂肪量による新生児体脂肪率の予測

正常単胎妊婦109例を対象とし、妊娠20週および30週に胎児上腕・大腿・腹部における脂肪量を計測した。具体的には、上腕・大腿正中での横断面像において、総面積から骨格筋および骨を含む面積を除き、脂肪面積を算出した。また、腹囲

計測断面における腹壁前面の脂肪厚を計測した。新生児体脂肪率は、倫理委員会承認のもと Dual Energy X-Ray Absorptiometry を用いて測定した。交絡因子として母体年齢、経産数、非妊時 BMI、母体体重増加量、在胎週数、児の性別を考慮し、妊娠 20 週および 30 週における胎児脂肪量と新生児体脂肪率の相関について、重回帰分析を用いて検討した。さらに ROC 解析を行い、胎児脂肪量による新生児体脂肪率高値 (≥ 90 パーセント) の予測能について検討した。

(ii) 胎児肝血流量と新生児体脂肪率の関連についての解析

正常単胎妊婦 62 例を対象として、妊娠 30 週に胎児肝血流量を測定した。肝血流量は既報に基づき、臍静脈血流量と静脈管血流量の差として算出した。交絡因子を考慮し、重回帰分析を用いて胎児肝血流量と新生児体脂肪率との相関について検討した。さらに、母体非肥満群 (非妊時 BMI < 25) と肥満群 (非妊時 BMI ≥ 25) に層別化し同様の解析を行った。

(iii) GDM における胎児四肢容積の発育についての解析

単胎妊婦 165 例 (GDM : 40 例, NGT : 125 例) について、妊娠 20 週から 37 週に胎児四肢容積を計測した。具体的には、上腕・大腿の中央 1/2 の領域を抽出し、長管骨と直交する 5 断面における上腕・大腿の断面積を積分することで上腕・大腿部分容積を算出した。交絡因子で補正を行った上で、GDM 群と NGT 群における上腕・大腿部分容積の発育を比較した。

【結果】

(i) 新生児体脂肪率は $13.9 \pm 5.7\%$ (平均 \pm SD) であり、妊娠 30 週における胎児上腕・大腿・腹部の

脂肪量と有意な相関を示した。特に胎児上腕の脂肪面積率は新生児体脂肪率の有用な予測因子であり、新生児体脂肪率 ≥ 90 パーセントの予測能は感度 72%、特異度 71% であった。一方で、妊娠 20 週における胎児脂肪量は新生児体脂肪率との相関を認めなかった。

(ii) 妊娠 30 週における胎児肝血流量は、新生児体脂肪率と有意な正の相関を示した。この相関関係は、特に非肥満群で有意差を認め、肥満群では有意差を認めなかった。一方で、胎児肝血流量は新生児骨格筋量とは有意な相関を認めなかった。

(iii) 単胎妊婦 165 例に対してのべ 287 計測 (GDM 群 : 82 計測, NGT 群 : 205 計測) を行った。多変量解析の結果、GDM 群では妊娠 32 週以降で上腕部分容積が有意に増加した。一方で大腿部分容積は、妊娠期間を通じて両群間で差を認めなかった。

【結論】

妊娠後期における胎児上腕の脂肪量は新生児体脂肪率の有用な予測因子であった。また、胎児肝血流量は非肥満妊婦における新生児体脂肪率の規定因子であると考えられた。さらに、母体糖代謝異常により胎児上腕の脂肪蓄積が促され、胎児上腕容積の増大をきたすことが示唆された。今後さらに、胎児脂肪量や肝血流量、四肢容積の規定因子 (糖代謝・脂質代謝に関連する内分泌因子や胎盤の糖質・脂質輸送体など) を解明していくことで、胎児発育への臨床的介入や治療戦略の確立が可能となりえる。さらに、本研究で検討した、胎児脂肪量に関連する新たなパラメーターを用いて胎児発育のより詳細な評価を行うことで、児の周産期予後のみでなく長期予後に関連する病態の解明や、早期発症メタボリックシンドロームの一次予防へとつながることが期待される。

Symposium 2 **P** Basic and clinical pathological understanding and treatment strategy for fetal and placental function associated with prognosis

1) Newer insights into fetal growth and body composition

IKENOUE Satoru

*Keio University***[Background]**

Already at birth, newborns exhibit substantial variation in fat mass. This inter-individual difference tracks across infancy into childhood, and relates to future risk of obesity and metabolic disorders. The elucidation of antecedent conditions that modulate fetal growth and fat deposition is an area of active investigation.

[Objectives]

The objective of the study was to investigate the ultrasound-based parameters that determine fetal fat mass and predict newborn adiposity. First, we investigated whether measures of fetal fat mass are associated with newborn adiposity. Next, we examined fetal umbilical venous blood flow as an index of nutrient substrate transport (including lipids) from the placenta to the fetal compartment, and to the fetal liver where nutrient inter-conversion occurs. Hence, we investigated whether fetal liver blood flow (fLBF) is a determinant of newborn adiposity. Finally, we examined the effect of maternal glucose intolerance on fetal fractional limb volume, which is an emerging parameter of fetal soft tissue volume including fat mass.

[Methods]

(1) In 109 low-risk pregnancies, cross-sectional arm and thigh percent fat area and anterior abdominal wall thickness were measured at 20 and 30 weeks. Newborn percent body fat was quantified by Dual Energy X-Ray Absorptiometry. The association between fetal fat mass and newborn adiposity was determined by multiple linear re-

gression.

(2) fLBF was quantified at 30 weeks by subtracting ductus venosus flow from umbilical vein flow in 62 uncomplicated pregnancies. Multiple regression analysis was used to determine the association between fLBF and newborn adiposity.

(3) Fetal fractional arm volume (AVol) and thigh volume (TVol) were assessed in 165 (125 normal glucose tolerance [NGT] and 40 GDM) pregnancies between 20 and 37 weeks. AVol and TVol were compared between the groups across gestation.

[Results]

(1) Fetal fat mass measures at 30 weeks, and not 20 weeks, was significantly associated with newborn percent body fat. Fetal arm percent fat area indicated the strongest association with newborn adiposity.

(2) fLBF at 30 weeks was significantly and positively associated with newborn total fat mass and percent body fat, and not with lean mass.

(3) Overall, 287 (205 NGT and 82 GDM) scans were performed. AVol was significantly larger in the GDM group than in the NGT group after 32 weeks. TVol was not different between the groups across gestation.

[Conclusions]

Fetal arm fat mass is an early indicator of newborn adiposity, which is affected by fetal liver blood perfusion. Maternal glucose intolerance could be one of the determinants of fetal arm fat and volume in late gestation. Elucidating the maternal and placental factors that influence fetal

fat mass, fLBF and fractional limb volume may help develop clinical intervention strategies for altered fetal growth, which potentially lead to

primary prevention of the metabolic dysfunction in later life.

シンポジウム 2 P 予後と関連づけた胎児・胎盤機能の基礎的・臨床的病態解明と治療戦略

2) 妊娠高血圧腎症の発症につながる妊娠初期絨毛の機能変化についての検討

昭和大学 川 嶋 章 弘

【目的】

妊娠高血圧腎症 (preeclampsia : PE) は妊娠初期の胎盤形成不全が原因の一つと考えられている。妊娠初期の絨毛細胞の機能として、酸化ストレスに対する耐性および血管新生の促進作用は胎盤形成に重要である。また、妊娠初期に起こる PE の発症につながる胎盤形成不全の病態を明らかにし、その評価法と介入法の開発につなげることは周産期管理の質の向上に不可欠である。そこで本研究では妊娠初期の絨毛機能に環境因子が関与することから、PE に関連する環境因子に伴う妊娠初期絨毛の機能変化を明らかにするとともに、その病態を無侵襲的に評価する分子マーカーの開発を目的に検討をした。

【方法】

検討 1 : 母体血清蛋白を用いた PE の発症予測

妊娠 11~13 週の妊婦血清 Placenta growth factor (PGF) 濃度を DELFIA アッセイ (PerkinElmer[®]) で測定し、前方視的にその後の臨床経過を確認した。また、母体背景、母体平均血圧、子宮動脈血流 (UtA-PI) を組み合わせて Fetal Medicine Foundation (英国) のアルゴリズムを用いた発症予測の精度を検討した。さらに妊娠 32 週未満に発症した高血圧を合併しない早発型胎児発育不全 (FGR) 症例の妊娠 26~31 週の妊婦血清中のサイトカインをマルチプレックス解析し、その後の早発型 PE 発症との関連を解析した。

検討 2 : 妊娠初期の酸化ストレスによる絨毛細胞の病態変化、絨毛細胞の機能に及ぼす抗酸化剤および母体環境の影響についての検討

妊娠 6~8 週の絨毛組織から低酸素環境下で接着性の絨毛細胞を抽出した。その細胞を低酸素環

境下で培養し、その後に細胞を酸素化することで妊娠初期の生理的な酸素化の環境を模倣した。酸素化に対する活性酸素種の産生や絨毛細胞の血管増殖因子およびアポトーシス関連遺伝子の発現の変化を検討した。さらに酸素化に対する抗酸化剤の効果および母体喫煙が及ぼす影響を検討した。検討 3 : PE を発症する妊婦における初期絨毛の DNA メチル化変化

環境因子である喫煙が胎盤の形成に関与していることから、エピゲノム修飾のひとつである DNA メチル化に注目した。妊娠 12 週に染色体検査の目的で絨毛穿刺を行った症例から余剰絨毛を採取し、凍結保存した。その後に PE を発症した 2 例と正常血圧 4 例の絨毛組織において Reduced representation bisulfite sequencing を行い、両者の DNA メチル化の違いを比較した。

上記の全ての研究は、当大学の医の倫理委員会またはヒトゲノム倫理審査委員会の承認を得た上で参加者に説明の上で文書による同意を得て実施した。

【成績】

検討 1 : 母体血清蛋白を用いた PE の発症予測

妊娠初期の母体血清 PGF 濃度を用いた PE の発症予測

妊娠初期評価を 913 例に実施し、その後の経過中に早産期 PE は 11 例を含む 26 例で PE を発症した。早産期 PE、満期 PE、非罹患での母体血清 PGF 濃度の中央値はそれぞれ 19.1, 36.5, 38.7 pg/mL であり、早産期 PE で有意に低値を示した。FMF アルゴリズムを用いた発症予測により早産期 PE の発症の検出率は 10% 偽陽性率水準で 91% であった。このことは妊娠初期絨毛では PE

の発症につながる病態が既に形成されていることを示すものであった。

早発型 FGR 症例における早発型 PE 発症と関連する因子の検討

早発型 FGR の 20 例中 14 例が 34 週未満に分娩を要し、その理由は 6 例で早発型 PE、残りの 8 例で胎児機能不全であった。早発型 FGR で PE の発症に関係なく母体血清 PGF 濃度は低値、sFLT-1、Endoglin および Leptin 濃度は高値を示したが、PE 発症に特異的な血清蛋白は抽出されなかった。その後の経過で胎児機能不全となる症例では sCD40L および EGF 濃度が高値を示した。PGF は妊娠初期の胎盤形成不全の病態は FGR と PE の双方の発症に関連すると考えられたが、PE の病態をより良く反映するマーカーの必要性が示唆された。

検討 2：妊娠初期の酸化ストレスによる絨毛細胞の病態変化、絨毛細胞の機能に及ぼす抗酸化剤および母体環境の影響についての検討

妊娠初期の酸化ストレスによる絨毛細胞の病態変化と抗酸化剤の影響

抗酸化剤 (VitC) の添加は酸素化に伴う絨毛細胞からの活性酸素種の産生を減少させ、アポトーシスに関連した *BCL2* 遺伝子発現量を増加させ、*TP53* の発現量と *BAX/BCL2* 比を低下させた。このことから抗酸化因子が絨毛細胞のアポトーシスを抑制し、妊娠初期のらせん動脈にリモデリングがすすむ段階での酸素化はアポトーシスを介して胎盤形成に重要な役割を担うことが示唆された。母体環境の影響の検討

喫煙妊婦より抽出された絨毛組織では *HIF1A*、*TP53* および *BAX* 遺伝子発現、および *BAX/*

BCL2 比は高値を示し、環境要因である喫煙が妊娠初期の絨毛組織でアポトーシスを促進していることは喫煙で FGR が増加する病態との関連を示唆する結果であった。また PGF 遺伝子発現は高値を示したことから、PGF を介した血管形成を促すことで胎盤形成を促進すると推察された。さらに喫煙妊婦より抽出された絨毛細胞では、急激な酸素化に対して PGF 遺伝子および PGF タンパクの発現が高値を示した。このことは環境要因がなくなった後にも PGF 産生亢進の影響が持続していることを示しており、母体環境に伴うエピゲノム変化の関与を示唆する結果であった。

検討 3：PE を発症する妊婦における初期絨毛の DNA メチル化変化

PE を発症する妊娠初期絨毛では、遺伝子のプロモーター領域で 56 遺伝子にメチル化変化を認め、エンリッチメント解析では胚性幹細胞の分化制御に重要なポリコム抑制複合体 2 の転写因子結合部位が抽出された。このことから、その後に PE を発症する妊婦の妊娠初期絨毛組織では、初期胚発生の転写結合に関連した DNA メチル化変化が PE の病態形成に関連があると示唆された。

【結論】

妊娠初期の胎盤形成はその後の PE などの妊娠合併症の発症に重要な影響を持つ。今回の検討で環境因子や抗酸化因子がこの過程に影響することが明らかになった。妊娠初期の胎盤形成を母体血清中 PGF 濃度でモニターできるものの、同時に胎盤形成不全と関連する絨毛のエピゲノム変化に着目することで、PE に選択性の高い新たな分子マーカーの開発が期待される。

2) First-trimester assessment of placenta function for the prediction of preeclampsia

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The aetiology of preeclampsia is multifactorial and recognizes the role of inflammation, oxidative and endoplasmic reticulum stress, and angiogenic dysfunction. The placenta is considered foremost in the pathophysiology of preeclampsia, as delivery of the placenta relieves the condition. Involvement of defects in extravillous trophoblast invasion and adaptation of spiral arteries in early-onset preeclampsia are now generally accepted. While genetic factors play a role, exposure to environmental contaminants has also been shown to have a profound influence in some cases, supporting mechanisms via the epigenome. Epigenetic mechanisms are believed to link environmental contaminant exposures to various phenotypes. Maternal exposures, such as smoking, antioxidants can strongly affect the fetal environment. Our present data drawn from human chorionic villi will emphasize develop-

mental windows of susceptibility. These preliminary data identified novel patterns of differential DNA methylation in genes regulating stem cell differentiation in the chorionic villi from women during the first trimester of pregnancy who were destined to develop preeclampsia in the third trimester. Further, some patterns of differential DNA methylation were also found in the common genes from cell-free DNA in the blood circulation of women during the first trimester, suggesting that the epigenomic patterns may predict preeclampsia and recognize subtypes of preeclampsia reached through different pathophysiological pathways. Identifying subtypes and revealing their different pathophysiologicals will provide specific targets for prevention, prediction, and treatment, addressing personalized care.

シンポジウム 2 P 予後と関連づけた胎児・胎盤機能の基礎的・臨床的病態解明と治療戦略

3) 食事由来母体炎症の胎児・胎盤機能不全への影響と長期予後改善を目指した治療・予防戦略 ビッグデータならびに羊胎仔慢性実験モデルから

福島県立医科大学 経塚 標

【背景】

母体の炎症は、早産の主な原因であることに加え、炎症が児に波及した場合、長期予後に関わる事がある。日常診療における胎児心拍数モニタリングの心拍数基線細変動 (Variability) や徐脈 (Deceleration) は胎児 wellbeing 評価における重要項目であるが、現時点では急性子宮内炎症時においてこれらがどのようなパターンで出現するかは明らかになっていない。子宮内炎症による胎児心拍数モニタリングパターンの解析は、その侵襲さから大動物を用いた基礎実験が必要である。一方で母体の慢性炎症は、胎盤形成、胎児胎盤循環を介した産科合併症に影響を与えるが、プレコンセプション期の炎症予防により周産期合併症を減少させるといった議論は今までになされていない。これまで我々は、大規模コホート調査 (エコチル調査) より、食事に起因する包括的炎症の指標である Dietary inflammatory index (DII) に着目し、プレコンセプション期としての妊娠1年前からの食事での DII 高値は妊娠初期の母体全身炎症と関連することを報告した。DOHaD 仮説に基づけば、妊娠期の炎症などのストレスは次世代に影響を与えることになるが、現在までに母体のプレコンセプション期の DII 値と、周産期短期長期予後に関する報告は非常に少ない。

【目的】

(1) 動物実験により子宮内炎症時における胎児心拍数モニタリングパターンを解析する (2) エコチル調査により妊娠前の炎症誘発食がもしくは炎症抑制食が新生児予後に与える影響について調べる。

【方法】

(1) 羊胎仔慢性実験モデルを用いた子宮内胎仔炎症における胎仔心拍数モニタリングの評価を行った。妊娠 118~120 日の妊娠羊 (n=7) を全身麻酔下に手術し、羊胎仔慢性実験モデルを作成した。子宮内炎症による胎仔 acidosis モデルは、羊水腔内に Lipopolysaccharide (LPS) を投与することにより作成した。術後 4 日、5 日に LPS : 40mg を羊水腔に投与した。子宮内胎仔死亡 (IUFD) に至るまでの胎仔心拍数の①基線細変動 (STV : Short term variability) 定量値、②圧受容体反射 (BRS : Baroreceptor sensitivity) を計測解析した。①-②ともに 1) control : 初回 LPS 投与前 24 時間、2) acute : 初回投与から 2 回目 LPS 投与前の 24 時間、3) acidosis : 2 回目 LPS 投与から胎仔死亡のまでの、3つの phase に分類し比較した。(2) コホート調査による研究は 2011 年から 2014 年にエコチル調査に参加した妊婦を対象とした。Food Frequency Questionnaire (FFQ) より各妊婦の DII を計算し、DII をもとにハイリスク症例を除外した経陰分娩妊婦を 5 分位化した (Q1 : Most anti-inflammatory group, Q5 : Most pro-inflammatory group)。多変量解析を用いて、Q5 グループにおける胎児機能不全の指標として分娩時臍帯動脈 pH < 7.20, pH < 7.10, pH < 7.00 のリスクを解析した。解析に当たっては分娩歴を考慮し初産婦、経産婦に層別化し解析した。

【成績】

(1) 胎仔はすべて 2 回目 LPS 投与後約 24 時間後に IUFD となった。絨毛膜羊膜、臍帯とも病理検査ではいずれも高度な炎症を認めていた。① STV 定量値は acidosis 期において、IUFD となる 3~6 時間前に有意な STV 上昇を認めた。② BRS

については control, acute, acidosis 期において BRS の平均値は control, acute 期に比較し, acidosis phase では BRS の有意な低下を認めた. (2) 22,289 人の初産婦経陰分娩症例 (Q1 : 3,495, Q2 : 4,051, Q3 : 4,463, Q4 : 4,788, Q5 : 5,492), 34,201 人の経産婦 (Q1 : 7,813, Q2 : 7,240, Q3 : 6,916, Q4 : 6,527, Q5 : 5,705) が解析対象となった. 妊娠前の DII 値 (pro-inflammatory diet) が高い母体は, 妊娠初期の母体白血球増多, 中期尿中活性酸素 (8OHdG) の増加を認めた. 多変量解析により, 初産婦経陰分娩症例の Q5 群において, 出生時臍帯動脈 pH < 7.10 のリスクは aOR : 1.64 (95% CI : 1.12-2.39) と増加した. このリスクは分娩所用時間を加味した解析モデルでも修正されることはなかった. 一方経産婦を対象とした多変量解析では, 高 DII 食事摂取と出生時胎児機能不全との関連は見られなかった.

【結論】

近年, 妊娠前の適切な時期に必要な知識・情報を妊娠希望女性やカップルを対象に提供し, 将来の妊娠のためのヘルスケアを行うプレコンセプションケアの概念が広まっている. もし母体個人

の日々の栄養内容が周産期合併症の発症や DOHaD 仮説に準ずる児の長期予後に関与するとなれば, プレコンセプションケアとして妊娠を希望する女性への妊娠前からの栄養指導により, 早期に女性自身が主体的に周産期医療の改善へ積極的に取り組める可能性が広がる. 今回大動物実験により, 子宮内炎症時において胎仔 variability は増加し, 徐脈の程度は減弱した. これは, ヒト胎児が子宮内低酸素を介した胎児機能不全となる時とは明らかに異なるパターンである. また慢性炎症状態から経陰分娩から出生した児は出生時アシドーシスのリスクが上昇することが大規模コホート調査から明らかになった. 当シンポジウムでは炎症というキーワードを用いて, 炎症による新生児短期長期予後改善の試みを動物実験, さらにビッグデータ解析の双方からアプローチし, 胎児心拍数モニタリングの重要性, プレコンセプションケアの重症性について述べる. また DOHaD 仮説に基づき, 食事に基づくプレコンセプションケアによる児の長期神経予後改善を試みた研究についても報告する.

Symposium 2 **P** Basic and clinical pathological understanding and treatment strategy for fetal and placental function associated with prognosis

3) Inflammatory diet during Pregnancy and fetal development : Study from Japanese birth cohort study and chronically instrumented fetal sheep

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[Objective] This study aimed to (1) analyze the pattern of fetal heart rate monitoring during intrauterine inflammation through animal experiments and (2) investigate the effect of inflammation-inducing diet prior to pregnancy on fetal development. **[Methods]** (1) We evaluated fetal heart rate monitoring in intrauterine fetal inflammation using an experimental chronic fetal sheep model. Pregnant sheep (n=7) at 118-120 days of gestation were operated under general anesthesia to create the chronic fetal sheep experimental model. The intrauterine inflammation-induced fetal acidosis model was created through administration of lipopolysaccharide (LPS) into the amniotic fluid cavity. On the fourth and fifth postoperative days, 40 mg of LPS was administered into the amniotic cavity. Short term variability (STV) and baroreceptor sensitivity (BRS) of fetal heart rate were measured and analyzed until intrauterine fetal death (IUFD). Both STV and BRS were classified and compared in three phases, namely control (24 hours prior to the first LPS administration), acute (24 hours from the first LPS administration to the second LPS administration), and acidosis (from the second LPS administration to IUFD). (2) The cohort study included pregnant women who participated in the Japanese cohort study from 2011 to 2014. The DII of each participant

was determined using the Food Frequency Questionnaire (FFQ). Participants were divided into five groups based on the DII (Q1 : most anti-inflammatory group, Q5 : most pro-inflammatory group). Using multivariate analysis, risk analysis was performed using umbilical artery pH at delivery (pH<7.20, pH<7.10, and pH<7.00). **[Results]** (1) All fetuses exhibited IUFD approximately 24 hours after the second LPS administration. STV showed a significant increase three to six hours before IUFD in the acidosis stage. Furthermore, significant decrease in BRS in the acidosis phase was observed. (2) High DII levels showed increased maternal leukocytosis in early pregnancy. In addition, multivariate analysis showed an increased risk of umbilical artery pH <7.10 at birth in the Q5 group of firsttime vaginal delivery with an aOR of 1.64 (95% CI : 1.12-2.39). **[Conclusion]** In this animal study, we observed an increase in fetal variability and a decrease in the degree of deceleration during intrauterine inflammation. In addition, a large cohort study has shown that pro-inflammatory diet was a risk factor for fetal acidosis among nulliparous women with vaginal delivery. In this symposium, we will discuss the importance of fetal heart rate monitoring and preconception diet to improve the long-term neurological prognosis of infants.

シンポジウム 2 P 予後と関連づけた胎児・胎盤機能の基礎的・臨床的病態解明と治療戦略

4) 胎児心不全の診断マーカー及び新規治療法の開発

国立循環器病研究センター再生医療部 三好剛一

1 胎児心不全の診断マーカーの開発

【目的】

胎児先天性心疾患及び不整脈は胎児心不全の主要な原因である。胎児心不全は胎児超音波検査に基づいて重症度診断されるが、その診断精度には限界があることから、より客観的な診断マーカーが望まれている。そこで、胎児心不全の診断に活用できる臍帯血、羊水、母体血中のバイオマーカー開発及び病態解明を目指して臨床研究を実施した。まずは、臍帯血、羊水を用いて、成人領域で心不全マーカーとして広く臨床応用されているナトリウム利尿ペプチド (ANP, BNP, NT-proBNP) の胎児胎盤循環における動態について検討した。次に、母体血中で胎児心不全時に変動するバイオマーカーについて探索した。

【方法】

2012~2016年に国立循環器病研究センターで周産期管理した胎児先天性心疾患・不整脈及び正常胎児において、分娩時に採取した臍帯血(血漿)及び羊水、同センターバイオバンクに保管された妊娠30週前後の母体血(血清)を用いて、以下について検討した。

- ①胎児心不全の重症度と臍帯血中ナトリウム利尿ペプチドの関連
- ②胎児心不全の重症度と羊水中ナトリウム利尿ペプチドの関連
- ③胎児心不全を反映する母体血中ホルモン及びサイトカイン類の探索 (hCG, AFP, Bio-Plex Pro Human Cancer Biomarker Panels 1, 2)

【成績】

①臍帯血中 ANP, BNP, NT-proBNP 濃度は胎児心不全で有意に上昇しており、胎児超音波検査による心不全重症度 (Cardiovascular profile score) と良好な相関性を示した。特に胎児頸脈性・徐脈

性不整脈や中等度以上の房室弁閉鎖不全症例で高値を示し、中心静脈圧の上昇との関連が考えられた。臍帯血中 ANP, BNP, NT-proBNP 濃度は、胎児不整脈治療の適応決定や治療効果判定にも有用であることが示唆された。また、逆相高速液体クロマトグラフィーによる臍帯血中 ANP, BNP の分子型解析の結果、ANP はほとんどが成熟型より構成され大部分が胎盤で代謝される一方、BNP は前駆体が主体で胎盤での代謝をほとんど受けないことが明らかになった。なお、臍帯血中 ANP, BNP 濃度は母体血中 ANP, BNP 濃度とは相関せず、母体循環と胎児胎盤循環は独立していると考えられた。

②羊水中では、NT-pro BNP 濃度は、臍帯血中濃度と良好に相関し、胎児心不全の重症度を反映した。一方で、羊水中 ANP, BNP 濃度は極めて低く、マーカーとしての利用は困難であった。

③母体血を用いたバイオマーカー探索では、まず主成分解析より、炎症性サイトカイン、アポトーシス・血管新生因子が、胎児心不全時に母体血中で変動していることが示された。多変量解析の結果、母体血中の胎児心不全バイオマーカーの候補因子として、TNF- α , VEGF-D, HB-EGF が同定された。これら3つを組み合わせた場合の診断精度は、感度 100%, 特異度 80.3%, 陽性的中率 33.3%, 陰性的中率 100% (AUC=0.90)であった。

【結論】

臍帯血中ナトリウム利尿ペプチドは、成人と同様に胎児においても心不全の重症度を反映することが示された。ナトリウム利尿ペプチドの上昇には、胎児の心形態異常自体ではなく、中心静脈圧の上昇が強く関与していた。一方で、母体循環と胎児胎盤循環は独立しており、胎児では成人とは異なるナトリウム利尿ペプチド分画を呈し、臍帯

血中で ANP より BNP の方が高い安定性を有することが示された。羊水中では、NT-proBNP 濃度が胎児心不全の診断マーカーとして応用可能と考えられた。さらに、胎児心不全時に母体血中で炎症性サイトカインや血管新生関連因子が変化することを初めて明らかにした。さらなる検証が必要であるが、胎児への侵襲性が無い新しい診断法として臨床応用が期待される。

2 胎児心不全の治療法の開発

【目的】

胎児先天性心疾患において心不全が進行した場合には、早期娩出して新生児治療に移行するしかないが、在胎週数が早ければ早いほど救命が難しくなるため、胎内で循環動態を維持する胎児治療法が望まれる。しかし、胎児心不全のモデル動物はなく、実験系が確立していないことから、胎児心不全治療法の開発はこれまで全く進んでいなかった。そこで、小動物用超音波高解像度イメージングシステム（Visual Sonics Vevo2100®）を用いて、胎仔期の心臓形態及び循環動態を経時的に評価することにより、胎児心不全モデルマウスを探索した。さらに、見出した胎児心不全モデルマウスを用いて、ホスホジエステラーゼ5阻害剤である Tadalafil の胎仔胎盤循環への効果を検討した。

【方法】

- ① *Hrt2* 遺伝子は Notch・ALK1 シグナル伝達系の下流で転写制御に関与し、胎生初期より心臓に強く発現している。*Hrt2* ホモ欠損マウスは心臓形態異常（心室中隔欠損症、三尖弁低形成など）を呈し、出生後早期にうっ血性心不全で死亡することが知られていた。小動物用超音波高解像度イメージングシステムを用いて、*Hrt2* ホモ欠損マウスの胎生期における心臓形態及び胎仔胎盤循環の評価を行った。
- ② Tadalafil は肺高血圧症の治療薬として小児・成人領域で用いられているが、心収縮能改善作用

や胎盤血管拡張作用を有することが近年報告されている。*Hrt2* ホモ欠損マウスの胎仔に対して、胎生期より Tadalafil を経胎盤的に投与することで、心臓形態異常や心不全の進行を抑制できるのではないかと考えた。*Hrt2* ヘテロ欠損マウス同士を交配し、無治療群、Tadalafil 0.04mg/mL 投与群、Tadalafil 0.08mg/mL 投与群の3群（各9匹）に分けて、胎生 10.5~18.5 日目にかけて母獣に飲水投与を行い、*Hrt2* ホモ欠損マウス胎仔における心臓形態及び循環動態への効果について検討した。

【成績】

- ① *Hrt2* ホモ欠損マウス胎仔では、心室中隔欠損症及び右室低形成が共通の表現型であった。また、胎齢が進むにつれて左室の拡大、左心室駆出率の低下、一部の胎仔で胸水貯留を認め、胎児心不全のモデルマウスとなりうる事が判明した。
- ② Tadalafil 0.04mg/mL 投与群において *Hrt2* ホモ欠損マウス胎仔の左室駆出率の改善効果が確認された。胎盤循環及び胎仔の心臓形態や容量負荷の変化を伴っていないことから、Tadalafil の胎仔心筋への直接作用が示唆された。また、用量反応性は示されず、Tadalafil には有効な治療域があると推察された。

【結論】

小動物用超音波イメージングシステムを用いて確立した評価系により、胎仔心臓形態及び胎仔胎盤循環を観察することで、*Hrt2* ホモ欠損マウス胎仔が胎児心不全モデルマウスとなることが示された。さらに、この胎児心不全モデルマウスを用いた解析により、Tadalafil の経胎盤的投与が胎児心不全治療法となりうる知見が得られた。Tadalafil の胎仔心臓に対する分子生物学的な作用機序、投与のタイミング、至適投与量など解明すべき課題は数多く残されているが、これまで全く治療法がなかった領域に光明をもたらす重要な研究成果と考える。

Symposium 2 P Basic and clinical pathological understanding and treatment strategy for fetal and placental function associated with prognosis

4) Development of diagnostic markers and treatment for fetal heart failure

MIYOSHI Takekazu

National Cerebral and Cardiovascular Center

1. Development of diagnostic markers for fetal heart failure

[Objective] It is difficult to appropriately diagnose the severity of fetal heart failure (HF) simply by ultrasonography. In adult cardiology, natriuretic peptides (NPs ; ANP, BNP, NT-proBNP) are the most useful biomarker of HF ; however, biomarkers for fetal HF in the fetal blood, amniotic fluid, and maternal blood are not established.

[Methods] We investigated NP levels in the umbilical cord blood and amniotic fluid in fetuses with congenital heart disease (CHD). The possibility of whether maternal serum biomarkers can diagnose fetal HF was also investigated.

[Results] Plasma NP levels in the umbilical cord blood reflect the severity of HF in fetuses with CHD. Elevated NP levels are mainly attributed to an increase in central venous pressure secondary to arrhythmia or atrioventricular valve regurgitation. Fetal plasma ANP comprises the mature form, and the placenta and umbilical vessels may be the major sites of ANP metabolism. Fetal plasma BNP predominantly consists of the precursor form, which may reduce BNP metabolism in the fetoplacental circulation. Meanwhile, NT-proBNP levels in the amniotic fluid increase according to the severity of fetal HF. Furthermore, maternal serum concentrations of TNF- α , VEGF-D, and HB-EGF were associated with HF in fetuses with CHD. The combination of these 3 cytokines showed sensitivity of 100%, specificity of 80.3%.

[Conclusion] The features of NPs in the umbilical cord blood and amniotic fluid provided a strong basis for their use as biomarkers for fetal HF. Maternal serum concentrations of TNF- α , VEGF-D, and HB-EGF can assess the severity of fetal HF.

2. Development of treatment for fetal heart failure

[Objective] There is no established transplacental treatment for HF *in utero*, and no animal models or experimental systems of fetal HF have been established. This study aimed to investigate the effect of maternal tadalafil administration on fetal cardiovascular function and utero-placental circulation in a murine model of fetal HF.

[Methods and Results] We first used an ultra-high-frequency ultrasound imaging system *in utero* and demonstrated that *Her2* KO embryos had marked left ventricular (LV) dilatation and worsening fractional shortening (FS) as gestation progressed, indicating that the embryos can be used as a murine model of fetal HF. Subsequently, we evaluated the effect of tadalafil treatment (0.04 or 0.08 mg/ml ; T0.04 or T0.08 groups, respectively) on fetoplacental circulation in *Her2* KO embryos. LV FS was significantly higher in the T0.04 group than in control, whereas LV dilatation, mitral E/A ratio, and umbilical artery resistance index were not significantly different among all groups.

[Conclusion] Maternal administration of tadalafil improved LV systolic function without

altering LV morphological abnormalities in *Her2* KO embryos. Our findings suggest that tadalafil

is a potential agent to treat impaired fetal ventricular systolic function.

教育講演 1

本邦の妊産婦死亡の現状と課題

宮崎大学 桂 木 真 司

日本産婦人科医会に登録された妊産婦死亡は年間40から60例であるが、2020年は29例と最も少ない数となった。国の人口動態統計でも、「妊娠、分娩及び産褥」の項目は2019年が32例であったのに対し、2020年は21例と激減した。妊産婦死亡率は、2台となり、わが国は世界でも最も妊産婦死亡の少ない国になった。

母体安全への提言2020年の統計部門で詳述されるように、有床診療所で死亡に関連した初発症状を発症した例が2016年から有意に減少した。また、救急車内での心停止例がほとんどなくなっている。これは2015年から始まった日本母体救命システム普及協議会(J-CIMELS)の母体救命コース(J-MELS)により生命の危険がある妊婦を適切な時期に高次施設に紹介、搬送する医療体制の改善の結果と考えられる。

死亡原因も、産科危機的出血の占める割合は少なくなり、なかでも子宮型羊水塞栓症の減少が顕著である。ショックインデックスを用いた危機的宣言の標準化や出血性ショック時の大量輸液プロトコルなど全国の産婦人科医師間での標準治療の普及と産科出血例の減少の時期が重なった事も興味深い。2010年には年間死亡例60例中、6例を占めていた弛緩出血の原因を、Thrombin(凝固異常)、Trauma(産道裂傷)、Tone(弛緩出血)などの比較的頭に入り易いフレーズを用いて多くの産婦人科医師が対処法/治療法を想起するような意識改革が起こった。それはそれまで最も死亡に繋がる頻度の高かった弛緩出血症例の初期対応を標準化し加速した。さらに産科危機的出血症例においてコマンダーを立てる事で、救急部、産科医師との連携医療の標準化が進んだ。2007年の奈良の大淀病院事件以降、周産期救急症の受け入れ態勢

整備が全国各地で行われた。東京、大阪、他の地域と地域地域で産科緊急症の受け入れ体制は異なるが、以前より広域を搬送ユニットとし、搬送用紙の事前配布や、次期への対策会議の定期開催などより効率的な母体搬送の改善が全国各地で2010年以降行われた。

脳出血、心肺虚脱型羊水塞栓症、心大血管疾患、感染症、肺疾患の重要性が相対的に増えてきた。今後、脳卒中発症直後の初期対応の徹底が脳卒中による後遺症を減少させる手立ての一步である。頭痛や意識障害、嘔吐、麻痺などの局所症状や痙攣などでは脳神経外科への連携を迅速に行うシミュレーションが重要である。脳出血のみならず脳梗塞も妊産婦の重症妊娠高血圧症候群の後遺症に大きく関与する。片側の手足のしびれ、倦怠感、めまい、視覚障害などに対して早期に脳神経外科へのコンサルトを行う事が肝要である。

産婦人科医師による周産期心筋症の早期発見が妊娠高血圧症候群の後遺症の軽減に繋がる。妊娠高血圧症候群、双胎妊娠、高齢妊娠、塩酸リトドリン使用が周産期心筋症のリスク因子である。倦怠感、息切れ、などは妊娠の随伴症状として見過ごされやすい。頻脈、体重増加、SpO₂、呼吸数などを心不全症状としてとらえる事ができるか否かが重症である。周産期心筋症を疑ったら自ら妊産婦の心エコーをして左室の動きが悪い場合、循環器内科医師へコンサルトを行う。産婦人科医師が循環器領域へ一步踏み出す事が今望まれている。

(1) 脳卒中、周産期心筋症の初期症状を見逃さない+鑑別しに行く診療、(2) 各専門医師へ医療連携するタイミングを逸さない、この二つが妊娠高血圧症候群による後遺症を減らすキーであると考えられる。

教育講演 2

AYA 世代婦人科がん患者における妊孕性温存治療 Up-to-date ～最善の治療選択を目指して～

名古屋大学 梶山 広明

がんが全死因の第1位となって久しいが、その約10%はAYA世代に発生すると言われている。男女ともに未婚率の増加を背景に出産の高齢化や少子化が急速に進んでいる。女性特有のがんには未婚や晩産化がリスクファクターとなるものも少なくない。初期婦人科がん患者のQOL維持の視点からもできるだけがんの根治性を損なわずに妊孕性を温存する重要性が増している。婦人科がんは主に子宮や卵巣、卵管に生じる悪性腫瘍である。この場合、妊孕性温存治療の基本は子宮と少なくとも片側の卵巣を残すことである。しかしながら、妊孕性温存に関する臨床病理学的な適応やその術式についても各種ガイドラインによって見解が異なっている現状がある。下記に代表的な初期婦人科がんにおける妊孕性温存治療の現状と臨床上的問題点を列記する。

初期子宮頸がんが妊孕性を温存する場合、微小浸潤癌(IA1期)で得られた摘出検体の病理検査において、切除断端が陰性であること、そして脈管侵襲を認めないことが重要となる。もし、脈管侵襲が認められた場合は骨盤リンパ節郭清術を含めた子宮全摘術が推奨されている。IA2期の場合、標準治療として確立してはいないがIA1期に準じて円錐切除が行われたり、広汎子宮頸部全摘術が適応される。IB1期で比較的腫瘍サイズが小さい(通常、長径2cm以下)症例に対して広汎子宮頸部全摘術が行われている。ガイドライン上での記載はないものの「IA2期およびごくわずかなIB1期の浸潤がんに対して円錐切除でどこまで対応可能なのか?」、あるいは「広汎子宮頸部摘出術でどこまで対応可能なのか?」などは実臨床の上で高頻度に

遭遇しうる疑問点である。

初期子宮体がんでは子宮内膜に限局していると考えられる高分化型類内膜癌が適応となる。現在本邦で子宮体がんの治療に使用することができる唯一のホルモン製剤はmedoxyprogesterone acetate (MPA)である。MPAは原則として600mgを連日経口投与し、寛解後は定期的に経腔超音波検査、内膜細胞診、内膜組織診で経過観察を行う。しかしながらMPA治療によって寛解に至るものも多いが同様に再発も多い。したがって臨床上的問題点としては「再発後のMPA再治療を行う場合、どの程度継続が可能か?」、あるいは「現行のガイドラインで規定されていないG1・内膜限局型を越える症例(例えばG2など)に対してMPA治療は許容されるのか?」などがあげられる。

上皮性卵巣癌に対する妊孕性温存手術の基本術式は患側付属器摘出術、大網切除術、および腹腔内細胞診である。臨床病理学的な必要条件として、原則、IA期かつ低異型度型という条件が掲げられている。本邦のガイドラインでは、IC1期かつ低異型度型の非明細胞癌、あるいはIA期明細胞癌に対する妊孕性温存の可能性を示唆しているが、未だ確立した適応基準ではない。ガイドライン上での適応はないものの「IC1期明細胞癌あるいは片側付属器に限局したIA期・高異型度型に対して妊孕性温存術式を選択することは可能か?」などは実臨床では遭遇しうる問題点である。

本教育講演では上記初期婦人科がんが焦点を当てて、妊孕性温存手術に関する現状と最近の知見を俯瞰し、現時点における運用上の課題と今後の方向性などを概説したい。

教育講演 3

骨盤臓器脱の診断と適切な術式の選択

東京医科大学 西 洋 孝

超高齢社会の到来とともに、高齢者のQOL疾患である骨盤臓器脱 (Pelvic Organ Prolapse: POP) が著しく増加している。骨盤底筋体操などの保存療法が奏功しない、または奏功しないであろうと思われるPOPに対する治療のファーストチョイスは手術療法であるが、治療のためには正しいPOPの診断と適切な術式の選択が重要となる。本邦では、多くの施設で従来法と呼ばれる腔式子宮全摘術+腔壁形成術+腔断端固定術が行われてきたが、30%以上という高い再発率が問題であった。2004年にTension-free Vaginal Mesh (TVM)手術が報告されると、その再発率の低さと手術の簡便さから、この術式はまたたく間に世界的に普及した。しかし、メッシュ露出、骨盤痛や性交痛などの合併症が少なくないこと、メッシュ感染を来すと重篤化する可能性があることなどから、2008年と2011年に米国FDAによる警告が発出された。これら合併症に対する十分な術前のインフォームドコンセントを取得すべき、というのがその主な趣旨だったが、その後、2019年には米国における全ての経腔手術用メッシュの発売が禁止となった。また、TVMの手術適応の判断にも種々の問題が指摘されていた。

TVM手術の衰退により、従来法、仙棘靭帯固定術や腔閉鎖術などのnative tissue repair (NTR)が見直されるようになった。性的活動がなく子宮摘出後や子宮頸がん検診の不要な高齢者には、その低再発率からも腔閉鎖術が適している。仙棘靭帯固定術は、DeLancyのレベルIの障害に

適した術式であるが、狭隘な腔奥の操作が必要なため技術的に難しいと言われてきた。ただし、近年ではそれを容易にする機器が開発され、技術的困難さは解決している。

元来、米国においては、その再発率の低さから仙骨腔固定術がPOP手術療法のゴールドスタンダードであるが、本邦でも2014年にその低侵襲術式である腹腔鏡仙骨腔固定術 (Laparoscopic Sacrocolpopexy: LSC)が保険収載された。この手術はDeLancyのレベルIの障害に適した術式で、腔を生理的な位置に矯正でき性機能温存の点で優れている。また、留置するメッシュを膀胱腔間や直腸腔間にまで延長すれば、レベルIIの障害である膀胱瘤や直腸瘤にも資する。再発率は低くQOLも有意に改善する。しかし、LSCは手技的に高難度であり、あまねく広く普及するには至っていない。これを克服する試みとして、2004年にはDi Marcoらによってはじめてロボット支援下仙骨腔固定術(RSC)が報告された。腹腔鏡は骨盤深部まで拡大して観察することができ、解剖学的構築を確認しながら行う必要のある骨盤臓器脱の手術に有用であるが、骨盤深部の結紮縫合のような腹腔鏡下では難しい操作もロボットの導入により容易となった。2020年にはRSCの保険収載がなされ、予想通り本邦でもその施行例が急増している。

本講演では、仙骨腔固定術のみならず、当科で行っていたTVM手術と現在行なっている仙棘靭帯固定術や腔閉鎖術についても解説したい。

教育講演 4

生殖医療の発展と今後の課題

徳島大学 岩 佐 武

近年の生殖医療の発展は目覚ましく、成功までに長い年月を要した体外受精・顕微授精に代表される生殖補助医療も、現在では一般的な治療として世界各国で実施されている。本邦において2019年に生殖補助医療によって誕生した子どもの数は6万人を超え、これはこの年に生まれた子どもの14人に1人に相当する。令和3年1月からは生殖補助医療に対する助成金が拡充され、また、令和3年10月現在において保険収載に向けての準備も進められていることから、生殖医療に対する世間の注目が高まりつつある。

生殖補助医療の成功とその後の発展を支えてきたのは、生殖内分泌学の進歩とそれにかかわった研究者達の探究心に他ならず、我々産婦人科診療を行う医師はこれらについての知識を持ち合わせておく必要がある。具体的には、生殖関連ホルモンの発見と測定技術の進歩、GnRH分泌機構の解明とそれを制御する手法の確立、およびホルモン製剤による卵巣刺激と子宮環境の調節の実現などがこれにあたる。一方、最近では凍結融解胚移植の技術が確立したことで、凍結した胚を時間およ

び空間を超えて使用することが可能となり、この技術と生殖内分泌学的・遺伝学的手法の組み合わせによって「がん生殖」や「着床前診断」などの新たな検査・治療法が開発された。同時にこれらの技術は「卵子提供」や「代理懐胎」など、第三者が関与する生殖医療を可能としたが、その是非や許容される範囲については未だ議論の渦中にある。また、これらの医療は現在の法制度では対応が困難な新たな問題を生み出しており、体制・規則の早急な整備が必要とされている。これらは社会全体で解決すべき課題であるとともに、実際に診療を行う医師一人一人が高い倫理観を持って真摯に向き合うべき事象と考えられる。

このように、これまでは生殖医療の発展のためにできること全てを行うことが許容されてきたが、生殖医療が完成形に近づきつつある今日においては、「できること」と「してよいこと」を明確に区別するという新たな姿勢が求められている。本講演を通じて生殖医療への知識を深めるとともに、現在議論されている諸問題について興味を持つきっかけとしていただきたい。

生涯研修プログラム 1 ホルモン調節機構 up-to-date

1) 視床下部キスペプチンニューロンによる生殖機能制御

島根大学 金 崎 春 彦

女性の生殖機能は視床下部—下垂体—性腺軸 (HPG axis) のより制御されるが、長年視床下部 GnRH ニューロンがその頂点に位置すると考えられたきた。2003年に特発性低ゴナドトロピン性性腺機能低下症の患者家系から GPR54 (後のキスペプチン受容体) 遺伝子変異が発見されたことからそのリガンドであるキスペプチンが GnRH 分泌を制御する重要な生理活性物質として登場し、その後視床下部にキスペプチンニューロンの存在が明らかになったことで現在では GnRH を制御するキスペプチンニューロンが HPG axis の頂点であると考えられている。少なくともげっ歯類において視床下部の異なる領域に局在するキスペプチン

ニューロンはエストラジオールに対して正反対の反応を示すという現象は、エストラジオールによる正及び負のフィードバック機構を説明できる。また、キスペプチンニューロンが様々な栄養代謝因子あるいはストレス関連因子の受容体を有し、その影響下にあるという知見は、視床下部性無月経をはじめとする月経異常の病態の解明に寄与している。治療薬としてのキスペプチンの使用や、キスペプチンニューロン制御による HPG axis の正常化の臨床研究も進められている。本講演では現在研究が進められているハブニューロンとしてのキスペプチンニューロンの役割について概説したい。

2) 生殖におけるメラトニンの役割

山口大学 田 村 博 史

女性の生殖では、卵胞発育、卵成熟、排卵、黄体形成、受精、子宮内膜増殖や脱落膜化、着床といったダイナミックな変化が、視床下部-下垂体-卵巣系の精巧な内分泌機構によって制御されている。鳥などの季節繁殖動物では、日照時間によって生殖活動が制御されるが、外界の光環境情報を体内の内分泌環境へ変換する脳ホルモンがメラトニンである。生殖腺刺激ホルモン放出抑制ホルモン (GnIH) の分泌を誘導することで、メラトニンは生殖機能を制御している。

一方で、メラトニンは血液中のみならず、脳脊髄液、唾液、卵胞液などの体液中に存在し、メラトニンの膜受容体は全身の多くの臓器に存在している。さらに、フリーラジカルなどの活性酸素種を消去する抗酸化作用を持つことも証明され、メラトニンは神経内分泌作用に加えて、膜受容体を介さない直接的な抗酸化作用で多様な生理作用を発揮している。

我々は、卵胞内に存在する抗酸化物質としてメラトニンに注目している。排卵過程では卵胞内において多量の活性酸素種が発生する。卵成熟や卵胞破裂には必要な刺激であるが、抗酸化機構とのバランスが崩れれば容易に卵子や顆粒膜細胞は酸化ストレスを受け、卵子の質の低下や顆粒膜細胞の機能低下につながる。メラトニンが卵胞液中に高濃度に存在することで、排卵過程で発生する活性酸素種から卵子を保護する可能性について研究し、また、不妊症患者に対してメラトニンを投与することで卵胞内の酸化ストレスを軽減し、卵子の質を向上させる臨床研究も行っている。さらに、アンチエイジングホルモンとしても注目されているメラトニンを長期投与することで、卵子数の減少、卵子の質の低下といった卵巣加齢の予防効果についても研究しており、これらについて解説したい。

生涯研修プログラム 1 ホルモン調節機構 up-to-date

3) オキシトシンの多彩な生理作用

産業医科大学医学部第1生理学¹⁾, 産業医科大学²⁾上田 陽 一¹⁾, 西村 和 朗²⁾, 吉野 潔²⁾

オキシトシンは視床下部室傍核および視索上核に局在する細胞体で産生され、下垂体後葉に投射した軸索終末から活動電位依存的に循環血液中に開口放出される。血中オキシトシンはオキシトシン受容体を介して子宮筋の収縮による分娩促進や授乳時の射乳反射に関与することはよく知られているが、骨形成・骨格筋維持、抗肥満、炎症抑制など多岐にわたる生理作用が報告されている。一方、脳内ではオキシトシン受容体が広範囲に存在しておりオキシトシンニューロンからの軸索の投射先で神経伝達物質として作用するのみならず、細胞体や樹状突起から分泌されたオキシトシンは中枢神経系を介して信頼・絆形成などに関与することが注目されている。私たちは、オキシトシン遺伝子に赤色蛍光タンパク (mRFP1) 遺伝子を挿入した融合遺伝子を用いてオキシトシンニューロンの可視化に成功し、オキシトシン産生の性周期

変化を含む種々の生理学的性質を明らかにしてきた。最近では、オキシトシン遺伝子に人工受容体 (hM3Dq) 遺伝子を挿入した融合遺伝子を用いて作出したトランスジェニックラットを用いて内因性オキシトシンニューロンを選択的に活性化したときの生理作用について検討している。例えば、オキシトシンニューロンの活性化により機械的刺激閾値が上昇することや慢性疼痛モデルでの疼痛緩和作用を見出した。オキシトシンニューロンは下垂体後葉に軸索を投射して血中にオキシトシンを分泌して末梢作用を発揮するのみならず延髄や脊髄へもその軸索を投射しており自律神経系や疼痛調整などに関わっており、オキシトシンニューロンの細胞体や樹状突起から脳内へ分泌されたオキシトシンは絆形成などの高次脳機能に関与しており、多彩な生理作用を発揮することが明らかになってきた。

生涯研修プログラム2 分娩に関わる新しいトピックス

1) 医学的介入のない分娩進行とは？ 分娩第1期活動期はいつから開始するとみなすべきか

横浜市立大学附属市民総合医療センター 青木 茂

分娩の進行を評価する上で、分娩第一期の潜伏期と活動期の考え方が非常に重要である。

潜伏期と活動期の境界については、従来わが国に明確な基準は無かったが、慣習的に、活動期はFriedman 曲線から子宮口開大3-4cm以降とされてきた。しかしながら、Friedman 曲線は1950年代に500人の初産婦の分娩経過から作成された曲線であり、現代の産科医療にそのまま合致するか疑問視されてきた。そこで、2010年にZhangらが62,415人の米国人のデータから現代の米国における標準的な分娩曲線を新たに作成し、Friedman 曲線が現代の分娩進行には合致しない事を報告した。その報告によると、分娩第一期はFriedman 曲線でいわれているよりも、緩徐に進む期間が長く、子宮口開大6cm以降を活動期とすることが提唱された。これを受けてACOGとSociety for maternity and fetal medicine

(SMFM)は2014年にSafe prevention of the primary cesarean deliveryを発表し、分娩進行の評価と対応について定義を修正した。

わが国の一部の施設では、ACOGの変更に伴い、6cm以降を活動期と考えた対応が行われ始めていたが、米国のデータはかなり多くの無痛分娩を含んでおり、日本の現状にそのまま合致するかどうかについては疑念があった。この問題を解決するために、日本産科婦人科学会周産期委員会では、日本における基準を作成するために医学的介入のない日本人の分娩データを用いた自然分娩曲線の作成を行い、子宮口開大5cm以降を分娩第一期の活動期とし、さらに5cmから6cmを加速期、6cm以降を極期とすることを提唱した。本講演では分娩進行曲線を提示し、分娩進行の評価と対応について概説する。

2) 頸管熟化法

浜松医科大学 伊東宏晃

産婦人科診療ガイドライン産科編2020では、「子宮頸管熟化が不良な場合（Bishop score6点以下と判断することが多い）には、子宮頸管熟化・拡張法を実施する」と記載されている。わが国では分娩誘発の際に子宮頸管熟化を促す方法として器械的頸管熟化処置が主に行われてきた歴史があり、臨床経験の蓄積も多い。わが国独自の臨床研究から、エストロゲン前駆物質〔プラステロン硫酸ナトリウム水和物〕の静注製剤や陰坐剤が子宮頸管熟化不全を適応として使用されてきたが、2020年に製造販売が中止された。本薬剤は海外で使用されたことはない。また、わが国では内服薬であるプロスタグランジンE₂製剤〔ジノプロストン〕が妊娠末期における陣痛誘発並びに陣痛促進の適応で用いられる。本薬剤は諸家により子宮頸管熟化作用もあるとされているが、子宮頸管熟化

不全に対する適応は無い。一方、諸外国のガイドラインでは、子宮頸管熟化が不良な場合にプロスタグランジン製剤の腔内投与を推奨するものと、子宮頸管熟化の良・不良に関わらず分娩誘発の第一選択としてプロスタグランジン製剤を腔内投与することを推奨するものがある。わが国でも2021年よりジノプロストン腔内留置用製剤の使用が可能となり、海外と同様の選択肢が選べる環境となった。わが国には器械的頸管熟化処置の手技に練達した産婦人科医師が多く、ジノプロストン腔内留置用製剤の登場により分娩誘発における頸管熟化方法の選択肢が1つ増えることで、これまで蓄積してきました器械的熟化処置の経験を生かし、日本の現状に即した新たな分娩誘発方法が生み出されることが期待される。

生涯研修プログラム2 分娩に関わる新しいトピックス

3) RPOC (Retained products of conception) の診断と管理

産業医科大学 柴田英治

RPOCとは流産或いは児娩出後の子宮内妊娠組織遺残物の総称である。発生頻度は妊娠中期の流産や中絶では40%にも上るが、正期産では1%程度と考えられている。分娩後の過剰出血で、子宮復古不全がない場合や出血開始時期が分娩後に数日から数か月経っている場合は、RPOCが原因であることが多い。RPOCの主要な構成成分は胎盤であり、子宮胎盤循環の豊富な血流の影響を受けて、大量出血を引き起こす。近年、超音波検査、CT、MRIによりRPOCの診断精度が向上し、RPOCに対する適切な管理や治療法が確立されつつある。

病理組織学的なRPOCの診断は、摘出組織中の浮遊絨毛の存在を基盤としてなされるが、臨床的RPOCの診断には超音波検査が有用である。RPOCは、超音波検査で子宮内膜肥厚増 (endometrial echo complex) や腫瘤像として検出される。カラードプラ法やパワードプラ法で病変内

に豊富な血流を検出した場合には、RPOCの確かな診断根拠となる。超音波検査で病変が分かりにくい場合は、CTやMRIが病変の検出に役立つ。注意すべき鑑別疾患には、子宮動静脈奇形、子宮内膜ポリープ、侵入奇胎、胎盤付着部に発生した子宮復古不全などがある。このため、RPOCの診断は、分娩時の状況、出血の開始時期などの臨床経過、および画像情報をもとに慎重になされるべきである。

RPOCの治療には、待機療法、子宮収縮剤投与、EP合剤による月経誘発、子宮内容除去術、子宮鏡下手術、子宮動脈塞栓術、および子宮全摘術や、これらの併用療法など多岐にわたり、治療法の選択に苦慮することが多い。RPOCの病変の状態、拳児希望の有無、施設毎の大量出血時の緊急医療体制を考慮して適切な治療法を選択することが必要である。

生涯研修プログラム3 センチネルリンパ節の保険適応に向けて

1) 子宮頸がん治療におけるセンチネルリンパ節生検の位置づけを考える

東北大学 永井 智之

早期子宮頸癌手術におけるセンチネルリンパ節 (SLN) 理論の妥当性は臨床試験を含めた多くの検証で示されており、国内外のガイドラインにおいても記載されている。SLN の術中迅速診断により転移陽性が判明した場合、根治手術を中止し放射線同時化学療法に移行するという治療戦略は海外では既に行われており、FIGO 分類の改訂に伴いリンパ節転移陽性症例がIIIC 期に分類されるため、本邦においても同様の治療戦略が導入される可能性がある。

一方、SLN 転移陰性症例に対する系統的リンパ節郭清省略手術の安全性は単施設での検討が複数報告されており、系統郭清群との比較において同等の予後が担保されること、術後リンパ浮腫の軽減が報告されている。近年では SLN 陰性症例に対

する系統的リンパ節郭清省略手術の安全性を検証する臨床試験が海外において複数行われており、その結果がまたれる。また、SLN を用いた妊孕性温存手術として、広汎子宮頸部切除術を含む子宮温存手術や子宮頸部円錐切除に SLN を組み合わせた治療戦略も小規模な検討ではあるが報告されており、高い妊娠率や生児獲得率を得ている。

SLN を用いてリンパ節転移の有無をより正確に診断することにより、様々な観点から早期子宮頸癌手術に対して適切な治療方針を選択できることが期待される。本発表では上述した臨床試験を含めた SLN の現状につき概説すると共に、SLN を標準治療に実装するための課題についても考察していきたい。

2) 子宮体癌におけるセンチネルリンパ節生検の現況

大阪医科薬科大学

田中 智人, 大道 正英

子宮体癌において、リンパ節郭清は治療的な役割のみならず、進期診断においても重要な術式の一つとなっている。リンパ節郭清が施行されていない場合、少なからずリンパ節転移例が混在し、リンパ節郭清や術後補助療法による治療効果の恩恵を享受できない症例が存在することとなる。しかしながら、再発リスクが低いと考えられる IA 期や類内膜癌 G1 および G2 では、実際にリンパ節転移をしている症例は少なく、リンパ節郭清による下肢リンパ浮腫などの合併症が問題となっている。

近年、センチネルリンパ節という概念が、乳癌をはじめ様々な癌種で考えられるようになり、臨床応用されている。センチネルリンパ節は、原発巣から流出するリンパ管が、最初に到達するリンパ節で、最も転移し易いリンパ節と考えられ、センチネルリンパ節に転移がなければ、他のリンパ節に転移している確率は極めて低い。センチネルリ

ンパ節は、微小転移の診断のためセンチネルリンパ節マッピングとして利用されたり、術中にリンパ節郭清の要否や郭清範囲を決定するため、センチネルナビゲーション手術として応用される。

NCCN ガイドラインでは、センチネルリンパ節生検に関する項目が記載されており、すでに標準的な術式として推奨されている。また、TNM 分類においてもセンチネルリンパ節生検や、微小転移などの表記方法が記載されており、世界的に広く臨床応用されていることが伺える。

残念ながら、本邦では、子宮体癌におけるセンチネルリンパ節生検は保険適応となっていないばかりか、使用薬剤が適応外使用にあたるため、臨床試験すら困難な状況である。本プログラムでは子宮体癌におけるセンチネルリンパ節生検の現状に加え、保険適応に向けた取り組みや、ハードル、問題点について周知を図る。

生涯研修プログラム 3 センチネルリンパ節の保険適応に向けて

3) 外陰がんに対するセンチネルリンパ節の保険適応に向けて

京都大学 山口 建

外陰がんの根治術には浅鼠径リンパ節郭清を行うことがあるが、下肢浮腫、リンパのう胞などの合併症が問題となる。諸外国では外陰がんに対するセンチネルリンパ節生検が行われており、予後を担保しつつ下肢浮腫などの軽減につながるエビデンスが蓄積されている。本邦ではセンチネルリンパ節生検は2010年に乳癌と悪性黒色腫に対して保険収載され、2018年に皮膚がん(悪性黒色腫、メルケル細胞癌、有棘細胞癌)へ拡大されたが、外陰がんに対しては保険収載されておらず試験的に行われている。以上の背景から現在、外陰がんに対して公知申請へ向けて動いている。NCCNガイドラインや本邦の外陰がん治療ガイドラインでは、大きさが2cmを超えるか間質浸潤が1mmを超えてIII期に至らない腫瘍に対して適応があるとしている。当院では2012年から医の倫理委員会承認の下、センチネルリンパ節の臨床試験を

行ってきた。外陰がん17例の経験から、本邦においても比較的 safely センチネルリンパ節生検を行うことができると考えられる。

これらの背景をもとに子宮頸癌、子宮体癌に対するセンチネルリンパ節生検と同時に先進医療申請を行うこととなった。しかし、厚生労働省のヒアリングにより先進医療Bで行う必要があると指摘を受け、今後はより可能性のある公知申請から保険収載を目指している。

本セッションでは、外陰がんに対するセンチネルリンパ節生検において、4cmを超える腫瘍、患側の鼠径リンパ節が陽性の場合の対側の鼠径リンパ節、局所再発など現在のガイドラインでは取扱いが定まっていない症例に対する取り扱いを既報とともに考察し、外陰がんに対するセンチネルリンパ節生検の必要性和現在の課題について述べる。

生涯研修プログラム 4 産科危機的出血の管理

1) 産科危機的出血の管理における凝固機能の把握

順天堂大学医学部附属浦安病院 牧野 真太郎

産科危機的出血は、常位胎盤早期剝離、前置胎盤、羊水塞栓症、弛緩出血などが原因疾患であり、前置胎盤を除けば、いずれも分娩前にその発生を予測することが困難な病態である。分娩時大量出血で心停止した産婦の70%以上は、発症から4時間以内に心停止に至っており、対応の遅れが母体生命の危機に繋がる病態であるため、迅速な対応が肝要となる。また産科大量出血では、希釈性凝固障害と消費性凝固障害が時として合併することがあり、その際には比較的少量の出血で凝固障害が発生する。産科危機的出血に対する治療の大原則は輸血療法、止血術であるが、凝固因子を速やかに上昇させることが可能であるクリオプレシピテートやフィブリノゲン濃縮製剤が注目されている。産科危機的出血での後天性低フィブリノゲン血症に対するフィブリノゲン製剤の適応拡大が

行われ、我々が持ちうる選択肢は日々増えていくことが期待される。

産科出血のほとんどは双手圧迫法、子宮収縮薬、タンポナーデ法などの低侵襲処置と、適切かつ迅速な輸液や輸血管理によってさらなる侵襲を回避できる。また、母体死亡回避や子宮温存のためにも、麻酔科や放射線科、輸血関連部署などとの協力体制を構築することが重要である。危機的状況下では、統括指揮者（コマンダー）を決め、コマンダーが輸血手配を含め、院内の関連部署と連携し、指揮をとることが大切である。コマンダーは全身状態、緊急度に応じて異型適合血輸血を選択することや、検査結果に依らずに輸血開始のタイミングを図ることなど、様々な状況判断が求められるため、あらかじめ手順を決めておいても良い。

2) 子宮内バルーンタンポナーデ

北九州市立医療センター総合周産期母子医療センター 高島 健

子宮内バルーンタンポナーデは、2006年の国際産婦人科連合（FIGO）や米国産婦人科学会（ACOG）、2009年の英国産婦人科学会（RCOG）などの分娩後出血（PPH：postpartum hemorrhage）に対する予防や治療に関するガイドラインにおいて、動脈塞栓術や開腹術に至る前に行う価値のある有用な止血法とされている。本邦では2017年に改訂された「産科危機的出血への対応指針2017」において、ショックインデックス1以上の分娩時異常出血の初期対応の1つとして、子宮内バルーンタンポナーデが追加された。しかしながら、バルーンの使用に関する具体的な方法が全く

示されていないため、個々の産婦人科医の嗜好や工夫に委ねられているのが現状である。

当院では、2007年5月から子宮内バルーンタンポナーデを開始した。当初は弛緩出血を対象としてメトロイリント（フジメトロ）を用いていたが、2013年からは前置胎盤を対象に加え、Bakri[®]分娩後バルーンを用いるようになった。2019年7月にはアトム子宮止血バルーンも使用している。

本セッションでは、当院での15年間の経験を基に、子宮内バルーンタンポナーデの基本的な手技や当院での工夫や成績について解説する。

生涯研修プログラム 4 産科危機的出血の管理

3) IVR を用いた止血法

慶應義塾大学 落合大吾

産科危機的出血は、我が国の妊産婦死亡の主な原因の一つである。したがって、産科危機的出血の治療は、今そこにある医療資源を迅速に現場に集中し行う必要がある。産科危機的出血への対応ガイドラインでは、直ちに輸血開始、次いで出血原因の検索、さらに子宮圧迫縫合、Interventional Radiology (IVR)、子宮摘出術などによる出血原因の除去を挙げている。また、産科危機的出血は時を選ばず突然に発生する。分娩に携わる医療者は、いつ産科危機的出血が生じて、周囲の状況を的確に判断しながら適切な治療を行う必要がある。

一般に、分娩取り扱い施設では、平日日中には産科医や関連部門のマンパワーは充実しているが、休日・夜間の体制は必ずしも満足するものではない。したがって、産科危機的出血のような「比

較的稀で急な事態」に対する対応は、施設の事情に応じて、事前に関連部署とのコンセンサスを形成しておく必要がある。

また、具体的な止血方法では、産後出血に対するIVRの有用性を示す報告は多く、低侵襲で妊孕性温存の可能が残されるなどの利点がある。しかし、血行動態の安定やDICの有無など、IVRの適応条件には統一見解が得られていない部分もある。

我々はこれまで、産科危機的出血に対して、短時間での大量輸血を目的とした「産科用 massive blood transfusion protocol の運用」と「IVRを用いた止血法」の2つを軸とした治療を行ってきた。本セッションでは、当院での実例を示しながら産科危機的出血の管理について概説する。

生涯研修プログラム5 HBOC 診療と RRSO ならびに RRM の実践

1) HBOC 診療と RRM の実践

高知大学乳腺内分泌外科/臨床遺伝診療部 杉本 健 樹

乳癌領域では2018年HER2陰性進行再発乳癌のオラパリブのコンパニオン診断(CDx)としてBRCA遺伝学的検査(GT),2020年乳癌既発症者のHBOC診断目的のGTとサーベイランス,リスク低減乳房切除(RRM),リスク低減卵管卵巣切除(RRSO)が保険収載となりHBOC診療へのニーズが急激に高まった。乳癌では1)45歳以下,2)多発乳癌(同時・異時,同側・両側を問わず),3)60歳以下のトリプルネガティブ,4)乳癌・卵巣癌の家族歴,5)男性乳癌でGTが保険適用となった。NCCNガイドライン等に準じた病的バリエーション(PV)検出率10%が基準となっているが,これはGTに要するコストや時間により将来変化する可能性がある。家族歴・病歴を問わず乳癌の4-5%にBRCAのPVを認めるため,全ての乳癌患者にGTを行うべきという意見もある。しかし,現状でも年間9万人超の乳癌患者の約40%がGTの適用となるため,現状のHBOC診療に対応できる体

制の整備が急務である。少なくとも保険適用患者すべてへの適正な情報と遺伝診療の提供は必須である。

当院では最大年間約40人であったGT受検者が2020年には100人を超えた。GTを受けた発端者320人中58人(BRCA1:19,2:39),未発症家系員17人(1:6,2:11)にPVを認めた。HBOCでは乳房温存が相対的禁忌で,対側乳房のMRIサーベイランス,RRM,リスク低減卵管卵巣切除(RRSO)が保険で提供できる。その中で,RRSO希望者は多いが,RRM希望者は少ない(RRSO19人,対側RRM6人)。卵巣癌患者や未発症者の両側RRMも施行例がない。乳癌は早期発見が可能で,RRSOと同等の死亡率減少効果はなく整容面で負担の大きいRRMの需要は高くないが,希望者に提供できる体制は重要である。RRSOの保険適用は乳癌患者のみのため,現時点でのRRSOの実践には乳癌のHBOC診療の充実が鍵となる。

2) HBOC 診療と RRSO の実践

慶應義塾大学 阪 埜 浩 司

遺伝性乳癌卵巣癌(hereditary breast ovarian cancer:HBOC)とは,生殖細胞系列のBRCA1あるいはBRCA2遺伝子の病的バリエーション(変異)に起因する遺伝性腫瘍であり,女性であれば高率に乳癌,卵巣癌に罹患する。BRCA1/2遺伝子の病的バリエーションを保持する女性における生涯の乳癌発症リスクは推定41~90%であり,高い対側乳癌リスクがあるとされている。また卵巣癌の発症リスクは,BRCA1遺伝子バリエーションでは39~46%,BRCA2遺伝子バリエーションでは12~27%であると報告されている。そのため,リスク低減乳房切除術や挙児の希望がなくなった時点でのリスク低減卵管卵巣摘出術(risk reducing salpingo-oophorectomy:RRSO)が,がんの一次予防法として推奨されている。

PARP阻害剤の登場により卵巣癌・卵管癌・原発性腹膜癌患者に対する抗癌剤の選択の必要性

から現在,それらの症例に対してHRD検査を含むBRCA遺伝学的検査が多く実施されている。このことは,ある一定頻度で存在するHBOC症例の同定を伴うことに他ならない。2020年4月からはHBOC乳癌既発症者に対するRRSOが保険適用となったことは,HBOC患者や家族の心理を大きく変容させ,RRSOを現実的に選択し得る医療へと変えつつある。しかしながら,RRSO施行に当たっては定められた算定要件と施設基準を遵守するだけでなく,術式の留意点,病理学的検査での留意点など婦人科腫瘍学への深い理解も求められる。さらに,術後の卵巣機能欠落症状に対して女性ヘルスケアを意識した臨床管理も必要となる等,様々な問題も存在している。今回,RRSO実施にあたり習熟しておくべきこれら診療知識,技術と現状の課題について解説する。

生涯研修プログラム 5 HBOC 診療と RRSO ならびに RRM の実践

3) RRSO ならびに RRM と臨床倫理

琉球大学病院地域・国際医療部 金城 隆 展

令和2年4月より遺伝性乳がん卵巣がん症候群(HBOC)の既発症者に対するリスク低減乳房切除術(RRM)およびリスク低減卵管卵巣摘出術(RRSO)が保険収載となり、その実施に関する倫理が現在注目を集めている。RRMおよびRRSOは、発症リスクを低減し患者の不安を軽減するために、現時点ではまだ発症していない(将来、必ずしも発症するとは限らない)乳房を切除/卵管卵巣を摘出する予防的介入であるが、これは患者を害してはならないと命ずる「無危害原則」に“二重に”抵触する可能性がある。RRMおよびRRSOは将来の発症という害を予見し、そのリスクを低減するという意味で、予見される害を予防することを促す無危害原則に即していると言えるがしか

し、そのために患者の(少なくともその時点で)健康な身体にメスを入れざるを得ないという点において無危害原則に抵触するからである。私たち専門家はこのような無危害原則的に矛盾せざるを得ない予防的切除をどう考え、予防的切除を希望される患者にどう向き合うべきだろうか?本講演では「最低限と最大限の倫理」および「似たケースは似た仕方に対応する」という公平性のルールを手がかりに、1)患者と専門家がリスクにどのように向き合い、評価し、そして、利益とのバランスをどのように取っていくべきか、2)どのように患者と共同意思決定していくべきか、を皆さんと共に考える時間としたい。

生涯研修プログラム6 コロナ禍における産婦人科診療

1) 新型コロナウイルス感染と妊娠出産

手稲溪仁会病院不育症センター 山田 秀人

2020年2月、武漢で新型コロナウイルスに妊婦が感染した報告以来、感染妊婦の情報が数多く集積された。妊婦のCOVID-19で、胎児異常、流産、死産のリスクが高いとする報告はこれまでにない。世界的に母子感染率は2~4%とされ、感染児の多くは無症状か軽症で分娩前の胎児感染は稀である。妊娠が重症化のリスクであり、早産リスクが高いとされる。一般的に、高齢、肥満、糖尿病、喘息は妊婦の重症化リスクである。日本のレジストリ解析でも、年齢やBMIが高く、呼吸器疾患やアレルギー歴のある妊婦、妊娠25週以降の感染では、重症化リスクが高いことがわかった。世界的にmRNAワクチンによって、不妊、流産、死産、早産、先天奇形、胎児発育不全が増える報告はない。妊婦の接種による発熱など副反応は、妊娠していない女性と同じである。妊婦は時期を問わず、パートナーもワクチン接種が推奨される。感染拡

大地域の方や、糖尿病、高血圧、気管支喘息など基礎疾患を合併している妊婦には、接種がより推奨される。アンケート調査によって、COVID-19流行下では、妊婦は不安を強く感じ、産後うつ病のリスクが高いことが判明した。注意を払い、必要であれば保健センター、主治医および精神科専門医との相談をすすめる。

厚生行政推進調査事業および日本産科婦人科学会として、「新型コロナウイルス感染症流行下における妊婦支援」のためのホームページ <https://www.med.kobe-u.ac.jp/cmv/covid/>を公開している。COVID-19妊婦の登録(レジストリ)によって感染妊婦の臨床情報を収集し、我が国における妊娠中のCOVID-19の頻度や重症化因子を調べ、妊婦の感染、重症化、母子感染の予防と対策、および周産期管理指針の作成につなげることを目的として、レジストリと解析を継続している。

2) 新型コロナウイルス感染症が国内外でがん診療・がん検診に与えた影響

日本大学 川名 敬

2020年3月からSARS-Cov2新型コロナウイルス(以下、新型コロナ)の感染が日本国内で拡大し、婦人科がん診療に影響が出てきた。不要不急の外出を控えることが求められた緊急事態宣言が発令された都道府県では、宣言下の2020年3-7月頃にはがん患者の受診行動すら制限され、対策型子宮頸がん検診は自治体でも一旦中止となっていた。病院によっては、院内クラスターのために初診患者の受け入れや手術の中止を余儀なくされた施設もあった。このような社会的、医学的制限が全国的に発生した経験はこれまでになかった。このような災害級のパンデミックが起こった時に、婦人科がん診療を中心的に担っているがん拠点病院や日産婦学会の基幹施設にはどのような影響を与えたのであろうか?日本婦人科腫瘍学会では、同学会の婦人科腫瘍訓練施設を対象とした全国調査を実施し、がん診療への影響を調査した。

さらに、子宮頸がん検診への影響について検討するために、大都市圏の自治体に対して子宮頸がん検診の検診数について実態調査を行った。いずれの調査においても前年比で患者数、手術件数、受診者数等を比較した。欧州のようなロックダウンしている都市や医療ひっ迫によってがん診療を制限した国ではがん診療への影響が多であり、欧州臨床腫瘍学会(ESMO)はパンデミック下での診療ガイドを発行し対応した。世界と日本国内の状況は大きく異なることが我々の実態調査からもわかったが、今後、さらなる新興感染症の災害級のパンデミックが起こることも想定したシミュレーションも必要であろう。本講演では、日本の実態調査結果をご紹介します。新型コロナの影響を振り返りつつ、新たな新興感染症パンデミックに対する備えを考察していきたい。

生涯研修プログラム 6 コロナ禍における産婦人科診療

3) COVID-19 と生殖医療

東京慈恵会医科大学 岸 裕 司

新型コロナウイルス感染症 (COVID-19) は、我々の生活全般に大きな影響を及ぼし、これに伴う行動変容を不可避のものとした。生殖医療もその例外ではなく、感染蔓延の最初期では、情報の不足する中で慎重な対応を余儀なくされた結果、治療周期の大幅な減少を招くこととなった。私達の施設も、ダイヤモンドプリンセス号に始まり、早期より COVID-19 症例を受け入れていたが、院内感染の発生を受け、生殖外来を含め、病院の多くの機能が、一時完全に停止する事態に陥った。さらに、学会よりの治療延期検討に関する声明等もあり、2020年の外来患者数は大きく減少した。その後、知識の蓄積による感染予防行動の徹底や、2021年に入ってのワクチン接種の普及に伴い、感染の制御が得られた結果、この抄録記載の時点では、本邦での患者数は激減を見ている。この一連の経験は、ほんの2年半前までは、自らがパンデ

ミックのただなかで医療をする事など想像すらしていなかった我々にとって、その認識・準備の甘さを痛感させるものであった。

本講演では、COVID-19が生殖医療へ与えた impact について、

- ・生殖医療が受けた影響 (患者動向、国内外の学会の対応)
- ・SARS-Cov-2が生殖機能に与える影響 (女性生殖機能に与える影響、男性生殖機能に与える影響、ARTへの影響)
- ・コロナワクチンが生殖機能に与える影響

等を中心に、これまでに得られた知見をもとにまとめることにより、この感染症が生殖医療に及ぼした影響の実態把握につとめる。そして、今後も起こりうるパンデミックへの対応についても考察する。

生涯研修プログラム7 卵巣予備能低下, 高齢, POI における不妊治療

1) 高齢不妊における卵巣刺激法, 採卵の工夫

歳本ウイメンズクリニック 歳本 武志

2019年の日本産科婦人科学会の統計によれば生殖補助医療(ART)を受けた40歳以上の高齢女性は全治療周期の41%を占めている。高齢化に伴う卵巣予備能低下(DOR)により発育卵胞数や採卵数は減少し, さらに卵子染色体異常数が増加して妊娠率は低下し流産率が上昇する。卵巣予備能の指標には抗ミュラー管ホルモン(AMH)と胞状卵胞数(AFC)があり, 高齢女性の卵巣刺激は卵巣予備能に応じた刺激法を選ぶのが適切である。高齢者でDOR症例の主な卵巣刺激法の選択は低刺激法で, クロミフェン+ゴナドトロピン(Gn)の隔日投与を行う。低刺激法で血中LH値が上昇する場合やGn製剤単独投与する場合はGnRHアンタゴニスト投与またはPPOS法(黄体ホルモン併用卵巣刺激法)を併用する。PPOS法は全胚凍結が前提となるがクロミフェン周期でも子宮内膜希薄化から全胚凍結をすることが多い。なお, 卵巣機能低下によりGn値が10mIU/ml以上と高値の症

例には卵巣の反応性を改善する目的で前処置としてエストロゲン製剤の投与やカウフマン療法を行い, 血中Gn値を平常化させた後に卵巣刺激を開始する。高齢女性は時に卵胞径14mm程度で早発LHサージにより早発排卵する症例があり, その場合は卵胞径が小さ目でトリガーを行い採卵する。卵巣予備能が十分にある高齢女性に対しては通常刺激であるGnRHアンタゴニスト法, PPOS法, GnRHアゴニスト法を行う。高用量Gn投与により卵質が低下することがあり, 卵質低下をきたした場合はGn投与量を減量するか低刺激法に変更する。採卵時に気をつけることとして高齢者の卵子は脆弱なものが多いため手引きよりはポンプ吸引が良い。採卵ポンプの吸引圧を通常より少し低めに設定する。以上のような工夫により高齢不妊患者には少しでも良質な卵子の採取を目指すことが望ましい。

2) IVA (in vitro activation)

順天堂大学 河村 和弘

近年の社会状況変化により晩婚化が進み高齢不妊女性が急増している。また, 40歳未満で閉経となる早発卵巣不全(POI: premature ovarian insufficiency)においても, 晩婚化により不妊となる症例が増加している。高齢不妊とPOIに共通した病態は卵巣内の残存卵胞数の減少による卵巣機能不全である。ヒトの卵胞は胎児期に形成され, 出生後は少なくとも体内においては再形成されないため, 卵巣機能不全患者は難治性の不妊となる。

我々はこれまで, POIに対し, 残存卵胞数の減少により体内では困難な休眠原始卵胞の活性化を, 卵巣組織の体外培養系を用いて行うことで, 閉経患者の卵胞発育を再生させる卵胞活性化療法(In Vitro Activation: IVA)を開発し臨床応用してきた(Kawamura et al. PNAS 2013, Hum Reprod 2015)。最近, さらに本法を応用し, 初期のPOIや月経不順と低AMH, 高ゴナドトロピン血

症を示す重度の卵巣機能不全患者に対し, 初期卵胞の発育を誘導可能な卵巣組織の体外培養系を含まないDrug-free IVAを開発し, 高い妊娠率をもたらすことに成功した(Kawamura et al. RMB online 2019, Tanaka, Kawamura et al. Fertil and Steril 2020)。

さらに, 高齢卵巣機能不全患者から得られた貴重な卵子/胚の体外受精治療の臨床成績を向上させるため, 卵子/胚が自ら産生する自己老化因子を同定し, その胚の老化作用を抑制する方法を見出し, アンチエイジングを可能とする胚の培養液の開発に成功した(Kawagoe, Kawamura et al. Aging Cell 2020, 国内・国際特許出願: 特願2016-187522, WO/2018/056461)。

本講演では卵巣予備能低下, 高齢, POIにおける不妊治療について, 我々が開発してきた治療を含め, 世界の趨勢について解説する。

生涯研修プログラム7 卵巣予備能低下, 高齢, POI における不妊治療

3) 挙児希望症例に対する子宮内膜症性卵巣嚢胞のマネジメント

—手術療法は本当に回避すべきなのか—

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【緒言】

子宮内膜症性卵巣嚢胞 (Endometrial cyst : EMC) に対する腹腔鏡手術は, 骨盤内環境の改善には有用であるが, 術後再発や卵巣予備能低下のリスクが問題となっている。本講演では, 当施設における解析結果をもとに, 子宮内膜症性卵巣嚢胞に対するマネジメント法を提案する。

【方法】

①2009-2015年に当科で腹腔鏡下卵巣嚢胞摘出術 (Laparoscopic cystectomy : LC) を施行した EMC 合併の 143 例において, 術後 6 か月以内に Bologna criteria より卵巣機能低下と診断した症例 (adverse diminished ovarian reserve : aDOR) の割合とリスク因子につき解析した。②2010-2017年に LC を施行した挙児希望のある 142 症例に対し, 術後の累積妊娠率と寄与因子に関して検討した。③2015~2019年に当科で採卵した LC 既往の EMC 合併不妊 49 例に対して, 獲得できた良好胚 (初期胚 \geq 7 cell G3 以上, 胚盤胞 \geq 3bb) 数と採卵回数の相関を解析した。

【結果】

①LC 後 6 か月以内に aDOR を呈したのは, 術前から aDOR を認めていた 31 例を除く 112 例のうち 33.9% (38/112) であり, そのリスク因子は両側性 EMC (OR : 3.71 ; p=0.006) と術前 AMH 値 (OR : 0.43 ; p<0.001) であった。②142 症例における累積妊娠率は, 術後 12, 24, 36 か月で 35.1, 59.1, 67.7% であり, 妊娠率に寄与する因子は術後再発 (HR 0.27, p=0.003) のみであった。③1 回目採卵における良好胚獲得率は 53.1% (26/49) であったが, 2 回目もしくは 3 回目の採卵ではそれぞれ 35% (7/20), 9.1% (1/11) と減少傾向にあった。

【結語】

嚢胞局在や術前 AMH 値によっては LC 後に卵巣機能低下を呈するリスクはあるが, 再発を回避できれば術後妊娠率は十分に高い。ただし良好胚獲得率は採卵回数に伴い低下する傾向もあるため, 当施設における新しいレスキュー法についてご紹介したい。

生涯研修プログラム8 プレコンセプションケア

1) 妊娠前からはじめる食生活改善に向けて
—「妊娠前からはじめる妊産婦のための食生活指針」について

医薬基盤・健康・栄養研究所栄養疫学・食育研究部 瀧本秀美

若年女性のやせは、早産や低出生体重などのリスクを高めることが報告されているにもかかわらず、我が国の若年女性ではエネルギー摂取量も少なく、20歳代で低体重（やせ）の割合が約5人に一人という現状がある。また、受胎前後に重要な葉酸の主な供給源である野菜摂取量も20歳代で最も少なく、1日に350g以上摂っている者の割合は最新の国民健康・栄養調査結果（2019年）では14.8%と、最も高い60歳代の35.7%に比べると大幅に少ない。また我が国の低出生体重児割合はOECD諸国の平均値6.5%よりも高い9.5%であり、1988年から1990年、2014年から2017年にかけて1.5倍に増加している。現在、胎児期や出生早期の成育環境が児の将来の健康状態や特定の疾患のかかりやすさに影響するというDevelopmental Origins of Health and Disease (DOHaD)の概念が注目されている。現在、UNICEFやWHO

では人生の最初の1,000日（受胎から満2歳の誕生日まで）の適切な栄養が将来の健康維持に重要であると提言している。我が国では「健やか親子21」推進検討会下の「食を通じた妊産婦の健康支援方策研究会」にて、2006年2月に「妊産婦のための食生活指針」が策定された。この指針策定から15年が経過し、この間に2005年の食育基本法制定や、2015年度から「健やか親子21(第2次)」が開始されるなどの政策が実施された。こうした国内の動きや国際的な動向を踏まえ、2019年度子ども・子育て支援推進調査事業「妊産婦のための食生活指針の改定案作成および啓発に関する調査研究」において、我々は指針の改訂を目的とした先行研究のレビューを実施した。本発表では、実施したレビューの内容とともに2021年3月に公表された「妊娠前からはじめる妊産婦のための食生活指針」について概説する。

2) 内分泌代謝疾患合併妊娠

国立成育医療研究センター周産期・母性診療センター母性内科 荒田尚子

糖尿病、甲状腺機能異常や肥満はプレコンセプションケアの有効性が証明されている代表的疾患である。

糖尿病合併妊娠では先天奇形、周産期死亡や巨大児のリスクが一般女性の3~5倍である。最近のメタ解析結果から、プレコンセプションケアは先天奇形、周産期死亡のリスクをそれぞれ半分もしくは半分以下に低下させた。具体的には、妊娠前にHbA1cを可能な限り6.5%未満のコントロールを目指し、糖尿病合併症の評価と管理を行う。高血圧、脂質異常症、心血管疾患等の合併症のチェックと管理を行う。メトホルミン以外の経口血糖降下薬はインスリンに変更し、妊娠中の禁忌薬（レニン・アンジオテンシン(RA)系抑制薬やスタチン系薬剤)を中止する。増殖前網膜症では光凝固療法を行い安定させ、糖尿病腎症では腎症2期(微量アルブミン尿)以下をめざし、場合によって妊娠成立までRA抑制薬で治療を行う。

明らかな甲状腺機能低下症では、流早産、妊娠高血圧症候群、常位胎盤早期剝離、帝王切開などのリスクが高く、機能亢進症も、流早産、常位胎盤早期剝離、甲状腺クリーゼ、低出生体重児、胎児・新生児甲状腺機能亢進症、死産などのリスクが高くなる。妊娠前の適切な治療によって、これらのリスクの軽減が明らかであり、プレコンセプションケアの必要性が強調される疾患である。また、抗甲状腺薬であるチアマゾールには催奇形性が明らかであり、特に妊娠5週~9週の薬剤使用と奇形症候群との関連性がいわれていることから、妊娠判明時の薬剤中止や変更について十分な説明と同意が必要である。

肥満も排卵障害による不妊や妊娠高血圧症候群、妊娠糖尿病、帝王切開分娩、巨大児などのリスクが高く、妊娠前に生活スタイルの修正によって健康な体重に到達することが重要である。

生涯研修プログラム 8 プレコンセプションケア

3) 心疾患・腎疾患女性に対するプレコンセプションケアとカウンセリング

福岡市立こども病院 日 高 庸 博

先天性心疾患に対する手術・管理技術の進歩はめざましく、以前では妊娠可能年齢に達しなかったかもしれない重症例が妊娠するようになってきた。多くの先天性心疾患女性では、行われるべき治療がすべて行われた後の状態にあるため、プレコンセプションケアが重要となるケースは多くない。しかし、特にハイリスク群においてプレコンセプションカウンセリングの重要性は高いものがある。一方、妊娠前のケアと加療が重要な心疾患もある。冠動脈狭窄を伴う川崎病では、適応があれば妊娠前の冠動脈インターベンション、バイパス術が推奨される。機械弁置換術後では可能な限り生体弁への入れ替え後に妊娠するのが望ましい。頻脈性不整脈に対しては妊娠前のアブレーションが考慮される。上行大動脈径の拡大したマルファン症候群では、妊娠に先立って外科手術が行われるべきである。

若年女性の腎疾患は多く、その経過中に妊娠出産に至ることはしばしばある。腎疾患女性に対してはより良い周産期予後を得るために妊娠前にできることが多く、プレコンセプションケアの重要性が高い。妊娠成立時点での母体の腎機能や血圧が周産期予後に大きく影響するため、妊娠前に原疾患の病勢を安定させておくこと、血圧をコントロールしておくことは重要である。透析患者の妊娠出産例も増え、その成績は以前と比して飛躍的に良化しているが、それでも産科合併症の頻度はきわめて高く、妊娠を考える慢性腎不全女性に対しては腎移植が勧められる。

プレコンセプションケアやカウンセリングの内容に注意を払うだけでなく、そのための場に疾患を有した生殖可能年齢女性が確実に辿り着いてくれる、その医療の流れを地域内に構築することは達成すべき今後の大きな課題である。

生涯研修プログラム9 産科手術における工夫

1) 経腹的子宮頸管縫縮術

長崎大学 原 田 亜由美

解剖学的に経膈アプローチによる子宮頸管縫縮術が困難な例に対して、経腹的頸管縫縮術が選択肢の1つとして考慮される。経腹的頸管縫縮術については、手術の実施時期(非妊娠時 vs 妊娠時)、アプローチ法(開腹術 vs 腹腔鏡手術)、縫縮糸の位置(子宮動脈分岐部の内側 vs 外側)、針の種類(直針 vs 曲針)などが議論され、それぞれにメリットとデメリットがある。私どもが行っている開腹術による経腹的頸管縫縮術では、膀胱を剝離したのち、術中超音波検査を用いて子宮動脈分岐部を同定し、分岐部内側の無血管野に曲針付きテフロンテープを子宮の腹側から背側へ運針している。開腹子宮頸管縫縮術を行った12例のうち11例の妊娠経過は順調で、いずれも妊娠37週以降に帝王切開で分娩した。したがって、開腹子宮頸管縫縮術は、経膈的子宮頸管縫縮術が困難な流早産ハイリスク例に対して有効かつ安全な手術手技と

考えられる。一方、開腹子宮頸管縫縮術は妊婦への侵襲が大きいため、私どもはより低侵襲な術式として妊娠初期の腹腔鏡下子宮頸管縫縮術に取り組んでいる。本術式のコツは、拡大視野で子宮動脈分岐部内側の無血管野を同定し、メリーランド型鉗子を無血管野の腹側から背側へ貫通させることで、針を用いることなくテフロンテープを背側から腹側へ誘導することである。腹腔鏡下子宮頸管縫縮術の出血量は開腹術によるそれと比較して有意に少量であり、低侵襲に子宮頸部を内子宮口の高さで縫縮することが可能になった。本講演では、私どもが行っている妊娠初期の経腹的子宮頸管縫縮術の工夫とコツについて術中ビデオを供覧しながら解説し、本術式が妊娠へ及ぼす影響の評価から手術実施に向けての留意点について紹介する。

2) 高度会陰裂傷 (3度裂傷・4度裂傷)

信州大学 菊 地 範 彦

高度会陰裂傷(3度裂傷・4度裂傷)はその発生頻度が1~5%程度と報告されている。初産年齢の高齢化、ハイリスク分娩の増加、無痛分娩の普及に伴い、高度会陰裂傷に遭遇する機会は避けられず、分娩に立ち会う産婦人科医師にはその対処法の知識や技術を有することが求められる。

高度会陰裂傷では創面が複雑なことも多く、肛門直腸裂傷では肛門括約筋や直腸の修復を必要とするなど、難易度の高い手技が必要となるが、その修復には縫合の技術のみならず会陰から膈の解剖を十分に理解しておくことも重要である。会陰裂傷と連続性のない直腸粘膜の損傷を認める場合もあり、創部の十分な観察も必要である。

縫合修復を成功させるためには、①十分な除痛、②創部の十分な洗浄、③創部の観察(解剖学的オリエンテーション)、④解剖学に基づく確実な4層縫合(直腸粘膜、肛門括約筋、直腸腔中隔、後腔壁)、⑤術後合併症の予防と早期発見が重要とな

る。

創離開や直腸腔瘻などの合併症が発生し再手術が必要になった場合には、一次的な対応が困難な症例もあり患者の負担も大きくなる。また、便失禁などQOLの低下につながる可能性もあり、分娩時の適切な初回修復が大切となる。このため、自身では修復困難と判断した場合には、経験のある医師への依頼や他施設への搬送も含めて考える事も大切である。

リスク因子を理解し出来るだけ高度会陰裂傷の発生を防ぐことや、日頃から縫合方法を習得するためのトレーニングを行っておくことも必要である。

また、高度会陰裂傷既往妊婦では分娩時の高度会陰裂傷発生率の増加が報告されており、次回妊娠時には高度会陰裂傷の再発に関連するリスクについて説明をした上で、患者の希望に基づいて分娩様式決定を決定する必要がある。

生涯研修プログラム 9 産科手術における工夫

3) 外陰腔壁血腫の治療・管理—手術療法と塞栓術—

沖縄県立中部病院 橋口 幹夫

産褥期に発生する血腫は、対症療法で経過観察するものから、積極的に止血コントロールを要する重篤症例もあり、その判断が臨床上重要となる。管理・治療のポイントは、血腫の発生部位の解剖学的同定と重症度判定を的確かつ迅速に行い、方針を速やかに決定することが大切である。診断は、症状、内診などの所見から判断するだけでなく、造影CT撮影による発生部位の同定と出血の活動性を確認し、治療方針を決定することが重要である。一般的に増大傾向がない、5cm以下の外陰・腔壁血腫は、疼痛コントロールのみで経過を観察し、血腫増大、裂傷合併例は、切開・開放し、縫合止血、ドレナージ留置という方法を行う。腔壁血腫は、術野の確保や責任血管の同定、結紮止血は、困難を極め、外科的治療に難渋することがある。さらに後腹膜への進展を伴うと循環動態の悪化が、管理を難しくする。近年では選択的動脈塞

栓術を行うことで飛躍的にその管理が容易になった。一方外陰血腫は、従来の外科的な対応が行われることが多い。しかし、産褥期の外陰血腫も、責任血管の殆どが内陰部動脈分枝、子宮動脈腔枝であり、動脈塞栓術が奏効することから、自院では、腔壁血腫にも塞栓術を外陰血腫にも適応し、良好な結果が得られている。また、重篤化しやすい後腹膜血腫は、その診断・治療に子宮破裂の合併を念頭に置く必要があり、開腹術の必要性を常に考えなければならない。IVR (Interventional Radiology) の普及で産褥期の血腫の治療は、「切開・開放・ドレナージ」から塞栓術による止血へと変化してきたが、従来の外科的なアプローチを否定するのではなく、両方の治療のメリットを理解し、適応することが大切である。過去に経験した症例を提示し、治療の方向性を述べたい。

生涯研修プログラム 10 不育症

1) 不育症，血液凝固系検査の最近の話題

杉ウイメンズクリニック不育症研究所 杉 俊 隆

昨年、「不育症管理に関する提言 2021」がまとめられ、公表された。厚生労働省のHP などから閲覧可能である。それによると、現在行われている不育症の検査において、エビデンスレベルの高い推奨検査は、子宮形態検査、抗リン脂質抗体検査、甲状腺検査、夫婦染色体検査、流死産胎児絨毛染色体検査しかなく、残念ながら20年前と変わらない。しかしながら、不育症分野に全く進歩が無いわけではなく、最近10年間で新しい原因を見つける努力がなされ、研究は進んできた。それは、提言の中で選択的検査として紹介されている。プロテインS、第XII因子、抗フォスファチジルエタノールアミン(PE)抗体、フォスファチジルセリン依存性抗プロトロンビン抗体(PS/PT)抗体など、その多くは血液凝固系の検査である。プロテインS欠乏は、日本では欧米の約10倍の頻度で

見られる。その理由は、プロテインS徳島と言う日本独特の遺伝子異常があるからで、欧米の知見を日本にそのまま当てはめる事は不適切である。日本独自の研究が必須である。ESHRE不育症ガイドライン(2017)では、先天性の血栓性素因検査は推奨されていないが、近年、プロテインS欠乏や第XII因子欠乏不育症患者に、プロテインSや第XII因子に対する自己抗体の存在が報告され、その病原性の検討が行われている。即ち、後天性の血栓性素因に関しては、これからの研究課題である。血液凝固系検査は、不育症検査としてエビデンスがまだ十分では無いが、検査不要と切って捨てて良いだけのエビデンスもまた無い。本講演では、血液凝固系検査の最近の動向につき、解説する。

2) 着床前胚遺伝学的検査(PGT-SR/A)の現状

名古屋市立大学 佐藤 剛

不育症の原因の主なものとして、抗リン脂質抗体症候群、子宮奇形、夫婦均衡型染色体構造異常、胎児染色体異常があげられるが、このうち、均衡型染色体構造異常を有する症例に対してはpre-implantation genetic testing for chromosomal structural rearrangements(PGT-SR)が、胎児染色体異常流産や原因不明の症例に対してはpre-implantation genetic testing for aneuploidy(PGT-A)が、それぞれ対処法の選択肢の1つとなりうる。

夫婦のどちらかが均衡型染色体構造異常を有する場合、自然妊娠での累積生児獲得率は64-83%、PGT-SRでの生児獲得率は27-77%と報告されているが、これらの検討には対照を設定したものはなく、PGT-SRの効果に関する十分なエビデンスはこれまで得られていない。わが国では、PGT-SRは、日本産科婦人科学会が公表している「『着床前診断』に関する見解」に則り、学会の倫理委員会

の承認を得た上で行われている。2015年までに729例に対して、PGT-SRでの解析後に569件の移植が行われ、84人の児の出生が報告されている。

不育症におけるPGT-Aの効果を検証した報告は多くない。不育症夫婦におけるPGT-Aと待機療法を比較した後方視的研究において、周期あたりの臨床妊娠率、流産率、生児獲得率、妊娠成立までの期間に差はなかったと報告されている。日本産科婦人科学会のPGT-Aの有用性に関する臨床研究のパイロット試験では、PGT-Aは、胚移植あたりの臨床妊娠率は向上させるが、症例あたりの継続妊娠率、臨床的流産率は非PGT-A群と同様であるという結果であった。

2021年11月現在進行中のPGT-A臨床研究本試験では均衡型染色体構造異常も対象に含まれており、その研究結果を元にPGT-A/SRに関する会告の改定が計画されている。

生涯研修プログラム 10 不育症

3) 子宮性不育症の外科的治療

東京女子医科大学 熊 切 順

本邦の子宮形態異常による不育症は不育症全体の7.9%を占めると報告されている。子宮形態異常による不育症は、先天的な中隔子宮、単核子宮、双角子宮などの子宮奇形、後天的な子宮筋腫、子宮腺筋症、子宮内膜ポリープ、アッシャーマン症候群などによる子宮内腔変形が要因となる。これらの要因のうち、幾つかの形態異常に対する外科的治療の推奨に関しては国外のガイドラインを参照することができる。さらに近年、本邦においても「不育症管理に関する提言2021」が公開され、国内の症例に合わせた治療選択が可能となったと考えられる。本提言によれば子宮形態異常による不育症に対しての外科的治療において中隔子宮を

要因とする不育症に対しての子宮鏡手術は積極的に推奨するとの結論に至っている一方、それ以外の病態についての推奨はなされていない。この背景には中隔子宮以外の病態に対しての比較対照研究の集積が困難であり、推奨に至るまでの結論が導き出せないことが理由であると考えられる。また子宮筋腫や子宮腺筋症などの比較的症例の多い病態により引き起こされる不育症に対しての外科的治療についても検討する必要があると考えられる。同研究班による今後の提言改定に大きく期待を寄せているが、本講演では不育症に関与する種々の子宮形態異常についての外科的治療の解析を行いその有用性について概説したい。

生涯研修プログラム 11 産婦人科医療における漢方の役割

1) 産婦人科医療における漢方の役割

富山大学附属病院和漢診療科 貝 沼 茂三郎

「血の道症」とは月経・妊娠・出産・産後・更年期など、女性ホルモンの変動により生じる精神不安やいらだちなどの精神神経症状および身体症状のことと定義されるが、古来よりこのような女性特有の不調に対して、漢方治療が行われてきた。急速な高齢化、女性の社会進出の増加などの社会構造の変化、そして生活様式の欧米化などの様々な要因によって、産婦人科においても疾病構造は変化し、産婦人科医療に対するニーズも多様化している。その結果、さまざまな場面でこれまで以上に産婦人科医療における漢方の果たす役割は極めて大きいと考える。一方、産婦人科領域での実臨床では三大処方といわれる当帰芍薬散、加味逍遙散、桂枝茯苓丸を中心に処方されているが、それ以外の方剤に関しては使用頻度が依然として低いように思われる。漢方医学の概念としての「気・血・水」では、身体の構成要素を3つに分け、そ

れぞれのバランスが崩れることで病気が発症すると考える。女性は月経があるために「血」の異常が病態を考える上で最も重要であり、女性の三大処方も「血」が滞った状態である「瘀血」の観点から処方選択される。しかし「気・血・水」の概念以外に、漢方医学的な概念では特に「陰・陽」について理解し、その観点から処方選択ができるようになると産婦人科領域で特に重要と思われる「冷え症」に対するアプローチも含めて処方選択の幅が広がると考える。本日の講演では「陰・陽」も含めた漢方医学的な観点から三大処方の解説と冷え症に対するアプローチをどのように産婦人科領域で活かしていくのかについてお話ししたい。産婦人科領域で漢方治療がその役割を十分に果たすためには漢方医学的な病態から診断そして処方選択できる産婦人科医が増えることを切望する。

2) 周産期疾患と漢方療法：免疫学的視点からのアプローチ

東京大学 永 松 健

妊娠中の母体では胎児発育に適した内部環境を確立するために内分泌、血液循環系を中心として様々な身体的変化が生じる。漢方ではこうした母体の変化は養胎優先の概念で表現される。そして、妊娠に伴う証の変化として気血水が血虚、腎虚、水毒など、いずれも陰虚証タイプに偏移するとされている。妊娠に伴い生じるつわり、便秘、めまい、貧血などのトラブルに対して、漢方薬を使用する場合にはそうした妊娠に伴う証の変化に合わせた薬剤選択が重要となる。妊娠中には胎児への安全性への考慮から薬剤選択が限定される。漢方薬は妊娠中にも概ね安全に使用できるとされているが、一部に妊娠に対する負の影響が懸念される生薬が存在することには注意が必要である。また、マイナートラブルの症状緩和という観点だけではなく、切迫流産、妊娠高血圧症候群などの周産期疾患に対しても、予防的あるいは治療的な目的

で漢方を利用する試みも行われている。

妊娠は父系抗原を有する胎児・胎盤に対して母体免疫システムが拒絶を生じることなく免疫寛容が維持されるという免疫学的に特殊な現象である。こうした適切な母児間免疫応答の破綻は不育症、胎児発育不全、妊娠高血圧症候群などの発症要因となる。安胎薬はそうした妊娠中の諸病を避け母児の健全な妊娠維持をサポートするための一連の漢方薬である。その中で当帰芍薬散は代表的な薬剤であるが、その安胎作用の分子生物学的機序については未解明の部分が多い。

本講演では、まず妊娠中の漢方薬の使い方のポイントについて概説する。そして、母児免疫異常への治療的効果という視点から、当帰芍薬散が発揮する安胎作用について近年の研究的な知見をもとに考察を行う。

生涯研修プログラム 11 産婦人科医療における漢方の役割

3) 女性ヘルスケアに活かす漢方治療 ～アンチストレスのための「新女性の3大処方」

近畿大学東洋医学研究所 武田 卓

地球温暖化による気候変動や頻発する大地震等による激甚自然災害の増加、COVID-19 感染症に代表される新興感染症のパンデミック等により、世界中の人々は持続的なストレス下にあると考えられる。そのなかで、最近の我が国における女性の自殺増が示すように、社会的弱者である女性はストレスの影響を受けやすく、特に高ストレス下にあることが想定される。そもそも女性は、月経・妊娠・分娩・閉経といった、劇的な内分泌環境の変化をとげ、そのため男性よりも心身の不調をきたしやすいとされている。更年期障害と月経前症候群がその代表的疾患であり、ストレスが増悪因子となることが知られている。西洋医学的にはホルモン補充療法と LEP・OC 製剤が標準治療となるが、我が国におけるホルモン製剤に対する一般における抵抗感の強さから、必ずしも治療が普及しているとは言いがたい。両疾患は古来より現在

に至るまで綿々と持続しており、歴史的には漢方治療が症状緩和に広く用いられてきた。これらの疾患に対する漢方治療の受け入れはよく、いわゆる「女性の3大処方」を中心とした薬剤が汎用されるが、現在の高ストレス社会においては、効果は十分とは言いがたい。そこで、アンチストレス生薬である「柴胡」を含有する薬剤群（柴胡剤）から、「加味逍遙散」「抑肝散」「加味婦脾湯」を「新女性の3大処方」として提唱する。本講演では、特別な漢方治療医学的な診断方法を用いることなく、これらの病名投与を用いた西洋医学への漢方治療応用を概説したい。さらに、最近明らかになりつつあるセロトニンやオキシトシンを介する分子レベルでの作用メカニズム解析と、「加味逍遙散」については更年期障害に対するプラセボ対照二重盲検比較試験の結果を併せてご紹介したい。

生涯研修プログラム 12 がん診療におけるメディカル AI 開発について

1) 深層学習を用いた子宮鏡における子宮体癌自動診断システムの開発について

東京大学 曾 根 献 文

人工知能は近年、深層学習の開発により飛躍的に進歩し、医療機器分野においてもその適用が検討されている。子宮体癌は進行期、再発症例であると難治性の事が多く早期発見が重要となる。このような背景の下、子宮体癌検診の重要なデバイスとして子宮鏡検査を一般化することを目的とし、人工知能 (AI) を用いた子宮鏡における子宮体癌自動診断システムの開発を目指した。また通常、深層学習を用いたモデル開発において精度を高めるためには膨大な症例数が必要であるが、医療用 AI 研究で疾患によっては必ずしも多い症例数を集められるわけではない。我々は、少ない症例数でも良好な正診率が得られる新たなアルゴリズムを開発した。177 症例 (正常子宮内膜: 60 例, 子宮筋腫: 21 例, 子宮内膜ポリープ: 60 例, 子宮内膜異型増殖症: 15 例, 子宮体癌: 21 例) を対象にし、約 40 万の静止画に変換し、それらの画像を

悪性グループ (子宮内膜異型増殖症, 子宮体癌), 非悪性グループ (正常子宮内膜, 子宮内膜ポリープ, 子宮筋腫) に分けて、深層学習を行った。また深層学習は3種類のネットワークモデル (Xception, MobileNetV2, EfficientNetB0) を用いた。まず、標準のアルゴリズムで評価したところ、正診率は約 80% 程度となり、さらに正診率を上げる方法として、ネットワークモデル組み合わせ法を開発した。この方法は3種類のネットワークモデルを同時に稼働させて、どれか一つのモデルが悪性と判定した場合、その症例を悪性と診断する方法である。この方法により正診率が 90% 以上と少ない症例においても良好な結果が得られた。今後、本研究で開発されたアルゴリズムが子宮体癌検診法の確立に大きく貢献する事が期待される。

2) コルポスコピーの AI 診断技術開発

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鈴 木 直 宏⁴⁾, 植 田 政 嗣⁵⁾, 万 代 昌 紀¹⁾

【目的】

子宮頸部細胞診異常を認めた症例に対するコルポスコピー検査 (コルポ診) において、子宮頸部上皮内腫瘍 (CIN) を (1) 高い診断精度かつ (2) 最小限の所要時間や組織採取で実施することは肝要であるが熟練を要する。本研究では専門医のコルポ診技術を、AI を用いて再現することで、検査者の熟練度に関わらず精度が高い CIN 病変の同定や診断的価値の高い組織採取部位の誘導を行う診断補助技術を開発することを目的とした。

【方法】

2013 年から 2019 年に実施されたコルポ診動画 8341 例のうち、生検により組織診断が為された CIN3 及び子宮頸がん 210 例に対し、酢酸加工後の病変部位の Annotation を行い、AI 学習を行うことで病変検知モデルを構築した。作成した病変検知モデルを CIN1 (121 例), CIN2 症例 (49 例) それぞれに適応し、軽度病変の検出精度を調べた。病変検知は病変面積 (感度, 特異度, Area under the curve (AUC)) 及び病変個数同定精度につい

て評価した。

【成績】

CIN3, 子宮頸がん 60 例で学習を行い、150 例で検証したところ病変面積は感度 85%, 特異度 73%, AUC 0.85, 病変個数同定精度は 95% と、高い精度で高度病変を同定するモデルを構築できた。また、同モデルを用いて CIN1, CIN2 症例も病変面積 (感度: 87%, 86%, 特異度: 70%, 67%, AUC: 0.81, 0.81), 病変個数同定精度 (97%, 93%) と軽度病変に対してもいづれも高い精度で予測できた。さらに病変予測確率に基づきヒートマップ表示することで視野内で最も病変強度が高い部位を生検推奨部位として可視化することができた。

【結論】

コルポ診における AI モデルを構築し、生検誘導に必要な高精度で CIN 病変を検知することができた。異常病変の可視化技術を応用し生検誘導を行うアプリを開発しており、検証実験結果と合わせて報告する。

生涯研修プログラム 12 がん診療におけるメディカル AI 開発について

3) インテリジェントながん治療支援システムのための人工知能技術の開発

国立がん研究センター研究所医療 AI 研究開発分野 小林 和馬

深層学習に代表される人工知能技術の登場によって、病院に大量に蓄積されてきた医用画像を貴重なデータ資源として利活用することで、画像診断支援、院内安全対策、診療スループットの向上といった、臨床における様々な課題解決を目的とした研究開発競争が世界的に激化している。特に本邦は、OECD 諸国の中でも人口あたりで最も多くの画像診断装置を有しており、超高齢社会を迎えてますます逼迫する医療の持続可能性という

観点からも、病院に蓄積されたデータ資源を価値創造の源泉として捉え、民間を巻き込んだ医療分野のイノベーション創出を志向する具体的な取り組みが急務であった。本演題では、人工知能技術を用いることによって、インテリジェントな医療システムを実現することを目的とした国立がん研究センター研究所における技術開発について紹介したい。

外科診療と医療安全

東海大学外科 森 正 樹

外科診療は医療安全がもっとも重視される分野の一つと思われる。本講演では医療安全を狭い意味ではなく、大きな範疇でとらえ、癌の早期診断、難治癌克服への取り組み、遠隔手術の3点について講演する。これらの点を研究して飛躍させることは、広い意味で医療安全に繋がっていると考えている。それら3点のポイントは以下のとおりである。

癌はポピュラーな疾患として捉えられるようになった。早期段階で診断できれば、多くの場合、治療により治癒が見込める。他方で、進行癌や再発癌の場合は、未だに完治からは程遠い場合が多い。癌の治療成績向上のためには、より早期の段階で診断することと、進行・再発癌の新しい治療法を開発することが重要である。他方で外科医不足は産婦人科医不足と同様に診療科偏在として社会問題化している。同時に地域医療偏在の問題も深刻になっている。これらの問題の解決法の一つとして遠隔手術の実現に向けて取り組んでいるので紹介する。

1) より早期の段階で診断できるように：特に膵臓癌は治療成績が極端に悪い。ただ膵臓癌の場合でも非常に早期の段階であれば、手術を含めた治療で完治できることも知られている。そこで膵臓癌の超早期診断法の確立を急いでいる。本講演ではマイクロRNAのメチル化を質量分析器で診断する方法について述べる。

2) 難治癌が難治である理由の一つとして癌幹細胞の存在が知られている。我々は癌幹細胞の観える化に成功し、さらにこれらを治療できる薬剤を開発した。他方で現在注目されている免疫チェックポイント阻害剤の弱点を克服できる制御性T細胞を標的とする治療法の開発に取り組んでいる。最後には体力のない患者さんのために癌の冬眠療法の可能性をしらべている。

3) 癌の手術を行う外科医が不足している状況下で、状況打開のために遠隔手術の開発に取り組んでいるので紹介する。

今回の講演が少しでも先生方のお役に立てればと願っている。

医療倫理講習会 

希少疾患の遺伝学的アプローチ：未解決症例への取り組みと医療倫理

横浜市立大学大学院医学研究科遺伝学 松本直通

2010年に次世代シーケンサー(NGS)を用いた初めてのヒト遺伝性疾患の原因解明以降、NGSを用いたメンデル遺伝性疾患の原因解明が爆発的に進行している。既に全エクソームシーケンス(Whole Exome Sequencing, WES)は、様々な遺伝性疾患の原因解明の第一選択技術となり広く施行されている。我々は、2009年よりWESを開始し、これまでに16700サンプル超のWES解析を進めた。そして76種類の疾患の原因について明らかにした。解析対象は多岐にわたる様々なヒト遺伝性疾患や未診断疾患(一部に自己炎症疾患等も含む)で、様々な解析手法を用いて原因解明を試みている。2020年3月末時点で、独立した7773例の解析において2745例(35.5%)で遺伝的な原因が解明されている。これは、WESを使用することで初め

て可能になった成果であるが、一方で64.5%の症例では、原因を特定できておらず、これらの未解明症例に対して、Whole Genome Sequencing(WGS)解析、Long-read WGS(LR-WGS)解析、RNA sequencing(RNA-seq)解析等の様々なアプローチを展開し解決を試みている。本講演では、これらの取り組みを紹介する。これら希少疾患の遺伝学的原因解明研究の倫理的手続きは、2021年6月30日に従来の三省の「ヒトゲノム・遺伝子解析研究に関する倫理指針」(いわゆる「ゲノム指針」)から「人を対象とする生命科学・医学系研究に関する倫理指針」(「生命・医学系指針」いわゆる「新統合指針」)に統合され施行されることとなった。本公演では本研究での倫理的手続きについても紹介する。

感染対策講習会 

知っておきたい予防接種の最新情報

福岡看護大学/福岡歯科大学医科歯科総合病院予防接種センター 岡田 賢 司

本学会が開催される頃には、ヒトパピローマウイルス（HPV）ワクチン接種希望者がこれまでより増えていることが予想されます。私たち小児科医が、日頃からHPVワクチン接種で気を付けている事項を紹介します。

ワクチン接種にあたっては、その効果と安全性について、事前に本人と保護者に十分に理解していただくことが大切です。かかりつけ医以外の医師が接種を行う場合、接種に不安のある方や基礎疾患で治療を受けている方には、まずかかりつけ医に相談することをお勧めしています。

(1) 予防接種を行う前：接種を受ける本人と保護者に対して、ワクチンの効果と安全性について改めて説明し、共有することをお勧めします。特に、接種後、数日以内に起きる可能性が高い有害事象（発熱などの全身反応や接種局所の痛みなど）について説明し、登校や課外活動に影響が出ることをあらかじめ伝えておくことが重要です。

(2) 予防接種を行う時：接種に際しては、落ち着いた環境で行い、痛みにも過敏な方に対しては、リラックスできるよう話しかけたり、痛みから気を

そらすように心がけています。血管迷走神経反射を起こしやすい世代ですので、横になった状態で接種を行い、接種後はすぐに立ち上がらせないなどの配慮を行っています。ワクチンは筋肉内接種（筋注）です。新型コロナウイルスワクチンで筋注は広く行われましたが、改めて接種手技を確認しておくことも必要です。

(3) 予防接種後：アナフィラキシーや血管迷走神経反射に備えて、接種後15～30分ほど観察を行います。ご承知のように、かつて接種後の全身の痛みや、手足の動かしにくさ、不随意運動等を中心とする「多様な症状」が報告されました。再開後、このような症状が出現した方が受診した際、接種医療機関、かかりつけ医療機関の医師は、まずその方の訴えに十分に傾聴することに心がけていただき、「HPVワクチン接種後に生じた症状に対する診療の手引き」等を参考に診察をお願いいたします。患者の症状や希望等を鑑み、必要に応じて各地域の協力医療機関もしくは専門医療機関を紹介することもご考慮ください。

教育奨励賞受賞講演

1) 全ての後期研修医が等しく教育を受けられる世界を目指して

自治医科大学附属さいたま医療センター 今井 賢

私は、自治医科大学産婦人科で後期研修医の期間を過ごしたが、熱心な指導医の教育を受け、専門医を取得する頃には、一人の産婦人科医師として責任を持てるレベルに成長できたと感じていた。しかし同時に、指導を受けた指導医の教育に対する熱意の度合いで、その後の知識量に差があることに気付いた。仮に同じ熱量であったとしても、その指導医の得意分野に知識が偏るため、満遍なく知識を深めるということは難しい。私はこの問題を解決したいと考え、「教育」に力を入れ取り組んできた。教育活動は2つの軸を基に行った。一つは教育の均一化を図るべく、産婦人科専門医として必要な知識を「広く浅く」教育する勉強会。二つめは、より専門性の高い知識を「深く」掘り下げる、手術に関する教育である。この2つの活動について、発表する。

【全国の後期研修医に向けたオンライン勉強会：SSS online (エスエスエス オンライン)】

教育の均一化として、まず院内の若手医師を教育しようと考え、医局の先輩である森澤宏行医師を中心に「若手勉強会」を発足した。しかし、2020年のコロナ禍の影響を受け対面の講義ができない状況に陥った。そこで、若手勉強会をオンラインで行うことを企画し、新たにSSS online (Step up Seminar for gain of Speciality) を立ち上げた。オンラインで行うことにより距離という壁がなくなった。本取り組みについて、SNSなどを通じて発信したところ、全国の医師からの参加希望をいただき、全国の後期研修医を対象とした勉強会に拡張した。現在は北海道から沖縄まで広くたくさんの先生にご参加いただき、2021年12月現在、のべ4200人の医師に参加登録をいただいている。本勉強会の特徴は3点ある。1つは定期開催であるという点である。毎月第4週に本講演があり、翌月

の第2週に再放送を行うようにしている。これにより自然に勉強のサイクルを作ることができ、学びの習慣ができる。2回聴くことで復習が可能であるメリットと、忙しい業務により参加できなくても再放送を視聴する機会があるというメリットがある。2つ目は、内容についてである。産婦人科領域の各疾患についての講演ではなく、明日からの臨床と結びつくような内容を心がけて計画している。例えば、腹式単純子宮全摘や卵巣腫瘍摘出術、産科領域では吸引分娩や鉗子分娩、帝王切開、生殖内分泌ではホルモン補充療法の使用方法などである。また、産婦人科領域に限らず、感染症の講義を総合内科の医師に講演いただき、さらには、医学に限らずスライドデザインや統計など、学会発表で使える知識を身につけられるようにしている。3つ目は、時間設定である。多くのオンラインセミナーが19時などに開催しているのに対して、開始時間を21時に設定している。これは、育児中の医師が子供の寝かしつけが終わってから参加しやすいようにするためである。また、本講演と再放送の曜日を分けることで、曜日が合わなくても参加できるように工夫した。さらに再放送ではYouTube Liveと連動することで、開始時間に間に合わなくても時間を戻して聴くことができるようにした。2021年11月にホームページ (<https://sss-online.net>) を開設した。今後もさらに利便性が高まるように工夫をしたいと考えている。

【自作手術シミュレーターを用いた手術教育：ウテリちゃんプログラム】

これまでの手術教育(特に腹腔鏡)は、ドライボックスでの個人トレーニング、手術動画を視聴するなど個人に任せる部分が多くあった。その上で実践的な部分は手術を行いながら指導する以外の方法がなかった。シミュレーターなどを用いる

ことでより実践的なトレーニングを行うことはできたが、シミュレーター自体が高価で簡単に手に入るものではないという問題があった。とはいえ、自主性に任せても予習をせずに手術を迎えてしまう医師もあり、そのまま手術を行うことで、患者に不利益を生じる可能性があるということが手術教育の大きな問題であった。実際の手術でしか学ぶことができなかつた on the job トレーニングを、シミュレーターを用いてドライボックス環境で行うことで、患者に不利益を生じることなく手術トレーニングを行うことができるようになると考えた。今回、自作 TLH (全腹腔鏡下子宮全摘) シミュレーター「ウテリちゃん」を用いた総合教育プログラム「ウテリちゃんプログラム」を作成し、後期研修に向けた TLH の手術教育を行った。ウテリちゃんは第 60 回日本産科婦人科内視鏡学会のワークショップでも発表した。自作シミュレーターとは言い、マニピュレーターを入れることができるように設計しており、綿を使って結合組織を再現し、剝離操作も可能となっている。それを用いて 1) 各腔の展開方法、2) マニピュレーターの操作、3) 腔管切開と腔断端縫合、4) まとめと総合演習という 4 つのパートからなる教育プログラムであるウテリちゃんプログラムを作成した。2 週間かけて 4 つのパートを理解し、達成することで TLH を理解できるようにした。各パートとも自分で説明ができるようになるまで修了にはせず、そのレベルを達成するまで私も付き合いとい

うことにした。さらにトレーニング中のメンタル面を考慮し、1on1 の面談を行うことにした。アドラー流メンタルトレーナーの資格を生かした面談を行うことで、モチベーションの維持に努めた。プログラムに参加した 4 名の後期研修医は全員プログラム修了し、前後の手術を技術評価ツールで採点すると、全員とも点数が上昇した。患者への合併症もなく、プログラム後の全例が出血少量で手術を終えることができ、何よりも、努力の結果としての成功体験を味わうことで、若手医師の目がキラキラと輝いている様子を見て、嬉しさを隠せなかつた。

以上の取り組みを通じて多くの若手医師と関わり、私自身も成長させていただいた。感謝の気持ちを忘れずに、今後も活動を続けたい。セミナーに参加した医師に教育の楽しさを伝え、教育に従事する医師を増やしたいと思う。そして、全ての後期研修医が等しく教育を受けられる世界を実現したいと考えている。これまで教育を評価されることはなく、無償の愛の元に成り立っていた部分が少なからずあった。私自身も、もうやめようと考えたこともあった。しかし、教育奨励賞が希望の光となり、同じように苦しみながらも活動を続けている医師の力になると感じている。その榮譽ある賞をいただき光榮に思うと同時に、受賞者としての責任を感じている。これからも活動を続け、産科婦人科学会のさらなる発展に貢献できれば幸いである。

教育奨励賞受賞講演

2) 機構専門医制度下における専攻医・若手医師に対し、多数ではない術者経験の下で効率よく腹腔鏡手術を教育するシステムの確立に向けた取り組み

大阪大学 角 田 守

本邦において、悪性疾患も含めて腹腔鏡下手術の需要は増える一方であるが、手術手技の複雑化・高度化に伴って、これまでの開腹手術の時代と異なり、若手の医師が術者として手術に携わる機会は減っている。手術の安全性を確保しつつ若手医師に効果的な手術トレーニングを行うことは共通の重要な課題である。特に医師一人あたりの症例数が少ない各施設においては切実な問題となっており、今回我々が行っている腹腔鏡手術教育の取り組みを報告する。

従来の開腹手術においては、対面に立って片側の手術手技を模倣してもらうことにより習熟を図ることができたが、限られた作業環境下で行う腹腔鏡手術教育においては同様に行うことは開腹手術と比較し難しいことが多い。しかし、大学病院のように若手医師在籍数が多く一人当たりの症例数が少ない施設においては手術の安全性を確保しつつ若手医師に効果的なトレーニングを行うことは重要な課題である。具体的な問題点としては、一人当たりの症例数が少ない、過去の腹腔鏡手術の症例経験数も様々である、悪性腫瘍症例の比率が高く専攻医が執刀できるような症例が少ない、習熟過程の中堅医師が多いなど多岐に渡り、自己完結型の腹腔鏡下子宮全摘出術（TLH）を執刀できる術者を育成することは多くの施設が直面している問題である。

腹腔鏡手術の習熟のためには、手術工程の細分化を行った上で、各手術工程における解剖の理解に基づいた術野展開を行い、その上で執刀医として手術手技の試行錯誤を行うことが重要である。そのため腹腔鏡手術教育における克服すべきポイントとして、(1) 定型化した手術工程を細分化し

て理解すること、(2) 少ない症例数を補うために如何に十分量のフィードバックを一例一例で適切に行えるかということが挙げられる。そこでこの2点を踏まえ、『手術工程の見える化』及び『上級医及び専攻医の理解の見える化』をポイントに手術教育システムの確立を目指し、少ない症例数の中でも個々の learning curve を上昇させることを目標とした。

定型化した手術手技を理解していく上で、従来の動画を見るという作業では、漠然と見てしまいポイントを理解しにくいという欠点がある。また成書などの静止画ではポイントは指摘しやすいが、その術野がどのように作成されているかなどを学ぶことは難しい。そこで両方の利点を活かすために、『手術工程の見える化』として、手術手順をセッティングから閉創までを細分化し、術中写真・解剖シエーマおよび術映像を添付したパワーポイント資料を、上級医の理解に基づいたポイントを学習しやすいように作成を行った。

『上級医及び専攻医の理解の見える化』としては実際の手術中に、フィードバックを行う側も受ける側も指摘できるポイントについては限界があるため、如何に簡便に多くのことをフィードバックできるかが重要である。細分化した手術工程において、専攻医は手術終了直後に自己評価を行い、これとは別に指導医もポイントごとに点数をつけて評価を行う。専攻医には指導医から指摘された箇所についてビデオを細かくポイントごとに復習することを促す双方向性のフィードバックを行えるようにした。

これまで漠然と行われていた手術教育を、上記の2点を押さえて『見える化』することにより細

かく手術工程を理解し復習をしていくこと、ならびに、評価についてコミュニケーションを取ることで各々の Learning Curve を上昇させることを目標とした。手技を習熟する上で、経験数より適切に学ぶことが重要である (Epstein et al. NBER Working Paper No. 18678) という報告もあり、若手のうちから適切に学び、試行錯誤することで Learning Curve を上昇させることで同じレベルに少ない症例数で到達することができ、それを繰り返していくことで将来、より Quality の高い手術を行うことができると考える。

上記のような腹腔鏡手術教育システムを構築し、効果の確認のために腹腔鏡手術経験の多い専攻医を『経験あり』群 (n=3)、腹腔鏡手術経験の少ない専攻医を『経験なし』群 (n=2) とし、研修開始時と終了時での点数の推移を観察した。当院赴任前の腹腔鏡手術件数は『経験あり』群で 45 ± 5 件であるのに対して、『経験なし』群では 20 ± 15 例と少なかった。それに伴い初回手術における点数は『経験あり』群で 48.7 ± 3.9 であるのに対し、『経験なし』群では 29.1 ± 3.1 と有意に低かったが、研修終了時の点数は『経験あり』群で 70.4 ± 9.4 であるのに対し、『経験なし』群は 81.9 ± 8.3 と両群間に有意差を認めないレベルに上昇させることができた。また、専攻医と上級医で評価の一致率も経験症例数とともに同様に正の相関を認め、上級医の視点を養うこともできた。これらの結果から、

この教育システムを用いて手術手技を細かくポイントを押さえて理解し、実際の手術において細かく問題点をフィードバックすることで、上級医と同じ視点・手術手技の習得を図ることができ、様々なレベルの医師が効率的に手術手技を習熟し経験の差を埋めるのに有用であった。上級医と同じ視点・思考力を養っていくことはいずれ専攻医が術者として成長していく上でも非常に重要であると考ええる。

今後の当教育システムの展開として、(1) 術式の拡大、(2) 導入施設の拡大、(3) 各施設において、指導医のレベルアッププログラムの開発の3つが挙げられる。この教育システムは子宮全摘のみならず、骨盤リンパ節郭清や広汎子宮全摘などにおいても同様にシステムを構築することができる。また大学病院に限らず他施設においても同様に当教育システムを導入していくことできる。実際に現在、関連病院においても導入することによって後期研修医のうちからポイントを押さえた Quality の高い TLH を実践することが可能となってきている。また同じ手術に対する各施設における上級医の評価の一致率を検証することによって、指導層のレベルアップも計ることができる。これらを押し進めることで様々な病院において技術の均てん化を図り、地域全体の技術の底上げが可能であると考ええる。

教育奨励賞受賞講演

3) 手術教育の innovation—Cadaver Surgical Training 導入と成果—

札幌医科大学 玉 手 雅 人

外科教育において「同僚・師・メンター」から直接学ぶ On the job training はかけがえのない時間である。一方で、シミュレーショントレーニングやアニマルラボを中心とした Off the job training も重要視されてきている。いずれも産婦人科においても効果が実証された教育方法である。しかし、頻度の少ない高難度手術（骨盤内臓全摘など）や新規術式の検証（子宮移植など）、希少手術の伝承（腔式手技など）には人体の解剖知識が必須であり、これらを実地臨床やシミュレーションだけで習得まで学ぶことは困難なこともある。そのような手術の習得を目的とした場合、献体を用いた解剖手術トレーニング=Cadaver Surgery Training（以下、CST）は有用である。札幌医科大学産婦人科では、2018年からCSTセミナーを全国規模で開始し教育効果を検証・還元している。CSTは実際の手術のようにチーム（術者・助手・器械・外回り）で行うため、実際の手術の臨場感が伝わり、OnとOffの中間的なMeso-the Job Trainingと位置付けた教育と言える。

Thiel法固定献体でのトレーニングは、実地臨床に近く、高難度手術習得に有効である。CST参加のハードルを突破して、高難度・希少手術の伝承や教育を実行できる教育を普及させたいと思い全国的なセミナーへと転換した。手術教育の評価は定性的側面と定量的側面があるため、評価が難しい。定性的な側面としては、外科医としての育った環境・性格・経験・サブスペシャリティなどが挙げられる。一方で、定量的な側面としては、解剖学的知識・縫合技術・手術機器の知識などが挙げられる。我々は定性的因子が定量的因子の交絡因子として、どのような影響を及ぼすか調べた。

CST外科教育システムの構築の意義は3点あると考えている。①若手産婦人科医の手術教育や

希少手術の伝承、②婦人科腫瘍外科医の高難度技能教育、③手術チームとしての向上である。昨今、高難度手術であっても合併症低減が求められる中で、解剖学講座・産婦人科主導のCSTセンターを作り、教育と評価を行う意義は非常に大きい。

札幌医科大学はCSTを年間15回ほど実施しており、2017年から婦人科単独で年間2回のCSTセミナーを実施できる環境にある。総務課・解剖学講座や倫理委員会と連携し、半年前の審査を通してCSTを実施した。日本外科学会・日本解剖学会へ事後報告書を提出した。CSTの前後で参加者から定性的・定量的データをとって、交絡因子の抽出などは回帰分析を用いて行った。そのようにしてデータ解釈し教育成果を評価した。そこから参加者に適した新規プログラムを考えて翌年のCSTに活用した。

その結果、産婦人科専門医を目指す医師にとっては、基本的な解剖の理解と婦人科手術手順の理解は進んだが、助手との協調や術中の気遣いが必要という意見が得られたため、自分の上司と組むようなプログラムが適していると考察した。

腫瘍専門医においては、研究や高難度手術の習得を目的とした場合が多く、モチベーションも高いことから、解剖知識の正答率は有意に上昇した。そのため、自由に手術を組み立てるグループワークが適していると考えられた。また、合併症を多く経験している医師が知識・技能の向上が得られており、解剖の研究目的より高難度手術を目的とした医師の方が解剖知識の正答率や技能が有意に上昇した。

以上のことから対象に合わせたCST教育プログラムは、知識と手術技能向上が得られるだけでなく、外科医の倫理的な成長とチーム力向上を与えたいと言える。そのような目と手と頭のトレーニ

ングに加えた心のトレーニング（チーム力・術中の緊張・助手の焦燥感）は他の Off the Job Training では難しく、産婦人科医の必要な要素の補完プログラムとも言える。そのような効果を4回にわたる CST セミナーで得られたことは大きな収穫であり、産婦人科医の周術期合併症低減や領域

を横断した卒後プログラムへの組み込みにも寄与する可能性が大きい。今後は CST 参加のハードルを下げて多くの産婦人科医が CST の恩恵を享受できるシステムの構築を行い、新規術式開発・医療機器開発へとつなげてゆきたい。

健康・医療活動受賞講演

開発途上国における母子保健・産婦人科医療向上のための人材育成制度強化活動～開発途上国とグローバルレベル、そして日本：産婦人科医のこれまでとこれから～

国立国際医療研究センター国際医療協力局

藤田 則子, 小原 ひろみ, 春山 怜

【背景】

2000年に、国連ミレニアム開発目標として「2015年までの妊産婦死亡率の削減」が世界目標となり、そのためには、開発途上国において、助産師・産婦人科医などの保健医療従事者の強化が必須と認識されるようになった。当時、日本は既に周産期医療提供体制が整っており、世界的にみても母子保健指標が優れていたことから、日本の産婦人科医による技術支援も求められた。しかし、個人ではなく複数の産婦人科医が継続して技術支援に関わる体制をもつ組織は日本には存在しなかった。

【組織概要】

国立国際医療研究センター国際医療協力局（以後 NCGM と略）は、1986年の創立以来、保健医療分野における日本を代表する国際協力機関として、厚生労働省や外務省、独立行政法人国際協力機構（JICA）、世界保健機関（WHO）等と連携し、開発途上国での技術協力事業への専門家派遣、国内外の保健医療人材の育成、国際保健医療の研究を通じて国際協力を行っている組織である。現在、76名の多様な職種（医師、看護助産師、薬剤師、検査技師、研究職、事務職等）の職員が在籍し、活動を行っている。過去20年、NCGMは継続して国際保健の学歴・職歴を持つ産婦人科専門医を確保し、開発途上国での人材育成事業実施を組織的に支援し、国際機関・政府機関とのネットワークを活用してその成果を発展・継続させることで、世界の女性の健康改善に貢献するための体制を構築・強化してきた。創立以来、NCGM 国際医療協

力局に在籍した産婦人科医は合計11名となっている。

【主な活動】

「開発途上国における母子保健・産婦人科医療向上のための人材育成制度強化活動」は、主に JICA の政府開発援助として実施された。具体的事業名は以下の通り。

- ・カンボジア：①「母子保健プロジェクト（フェーズ1、フェーズ2）」（1998-2005年）、②「地域における母子保健サービス向上プロジェクト」（2007-2010年）、③「医療技術者育成システム強化プロジェクト」（2010-2015年）、④「工場労働者のための子宮頸がんを入口とした女性のヘルスケア向上プロジェクト」（2015-2018年）、⑤「女性のヘルスプロモーションを通じた包括的子宫頸がんサービスの質の改善プロジェクト」（2019年-現在）。
- ・アフガニスタン：「リプロダクティブ・ヘルスプロジェクト」（2005-2008年）。

これら事業に長期・短期に派遣された産婦人科医は、国際的技術専門家として、日本の他職種の専門家や現地援助団体らと協力し、女性の健康改善にむけて、現地の医療従事者・保健行政官の能力強化・人材育成制度策定・強化を行った。2015年からの日本とカンボジア産婦人科学会が実施しているプロジェクトでは、NCGM 事業担当者は学会員として両学会をつなぐ役割を務めている。

【成果】

各事業で現地の産婦人科医・助産師を中心とする保健医療従事者の能力・人材育成制度が強化されたことは、終了時・終了後の評価報告書に記載

のとおり確認されている。カンボジアにおいて、医療従事者介助分娩率の向上や妊産婦死亡率低下が認められる。具体的な成果詳細と活動時の工夫については発表時に紹介する。

NCGMは、これら事業管理を組織的に実施することで、日本の産婦人科医が国際的環境において産婦人科医療向上を技術支援する能力を強化するとともに、開発途上国の健康課題を理解する日本の産婦人科医数を増加させてきた。また、開発途上国の健康課題に関する論文・学会発表を行い国際的に発信するとともに、技術専門委員等としてWHOの世界戦略やガイドライン等に助言を行い、グローバルレベルを通じて世界の健康課題改善への貢献を継続している。

【今後の展望】

1. 開発途上国の女性のさらなる健康改善への技術貢献：

2030年までのユニバーサル・ヘルス・カバレッジの達成が持続可能な開発目標となっている現在、全ての年代の女性の健康改善と公平性改善が必要である。各国政府や援助団体等により取組みは行われているものの、新型コロナウイルス感染症の影響により、近年の改善が逆戻りしてしまうことが懸念されている。また、既存の国連組織・援助団体に働いている産婦人科医は少なく、特に疾病構造の変化による新たな健康課題（子宮頸がん対策等）に対し技術支援可能な専門家は乏しい。外部支援なくとも現地産婦人科医・保健医療従事者の人材育成制度が機能するまでの間、女性の健康改善に包括的に知見のある日本の産婦人科専門医が、現地人材育成制度強化に貢献することは意義がある。

2. グローバルなレベルを通じての世界と日本への貢献：

開発途上国の健康課題を理解した上で、国際的な規範・基準設定に参画できる日本人技術専門委員は限られている。女性の健康改善に関する世界戦略やガイドライン策定において、日本の産婦人

科医がグローバルレベルの技術専門委員等となることにより、世界規模課題の解決に貢献する余地は大きい。また、新型コロナウイルス感染症の流行と対応を経験する近年、限られた資源の有効活用という点では開発途上国と先進国の課題が実は共通であることも明らかとなった。開発途上国という資源の限られた中での国際的な推奨や対策オプションを理解することは、日本の改善策の検討にも資する。

3. 開発途上国学会等との接点による日本産科婦人科学会のさらなる国際化推進と世界規模課題への貢献：

開発途上国でも、学会に求められる役割は、倫理面や技術面での規範設定や継続教育など多岐にわたっている。職能団体である産婦人科学会をプラットフォームとし技術支援することにより、公的セクターと民間セクター双方の保健医療人材を対象とすることが可能である。上記の日本とカンボジアの学会の共同事業は子宮頸がんという女性の新たな健康課題解決に向けた国際協力のあり方として注目されている。参加する日本側学会員も開発途上国の健康課題と現況を理解することで視野も広がり、今後は、その課題を解決することを念頭においた研究・発信を行うことにより、世界規模課題の解決に向けてさらに貢献することが可能である。

【結語】

国際協力とは「健康に関する格差をなくすための国際的なパートナーシップと財政的技術的支援」であり、一方向の貢献ではなく双方向に影響を及ぼしあうものである。日本は世界の一員としての役割を期待されている。高い専門性と職業規範をもつ日本の産婦人科医は、開発途上国における女性の健康課題も理解しスコープとすることにより、日本を含む世界の女性の健康課題改善にさらに貢献することが可能である。学会員として引き続き日本と世界をつなぐ活動を継続したい。

学術奨励賞受賞講演

1) ヒト子宮内膜間質細胞の脱落膜化における遺伝子発現調節機構の解明

山口大学 田 村 功

学術奨励賞
受賞講演

プロゲステロンにより誘導される子宮内膜間質細胞 (endometrial stromal cell ; ESC) の脱落膜化は妊娠の成立, 維持に重要な役割を果たしている。この過程において, 劇的な遺伝子発現変化が起こり細胞機能が変化する。これまで脱落膜化における遺伝子発現調節は主に転写因子による制御のみに着目され研究が行われてきた。しかし, 遺伝子発現は, 単に転写因子のみで調節されているのではなく, その受け手側である DNA promoter 側の状態によっても調節されている。すなわちヒストン修飾に代表される epigenetics 調節機構がクロマチン構造を変化させ, 転写因子の DNA 結合を規定している。そこで, 脱落膜化における遺伝子発現調節を「転写因子による調節」だけでなく「epigenetics による調節」の視点からの解明を行った。

【1. ヒト子宮内膜間質細胞脱落膜化における遺伝子発現調節と epigenetics】

まず, 脱落膜化マーカー遺伝子である IGFBP-1 と PRL の promoter 領域の解析を行い, 同領域はヒストンアセチル化により, 脱落膜化刺激で誘導される転写因子 C/EBP β が結合しやすいクロマチン構造状態になっていることを明らかにした。脱落膜化過程では, これらのマーカー遺伝子のみならず多くの遺伝子発現変化が起こる。よって, ゲノムワイドな視点から脱落膜化における epigenetics 調節機構の解明を行った。我々は ChIP-sequence によるゲノムワイドヒストン修飾解析を行い, 脱落膜化におけるエピゲノム情報を世界に先駆けて報告した。脱落膜化により多くの遺伝子で H3K27ac 修飾が誘導され遺伝子発現が上昇することを見出した。興味深いことにこれらの変化は, これまで着目されていた転写開始点近傍のみならず, 遠位 enhancer 領域にも広く分布

していることが明らかとなった。以上より, 脱落膜化という現象はゲノムワイドな H3K27ac 誘導により様々な領域での転写活性メカニズムが起こる変化であることを明らかにした。

【2. エピゲノム解析とゲノム解析を合わせた脱落膜化における新規 enhancer の同定】

ChIP-sequence 解析により同定された遠位 H3K27ac 修飾領域は, これまで着目されていない未知の enhancer 領域であると考えられた。IGFBP-1 遺伝子にも, 転写開始点より 5kb 上流の領域に脱落膜化により H3K27ac 修飾が上昇する領域が存在したので, この領域が新規 enhancer 領域であると考え解析を行った。これまで, 遠位 enhancer 領域の転写活性を示す方法としては, reporter assay が行われるのが一般的であったが, 我々は, ゲノム編集を用いることで内在性の enhancer 領域を欠失した細胞を作製するという画期的な方法で, 直接的な enhancer 活性を証明した。さらに, これらの enhancer 領域には C/EBP β , FOXO1, p300 といった様々な転写因子が結合し, クロマチン構造を dynamic に調節し, IGFBP-1 遺伝子の発現を制御していることを明らかにした。このように, ヒストン修飾解析やクロマチン構造解析 (エピゲノム解析) とゲノム編集を組み合わせたエピゲノム・ゲノム解析という新たな手法を用いることで, 脱落膜化における遺伝子発現に関連した新たな enhancer 領域を同定することに成功した。

【3. ゲノムワイドヒストン修飾誘導のメカニズムの解明】

H3K27ac 修飾変化は, 凝集したクロマチン構造領域に pioneer factor と呼ばれる転写因子が結合し, そこに histone acetyltransferase (HAT) 活性をもった cofactor がリクルートされることで誘

導される。IGFBP-1, PRL 遺伝子の promoter や enhancer 領域では, H3K27ac 誘導を担う pioneer factor が C/EBP β であること, HAT 分子が p300 であることを明らかにした。さらに, ゲノムワイドな解析も行い, C/EBP β が pioneer factor として働きそこに p300 がリクルートされるという機序が, 脱落膜化における H3K27ac 誘導の主なメカニズムであることを明らかにした。

【4. ゲノムワイドヒストン修飾解析から解明された脱落膜化におけるグルコースの重要性】

脱落膜化においてヒストン修飾変化が起こる遺伝子は, インスリンシグナリングに関連する遺伝子に特に集中していた。この知見から脱落膜化におけるグルコースの重要性に着目し解析を行った。脱落膜化が誘導されるにはグルコースが必須なこと, また脱落膜化過程では ESC 内へのグルコース取り込みが増加することを明らかにした。また, このグルコース取り込みにはグルコーストランスポーターである GLUT1 が関与していることも明らかにした。さらに, GLUT1 の発現も, C/EBP β が promoter 領域に pioneer factor として結合し p300 をリクルートし, H3K27ac を誘導させていた。

【5. 脱落膜化における転写因子 WT1 の役割】

前述の C/EBP β 制御下遺伝子を詳細に解析し

たところ, C/EBP β は多くの転写因子の発現を制御する上流転写因子であることが分かった。そこで, C/EBP β の制御下にある転写因子のうち, Wilms Tumor 1 (WT1) に着目し, WT1 と脱落膜化の関係を解析した。WT1 は脱落膜化で発現が上昇すること, この上昇は C/EBP β が新規 enhancer 領域に結合することで誘導されることを前述のゲノム編集法を用いて解明した。さらに, WT1 制御下遺伝子をマイクロアレイにて解析したところ, WT1 は脂質代謝関連遺伝子を多く制御していた。そこで, 脱落膜化における脂質代謝を解析したところ, 脱落膜化過程では細胞内の脂質蓄積が増加することが分かった。この増加はコレステロールのトランスポーターである VLDLR の発現を WT1 が誘導していることを明らかにした。このように, WT1 の脱落膜化における重要性を証明するとともに, 脱落膜化における脂質代謝の調節機構を明らかにした。

【6. 結語】

ESC の脱落膜化においては劇的な epigenetic 変化が起こり, 多くの遺伝子発現変化が誘導される。そして, これらの変化により脱落膜化における細胞機能変化が誘導され, 妊娠の成立・維持に貢献していると考えられた。

学術奨励賞受賞講演

2) 胎児頻脈性不整脈の臨床試験および胎児心不全バイオマーカーの開発

国立循環器病研究センター再生医療部 三好 剛 一

本邦の周産期医療の成績は世界最高水準を維持している一方で、周産期・小児領域の臨床研究は質量とも欧米諸国の後塵を拝しているという現状がある。周産期領域において質の高い臨床研究を実施するためには、(1) 本邦における自然歴データに基づき、(2) 明確な研究仮説に基づく優れた研究計画を立案し、(3) 多施設での臨床試験実施体制を構築する必要がある。このコンセプトに則り、世界でも初となる胎児頻脈性不整脈の臨床試験を実施し、本邦発のエビデンスとして世界へ発信した。さらに、そこから得られたクリニカルクエスチョンに基づき、胎児心不全の診断バイオマーカーの開発を目指した臨床研究を展開している (Front Physiol 2021)。

【1. 胎児頻脈性不整脈の臨床試験】

胎児頻脈性不整脈は稀な疾患であるが、持続すると心不全より胎児水腫に至るため、経胎盤的な抗不整脈薬投与による胎児治療が試みられてきた。胎児治療の有効性に関してはコンセンサスが得られてきていたが、国内外とも適応外で実施されているという状況であった。

(1) 本邦における胎児頻脈性不整脈の全国調査(後方視的研究)

まずは系統的に文献をレビューするとともに、胎児頻脈性不整脈に対する胎児治療に関する全国アンケート調査(厚労科研, 主任研究者: 左合治彦, 研究責任者: 池田智明)を施行し、本邦での診療実態の把握を行った。2004~2006年の3年間において、胎児頻脈性不整脈82例中41例で胎児治療がなされ、そのうち37例が頻脈の改善を認めた(奏効割合90%) (J Matern Fetal Neonatal Med 2018)。胎児治療薬として、主としてジゴキシン、ソタロール、フレカイニドが用いられていた。

(2) 胎児頻脈性不整脈に対する臨床試験の立案(介

入研究のプロトコール作成)

2010年に「胎児不整脈に対する胎児治療の臨床研究」(厚労科研, 研究代表者: 左合治彦, 研究責任者: 池田智明)で、最も効果的であると考えられる治療プロトコールを立案し、胎児頻脈性不整脈に対する胎児治療のエビデンス確立をめざす臨床試験を計画した(BMJ Open 2017)。その後、2014年に米国心臓学会よりステイトメントが発出され、胎児頻脈性不整脈に対する胎児治療は強く推奨されたものの、ほとんどが後方視的研究に基づいており、検証された治療プロトコールがないという問題が依然として残っていた。

(3) 胎児頻脈性不整脈に対する多施設共同臨床試験(介入研究の実施)

胎児頻脈性不整脈に対する世界初の多施設共同臨床試験「胎児頻脈性不整脈に対する経胎盤的抗不整脈薬投与に関する臨床試験(厚労科研, 研究代表者: 左合治彦, 研究責任者: 池田智明)」を先進医療Bで実施した。全国より15施設が参加し、2011~2017年の6年間で目標とした50症例を集積し、胎児治療が実施された。約90%で胎児頻脈性不整脈が消失し、プロトコール治療の高い有効性が確認された(J Am Coll Cardiol 2019)。安全性に関しては、母体では治療薬剤との因果関係が否定できない有害事象が約80%と高頻度で発現したが、ほとんどが軽微であり、薬剤減量等により治療の継続は可能であった。胎児では治療薬剤との因果関係が否定できない有害事象が約25%で確認され、胎児死亡例および重篤な有害事象のため治療中止となった症例も少数ながら含まれたことから、産科、小児循環器科、新生児科の共同による慎重なモニタリングおよび迅速な対応が必要と考えられた。現在、出生後3歳までの神経発達予後について解析するとともに、胎児頻脈性不整

脈に対する抗不整脈薬の適応拡大に向けた申請準備を進めている。

【2. 胎児心不全バイオマーカーの開発】

胎児先天性心疾患と不整脈は胎児心不全の主要な原因である。胎児心不全は胎児超音波検査に基づいて重症度診断されるが、その診断精度には限界があることから、より客観的なマーカーが望まれている(J Obstet Gynaecol Res 2019)。そこで、胎児心不全の診断に活用できる臍帯血、羊水、母体血中バイオマーカーの開発および病態解明を目指して臨床研究を実施した。2012~2016年に国立循環器病研究センターで周産期管理した胎児先天性心疾患・不整脈および正常胎児を対象として、分娩時に採取した臍帯血(血漿)および羊水を用いて、成人領域で心不全マーカーとして広く臨床応用されているナトリウム利尿ペプチド(ANP, BNP, NT-proBNP)の胎児胎盤循環における動態について検討した。次に、同センターバイオバンクに保管された妊娠30週前後の母体血(血清)を用いて、母体血中で胎児心不全時に変動するバイオマーカーについて探索した。

(1) 臍帯血中バイオマーカー

臍帯血中 ANP, BNP, NT-proBNP 濃度は胎児心不全症例で有意に上昇しており、胎児超音波検査による心不全重症度(Cardiovascular profile score)と良好な相関性を示した(Ultrasound Obstet Gynecol 2018)。ANP, BNP, NT-proBNP の上昇には、胎児心不全の重症度のほか、早産、アシデミア、胎児頻脈性・徐脈性不整脈が関与していた。特に胎児頻脈性・徐脈性不整脈や中等度以上の房室弁閉鎖不全を有する症例で高値を示し、胎児の心形態異常自体ではなく、中心静脈圧の上昇が病態として重要であることが示唆された。また、臍帯血中 ANP, BNP, NT-proBNP 濃度は、胎児不整脈治療の適応決定や治療効果判

定にも応用可能と考えられた(J Matern Fetal Neonatal Med 2021)。さらに、逆相高速液体クロマトグラフィーによる臍帯血中 ANP, BNP の分子型解析の結果、ANP はほとんどが成熟型より構成され大部分が胎盤で代謝される一方、BNP は前駆体が主体で胎盤での代謝をほとんど受けないことが明らかになった(Placenta 2019)。なお、臍帯血中 ANP, BNP 濃度は母体血中 ANP, BNP 濃度とは相関せず、母体循環と胎児胎盤循環は独立していると推察された。

(2) 羊水中バイオマーカー

羊水中 NT-pro BNP 濃度は、臍帯血中濃度と良好に相関し、胎児心不全の重症度を反映した(Circ J 2018)。一方で、羊水中 ANP, BNP 濃度は極めて低く、診断マーカーとしての利用は困難であった。羊水中 NT-pro BNP の産生源としては、卵膜からの分泌と胎児からの尿中排泄が知られているが、妊娠初期・中期には前者が、妊娠後期には後者が主たる起源であると推察された。

(3) 母体血中バイオマーカー

胎児心不全を反映する母体血中ホルモンおよびサイトカイン類(hCG, AFP, Bio-Plex Pro Human Cancer Biomarker Panels 1, 2)を網羅的に探索した。まず主成分解析より、炎症性サイトカイン、アポトーシス・血管新生因子が、胎児心不全時に母体血中で変動していることが示された(Am J Obstet Gynecol 2019)。多変量解析の結果、母体血中の胎児心不全バイオマーカーの候補因子として、TNF- α , VEGF-D, HB-EGF が同定された。これら3つを組み合わせた場合の診断精度は、感度100%、特異度80.3%、陽性的中率33.3%、陰性的中率100%(AUC=0.90)であった。再現性も含めてさらなる検証が必要であるが、胎児への侵襲性が無い新しい診断法として臨床応用が期待される。

学術奨励賞受賞講演

3) 正常子宮内膜のゲノム異常に注目した子宮内膜関連疾患の発症メカニズムの解明

新潟大学 吉原弘祐

子宮内膜は、月経により剥奪と増殖を繰り返す再生能の高い組織であり、その異常は子宮内膜症、子宮腺筋症、子宮内膜ポリープなどの良性疾患から、子宮内膜癌・子宮内膜症関連卵巣癌などの悪性疾患にいたるまで多岐にわたる。我々は、多段階発がんモデルに注目し、正常子宮組織から子宮内膜症・内膜症関連卵巣癌への進展メカニズムの解明を進めてきた。

【1. 子宮内膜症および正常子宮内膜における癌関連遺伝子変異】

臨床検体からレーザーマイクロダイセクション法で子宮内膜症上皮や正常子宮内膜上皮を選択的に回収し、全エクソンシーケンスおよびターゲットシーケンスを実施した。その結果、①PIK3CA・KRASなどの癌関連遺伝子が、子宮内膜症上皮や正常子宮内膜上皮ですでに高頻度に体細胞変異を起こしていること、②正常子宮内膜の癌関連遺伝子変異は腺管単位で生じ、腺管ごとに多様な遺伝子変異を有していること、③癌関連遺伝子変異は子宮内膜上皮・内膜症上皮に認めるが、子宮内膜間質・内膜症間質に認めないことを明らかにし、正常子宮内膜から子宮内膜症、内膜症関連卵巣癌への進展には、ゲノム異常の蓄積が重要であることを提唱した。

【2. 正常子宮内膜から内膜症関連卵巣癌へのゲノム異常の連続性】

卵巣明細胞癌症例内における子宮内膜上皮・卵巣子宮内膜症上皮・癌近傍の異型内膜症上皮・癌上皮に対して全エクソンシーケンス解析を実施した。興味深いことに、遺伝子変異数は子宮内膜から、内膜症上皮、異型内膜症上皮、明細胞癌に進むにつれて減少するのに対し、変異アリル頻度

は子宮内膜から明細胞癌に進展するにつれて増加していた。子宮内膜から明細胞癌まで NRAS 変異・PIK3CA 変異を、内膜症から明細胞癌まで ARID1A splicing を、異型内膜症から明細胞癌まで ARID1A フレームシフトを共有しており、正常子宮内膜でのゲノム異常の蓄積が子宮内膜症、内膜症関連卵巣癌発症に寄与していることを明らかにした。

【3. 正常子宮内膜の3次元構造とゲノム異常】

独自の組織透明化技術を用いて子宮内膜腺の3次元構造解析を行い、人体組織学の誕生以来、分岐単一管状構造であると考えられてきた子宮内膜腺は、①基底層で子宮内膜腺管が地下茎様の網目状構造を呈し、この網目状構造は月経期にも構造が保たれていること、②増殖期には地下茎様構造から機能層に向けて複数の腺管が同時に発育することを見出した。また、子宮腺筋症においては、地下茎構造から子宮筋層に直接侵入する腺管を同定することが可能であった。次に、地下茎構造を形成している水平方向に伸びる腺管と、地下茎構造から垂直に伸びている腺管をレーザーマイクロダイセクション法で分離し、それぞれの腺管について全ゲノムシーケンス解析を実施した。その結果、地下茎構造を共有する腺管は、モノクローナルで同一起源であることを明らかにした。

【結語】

我々が発見した地下茎構造は、繰り返される月経に対応するために子宮内膜が獲得した機能的な構造であると同時に、月経による内膜剝離時の子宮内膜幹細胞の保護に有利に働く可能性がある。一方で、地下茎構造を構成する子宮内膜腺管にゲノム異常が出現・蓄積することで、子宮内膜症や

子宮腺筋症、内膜症関連卵巣癌に進展していくと推察される。子宮内膜の新しい3次元構造や正常子宮内膜腺管における癌関連遺伝子変異の発見

は、子宮内膜の生理及び良性疾患・悪性疾患の病態解明に大きく貢献すると考えている。

J-CIMELS ワークショップ

さらなる妊産婦死亡の減少に向けた J-MELS コース開催のこれから

日本母体救命普及協議会の運営するシミュレーションコース (J-MELS) は、分娩の安全性を更に高めるため、そして妊産婦死亡を更に減少させる取り組みとして 2015 年に活動がスタートした。本コースは、産婦人科医師のみでなく、救急医、麻酔科医、メディカルスタッフ等との協働を目的とした実践教育、最新の知見に基づいた救命処置を基本にしているため、実際の産科医療に関わる臨床現場においても、関連各科、スタッフとのコラボレーションの醸成に役立っている。発足から 6 年が経ちベーシックコースの受講者は 15000 人、遅れて始まったアドバンスコースは 400 人、硬膜外無痛鎮痛コースは 250 人を超えている。

その成果もあって、妊産婦死亡の減少、特に産科危機的出血によるものの減少、搬送までの時間

の短縮は明らかなものとなっている。その一方、それ以外の急変による妊産婦死亡数は不変であることや、間接産科的死亡の比率が増えていることもあり、産科急変の対応は複雑多岐となっている。昨年はコロナ感染症の拡大によって、直接対面でのシミュレーションを実践する本コースの開催に困難性が生じた。また、本会のコース認定期間は 5 年と定められており、更新年に達している認定者に対して暫定的な対応をとらざるを得なくなった。このような中、今後 J-MELS をどの様に開催すべきか、どのような新しい視点を盛り込んでいくのか、開催する上での注意や認定更新など、全国のインストラクター、認定者、今後受講を考えている医療従事者へ向けて情報を発信することを目的にワークショップを開催する。

海外招請講演 1 (Overseas Invited Lecture 1) **ST**

Leading For the Future : Beyond Diversity and Space

Conry Jeanne A.

FIGO President, USA

I have the distinct honor to address my colleagues in Japan about leadership. I will provide an overview of leadership opportunities in our lives and describe four of the steps I believe are essential. The most important and first step is to recognize yourself as a leader right now, in your current stage in life. Leaders change, leaders evolve, but it is that first step in recognition that you are a leader is most critical. Second, we must say Yes to all opportunities that arise before us, because quite often we do not appreciate where our work will take us. By saying YES to opportunities, we broaden our horizons and achieve much more. Third, we must follow our passions. If we have an innate interest in one area of medicine, we should follow that path. We then engage

our energy and our interests more fully. And, we will accomplish much more personally and professionally. Finally, we must appreciate that leadership paths are not linear, and each time we take a path to the side or on a different direction it contributes to our growth. Leaders must be flexible and help those around them grow. I will discuss FIGO and its strategic plan, that relies on Member Societies and Regional Federations to guide global health. I will close my remarks with what it means for FIGO and JSOG to be global leaders in women's health. This role will require more than just a diverse perspective, it will require partnerships, it will require focus, and it will require collaboration around the world.

海外招請講演 2 (Overseas Invited Lecture 2) **ST**

Targeting aberrant ERK mitogen-activated protein kinase signaling for cancer treatment

Der Channing J.

University of North Carolina, Lineberger Comprehensive Cancer Center, USA

Oncogene activation (e.g., receptor tyrosine kinases, RAS, BRAF) and tumor suppressor loss (e.g., NF1, FBXW7) drive cancer growth through aberrant hyperactivation of the RAF-MEK-ERK mitogen-activated protein kinase (MAPK) signaling network. Key consequences of aberrant ERK MAPK signaling include activation of the MYC transcription factor and inactivation of the RB tumor suppressor. Therefore, therapeutic targeting of each of the nodes of the three-tier ERK MAPK cascade is intensively pursued for cancer treatment, with many inhibitors approved or under clinical evaluation. However, clinically effective therapeutic targeting of ERK signaling has

been limited by normal cell toxicity and cancer cell innate and acquired resistance. To facilitate the development of more effective therapies to target ERK MAPK signaling for cancer treatment, our studies have taken two complementary approaches. One involves chemical and genetic library functional screens to identify drug combinations that enhance the cytotoxic activity of ERK inhibitor therapies. The second involves systemwide profiling of the ERK-dependent transcriptome, phosphoproteome and metabolome. Together, these studies have identified novel combination therapies for the treatment of ERK hyperactivated cancers.

海外招請講演 3 (Overseas Invited Lecture 3) **ST**

Circulating Trophoblast Extracellular Vesicles as markers of obstetric disease

Vatish Manu

University of Oxford, UK

The syncytiotrophoblast, a fused single-cell layer between mother and fetus, constitutively releases extracellular vesicles (STBEV) directly into the maternal circulation. STBEV contain a variety of proteins and RNA which can be targeted to specific cells. In preeclampsia, asymptomatic placental oxidative stress is a precursor to later multi-organ dysfunction in the mother. Increased STBEV release in preeclampsia is considered a manifestation of syncytiotrophoblast stress, which may play a key role in signalling between fetus and mother. STBEV release in

preeclampsia changes, both in terms of volume and content. In this talk I will discuss how STBEV fit into the pathophysiology of the heterogeneous syndrome of preeclampsia. The key unifying concept in early- and late-onset preeclampsia is syncytiotrophoblast stress. I will propose that STBEV are the key stress signal in preeclampsia and that further investigation of STBEV release, content and actions may offer valuable insights into preeclampsia pathophysiology and offer potentially valuable clinical diagnostics and therapeutic targets.

海外招請講演 4 (Overseas Invited Lecture 4) **ST**

INTERGROWTH-21st : A set of clinical tools for monitoring human growth and development from early pregnancy to 2 years of age

Kennedy Stephen

University of Oxford, UK

INTERGROWTH-21st is a multinational research project, involving nearly 70,000 mothers and babies established to : 1) assess human growth, development and associated behaviours from early pregnancy to age 2 under healthy conditions and 2) characterise the highly heterogeneous syndromes, preterm birth (PTB) and small for gestational age (SGA), using a comprehensive set of characteristics including measures of intrauterine growth, aetiological factors, exposure to environmental conditions and postnatal outcomes to early childhood.

INTERGROWTH-21st consisted of five complementary studies, based conceptually on the prescriptive approach that produced the WHO Child Growth Standards. It took place across eight urban areas worldwide, geographically delimited to ensure the project was population-based. We enrolled a large cohort of healthy pregnant women <14weeks' gestation and monitored their babies prospectively until age 2. The participants had, at population and individual levels, the health, nutritional and socio-economic status needed to construct international standards, i.e. healthy, well-nourished, well-educated women living in environments with minimal constraints on fetal growth, whose antenatal care was evidence-based.

The principal findings were that early growth and development are similar across diverse settings when environmental constraints on growth

are low, and mothers' nutritional and health needs are met - irrespective of their ancestry, ethnicity or place of birth.

These studies led us to construct international standards to replace multiple local reference charts for : 1) monitoring gestational weight gain ; 2) measuring symphyseal-fundal height ; 3) using ultrasound to : a) estimate gestational age in early and late pregnancy and b) measure fetal size and estimated fetal weight to monitor intrauterine growth ; 4) evaluating newborn size at birth, and 5) monitoring the postnatal growth of preterm infants. Uniquely, the same healthy cohort was used to produce all the clinical tools - the largest population ever assembled for such a longitudinal study.

The children, whose ultrasound data were used to construct the fetal growth standards, remained healthy with satisfactory growth and motor development up to age 2, supporting the cohort's appropriateness for constructing international standards. The sequence and timing of attainment of key neurodevelopmental milestones and associated behaviours among these children at age 2 were assessed using the INTER-NDA, specifically produced for the project for implementation by non-specialists across international settings. The children's developmental patterns were similar across these diverse populations in keeping with the associated low health, nutritional and environmental risks.

In addition, we have demonstrated that PTB and SGA consist of aetiologically-based phenotypes with differential neonatal morbidity, growth and neurodevelopment up to age 2. These novel phenotypic classification systems and the international standards, which comple-

ment the WHO Child Growth Standards, provide a unique set of clinical tools for use across all healthcare systems to diagnose impaired growth and development and standardise the care of pregnant women and their children globally.

海外招請講演 5 (Overseas Invited Lecture 5) **ST**

Testosterone, physiology and clinical significance for women

Davis Susan R.

Monash University, Australia

Testosterone has long been recognised as a critical hormone for women. In healthy, regularly menstruating premenopausal women, median serum testosterone concentrations are similar to those of oestradiol. However, in premenopausal women testosterone levels decline by approximately 25% between the 3rd to 5th decades of life, so that by the time women reach the average age of natural menopause their testosterone levels are substantially lower than when they were younger. Following a nadir in serum testosterone in women at the start of the 7th decade of life, serum testosterone concentrations increase. Hence, the median serum testosterone concentration of women in their seventies is the same as for premenopausal women. In contrast, blood concentrations of DHEA the main precursor for testosterone and oestrogen production in postmenopausal women, and DHEA-sulphate, the circulating reservoir of DHEA, decline almost linearly with age, with no increase in the latter years. The increase

in blood testosterone concentrations in elderly women suggests that either having higher testosterone offers a survival advantage, or is a marker of longevity.

Clinical trials of testosterone therapy for women have primarily focussed on treatment of female sexual dysfunction, with the largest placebo-controlled studies being of transdermal testosterone in postmenopausal women. Based on the cumulative data from these studies, loss of sexual desire with associated personal distress is presently the only agreed upon indication for judicious testosterone supplementation for postmenopausal women. However, there are data that suggests testosterone has important roles in cardiovascular and musculoskeletal health, and cognitive function, but available data is limited. This presentation will review the latest information pertaining to testosterone physiology and the consequences of testosterone depletion and replacement in women.

海外招請講演 6 (Overseas Invited Lecture 6) **ST**

Differential Regulation of Ovarian Function by Salt Inducible Kinases

Stocco Carlos O.

Department of Physiology and Biophysics, The University of Illinois at Chicago, USA

Infertility is a significant public health problem affecting 15% of couples, of which approximately 40% are unable to produce or release mature eggs at ovulation. Ovulation is the pinnacle of folliculogenesis, a process that requires granulosa cell (GC) proliferation and differentiation, both needed for preovulatory follicle formation. Steady follicle growth towards the preovulatory stage and prevention of follicular atresia depends on follicle-stimulating hormone (FSH), a prevailing drug for infertility treatments. However, a significant number of patients respond poorly to FSH; therefore, the doses and total FSH needed for optimal follicle growth differ considerably between patients undergoing controlled ovarian hyperstimulation. This uncertainty is of great concern as the effects of high doses of FSH are questionable if not harmful. Seeking to solve this significant clinical problem, we looked for regulators of FSH action in the ovary. We show that salt-inducible kinases (SIKs) interact with FSH to regulate GC function. All SIK isoforms are expressed in human and rodent GCs and theca cells at different levels (SIK3>SIK2>SIK1). Pharmacological inhibition of SIK activity potentiates the stimulatory effect of FSH on markers of GC differentiation

and estradiol production. In humans, SIK inhibition strongly enhances FSH actions in GCs of patients with normal or abnormal ovarian function. The knockdown of SIK2, but not SIK1 or SIK3, synergizes with FSH on the induction of markers of GC differentiation. In vivo, SIK inhibition boost gonadotropin-induced GC differentiation, while the genomic knockout of SIK2 leads to a significant increase in the number of ovulated oocytes. Conversely, SIK3 knockout females are infertile, FSH insensitive, and have abnormal folliculogenesis. These findings establish SIKs as critical regulators of ovarian function and show that SIK2 and SIK3 have opposite effects on female fertility. Our findings reveal novel roles for SIK2 in regulating folliculogenesis and ovulation in rodents and the control of GC differentiation in humans. Since SIK activity can be modulated pharmacologically, a better understanding of SIK-controlled mechanisms and pathways may facilitate the development of novel therapies to advance fertility, allowing safer and more effective ovulation induction in assisted reproductive technologies. SIK regulated mechanisms could also reveal new targets for the development of innovative contraception methods.

海外招請講演 7 (Overseas Invited Lecture 7) **ST**

En bloc deep endometriosis excision

Chalermchockcharoenkit Amphan

TG-MET Center/Siriraj Hospital, Mahidol University, Thailand

Endometriosis is one of the most common problems encountered in Gynecology. It causes seriously impair woman health and huge economic and social consequences. Regarding the surgical treatment of endometriosis, laparoscopic surgery has dominated in recent decades. It has become gold standard for diagnosis and surgical treatment in many centers because of less morbidity and more effectiveness for both of conservative and radical surgical treatment when it is compared with the traditional open surgery.

However, inadequate laparoscopic DE excision

is still common, it can only produce good short-term outcomes but has a high recurrent and re-operation rate. En bloc deep endometriosis excision was developed to get better outcomes. Addition to an appropriate preoperative approach and acknowledgement of intraperitoneal and retroperitoneal pathological findings, this presentation also demonstrates an appropriate systemic approach of this surgical procedure for both conservative and radical surgery including the respective intraperitoneal and retroperitoneal anatomical landmarks, tactic of retroperitoneal approach and microsurgical dissection.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

1. 周産期 (Perinatology)

1) Wound healing of ruptured fetal membranes

Mogami Haruta

Kyoto University/JSOG

Fetal membrane rupture has been believed to be irreversible. However, spontaneous “re-seal” of fetal membranes sometimes occurs. This suggests that amnion has the capacity of regeneration. We investigated the mechanism of healing of ruptured fetal membranes.

1. Macrophages migrated in the edge of ruptured human amnion.

In the edge of ruptured amnion in pPROM, proliferation of amnion mesenchymal cells was observed. The surface of the edge was covered by monolayer amnion epithelial cells, and CD68+ macrophages migrated to the ruptured amnion.

2. Preclinical mouse model of ruptured fetal membranes.

On 15th days of pregnancy, fetal membranes of mice were mechanically ruptured. Healing of amnion started within 24 h, and closure was complete within 48-72 h. Histologically, aggregation of amnion mesenchymal cells was observed in the edge of the amnion, and this thickened edge was covered by a monolayer of epithelial cells. Macrophages were migrated to the ruptured site, where they released TGF- β at the ruptured site. In the later part of healing of amnion, extracellular matrix of the wounded amnion was re-modeled.

3. Healing of amnion and epithelial-mesenchymal transition (EMT)

Next, we asked the role of TGF- β at the ruptured amnion *in vitro*. Co-culture of human amnion epithelial cells (AECs) with human macrophages significantly accelerated the migration of AECs. TGF- β was released from macrophages, not from AECs. The treatment with TGF- β also increased the migration of AECs. Remarkably,

shape of AECs changed to a more spindle-like configuration at the edge of migration, and these cells were immunoreactive for vimentin, suggesting EMT. Similarly, vimentin-positive cells were scattered in the epithelial layer of ruptured amnion in both human and mice, suggesting EMT *in vivo*.

4. Healing of amnion is compromised in macrophage-depleted mice

We generated macrophage-depleted fetuses using Cre-loxP system. We used *Cx3cr1*^{CreER/+} : *Csflr*^{Flox/Flox} mice as conditional knockout mice (cKO). Intraperitoneal tamoxifen to pregnant mice induced deletion of *Csflr* in CX3CR1+ fetal cells, which led to depletion of CX3CR1+ fetal macrophages. In flowcytometry, proportion of CX3CR1+ macrophages in cKO was significantly decreased in fetal membranes and lungs. In cKO, healing of amnion significantly delayed and EMT was rarely observed. Moreover, pSmad3 positive cells at ruptured amnion were diminished in cKO, as well as the decreased *Tgfb1* mRNA. Therefore, fetal macrophages is inevitable for the healing of ruptured amnion.

5. Conclusion

Fetal macrophages migrate to the ruptured amnion, which release TGF- β . Amnion epithelial cells differentiate into mesenchymal cells through EMT. EMT speeds up migration of AECs which is required to close the wound faster, and it provides more mesenchymal cells to the wounded amnion which synthesize and release extracellular matrices to strengthen the injured site. Collectively, macrophages play a central role in the healing of amnion.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

1. 周産期 (Perinatology)

2) Changes in Birthweight During the SARS-CoV-2 Pandemic :
A Nationwide Study in South Korea

Cho Geum Joon¹⁾, Jeongeun Hwang²⁾

Korea University Guro Hospital, Korea/KSOG¹⁾,

Department of Biomedical Research Center, Korea University Guro Hospital, Korea²⁾

Objective

COVID-19 pandemic has brought major changes in the medical delivery system, socio-economic stress, and in behavioral aspects of individuals, and direct or indirect impacts on the adverse birth outcomes including stillbirths, maternal deaths, and preterm births have been studied previously. Birthweight is a strong determinant of a neonate's health. However, the impact of COVID-19 pandemic on birth weights has not been investigated in detail, and the conclusions of initial studies are inconsistent. We aimed to evaluate the effects of COVID-19 pandemic on birthweights.

Methods

The birth micro-data, which is an exhaustive census of all births in South Korea provided by Korean Statistical Information Service was used to examine whether the mean birthweight and the rates of under/overweight births have significantly changed during the COVID-19 pandemic year (2020) compared to the pre-pandemic period (2011-2019). Only singleton birth cases were analyzed. Low birthweight (LBW) and macrosomia were defined as birthweight less than 2.5 kg and more than or equal to 4.0 kg, respectively. Small for gestational age (SGA) and large for gestational age (LGA) were defined as birth-

weight below 10th and above 90th percentile for sex- and gestational age, respectively. Generalized linear models predicting LBW, macrosomia, SGA, and LGA births were built adjusting for maternal and paternal age, maternal and paternal education level, marital status of parents, parity, gestation age, and months from January 2011.

Results

There were 3,481,423 singleton births in pre-pandemic period and 255,024 delivery occurred during the pandemic period. Multivariate generalized linear models estimated negative associations between pandemic period and LBW (Odds Ratio, OR : 0.967, 95% Confidence Interval, CI : 0.956-0.979), macrosomia (OR : 0.899, 95% CI : 0.886-0.912), SGA (OR : 0.974, 95% CI : 0.964-0.984), and LGA (OR : 0.952, 95% CI : 0.945-0.959), indicating decline in pandemic period compared to pre-pandemic period.

Discussion

To our knowledge, this is the largest and most comprehensive national-wide study to date of the impact of the COVID-19 pandemic on birth weight. Our study found paradoxical results that a birth in pandemic period was associated with lower odds of being both underweight and overweight. Further studies are needed to understand the dynamics underlying this phenomenon.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

1. 周産期 (Perinatology)

3) Placental Function in Intrauterine Growth Restriction

Chen Yi-Yung

MacKay Memorial Hospital, Taiwan/TAOG

Fetal growth and development is the result of complex interactions between the genetic growth potential of the fetus, placental development, and the maternal environment. Intrauterine growth restriction (IUGR) can generally be defined as a failure of the fetus to achieve its genetically determined growth potential. Changes in placental function, which are often referred to as placental dysfunction or placental insufficiency, are believed to cause or directly contribute to most cases of asymmetric IUGR. A better understanding of the molecular and cellular

mechanisms underlying the changes in placental function leading to IUGR may provide us with better tools for early diagnosis and intervention. Reported functional changes in the IUGR placenta include inhibition of insulin/IGF-I and mTOR signaling ; activation of ER stress pathways ; decreased activity of transporters for amino acids, folate, protons, and sodium ; and increased activity of the calcium pump. The focus of this talk is to discuss these alterations in detail.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

2. 不妊 (Reproduction)

1) Insights into the development of polycystic ovary syndrome (PCOS)

Harada Miyuki

The University of Tokyo/JSOG

The pathophysiology of PCOS tends to focus on reproductive dysfunction due to its name and current diagnostic criteria, but it is essentially shaped by the interaction between reproductive dysfunction and metabolic disorders. The identity of the disease in each region was often questioned because of ethnic variation in the presentation and manifestations of PCOS. However, genome-wide association studies (GWAS) have revealed the same polymorphism in disease-related genes in Han-Chinese and European descents ; PCOS is presumed to be a disease that occurred at the latest 60,000 years ago and spread to various places. It has also become clear that there is no regional difference in prevalence when the most widely used definition, Rotterdam criteria, is applied. PCOS is a common disease affecting 10-15% of females of reproductive age, and the first international guideline for the assessment and management of PCOS, published in 2018, points out the need for lifelong management of patients diagnosed with PCOS, as it has a wide range of effects on the health of affected women, that includes reproductive and metabolic function, as well as mental health.

Then, what is the cause of PCOS? Recent studies have shown that PCOS exhibits high familial aggregation. On the other hand, although multiple disease-related genes have been identified by GWAS, less than 10% of these genetic factors

contribute to its familial aggregation ; over 90% of the pathogenesis of PCOS is now considered to be regulated by environmental factors. Possible environmental factors include the intrauterine environment of the PCOS mother, local follicular microenvironment, and lifestyle. In this presentation, I will introduce our research focusing on the role of endoplasmic reticulum stress (ER stress), activated in follicular microenvironment, in pathophysiology of PCOS. In addition, the results of our latest research will also be presented, focusing on the effects of intrauterine hyperandrogenism of PCOS mother on the development of gut microbiome and PCOS in their infants. Finally, I'd like to discuss the future perspective on basic research on pathophysiology of PCOS, as well as new treatment strategies based on these results.

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日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

2. 不妊 (Reproduction)

2) The Impact of Robotic Surgery on Ovarian Reserve

Park So Yun

Ewha Womans University, Korea/KSOG

The introduction of the da Vinci[®] system (Intuitive Surgical Inc., Sunnyvale, CA, USA) made it possible to overcome these prior known weaknesses of the laparoscopic approach. Robotic single site surgery (RSSS) using the da Vinci Si or Xi system has been incorporated into urological surgery since 2009, due to the advantages of single-port laparoscopy in reducing pain and improving patient satisfaction. Elsewhere, since Kane and Stepp first reported that the use of RSSS was feasible in 2010 in the gynecologic field, the approach has been applied to a wide range of gynecological procedures for treating both benign and malignant indications. Although it is clear that the da Vinci Si or Xi system has greatly improved surgeon dexterity, surgical precision, visualization, and ergonomics. Recently, a fourth-generation model, the da Vinci SP surgical system, was developed and introduced to perform robotic single port surgery (RSPS). Of note, all instruments for the SP system have two joints ; it was postulated therefore that surgeons might be able to overcome the limitations of RSSS observed when using the da Vinci Si or Xi systems because of the existence of various instruments with the new da Vinci SP

surgical system that have sufficient articulation, proper power, and less crowding.

Many studies have shown that the AMH can decrease due to ovarian damage after laparoscopic ovarian cyst resection especially in endometriosis cases. As in laparoscopic ovarian cyst resection, the AMH value decreased postoperatively in robotic ovarian cystectomy. The study also showed that the decrease in AMH was remarkable in surgery to remove bilateral endometriosis, whether using a robot or laparoscopy. There are various studies and opinions on what factors are helpful in preserving ovarian function during laparoscopic ovarian cyst resection. There was a study that concluded that bi-laterality of ovarian cyst was the only effect on AMH reduction after surgery. The degree of postoperative AMH reduction was not related to pathologic result of ovarian cyst such as endometriosis or other types of ovarian cyst. In particular, few studies have been conducted on the factors affecting the decrease in ovarian function during ovarian cyst resection using a da Vinci robot system or laparoscopic surgery.

In this lecture, I will give a talk regarding the impact of robotic surgery on ovarian reserve.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

2. 不妊 (Reproduction)

3) Infertility Treatment Challenges of Reproductive Aging : From Basic to Clinics

Kuan Hao Tsui

Kaohsiung Veterans General Hospital, Taiwan/TAOG

Ovarian aging in women is associated with a progressive loss of oocyte quantity and quality. When these processes occur early or are accelerated, their clinical correlates are reduced ovarian reserve and/or ovarian insufficiency. Both of these conditions have important implications for women's reproductive health and general health, including infertility. Optimal maturation of the oocyte depends on its environment and determines embryo competence, because the embryonic genome is not active until the cleavage stage and new mitochondria are not produced until blastulation. Mitochondrial function and energy production deteriorate with age, adversely affecting ovarian reserve, and embryo competence. In this talk, we will share the mtDNA damage, telomere changes, reactive oxygen species, and mitochondrial dysfunction associated

with ovarian aging, as well as the well-known genetic mutations associated with primary ovarian insufficiency and reduced ovarian reserve. We screened for genes potentially associated with ovarian aging through a multi-omics and confirmed them in granulosa cells, ovaries of aging mice, and cumulus cells from aging patients. Focusing on the target genes, we further tested the energy metabolism and microenvironmental alterations of common supplements on germ cells of aged infertility patients from *in vitro* studies to clinical trials. A better understanding of the molecular basis of ovarian aging through translational medicine will ultimately lead to diagnostic and therapeutic advances that will provide women with information to make earlier choices about their reproductive health.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

3. 婦人科腫瘍 (Gynecology)

1) Differential diagnosis and management of cervical multicystic disorders and application of artificial intelligence

Miyamoto Tsutomu

Shinshu University/SOG

[Objective]

Multicystic diseases of the uterine cervix encompasses various disorders ranging from benign to malignant lesions, such as gastric-type mucinous carcinoma (GAS), including minimal deviation adenocarcinoma (MDA), lobular endocervical glandular hyperplasia (LEGH), and Nabothian cyst (NC). GAS/MDA is a human papillomavirus (HPV)-independent, aggressive phenotype of cervical adenocarcinoma. LEGH is, in principle, a benign disorder clinically and pathologically mimicking MDA but a potential precursor of MDA/GAS. NCs are utterly benign retention cysts showing multiple cysts. However, the precise preoperative diagnosis of these diseases is often challenging when a cervical multicystic lesion (CMCL) is observed. To address this issue, we performed a multicenter study of 112 cases of MDA and related disorders from 24 hospitals in Japan. Based on this study, we developed a diagnostic protocol to classify CMCL into three categories, i.e., suspicious of Nabothian cyst (sNC), LEGH (sLEGH), and MDA/GAS/adenocarcinoma (sGAS), according to MRI findings, cervical cytology, and gastric mucin detection. We also explored the application of AI for MRI diagnosis.

[Methods]

Using our protocol, we first clinically diagnosed patients with CMCL and then evaluated

the diagnostic accuracy by the following hysterectomy. We also followed-up the conservatively managed sLEGH patients to determine the incidence and signs of malignant transformation. In addition, we studied the application of artificial intelligence (AI), Pre-Learning Convolutional Neural Networks (CNN), to MRI diagnosis using 121 CMCL cases (64 LEGHs and 57 NCs).

[Results]

We clinically diagnosed 175 CMCL patients using our diagnostic protocol, and the diagnostic accuracy was 67% (10/15) for sGAS and 90% (19/21) for sLEGH. In sLEGH patients, 69 were followed-up more than six months (mean follow-up period : 57.1 months), and only one patient (1.4%) developed MDA. This patient showed glandular cell atypia and lesion enlargement which seemed to be important signs of malignant change. After deep learning of MRI T2-weighted images of LEGH and NC, CNN showed a similar differential diagnostic accuracy of these lesions compared with two diagnostic radiologists (0.76 vs. 0.79).

[Conclusion]

Our diagnostic protocol is helpful for the management of CMCL, and the malignant change of LEGH is rare in the short term. AI can contribute to improving the diagnostic accuracy of MRI for CMCL.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

3. 婦人科腫瘍 (Gynecology)

2) Long-term efficacy of consolidation hyperthermic intraperitoneal chemotherapy (HIPEC) for patients with epithelial ovarian cancer

Lee Sung Jong¹⁾, Yoo Jigeun³⁾, Lim Myong Cheol²⁾, Lee Joon Mo¹⁾, Lee Keun Ho¹⁾,
Hur Soo Young¹⁾

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National Cancer Center, Korea²⁾,

Daejeon St. Mary's Hospital, The Catholic University of Korea, Korea³⁾

Objective : We aimed to evaluate the long-term efficacy of consolidation hyperthermic intraperitoneal chemotherapy (HIPEC) for patients with epithelial ovarian cancer.

Methods : This retrospective study included patients who received consolidation HIPEC at Seoul St. Mary's Hospital between January 1991 and December 2003. Consolidation HIPEC was performed during second-look operation for patients who had complete or partial response after primary cytoreductive surgery (CRS) and adjuvant platinum-based chemotherapy. HIPEC was performed by perfusion of 6L of lactated Ringer's solution and paclitaxel 175 mg/m² or carboplatin 350 mg/m² at 43-44°C for 90 minutes. Ten-year progression-free survival (PFS) and overall survival (OS) were analyzed and compared with patients who underwent second-look operation without HIPEC.

Results : A total of 87 patients were included. Of these, 44 patients (50.6%) received consolidation HIPEC, and the other 43 (49.4%) received second-look operation only (No HIPEC). The 10-year PFS rate was significantly longer in the HIPEC group compared to the control group (59.1% vs. 34.9%, $p=0.032$), and there was a marginal significance in the 10-year OS rate in between the

two groups (59.1% vs. 37.2%, $p=0.054$). In a subgroup of patients with stage III, HIPEC group showed significantly longer 10-year PFS and OS rate compared with the control group (PFS, 53.8% vs. 14.8%, $p=0.001$; OS, 38.5% vs. 11.1%, $p=0.036$). Multivariate analysis identified HIPEC as an independent favorable prognostic factor for the 10-year PFS (adjusted HR 0.49, 95% CI 0.25-0.96, $p=0.039$), although not for the 10-year OS (adjusted HR 0.60, 95% CI 0.31-1.17, $p=0.133$). Patients who underwent HIPEC with paclitaxel showed a trend of higher PFS and OS compared with those who underwent HIPEC with carboplatin, although the result was not statistically significant (PFS, adjusted HR 0.39, 95% CI 0.13-1.2, $p=0.102$; OS, adjusted HR 0.31, 95% CI 0.03-1.1, $p=0.070$). Adverse events more common in the HIPEC group were thrombocytopenia, elevated liver enzyme, and wound complications. However, these adverse events were reversible and did not delay subsequent consolidation chemotherapy.

Conclusion : The consolidation HIPEC demonstrated a significant improvement in 10-year PFS and a marginally significant improvement in 10-year OS in patients with epithelial ovarian cancer, with acceptable toxicity.

日韓台ジョイントカンファレンス (5th J-K-T Joint Conference) **ST** :

3. 婦人科腫瘍 (Gynecology)

3) The guideline of gynecologic cancer in Taiwan

Chang Cherry Yin-Yi

China Medical University Hospital, Taiwan/TAOG

Clinical practice guidelines are systematically developed statements to assist clinical care professional and patient in decision making about appropriate health care for specific clinical circumstances. Initially, this comes from the “Clinical Practice Guidelines : Directions for a New Program” written by Field MJ and Lohr KN and published in 1990. Since then, clinical guidelines have gradually become the standard of diagnosis and treatment, and have also become one of the criteria for evaluation of medical quality. However, the development and application of guidelines has its advantages as well as disadvantage. Only if the clinical practice guidelines were developed cautiously and objectively can improve the quality of medical care and minimize its potential harm. Evidence-Based Guideline (EBG) is established objectively which based on evidence-based medicine. EBG was the comprehensive result of medical research which could provide treatment advice, improve doctor-patient communication and medical quality. It is also a good educational material for healthcare professional. The development of clinical practice guidelines has begun since the concept of evidence-based medicine was introduced into Taiwan in 1996. Bureau of National Health Insurance, National Health Research Institutes, and Joint Commission of Taiwan have built up the promotion process for clinical practice guidelines which based

on evidence-based medicine. With the development of national medical knowledge and income, people have higher expectations for understanding their own diseases. However, healthcare professional in different medical institutions or even in the same department inconsistent diagnosis and treatment for some disease. In Taiwan, the principles of diagnosis and treatment of diseases must comply with the provisions of National health insurance. Therefore, the clinical practice guidelines of medical institutions should not have too much difference from the national guidelines and also from the other developed countries. The Taiwanese clinical practice guidelines in the management of gynecologic cancer was prepared by the team of Taiwan Gynecology Oncology Group. The guidelines are divided into chapters including cervical cancer screening, clinical practice guideline of cervical cancer, endometrial cancer, uterine sarcoma, epithelial ovarian cancer, fallopian tube cancer, peritoneal cancer, malignant ovarian germ cell tumors, gestational trophoblastic disease, vulvar and vaginal cancer. As the implementation of new diagnosis technology and medication, the written of clinical practice guidelines is a long-term work, so the revision of the guidelines requires the participation of many experts to keep the guideline updated.

Joint Conference JSOG-DGGG **ST**

1) The future of Laparoscopy for Cervical Cancer

Becker Sven

Frankfurt University Women's Hospital, Germany/DGGG

Minimally invasive surgery - either by laparoscopy or by robotically assisted surgery - has revolutionized surgical gynecology. Gynecologic surgery is today - essentially - minimally invasive surgery : Operative Hysteroscopy, Diagnostic Laparoscopy, Laparoscopic Adnexal Management, Myomectomy, Hysterectomy, Sacrocolpopexy, Adhesiolysis, Endometrial Cancer Management, Endometriosis-Surgery and - finally - Cervical Cancer Management. One prospective study in 2018 put into question the oncologic safety of laparoscopy and minimally invasive surgery for cervical cancer, forcing surgeons to revert to a technique from the 19th century for their surgical care. This lecture re-visits the original study critically, reviews the evolving literature since then and looks at different approaches taken in different cultural contexts.

The lecture will look at interesting aspects of reporting of scientific facts and review current and historic scientific controversies. The role of the lay media is examined and the myth of "objective" scientific evidence reviewed. The human factor of scientific research and reporting is explored and again, historic evidence is provided. The concept of the prospective randomized trial for surgical interventions will be critically analyzed, particularly with regard to questions surrounding the learning curve of the individual surgeon. This will lead to a discussion about centralization of oncologic and specialized care and the obstacles that lie in the way. Finally, the role of the legal system in different countries will be elucidated. Current existing studies will be reviewed and a general outlook offered.

2) Ovarian tumors in pregnant women

Fehm Tanja

University Hospital of Düsseldorf, Germany/DGGG

Approximately 0.05% up to 2.4% of women are diagnosed with an ovarian tumor during pregnancy, mostly in the first trimester due to the vaginal ultrasound performed to evaluate the fetus. In a small subset of pregnant patients an ovarian torsion may occur due to the enlarged ovary which is associated with acute abdominal pain. The majority of ovarian torsions occurs between the 10th and 17th week of gestation. Ovarian tumors not been diagnosed antepartum may be diagnosed when the cesarean section is performed.

Over 90% of the ovarian tumors are benign including corpus-luteum cysts, teratomas or endometriomas. The most common malignant tumors during pregnancy are dysgerminomas followed by borderline tumors, ovarian cancers and granulosa cell tumors.

The diagnostic work-up includes vaginal and abdominal ultrasound. Sonomorphological criteria for malignancy are tumors >10 cm, containing solid and cystic areas, having papillary areas or septae. If the ultrasound imaging cannot distinguish between a benign or malignant finding, a MRI can be performed without gadolinium. The determination of serum tumor markers including CA 125, β -HCG, CEA and AFP may not be helpful since they are normally elevated during pregnancy. Indications for timely surgery are symptomatic cysts, tumors suspicious for malignancy, increasing size of the tumor and increasing tumor marker during expectant man-

agement. Surgery should preferably be performed in the second trimester. In the first trimester ovarian tumors may have a functional history and disappear at the end of first trimester. Moreover, an increase of spontaneous pregnancy loss has been described by ovarian surgery within the first 12 weeks. A laparoscopic approach can be offered to pregnant patients but the size of the uterus should be taken into account when accessing the abdomen. The Palmer's point should be preferably used for abdominal entry. In case of ovarian cancer or malignant ovarian tumors open surgery is mandatory to perform an adequate staging. If the patient is diagnosed at an advanced stage, neoadjuvant chemotherapy with carboplatin/taxol may be discussed. The administration of chemotherapy after the first trimester is safe and does not impair the cardiac, cognitive or general development of children in early childhood. However, in utero exposure to chemotherapy is associated with a higher rate of preterm prelabor rupture of membranes, intrauterine growth restriction and low-birth weight. Bevacizumab is not allowed during pregnancy. The prognosis of pregnant patients with ovarian cancer or non-epithelial malignant tumors seems similar to non-pregnant patients, however data are limited. An important prognostic factor for these patients is a treatment which follows as closely as possibly the current guidelines for the diagnosis and treatment of malignant ovarian tumors.

3) Chronic endometritis and its effect on reproduction

Kimura Fuminori

Nara Medical University/JSOG

[Objective]

Restoration of endometrial receptivity is thought to provide a new therapeutic strategy for many patients with implantation failure. We focused on chronic endometritis (CE) as a cause of implantation failure.

[Methods]

In this session, we will report our study on the effects of CE on implantation and pregnancy outcome, the effects of CE on endometrial function, and the effects of progestogen as treatment for CE according to our research results.

[Results]

The results of the prospective study showed that the pregnancy and live birth rates were significantly lower and the miscarriage rate was significantly higher in patients with CE. In addition, a retrospective study revealed that patients diagnosed with CE had a higher rate of miscarriage and preterm birth after pregnancy.

When endometrial stromal cells were isolated from the implantation stage endometrium and cultured with estradiol and progesterone, the secretion of $TNF\alpha$, $IL1\beta$, and $IL6$ was significantly increased in CE. The secretion of the decidualization markers, PRL and IGFBP1, were both significantly decreased and the number of

cells significantly increased in the CE group after the culture for 2 weeks. Similarly, when the endometrium during implantation was collected and helper T cells were isolated and their subpopulations examined, the ratio of Th1 was higher and the ratio of Th2 was lower in the CE group than in the non-CE group, but there was no difference in Tregs and Th17.

Based on the results of bench studies, we hypothesized that an altered administration route and increased dosage of progestogen may improve clinical outcomes. The clinical outcomes of patients who underwent single frozen-thawed blastocyst transfer were examined for each hormone replacement therapy. It was found that using a progesterone vaginal suppository in combination with an oral progestin for hormone replacement improved the pregnancy rate and live birth rate in CE patients when compared with using an oral progestin alone.

[Conclusion]

CE may cause implantation failure and affect pregnancy outcomes. CE altered the decidualization and subpopulation of immune cells in the endometrium. Devising luteal support improved the pregnancy rate.

4) A treatment strategy for the gastrointestinal development of premature infants by administration of micelles derived from pulmonary surfactants and the vernix caseosa

Nishijima Koji

Niigata University Medical & Dental Hospital/JSOG

We have shown that human pulmonary surfactant micelles can induce detachment of the vernix caseosa under *in vitro* conditions. Micellization is an important step in postnatal lipid absorption, with micelles being present both in the amniotic fluid swallowed by the fetus and in human breast milk. Our study aimed to establish a treatment strategy to ensure the gastrointestinal development of premature infants, by focusing on the presence of micelles in the intake environment of fetuses and neonates. We first examined the presence of micelles of pulmonary surfactant in human amniotic fluid at term. In order to assess the kinetics of micelles in amniotic fluid, we then prepared fluorescently and gold colloid labeled liposomes with morphology similar to that of pulmonary surfactant micelles, and continuously infused these liposomes into the amniotic fluid of pregnant rabbits. The intra-amniotically infused liposomes were absorbed into the fetal intestinal epithelium, but were not transported to the livers of fetal rabbits. Subsequently, we prepared bovine pulmonary surfactant (surfactant TA) and vernix caseosa complexes and introduced them into the amniotic fluid of pregnant rabbits. The fetal intestinal villous heights and palmitic acid uptake rates were greater in

the group receiving surfactant TA-vernix caseosa infusion than in the normal saline infusion group ($P < 0.05$). The continuous administration of surfactant TA-vernix caseosa micelles influenced the intestinal morphology and lipid absorption of the rabbit fetus, thus protecting the enterocytes from damage due to surgical intervention. We focused on a necrotizing enterocolitis (NEC) newborn rat model induced by loading enteral special formula feeding and exposure to hypoxia after cold stress and hyperoxygenation. Surfactant TA-vernix caseosa complexes reduced the severity of NEC by intervening in the apoptotic pathway. The fetal and neonatal gut is constantly exposed to micelles during the perinatal period. Amniotic fluid micelles intake *in utero* might prepare the gut for the dramatic shift from a highly controlled *in utero* environment to the heavily burdened environment encountered immediately after birth. Although further studies are needed to confirm our findings, our results shed light on the physiological interactions among pulmonary, dermal-epidermal, and gastrointestinal developmental processes, and raise the intriguing possibility for the improved nutritional care of preterm infants immediately after birth.

海外名誉会員講演・表彰式 **ST**1) Ovarian cancer treatment over the last decades, perspectives
for the future

Kuhn Walther C.

DonauIsarKlinikum Deggendorf, Academic Hospital of the University of Hannover, Germany

Ovarian cancer is correlated with the highest mortality due to gynecologic cancer, the 5-year survival for all stages is 20%, screening programs are not yet efficient enough to reduce the 80% rate of advanced tumor stages at the time of diagnosis.

Multiple efforts of different disciplines have been performed during the last 50 years to improve the outcome : in the 60s of the last century the intraperitoneal instillation of radioactive agents (“radio-gold”) turned out to be palliative, even the external, percutaneously applied radiation had no long lasting effect. In the 70s the surgical approach by tumor resection procedures led to better survival rates, even if these findings were not generated by randomized trials. In the following time the adjuvant chemotherapy was state of the art, firstly alkylating agents, later in the 80s and 90s platinum compounds (cisplatin followed by carboplatin) combined with taxanes significantly improved patient outcome. In the 90s and in the beginning of this century multiple national and international multicenter trials investigated different agents, drug combinations, dosages and application routes coming to the conclusion, that the combination of i.v. application of carboplatin and paclitaxel represents the gold standard. Dose intensification and local, intraperitoneal application of the compounds (heated or unheated) are still matter of debate. During the last 15 years new therapeutical principles were integrated in the standard treatment protocols : anti-VEGF agents were approved, at

first in the relapse situation later for extended adjuvant application ; patients in advanced stages with residual tumors profit the most from this antibody treatment. Recently, compounds interfering with the DNA repair mechanism of the tumor cells (PARP-inhibitors) demonstrated significant and better effects on tumor response, especially in tumor tissue with BRCA1/2 mutations and genetic instability (Homologous Recombination Deficiency).

Concerning the surgical approach, multiple clinical studies could demonstrate during the last years, that radical surgical procedures with pelvic, middle and upper abdomen as well as thoracic surgery (“debulking” surgery) can realize a complete tumor resection, a prerequisite for better outcome, even if morbidity and mortality are to be respected. The debate about the timing of surgery (primary surgery vs. interval surgery vs. surgery after primary chemotherapy) is still going on.

In conclusion, the above mentioned treatment options led to better patient outcome, even if the 5-year survival rate of 25% is disappointing. The “one fits all” -strategy (radical surgery followed by chemotherapy) is no longer standard of care, there are molecular based predictive markers (e.g. mutations, HRD, immunogenicity), leading to an individualized specific treatment. In future studies these markers should be analysed (by laparoscopy or interventional procedure) to define tumor biology and response-probability before beginning the burdensome treatment.

2) A bridge connecting Korean and Japan Society

Kang Soon B.

Professor Emeritus of Seoul National University Hospital/Hosan Women's Hospital, Korea

History can help guide people away from repeating mistakes of the past. Indeed only through an understanding of history we can continue to improve ourselves.

Remembering the past over thirty years, I would like to memorize the 1st Korea-Japan Joint Conference of Ob/Gyn (1989) in Seoul which was organized by Prof. Chang and I also assisted as the Secretary General of KSOG. Twenty years later, The 11th K-J Joint Conference (2009) in Seoul which was hosted by myself as Chairman of the Board of KSOG. And we'd published the "History Book of 20 years of the K-J Joint Conference of Ob/Gyn" to be part of celebration.

All of these were fortunate occasions for me to

be involved and contributed to achievement and advancement of academic field and friendly relationships of both societies.

This meaningful project has led the relevant societies to collaborate and promote international relationships in both countries. They have been with us for very productive years in Maternal-Fetal Medicine, Reproductive Endocrinology, Gynecologic Oncology and General Gynecology.

Now I review the history of Korea-Japan Joint Conference of Ob/Gyn and consider the ability to play the role of bridging our two nations and their people.

3) Paradigm Change in the Management of Gynecologic Cancer

Kim Young-Tak

University of Ulsan, Asan Medical Center, Korea

For cervical cancer surgery Dr. Ernst Wertheim in Austria standardized the full extended Radical Hysterectomy (RH) in 1898 and Dr Friedrich Schauta performed his first extensive Radical Vaginal Hysterectomy (RVH) in 1901 with operative mortality of 9.8% for 7 years afterwards.

Original cancer surgeries had focused on the radicality of surgery that might compensate for the inevitable complications and surgical morbidity. Dr. Okabayashi in Japan first performed nerve sparing RH in 1921 that might be the first approach considering the quality of life.

Since 1940's until recent years there had been remarkable improvement in surgical skills with less morbidity including Dr. Joe Vincent Meigs' modified Wertheim RH in 1944, Alexander Brunschwig's pelvic exenteration in 1948 and Kobayashi RH method in 1961.

Pelvic exenteration was considered one of the breakthroughs in gynecologic oncology of the last-quarter century hypothesizing that ultraradical dissection of organs in the pelvic area might eradicate the disease. The hypothesis also might has been applied to ovarian cancer cytoreductive debulking surgery to no residuals in recent years.

However, for the past several decades Quality

of life (QOL) became a fundamental consideration for management patients even with life threatening diseases. Major evolving paradigms with improved QOL are such as minimally invasive surgery for nerve sparing and fertility preservation or sentinel lymph node mapping to lessen the extensive lymphadenectomy with laparoscopy and Robot.

Now there are more clinical trials to introduce computers to integrate multimodal data and artificial intelligence (AI) to augment surgical decision.

The goals of treatment for most patients with advanced gynecologic tumors remain largely palliative, and patient reported QOL is the primary outcome determining the utility of treatment. Particularly QOL endpoints are increasingly important in clinical trials and in the evaluation of interventions.

Now the systemic management gynecologic cancer has evolved from a "one-size-fits-all" approach to one in which we are becoming more precise and targeted therapy.

In the future, there would be paradigm change toward selecting sub-groups of cancer patients with diverse genetic/biochemical abnormalities and physical status who might benefit from personalized surgical or systemic approach.

会長特別企画 1 (AOFOG Presidential Lectures) **ST**

1) On the shoulders of giants

Chandran Ravi

AOFOG Past President/Gleneagles Hospital Kuala Lumpur, Malaysia

The concept of the Asia Oceania Federation of Obstetrics & Gynaecology (AOFOG) was first mooted in 1954 and eventually materialised in April 1957 in Tokyo at its inaugural meeting, with Professor Hideo Yagi ensconced as its first President. Throughout its 65 years of existence, the AOFOG has always strived to improve the healthcare of women in our region. And throughout this time, we have fiercely and proudly remained an autonomous body as envisioned by our founding fathers. Without doubt, AOFOG has had its share of ups and downs with its “golden years” overseen by giants such as Professors Sakamoto and Mizuno from Japan, Professor Shan Ratnam from Singapore and Professor Bishop from Australia. Since 2017, we have

worked to recapture some of our past glory and reinstate AOFOG to its rightful and proper status among the international community of Obstetricians & Gynaecologists. We strengthened our internal processes, improved communication within our administration as well as with our National Society members, built bridges with other like-minded organisations and above all, focused on key health issues impacting our region via research, advocacy and projects. We were not reinventing the wheel as, in essence, the building blocks had already been laid previously by our predecessors. We were merely “re-polishing the diamond” and although much has been achieved, it is still a work in progress.

会長特別企画 1 (AFOG Presidential Lectures) **ST**

2) My voyage drifting in the waves of COVID-19 with AFOG

Ochiai Kazunori

AFOG President/Shin-Yurigaoka General Hospital

In a nutshell, the characteristic of my president's term is "the fight against COVID-19." Especially, between 2020 and 2021, AFOG spent completely different years from normal AFOG activities since it has been established in 1957. That is because, of course, the COVID-19 pandemic raged around the world repeatedly. Under these circumstances, the first thing that welcomed us who starting to row in the rough seas of COVID-19 was the issue of the AFOG congress, which is usually held every two years. The momentum of the COVID-19 pandemic at that time was tremendous, and we decided to postpone the AFOG congress 2021 originally scheduled for March 2021 to May 2022. Initially, some said the 14-month postponement was too long, but we thought it was necessary and sufficient for global control of this infection to spread.

While we were overcoming several big waves, vaccines were developed, and vaccination progressed around the world. New infections have plummeted, lockdowns have been lifted in many countries, and citizens have been able to regain their normal lives. However, mutations in the COVID virus are endless. Recently, the new VOC "Omicron" has begun to rage around the world.

During this period, all meetings related to the

operation of AFOG were held online, and the seminars organized by each Committee were also held virtually. The advantage of the web meeting is that you can attend meetings and seminars without going to the venue, but unfortunately the enthusiasm in the venue is not transmitted through the web. Is it an old idea that face-to-face is the basis of meetings, conferences, and seminars? The purpose of attending an international conference is not just about going to the conference venue. It is also an opportunity to experience the culture of the host country and is an irreplaceable place for other members to get to know each other. It is a good chance to deepen friendships with old friends and at the same time make new friends. This Omicron strain is highly infectious, but fortunately it is said that it is unlikely to become severe.

For the past two years, I was able to survive the rough sea voyage safely with the seniors who showed me the right direction, the executive board members who steered with me, and the chairs and members of standing committee who rowed the boat together. I have been enjoying voyage with NS members who were on board joined a trip with us. I would like to look back my term by thanking to everyone's support and cooperation.

会長特別企画 1 (AOFOG Presidential Lectures) **ST**

3) Future focus of AOFOG in 2022-2024

Lumbiganon Pisake

AOFOG President Elect/Khon Kaen University, Thailand

COVID-19 pandemic limits our AOFOG activities so much. I hope that in 2022 COVID-19 situation will allow us to do more AOFOG onsite activities. AOFOG executive board will do our best to make the AOFOG 2024 Congress in Korea to be very attractive, useful and attended by as many participants as possible. We will support our standing committees to organize evidence based scientific activities in collaboration with national societies. Although there are many important reproductive health issues in our AOFOG, I would like to focus on three challenging issues including :

1) Elimination of cervical cancer

AOFOG has been addressing this issue since 2015 before WHO and FIGO. In May 2018, the WHO Director-General announced a global call for action to eliminate cervical cancer. There are many countries in AOFOG that still facing this preventable and effectively treatable disease. We have to work harder to get 90% of girls fully vaccinated with the HPV vaccine by the age of 15 ; 70% of women screened using a high-performance test by the age of 35, and again by the age of 45 ; and 90% of women with pre-cancer treated and 90% of women with invasive cancer managed. Each country should meet the 90-70-90 targets by 2030 to eliminate cervical cancer within the next century.

2) Appropriate use of Cesarean section

Caesarean section rates have been increasing steadily worldwide over the last decades. This is

also true for many countries in AOFOG. Caesarean birth is associated with short- and long-term risks and affect the health of the woman, the child and future pregnancies. High rates of caesarean section are associated with substantial health-care costs. Japan is one of the best country in AOFOG in keeping cesarean section rate at a very low level whilst one of the lowest maternal and perinatal mortalities in the world. Japan should advise other AOFOG countries with high cesarean section rates how to use cesarean section appropriately.

3) Violence against women

Violence against women, particularly intimate partner violence and sexual violence is a major public health problem. WHO indicated that globally about 1 in 3 of women have been subjected to violence in their lifetime. Violence can negatively affect women's physical, mental, sexual, and reproductive health. AOFOG should address this very important reproductive health issue more aggressively.

The other general concept that I would like to promote is the "evidence based reproductive health practices". It is very important for us to use trusted evidence to inform our practice for better health of our population. Cochrane is an internationally recognized that produces trusted synthesized evidence, make it accessible to all, and advocate for its use. There are already some Cochrane entities in AOFOG countries. AOFOG should collaborate more with Cochrane.

会長特別企画 1 (AOFOG Presidential Lectures) **ST**

4) 【Video Letter】 JOGR matter : for the future

Kato Kiyoko

Editor-in Chief, Journal of Obstetrics and Gynecology/Kyushu University

JOGR is the official journal of Asia and Oceania Federation of Obstetrics and Gynecology (AOFOG) and Japan Society of Obstetrics and Gynecology (JSOG) issued monthly. It is an online only journal. It is an online only journal, and the current volume is 47.

Journal scope are Original, Peer-Reviewed papers in all area of Obstetrics and Gynecology, including perinatology, oncology, reproductive endocrinology and infertility, urogynecology and women's health care. We have recently 100 Japanese associated editors' members and editorial board members from each country belonged to AOFOG.

Submission has been increasing year by year. In 2020, submission increased significantly, which might have been caused because of the COVID-19 pandemic and it reached to 2581 and acceptance rate was 20%. Impact Factor is slightly increasing, and it is 1,122 in 2018, 1,392 in 2019 and 1,710 in 2020. To improve impact factor, we would increase review articles by experts such as invited articles, report the activities of national societies in AOFOG area (Country report) and report products from the activities of AOFOG Committees such as clinical suggestions from the committees. In 2019, 7,380 institutions offered access to the latest content in your jour-

nal via either a Wiley License or a traditional (title-by-title) subscription. Philanthropic initiatives extended low-cost or free access to current content to 6,193 developing world institutions. Distribution our journal is to all over the world, not only AOFOG area but also Europe, UK, United States and Canada. This means JOGR is now an international scientific journal. The number of full-text article downloads is also increasing (386,897 in 2019) and the percentage of total usage top three countries is 22% United States, 11% China and 9% Japan. In AOFOG award, Young Scientist Award (the first named author and must have been 45 years or below when the article was submitted), Y S Chang Endowment Award (articles in Reproductive Endocrinology and Infertility) and Yuji Murata Endowment Award (articles in Maternal Fetal Medicine) are selected from the articles of JOGR.

However, we found many inappropriate acts during the Journal publication process including plagiarism, repetitive publication, and salami publication. Recently, the inappropriate acts in the publication process have drawn a great deal of attention. We introduce the systems which find inappropriate acts during review process and discuss about sanction in the editorial meeting.

会長特別企画 2 P 旧優生保護法を考える

基調講演：旧優生保護法の歴史と倫理的課題

立命館大学科学史・生命倫理学 松原洋子

【概要】

この講演では、旧優生保護法の歴史を概観し、その倫理的課題を明らかにする。前身である国民優生法（1940年）と旧優生保護法（1948年）の共通点と相違点、敗戦後の占領期に旧優生保護法が成立した背景、1970年代の胎児条項導入をめぐる論争、1980年代の政府による優生条項削除の失敗、母体保護法（1996年）改正の経緯、その後現在に至る展開、またこの過程における産婦人科医の関与について述べる。

【旧優生保護法の「優生保護」】

旧優生保護法は、敗戦後間もない1948年に公布された。「この法律は、優生上の見地から不良な子孫の出生を防止するとともに、母性の生命健康を保護することを目的とする」（第1条）とあるように、旧優生保護法は「優生保護」と「母性保護」の二つの特徴を備えていた。このうち「優生保護」については、障害者差別であるという強い批判や、「優生手術」の基準に対する医学的な疑問が、すでに1970年代から提起されていた。1980年代には政府が優生条項を削除する法改正を検討していたが、改正案が提出されることはなかった。議員立法により、旧優生保護法が「母性保護」のみを残して現在の母体保護法に改正されたのは、1996年のことである。被害を受けた女性が2018年1月に仙台地裁に国家賠償請求訴訟を起こしてから、メディアによる集中的な調査報道を通じて、旧優生保護法のもとの強制的な不妊手術や人工妊娠中絶の実態がようやく社会に広く知られるようになった。戦後の日本で強制不妊手術が国の政策として進められていた事実は社会に大きな衝撃を与え、旧優生保護法一時金支給法の成立（2019年4月）や、日本医学会連合による「旧優生保護

法の検証のための検討会報告書」の公表（2020年6月）につながった。1996年の母体保護法への改正から、医学界を含む社会が旧優生保護法下での被害の実態に目を向けるようになるまで、20年以上の歳月を要した。このことは、優生条項の削除という法的対応だけでなく、優生条項の倫理的問題を広く社会に共有することが重要であることを示唆している。

【「母性保護」と「新優生学」】

さらに、出生前診断の結果にもとづく人工妊娠中絶が、旧優生保護法の「母性保護」を引き継いだ母体保護法のもとで実施され続けていることにも留意しなければならない。旧優生保護法において、「母性保護」は「良い子」を産むための「優生保護」の理念と密接に関わっていた。例えば1960年に母子保健法が公布されると、旧優生保護法と連動しながら、地方自治体による「不幸な子どもの生まれない運動」が展開された。この運動では周産期医療および母子保健の拡充を目指すと同時に、障害をもって生まれる子を「不幸な子ども」とみなし、その発生予防・出生予防を推進した。現在、生殖技術と遺伝子技術の進展を背景に、健康な子どもを産むのは親の道徳的義務であると主張する「新優生学」が論議を呼んでいるが、「不幸な子どもの生まれない運動」と「新優生学」は、基本的な理念を共にしている。過去の優生学と現在の新優生学の関係、さらに「優生学」の何が問題なのかが、ゲノム編集ベビーの是非をめぐる国際的な議論においても倫理的課題として真剣に問われている。女性はもとより医療者もすでに新優生学の渦中にあり、その点でも旧優生保護法の倫理的課題を考える必要がある。

会長特別企画 2 P 旧優生保護法を考える

1) 不妊手術について、もう一度考えてみる機会に

京都医療センター 小西郁生

旧優生保護法の下で、障がいをもつ方々が、本人の同意の有無にかかわらず不妊手術を受けていたことが大きく報道され、「強制不妊手術」という用語が一人歩きを始めました。その影響で、国民の間に「不妊手術」はとても嫌な手術であるというイメージが植えつけられたのではないかと危惧いたします。私自身、令和元年6月から厚労省の旧優生保護法一時金認定審査会の委員となり、その実態を目の当たりにし、このようなことが二度とあってはならないという思いとともに、不妊手術に至った子どもたちのご両親の思いを感じることができました。現在までの一時金申請者の内訳をみる限りにおいて、ハンセン氏病の方々を除くと、実際に不妊手術を受けたのは圧倒的に女性なのです。当初はジェンダー差別かと思いましたが、必ずしもそうではなく、やはり女性こそが妊娠・分娩のリスクを担う性であり、子育てに全責任を負う立場であったことに起因します。ご両親の「この子の障がいを遺伝させない方がよいのか?」という考えとともに、「この子には妊娠や出産、まして子育てはとても無理」という思いが、法律の後押しを受けて一気に不妊手術へと繋がったのではないかと推察いたします。また当時は、妊産婦死亡率も10万人あたり100~150と非常に高く、女性のもつ妊娠・出産のリスクと子育て負担を抜きにして、旧優生保護法は語れないと思いました。

ヒトはその進化のなかで妊娠・出産のリスクを内包することとなります。約600万年前のアフリ

カでヒトは二本足で直立歩行を開始しますが、四つ足から二本足で直立したことで骨盤形態に劇的な変化がもたらされ、女性は未熟な子どもしか生めなくなり、子育て負担が著しく増加します。その環境において、女性の発情期消失という決定的な適応進化があり、その結果、互いにパートナーを得るための文化が開き、いつでもセックスができ、男女の愛情を格段に深め、主として一夫一婦制をとりながら両性が協力して子育てを行う社会が形成されてきました。しかし一方で、女性は難産となり死亡リスクが高まり、受胎時期が不明瞭となったことで望まない妊娠や人工妊娠中絶も不可避となり、避妊・不妊法を必要とするようになります。ヒトの進化はまさしく産婦人科の歴史です。避妊・不妊法の開発では、私たちの大先輩である荻野久作先生、太田典礼先生、内田一先生らが世界的にも大きな役割を果たしています。そのような背景のなかで、近年、女性のセクシャル・リプロダクティブヘルス/ライツの考え方が生まれ、現在に至っています。わが国は、男女共同参画社会の実現にはまだ遠く、現在も子育て負担の多くを女性が背負う形となっています。その意味で、旧優生保護法下の大きな問題は、その法律は廃止されたとはいえ、現在も持続しているといえます。私たち産婦人科医こそが、女性のヘルスケアに責任をもつ立場から、女性のセクシャル・リプロダクティブヘルス/ライツを大いに啓発していくことが大切です。

会長特別企画2 **P** 旧優生保護法を考える

2) 旧優生保護法と精神医学・医療の関係

—日本精神神経学会の調査研究から見えてきたこと—

仙台医療センター精神科 岡崎 伸郎

2018年1月、旧優生保護法にもとづいて強制不妊手術を受けた女性（宮城県）が国家賠償請求訴訟を提起した。これをきっかけに各地で同趣旨の提訴が続き、旧優生保護法について社会的関心が高まった。そして2019年4月には、被害者に一時金を支給する救済法が成立し施行されたが、該当者の掘り起こしは容易でなく、申請者数は伸び悩んでいる。旧優生保護法（1948～1996年）によって強制不妊手術を施行された人は16,475人（女性11,312人、男性5,163人）にのぼる。その件数は1955年頃をピークとして漸減した。最も件数の多かったのは北海道、次いで宮城県である。確認できる最後の事例は、母体保護法に改組される4年前の1992年（福岡県）である。例えば1970年代に20歳代で手術を施行された人が今日生存していれば70歳代となるが、そのことから今日生存している旧法の被害者は少なくないと考えられる。

（公社）日本精神神経学会は、最初の訴訟以前から、旧優生保護法およびそれを支えた優生思想とは何かという問題に注目し、学術総会でのシンポジウム等を通じて会員の関心を喚起してきた。この間、2016年に相模原市で起きた障害者施設入所者大量殺傷事件において、極端な優生思想が犯行の動機であったとされたことも大きな契機となった。その後、当学会法委員会（演者ら）が理事会の負託を受ける形で調査研究に着手し、現在進行中である。メンバーには精神科医のほか社会学や歴史学の研究者も加わり、人文社会科学的手法を備えた体制としている。調査研究項目としては、(1) 文献のレビュー、(2) 公文書の調査、(3) 会員を対象とした旧法への関与や問題意識についての質問紙調査、(4) 優生手術に関与した会員への任意の聞き取り調査、(5) 過去の診療録の調査、

である（当日、一部を紹介する）。

これまでの調査研究で、旧優生保護法は精神科医の関与なしには運用され得なかったことが明らかになっている。具体的には、国レベルでは公衆衛生審議会優生保護部会委員として、都道府県レベルでは優生保護審査会委員として、そして個別ケースでは優生手術の主たる申請者として、精神科医はこの制度運用の各プロセスにおいて重要な役割を担ったのである。一方、当学会自体は、研究と人権問題委員会が1991年に「優生保護法に関する意見」をまとめて強制断種に関わる条文の削除を提起し、理事会がそれを学会見解として厚生省（当時）に送付しているが、会員の大勢を巻き込むような動きには結びつかなかった。精神科医の多数が加盟する基幹学会であり、医学の発展による社会貢献を目的とする学術団体でありながら、旧優生保護法体制の存続を長きにわたって看過してきたこと、また法の廃止後も積極的な検証作業を行ってこなかったことへの社会的道義的責任は極めて大きい。学会も、個々の精神科医も、自らが主体的に取り組まなければならない問題であるとの自覚に乏しかったと言わざるを得ないのである。

調査活動を通じて醸成されてきた演者らの仮説であるが、戦後の復興期において公益重視の名のもとに行われた国策として、優生政策（優生保護法として具現化）と隔離収容の精神医療政策（精神衛生法として具現化）とが深いところで結びついていたという歴史的視点が浮かび上がってきた。

旧優生保護法への精神科医の関与という歴史的な人権問題に対して、日本精神神経学会は近い将来の見解の取りまとめに向けて検討を続けている。

会長特別企画 2 P 旧優生保護法を考える

3) 旧優生保護法について

関内法律事務所弁護士 平 岩 敬 一

旧優生保護法は、平成8(1996)年に強制優生手術条項等の優生思想に基づく条項を削除して改正され、現行の母体保護法となった。

同法が改正された22年後である平成30(2018)年、本人の同意なく優生手術を受けさせられた被害者らが、国を被告として国家賠償訴訟を提起している。一方、強制不妊手術が社会問題化していることを受け、平成31(2019)年4月、「旧優生保護法一時金支給法」が成立している。

前記裁判については、令和元(2019)年5月仙台地裁が、子を生み育てることは、憲法上保証された個人の基本的権利であり、何人にとってもリプロダクティブ権を奪う事は許されない。本件規定は、憲法13条に違反し無効である。と判示している。また、東京地裁でも、令和2年6月同旨の判決があった。しかし、両判決とも国家賠償については、20年の除斥期間の経過を理由に請求を棄却している。

現在では、誰もが強制不妊手術は被害者の基本的人権を侵害するものだと考えるに違いない。何故、敗戦後の占領下であるとはいえ基本的人権尊重主義を基本原理の一つとする日本国憲法が施行された翌23年に、旧優生保護法は成立したのであるか。

立法当時の関係者は、皆、天皇を主権者とする大日本帝国憲法下で教育を受けていた。主権者を国民とする日本国憲法の定める基本的人権に対する理解が不十分であったことは否定できない。敗戦後の日本が範とした欧米諸国でも強制不妊手術は行われていた。戦後の荒廃した国土に大量の復員者、引揚者が帰還し、類例のない過剰人口問題や食糧難などから人口抑制が課題となっていた。民族の逆淘汰を防止する必要があった。等が、同法成立時の立法事実であると考えられる。

同法は、制定の翌年改正され、強制不妊手術の審査の申請を任意から、罰則はないものの医師の法的義務としている。その後、手術数は急増したが、昭和30(1955)年をピークに漸減し、法改正の6年前には零になった

一方1970年代には、欧米各国で優生思想に対する批判が高まり、断種法も廃止されていった。我が国でも高度経済成長により、国民生活も安定して権利意識も向上し、障害者の福祉も改善している。法律制定時の立法事実は消滅していると考えられるのに、何故、法改正までに、欧米各国から20年以上も遅れを取ったか。一旦法が制定され、制度が出来たとしても時代と共に価値観・倫理観は変化する。日本国憲法は、「この憲法が国民に保障する自由及び権利は国民の不断の努力によって、これを保持しなければならない」(憲法第12条)と定めることを重く受け止める必要がある。

強制不妊手術を申請した医師、施術をした医師は、法の定めに従ったものであり、法的責任はない。しかし、手術件数は、漸減している。医師の間にも強制不妊手術について問題があるとの認識があったのではないか。一方、昭和45(1970)年に成立した「心身障害者対策基本法」は、目的に心身障害の発生予防に関する施策を挙げている。また、「不幸な子どもが生まれない運動」も全国規模で行われていた。このようなことから、医師側の懸念が行動にあらわれなかったと思われる

医療の進歩は目ざましい。現在、日産婦学会は、新型出生前診断、着床前診断等の問題に真剣に取り組んでいる。東京地裁は、平成19(2007)年5月日産婦学会の「着床前診断に関する見解」に対する無効確認請求を却下している。一方、ユーロの人権裁判所、イタリアの憲法裁判所は、着床前診断を禁じるイタリアの法が、自己決定権に反し、

違法・違憲であるとの判決を下した。これからは
リプロダティブヘルス・ライツと公共の福祉をど
のように調和させるのか、学会の自律権の限界は

どこか等が大きな課題になると思われる。旧優生
保護法に対する検証を十分に行い今後の教訓にし
ていくことが大切である。

医会・学会共同企画 「生涯研修プログラム」 生涯研修プログラム 13 後遺症なき児の発育を目指して

1) 産科医療補償制度の現状

大分県立病院 佐藤昌司

2009年の制度導入以降13年を経て、加入分娩機関は3,176施設(全分娩機関の99.9%)で、全審査件数4,456件のうち3,374件(75.7%)(2021年6月末現在)が補償対象となっている。この間、分娩週数(在胎32週以上)と出生体重の引き下げ(1400g以上)を経て、制度開始時よりも‘より軽い、より早い’事例が増加した。原因別にみると、常位胎盤早期剥離あるいは胎児心拍数陣痛図所見から臍帯因子と思われる例など、分娩中発症の胎児低酸素・酸血症および胎盤機能不全の事例は、頻度は不変ながら原因に占める割合が漸増してきている。一方で、いわゆる分娩中の低酸素・酸血症に起因する事例は漸減してきている。妊娠中から分娩時に異常なエピソードを認めない「原因不明」例が約40%に及び、さらに早産例の増加に伴って一絨毛膜性双胎における一児/両児の脳性麻痺例、ビリルビン脳症、あるいは胎児酸血症や

新生児仮死は軽度であったにもかかわらずPVLに至った事例の頻度および比率が増加してきている。産科管理面から見ると、臍帯因子あるいは常位胎盤早期剥離の事例では、産科管理は適切であったにもかかわらず脳性麻痺の転帰に至った事例も少なくない。また、早産例では胎児心拍数陣痛図との関連から一義的に原因および受傷時期を決定できない事例、顕著な脳画像所見にもかかわらず胎児心拍数陣痛図所見の異常がない、など、正期産児と異なり胎児期の臨床所見、分娩時データおよび脳画像所見の間に一義的な関係が不明確な事例が多いことが分かる。2022年1月からは、補償対象条件から体重要項が削除され「在胎週数が28週以上であること」のみとなり、脳性麻痺の原因あるいは背景要因がさらに多角化する可能性がある。

2) 双胎妊娠と脳性麻痺

東邦大学 中田雅彦

双胎妊娠などの多胎妊娠は単胎妊娠に比較して早産率が高く、胎児発育不全や先天性構造異常の合併率も高い。さらに一絨毛膜双胎では、双胎間輸血症候群やSelective fetal growth restriction (FGR), Twin anemia-polycythemia sequence (TAPS)といった一絨毛膜双胎固有の合併症や一児胎児死亡による胎児間失血などの問題を合併する可能性が高い。本講演では、我が国の大規模な統計データを用いた解析による双胎妊娠の妊娠週数別の周産期死亡率の検討結果を提示する。さらに、産科医療補償制度の脳性麻痺分析結果より、

双胎妊娠における脳性麻痺原因の特徴について提示する。特に、膜性診断別の解析では、二絨毛膜双胎に比較して一絨毛膜双胎では、単胎や二絨毛膜双胎とは異なる特徴が認められることが明らかとなった。具体的には前述の一絨毛膜双胎固有の合併症が脳性麻痺発症に大きく関与していることが判明した。

上記のデータを踏まえ、脳性麻痺の発症を可能な限り防ぐための双胎妊娠の管理法と対策について概説する。

3) 無痛分娩における脳性麻痺症例について

昭和大学 新 垣 達 也

無痛分娩は産婦にとってメリットがある一方、分娩管理において適切な母児の管理、医療介入が必要である。わが国の無痛分娩の頻度は漸増傾向にあり、無痛分娩に関連した脳性麻痺発症例の特徴を明らかにすることを目的に検討をおこなった。2009～2019年までに産科医療補償制度に報告された脳性麻痺例2,457例の内、無痛・和痛分娩102例の原因分析報告書全文版(マスキング版)の臨床経過、問題点を解析した。硬膜外鎮痛法による無痛分娩を実施した症例は85例(脳性麻痺事例の3.5%)あった。脳性麻痺に関連したイベントが分娩中であったのは52%(44)であった。そのうち15例は早剥、臍帯脱出・下垂、子宮破裂、羊水塞栓症、子宮内感染などに関連したが、66%(29)は無痛の分娩管理に関連したと考えられた。そのうち、硬膜外麻酔が直接的に関連したものが3例(全脊椎麻酔1例、麻酔薬投与に伴う子宮胎盤循環

不全2例)あったが、それ以外の26例には無痛の分娩管理が関連していた。それらに微弱陣痛は20例あり、6例はなかった。不適切な急速遂娩に関連したのが(鉗子・吸引失敗で帝切、要約を満たさない鉗子・吸引分娩など)18例、子宮収縮薬、CTG判読に関連したのが4例、その他4例であった。本検討によって、無痛分娩中のイベントに関連して脳性麻痺になったと考えられる事例の3分の2に無痛分娩の管理、医療行為の影響があることが明らかになった。麻酔自体が直接的に影響を与えた例もあったが、多くは無痛分娩によって生じた微弱陣痛に対する陣痛促進、器械分娩の施行方法、CTGの判読、子宮収縮薬の使用法の問題も含まれていた。医療行為に関連した脳性麻痺を減ずるために、適切な母児のモニタリング、子宮収縮の評価、子宮収縮薬の使用、産科手術法の選択と実施が必要である。

医会・学会共同企画 「生涯研修プログラム」 生涯研修プログラム 14 後遺症なき出産を目指して

1) 妊産婦死亡の現状と再発防止

聖マリアンナ医科大学 長谷川 潤 一

2010年わが国の妊産婦死亡事例を検討して再発防止へ繋げることを目的に妊産婦死亡報告事業が発足した。毎年、再発防止のための提言を掲載した冊子「母体安全の提言」を発刊しているが、創刊号で強調されたのは産科危機的出血による死亡を減ずるためのバイタルサインへの注意、Shock indexの計算という今では極めて初歩的と感じられる内容であった。その後、診療科や病診の垣根を超えた協働による母体救命の必要性が強調され、その教育システムの構築のため2015年に母体救命普及協議会(J-CIMELS)が発足した。このような経緯の中、妊産婦死亡の原因のトップであった産科危機的出血は年々顕著な減少傾向を示し、現在では妊産婦死亡報告事業の立ち上がった時の1/3になった。これは、ひとえに産科医療に関わる医療者のバイタルサインの意識や速やかな

初期対応への意識改革と実践、シミュレーションの実施、速やかな輸血や母体搬送、コミュニケーションなどの改善の結果であると考えられる。そのため、妊娠や分娩に関連する異常で死亡に至った直接産科的死亡の減少傾向の一方、間接産科的死亡の割合が増え、妊産婦死亡事例の原因究明はより複雑になっている。さらなる母体安全の向上のための課題として、妊娠高血圧症候群、肺血栓塞栓症、羊水塞栓症、劇症型A群溶連菌感染症、心大血管疾患の克服がある。搬送前の心肺停止例への救急救命士の関わり、精神疾患関連による自殺、産科麻酔管理などの問題にも改善が必要である。様々な原因で死亡している妊産婦を一人でも救っていくために、地道な努力を続けていく必要がある。本講演では、妊産婦死亡の現状と今後の再発防止の方向性について論じる。

2) 妊娠高血圧症候群への対応

宮崎大学 桂 木 真 司

妊娠高血圧症候群は妊産婦の年齢と関連して発生頻度、後遺症頻度が高くなる。妊産婦の後遺症に関連する病態には脳卒中が約9割、周産期心筋症が約1割関与している。妊娠高血圧症候群による死亡例の約8割は妊娠35週以降に発症し入院時期や分娩時期、診断の遅れが指摘されている。近年、高齢の妊産婦は脳神経外科医師のいる二次、三次施設での分娩数が高くなっている事が報告されており、今後、脳卒中発症直後の初期対応の徹底が脳卒中による後遺症を減少させる手立ての一步である事が期待される。頭痛や意識障害、嘔吐、麻痺などの局所症状や痙攣などでは脳神経外科への連携を迅速に行うシミュレーションの重要性がクローズアップされる。脳出血のみならず脳梗塞も妊産婦の重症妊娠高血圧症候群の後遺症に大きく関与する。片側の手足のしびれ、倦怠感、めまい、視覚障害などに対して早期に脳神経外科へのコン

サルトを行う事が肝要である。

産婦人科医師による周産期心筋症の早期発見が妊娠高血圧症候群の後遺症の軽減に繋がる。妊娠高血圧症候群、双胎妊娠、高齢妊娠、塩酸リトドリン使用が周産期心筋症のリスク因子である。倦怠感、息切れ、などは妊娠の随伴症状として見過ごされやすい。頰脈、体重増加、SpO₂、呼吸数などを心不全症状としてとらえる事ができるか否かが重症である。周産期心筋症を疑ったら自ら妊産婦の心エコーをして左室の動きが悪い場合、循環器内科医師へコンサルトを行いたい。産婦人科医師が循環器領域へ一歩踏み出す事が今望まれている。(1)脳卒中、周産期心筋症の初期症状を見逃さない+鑑別しに行く診療を行う、(2)各専門医師へ医療連携するタイミングを逸さない、この二つが妊娠高血圧症候群による後遺症を減らすキーであると考えられる。

3) 妊産婦の重症感染症への対応

東邦大学 早田 英二郎

妊産婦死亡症例検討評価委員会の分析では、2010年～2020年に発生した妊産婦死亡のうち、感染症が原因と判定されたものは全体の8.8% (42/477)を占め、その割合は増加傾向にある。同委員会は、一般的には稀であるが、死亡原因として頻度の高い疾患に関して、生存者の診療情報を集積し、死亡者との比較・分析を行う研究を開始した。本項では、その先行研究として、感染症による妊産婦の死亡例・生存例の症例を全国から集積し、後方視的観察研究を実施した成果、および今後の展望について報告する。

感染症による妊産婦死亡の原因として、劇症型A群溶連菌感染症 (Streptococcal Toxic Shock Syndrome; STSS)が52.3% (22/42)で最多であった。STSSによる生存者と死亡者の診療記録を用いた後方視的研究では、STSSによる死亡者と生

存者で、予後と関連するような背景因子 (年齢、経産回数、季節等)は認められなかった。また、劇症化後速やかに (1時間以内)に抗菌薬の全身投与を含む集中治療が生存に寄与している可能性が示唆された。さらに、早期の治療介入のために、臨床症状に加え GAS 感染症の家族歴聴取や GAS 迅速抗原検査の重要性が示唆された。

日本産婦人科医会では、STSSを含む6疾患の妊産婦死亡数の減少が限定的であるとして、死亡数の減少を図る目的で、2021年4月から「妊産婦重篤合併症報告事業」を開始した。今後救命しえた STSS 症例について、妊産婦死亡の減少につながることを目的として、多くの事例を集積して詳細な分析・評価を行うことで、これらの疾患に関連した管理法について発信していく予定である。

4) 肺血栓塞栓症への対応

三重大学 田中 博明

妊娠中は①血液凝固能亢進、線溶能低下、血小板活性化、プロテインS (PS) 活性低下、②エストロゲンによる静脈平滑筋弛緩作用、③増大した妊娠子宮による腸骨静・下大静脈の圧迫により、静脈血栓塞栓症 (VTE)が生じやすくなっている。また、妊娠の時期によって、妊娠初期の妊娠悪阻、中期の切迫早産による安静、後期の帝王切開などが、脱水や安静臥床を伴うため VTE の危険因子として認識されてきた。

欧米と比較すると人種的な問題から、日本人における肺血栓塞栓症の発症頻度は必ずしも高くはない。日本産婦人科・血液学会により、1991年から2000年までの10年間の産婦人科領域における VTE 発症の全国調査を行ったところ、肺血栓塞栓症 (PTE) の発症は、経陰分娩では9例/34.8万分娩 (0.003%)、帝王切開では50例/8.7万分娩

(0.06%)であった。また、同調査から VTE は年々増加傾向にあることが示された。

これまで、周産期に携わる産婦人科医は、従来からリスクとされている肥満、高齢、脱水、安静臥床などに留意し、VTE・PTEの予防に努めてきた。しかし、妊産婦死亡報告事業や肺血栓塞栓症に関する全国悉皆調査からは“高リスクと認識されていない”PTEによる妊産婦死亡例があり、日本における肺血栓塞栓症による妊産婦死亡は減少していないことが示されている。これまでの妊産婦死亡報告事業や肺血栓塞栓症に関する全国悉皆調査から得られた情報をもとに、現在の肺血栓塞栓症予防のための問題点について述べる。また、実際に肺血栓塞栓症を発症した際に、どのように対応すべきかについても述べたい。

医会・学会共同企画 「生涯研修プログラム」 生涯研修プログラム 14 後遺症なき出産を目指して

5) 産科麻酔急変への対応

日本医科大学 鈴木俊治

産科麻酔における不測の事態は緊急的突発的に発生するが、その対応に必要なことは、母体に対しては呼吸・循環状態を監視しながら適切な処置を行うための人員配置であり、そして十分なトレーニング・シミュレーションを行っておくことである。日本産婦人科医会「母体安全への提言」では、麻酔が原因となった母体死亡例では、全例で麻酔科医以外のスタッフが麻酔を担当していたことが報告されている。特に硬膜外麻酔を用いた無痛分娩などにおいては、麻酔および患者モニタリ

ングの記録を残すことに留意し、さらに全脊髄くも膜下麻酔、局所麻酔薬中毒などの生命を脅かす合併症に対するシミュレーションを定期的を実施することが重要である。また、帝王切開における区域麻酔後の気道トラブルなども母体死亡原因となっている報告例があることから、高度肥満や重症妊娠高血圧症候群などの気道確保困難が予測される場合は、麻酔科専門医のいる総合施設への事前紹介を考慮する必要がある。

AOFOG Symposium 1 ST : Elimination of Cervical Cancer in AOFOG Region

1) Trend of cervical cancer in Asia-Oceania

Pariyar Jitendra

AOFOG Committee Member/Civil Service Hospital, Nepal

Cervical cancer is a global public health problem based on the estimate that 604000 women worldwide were diagnosed to have this disease and 342,000 women died from it in 2020. About 50% of these cases and deaths occur in low- and middle-income countries (LMICs) of Asia-Oceania region. Low incidence and mortalities reported in Japan, Australia and New Zealand and high incidence and mortalities reported in Nepal, India and Papua New Guinea reflect the existing inequity in the cervical cancer burden between high-income countries (HICs) and low- and middle-income countries (LMICs) in Asia-Oceania region.

Cervical cancer, caused by human papilloma virus, is preventable with vaccination and treatment of preinvasive cervical lesions detected by reliable screening tests. However, due to lack of HPV vaccination and low population based cervical screening uptake in LMICs of Asia-Oceania,

the disease incidence has not decreased as satisfactorily as observed in the western countries. Cure of cervical cancer is also possible through early detection and appropriate treatment. However, due to lack of diagnostic and imaging services, comprehensive centers with onco-surgery, radiation and medical oncology facilities and allied departments, many cases in LMICs of Asia-Oceania are diagnosed in late stage when cure not possible.

Many Asian-Oceania countries have focused on including HPV vaccination in national program, scaling up the cervical cancer screening, and enhance the management of precancers and advanced cancers. Capacity building through training and courses are also crucial in the effort of achieving the WHO call for cervical cancer elimination which many countries in the region are striving for.

AOFOG Symposium 1 ST : Elimination of Cervical Cancer in AOFOG Region**2) HPV vaccination : How far has it worked?****Domingo Efren J.***AOFOG Deputy Committee Chair/University of the Philippines, Philippine General Hospital, Philippines*

Human Papillomavirus vaccination has been in the forefront of cervical cancer prevention for the past 15 years. For most affluent countries the efficacy and safety of the HPV vaccines have been widely accepted and disseminated through various government and private vaccination strategies integrated with screening procedures. However, for the poor countries, the efficacy and safety has yet to be tried and proven because of the difficulties in implementation as a result of the allocation of limited resources. Various real-

world experiences from Asia-Pacific have been tried and proven to have shown benefits. The school-based programs as well as the municipal and district coverage programs of HPV vaccination equally promote the integration of the benefits into the primary prevention outcomes for Cervical Cancer. The challenge left to be hurdled include the allocation of more HPV vaccines as well as the affordability of these in settings where the poorest of the poor exist.

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3) Cervical cancer screening : How could we maximize them in Japan?

Ushijima Kimio

AOFOG Committee Member/Kurume University Hospital

Uterine cervical cancer is one of the cancer which can be detected early by screening.

On the other hand, the increasing of incidence of uterine cervical cancer in young women is a serious problem. Furthermore, the number of deaths by cervical cancer is increasing, and the most of the survivor have lost their fertility.

The only way to improve this bad situation is to increase the number of people undergoing screening.

The environment of screening system or cervical cancer varies greatly depending on Asian countries. The Japanese screening system is probably well developed. All women more than 20 years of age can undergo cervical cancer screening with very low cost every 2 years.

Nevertheless, the screening rate of Japan is only about 40%, which is lower than other devel-

oped countries, especially in younger age,

What is the reason low screening rate in Japan?

The first, the information to the citizen about cervical cancer is not enough. Most Japanese young girls are unaware of the crisis of cervical cancer.

Second, despite the recommendation of the guidelines of many countries, HPV screening system in Japan has not adapted. The main reason of this is a cost and also the call-recall system is not functioning. If it is possible to control the number of unnecessary screening examinee, it will reduce the cost.

Active recommendation of HPV vaccine finally resumed the first in these 8 years. So, we must go to the next step to prevent and early detect of cervical cancer.

AOFOG Symposium 1 **ST** : Elimination of Cervical Cancer in AOFOG Region

4) AOFOG efforts in Elimination of Cervical Cancer

Wilailak Sarikapan

AOFOG Committee Chair/Ramathibodi Hospital, Mahidol University, Thailand

Cervical cancer is still one of the most common cancers in women in Asia-Oceania. The incidence rate is discrepancy across Asia-Oceania region, with continued high incidence in some area, for example, South-East Asia, South-Central Asia, etc. Worldwide, cervical cancer is the fourth most common cancer in women.

In November 2020, WHO launched the Global strategy following targets of the three pillars for 2030 : 90% of girls fully vaccinated with HPV vaccine by 15 years of age, 70% of women are screened with a high-performance test by 35 and 45 years of age, and 90% of women identified with precancer or cancer receive treatment and care. WHO comprehensively cooperated a health policy with other organizations including Asia & Oceania Federation of Obstetrics & Gynecology (AOFOG) toward the elimination of cervical cancer.

AOFOG launched Manila declaration in November, 2019, during AOFOG Congress, Manila, Philippines. The aim is to collaborate health care professionals with the civil societies, the academic and public health communities among AOFOG countries to prevent cervical cancer. AOFOG position of cervical cancer control have provided scientific and technical supports for their members, encouraged national societies and professional education as well as encouraging gynecologists to do more primary and second-

ary prevention. In Philippines, the 9th HPV summit highlighted Asia-Oceania's commitment for cervical cancer elimination. This HPV summit is the annual meeting gathering healthcare professionals, medical societies, patient groups, advocates, health program officers, policymakers, media, civil society organizations, and private sector to discuss key developments and strategies to eliminate cervical cancer. In Cambodia, HPV vaccination program was initiated in 2017 aiming to reach as many girls as possible and to implement in primary school (98% of girls aged 9 years old). The vaccination took place in six districts in two provinces as a pilot program. The Vaccine Alliance has provided financial support to purchase the HPV vaccine for free vaccination to girls. In Thailand, there is a Memorandum of Understanding between the Royal Thai College of Obstetricians and Gynaecologists (RTCOCG) and the Ministry of Public Health (MOPH) of the Kingdom of Thailand on the Cooperation in Prevention of Cervical Cancer. In 2017, the MOPH implemented free two-dose vaccines for girls aged 11-12 years old.

In conclusion, AOFOG uses dual track strategy : Primary and secondary prevention, health provider and women, government and public, AOFOG and national societies of member countries. Hopefully, we will win the war to eliminate cervical cancer from our region and global soon.

AOFOG Symposium 2 (Committee Symposium of MIGS) **ST :**
Ideal educational exchange program for MIGS training in this era : In the AOFOG society, what did we learn and what should we continue?

1) **【Keynote】 Missions and Activities of AOFOG Minimally Invasive Gynecologic Surgery Committee**

Mandai Masaki¹⁾, Baba Tsukasa²⁾

Past Chair of AOFOG MIGS Committee/Kyoto University¹⁾,

Chair of AOFOG MIGS Committee/Iwate Medical University²⁾

AOFOG, Asia-Oceania Federation of Obstetrics and Gynecology, is an important organization for communication and education of OBGY societies in this region. Since this field covers wide area of woman's health care, AOFOG runs several committees, including MIGS (Minimally Invasive Gynecologic Field) Committee.

MIGS is obviously very important field of gynecologic surgery, especially in recent advances of surgical technique including robotic surgery. However, its prevalence and maturity are significantly differ from country to country in this region. In addition, educational system is also quite different among countries. In order to accomplish the primary mission of the MIGS Committee, that is, to facilitate the prevalence of MIGS safely in this region, the most important factor is mutual understanding of the status of each country. For this purpose, the MIGS Committee conducted a survey to explore the prevalence of MIGS, the levels of general skills, facilities, product supply and education system in each country. The result demonstrated the demand and supply of MIGS education in this region, namely, which country has sufficient resource to provide educational program and which country really needs it.

One of the obstacles of MIGS education is that

MIGS is not necessarily essential for the woman's basic healthcare. In surgical intervention in OBGY field, MIGS is not the first priority comparing more basic surgeries such as cesarian section or cancer prevention surgeries, or laparotomy. Therefore, maintaining motivation for MIGS training of both society and each surgeon, especially young surgeon, is somehow difficult. On the other hand, development in MIGS technology is so rapid, and discrepancies between MIGS-fully developed countries and MIGS-developing countries seems more and more apart. Considering that surgical education takes time, AOFOG should offer effective training opportunity for the future of young doctors in this region. There are several factors that AOFOG can take initiative for this purpose. First, making mutual relationship between societies as well as personal levels via AOFOG activities. Second, mutual understanding of each society's situation, and effective matching according to the real needs. Third, establishing long-standing relationship/program including continuous follow up. Additionally, to build an effective training system on line is urgent under corona situation. Readership of AOFOG is expected to lead to the base-up of total skills of MIGS in this region.

AOFOG Symposium 2 (Committee Symposium of MIGS) **ST :**
Ideal educational exchange program for MIGS training in this era : In the AOFOG society, what did we learn and what should we continue?

2) The Learning Curve of Laparoscopic Sacrocolpopexy

Meutia Alfa P.

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Sacrocolpopexy is the treatment of choice for vaginal vaults, and the laparoscopic approach is preferred. Compared with open sacrocolpopexy, laparoscopic sacrocolpopexy (LSC) shows lower morbidity, shorter recovery and better anatomic resistance as it is known as the gold standard therapy for apical prolapse. Regardless of these advantages, learning LSC is still proven to be a challenge for unexperienced surgeons.

Numerous studies have been done in order to show the effect of learning curve to LSC operative time. Claerhout et al suggested that 31 procedures are needed to reduce time difference between trainee and expert surgeon, while Mustafa et al showed 15 procedures have already significantly reduced operative time. The number of

procedure in these studies varies between 10 to 90 cases with operating time between 162 minutes to 240 minutes.

Mowat did another study to know whether the learning curve for laparoscopic sacrocolpopexy could be further reduced with a structured learning program consisted of assisting in 20 LSCs, video-edit 2 procedures, and practicing laparoscopic and knot tying. Using this structure learning program, the fellow included in this study only needed 90 minutes or less to perform five consecutive LSC without intraoperative or post-operative complication by case 18. This result shows that structured learning program could help in reducing the learning curve for laparoscopic sacrocolpopexy.

AOFOG Symposium 2 (Committee Symposium of MIGS) **ST** :
Ideal educational exchange program for MIGS training in this era : In the AOFOG society, what did we learn and what should we continue?

3) 【Keynote】 International exchange for MIGS training : from Asia to Thailand

Chalermchockcharoenkit Amphan

TG-MET Center/Siriraj Hospital, Mahidol University, Thailand

Today, laparoscopy is one of the most common surgical procedures performed in many parts of the world. Compared with laparotomy, multiple studies have shown laparoscopy to be safer, to be less expensive, and to have a shorter recovery time. Historically, main gynecologic surgical approaches were achieved at open surgery but laparoscopic surgery has dominated for benign and early stage of malignant diseases in recent decades. However, unique psychomotor and perceptual challenges of laparoscopy - such as marred depth perception, the requirement for advanced hand-eye coordination and the use of long instruments - mean that laparoscopic trainees face a steep learning curve.

The Thai -German Multidisciplinary Endo-

scopic Training center (TG-MET center), Faculty of medicine Siriraj Hospital is a pioneer of MIGS training center in Thailand, started to set up the training curriculums of fellowship and workshop in the year 2000. Not only academic field, but promoting international friendship and cultural exchange are also our main objectives. With a great number of MIGS, good MIGS training curriculums and great affiliation to many international associations, these lead us to promote our training curriculums for international fellowship and annual International workshop.

Thailand, a smile land with a great variation of geography, food and culture, prompts to welcome all of you to explore and learn more your life.

AOFOG Symposium 2 (Committee Symposium of MIGS) **ST** :
Ideal educational exchange program for MIGS training in this era : In the AOFOG society, what did we learn and what should we continue?

4) **【Comments】** International exchange for MIGS training :
from Japan to Thailand

Yahata Hideaki

Kyushu University

Speaking of gynecological tumor surgery, laparotomy was the norm a long time ago. Since I became an obstetrician/gynecologist, I have progressed my surgical techniques such as adnexal resection for benign ovarian tumors, simple total hysterectomy for uterine fibroids, radical hysterectomy for malignant tumors, and radical surgery for ovarian cancer with dissemination. When I was young, laparoscopic surgery was performed by reproductive and endocrine surgeons, and as a specialist in gynecological oncology, laparoscopic surgery was another world of surgery. However, the wave of minimally invasive surgery has arrived in the world of gynecological malignancy surgery, and at Kyushu University Hospital, laparoscopic surgery for uterine corpus cancer was introduced in 2015, and laparoscopic radical hysterectomy for cervical

cancer was introduced in 2017 as a clinical trial. As I had already been doing laparotomy for 20 years, laparoscopy was technically a very high hurdle for me. However, with a sense of crisis that gynecological oncologists in the future would be eliminated from only doing laparotomy, I decided to go to the TG-MET center of Siriraj Hospital in Bangkok for one year of training in the basics of laparoscopy. In Bangkok, I spent my days immersed in laparoscopy and was able to be involved in about 400 laparoscopic surgeries a year. In addition to laparoscopic training, I had many good experiences in Thailand, such as delicious Thai food and golf in a wonderful environment. Now I also perform laparoscopic radical hysterectomy and laparoscopic para-aortic lymph node dissection but my original laparoscopic technique is made in Thailand.

AOFOG Symposium 2 (Committee Symposium of MIGS) **ST :**
Ideal educational exchange program for MIGS training in this era : In the AOFOG society, what did we learn and what should we continue?

5) What we can do for surgical education

Hada Tomonori

Kurashiki Medical Center

Surgical competence has been described as a collection of skill, knowledge and judgment required to complete new and familiar tasks incorporating both technical and non-technical components. For MIGS training, first problem is sufficient hand-eye coordination, and it would be trained by using dry-box training. We have tried to teach and learn basic laparoscopic suturing skills by using YouTube and Google form. Asynchronous communication is one of good way on this internet society. Japan Society of Gynecologic and Obstetric Endoscopy and Minimally

Invasive Therapy (JSGOE) organizes training courses by dividing the area into three parts and connecting them online at the same time. Trainers and trainees participated in each area, but the number of people was small and it was avoided to form a group. Lectures were given online at the same time, and box training was conducted in each region, but by connecting the boxes in each region, we were able to grasp the progress of each other. Combination of web-based lectures and on-site training would become a new style of MIGS training.

International Workshop for Junior Fellows 1 **ST** :
HPV vaccination for cervical cancer

1) HPV-Vaccination for Cervical Cancer - The European Perspective

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DGGG

Cervical Cancer is the seventh most common cancer disease among women in Europe and the second most common gynecological cancer (after breast cancer) for women aged 15 - 44 years. Among European countries the mortality rates differ, socio-economic and health care standards determine the oncological outcome. In most cases middle-aged patients are affected. Besides risk factors like immunosuppression or smoking an HPV infection is the most frequent cause.

The family of human papilloma virus comprises several low and high risk types, both are sexually transmitted. Malign lesions of the cervix, but also other squamous cell tissues are caused mainly by the high risk types 16 and 18 (also 31, 33, 35, 39, 45, 51, 52, 56, 58, 59). In 90 - 95% HPV can be found in cervical cancer. Consequently, by preventing HPV infections and transmission, the risk for cervical cancer can be significantly reduced. Countries offering screening programmes have decreased cervical cancer incidence and mortality.

Among Europe three HPV vaccines are authorised. At first the vaccine Gardasil targeting HPV types 6, 11, 16 and 18 was used. In recent

years two other vaccines were authorised, Gardasil 9 (HPV types 6, 11, 16, 18, 31, 33, 45, 52) and Cefarix (HPV types 16, 18). HPV vaccination is recommended for male and female patients aged from 9 - 12 years and should be completed before first sexual contact. Two shots are recommended when the patient is younger than 15 years, older patients need three vaccinations.

Currently 13 out of 27 European countries made the vaccination gender neutral, though the success rate in obtaining completion by getting the final dose is lower in boys. The general aim of vaccinating at least 90% of the European target population is not yet reached with low vaccination rates varying from 14% in Luxembourg (2019) to 53% in the Netherlands. In general the success of the campaign suffered from the recent pandemic. Educational work with the children and their parents is needed to increase the knowledge about the benefit of a HPV vaccination and consequently lead to higher rates of parents agreeing on the vaccination of their child. To sum up, vaccination rates and prevalence of cervical cancer differ a lot among the European population.

International Workshop for Junior Fellows 1 **ST** :
HPV vaccination for cervical cancer

2) Cervical cancer screening and HPV vaccination in elderly women in Korea

Cho Sumin, Cho Hyun Woong, Min Kyung Jin, Lee Sanghoon, Hong Jin Hwa,
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KSOG

[Objective] Cervical cancer is expected to decrease through a combination of HPV vaccination and screening program. The purpose of this study was to evaluate the effectiveness of cervical cancer screening in elderly women in Korea.

[Methods] The data of 2079 women, who underwent CCS followed by liquid-based Pap, HPV test, and colposcopic biopsy at Korea University hospital from May, 2008 to May, 2018, were retrospectively evaluated. Age groups were classified as <25 (n=61), 25-65 (n=1736), and >65 (n=459). To evaluate the value of CCS in women older than 65, age groups were simply divided into <65 or 65.

[Results] The mean age was 49.02 (range from 15 to 91). There was a difference in the distribution of LBP results between age groups ($p <$

0.001). The incidence of HSIL (39.7%) and \geq CIN 3 (40.2%) were significantly higher in the age group of over 65. There was no difference in HPV results between the groups ($p=0.163$). However, in HSIL and HPV negative group, \geq CIN 2 was increased by age in women older than 65 (93%).

[Conclusion] Annual screening for CIN or cancer is still necessary in Korean women older than 65 due to higher incidence of CIN 2, in terms of Korea's low medical fee and easy access to medical care. Also, relatively low overall participation rate for 10 years in CCS program and low HPV vaccination rate in this population should be considered. In addition, primary HPV test alone for those aged 65 or older needs further evaluation.

International Workshop for Junior Fellows 1 **ST** :
HPV vaccination for cervical cancer

3) HPV vaccination for cervical cancer in Taiwan

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TAOG

Human papillomavirus (HPV) is known to be the leading cause of cervical cancer with high-risk strains of 16 and 18 causing 70% of the cervical cancer and pre-cancerous cervical lesions. Cervical cancer is the fourth most common cancer among women in the world. It is a preventable disease that is curable if detected early and treated promptly. HPV is also responsible for a high proportion of anal, penile, vaginal, vulvar and oropharyngeal cancer.

In Taiwan cervical cancer was the leading cause of malignant -related death in 1995. The national program of annual pap smear screening was then initiated for all women over the age of 30. Most common types of HPV in Taiwan are 52, 18, 58 and type 16 is the strain most likely to cause cancer. The estimated age-standardized incidences of cervical cancer was 25.1 per 100,000 women in 1995 and declined to 7.9 per 100,000 women in 2018. The standardized death rate has also dropped from 11 per 100,000 women to 3.1 per 100,000 women. However, cervical cancer is still the 8th leading cause of malignant-related death in Taiwan nowadays under a Pap smear

annual participation rate 26.7%, 3-year coverage rate 50.5% and 6-year coverage rate 66.4%.

The HPV vaccine was first approved in Taiwan in 2006. It is expected to prevent an estimated 70% of cervical cancer cases and protect against HPV-related cancer. The national HPV vaccination program in Taiwan was introduced in late 2018. The focus of the program is school-based for girls entering junior high (age 13). Approximately 90,000 young girls benefit from this program each year. In Taiwan 260,000 girls have received the HPV vaccine since 2018 and there were 210 reported adverse events from all the cases (incidence rate was 8 per 10,000). Most of the reported adverse events were injection site reaction, fever, dizziness and headache. The vaccination rate was 73% in 2019. Hopefully with the proper health education and promotion the vaccination rate will reach 92% by 2030.

With the increased rate of vaccination and regular pap smear screening, the incidence of cervical cancer and HPV-related diseases will continue to decline over time in Taiwan.

International Workshop for Junior Fellows 1 **ST** :
HPV vaccination for cervical cancer

4) HPV vaccination in Japan : learn from the past, learn from the other
countries, and think about the future

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JSOG

Cervical cancer is an increasing malignancy in Japan, with around 10,000 recorded cases and around 3,000 women deaths from it every year. As more than 90% of cervical cancers are caused due to human papillomavirus (HPV), the development of the HPV vaccine in 2006 tremendously changed the cervical cancer prevention program. However, there is great variation worldwide in primary HPV vaccination coverage, and Japan has the lowest HPV vaccination coverage in the world.

In Japan, the bivalent HPV vaccine (HPV 16, 18) was approved in October 2009. With the expectation as an effective preventive measure against cervical cancer, some local authorities started subsidizing vaccination in 2010 and the quadrivalent vaccine (HPV 6, 11, 16, 18) was also approved in 2011. Afterward, the Japanese government included the HPV vaccination in the national routine vaccination program, which takes no cost to the recipient, in April 2013. However, repeated news in media arose soon regarding so-called adverse events such as chronic pain, motor impairment and convulsions, bringing public to doubt the safety of the vaccine. As a result, the

Japanese Ministry of Health Labour and Welfare (MHLW) suspended its proactive recommendations for the vaccination in June 2013 and instructed local authorities to stop promoting the use of the vaccine. It led to a rapid and dramatic decrease in vaccination coverage from 70% to less than 1%. This “no active-recommendation” situation continued for 8 years, and it is called the “HPV vaccination crisis.” Due to this vaccination hesitancy, 24,600 preventable cervical cancer cases and 5,000 preventable cervical cancer deaths are estimated to occur by missed vaccination.

On the other hand, much evidence regarding HPV vaccination is reported in this decade worldwide. HPV vaccination was reported to prevent 47%-100% high-grade squamous intraepithelial lesions, 60%-70% of future cervical cancers, and catch-up vaccination for adolescents and young adults is also reported as effective. Approximately 99.993% of the vaccinations ended in safe, and adverse events were similar to the other vaccines.

With the accumulations of this evidence on efficacy and safety of HPV vaccination, the MHLF

decided to resume “active recommendation” of the HPV vaccination and announced to consider about catch-up vaccination for women who missed the opportunity for vaccination in November 2021.

The situation in Japan is expected to get better. However, we gynecologists have some works to do regarding this resumption of HPV vaccina-

tion. We not only need to update recent medical evidence, but also need to learn from the past and learn how the other countries are dealing with HPV vaccination. Next, we need to think about how we can carry out this HPV vaccination strategy to protect women from this preventable cancer.

International Workshop for Junior Fellows 2 **ST** :
Impact of the COVID-19 pandemic on OB/GYN practice

1) Impact of the COVID-19 pandemic on OB/GYN practice

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DGGG

The COVID-19 pandemic has undoubtedly influenced everyone's lives at least to some extent. As physicians in the field of obstetrics and gynecology we have not been left out. With regards to obstetrics a lot of effort has been made to research the impact of SARS-CoV-2 on pregnancy outcome and neonatal development.

Although pregnancy itself does not lead to a higher susceptibility to the disease, the clinical course of the infection appears to be worse. Risk factors include older age, obesity, gestational diabetes, preeclampsia, and other preexisting comorbidities, such as hypertension or diabetes. Hence, an elevated risk of an adverse pregnancy outcome can be shown in patients with a symptomatic infection, especially in severe/critical cases. Patients with a severe or critical course are at risk of preterm birth, cesarean section and lower birth weight compared to a mild to moderate or asymptomatic infections. Asymptomatic infections influence the pregnancy to a lesser extent. However, even an asymptomatic infection can result in the development of a preeclampsia. Fortunately, there is no evidence of more frequent miscarriages or congenital anomalies.

Consequently, to prevent a severe-critical

course the vast majority of the medical community recommends vaccinations with a mRNA based vaccine, even during pregnancy, puerperium or while breastfeeding. There is no evidence that a vaccination affects fertility of women in a reproductive age.

In terms gynecology and more specifically gyneco-oncology there is data that suggests an increase in postoperative mortality rates in SARS-CoV-2-positive patients with an infection 7 days prior or 30 days after surgery. That, and an already burdened health-care system, inevitably led to postponements of not only elective, but also oncological surgeries. Furthermore, to reduce patient contact with health care facilities, routine cancer screening procedures were recommended to be postponed during times of high infection rates, unless clinically a cancer is suspected. Subsequently, there was a drop in screening procedures of approximately 60 to 99 percent between January and June 2020. The resulting delayed diagnosis will possibly have a huge effect on cancer mortality and morbidity, if the duration of the pandemic and its effects last longer.

International Workshop for Junior Fellows 2 **ST** :
Impact of the COVID-19 pandemic on OB/GYN practice

2) Impact of the COVID-19 pandemic on OB/GYN practice

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KSOG

[Objective] In South Korea, the first case of COVID-19 was confirmed on 2020 January 20. The general COVID-19 protocol in South Korea is as follows. When the patient has a fever or respiratory symptoms, the COVID-19 PCR test must be completed and have a negative test result 3 days before admission. If COVID-19 infected patient needs surgery, a minimum number of surgeons must wear personal protective equipment (PPE) and operate in a negative pressure room, making the surgery exceedingly uncomfortable and difficult.

[Methods] This was prepared based on South Korea quarantine guidelines and tertiary hospitals standards.

[Results] In the field of obstetrics, most pregnant women in South Korea were unwilling to take the COVID-19 vaccine due to safety concerns. Recently, however, the ACOG recommended that all pregnant and lactating individuals re-

ceive a COVID-19 vaccine. Therefore, obstetricians expect maternal vaccination rates to increase. Secondly, another issue is an unsafe delivery environment for pregnant women who are suspected of or are confirmed of coronavirus. Two full-term pregnant women were suspected of COVID-19 due to a fever in Chung-Ang University Hospital, so obstetricians were forced to oversee delivery at the ER wearing PPE. Both women and infants had no complications, but, it would be dangerous, and could lead to a medical accident in a poorly prepared labor environment.

[Conclusion] In short, the COVID-19 pandemic has affected particularly in medical institutions. While vaccines are aiding in a return to normal medical protocols, several issues still exist in the field of obstetrics. As such, there is a need for safer healthcare system for pregnant women that should be considered in the current situation.

International Workshop for Junior Fellows 2 **ST** :
Impact of the COVID-19 pandemic on OB/GYN practice

3) Impact of the COVID-19 pandemic on OB/GYN practice

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TAOG

The coronavirus disease 2019 (COVID-19) has struck our lives and clinical works ever since the pandemic broke out in the early 2020. People were told to stay at home and patients withdrew appointments with doctors. Among all the practices, pregnant women were one of the most vulnerable groups that might develop severe complications if infected with the coronavirus, SARS-CoV-2, compared to the nonpregnant counterparts. Taiwan Association of Obstetrics and Gynecology (TAOG) has released and updated the guideline for management of pregnant women at the beginning of the COVID-19 pandemic since Feb 2020. Antenatal care was provided at outpatient clinic as usual, but the return timing could be adjusted to a longer interval with targeted examinations if the pandemic got severe. In prevention of deliveries under unknown status of infection, scheduling for induction of labor is recommended if vaginal delivery is planned. Aside from the similar recommendations for avoidance of exposure by quarantine as nonpregnant patient, pregnant women who were suspected or confirmed to be infected with COVID-19 were treated with high quality airborne precaution, or at least droplet and contact precaution in an iso-

lated negative pressure room if they progressed into labor or any other conditions that deliveries were inevitable. Until now, given that several pregnant patients were diagnosed of COVID-19, there was no mortality nor vertical transmission to the newborn reported. Vaccination was suggested and provided to pregnant women since Jun 2021. The available vaccines in Taiwan include mRNA-1273 (Moderna), BNT162b2 (Pfizer-BioNTech), ChAdOx1 nCoV-19/AZD1222 (University of Oxford, AstraZeneca, and the Serum Institute of India) and MVC-COV1901 (Medigen Vaccine Biologics Corporation, Dynavax, National Institutes of Health of the United States). Most of the them received mRNA-1273 (Moderna).

Under the COVID-19 pandemic, none of us could keep out of the crisis. While hospitals were overwhelmed by the COVID patients and anxious people came for COVID screening, patients with other problems either declined the scheduled return appointment or delayed the examinations for diseases that may or may not threaten life immediately. We hope that the pandemic could subside soon and that all of us can return to ordinary life in the near future.

International Workshop for Junior Fellows 2 **ST** :
Impact of the COVID-19 pandemic on OB/GYN practice

4) Impact of the COVID-19 pandemic on the practice of obstetrics and
gynecology in Japan

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JSOG

The COVID-19 pandemic since 2020 has brought about many changes in the behavior and lifestyle of the people all around the world. In response to the pandemic that broke out in Japan in April 2020, the government has declared a state of emergency. Since then, Japan has experienced the fifth wave of infection around August 2021, with a total of approximately 1,726,000 cases and 18,000 deaths to date. The pandemic has also caused big changes in the practice of obstetrics and gynecology in Japan. Due to the lack of medical equipment and consumables, the demand of precautionary measures against hospital-acquired infections, and COVID-19 infections of medical staff themselves, the number of surgeries of gynecological diseases was forced to be considerably reduced. Also, the number of patients in infertility clinics showed temporary decrease because of the unknown effects of COVID-19 on their pregnancy course and fetus. Particularly, the pandemic has posed a great impact on the obstetrics practice. Medical staff have been obligated to execute the rigid enforcement of personal protective equipment and movement lines specified in each hospital. On top of that, expectant mothers awaiting planned

birth including Caesarean section have been asked to get tested for COVID-19 before admission, and been highly recommended to wear masks even during delivery. In agreement with the worldwide report that expectant mothers in late gestation tend to become severe by COVID-19 infection, the figures of Japan Society of Obstetrics and Gynecology shows increased demand of oxygenation for pregnant women with COVID-19 infection in late gestation. Moreover, obstetrician has been confronted with the issue of the hypoxia in mothers and ensuing forced preterm delivery. We experienced an unfortunate case of neonatal death who was delivered at 29 weeks gestation at home because of the inaccessibility of hospitals capable of managing both COVID-19 infection and premature infant simultaneously. As of November 2021, Japan has gone through the fifth wave of COVID-19, and been preparing for the coming wave of pandemic in national and local scales, making the most of previous lessons. The government is actively recommending COVID-19 vaccine to all people including expectant mothers and children, and has just decided the promotion of a third dose. Also, the government is trying to improve the medical

service for COVID-19 infection by increasing the beds and allowance for medical staff. In addition, local cooperation systems of the emergency care for preterm expectant mothers with COVID-19 infection are now under discussion among insti-

tutions. Further accumulation of statics and international exchange of opinions are warranted to gain a promising outlook for the practice of obstetrics and gynecology in an age of COVID-19.

指導医講習会 サステイナブル医療体制確立委員会企画 

激論！2024年に向けた産婦人科医の働き方改革（仮）

指導医
講習会

2024年度より医師の働き方改革が開始されることが決定され、行政、病院、診療科それぞれのレベルで準備が進められている。サステイナブル産婦人科医療体制確立委員会企画においては、前半のシンポジウムにおいて、1年半後に迫る働き方改革について行政、病院、診療科それぞれのレベルでの準備に必要な情報を厚生労働省、専門家、サステイナブル委員会より提供する。また、2022年4月に行われた拡大サステイナブル委員会の報

告を通して、各地域レベルでの課題を概説する。これらを踏まえて現場レベルでどのような準備や対応が必要かということをはっきりさせるためのアンケート調査結果やQ&Aを報告する。後半のパネルディスカッションにおいては、指導医、若手、子育て中など様々な立場から医師の働き方改革に対して望むものに対して、今後、本委員会としてどのような情報提供や取り組みが必要かオープンディスカッションを行う。

婦人科腫瘍委員会企画 **P** 卵巣がん診断・治療のパラダイムシフト

1) 婦人科腫瘍登録の活用と課題

慶應義塾大学 山 上 亘

日本産科婦人科学会婦人科腫瘍登録では、従来子宮頸癌、子宮体癌、卵巣腫瘍の登録が行われてきたが、2014年に卵巣腫瘍・卵管癌・腹膜癌取扱い規約臨床編が発刊されたことに伴い、2015年症例より卵管腫瘍や原発性腹膜癌も登録対象となり、また漿液性卵管上皮内癌 (STIC) の有無や分子標的治療薬の治療の有無も登録項目に追加された。その後、2016年に同取扱い規約病理編が発刊されたことに伴い、2017年症例より組織分類が現行のものに変更となり、現在に至っている。登録された臨床病理学的因子は患者年報としてまとめられ、また5年目の予後情報は治療年報として解析され、それぞれ日本産科婦人科学会雑誌およびホームページで公表されている。

卵巣・卵管・腹膜癌の初回治療は、子宮悪性腫瘍に比してしばしば複雑な場合が多く、そのため術式については詳細な登録項目を設けており、primary debulking surgeryのみならず、interval debulking surgeryについても、術式や完遂度を登録項目としているが、一方で、薬物療法につい

ては、化学療法と分子標的治療薬の併用、維持については収集しているものの、具体的なレジメンやサイクル数、治療効果については登録項目に含めていない。近年、婦人科腫瘍登録データを用いた解析結果がいくつか報告されており、全国多施設から収集されたデータを活かした本邦の特性を明らかにするような臨床研究に有用であったものの、項目が限定されているため解析できる項目も自ずと限定されてしまい、「かゆいところに手が届く」とは言い難いことが問題点となっている。微に入り細を穿つような登録項目はかえってデータの品質が低下するリスクがあるものの、昨今の治療法の変化を考慮すると、登録項目の見直しを要するのではないかと考えられる。

現在、婦人科腫瘍委員会では日本婦人科腫瘍学会と連携し、統合入力システムの開発を進めている。これにより詳細なデータが蓄積されるシステムを構築できることが想定されているので、期待したい。

婦人科腫瘍
委員会企画

2) 卵巣腫瘍・卵管癌・腹膜癌取扱い規約病理編の改訂ポイント

岩手医科大学 馬 場 長

2020年のWHO分類改訂を受け、婦人科腫瘍委員会では「婦人科癌の取扱い規約改訂に関する小委員会」を置き日本病理学会と共同で改訂委員会を設け、同時並行で子宮頸癌、子宮体癌、卵巣腫瘍・卵管癌・腹膜癌のそれぞれの取扱い規約の病理編の改訂作業に着手した。これら3つの病理編では以前より、1. 病理診断報告書の記載法、2. 切除・摘出検体の取扱い、3. 術中迅速組織診断、4. 進行期分類、5. 組織学的分類、6. 図譜、の構成は統一されていたものの、改訂時期がずれていたことで詳細についてはそれぞれの規約で違いがあった。

違いが生まれる原因として、FIGO 進行期分類とTNM分類 (UICC) の改訂時期に多少のずれがあることがある。実際、10年ぶりのFIGO分類の改訂 (FIGO2018) を受けて2020年に上梓された子宮頸癌取扱い規約 臨床編第4版では、FIGO2018に対応した日産婦2020が進行期分類として示された一方、TNM分類はFIGO2008に対応するUICC第8版しか掲載できなかった。昨年、FIGO2018に対応したTNM分類 (UICC2021) が

出版され、病理編第5版ではようやく2つの病期分類が対応した形で掲載される見込みである。卵巣腫瘍・卵管癌・腹膜癌取扱い規約病理編第1版作成時もTNM分類はUICC第7版でFIGO2014に対応しておらず第8版案を掲載した経緯がある。取扱い規約は揺るがせない診療の柱であると共に、現場の混乱を避けて随時更新する必要がある。臨床編と病理編で進行期分類の違いが今後生まれうる。

今回のWHO改訂は婦人科癌の疾患概念を発病過程と癌ゲノムで捉えなおしたのが大きな特徴である。しかし、卵巣癌の発病過程や癌ゲノムによる階層分けは多分に研究者の概念に左右され、これまでも臨床現場で取扱う感覚とずれを生じてきた。WHOによる組織学的分類は改訂のたびに疾患概念の変化と揺り戻しを繰り返しており、逐次対応すると、がん登録で本邦の婦人科癌の年次推移を追うことができない。改訂委員会では本邦での統一性にも配慮して組織学的分類の更新を進めている。

婦人科腫瘍委員会企画 **P** 卵巣がん診断・治療のパラダイムシフト

3) 卵巣がんの手術療法

神戸大学 寺井 義人

近年、卵巣癌に対する手術療法は、初回手術における LION study の結果から、進行卵巣癌に対し、staging laparotomy としての骨盤・傍大動脈リンパ節郭清術の有無による予後に差はないことが発表され、卵巣癌治療ガイドライン 2020 年版では、II 期以上の卵巣癌に対しては、骨盤・傍大動脈リンパ節郭清術が省略されるようになってきた。また、再発卵巣癌に対する手術療法として、DESKTOP III study の結果から、プラチナ感受性初回再発に対する手術で腫瘍を肉眼的にすべて切除することができた場合、手術療法は予後の改善に寄与するという結果が報告され、再発卵巣癌に対する手術療法もクローズアップされた。一方、子宮頸がん、子宮体癌や他癌種では、腹腔鏡下手術やロボット支援下手術が導入され、鏡視下手術が普及し開腹手術から鏡視下手術に置き換わりつ

つあるが、卵巣癌に対する鏡視下手術においては、標準治療にはなっていないが、欧米のガイドラインでは手術選択肢の一つに鏡視下手術が導入されつつある。このように近年の卵巣癌に対する手術療法は、遺伝子診断の導入や各種分子標的薬の導入と同様にまさにパラダイムシフトを迎えているといえる。一方、LION study, DESK TOP III などの study は欧米のデータであり、本邦に多い明細胞癌など他の組織型に当てはめてよいのか、両 study とも高い complete surgery 率を上げており、本邦の婦人科腫瘍医のレベルと同様の手術を行うことができるのか。鏡視下手術においては、保険適用の問題点などを解決していかなければならない。このような変革期の卵巣癌治療をもとに、現時点の検証と将来の卵巣癌治療の方向性について考えたい。

4) 卵巣がんの初回薬物療法

東京女子医科大学 田畑 務

2020 年 8 月に「卵巣がん、卵管癌、腹膜癌治療ガイドライン」が発刊され、その約 3 か月後にガイドライン Up date 版が Web 公開された。その主な理由は、卵巣癌に対する初回治療に PARP 阻害薬を用いた臨床試験が多数報告され、治療方針に大きな影響を及ぼしたからである。卵巣癌の初回治療は PDS が基本であるが、Optimal surgery が困難な場合、NAC+IDS が推奨されている。しかし、これまでの PDS と NAC+IDS を比べた無作為化第三相比較試験は EORTC55971/NCIC-OV13 試験、CHORUS 試験、JCOG 0602 試験、SCORPION 試験の 4 試験であるが、残念ながら PDS での完全切除率がすべて 50% 以下である。現在、PDS にて完全切除率を 50% 以上達成できる施設に限定して、PDS と NAC+IDS を比べる SUNNY 試験が進行中であり、その結果が待たれている。卵巣癌の初回薬物療法は TC 療法が基本である。そして、III/IV 期症例では、TC 療法にベバシズマブを併用するかどうかを検討することとなる。また、薬剤の選択に当たっては、BRCA 検査、HRD 検査が大きく関与する。すなわち、

BRCA 変異陽性群、HRD 群では PARP 阻害薬の治療効果が高いことから、進行症例では PARP 阻害薬の維持療法が推奨される。これまでの臨床試験として、SOLO-1 試験では、BRCA 変異陽性症例を対象にした高異型度漿液性癌 (HGS) でオラパリブの有効性が示され、PAOLO-1 試験では、HRD 症例を対象にベバシズマブ+オラパリブの維持療法の有効性が示された。一方、PRIMA 試験では、HRD 症例だけでなく HRD のない症例に対してもニラパリブの維持療法の有効性が示された。PARP 阻害薬の有効性が示された臨床試験では、主に HGS を対象に臨床試験が行われている。しかし、本邦では明細胞癌が多いことが特徴であり、今後、非 HGS に対する PARP 阻害薬の治療効果を検証する必要がある。進行卵巣癌はその再発率は 50% 以上と高く、しかも、再発卵巣癌は完治を望むのが困難である。そのため、進行卵巣癌では初回治療として、手術療法と薬物療法を併せた集学的治療を用いて、いかに PFS を延長させるかが重要である。

婦人科腫瘍委員会企画 **P** 卵巣がん診断・治療のパラダイムシフト

5) 再発卵巣癌の実態と管理

東北医科薬科大学 渡 部 洋

近年の分子生物学的手法を用いた癌の遺伝子学的検討は飛躍的な進歩を遂げており、生殖細胞変異を含む変異遺伝子診断の展開、遺伝子異常情報に基づいた新規予後因子の検索、さらには分子生物学的異常を標的とした新たな薬理効果を有する分子標的薬の開発など、癌治療戦略は急速な進歩と共に大きなパラダイムシフトを迎えている。

進行卵巣癌の長期予後改善は婦人科癌治療における喫緊の課題であるが、特に再発卵巣癌に対する総合的かつ有効な管理は、生存のみならず患者 quality of life の維持の面からも極めて重要な位置を占めている。これまでの再発卵巣癌治療においては腫瘍の縮小あるいは消失を目的とした殺細胞性薬剤の選択を主体とした治療戦略がとられて

きたが、分子標的薬の登場によってその治療概念が変わりつつある。また、再発卵巣癌に対する総合的治療戦略の策定や効果的な新規治療法開発および検証を目的とした臨床研究実施のためには、臨床病理学的特徴の把握が必須であるが、本邦における再発卵巣癌に対する全国的な調査報告はなく、その病態の詳細は不明であった。そこで、婦人科腫瘍委員会では委員会内臨床研究の一環として委員会所属施設を対象とした再発卵巣癌における診断ならびに治療の実態調査を計画した。本講演においては再発卵巣癌調査成績の報告と共に、調査結果に基づいた再発卵巣癌の管理の方向性と展望について述べてみたい。

SARS-CoV2 (新型コロナウイルス) 感染対策委員会企画

新型コロナウイルス感染症とどう向き合うか? ~パンデミックが起こった時, どうする?

1) パンデミックの歴史から学ぶ

日本大学医学部病態病理学系微生物学分野 早川 智

我々の先祖が狩猟採集を業としていたころは大規模な感染症の集団発生はなかった。約1万年前から農業の成立とヒトの定住化, そして家畜飼育による人獣共通感染症から様々な感染症が現れた。メソポタミアの楔形文字やエジプトの象形文字による記録だけでなく古人骨やミイラのDNA解析から様々な感染症が人類を襲ってきたことが判明した。そしてこれに対抗することで現代の社会が存在する。様々な歴史資料にみられるように古くは13世紀, 元によるシルクロード開通とペスト, 16世紀コロンブス交換と梅毒, 前世紀初頭のスペインインフルエンザ, 1980年代以降のエイズそして現在のCOVID-19と様々な感染症が人類を襲った。しかし我々は医学と社会システムの進歩によってこれを乗り越えてきた。特に19世紀から

20世紀は様々な病原体の同定とワクチン開発, 抗微生物薬といった感染症学の黄金時代であった。今回のCOVID-19は我々が予想していたよりもはるかに短い期間で人獣共通感染症からパンデミックに進展したが, これも予想以上の速さでウイルス遺伝子の同定とワクチン開発, さらに特異的な治療薬の開発がなされた。特に今回のパンデミックでは医学以外の様々な問題が生じた。実際, 経済対策や政治社会的安全性, 医療供給体制の構築, 無責任なデマと集団心理への対策など医師以外の専門家の力を借りる必要がある。今回のCOVID-19を教訓により安全な社会の構築と維持に我々医学者がいかに貢献できるかを考えてゆきたい。

2) 新型コロナウイルス感染症の疫学と積極的疫学調査・クラスター防止策

川崎市健康安全研究所 岡部 信彦

2021年11月, 私たちは新型コロナウイルス感染症(COVID-19)の世界的流行(パンデミック)の真ただ中にいる。国内においてはこれまで5回の流行の波を経験し, 一般「第5波」と称される今夏の流行は, これまでにない感染者数の急増とそれに伴う重症者数の増加が見られた。7~8月の東京オリンピック・パラリンピックは, 流行中の開催が是か非かで意見が分かれたが, 最終的には無事パラリンピックの閉会式が行われ, 幕は閉じた。新規感染者数はこの頃からピークアウトが始まり, 9~10月と急速に感染者数の低下がみられ, 11月中旬には今年に入って最も少ない新規感染者数が国内各地で見られている。医療機関・保健所等は少し息をつき, 一般生活も少しずつ制限等の解除が進み始めているが, 安心が油断につながらないよう, 注意が必要である。また世界で

は, ワクチン接種が進んだにもかかわらず大きなリバウンドが生じている国もあり, 予断は許されない。

今回のCOVID-19の流行の中, 「積極的調査」「クラスター」という語が一般にも知られるようになった。感染症のアウトブレイクの際に, 集団発生(クラスター)を早期に検知しその端緒を知ることが, その後の感染拡大を抑え込むのに重要なヒントとなるが, そのためには感染源・感染経路の探索を積極的疫学調査によって行うことが必須である。

今回のシンポジウムの中で, 国内におけるCOVID-19の疫学的現状の紹介に加えて, 積極的疫学調査に基づくクラスター対策などについても触れてみたいと考えている。

SARS-CoV2 (新型コロナウイルス) 感染対策委員会企画

新型コロナウイルス感染症とどう向き合うか?～パンデミックが起こった時、どうする?

3) 新型コロナウイルス感染症の臨床

国立国際医療研究センター病院国際感染症センター 大曲 貴夫

新型コロナウイルス感染症は、2019年12月に中国の武漢市で初めて患者が報告され、新型コロナウイルスが病原体であることが確認された。患者から検出されたコロナウイルス SARS CoV-2 と呼ばれるようになり、WHO は本ウイルスによる感染症の呼称を Coronavirus Disease 2019 (COVID-19) と決定した。COVID-19 では多くの場合は咽頭痛は微熱などの軽い風邪の症状が1週間程度続いた後徐々に軽快していく。しかし一部の患者では発症後1週間前後から咳や高熱が開始、肺炎を起こす。甚だしい場合には進行性の呼吸不全を来し、人工呼吸や膜型人工肺による治療必要になる場合がある。COVID-19 の重症化の機序として、疾患の進行の過程でウイルスの過度の増殖の結果肺胞上皮細胞等が感染して感染した

細胞の壊死が進行して様々な物質が体内に放出され、これを刺激として免疫系の調整不全が起こってサイトカインの異常放出が起こり、結果として全身で細胞障害が進行することが考えられている。

COVID-19 の大流行下では中等症Ⅱおよび重症の例を如何に早期に入院させて対応するかが重要である。当院でも一般医療を一部縮小してこの対応にあたった。今後は重症化を防ぐための自宅療養者への医療提供、およびハイリスク者への抗体製剤や内服薬の投与、大流行時に一刻も早く患者に治療を施すための臨時的医療施設の開設、中等症Ⅱおよび重症の例を収容できるためのベッド数の拡充が求められる。

4) ワクチンと治療薬

愛知医科大学大学院医学研究科臨床感染症学 三 鴨 廣 繁

COVID-19 の診療においては発症早期に抗ウイルス薬が、発症7日以降には抗炎症薬が重要な役割を担っている。COVID-19 の病態解明と各種薬剤の臨床試験の集積により、COVID-19 に対する推奨薬も大きく変化してきた。日本感染症学会が発表している COVID-19 に対する薬物治療の考え方は、第10版を超え、抗ウイルス薬としてレムデシビル、ファビピラビル、ステロイド薬としてデキサメタゾン、免疫抑制薬として JAK 阻害薬のバリシチニブや抗 IL-6 モノクローナル抗体のトシリズマブ、中和抗体薬のカシリビマブ・イムデビマブ、ソトロビマブなどが提示されている。

内服の抗ウイルス薬についてもモルヌピラビルをはじめとして至適使用に関する研究が進められている。また、SARS-CoV-2 はヒトからヒトへと飛沫および接触感染するため、個人予防に加え、他者に伝播させないためにワクチンを接種することが推奨される。ワクチン接種にあたっては、規定量を規定回数接種すること、副反応の症状や頻度、出現する時期などの知識を共有した上で、副反応に対する対応を考慮した勤務体制を整えることも重要となる。また、ワクチン差別に対する配慮も必要である。

医学教育活性化委員会企画 **P**

産婦人科医が考える学生・研修医教育のコツ

医学生に対する臨床参加型実習の導入と、臨床研修における産婦人科再必修化を受け、産婦人科教育の充実が喫緊の課題となっている。多忙な臨床現場で医学教育に携わる多くの会員のサポートを目指し、2021年6月に教育委員会内に医学教育活性化委員会（以下、本委員会）が新たに設置された。本委員会では、1. 医学生、臨床研修医に対する教育ツールとして講義資料や動画コンテンツなどを拡充していくこと、2. 指導医の教育、FD (Faculty Development) に積極的に取り組んでいくこと、3. 各施設で教育に取り組んでいる医師のコミュニティを形成し繋がりを強化していくこと、を具体的な目標としている。学習者と指導者双方に、産婦人科学の面白さと魅力を再認識してもらえるよう新たな革命を起こしたい。

教育に携わる産婦人科医の中には、情熱を持っているものの多忙な日常業務との両立が困難であ

ると感じている者が少なくない。そこで本委員会企画では、会員を対象に医学生・研修医教育に関する事前アンケート調査を行う。アンケート調査から浮かび上がってきた問題点を共有し、医学教育の専門家とともに議論する中で、解決へのヒントを提示したい。また、自施設の教育現場で活用可能な取り組みのきっかけを掴んでいただけるよう、種々の施設での医学教育の実際を紹介する。

医学教育は、指導医や医学教育専門家のみが行うものではなく、また情熱を持つ一部の者のみが行うものでもない。産婦人科全体として医学教育に取り組む風土が形成されることが重要である。教育が充実すれば、産婦人科医の増加に寄与するだけでなく、女性診療の理解が深まった他科医師が増加し、結果として社会に大きな貢献ができる可能性がある。本委員会企画をその契機としたい。

災害に強靱でしなやかな産婦人科医療体制を構築する

阪神淡路大震災（1995）、東日本大震災（2011）の大きな災害を経験して医療における災害対策は大きく変化した。とくに東日本大震災以降は母子に対する災害時の対応について様々な議論がされ対策が考えられてきた。その中で都道府県の災害時医療調整本部で指揮を執る災害医療コーディネータが配置され、さらに災害時医療コーディネータに妊婦・小児の医療提供などについての助言を行いながら協働していく災害時小児周産期リエゾンの養成が始まり、都道府県としての災害時の小児・妊産婦を守っていく体制の整備は進んできているが、行政組織だけでは医療提供はできない。災害時に個々の医療機関の機能維持は依然として大きな課題であり、特に分娩を取り扱う産科診療においては、分娩の開始を予定できず、いつでもどこでも対応しなければならないため、災害

時は特別な対応が必要とされる。個々の医療機関では被災状況を確認し、それに合わせた地域としての医療提供体制の再構築、妊婦の遠隔地への移送などの迅速な対応策の策定が必要である。産科だけでなく婦人科悪性疾患、不妊生殖医療をはじめ、女性診療で継続診療が必要な疾患でも即時対応ではないが同様の対応が不可欠である。都道府県については災害医療コーディネータを中心に様々な施策がされているが、二次医療圏、災害時に医療提供の中核となる保健所圏域、さらに個々の医療機関、保健所と医療機関の連携はまだまだ課題が残っているところである。今回のCOVID-19パンデミックで明らかになって3次医療圏、2次医療圏、保健所との連携などにおける様々な課題解決を共有し、各段階におけるBCRP策定を促すような議論ができればよいと考える。

産婦人科未来委員会企画 **P**

働き甲斐のある職場はリクルート最大の武器である

～ダイバーシティ&インクルージョン推進戦略～

ダイバーシティ&インクルージョン推進とは、組織メンバー一人ひとりの多様性（ダイバーシティ）を高めるだけでなく、各々の個性や違いを活かし個人として尊重されながら力を発揮できるよう（インクルージョン）、積極的に環境整備や働きかけを行っていくことである。労働人口の減少が問題となる現代社会において、成功戦略として多くの企業でダイバーシティ&インクルージョンが重要視されるようになってきているが、医療業界ではそれほど認知されていない。2019年4月からの『働き方改革関連法』の施行後、医師については時間外労働の上限規制が猶予されてきたが、2024年4月より医師にも適応される。時間外労働を減らすためには常勤医師の確保が必要であるが、産婦人科においては慢性的な人材不足に悩まされている大学医局や市中病院も多い。人材を確保するためには、新規の人材をリクルートすることに加え、離職防止を図ることも重要である。ダイバーシティ&インクルージョンという概念を普及させ

ることで「働き甲斐のある職場」の構築が可能となり、リクルートと離職防止に対して非常に効果的な手段となる可能性がある。また、「働き甲斐のある職場」の構築には、メンタルサポートも重要である。

本企画は産婦人科における人材不足解決に向けたダイバーシティ&インクルージョン推進を目的とする。産婦人科医にとって働きがいのある職場づくりを目指すことで、新規リクルートをより効果的にするとともに、やめない職場づくりを促す。第一部では、事前に実施した全国の産婦人科医師の働き方に関するアンケート結果を共有する。第二部のシンポジウムでは、ダイバーシティ&インクルージョン推進戦略について専門家よりご講演頂く。第三部のパネルディスカッションでは、産婦人科において働きがいのある職場を目指すために、どのような戦略や取り組みが必要なのかについて、メンタルサポートを含め、様々な立場から議論する。

渉外委員会企画 

若手医師の国際交流促進の取り組み—過去から未来へ

日本産科婦人科学会では若手医師の国際交流の活性化のため、今まで長きにわたり各国との国際交流プログラムを実施してまいりました。現在も、韓国 KSOG、台湾 TAOG、ドイツ DGGG、英国 RCOG とのプログラムが実施されています。そのプログラムの中では日本の若手医師が、交流相手国での学会に参加して、その国の産婦人科医療を直接体験する機会が提供されています。

また、日本産科婦人科学会学術講演会では毎年 international workshop for junior fellows (IWJF) 企画が実施されており JSOG と国際交流プログラムを実施している各国を中心に海外からの若手医師を招いて共通のテーマについて討論を行いお互

いの交流を深めるという場が設けられてきました。

こうした、国際交流プログラムや IWJF における取り組みは、参加した若手産婦人科医に多くの刺激を与えて、海外に目を向けた国際的な活動を開始するきっかけを提供してきました。残念ながら、最近の2年間は COVID-19 の感染下で国際交流が困難に直面してきました。しかし、本企画では改めて JSOG における若手医師の国際交流について、その歴史と意義を振り返りポストコロナ時代における若手医師による国際交流の課題および展望などについて話し合う場として本企画を実施いたします。

女性ヘルスケア委員会企画 **P**

産婦人科細菌感染症の新たな展開

【1】梅毒の現状と治療方針】

愛知医科大学 三嶋廣繁

梅毒は全数把握疾患5類感染症である。1967年以降減少傾向を示していたが、2013年以降増加傾向に転じている。梅毒の治療においては従来からアモキシシリンが用いられてきたが、神経梅毒を除く活動性梅毒の治療薬としてベンジルペニシリンベンザチン水和物が日本でも承認され、治療ストラテジーも大きく変化した。

【2】淋菌の薬剤耐性】

札幌医科大学 安田満

淋菌は推奨されてきたほとんどの抗菌薬に対し耐性を獲得し、現在わが国でCTRXとSPCMのみが初期治療薬に推奨されているにすぎない。そのため新規抗菌薬の開発が望まれている。また既存抗菌薬の有効利用が考えられているが同時にPOCTの開発も必要である。さらに感染予防およびその教育・啓発活動も重要である。

【3】*Mycoplasma genitalium* による女性生殖器感染症】

新小倉病院 濱砂良一

Mycoplasma genitalium は Mollicutes 綱に属する細菌である。男性の尿道炎、女性の子宮頸管炎、骨盤内臓器感染症の原因となることが証明され、早産、流産、早期破水、不妊などとの関連も検討されている。本菌の薬剤耐性化は著しく、マクロライドは70%以上の症例で耐性であり、ニューキノロンへの耐性化も進んでいる。2021年の段階では、我が国ではその検出法は保険未承認であるが、緊急に治療法などを検討する必要がある。

【4】グラム陰性桿菌の薬剤耐性～ESBL 産生菌、CRE と CPE, AmpC 産生菌～】

小倉記念病院 宮崎博章

大腸菌などのグラム陰性桿菌は、産婦人科領域において重要な起炎菌である。近年、基質特異性拡張型 β ラクターマーゼ (ESBLs) 産生菌、カルバペネム耐性腸内細菌科細菌 (CRE), AmpC 産生菌と、グラム陰性桿菌の耐性化は深厚な状況となっている。今回、これらの耐性菌と直面する産婦人科感染症について解説を行う。

リプロダクティブ・ヘルス普及推進委員会企画 **P** いまセクシュアル・リプロダクティブヘルス/ライツ (SRHR) を考える

1) SRHR に関する我が国の現状と課題

女性クリニック We! TOYAMA 種部 恭子

1994年国連人口開発会議（カイロ）において、「リプロダクティブ・ライツ」は全てのカップルと個人が自分たちの子供の数、出産間隔、ならびに出産する時を責任を持って自由に決定でき、そのための情報と手段を得ることができるという基本的権利と定義され、人口政策は国家による強制的なプログラムから、人権とジェンダー平等を主流にする方向へ転換された。

翌年の第4回世界女性会議（北京）で「リプロダクティブ・ヘルス」が定義され、採択された行動綱領では、リプロダクティブ・ヘルスケア・サービスとして、安全で満ち足りた性、生殖機能、避妊、中絶、安全な妊娠・出産、思春期、性感染症、過重労働、DV・ジェンダーに基づく暴力、薬物乱用、貧困、乳がん・子宮頸がんその他の生殖器系がん、不妊症、生殖に関する決定を行える権利、差別的な社会慣習、教育、高齢女性のヘルスケアなどに包括的に取り組むよう、各国政府に要請された。

産婦人科医療はリプロダクティブ・ヘルスケ

ア・サービスそのものであり、このアジェンダのうち生殖器系がん、安全な妊娠・出産、生殖医療、更年期を中心としたヘルスケアに主に注力してきた。しかし、ジェンダーに基づく暴力や、生殖に関する自己決定権、セクシュアリティなど、妊娠・出産に深くかかわりかつジェンダー不平等の根幹をなす課題に取り組んできたとは言えない。そのアウトカムが0日目の虐待死や産後の自殺、少子化、HPVワクチンやセクシュアリティを肯定的に捉える性教育の後退だ。

せっかく医療技術を向上させても、セクシュアル&リプロダクティブ・ヘルス/ライツ (SRHR)、とくに暴力や格差、ジェンダー不平等を無視することは、教育及び経済的・政治的エンパワーメントの機会を含む女性の機会も著しく制限し、社会の持続可能な発展を阻害する。フロントラインを知る産婦人科医こそ、SRHRの課題解決をもってジェンダー平等を目指す推進力となるべきではないか。

2) コロナ禍で顕在化した SRHR の諸問題

東京女子医科大学 水主川 純

新型コロナウイルス感染症 (coronavirus disease 2019: COVID-19) の感染拡大は、社会に大きな影響を及ぼした。すなわち、社会活動の停止・抑制、移動の制限、休業や自粛に伴う経済基盤への影響、在宅勤務などに伴う生活様式の変化により、社会生活が大きく変化した。この変化による精神的ストレスは喫煙や飲酒などの健康に関連する行動に影響し、本邦における domestic violence (DV) の相談件数がコロナ禍において増加したことも報告されている。DV被害は性感染症、避妊、予期しない妊娠などに関連し、被害者が妊産婦である場合は早産、産後うつ病などの周産期異常の

リスクが上昇するとされている。また、DV被害者と同居する子どもは、COVID-19の影響により見守り機会が減少し、児童虐待のリスクが高まっている。このようにコロナ禍では性と生殖に関することにおいて、社会的、精神的、身体的に良好な状態で生活することができない事態が生じた。すなわち、Sexual Reproductive Healthを確保することが困難であり、Sexual Reproductive Rightsに影響が及び、Sexual Reproductive Health/Rights (SRHR) の諸問題が顕在化された。したがって、すべての人が社会情勢によらず SRHR を享受できる体制の確保が望まれる。

リプロダクティブ・ヘルス普及推進委員会企画 **P** いまセクシュアル・リプロダクティブヘルス/ライツ (SRHR) を考える

3) 幼少期からの包括的性教育の実践の重要性

女性ライフクリニック銀座・新宿 対馬 ルリ子

2009年ユネスコの「国際セクシャリティ教育ガイドダンス」において、comprehensive sexuality education が提唱されて以来、日本でも「包括的性教育」が知られるようになった。そもそも包括的とは、総合的な、全てを含めたという意味であるが、このガイドダンスは、単に性や生殖に関する知識や技術的な教育だけではなく、子どもや若者が生涯にわたる健康とウェルビーイング、自立した人間として尊厳を実現してゆくための知識、スキル、態度、価値観を身につけさせること、自己と他者との関係をより良いものとし互いに尊重しあう関係性や社会環境の実現も目的としている。

もちろん、SRHR の理解がその前提にあり、性と生殖のしくみに関する基本的な理解、妊娠のなりたちや避妊、性感染症の予防など、知らなければ

行動に結びつけられないことは多々存在する。

コロナ禍以降、世界は、多様な性のあり方を認め合い助け合う SDGs の時代にシフトしている。特にジェンダーの平等と DV・性暴力への対処など、これまで我が国では扱われていなかった人権に関する教育は、出産や子供の安全、人々のウェルビーイングのために急務となっている。SRHR のエッセンシャル薬剤と言われる緊急避妊薬も、知識やアクセス性の整備がなければ必要な女性には届かず、乳児虐待のリスクとなる。

世界ではゼロ歳からの性教育という考え方もある。教育が次世代にとって真に役立つ生きる力になるために、幼少時からの性教育の実践の重要性について述べたい。

4) SRHR の実現に向けて私たちがいまできること

丸の内の森レディースクリニック 宋 美 玄

2019年に行われた日本産科婦人科学会の調査によると産婦人科医の間でSRHRという言葉の認知度は高かったが、現実の産婦人科診療や女性を取り巻く社会システムはSRHRの実現にはまだまだ程遠い部分が多い。言葉だけではなく内容の本質を知り、一段上から指導したり判断したりするのはなく、患者さんのSRHRの実現を手伝うことが本来の産婦人科診療であるという心得についても専門医研修で学ぶ必要がある。また、すでに研修を終えた世代にも意識をアップデートしパターンナな診療から脱却する機会が必要であ

る。

また、SRHRを当然のものとして認識できるようになるためには、SRHRに関わる仕事をする産婦人科医療従事者自身のSRHRを実現していく必要がある。女性の多い職場でありながら、医療従事者自身が生殖と性の健康や自己決定権を、職場及び家庭のジェンダーギャップや環境により実現を阻まれている現状を直視し、医療従事者のSRHRも蔑ろにしないための改革が必要だと考えられる。

倫理委員会企画

PGT-A 臨床研究の結果報告と PGT-M および NIPT の現状について

本企画では着床前胚遺伝子検査 (PGT-M) および着床前胚染色体異数性検査 (PGT-A)・着床前胚染色体構造異常検査 (PGT-SR), non-invasive prenatal testing (NIPT) を中心に, それらの技術に関する現状と将来的なあり方について倫理委員会での活動を紹介しつつ解説を行う。

【1】 PGT-M の現状の報告と今後

2020 年から 2021 年にかけての 3 回にわたる倫理審議会での議論を踏まえ, 新しい「重篤性」の基準の設定, 新しい審査システムの導入などを加えた「着床前診断に関する見解」の改定を行った。今回の講演では PGT-M の現状の報告と今後について解説したい。

【2】 PGT-A・SR 臨床研究の結果報告

探索的パイロット試験を踏まえ, 不妊症・不育症の治療への応用を目的として, 2020 年からは臨床研究として多施設共同研究を進めてきた。今回の講演では PGT-A・SR 臨床研究の結果報告を行

い, 海外のデータとの比較とともに PGT-A・SR の有効性についても検討したい。

【3】 公聴会の結果報告と PGT-A 実臨床に向けて

PGT-A・SR 臨床研究の中間報告を踏まえ, 倫理社会問題の課題も含めて広く意見を拝聴するため, 「PGT-A・SR 臨床研究に関する公開シンポジウム」をオンライン形式で 2 回開催した。今回の講演ではシンポジウムの結果報告と PGT-A 実臨床に向けて今後の進め方を示したい。

【4】 NIPT に関する今後の展望

遺伝カウンセリングの質を保ちつつ妊婦のニーズに対応できる新たな体制づくりを目指した改定が進められたが, 厚生労働省からの要請により新指針は凍結の状態となった。その後厚生労働省において議論が進められ, 日本医学会において NIPT 実施に関して新たな体制での運用が予定されている。本企画では国内の NIPT に関する問題点, 今後の展望について議論を進める。

臨床研究審査委員会企画 **P**改訂された「人を対象とする生命科学・医学系研究に関する倫理指針」
について

「人を対象とする生命科学・医学系研究に関する倫理指針」(以下新統合指針)の施行に伴い、令和3年6月30日をもって、「人を対象とする医学系研究に関する倫理指針」と「ヒトゲノム・遺伝子解析研究に関する倫理指針」は廃止された。一方、すでに廃止された2つの倫理指針によって過去に開始された研究については、ここから数年は旧指針に沿って、変更申請、終了報告、年次報告などを行うことが許容されている。このような状況に対応するため、令和3年度、日本産科婦人科学会においては、倫理委員会内にあった臨床研究審査小委員会から、臨床研究審査委員会が独立し、活動を開始している。

新統合指針においては、研究責任者の役割がより厳しく規定され、多機関共同研究を実施する場合には一括審査が原則となっている。また、研究の実施又は継続の適否その他研究に関し必要な事

項について、倫理的及び科学的な観点から調査審議するために設置された合議制の機関として倫理委員会が規定されている。日本産科婦人科学会がこの新統合指針に適合した倫理委員会を設置することは困難であるため、新統合指針の倫理審査は実施しないこととなった。しかし、本学会が所有するデータベースを用いた研究と、学会内の委員会・小委員会から提案される研究については、新統合指針に適合する倫理審査の前に、本委員会においてその妥当性を審査することとなった。

今回の臨床研究審査委員会企画は、産婦人科医が臨床研究を企画、遂行するうえでの新統合指針に関する留意点、新たな個人情報保護法に対応した研究計画のポイントを解説いただくとともに、本委員会での研究審査の方法の変更点について、会員にお伝えすることを目的とする。

専攻医教育プログラム 1 総論

1) 周産期画像診断

九州大学 藤田 恭之

今日の周産期医療において、超音波検査のみならず、MRI 検査、CT 検査は欠くことができない診断手法である。

妊婦に対する超音波検査は、通常超音波検査と胎児精密検査に二分される。通常超音波検査は、妊婦健診の際に行う超音波検査で、胎児発育や羊水量を評価することが主な目的である。胎児発育不全や羊水量異常を疑う所見を認めた際は、胎児血流波形解析や胎児超音波スクリーニング検査を行う。胎児精密超音波検査では、スクリーニング陽性である胎児に対して、妊娠中の管理、新生児医療への潤滑な移行、本人・家族へのカウンセリングを念頭において胎児診断を行う。

前置胎盤や頸管無力症の診断には経陰超音波検査が有用であるが、画像診断を行う上で、施行時期や手技において注意すべき点があることも認識しておく必要がある。

MRI 検査は、胎児の中樞神経系の異常や胸部疾

患の診断・鑑別に有用である。新生児治療に携わる他科の医師と情報共有する際には、超音波画像所見よりも MRI 画像所見の方が理解を得やすく、また、超音波検査のみでは鑑別が困難な腫瘍性病変を有する胎児疾患の診断にも用いられる。胎児疾患以外では、前置癒着胎盤や分娩障害となり得る子宮筋腫合併妊娠、嵌頓子宮といった症例においては、MRI 検査によって術前に情報を収集することが手術に対する十分な準備が可能となる。

CT 検査に関して、妊娠中の胎児の被ばくの問題があるが、一般的な骨盤 CT 検査においては、胎児への影響は少ないと考えられている。胎児の骨系統疾患などでは、CT 検査によって得られる 3 DCT 画像が、疾患の理解や家族への説明に用いる際に、超音波画像よりも優れていることがしばしばある。

本講演では、それぞれの検査法における画像診断について、概説する。

2) 産婦人科と血栓塞栓症

奈良県立医科大学 川口 龍二

静脈血栓塞栓症 (venous thromboembolism ; VTE) は、深部静脈血栓症 (deep vein thrombosis ; DVT) と肺血栓塞栓症 (pulmonary embolism) をあわせた概念であり、エコノミークラス症候群として一般にも広く認知されている。PE の原因として下肢に発生した DVT は重要である。VTE の病態は、Virchow の三徴、すなわち血流の停滞、血液凝固能の亢進、血管内皮細胞の障害の点から理解することが重要である。

妊娠中は凝固・線溶系がダイナミックに変化し、子宮も増大することなどから、VTE 発症リスクは高くなり、その頻度は非妊娠時に比べ 4~5 倍になるとされている。とくに、妊娠初期における重症妊娠悪阻と帝王切開術後は VTE 発症のリスク因子として重要である。婦人科疾患では悪性

腫瘍のみならず、骨盤腔を占拠する巨大な子宮筋腫や卵巣腫瘍などの良性疾患でも VTE 発症リスクは高い。悪性腫瘍では、周術期だけでなく、抗がん剤や放射線治療を行っている際、また、がんの終末期においても VTE 発症のリスクが上昇する。

VTE の診療についてもっとも重要なことは、「VTE を疑う」ことである。VTE の臨床症状の注意深い観察を行い、早期診断・治療を行うことが VTE による死亡を防ぐことにつながると考えられる。そのためには、各施設の実情にあった VTE 予防プロトコルを作成し、他診療科と連携しながら病院全体としてリスクマネジメントを整えておくことが重要である。

専攻医教育プログラム 1 総論

3) 産婦人科に関する医療制度—産科医療補償制度と医療事故調査制度—

大分県立病院 佐藤昌司

産科医療補償制度は、分娩に関連して発症した重度脳性麻痺児及びその家族の経済的負担を速やかに補償するとともに、原因分析により同じような事例の再発防止に資する目的で2009年に設立された。制度導入以降13年を経て、加入分娩機関は3,176施設(全分娩機関の99.9%)で、全審査件数4,456件のうち3,374件(75.7%)(2021年6月末現在)が補償対象となっている。原因別には常位胎盤早期剝離あるいは臍帯因子と思われる例など、急性発症の胎児低酸素・酸血症の事例は、頻度は不変ながら原因に占める割合が漸増し、いわゆる分娩中の低酸素・酸血症(胎児機能不全)に起因する事例は漸減してきている。また、妊娠中から分娩時に異常なエピソードを認めない「原因不明」例が約40%に及ぶことがわかってきている。一方、医療事故調査制度は、医療に起因また

は起因すると疑われる死亡または死産で、当該者が転帰を予期しなかった事例を対象に、医療事故の再発防止を目的に2015年に設立された制度で、2020年までに1,850件の報告がなされている。2020年の報告では、起因した医療として手術(分娩を含む)が157件(48.4%)と最も多く、次いで処置、投薬・注射、診察の順となっている。双方ともに第三者機関(日本医療機能評価機構、日本医療安全調査機構)により運営され、再発防止を目的とする点、さらに検討事項が大きく原因の考察、医療行為に対する評価および今後に向けての検討・提言の3つの視点からなされるといった点は類似している。一方で、金銭的補償の有無、院内調査義務の有無、事例調査の手順など似て異なる点も多い。本発表では、両制度の概要および現状について概説する。

専攻医教育プログラム2 生殖・内分泌

1) 無月経の診断と治療

弘前大学医学部保健学科 樋口 毅

無月経を考える前に、月経はどのようにしておこなうかの理解が必要である。視床下部から性腺刺激ホルモン放出ホルモン、続いて下垂体から性腺刺激ホルモンが分泌され、正常に分化した性腺である卵巣が呼応して女性ホルモンの分泌する。女性ホルモンは子宮内膜の周期的変化を誘導するが妊娠が成立しない場合には、女性ホルモンの消退とともにはがれ落ちる子宮内膜からの出血が起こる。このほぼ1か月の間隔で生じる限られた日数の周期的な出血が月経である。子宮からの出血は、腔を通過して体外に至り、「月経が来た」ことになる。以上の流れのどの部分に障害が生じても無月経となりうる。

WHOでは、無月経を、FSHとエストロゲンの血中の値からおおよその障害部位別にタイプIからIVに分類している（高プロラクチン血症によ

るものは別カテゴリー）が、本邦ではゴナドトロピンの値から分類するのが一般的である。原発無月経も続発無月経も視床下部性、下垂体性、卵巣性、子宮・腔性に分類される。

本講演では、原発、続発無月経についてそれぞれの疫学、診断及び治療を説明してゆく。低エストロゲン状態によりおこる障害に対する管理の重要性も強調したい。無月経というと思春期周辺の年齢層でおきる病態をまずイメージしやすいが、早発卵巣不全（primary ovarian insufficiency, POI）という広範な概念がある。POIは40歳未満の高ゴナドトロピン性、6か月以上の続発性無月経の総称であり、症例によっては挙児希望がある。このような場合には生殖医療の視点からのアプローチも必要となってくる。この分野での最近の治療についても紹介する予定である。

2) 月経困難症/月経前症候群の診断と治療

東京歯科大学市川総合病院 小川 真里子

月経困難症は、「月経期間中に月経に随伴して起こる病的症状」と定義され、器質的疾患の有無により、機能的月経困難症と器質性月経困難症に分類される。一般的には機能的月経困難症は初経後早期より始まり、月経の初日～2日目に強く痛みの性質は痙攣性、周期性であり、一方、器質性月経困難症は、月経前から月経後まで持続する持続性の鈍痛のことが多いとされる。患者自身が月経痛のために支障をきたしていれば治療対象と考え、診察や画像検査などにより器質的疾患の有無を確認し、器質的疾患があり手術適応と考えられる場合は手術を、そうでない場合は薬物療法を優先する。薬物療法としては、NSAIDsなどの鎮痛薬、鎮痙薬、漢方薬、低用量エストロゲン・プロゲステン配合薬、プロゲステン、レボノルゲステル放出子宮内システムが選択可能であり、患者の年齢や挙児希望の有無、環境、好みなどを鑑み

て選択する。

月経前症候群（premenstrual syndrome : PMS）は、「月経前3～10日の黄体期のあいだ続く精神的あるいは身体的症状で、月経発来とともに減退ないし消失するもの」と定義されている。排卵を伴う月経のある女性において、なんらかの症状が月経前に限局して出現しており、月経後に症状が消失し、その症状により日常生活に支障をきたしている場合に診断されるが、それらのことが前方視的記録により確認されることが原則として求められる。治療法としてはカウンセリング・生活指導、運動療法、利尿薬、漢方薬、ドロスピレノン・エチニルエストラジオール錠などの低用量エストロゲン・プロゲステン、選択的セロトニン再取り込み阻害薬（SSRIs）などが使用される。やはり挙児希望の有無を含む患者の置かれる状況を考慮し、治療法を選択する必要がある。

専攻医教育プログラム 2 生殖・内分泌

3) 不育症の診断と治療

神戸大学 谷 村 憲 司

不育症は、「妊娠するが2回以上の流産・死産もしくは生後1週間以内に死亡する早期新生児死亡によって児が得られない状態」と定義される。

リスク因子として、子宮形態異常、内分泌・代謝異常(甲状腺機能異常等)、夫婦染色体異常、抗リン脂質抗体症候群(APS)、血栓性素因(プロテインS欠乏症等)等が挙げられる。

これらリスク因子を検索する検査が治療法決定に重要だが、各国のガイドライン毎に推奨検査項目や推奨度が異なる。

各ガイドラインに共通して、不育症との関連が認められているリスク因子とその検査・治療法等を下に記す。

①子宮形態異常：特に中隔子宮が関連する。診断には3D超音波やMRI検査が有用で、子宮鏡下中隔切除術により生児獲得率が上昇する可能性がある。

②甲状腺機能異常：甲状腺機能検査(TSH, fT4)、抗甲状腺ペルオキシダーゼ抗体(TPOAb)測定が

推奨される。しかし、潜在性甲状腺機能低下症やTPOAb陽性者に対するレボチロキシン投与の有効性に関するエビデンスはない。

③夫婦染色体異常：均衡型転座が主で、夫婦染色体Gバンド法が推奨される。しかし、異常があっても自然経過での累積生児獲得率は約7~8割に上る。

④APS：抗カルジオリピン抗体-IgG/M, 抗β2 GPI抗体-IgG/M, ループスアンチコアグラントを測定する。12週間以上の間隔をあけて2回以上陽性であれば、APSと診断され、低用量アスピリンとヘパリン併用療法(LDA+hep)が確立した治療法である。一方、偶発的陽性例に対するLDA+hepの有効性のエビデンスはない。

推奨のないリスク因子についても、カウンセリングを行い、同意を得た上で検査・治療を行うことも許容される。

一方、不育症女性には、抑うつや不安症が高頻度にみられ、精神的支援も重要である。

専攻医教育プログラム3 周産期

1) 妊娠とくすり

国立研究開発法人国立成育医療研究センター妊娠と薬情報センター 村 島 温 子

医師が薬剤を処方する際には、リスク(副作用)とベネフィット(効果)のバランスをみて判断される。その際に添付文書の注意事項を参照するのだが、妊婦・授乳婦についての安全性に関する情報が少ないために「妊娠中の薬の使用はできるだけ避けたい」と思わせるような表現になっている。従って、慢性疾患を抱えた女性が妊娠を考えた際には、妊娠前から薬で原病をしっかりコントロールされている事が良好な妊娠転帰につながるという事実もあるにもかかわらず妊娠をきっかけに休薬してしまう例、薬物治療をしているがために妊娠を先延ばしにし、気が付くと妊孕性が落ちてしまっていたという例にしばしば遭遇する。また、妊娠していると知らずに服薬してしまった場合に児への影響を過剰に心配して妊娠継続について悩

む女性も多い。添付文書は製薬会社が作成する製品取り扱い説明書であり、本来なら医療者はエビデンスないしは科学的思考に基づいた判断をすべきである。そのための参考書として国内外の成書や産科ガイドライン2020年版が有用である。2005年厚労省の事業として開設された妊娠と薬情報センターでは、全国47都道府県53病院に拠点病院として相談外来を分担していただいている。相談の利便性を高めるために新たにシステムを構築中で、2022年春からは拠点病院を中心とした当該分野の情報提供が推進されていくと思われる。当日は母性内科医と妊娠と薬情報センターの立場から、妊娠・授乳中の薬物治療の基本的な考え方と、頻用薬の具体的な使い方をお話しするとともに、当該分野の現状と課題についても言及したい。

2) 切迫早産/早産の診断と管理

昭和大学 松 岡 隆

我が国の早産率は5~6%で、世界でも低水準である。しかし、形態異常を除く周産期死亡原因の約3/4は早産児であり、早産抑制が周産期予後改善の最大要因と言える。

切迫早産とは、妊娠22w0d~36w6dまでの妊娠中に、規則的な子宮収縮が認められ、かつ子宮頸管の開大度・展退度に進行を認める場合、あるいは初診時の診察で子宮頸管の開大が2cm以上となっているなど、早産となる危険性が高いと考えられる状態である。一方、頸管無力症は外出血や子宮収縮などの切迫流産徴候を自覚しないにも関わらず子宮口が開大し、胎胞が形成されている状態である。つまり、外来経膈超音波検査における子宮収縮を伴わない頸管長短縮は狭義では切迫早産には当たらない。

治療：子宮収縮抑制薬が用いられる。我が国では塩酸リトドリン長期使用が多いが、コルチコステロイド1クール48時間を超えての長期使用は妊

娠期間延長より副作用の指摘も多く、国際的には一般的とは言えない。硫酸マグネシウムは胎児脳保護効果が認められているが、長期投与による妊娠期間延長効果は明らかでない。母体副作用の少ないニフェジピンが海外で使用されているが我が国では保険適応はない。

予防：頸管長短縮症例に対する早産予防として、頸管縫縮術や経膈黄体ホルモン投与がある。頸管縫縮術の効果には一定の見解がない。一方、経膈黄体ホルモン投与は頸管長短縮例と早産既往に対して効果を示した結果があり、予防薬として期待されている。

管理：産科診療ガイドライン2020年では、早産ハイリスク群の認識、妊娠18~24w頃の頸管長、常位胎盤早期剥離の鑑別、児の肺成熟や頭蓋内出血予防を目的のコルチコステロイド、妊娠26w以降に母体が臨床的絨毛膜羊膜炎と診断された場合は24時間以内の娩出などが推奨されている。

専攻医教育プログラム 3 周産期

3) 胎児機能不全/胎児発育不全の診断と管理

大阪母子医療センター 石井 桂介

胎児発育不全 (fetal growth restriction ; FGR) 児は、周産期におけるハイリスクであり、周産期死亡や神経学的後遺症のリスクがある。胎内での低酸素に伴う胎児状態悪化のリスクと妊娠終結 (人工早産) による未熟性のリスクがあり、分娩時期の決定には難渋する。在胎週数や出生体重が予後に関連するが、最適な分娩時期の決定を含めて管理指針は確立していない。現在も主に超音波ドプラ法による血流異常を重視した、FGR 症例の最適な分娩時期についての議論が続いている。

本邦では胎児推定体重が-1.5SDを下回る場合に FGR と診断するが、FGR の診断基準は国際的には統一されていない。海外の主要なガイドライン (the Society for Maternal-Fetal Medicine

(SMFM), International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)) に示されている診断基準を参照しつつ、病的な FGR といわゆる constitutional small 児の違いについても言及する。

最適な分娩時期を考えるうえでは、FGR 児の予後因子を明らかにすることが望まれる。本邦のコホート研究の結果も含めて予後因子に関するこれまでのエビデンスを概説する。また超音波ドプラ法による臍帯動脈、中大脳動脈、および静脈管の血流計測の適切な計測方法と結果の解釈について理解する必要がある。また、早発型 FGR と遅発型 FGR では求められる評価方法が異なるため、それぞれの特徴を解説する。

4) 急速遂娩法と子宮底圧迫法

北海道大学 馬 詰 武

急速遂娩や子宮底圧迫が必要な状況下では緊張感が張り詰める。分娩立ち合いをしている医師には、分娩の緊急度や施設の対応能力に応じた判断と現場の統率が求められ、もっとも緊張する臨床現場の一つである。急速遂娩法には吸引分娩、鉗子分娩、緊急帝王切開術があり、吸引分娩と鉗子分娩の補助手段として子宮底圧迫法が位置づけられている。

吸引分娩か鉗子分娩のいずれの手技に長けているかは教育を受けた環境により異なるが、手技の習得が容易なことから吸引分娩が広く普及している。電動吸引器を用いたシリコン製のソフトバキュームカップや金属製のハードカップに加えて、キウイ娩出吸引カップに代表される操作の容易な手動式分娩用吸引器も導入され、安全な分娩

の一助となっている。

子宮底圧迫法は器具を使用せずに実施できる容易さから急速遂娩の第一選択として認識されることもあるが、産婦人科診療ガイドライン産科編 2020 では原則的に補助的手段として位置づけられていることに留意したい。しかし、突然の胎児徐脈などに対してやむを得ず子宮底圧迫法単独で対応することについてもガイドライン内に記載されており、本講演でも確認をしていく。

北海道大学産婦人科では、速やかな娩出が必要な場合には吸引分娩と子宮底圧迫を併用した分娩を行っており、本講演では手技の実際と緊張した現場を乗り切るために筆者が大切にしているポイントなどを中心に解説する。

専攻医教育プログラム4 腫瘍

1) 子宮筋腫，腺筋症の診断と治療

川崎医科大学

太田 啓明, 佐野 力哉, 塩田 充

子宮筋腫・腺筋症の診断は経膈超音波とMRI検査が用いられる。超音波はリアルタイムに周辺臓器との癒着の有無や血流や最近ではエラストグラフィを用いて組織の硬さを診断できる。また手術用プローベを用いれば腹腔鏡手術中に腫瘍の局在診断まで行える。一方MRIはコントラストに優れ、正常組織との位置関係をより詳しく診断することができる。子宮筋腫ではこれら画像検査から国際産科婦人科連合(FIGO)によるfibroid subclassification systemにより7つのtypeに分類される。子宮腺筋症に対してはその発生部位によりKishiらが4つのtypeに分類している。

子宮筋腫に対するホルモン療法はGn-RHアゴニストおよびアンタゴニストが使用できるが骨量減少の副作用により連続使用が6か月に限定されるために、基本的には手術療法が基本となる。子宮腺筋症に関しては加えてジエノゲストが使用可能だが子宮筋層が5cmを超えるような症例には大

出血のリスクを伴う。

手術療法は妊孕能温存の場合には子宮筋腫核出が腹腔鏡で行われることが近年多くなった。腹腔鏡手術では筋腫を体外に搬出する工程を経る必要がある。その方法の一つとして電動モルセラータを使用することがある。米国食品医薬品局(FDA)は想定されない子宮肉腫を播種させるリスクを危惧し使用規定を設けた。わが国でも対応準備中である。子宮腺筋症に対する妊孕能温存手術は妊娠中の子宮破裂リスクに対して十分なインフォームドコンセントを得る必要がある。両疾患に対する根治術として子宮全摘が行われ、従来の腹腔鏡子宮全摘術に加え、2018年よりロボット支援手術が保険適用となった。これら鏡視下手術は整容性に優れ社会復帰も早い尿管損傷のリスクが高い術式とされ、開腹手術とは違う術式と考える必要がある。

2) 婦人科がん予防 (HPV ワクチンなど)

大阪大学 上田 豊

予防できる婦人科がんとしては子宮頸がんが挙げられる。1次予防としてのHPVワクチンと2次予防としての子宮頸がん検診によりそのほとんどが予防可能とされる。WHOは、90%の女子が15歳までにHPVワクチンを接種し、70%の女性が35歳・45歳で子宮頸がん検診を受け、90%の子宮頸部病変患者が適切な診療・ケアを受けることを2030年までの介入目標として設定し、これを達成することにより「子宮頸がんのない世界」を構築することを目指している。海外ではすでにHPVワクチンによる子宮頸がん(浸潤がん)の予防効果が示され、男子への接種も進みつつある。また、HPV検査の検診への導入も進んできている。一方、本邦ではHPV検査の導入はまだ定まっておらず、HPVワクチンも長期に渡って停止状態となっていた。本セミナーでは、子宮頸がん検診

やHPVワクチンの最新の知見を整理する。またHPVワクチンが停止状態であった本邦固有の問題として、HPVワクチンの再普及に向けた課題も検討したい。

卵巣がんに関しては経膈超音波検査や血清CA125を用いたスクリーニングによる死亡率減少効果は認められていない。一方、BRCA1/2遺伝子バリエーション保持者では、乳がんや卵巣がん・卵管がん・腹膜がんの生涯発症リスクが高率であり、リスク低減卵管卵巣摘出術(RRSO)が最も確実な予防法として保険収載されている。ただし、RRSO施行後も数%の確率で腹膜がんの発生が認められることには留意が必要で、適切な経過観察が求められる。本セミナーではこれら卵巣がんの予防についても概観する。

専攻医教育プログラム 4 腫瘍

3) 子宮体部悪性腫瘍の疫学・診断・治療（内膜増殖症/体癌/肉腫など）

三重大学 近 藤 英 司

本邦における2016年の女性のがん罹患数は多い順に、乳房(94,848)、大腸(68,476)、胃(41,959)、肺(41,634)、子宮(28,076)子宮頸部11,283、子宮体部16,304であり、子宮体がんは年々罹患率および死亡率も増加している。一般的なスクリーニングが可能な子宮頸がん検診と異なり、子宮内膜細胞診は本邦では検出感度はほぼ90%、特異度は84-100%と報告されているが、海外では一般的なスクリーニングとして施行されていないのが現状である。最近では次世代シーケンサーによる遺伝子解析は婦人科がんでも進歩しており、TCGAのゲノム解析①polymerase ϵ (POLE) ultramutated, ②microsatellite instability (MSI) hypermutated, ③copy number low (endometrioid), ④copy-number high (serous like)から、子宮体がんは4つのサブタイプに分類された。高頻度マイクロサテライト不安定性(MSI-H)は子宮体癌患者

の約15%に認められる。また、遺伝性腫瘍も着目され、Lynch Syndromeは子宮体癌患者の2-5%を占め、MMR genes(MLH1, MSH2, MSH6, PMS2) or EPCAMの異常が原因とされる。

治療は、手術療法が基本であり、現在は海外でもMinimally invasive surgery (MIS)が標準治療であり、ロボット手術が主流となりつつある。また、子宮内膜異型増殖症または類内膜癌、G1症例に対しては妊孕性温存希望であれば黄体ホルモン療法が提案されるが、再発率は高率である。術後再発のリスク分類により、本邦では化学療法が術後補助療法として用いられており、進行・再発症例と同様にAP療法(アドリアマイシン・シスプラチン)あるいはTC療法(パクリタキセル・カルボプラチン)が勧められる。また治療法も抗PD-1抗体チェックポイント阻害剤のペムプロリズマブの治療も期待できる。

4) 外陰/腔の腫瘍の診断・治療

国立病院機構仙台医療センター 新 倉 仁

外陰の疼痛、搔痒感、腫瘤感を訴えて受診した場合に初期の悪性病変を見逃さないためには外陰部の丁寧な視診、触診が必要であり、日常診療から心がけることが重要である。さらに外陰部に発生する腫瘍には様々なものが存在し、日常診療で経験することの多い尖圭コンジローマや前庭扁平乳頭腫、腺系の良性病変としては最も頻度の高い乳頭状汗腺腫などの良性病変であっても肉眼的に様々な形態を呈する扁平上皮内病変(VIN)との鑑別が問題となることもあり、生検による診断を躊躇せず行うことは重要である。現在、外陰扁平上皮癌の発生機序には2つの異なる経路が考えられているが、非角化型扁平上皮癌の前癌病変と考えられ高リスクHPVと関連が強いとされる高度扁平上皮内病変と角化型扁平上皮癌の前癌病変として考えられ硬化性苔癬を背景に発生する分化型外陰上皮内腫瘍(dVIN)の理解も必要である。また、

診断の際には外陰Paget病や悪性黒色腫の存在も忘れてはならない。治療に関しては「外陰がん・腔がん治療ガイドライン2015年版」にも示されるように、外陰がんの標準治療は手術であり、その病期に応じた術式の選択が重要である。最も強い予後因子は鼠径リンパ節転移であり、鼠径リンパ節の系統的郭清は基本術式に含まれるものの、欧米においては早期外陰がんにおいてはセンチネルリンパ節生検により転移陰性例には系統的郭清の省略が標準治療となってきた。腔がんの前癌病変であるVAINの大部分はHPVに関連しているとされる。腔がんは腔の上部1/3が好発部位であるが、発生部位によりリンパ節転移経路が異なるので治療の際には注意が必要である。本プログラムでは専攻医が理解すべき、外陰・腔の腫瘍の診断と治療に関する内容を概説する。

専攻医教育プログラム5 女性のヘルスケア

1) 性的マイノリティ, 性暴力被害への対応

女性クリニック We! TOYAMA 種部 恭子

性的マイノリティは、性的指向・性自認が従前のカテゴリーに属さないものの総称であり、それぞれ抱える課題や生きづらさは異なる。同性愛は、婚姻ができず医療同意や契約等で親族とみなされないこと、拳児が困難なこと等が課題である。一方、性自認が身体の性と異なるトランスジェンダーは、二次性徴や社会の中で割り当てられた性別役割（制服、髪型、トイレの使用等）が苦痛であり、就学・就労にも困難が生じる。2004年特例法が施行され、性別適合手術を行うことで戸籍の性別の変更が可能となったが、診療にかかわる医療機関は少ない。日本精神神経学会のガイドラインに則って診断治療を行う場合、産婦人科医はジェンダー判定チームの一員として、身体的性別の診断を行い、見た目を自認する性に近づけるためのホルモン治療等にかかわる。同時に、社会的摩擦や葛藤を解消するための働きかけも求められる。

本邦の女性の6.9%が性暴力被害経験を持つ。加害者の約9割がパートナーや親や知人などの顔見知りであるため、被害届が出せず、性犯罪として刑事事件化されるものは僅かである。加害者の処罰を望む場合、刑法強姦性交等罪を見据えて産婦人科医が捜査に協力する。外傷や薬物使用の医学的証明により被害者が抗えない状況であったことを裏付け、また、性交が行われたことを客観的に証明するため、被害者の体に残された損傷や加害者のDNA等の証拠を保全する。子どもへの性暴力の場合は所見の取り方等の診察技術が裁判の争点になることがあり、産婦人科診療ガイドラインに則った対応が求められる。国の方針で全都道府県に性暴力被害者のためのワンストップセンターが設置され、産婦人科医が急性期に関わる体制作りが進められており、多くの先生方の協力をお願いしたい。

専攻医教育
プログラム

2) 骨盤臓器脱の診断と治療

産業医科大学若松病院 吉村 和晃

超高齢化社会の日本において、骨盤臓器脱（pelvic organ prolapse：POP）は重要なQOL疾患となりつつある。POPは多彩な病型を呈し、患者背景も様々であるため、症例毎にリスク&ベネフィットを考慮し、QOLを改善させる最善の治療法を考えることが重要である。

まず内診台の理学的所見でPOP-Q（pelvic organ prolapse quantification）システムにより骨盤底の損傷部位と程度を正確に診断する。リングベッサリーの保存的治療が可能なら、リングフィッティングと自己着脱指導を行う。患者がリスクを十分理解し、手術を希望している場合は手術療法を選択する。術式を決める上で重要な、POP手術の3大原則を挙げる。

1. POP手術は解剖学的修復と、排尿・排便・性機能を回復することにより、QOLを改善させるのが目的である。
2. QOL疾患の手術で致命的な合併症を起こして

はならない。POPは悪性腫瘍や心疾患と違い、放置しても命に関わらないQOL疾患であるため、なるべく低侵襲で有効な術式を検討する。

3. 患者を手術に合わせるのではなく、手術を患者に合わせる。術者の得意な術式を全症例に行うのではなく、自分が提供できる術式を増やし、症例毎に最適な術式を施行できるようにする。

これまでPOP手術と言えば経膈手術であったが、現在では腹腔鏡手術の選択肢もある。また非吸収性メッシュを用いる手術も確立され、POP手術には経膈/腹腔鏡アプローチがあり、それぞれにメッシュ/ノンメッシュ手術の選択肢がある。よりよいPOP治療のためには、少なくとも1種類ずつの手術を提供できるようにトレーニングを行う。またPOP治療には尿失禁や過活動膀胱などの下部尿路症状への対処が不可欠で、術前後の対応や治療ができるようにすべきである。

IS-AC-1-1

Serine/threonine kinase 31 (STK31) expression is a potential favorable biomarker in patients with ovarian clear cell carcinoma Chiang Ying-Cheng¹, Hsu Heng-Cheng², Tai Yi-Jou¹, Chen Chi-An¹, Cheng Wen-Fang¹ *National Taiwan University Hospital, Taiwan¹, National Taiwan University Hospital, Hsin-Chu Branch, Taiwan²*

[Objective] The incidence of ovarian clear cell carcinoma is estimated to be 15% in East Asia, especially in Japan and Taiwan. *STK31* is one of the novel cancer/testis antigens for which its biological functions remain largely unclear. In the study, we investigated the *STK31* expression in ovarian clear cell carcinoma and correlated with the clinical outcomes. **[Methods]** We investigated the expression of *STK31* in 88 clear cell carcinomas by real-time Q-PCR method. **[Results]** The median expressions of *STK31* were significantly different in FIGO stage (Early versus Advanced : 1.96 versus 0.66 : Kruskal-Wallis test, $p=0.013$), lymph node metastasis (No versus Yes : 1.12 versus 0.11, $p=0.009$), recurrence (No versus Yes : 2.63 versus 0.62, $p=0.005$), chemo-response (Sensitive versus Resistant : 1.90 versus 0.23, $p=0.010$) and prognosis (Alive versus Death : 2.16 versus 0.11, $p<0.001$). The patients with high *STK31* expression had better progression free survival and overall survival than those with low *STK31* expression. The Cox regression models for evaluating the risk of recurrence and death were performed. Advanced FIGO stage (H.R. : 4.02, 95% C.I. : 1.84-8.81), optimal debulking surgery (H.R. : 0.45, 95% C.I. : 0.21-0.97) and *STK31* expression (H.R. : 0.37, 95% C.I. : 0.16-0.83) were independent factors for disease recurrence. Also, advanced FIGO stage (H.R. : 5.11, 95% C.I. : 1.59-16.31), optimal debulking surgery (H.R. : 0.29, 95% C.I. : 0.12-0.71) and *STK31* expression (H.R. : 0.27, 95% C.I. : 0.08-0.96) were independent factors for disease related death. **[Conclusion]** *STK31* expression is a potential favorable biomarker in patients with ovarian clear cell carcinoma.

IS-AC-1-2

Serum neurofilament light chain levels as a biomarker for paclitaxel-induced peripheral neuropathy : preliminary results of a prospective study Lim Myong Cheol¹, Kim Su-Hyun², Kim Ji Hyun³, Park Na Young², Kim Ji Hee², Woo Min-Ki², Kim Ki Hoon², Hyun Jae-Won², Kim Ho Jin², Seo Sang-Soo¹, Park Sang-Yoon¹ *National Cancer Center, Korea¹, Department of Neurology, National Cancer Center, Korea²*

[Objective] Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect occurring in gynecological cancer patients treated with paclitaxel-based chemotherapy. Accurate assessment of neurotoxicity severity is critical in neuronal injury monitoring during chemotherapy and successful identification of risk factors associated with CIPN. We aimed to determine the utility of serum neurofilament light chains (sNfL) and serum brain-derived neurotrophic factor (sBDNF) as reliable biomarkers of progression in paclitaxel-induced peripheral neuropathy. **[Methods]** Thirty-five patients who were scheduled to undergo paclitaxel/carboplatin combination therapy were assessed using the following clinical assessment scales : National Cancer Institute-Common Toxicity Criteria (NCI-CTC) and EORTC QLQ-Chemotherapy-Induced Peripheral Neuropathy 20 module (EORTC-CIPN20). Furthermore, the patients underwent sNfL and sGFAP level measurements. **[Results]** With the application of the NCI-CTC, CIPN was classified as Grade 0-1 in 9 (25%) patients, Grade 2 in 17 (49%), and Grade 3 in 9 (26%) at 6 cycles of chemotherapy. Mean sensory, motor, and autonomic scores of EORTC QLQ-CIPN20 were increased with repeated treatment cycles. Moreover, median sNfL levels increased during paclitaxel administration with the following measurements : baseline (median : 78.9 pg/mL, IQR : 55-111) ; and at

the end of treatment (median : 165 pg/mL, IQR : 99-332). Notably, Grade 3 CIPN patients showed significantly higher mean sNfL levels than Grades 0-2 CIPN patients at the end of treatment, whereas sBDNF levels did not show significant differences between Grade 3 and Grades 0-2 CIPN patients. **[Conclusion]** The study's preliminary results suggest that sNfL monitoring during chemotherapy can indicate an ongoing neuroaxonal injury and help determine the severity of paclitaxel-induced peripheral neuropathy.

IS-AC-1-3

Long-term oncologic outcome and pattern of recurrence of abdominal radical trachelectomy (ART) : updated series of 297 cases Shiina Miki, Nishio Hiroshi, Iwata Takashi, Ohno Ayumi, Yokota Megumi, Tanaka Ikumo, Sugawara Yo, Tanaka Mamoru, Aoki Daisuke *Keio University Hospital*

[Objective] There has been a growing trend in increasing number of cervical cancer patients diagnosed during their child-bearing ages and abdominal radical trachelectomy (ART) has offered fertility preserving for selected patients. This study is to assess the long-term oncologic outcomes and pattern of recurrence after ART at a single institution. **[Methods]** We identified early-stage cervical cancer patients with FIGO2008 stage IA1 to IB1 (tumor size ≤ 2 cm) who underwent ART from the year of 2003 to 2020. We reviewed clinical demographics including FIGO stage, age, histology, and recurrent cases. **[Results]** A total of 323 patients were initially planned ART and 297 patients underwent ART. The median age was 33 (22 to 44) years old, and the median follow up period was 74 (9-214) months. Clinical stages were 29 with stage IA1, 30 with stage IA2 and 238 with stage IB1. Histology distribution revealed that 237 (79%) with squamous cell carcinoma and 60 (21%) with adenocarcinoma. Twenty patients had adjuvant treatment and sixteen recurrent cases (5.4%) were recognized. The location of recurrent sites included seven (50%) with residual cervix, six (37.5%) with pelvic regional lymph nodes, one (6.3%) with peritoneal dissemination, and two (12.5%) with distant metastases. The median time of recurrence was 26 months (4-156months) and two cases were found to have recurrent diseases more than 10 years after surgery (128 and 157 months respectively). **[Conclusion]** This updated analysis showed that for patients with early-stage cervical cancer, ART provided acceptable long-term oncologic outcomes. Long-term follow up should be considered following this procedure.

IS-AC-1-4

Clinical Research to Improve the Quality of Life of Gynecological Cancer Patients : Managing Quality of Life with Lifelogs Higashiyama Nozomi, Yamaguchi Ken, Ueda Akihiko, Ukita Masayo, Taki Mana, Yamanoi Koji, Egawa Miho, Hamanishi Junzo, Mandai Masaki *Kyoto University*

[Objective] The decline in quality of life (QOL) of gynecological cancer patients has become a social problem. However, there is no objective and simple method to evaluate QOL. In this study, we extracted the worst symptom affecting the QOL in gynecological cancer patients and examined whether QOL can be evaluated through lifelogs. **[Methods]** Lifelogs (heart rate variability, voice, etc.) and QOL questionnaires (EORTC-qlq-c 30, PHQ9 etc.) were collected from 120 gynecological cancer patients at our hospital using a mobile application. Symptoms and functions that contributed most to the Global Health Status, an overall QOL index, were examined. Fatigue-related metabolites in patient serum were measured using ELISA. Correlations between each lifelog, fatigue score, and fatigue-related metabolites were examined. A model to predict fatigue (high/low) from lifelogs was developed. **[Results]** Fatigue was found to be the

most severe symptom in all treatment periods, and this deteriorated the QOL of gynecological cancer patients most frequently. The fatigue scale and blood concentration of fatigue-related metabolites were significantly correlated with multiple lifelogs ($p < 0.05$, $r = -0.25$ to -0.15 for each and $p < 0.05$, $r = -0.44$ to -0.37 , respectively). A prediction model for fatigue (high/low) was developed from the lifelogs (AUC=0.67). We found two cases of persistent high fatigue during chemotherapy that led to depression and depressive relapse [**Conclusion**] Gynecological cancer patients have problems with fatigue, which can possibly be assessed by objective data using lifelogs. Persistent high fatigue may progress to depression.

IS-AC-1-5

Application of sono-elastography in differentiating endometrial carcinoma from benign endometrial lesions : A cross-sectional study Santos Catherine M, Pangilinan Nelinda Catherine P, Franada Maria Cristina C *Section of Ultrasound, Rizal Medical Center, Philippines*

[**Objective**] To evaluate the diagnostic value of sono-elastography to distinguish endometrial cancer from benign endometrial lesions. [**Methods**] A cross sectional study was conducted and included 31 subjects with abnormal uterine bleeding who required endometrial sampling. Sono-elastography assessment was done qualitatively and quantitatively using Tsukuba elasticity score and strain ratio, respectively. Results were compared between those with endometrial cancer and those with benign endometrial lesions (hyperplasia and polyp) using Kruskal-Wallis test and Mann-Whitney U test. Diagnostic accuracies of Tsukuba elasticity score and strain ratio in differentiating endometrial cancer from benign endometrial lesions were determined with cut-off values derived from ROC analysis. [**Results**] Both the Tsukuba elasticity score and strain ratio value were significantly higher among patients with endometrial cancer ($n=15$; mean age : 55.07 ± 8.53 years) compared to those with benign endometrial lesions ($n=16$; mean age : 41.63 ± 8.02 years) ($P < 0.0001$). A Tsukuba elasticity score of ≥ 3 showed the highest diagnostic accuracy at 93.5% (95%CI : 79.3%-98.2%), with sensitivity of 86.7% (95%CI : 62.1%-96.3%), specificity of 100% (95%CI : 80.6%-100%), PPV of 100% (95%CI : 77.2%-100%), NPV of 88.9% (95%CI : 67.2%-96.9%), positive LR of undefined indicating high value and negative LR of 0.10 (95%CI : 0.05-0.40). A Strain ratio value of ≥ 2 showed the highest diagnostic accuracy at 93.5% (95%CI : 79.3%-98.2%), with sensitivity of 93.3% (95%CI : 70.2%-98.8%), specificity of 93.8% (95%CI : 71.7%-98.9%), PPV of 93.3% (95%CI : 70.2%-98.8%), NPV of 93.8% (95%CI : 71.7%-98.9%), positive LR 14.9 (95%CI : 2.1-107.1), and negative LR of 0.07 (95%CI : 0.01-0.51). [**Conclusion**] The results indicate that sono-elastography can distinguish endometrial cancer from benign endometrial lesions. However, external validation on a larger scale of population should be done.

IS-AC-1-6

A novel development of deep neural network model for diagnosis of uterine sarcomas Toyohara Yusuke, Sone Kenbun, Noda Katsuhiko, Yoshida Kaname, Tanimoto Saki, Takahashi Yu, Inoue Futaba, Kukita Asako, Kawata Yoshiko, Taguchi Ayumi, Furusawa Akiko, Miyamoto Yuichiro, Tsukazaki Takehiro, Tanikawa Michihiro, Mori Mayuyo, Tsuruga Tetsushi, Oda Katsutoshi, Yasugi Toshiharu, Takechi Kimihiro, Osuga Yutaka *Graduate School of Medicine, The University of Tokyo, SIOS Technology, Inc., Showa General Hospital and Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital*

[**Objective**] Magnetic Resonance Imaging (MRI) is efficient for diagnosing uterine sarcomas ; however, it is not accurate. Re-

cently, artificial intelligence (AI), including deep neural networks (DNN), has been introduced to medical fields. The use of DNN for the evaluation of uterine sarcomas has not been investigated yet ; therefore, we aimed to investigate it in this study. [**Methods**] Sixty-two cases of uterine sarcomas including uterine leiomyosarcomas, endometrioid stromal sarcomas, etc., and 200 cases of uterine leiomyomas from three institutions were included. Our DNN model learned 15 types of MRI sequences. The ratio of learning and evaluation set was 5 : 1, which was cross-validated. Moreover, six radiologists (three specialists and three practitioners) validated the quality by diagnosing the same MRI images. [**Results**] The most important individual MRI sequences were axial T2WI, sagittal T2WI, and DWI, and the accuracy was 83-85%. The most accurate combination of MRI sequences included axial T2WI, sagittal T2WI, and DWI (accuracy : 91.3%), with a similar quality of diagnostic ability to that of specialists (accuracy : 88.4%) and was superior to that of practitioners (accuracy : 81.3%). Moreover, when AI-supported radiologists (with the results of AI analysis) diagnosed it, the accuracy improved (89.6% in specialists, 92.2% in practitioners). [**Conclusion**] The combination of MRI sequences contributed better results, which are meaningful when used for clinical diagnosis. DNN is a valuable method to improve the diagnostic accuracy for uterine sarcomas, especially in filling the gap between well-trained specialists and practitioners. This development can be expected to be clinically implemented in the future.

IS-AC-2-1

Impact of the COVID-19 pandemic on preterm birth in Japan Ohashi Mizuki, Tsuji Shunichiro, Kasahara Kyoko, Kasahara Makiko, Murakami Takashi *Shiga University*

[**Objective**] People are adopting a sedentary lifestyle after the World Health Organization declared the coronavirus disease outbreak a pandemic. The resulting inactivity was observed across age groups and had implications in pregnant women. Thus, the aim of our study was to evaluate the impact of this change on the perinatal condition in Japan. [**Methods**] We evaluated differences in pregnancy complications at childbirth from October to December 2018, 2019, and 2020 using International Classification of Diseases 10 codes in the JMDC Claims Database. The data from this database, which was hosted at JMDC Inc., were sourced from patient's health insurance claims from various medical institutions. Comparison analysis was performed using the chi-square test followed by Bonferroni correction, wherein a p value < 0.05 indicated statistical significance. [**Results**] The incidence of threatened preterm labor (TPL) had significantly decreased in 2020 ($n=2458$, 41.3%) compared with that in 2018 ($n=2507$, 45.3%) and 2019 ($n=2781$, 44.5%) ($p < 0.001$ and $p=0.001$, respectively). Furthermore, the incidence of pre-mature birth in 2020 ($n=154$, 2.6%) had declined in comparison to that in 2018 ($n=218$, 3.9%) and 2019 ($n=238$, 3.8%) ($p < 0.001$ and $p < 0.001$, respectively). Meanwhile, there was no significant difference in the frequency of hypertensive disorder pregnancy, HELLP syndrome, emergency transfer, and cesarean section. [**Conclusion**] Although the effect of home rest to prevent TPL is controversial, our results suggest that maternal bed rest as a shift in lifestyle pattern might ameliorate TPL and, consequently, reduce the likelihood of premature birth.

IS-AC-2-2

Cervical MUC5B and MUC5AC protect pregnant uterus from ascending pathogens Ueda Yusuke¹, Mogami Haruta¹, Takakura Masahito¹, Matsuzaka Yu¹, Yasuda Eriko¹, Inohaya Asako¹, Kawamura Yosuke¹, Chigusa Yoshitsugu¹, Kondoh Eiji², Mandai Masaki¹ *Kyoto University¹, Kumamoto University Hospital²*

[Objective] Cervical conization and trachelectomy are risk factors of preterm birth and preterm PROM. This implies that cervical epithelium is a functional barrier to pregnant uterus. Here, we investigated the role of cervical epithelium by proteomic analysis of cervicovaginal fluid (CVF) in the patients after trachelectomy. **[Methods]** Proteome compositions of CVF from pregnant women at 18-24 weeks after trachelectomy were compared to those from pregnant women without surgery. In immunohistochemistry, localization of the screened molecules was identified using the uterine sections from pregnant women and non-pregnant women after trachelectomy, compared to non-pregnant women without cervical surgery. Primary epithelial cells from human endocervix were utilized to assess the regulation of these molecules. **[Results]** In CVF proteomic analysis, normalized abundance of MUC5B and MUC5AC was significantly less in the women after trachelectomy (0.44-fold, $P=0.033$ and 0.36-fold, $P=0.030$, respectively). When MUC5B or MUC5AC in CVF was below the mean normalized abundance of control, all the women after trachelectomy delivered preterm. In immunohistochemistry, these two mucins were expressed ubiquitously in the columnar epithelium of endocervix. MUC5B-positive area was larger in pregnant women (4.2-fold, $P=0.007$), while MUC5AC-positive area was not changed. Both MUC5B-positive and MUC5AC-positive area were smaller in non-pregnant women after trachelectomy (0.12-fold, $P=0.002$). In primary endocervical cells, estradiol and progesterone increased MUC5B mRNA expression (1.8-fold, $P<0.001$); MUC5AC mRNA expression was not changed. IL-1 β increased MUC5AC mRNA expression (3.9-fold, $P<0.001$). **[Conclusion]** The endocervical MUC5B increases during pregnancy, and MUC5AC increases responding to inflammation. This double-barreled physiological barrier would contribute to protect pregnant uterus from ascending pathogens.

IS-AC-2-3

Effects on Perinatal Outcomes of External Radiation Dose to Pregnant Women from the Fukushima Daiichi Nuclear Power Plant Accident after the Great East Japan Earthquake: the Fukushima Health Management Survey (FHMS) Yasuda Shun *Fukushima Medical University*

[Objective] This study aimed to investigate the effects of maternal exposure to external radiation on perinatal outcomes among women who experienced the Fukushima Daiichi Nuclear Disaster (FDND) using the Fukushima Health Management Survey (FHMS). **[Methods]** Data from the pregnancy and birth and basic surveys, respectively, in the FHMS were combined to analyze external maternal radiation exposure following the FDND, and the relationship between radiation dose and perinatal outcomes was analyzed using binomial logistic regression analysis. Missing dose data were supplemented using multiple imputation. **[Results]** A total of 6,875 individuals responded to the survey. Congenital anomalies occurred in 2.9% of patients, low birth weight (LBW) in 7.6%, small for gestation age (SGA) < 10th percentile) in 8.9%, and preterm birth in 4.1%. The median maternal external radiation dose was 0.5 mSv (maximum, 5.2 mSv). Doses were classified as follows: 0-1 mSv (reference), 1-2 mSv, and ≥ 2 mSv. For congenital anomalies, the crude odds ratio for 1-2 mSv was 0.81 (95% confidence interval [CI] 0.56-1.17) (no participants with congenital anomaly were exposed to ≥ 2 mSv). At 1-2 mSv and ≥ 2 mSv, the respective adjusted odds ratios were 0.91 (95% CI 0.71-1.18) and 1.21 (95% CI 0.53-2.79) for LBW, 1.14 (95% CI 0.92-1.42) and 0.84 (95% CI 0.30-2.37) for SGA, and 0.91 (95% CI 0.65-1.29) and 1.05 (95% CI 0.22-4.87) for preterm birth. **[Conclusion]** External radiation dose due to the FDND was not associated with congenital anomalies, LBW, SGA, or preterm birth.

IS-AC-2-4

Maternal thyroid function at first trimester of twin pregnancy: A retrospective study in China Hu Jing, Wang Haining, Zeng Lin, Guo Xiaoyue, Zhao Yangyu, Wang Yan *Peking University Third Hospital, China*

[Objective] The aim of this study was to set up reference ranges of maternal thyroid function in the first trimester for twin pregnancy. **[Methods]** This was a retrospective study of pregnant women with two live fetuses in the first trimester. A total of 248 twin-pregnant women who met the National Academy of Clinical Biochemistry criteria were enrolled to establish reference ranges in the first trimester. The levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT_4) were compared and shown as median and 2.5th and 97.5th percentiles. **[Results]** Twin-pregnancy thyroid function reference ranges at gestational weeks 4-13 for TSH and FT_4 were 1.02 (0.01-3.51) mIU/L and 1.32 (1.00-2.01) ng/dL, respectively. The median twin-pregnancy TSH level at gestational weeks 7-13 (0.72 [0.01-2.89] mIU/L) was significantly lower than that at gestational weeks 4-6 weeks (1.65 [0.14-3.95] mIU/L, $P<0.001$) and that for singleton pregnancy at gestational weeks 4-12 (1.12 [0.13-3.93] mIU/L, $P<0.001$). There were no significant differences in TSH and FT_4 levels between the mono- and di-chorionic twins as well as between different outcome groups in monochorionic twins. Using reference ranges for singleton pregnancy in twin pregnancy could misdiagnose hypothyroidism in twin pregnancy (0.4% vs 2.1%). **[Conclusion]** The reference ranges for TSH and FT_4 in the first trimester of twin pregnancy differed from those in singleton pregnancy, especially after the seventh gestational week. The establishment of specific reference ranges is needed to avoid misdiagnosing hypothyroidism in the first trimester of twin pregnancy.

IS-AC-2-5

Developing a targeted delivery system to improve placental function in Intrauterine Growth Restriction Mazey Emily E¹, Matsumiya Yosuke^{1,2}, Kandzija Neva¹, Zhang Wei¹, Arai Manae³, Hibino Mitsue³, Yamada Yuma³, Vatish Manu¹ *University of Oxford, UK¹, LUCA Science Inc.², Biopharmaceutical Sciences and Pharmacy, Hokkaido University³*

[Objective] Intrauterine growth restriction (IUGR) affects ~10% of pregnancies and carries a high risk of perinatal morbidity and mortality. The key causes of IUGR are placental insufficiency and malnutrition; currently the only treatment is carefully timed delivery. Our research aims to address this treatment gap, with the ambition of creating a targeted delivery system in which liposomes containing a therapeutic cargo that improves placental function can be delivered directly to the placenta. **[Results]** Placental explants and mammary epithelial cells were treated with DiI (fluorescent dye) -liposomes labelled with the supposedly placenta-targeting CGK peptide. Contrary to the previous literature, fluorescent microscopy showed low uptake of the CGK-liposomes into the placental explants. Importantly, we also observed high off-target uptake into mammary epithelial cells. The VAR2CSA-derived EC peptide, which is implicated in the pathophysiology of pregnancy-associated malaria due to its affinity for the chondroitin sulfate A receptor, was also trialled as a placenta-targeting peptide. Placental explants, mammary epithelial cells and endometrial tissue were treated with TAMRA (fluorescent dye) -labelled EC peptide. In agreement with the previous literature, fluorescent microscopy showed high uptake of the EC peptide into the syncytiotrophoblast layer of the placental explants, with no off-target uptake into mammary epithelial cells or endometrial tissue. Our data suggests that the EC peptide is an effective peptide for placenta-targeted delivery. **[Conclusion]** We will present data

showing that liposomes labelled with EC peptide can successfully deliver cargo to the syncytiotrophoblast layer of the placenta. This will be the first step in bridging the treatment gap in IUGR.

IS-AC-3-1

Differentiation of the functional lactotrophs in the induced adenohypophysis differentiated from human-induced pluripotent stem cells Miyake Natsuki¹, Nagai Takashi², Osuka Satoko¹, Sonehara Reina¹, Murakami Mayuko¹, Yoshita Sayako¹, Muraoka Ayako¹, Nakanishi Natsuki¹, Nakamura Tomoko¹, Goto Maki¹, Iwase Akira³, Kajiyama Hiroaki¹ *Nagoya University¹, Handa Hospital², Gunma University³*

[Objective] A method for generating functional adrenocorticotropic hormone-producing cells from human-induced pluripotent stem cells (hiPSCs) has been described. However, prolactin (PRL)-producing cells derived from hiPSCs have not been investigated. Therefore, the present study aims to identify and functionally evaluate PRL-producing cells in a hiPSC-derived anterior pituitary. **[Methods]** Pituitary cells were differentiated from hiPSCs using serum-free aggregate suspension culture, and the appearance and function of PRL-producing cells were evaluated and the resulting values were represented as mean \pm SEM. **[Results]** PRL secretion from aggregates derived from hiPSCs was confirmed to increase with further cultures (day 81 0.89 ± 0.08 ng/mL ; day 93 4.79 ± 0.71 ng/mL ; day 111 39.6 ± 5.57 ng/mL, $p < 0.01$, respectively). The secretion was promoted by prolactin secretagogues (PRL-releasing peptide $116 \pm 0.04\%$; vasoactive intestinal peptide $155 \pm 0.17\%$; tyrosine-releasing hormone $267 \pm 0.36\%$, $p < 0.05$, respectively) and was inhibited by bromocriptine ($71 \pm 0.04\%$, $p < 0.01$). Fluorescence immunostaining and immunoelectron microscopy confirmed the presence of PRL-producing cells and secretory granules. Additionally, the fluorescent immunostaining revealed the presence of tyrosine hydroxylase-positive dopaminergic nerves, suggesting a connection between dopamine and PRL production. **[Conclusion]** Pituitary PRL-producing cells that were generated from hiPSCs, exhibited secretory responsiveness that are similar to that of human cells *in vivo*. The generated cells can be used as a model of human PRL-producing cells and are expected to play an important role in future research, including drug discovery, side effect prediction, and the elucidation of tumorigenic mechanisms. This work may also promote the development of regenerative medicine for the pituitary gland.

IS-AC-3-2

Suppression of uterine and placental ferroptosis in a rat model of polycystic ovary syndrome by N-acetylcysteine Shao Linus *Reproductive Endocrinology Department of Physiology and Endocrinology, The Sahlgrenska Academy at Göteborg University, Sweden*

[Objective] Hyperandrogenism and insulin resistance constitute the central pathophysiological mechanisms that contribute to the reproductive dysfunctions such as miscarriage seen in women with polycystic ovary syndrome (PCOS). To determine whether N-acetylcysteine (NAC) has an effect in 5 α -dihydrotestosterone (DHT) and insulin (INS)-exposed pregnant rats, and if so to investigate the molecular mechanism of action of NAC in the gravid uterine and placental ferroptosis *in vivo*. **[Methods]** Maternal exposure of pregnant rats to DHT and INS, and addional treatment with NAC. **[Results]** In the present study, we report that treatment with NAC differentially suppresses ferroptosis between the gravid uterus and placenta under conditions of maternal hyperandrogenism and INS resistance. We found that NAC attenuated DHT+INS-induced uterine ferroptosis. Changes in other molecular factors after NAC treatment

were also observed in the placenta exposed to DHT and INS. However, NAC was not sufficient to rescue DHT+INS-induced mitochondrial abnormalities in the uterus whereas the same treatment partially reversed such abnormalities in the placenta. NAC dose-dependently increased JNK phosphorylation, but not ERK1/2 phosphorylation, which was in contrast to what was seen in the placenta. In control pregnant rats NAC treatment compromised the uterus and placenta with decreased GSH protein content, increased iron deposition, and abnormal mitochondrial structure indicating that NAC treatment in healthy pregnancy should be avoided. **[Conclusion]** Our data provide insight into how NAC exerts beneficial effects on attenuating uterine and placental ferroptosis through reduced iron accumulation, elevated GSH and/or GPX4 levels, and decreased lipid peroxidation in a PCOS-like rat model with fetal loss.

IS-AC-3-3

Risk factors associated with major complications of total laparoscopic hysterectomy Chuthong Juthamas, Srichaikul Pisutt, Boriboonhirunsarn Dittakarn *Siriraj Hospital, Mahidol University, Thailand*

[Objective] To determine risk factors associated with major complications of total laparoscopic hysterectomy (TLH). **[Methods]** A case-control study was conducted in 275 women underwent TLH at a university based tertiary care hospital. Cases consisted of 55 women with major intraoperative complications. Controls were 220 women with uneventful operation, randomly selected from those who underwent TLH during the same period as cases. Data was retrieved from medical records, including baseline and operative characteristics, diagnosis and indications, surgeon experience, and characteristics of the complications. **[Results]** Cases and controls were comparable in terms of baseline characteristics, including age, BMI, diagnosis, and surgeon's experience. Cases were significantly more likely to have previous abdominal surgery, and have preoperative diagnosis of endometriosis. (41.8% vs. 25%, $p=0.013$ and 47.3% vs. 29.5%, $p=0.012$, respectively). In addition, cases were significantly more likely to have higher specimen weight, longer operative time, and estimated blood loss ($p < 0.001$). Among those with major complications, internal organ injuries occurred in 30 cases (54.5%) including injuries to bowel (21.8%), bladder (18.2%), and ureters (16.4%). Conversion to abdominal operation occurred in 32.7%. Multivariate analysis showed that, after adjusting for potential confounders, having had previous abdominal surgery and preoperative diagnosis of endometriosis independently increased risk of major complications (adjusted OR 2.2, 95%CI 1.2-4.29, $p=0.015$ and adjusted OR 2.1, 95%CI 1.1-4.1, $p=0.019$, respectively). **[Conclusion]** Having had previous abdominal surgery and preoperative diagnosis of endometriosis independently increased risk of major complications of TLH procedure.

IS-WS-1-1

The establishment of a cervical gastric type cancer cell line
Tsuda Naotake *Kurume University Hospital*

[Objective] We planned to establish a gastric cervical cancer cell line to examine the mechanism of the resistance ability to conventional chemotherapy. **[Methods]** The patient was stage IIb cervical gastric type cancer with lymph node and ovarian metastasis. We checked gene mutations of the cancer tissue (AmpliSeq Cancer Hotspot Panel v2) by the next-generation sequencer (Ion S5). Five months after first-line chemotherapy (TC six cycles), the recurrence was observed as carcinoma peritonitis. We extracted the gastric cancer cells from the ascites and started long-term culture. We repeated more than twenty times passages to establish the cancer cell line (KCGAS-1). To examine the population of cancer stem cells, we examined the percentage of ALDH, CD44, CD133, EpCAM by flowcytometry. To explore the response to conventional chemotherapy to cervical cancer, we performed MTT assay of paclitaxel and CBDCA to KCGAS-1 and the usual type cervical adenocarcinoma cell line (Hela). **[Results]** we detected p53 and APC mutations in the cancer tissue. We confirmed a high population of cancer stem cell characteristics (ALDH : 58%, CD44 : 97%, CD133 : 0%, EpCAM : 19%). Regarding the response to the conventional chemotherapeutic reagents of cervical cancer, KCGAS-1 has a poor response (maximal inhibition were 11% to PTX, 20% to CBDCA) compared with Hela (maximal inhibition were 56% to PTX, 62% to CBDCA). **[Conclusion]** We confirmed high cancer stem cell populations and a poor response to conventional chemotherapy reagents to cervical gastric cancer cells.

IS-WS-1-2

Genomic alteration profiles of Gastric-type cervical adenocarcinoma
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[Objective] Recent studies have revealed that endocervical adenocarcinoma (ECA) is etiologically divided into HPV-associated and HPV-independent (HPVI) types. Gastric-type carcinoma (GAS) is a distinct subtype of ECA, being the most frequent HPVI type, that has aggressive behavior. Lobular endocervical glandular hyperplasia (LEGH) is one of the postulated precursors of GAS. The pathogenesis of GAS has yet to be elucidated. There have been few reports of genomic alterations of LEGH, and the mechanism of carcinogenesis from LEGH to GAS remains to be unraveled. **[Methods]** Fourteen cases of surgically resected GAS were included in the present study. Review of the pathology slides of 14 cases confirmed the histological type of the tumor, three of which had an associated LEGH component. In each case, DNA of GAS, normal tissues, and LEGH (if present) was extracted separately using formalin-fixed paraffin-embedded tissue. The molecular characteristics of both GAS and associated LEGH were examined by whole exome sequencing to assess single-nucleotide and insertions/deletions. **[Results]** In total, 1,611 variants were called across the 14 tumor samples tested. *MUC19* was the most recurrently mutated gene followed by *FLG*, *MUC17*, *LILRB3*, *MUC5B* and *TP53*. 486 variants were detected in three LEGH samples coexistence to GAS. **[Conclusion]** Our study shows the genomic alteration profile of GAS with some potentially actionable molecular alterations, which highlights the importance of further molecular characterization for better identification of this rare entity, and hence better clinical management.

IS-WS-1-3

DDIT4 acts as a driver of lymph node metastasis of cervical cancer through activation of epithelial-mesenchymal-transition

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[Objective] Lymph node metastasis remains a serious problem in the management of cervical cancer (CC). Our aims were to identify a gene that promotes lymph node metastasis in cervical cancer, and to evaluate its potential as a diagnostic marker and a therapeutic target. **[Methods]** Public database was used to identify specific tumor markers. The expression in immunohistochemistry and clinical features were analyzed in patients with CC who underwent surgical resection at our institute. The function of DDIT4 was evaluated by siRNA and shRNA. The ability of cells to proliferate, migrate, and invade were analyzed in vitro and in vivo. **[Results]** Expression analysis using GEO database and ONCOMINE database revealed that DDIT4 was upregulated in CC tissues compared to normal cervix. High DDIT4 expression in immunohistochemistry was significantly correlated with lymph node metastasis and lymphovascular infiltration ($P < 0.05$). High expression of DDIT4 also correlated to short overall survival in both our cohort ($n=70$) and TCGA ($n=174$). DDIT4 knockout attenuated the migration and invasion ability of CC cells, with increased expression of E-cadherin and decreased expression of Vimentin. DDIT4 expression was upregulated by hypoxia and hypoxia-inducing malignant phenotype was attenuated by DDIT4 knockout. Comprehensive RNA sequencing revealed the association between DDIT4 expression and activation of multiple pathways including NF κ B pathway. Finally, our mouse xenograft tumor model revealed DDIT4 was required for lymph node metastasis. **[Conclusion]** DDIT4 can be a tool for prediction of lymph node metastasis from CC as well as being a promising therapeutic target.

IS-WS-1-4

Identification of the characteristics and oncogenesis of HPV 18-related cervical adenocarcinoma using induced reserve like cells

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[Objective] Difference of carcinogenesis between Human papillomavirus (HPV) type 18 and 16 remains unknown. We aimed to identify the clinically significant genes between HPV 18 and 16 using the original induced reserve cell-like (iRC) cells generated from iPSC cells under specific culture conditions, then aimed to perform functional analysis of identified gene. **[Methods]** HPV18 E6/E7-iRC (iRC18) and HPV16 E6/E7-iRC (iRC16) were generated by transfecting each E6 and E7. For comparison, HCK (Human cervical keratinocytes) cells prepared from the cervical epithelium of clinical specimens were also transfected with E6 and E7. Gene expression statuses in iRC16 and iRC18 were examined by RNA sequencing. Both iRC cells group and HCK cells group were injected with matrigel subcutaneously into the immunocompromised mice (NOD-scid). Extracted tumors were evaluated by immunohistochemistry. **[Results]** RNA sequencing revealed expression levels of both stem cell and adenocarcinoma markers were much higher in iRC18 than iRC16. iRC cells group formed tumors, however not in HCK cells group. Tumor growth speed was faster in iRC18 than iRC16. Adenocarcinomatous lesions were observed in both iRC16 and iRC18 cell-tumors, but not in HPV-negative iRC control-tumor. Immunohistochemistry revealed the glandular epithelial part had the expression of cancer stem cell markers (CD44, ALDH, Musashi-1) and adenocarcinoma markers (Keratin8, Keratin18, Claudin 7). **[Conclusion]** iRC cells revealed HPV16 E6/E7 and HPV18

E6/E7 have the property of differentiating CSC marker-positive glandular structures. HPV18-related tumors are characterized by faster progression than HPV16. This study might provide a new therapy strategy for HPV18-related cancer.

IS-WS-1-5

Establishment of organoid culture from HPV18-positive small cell carcinoma of the uterine cervix : Identification of two therapeutic targets for precision medicine Kusakabe Misako¹, Taguchi Ayumi¹, Tanikawa Michihiro¹, Tsuchimochi Saki¹, Toyohara Yusuke¹, Kawata Akira¹, Sone Kenbun¹, Mori Mayuyo¹, Tsuruga Tetsushi¹, Oda Katsutoshi², Kawana Kei³, Osuga Yutaka¹ *The University of Tokyo¹, Department of Integrative Genomics, The University of Tokyo², Nihon University³*
[Objective] Genome-based precision medicine is prevalent in various types of cancers. For HPV-associated cancer, where genes around the HPV genome integration sites are usually activated and can be another target for anti-cancer medicine. Small cell carcinoma of the uterine cervix (SCCC) is highly malignant HPV-associated cancer. However, its carcinogenesis still remains unclear. Here, we aimed to establish workflow for precision medicine by focusing on cancer specific carcinogenesis. **[Methods]** The patient-derived organoid (PDO) was established from HPV18-positive SCCC. Therapeutic targets were identified by whole exome sequencing (WES) and RNA-seq analysis. Drug susceptibility tests (DST) were performed using established organoids. **[Results]** Pathological examination showed that the established SCCC organoid was morphologically similar to the original tumor and retained the expression of CD56 and chromogranin A. Genetic analysis by WES revealed that both original tumor and organoid had common 19 somatic variants, including KRAS p.G12D pathogenic variant. Analysis of the human-viral fusion RNA identified that HPV18 was integrated into chromosome 8, at 8q24.21. RNA-seq analysis revealed the increased expression of the proto-oncogene MYC, downstream of the integration site. DST revealed the sensitivity of SCCC organoid to a MEK inhibitor (a KRAS pathway inhibitor) and MYC inhibitor. **[Conclusion]** In this study, we confirmed two strategies for identifying therapeutic targets of HPV-derived SCCC. WES for identifying pathogenic variants and RNA-seq for identifying HPV integration sites. Organoid culture is an effective tool for unveiling the oncogenic process of rare tumors and can be a breakthrough for the development of precision medicine for patients with HPV-positive SCCC.

IS-WS-1-6

The difference in the effectiveness of HPV vaccine based on smoking status Hikari Takako¹, Nakao Yoshifumi², Hashiguchi Mariko², Yasunaga Makio¹, Ookuma Emi², Ookuma Ryoichi², Umezaki Yasushi², Fukuda Asako², Tokunaga Mariko², Hideshima Misako², Kurihara Makiko², Yokoyama Masatoshi² *Saga-ken Medical Centre Koseikan¹, Saga University Hospital²*
[Objective] This study aimed to clarify whether there is a difference in the effectiveness of HPV vaccine based on smoking status. **[Methods]** This retrospective cross-sectional study considered women aged 20-24 who underwent cervical cancer screening in Saga City from April 2014 to March 2020. Cervical cytology and histological diagnosis were compared with or without HPV vaccination and smoking. **[Results]** The study included 7,253 women (2,467 vaccinated and 4,786 unvaccinated). Among the vaccinated women, 462 were smokers, 2,003 were non-smokers : among the non-vaccinated women, the numbers were 1,217 and 3,554, respectively. 0.28% (7/2,467) of participants with vaccination had HSIL+ compared to 0.77% (37/4,786) without vaccination (odds ratio (OR) 0.36, 95% confidence interval (CI), 0.16-0.81). 0.32% (8/2,467) with vaccination had cervi-

cal intraepithelial neoplasia (CIN) 2+ compared to 0.69% (33/4,786) without vaccination (OR 0.46, 95% CI, 0.21-1.00). Four women without vaccination had CIN3+. In non-smokers, HPV vaccination significantly suppressed the incidence of HSIL+ from 0.42% (15/3554) to 0.1% (2/2003) (OR 0.21, 95% CI, 0.05-0.95), but the suppressive effect was not significant in smokers (OR 0.59, 95% CI, 0.22-1.56). In vaccinated women, the incidence of CIN2+ was 0.20% (4/2,003) in non-smokers and 0.87% (4/462) in smokers (OR 0.22, 95% CI, 0.05-0.89, p=0.02). **[Conclusion]** HPV vaccination is effective in protecting against uterine cervical abnormality. The vaccine effectiveness is, however, reduced in smokers compared to non-smokers. The 9-valent vaccine may solve this problem, but at this point, it will be important to give instructions to young women not to smoke.

IS-WS-1-7

Trends in HPV infection rates and changes in HPV infection type profiles Kurosawa Megumi¹, Sekine Masayuki¹, Yamaguchi Manako¹, Kudo Risa¹, Adachi Sosuke¹, Yagi Asami², Ikeda Sayaka¹, Ueda Yutaka², Miyagi Etsuko³, Enomoto Takayuki¹ *Niigata University Medical & Dental Hospital¹, Osaka University², Yokohama City University³, National Cancer Center Hospital⁴*
[Objective] HPV vaccination rate was dramatically decreased for women born in the 2000 birth year due to suspension of proactive recommendation in 2013. As a result, it is predicted that HPV 16/18 infections, which had temporarily decreased, will increase again. But It is necessary to verify whether it actually happens in the real world. **[Methods]** In this study, we investigated HPV infection rates among women aged 20-21 years who underwent cervical cancer screening from April 2014 to September 2021. **[Results]** HPV vaccination rates ranged from 30.8% (2014) to 87.8% (2015), 90.0% (2016), 92.9% (2017), 89.6% (2018), and 89.2% (2019). However, the vaccination coverage decreased sharply to 42.4% in 2020. The HPV 16/18 infection rate decreased from 1.3% (2014) to 0.4% (2015), 0.4% (2016), 0% (2017), 0.4% (2018), and 0.5% (2019), but increased to 1.7% (2020) and 0.8% (2021). The HPV 16/18 infection rates, which had previously decreased due to increased HPV vaccination coverage also increased significantly due to decreased vaccination coverage after the suspension of proactive recommendations (p=0.002). **[Conclusion]** This indicates that the impact of the suspension of proactive recommendation is real-world. We would also like to add new data on the annual trend of HPV 16/18 infection and how HPV infection profiles are changing as HPV vaccination rates increase and decrease.

IS-WS-1-8

Effectiveness of the Systemic Immuno-inflammatory Index for Assessing the Prognosis of Elderly Patients with Cervical Cancer Hikino Kouhei, Okawa Masayo, Iida Yuki, Osaku Daiken, Komatsu Hiroaki, Kudoh Akiko, Chikumai Jun, Sato Shinya, Taniguchi Fuminori, Harada Tasuku *Tottori University*
[Objective] To investigate the efficacy of the systemic immune-inflammation index (SII), calculated by lymphocyte, neutrophil, and platelet counts, in assessing the prognosis of elderly patients with cervical cancer. **[Methods]** Eighty-nine patients with cervical cancer over 65 years old treated in our hospital between 2002 and 2017 were enrolled. The cut-off SII was determined using the ROC curve, and the patients were classified either the high or low SII group. Using univariate and multivariate Cox regression analyses, we examined the association between overall survival (OS) or progression-free survival (PFS), and clinicopathological factors. **[Results]** The median age was 75 (65-90) years. Thirty-two patients (36%) were diagnosed FIGO stages III or IV. Both OS and PFS rates were significantly

lower in the high SII group than those in the low SII group (5-year OS rate : 35% vs. 84%, $p < 0.01$; 5-year PFS rate : 21% vs. 78%, $p < 0.01$). Multivariate analysis showed that the high SII (hazard ratio : 2.67, 95% CI : 1.12-6.33, $p < 0.05$) and the advanced stage (FIGO stages III and IV) (hazard ratio : 6.65, 95% CI : 0.061-0.37, $p < 0.01$) were the independent prognostic factors. In terms of PFS, a high SII was also an independent prognostic factor (hazard ratio : 2.40, 95% CI : 1.06-5.41, $p < 0.05$). **[Conclusion]** High SII could be associated with the poor prognosis in elderly cervical cancer patients.

IS-WS-2-1

Deep neural network-based classification of cardiocograms outperformed conventional algorithms Ogasawara Jun¹, Ochiai Daigo², Ikenoue Satoru², Yamamoto Hiroko³, Kasuga Yoshifumi², Aoki Daisuke², Tanaka Mamoru² *Department of Pharmacology, Keio University School of Medicine¹, Keio University School of Medicine², Department of System Design Engineering, Faculty of Science and Technology, Keio University³*
[Objective] Cardiotocography records fetal heart rates and their temporal relationship to uterine contractions. To identify high risk fetuses, obstetricians inspect cardiocograms (CTGs) by 'eyeballing' (subjective pattern recognition). Therefore, CTG traces are often interpreted differently among obstetricians, resulting in inappropriate interventions. However, few studies have focused on quantitative and nonbiased algorithms for CTG evaluation. In this study, we propose a newly constructed deep neural network model (CTG-net) to detect compromised fetal status. **[Methods]** CTG-net consists of three convolutional layers that extract temporal patterns and interrelationships between fetal heart rate and uterine contraction signals. We aimed to classify the abnormal group (umbilical artery pH < 7.20 or Apgar score at one minute < 7) and the normal group from the last 30 minutes of CTG data from 324 vaginal deliveries. We evaluated the classification performance of the CTG-net and compared it with conventional algorithms (Support Vector Machine and k-means clustering) and another deep neural network model (long short-term memory). We applied CTG-net to the open-access CTG Database to confirm its generalization performance. **[Results]** CTG-net showed significantly higher F1 score (0.67 ± 0.03) than SVM (0.55 ± 0.05) and k-means clustering (0.52 ± 0.12), and area under the receiver operating characteristic curve (0.73 ± 0.04) than long short-term memory (0.62 ± 0.03). CTG-net showed comparable performance (AUC-ROC of 0.68 ± 0.03) for the open-access CTG data. **[Conclusion]** CTG-net, a quantitative and automated diagnostic aid system, showed consistent and high performance for the classification of normal and abnormal deliveries. It could enable early intervention for putatively abnormal fetuses.

IS-WS-2-2

Explainable artificial intelligence to support examiners for abnormality detection in fetal cardiac ultrasound screening Komatsu Masaaki^{1,2}, Sakai Akira^{2,3,4,5}, Komatsu Reina^{4,6}, Matsuoka Ryu^{4,6}, Yasutomi Suguru^{3,4}, Dozen Ai², Shozu Kanto², Aizawa Rina^{2,6}, Arakaki Tatsuya², Sekizawa Akihiko⁶ *Cancer Translational Research Team, RIKEN Center for Advanced Intelligence Project¹, Division of Medical AI Research and Development, National Cancer Center Research Institute², Artificial Intelligence Laboratory, Fujitsu Ltd.³, RIKEN AIP-Fujitsu Collaboration Center, RIKEN Center for Advanced Intelligence Project⁴, Biomedical Science and Engineering Track, Tokyo Medical and Dental University⁵, Showa University⁶*
[Objective] Congenital heart disease (CHD) is the most frequent malformation and the major prognostic determinant of neonatal outcome. However, the prenatal diagnosis rate remains low due

in part to the difficulty of primary screening. Explainable artificial intelligence (AI) is expected to elucidate medical diagnostic processes. Here, we assessed our novel explainable AI to help examiners identify abnormalities in fetal cardiac ultrasound screening videos. **[Methods]** We used a total of 160 cases and 344 fetal ultrasound videos (18-34 weeks gestation), of which 13 CHD cases and 26 videos are abnormal data. We proposed a graph chart diagram representing the information of 18 cardiac substructures for each video using simple auto-encoder and novel techniques : cascade graph encoder and view-proxy loss. We then conducted a comparative study to evaluate the performance of examiners to screen 40 randomized videos with or without AI assistance. Eight experts, ten fellows, and nine residents were enrolled in this study. **[Results]** We evaluated the experiment using the mean area under the curve (AUC) of the receiver operating characteristic (ROC) curve. The combination of cascade graph encoder and view-proxy loss improved the screening performance of AI from 0.798 to 0.861. Furthermore, the performance is improved from 0.966 to 0.975 for experts, 0.829 to 0.890 for fellows, and 0.616 to 0.748 for residents, respectively. Performance enhancement was shown in examiners with all experience levels. **[Conclusion]** To our knowledge, this is the first demonstration that examiners use a deep learning-based explainable representation to improve their performance of fetal cardiac ultrasound screening.

IS-WS-2-3

Glucocorticoids increase the risk of preterm premature rupture of membranes possibly by inducing ITGA8 in the amnion Okazaki Yuka^{1,2,3}, Taniguchi Kosuke¹, Miyamoto Yoshitaka¹, Nakabayashi Kazuhiko¹, Kaneko Kayoko¹, Hamada Hiromi³, Satoh Toyomi³, Murashima Atsuko², Hata Kenichiro¹ *Department of Maternal-Fetal Biology, National Research Institute for Child Health and Development¹, Center for Maternal-Fetal, Neonatal and Reproductive Medicine, Division of Maternal Medicine, National Center for Child Health and Development², University of Tsukuba³, Department of Reproductive Biology, National Research Institute for Child Health and Development⁴*
[Objective] We previously reported an association between glucocorticoids and preterm premature rupture of membranes (pPROM) with non-infectious etiology through clinical data from patients with systemic lupus erythematosus (SLE). However, the mechanism remains disputed. We hypothesized that glucocorticoid exposure weakens the fetal membranes and increases the pPROM risk. **[Methods]** To assess the hypothesis, we used human primary amnion mesenchymal cells (hAMCs) to examine the effects of the glucocorticoid dexamethasone (DEX) on the amnion by electrophysiological measurements and RNA-seq. Then, the amnion samples from patients with SLE were analyzed by RNA-seq. **[Results]** Glucocorticoid-treated hAMCs showed decreased electric resistance between cells, indicating increased permeability. Differentially expressed genes in hAMCs with glucocorticoid treatment and in the amnion from patients with SLE were significantly enriched with cell adhesion-related genes compared to controls. Among them, *ITGA8*, which is known as a fibrotic remodeling marker, was a most upregulated gene both in hAMCs and amnion in SLEs. Using quantitative PCR, we found that DEX-induced *ITGA8* upregulation was normalized by a glucocorticoid inhibitor. **[Conclusion]** Our findings indicate that glucocorticoids increase amnion permeability and modulate cell-adhesion related genes. *ITGA8* could be one of the candidates that triggers pPROM through fibrotic remodeling and preventing resealing of the rupture site in fetal amnion.

IS-WS-2-4

Neurodevelopmental disorders and fetal electrocardiographic changes in maternal immune activation (MIA) mice Momono Yuta^{1,2}, Kimura Yoshitaka^{2,3}, Yaegashi Nobuo¹, Saito Masatoshi^{1,2} *Tohoku University¹, Department of Maternal and Fetal Therapeutics, Tohoku University², South Miyagi Medical Center³*

Maternal immune activation (MIA) is caused by inflammation during pregnancy. Prenatal exposure to MIA causes neurodevelopmental disorders, including autism spectrum disorders (ASD), in children. The relationship between neurodevelopmental disorders caused by MIA and inflammatory cytokine interleukin (IL) 17A expression has attracted attention recently. Some patients with ASD are characterized by autonomic nervous system instability, and if autonomic nervous system abnormalities occur from the fetal period, they could be detected using fetal electrocardiography (ECG). **[Objective]** We used fetal ECG to detect autonomic nervous dysfunction in MIA. **[Methods]** Pregnant mice that received gene-transferred IL-17A via the hydrodynamics-based delivery method on embryonic day (E) 12.5 were used as MIA mouse models in this study. Behavioral tests performed in the offspring of such mice. Fetal ECG signals were measured on E 18.5. **[Results]** Behavioral tests showed behavioral abnormalities that suggested deteriorating sociality and exploratory behaviors. In fetal ECGs, the low and high frequency component of heart rate variability, low frequency to high frequency ratio, and short-term variability were significantly increased in comparison with those in the controls. Increased fetal brain gene expression levels are involved in the integrin-ligand extracellular matrix and PI3K/Akt signaling pathways associated with synaptic numbers. Such changes in the fetal brain gene expression levels could be involved in the autonomic and behavioral phenotypes of MIA mice. **[Conclusion]** Inflammation with elevated IL-17A levels during pregnancy may cause autonomic neuropathy from the fetal period and can be detected using fetal ECG.

IS-WS-2-5

Protein Kinase C-mediated alteration of placental angiogenic and antiangiogenic factors in pregnant diabetic mice Mitsui Takashi, Mishima Sakurako, Tani Kazumasa, Masuyama Hisashi *Okayama University Hospital*

[Objective] The activation of protein kinase C (PKC) is implicated in the development of diabetic angiogenic complications and deeply involved in the production of angiogenic and antiangiogenic factors. Activated PKC might also play a pivotal role in the production of angiogenic and antiangiogenic factors in the placenta of pregnant women with aberrant glucose metabolism. Therefore, we examined the activated PKC-mediated production of angiogenic and antiangiogenic factors in the placenta of pregnant diabetic mice. **[Methods]** Blood samples and placentas were collected from pregnant diabetic (KK) and pregnant control mice (C57BL/6) on day 15.5 of gestation to evaluate PKC activity in placentas. Phosphorylation of PKC isozymes were analyzed by western blotting. To assess the balance between angiogenic and antiangiogenic factors in placentas and plasma, levels of placental growth factor and soluble fms-like tyrosine kinase-1 (sFlt-1) were measured via quantitative polymerase chain reaction and enzyme-linked immune-sorbent assay. Furthermore, PKC inhibitor was orally administered to diabetic mice from day 7.5 to day 14.5 of gestation, and its effect was examined. **[Results]** PKC activity and the expression of sFlt-1 mRNA were significantly elevated in the placentas of diabetic mice compared to that in control mice. Plasma sFlt-1 levels were also high in pregnant diabetic mice, and increased sFlt-1 expression was suppressed by the oral administration of PKC inhibitor. **[Con-**

clusion] PKC activation might be associated with the production of angiogenic and antiangiogenic factors in the placenta of pregnant diabetic mice.

IS-WS-2-6

Prenatal testing for confined placental mosaicism associated with severe fetal growth restriction by analysis of cfDNA in maternal plasma Miyagami Keiko¹, Shirato Nahoko¹, Izumi Mikiko¹, Hirose Tatsuko¹, Yasui Osamu¹, Hamada Shoko¹, Matsuoka Ryu¹, Suzumori Nobuhiro², Sekizawa Akihiko¹ *Showa University¹, Nagoya City University²*

[Objective] We examined the influence of confined placental mosaicism (CPM) as a cause of fetal growth restriction (FGR) and whether CPM can be screened using cell-free DNA (cfDNA) analysis of the maternal plasma. **[Methods]** Among pregnant women at >21 weeks of gestation who visited our hospital between March 2017 and July 2021, 45 cases with an estimated fetal weight of less than -2.0 SD and a diagnosed with FGR by ultrasonography were included in the present studies. We analyzed cfDNA in the maternal plasma using massively parallel sequencing to detect chromosomal aberrations. Fetal and placental genotyping was performed to confirm CPM cases. This study was approved by the Institutional Ethics Committee. **[Results]** cfDNA analyses of maternal plasma detected suspected CPM cases with chromosomal aneuploidy or copy number variations in 6 of 45 cases (13.3%). For 4 cases in which the entire placenta consisted of cells with chromosomal aneuploidy, fetal growth was severely restricted. **[Conclusion]** CPM can be screened by cfDNA analysis in maternal plasma, accounting for more than 10% of causes of FGR smaller than -2.0SD, and the higher the proportion of abnormal karyotype cells in the placenta, the more severe placental dysfunction and FGR.

IS-WS-2-7

A study on the diagnosis of fetal inflammation using fetal heart rate variability in preterm fetal sheep Magawa Shoichi, Nii Masafumi, Ikeda Tomoaki *Mie University*

[Objective] Perinatal infection/inflammation can trigger preterm birth and contribute to neurodevelopmental disability. There are currently no sensitive, specific methods to identify perinatal infection. We investigated the utility of time, frequency and non-linear measures of fetal heart rate (FHR) variability (FHRV) to identify either progressive or more rapid inflammation. **[Methods]** Chronically instrumented preterm fetal sheep were randomly assigned to one of three different 5d continuous i.v. infusions : 1) control (saline infusions : n=10), 2) progressive lipopolysaccharide (LPS ; 200ng/kg over 24h, doubled every 24h for 5d, n=8), or 3) acute-on-chronic LPS (100ng/kg over 24h then 250ng/kg/24 h for 4d plus 1μg boluses at 48, 72, and 96h, n=9). **[Results]** Both LPS protocols triggered transient increases in multiple measures of FHRV at the onset of infusions. No FHRV or physiological changes occurred from 12 h after starting progressive LPS infusions. LPS boluses during the acute-on-chronic protocol triggered transient hypotension, tachycardia and an initial increase in time and frequency domain measures of FHRV, with an asymmetric FHR pattern of predominant decelerations. Following resolution of hypotension after the second and third LPS boluses, all frequencies of FHRV became suppressed. **[Conclusion]** These data suggest that FHRV may be a useful biomarker of rapid but not progressive preterm infection/inflammation.

IS-WS-2-8

Effect of Thrombopoietin receptor agonist (TPO-RA) on pregnant mice and fetus Nakai Kensaku¹, Tahara Mie¹, Hamuro Akihiro¹, Misugi Takuya¹, Nakano Akemi¹, Tachibana Daisuke¹,

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Ishikiriseiki Hospital²

[Objective] TPO-RA is an effective treatment for refractory idiopathic thrombocytopenic purpura (ITP), however the use of TPO-RA is limited for ITP in pregnant women pregnancy due to concerns about fetal toxicity. Little is known about the maternal and fetal effects of the use of TPO-RA during pregnancy. In this study, we administered TPO-RA to pregnant mice and examined the effects on pregnant mice and newborn. **[Methods]** Pregnant ICR mice (8-12 weeks old) were injected subcutaneously with romiplostim (Nplate[®], Amgen; 1, 5, 10, 30, 100 µg/kg) at gestational day (GD) 1, GD8, and GD15. On GD18, pregnant mice were sacrificed and blood from maternal and newborn pregnant mice and was collected (6 µL) and counted the number of peripheral platelet. Maternal femoral bone and liver of newborns, and placenta were collected and morphological evaluation was performed. The rate of resorption or the number of pups per litter, and the weight of the fetuses and placenta were also recorded. **[Results]** TPO-RA increased platelet counts in pregnant mice and newborn dose-dependently. The increased platelet counts also correlated with increased megakaryocyte (MK) numbers in the bone marrow of pregnant mice and the liver of newborn. TPO-RA significantly reduced the body weight of newborns, but did not significantly affect the rate of absorption or the number of pups per litter. **[Conclusion]** In this study, it is indicated that TPO-RA pass through placenta and increased fetal platelet, and it is necessary to accumulate further consideration.

IS-WS-3-1

Impact of ProMisE molecular classification on prognosis among Japanese patients with endometrial cancer Asami Yuka^{1,2}, Hiranuma Kengo^{2,3}, Kato Mayumi^{2,4}, Nagashima Minoru¹, Terao Yasuhisa³, Sekizawa Akihiko¹, Matsumoto Koji¹, Kato Tomoyasu¹ Showa University¹, Division of Genome Biology, National Cancer Center Research Institute², Juntendo University³, National Cancer Center Hospital⁴

[Objective] Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) is a clinically applicable molecular classification system to identify four Cancer Genome Atlas molecular subtypes with different prognoses. To date, most reports submitted to the Cancer Genome Atlas come from within Caucasian populations. Thus, we investigated whether ProMisE is useful for predicting prognosis in Japanese women with endometrial cancer (EC). **[Methods]** Paraffin-embedded tissues were collected from 265 patients treated for EC at our hospital. Immunohistochemistry for p53 and mismatch repair (MMR) proteins and DNA sequencing of the *POLE* exonuclease domain were used to classify each sample for *POLE* exonuclease domain pathogenic mutation (*POLE*-EDM, n=28) status, MMR deficiency (MMR-d, n=71), altered p53 expression (p53abn, n=57) and no specific molecular profile (NSMP, n=109). Primary and secondary end points were progression-free survival (PFS) and overall survival (OS), respectively. Kaplan-Meier plotting, log-rank test, and Cox hazard model were used for analyses. **[Results]** Five-year PFS was 48.0% for EC patients with p53abn, 96.4% for *POLE*-EDM, 74.5% for MMR-d, and 77.2% for NSMP (P<0.01). Five-year OS was 63.9% for EC patients with p53abn, 100% for *POLE*-EDM, 84.8% for MMR-d, and 87.3% for NSMP (P<0.01). Using Cox hazard models, adjustments for FIGO clinical stage and age did not change our findings. **[Conclusion]** We confirmed that EC patients with *POLE*-EDM had excellent PFS and OS, while those with MMR-d and NSMP exhibited intermediate prognosis. Molecular classification using ProMisE is a useful method to retrieve independent prognostic information regardless of ethnicity.

IS-WS-3-2

Epigenome modifier, Protein arginine methyltransferase (PRMT) 6 in endometrial cancer cells using epigenome multi-omics analysis reveals PRMT6 inhibition induces apoptosis via activating interferon signaling Inoue Futaba^{1,2}, Sone Kenbun¹, Tanimoto Saki¹, Toyohara Yusuke^{1,2}, Takahashi Yu¹, Kukita Asako¹, Taguchi Ayumi¹, Tanikawa Michihiro¹, Tsuruga Tetsushi¹, Mori Mayuyo¹, Oda Katsutoshi¹, Osuga Yutaka¹ The University of Tokyo¹, Project for Cancer Epigenomics, The Cancer Institute of Japanese Foundation for Cancer Research², Department of Integrative Genomics, The University of Tokyo³

[Objective] Histone modification is a major epigenetic mechanism and regulates gene expression by chromatin remodeling, which introduces dynamic changes in chromatin architecture. Recently, it was reported that the epigenome regulates endogenous retrovirus (ERV) expression, which activates interferon signaling, is related to cancer. Protein arginine methyltransferase (PRMT) 6 is a histone arginine methyltransferase reportedly overexpressed in various types of cancers. We investigated the antitumor effects of PRMT6 inhibition and the role of PRMT 6 in endometrial cancer (EC), using epigenome multi-omics analysis including Assay for Transposase-Accessible Chromatin with high-throughput sequencing (ATAC-seq) and Chromatin Immunoprecipitation sequencing (ChIP-seq). **[Methods]** We analyzed PRMT6 expression in EC using RT-qPCR. The prognostic impact of PRMT6 expression was evaluated using the TCGA database. We investigated the effects of PRMT6-knockdown (KD) on EC cells by cell viability assay and apoptosis assay, and its effects on epigenome using ATAC-seq, ChIP-seq, and RNA-seq. Finally, we evaluated the downstream targets identified by multi-omics analysis. **[Results]** PRMT6 was overexpressed and associated with poor prognosis. PRMT6-KD induced histone hypomethylation and suppressed cell growth and apoptosis. ATAC-seq revealed genome-wide changes in chromatin remodeling. ChIP-seq revealed PRMT6 regulated genomic regions related to interferon and apoptosis through histone modifications. Multi-omics analysis identified 19 overlapping genomic regions, which include interferon, apoptosis, and cancer-related genes. RT-qPCR showed eight ERV genes, which activate interferon signaling, was upregulated by PRMT6-KD. **[Conclusion]** Our data suggested PRMT6 inhibition induces apoptosis through interferon signaling activated by ERV and PRMT6 regulates cancer-related genes by chromatin remodeling. PRMT6 may be a novel therapeutic target in EC.

IS-WS-3-3

Investigation of the frequency of BRCA pathogenic variants in endometrial cancer Imaeda Keiyo¹, Kobayashi Yusuke^{1,2}, Masuda Kenta^{1,2}, Nakamura Kohei³, Aimoto Eriko³, Ueki Arisa², Chiyoda Tatsuyuki¹, Yamagami Wataru¹, Banno Kouji¹, Nishihara Hiroshi³, Tanaka Mamoru¹, Aoki Daisuke¹ Keio University¹, Center for Medical Genetics, Keio University², Division of Clinical Cancer Genomics, Keio University³

[Objective] While the prevalence of *BRCA* pathogenic variants in ovarian cancer has been clarified, the relationship between endometrial cancer, particularly serous carcinoma, and *BRCA* pathogenic variants is controversial. We aimed to determine the relationship between endometrial cancer and *BRCA* pathogenic variants by using PleSSision-Rapid, cancer gene panel testing, and genetic testing. **[Methods]** Among patients with endometrial cancer who underwent initial surgery at our institution between 2019 and 2020, we performed germline genetic testing on tumor *BRCA* pathogenic variant-positive cases from 116 patients who underwent PleSSision-Rapid testing using tumor paraffin-embedded sections, and retrospectively examined the association between endometrial cancer and *BRCA* patho-

genic variants. **[Results]** Among 116 patients with endometrial cancer, 9 had serous carcinoma, 105 had endometrioid carcinoma (G1 : 66, G2 : 21, and G3 : 18), and 2 had others. Tumor *BRCA* pathogenic variants were detected 9 patients (7.8%) overall, and in 2 (22.2%), 4 (6.1%), and 3 (16.7%) patients with histologic subtypes of serous, endometrioid G1, and G3, respectively. Germline *BRCA* pathogenic variants were detected in 4 patients (3.4%) overall, and in 1 (11.1%), 2 (3.0%), and 1 (5.6%) patient with histologic subtypes of serous, endometrioid G1, and G3, respectively. Pathogenic variants included *BRCA1* in 1 patient with endometrioid G1 and *BRCA2* in a total of 3 patients with serous, endometrioid G1, and G3 (1 patient each). **[Conclusion]** In endometrial cancer, the rate of positive tumor *BRCA* pathogenic variants was higher in serous and endometrioid carcinoma G3, and in germline, this was higher in serous carcinoma.

IS-WS-3-4

The modified molecular classifier combined with conventional clinicopathologic risk factors well stratify the prognosis of the patients with endometrial cancer treated with complete staging surgery and adjuvant chemotherapy Yamazaki Hiroyuki, Asano Hiroshi, Yoshikawa Hiroaki, Kurosu Hiroyuki, Ihira Kei, Endo Daisuke, Mitamura Takashi, Konno Yosuke, Kato Tatsuya, Watari Hidemichi *Hokkaido University*

[Objective] We aimed to validate a modified TCGA classification, ProMisE, for patients who received adjuvant chemotherapy at intermediate or high risk of recurrence following radical surgery. **[Methods]** From 2003 to 2015, the patients who underwent systematic lymphadenectomy were enrolled. We prepared tissue-microarrays from surgical specimens and classified them using the conventional clinical risk classifier, IHC for MMR proteins (MLH1, MSH2, MSH6, PMS2), LICAM, and p53, and direct sequencing for hotspot mutations in *POLE* (exon 9, 13, and 14). The 5-years disease-specific survival (5y-DSS) was estimated by the Kaplan-Meier method. **[Results]** A total of 184 patients were analyzed. The median age and follow-up period were 57.5 years old and 109 months. The number of patients classified as low-risk was 41, *POLE*-mutated 13, LICAM+ 45, Abn-p53 5, MMRd 34, and Others 46. The prognosis was stratified into three groups with statistically significant differences ($p < 0.05$, log-rank test) : favorable, low-risk, and *POLE*-mutated ; intermediate, MMRd and Others ; unfavorable, LICAM+ and Abn-p53. The 5y-DSS was 100%, 93.8%, and 75.1%, respectively. Low-risk and *POLE*-mutated predicted a quite favorable prognosis. **[Conclusion]** The modified TCGA classification can stratify the prognosis in combination with conventional recurrent risk, IHC for LICAM, MMR, and p53, and sequencing for *POLE* hotspot mutation.

IS-WS-3-5

Development of a prognostic biomarker of fertility-preserving hormonal therapy based on multi-gene panel testing for endometrial cancer or atypical endometrial hyperplasia Hirano Takuro^{1,4}, Yamagami Wataru¹, Yoshimura Takuma¹, Sakai Kensuke¹, Chiyoda Tatsuyuki¹, Nakamura Kohei², Aimoto Eriko², Kawaida Miho³, Nishihara Hiroshi², Aoki Daisuke¹, Tanaka Mamoru¹ *Keio University School of Medicine¹, Genomics Unit, Keio Cancer Center, Keio University School of Medicine², Department of Pathology, Keio University School of Medicine³, Saiseikai Yokohamashi Tobu Hospital⁴*

[Objective] Medroxyprogesterone acetate (MPA) therapy for atypical endometrial hyperplasia (AEH) and early grade 1 endometrioid carcinoma (G1) has a high recurrence rate. Furthermore, some patients relapse before pregnancy and it is difficult to predict recurrent cases based on clinical-pathological factors

alone. This study aimed to develop a prognostic biomarker of MPA therapy based on multi-gene panel testing. **[Methods]** Sixteen patients with AEH and 20 patients with stage IA G1 without myometrial invasion who underwent first-line MPA therapy at our institution were enrolled. Genomic DNA extracted from formalin-fixed paraffin-embedded tissue samples, which was obtained from endometrial biopsy or curettage, were subjected to multi-gene panel testing using the PleSSision-Rapid. The relationship between cancer-related genes and treatment outcomes was retrospectively analyzed under the approval of the ethics board at our institution. **[Results]** The median age at initial treatment was 34 (19-43) years, and the median follow-up period was 38 (8-62) months. Actionable variants of cancer-related genes were detected in 35 patients (97%). The genes with high frequency were *PTEN* (23 cases), *CTNNB1* (19 cases), and *PIK3CA* (10 cases), whereas *POLE* and *MSH2* were detected in one case, respectively. Furthermore, the period until tumor disappearance was significantly longer in patients who had pathogenic variants of *PTEN* and *CTNNB1* ($p=0.035$). The results also showed that the recurrence rate was significantly higher in patients who had pathogenic variant of *PTEN* or *CTNNB1* ($p=0.043$). **[Conclusion]** The pathogenic variants of *PTEN* or *CTNNB1* may be prognostic biomarkers for MPA therapy.

IS-WS-3-6

Multicenter phase II investigator initiated trial (STATICE TRIAL, NCCH1615, UMIN 000029506) : A novel anti-HER2 therapy of trastuzumab deruxtecan in HER2-expressing uterine carcinosarcoma Yasui Hiroaki, Nishikawa Tadaaki, Hasegawa Kosei, Mori Masahiko, Hirashima Yasuyuki, Takehara Kazuhiro, Ariyoshi Kazuya, Kato Tomoyasu *STATICE TRIAL GROUP*

[Objective] Uterine carcinosarcoma (UCS) is an aggressive malignant tumor. Previous studies reported that human epidermal growth factor receptor 2 (HER2) expression was detected in 20-50% of UCS patients. Here, we conducted a phase 2, multicenter clinical trial to evaluate the efficacy of trastuzumab deruxtecan (T-DXd) by targeting HER2. **[Methods]** Between February 2018 and June 2020 at 7 institutions in Japan, we enrolled standard chemotherapy-refractory UCS patients with HER2-expression assessed by immunohistochemistry. T-DXd was administered every 3 weeks until progressive disease (PD) or intolerable toxic effects were confirmed. The primary endpoint was overall response rate (ORR) in HER2 2+/3+ (2+/3+) on central review, and the secondary endpoints were ORR in HER2 1+(1+) or more, progression-free survival, overall survival and incidence of adverse events. The trial design was based on the Bayesian strategy. **[Results]** 34 patients were enrolled, 22 patients with 2+/3+ and 10 patients with 1+ were included in the efficacy analysis. The number of complete response and partial response (PR) was 12 (55%), stable disease (SD) was 10 (45%) and no PD in 2+/3+, therefore, it exceeded the minimum required number of responders (4 out of 22 patients). In 1+ patients, the number of PR was 7 (70%), SD was 3 (30%) and no PD. Pneumonitis or interstitial lung disease with grade 1 to 3 occurred in 9 patients (27%) and no grade 4/5 events were reported. **[Conclusion]** The primary endpoint of ORR in 2+/3+ patients was met. T-DXd has also shown a promising efficacy in 1+ patients.

IS-WS-3-7

Identification of novel therapeutic candidates for uterine leiomyosarcoma based on integrated biological analyses Yoshida Kosuke¹, Yokoi Akira¹, Kitagawa Masami², Kato Tomoyasu², Kajiyama Hiroaki¹ *Nagoya University¹, National Cancer Center Hospital², Bell Research Center, Nagoya Univer-*

sity³

[Objective] Uterine leiomyosarcoma is one of the most aggressive gynecological malignancies. In the past decade, novel agents such as trabectedin and pazopanib have been approved, but the prognosis of patients remains unsatisfactory. Moreover, due to the low incidence, the molecular biological features have been less understood. Therefore, the purpose of this study is to identify potential therapeutic agents for uterine leiomyosarcoma based on next-generation sequencing. **[Methods]** Using fresh-frozen tumor tissues of six uterine leiomyosarcomas and three leiomyomas, mRNA sequencing was performed. Based on pathway analysis using IPA software, target genes were identified, and the anti-cancer effects of ten selective inhibitors for the genes were evaluated using three leiomyosarcoma cell lines. Moreover, the *in vivo* efficacy of the inhibitors was assessed using SK-UT-1 bearing mice. **[Results]** Through mRNA sequencing, 512 significantly differentially expressed genes were identified. Subsequent pathway analysis revealed that the functions of cell cycle-related kinases were significantly activated in uterine leiomyosarcoma. *In vitro* analyses showed that inhibitors targeting CDK1/2, CHEK1/2, or PLK1 induced cell cycle arrest and DNA damage, resulting in cell death. Especially, the IC50s of the three inhibitors were below ten nanomolar. Moreover, the inhibitors suppressed tumor growth by about 75% *in vivo* and significantly prolonged the survival of mice ($p < 0.001$). **[Conclusion]** CDK1/2, CHEK1/2, and PLK1 inhibitors exerted an excellent anti-cancer effect and can be novel therapeutic agents for uterine leiomyosarcoma. The inhibitors are under clinical trials in other malignancies, and their toxicity is tolerable. Therefore, we are now planning to conduct a clinical trial.

IS-WS-4-1

Risk factors for disease severity among COVID-19 pregnant women : a nationwide questionnaire survey in Japan Arakaki Tatsuya¹, Sekizawa Akihiko¹, Hasegawa Junichi^{1,2}, Ikeda Tomoaki³, Ishiwata Isamu¹, Kinoshita Katsuyuki⁵ *Showa University¹, St. Marianna University², Mie University³, Ishiwata Obstetrics and Gynecology Hospital⁴, Seijo Kinoshita Hospital⁵*

[Objective] To clarify the clinical risk factor to severity of COVID-19 pregnant women in Japan. **[Methods]** A nationwide questionnaire-based survey for all 2,135 maternity services in Japan was conducted between July and August 2021. Information regarding maternal characteristics and clinical course of pregnant women diagnosed with COVID-19 between July 2020 and June 2021 were collected. The presence of maternal complications, maternal age, and the gestational age of diagnosis were examined with univariate and multivariate logistic regression analyses for risk factors for severe cases. **[Results]** Responded 1,288 institutions were assessed (60.3% of all delivery institutions in Japan). One thousand fifty infected pregnant women were reported, with 832 symptomatic and 218 asymptomatic. Of the symptomatic patients, 69 patients (8.3%) required oxygen, 56 (6.7%) had severe respiratory symptoms, of whom five (0.6%) were the most severe cases, and there were no maternal deaths. The proportion of gestational age at diagnosis over 24 weeks ($GA \geq 24w$) (89.3% vs. 51.7% : $p < 0.001$) and maternal age over 32 years ($Age \geq 32y$) (66.1% vs. 39.5% : $p < 0.001$) were significantly higher in severe cases, respectively. Using a multivariable logistic regression analysis, $GA \geq 24w$ (aOR 6.8 ; 95% CI 2.9-16.2 ; $p < 0.001$) and $Age \geq 32y$ (aOR 2.5 ; 95% CI 1.4-4.6 ; $p = 0.002$) were independently associated with severe respiratory symptoms. **[Conclusion]** After the middle of the second trimester of pregnancy and higher maternal age were associated with severe cases of COVID-19. Pregnant women after 24 weeks of gestation or over 32 years old with symptomatic COVID-19 need careful observation and follow-up.

IS-WS-4-2

Outcomes of pregnant women with COVID-19 in Japan : a retrospective study Takahashi Ken, Kobayashi Yukari, Sato Mariko, Nagae Seika, Kondo Ibuki, Funaki Satoru, Sato Taisuke, Konishi Akiko, Ito Yuki, Kamide Taizan, Samura Osamu, Okamoto Aikou *The Jikei University Hospital*

[Objective] We aimed to investigate the outcomes of pregnant women with COVID-19 in Japan. **[Methods]** In this retrospective study, we collected data from medical records of pregnant women with COVID-19 who were treated at our hospital between April 2020 and April 2021. The data included clinical information, mode of delivery, clinical courses, neonatal outcomes, quantitative reverse transcription-polymerase chain reaction results from pregnancy-related samples, and placental pathological findings. **[Results]** The most common symptom of 31 pregnant women with COVID-19 was a fever ; approximately 10% of patients were asymptomatic. One patient with rapidly worsening pneumonia needed a cesarean section at 30 weeks and was admitted to intensive care. All patients recovered from COVID-19. Twelve patients received perinatal care in our hospital, including 10 live births, one stillbirth, and one artificial abortion. Six patients delivered vaginally ; the others delivered via cesarean section. Two patients had complications, including severe hypertensive disorders and preeclampsia. The 10 newborns had no severe adverse outcomes. Severe acute respiratory syndrome coronavirus 2 was not detected in the placenta, umbilical cord, cord blood, amniotic fluid, vaginal fluid, or breast milk in any patient. Placental pathology revealed no COVID-19-specific findings. No medical staff member had COVID-19 symptoms. **[Conclusion]** Although most pregnant women with COVID-19 recovered without treatment, pneumonia rapidly worsened in some patients. Hypertensive disorders and preeclampsia were observed ; there were no neonatal adverse outcomes. The possibility of transmitting the coronavirus to pregnancy-related samples was low. Some pregnant women had severe pneumonia, which could increase the risk of perinatal complications.

IS-WS-4-3

Maintaining critical safe delivery services for pregnant women during the COVID-19 pandemic in National Maternal and Child Health Center (NMCHC) Sothy Pech¹, Ratana Kim¹, Sovanara Hang¹, Rayounette Krouch² *National Maternal and Child Health Center¹, Ministry of Health²*

[Introduction] The COVID-19 pandemic poses challenges and its response has become top priority of every government worldwide. Royal Government of Cambodia has mobilized resources to combat the pandemic. Ministry of Health is responsible for ensuring continuity of safe delivery services with reduced risk of COVID-19 infection to mothers, infants and health staffs. **[Objective]** The objective of this presentation is to 1) describe actions taken at National Maternal and Child Health Center (NMCHC) to ensure safe delivery and 2) examine clinical outcomes of pregnant women with COVID-19 infection at NMCHC. **[Methods]** We retrospectively reviewed the preventive measures taken at NMCHC and clinical outcomes of pregnant women with COVID-19 admitted to NMCHC between April to August 2021. **[Results]** In April 2021, we established a triage system, through which we screened all pregnant women with rapid antigen test and provided health education to pregnant women to prevent COVID-19 transmission. We also formed health staff teams (doctors, nurses and midwives) and created isolated building for COVID-19 infected pregnancy. By applying these interventions, NMCHC was able to provide safe delivery services to COVID-19 infected pregnant women, who otherwise would not have access to this service due to fear of discrimina-

tion. As of August 2021, a total of 305 pregnant women with COVID-19 had safely delivered including 68 by cesarean section. **[Conclusion]** Ensuring continuity of safe delivery services is critical in order to prevent maternal death during COVID-19 pandemic. Our unique experience in receiving and providing maternity care and lessons learned will guide practice through this challenging time in Cambodia.

IS-WS-4-4

Pregnancy outcomes in women with aortic stenosis Kakigano Aiko, Kamiya Chizuko, Ogawa Moe, Lee Koichiro, Ogawa Ayana, Tabuse Mari, Tsukimura Eriko, Temukai Mai, Shionoiri Tadasu, Nakanishi Atsushi, Iwanaga Naoko, Yoshimatsu Jun *National Cerebral and Cardiovascular Center*

[Objective] Experts recommend avoiding pregnancy with severe aortic stenosis (AS) because of its high morbidity. According to the guidelines of Japanese Circulation Society, women with an aortic valve mean pressure gradient (AVmPG) greater than 40-50 mmHg are recommended to avoid pregnancy. However, there is insufficient evidence how to manage severe AS wishing for childbearing. **[Methods]** We retrospectively reviewed pregnancy with AS which were managed in our institution from 2004 to 2021. Pregnancies after prosthetic valve replacement, those with trivial AS, and miscarriage cases were excluded. Perinatal outcomes and cardiac complications were compared in each severity of AS. **[Results]** Thirty pregnancies complicated with AS were included. Seven had mild AS, 13 had moderate AS, and 10 had severe AS. AVmPG were less than 50 mmHg in all cases either by ultrasonography or catheterization. No significant difference was seen in gestational age at delivery or birthweight among the three groups. One case complicated with severe AS delivered preterm because of maternal aortic dilatation, and three delivered preterm for obstetrical reason such as hypertensive disorders in pregnancy. No significant difference was seen in the rate of preterm birth among the three groups. Arrhythmia requiring medication occurred in four cases, without significant difference among the three groups. Heart failure did not develop in any cases. **[Conclusion]** Pregnancy outcomes in severe AS with AVmPG less than 50 mmHg were comparable to those in mild or moderate AS. With careful management, good pregnancy outcomes can be expected in severe AS cases with AVmPG of 40-50 mmHg.

IS-WS-4-5

Effectiveness of external cephalic version using combined spinal epidural anesthesia Takeda Jun, Takahashi Mayu, Masaoka Ryu, Kawata Misato, Masaoka Shun, Ando Hitomi, Ueki Norikazu, Sei Kiguna, Yamamoto Yuka, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] The study was conducted to assess the effectiveness of external cephalic version (ECV) under combined spinal epidural anesthesia (CSEA). **[Methods]** From 2021, all of the pregnant women with non-cephalic fetal position were informed whether to perform ECV. The medical chart review was performed. Risk factor to fail ECV were assessed with the data of patient and fetal characteristics. The impact of the ECV to the medical expenses was also examined. **[Results]** Sixty-three percent of pregnant women with non-cephalic fetus was agreed to perform ECV. One patient had urgent cesarean delivery due to onset of labor before attempting ECV. The success rate of ECV under CSEA was 87%. There was no difference in maternal or fetal background to the success of ECV. Except for three cases that had not yet delivered, 53% had vaginal delivery after successful ECV. From the above data, medical expenses could be reduced by 77,483 yen per one ECV case. **[Conclusion]** ECV had a high success rate under the CSEA. Minimal invasiveness to

the patient and the reduction of medical expenses were achieved by avoiding cesarean delivery. Increasing the ECV consent rate and increasing the success rate of vaginal delivery after successful ECV seemed to lead to further reductions in medical costs.

IS-WS-4-6

Prevalence and trends of pelvic floor disorders after epidural delivery in Japanese women using the PFDI-20: A single-center retrospective cohort survey Suemitsu Tokumasa¹, Mikuni Kazumi², Suzuki Makoto³ *Kameda Medical Center¹, Gastroenterological Surgery, Kameda Medical Center², Asahi General Hospital³*

[Introduction] Female pelvic floor disorders (PFD) include various clinical conditions, such as urinary and fecal incontinence and pelvic organ prolapse. Pregnancy and labor are known as risk factors for PFD. Previously we reported 73.6% (n=157/333) patients manifested PFD symptoms even postpartum 6-15 months. The association between PFD risk and the mode of delivery is controversial. Not many studies have reported the association of PFD prevalence with epidural anesthesia, especially in postpartum Japanese women. **[Objective]** We analyzed the association between PFD risk and the mode of delivery (epidural delivery, non-epidural delivery, and cesarean section) in Japanese women, especially 6-15 months after delivery. **[Methods]** We conducted a retrospective cohort study of patients who gave birth at our institution. The Pelvic Floor Distress Inventory-20 (PFDI-20) questionnaire (validated in the Japanese language) evaluated PFD symptoms 6-15 months postpartum, and their medical information was obtained from the medical records. **[Results]** Of 333 patients, 212 (63.7%) completed the questionnaire. The prevalence of PFDI-20 was statistically different (p=0.037) in all groups, and the readings were as follows: epidural 19 (90.5%), non-epidural 110 (74.8%), and cesarean section 27 (61.4%). Multivariable regression for disease burden score showed the epidural group had 8.67 points higher disease burden score (estimate: 8.67 (0.03 to 17.3)), and the cesarean section group had -7.61 points (estimate: -7.61 (-14.2 to -1.03)), as compared to the non-epidural group. **[Conclusion]** The epidural delivery would risk PFD even 6-15 months after delivery. Therefore, healthcare workers should inform pregnant women who are planning epidural delivery.

IS-WS-4-7

Episiotomy and Risk Factors for Obstetrical Anal Sphincter Injuries During Vaginal Birth in Korean Women Moon Hanna, Kwon Ja-Young, Jung Yun Ji, Lee Joon Ho, Kim Young-Han, Kwon Hayan *Yonsei University College of Medicine, Yonsei University Health System, Korea*

[Objective] Obstetric anal sphincter injuries (OASIS) during vaginal birth are the leading cause of pelvic floor dysfunctions. This study aimed to evaluate the risk factors for OASIS according to use of episiotomy and type of episiotomy in Korean women **[Methods]** A retrospective cohort study in women with vaginal delivery of term, singleton, and cephalic presentation at tertiary hospital in Korea was performed. The data on maternal characteristics, neonatal, and maternal outcomes were collected. OASIS was defined as third- and fourth-degree perineal lacerations. Logistic regression analysis was performed to assess the potential risk factors according to use of episiotomy and type of episiotomy. **[Results]** 5,966 women were included, and 194 women (3.3%) experienced OASIS. Factors independently associated with OASIS included nulliparous (OR 3.23; 95% CI, 2.23-4.68), duration of 2nd stage of labor (OR 1.01; 95% CI, 1.01-1.02), head circumference of neonate (OR 1.16; 95% CI, 1.04-1.30), birthweight ≥ 3500 g (OR 1.45; 95% CI, 1.06-1.97), along with in-

creasing gestational age (OR 1.24 ; 95% CI, 1.07-1.44). The risk of OASIS wasn't higher in women with the use of episiotomy, however, the median episiotomy was independent risk factor for OASIS compared to no-episiotomy (OR 2.30 ; 95% CI, 1.61-3.28). In subgroup analysis by parity, dissimilar to overall and nulliparous women, pre-pregnancy BMI (OR 1.13 ; 95% CI, 1.05-1.23) was the risk factor for OASIS in multiparous women. **[Conclusion]** In Korean women, the risk of OASIS related with episiotomy varies depending on other risk factors. Therefore, different risk factors should be considered to reduce the risk of OASIS.

IS-WS-4-8

Pregnancy-related maternal deaths due to cardiovascular diseases in Japan from 2010 to 2019 : an analysis of the Maternal Death Exploratory Committee data in Japan Matsushita Tomomi¹, Arakaki Tatsuya¹, Sekizawa Akihiko¹, Hasegawa Junichi^{1,2}, Tanaka Hiroaki³, Katsuragi Shinji⁴, Nakata Masahiko⁵, Murakoshi Takeshi⁶, Ikeda Tomoaki³, Ishiwata Isamu⁷ *Showa University¹, St. Marianna University², Mie University³, University of Miyazaki⁴, Toho University⁵, Seirei Hamamatsu General Hospital⁶, Ishiwata Obstetrics and Gynecology Hospital⁷*

[Objective] To assess characteristics of maternal deaths due to cardiovascular diseases and quality of care provided to the patients to identify elements to improve maternal care in Japan. **[Methods]** Patients who died during pregnancy or within a year after delivery, between January 2010 to December 2019 in Japan, whose detailed reports were analyzed by The Maternal Deaths Exploratory Committee, were enrolled in the present study. Information regarding maternal characteristics and clinical course were extracted. **[Results]** Of 445 eligible pregnancy-related maternal deaths, 44 (9.9%) were attributed to cardiovascular diseases. The most frequent causes were aortic dissection (18 cases, 40.9%), followed by peripartum cardiomyopathy (8 cases, 18.2%) and pulmonary hypertension (5 cases, 11.4%). In 31.8% of cases, cardiopulmonary arrest occurred within 30 minutes after initial symptoms. About 60% had initial symptoms in the prenatal period. The most frequent symptoms were dyspnea (18.2%), or chest and abdominal pain (13.6%). More than half of patients had known risk factors : aged 35 or older, hypertensive disorder, and obesity were the commonest. Quality of care was assessed as suboptimal in nine patients (20.5%), in which cardiac risk assessment was insufficient in three cases with a pre-existing cardiac disease, and the remaining six cases with symptoms and risk factors warranting intensive monitoring and evaluation. **[Conclusion]** The leading cause of maternal deaths due to cardiac disease was aortic dissection. Rapid cardiovascular collapse after onset of the initial symptom was found in one-third of cases. Intensive monitoring and comprehensive assessment would be the key to improving maternal care in limited cases.

IS-WS-5-1

A novel mechanism of ovarian cancer cell phagocytosis by mesothelium and possible immunosuppressive effect in peritoneal dissemination : Are mesothelial cells foe or friend?

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[Objective] Mesothelial cells (MCs), the largest component of the peritoneal cavity, are capable of phagocytosis. Recently, the importance of by-stander but amateur phagocytes has been reported in various fields including neural injury. In this study, we aimed to clarify the significance of cancer cell phagocytosis by MCs and its involvement in cancer immunity. **[Methods]** We conducted a mesothelial lineage tracing using Wt1^{CreERT2}/ROSA26-LSL-tdTomato mouse model of peritoneal dissemination and evaluated phagocytosis by MCs. Mouse-MCs and apoptosis-induced mouse-ovarian cancer (mOvCa) cells were co-cultured, and the phagocytic MCs were sorted by FACS. The expression of immune-related gene was examined using qPCR. Mouse-MCs which phagocytized mOvCa cells were intraperitoneally injected to allogeneic immune normal mice, and then mOvCa cells were injected into their peritoneal cavity to evaluate tumor growth and immunocompetence. **[Results]** The 3D-construction imaging using multiphoton microscopy of mice peritoneal wall showed phagocytosis rate of 6.4% (88/1,365). Although MCs did not phagocytize viable cancer cells, MCs phagocytized apoptotic cancer cells in vitro (3.5%). The qPCR analysis showed significant upregulation of immune co-suppressor genes : PD-L1 ($p < 0.01$, 3.2-fold), CD86 (ligand of CTLA4, $p < 0.05$, 3.4-fold), B7-H3 ($p < 0.05$), and B7-H4 ($p < 0.05$) and significant downregulation of immune co-stimulatory gene : ICOSL ($p < 0.01$, 5.5-fold). Cancer-associated mesothelial cells, which were induced mesothelial-mesenchymal transition (MMT) by TGF- β 1 secreted from cancer cells, also showed significant upregulation in immune co-suppressor gene : B7-H4 ($p < 0.05$) and downregulation in immune co-stimulatory gene : ICOSL ($p < 0.05$). **[Conclusion]** MCs which phagocytized cancer cells and cancer-associated mesothelial cells were suggested to be involved in immune escape of ovarian cancer cells.

IS-WS-5-2

Establishment and characterization of reversibly immortalized ovarian epithelial cell lines using the Sendai virus

Komatsu Hiroaki, Okawa Masayo, Hikino Kouhei, Iida Yuki, Osaku Daiken, Kudoh Akiko, Chikumi Jun, Sato Shinya, Oishi Tetsuro, Taniguchi Fuminori, Harada Tasuku Tottori University

[Objective] To establish reversibly immortalized cells without induction of mutations in the genome from human ovarian non-cancerous tissue using the Sendai virus (SeV) vector. **[Methods]** Superficial ovarian epithelial cells (normal epithelium : OVn), endometrioid cysts : OVC), and ovarian mucinous cystadenoma (Ovm), dissected at the time of surgery with patient consent, were infected with temperature-sensitive SeV vectors carrying three immortalization genes (Bmi-1, hTERT, and SV40T). The presence of infection was confirmed based on GFP and mCherry fluorescence. Immunoreactivity of anti-EpCAM antibody (marker derived from epithelial carcinoma) in each SeV-infected cell was confirmed by flow cytometry. Chromosomes were karyotyped for the presence of numerical and structural abnormalities. Exosomes were extracted from each cell supernatant by ultracentrifugation, particle size was measured using a nanoparticle analysis system, and the presence of CD9 and CD63 was confirmed by western blotting. **[Results]** SeV-infected

cells showed GFP and mCherry fluorescence, while non-infected cells did not. SeV infection allowed all primary cell lines to grow for at least 10 generations, while non-infected SeV cells lacked the proliferative capacity and showed senescence-like morphology. SeV-infected cells senesced in a temperature-dependent manner. Particles approximately 100 nm in size could be accumulated from the recovered exosomes and showed CD9 and CD63 responses. **[Conclusion]** We have succeeded in the reversible immortalization of proliferative ovarian epithelial cells using SeV for the first time. It was possible to extract exosomes from the supernatant of cultured cells. In addition to chromosome analysis, we will analyze exosome-miRNA profiles, identify characteristic expression patterns, and search for biomarkers.

IS-WS-5-3

Detecting ovarian cancer specific extracellular vesicles isolated by polyketone-coated nanowires Onono Mayu¹, Yokoi Akira¹, Yoshida Kosuke¹, Kitagawa Masami², Koya Yoshihiro², Nawa Akihiro², Kajiyama Hiroaki¹ Nagoya University Hospital¹, Laboratory of Bell Research Center, Nagoya University Hospital²

[Objective] Ovarian cancer (OV) cell derived extracellular vesicles (EVs), including exosomes, have unique profiles and those EVs are promising targets as disease biomarkers. However, for clinical application, highly specific EV markers and simple EV preparation steps are required. In this study, we aimed to identify OV specific membrane proteins on EVs and develop novel EV preparation platform. **[Methods]** To globally analyze proteins in OV, shotgun proteomics were performed. EVs were isolated as small and large EVs by serial centrifugation methods from 10 cell culture supernatants and over 20 patient serum and ascites. CPTAC database for OV tissue proteins was referred. Polyketone-coated nanowires (pNW) were developed, validated and used for isolation of EVs. Exoview, multiplexed array assays, was used for detecting specific OV-EVs. **[Results]** Proteomic analyses for 50 samples reveal that small EVs and large EVs have distinct profiles and OV derived EVs has unique characteristics. In the process of selection, gene expression profile in 514 cases were also considered, and we identified 3 proteins, specifically located on small EVs derived from OV patients. For easily isolating EVs, pNW was developed and the device well purify the EVs comparing to conventional methods. By using pNW, clinical utility of the 3 markers were tested and Exoview system reveal that they are specifically detected in cancer patients and may predict their drug response. **[Conclusion]** OV specific EVs were newly identified and pNW were used for simple EV isolation. These insights provides further potential application in the aspect of EV heterogeneity and clinical uses.

IS-WS-5-4

High-resolution analysis of molecular subtypes in high-grade serous ovarian carcinoma using single-cell RNA sequencing Takamatsu Shiro¹, Taki Mana¹, Yamanoi Koji¹, Yamaguchi Ken¹, Hamanishi Junzo¹, Matsumura Noriomi², Mandai Masaki¹ Kyoto University Hospital¹, Kindai University Hospital²

[Objective] Single-cell RNA sequencing (scRNA-seq) is a method for genome-wide, unbiased gene expression analysis by separating tissues into individual cells, which allows for a more detailed analysis of cancer molecular pathology than conventional bulk RNA-seq. This study aims to re-evaluate the classical molecular subtype classification of high-grade serous ovarian carcinoma (HGSOC) at the cellular level. **[Methods]** From previous reports, we analyzed scRNA-seq data of 95151 cells derived from 28 HGSOC samples, collected from primary, peritoneal, and omental tumors. **[Results]** Based on the transcriptional analysis of 17103 genes shared among the datasets, including the

batch correction, we grouped the cells into epithelial, stromal, immune, and the other cell types. We also performed per-sample pseudo-bulk expression analysis, where the samples were classified into the four molecular subtypes: immunoreactive, mesenchymal, proliferative, and differentiated. The subtypes correlated strongly with the composition of cell types in the tumor; the immunoreactive, differentiated, and mesenchymal samples contained a higher proportion of immune, epithelial, and stromal cells, respectively. Gene set enrichment analysis restricted to epithelial (cancer) cells showed that cells of the immunoreactive subtype showed a higher gamma interferon response signature, and those of the mesenchymal and proliferative higher epithelial-mesenchymal transition and angiogenesis signatures. Unexpectedly, cells of the mesenchymal subtype exhibited the lowest cell cycle score. No differences in the results were observed among the sampling sites. **[Conclusion]** The classical molecular subtypes of HGSOV are not only strongly dependent on differences in the tumor microenvironment but may also depend on intrinsic factors of tumor cells.

IS-WS-5-5

Extracellular DNA from neutrophils (NETs) may promote peritoneal dissemination of ovarian cancer Bun Michiko¹, Kawano Mahiru², Shimura Koutarou³, Toda Aska¹, Nakamura Koji¹, Kinose Yasuto¹, Kodama Michiko¹, Hashimoto Kae¹, Sawada Kenjiro¹, Kimura Tadashi¹ *Osaka University¹, Department of Cell Biology, Duke University Medical Center, USA², Osaka Rosai Hospital³*

[Objective] Neutrophil extracellular traps (NETs) are extracellular neutrophil-derived DNA released in response to inflammation. In contrast to their primary host-defensive role, NETs are recently reported to promote cancer progression. The aim of this study is to investigate the role of NETs in peritoneal dissemination of ovarian cancer. **[Methods]** The clinical data of patients treated for ovarian cancer at our hospital were retrospectively analyzed to examine the relationship between neutrophilia, peritoneal dissemination and prognosis. The omental tissue was examined for NETs pathologically to find basophilic web-like structure associated with neutrophils by H&E-staining. NETs were formed in vitro by stimulating human peripheral blood neutrophils with PMA. Then human ovarian cancer SKOV3 cells were co-cultured with NETs to evaluate the effect of NETs on cancer cell proliferation, adhesion, migration and invasion. Peritoneal dissemination model was generated by injecting murine ovarian carcinoma ID8 cells intraperitoneally into C57BL/6 mice. As a model of neutrophilia, G-CSF-producing tumor cells were used. The formation of NETs and cancer progression were assessed. **[Results]** Neutrophilia (neutrophils > 7000/ μ l) was associated with advanced disease accompanied by peritoneal dissemination and compromised survival. Omental tissues from patients with neutrophilia showed NETs-like structures. The adhesion of ovarian cancer cell was increased by co-incubation with NETs. G-CSF-producing tumor bearing mice exhibited greater peritoneal dissemination and significantly shorter survival. Neutrophils were markedly increased in the ascites and NETs foci were observed in the metastatic sites. **[Conclusion]** Neutrophilia is associated with peritoneal dissemination and poor prognosis in ovarian cancer. Increased neutrophils might promote peritoneal dissemination by forming NETs.

IS-WS-5-6

Spatial heterogeneity of the actionable genomic alterations in ovarian clear cell carcinoma Kamii Misato, Takenaka Masataka, Kuroda Takafumi, Kawabata Ayako, Takahashi Kazuaki, Iida Yasushi, Yanaiharu Nozomu, Takano Hirokuni,

Okamoto Aikou *The Jikei University*

[Objective] Spatial heterogeneity in malignant tumors (heterogenous distribution of genomically diverse tumor subpopulations across different sites) is associated with resistance to treatment. The current study aimed to identify the spatial heterogeneity of the actionable genomic alterations in ovarian clear cell carcinoma (OCCC). **[Methods]** Advanced OCCC with four or more metastatic lesions resected at primary debulking surgery were included. Genomic DNA extracted from the formalin-fixed paraffin-embedded (FFPE) blocks of multiple cancerous lesions was analyzed by targeted deep sequencing with the custom panel including 84 OCCC-related genes. The genomic profiles in multiple cancerous lesions were compared to identify the spatial heterogeneity of the actionable genomic alterations for each case. **[Results]** Fifty-seven cancerous lesions obtained from nine OCCC were analyzed, and 198 potentially pathogenic variants (31 genomic alterations in 18 genes) were identified in seven cases. Twenty-two genomic alterations in 14 genes including *KRAS* and *TP53* were shared across the primary and all metastatic lesions, whereas nine in four genes consisted of *ARID1A*, *PIK3CA*, *PIK3R1* and *FGFR2* showed the heterogenous distribution. 40% (2/5) of *ARID1A* mutations and 60% (3/5) of *PIK3CA* mutations were not detected in lymph node metastases. Moreover, in one case, the *PIK3CA* mutation was found only in the omental dissemination in which *KRAS* mutations were shown in all cancerous lesions. **[Conclusion]** A part of the actionable genomic alterations showed the spatial heterogeneity in advanced OCCC, suggesting that the therapeutic strategies considering the spatial heterogeneity of the actionable genomic alterations will be required in OCCC.

IS-WS-5-7

Analysis of anti-cancer effects of metformin on ovarian clear cell carcinoma cells Takemori Satoshi, Morisada Tohru, Osaka Makoto, Watanabe Momoe, Tajima Atsushi, Tanigaki Shinji, Kobayashi Yoichi *Kyorin University*

[Objective] Metformin (MET), which is a biguanide oral medicine for diabetes mellitus, has recently been identified to have growth inhibitory effects and enhancing chemosensitizing on cancer. However, its effects on ovarian clear cell carcinoma (OCCC) still remain unclear. So, we evaluated the effect of MET on ovarian clear cell carcinoma cell line. **[Methods]** Using RMG-I, derived from OCCC, we prepared two groups of with or without MET in the culture supernatant. Then, each group was further divided into two groups depending on whether to add Cisplatin (CIS). We evaluated the proliferation of each well using WST-1 cell proliferation assay by measuring the absorbance of each sample. In addition, we evaluated apoptosis of two groups with and without MET by AnnexinV-APC/7 ADD flow cytometry. **[Results]** In the group with MET, the absorbance was significantly reduced compared to those without MET ($p < 0.01$). In the group with CIS, the absorbance was significantly reduced compared to the group of without CIS ($p < 0.01$). The absorbance of the group with both CIS and MET was significantly reduced compared to each group of without any drugs or with CIS only ($p < 0.01$). According to the results of flow cytometry, in the group with MET, the rate of apoptosis was significantly increased compared to the group without MET ($p = 0.026$). **[Conclusion]** These results suggest that MET has growth inhibitory effect, and enhancing chemosensitivity in the cell line of OCCC, and suggested that induction of apoptosis is involved in growth-inhibitory effect of MET.

IS-WS-5-8

Does chemotherapy diminish the negative impact of positive ascites cytology in patients with epithelial ovarian carcinoma

noma? : A large-scale multi-institutional study based on propensity-score-based matching analysis Fujimoto Hiroki, Yoshihara Masato, Kitami Kazuhisa, Iyoshi Shohei, Uno Kaname, Mogi Kazumasa, Tano Sho, Yoshikawa Nobuhisa, Kajiyama Hiroaki *Nagoya University*

[Objective] Positive ascites cytology is a robust prognostic factor in patients with early-stage epithelial ovarian cancer (EOC). However, it is still unclear how the positive ascites cytology affects the prognosis of advanced-stages. We investigated the comprehensive impact of positive ascites cytology on patients with EOC and the effectiveness of additional therapeutic interventions, including complete-staging surgery and chemotherapy. **[Methods]** We analyzed 4,730 patients with malignant ovarian tumors, which included 1,906 of EOC. Baseline data of the cohort were adjusted with propensity score (PS) -based inverse probability of treatment weighting (IPTW) adjustment. Subgroup analysis was also undertaken to assess the interaction effect of chemotherapy and complete-staging surgery with positive ascites cytology. **[Results]** Multivariate analysis showed positive ascites cytology significantly correlated with poor prognosis (hazard ratio (HR) : progression-free survival (PFS), 1.541, $P < 0.001$; overall survival (OS), 1.666, $P < 0.001$). Kaplan-Meier curves with PS-based IPTW adjustment also indicated patients with positive ascites cytology had significantly worse PFS and OS (Log-rank test on PFS and OS : $P < 0.005$). In contrast, positive ascites cytology did not affect the prognosis of patients with stage IV tumors and mucinous histology. Besides, the introduction of chemotherapy significantly extended PFS (HR : 0.163, $P < 0.001$) and OS (HR : 0.128 (0.060-0.273), $P < 0.001$), while complete-staging surgery did not improve the prognosis of patients with positive ascites cytology. **[Conclusion]** Our data suggested positive ascites cytology negatively influenced the prognosis of the patients with EOC except for stage IV tumors or mucinous histology. Additionally, chemotherapy may effectively diminish the negative impact of positive ascites cytology on survival outcomes.

IS-WS-6-1

Lipid storage myopathy with hypoplastic lung and diaphragmatic eventration in two siblings : case report Yamada Naoshi¹, Kodama Yuki¹, Aman Murasaki², Tsuzuki Yasue¹, Muraoka Junsuke¹, Yamashita Rie¹, Doi Koutarou¹, Kaneko Masatoki¹, Yamaguchi Masatoshi^{1,3}, Sameshima Hiroshi¹, Katsuragi Shinji¹ *University of Miyazaki¹, Department of Diagnostic Pathology, Division of Pathology, University of Miyazaki², Department of Clinical Genetics, University of Miyazaki³*

Here we report two siblings with rare lipid storage myopathy with hypoplastic lung and diaphragmatic eventration. The first female baby was born by vaginal delivery. Her birth weight was 2,526g at 40 and 3/7 of gestation. After birth, she was intubated immediately after birth due to respiratory distress with floppy infants, and treated for persistent pulmonary hypertension of the newborn (PPHN). She died 9 hours of life. On autopsy, she was diagnosed hypoplastic lung and diaphragmatic eventration, revealed markedly various-sized muscle fibers in diaphragm. The second male baby was healthy. The third female baby was born at 37 and 1/7 of gestation. She was also in respiratory distress with floppy infants showing PPHN, and died 6th days of life. Autopsy revealed that lung-body weight ratio was 0.0014%, and increased capillaries in the alveolar wall such as Pulmonary capillary hemangiomatosis. There were also markedly various-sized muscle fibers and fibrosis of interstitium in the diaphragm, biceps brachii, and upper vertical tongue muscle. No specific inflammation was shown on muscle tissue, however increased lipid droplets were observed in muscle fibers with oil red stain. We speculated that 1st and 3rd neonates died of lipid storage myopathy. Targeted gene panel sequencing of 41 causa-

tive genes for congenital metabolic myopathies identified only heterozygous pathologic variant of *SLC22A5* gene. Moreover, serum concentration of carnitine was normal in tandem mass spectrometry suggesting this case is not a carnitine metabolism related disease. Trio analysis with initiative on rare undiagnosed disease (IRUD) is now under analysis.

IS-WS-6-2

The Use of the Interischial Distance Sonographic Measurement of the Fetal Pelvis for the Estimation of Gestational Age in a Tertiary Hospital : A Prospective Study Ng-Go Vanessa Jam T, Balita Berly B *Section of Ultrasound, Rizal Medical Center, Philippines*

[Objective] Accurate assessment of gestational age is an integral part of antepartum care for adequate planning of proper intervention during pregnancy. The study aims to evaluate that interischial distance (IID) sonographic measurement is a reliable parameter for gestational age estimation during the 2nd and 3rd trimester of pregnancy. **[Methods]** The study was conducted in a tertiary hospital from September 2020 - February 2021. Three hundred fifty-five pregnant women of gestational age (GA) 16-40 weeks of pregnancy referred for antenatal scan who fit in the inclusion criteria comprised our study sample. **[Results]** Age of women ranged from 19 to 45 years with a mean of 28.69 years. In our experience, IID measurement is relatively simple and can be easily performed in daily practice with good reliability. The study demonstrated that IID showed a linear relationship with GA which grows at a constant rate of 1 mm per week that was statistically significant (with a correlation coefficient of 0.992) and was found to be the most accurate as compared to the other traditional biometric parameters : Biparietal Diameter, Head Circumference, Abdominal Circumference and Femur Length. **[Conclusion]** Interischial distance ultrasonographic measurement may be used as a valuable alternative biometric parameter during the second and third trimesters of gestation. However, more studies should be done to determine its possible use not only during normal pregnancy, but also in fetuses that have conditions which are known to affect fetal growth and development.

IS-WS-6-3

Association between fetal sex and pregnancy outcomes among women with twin pregnancies : a multicenter cross-sectional study Funaki Satoru, Matsumoto Natsuki, Oka Kazuhiko, Mori Shin, Nagao Takeshi, Kitamura Naoya, Hasegawa Akihiro, Inoue Momoko, Ito Yuki, Takahashi Ken, Miya Michiko, Samura Osamu *The Jikei University*

[Objective] Some studies on the association between fetal sex and pregnancy outcomes in twin pregnancies have been conducted. However, most of them only focused on limited outcomes, and chorionicity has been rarely considered. This study aimed to examine the frequency and to what extent fetal sex is associated with pregnancy outcomes among twin pregnancies, as stratified by chorionicity. **[Methods]** This registry-based multicenter cross-sectional study was conducted using the Japan Society of Obstetrics and Gynecology perinatal database between 2007 and 2016. The sample population was restricted to women with twin pregnancies. The main pregnancy-related outcomes included preterm birth, very preterm birth, extremely preterm birth, preeclampsia, twin-to-twin transfusion syndrome (TTTS), and selective intrauterine growth restriction (s-IUGR). A multivariable Poisson regression analysis was used to examine the association between fetal sex and pregnancy complications. **[Results]** The primary analysis was performed based on including 23,804 women with dichorionic diamniotic (DD) twins and 14,149 women with monochorionic diamniotic (MD) twins.

Women with male/male DD twins had a significantly higher preterm birth risk (adjusted risk ratio [aRR] : 1.07, 95% confidence interval [CI] : 1.03-1.10) and a lower preeclampsia risk (aRR : 0.74, 95% CI : 0.62-0.88) than women with female/female DD twins. Women with male/male MD twins also had a significantly higher preterm birth risk (aRR : 1.06, 95% CI : 1.04-1.09) than the latter women. Preeclampsia, TTTS, and s-IUGR risks did not differ by sex among MD pregnancies. **[Conclusion]** This study demonstrated significant associations between fetal sex and several pregnancy outcomes in twin pregnancies, some of which differed by chorionicity.

IS-WS-6-4

Alteration of insulin and glucose in cord blood according to the delivery mode Lee Sul, Jo Hyun-Bin, Kim In-Hye, Kang Seung-Wan, Kim Seung-Chul *Pusan National University Hospital, Korea*

[Objective] Through the process of labor and delivery, the pregnant women are affected by various hormones which results in changes in glucose and insulin concentrations. The altered maternal glucose level is transmitted to the fetus through the cord blood, which affects fetal glycogenesis and glycolysis. These alterations may result to affect the initial glucose level of the newborn. Therefore, the purpose of this study is to examine the differences in cord blood glucose and insulin concentrations according to delivery methods. **[Methods]** In this study, maternity and fetus scheduled for delivery after 36 weeks were enrolled and a total 89 patients participated (11 of vaginal delivery and 78 of cesarean delivery). Concentration of glucose and insulin were quantified from cord blood collected immediately after delivery. Independent *T*-test was used to compare glucose and insulin concentrations between the groups. **[Results]** The average of the glucose concentration in vaginal delivery was 129.1 (\pm 47.18) mg/dl and in cesarean delivery was 73.8 (\pm 13.2) mg/dl. The average of the insulin concentration in vaginal delivery 5.13 (\pm 3.04) μ IU/ml and in cesarean delivery was 11.34 (\pm 6.01) μ IU/mL. The concentration of glucose and insulin are statistical significance between vaginal delivery and cesarean delivery. **[Conclusion]** It is consider that the concentration of maternal and fetal glucose increase under stressful conditions such as labor, and it would be further promoted through a decrease secretion of insulin in fetus.

IS-WS-6-5

Efficacy of daily rectal micronized progesterone for prevention of preterm delivery : a randomized clinical trial Khashanian Maryam, Karamiabd Tayyebah *Iran University of Medical Sciences, Iran*

[Objective] To determine the efficacy of rectal progesterone as a maintenance tocolytic after arresting preterm labor, for increasing the duration of pregnancy, and postponing preterm birth. **[Methods]** The study was performed as a double-blind randomized clinical trial on women with preterm labor in whom contractions have been stopped. The eligible women were randomly divided into two groups. In the intervention group (progesterone group), progesterone was administered rectally as a dose of 200mg daily until 36th weeks or spontaneous delivery before that time, whichever came first ; and in the placebo group, placebo was administered similarly. Primary outcomes were the number of deliveries before 37 weeks of gestation and time to delivery interval in two groups. Secondary outcomes were neonatal Apgar score and weight, and need for NICU admission. **[Results]** 160 women finished the study (80 women in each group). The women of the two groups did not have significant differences according to the baseline characteristics. Frequency of preterm labor (earlier than 37 weeks) and mean gestational

age at the time of delivery did not show a significant difference in the two groups. Also, neonatal outcomes including Apgar score, birth weight, NICU admission, and neonatal complications were not different between the two groups. The pregnancy length was longer in the progesterone group (28.84 \pm 3.36 VS 21.19 \pm 4.62 days), [p=0.001, CI 95% : 3.71-4.83]. **[Conclusion]** Rectal progesterone as a maintenance tocolytic agent, cannot lower the frequency of preterm birth, but was suggested to prolong pregnancy length.

IS-WS-6-6

Tocolytic treatment for prevention of preterm birth from a Taiwanese perspective : A survey of Taiwanese obstetricians Lee Howard Hao¹, Yeh Chang-Ching², Wang Peng-Hui^{1,2,3} *Taipei Veteran's General Hospital, Taiwan¹, Institute of Clinical Medicine, National Yang-Ming Chiao Tung University, Taiwan², Department of Medical Research, China Medical University Hospital, Taiwan³*

[Objective] : To understand the practice patterns and beliefs regarding tocolysis in Taiwan. **[Methods]** : We conducted a paper-based survey at the 2020 Taiwan Society of Perinatology Conference on December 8th, 2020. The survey consisted of different clinical scenarios such as short cervix, preterm labour, maintenance tocolysis, premature preterm rupture of membrane etc. The respondents were asked whether they would prescribe tocolytics for each scenario as well as the choice of tocolytic. **[Results]** : 77 obstetricians responded to the survey. According to the survey, tocolysis widely accepted and practiced in Taiwan. This is also true for less evidence-based indications such as abdominal tightness (22%), short cervix (46%), maintenance tocolysis (60%) and repeat tocolysis (89%) with the preferred first line medication being nifedipine and ritodrine. **[Conclusion]** : Tocolysis is widely accepted and practiced in Taiwan. More research is needed to include Taiwan specific economical and cultural factors as well as associated adverse effects and patient outcomes.

IS-WS-6-7

Maternal ritodrine hydrochloride administration and childhood wheezing in the offspring up to three years of age : The Japan environment and children's study Murata Tsuyoshi¹, Kyojuka Hyo¹, Yasuda Shun¹, Fukuda Toma¹, Yamaguchi Akiko¹, Nishigori Hidekazu², Fujimori Keiya¹ *Fukushima Medical University¹, Fukushima Medical Center for Children and Women, Fukushima Medical University²*

[Objective] The effect of maternal ritodrine hydrochloride administration (MRA) on the offspring remains unclear. This study aimed to evaluate the association between MRA and corresponding offspring's childhood wheezing using data from a Japanese nationwide birth cohort study. **[Methods]** Data of participants enrolled in the Japan Environment and Children's Study, a nationwide prospective birth cohort study, between 2011 and 2014 were analyzed. Data of women with singleton live births at and after 22 weeks of gestation were enrolled. The participants were divided according to the MRA status. A logistic regression model was used to calculate odds ratios for "wheezing ever," diagnosis of asthma in the last 12 months, and "asthma ever" in women with MRA, considering offspring's childhood factors affecting the incidence of wheezing, including smoking environment and childhood viral infections. Women without MRA served as the reference. Additionally, participants were stratified by term births, and odds ratios for outcomes were calculated using a logistic regression model. **[Results]** A total of 68,123 participants were analyzed. The adjusted odds ratio (aOR) for wheezing was 1.17 (95% confidence interval, 1.12-1.22). The aORs for the other outcomes did not increase signifi-

cantly after adjusting for the childhood factors. The same tendency was noted among women with term births. **[Conclusion]** MRA was associated with a slightly increased incidence of childhood wheezing in the offspring up to 3 years of age, irrespective of the term or preterm birth status. It is important that perinatal physicians consider the potential effects of MRA on the offspring's childhood health.

IS-WS-6-8

Evaluation of Serum MicroRNAs, miR-4535 and miR-191-5p, as Predictive Non-Invasive Biomarkers for Chorioamnionitis Ishida Koko, Kiyoshima Chihiro, Kurakazu Mariko, Izuchi Daisuke, Fukagawa Satoshi, Urushiyama Daichi, Sanui Ayako, Kurakazu Masamitsu, Miyata Kohei, Miyamoto Shingo *Fukuoka University Hospital*

[Objective] We had previously reported that miR-4535, miR-1915-5p and miR-191-5p in amniotic fluid are potential biomarkers for severe chorioamnionitis (CAM). Therefore, we evaluated these micro RNA (miR) in serum could be non-invasive biomarkers for CAM or fetal infection. **[Methods]** 40 pregnant who suspected and treated as CAM and those 37 newborns admitted in our hospital were enrolled. Maternal blood and amnion miR-4535, miR-191-5p, and miR-1915-5p were elevated with semi-quantitative real-time PCR. Categorize the patients depend on Blanc's classification into Stage 0-I (n=12), Stage II (n=17) and Stage III (n=11) or each infectious feature such body temperatures, heart rate, WBC, or CRP. Compare the each three miR expression and analyze statistically using with Simple regression analysis, Fisher's exact test, and Receiver Operating Characteristic Analysis (ROCA). **[Results]** Serum miR-4535 (p=0.0021) and miR-191-5p (p=0.0051) expression were elevated in stage III CAM compared to stage 0-I. Serum miR-4535 expression was correlated positively with amniotic miR-4535 (p=0.0105) and maternal WBC (p=0.0027). Serum miR-191-5p was correlated positively with maternal and fetal CRP. ROCA revealed that probability of miR-4535 and miR-191-5p as predictor of fetal infection with area under the ROC curve (AUC) 0.922 and 0.745, respectively. **[Conclusion]** Serum miR-4535 and miR-191-5p have potential for the non-invasive biomarkers to predict the CAM and newborn infection, without amniocentesis.

IS-WS-6-9

Individual low dose betamethasone acetate therapy improves fetal lung maturation response with reduced HPA axis and growth suppression in a sheep pregnant model Takahashi Tsukasa^{1,2} *Tohoku University Hospital¹, The University of Western Australia, Australia²*

[Objective] Antenatal corticosteroid therapy has not been optimized yet. We hypothesized that quick-release betamethasone phosphate (Beta-P) reduced the efficacy of therapy when it was administered in combination with slow-release betamethasone acetate (Beta-Ac) in sheep pregnant model. **[Methods]** Ewes carrying a single fetus were randomized either : i) 0.125 mg/kg Beta-Ac (n=11), ii) 0.25 mg/kg Beta-P+Ac (n=12) ; or iii) sterile saline (n=12) two days and one day before delivery at 123 or 124 days' gestation (term 150 days). Lambs were ventilated for 30 minutes before being euthanized. Lung maturation was assessed by cord blood pH, PaO₂ PaCO₂ at 30 minutes ventilation and statistic lung compliance. Fetal birth weight (BW) and fetal ACTH at delivery were measured. ANOVA was used to compare mean differences between groups. **[Results]** Functional lung maturation was better in both of treatment groups than saline group. However, there was not significantly different between Beta-Ac and Beta-P+Ac group animals. The response rate which was defined by the arbitrary cut-off, being a PaCO₂ level more extreme than 2SD from the mean value of Saline

Group, was higher in Beta-Ac Group (82%) than Beta-P+Ac Group (33%). BW and ACTH were significantly lower in Beta-P+Ac Group than Saline Group (BW : 2.38 ± 0.29 vs 2.80 ± 0.35 kg, p<0.01) and Beta-Ac Group (ACTH : 6.7 ± 1.2 vs 13.2 ± 6.6 pg/mL, p=0.01), respectively. **[Conclusion]** Low dose Beta-Ac therapy was sufficient for fetal lung maturation. Inclusion of Beta-P did not additionally improve lung maturation, but was associated with greater HPA axis suppression, a lower steroid treatment response rate, and lower birth weight.

IS-WS-7-1

Reduced innate lymphoid cells in the endometrium of women with endometriosis Sugahara Takuya, Tanaka Yukiko, Fujii Maya, Shimura Koki, Tarumi Yosuke, Ogawa Kanae, Okimura Hiroyuki, Koshiba Akemi, Khan Khaleque, Kusuki Izumi, Mori Taisuke, Kitawaki Jo *Kyoto Prefectural University of Medicine*

[Objective] Innate lymphoid cells (ILCs), a recently discovered family of innate immune cells, are responsible for the early immune response, and control both innate and adapted immune system via cytokine secretion. The role of ILCs in endometriosis has not been investigated ; therefore, here, we aimed to investigate how the proportion of ILCs changes in endometriosis. **[Methods]** The percentage of each ILC group in CD45+ cells was examined in the peripheral blood, peritoneal fluid, endometrium, and ovarian endometrioma obtained from women with and without endometriosis (ERB-C-1216) using flow cytometry. **[Results]** Specimens were obtained from 19 women with endometriosis and 15 without endometriosis. In the endometrium, patients with endometriosis had lower proportion of ILC2 and 3 compared to control specimens (ILC2 : 0.02 ± 0.01% vs 0.07 ± 0.03% ; P<0.05, ILC3 : 0.31 ± 0.14% vs 1.10 ± 0.93% ; P<0.05). There was no significant change in the peripheral blood or the peritoneal fluid between the two groups. Additionally, ovarian endometrioma increased the proportion of ILCs (ILC1 : 0.92 ± 1.12%, ILC2 : 0.08 ± 0.08%, ILC3 : 0.70 ± 0.39%) compared to the endometrium samples of patients with endometriosis each with P<0.05. Immunohistochemistry of IL-1β and IL-23, which are ILC3 inducing factors, showed no significant change in the H-score of the epithelium of the two groups, but a significant increase was found in ovarian endometrioma. **[Conclusion]** The proportion of ILC2 and 3 was reduced in the endometrium of patients with endometriosis, and ILCs were increased in ovarian endometrioma. Our findings may indicate a new immunological approach to understand the pathophysiology of endometriosis.

IS-WS-7-2

Tracing location by applying emerald luciferase in early phase of murine endometriotic lesion formation Wada Ikumi, Taniguchi Fuminori, Nagata Hiroki, Nakaso Takaya, Ikebuchi Ai, Moriyama Maako, Yamane Emiko, Nagira Kei, Azuma Yukihiko, Sato Eri, Harada Tasuku *Tottori University*

[Objective] Although the pathogenesis of endometriosis remains unclear, several hypotheses have been proposed, such as retrograde menstruation, Müllerian remnants, apoptosis defects, epigenetics, and genetics. We focused on the behavior of the ectopic endometrium, in the early period of endometriotic lesion formation. To observe the lesion formation non-invasively, we developed the novel endometriosis animal model using bioluminescence technology. **[Methods]** We established the transgenic mouse that expressed the Emerald luciferase (ELuc) derived by CAG promoter. The mice were ovariectomized and injected with E2 (0.5 or 0.2 μg/mouse). They were intraperitoneally injected with D-luciferin, and the bioluminescence of the whole body was detected using IVIS[®] Lumina imaging system. The correspondent rates between the location of bioluminescence

and that of actual observation were assessed. **[Results]** The accuracy of tracing by ELuc was high and depended on the dosage of E2 administration (100% of correspondent rate on Day3 at 0.5 µg/mouse of E2 dose). The correspondent rates at 0.2 µg/mouse of E2 dose were lower compared to the 0.5 µg/mouse both on Days 3 and 14. The bioluminescence signals of ELuc could be detected non-invasively over time. Signals on the pancreas and suture site were detected on Day 1, and on the pancreas, they remained almost at the same position on Day 7. In contrast, the signals around the suture sites were decreased. **[Conclusion]** In the early phase after transplantation, the process of lesion formation can be observed non-invasively and chronologically. Our mouse model has the advantage of tracing the migration of grafts, because even small grafts possess strong emissions.

IS-WS-7-3

Increased CCL26 expression and its involvement with epithelial-mesenchymal transition in human endometrium with adenomyosis Ikebuchi Ai, Taniguchi Fuminori, Wada Ikumi, Nagata Hiroki, Nakaso Takaya, Moriyama Maako, Yamane Emiko, Azuma Yukihiro, Sato Eri, Harada Tasuku *Totomi University*

[Objective] Adenomyosis is a common gynecologic disorder characterized by symptoms of dysmenorrhea, abnormal uterine bleeding, and infertility. We sought to analyze the expression profile of key factors concerning inflammatory cytokines in the endometrium with adenomyosis, and the involvement with epithelial mesenchymal transition (EMT). **[Methods]** Eutopic endometrial tissues in secretory phase from premenopausal women with (n=3) or without (n=3) adenomyosis were applied to the DNA array for inflammatory cytokines. Gene and protein expression were re-evaluated by RT-PCR (n=19) and immunohistochemistry (n=56). Immunohistochemical analyses using H-score of CCL26 and EMT related factors were performed in the uterine tissues resected for adenomyosis (n=37), including the cases operated after GnRHa treatment. **[Results]** Using the DNA array, we found the upregulated genes of *CCL26*, *IL-1B*, *CCL3* and downregulated genes of *C5*, *CXCL-9*. Within the upregulated genes, *CCL26* mRNA expression was obviously enhanced in the endometrium with adenomyosis than those without adenomyosis, in addition, H-score of CCL26 was increased in patients with severe pelvic pain. Immunohistochemical analysis revealed that CCL26 expression was markedly higher in the basal layer of endometrium with adenomyosis compared with those without adenomyosis, regardless of GnRHa treatment. CCL26 expression in the basal layer of endometrium positively correlated with the enhanced N-cadherin and ZEB1 expression. **[Conclusion]** CCL26 may be deeply involved in the pathogenesis of adenomyosis by inducing EMT in the basal layer of the endometrium.

IS-WS-7-4

Study for tissue origin of endometriosis by DNA methylome and histological findings Maekawa Ryo¹, Mihara Yumiko¹, Tamura Isao¹, Taketani Toshiaki¹, Tamura Hiroshi¹, Ota Yoshiaki², Ota Ikuko², Sugino Norihiro¹ *Yamaguchi University¹, Kawasaki Medical School², Kurashiki Heisei Hospital³*

[Objective] There are two hypotheses for the pathogenesis of endometriosis. One is endometrial implantation by retrograde of menstrual blood, and the other is celomic metaplasia, in which visceral and parietal peritoneum undergo metaplastic change. However, the conclusion has not been reached. **[Methods]** 1) DNA methylome were compared among the cystic wall and peritoneal adhesion regions of ovarian endometrioma (OE-cyst and OE-adhesion, respectively), blueberry spots, and normal tissues of the endometrium, peritoneum, and ovary by hierarchical

clustering analysis. 2) The lesions from OE-adhesion to OE-cyst were histologically examined. **[Results]** 1) OE-cyst and OE-adhesion were distinctly different from the endometrium. OE-cyst was close to the ovary. OE-adhesion and blueberry spot presented the same profile and were close to the peritoneum. 2) OE-cyst showed an ovarian surface epithelium (OSE)-like structure near the OE-adhesion, which was continuously connected to a cylindrical epithelium structure. Expression of calretinin, a mesothelial marker, was strong in the OSE-like region but decreased in the cylindrical epithelium. The estrogen receptor (ER) expression was absent in the OSE-like region but was clearly expressed in the cylindrical epithelium region. OE-adhesion showed an endometrial glands-like structure with ER expression. **[Conclusion]** The implanted endometrium is unlikely to grow and form OE. We hypothesize that OE is caused by 1) Endometrium implants to the peritoneum and forms the peritoneal lesion. 2) Ovary adheres to the peritoneal lesion. 3) Repeated bleeding from the peritoneal lesion and inflammation forms inclusion cyst in the ovary, which is OE. The cyst wall is lined by OSE cells with partial metaplasia.

IS-WS-7-5

Different DNA methylome, transcriptome, and histological features in uterine leiomyomas with and without MED12 mutations Tamehisa Tetsuro, Maekawa Ryo, Sato Shun, Sakai Takahiro, Mihara Yumiko, Taketani Toshiaki, Tamura Hiroshi, Sugino Norihiro *Yamaguchi University Hospital*

[Objective] Somatic mutations in Mediator complex subunit 12 (MED12) have been reported as a biomarker of uterine leiomyomas (ULs), being detected in 70% of ULs. However, the role of MED12 mutations is still unclear in the pathogenesis of ULs. Here, we investigated the differences in DNA methylome, transcriptome, and histological features between ULs with and without MED12 mutations. **[Methods]** DNA methylomes and transcriptomes were examined in MED12m-positive (n=6) and -negative (n=9) ULs and myometrium (n=6). 1) Hierarchical clustering profiled the tissues based on DNA methylomes. 2) Differentially expressed genes in comparison with the myometrium were subjected to gene ontology enrichment analysis (GO). 3) Genes that contribute to key functions in each MED12m-positive and -negative ULs were detected by weighted gene co-expression network analysis and subjected to GO. 4) The amounts of collagen fibers and the number of blood vessels were histologically evaluated. **[Results]** 1) The myometrium, MED12m-positive, and MED12m-negative ULs were independently clustered. 2), 3) MED12m-positive ULs had increased extracellular matrix formation activities and decreased angiogenic activities. On the other hand, MED12m-negative ULs had increased angiogenic activities and decreased extracellular matrix formation activities. 4) MED12m-positive ULs had a higher collagen amount than MED12m-negative ULs, whereas MED12m-negative ULs had more blood vessels than MED12m-positive ULs. **[Conclusion]** MED12m-positive and -negative uterine fibroids had different profiles of DNA methylation and gene expression, and different histological features. MED12m-positive ULs form the tumor with a rich extracellular matrix and poor blood vessels compared to MED12m-negative ULs, suggesting MED12 mutations affect the tissue composition of ULs.

IS-WS-8-1

Establishment of a Novel In Vitro Model of Endometriosis with Oncogenic KRAS and PIK3CA Mutations for Understanding the Underlying Biology and Molecular Pathogenesis Kanno Kousuke, Nakayama Kentaro, Hossain Mohammadmahmud, Shanta Kamrunnahar, Sultana Razia,

Ishikawa Masako, Ishibashi Tomoka, Yamashita Hitomi, Sato Seiya, Iida Koji, Kyo Satoru *Shimane University Hospital*
[Objective] Endometriosis-harboring cancer-associated somatic mutations of PIK3CA and KRAS provides new opportunities for studying the multistep processes responsible for the functional and molecular changes in this disease. We aimed to establish a novel in vitro endometriosis model to clarify the functional behavior and molecular pathogenesis of this disorder. **[Methods]** Immortalized HMOsisEC10 human ovarian endometriotic epithelial cell line was used in which KRAS and PIK3CA mutations were introduced. Migration, invasion, proliferation, and microarray analyses were performed using KRAS and PIK3CA mutant cell lines. **[Results]** In vitro assays showed that migration, invasion, and proliferation were significantly increased in KRAS and PIK3CA mutant cell lines, indicating that these mutations played causative roles in the aggressive behavior of endometriosis. Microarray analysis identified a cluster of gene signatures; among them, two significantly upregulated cancer-related genes, lysyl oxidase (LOX) and pentraxin3 (PTX3), were associated with cell proliferation, invasion, and migration capabilities. Furthermore, siRNA knockdown of the two genes markedly reduced the metastatic ability of the cells. These results suggest that endometriosis with KRAS or PIK3CA mutations can significantly enhance cell migration, invasion, and proliferation by upregulating LOX and PTX3. **[Conclusion]** We propose that LOX and PTX3 silencing using small molecules could be an alternative therapeutic regimen for severe endometriosis.

IS-WS-8-2

Evaluation of bioavailable testosterone in female athletes with low dose estrogen-progestin Kawasaki Yu¹, Ozaki Rie¹, Matsumura Yuko¹, Ochiai Asako¹, Kitamura Eri¹, Takeuchi Shiori¹, Ikuma Shinichiro¹, Okada Yukiko¹, Murakami Keisuke¹, Kitade Mari¹, Itakura Atsuo¹, Matsuda Takao² *Juntendo University Hospital, Juntendo University¹, Institute of Sport Medicine, National Hospital Organization Nishibeppu National Hospital²*
[Objective] The use of Low-dose estrogen-progestin (LEP) for female athletes with menstrual symptoms is becoming more common. While there are tremendous benefits to avoiding the effects of menstruation on athletic performance and improving dysmenorrhea, the decrease in testosterone associated with LEP medication can reduce athletic performance. In testosterone assessment, it is not sufficient to measure total testosterone (TT) or evaluate free testosterone (FT), but it is essential to evaluate calculated bioavailable testosterone (cBAT). **[Methods]** Patients who visited the outpatient clinic for female athletes with dysmenorrhea were included in this study. We measured TT, FT, albumin, and SHBG, calculated cBAT, and evaluated the changes before and 3 to 6 months after treatment with LEP containing levonorgestrel (group L : n=8) and LEP containing drospirenone (group D : n=7) **[Results]** There was no significant difference in TT and FT decrease between D and L groups (TT, D : -27.4 ± 29.7% vs. L : -15.5 ± 22.7% p=0.40 and FT, D : -43.6 ± 22.7% vs. L : 87.7 ± 330.5% p=0.32). In SHBG, the D group showed a significant increase after oral administration over the L group (D : 183.3 ± 147.5% vs L : 17.4 ± 73.7% p=0.01), resulting in a significant decrease in cBAT in the D group (D : -64.6 ± 17.3% vs L : -4.20 ± 37.6% p<0.01). **[Conclusion]** LEP containing drospirenone causes a reduction in cBAT compared to LEP containing levonorgestrel. In the case of female athletes whose performance is affected by LEP medications, the choice of LEP may need to be made with reference to cBAT.

IS-WS-8-3

Novel Myoma Score to Aid Selection of the Optimal Minimally Invasive Surgery Platform for Myectomy Huang

Kuan-Ju¹, Li Ying-Xuan², Wu Chin-Jui³, Chang Wen-Chun², Wei Lin-Hung², Sheu Bor-Ching² *National Taiwan University Hospital Yunlin Branch, Taiwan¹, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan², National Taiwan University Hospital Hsin-Chu Branch, Taiwan³*

[Objective] Minimally invasive myomectomy has evolved over the recent years, including single-incision laparoscopic surgery (SILS), 2-port laparoscopic surgery (TPA), conventional laparoscopic surgery (CL), and robotic-assisted myomectomy (RM). However, the indications of each surgical platform remain undefined. **[Methods]** The study retrospectively evaluated patients receiving minimally invasive myomectomy within a single tertiary hospital between 2015 and 2019. A myoma score was developed based on contributing factors and used to compare groups. **[Results]** 322 patients (35, 155, 48, and 84 patients in SILS, TPA, CL, and RM, respectively) were included. The baseline characteristics were similar, but myoma burden, including size, number, weight and volume, was the greatest in RM group. Operation time also differed significantly (RM 184.11, SILS 141.14, CL 125.96, and TPA 104.31 minute). Linear regression was used to calculate the association between major factors and operation time, and 3 tiers were applied to myoma size and number, whereas 2 tiers were used for BMI and FIGO subclassification. In total, the myoma score for each patient ranged from 4 to 10. The myoma score not only matches operation time within the cohort, but also in the range of estimates for most published literature. **[Conclusion]** The myoma score is useful in preoperative evaluation and referral to specialists. SILS is the method of choice when considering cosmetic outcome. TPA is easy to perform, easily available, and cost-effective. For difficult myomas, CL remains of critical value; in cases when CL is not considered, RM may be preferred if cost is agreeable.

IS-WS-8-4

The learning curve in vaginal pelvic reconstruction surgery for severe pelvic organ prolapse : Analysis of the cumulative summation test (CUSUM) Wu Chin-Jui *National Taiwan University, HsinChu Branch, Taiwan*

[Objective] Determination of the learning curve in vaginal pelvic reconstructive surgery. **[Methods]** With cumulative summation (CUSUM) analysis of surgical failure and operation time, we assessed the learning curve of vaginal pelvic reconstructive surgery, including sacrospinous ligament fixation, anterior colporrhaphy, posterior colporrhaphy, optional vaginal hysterectomy with or without mesh placement. **[Results]** Two hundred and sixty-four women with stage III or IV pelvic organ prolapse underwent vaginal pelvic reconstructive surgery procedures. Based on surgical failure and operation time, surgical proficiency was achieved in 32-54 vaginal pelvic reconstructive surgery procedures without mesh and 37-61 procedures in the same surgery with mesh. The surgical success rate for surgeons A and B were 82.2% and 94.1%, with a median follow-up time of 60 and 33 months, respectively. **[Conclusion]** The learning phase of vaginal pelvic reconstructive surgery in advanced pelvic organ prolapse in this institutional cohort required 54 and 61 procedures, respectively. A higher number of procedures were required for the learning curve of vaginal pelvic reconstructive surgery with mesh. Having crossed the boundary of proficiency, surgical success rate and operation time were improved.

IS-WS-8-5

Clinical outcome of a Multidisciplinary Team for Long-term Management of Cloacal Anomalies : vaginoplasty for persistent cloaca Kobayashi Akiko, Nishikawa Nobumichi, Yachida Nozomi, Shima Eiri, Ishiguro Tatsuya, Sekine Masayuki,

Enomoto Takayuki *Niigata University Medical & Dental Hospital*

[Objective] Cloacal anomalies require treatment and care according to the life stages of infancy, childhood, and adolescence. The treatment should primarily secure the defecation and urinary organs, which is related to life support, but when the life stage advances, it can necessitate reconstructive surgery at adolescence for preventing menstrual obstruction. However, each case presents as a unique anomaly. To cope with these problems, a multidisciplinary team was formed in October 2018 followed by examination and treatment of each case. **[Results]** We had been discussed about 33 cases of cloacal anomalies, 9 cases of Persistent Cloaca, 6 cases of Cloacal exstrophy, 9 cases of Urogenital Sinus, 4 cases of MRKH type II, 4 cases of PORD. After the team was formed, two new children were born with cloacal exstrophy, two urogenital sinuses, and one with PORD. The team went through 21 joint surgeries. Of these, 7 were joint examinations under general anesthesia and 7 were gynecological surgeries. The gynecological procedures included unilateral hysterectomy, vaginoplasty, and cervicoplasty. We actively discussed the uterus, vagina, fallopian tubes, and ovaries under general anesthesia and in the presence of urologists and pediatric surgeons and were able to develop a treatment plan for the entire life of the patient. **[Conclusion]** Neonatal assessment of the urogenital tract accompanied by early identification of abnormal structure and function is therefore fundamental to minimize the impact of any urogenital condition on the child's overall health.

IS-WS-8-6

Epidemiological, Clinical Aspects and Treatment of Victims of Child Sexual Abuse in the Gynaecology and Obstetrics Department of Karnataka Institute of Medical Sciences Hubballi Raju Sowrirajalu Ashwini, Puneetha Naik *Karnataka Institute of Medical Sciences, India*

[Objective] Draw up an epidemiological profile of Child Sexual Abuse victims Develop the treatment protocol **[Methods]** This is a 2-year descriptive retrospective study. Included in this study were patients who were the victims of child sexual abuse. For each case, the following parameters were studied: the epidemiological characteristics (age, gestation, parity and place of residence), the circumstances of the abuse (time and place), the characteristics of the aggressor (age, link with the victim, number of aggressor), the type of sexual contact, the possible lesions found during the physical examination (genital and extragenital), the mode of admission, the delay of the consultation, the attitude after the sexual abuse, the gynecological and obstetrical status of the victim, the repercussions and psychological follow-up, the paraclinical assessment, the treatments administered. Data were collected using a survey form and analysed with SPSS software. **[Results]** 15 to 17 age group was the most represented. Students were the most represented among victims of sexual abuse (87.4%). The average age of the alleged attackers was 20-30 when they were known to their victim. Among those who were in genital activity, 38 cases of pregnancy were reported; which represented 33.33% of cases. After the clinical examination, 50% of the victims had received antibiotic prophylaxis. **[Conclusion]** Child Sexual abuse is currently a real socio-cultural drama. Preventing them involves raising public awareness. Obstetricians and other specialists should be aware of their early management and should adapt proper treatment protocols in order to prevent sexually transmitted infections and psychological consequences.

IS-WS-9-1

Elucidation of the Mechanism of Intrauterine Administration

of Peripheral Blood Mononuclear Cells (PBMC) Treatment for Recurrent Implantation Failure Kitawaki Yoshimi, Yanai Akihiro, Ohara Tsutomu, Nakakita Baku, Sagae Yusuke, Okunomiya Asuka, Horie Akihito, Mandai Masaki *Kyoto University*

[Objective] We have been providing intrauterine cavity administration of PBMC (IC-PBMC) treatment for recurrent implantation failure (RIF) patients, which improved IVF success rate. However, the precise mechanisms of the effect have been poorly elucidated. The aim of this study is to investigate responsible factors and in vivo effect of IC-PBMC. **[Methods]** PBMCs are cultured with hCG for 48 hours before intrauterine administration. Therefore we examined cell populations in human PBMCs cultured for 48 hours by flow cytometry (i) and cytokine profiles in PBMC conditioned media (CM) by cytokine arrays (ii). We also evaluate the efficacy of IC-PBMC in a RIF mouse model injected with progesterone antagonist RU486. In these experiments, PBMCs were cultured with or without hCG to examine the effect of hCG-activated PBMCs. **[Results]** (i) Lymphocytes, especially T-cell populations were higher, while classical monocytes were lower in cultured PBMCs compared with fresh PBMCs. Cell populations did not change by hCG. (ii) Cytokines (IL-8, RANTES, MIP-1beta, EGF, LIF) which were presumed to promote embryo implantation were detected in PBMCs CM. The expression of these cytokines tended to increase in hCG-activated PBMCs CM, but the difference was not significant. (iii) IC-PBMC with/without hCG significantly improved pregnancy rate of RIF model mice (69%, 61% vs 15%, respectively). The number of implantation sites was highest in PBMCs-with-hCG treatment group. **[Conclusion]** Our data suggest that IC-PBMC can contribute IVF success in RIF patients with progesterone effect insufficiency, and hCG could enhance this IC-PBMC effect.

IS-WS-9-2

The essential glucose transporter GLUT1 is epigenetically upregulated by C/EBP β and WT1 during decidualization of human endometrial stromal cells Tamura I Sao, Fujimura Taishi, Tanaka Yumiko, Shirafuta Yuichiro, Mihara Yumiko, Maekawa Ryo, Taketani Toshiaki, Tamura Hiroshi, Sugino Norihiro *Yamaguchi University*

[Objective] We previously reported that glucose uptake by human endometrial stromal cells (ESCs) increases during decidualization, and that glucose is indispensable for decidualization. Although glucose transporter 1 (GLUT1) is up-regulated during decidualization, it remains unclear whether it is involved in glucose uptake. Here, we attempted to determine the role of GLUT1 during decidualization as well as the mechanisms underlying its up-regulation. **[Methods]** Primary ESCs were incubated with cAMP to induce decidualization. Knockdown was performed with siRNA. Glucose uptake was examined by a 2-deoxyglucose uptake assay. GLUT1 promoter analysis was performed by ChIP assay and luciferase assay. **[Results]** cAMP increased glucose uptake with the induction of IGFBP-1 and PRL, specific markers of decidualization. Knockdown of GLUT1 suppressed them. To investigate the regulation of GLUT1 expression, we focused on CCAAT enhancer-binding protein β (C/EBP β) and Wilms tumor 1 (WT1) as the upstream transcription factors regulating GLUT1 expression. Knockdown of either C/EBP β or WT1 suppressed cAMP-increased GLUT1 expression and glucose uptake. cAMP treatment also increased the recruitment of C/EBP β and WT1 to the GLUT1 promoter region. Interestingly, cAMP increased the H3K27 acetylation (H3K27ac) and p300 (a cofactor with histone-acetyltransferase) recruitment in the GLUT1 promoter region. Knockdown of C/EBP β or WT1 inhibited these events, indicating that both C/EBP β and WT1 work as pioneer factors inducing H3K27ac by recruiting p300 to the

GLUT1 promoter region during decidualization. **[Conclusion]** GLUT1 is involved in the glucose uptake in ESCs during decidualization. C/EBP β and WT1 are up-regulators of GLUT1 through the induction of epigenetic changes in the GLUT1 promoter by recruiting p300.

IS-WS-9-3

Role of PROK1 in decidua of patients with unexplained recurrent pregnancy loss showing insulin hypersecretion Goto Shinobu^{1,2}, Ozawa Fumiko², Kitaori Tamao^{1,2}, Yoshihara Hiroyuki^{1,2}, Ozaki Yasuhiko^{2,3}, Sugiura Mayumi^{1,2} Nagoya City University Hospital¹, Research Center for Recurrent Pregnancy Loss, Nagoya City University Hospital², Nagoya City University West Medical Center³

[Objective] Prokineticin1 (PROK1) is an angiogenic factor that is regulated by hypoxia and insulin. PROK1 is produced during endometrial decidualization and plays an important role in embryonic implantation and placentation. In this study, we investigated the role of PROK1 in decidua in patients with unexplained recurrent pregnancy loss (RPL) with relation to the HOMA- β index (a measure of insulin secretion calculated by fasting blood glucose and insulin levels). **[Methods]** Forty patients with unexplained RPL were included. The expression of PROK1 in decidua was examined by immunohistochemistry (IHC). According to the combination of high or low HOMA- β levels and normal (NC) or abnormal (AC) chorionic chromosomes, 40 cases were divided into four groups (HOMA- β high-NC : 8 cases, low-NC : 12 cases, high-AC : 8 cases, low-AC : 12 cases). The expression levels of PROK1 and IGFBP-1, which is an indicator of decidualization, were measured by ELISA, and the PROK1/IGFBP-1 ratio was compared in each group. All samples were collected with informed consent under the approval of the university ethical committee. **[Results]** The co-localization of PROK1 and IGFBP-1 was observed in decidua by IHC. The PROK1/IGFBP-1 ratio was significantly higher in the group with high HOMA- β and normal chorionic chromosomes compared to the other three groups ($p < 0.001$). **[Conclusion]** We reported for the first time that the PROK1/IGFBP-1 ratio in decidua was elevated in RPL patients showing insulin hypersecretion with normal chromosome miscarriage. It was suggested that insulin overproduction may cause impaired decidualization and excessive PROK1 production.

IS-WS-9-4

Distribution of the follicular and luteal phase length and their age-dependent change in Japanese women : an analysis of big data Mitake Sawa¹, Hiraike Osamu¹, Fujii Tomoyuki², Osuga Yutaka¹ The University of Tokyo¹, Sanno Hospital²

[Objective] Current definition of normal menstrual period is defined as 25-38 days in Japan, but the original data is apparently outdated. We aimed to establish exact length of follicular and luteal phase using a big data. **[Methods]** More than 300,000 subjects' data registered with a smartphone application were collected from January 1, 2015, to December 31, 2019, and were analyzed in this retrospective study. Data showing biphasic basal body temperature were extracted based on the Sensiplan method ; data with a high temperature that lasts no less than 10 days were defined as luteal phase, and data with a low temperature that lasts more than 3 days was defined as follicular phase. Appropriate period was defined as no longer than 80 days. **[Results]** We extracted more than 8 million data from more than 80,000 subjects that met our criteria. The mean duration of the luteal phase was 13.0 (range : 11-15) days, and the mean duration of the follicular phase was 17.1 (range : 12.5-22.2) days. The duration of the follicular phase was found to shorten as participants age, and this tendency became evident in their 40s. **[Conclu-**

sion] Although there are several limitations, this study revealed current distribution of the follicular and luteal phases, which may help women in reproductive age to understand the status of their own menstrual cycle. In addition, the shortening of the duration of the follicular phase in women in their 40s might suggest that there may be a relationship between the duration of the follicular phase and fecundity.

IS-WS-9-5

Involvement of BMP-15 in glucocorticoid actions on ovarian steroidogenesis by rat granulosa cells Kashino Chiaki¹, Hasegawa Toru^{1,2}, Kamada Yasuhiko¹, Masuyama Hisashi¹, Otsuka Fumio² Okayama University Hospital¹, Department of General Medicine, Okayama University Hospital²

[Objective] To elucidate the impact of glucocorticoids on ovarian steroidogenesis and its molecular mechanism by focusing on bone morphogenetic proteins (BMPs). **[Methods]** Granulosa cells isolated from female immature rats were treated with follicle-stimulating hormone (FSH) in the presence of dexamethasone (Dex) in serum-free conditions. After treatment with Dex for 48 h, the changes of estradiol and progesterone production and cAMP synthesis induced by FSH treatments were measured by ELISA. Total RNAs of granulosa cells treated with FSH, Dex and BMPs were extracted and mRNA levels of steroidogenic factors and enzymes, BMP receptors, Id-1 and glucocorticoid receptor (GR) were quantified by real-time RT-PCR. Phosphorylation of Smad1/5/9 induced by BMPs was evaluated by Western blotting in the presence or absence of Dex. **[Results]** Dex treatment dose-dependently decreased estradiol production but increased progesterone production induced by FSH. In accordance with the effects of Dex on estradiol synthesis, Dex suppressed P450arom mRNA expression and cAMP synthesis induced by FSH. Dex treatment in turn enhanced basal as well as FSH-induced levels of mRNAs encoding the enzymes for progesterone synthesis including P450scc and 3 β HSD. Of note, Dex treatment significantly upregulated transcription of the BMP target gene Id-1 and Smad1/5/9 phosphorylation in the presence of BMP-15 among the key ovarian BMP ligands. It was also found that Dex treatment increased the expression level of BMP15 type-I receptor ALK-6. On the other hand, BMP-15 treatment upregulated GR expression in granulosa cells. **[Conclusion]** It was revealed that glucocorticoids elicit differential effects on ovarian steroidogenesis, in which GR and BMP-15 actions are mutually enhanced in granulosa cells.

IS-WS-9-6

Deletion of a mouse retrovirus-derived cell fusion suppressor gene induces abnormal placental formation Sugimoto Jun, Kudo Yoshiki Hiroshima University

[Objective] Suppressyn is one of the first human proteins to be identified that inhibits cell-cell fusion. Its limited expression in the placenta and ability to inhibit the syncytin-1 induced cell fusion suggests possible involvement in normal and abnormal placental development. Here, we assessed fetal and placental development in a knockout mouse lacking a gene encoding a cell fusion inhibitor to further evaluate a potential *in vivo* function for human suppressyn. **[Methods]** Previously, we isolated a mouse ERV-derived gene sequence (C11). It is not homologous to human suppressyn gene but has same functional effects at the protein level. The mice with homozygous deletions of this gene were mated to assess fetal and placental development. Immunohistochemical analysis was performed using mouse placentas that isolated across E8.5-E18.5 of gestation. **[Results]** The progeny of C11 deficient mouse displayed intrauterine fetal death and/or intrauterine fetal growth restriction. Abnormalities in fetal growth were associated with abnormal placental develop-

ment, most notably detected at E12.5-14.5 and affecting trophoblast cells in labyrinth zone, as confirmed by staining for E-cadherin. **[Conclusion]** ERV-derived anti-fusogens appear to be involved in human and murine placental and fetal growth development. Further analysis of those mechanisms should expand our understanding of the role of ERV-derived proteins in murine as well as human placental development. It should help to define the role for human suppressin in placental health and disease.

IS-WS-10-1

Are ovarian cancer spheroids composed of only cancer cells? : the detailed observational findings with multi-photon microscopy Uno Kaname¹, Yoshihara Masato¹, Sugiyama Mai², Koya Yoshihiro², Fujimoto Hiroki¹, Mogi Kazumasa¹, Kitami Kazuhisa¹, Iyoshi Shohei¹, Yamakita Yoshihiko², Nawa Akihiro², Kajiyama Hiroaki¹ *Nagoya University Hospital¹, Bell Research Center, Nagoya University Hospital²*

[Objective] More than 50% of ovarian cancer (OvCa) patients are diagnosed with ascites full of cancer spheroids, which are recently thought to comprise hetero-cellular components. We aimed to reveal the component and characteristics of OvCa spheroids. **[Methods]** We have evaluated the differences of OvCa spheroids in PDS and IDS samples. OvCa spheroids were evaluated by using multiphoton microscopy. Invasion ability to collagen or mesothelial monolayer were investigated. We also performed apoptosis detection assay and RNA sequence for these OvCa spheroids. **[Results]** OvCa spheroids in IDS were more strict and round shape than those in PDS (33vs23cells/2,000 μm^2 , $p=0.002$, roundness 0.71vs0.54/sphere, $p<0.001$). We revealed that almost all OvCa spheroids included mesothelial cells (MCs) which could be identified with HBME-1 staining. The rate of MCs in spheroids were higher in IDS spheroids (4% vs16%, $p<0.01$). OvCa cells rapidly generated strict spheroids with MCs compared with OvCa cells alone (fluorescence-area 320vs460 μm^2 /24hrs, $p=0.002$). OvCa spheroids with MCs rapidly invaded into collagen gels (933vs312 μm /72hrs, $p<0.001$). Surprisingly, MCs invaded at first, and then OvCa cells followed. The percentage of apoptosis of OvCa cells with cisplatin were significantly less when they made spheroids with MCs than OvCa cells alone (5.7%vs25.2%, $p<0.001$). RNA sequence revealed high level of TGF- β -related pathway and FSCN1 was upregulated in mesothelial cells in spheroids (gene-counts : 23.5%, $p=0.013$). Blocking FSCN1 in MCs showed decrease of these aggressive features. **[Conclusion]** We revealed that OvCa cells and MCs compose cancer spheroid. These hetero-cellular spheroids are aggressive invasion and migration via TGF- β -FSCN1 axis, and resistant for conventional chemotherapy.

IS-WS-10-2

How peritoneal microenvironment promotes ovarian cancer dissemination?—A mesothelial cell lineage tracing using conditional knock-in mouse— Mogi Kazumasa¹, Yoshihara Masato¹, Uno Kaname¹, Kitami Kazuhisa¹, Iyoshi Shohei¹, Fujimoto Hiroki¹, Sugiyama Mai², Koya Yoshihiro², Yamakita Yoshihiko², Nawa Akihiro², Kajiyama Hiroaki¹ *Nagoya University Hospital¹, Bell Research Center, Nagoya University²*

[Objective] Cancer-associated mesothelial cells (CAMs) have been reported to promote ovarian cancer (OvCa) progression in the peritoneal microenvironment. In this study, we evaluated how CAMs behaved and promoted tumor microenvironment with conditional knock-in mouse and various *in silico* omics analyses. **[Methods]** We established an *in vitro* peritoneal metastatic invasion model and visualized fluorescent labeled-cell behavior by 3D-construction. Wt1^{CreERT2}/ROSA26-LSL-tdTomato mice were conditional knock-in mice that selectively expressed tdTomato (red-fluorescent protein) in mesothelial cells (MCs).

We intraperitoneally injected ID8 cells to these mice and observed the behavior of MCs in peritoneally disseminated tumors. In addition, cell viability of OvCa cells co-cultured with CAMs and normal MCs were evaluated by apoptosis detection assay and transcriptome analysis was performed. **[Results]** Morphological changes and elevation of mesenchymal markers were observed in CAMs and its relevance was confirmed by proteome analysis. The 3D-construction imaging demonstrated that OvCa cells invaded with CAMs into extracellular matrix beneath the layer of MCs (846 μm vs 261 μm , $p<0.05$). In conditional knock-in mouse, histopathology of ID8 peritoneal tumors revealed that tdTomato-positive MCs were recruited into the tumor (account for 20.6% area). Transcriptome analysis suggested PI3K/Akt pathway played a crucial role in OvCa cells induced by stimulation of CAMs (3.84-fold change). Moreover, we found acquired platinum-resistance in OvCa cells co-cultured with CAMs by apoptosis detection assay (24.6% vs. 9.93%, $p<0.05$). **[Conclusion]** Our results suggest that CAMs transform into tumor stromal cells, promoting the progression of peritoneal dissemination of OvCa and the acquisition of platinum-resistance.

IS-WS-10-3

Docetaxel-mediated TNF-alpha upregulation synergistically enhances SMAC Mimetic activity in Ovarian Cancer Shibuya Yusuke *Sendai City Hospital*

[Objective] Inhibitor of apoptosis (IAP) proteins are frequently upregulated in ovarian cancer, resulting in the evasion of apoptosis and enhanced cellular survival. Birinapant, a synthetic second mitochondrial activator of caspases (SMAC) mimetic, suppresses the functions of IAP proteins in order to enhance apoptotic pathways and facilitate tumor death. Despite on-target activity, however, pre-clinical trials of single-agent birinapant have exhibited minimal activity in the recurrent ovarian cancer setting. The objective of this study is to augment the therapeutic potential of birinapant. **[Methods]** We utilized a high-throughput screening matrix to identify synergistic drug combinations. **[Results]** Of those combinations identified, birinapant plus docetaxel was selected for further evaluation, given its remarkable synergy both *in vitro* and *in vivo*. We show that this synergy results from multiple convergent pathways to include increased caspase activation, docetaxel-mediated TNF- α upregulation, alternative NF- κB signaling, and birinapant-induced microtubule stabilization. **[Conclusion]** Docetaxel-mediated TNF- α upregulation synergistically enhances SMAC Mimetic activity in Ovarian Cancer. These findings provide a rationale for the integration of birinapant and docetaxel in a phase 2 clinical trial for recurrent ovarian cancer where treatment options are often limited and minimally effective.

IS-WS-10-4

Repurposing penfluridol in combination with paclitaxel for treatment of epithelial ovarian cancer Chang Chi-Son, Ryu Ji-Yoon, Lee Yoo-Young, Choi Chel Hun, Kim Tae-Joong, Kim Byoung-Gie, Lee Jeong-Won *Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*

[Objective] Epithelial ovarian cancer (EOC) has a poor prognosis because of high recurrence rate due to chemoresistance, and there is a need to find new therapeutic drugs. Previous studies showed antipsychotic drugs to have anticancer effects. In this study, we investigated the anticancer potential of penfluridol, an antipsychotic drug used in schizophrenia, on ovarian cancer cell lines. **[Methods]** *In vitro*, EOC cell lines were treated with penfluridol and cell survival was assessed using MTT assay. Furthermore, we evaluated the synergistic effect of penfluridol with paclitaxel on EOC cell lines. *In vivo* experiments were performed to test the effect of penfluridol and paclitaxel combina-

tion on tumor growth in orthotopic mouse xenografts of EOC cell lines. **[Results]** Penfluridol significantly reduced cell proliferation in chemosensitive (A2780, HeyA8, SKOV3ip-1) and chemoresistant (A2780-CP20, HeyA8-MDR, SKOV3-TR) EOC cells with time and dose dependent manner. In chemoresistant cell lines (HeyA8-MDR, SKOV3-TR), penfluridol and paclitaxel combination showed significantly reduced cell proliferation compared to the control, paclitaxel alone, or penfluridol alone. In xenograft mouse models of EOC using HeyA8, mice treated with penfluridol showed significantly reduced tumor weight compared to control group, but showed similar effect with paclitaxel alone or penfluridol and paclitaxel combination group. In model with HeyA8-MDR, mice treated with the combination of penfluridol and paclitaxel had significantly decreased tumor weight than the control, paclitaxel alone, or penfluridol alone groups. **[Conclusion]** Penfluridol might be a potential therapeutic drug for EOC, especially by combination with paclitaxel in chemoresistant ovarian cancer.

IS-WS-10-5

The identification of miRNAs associated with bevacizumab resistance in ovarian cancer Yagi Taro, Sawada Kenjiro, Miyamoto Mayuko, Nakamura Koji, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Kimura Tadashi *Osaka University*

[Objective] Bevacizumab (Bev) plays a key role in ovarian cancer (OC) treatment; however, Bev resistance is often seen in clinical setting. The aim of this study is to identify miRNAs associated with resistance and elucidate its mechanism. **[Methods]** ID-8 murine ovarian cancer cells were injected intraperitoneally into C57BL/6 mice: after Bev or control IgG administration was conducted twice weekly for 6 weeks, mice were sacrificed and RNA was extracted from the disseminated tumors. We performed miRNA microarray and TaqMan assays to identify miRNAs and genes which were altered by Bev treatment. We chose miR-143-3p and elucidated its role during the acquisition of Bev resistance. **[Results]** We selected miR-143-3p because TCGA database revealed low expression of miR-143-3p was significantly associated with poor prognosis. In silico and functional analyses revealed miR-143-3p targeted SERPINE1 and negatively regulated PAI-1 expression. In TCGA, higher PAI-1 expression was associated with poor prognosis of patients who received Bev, suggesting its role in Bev resistance. Recombinant PAI-1 treatment to HUVECs enhanced in vitro tube formation despite of Bev treatment. Transfection of miR-143-3p suppressed PAI-1 secretion from OC cells and inhibited HUVECs' in vitro angiogenesis. MiR-143-3p overexpressing ID-8 cells were constructed, intraperitoneally inoculated into C57BL/6 mice. ID-8/miR-143-3p cells revealed PAI-1 downregulation in tumor, attenuated angiogenesis and significantly inhibited intraperitoneal tumor growth by Bev treatment. **[Conclusion]** Continuous Bev treatment downregulates miR-143-3p which causes PAI-1 upregulation leading to alternative angiogenesis in OC. The substitution of this miRNA during Bev treatment may suppress Bev resistance, suggesting novel strategy for clinical settings.

IS-WS-10-6

Metastatic unit in ascites mediates progression of peritoneal dissemination and therapeutic resistance of advanced ovarian cancer Yoshihara Masato¹, Uno Kaname¹, Kitami Kazuhisa¹, Mogi Kazumasa¹, Iyoshi Shohei¹, Fujimoto Hiroki¹, Sugiyama Mai², Koya Yoshihiro², Yamakita Yoshihiko², Nawa Akihiro², Kajiyama Hiroaki¹ *Nagoya University¹, Bell Research Center, Nagoya University²*

[Objective] Positive ascites-cytology is one of the most negative prognostic factors in ovarian cancer (OvCa); however, we

hardly recognize its biologic impact for peritoneal progression and therapeutic resistance in advanced-stage. This study investigated the existence of metastatic unit (MU), cluster of OvCa cells, in ascites and how MU mediates development of refractory OvCa. **[Methods]** We microscopically evaluated morphology of MU in ascites cytology among patients with stage IIIC OvCa, who received primary debulking surgery (PDS) or neoadjuvant chemotherapy followed by interval debulking surgery (NAC-IDS) with immunofluorescence. Additionally, we clinically investigated prognostic impact of presence of MU in patients received PDS or NAC-IDS among 4730 OvCa patients under central pathological review. **[Results]** In all slides of positive ascites-cytology, MU comprised 25 or more OvCa cells, were identified (n=56). Interestingly, circularity-index and cell-density were significantly higher in NAC-IDS than PDS patients (circularity-index: 0.708 vs. 0.545, p<0.001; cell-density: 16.4x 10³ vs. 11.1x10³/μm², p<0.001), which implied that chemotherapy induced MU to be mechanistically condensed. In clinical analysis, presence of MU, positive ascites-cytology, was independently associated with poor prognosis regarding progression-free and overall survival in both PDS (n=191) and NAC-IDS patients (n=59). Surprisingly, the hazard of progression and death was higher in NAC-IDS than PDS patients (progression-free survival: 2.021 vs. 1.495; overall survival: 3.244 vs. 1.692), which indicated that presence of MU in NAC-IDS highly likely lead worse prognosis compared to that in PDS. **[Conclusion]** Collectively, the results highlighted the fact that MU promoted progression of peritoneal metastasis and therapeutic resistance of advanced OvCa.

IS-WS-10-7

Clinical indicators useful in decision-making about palliative chemotherapy for end-of-life ovarian cancer patients Hasegawa Kiyoshi, Wakai Kaori, Motegi Emi, Kousaka Nobuaki, Mitsuhashi Akira *Dokkyo Medical University Hospital*

[Objective] Palliative chemotherapy for end-of-life ovarian cancer patients is a complex and delicate problem. We evaluated whether active chemotherapy is beneficial for such patients using immune-inflammatory or nutritional parameters, and the PPI (Palliative Prognostic Index). **[Methods]** Forty-eight patients whose clinical data just before starting the last chemotherapy could be obtained among 65 patients who died from ovarian cancer from 2014 to 2020 were enrolled. Associations between the time from last chemotherapy to death and the following parameters were investigated: age, PS (performance status), NLR (neutrophil/lymphocyte ratio), PLR (platelet/lymphocyte ratio), mGPS (modified Glasgow prognostic score), PNI (prognostic nutritional index) score, CONUT (controlling nutritional status) score, and PPI score. **[Results]** The median age was 57 (range, 19-80) years. The median time from last chemotherapy to death was 45 (range, 11-110) days. Eleven patients (24.4%) died within 30 days of their last chemotherapy. In univariate analysis, median survival time was significantly shorter in patients with age ≥70, PS 3-4, higher NLR, mGPS 2, CONUT score ≥3, and higher PPI values. In multivariate analysis, mGPS 2 was only identified as independent prognostic factors for survival (hazard ratio: 4.25, 95% confidence interval: 1.20-13.45, p=0.022). **[Conclusion]** Parameters such as age, PS, NLR, mGPS, CONUT score, and PPI score may be indicators for discontinuation of palliative chemotherapy, and especially mGPS, evaluated by combining C-reactive protein and albumin values, may be simple and useful for predicting life expectancy for ovarian cancer patients.

IS-WS-11-1

Effect of Porphyromonas gingivalis infection of the placenta

on the risk of hypertensive disorders of pregnancy Oomori Yuriko, Nakamoto Kosuke, Tsunakake Megumi, Morioka Hirohiko, Teraoka Yuko, Nosaka Suguru, Sekine Masaki, Tomono Katsuyuki, Yamazaki Tomomi, Mukai Yurika, Koh Iemasa, Kudo Yoshiki *Hiroshima University*

[Objective] Periodontal disease has been reported to be associated with various systemic diseases. Inflammatory cytokines produced by periodontal disease and periodontal pathogens are thought to cause various systemic diseases by hematogenously spreading throughout the body. In obstetrics, periodontal disease has been reported to be one of the risk factors for hypertensive disorders of pregnancy (HDP), which can lead to serious prognosis for both mother and fetus. We also reported that the area of periodontal pockets showing inflammation was larger and serum *Porphyromonas gingivalis* (*P.g.*) antibody titer was higher in cases with HDP. However, the mechanism by which periodontal disease is involved in the development of HDP has not yet been clarified. In this study, we focused on *P.g.*, a major periodontal pathogen, and examined the effects of *P.g.* infection on the placenta. **[Methods]** In the cases of the patients who delivered at our hospital and had periodontal examination and serum *P.g.* antibody titer measurement as described above, immunohistochemical staining of the placenta for *P.g.* was performed. **[Results]** In the cases with HDP, *P.g.* colonization was observed in the placental tissues. *P.g.* was found in the villous interstitium and in the intravillous blood vessels. **[Conclusion]** We found that *P.g.*, a major periodontal pathogen, colonizes in the placenta of cases with HDP. *P.g.* may be hematogenously transferred to the placenta in cases of periodontal disease, and this may be involved in the development of HDP.

IS-WS-11-2

Simvastatin, a lipophilic statin, ameliorates preeclampsia in mice more potently than pravastatin, a hydrophilic statin Inaba Kei¹, Kumasawa Keichi¹, Miyatake Risa¹, Kanda Masako¹, Fujii Tatsuya¹, Sayama Seisuke¹, Seyama Takahiro¹, Iriyama Takayuki¹, Nagamatsu Takeshi¹, Fujii Tomoyuki^{1,2}, Osuga Yutaka¹ *The University of Tokyo Hospital¹, Sanno Hospital²*

[Objective] Pravastatin, a hydrophilic statin, is a promising agent for preeclampsia treatment. However, according to recent reports, the action of pravastatin is not immediate, thus necessitating alternative therapeutics in severe or rapidly deteriorating cases. We focused on simvastatin, a lipophilic statin that is more quickly absorbed and potent than pravastatin. This study investigated whether simvastatin is a potential therapeutic agent for preeclampsia when compared with pravastatin. **[Methods]** A mouse model of preeclampsia, established by narrowing both the abdominal aorta and vein (NAV), was administered simvastatin or pravastatin intraperitoneally daily. Blood pressure was measured by the tail-cuff method; the fetuses and placentas were weighed, and blood and organ tissues were collected at embryonic day 18.5 (E18.5). **[Results]** Mean arterial pressure at E18.5 significantly decreased in both simvastatin- and pravastatin-administered mice compared with that in NAV mice (79.3 ± 2.7 , 80.2 ± 3.5 , and 86.9 ± 2.0 mmHg; $n=8, 7$, and 14 ; $p < 0.001$ and $p < 0.001$, respectively). Fetal weight was also improved by simvastatin and pravastatin. The lowest dose of simvastatin was the most potent and reduced serum soluble fms-like tyrosine kinase-1 (sFlt-1) by 68.0% ($n=10$) of the average level in untreated NAV mice; pravastatin reduced it by 32.8% ($n=7$). Furthermore, simvastatin exhibited an antihypertensive effect even when its dosing was initiated at a later stage of gestation than that of pravastatin. **[Conclusion]** These results demonstrate that simvastatin can ameliorate preeclampsia in mice with enhanced therapeutic activity when compared with pravastatin, thereby confirming its potential as a potent treatment for preeclampsia.

IS-WS-11-3

Prediction of outcomes using the sFlt-1/PlGF ratio in pregnant women with fetal growth restriction Yamazaki Tomomi¹, Oomori Yuriko¹, Mukai Yurika¹, Koh Iemasa¹, Kawasaki Masaya², Nakagawa Hitoshi³, Yorishima Makoto⁴, Tanaka Norifumi⁵, Date Kenjiro⁶, Nakanishi Yoshinobu⁷, Sugimoto Jun¹, Kudo Yoshiki¹ *Hiroshima University¹, Kawasaki Clinic², Nakagawa Clinic³, Yorishima Clinic⁴, Higashihiroshima Medical Center⁵, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital⁶, JA Hiroshima General Hospital⁷*

[Objective] Our objective is to evaluate the trends of sFlt-1/PlGF ratio in pregnant women with fetal growth restriction (FGR) with different prognoses. **[Methods]** We did a secondary analysis of a prospective observational cohort study of high risk pregnant women with preeclampsia. We selected women diagnosed with FGR and underwent assessment of maternal serum sFlt-1/PlGF ratio. We compared the values and trends of the sFlt-1/PlGF ratio between cases with FGR only and those that additionally developed PE. **[Results]** 27 women were diagnosed with FGR between 18 and 36 weeks of gestation. Among the 27 women with FGR, 9 were excluded because they had been diagnosed with preeclampsia (PE) at the same time or already. 18 women were classified into the FGR only cases (FGR, $n=14$) and the FGR cases that additionally developed PE (FGR→PE, $n=4$). In the FGR→PE cases, the sFlt-1/PlGF ratio at the time of FGR diagnosis was higher than the FGR cases (130.9 versus 14.4, $P < 0.005$). In the FGR→PE cases, sFlt-1/PlGF was already elevated before the onset of FGR. All women with sFlt-1/PlGF < 38 at the time of FGR diagnosis ($n=11$) resulted in FGR only. All women with sFlt-1/PlGF ≥ 85 at the time of FGR diagnosis ($n=3$) developed PE. **[Conclusion]** The sFlt-1/PlGF ratio at the time of FGR diagnosis is very useful in predicting pregnancy outcomes.

IS-WS-11-4

Shear stress in the intervillous space plays a key role in syncytial formation of human trophoblasts Inohaya Asako¹, Chigusa Yoshitsugu¹, Matsuzaka Yu¹, Yasuda Eriko¹, Takakura Masahito¹, Ueda Yusuke¹, Kawamura Yosuke¹, Mogami Haruta¹, Kondoh Eiji², Mandai Masaki¹ *Kyoto University¹, Kumamoto University²*

[Objective] In the intervillous space, trophoblasts are continuously exposed to the shear stress generated by maternal arterial blood flow. However, the effect of shear stress on placental formation has yet to be elucidated. Here, we sought to assess the effects of shear stress on trophoblasts in early pregnancy, and to manifest its physiological role in placental development. **[Methods]** The cytotrophoblast stem cells derived from human naïve induced pluripotent stem cells (iPSCs) were incubated on the micro chamber slide under the shear stress (10 dyn/cm², or static condition: 0 dyn/cm²). **[Results]** The shear stress up-regulated the mRNA expressions of placental growth factor, and ERVV-1, (which can serve as marker of trophoblastic invasion and formation of the syncytium), (6- and 3-fold higher, respectively, $p < 0.05$). Concomitantly, the fusion index was significantly increased by flow condition compared to static condition (3-fold, $p < 0.05$). In immunofluorescence, hCG positive cell area was increased (3-fold, $p < 0.05$). In RNA sequence, principal component analysis revealed that cytotrophoblast stem cells are time-dependently differentiated, and the differentiation was further promoted by shear stress, which stimulated syncytiotrophoblast-like gene expression pattern. **[Conclusion]** The appropriate shear stress generated by maternal blood flow in the intervillous space would be necessary for syncytial formation of trophoblasts.

IS-WS-11-5

Perinatal outcome of the subsequent pregnancy following abruptio placenta : the earlier, the worse Takahashi Sara, Iwama Noriyuki, Kudo Rie, Tagami Kazuma, Tomita Hasumi, Hamada Hiroataka, Hoshiai Tetsuro, Saito Masatoshi, Yaegashi Nobuo *Tohoku University Hospital*

[Objective] Abruptio placenta (AP) is widely recognized to be associated with poor perinatal outcomes, and moreover known as the greatest predictor of recurrent AP in the following pregnancy. However, little is known about the association between gestational age (GA) of the previous AP and perinatal outcomes of the subsequent pregnancy. Here, we investigate the perinatal outcome of the subsequent pregnancy following AP. **[Methods]** A case-accumulation study was conducted on singleton pregnancies with a history of AP managed at our facility from January 2008 to September 2021. Cases were divided into two groups : preterm-AP (previous AP before 37 weeks GA) and term-AP (previous AP after 37 weeks GA). Composite adverse perinatal outcome (abruption, abortion, preterm birth and stillbirth) were analyzed using Firth logistic regression model. **[Results]** Among 12177 deliveries, 52 (0.42%) had a history of AP. The median (range) of GA for AP during the previous pregnancy was 35 (19-39) weeks, and 37 cases (80.4%) were preterm-AP. 19 cases (41.3%) had adverse perinatal outcomes during the current pregnancy : repeated abortion (n=5), abortion or preterm birth (n=19) and stillbirth (n=2). Adverse perinatal outcome was 19 (51.4%) and 0 (0%), in preterm-AP and term-AP, respectively. Preterm-AP had significantly higher risk of composite adverse perinatal outcomes than term-AP with an adjusted odds ratio of 16.7 [95% confidence interval : 1.50-2277]. **[Conclusion]** Pregnant women with history of preterm AP is associated with adverse perinatal outcomes, thus, conservative management would be suggested. Additionally, we should take into consideration that preterm and term AP might have different pathogenic mechanisms.

IS-WS-11-6

PEG-conjugated recombinant Thrombomodulin ; a Novel Placenta-Targeting Nanomedicine Ameliorates Preeclampsia in Mice—A Challenge for Clinical Application of Organ Targeting Drug Delivery Nanotechnology Aimed to Treat Placental Dysfunction Oda Hiroko, Nagamatsu Takeshi, Sayama Seisuke, Seyama Takahiro, Kumasawa Keiichi, Iriyama Takayuki, Osuga Yutaka *The University of Tokyo*

[Objective] Thrombomodulin (TM) is a transmembrane glycoprotein expressed on trophoblast cells that plays a role in anti-coagulation and organ protection. Although recombinant-TM (rTM) : an anticoagulant composed of TM domains, is reported to attenuate placental damage in preeclamptic (PE) patients, there is a concern for use due to the risk of maternal systemic hemorrhage. Drug delivery nanotechnology is a strategy to regulate drug distribution and avoid adverse effects. We created a polyethylene-glycol (PEG) conjugated rTM as a novel placenta-targeting nanomedicine and examined its efficacy on PE mouse model. **[Methods]** Seven rTM molecules were conjugated to PEG as rTMPEG nanomedicine. As previously reported, PE mouse was created by continuous infusion of angiotensin2 (Ang2) to pregnant mice from pc10. rTMPEG was administered intravenously for 4 days. Blood pressure (BP), blood and urine analysis were conducted before and after the treatment. On pc17, histological changes and drug distribution were evaluated in maternal organs by immunohistochemistry and fluorescence imaging studies. **[Results]** rTMPEG was adjusted to 20nm-size, targeting the placenta. Imaging analysis showed placenta restricted accumulation of rTMPEG accompanied by significant improvement of placental vasculature. rTMPEG at-

tenuated Ang2-induced PE symptoms by pc17 : systolic-BP (mmHg) : rTMPEG : 129.7 ± 4.1, control : 160.4 ± 7.4, $p < 0.001$, proteinuria (mg/g · creatinine) : rTMPEG : 28.2 ± 16, control : 96.1 ± 25, $p < 0.001$, and fetal weight (g) : rTMPEG : 0.89 ± 0.1, control : 0.6 ± 0.07, $p < 0.001$. Therapeutic effects of rTMPEG were significantly enhanced compared to non-PEG conjugated rTM. **[Conclusion]** rTMPEG selectively accumulated to the placenta which attenuated placental damage and subsequent PE symptoms. rTMPEG can be a novel approach for PE that enables to treat its underlying placental dysfunction.

IS-WS-12-1

Effectiveness of NLRP3 Inhibitor as a Non-Hormonal Treatment for Ovarian Endometriosis Murakami Mayuko, Osuka Satoko, Tanaka Hideaki, Yabuki Atsushi, Sonehara Reina, Miyake Natsuki, Yoshita Sayako, Muraoka Ayako, Nakanishi Natsuki, Nakamura Tomoko, Goto Maki, Kajiyama Hiroaki *Nagoya University*

[Objective] Because hormonal treatments for endometriosis suppress ovulation, they are not compatible with fertility treatment. Therefore, the aim of the present study was to evaluate non-hormonal therapies for ovarian endometriosis (OE), such as inhibitors of the NLRP3 inflammasome, which contributes to the activation of IL1 β . **[Methods]** The expression of NLRP3 was measured in OE and utopic endometrium (EM) from patients with endometriosis and in OE- and EM-derived stromal cells (CSCs and ESCs, respectively). The effect of a NLRP3 inhibitor (MCC950) on CSC and ESC survival was evaluated, and MCC 950 was also evaluated histologically using a murine model. **[Results]** The NLRP3 gene and protein expression levels were higher in OE and CSCs than in EM and ESCs respectively, and 24 h MCC950 (100 μ M) treatment significantly reduced the survival of CSCs (73 ± 5.8%, compared to 0M, $P < 0.01$) but not ESCs. Moreover, MCC950 treatment reduced the co-staining rate of NLRP3 and IL1 β in CSCs and reduced the IL1 β concentrations of CSC supernatants. In the murine model, MCC950 treatment reduced OE lesion size (89 ± 15 vs. 49 ± 9.3 mm² per ovary ; $P < 0.05$), IL1 β and Ki67 staining in the OE-associated epithelia, oxidative stress markers of granulosa cells, and increased follicle counts when compared to PBS treatment. Data are shown as the mean ± SEM. **[Conclusion]** These results indicate that NLRP3/IL1 β is involved in the pathogenesis of endometriosis and that NLRP3 inhibitors may be useful for suppressing OE and improving the functions of ovaries with endometriosis.

IS-WS-12-2

Effect of Tokishakuyakusan on infertility in endometriosis model mice Maki Eiko, Izumi Gentaro, Koga Kaori, Mohammed Elsherbini Elshal, Satake Erina, Takeuchi Arisa, Makabe Tomoko, Taguchi Ayumi, Hirata Tetsuya, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] Endometriosis is known to decrease fertility ; however, there is no adequate therapy or prevention. We evaluated the effect of Tokishakuyakusan (TSS) on fertility in a murine model of endometriosis. **[Methods]** Mice were divided into four groups : control group, control+TSS group, endometriosis group and endometriosis+TSS group (n=10). The TSS group and the endometriosis+TSS group were fed food containing 1% TSS. Endometriosis mouse models were created by intraperitoneal injection of minced uterus taken from homogeneous mice. Mating with healthy male was initiated the day after the creation of the endometriosis, and the time to birth was compared using the Kaplan-Meier method. Mice were sacrificed on day 3 post-partum and the longest diameter of the lesion was measured. **[Results]** During an observation period of 50 days from the start of mating, pregnancies were established in all mice ex-

cept one in the endometriosis group. Although there were no significant differences between the groups, the time to delivery in the endometriosis group tended to be longer than in the control group (median : 27 days vs 23 days, $P=0.30$), and that in the endometriosis+TSS group tend to be shorter than in the endometriosis group (median : 24 days vs 27 days, $P=0.85$). The total diameter of lesion was significantly shorter in the endometriosis+TSS group than in the endometriosis group (median : 4.54 mm vs 7.76 mm, $P=0.03$). **[Conclusion]** TSS reduced the growth of endometriotic lesion and may improve fertility. Further study is needed to understand its mechanism.

IS-WS-12-3

Association between neonatal uterine bleeding and early onset endometriosis Ogawa Kanae¹, Khan Khaleque¹, Koshiha Akemi¹, Kitawaki Jo², Mori Taisuke¹ *Kyoto Prefectural University of Medicine¹, Otsu City Hospital²*

[Objective] We previously confirmed that neonatal uterine bleeding (NUB) occurs in 3.1% of newborns during the period of 2013-2017. In an attempt to identify various symptoms related to endometriosis, we performed an online questionnaire survey among young women who were born 20 years before with and without NUB in our hospital. **[Methods]** We retrospectively searched medical records of female babies born between 1996 and 2000. After informed consent, an online questionnaire survey of symptoms related to endometriosis was performed among women who were born with and without NUB. Fisher's exact test was applied to identify any difference in endometriosis-related symptoms between NUB (+) and NUB (-) cases. **[Results]** Among 1083 female babies, 105 cases showed NUB with a prevalence of 9.7%. Multiple logistic regression analysis indicated that per week increase of gestational age was significantly associated with the occurrence of NUB (OR 1.47, [95%CI, 1.23, 1.81], $P<0.0001$). We finally collected questionnaire response from 31 NUB (+) cases and 52 NUB (-) cases. We found that women with a history of NUB equally suffer from various symptoms related to endometriosis such as constant cyclic pain, severe cyclic/acyclic pain (VAS score 7-10), disturbance of daily life activity, absence from school or work during pain, similar to women who had no history of NUB. **[Conclusion]** An online questionnaire survey revealed that young women who had a history of NUB equally suffer from various endometriosis-related symptoms similar to women without NUB. These findings may clarify a possible association between NUB and early onset endometriosis.

IS-WS-12-4

Physicians-Patient communication : Assessing physician strategies for informing children and adolescents about their cancer diagnosis and the risk of gonadal dysfunction in Japan and the US Iwahata Yuriko, Takae Seido, Iwahata Hideyuki, Tozawa Akiko, Hasegawa Junichi, Suzuki Nao *St. Marianna University*

[Objective] Over the last 15 years, direct communication about cancer with children seems to have shifted. Less is known about communication regarding to discussion of future infertility risk due to cancer therapy. Present survey is cross-cultural comparison between Japan and the US, to verify the patterns of communication of them in these countries. **[Methods]** An online survey was distributed to the member of Japanese Society of Pediatric Hematology/Oncology (JSPHO) in July 2019, and the American Society of Pediatric Hematology/Oncology (ASPHO) in July 2020. **[Results]** We analyzed 325 physicians in Japan, while 46 in the US. In Japan, 80.5% of physicians notified cancer diagnosis directly to 7-9y.o., and 91.7% (10-14y.o.), and 92.1% (15-17y.o.). In comparison, in the US, 100% of physicians tell cancer

diagnosis regardless of age. In the study in 2006, only 9.5% of physicians 'always' tell cancer diagnosis in JAPAN, while 65% in the US. Regarding to fertility risk discussion, 9% of Japanese physicians and 45% in the US directly tell child patients 7-9y.o., 41% and 75% (10-14y.o.), 72% and 85% (15-17y.o.). The factors influence to physicians whether to discuss fertility issues were patient's age and parental request. In Japan, 73% have their low confidence in knowledge of infertility risks for fertility issues, while 20% in the US. **[Conclusion]** Present study suggests direct communication about cancer with children has been significantly increased in this decades. While the frequency of fertility risks discussion is not so often. We think it need to develop preparation tools to overcome the communication barriers.

IS-WS-12-5

Fertility preservation by ovarian tissue cryopreservation for pediatric cancer patients in our department Wakimoto Yu, Ogino Nana, Kamei Hidetake, Sugiyama Yukiko, Kato Toru, Yamaya Ayano, Fukui Atsushi, Hasegawa Akiko, Shibahara Hiroaki *Hyogo College of Medicine*

[Objective] Ovarian tissue cryopreservation (OTC) is the only method to preserve fertility in pediatric cancer patient who have not yet undergone menstruation. After we established a regional onco-fertility network, we have experienced some OTC cases for pediatric cancer. Here, we outlined the fertility preservation by OTC for pediatric cancer patients in our department. **[Methods]** OTC was performed obtaining informed consent in 32 cases at our institution between February 2017 and October 2021. 12 out of 32 cases were pediatric cancer patients younger than 15 years. We evaluated primary disease, mean age, serum AMH level, history of chemotherapy, and ovarian histopathological evaluation. **[Results]** Primary diseases were hematological cancer in 6 cases, germ cell tumor in 3 cases, bone and soft tissue tumor in 2 cases, and medulloblastoma in 1 case. The mean age was 10.9 ± 3.7 years (range : 2-14 years), the mean AMH level was 1.32 ± 1.79 ng/mL, 10 patients had a history of chemotherapy before OTC, and 2 patients had no history of chemotherapy. The mean densities of primordial, transitional, primary, and secondary follicles in ovarian tissue were 2726.74 ± 3254.1 , 0.12 ± 0.29 , 0.13 ± 0.28 , and 0.03 ± 0.09 follicles/mm³, respectively. **[Conclusion]** It has been reported that the density of primordial follicles in children is higher than that in adults. We showed the density of primordial follicles were relatively high even after chemotherapy. This result is supported by the report that primordial follicles are dormant and are therefore not susceptible to chemotherapy.

IS-WS-13-1

Performance of ROMA based on CA125 and HE4 values in Japanese women presenting with epithelial ovarian tumors Iizuka Makoto, Irie Taichi, Hamano Ai, Nemoto Kohei, Saito Kanami, Kondo Ibuki, Saito Yoko, Yamaguchi Noriko, Sakamoto Shuichi, Takakura Satoshi *Dokkyo Medical University Saitama Medical Center*

[Objective] We investigate the clinical utility of HE4, CA125, and risk of malignancy algorithm (ROMA) in Japanese patients with epithelial ovarian tumors (EOT). **[Methods]** 313 Japanese patients with EOT by pathological assessment after surgery were included in this study. The retrospective study validated the diagnosis performance of CA125, HE4, and ROMA. **[Results]** 1) The serum level of CA125, HE4 and ROMA were shown more than cut-off value in 64 (35%), 7 (4%), and 18 (10%) of 181 benign EOT (BEOT) patients, in 16 (44%), 1 (2%), and 6 (16%) of 36 borderline-malignant EOT (BMEOT), and in 67 (69%), 52 (54%), and 67 (54%) of 96 malignant EOT (MEOT), respectively. 2) For identifying BMEOT and MEOT, AUC/sen-

sitivity/specificity/positive productive value (PPV) /negative productive value (NPV) /accuracy of CA125, HE4, and ROMA were 0.74/67%/64%/58%/73%/65%, 0.77/40%/97%/91%/69%/73%, and 0.80/55%/90%/80%/73%/75%, respectively. 3) ROMA were shown more than cut-off value in 6 (11%) of 54 serous BEOT, 2 (25%) of 8 serous BMEOT, and 26 (90%) of 29 serous MEOT, respectively, in 9 (14%) of 61 mucinous BEOT, 3 (12%) of 25 mucinous BMEOT, and 4 (36%) of 11 mucinous MEOT, respectively, and in 3 (4%) of 61 endometriotic cyst, 0 of 1 endometrioid BMEOT, 21 (76%) of 27 endometrioid MEOT, and 16 (55%) of 29 clear cell MEOT, respectively. 4) For identifying BMEOT and MEOT, AUC/sensitivity/specificity/PPV/NPV/accuracy of ROMA were 0.90/76%/89%/82%/84%/84% in serous EOT, were 0.55/22%/85%/47%/65%/62% in mucinous EOT, and were 0.93/65%/95%/93%/74%/77% in endometrioid and clear cell EOT, respectively. **[Conclusion]** In Japanese patients with EOT, ROMA was useful clinical biomarker for identifying BMEOT and MEOT, except for mucinous BMEOT and MEOT.

IS-WS-13-2

Outcomes after fertility-sparing surgery of early-stage ovarian cancer: a nationwide population-based study Lee Chia-Yi¹, Chiang Chun-Ju², Cheng Wen-Fang³ *National Taiwan University Hospital, Hsin-Chu Branch, Taiwan¹, Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University; Taiwan Cancer Registry, Taipei, Taiwan², National Taiwan University Hospital, Taipei, Taiwan³*

[Objective] To compare the outcomes of early-stage epithelial ovarian cancer (EOC) patients undergoing fertility-sparing surgery (FSS) and radical comprehensive staging surgery (RCS) and the suitability of FSS. **[Methods]** There were 1297 patients with a newly-diagnosed early-stage EOC in Taiwan Cancer Registry (TCR) database between 2009 and 2017 recruited. Site-specific surgery codes were used to distinguish patients in FSS group or RCS group. Cancer-specific survival (CSS) was evaluated using Kaplan-Meier method with log-rank test and Cox models. **[Results]** There were 401 and 896 women in FSS and RCS group. Patients in FSS group were with younger age and mostly had stage I disease. In contrast, patients in RCS group were older. There were more stage II, high grade (grade 3) disease, and adjuvant chemotherapy in RCS group. Stage and tumor grade were two independent factors correlating with CSS and the type of surgery showed no effect on CSS (HR : 0.73, 95% CI : 0.66-1.77, p=0.73) in multivariate analysis. Clear cell carcinoma group underwent FSS had better CSS than those in RCS group in multivariate analysis (HR : 0.28, 95% CI : 0.06-0.82, p=0.04). There were 17 women underwent FSS developed second malignancies of uterine corpus or contralateral ovary. **[Conclusion]** FSS could be a safe alternative procedure in selected young patients of early-stage EOC who had fertility desire. Endometrial biopsy before or during FSS surgery and regular surveillance to early detect recurrence were mandatory for ovarian cancer women undergoing FSS.

IS-WS-13-3

Does limited-staging surgery lead to the poorer prognostic outcome for patients with stage IA epithelial ovarian cancer: a multi-center study with propensity-score-adjusted analysis Suzuki Hironori¹, Yoshihara Masato², Mogi Kazumasa², Kitami Kazuhisa², Uno Kaname², Iyoshi Shohei², Fujimoto Hiroki², Yoshikawa Nobuhisa², Kajiyama Hiroaki² *Shizuoka Saiseikai General Hospital¹, Nagoya University Hospital²*

[Objective] This study examines the influence of complete- and limited-staging surgery on stage IA epithelial ovarian cancer

(EOC) recurrence. **[Methods]** This is a regional population-based study between 1986 and 2019, collecting clinicopathological data of 4,730 women with EOC and 293 patients were enrolled. Limited-staging surgery was defined as surgery without at least one following procedure: 1) hysterectomy (fertility-sparing surgery), 2) systematic retroperitoneal lymphadenectomy, 3) ascites cytology. We evaluated characteristics, and clinical and survival outcomes of the patients. Additionally, baseline imbalance between patients with and without complete-staging was adjusted using an inverse probability of treatment weighting using propensity scores composed of independent clinical variables. **[Results]** Among the study cohort, 176 patients (60.1%) received limited-staging surgery. Median follow-up period was 70.2 months. In total, 30 recurrence (10.2%) and 12 death (4.1%) were detected during the study periods. In multivariate analysis, serous carcinoma was the strongest prognostic factor, but limited-staging surgery did not significantly deteriorate both recurrence-free survival (RFS) and overall survival (OS) [RFS : HR 1.297, P=0.353 ; OS : HR 1.622, P=0.322]. With propensity score-adjustment, there were also no significant difference of survival outcomes between patients with complete- and limited-staging surgery regarding both PFS and OS (10-year RFS rate : 89.8% vs. 85.6%, log-rank p=0.337 ; 10-year OS rate : 95.8% vs. 92.7%, log-rank p=0.115). **[Conclusion]** Based on the results, limited-staging surgery, including uterine preservation, was not associated with poorer prognosis in stage IA EOC. This finding also supported the feasibility of limited operation, such as fertility-sparing surgery, especially for stage IA disease.

IS-WS-13-4

Oncological and reproductive outcomes in patients with seromucinous borderline ovarian tumors: results of a large retrospective study Wang Dan¹, Jia Congwei², Cao Dongyan¹, Yang Jiaxin¹, Xiang Yang¹ *Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, China¹, Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, China²*

[Objective] : To evaluate the oncological and reproductive outcomes in patients with seromucinous borderline ovarian tumors (SMBOT) treated with fertility-sparing surgery (FSS). **[Methods]** : The medical records of patients with SMBOT who underwent surgery between 2000 and 2019 were reviewed retrospectively. A centralized histological review was performed. The recurrence rates were compared between different surgical procedures. **[Results]** : One hundred and four patients fulfilled the inclusion criteria, of whom 66 underwent FSS and 38 were treated with radical surgery. After a median follow-up time of 59.7 months (range : 22.1-256.8 months), 19 patients had recurrent disease. All but one relapsed in the form of SMBOT. Multivariate analysis showed no significant difference in disease-free survival between groups who underwent FSS or radical surgery (P= 0.324). In the subgroup of conservatively treated patients, the recurrence rate in cystectomy group was higher than that in the unilateral salpingo-oophorectomy (36.1% vs 13.3%, P= 0.015). However, all of the relapses were successfully salvaged with surgery. Fourteen of the 17 relapsed patients after FSS received a second conservative surgery. Seven of these patients became pregnant after the treatment of their first recurrence (six with normal outcomes and one with spontaneous abortion). **[Conclusion]** : The overall prognoses are favorable in patients with SMBOT. FSS is feasible for young patients who wish to preserve their fertility. Patients who were treated with ovarian cystectomy initially may be managed by close surveillance if post-operative imaging were negative. A second FSS remains a valuable alternative for young patients

with recurrent SMBOT after a through communication.

IS-WS-13-5

p53 dysfunction hampers the differentiation and causes the precancerous potency in mouse fallopian tube organoids

Nagai Shimpei, Masuda Kenta, Tamura Tomohiro, Akahane Tomoko, Chiyoda Tatsuyuki, Kobayashi Yusuke, Banno Kouji, Tanaka Mamoru, Aoki Daisuke *Keio University*

[Objective] The fallopian tube epithelium is considered the origin of high-grade serous carcinoma (HGSC). As precancerous lesions of HGSC and serous tubal intraepithelial carcinoma (STIC) with abnormal staining of p53 are found in the fallopian tube, the alteration of p53 function is considered an early event of HGSC development. This study aimed to examine the biological effects of p53 dysfunction on the fallopian tube epithelium using mouse fallopian tube organoids, a three-dimensional culture system that mimics the structure of fallopian tube. **[Methods]** We established mouse fallopian tube organoids and knocked out (KO) *Trp53* by CRISPR/Cas9 system. After the single cell cloning and confirmation of biallelic mutations of *Trp53*, we evaluated the cell proliferation, differentiation capacity, and gene expression profiles in *Trp53* wild type (WT) and KO organoids by cell proliferation assay, RT-PCR, immunohistochemistry, and RNA-sequencing. **[Results]** *Trp53*KO organoids showed increased cell proliferation, loss of α -tubulin and reduced cilia markers, which indicated that differentiation into cilia was suppressed. Gene set enrichment analysis of RNA-Seq data showed that *Trp53*KO organoids increased the expression of stem cell markers and decreased the expression of cilia markers (*Foxj1*, *Ccdc17*) compared to *Trp53*WT organoids. The inhibition of NOTCH signaling which controls cell fate of fallopian tube epithelial cells promoted ciliated differentiation in *Trp53*WT organoids but not *Trp53*KO organoids, suggesting that p53 is involved in the NOTCH-regulated cellular differentiation in the fallopian tube. **[Conclusion]** Our results thus suggested that p53 dysfunction contributed to cancer initiation by affecting the proliferative and differentiation capacities of fallopian tube epithelial cells.

IS-WS-13-6

Whole-Exome Sequencing of Rare Site Endometriosis-Associated Cancer Makihara Kan, Nakayama Kentaro, Kanno Kousuke, Sawada Kiyoka, Yamashita Hitomi, Ishibashi Tomoka, Ishikawa Masako, Sato Seiya, Kyo Satoru *Shimane University Hospital*

[Objective] Malignant transformation of extraovarian endometriosis is rare, with the carcinogenesis mechanism unclear. **[Methods]** To clarify the actionable variants of rare-site endometriosis-associated cancer (RSEAC), we performed whole-exome sequencing for the tumor, in two patients. The intestine was affected in both cases, although the histology was that of clear cell carcinoma and undifferentiated carcinoma, respectively. Therefore, the cases were referred to as endometriosis-associated intestinal tumors (EIATs). **[Results]** Actionable variants (all frameshift mutations) were identified in tumor suppressor genes ARID1A, PTEN, and p53; however, no oncogenic variants were identified. Both cases were microsatellite stable. The patient with undifferentiated carcinoma exhibited hypermutator and homologous recombination deficiency phenotypes. The dominant mutation signatures were signature 30 (small subset of breast cancers) and 19 (pilocytic astrocytoma) in patient 1, and signature 5 (small subset of breast cancers) and 3 (breast, ovarian, and pancreatic cancers) in patient 2. Immunohistochemistry revealed positive CD8 and PD-1 expression in both patients; patient 1 also showed positive PDL-1 expression. **[Conclusion]** Our results suggest that RSEAC is associated with

variants of tumor suppressor genes as epigenetic alterations. Mutation signature-based whole-exome sequencing could be useful to select an adjuvant chemotherapy regimen. High CD8 and PD-1 expression in RSEAC suggests that immune checkpoint inhibitors are useful for treatment.

IS-WS-13-7

Activated neutrophils inhibit chemotactic migration of activated T lymphocytes by multiple mechanisms Tamura Kohei¹, Saga Yasushi¹, Takahashi Yoshifumi¹, Koyanagi Takahiro¹, Yoshida Takahiro¹, Takahashi Suzuyo¹, Taneichi Akiyo¹, Takei Yuji¹, Kitayama Joji², Fujiwara Hiroyuki¹ *Jichi Medical University Hospital¹, Gastrointestinal Surgery, Jichi Medical University Hospital²*

[Objective] High density of tumor-infiltrating lymphocytes (TILs) in the tumor correlates with good prognosis of the gynecological cancer patients, while that of tumor-associated neutrophils (TAN) shows inverse correlation with outcome. We examined the effects of activated neutrophils on chemotactic migration of activated T cells in vitro. **[Methods]** Neutrophils and mononuclear cells (PBMC) were collected from the blood of healthy donor. Neutrophils were stimulated with PMA (1 μ M) or LPS (10ng/ml) for 15 min, washed extensively, and incubated for another 4 hours. PBMC were cultured on anti-CD3mAb coated plate with r-IL-2 (10ng/ml) for 7-14days. The activated T cells were placed in culture inserts and migration to CXCL11 (1000ng/ml) in lower chamber with or without activated neutrophils were examined after 2 hours. **[Results]** PMA stimulated with PMA or LPS produced neutrophil extracellular traps (NETs). Migration of T cells to CXCL11 was drastically inhibited in the presence of PMA-activated neutrophils. The inhibition was similarly detected when NETs was degraded by DNase I or removed by centrifugation. Timelapse analysis also showed supernatant of PMA-activated neutrophils inhibited migration, which was canceled by the pretreatment with 800U/ml catalase. T cell migration was significantly inhibited by LPS-activated neutrophils (p=0.02) but not by NET-depleted supernatant (p=0.99). In western blotting, CXCL11 was degraded by NETs derived from LPS-stimulated neutrophils which was restored by protease inhibitor, phenylmethylsulfonyl fluoride (PMSF). **[Conclusion]** Activated neutrophils inhibit chemotactic migration of activated T cells through multiple mechanisms including ROS production and chemokine degradation. TAN may have suppressive effects of the accumulation of TILs in tumor tissue.

IS-WS-13-8

Establishment of a patient-derived xenograft (PDX) mouse model of rare gynecologic tumor for precision medicine. An example of mesonephric adenocarcinoma Kasuya Kanako, Kinose Yasuto, Toda Aska, Nakamura Koji, Kodama Michiko, Hashimoto Kae, Sawada Kenjiro, Kimura Tadashi *Osaka University Hospital*

[Objective] Mesonephric carcinoma (MC) is a rare tumor of the female genital tract which originates from mesonephric remnants. Because of its rarity, there is no standard treatment established. Here, we aim to develop a precision medicine platform for MC using the PDX model. **[Methods]** We orthotopically implanted the patient's tumor obtained from the surgery onto the left ovary/distal of the left uterine horn of nude mice. The PDX tumors were harvested when they expanded over 1000 mm³. With the first mouse passage tumors (MP1), we made the second mouse passage PDX models (MP2). For drug testing, we performed patient-derived explant (PDE) experiments using the MC PDX fragments on medium-soaked gelatin sponges exposed to chemotherapeutic agents. As another drug testing model, we tried to establish organoids of MC. To search for the therapeutic

target, we did whole exome sequencing (WES) of the patient original tumor. **[Results]** The MC MP1 and MP2 PDX tumors were collected 118 days after the transplant on average. All PDX tumors represented similar histological findings to the original patient tumor. In PDE models, MC showed the dose-dependent response to carboplatin or paclitaxel. WES results showed *KRAS* and *PIC3CA* pathogenic variants in the patient's tumor. **[Conclusion]** We established a PDX model of MC and the PDE platform. PDX models enabled us to expand tumor samples of the rare cancer for developing precision medicine platform. We are going to test molecular-targeted drugs in the PDE, organoid, and PDX models.

ISP-1-1

Management of patients with atypical glandular cell cytology of uterine cervix Sasa Hidenori, Matsuura Hiroko, Iwahashi Hideki, Kakimoto Soichiro, Miyamoto Morikazu, Takano Masashi *National Defense Medical College*

[Objective] It is difficult to manage patients with atypical glandular cell (AGC) cytology, as the diagnostic criteria for suspected adenocarcinoma in situ (AIS) or invasive adenocarcinoma in the presence of AGC may be unclear. We report the management of patients with AGC cytology at our hospital. **[Methods]** Data of a total 66 patients (mean age : 44.2 years old) referred for AGC cytology over the past 11 years were retrospectively analyzed. The results of cytology and biopsy performed under colposcopic guidance were compared with the clinical course and histological diagnosis in the patients with AGC cytology. **[Results]** The results of repeat cytology in the 66 patients revealed AGC in 27 cases, AIS in 3 cases, high-grade squamous intraepithelial lesion (HSIL) in 8 cases, and AGC+HSIL in the Bethesda system in 11 cases. The biopsies performed under colposcopic guidance revealed a total of 30 cases (45%) with high lesions (i.e. cervical intraepithelial lesion 2+ or AIS), which was significantly lower than the number yielded by cytology. Conization was performed in 40 patients, and histopathologic examination revealed high lesions in 36 of the 40 patients. Seven patients (17.9%) had squamous and glandular lesions. Seven patients showed positive cytology, negative biopsy and positive conization histology. Human papillomavirus (HPV) genotype was examined in 27 patients and 13 were found to be positive for high-risk genotypes. **[Conclusion]** Since more than half of the patients with AGC cytology showed latent malignant lesions, diagnostic conization could be considered, especially in cases positive for high-risk HPV genotypes.

ISP-1-2

Attitudes and behaviors toward HPV vaccination : a 7-year follow-up survey of obstetricians and gynecologists in Japan Oka Emiko¹, Ueda Yutaka¹, Nagase Yoshikazu¹, Sawada Masaaki², Takata Tomomi³, Yagi Asami¹, Miyoshi Ai¹, Kimura Tadashi¹ *Osaka University¹, Osaka General Medical Center², Kansai Rosai Hospital³*

[Objective] In Japan, the government suspended HPV vaccine recommendation in 2013, resulting in dropping vaccination uptake to almost zero. We conducted four serial surveys on our colleague's attitude to HPV vaccination between 2014 to 2021. Here, we evaluate the result of the survey in 2021 and compare it to previous surveys. **[Methods]** The subjects were 567 obstetricians and gynecologists who had been trained in our university hospital or our affiliated hospitals. We used a questionnaire similar in format to those used in 2014, 2017, and 2019. **[Results]** A total of 340 doctors (60.0%) completed the survey. Among them, 93.2% (317/340) of respondents thought that the government should restart HPV vaccination recommendation, and that 65.0% (215/331) think male teenagers should also vaccinate against HPV. The percentage of teenaged daughters inoculated with HPV vaccination after Japanese government had suspended its recommendation was 43.5% (20/46), an increasing trend from the previous surveys. Among 340 doctors, 14 have 15 daughters aged 12 or 13 in total. Although they have inoculated only 1 (6.7%) of 15 daughters, they replied that they would inoculate HPV vaccine to 13 (92.9%) of 14 daughters who were not got vaccinated yet, either after they take junior high school entrance examination or after 9-valent HPV vaccination is designated as a national routine-immunization. **[Conclusion]** This study revealed increasing number of our colleagues think HPV vaccination is necessary for prevention of cervical cancer. We strongly suggest that the Japanese government resume its rec-

ommendation of HPV vaccination.

ISP-1-3

Evaluation of clinical significance and establishment of follow-up strategy for positive surgical margin after cervical conization Sugi Toshihiro, Ikeda Yuji, Katoh Kanoko, Kobayashi Osamu, Nakajima Takahiro, Kawakami Kaori, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] The aim of this study was to identify the clinicopathological factors affect to the recurrence to establish the follow-up strategy in patients with positive surgical margin (PSM) after cervical conization. **[Methods]** Total of 226 patients who underwent conization at our hospital in the past 5 years was examined. PSM was defined as pathologically confirmed as CIN3 or worse (CIN3+) on the margin. The Kaplan-Meier analysis and log-rank test was performed to evaluate the duration for recurrence. The clinicopathological factors affect to the recurrence in cases with PSM was evaluated by univariate analysis. **[Results]** Among 22 out of 226 cases (9.7%) were PSM. The recurrence of CIN3 was found in 3 cases (13.6%) and 3 cases (1.5%) in PSM and negative surgical margin, respectively. The recurrence of CIN1 and CIN3 after conization were significantly higher in PSM group ($p < 0.0001$, $p = 0.0003$). All of recurrence cases in PSM found pathological abnormalities until 610 days after surgery. Focusing on 22 cases with PSM, operation time was significantly associated with recurrence ($p = 0.0383$). **[Conclusion]** The patients with PSM should be followed carefully up to about 20 months after surgery. Longer operative time, significantly associated with high recurrence, may be affected by surgically difficult cases by any factors such as expanded area of disease or field of surgical view. These cases may be particularly and carefully followed up.

ISP-1-4

Aptima HPV correlate with changes in CIN lesions? Shiomi Mayu¹, Kakuda Mamoru², Nakagawa Satoshi², Hiramatsu Kosuke², Miyoshi Ai², Kobayashi Eiji², Kimura Toshihiro³, Ueda Yutaka², Kimura Tadashi² *Osaka Police Hospital¹, Osaka University²*

[Objective] Aptima HPV, which detects 14 high-risk HPV types by TMA method, detects mRNA derived from E6/E7 gene, and HPV typing test is covered by insurance for CIN1 and CIN2. The purpose of this study was to analyze whether Aptima HPV correlates with changes in CIN lesions. **[Methods]** Cytology, colposcopy, HPV typing, and HPV E6/E7 expression analysis were performed every 6 months in patients whose cervical histology led to the diagnosis of CIN1 and CIN2 for the first time. **[Results]** A total of 183 patients were enrolled. The median age was 37 years (range : 20-84). The ratio of HPV E6/E7 expression in the group whose biopsy results were upgraded from CIN1 to CIN2 or CIN to CIN3 or CIN2 to CIN3 was significantly increased compared to the group whose biopsy results were downgraded or unchanged from CIN1 or CIN2 (2.80 vs 0.93 ; $p = 0.022$). **[Conclusion]** HPV E6/E7 expression levels correlate with changes in CIN. The use of Aptima HPV may obviate the colposcopic biopsy. Further analysis will be reported.

ISP-1-5

Observation of three-dimensional Immunostained-virus particles of formalin-fixed, paraffin-embedded (FFPE) sections by Scanning Electron Microscopy Itoh Toshiya¹, Todo Yusuke¹, Oda Tomoaki¹, Matsuya Madoka¹, Adachi Masashi¹, Shibata Toshiaki¹, Murakami Hirotake¹, Abe Masakazu¹, Itoh Hiroaki¹, Kanayama Naohiro², Kawasaki Hideya² *Hamamatsu University School of Medicine¹, Institute for NanoSuit Research, Preemi-*

ment Medical Photonics Education & Research Center, Hamamatsu University Hospital², Shizuoka College of Medicalcare Science³

[Objective] Light microscopy can show human papillomavirus (HPV) infected nuclei with immunohistochemistry (IHC) staining but not numerous numbers of HPV particles in the nuclei. Conventionally, exceedingly small particles, such as viral pathogens, have been demonstrated by transmission electron microscope (TEM) observation. We have reported "NanoSuit method" that enables to observe living and wet organisms under electron microscope and that can be applied to the field emission (FE) sequential electron microscopy (SEM) of paraffin sections. In this study, we aimed to observe HPV particles in the nucleus of cervical intraepithelial neoplasia (CIN) of paraffin sections with FE-SEM using NanoSuit method. In addition, we applied this technique to the observation of Cytomegalovirus (CMV), Varicella-Zoster Virus (VZV) and SARS-CoV-2. **[Methods]** Immunohistochemical staining of paraffin sections were performed, and they were visualized with 3,3'-diaminobenzidine (DAB). The DAB-stained slides were incubated with 2% osmium solution and NanoSuit solution was dropped on the glass slides or osmium coating was applied to them. Ultra-thin sections were made from the sections observed by NanoSuit method to observe them with TEM. **[Results]** A vast number of HPV in the nucleus of CIN were demonstrated in three-dimension with FE-SEM. Incubation of DAB-stained sections with OsO₄ (osmium) enhanced the structure of HPV particles. Large amounts of HPV particles were confirmed by TEM observations in the same nucleus where observed with a light microscope or FE-SEM. CMV, VZV, and SARS-CoV-2 could also be depicted by FE-SEM in the same technique. **[Conclusion]** This new method can be a novel method to observe various virus particles in paraffin sections.

ISP-1-6

Comparison of Roche Linear array and next generation sequencing in human papillomavirus (HPV) genotyping Niiya Akari¹, Yamasaki Kentaro², Abe Shuhei¹, Hamaguchi Daisuke³, Kotera Kohei⁴, Sameshima Tetsuro⁵, Nakayama Daisuke⁶, Murakami Makoto⁷, Kitajima Yuriko⁸, Hasegawa Yuri¹, Kitajima Michio¹, Miura Kiyonori¹ *Nagasaki University Hospital¹, Yamasaki Clinic², Isahaya General Hospital³, Nagasaki Harbor Medical Center⁴, Japanese Red Cross Nagasaki Genbaku Hospital⁵, Sasebo City General Hospital⁶*

[Objective] High-risk HPV is frequently detected in severe cervical dysplasia cases. HPV genotyping test have been used to determine the follow-up intervals for moderate and mild cervical dysplasia. The purpose of this study was to analyze HPV DNA using a next-generation sequencer (NGS) in addition to Roche linear array test and to clarify the sensitivity and specificity of the linear array test. **[Methods]** The patients who were diagnosed with cervical dysplasia between 2007 and 2008 were included. HPV DNA was extracted from patient vaginal secretion and typed by Roche Linear array genotyping assay and NGS : MiSeq. **[Results]** 325 cases were included. 13 high-risk HPV types were targeted for testing. In 240 cases (74%), multiple HPV types were detected. 35 cases were positive for both linear array test and NGS, 523 cases were positive for NGS only, 68 cases were positive for linear array test only, and 3399 cases were negative for both. The sensitivity and specificity of the linear array test were 31% and 98%, respectively. The median coverage of the 68 cases, positive for linear array test only, was 53.3%. Coverage was less than 30% in 19 cases, and less than 10% in 9 cases. **[Conclusion]** Roche linear array test was found to be a highly specific test method. There were some cases that were judged positive by the linear array method even though the coverage was less than 30%. It is suggested that a small amount of DNA fragments may have been amplified by PCR

and judged positive.

ISP-1-7

Use of Novel 'Hands free' Magnification device (Bi-Scope) aided visual inspection with Acetic acid (VIA Bi-Scope) in Cervical Intraepithelial Neoplasia Agrawal Sudesh Sardar Patel *Medical College, Bikaner, Rajasthan, India*

[Objective] To find out the efficacy in terms of sensitivity, specificity, positive predictive value and negative predictive value of Novel Hands free Magnification device (Bi-Scope) aided visual inspection with Acetic acid (VIA Bi-Scope) in Cervical intraepithelial Neoplasia. **[Methods]** The A total of 100 symptomatic women attending Gynecologic Out-patient department were enrolled for the study after obtaining informed consent. The cervix was visualized with naked eye (per speculum examination), visual inspection with acetic acid (VIA-UAE). Later examination was repeated with Bi-Scope. Bi-Scope is a low cost, light weight, portable, hands free (worn as a head gear or as spectacles), illuminated with LED light, chargeable, magnifier lenses 1.5 to 4 times with image capturing facility. Images can be stored in data card or transferred via USB port. Colposcopy and biopsy were done if indicated. Statistical analyses were carried out. **[Results]** The detection rate for VIA-UAE positive lesions was 11% (11/100), while it was 18% (18/100) for VIA Bi-Scope positive lesions. The sensitivities of detection of cervical intraepithelial neoplasia (CIN) 2 and higher lesions were 55% for VIA-UAE, 86% for VIA-BiScope with a specificity of 53% for VIA-UAE and 60% for VIA Bi-Scope. **[Conclusion]** VIA Bi-Scope will be useful device in cervical cancer screening programmes especially in low and middle income countries. Captured images can be stored, compared and used for research and teaching with possibility of automation with application of deep neural networks in future.

ISP-2-1

The characteristics of prognosis of cervical cancer patients with new stage IIIC (pN1) and the validation of new staging classification FIGO 2018 Itoda Yukiko, Kawatake Rina, Kobayashi Osamu, Katoh Kanoko, Nakajima Takahiro, Ikeda Yuji, Kawakami Kaori, Takeya Chiaki, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] According to the new FIGO stage of cervical cancer (2018), cases of lymph node metastasis are classified as stage IIIC. We here validated the new staging classification focusing on patients with new stage IIIC (pN1) who received radical hysterectomy. **[Methods]** 177 patients of cervical cancer (stage IB : 87, stage II : 44, stage III : 46 by FIGO2008) received primary treatment at our hospital during 2016-2021 were enrolled. Of FIGO2008 stage IB/II patients, 118 (90%) underwent radical hysterectomy, and pelvic lymph nodes were pathologically evaluated. High-risk patients received concurrent chemoradiotherapy after surgery. The Kaplan-Meier method was used to determine the 3-year overall survival (OS) and the log-rank test was performed. **[Results]** Among the former IB-II stage, 39 patients (29.8%) had the new stage IIIC while 21 former stage III patients (45.7%) had the new stage IIIC. By FIGO2018, stage IIIC accounted for 34% (60 patients) of all cases. OS was 97%, 74%, 62% in FIGO2008 stage IB, II, and III, and 98%, 83%, and 65% in FIGO2018 stage IB, II, and III, respectively. The prognosis of 118 patients (OS=89%) who underwent radical hysterectomy in the former IB-II stage was clearly distinguished into new stages IB-II (OS=94%) and IIIC (OS=74%). In stage IIIC, OS was significantly higher in patients with pT1b, 2a, 2bN1 than those with T 3N1. **[Conclusion]** Classification of pN1 patients with poor prognosis into stage IIIC improved OS in new stage IB-II. Our data

suggested it should be noted that the prognosis in stage IIIC differs depending on T1/2 or T3.

ISP-2-2

Cervical dilation is effective for conception in the post-trachelectomy patients Matsuda Erina, Kobayashi Osamu, Okuma Yuki, Tanaka Yuria, Katoh Kanoko, Nakajima Takahiro, Kawakami Kaori, Ikeda Yuji, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] Since, in generally, the pregnancy rate among women who underwent radical trachelectomy is approximately 20-45% and the preterm birth rate is approximately 40-60%, the procedure has limitations regarding fertility and obstetrical outcome. We here examined the factors for conception in the post-trachelectomy patients and then the effectiveness of cervical dilation. **[Methods]** We investigated 50 patients who underwent trachelectomy during 2009-2021. Patient personal background, pathological factors, post-operation status (cervical stenosis, cervical and uterine lengths) were analyzed by Unpaired t-test, Fisher exact test and Tukey-Kramer test. Patients with cervical stenosis who desire to get pregnant underwent cervical dilation under anesthesia. The pregnant women after trachelectomy were managed in hospital after 28 gestation-weeks even with no symptom. **[Results]** Fourteen (74%) among 19 patients who desire to have a child became pregnant. 12 patients had live births and two were currently pregnant. A half of them was natural pregnancy. Of the 12 patients, seven (58%) and five (42%) were delivered after 34 and 37 gestation-weeks, respectively. The patients without cervical stenosis were likely to become pregnant ($p < 0.05$). Among patients with cervical stenosis, all patients who underwent cervical dilatation became pregnant. Cervical stenosis, cervical dilation, cervical and uterine lengths and vaginal flora was not associated with preterm birth. **[Conclusion]** The pregnancy rate after trachelectomy in our hospital was clearly higher than the generally reported rate. Cervical dilation may further improve pregnancy rates in the post-trachelectomy patients.

ISP-2-3

Obstetrical and oncological results of patients with early invasive uterine cervical cancer who underwent vaginal simple trachelectomy (ST) Shinkai Shota *Sapporo Medical University*
[Objective] RT with pelvic lymphadenectomy has become a new treatment option for patients with uterine cervical cancer stages IA2-IB1 who desire the preservation of their fertility. However, pregnancy after RT is a high risk of miscarriage and preterm birth. We started vaginal ST for patients with low risks in stage IA2-IB1. The objective of this study is to evaluate the oncological and obstetrical results of pregnant patients after vaginal ST in comparison with those after vaginal radical trachelectomy (RT). **[Methods]** Both obstetrical and oncological results of three patients who underwent vaginal ST in our institute between 2018 and 2021 (Group A), and those of five patients who underwent RT with pelvic lymphadenectomy during the same period (Group B) were reviewed based on their medical charts. **[Results]** One patient in Group A terminated due to a psychological disease in her 2nd trimester of the pregnancy. Also one patient in group A experienced 2 pregnancies after ST. Three pregnancy courses of Group A were well and they could undergo scheduled cesarean section after 36 weeks of pregnancy except for a terminated case. None of them showed any signs of the recurrence up till now. Patients with Group B also showed good obstetrical and clinical courses. There were no significant differences in both oncological and obstetrical results between Group A and Group B. **[Conclusion]** Vaginal ST appear

to be a safe fertility-preserving surgery in well-selected patients with small-volume cervical cancer. Obstetric outcome also appears favorable.

ISP-2-4

Reassessment of recurrence risk factors for cervical cancer in patients who underwent radical hysterectomy Okawa Masayo, Komatsu Hiroaki, Hikino Kouhei, Iida Yuki, Osaku Daiken, Kudoh Akiko, Chikumi Jun, Sato Shinya, Oishi Tetsuro, Taniguchi Fuminori, Harada Tasuku *Tottori University*

[Objective] To reassess significance of postoperative recurrence risk factors for cervical cancer **[Methods]** We enrolled patients with stage IBI-IIB (FIGO 2008) cervical cancer who underwent radical hysterectomy (RH) in our hospital for 2006-2016. Postoperative recurrence risk was defined as : high-risk (pelvic lymph node metastasis or parametrium invasion), intermediate-risk (preoperative tumor size ≥ 4 cm in diameter, muscle layer invasion $\geq 1/2$, vascular, or interstitial invasion), and low-risk (others). All High-risk cases received adjuvant therapy. We evaluated the overall survival (OS) and progression-free survival (PFS), and determined the recurrence risk factors by multivariable analysis. **[Results]** One hundred and fifty-two cases (IB1, 87 ; IB2, 26 ; IIA, 11 ; IIB, 28) were classified into two groups : with or without neoadjuvant chemotherapy (NAC+ or NAC-). The NAC+ group included 55 cases (high-risk, 25 ; intermediate-risk, 9 ; low-risk, 21), and the NAC- group, 97 cases (high-risk, 18 ; intermediate-risk, 23 ; low-risk, 56). In the NAC-group, PFS in the high- and intermediate-risk cases were shorter than that in the low-risk cases ($p = 0.02$, $p = 0.01$), and OS in the high-risk cases ($p = 0.01$) was inferior to that in the low-risk cases. Similarly, in the NAC+ group, PFS in the high- and intermediate-risk cases ($p = 0.01$, $p < 0.05$) were worse, and OS in the high-risk cases ($p = 0.01$) was obviously shortened, compared with the low-risk cases. Although no independent prognostic factor was observed, vascular invasion tended to be the poor prognosis factor in the intermediate-risk cases (HR : 2.25, 95% CI : 0.351-13.7). **[Conclusion]** Adjuvant therapy may be needed in the intermediate-risk cases after RH and is further intensified in the high-risk cases.

ISP-2-5

Surgical, oncological and obstetrical outcomes of Shimodaira-Taniguchi conization method Higami Shota, Tanaka Yusuke, Jitsumori Mariko, Shimura Koutarou, Deguchi Tomomi, Shiraishi Mariko, Shiki Yasuhiko *Osaka Rosai Hospital*

[Objective] To investigate surgical, oncological and obstetrical outcomes of Shimodaira-Taniguchi conization. **[Methods]** A total of 829 cases of therapeutic conization (Shimodaira-Taniguchi method) for CIN2 or CIN3 performed in Osaka Rosai Hospital from January 2010 to December 2018 were retrospectively reviewed. Risk factors associated with recurrent disease were investigated by univariate and multivariate analysis. Surgical complications and obstetrical outcomes were also analyzed. **[Results]** The median age of patients was 38 years old (interquartile range (IQR) : 33-45). The median operative time was 5 minutes (IQR : 3-8). The intraoperative blood loss was small amount (less than 50ml) in 97% (805 cases) of 829 cases. Postoperative bleeding and cervical stenosis were observed in 8.4% (70 cases) and 2.2% (18 cases), respectively. Recurrent disease occurred in 4.9% of 829 cases. The independent risk factors of recurrent disease were age ≥ 45 [hazard ratio (HR) 3.40, 95% CI 1.832-6.33] and positive surgical margin status [hazard ratio (HR) 6.63, 95% CI 3.53-12.4]. The 4-year recurrence rate in patients aged ≥ 45 with positive surgical margin was significantly higher compared to that of patients aged ≤ 44 (29.9% vs. 10.1%, $P = 0.009$). Of 74 cases of live births, 95.9% (71 cases) was term

delivery and 2.7% (2 cases) was extremely or very preterm birth (≤ 32 weeks). [**Conclusion**] Shimodaira-Taniguchi conization method is effective in terms of surgical, oncological and obstetrical outcomes. However, careful follow-up is required for patients aged ≥ 45 with positive surgical margin.

ISP-2-6

Surgical treatment for bulky cervical cancer : from single institution experience Kawatake Rina, Ikeda Yuji, Itoda Yukiko, Katoh Kanoko, Kobayashi Osamu, Nakajima Takahiro, Kawakami Kaori, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[**Objective**] The aim of this study is to evaluate the prognostic significance of surgery for operable bulky cervical cancer. [**Methods**] From 223 cases diagnosed with cervical cancer for 5 years, 34 cases with maximum tumor diameter ≥ 4 cm with stage IB-IIIB (FIGO 2008) was analyzed. Patients were classified by treatment method and clinicopathological factors, then evaluated by Chi square test or Fisher's exact test. The Kaplan-Meier and Log-rank test were used to evaluate disease-free survival (PFS) and overall survival (OS). Association of clinicopathological factors into prognosis were evaluated by univariate analysis. [**Results**] Among 34 cases with bulky cervical cancer, 27 and 7 cases were treated by surgery (SUR) and CCRT/RT (RT), respectively. In SUR, 24 of 27 patients (88.9%) received additional CCRT/RT following to surgical procedure, and 1 patient (3.7%) received chemotherapy as an adjuvant therapy. Recurrence was found in 8 cases (29.6%), and 3 cases (42.9%) in the SUR and RT, respectively. There was no significant difference between SUR and RT in PFS ($P=0.779$), as well as OS ($P=0.457$). Among 19 cases of cN0 in SUR, pN1 was found in 8 cases (42%). Squamous cell carcinoma was in 17 of 27 cases (63%) and all cases (100%) in SUR and RT, respectively. Significant survival difference was not found by sub-analysis in squamous cell carcinoma. [**Conclusion**] In Bulky cervical cancer, no significant difference was found by treatment method. As this study include several biases, additional analysis is required to identify the treatment method for bulky cervical cancer.

ISP-2-7

Cusum analysis for learning curve of robotic-assisted hysterectomy in initial experience at a single institution Yotsumoto Fusanori, Ito Tomohiro, Miyahara Daisuke, Yoshikawa Kenichi, Shigekawa Koichiro, Miyamoto Shingo *Fukuoka University Hospital*

[**Objective**] The aim of this study was to evaluate the learning curve and perioperative outcomes of robot-assisted hysterectomy (RAH). [**Methods**] This retrospective study included 45 patients underwent RAH using the da Vinci Xi surgical system. The learning curve was evaluated using cumulative summation method (CUSUM). Demographic data and various perioperative parameters including docking time, hysterectomy time from round ligament dissection to vaginal cuff closure and total operative time from skin incision to skin closure were reviewed from the medical records. [**Results**] CUSUM analysis reached to proficiency at 33 cases for hysterectomy time. Two unique phases of the learning curve for hysterectomy time were derived : phase A identified by the bottom point in the curve and phase B identified by an upward line after the bottom point in the curve. There was no significant difference between the two phases in terms of age and body mass index. The median perioperative parameters in phase A and phase B group were as follows, respectively : docking time, 48 minutes [range, 29-97] vs 38 minutes [21-46] ($p=0.0009$) ; total operative time, 330 minutes [range, 169-443] vs 255 minutes [184-303] ($p=0.002$) ; intraoperative blood loss, 70 g [1-672] and 20 g [1-155] ($p=0.0473$). Pe-

rioperative complication rates were 30.3% and 0% ($p=0.0423$). No conversion to laparotomy occurred in both groups. [**Conclusion**] Improvement of surgical performance in RAH can be achieved after 33 cases. The two phases identified by CUSUM analysis showed significant reduction in docking time, operative time, blood loss, and complication rates at the proficient phase of learning curve.

ISP-3-1

Comparison of response to definitive radiotherapy for locally advanced cervical cancer by histological subtypes Kuruma Airi, Kodama Michiko, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Miyoshi Ai, Kobayashi Eiji, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Tomimatsu Takuji, Kimura Tadashi *Osaka University*

[**Objective**] Response and poor prognostic factors of definitive radiotherapy for locally advanced cervical cancer were investigated by histological subtypes. [**Methods**] The characteristics and treatment outcome of patients with locally advanced cervical cancer, who underwent definitive radiotherapy between January 2010 and July 2020, were retrospectively reviewed. WHO classification and FIGO2018 were used for histopathological classification and staging, respectively. The patient characteristics of complete response (CR) and non-CR cases were compared using Fisher's exact probability test, Pearson's chi-square test and Mann-Whitney U test, and prognostic factors associated with non-CR were examined by logistic regression analysis. [**Results**] Among 230 patients, 188 patients had squamous cell carcinoma (SCC) and 42 patients had glandular tumors, which were classified into 16 adenocarcinoma, 9 gastric type, 4 endometrioid, 3 poorly differentiated, 2 clear cell type, 2 adenosquamous, and 6 unknown. One hundred seventy two patients (91.5%) with SCC achieved CR and 20 patients (47.6%) with adenocarcinoma (AC)/adenosquamous carcinoma (ASC) achieved CR. Among AC/ASC, the proportion of gastric type adenocarcinoma, and FIGO stage \geq IIB were significantly higher in non-CR than in CR group (36.4% vs. 5.0%, $P=0.02$ and 86.4% vs. 50.0%, $P=0.04$). The prognostic factor associated with non-CR in multivariate analysis was gastric type (adjusted odds ratio 15.2 ; 95% confidence interval 1.4-158.3 ; $P=0.02$). [**Conclusion**] Definitive radiotherapy for locally advanced cervical cancer was significantly more effective in SCC than AC/ASC. Among AC/ASC, the only factor associated with non-CR was gastric-type adenocarcinoma.

ISP-3-2

Development of a novel transvaginal laser hyperthermia device for cervical cancer Matsukawa Tetsuya, Yoshikawa Nobuhisa, Yoshihara Masato, Tamauchi Satoshi, Yokoi Akira, Ikeda Yoshiki, Kajiyama Hiroaki *Nagoya University Hospital*

[**Objective**] There is an intensive need for curative treatment for local residual disease or local recurrent disease of cervical cancer after radiotherapy, which is difficult to eradicate with additional radiotherapy or chemotherapy. This study was aimed to evaluate efficacy and safety of a novel transvaginal laser hyperthermia device. [**Methods**] We developed a novel transvaginal laser thermotherapy device in collaboration with Asuka Medical Inc.(Kyoto, Japan). This system is compact and integrated with a camera at the tip $^{\circ}$ C of probe. The temperature on the top of probe was monitored and controlled about 43 by thermo control unit. [**Results**] Three cervical cancer patients were included. A 4Xyears old woman with squamous cell carcinoma in stage IIB had residual disease on after concurrent chemoradiotherapy (CCRT). Because of the cerebral infarction, CCRT was discontinued, and laser hyperthermia was administered. After hyperthermia, residual tumor on uterine cervix

vanished. A 7X years old woman with squamous cell carcinoma in stage IIB underwent hysterectomy followed by CCRT. After CCRT, recurrent tumor at the vaginal margins was treated by hyperthermia. Her residual tumor did not vanish, but she is still alive for more than 5 years. A 4X years old woman with adenocarcinoma in stage IIB underwent CCRT followed by salvage hysterectomy with positive vaginal margin. After hyperthermia, mucosal ulcer was found on the vaginal end, and hyperthermia was cancelled. **[Conclusion]** We developed a novel laser hyperthermia device for residual or recurrent cervical cancer after radiotherapy. Further study is necessary for clinical application.

ISP-3-3

Efficacy and safety of concurrent chemoradiotherapy after type III radical hysterectomy for high-risk cervical cancer Suzuki Eitaro, Tanabe Hiroshi, Kato Sayako, Yamauchi Kishihito, Yokosu Kouta, Saito Motoaki, Takano Hirokuni, Yamada Kyosuke, Okamoto Aikou *The Jikei University*

[Objective] Type III radical hysterectomy (RH) followed by concurrent chemoradiotherapy (CCRT) for high-risk cervical cancer is a standard treatment as specified in the guidelines. Nevertheless, due to lack of data on efficacy and adverse events of CCRT, many institutions choose chemotherapy as adjuvant therapy. The aim of this study is to confirm the efficacy and safety of CCRT after RH for high-risk cervical cancer. **[Methods]** Patients initially treated with RH and pelvic lymphadenectomy between 2012 and 2020, and whom had high-risk for recurrence (positive lymph nodes and/or parametrium invasion and/or positive margin) were eligible for the study. Eligible patients received external beam radiotherapy of 45-50.4 Gy and weekly cisplatin consisted of 40mg/m² for 5-6 courses concurrently. **[Results]** 133 patients were eligible for the study. Among whom 34 (25.6%) had non squamous cell histological type, 109 (82.0%) had positive nodes and 67 (54.0%) had parametrium invasion. The median follow-up period among surviving patients was 49 months. The 4-year progression free survival and overall survival were 72.7% and 80.5% respectively. 35 (26.7%) patients experienced recurrence during the follow-up period and site of recurrence was intra-pelvis 22.9%, extra-pelvis 62.6% and both intra and extra 11.4%. Significant factors for recurrence in univariate and multivariate analyses were non squamous cell histologic type and parametrium invasion. Patients experiencing grade 3, 4 bowel obstruction, leg lymphedema and hydronephrosis were 13.0%, 6.1% and 3.8% respectively. **[Conclusion]** CCRT after RH remains a challenge in suppressing extra-pelvis recurrence. Some adverse events also need improvement, and further studies are warranted.

ISP-3-4

Clinical outcomes of neoadjuvant chemotherapy for neuroendocrine carcinoma of the uterine cervix Nagasawa Saya¹, Fujihara Risa², Ito Yosuke¹, Okumura Toshiyuki³, Hirayama Takashi², Hamamura Kensuke¹, Ujihira Takafumi³, Fujino Kazunari², Kaneda Hiroshi¹, Terao Yasuhisa², Ogishima Daiki¹, Itakura Atsuo² *Juntendo University Nerima Hospital¹, Juntendo University Hospital, Juntendo University², Juntendo University Urayasu Hospital³, Juntendo University Shizuoka Hospital¹*

[Objective] In 2014, the Gynecologic Cancer International Group published a consensus review on the treatment of small cell neuroendocrine carcinoma of the uterine cervix (NECC). They recommend radical surgery for FIGO 2009 stage I-IIA disease, whereas chemoradiation or systemic chemotherapy consisting of etoposide and cisplatin were recommended for stage IIB or more. The purpose of the present study is to verify the clinical outcomes of current treatment for NECC in our hospital. **[Methods]**

[Results] Clinical data was collected from 27 NECC patients treated in three Juntendo branch hospitals from January 2002 through December 2020. **[Results]** FIGO 2018 stage I-II and III-IV disease presentation were distributed with 12 (44%) and 15 (56%) cases, respectively. NECC was basically diagnosed with immunohistochemical examination. The most common primary treatment was neoadjuvant chemotherapy (NAC) -combined radical surgery followed by adjuvant chemotherapy, and systemic chemotherapy, those described in 7 cases each. Cisplatin and irinotecan (IP) were the most common-used regimen. Regarding NAC, CR/PR rate was 56% in IP regimen, which was much better than the other regimens (0%) including cisplatin/carboplatin combined with etoposide. Among stage IVB group, three of 10 patients are in NED or AWD status, with their median PFS and OS as 63.4 and 96.7 months, respectively. Overall, the median PFS and OS of 27 patients was 10.6 and 25.2 months, respectively. **[Conclusion]** NAC using IP regimen could be effective for late stage NECC patients. If it became CR/PR, stage IVB patients possibly have chance to survive.

ISP-3-5

Survival impact of adjuvant concurrent chemoradiotherapy after radical hysterectomy in FIGO stage IIIc1 cervical adenocarcinoma Suzuki Kazuhiro¹, Nagao Shoji³, Narita Moyu², Nakazawa Hiroshi², Shibutani Takashi², Jimi Tomoatsu², Yano Hiroko², Kitai Miho², Shiozaki Takaya², Yamaguchi Satoshi², Kajiyama Hiroaki¹ *Nagoya University Hospital¹, Hyogo Cancer Center², Okayama University Hospital³*

[Objective] We evaluated the survival effect of adjuvant concurrent chemoradiotherapy after radical hysterectomy in patients with clinical pelvic node-positive cervical adenocarcinoma. **[Methods]** Patients with pelvic node-positive cervical adenocarcinoma diagnosed between 2000 and 2016 were identified. Survival was compared between patients who underwent radical hysterectomy alone and those who received concurrent chemoradiotherapy as an adjuvant treatment. Survival analysis using log-rank test and Cox proportional hazards model was performed. **[Results]** We identified 80 patients who underwent radical hysterectomy for clinical pelvic node-positive cervical adenocarcinoma; of these, four with pathological pelvic node-negative adenocarcinoma were excluded. Of the 76 patients, 27 underwent radical hysterectomy alone and 49 received radical hysterectomy followed by concurrent chemoradiotherapy. With a median follow-up of 53 months, the 5-year overall survival rate was 51.0% in patients who underwent radical hysterectomy alone versus 53.0% in patients who received additional concurrent chemoradiotherapy (log-rank p=0.455). **[Conclusion]** The addition of concurrent chemoradiotherapy after radical hysterectomy did not significantly improve survival among patients with pelvic node-positive cervical adenocarcinoma. More appropriate treatment strategies are needed to improve the survival outcomes of these patients.

ISP-3-6

The characterization of the elderly patients with cervical cancer over the age of 65 Kotani Kiriko, Mitani Takeji, Ichikawa Ryoko, Nomura Hiroyuki, Nakamura Masaru, Fujii Takuma *Fujita Health University*

[Objective] Japan is the most aged society worldwide. Approximately 20% of patients with invasive cervical cancer was diagnosed in women over the age of 65. This study aims to characterize elderly patients with cervical cancer in our hospital by retrospective analysis. **[Methods]** The patients with cervical cancer who attended at our hospital from 2012-2015 were classified into younger (≤65) and elderly group (66≥). The motivation for the attendance, clinical stage, treatment method and five

year progression-free survival were compared in two groups. Statistical analysis was performed using the Fisher's exact test, Pearson's Chi-Square test and Kaplan-Meier method. **[Results]** Genital bleeding for the motivation of the first attendance was 50.5% (51/101) and 72% (18/25) in younger and elderly group ($p=0.053$), respectively. Predominantly staging of younger and elderly group was stage I (57% : 60/105) and stage III/IV (48% : 13/29), respectively. Patients (72% : 75/105) under 65 years underwent surgery, while patients (76% : 22/29) over 66 years concurrent chemoradiotherapy or radiation alone, showing a significant difference in treatment methods between two groups (p -value 4.1×10^{-9}). progression-free survival was 80.1% and 53% in younger and older group, respectively ($p=0.01$). **[Conclusion]** Elderly patients with cervical cancer are diagnosed in advanced stages and treated with concurrent chemoradiotherapy or radiation only, and have a poor prognosis. The number of population over 65 year is expected to increase by 17% over the next 10 years : thus, there is an urgent need to re-evaluate screening and treatment practices in this population.

ISP-3-7

Lobular endocervical glandular hyperplasia presenting as a hemorrhagic bulky mass clinically mimicking cervical malignancy—A case report Onuma Kazuya, Fukuda Takanori, Shibuya Mari, Shibasaki Satoshi, Aoyagi Ryo, Watanabe Remi, Uzawa Yoshie, Kohata Yutaka, Inoue Hiromi *Shonankamakura General Hospital*

Introduction A hemorrhagic large mass of the uterine cervix is usually suspicious for cervical carcinoma, and not a typical finding of lobular endocervical glandular hyperplasia (LEGH). **Case** A 42 year-old woman with a large cervical mass was referred to us for further investigation. Colposcopic examination revealed a bulky mass with atypical vascularization replacing the anterior cervix. The mass was hemorrhagic and biopsy caused significant bleeding needing active hemostatic procedure. MRI demonstrated a 6cm mass consisting of multiple cysts in various size and shape. No solid component or enhancement was noted. Review of the previous MRI of 12 years ago revealed a small multicystic lesion measuring 23 mm in the upper cervix suggestive of LEGH. Despite the clinical findings and presentation highly suspicious for malignancy, biopsy showed benign glandular proliferation, and diagnostic conization revealed LEGH with inflammation and erosion. Total laparoscopic hysterectomy was performed for complete pathologic evaluation and treatment, and showed LEGH without atypical features or carcinoma. Immunohistochemistry showed the lesional glandular cells positive for MUC6, negative for CEA, p53 and low ki-67 index. **Discussion** Although growing in size and hemorrhagic nature of the cervical cystic mass is worrisome for malignancy, a bulky LEGH may cause surface irritation and present as a hemorrhagic mass, leading to deceptive clinical picture. Entire removal of the lesion is necessary for complete histopathologic assessment.

ISP-3-8

A case of uterine-sparing treatment for giant angiomyofibrosarcoma of the uterine cervix Takezawa Miki, Watanabe Zen, Toratani Junpei, Hiraga Hiroaki, Yokoyama Emi, Ishibashi Masumi, Shiga Naomi, Tokunaga Hideki, Tachibana Masahito, Yaegashi Nobuo *Tohoku University Hospital*

Introduction : Angiomyofibrosarcoma (AMFB) is a benign mesenchymal tumor that develops most commonly in the external genitalia of women, first reported by Fletcher in 1992. AMFBs often grow slowly and are less than 10 cm in diameter. Here we report a case of giant AMFB of the uterine cervix which could preserve uterus. **Case :** A 33-year-old patient, gravida two, para two, detected cervical fibroid of 35mm in last

pregnancy. She has had worsening of the intravaginal mass feeling, an increase of discharge and dysuria and was referred to a secondary medical institution for tumor infection. MRI revealed a 598 mm³, T1WI low signal, T2WI heterogeneous high signal, well-defined tumor in the posterior lip of the cervix. Histological examination by transvaginal tumor biopsy revealed AMFB (positive for both estrogen and progesterone receptors). According to her desire for fertility preservation and the histological examination result, we inducted pseudo-menopause using GnRH antagonist followed by uterine-sparing surgery. The preoperative MRI showed the tumor had shrunk to 457 mm³. Considering the need for intraperitoneal approach and hemostasis by uterine artery ligation, laparoscopy was also introduced. Under general anesthesia, the entire tumor could pull out from vagina and thus, resection was performed transvaginally. The boundary between the tumor and normal muscular layer was clear and was bluntly exfoliated. Her symptoms improved and post-operative course was uneventful. **Conclusion :** We successfully performed uterine-sparing surgery for giant AMFB. A key for success of treatment might be induction of preoperative pseudo-menopause whereby reduction of both size and vascularization of the tumor.

ISP-4-1

p16INK4A expression might be associated with a favorable prognosis for cervical adenocarcinoma via dysregulation of the RB pathway Ishikawa Masako, Nakayama Kentaro, Sawada Kiyoko, Nonomura Yuki, Yamashita Hitomi, Fukushima Ruriko, Ishibashi Tomoka, Sato Seiya, Iida Koji, Kyo Satoru *Shimane University*

[Objective] Previous studies have largely failed to clarify the relationship between p16^{INK4A} status and cervical adenocarcinoma prognosis. The current study aimed to examine the clinical and pathological significance of p16^{INK4A} expression in several cervical adenocarcinoma subtypes. **[Methods]** Eighty-two samples collected from patients with cervical adenocarcinoma were formalin fixed and paraffin embedded. Next, p16^{INK4A} levels were analyzed with immunohistochemistry. Additionally, the relationship between p16^{INK4A} expression and clinicopathological factors as well as prognosis was evaluated. **[Results]** The expression of p16^{INK4A} was mostly detected in all usual cervical adenocarcinoma subtypes. In the gastric type, only a few cases were positive for p16^{INK4A} expression. Results of the Kaplan-Meier analysis indicated that the positive p16^{INK4A} expression in tumor cells was significantly associated with favorable progression-free survival and overall survival in patients with cervical adenocarcinoma ($p=0.018$ and $p=0.047$, respectively, log-rank test). Our findings suggest that the status of p16^{INK4A} expression may influence prognosis. **[Conclusion]** Thus, p16^{INK4A} expression could be used as a biomarker for improving the prognosis of patients with cervical adenocarcinoma.

ISP-4-2

Estrogen induces genomic instability under high-risk HPV infection in cervical adenocarcinoma Ogawa Minori, Hashimoto Kae, Kitano Saki, Toda Aska, Nakamura Koji, Kinose Yasuto, Kodama Michiko, Sawada Kenjiro, Kimura Tadashi *Osaka University*

[Objective] Cervical cancer was believed to be estrogen-insensitive neoplasms, however some epidemiological studies suggested postmenopausal estrogen-progestogen therapy increase prevalence of cervical adenocarcinoma (CA). We hypothesized that, in CA, estrogen-induced carcinogenesis was increased under DNA repair deficiency caused by HPV infection. The purpose of this study is to elucidate the role of estrogen in the carcinogenesis of CA. **[Methods]** The expression of estrogen

receptors, GPR30 and ER α was examined in clinical samples by immunohistochemistry. Cellular proliferation was measured by MTS assay using cell lines, HCA-1, NCC16-P11 and HeLa. γ H2AX and Rad51, the DNA damage and repair marker, were evaluated by fluorescent immunostaining. γ H2AX also evaluated by fluorescence-activated cell sorting. Chromosomal aberration was examined by Giemsa stain. **[Results]** The GPR30 was expressed in 73% of normal endocervical glands and 7% of squamous epithelium; ER α was expressed in 33% of normal endocervical glands and 67% of squamous epithelium. Cell proliferation was increased by estradiol and GPR30 agonist compared to negative control (NC) in five-day (25% and 23%). Estradiol increased the expression of γ H2AX than NC in HPV16 E6-positive cells (14.0 vs. 3.5, $p < 0.01$) and si-E6 counteracted that. In HPV16 E6-positive cells, the mislocation of Rad51 to γ H2AX was increased than NC (65% vs. 20%, $p < 0.01$), suggesting the homologous recombination function of Rad51 was reduced. Giemsa staining showed chromosomal aberration in HPV16 E6-positive cells with estradiol. **[Conclusion]** Estrogen increased genomic instability under high-risk HPV infection. This genomic instability is thought to induce the carcinogenesis of CA.

ISP-4-3

Itraconazole inhibits intracellular cholesterol trafficking and decreases phosphatidylserine level in cervical cancer cells Takimoto Yumi, Isono Roze, Tsubamoto Hiroshi, Ueda Tomoko, Inoue Kayo, Shibahara Hiroaki *The Hospital of Hyogo College of Medicine*

[Objective] Itraconazole shows anticancer activity in various types of cancer but its underlying mechanism is unclear. We investigated the effect of itraconazole on membrane-associated lipids. **[Methods]** To investigate the influences of itraconazole on cholesterol trafficking, cervical cancer CaSki cells were cultured with itraconazole and analyzed by Filipin staining followed by confocal microscopy. Effect on the glycerophospholipid profiles was analyzed by liquid chromatography/mass spectrometry (LC/MS). **[Results]** After itraconazole treatment, Filipin staining revealed cholesterol accumulation in the intracellular compartments, which was similar to the distribution after treatment of U18666A (cholesterol transport inhibitor). LC/MS analysis showed a significant decrease in phosphatidylserine levels and an increase in lysophosphatidylcholine levels in CaSki cells. **[Conclusion]** Itraconazole inhibited cholesterol trafficking and altered the phospholipid composition. Alterations in the cell membrane can potentiate the anticancer activity of itraconazole.

ISP-4-4

Poorly differentiated cervical squamous cell carcinoma resembling giant cell carcinoma of the lung : Extreme morphology of this tumor and its clinical course Kurita Tomoko¹, Shibahara Mami¹, Tooyama Atsushi¹, Aoyama Yoko¹, Kuwazuru Tomoichiro¹, Hoshino Kaori¹, Nishimura Kazuaki¹, Harada Hiroshi^{1,2}, Ueda Taeko¹, Kagami Seiji³, Matsuura Yusuke², Yoshino Kiyoshi¹ *University of Occupational and Environmental Health¹, Nursing of Human Broad Development, University of Occupational and Environmental Health², Kyushu Rosai Hospital³*

[Objective] Giant cell carcinoma is a distinctive, highly aggressive tumor characterized by the striking proliferation of pleomorphic, bizarre giant cells usually observed in the lung. The importance of histopathological imaging and the clinical course of this tumor are unknown. To investigate whether this component affects treatment outcomes and prognosis compared to conventional cancers. **[Case report]** A 40-year-old woman with

cervical cancer showed leukocytosis and elevated G-CSF. An extensive work-up revealed that the clinical diagnosis was stage IIA2 cancer of the uterine cervix. The patient underwent a radical abdominal hysterectomy. Pathological examination revealed poorly differentiated cervical squamous cell carcinoma resembling giant cell carcinoma. Immunohistochemically, these neoplastic cells were positively reactive to p16, and they were focally positive for p40 and CK5/6, whereas they were negative for CK20, CDX-2, and TTF-1. The final pathological diagnosis was poorly differentiated cervical squamous cell carcinoma. The patient was alive with no evidence of disease 37 months after CCRT. After treatment, leukocytosis and G-CSF were normalized. **[Conclusion]** To date, there have been few reports of giant cell carcinoma in gynecologic cancer. It is unclear whether the tumor is extremely rare or if it was unrecognized and treated as poorly differentiated or undifferentiated cancer. Cumulative data on giant cell carcinoma are limited, thus we considered the prognostic significance of the presence of giant cell carcinoma in uterine carcinoma.

ISP-4-5

FYN expression predicts the efficacy of neoadjuvant chemotherapy for locally advanced uterine cervical cancer Nanno Shigenori, Fukuda Takeshi, Noda Takuya, Uchikura Eijiro, Awazu Yuichiro, Imai Kenji, Yamauchi Makoto, Yasui Tomoyo, Sumi Toshiyuki *Osaka City University Hospital*

[Objective] We examined the correlation between FYN (a member of the Src family) expression and the efficacy of neoadjuvant chemotherapy (NAC) for locally advanced uterine cervical cancer. **[Methods]** We reviewed 53 cases of locally advanced uterine cervical cancer (stage IIIA and IIIB, FIGO2008) from 1996 to 2010. Cases were divided into two groups: one group in which NAC was effective, surgery was possible and radiotherapy was performed (group A; n=28), and the other group in which NAC was ineffective and radiation therapy was performed (group B; n=25). FYN expression was examined immunohistochemically in paraffin-embedded sections. The effect of the small interfering RNA-mediated knockdown of FYN on the sensitivity of cervical cancer cells to cisplatin was investigated *in vitro*. This study was approved by the institutional review board in our facility. **[Results]** The expression of FYN was significantly higher in group B than in group A ($p=0.0038$). Cases were divided into two groups: one group in which FYN expression was low level (weighted score ≤ 3 , n=31), and the other group in which FYN expression was high level (weighted score ≥ 4 , n=22). The low FYN expression group might be more responsive to NAC than the high expression group ($p=0.0023$). The low FYN expression group had a more favorable overall survival compared with the high FYN expression group ($p=0.0372$). Furthermore, knockdown of FYN expression significantly increased cancer cell sensitivity to cisplatin *in vitro*. **[Conclusion]** FYN expression may be a useful indicator of the response to NAC for patients with locally advanced uterine cervical cancer.

ISP-4-6

Microarray analyses of HPV oncogene E7-specific pathways in cervical carcinogenesis Qi Nan², Minaguchi Takeo¹, Xu Chenyang², Fujieda Kaoru¹, Suto Asami¹, Itagaki Hiroya¹, Shikama Ayumi¹, Tasaka Nobutaka¹, Akiyama Azusa¹, Nakao Sari¹, Ochi Hiroyuki¹, Satoh Toyomi¹ *University of Tsukuba¹, Graduate School of Comprehensive Human Sciences, University of Tsukuba²*

[Objective] The molecular mechanisms whereby the E7 oncogene contribute to the development of cervical lesions with more malignant natures than the E6 oncogene are yet to be

fully clarified. The aim of our study was to investigate E7-specific pathways in cervical carcinogenesis. **[Methods]** We knocked down the E6 and E7 genes by gene-specific siRNAs in CaSki and HeLa cells. Microarray analyses were conducted using mRNAs extracted from the cells, and differentially expressed genes (DEGs) were identified by the BRB-Array tools. E7-specific DEGs were extracted by the FunRich program. Protein-protein interactions (PPI), hub genes, modules, and pathway interactions were analyzed by the Cytoscape program. **[Results]** Seven genes were extracted as E7-specific DEGs. In the PPI analysis based on those DEGs, the identified hub genes included *CCND1*, *HDAC1* and *ESR1*, all of which were found in the same module. This module involved cell cycle, apoptosis, DNA damage response, DNA repair, and estrogen signaling pathways, etc. **[Conclusion]** The above identified hub genes may be playing important roles in the E7-specific cervical carcinogenic mechanisms.

ISP-4-7

CLPTMIL expression predicts recurrence of intermediate- and high-risk stage IB-IIB cervical cancer undergoing radical hysterectomy followed by TP as adjuvant chemotherapy Awazu Yuichiro, Fukuda Takeshi, Noda Takuya, Uchikura Eijiro, Nanno Shigenori, Imai Kenji, Yamauchi Makoto, Yasui Tomoyo, Sumi Toshiyuki *Osaka City University Hospital*

[Objective] We examined the correlation between CLPTMIL (Cleft lip and palate transmembrane protein 1-like) expression and recurrence of intermediate- and high-risk stage IB-IIB (FIGO2008) cervical cancer undergoing radical hysterectomy followed by TP (paclitaxel plus cisplatin). **[Methods]** We reviewed 91 cases of intermediate- and high-risk stage IB-IIB cervical cancer patients who underwent TP after radical hysterectomy from 2014 to 2019. Cases were divided into two groups, one group in which the patients didn't recur within 2 years after initialization of treatment (group A : n=76), and the other group in which the patients recurred within 2 years (group B : n=15). CLPTMIL expression was examined immunohistochemically in paraffin-embedded sections. Multiple logistic regression analysis was performed to identify independent predictor of recurrence. This study was approved by the institutional review board. **[Results]** The expression of CLPTMIL was significantly higher in group B than in group A ($p<0.001$). Cases were divided into two groups according to a cutoff value of 6 which was calculated using a receiver operating characteristic curve ; one group in which CLPTMIL expression was low level (weighted score ≤ 4 , n=59), and another group in which CLPTMIL expression was high level (weighted score ≥ 6 , n=32). Low CLPTMIL expression was more likely related to recurrence after adjuvant TP than high expression ($p<0.01$). And multivariate analysis revealed that CLPTMIL expression was an independent predictor of recurrence ($P=0.003$). **[Conclusion]** High CLPTMIL expression might be associated with cancer recurrence of intermediate- and high-risk stage IB-IIB cervical cancer undergoing radical hysterectomy followed by TP.

ISP-4-8

Development of on-chip p16/Ki67 double immunostaining system using microfluidic device technology for cervical cancer screening Hashimoto Kei¹, Miyagawa Yuko¹, Kumagai Tomoo¹, Koike Ryoko¹, Takahashi Yuko¹, Nishida Haruka¹, Ichinose Takayuki¹, Kihira Chikara¹, Hiraike Haruko¹, Kim Soo Hyeon², Nagasaka Kazunori¹ *Teikyo University¹, Department of Mechanical and Biofunctional Systems, Institute of Industrial Science, The University of Tokyo²*

[Objective] p16/Ki-67 double-stained cytology is considered high clinical significance and is expected to be a triage method

for high-risk HPV-positive women. p16/Ki-67 double staining can reduce the number of unnecessary tests. However, p16/Ki-67 double-staining cytology requires advanced diagnostic skills to be acquired by specialized cytotechnicians. In this study, we aim to develop an automated on-chip immunostaining method using a microfluidic device. **[Methods]** This study used a microfluidic device called electroactive microwell array (EMA), patterned thin-film electrodes at the bottom of each microwell for single-cell capture by dielectrophoresis (DEP). Immunostaining was performed on diagnosed cytology samples stored on a liquid basis and examined by double staining for p16/Ki-67 with the EMA device. We measured the number of p16/Ki-67 double-stained cells captured by the EMA device. The proportion of double-stained positive cells from cervical intraepithelial neoplasia (CIN) lesions was then examined. **[Results]** We examined three samples from cervical carcinoma in situ (CIS), ten samples from CIN3, and five samples from CIN2. A total of 5,000 positive cells were counted using an automated cell counting program (BZ-X800, KEYENCE). The percentage of double-positive cells was 7.2% for CIN2, 17.5% for CIN3, and 32.1% for CIS. All experiments were repeated three times. The positive staining for p16/Ki-67 in the population significantly increased with the severity of the cervical lesions. **[Conclusion]** The p16/Ki67 double immunostaining using the EMA device is as sensitive as the conventional method in confirming the histopathological diagnosis without losing valuable cervical samples and allows quantified parallel analysis at the individual cell level.

ISP-5-1

BHLHE40 regulates glycolysis and oxidative phosphorylation mediated by a phosphatase-AMPK axis in endometrial cancer cells Asanoma Kazuo, Yagi Hiroshi, Onoyama Ichiro, Kodama Keisuke, Kawakami Minoru, Yasutake Nobuko, Maenohara Shoji, Yasunaga Masafumi, Ohgami Tatsuhiro, Okugawa Kaoru, Yahata Hideaki, Kato Kiyoko *Kyushu University Hospital*

[Objective] Cancer cells are known to depend on glycolysis for energy production. However, regulatory mechanism of metabolism in cancer cells remains largely unknown. In this study, we studied a regulation of glycolysis and oxidative phosphorylation (OXPHOS) by a tumor suppressive transcription factor, BHLHE40 in endometrial cancer cells. **[Methods]** We used endometrial cancer cells to knockdown or overexpress BHLHE40 to examine their cellular glycolysis and OXPHOS using a flux analyzer. The expression of AMP-activated protein kinase alpha, AMPKA ; lactate dehydrogenase A subunit, LDHA ; and pyruvate dehydrogenase E1 subunit alpha 1, PDHA1 were examined by antibodies to detect total and phosphorylated forms of each protein. The activity of PDH and LDH was also examined. PPM1 family of phosphatase was examined to regulate AMPK activity. Transcriptional regulation of PPM1 family by BHLHE40 was also examined using a reporter assay. **[Results]** Knockdown of BHLHE40 in the cancer cells resulted in upregulation of glycolysis accompanied with activation of LDH, and downregulation of OXPHOS accompanied with suppression of PDH. Remarkable suppression of AMPK activity was observed. On the contrary, forced expression of BHLHE40 in the cancer cells exert the reverse effects. We also discovered BHLHE40-regulated phosphatase suppressed AMPK activity. **[Conclusion]** BHLHE40 is suggested to regulate the activity of AMPK to control the metabolic balance between glycolysis and OXPHOS in endometrial cancer cells. Understanding the mechanism of energy production in cancer cells might lead to a new strategy to control the development of endometrial cancer.

ISP-5-2

Anti-LSR monoclonal antibody for endometrial cancer : Pre-clinical study as a potential therapeutic agent Nagase Yoshikazu¹, Hiramatsu Kosuke¹, Funauchi Masashi^{1,2}, Kakuda Mamoru¹, Nakagawa Satoshi¹, Miyoshi Ai¹, Matsuzaki Shinya¹, Kobayashi Eiji¹, Kimura Toshihiro¹, Ueda Yutaka¹, Naka Tetsuji², Kimura Tadashi¹ *Osaka University¹, Division of Clinical Immunology, Department of Internal Medicine, Iwate Medical University²*

[Objective] Advanced and recurrent endometrial cancer (EC) has a poor prognosis. Since the efficacy of current chemotherapy is limited, new therapeutic agents are needed. We focused on lipolysis-stimulated lipoprotein receptor (LSR), a membrane protein highly expressed in EC cells, and developed a new anti-LSR monoclonal antibody (mAb). In this study, we aimed to investigate the antitumor effect of anti-LSR mAb and the function of LSR in EC cells. **[Methods]** Survival and clinicopathological analysis based on immunohistochemistry for LSR was performed in 228 EC patients. We developed a chimeric chicken-mouse anti-LSR mAb and evaluated its antitumor activity in EC cell xenograft mouse model. To clarify the function of LSR, we conducted in vitro assays using EC cell lines (HEC1 and HEC116) and pathway enrichment analysis using protein expression data of EC samples. **[Results]** High expression of LSR was significantly associated with decreased 5-year overall survival rate (hazard ratio 3.53, 95% confidence interval 1.35-9.24), deep myometrial invasion, and metastasis in EC patients ($p < 0.05$, respectively). Our anti-LSR mAb inhibited the tumor growth in HEC1 xenograft mouse model (tumor volume, 407.1 mm³ versus 726.3 mm³, $p = 0.019$). In vitro assays and pathway enrichment analysis showed that LSR promoted EC cell proliferation, invasion, and migration and that the ERK/MAPK signaling pathway and subsequent matrix metalloproteinases (MT1-MMP and MMP2) are significantly involved in these mechanisms. **[Conclusion]** LSR is associated with tumor growth, invasion, metastasis, and poor prognosis in EC. Our preclinical study proposes an anti-LSR mAb as a potential antitumor agent against EC.

ISP-5-3

Fibronectin mediates activation of stromal fibroblasts by SPARC in endometrial cancer cells Yoshida Sachiko¹, Asanoma Kazuo², Yagi Hiroshi², Onoyama Ichiro², Okugawa Kaoru², Yahata Hideaki², Kato Kiyoko² *Tagawa Municipal Hospital¹, Kyushu University Hospital²*

[Objective] Matricellular glycoprotein, SPARC is a secreted molecule, that mediates the interaction between cells and extracellular matrix. SPARC functions as a regulator of matrix organization and modulates cell behavior. In various kinds of cancer, strong SPARC expression was observed in stromal tissues as well as in cancer epithelial cells. The function of SPARC in cancer cells is somewhat controversial and its impact on peritumoral stromal cells remains to be resolved. **[Methods]** We investigated the effects of SPARC expression in endometrial cancer cells on the surrounding stromal fibroblasts using in vitro coculture system. Changes in characteristics of fibroblasts were examined by analysis of fibroblast-specific markers and in vitro contraction assay. **[Results]** SPARC induced AKT phosphorylation and epithelial-to-mesenchymal transition, consistent with previous reports. Cancer-associated fibroblasts of endometrial cancer expressed higher levels of mesenchymal- and fibroblast-associated factors and had a stronger contraction ability. Unexpectedly, cancer-associated fibroblasts expressed comparable levels of SPARC compared with fibroblasts from normal endometrium. However, co-culture of normal fibroblasts with SPARC-expressing Ishikawa cells resulted in activation of the fibroblasts. Immunodepletion of SPARC did not affect the acti-

vation of fibroblasts. **[Conclusion]** Our data indicated that SPARC activated fibroblasts only in the presence of fibronectin, which was abundantly secreted from SPARC-expressing endometrial cancer cells. These results suggested that a SPARC-fibronectin-mediated activation of fibroblasts might be involved in enhanced mobility and invasion of cancer cells.

ISP-5-4

Long non-coding RNA DLEU2 drives EMT and glycolysis in endometrial cancer through HK2 by binding with miR-455 Dong Peixin, Ihira Kei, Konno Yosuke, Watari Hidemichi *Hokkaido University*

[Objective] Although increasing evidence demonstrates an association between epithelial-to-mesenchymal transition (EMT) and enhanced aerobic glycolysis in human cancer, the mechanisms linking these two conditions in endometrial cancer (EC) cells remain poorly defined. **[Methods]** We characterized the role and molecular mechanism of the glycolytic enzyme hexokinase 2 (HK2) in mediating EMT and glycolysis and investigated how long noncoding RNA DLEU2 contributes to the stimulation of EMT and glycolysis via upregulation of HK2 expression. **[Results]** HK2 was highly expressed in EC tissues, and its expression was associated with poor overall survival. Overexpression of HK2 effectively promoted EMT phenotypes and enhanced aerobic glycolysis in EC cells. Moreover, microRNA-455 (miR-455) served as a tumor suppressor by directly interacting with HK2 mRNA and inhibiting its expression. Furthermore, DLEU2 displayed a significantly higher expression in EC tissues, and increased DLEU2 expression was correlated with worse overall survival. We found that DLEU2 acted as an upstream activator for HK2-induced EMT and glycolysis in EC cells by inducing HK2 expression through binding with miR-455. **[Conclusion]** This study identified DLEU2 as an upstream activator of HK2-driven EMT and glycolysis in EC cells and provided significant mechanistic insights for the potential treatment of EC.

ISP-5-5

The antitumor effect of alpha-particle emitting astatine-211-labeled trastuzumab for uterine serous carcinomas which overexpress HER2 Anko Mayuka^{1,2}, Banno Kouji¹, Kobayashi Yusuke¹, Nogami Yuya¹, Tsuji Kosuke¹, Masuda Kenta¹, Hasegawa Sumitaka², Tanaka Mamoru¹, Aoki Daisuke¹ *Keio University¹, Radiation and Cancer Biology Group, National Institutes for Quantum and Radiological Science and Technology²*

[Objective] Astatine-211 (At-211), an alpha-particle emitting radionuclide, is characterized by its short range and high linear energy transfer, which allows it to cause effective damage to tumor tissue and little damage to normal tissue. Although almost 35-44% of uterine serous carcinomas (USCs) have HER2 overexpression or gene amplification, the efficacy of the anti-HER2 antibody, trastuzumab, as a single agent has not been clear to date. We aimed to evaluate the efficacy of At-211-labeled trastuzumab (²¹¹At-trastuzumab) on HER2 high expressing (HER2-high) human USC cell lines. **[Methods]** Five human USC cell lines, three HER2-high and two HER2-low, were used for our experiments. One hour after administration, the cell binding ability was evaluated by measuring the radioactivity of ²¹¹At-trastuzumab bound to the cells. Specific binding capacity was also measured by preadministering trastuzumab to block HER2 before administering ²¹¹At-trastuzumab. Furthermore, the cytotoxicity of ²¹¹At-trastuzumab for 24 hours was evaluated by measuring cell viability. **[Results]** In HER2-high cell lines, ²¹¹At-trastuzumab specifically bound to cells at 2.9-9.5 times more than the control group ($n = 3$, $P < 0.05$; Student t-test). Moreover, in HER2-high cell lines, the cell survival rates were 22.1-

40.9% in ²¹¹At-trastuzumab 1.85kBq group and 96.5-110.7% in trastuzumab group (n=3, P<0.05; Tukey-Kramer HSD test). **[Conclusion]** The efficacy of ²¹¹At-trastuzumab for HER2-high USC cell lines was demonstrated in vitro. These experiments may be a precursor to targeted alpha-particle therapy, in which alpha-particle emitting nuclides are specifically delivered to cancerous cells for treatment.

ISP-5-6

ARID1A deficiency is not suitable as a biomarker for immune checkpoint inhibitors in endometrial cancer Yamashita Hitomi, Nakayama Kentaro, Kanno Kousuke, Nonomura Yuki, Sawada Kiyoka, Fukushima Ruriko, Ishibashi Tomoka, Ishikawa Masako, Sato Seiya, Iida Koji, Kyo Satoru *Shimane University Hospital*

[Objective] ARID1A deficiency is currently recognized as a biomarker for immune checkpoint inhibitors (ICIs) because ARID1A has been reported to interact with one of the mismatch repair (MMR) proteins, MSH2. Cases in which at least one of the four MMR proteins by immunostaining was negative were excluded. There were no significant differences in the expression levels of tumor-infiltrating lymphocytes (CD8), PD-L1 and PD-1 between ARID1A deficient group and ARID1A expression group. Therefore, we conducted additional analyses to determine if ARID1A deficiency is suitable as a biomarker for ICIs. **[Methods]** We performed MSI analysis of ARID1A knockout human ovarian endometriotic epithelial cells (HMOsIEC7). In cases of positive ARID1A immunostaining, Sanger sequencing of ARID1A was performed at the regions that binds to MSH2. We added cases with ARID1A mutations detected using Sanger sequencing to ARID1A deficient group, and re-evaluated the expression of CD8, PD-L1 and PD-1 between ARID1A deficient group and ARID1A expression group. **[Results]** ARID1A knockout in HMOsIEC7 was negative for all microsatellite markers at both 3 and 78 population doubling. Three of 78 cases showed ARID1A mutations. There were no significant differences in the expression levels of CD8, PD-L1 and PD-1 between the two groups. **[Conclusion]** ARID1A deficiency is not suitable as a biomarker for ICIs. The previous reports that ICIs are effective in ARID1A deficient tumors have not examined the expression of MMR proteins. Therefore, MMR deficiency may have influenced previous reports that ICIs are effective in ARID1A deficient tumors.

ISP-5-7

Claudin-9 is a novel biomarker of the prognosis of Endometrial cancer Endo Yuta, Kojima Manabu, Kato Asami, Okabe Chikako, Sato Tetsu, Ueda Makiko, Kamo Norihito, Furukawa Shigenori, Soeda Shu, Watanabe Takafumi, Fujimori Keiya *Fukushima Medical University*

[Objective] Claudins (CLDNs) are major tight junction proteins. There are more than 20 CLDNs. Some are aberrantly expressed in various types of cancers and are utilized as cancer biomarkers. Recently, we reported that aberrant CLDN6 expression predicts poor prognosis in endometrial cancer (EC). CLDN9, the closest member to CLDN6, is also expressed at the mRNA level in patients with poor prognosis. We aimed to evaluate the prognostic significance of CLDN9 protein in EC. **[Methods]** A monoclonal antibody against human CLDN9 was generated and its specificity was verified. Immunohistochemical staining and semi-quantification were performed to evaluate the relationship between CLDN9 expression and clinicopathological parameters in tissues from 134 cases of EC. Additionally, CLDN9 and CLDN6 expressions were compared. **[Results]** Twenty-four cases (17.9%) displayed high CLDN9 expression. The 5-year overall survival (OS) rate in the high and low CLDN9 group was 62.5%

and 90.0%, respectively. High CLDN9 expression was associated with significantly poor disease specific survival (DSS) and with high CLDN6 expression. The 5-year OS rate was approximately 30% in the high CLDN6 group regardless of CLDN9 expression. In the low CLDN6 group, the 5-year OS rate in the high and low CLDN9 group was 76.5% and 91.6%, respectively, and high CLDN9 expression was associated with poor DSS. **[Conclusion]** Aberrant CLDN9 expression predicts poor prognosis for EC. Especially, CLDN9 protein is produced in CLDN6-negative patients with poor prognosis. The combination of CLDN6 and CLDN9 could be advantageous to identify patients with EC with a poor prognosis.

ISP-6-1

Development of a rapid preoperative diagnosis method using isothermal nucleic acid amplification technology, and novel predictive model of combining the mRNA biomarkers and clinical variables for diagnosis of lymph node metastases in endometrial cancer Yoshida Emiko¹, Terao Yasuhisa¹, Ueno Yuta¹, Kato Hisamori², Kato Tomoyasu³, Ito Yosuke⁵, Notomi Tsuguto², Fujihara Risa¹, Hirayama Takashi¹, Fujino Kazunari¹, Itakura Atsuo¹ *Juntendo University¹, Kanagawa Cancer Center², National Cancer Center Hospital³, Nippon Medical School Chiba Hokusoh Hospital⁴, Juntendo University Nerima Hospital⁵*

[Objective] The therapeutic role of lymphadenectomy in surgical management of endometrial cancer remains controversial. Noninvasive and high-precision diagnosis method for lymph node metastatic state which supplants lymphadenectomy is highly demanded. Here, we attempted to accelerate gene quantitative analysis in order to realize intraoperative diagnosis, and to develop a novel predictive model using clinical variables and quantitative values of biomarkers. **[Methods]** Four mRNA biomarkers including SEMA3D, TACC2 novel isoform and two companion-markers, were quantified by real-time reverse transcription polymerase chain reaction. Logistic regression analysis was used to calculate probability of LNM by using biomarker quantitative values and clinical variables including Kanagawa cancer center scoring parameters, and biomarker quantitative values. Then we assessed whether RT-SmartAmp method, which can detect nucleic acids in one step consisting of a reverse transcription and an isothermal amplification of DNA, could quantify our biomarker RNA rapidly. We measured the speed of amplification and target specificity based on biomarker RNA as the template in one step containing reverse transcription step. **[Results]** First, we validated the diagnostic accuracy by using previous single-facility data set of 115 patients. Secondary, the reproducibility was confirmed using the validation data set of 650 patients collected in multi-facilities. The accuracy was very high (AUC 0.83) even if all cases were targeted. Additionally, we also succeeded to develop a promising primer set to quantify biomarker genes by using SmartAmp. This novel method can detect RNA quantitatively within 30 minutes. **[Conclusion]** Our findings pave the way for support clinical decisions that minimize irrelevant lymphadenectomy.

ISP-6-2

Molecular Pathological analysis of uterine rhabdomyosarcoma Hayashi Takuma, Tamura Saya, Ichimura Tomoyuki, Abiko Kaoru, Yaegashi Nobuo, Konishi Ikuro *PRUM IBio Study*

[Objective] Uterine sarcoma is classified into carcinosarcoma, which is a mixed epithelial and mesenchymal tumor, and mesenchymal tumor (leiomyosarcoma, endometrial stromal sarcoma, adeno-sarcoma, etc.). In addition, among the ectopic mesenchymal tumors that develop in the uterus, rhabdomyosarcoma may develop as a component of mesoderm mixed tumors. The frequency of rhabdomyosarcoma in uterine malignancies is less

than 0.1%, and rhabdomyosarcoma is considered to be a very rare tumor. Therefore, rhabdomyosarcoma has unclear points in terms of molecular pathology. **[Methods]** Based on the markedly reduced expression of LMP2, candidate factors as biomarkers specifically expressed in uLMS have been sought by genome-wide experimental methods. As a result, CAVEOLIN, CYCLIN B, CYCLIN E, Ki-67 and LMP2 were identified as biomarker candidate factors specifically expressed in uterine mesenchymal tumors including uLMS. We examined the oncological properties of rhabdomyosarcoma by molecular pathological analysis including the expression status of these biomarkers. **[Results]** Previous clinical studies suggest that rhabdomyosarcoma patients with high expression of Cyclin E and Ki-67 may have a poor prognosis. In addition, unlike uterine leiomyosarcoma, expression of LMP2 was observed in uterine rhabdomyosarcoma. **[Conclusion]** The expression status of Cyclin E and Ki-67 is considered to correlate with the malignancy of uterine rhabdomyosarcoma. The results of molecular pathological analysis of rhabdomyosarcoma may contribute to the development of new therapies.

ISP-6-3

Identification of companion markers for endometrial cancer risk assessment Ito Yosuke¹, Yoshida Emiko², Terao Yasuhisa² *Juntendo University Nerima Hospital¹, Juntendo University Hospital, Juntendo University²*

[Objective] In a previous study, we reported a biomarker that assesses lymphatic metastasis based on SEMA3D and TACC2 gene expression patterns in primary lesions in the low to moderate recurrence risk group of endometrial cancer. Since this biomarker is intended only for low to moderate recurrence risk groups, it is necessary to distinguish low to moderate recurrence risk groups from all patients in advance. So we searched other companion marker to distinguish between the two risk groups. We identified the companion markers. And we report on their evaluation. **[Methods]** We performed screening analysis in Low risk lymph node metastasis minus group vs High risk lymph node metastasis positive group using the CAGE method, which can comprehensively capture the transcription initiation site and analyze gene expression in the entire genome. Furthermore, based on TCGA data, candidate genes with significantly different expression levels between the high recurrence risk group and the low to medium recurrence risk group were identified. Next, discrimination was performed based on the relative expression level by mRNA quantification. **[Results]** PR was listed as a candidate gene from CAGE analysis. There were significant differences in PR and ER mRNA quantification between the Endometrioid G1/G2 group and other histological groups. **[Conclusion]** It was shown that ER and PR can be evaluated quantitatively compared with the qualitative evaluation by immunohistochemistry performed for endometrial cancer. It was suggested that evaluation in combination with SEMA3D and TACC2, which are predictive markers for lymph node metastasis, may contribute to appropriate surgical procedure selection.

ISP-6-4

New treatment strategies for uterine sarcoma by secreted frizzled-related protein Kagawa Tomohiro, Mineda Ayuka, Nishimura Masato, Irahara Minoru, Iwasa Takeshi *Tokushima University*

[Objective] Secreted frizzled-related protein (SFRP) has been reported to be involved in the development of various cancer types by suppressing the Wnt signaling pathway. To clarify the clinical implications of SFRP in uterine sarcoma, expression level of SFRP and the effects of SFRP on uterine sarcoma cells were examined. **[Methods]** Immunostaining of SFRP was per-

formed in the tissues of uterine smooth muscle, uterine fibroid, and uterine leiomyosarcoma. Intensity score (0-3) and proportion score (0-3) were evaluated and compared among these tissues. In addition, the effects of SFRP4 administration on the cell concentration, proliferation and adhesion ability were evaluated in uterine sarcoma cells (SKN and MES-SA). **[Results]** The mean intensity of SFRP4 expression in uterine smooth muscle, uterine fibroid, and uterine leiomyosarcoma were 2.25, 2.75, 1.25, and mean proportion were 2.75, 3.0, 1.75, respectively. Expression level of SFRP4 in uterine leiomyosarcoma tissue was lower than those in normal smooth muscle and uterine fibroids tissues ($p < 0.05$). SFRP4 suppressed the cell concentration and proliferation, and increased the adhesion ability in uterine sarcoma cells, i.e. SKN and MES-SA, compared with control cells ($p < 0.05$). **[Conclusion]** SFRP4 expression was low in uterine sarcoma cells, and SFRP4 administration suppressed sarcoma cell proliferation and increased adhesion ability. These results suggest that SFRP4 may be a new therapeutic target for uterine sarcoma.

ISP-6-5

ProMisE is a useful molecular classification for prognostic evaluation of Japanese patients with endometrial carcinoma Masuda Sayaka¹, Nakayama Kentaro², Kanno Kousuke², Makihara Kan², Sawada Kiyoka², Nonomura Yuki², Yamashita Hitomi², Ishibashi Tomoka², Ishikawa Masako², Sato Seiya², Kyo Satoru² *Kurashiki Medical Center¹, Shimane University Hospital²*

[Objective] Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) is a clinically useful, simplified molecular classification based on a combination of immunohistochemistry for mismatch repair (MMR) proteins and tumor protein 53 (*p53*) and sequencing of polymerase epsilon (*POLE*) mutation. The four subgroups identified by ProMisE are prognostically comparable to the genomic subgroups in the The Cancer Genome Atlas (TCGA). We investigated whether ProMisE could be a useful assessment tool for predicting the prognosis of Japanese patients with endometrial carcinoma. **[Methods]** We retrospectively assessed patients treated for endometrial carcinoma between 2006 and 2017. Immunohistochemistry for MMR proteins (MSH2, MSH6, PMS2, and MLH1) and *p53*, and sequencing for *POLE* exonuclease domain hotspot mutations (exon 9-14) were performed and four subgroups (MMR deficiency, *p53* mutation, *p53* wild type, and *POLE* mutation) were identified. We compared the overall survival (OS) and progression-free survival (PFS) among four subgroups. **[Results]** There were 148 cases of endometrial carcinoma, 44 (29.7%) with MMR deficiency, 28 (18.9%) with *p53* mutation, 71 (48.0%) with *p53* wild type, and 5 (3.4%) with the *POLE* mutation. There was a significant difference in OS ($P=0.0019$) and PFS ($P=0.00185$) among the four ProMisE subgroups. The *POLE* mutation group had the best prognosis, while the *p53* mutation group had the worst prognosis, similar to the survival curve shown by the TCGA genomic subgroup. **[Conclusion]** ProMisE is useful for the stratification of prognostic inference in patients with endometrial carcinoma.

ISP-6-6

Mutational analysis of KRAS/PIK3CA gene in a normal endometrial epithelium Sato Seiya, Nakayama Kentaro, Ishikawa Masako, Ishibashi Tomoka, Yamashita Hitomi, Fukushima Ruriko, Sawada Kiyoka, Nonomura Yuki, Saito Hikaru, Kanno Kousuke, Makihara Kan, Kyo Satoru *Shimane University*

[Objective] This study aimed to clarify the frequency and biological significance of *KRAS/PIK3CA* driver mutations in normal endometrial epithelium. **[Methods]** This study was conducted using resected uteri diagnosed with benign gynecologi-

cal disease (n=3). The endometrium was macroscopically divided into nine regions, and ten endometrial single glands were randomly separated from each region under a microscope. Another 30 glands were subjected to a long-term spheroid culture for each region, and spheroids grown to a diameter of ≥ 2 mm were collected. DNA was extracted from a single gland and spheroids. *KRAS* or *PIK3CA* driver mutations were assessed using the Sanger method, and the relationship between the frequency of each endometrial region and the efficiency of spheroid formation was analyzed. **[Results]** The mutation detection rate in single glands was 9.3% (25/270), and the mutation frequency in each endometrial region varied from 0% to 50%. Thirty-three spheroids were collected; however, there was no correlation between the frequency of mutation in each endometrial region and the number of spheroids generated. The mutation detection rate in spheroids was 63.3% (21/33), which was significantly higher than that in single glands; all of these were *PIK3CA* mutations, and no *KRAS* mutation was observed. **[Conclusion]** There is a regional diversity in genetic mutations in a normal endometrial epithelium. Considering the characteristics of spheroid cultures that provide a stem cell-rich environment, the aberrant proliferation of endometrial epithelial stem cells was suggested to be associated with *PIK3CA* mutations.

ISP-7-1

A role of vaginal cytology for postoperative surveillance of endometrial cancer

Watanabe Yuko, Kobayashi Eiji, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Miyoshi Ai, Kodama Michiko, Hashimoto Kae, Ueda Yutaka, Sawada Kenjiro, Tomimatsu Takuji, Kimura Tadashi *Osaka University*
[Objective] Although there are many skeptical reports about the significance of vaginal cytological examination, which is routinely performed in the postoperative surveillance of uterine cancer in daily practice. In this study, we aimed to investigate a role of postoperative vaginal cytology as follow up surveillance for endometrial cancer. **[Methods]** We conducted a retrospective analysis for the endometrial cancer patients who underwent hysterectomy from Jan 2010 to Dec 2019. Clinicopathological factors, postoperative treatments, recurrence sites, and the timing of diagnosis of recurrence were extracted from medical records. **[Results]** During the study period, 759 patients underwent hysterectomy for endometrial cancer. Recurrence was observed 88 out of 759 patients (11.6%). Vaginal recurrence was occurred in 20 out of 88 patients (22.7%). Among the solitary recurrences, the most common site was vagina in 12 cases (13.6%), followed by lung in 10 cases (11.4%). Vaginal recurrences were detected by subjective symptoms or pelvic examination, except one case. There was one exceptional case revealing cytological abnormality. After a month, her recurrent tumor was visible at her stump by inspection and palpated. **[Conclusion]** Although vaginal recurrence is the most common pattern of endometrial cancer recurrence, a role of vaginal cytology was negligible. We reaffirmed that interview, inspection by speculum and bimanual examination at follow up visits are more important than cytology for early detection of vaginal recurrence.

ISP-7-2

Retrospective analysis of postoperative complications of para-aortic lymphadenectomy in Endometrial Cancer

Sato Chihiro¹, Tanabe Hiroshi^{1,2}, Tomita Yuna¹, Tomita Keisuke¹, Kato Sayako¹, Kamii Misato¹, Yamauchi Kishihito¹, Takenaka Masataka¹, Saito Motoaki¹, Takano Hirokuni¹, Yamada Kyosuke¹, Okamoto Aikou¹ *The Jikei University¹, National Cancer Center Hospital East²*

[Objective] Systematic lymphadenectomy including para-aortic lymphadenectomy (PANx) is considered necessary for accurate

surgical staging. On the other hand, para-aortic lymphadenectomy is associated with increased perioperative complications. The aim of this study is to examine and compare the incidence rates of postoperative complications retrospectively between with and without PANx in patients with endometrial cancer at our hospital. **[Methods]** Patients with endometrial cancer who underwent radical surgery at our 4 affiliated hospitals from 2016 to 2020 were reviewed. A total of 180 patients underwent pelvic lymphadenectomy (PELx) and PANx, 149 patients underwent PELx alone, and 53 patients underwent total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO). We compared the incidence rates of postoperative complications in each group. **[Results]** The median operation time was 282 min. in the PELx and PANx group, and 188 min. in the PELx group. In the TAH+BSO group, one case of thrombosis and one case of abdominal incisional hernia were observed as postoperative complications. In the PELx and PANx group and the PELx group, the most frequent observed postoperative complication was lymphedema. Comparing the 2 groups, the PELx and PANx group had a significantly higher incidence of lymphedema (18.8% vs 7.3%; $p=0.003$). There were no significant differences in the incidence rates of ileus (10.0% vs 5.3%) and other postoperative complications. **[Conclusion]** This study suggests that lymphedema increase in the PELx and PANx group as a postoperative complication rather than the PELx group. We report on postoperative complications of para-aortic lymphadenectomy with further literature review.

ISP-7-3

Effectiveness of hysteroscopic transcervical resection in the diagnosis of diseases near the internal os of the uterine canal

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[Objective] Collecting tissue near the internal os in the uterine canal with conization or curettage is often difficult and insufficient. The aim of this study was to evaluate efficacy of hysteroscopic transcervical resection (TCR) for the pathological diagnosis of diseases located near the internal os. **[Methods]** We performed a retrospective review of 9 patients who were operated with TCR for diagnosis of diseases in the uterine canal located near the internal os between 2017 and 2021. Clinical features and pathological diagnosis were evaluated. **[Results]** Multiple-cystic lesions were observed and lobular endocervical hyperplasia (LEGH) or mucinous carcinoma, gastric type (GAS) was suspected in 8 patients according to preoperative MRI findings. The cytological findings of the uterine cervix were NILM in 7 patients and AGC in 1 patient. Thickness of the endometrium in the cervix was observed in 1 patient whose cytological finding was adenocarcinoma, endocervical adenocarcinoma was suspected. Operating with TCR, biopsy of the target point was possible in all cases. Pathological findings using TCR for biopsy were normal endocervical tissue in 3 patients, Nabothian cysts in 2 patients, LEGH in 2 patients, adenomyosis in 1 patient and adenocarcinoma in 1 patient. 1 patient diagnosed as LEGH and 1 patient diagnosed as adenocarcinoma were treated with hysterectomy, the pathological findings of the uterus were same as the result of TCR. Other patients were followed with only observation, disease progression was not found. **[Conclusion]** Biopsy with TCR may be effective for the pathological diagnosis of diseases located near the internal os of the uterine canal.

ISP-7-4

Adverse events and outcomes of cervical cancer patients treated with definitive radiation therapy with weekly paclitaxel and carboplatin or nedaplatin Ishii Saki¹, Kodama Michiko¹, Miyoshi Ai¹, Mabuchi Seiji², Kimura Tadashi¹ *Osaka University Hospital¹, Osaka International Center Institute²*

[Objective] The study aims to assess the clinical outcomes and adverse events of cervical cancer patients treated with concurrent chemoradiotherapy (CCRT) involving weekly paclitaxel and carboplatin (TC) or nedaplatin. **[Methods]** Age, FIGO2008, TNM classification, histology, response to CCRT, serious adverse events (SAE) defined as grade 3 or above according to Common Terminology Criteria for Adverse Events, and survival outcome were retrospectively collected from electrical records, of whom underwent TC-based or nedaplatin-based CCRT between 2016 January and 2018 December in our hospital. Exclusion criteria were missing information on response to CCRT, and cases requiring extended field radiotherapy. The treatment completion and response rate, and SAE incidence were analyzed via Fisher exact test. **[Results]** Eleven and 40 patients underwent TC, and nedaplatin-based CCRT, were eligible for analyze. Concurrent TC were performed on advanced (IIB-IVA) cases, while nedaplatin was for IA2-IIB. Chemotherapy could be completed as scheduled in 8 patients (72.7%) and 34 patients (85%) in the TC and nedaplatin group, respectively (NS). Nine patients (81.8%) achieved complete response to CCRT in the TC group and 33 patients (82.5%) in the nedaplatin group. SAE occurred in 6 patients (54.5%), showing 3 neutropenia, 1 allergy, 1 appetite loss, and 1 infection, in the TC group and 11 patients (27.5%), showing 10 neutropenia, and 1 diarrhea, in the nedaplatin group (NS). **[Conclusion]** TC-based CCRT tended to show higher rate of SAE, resulted in lower completion rate of concurrent chemotherapy. We further plan to analyze more cases to clarify the feasibility of TC-based CCRT.

ISP-7-5

Case reports of obese endometrial cancer patients with levonorgestrel IUS to reduce the risk of laparoscopic surgery Isono Roze, Nakagawa Kohei, Takimoto Yumi, Ueda Tomoko, Yamaguchi Momoko, Saeki Shinichiro, Takeda Kazuya, Inoue Kayo, Tsubamoto Hiroshi, Shibahara Hiroaki *The Hospital of Hyogo College of Medicine*

We report on highly obese patients with endometrial cancer (EC) or atypical endometrial hyperplasia (AEH) who underwent implantation of Mirena (IUS) and weight loss guidance (WLG) to reduce perioperative risks. **[Case 1]** EC G1 stage IA, BMI 36.6. She had DVT in the IVC due to protein S deficiency. Four months after IUS+WLG and anticoagulation therapy, BMI decreased to 30.6 with residual EC tissue. Because IVC filter placement was not possible due to residual central DVT, laparoscopic surgery (TLH+BSO) was performed under anticoagulation. There were no perioperative complications. **[Case 2]** EC G1 stage IA, BMI 42.3. She had history of thyroid cancer, transverse colon cancer, and HT. After 3 months of IUS+WLG, BMI decreased to 36.2 and EC tissue remained. She underwent TLH+BSO without perioperative complications. **[Case 3]** AEH, BMI 52.2. She had coronary artery disease, Hashimoto's disease, antiphospholipid antibody syndrome, DM, and was unable to maintain supine position due to respiratory impairment. After 6 months of IUS+WLG, her BMI decreased to 38 and she was able to lie supine. We recommended surgery as planned, but the atypical cells disappeared, and the patient requested follow-up. No recurrence was observed after 5 years.

ISP-7-6

Uterine tumor resembling ovarian sex cord tumor : A case

report Shibahara Mami¹, Kurita Tomoko¹, Murakami Midori¹, Aoyama Yoko¹, Kuwazuru Tomoichiro¹, Hoshino Kaori¹, Nishimura Kazuaki¹, Harada Hiroshi¹, Ueda Taeko¹, Kagami Seiji², Matsuura Yusuke³, Yoshino Kiyoshi¹ *University of Occupational and Environmental Health¹, Kyushu Rosai Hospital², Nursing of Human Broad Development, University of Occupational and Environmental Health, Japan³*

Introduction : Uterine tumor resembling ovarian sex cord tumor (UTROSCT) is rare type of uterine neoplasm. Although most UTROSCT cases exhibit benign behavior, a few cases had metastasis or recurrence. The therapeutic strategies based on prognosis have not been established. **Case :** A 77-year-old woman was referred to our department with postmenopausal bleeding. Magnetic resonance imaging revealed a 25×27×22 mm mass in the anterior uterine wall. No metastasis was detected on a systemic computed tomography scan. Endometrial cytology revealed atypical cells that showed resembling stromal cell. We performed a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO). Microscopically, the nodular lesion composed of a mildly cellular proliferation of epithelioid polygonal, oval or spindle cells having eosinophilic cytoplasm arranged in fascicles, cords or small nests focally displaying an invasive or pseudoinvasive manner with thick-walled blood vessels, a myxoid stroma and hemorrhage. Immunohistochemically, the tumor cells were positively reactive to markers of sex cord differentiation such as calretinin and CD99. The pathologic diagnosis was UTROSCT with no metastasis. No recurrence was observed in the patient since the initial treatment (12 months). **Conclusion :** We experienced a case of UTROSCT treated with TAH+BSO. Based on previous cases of UTROSCTs, we discuss the diagnosis, treatment and prognosis.

ISP-7-7

A case of uterine rhabdomyosarcoma, embryonal type in adult Matsumoto Yuka, Kinose Yasuto, Nakagawa Satoshi, Takiuchi Tsuyoshi, Miyoshi Ai, Kodama Michiko, Hashimoto Kae, Kobayashi Eiji, Ueda Yutaka, Sawada Kenjiro, Tomimatsu Takuji, Kimura Tadashi *Osaka University*

[Objective] Most rhabdomyosarcoma develops from striated muscle in childhood. Rhabdomyosarcoma derived from uterus is extremely rare and occurs only about 5 cases a year in Japan. Here we report a case of an adult woman with uterine rhabdomyosarcoma. **[Methods]** A 52-year-old woman complained of lower abdominal pain. Pelvic magnetic resonance imaging showed a 9-cm uterine mass with heterogeneous signaling containing intratumoral hemorrhage. Positron emission tomography demonstrated FDG accumulation at the uterus and a 2-cm right lung nodule, suggesting uterine sarcoma with and pulmonary metastasis. Surgery with complete resection was performed : abdominal simple hysterectomy, bilateral salpingo-oophorectomy, partial omentectomy, and thoracoscopic partial pneumonectomy (S6). Pathological findings of the uterus represented proliferating atypical and spindle cells with mucinous stroma background. Immunohistochemical study showed partial positive patterns with MyoD1 and Myogenin staining, suggesting the tumor was developed from immature striated muscle. With advice from expert pathologists in other hospitals, she was diagnosed with uterine rhabdomyosarcoma, embryonal type. The pulmonary lesion was benign hamartoma. Japan Rhabdomyosarcoma Study Group risk classification was Group A. **[Results]** We discussed with experienced pediatricians and orthopedic oncologists and planned to conduct 8 cycles of VAC chemotherapy (Vincristine, Actinomycin D, and Cyclophosphamide). She suffered from febrile neutropenia in 1st cycle and the dose reduction was required since 2nd cycle. CT findings showed no evidence of recurrent disease after the 4th cycle. **[Conclusion]** Rhabdomyosarcoma is a rare malignant tumor and the adjuvant

chemotherapy depends on the subtype and the disease sites. It is essential to cooperate with doctors who are familiar with rhabdomyosarcoma.

ISP-7-8

Age-related characteristics of endometrial cancer accompanied with endometriosis Ishizaka Aya *The University of Tokyo Hospital*

[Objective] Endometriosis (EM) is sometimes accompanied with endometrial cancer (EC) even in postmenopausal patients. However, little is known about characteristics of EC with EM. We investigated age-related clinicopathological features of EC accompanied with EM. **[Methods]** Under approval of IRB, 374 patients (median age : 55 y.o.) with EC who underwent hysterectomy between 2007 and 2015 were retrospectively evaluated. Patients were divided into EM and non-EM (control) groups according to the presence of pathologically confirmed EM. Clinicopathological characteristics and progression free survival (PFS) were compared between two groups. The comparisons were also conducted in young (<55 y.o.) and elderly patients (≥ 55 y.o.). **[Results]** Number of EC patients with EM were 55 (14.7%), 33 (18.0%), and 22 (11.4%), in total, young, and elderly groups, respectively. In the total cohort, there were no differences in clinicopathological features and PFS between EM and control groups. In young patients, no patients in EM group had lymph node metastasis (LMN), whilst 19 of control group had (0% vs 13%, $p=0.0046$). In contrast, in elderly patients, LNM ratio was significantly higher in EM group than control group (36% vs 13%, $p=0.0099$). Moreover, in elderly patients, EM group had significantly worse PFS than control group (5-year PFS : 66% vs 86%, $p=0.0038$). **[Conclusion]** Our results suggest that characteristics of EC with EM are influenced by age. Young patients with EM had favorable pathological features, whilst elderly patients with EM did not. Long time exposure of estrogen and inflammation might be associated with unfavorable clinicopathological characteristics in elderly patients.

ISP-7-9

A case of large uterine endometrial polyp involving atypical endometrial hyperplasia in postmenopausal elderly woman Yoshida Shozo, Yamanaka Shoichiro, Morita Sayuri, Onogi Akira *Osaka Gyoumeikan Hospital*

A 80 year-old nonparous female patient, was referred to our hospital. It had been pointed out that enlarged uterus in her pelvis by CT scan taken for screening purposes at another facility. She had no subjective symptoms until she visited our hospital. At the time of the first visit, transvaginal ultrasound showed a hyperechoic echogenic image suggestive of marked thickening of the endometrium. Endometrial cytology was collected, but it was negative. Although the ultrasound images had not changed after careful follow-up, images were so unusual and needed marked attention. Pelvic contrast enhanced MRI was done and showed the lesion seemed to be an endometrial polyp with a diameter of 5 cm. Since the imaging was so atypical, surgical treatment was proposed and laparoscopic total hysterectomy and bilateral adnexectomy were performed. The mass was a stalked endometrial polyp originating from the uterine fundus, and many cysts were found on the circumferential surface. Histopathological examination revealed benign endometrial polyps, but atypical endometrial hyperplasia was found in the endometrium on the surface of the polyps. Uterine endometrial polyps are common in women of reproductive age and elderly cases are rarely encountered. We report this case with a discussion of the literature.

ISP-8-1

Development of TIE-1 target therapy for ovarian cancer Ishibashi Masumi, Hashimoto Eifumi, Shigeta Shogo, Tokunaga Hideki, Shimada Muneaki, Yaegashi Nobuo *Tohoku University*

[Objective] To establish a novel therapeutic strategy for ovarian cancer. **[Methods]** The candidate gene sensitize cisplatin sensitivity was selected from siRNA high-throughput screening using ovarian cancer cell line. Furthermore, we investigated the tumor biological functions of the candidate gene in ovarian cancer. **[Results]** High-throughput functional siRNA screening identified tyrosine kinase with immunoglobulin-like and EGF-like domains 1 (TIE-1) as a gene that confers cells resistant to cisplatin. Conversely enforced over-expression of TIE-1 was validated to decrease cisplatin sensitivity in multiple ovarian cancer cell lines. Mechanistically, TIE-1 up-regulated the nucleotide excision repair (NER) system mediated by xeroderma pigmentosum complementation group C (XPC), thereby leading to decreased susceptibility to cisplatin-induced cell death without affecting cisplatin uptake and excretion. Moreover, the treatment of ovarian-cancer cells with siRNA against TIE-1 decreased the expression of key molecules in the PI3K/Akt signaling pathway, such as p110 α and phospho-Akt. The knockdown of TIE-1 significantly decreased cell proliferation in high-PI3K-expressing cell lines but not low-PI3K-expressing cell lines. These results suggested that inhibition of TIE-1 decreases cell growth in high-PI3K-expressing cells. **[Conclusion]** TIE-1 regulates nucleotide excision repair system and contributed to cisplatin resistance. Moreover, TIE-1 participates in cell growth and proliferation by regulating the PI3K/Akt signaling pathway. Taken together, our findings strongly implicate TIE-1 as a novel therapeutic target in platinum-resistant ovarian cancer or high-PI3K-expressing ovarian cancer. TIE-1 target therapy must be promising to overcome chemo-resistance and poor prognosis of ovarian cancer.

ISP-8-2

Development of cisplatin-loaded nanogel through a hybrid system containing alginate-based nanogel and in-situ cross-linkable hydrogel and its preclinical evaluation for the treatment of disseminated ovarian cancer Yamaguchi Kohei, Hiraike Osamu, Sone Kenbun, Osuga Yutaka *The University of Tokyo*

[Objective] Intraperitoneal chemotherapy can be an alternative to systemic chemotherapy for peritoneally disseminated ovarian cancer because the maintenance of higher concentrations of anticancer drugs is speculated, while the side effects including bone marrow suppression are relatively limited. However, a large proportion of drugs, particularly micromolecular and hydrophilic drugs including cisplatin (CDDP) are often excreted through glomerular filtration rapidly. To effectively deliver CDDP into peritoneally disseminated lesions, we developed an alginate (AL)-based hybrid system in which CDDP-loaded AL nanogels (AL/CDDP-nanogel) were physically encapsulated in and chemically conjugated to injectable AL-hydrogel (AL/CDDP/Ca hydrogel). **[Methods]** We measured the sustained release of CDDP from AL/CDDP/Ca hydrogel in the abdominal cavity of the mouse model. Furthermore, we constructed a peritoneal disseminated ovarian cancer mouse model using ovarian cancer cell lines with KRAS mutations (ID8-KRAS : KRASG12V) and injected free-CDDP or AL/CDDP/Ca hydrogel intraperitoneally. **[Results]** This system enabled the sustained release of the AL/CDDP-nanogels from the AL-hydrogel matrix for over a week. The AL/CDDP-nanogel/AL-hydrogel hybrid system prolonged the overall survival and showed significant antitumor activity in the mouse model with peritoneally disseminated ovarian cancer. **[Conclusion]** The AL/CDDP-nanogel/AL-hydrogel

hybrid system that showed significant antitumor activity *in vivo* could be a novel strategy for advanced-stage ovarian cancer with peritoneal dissemination. Future evaluation for the inhibition of tumor recurrence post-surgery in clinical setting is warranted.

ISP-8-3

Fluorescence-guided detection using sensitive beta-Galactosidase targeting fluorescence probe in ovarian clear cell cancer Kukita Asako¹, Hiraike Osamu¹, Tsuchimochi Saki¹, Sone Kenbun¹, Oda Katsutoshi², Tanimoto Saki¹, Toyohara Yusuke¹, Taguchi Ayumi¹, Tanikawa Michihiro¹, Mori Mayuyo¹, Tsuruga Tetsushi¹, Osuga Yutaka¹ *The University of Tokyo Hospital¹, Department of Integrated Genomics, The University of Tokyo Hospital²*

[Objective] Fluorescence-guided detection using sensitive enzyme-targeting fluorescence probe is becoming a promising tool for fluorescence-guided surgery. β -Galactosidase (β Gal : *GLBI*) is an enzyme which is overexpressed in several cancers. A highly sensitive probe targeting β Gal/ β -Galactosidase (β Gal : *GLBI*), an enzyme overexpressed in several types of cancers, has enabled us to visualize human peritoneal ovarian cancer dissemination in mouse models. In this study, we aimed to validate the potential of fluorescence-guided detection using highly sensitive β Gal probe by evaluating *GLBI* expression level and β Gal activity with clinical tissues of ovarian cancer. **[Methods]** We evaluated the expression level of *GLBI* with freshly frozen tissues of ovarian cancer including control by quantitative real time PCR (qRT-PCR). We performed fluorescence imaging with a set of freshly frozen tumor tissues of ovarian clear cell cancer (OCCC) and freshly frozen normal tissues (ovary and/or endometrium) for 10 patients and visualized fluorescence using two highly sensitive β Gal probes (SPiDER- β Gal and HMRRef- β Gal) by the Maestro EX[®] *in vivo* imaging system. **[Results]** The mRNA expression level of *GLBI* was significantly higher in high grade serous ovarian cancer and OCCC compared to normal ovary ($p=0.009$ and $p=0.002$, respectively) but not in endometrioid ovarian cancer. Fluorescence imaging of freshly frozen OCCC tissues exhibited potent fluorescence signature compared to normal tissues. **[Conclusion]** We showed that mRNA expression and β Gal activity paralleled in OCCC freshly frozen tissues. Further investigations are warranted to give insights into fluorescence-guided detection of lesions using β Gal probe, and this method can be applicable for ovarian clear cell cancer surgery.

ISP-8-4

Oral intake of luteolin is a novel therapeutic approach for refractory ovarian cancer Tamauchi Satoshi, Chang Xuboya, Yoshihara Masato, Yokoi Akira, Ikeda Yoshiki, Yoshikawa Nobuhisa, Kajiyama Hiroaki *Nagoya University Hospital*

[Objective] Luteolin is a flavonoid contained in green and yellow vegetables. In the present study, we examined the anti-tumor effect of luteolin for epithelial ovarian cancer using cell lines and a patient-derived xenograft (PDX) model. **[Methods]** To show the anti-tumor effect of luteolin and the mechanism, time-lapse cell proliferation assay, multiplex fluorescence staining of EMT markers, western blotting, cell migration assay, phospho-kinase array, RNA sequence were utilized. *In vivo* experiments, patient tumors were divided and transplanted into 50 immunodeficient mice to make "xenopatient". Half of them were fed a 50 ppm luteolin mixture, and half were fed a control diet. Tumor size was measured, and the removed tumors were analyzed by immunochemistry. **[Results]** Luteolin inhibited the proliferation of cell lines A2780 and ES-2 in a concentration-dependent manner by inhibiting mitosis ($p<0.01$). In the

phospho-kinase array, phosphorylation was suppressed in MAPK pathway. EMT status of the cells was significantly suppressed by luteolin treatment ($p<0.01$). In PDX experiment, tumor growth was significantly suppressed by oral intake of luteolin ($p<0.05$). Furthermore, combination treatment of luteolin and cisplatin showed an additive effect of these two ($p<0.01$). There were no obvious adverse effects of the treatment, such as body weight loss. Immunostaining of excised tumors showed that phosphorylation of histone H3 (Ser10), a marker of cell cycle M phase, and MAPK were markedly suppressed ($p<0.05$). **[Conclusion]** We showed the antitumor effect of food-containing flavonoid for ovarian cancer using an oral intake assay. Clinical application is expected as a safe and inexpensive therapeutic substance.

ISP-8-5

Identification of circular RNAs which are elevated in ovarian cancer and elucidation of their roles Oi Yukako, Sawada Kenjiro, Yamamoto Misa, Nakamura Koji, Kinose Yasuto, Kodama Michiko, Hashimoto Kae, Kimura Tadashi *Osaka University*

[Objective] Circular RNA (circRNA) is a single-stranded RNA which, unlike linear RNA, forms a covalently closed continuous loop. Due to the lack of poly-A ends, it is resistant to exonuclease-mediated degradation and can stably exist in cells. Recent reports suggested indispensable roles of circRNA in cancer biology. Herein, we intended to examine circRNAs specific to ovarian cancer tissues and identify their roles in cancer progression. **[Methods]** Through RNA microarray (Arraystar V2.0) using extracted RNAs from two high grade serous carcinomas (HGSOCs) and two clear cell carcinomas (CCCs) with each corresponding normal ovarian tissue, we identified candidates of circRNAs highly expressed in HGSOCs and CCCs. Their expression in 13 HGSOC and 21 CCC cases was validated using RT-qPCR. Further, the roles of these circRNAs were examined using *in vitro* proliferation and invasion assays using ovarian cancer cell lines representative to HGSOC (HeyA8 and OVCAR-3) and CCC (RMG-I and OVISe). **[Results]** Among candidate circRNAs, circ_0084927 and circ_0004203 were highly expressed in HGSOCs, while circ_0059665 and circ_0004662 were elevated in CCCs. qPCR assays with other cancer tissues as well as 4 ovarian cancer cell lines validated these results. Among those, silencing circ_0084927 significantly inhibited cell proliferation of HeyA8 and OVCAR-3 and silencing circ_0004662 significantly suppressed cell invasion of RMG-I and OVISe. **[Conclusion]** Through comprehensive analyses, a set of circRNAs which are highly expressed in ovarian cancer were identified. Silencing circ_0084927 suppressed cancer cell proliferation and silencing circ_0004662 alleviates cancer cell invasion, suggesting their roles in ovarian cancer progression.

ISP-8-6

RNA sequencing analysis of ovarian cancer minimal residual disease revealed a metabolic signature as a new therapeutic target Masuda Kenta¹, Ahmed Ahmed Ashour², Tamura Tomohiro¹, Nagai Shimpei¹, Nogami Yuya¹, Tsuji Kosuke¹, Kobayashi Yusuke¹, Banno Kouji¹, Tanaka Mamoru¹, Aoki Daisuke¹ *Keio University¹, University of Oxford, UK²*

[Objective] High-grade serous carcinoma (HGSC), the most common and aggressive subtype of ovarian cancer, has high mortality and a high recurrence rate. Most HGSC patients at stage III or IV respond well to the chemotherapy, but will eventually relapse. This indicates that the survival of minimal residual disease (MRD) is thought to be the origin of ovarian cancer recurrence. This study aimed to investigate the mechanisms through which MRD cells survive chemotherapy. **[Methods]**

Paired samples at the time of diagnostic laparoscopy and the interval debulking surgery after neoadjuvant chemotherapy were collected from advanced ovarian cancer patients and RNA sequencing analysis on cancer islets isolated through laser capture microdissection (LCM) were performed. We established MRD models using a HGSC organoid model developed from mouse fallopian tubes and ovarian cancer cell lines (OVCAR5, OVCAR8, KURAMOCHI) to mimic the gene expression of MRD by long-term treatment of cytotoxic agents and evaluated the gene expression and chemosensitivity of these models. **[Results]** RNA sequencing analysis revealed that ovarian cancer cells in MRD had higher expression of fat metabolism genes, stem-cell marker genes, and EMT genes than chemotherapy-naïve samples. Established MRD models recapitulated the transcriptomic signature of MRD and MRD models were dependent on fatty acid oxidation for survival. Blocking fatty acid oxidation sensitized the effect of cytotoxic agents in MRD models compared to cytotoxic agents only ($p < 0.05$). **[Conclusion]** These findings revealed the molecular signatures of MRD showed the attractive target to eradicate MRD in ovarian cancer.

ISP-8-7

Preclinical Activity of Plitidepsin Against Clear Cell Carcinoma of the Ovary Miyake Ryuta¹, Mabuchi Seiji², Matsubara Sho¹, Yamanaka Shoichiro³, Iwai Kana¹, Yamada Yuki¹, Kawaguchi Ryuji¹, Kimura Fuminori¹ *Nara Medical University¹, Osaka Medical Center for Cancer and Cardiovascular Diseases², Osaka Gyomeikan Hospital³*

[Objective] Eukaryotic Translation Elongation Factor 1 Alpha 2 (eEF1A2) is frequently over-expressed in ovarian clear cell carcinoma (CCC). Although the detailed mechanisms underlying the action remain unclear, Plitidepsin, a novel anti-cancer drug, has been suggested to exert its antitumor activity by interacting with eEF1A2. We therefore explored the antitumor effects of Plitidepsin against CCC of the ovary. **[Methods]** The eEF1A2 expression in ovarian cancer was assessed using surgically resected tissue from our hospital. Using ovarian CCC cell lines, the antitumor effect of Plitidepsin was assessed. By over-expressing or knocking down the eEF1A2 expression, the role of eEF1A2 in the sensitivity of CCC cells to Plitidepsin was investigated. **[Results]** Moderate to high immunoreactivity to eEF1A2 was observed in 16 of 19 cases (76.2%) of ovarian CCC, a significantly higher rate than in other histological subtypes of ovarian cancer. Plitidepsin exerted significant antitumor activity toward chemo-naïve and chemoresistant CCC cells *in vitro*. An MTS cell growth assay showed that treatment with Plitidepsin inhibited the proliferation of CCC cells in a dose-dependent manner. The IC₅₀ values obtained for ovarian CCC cell lines were 2.51-4.97 nM. An increased percentage of G1 phase and cleaved PARP was shown following Plitidepsin treatment by flow cytometry and Western blotting, respectively. Ectopic expression of eEF1A2 in CCC cells resulted in increased sensitivity to Plitidepsin, whereas eEF1A2 knockdown decreased the sensitivity of CCC cells to plitidepsin. **[Conclusion]** Plitidepsin may be a promising agent for treating ovarian CCC.

ISP-8-8

A new biomarker by measuring circulating tumor DNA of ovarian cancer patients using Digital Droplet PCR Minato Takamichi *Tohoku University*

[Objective] Ovarian cancer (OC) is an intractable gynecological tumor, and frequent recurrence is experienced within a few years even after the complete eradication of tumor tissues by radical resection and neo-adjuvant chemotherapies. The conventional recurrence marker, CA125, is widely used for follow-up after resection of OC, but CA125 has a long half-life in blood and

lacks dynamic responses to tumor recurrence. Recent developments in liquid biopsy procedures are expected to overcome the difficulties in early diagnosis of OC recurrence after surgery. **[Methods]** We applied droplet digital PCR (ddPCR) technology to detect circulating tumor-derived DNA in OC patients' plasma during follow-up. Exome sequencing of 11 tumor-normal pairs of genomic DNA from consecutive OC patients identified tumor-specific mutations, and ddPCR probes were selected for each sample. **[Results]** Six of 11 cases showed apparent recurrence during follow-up (mean progression-free survival was 348.3 days) and all six cases were positive in ddPCR analyses. In addition, ddPCR became positive before increased plasma CA125 in five out of six cases. Increased allele frequency of circulating tumor DNA (ctDNA) is associated with increased tumor volume after recurrence. ddPCR detected ctDNA signals significantly earlier than increased CA125 in the detection of OC recurrence by imaging (49 days and 7 days before, respectively; $p < 0.05$). No ctDNA was detected in the plasma of recurrence-free cases. **[Conclusion]** Our results demonstrate the potential of identifying ctDNA by ddPCR as an early detection tool for OC recurrence.

ISP-9-1

Examination of LAT1-mediated leucine transport in clear-cell ovarian carcinoma strain JHOC9 cells Nakamoto Kosuke¹, Sadakane Takako², Oomori Yuriko¹, Teraoka Yuko¹, Sekine Masaki¹, Tomono Katsuyuki¹, Nosaka Suguru¹, Yamazaki Tomomi¹, Mukai Yurika¹, Koh Iemasa¹, Sugimoto Jun¹, Kudo Yoshiki¹ *Hiroshima University¹, Higashihiroshima Medical Center²*

[Objective] It is known that cancer cells have enhanced uptake of glucose and amino acids necessary for their active cell proliferation. Among the amino acid transporters, L-type amino acid transporter 1 (LAT1) is found in normal cells, although the expression level is relatively low, it is highly expressed in proliferative cells such as cancer, and it has been reported that it is overexpressed in various cancers. Clear-cell ovarian carcinoma is a disease that is resistant to chemotherapy and has a poor prognosis, and the development of new therapeutic strategies is required. So far, We confirmed that LAT1 is also expressed in clear cell ovarian carcinoma strains. Leucine, one of the amino acids involved in cell proliferation, is transported intracellularly mainly via LAT1. Therefore, we investigated whether leucine is transported via LAT1 in clear cell ovarian carcinoma. **[Methods]** JHOC9 cells in which LAT1 expression was observed at the RNA and protein levels, were incubated with [³H] Leucine, and the amounts taken up by the cells were measured by liquid scintillation counting. We also analyzed the effect of JPH203, a selective inhibitor of LAT1, on leucine transport. **[Results]** Leucine transport in JHOC9 cells was time-dependent, Na-independent, and concentration-dependent saturation, suggesting transport-mediated transport. In addition, the LAT1 selective inhibitor JPH203 suppressed leucine transport in a concentration-dependent, and suppressed leucine transport by up to about 90%. **[Conclusion]** In JHOC9 cells, the intracellular transport of leucine was markedly inhibited by LAT1 selective inhibitors. It is suggested that LAT1 is involved in Leucine transport in JHOC9 cells.

ISP-9-2

The immune profile of ovarian clear cell carcinoma is different from that of high-grade serous carcinoma, with high expression of poliovirus receptor on tumor cells Murakami Kosuke¹, Miyagawa Chiho¹, Takamatsu Shiro², Yamaguchi Ken², Hamanishi Junzo², Mandai Masaki², Matsumura Noriomi² *Kindai University¹, Kyoto University²*

[Objective] According to clinical trials in ovarian cancer, immunotherapy may respond better to clear cell carcinoma (CCC) than high-grade serous carcinoma (HGSC). The aim of this study is to explore the differences in immune profiles of CCC and HGSC by gene expression profiling (GEP) and immunohistochemistry (IHC). **[Methods]** GEP and IHC were performed on clinical samples of CCC and HGSC. In addition, public data sets of ovarian cancer and ovarian cancer cell lines were used for analysis. **[Results]** GEP of 40 CCCs and 13 HGSCs showed that there were few CD8⁺Tcells and a high proportion of CD4⁺Tcells and M2 macrophages, but no difference by histological type. Among CD4⁺Tcell subsets, Th17 (RORC) were more abundant in CCC ($p < 0.001$) and mutually exclusive with Th2 (GATA 3) and Treg (FOXP3). The expression of IL-6 and PD-L1 was positively correlated ($p = 0.038$) in the IHC of 15 CCCs. In addition, the expression of PVR (poliovirus receptor), which is involved in DNAM1-axis, was higher in CCC compared to HGSC in GEP ($p < 0.0001$). Furthermore, the expression of PVR was significantly higher in CCC in all five public data sets. In ovarian cancer cell lines (13 CCC and 24 non-CCC), PVR expression was significantly higher in CCC than in non-CCC ($p = 0.036$). 15 CCCs were all positive for PVR in tumor epithelium. **[Conclusion]** CCC showed different immune profiles from HGSC in CD4⁺Tcell subsets, and high PVR expression in tumor cells may lead to anti-TIGIT antibody acting on DNAM1-axis, or oncolytic virus therapy and CAR-T therapy targeting PVR itself.

ISP-9-3

Stearic acid, a long-chain fatty acid, may induce apoptosis through the accumulation of DNA damage in ovarian cancer cells Ogura Jumpei, Yamanoi Koji, Taki Mana, Ukita Masayo, Yamaguchi Ken, Hamanishi Junzo, Mandai Masaki *Kyoto University*

[Objective] Long-chain fatty acids (LFAs) are involved in various biological reactions and have been reported to be involved in malignant phenotypes of cancer. Still, the detailed mechanisms remain to be unclear. In this study, we explored the effects of stearic acid (SA) and oleic acid (OA), a type of long-chain fatty acid, on the malignant phenotypes of cancer. **[Methods]** We used the human ovarian cancer cell lines OVCAR5 and SKOV3 for the subsequent studies. In vitro, cell proliferation assay, sphere formation assay, and soft agar colony formation assay were used to evaluate cell functions. The apoptotic cells were analyzed by flow cytometry, and the expression of apoptotic proteins and the marker of DNA damage, γ H2AX, were evaluated by Western blotting. In vivo, tumor initiation/proliferation ability under SA-rich (S-HFD) or OA-rich (O-HFD) high-fat diet was evaluated by mice models subcutaneously inoculated with SCD knock-down cell lines established by shRNA technique. **[Results]** In both cell lines, the addition of SA significantly inhibited malignant phenotypes such as cell proliferation, sphere formation, and soft agar colony formation. Still, these effects were canceled when OA was added. The addition of SA significantly induced apoptosis and elevation of γ H2AX expression levels in a concentration-dependent manner, but when OA was added, neither apoptosis nor γ H2AX increased. In vivo, tumor growth was significantly restricted in the S-HFD group and the SCD knock-down strain model but not in the O-HFD group. **[Conclusion]** These findings suggest that SA induces apoptosis of tumor cells through DNA damage.

ISP-9-4

Rapid ovarian cancer cell death induced by non-genomic action of progesterone via membrane receptors Koyanagi Takahiro, Saga Yasushi, Takahashi Yoshifumi, Yoshida Takahiro, Tamura Kohji, Takahashi Suzuyo, Taneichi Akiyo,

Takei Yuji, Fujiwara Hiroyuki *Jichi Medical University*

[Objective] Progesterone therapy is a relatively inexpensive treatment option with few side effects for endometrial and breast cancers. We examined the effect of progesterone and its mechanism of action on ovarian cancer cells. **[Methods]** 1) Expression of progesterone receptor (PR) was examined in six serous ovarian cancer cell lines by western blot using rabbit anti-human antibody. 2) Ovarian cancer cells were exposed to 0.005-0.2 mM progesterone for 1 hour and cell viability was subsequently assessed using the WST-1 assay. 3) Expression of pro-apoptotic protein BAX following exposure to progesterone was examined over time in ovarian cancer cells by western blot using rabbit anti-human antibody. 4) Expression of membrane PR (mPR) in ovarian cancer cells was examined by RT-qPCR. 5) mPR on ovarian cancer cells was knocked down by CRISPR/Cas9 to determine changes to progesterone sensitivity. **[Results]** 1) PR was not expressed in six ovarian cancer cell lines. 2) Progesterone induced cell death in all cell lines in a dose-dependent manner following 1-hour exposure. 3) Expression of BAX increased 1 minute after exposure to progesterone. 4) All six ovarian cancer cell lines expressed mPR. 5) mPR-knockout decreased the sensitivity of cells to progesterone. **[Conclusion]** We demonstrated that progesterone was effective in rapidly inducing cell death in PR-negative ovarian cancer cells. Our findings also indicated that this was a non-genomic effect induced via mPR. Progesterone therapy may be established as an inexpensive and safe treatment option for ovarian cancer.

ISP-9-5

Development of a novel gene immunotherapy targeting PD-L1 gene in mouse ovarian cancer using the adeno-associated virus-CRISPR/Cas9 system Yahata Tamaki, Ino Kazuhiko *Wakayama Medical University*

[Objective] The response rate of antibody therapy targeting immune checkpoint molecules in ovarian cancer is not sufficient, and it is needed to develop new inhibitory methods. We have previously reported that knockout of programmed cell death ligand 1 (PD-L1) using CRISPR/Cas9 suppresses tumor growth in a mouse model of ovarian cancer. In this study, we developed a novel gene immunotherapy model targeting PD-L1 in ovarian cancer using adeno-associated virus-CRISPR/Cas9 (AAV-CRISPR/Cas9) and investigated its efficacy. **[Methods]** All protocols were approved by the ethics committees. In vitro, we produced AAV-PDL1 particles for knockout of PD-L1. AAV-PDL1 particles were transduced into murine ovarian cancer cell lines, ID8, and the expression of PD-L1 was confirmed at the protein level on flow cytometry. In vivo, PD-L1-AAV particles were intraperitoneally injected into the mouse peritoneal dissemination model, and the tumor progression and survival time were compared with those injected with control-AAV particles. **[Results]** We demonstrated that PD-L1-AAV particles reduced PD-L1 expression in a dose-dependent manner under the treatment of IFN- γ . In the peritoneal dissemination model, the survival time was significantly longer in the PD-L1-AAV particles-treated group compared to the control group. Tumor weights were significantly lower in the PD-L1-AAV particles-treated group compared to the control group. There were no specific severe adverse events in the organs such as lungs, livers, kidneys, and spleens. **[Conclusion]** AAV-CRISPR/Cas9 may be a potential gene immunotherapy targeting PD-L1 in ovarian cancer.

ISP-9-6

Inhibition of Src abrogates polarity switching and adhesion to extracellular matrix of ovarian cancer cell clusters Kawata Mayuko^{1,2}, Kimura Tadashi², Inoue Masahiro¹ *Department of Clinical Bio-resource Research and Development, Kyoto*

University¹, Osaka University²

[Objective] Peritoneal dissemination of ovarian cancer (OC) is commonly seen in advanced ovarian cancer patients. Recently, it is reported that cancer cell clusters play an important role as a source of metastasis. Our group reported that cancer cell cluster has apico-basal polarity and the dynamic conversion of the polarity, or “polarity switch”, is related to metastasis in colorectal cancer. This study was aimed to evaluate the mechanism of polarity switch and its contribution to adhesion to ECM in OC. **[Methods]** We used various histological types of OC patient-derived cancer organoids, tissue-originated spheroid (CTOS), as a model of OC cell clusters floating in ascites. Apico-basal polarity of OC tissue and ovarian CTOS was evaluated by immunostaining. ZO1 and ITGB4 were used as markers for apical and basolateral membrane, respectively. Marigel coated plates were used to evaluate the adherence of OC CTOS to ECM. **[Results]** Both OC tissue and ovarian CTOS exhibited apico-basal polarity. CTOS in suspension culture showed apical-out/basal-in polarity status, while once embedded in ECM, CTOSs switched its polarity to basal-out/apical-in. This polarity switch was accompanied by Src phosphorylation, and was inhibited by Src inhibitors. When CTOS was cultured on the ECM coated plastic surface, CTOSs adhered to the bottom of the dish, which was also abrogated by Src inhibitors. **[Conclusion]** Inhibition of Src in OC cell clusters prevented polarity switch and adherence to ECM. Src can be a potential target to suppress OC implantation in peritoneal wall.

ISP-9-7

Comprehensive genomic profiling of borderline ovarian tumors Takahashi Mio¹, Chiyoda Tatsuyuki¹, Nakamura Kohei², Yamagami Wataru¹, Nishihara Hiroshi², Tanaka Mamoru¹, Aoki Daisuke¹ *Keio University¹, Genomics Unit, Keio Cancer Center, Keio University²*

[Objective] Cancer genomic medicine has been gaining traction recently, and genetic profiles of ovarian cancer have been obtained. Reports providing genetic profiles of borderline ovarian tumors (BOT) using whole exome sequencing remain scarce. We aimed to identify genetic mutations in BOT. **[Methods]** We investigated BOT cases among patients registered in a multi-center study to construct a database curating whole exome sequences from tumors and blood samples from Japanese patients. This database was used to clarify correlations between genetic changes, pathological/biological characteristics, and treatment effects. We reviewed the database and obtained clinical data from medical records. **[Results]** Seven patients participating in the study were histopathologically diagnosed with BOT. Their median age was 48 (range 36-67) years. Histological types were : 4 cases of serous, 1 mucinous, 1 endometrioid, and 1 seromucinous. Median tumor mutation burden was 67 (range 56-94) non-synonymous single nucleotide variants (SNVs). Actionable mutations were found in *BRAF* (57.1%), *KRAS* (42.9%), *ARID1A* (28.6%), *PIK3CA* (7.1%), and *PTEN* (7.1%). Mutations were also observed in *CTNNB1*, *CDKN2A*, and *MSH2*, and a homozygous deletion in *RECQL4* was also observed. All serous BOT cases had a mutation in either *BRAF* or *KRAS*. One case of mucinous BOT had co-mutation of *KRAS* and *BRAF*. No cases of high microsatellite instability were found, and no cases were found to have *BRCA1/2* or *TP53* mutations. **[Conclusion]** Most cases had mutations in genes associated with the RAS/MAPK signaling pathway, such as *KRAS* and *BRAF*. Serous BOT cases in particular displayed genetic profiles similar to low-grade serous carcinoma.

ISP-10-1

The utility of FS-C4BP as a prognostic biomarker for epithelial ovarian cancer Hayashi Io¹, Momose Hiroaki¹, Kashiwagi Hirofumi¹, Hayashi Masaru¹, Machida Hiroko², Ikeda Masae¹, Ishimoto Hitoshi¹, Mikami Mikio¹ *Tokai University Hospital¹, Toyohashi Municipal Hospital²*

[Objective] Fully-sialylated C4-binding protein (FS-C4BP) is a member of the glycoprotein, and we reported that serum levels of that were elevated in epithelial ovarian cancer (EOC) patients in contrast to non-cancer control (Gynecol Oncol. 2015 ; 139 : 520-8). This study aimed to examine the utility of FS-C4BP as a prognostic biomarker for EOC. **[Methods]** This was a retrospective study that plasma samples from EOC patients collected between 2009 and 2019 (IRB : 09R-082). A total of 151 patients were enrolled in this study. The Kaplan-Meier method was used to estimate the survival curves of groups and multivariate Cox regression analyses were performed to identify independent predictors for cause-specific survival (CSS). **[Results]** The mean age of the EOC patients was 56.0 ± 11.1 years old. The most common histologic subtype was clear cell carcinoma (n=71, 47.0%), followed by serous carcinomas (n=27, 17.9%) and endometrioid (n=21, 13.9%). The majority of our study population had early disease (stage I-II in 66.9%), and the 5- or 10-year CSS rate were 79.8% and 67.8%, respectively. Patients with high FS-C4BP (≥ 0.43) had a lower 5- or 10-year CSS, compared to their counterparts (69.2% versus 88.3% at 5-year, 62.8% versus 75.5% at 10-year, P=0.001). Multivariate analysis revealed that high FS-C4BP levels were an independent predictor for CSS (HR 3.23, CI 1.51-6.90, P<0.01) in addition to high stage (III-IV). **[Conclusion]** Our study revealed that higher pretreatment levels of FS-C4BP predicts poor survival, and FS-C4BP can be a novel prognostic biomarker for EOC.

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ISP-10-2

Establishment and characterization of a cell line (HCH-2) originating from human mixed germ cell tumor of the ovary Yamada Takashi *Department of Pathology, Osaka Medical and Pharmaceutical University Hospital*

[Objective] Cell lines are very useful for clinical and basic research. Due to the scarcity of information, the establishment of an ovarian malignant tumor cell line with distinctive characteristics is particularly important to study this disease. Thus, this study was undertaken to establish and characterize a new human mixed germ cell tumor cell line of the ovary. **[Methods]** The cell line HCH-2 was established from an ovarian tumor of a 42-year-old woman. Features of the cell line studied included morphology, chromosome analysis, heterotransplantation, tumor markers, chemosensitivity, and cancer genes. **[Results]** The original tumor was consisted of yolk sac tumor, teratoma, and adenocarcinoma. HCH-2 was successively subcultured in 20 years. The monolayer cultured cells appeared to be non-epithelial and tendency to pile up without contact inhibition. The cytology revealed anaplastic and pleomorphic features. The chromosomal number shows aneuploidy and the modal chromosomal number is in the triploid range. The population doubling time was 124 hours, the saturation density was 3.7 × 10⁴ cells/cm², the plating efficiency was 6.5% and the mitotic index was 0.8%. The HCH-2 cells were transplanted subcutaneously to nude mice and produced tumors that resembled the original tumor. HCH-2 cells were sensitive to actinomycin D and cisplatin in vitro. Ten thousand HCH-2 cells produced tissue polypeptide antigen (TPA) during 7 days in culture media. KIT, HRAS and TP53 mutations were found in hotspot locations of 50 cancer genes. **[Conclusion]** HCH-2 may be useful in investigating mixed germ cell tumor of the ovary.

ISP-10-3

Establishment of an inbred mouse model of ovarian clear cell

carcinoma, analysis of tumor immunity and investigation of therapeutic effects of anti-IL-6 antibody Miyagawa Chiho, Murakami Kosuke, Matsumura Noriomi *Kindai University Hospital*

[Objective] Based on clinical trial data in ovarian cancer, immune checkpoint inhibitors have shown promise against ovarian clear cell carcinoma (OCCC). In OCCC, overexpression of IL-6 has been suggested to be involved in immune-mediated tumor growth. The purpose of this study was to establish the mouse model of OCCC suitable for the analysis of tumor immunity, to analyze the tumor immune response associated with carcinogenesis, and to investigate the anti-tumor effect of anti-IL-6 antibody. **[Methods]** Backcrossing was performed from Cre/loxP-based conditional ARID1A knockout/PIK3CA overexpression CD-1 mice to inbred C57BL/6 mice. After Cre adenovirus was administered to cause carcinogenesis, the immune responses of the tumor and ascites over time were analyzed by flow cytometry. In addition, anti-IL-6 antibody was administered, and survival was examined. **[Results]** Administration of Cre adenovirus to C57BL/6 mice with oncogenic gene mutations resulted in carcinogenesis and the tumors showed characteristics like human OCCC. The number of CD8+ T cells in the tumors increased over time and the expression of PD-1 on CD8+ T cells was increased from the early stage of carcinogenesis. Comparing the anti-IL-6 antibody group (3 cases) with the control group (6 cases), the overall survival was 14 days (12-29 days) and 8 days (2-9 days), respectively, and the survival time was significantly prolonged in the anti-IL-6 antibody group ($p=0.0079$). **[Conclusion]** We established an inbred OCCC mouse model. The analysis of tumor immunity in these mice may lead to the search for biomarkers and the development of strategies. Anti-IL-6 antibody may be effective for OCCC.

ISP-10-4

Performance of HE4, CA125 and CA19-9 values in Japanese women presenting with mucinous ovarian tumors Irie Taichi, Iizuka Makoto, Ichikawa Teppei, Kimata Ayaka, Hamano Ai, Tsuchiya Kei, Kouroku Yasumasa, Saito Yoko, Sakamoto Shuichi, Takakura Satoshi *Dokkyo Medical University Saitama Medical Center*

[Objective] We investigate the clinical utility of HE4, CA125, and CA19-9 in Japanese patients with mucinous ovarian tumors (MOT). **[Methods]** 97 Japanese patients with MOT by pathological assessment after surgery were included in this study. The retrospective study validated the diagnosis performance of CA125, HE4, and CA19-9. **[Results]** 1) The serum level of HE4, CA125 and CA19-9 were shown more than cut-off value in 1 (1%), 15 (24%), and 16 (26%) of 61 benign MOT (B-MOT) patients, in 0, 10 (40%), and 13 (52%) of 25 borderline-malignant MOT (BM-MOT), and in 3 (27%), 7 (63%), and 6 (54%) of 11 malignant MOT (M-MOT), respectively. 2) The serum level of CA125 and CA19-9 were significantly higher in BM-MOT and M-MOT than those in B-MOT [CA125 : median 26.6 (interquartile range 16.8-81.3) U/mL vs. 18 (9.5-34.8) U/mL, $p=0.028$; CA19-9 : 50.5 (11.7-860.4) U/mL vs. 13.8 (6.5-37.8) U/mL, $p=0.003$]. No significant difference was observed in HE4 (data not shown). 3) For identifying BM-MOT and M-MOT in MOT, AUC/sensitivity/specificity/PPV/NPV/accuracy of HE4, CA125 and CA19-9 were 0.55/8%/98%/75%/64%/64%, 0.68/47%/75%/53%/70%/64%, and were 0.68/52%/73%/54%/72%/65%, respectively. 4) The serum level of HE4 and CA125 were significantly higher in M-MOT than those in B-MOT and MB-MOTT [HE4 : 70.8 (56.8-93.8) pmol/L vs. 42.0 (30.8-58.8) pmol/L, $p=0.006$; CA125 : 64.3 (21.7-178.5) U/mL vs. 20.6 (12.2-41.6) U/mL, $p=0.01$]. Nonsignificant difference was observed in CA19-9 (data not shown). 5) For identifying BM-MOT in MOT, AUC/sensitivity/specificity/positive productive value (PPV) /negative produc-

tive value (NPV) /accuracy of HE4, CA125 and CA19-9 were 0.61/27%/98%/75%/91%/90%, 0.79/63%/70%/21%/93%/70%, and were 0.63/54%/66%/17%/91%/64%, respectively. **[Conclusion]** In Japanese patients with MOT, HE4 and CA125 were useful clinical biomarker for identifying M-MOT, and CA125 and CA19-9 were useful clinical biomarker for identifying BM-MOT and M-MOT, respectively.

ISP-10-5

Amigo-2 expression and prognosis of ovarian cancer Iida Yuki, Sato Shinya, Okawa Masayo, Hikino Kouhei, Osaku Daiken, Komatsu Hiroaki, Kudoh Akiko, Chikumi Jun, Oishi Tetsuro, Taniguchi Fuminori, Harada Tasuku *Tottori University*

[Objective] Amphoterin-induced gene and open reading frame 2 (Amigo-2) is reported to be associated with the prognosis of colorectal and gastric cancer. The aim of this study was to clarify the role of Amigo-2 in ovarian cancer. **[Methods]** The study included 131 patients with ovarian, fallopian tube, and peritoneal cancer who underwent surgery at our hospital from 2009 to 2018. The tumor tissue samples were assessed by immunohistochemical staining for Amigo-2 expression before chemotherapy. Clinicopathological factors, progression free survival (PFS), and overall survival (OS) were analyzed based on Amigo-2 expression. **[Results]** The expression of Amigo-2 was high in 71 (54%) of 131 patients, and the high-expression group predominantly had serous carcinoma. PFS and OS were significantly shorter in those with high expression of Amigo-2 in both serous carcinoma (high vs. low, PFS 30% vs. 60%, OS 47% vs. 87%) and clear cell carcinoma (high vs. low, PFS 39% vs. 70%, OS 45% vs. 88%) groups. High expression of Amigo-2 was a prognostic factor in the multivariate analysis of PFS (hazard ratio [HR] 2.36 [95% confidence interval (CI) : 1.29-4.51]) and OS (HR 3.28 [95% CI : 1.56-7.55]). **[Conclusion]** Amigo-2 expression was associated with the prognosis of serous and clear cell carcinoma. Additionally, high expression of Amigo-2 was an independent prognostic factor for both PFS and OS.

ISP-10-6

Filopodia Play an Important Role in the Trans-mesothelial Migration of Ovarian Cancer Cells Yamakita Yoshihiko¹, Yoshihara Masato², Koya Yoshihiro¹, Sugiyama Mai¹, Mogi Kazumasa², Uno Kaname², Kitami Kazuhisa², Iyoshi Shohei², Fujimoto Hiroki², Yamashita Mamoru¹, Nawa Akihiro¹, Kajiyama Hiroaki² *Bell Research Center, Nagoya University¹, Nagoya University²*

[Objective] Ovarian cancer cells shed from primary tumors can spread easily to the peritoneum via the peritoneal fluid. To allow further metastasis, the cancer cells must interact with the mesothelial cell layer, which covers the entire surface of the peritoneal organs. Although the clinical importance of this interaction between cancer and mesothelial cells has been increasingly recognized, the molecular mechanisms utilized by cancer cells to adhere to and migrate through the mesothelial cell layer are poorly understood. **[Methods]** : We set up an *in vitro* trans-mesothelial migration assay using primary peritoneal mesothelial cells. Ovarian cancer cell line, ES-2 or SK-OV-3, was labeled and microscopically assessed through the detailed invasion process. We also examined whether the *in vitro* assays represented the *in vivo* environment. **[Results]** : We found that downregulation of filopodial protein fascin-1 or myosin X expression in ES-2 cells significantly inhibited the rate of trans-mesothelial migration of cancer cells, whereas upregulation of fascin-1 in SK-OV-3 cells enhanced this rate. Furthermore, downregulation of N-cadherin or integrin $\beta 1$ inhibited the rate of cancer cell trans-mesothelial migration. Conversely, down-

regulation of cortactin or TKS5 or treatment with the MMP inhibitor GM6001 or the N-WASP inhibitor wiskostatin did not have any effect on cancer cell trans-mesothelial migration. In mice xenograft model, fascin-1-expressing SK-OV-3 cells exhibited more elongated processes than the control, and the processes appeared to be inserted between the mesothelial cells. **[Conclusion]** : These results suggest that filopodia, but not lamellipodia or invadopodia, play an important role in the trans-mesothelial migration of ovarian cancer cells.

ISP-10-7

Copy Number Variation Status in Extracellular Vesicles DNA as a Novel Biomarker of High Grade Serous Ovarian Carcinoma Uekusa Ryosuke¹, Yokoi Akira¹, Ono Mayu¹, Kitagawa Masami², Yoshida Kosuke¹, Yoshihara Masato¹, Tamauchi Satoshi¹, Ikeda Yoshiki¹, Yoshikawa Nobuhisa¹, Kajiyama Hiroaki¹ *Nagoya University¹, Nagoya University Bell Research Center²*

[Objective] High-grade serous ovarian carcinoma (HGSOC) is the most common subtypes and is basically originated from chromosomal instability caused by *TP-53* mutation and multiple somatic copy number variations (CNVs). Extracellular vesicles (EVs) are released by all living cells and contain diverse bioactive molecules including genomic DNA. We aimed to reveal the significance of EV-DNA as a novel biomarker for HGSOC patients. **[Methods]** A total of 24 samples from HGSOC patient samples and cell lines was analyzed. Comprehensive CNV statuses were analyzed by whole genome sequencing (WGS) and SNP array, and CNV statuses of specific genes were analyzed by droplet digital PCR (ddPCR). **[Results]** S-EVs, including exosomes and L-EVs from human serum and ascites and culture supernatant of HGSOC cells were successfully isolated, and DNA in tissues, cells and EVs were extracted. In both WGS and SNP array, there were high correlations of CNV between cell and L-EV and S-EV in cell line samples. However, correlation of CNV between tissue and EVs was not confirmed regarding human samples. For selecting dominant CNVs in HGSOC, The Ovarian Cancer Moon Shot database was referred, and selected 28 genes as the panel for analyzing by ddPCR. Most CNV statuses of cell lines were detected in both L-EV and S-EV by ddPCR and part of the CNV statuses of human tissues was also detected in EV-DNA. **[Conclusion]** Detection of CNV in EV-DNA was confirmed by ddPCR method, and this concept provides a novel strategy for predicting HGSOC patient status as a novel cancer biomarker.

ISP-11-1

Initial reduction of CA125 is predictive biomarker of Olaparib response for recurrent ovarian cancer Nishijima Akira, Tanikawa Michihiro, Kawata Akira, Taguchi Ayumi, Eguchi Satoko, Miyamoto Yuichiro, Sone Kenbun, Tsuruga Tetsushi, Mori Mayuyo, Osuga Yutaka *The University of Tokyo*

[Objective] The treatment of recurrent ovarian cancer has dramatically changed with the introduction of PARP inhibitors. Evaluation of the clinical traits of recurrent cases treated with PARP inhibitor is significant to further establish the strategy for the forefront therapy and recurrent therapy for ovarian cancer. **[Methods]** The platinum-sensitive recurrent ovarian cancer cases diagnosed from 2018 to 2020 in our hospital were enrolled in this study. We retrospectively analyzed the clinical characteristics and the efficacy of PARP inhibitors for these cases under the approval of ethics committee. **[Results]** Forty patients used the PARP inhibitor was enrolled. Median progression free interval was 337 days. Comparing 10 cases of recurrence within 6 months and 30 other cases, there was a significant difference in the initial change of CA125 at 2 months after the introduction

of Olaparib (1049 U/ml [95%CI : 222,1876] vs 9.9 U/ml [95% CI : -467,487], $p=0.034$), though no significant difference in the change of CA125 at previous platinum recombinant therapy (-363 U/ml vs -175 U/ml, $p=0.27$) and treatment-free interval before the relapse (427days vs 735 days, $p=0.2$). Pathology, stage, number of recurrence regimens and maintenance therapy of bevacizumab did not show significant differences by Cox-hazard model. Three patients administered the niraparib therapy after progressive and relapsed condition after olaparib, and none of them continued more than 6 months. **[Conclusion]** Our data suggest that the initial change in CA125 after the introduction of olaparib is significant predictive marker for the response. We also showed limited efficacy of re-challenge of PARP inhibitors for platinum sensitive recurrence.

ISP-11-2

Clinical outcome of platinum sensitive ovarian cancer patients after PARP inhibitors maintenance therapy Tanaka Hiroataka, Yasunaga Masafumi, Hachisuga Kazuhisa, Yasutake Nobuko, Maenohara Shoji, Yagi Hiroshi, Ohgami Tatsuhiro, Onoyama Ichiro, Okugawa Kaoru, Asanoma Kazuo, Yahata Hideaki, Kato Kiyoko *Kyushu University Hospital*

[Objective] Platinum responsiveness has been recognized as a surrogate marker for usefulness of PARP inhibitors for ovarian cancer. However, there has been a limited data about effectiveness of re-treatment by platinum doublet for platinum-sensitive relapse ovarian cancer patients under PARP inhibitors maintenance therapy. Herein, we report six platinum-sensitive relapse cases under PARP inhibitors maintenance therapy with a focus on platinum responsiveness. **[Methods]** A retrospective analysis was conducted on six platinum-sensitive relapse ovarian cancer patients of 35 patients treated with PARP inhibitors maintenance therapy between 2018 and 2020 at our hospital. The data of best overall response based on RECIST criteria, accompanied by clinical information, were collected. **[Results]** The patient's age ranged 42 -77 years old. One of 6 patients performed by BRCA analysis had germline BRCA 1 mutation. Median platinum free interval was estimated 11.3 months on 6 patients. Three patients received paclitaxel plus carboplatin as post progression therapy. The others were treated by other platinum-based regimens such as docetaxel plus cisplatin, docetaxel and carboplatin, and gemcitabine and carboplatin respectively. Overall response rate was 16.6%. **[Conclusion]** Response rate has been reported to be 30 - 60% in treating conventional platinum sensitive relapse ovarian cancer patients with platinum doublet. The best overall response rate of re-treatment by platinum doublet for platinum-sensitive relapse ovarian cancer patients with PARP inhibitors failure were inferior to that of conventional platinum sensitive relapse patients by our small case series. Another treatment strategy may be urgently needed to treat platinum-sensitive relapse ovarian cancer after PARP inhibitors maintenance therapy.

ISP-11-3

Current situation of homologous recombination deficiency (HRD) testing at our department Fujihara Risa¹, Hirayama Takashi¹, Yoshida Emiko¹, Fujino Kazunari¹, Sekine Hanae², Ujihira Takafumi³, Kaneda Hiroshi¹, Miyai Kentaro³, Ogishima Daiki², Terao Yasuhisa¹, Itakura Atsuo¹ *Juntendo University Hospital, Juntendo University¹, Koshigaya Municipal Hospital², Juntendo University Urayasu Hospital², Juntendo University Shizuoka Hospital¹, Tobu Chiiki Hospital³, Juntendo University Nerima Hospital⁶*

[Objective] Homologous recombination deficiency (HRD) testing as companion diagnostics for ovarian cancer became insurance coverage from January 2021. Since then, therapeutic strat-

egy for initial advanced ovarian cancer and recurrent ovarian cancer has expanded. The aim of this study is to clarify how clinical practice has changed with the advent of HRD testing. **[Methods]** Subjects of this research are 22 ovarian cancer patients who underwent HRD testing between January 2021 and August 2021 at our department. Patient characteristics, operative methods, presence or absence of staging laparoscopy, histology, results of HRD testing, and treatment post HRD testing were analyzed retrospectively. **[Results]** The age of the patients was 63.5 ± 10.8 (mean \pm SD) years, and initial advanced ovarian cancer was 19/22 (86.4%). Primary and interval debulking surgery was performed on 11/22 (50.0%) and 9/22 (40.9%), respectively. Staging laparoscopy was performed on 5/22 (22.7%). Histological types were mainly high-grade serous carcinoma 14/22 (61.1%) and clear cell carcinoma 3/22 (13.6%). The HRD testing results were positive on 11/22 (50.0%) and unsuitable samples were seen on 4/22 (18.1%). Four of the five patients with primary advanced ovarian cancer who were positive for HRD testing and were already on maintenance therapy received olaparib and bevacizumab. **[Conclusion]** After emergence of HRD testing, PARP inhibitor usage became more frequent. It is likely that HRD testing advance personalized treatment of ovarian cancer. Inability of HRD testing required to be reduced to provide appropriate treatment. It is necessary to continue to accumulate cases and follow up the prognosis.

ISP-11-4

Comparison of the toxicity between olaparib and niraparib for the treatment of the patients with ovarian, fallopian, and peritoneal cancer : A single-institution retrospective analysis

Endo Shun, Shigeta Shogo, Hashimoto Eifumi, Shimizu Takanori, Minato Junko, Shibuya Yusuke, Ishibashi Masumi, Hashimoto Chiaki, Tomoyuki Nagai, Tokunaga Hideki, Shimada Muneaki, Yaegashi Nobuo *Tohoku University Hospital*

[Objective] PARP inhibitors olaparib and niraparib are now available for the maintenance therapy for the patients with advanced ovarian, fallopian and peritoneal cancer in Japan. In this study, we retrospectively reviewed the toxicity profile common or unique to olaparib or niraparib for the better understanding of the PARP inhibitors among Japanese population from a view of adverse events. **[Methods]** Clinical information of the patients with ovarian, fallopian, and peritoneal cancer who have started maintenance therapy with PARP inhibitors by October 2022 at our hospital were extracted. Toxicity profile was retrospectively reviewed and assessed complying with Common Terminology Criteria for Adverse Events v5.0. **[Results]** Fifty-eight patients were treated with olaparib and twenty-two patients with niraparib. When limited to the Grade 3 or Grade 4 hematological toxicity, 27.6% (16/58), 15.5% (9/58), and 3.4% (2/58) of the patients treated with olaparib experienced anemia, neutropenia, and thrombocytopenia, respectively. The corresponding numbers were 22.7% (5/22), 9.0% (2/22) and 13.6% (3/22) among the patients treated with niraparib, respectively. Adverse events that require dose de-escalation were more frequently observed within 8 weeks from the introduction of the maintenance therapy in both olaparib and niraparib (34.5% and 36.4%, respectively) with statistically significant difference compared to the frequency after 8 weeks (17.2% and 4.5%). **[Conclusion]** We clarified the common and the characteristic toxicity profiles of the PARP inhibitors in Japanese population. We consider that understanding of the toxicity profile helps clinicians select appropriate PARP inhibitor for each patient.

ISP-11-5

A retrospective study of olaparib maintenance therapy for the treatment of platinum-sensitive recurrent ovarian cancer

in the real world Katsuda Takahiro, Nishio Shin, Park Jongmyung, Nasu Hiroki, Tasaki Kazuto, Terada Atsumu, Tsuda Naotake, Ushijima Kimio *Kurume University Hospital*

[Objective] More than three years have passed since Japan introduced olaparib maintenance therapy for platinum-sensitive recurrent ovarian cancer. In addition, the test for homologous recombination deficiency (HRD) has been included in the insurance coverage for ovarian cancer treatment, and the number of patients with known HRD status has been increasing. This study investigated the treatment effect and prognostic factors of patients with platinum-sensitive recurrent ovarian cancer treated with olaparib maintenance therapy at our hospital. **[Methods]** From April 2018 to October 2021, 50 patients who started olaparib maintenance therapy for recurrent ovarian cancer at our hospital were retrospectively evaluated: patient background, treatment effect, HRD, and other prognostic factors were evaluated from medical records. **[Results]** The most common histological type was serous carcinoma (45 patients). HRD testing was performed in 28 of 50 patients, of which 21 were HRD positive. The median PFS/OS of olaparib maintenance therapy was 8.2 months and 35.2 months, respectively. The median PFS/OS of the HRD-positive group was 16 months and not reached, respectively, and the median PFS/OS of the HRP/Unknown group was 6.5 months and 23.2 months, respectively, which were significantly different ($P=0.006$, $P=0.003$). Other prognostic factors, such as the efficacy of chemotherapy before olaparib treatment and CA125 level, were not significant. Treatment was discontinued due to adverse events in 1 of the 50 patients. **[Conclusion]** HRD status showed a significant difference in prognosis for olaparib maintenance therapy in platinum-sensitive recurrent ovarian cancer.

ISP-11-6

Experience of treatment by Olaparib for platinum-sensitive relapsed ovarian cancer

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[Objective] To report on our experience of treatment by Olaparib for platinum-sensitive relapsed ovarian cancer. **[Methods]** Fifteen patients with platinum-sensitive relapsed ovarian cancer treated by Olaparib from July 2018 to August 2021 were enrolled. We analyzed about administration status and adverse events retrospectively. **[Results]** The histological types were high grade serous carcinoma in 13 cases and endometrioid carcinoma in 2 cases. The median number of previous regimens was 2 (2-6). Pretreatment PFI were 6-12 months in 4 cases and more than 12 months in 11 cases. The latest chemotherapy were ddTC in 14 patients and CBDCA in 1 patient, resulting CR or NED in 7 patients and PR in 8 patients. The median administration period of Olaparib was 61 weeks (6-145) and 9 cases exceeded the pretreatment PFI. 6 cases had discontinued due to disease progression in 3 cases, patient's refusal in 2 cases and anemia in 1 case. Moreover, 9 patients were required interruption and 5 patients were required dose reduction. Among adverse events, non-hematologic toxicities of G2 were nausea in 3 cases, increased creatinine level in 2 cases and each fatigue, increased liver enzyme, oral mucositis, pneumonia in 1 case. Hematologic toxicities of G3 were anemia in 5 cases, neutropenia in 1 case, and thrombocytopenia in 1 case. **[Conclusion]** We had experienced that patients treated by Olaparib did not suffer from severe adverse events and 60% of them could continue over their pretreatment PFI. We need to improve the management of side effects when continuing the administration of Olaparib longer.

ISP-12-1

A retrospective study of surgically treated 32 ovarian endometrioma with preoperative suspicion of ovarian malignancy Takeuchi Arisa, Taguchi Ayumi, Koga Kaori, Satake Erina, Kawata Akira, Miyamoto Yuichiro, Tanikawa Michihiro, Sone Kenbun, Mori Mayuyo, Tsuruga Tetsushi, Osuga Yutaka
The University of Tokyo

[Objective] The differential diagnosis between ovarian endometrioma (EM) and ovarian malignancy is important in determining the therapeutic strategy. MRI is commonly used for the diagnosis, and although the presence of contrast-enhanced nodules is characteristic of malignancy, their specificity is not clear. This study aimed to clarify the characteristics of cases in which malignancy was suspected by preoperative MRI but the postoperative diagnosis was EM. **[Methods]** Under IRB approval, we retrospectively reviewed 32 patients who underwent surgery with a diagnosis of malignancy but were diagnosed with EM on postoperative pathology between 2015 and 2020. In particular, preoperative MRI findings were compared with the intraoperative findings. **[Results]** The mean age of the patients was 40.6 ± 1.3 years. The mean size of the tumors was 68.5 ± 17.2 mm. Malignancy was suspected due to the presence of contrast-enhanced nodules (MRI-detected nodules) in 24 (75%), thickening of the cyst wall 3 (9%), and increase in tumor size in 12 (38%). Surprisingly, none of MRI-detected nodules ($n=24$) were identified as macroscopic nodules in the resected specimen. Patients with MRI-detected nodules had severe endometriosis with a mean rASRM score of 60.3 ± 10.5 . In addition, all MRI-detected nodules were presented in dense adhesion areas. **[Conclusion]** This study revealed that in patients with severe endometriosis, peri-ovarian adhesion may be depicted as "pseudo-nodules" on MRI. Further research are warranted to distinguish this "pseudo-nodules" from true nodules.

ISP-12-2

Utility of Cell Blocks for Determining the Homologous Recombination Deficiency (HRD) Status in Stage IVA Ovarian Cancer : A Case Report Saijo Masayuki, Seki Noriko, Sanada Chika, Omae Ayano, Aimoto Noritoshi, Hirata Tomoko, Nishida Tomomi, Kawai Sayaka, Nakayama Tomoko, Odaka Koji, Mizutani Yasushi
Japanese Red Cross Society Himeji Hospital

Background : With advancement in cancer genome medicine, HRD testing prior to initiating chemotherapy for managing advanced ovarian cancer has gained prominence. The cell block technique can help determine the histological type and primary site of the tumor. We present a case of stage IVA ovarian cancer in which a cell block of pleural effusion confirmed high-grade serous ovarian carcinoma (HGSOC) and HRD positivity, thus helping in administering the appropriate treatment. **Case :** A 47-year-old woman presented with dyspnea. Chest radiography showed a massive right pleural effusion, and CT showed bilateral ovarian tumors and peritoneal dissemination. Cytology revealed a Class V classification. The patient was in a critical condition and could not tolerate diagnostic laparoscopy. Therefore, immunostaining of cell blocks was performed and HGSOC was suggested. The CA125 level was extremely high, and no other primary lesions were detected on endoscopy or PET/CT. Thus, a diagnosis of stage IVA ovarian cancer was made. Four cycles of NAC (TC + Bev) were initiated, followed by IDS, two additional cycles of adjuvant chemotherapy, and maintenance therapy with Bev. The percentage of tumor cells in the specimen obtained through IDS was insufficient for HRD testing. The gBRCA1/2 mutation was negative on BRACAnalysis[®]. Testing of a former cell block using the myChoice[®] Diagnostic System revealed HRD positivity/tBRCA negativity ; consequently, the maintenance therapy was changed from Bev to the PAOLA

regimen. **Conclusion :** If the patient's condition is critical to perform a diagnostic laparoscopy, cell blocks may be used for both diagnosis and HRD status determination.

ISP-12-3

Recurrent serous borderline tumor after fertility-preserving surgery following twin pregnancy and resumption of menstruation Morita Noriko¹, Matsushita Hiroshi¹, Yabushita Hiromitsu², Wakatsuki Akihiko¹
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Approximately 40% of women with gynecologic malignancies are pre- or perimenopausal. Cancer therapies tend to predispose women to premature menopause ; therefore, hormone therapy (HT) is strongly recommended to prevent menopause-induced health concerns. However, the use of HT is sometimes limited due to estrogen sensitivity of the tumor. A 37-year-old woman who wished to conceive consulted a gynecologist and underwent evaluation, which showed bilateral adnexal masses. Magnetic resonance imaging revealed a multiloculated ovarian tumor with intracystic papillary projections, and she was referred to us for further evaluation of suspected ovarian cancer. Exploratory laparotomy was performed, and frozen section diagnosis revealed a serous borderline tumor (BT) with non-invasive peritoneal implants. We performed fertility-preserving surgery consisting of left salpingo-oophorectomy and right ovarian tumor resection. Postoperative in-vitro fertilization and embryo transfer resulted in twin pregnancy, and she delivered healthy infants at 34 weeks' gestation, 2 years postoperatively. The patient experienced amenorrhea over a year without recurrence during the postpartum amenorrheic period. Ultrasonography at the first visit after resumption of menstruation revealed a right ovarian cyst with intracystic papillary projections. Laparotomy also revealed a serous BT, and she underwent right salpingo-oophorectomy with total hysterectomy and omentectomy. The patient has been closely observed postoperatively without HT administration because the tumor recurred soon after resumption of menstruation, which suggests possible estrogen sensitivity of the tumor. The Society of Gynecologic Oncology clinical practice statement does not recommend HT for patients with low-grade serous ovarian cancers, although those with high-grade serous ovarian cancer may receive HT.

ISP-12-4

A Study of Factors Determining the accuracy of Intraoperative frozen section of Ovarian Tumors Shimogawa Saori, Nakajima Takahiro, Kobayashi Osamu, Katoh Kanoko, Tanaka Yuria, Ikeda Yuji, Kawakami Kaori, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei
Nihon University

[Objective] The preoperative diagnosis of ovarian tumors has become accurate due to advances in imaging and tumor markers, but intraoperative frozen section has been performed for the purpose of more appropriate surgical selection. In this study, we evaluated the accuracy of intraoperative frozen section in surgical cases of ovarian tumors and retrospectively examined factors associated with discordant groups. **[Methods]** The study consisted of 168 cases who performed for the diagnosis of ovarian tumors. The cases in which the intraoperative frozen section and permanent histology reports were completely agree were classified as the concordant group ($n=138$), and the cases in which it was difficult to determine histology by intraoperative frozen section or misdiagnosis cases were classified as the discordant group ($n=30$). **[Results]** The permanent histology reports were benign ($n=65$), borderline malignant ($n=39$), and malignant ($n=64$). The overall accuracy for intraoperative frozen section was 82%, benign was 95.4%, borderline malignant was 64.1%, and malignant was 79.7%. Univariate analysis showed

that tumor size of more than 10 cm and borderline malignant tumors were significantly more likely to be discordant. Of the discordant group, 5 cases were over diagnosis and 22 cases (81.5%) were under diagnosis. **[Conclusion]** In cases of tumors size greater than 10 cm, especially those that require differentiation between borderline malignant and malignant tumors, it is important to inform the pathologist of the clinical information so that they can consider the number of cutouts. It is also necessary to explain the accuracy of intraoperative frozen section to the patient before surgery.

ISP-12-5

Efficacy and safety of Bevacizumab beyond progressive disease in patients with platinum-sensitive recurrent ovarian and primary peritoneal cancer Ichikawa Teppei, Hamada Yoshinobu, Kosugi Satoshi, Ogasawara Megumi, Suzuki Keisuke, Irie Taichi, Yamaguchi Noriko, Iizuka Makoto, Sakamoto Shuichi, Takakura Satoshi *Dokkyo Medical University Saitama Medical Center*

[Objective] The aim of this study was to evaluate the efficacy and safety of continuation or reintroduction of bevacizumab (Bev) in Japanese patients with platinum-sensitive recurrent (PSR) ovarian and primary peritoneal cancer pretreated with Bev, which had been showed by only one phase III study **[Methods]** We performed a retrospective review of 36 patients with PSR ovarian and primary peritoneal cancer treated with Bev combined with second-line chemotherapy. **[Results]** In 36 patients, 16 had been treated with Bev combined with front-line chemotherapy (the Bev beyond PD Group) and 20 had been treated with front-line chemotherapy alone (the Post-relapse Bev-initiation Group). In the Bev beyond PD Group and the Post-relapse Bev-initiation Group, the median Progression-free survival (PFS) was 14 and 15 months, respectively, the median PFS2 was 36 and 46 months, the median Overall survival (OS) was not reached and 79 months, and the objective response rate (ORR) was 86% and 88%, respectively. No significant difference was found in PFS, PFS2, OS, and ORR between these two groups. Grade 2 or more hypertension, grade 2 or more proteinuria, and grade 3 thromboembolic events were found in 4 (25%), 5 (31%), and 1 (6%) in the Bev beyond PD Group, respectively, and in 5 (25%), 5 (25%), and 2 (10%) in Post-relapse Bev-initiation Group, respectively. **[Conclusion]** It is suggested that there are the efficacy and safety of continuation or reintroduction of Bev as well as post-relapse Bev-initiation in Japanese patients with PSR ovarian and primary peritoneal cancer.

ISP-12-6

Bevacizumab may improve outcomes on the subsequent treatment after progression of olaparib maintenance in patients with platinum sensitive recurrent ovarian cancer Okame Shinichi, Fujimoto Etsuko, Hibino Yumi, Yokoyama Takanori, Sakai Mika, Takehara Kazuhiro *National Hospital Organization Shikoku Cancer Center*

[Objective] Olaparib is approved as maintenance therapy in patients with platinum sensitive recurrent ovarian cancer after response to last platinum-based therapy. Not many data on the subsequent treatment after progression of olaparib maintenance are available. **[Methods]** In this retrospective study, patients treated with olaparib and who had progression during the treatment at our institution as of 2018 through 2020 were reviewed. We compared progression free survival (PFS) of subsequent treatment with or without bevacizumab (Bev) after olaparib, and compared them with PFS of previous treatment including olaparib. **[Results]** 35 patients were analyzed. All patients received olaparib after 2 or more lines of platinum-based chemotherapy achieving a radiologic complete or partial response.

Among 16 patients received further treatment after progression of olaparib maintenance, overall response rate for the treatment with Bev (n=10) was 78% and that for the treatment without Bev (n=6) was 17%. Median PFS of the subsequent treatment was 9.4 months and 5.7 months, prospectively, and that of the previous treatment was 14.3 months. A significant difference was shown between the treatment without Bev and the previous treatment. **[Conclusion]** Bevacizumab may improve PFS on post-progression, though overall subsequent treatment was less effective than previous treatment. Further research is needed to be confirmed the effect of subsequent treatment and find out new therapeutic regimen.

ISP-12-7

Incorporation of Bevacizumab in the management of early-stage ovarian clear cell carcinoma Hsu Ching, Huang Kuan-Ju, Sheu Bor-Ching, Wu Chin-Jui, Chang Wen-Chun, Pan Chen-Yu, Li Ying-Xuan, Huang Ruby Yun-Ju, Wei Lin-Hung *National Taiwan University Hospital, Taiwan*

[Objective] Ovarian clear cell carcinoma (OCCC) is distinct from the most common serous subtype of epithelial ovarian cancer (EOC). OCCC patients usually have a worse prognosis upon recurrence due to lower sensitivity to platinum-based chemotherapy. Bevacizumab has been shown to have clinical benefits in advanced EOC. However, its efficacy in early-stage OCCC is mostly unknown. This study aims to evaluate bevacizumab's effects on survival outcomes in stage I/II OCCC patients. **[Methods]** This is a retrospective case-controlled cohort study of early-stage OCCC patients. Progression-free survival (PFS) and overall survival (OS) of three cohorts, observation, standard (with adjuvant chemotherapy only), and bevacizumab (BEV) group (with adjuvant chemotherapy plus bevacizumab), were compared with univariate and multivariate analysis. **[Results]** 160 OCCC patients were identified (16 in the observation group, 131 in the standard group, and 13 in the BEV group). The standard group's median age was younger (51.7, 49, and 55.96, respectively). The platinum/taxane doublet were the most common adjuvant chemotherapy used (0%, 90.84%, and 76.92%), and some patients received platinum/gemcitabine doublet (0%, 0%, 23.08%). Upon 1:2 matching of 12 patients from the BEV group with 24 patients from the standard group based on multivariate factors, the 5-year PFS was significantly higher in the BEV group (91.67% vs. 54.17%, $p=.03$). There was a trend toward improved 5-year OS (100% vs. 75%, $p=.08$) in the BEV group. **[Conclusion]** Among early-stage OCCC patients, there might be better PFS and OS by incorporating bevacizumab with current adjuvant chemotherapy.

ISP-13-1

Gynecological management of ovarian tumor arising from colorectal cancer ; experience in single institution Deguchi Satoki, Nakagawa Satoshi, Kinose Yasuto, Takiuchi Tsuyoshi, Miyoshi Ai, Kodama Michiko, Hashimoto Kae, Kobayashi Eiji, Ueda Yutaka, Sawada Kenjiro, Tomimatsu Takuji, Kimura Tadashi *Osaka University Hospital*

[Objective] The management of metastatic ovarian tumors arising from colorectal cancer is controversial. Many surgeons believe that ovarian metastases are less likely to responsive to chemotherapy than other metastases of colorectal cancer and tend to choose surgical resection. The purpose of this study is to discuss the utility of surgery with our experience cases and treatment outcomes. **[Methods]** Ten cases with pathologically confirmed metastatic ovarian carcinoma arising from colorectal cancer, who were surgically treated between 2010 and 2021 at our hospital, were reviewed. **[Results]** There are 10 operated cases of ovarian tumor arising from of colorectal cancer. Four

were diagnosed simultaneously as metastasis, and six were asynchronous recurrence. In metastatic cases, the median survival period is 13 months (5months - 63 months). In recurrence cases, the median period to ovarian recurrence was 21.5 months (7 months - 27 months) and the median survival period was 26 months (14 months - 78 months). **[Conclusion]** Due to the limited number of cases, no definite conclusion can be drawn. But surgical treatment for ovarian cancer arising from colorectal cancer can be an option.

ISP-13-2

Granulocyte colony-stimulating factor producing ovarian mucinous carcinoma with mural nodules : A case report Kagami Seiji, Urakawa Ruka, Kitajima Mitsuyasu, Toki Naoyuki *Kyushu Rosai Hospital*

[Background] Ovarian mucinous tumors with mural nodules are rare. The mural nodules are histologically divided into a wide variety, such as sarcoma-like, anaplastic carcinoma, true sarcoma and carcinosarcoma. There is no report of mucinous ovarian cancer with a mural nodule capable of producing granulocyte colony-stimulating factor (G-CSF). **[Case]** A 48-year-old woman presented to the emergency clinic for evaluation of strong abdominal pain. A 20cm-sized pelvic cystic mass was found on computed tomography. Emergent surgery was performed with a diagnosis of ovarian tumor torsion. Histological diagnosis of ovarian mucinous carcinoma with mural nodules of anaplastic carcinoma and myxofibrosarcoma-like tumor. The tumor was staged as FIGO IA. Evaluation after two courses of postoperative paclitaxel and carboplatin therapy revealed multiple lung metastases and para-aortic lymph node metastases. Severe leukocytosis was noted, G-CSF expression was positive on the tumor, and serum G-CSF was high (171pg/ml). The tumor progressed rapidly during two courses of liposomal doxorubicin therapy, so treatment was changed to docetaxel and gemcitabine therapy. Although the disease was suppressed up to the four courses, the chemotherapy became ineffective. Nine months after the operation the patient died of disease. **[Conclusion]** Anaplastic carcinomas in mucinous ovarian tumors has been shown to have a poor prognosis. However, the report suggested patients with stage IA tumors were not essentially associated with poor clinical outcomes. Recent reports suggest that KRAS mutation and SWI/SNF protein loss have some effect on poor prognosis. In this case, the ability to produce G-CSF was considered to have contributed to a further poor prognosis.

ISP-13-3

Validation of D-dimer cut-off values for diagnosis of venous thromboembolism in ovarian cancer patients : retrospective analysis Furukawa Shigenori¹, Ueda Makiko¹, Kato Asami¹, Okabe Chikako¹, Sato Tetsu¹, Kamo Norihito¹, Endo Yuta¹, Kojima Manabu², Nomura Shinji³, Soeda Shu¹, Watanabe Takafumi¹, Fujimori Keiya¹ *Fukushima Medical University Hospital¹, Takeda General Hospital², Jusendo Hospital³*

[Objective] To explore the clinical significance of D-dimer levels for the diagnosis of venous thromboembolism (VTE) on ovarian cancer patients. **[Methods]** 171 patients with ovarian cancer or peritoneal cancer that were treated at our hospital from January 2008 to December 2018 were enrolled. The relationship between the elevated D-dimer level and the presence of VTE was researched. 171 patients were divided into three groups : Group A (30 patients with thrombosis), Group B (51 patients without thrombosis), and Group C (90 patients who were not performed the imaging examination for the detection of VTE). In three groups, the comparison of D-dimer level was done by t-test. The cut-off values of D-dimer for diagnosing VTE and performing imaging studies for detecting VTE were calculated by using the

ROC curve and Youden's Index. **[Results]** The mean D-dimer level in Group A was significantly higher than Group B (24.8 ± 23.0 vs. 12.2 ± 16.5 , $P < 0.05$). The mean D-dimer level in Group B was significantly higher than Group C (12.2 ± 16.5 vs. 6.93 ± 14.0 , $P < 0.05$). The cut-off value of D-dimer for discovering VTE, sensitivity and specificity were $11.6 \mu\text{g/ml}$, 90% and 70.6%. The cut-off value of D-dimer for performing imaging studies for detecting VTE, sensitivity and specificity were $5.1 \mu\text{g/ml}$, 81.5% and 75.0%. **[Conclusion]** Although the prediction of VTE needs more clinical findings in addition to the D-dimer value, our data suggested that the additional imaging studies for detecting the VTE might be omitted in the patients of which the D-dimer value were less than $5.1 \mu\text{g/ml}$.

ISP-13-4

Genetic characteristics of platinum-sensitive ovarian clear cell carcinoma Saito Ryosuke^{1,2}, Shoburu Yuichi¹, Tsuda Akina¹, Kuroda Takafumi¹, Saito Motoaki¹, Tanabe Hiroshi¹, Takano Hirokuni¹, Yamada Kyosuke¹, Kiyokawa Takako³, Kato Tomoyasu⁴, Kohno Takashi², Okamoto Aikou¹ *The Jikei University¹, Division of Genome Biology, National Cancer Center Research Institute², Department of Pathology, The Jikei University School of Medicine³, National Cancer Center Hospital⁴*

[Objective] Ovarian clear cell carcinoma (OCCC) is known to be more resistant to platinum-based chemotherapy compared to high-grade serous carcinoma (HGSC) ; however, a small fraction of cases are platinum-sensitive. We retrospectively selected such platinum-sensitive OCCCs from two hospital cohorts and examined their pathological and genetic characteristics. **[Methods]** Of 136 patients with advanced OCCC who underwent primary surgery, complete resection was not achieved in 53 patients. By reviewing their clinical information, patients who responded to platinum based chemotherapy was selected. Immunohistochemical staining (IHC) ; and NCC Oncopanel and myChoice[®] HRD tests were performed for platinum-sensitive OCCC. **[Results]** Of the 53 cases with residual tumors after initial surgery, 11 (21%) were judged platinum-sensitive. These cases showed significantly better progression-free and overall survival than platinum-resistant cases. Eight of the 11 sensitive cases were subjected to molecular profiling. Six cases were pathologically validated as being as OCCC, while the remaining two cases were re-diagnosed as HGSC. The six OCCCs lacked *BRCA1/2* mutations, while three (50%) had somatic *ATM* mutations. Only one of the six OCCCs showed a high genomic instability score (GIS) suggestive of homologous recombination deficiency (HRD). Both two HGSCs had high GIS as well as *BRCA1* or *BRCA2* mutation. **[Conclusion]** Platinum-sensitive OCCCs may have different genetic characteristics from HGSC with frequent *ATM* mutations and infrequent HRD phenotype. Further study is planned to confirm the genetic status of *ATM* mutations and HRD phenotype.

ISP-13-5

Sarcopenic factors may have no impact on outcomes in ovarian cancer patients Ishibashi Tomoka, Nakayama Kentaro, Sato Seiya, Ishikawa Masako, Yamashita Hitomi, Fukushima Ruriko, Nonomura Yuki, Sawada Kiyoka, Makihara Kan, Kanno Kousuke, Kyo Satoru *Shimane University Hospital*

[Objective] Although the prognostic value of sarcopenic factors, such as loss of muscle mass and quality, have been widely reported in patients with cancer during the last decade, the value in those with ovarian cancer remains unclear. Therefore, this study evaluated the prognostic impact of sarcopenic factors in patients with ovarian cancer. **[Methods]** We retrospectively evaluated the data of 94 ovarian cancer patients who underwent surgery and chemotherapy between March 2006 and 2013. Pre-

operative computed tomography scan at the level of the third lumbar vertebra was used to evaluate skeletal muscle volume and quality based on the skeletal muscle index (SMI) and intramuscular adipose tissue content (IMAC), respectively. **[Results]** The impact of preoperative SMI and IMAC on outcomes was subsequently investigated. Low SMI and high IMAC were not significantly associated with disease-free survival ($p=0.329$ and $p=0.3370$, respectively) or poor overall survival ($p=0.921$ and $p=0.988$, respectively). **[Conclusion]** Neither preoperative low muscle volume nor low muscle quality was a poor prognostic factor in ovarian cancer.

ISP-13-6

Definitive Radiation Therapy for Recurrent Epithelial Ovarian Cancer Kato Asami, Endo Yuta, Sato Tetsu, Okabe Chikako, Ueda Makiko, Kamo Norihito, Kojima Manabu, Furukawa Shigenori, Soeda Shu, Watanabe Takafumi, Fujimori Keiya *Fukushima Medical University*

[Objective] Few retrospective studies have shown a benefit for radiation therapy (RT) use in patients with recurrent epithelial ovarian carcinoma (REOC). This study aimed to evaluate the efficacy and toxicities of definitive RT (DRT) for REOC. DRT was defined as irradiation that included all measurable lesions in the treatment field. **[Methods]** The medical records of patients who were treated with DRT for REOC from January 2008 to December 2018 were reviewed. Response rate, overall survival after initial therapy and DRT, and toxicities were analyzed. **[Results]** Seventeen patients and 23 irradiated sites were included. The median age at initial DRT was 60 years (range, 36-87 years). Sixteen patients had stage III or IV disease, and 15 patients had high-grade serous carcinoma. Of the 23 irradiated sites, 14 were lymph nodes and 7 were brain lesions. The median total dose was 50 Gy (range, 23-60 Gy). Six and 11 sites achieved complete response (CR) and partial response (PR), respectively. The response rate (CR+PR) was 73.9%. The response rates were 100% and 71.4% for the brain and lymph nodes, respectively. The median overall survival after initial therapy and DRT was 70 months (range, 17-139 months) and 19 months (range, 3-69 months), respectively. Only one patient developed grade 4 toxicity (sigmoid-vesical fistula which required colostomy). **[Conclusion]** DRT was associated with excellent local control for REOC in the brain and lymph nodes, and the toxicity level was tolerable.

ISP-14-1

Uterine torsion in non-gravid women : A case report and review of cases reported in the last 20 years Matsumoto Harunobu^{1,2}, Aoyagi Yoko², Morita Taisuke^{1,2}, Nasu Kaei² *Nakatsu Municipal Hospital¹, Oita University²*

(Introduction) Uterine torsion is defined as a rotation of $>45^\circ$ around the long axis of the uterus. It is generally rare but particularly rarer in non-gravid women, with only 25 cases reported in the last 20 years. Here, we report a case of uterine torsion associated with uterine leiomyomas in a non-gravid older woman and present a review of all cases of uterine torsion in non-gravid women reported in the last 20 years. **(Case)** An 83-year-old woman presented at the hospital with lower abdominal pain, and a computed tomography scan revealed multiple uterine leiomyomas with calcifications. Subsequent magnetic resonance imaging raised suspicion for torsion of subserosal uterine leiomyomas. Emergency laparotomy was performed, and the patient was diagnosed with uterine torsion with multiple subserosal uterine leiomyomas. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The patient's postoperative course was uneventful. **(Discussion)** According to the review of cases reported in the last 20 years, uterine torsion

in non-gravid women was often diagnosed late, resulting in fertility and life-threatening complications. CT scan and MRI often revealed characteristic findings ; specifically, the "whirl sign" of the uterine cervix may be useful for early diagnosis. Uterine torsion should be considered a differential diagnosis for acute abdominal pain in women of all ages, as early imaging and surgical intervention may preserve fertility and prevent life-threatening complications.

ISP-14-2

Relationship between vaginal microbiota and clinical findings in the patients with endometriosis Nishimura Masakuni, Katoh Kanoko, Kobayashi Osamu, Nakajima Takahiro, Ikeda Yuji, Komatsu Atsushi, Takeya Chiaki, Chishima Fumihisa, Sato Mikiko, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] The relationship between endometriosis and bacterial vaginosis have been reported. In addition, the bacterial colonization is shown in the menstrual blood of women with endometriosis by the detection of *E. coli*. The purpose of this study is to investigate the relationship between vaginal microbiota and clinical findings in the patients with endometriosis. **[Methods]** Among 179 patients who underwent surgery and were histopathologically diagnosed with endometriosis in our hospital from 2016 to 2021, 30 patients who were checked preoperative vaginal secretion culture testing are included. Among 410 patients who underwent surgery during the same period and were diagnosed with uterine fibroids or benign ovarian tumors, 30 patients who were checked vaginal secretion culture testing were included in the control group. **[Results]** There were 18 cases of some kind of pathogens in the endometriosis group, compared to 9 cases in the control group, which was significantly higher in the endometriosis group ($p<0.05$). *E.Coli* ($n=7$) and *Candida sp.* ($n=7$) were more common in the endometriosis group, while *St. agalactiae* ($n=4$) and *Candida sp.* ($n=3$) were more common in the control group. Comparison of ASRM scores according to the presence or absence of *E.coli* in the endometriosis patients showed that the ASRM scores of *E.coli* (+) patients was significantly higher than those of *E.coli* (-) patients ($p<0.05$). **[Conclusion]** The presence of some pathogenic bacteria in the endometriosis group were higher than in the control group, suggesting that a relationship between the vaginal microbiota and endometriosis.

ISP-14-3

A case of a recurrence of deep soft tissue leiomyoma extending to inferior vena cava (IVC) Yano Yoko, Nishimoto Masashi, Nagamata Satoshi, Kaji Takahiro, Yamanaka Keitaro, Azumi Maho, Washio Keiichi, Sasagawa Yuuki, Yamasaki Yui, Terai Yoshito *Kobe University Hospital*

Mesenchymal tumor extending to inferior vena cava (IVC) is extremely rare. Since the low prevalence, there are no definite guideline of this disease. However, we need to treat such patients multidisciplinary due to the possibility of life-threatening clinical cause caused by tumor embolism. We present a case of recurrence of deep soft tissue leiomyoma with intravenous extension two years after the primary surgery. A 34-year-old female presented an abdominal distension to the previous hospital. MRI (magnetic resonance imaging) showed 15cm pelvic mass suspected unrelated to gynecological organs. At the primary surgery, only the pelvic mass was removed because the tumor disconnected to the gynecological organs. Postoperative pathological diagnosis was deep soft tissue leiomyoma, and she was followed up with imaging test after surgery. Follow up CT (computed tomography) scan at 2 years after surgery indicated a tumor recurrence and she was referred to our hospital. Detailed imaging examination revealed the pelvic tumor invaded

IVC from the left internal iliac vein and surrounded the ureter. But the tumor seemed to have no connection with endometrium. We carried out CT-guided biopsy, and its findings were similar to the previous pathological features. Therefore, we diagnosed a recurrence of deep soft tissue leiomyoma, and performed an operation. Because estrogen was thought to be involved as a cause of recurrence, the operation included radical hysterectomy, bilateral salpingo-oophorectomy, and removal of retroperitoneal and intravascular tumor. Our case highlights the importance of a multidisciplinary approach in treating this rare case through preoperative assessment to an operation.

ISP-14-4

The clinical outcomes of dienogest treatment more than two years in women with endometrioma Kajimura Itsuki, Kitajima Michio, Matsumura Asako, Miyashita Noriko, Matsumoto Kanako, Harada Ayumi, Kitajima Yuriko, Miura Kiyonori *Nagasaki University Hospital*

[Objective] Dienogest is a fourth-generation progestin which alleviate pain symptoms associated with endometriosis. Moreover, it may reduce the size of endometrioma and prevents recurrence after conservative surgery. However, clinical knowledge on long-term treatment with dienogest are limited. Thus, we investigated the effectiveness and possible side effects of long-term treatment of dienogest in women with endometrioma. **[Methods]** From January 2015 to August 2021, we retrospectively analyzed 57 women treated with dienogest 2mg/day continuously at least 2 years at our hospital. We evaluated clinical variables, such as duration of medication, side-effects, size of endometrioma, recurrence during medical treatment. **[Results]** The mean age at initiation of the treatment was 35.9 years and the mean duration of continuous treatment was five years and two months, and longest treatment period was thirteen years. Out of 57 patients, 33 patients had ovarian endometrioma at the start of treatment, in which 31 patients (93.9%) had cyst size reduction after 2 years of treatment. Among 24 women had conservative surgery for endometrioma, four women (16.7%) were diagnosed as having recurrence. Various degrees of irregular uterine bleeding and estrogen deficient symptom were reported in 48 women (84.2%). Among 31 women examined bone mineral density (BMD), three women showed decreased BMD. **[Conclusion]** The treatment for endometrioma with dienogest more than two years is effective in cyst size reduction and prevention of post-surgical recurrence. The most symptom associated with dienogest during treatment are tolerable though careful follow-up is needed to avoid serious side effects.

ISP-14-5

Concurrence of Endometrial Cancer and Ovarian Cancer during Hormonal Therapy of Dienogest : A Case Report Ojima Tetsu¹, Takaoka Osamu¹, Koshiha Akemi¹, Aoyama Kouhei¹, Tarumi Yosuke¹, Kataoka Hisashi¹, Kokabu Tetsuya¹, Yoriki Kaori¹, Khan Khaleque¹, Kusuki Izumi¹, Kitawaki Jo², Mori Taisuke¹ *Kyoto Prefectural University of Medicine¹, Otsu City Hospital²*

[Objective] Dienogest (DNG) has been shown to be efficacious for the treatment of endometriosis-related symptoms. We report a case of concurrence of uterine endometrial cancer and ovarian cancer arising from the endometrioma during DNG treatment. **[Case]** A 45-year-old, nulligravid, Japanese woman was referred to our hospital for adenomyosis. She began receiving GnRH analog treatment before DNG therapy. At two years of DNG treatment, a right ovarian endometrioma (35 mm) was newly noted. At four years of DNG treatment, the patient had atypical genital bleeding and endometrioid carcinoma G1 after a complete endometrial curettage. PET-CT showed accumulation within the

uterine cavity and the right ovarian endometrioma. Operation was performed. On histopathological examination, the patient was diagnosed with endometrioid carcinoma G1 and ovarian cancer arising from endometrioma. Since then, no postoperative complications and cancer recurrence have been observed. **[Discussion]** Endometrioid carcinoma with in-situ lesions and subsequent endometriotic lesions was found in the same ovarian section. On the other hand, continuity with uterine adenomyosis lesions was not observed. However, atypical glandular duct proliferation in the endometrium as the main locus was observed. Taken together, this case was diagnosed as a double cancer of endometrial and ovarian cancers. As a result of examining the previous research reports of cancer formation during DNG treatment, there was a tendency for cancer to develop even if the ovarian tumor size was not huge. **[Conclusion]** Even though DNG treatment seems to be effective in regulating endometriomas, careful observation is needed to follow-up patients.

ISP-14-6

Disseminated peritoneal leiomyomatosis without history of uterine surgery : A case report Goto Takeshi *Osaka University Hospital*

[Background] Disseminated peritoneal leiomyomatosis (DPL) is a rare benign disease which is characterized by the dissemination of multiple fibroid-like nodules throughout abdominal cavity. Though iatrogenic DPL has been reported following laparoscopic procedures with morcellation technique of uterine fibroid there are few reports of DPL with no history of uterine surgery. The present report describes a case of a woman without history of uterine surgery had extensive lesions of DPL. **[Case]** A 30-year-old woman, gravida 0, was referred to our hospital with growing uterine myomas and suspicion of peritoneal dissemination. She had history of taking oral contraceptive for several years. Magnetic resonance imaging (MRI) and computed tomography revealed uterine myomas, extensive disseminated lesions in the pelvis and upper abdomen, including the diaphragmatic plane, and ascites. As the patient wanted to preserve her fertility, we planned laparoscopic biopsy of the lesions for pathological diagnosis. We observed innumerable disseminated nodules on the peritoneum of pelvic cavity and upper abdominal wall, diaphragm, omentum, serosal surface of small intestine, and colon. We biopsied some nodules of peritoneum and omentum. Histopathological examination showed features compatible with leiomyoma, and there was no findings of malignancy. As the lesions were too extensive to remove completely, gonadotropin-releasing hormone antagonist (relugolix) is being administered for tumor reduction. Future MRI examination and second look laparoscopy will be considered depending on her symptoms.

ISP-14-7

The omental cystic endometriosis that recurred 8 years after initial treatment : A case report Katakura Masafumi *Toho University Omori Medical Center*

[Introduction] Recently, a report of omental cystic endometriosis was published in *The New England Journal of Medicine* (Arakawa T et al. *N Engl J Med.* 2021). We report a case of omental endometrioma that recurred after 8 years of initial treatment. **[Case]** A 47-year-old woman, G1P1, had a history of a laparoscopic omental tumorectomy, and histopathological diagnosis was omental endometriosis when she was 39 years old. She had occasional lower abdominal pain for several days. She visited our hospital and underwent an ultrasound examination, which revealed a 40-mm pelvic mass on the left side of the vesicouterine pouch. She was admitted to the hospital as an emer-

gency. On contrast-enhanced MRI, the T2-weighted image revealed a 45-mm-large cystic lesion in the left adnexal region, with clear borders and fluid formation, and the T1-weighted image showed a mildly hypertense cyst, and no other structures that could be considered the left ovary were noted, so left cystic endometriosis was suspected. She was diagnosed with peritonitis because of severe abdominal pain, and emergency laparoscopic surgery was performed the day after admission. Surgical findings showed that the uterus and bilateral adnexa were not enlarged, and the cystic lesions originated from the omentum. The omental cyst was removed. Histopathological diagnosis showed fibrosis and endometriosis-like tissue in part of the fatty tissue, consistent with endometriosis, similar to the findings of the previous surgery. [Discussion] Omental endometrioma is very rare, and its pathogenesis is unknown. Moreover, recurrent omental endometrioma is a very valuable case.

ISP-14-8

Effectiveness and safety of Relugolix (gonadotropin-releasing hormone antagonist) on uterine leiomyomas : A retrospective cohort study Wada Yoshimitsu^{1,2}, Takei Yuji², Minezumi Takumi^{1,2}, Tsukahara Arisa^{1,2}, Yamamoto Kazuki^{1,2}, Izumi Ryo^{1,2}, Hirashima Hiroto^{1,2}, Baba Yosuke^{1,2}, Taneichi Akiyo², Fujiwara Hiroyuki² *Sanokousei General Hospital¹, Jichi Medical University²*

[Objective] To clarify the effectiveness and safety of Relugolix for the treatment of uterine leiomyomas, and predictors of size reduction. [Methods] We retrospectively reviewed medical records of patients who underwent treatment for uterine leiomyoma with Relugolix from December 2019 to September 2021 in our single institute. The patient's background, treatment period, size of leiomyoma before and after treatment, location of leiomyoma, hemoglobin, and adverse events were reviewed. If a patient had multiple leiomyomas, we evaluated the location and size of the largest leiomyoma. The size reduction rate was calculated by the maximum diameter of the leiomyoma measured on ultrasounds or magnetic resonance imaging. [Results] Sixty-seven patients who underwent treatment for uterine leiomyoma with Relugolix were included. The median (range) size reduction rate was 22.9 (12.7-28.4) %. Compared to the patients with leiomyomas less than 150 mm in size before treatment (62/67), the patients with leiomyomas greater than 150 mm in size (5/67) showed a significantly lower size reduction rate (median [range] : 23.6 [13.8-30.5] vs. 11.6 [4.2-14.0] %, respectively : P = 0.011). Post-treatment hemoglobin was significantly elevated, comparing with pre-treatment (median [range] : 13.5 [12.7-14.0] vs. 10.4 [7.6-12.2] g/dL, respectively : P < 0.001). Two patients received emergency surgery due to severe hemorrhage with prolapse of pedunculated myoma through the cervix. [Conclusion] Relugolix was effective for size reduction of leiomyomas and elevation of hemoglobin. However, the effectiveness of size reduction may be low for patients with leiomyomas with a maximum diameter of 150 mm or greater.

ISP-14-9

Cancer-associated mutations in adenomyosis Suda Kazuaki¹, Yoshihara Kosuke¹, Ishiguro Tatsuya¹, Yamaguchi Manako¹, Yachida Nozomi¹, Yokota Yuki², Kase Hiroaki², Enomoto Takayuki¹ *Niigata University Medical & Dental Hospital¹, Nagaoka Chuo General Hospital²*

[Objective] Adenomyosis is characterized by the presence of endometrial glands and stroma within the myometrium. The aim of this study is to reach a further understanding of the somatic landscape in adenomyosis. [Methods] After ethical committee approval and written informed consents, we performed target-gene sequencing for 44 adenomyotic epithelium samples,

13 adenomyotic stroma samples and 57 normal endometrium samples from 23 adenomyosis patients. All samples were isolated from frozen sections by using laser-microdissection. Sequencing data from paired blood samples was used for reference. [Results] The representative genes mutated (frequency) in the adenomyotic epithelium samples were *KRAS* (34%), *ARID1A* (20%), *ARHGAP35* (16%), and *PIK3CA* (11%) with the average mutant allele frequency (MAF) of 0.38, 0.24, 0.19 and 0.37, respectively. Furthermore, the adenomyotic epithelium samples, which were obtained by multiregional sampling, shared common mutation profiles in several patients. Adenomyotic stroma samples shared scarce mutations with the adjacent adenomyotic epithelium. Normal endometrium samples, which were obtained from adenomyosis patients, harbored mutations in *PIK3CA* (68%), *ARHGAP35* (60%) and *KRAS* (53%) with the average MAF of 0.10, 0.09 and 0.17, respectively. The identical mutation of *KRAS* was detected in paired samples of adenomyotic epithelium and normal endometrium in 3 of 23 patients. [Conclusion] We clarified that adenomyotic epithelium harbored cancer-associated mutations with a manner of clonal proliferation. The commonality in somatic mutations in the adenomyotic epithelium and normal endometrium could be further molecular evidence that adenomyosis derives from normal endometrium.

ISP-14-10

Evaluation of 83 cases of single-port laparoscopic adnexal surgery (SPLAS) in a single institutional training program

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[Objective] Single-port laparoscopic adnexal surgery (SPLAS) has frequently been used in gynecologic fields as its advantage of minimizing incision scars, aesthetically benefit and patient satisfaction. However, as it provided narrow surgical field, thus surgical skills mastering delicate manipulations must be applied. This study was conducted to evaluate the improvement of our fellow residents during the training program of SPLAS. [Methods] This a single institutional study of a total 83 patients with adnexal lesions who received single-port laparoscopic adnexal surgery between January 2019 and August 2021. SPLAS was performed by fellow doctors under supervision of single attending physician. Data were collected and analyzed. Operative time, estimated blood loss, intra- and post-operative complications according to seniority of fellowship were analyzed. [Results] The mean operative time is 64.0 mins. Mean blood loss was 7.0 mL. Only two patients (2.4%) need additional ports to complete the surgery. Subgroup analysis among performance between fellow 1 and fellow 2 surgeon showed shorter operative time among those senior doctors (53.1mins vs 67.1 mins : p=0.0082). No major intra-operative and post-operative complication was noted among both groups. [Conclusion] With proper training program, single-port laparoscopic adnexal surgery is feasible and safe as initial approach for young doctors to adnexal lesions. Further learning curve study yet need to be conduct for guiding optimization and modification of the training protocol.

ISP-14-11

LigaSure in two-port laparoscopic subtotal hysterectomy Li Yingxuan¹, William Yu Lee¹, Kuan-Ju Huang², Chin-Jui Wu², Lin-Hung Wei¹, Bor-Ching Sheu¹, Wen-Chun Chang¹ *National Taiwan University Hospital, Taiwan¹, National Taiwan University Hospital, Hsin-Chu Branch, Taiwan², National Taiwan Uni-*

versity Hospital, Yun-Lin Branch, Taiwan³

[Objective] Two-port laparoscopic subtotal hysterectomy is a way to manage symptomatic benign uterine lesions, and it takes shorter operative time and less postoperative pain than conventional laparoscopy. Ligasure™ is a kind of energy device that can seal the vessels less than 7mm without much smoke and cut tissue simultaneously. Here we presented a study about two-port laparoscopic subtotal hysterectomy with LigaSure™. **[Methods]** This was a retrospective study to enroll those who underwent two-port laparoscopic subtotal hysterectomy with LigaSure™ between May 2018 and February 2021. The data about the patient's characteristics, histopathology results, complications, operative time and estimated blood loss were collected. Those data was presented by percentage, mean \pm standard deviation and multivariable linear regression. **[Results]** There were seventy-one cases were enrolled after excluding three converted laparotomy cases. The mean age was 45.6 ± 4.6 (33-61). The mean BMI was 24.7 ± 5.1 (18-43). The most frequent histopathology was leiomyoma (80.2%). The mean of the operating time was 100.8 ± 35.6 (49-230) minutes. The mean of the estimated blood loss was 327.3 ± 278.5 (0-1100) ml. The operative time was related to the uterine weight, followed by surgeon, isthmus area, using uterine manipulator and adhesion to the uterus. The estimated blood loss was also related to uterine weight, followed by the area of isthmus. Four cases had constipation and all resolved after conservative treatments. **[Conclusion]** Two-port laparoscopic subtotal hysterectomy performed by LigaSure™ is a feasible choice to manage uterine benign tumors.

ISP-15-1

A case of unresectable adenoid cystic carcinoma of Bartholin's gland with multiple metastases Adachi Takaki^{1,2}, Nakatani Makiko¹, Matsumoto Sachiko¹, Nakajima Ayako¹, Yamada Hideto¹, Fujino Takafumi¹, Wada Shinichiro¹ *Teine Keijinkai Hospital¹, Sapporo Medical University Hospital²*

There are few reported cases and no established nonsurgical treatment for Bartholin's gland carcinoma, an extremely rare tumor accounting for 0.1% of female genital tumors and 2-7% of malignant vulvar tumors. We report a case of unresectable adenoid cystic carcinoma of Bartholin's gland with multiple metastases. A 74-year-old woman presented with a six-year-old slow-growing left vulvar tumor. For the previous two years, she had endured increasingly intense pain. A physician referred her to our hospital when the pain rendered her unable to sit. Upon examination, we observed vaginal compression by a left vulvar mass (8 cm \times 4 cm) beyond the left labia majora. A biopsy identified it as adenoid cystic carcinoma of Bartholin's gland. Magnetic resonance imaging revealed a mixed-density mass (8.5 cm \times 7.5 cm \times 7.0 cm) on the left side of the perineum. Enhanced positron emission tomography-computed tomography showed multiple pulmonary, hepatic, and bilateral renal metastases, leading to a classification of FIGO (International Federation of Gynecology and Obstetrics) Stage IVB. As it was unresectable, she underwent palliative chemoradiotherapy to enable her to sit. After two courses of chemotherapy (cisplatin 63 mg/m²) combined with radiation (30Gy/10Fr), the tumor shrank slightly and the pain eased. She is undergoing cancer gene panel testing and will continue to receive Paclitaxel/Carboplatin therapy until those results are available. Few studies have reported effective treatments for adenoid cystic carcinoma of Bartholin's gland. We will proceed with treatment based on the results of cancer gene panel testing.

ISP-15-2

Effectual surgical pelvic restoration of malignant mucosal vulvar melanoma Sheen Jiun-Yi¹, Li Ying-Xuan¹, Chang

Wen-Chun¹, Huang Kuan-Ju¹, Wu Chin-Jui^{1,2}, Wei Lin-Hung¹, Sheu Bor-Ching¹ *National Taiwan University Hospital, National Taiwan University, Taiwan¹, National Taiwan University Hospital Hsin-Chu Branch, Taiwan²*

Objective : To demonstrate successful surgical treatment and reconstruction in a case of malignant mucosal vulvar melanoma. **Case report :** A 52-year-old woman had stage II bulky malignant mucosal vulvar melanoma and received wide surgical excision with partial vulvectomy. She underwent 2-steps pelvic reconstructive vulvoplasty and vaginoplasty with skin grafting 1 year after initial surgical treatment. There was no evidence of recurrence after 3 years of follow-up. **Conclusion :** Vulvar melanoma is a rare malignant neoplasm. Wide local excision with pelvic reconstructive operations can relieve pelvic discomfort and restore local function after the surgery.

ISP-15-3

Low-grade endometrial stromal sarcoma arising in the vulvovaginal transition Harada Hiroshi¹, Matsuno Mariko¹, Shibahara Mami¹, Aoyama Yoko¹, Kuwazuru Tomoichiro¹, Hoshino Kaori¹, Nishimura Kazuaki¹, Ueda Taeko¹, Kurita Tomoko¹, Kagami Seiji², Matsuura Yusuke³, Yoshino Kiyoshi¹ *University of Occupational and Environmental Health¹, Kyushu Rosai Hospital², Department of Nursing of Human Broad Development, University of Occupational and Environmental Health, Japan³*

Introduction : Low-grade endometrial stromal sarcoma (Low-grade ESS) is rare, with some reports of its ectopic occurrence outside the uterus. We report an extremely rare case of Low-grade ESS originating from the vulvovaginal area. **Case history :** 22 years old, 0 gravida, 0 para. The patient was aware of a vulvar mass and referred to our department 5 months later. A solitary 4cm tumor was originated from the vulvovaginal area, without neoplastic lesions in the upper vaginal area or uterine cervix. Scraping cytology of the tumor surface was negative, and tumor biopsy was diagnosed as granulation tissue, thus a tumor resection was performed. On H&E staining, a subcutaneous tumor was formed with somewhat indistinct borders. Those tumor cells were oval- or short spindle-shaped and arranged in irregular cellular islands in the fibrous stroma. Based on these findings, Low-grade ESS was diagnosed. No other neoplastic lesions were noted on imaging studies, and the vulvovaginal transition area was determined as primary. The patient was young and the surgical margin was negative, thus no additional treatment was administered. **Discussion :** This is the first report of an ectopic Low-grade ESS arising in the vulvovaginal area. This tumor may have originated from ectopic endometriosis or stray Müllerian duct tissue. Low-grade ESS originated from the uterus is characterized by a gradual development and a good prognosis with a median overall survival over 5 years, whereas long-term follow-up is recommended. **Conclusion :** There are limited reports of ectopic Low-grade ESS, and its prognosis and therapeutic efficacy require further follow-up.

ISP-15-4

Imiquimod for vaginal intraepithelial neoplasia 2-3 : A single-center-experience and a systematic review and meta-analysis of reported cases Inayama Yoshihide^{1,2}, Yamanishi Yukio¹, Aratake Junichi¹, Sasagasako Nanayo¹, Yamada Kaori¹, Gou Rei¹, Kawamura Atsuko¹, Yamanishi Megumi¹, Yamaguchi Ken², Hamanishi Junzo², Mandai Masaki², Kosaka Kenzou¹ *Shizuoka General Hospital¹, Kyoto University Hospital²*

[Objective] Vaginal intraepithelial neoplasia (VaIN) 2-3 is a rare premalignant condition without an established treatment strategy. This study was conducted to investigate the efficacy of imiquimod in VaIN 2-3. **[Methods]** The clinical records of

women with VaIN 2-3 who were treated with imiquimod in our hospital from January 2016 to May 2020 were investigated. Also, electronic databases (PubMed, EMBASE, ClinicalTrials.gov, and Cochrane Central Register of Controlled Trials) were searched and articles reporting imiquimod treatment for VaIN 2-3 were identified. The last search was conducted on October 10, 2019. The data from the systematic search and our hospital were analyzed, and a pooled complete response (CR) rate and response rate of imiquimod treatment for VaIN 2-3 were estimated. **[Results]** Imiquimod was used in nine women with VaIN 2-3 in our hospital. Five articles described 28 women with VaIN 2-3 who were treated with imiquimod. The discontinuation of the treatment was required in only one patient of the reported cases. The pooled CR rate and response rate of imiquimod for VaIN 2-3 was 0.76 (95% CI, 0.59-0.87) and 0.89 (95% CI, 0.71-0.97), respectively. In the subgroup analysis, the CR rate in patients with hysterectomy was 0.98 (95% CI, 0.11-1.0) while those without hysterectomy was 0.60 (95% CI, 0.30-0.84), and the rate ratio was 0.83 (95% CI, 0.48-1.19). **[Conclusion]** Imiquimod can be an effective treatment for vaginal intraepithelial neoplasia 2-3.

ISP-15-5

Histone deacetylase inhibitors as novel therapeutic agents for choriocarcinoma by inducing ferroptosis Watanabe Eri¹, Yokoi Akira^{1,2}, Yoshida Kosuke^{1,2}, Sugiyama Mai³, Kitagawa Masami³, Nishino Kimihiro¹, Niimi Kaoru¹, Kajiyama Hiroaki¹ Nagoya University¹, Institute for Advanced Research, Nagoya University², Bell Research Center, Nagoya University³

[Objective] The response rate of current standard chemotherapy for choriocarcinoma is high, but the prognosis of refractory choriocarcinoma remains very poor. In this study, we aimed to identify novel therapeutic agents for choriocarcinoma from clinically available drug library. **[Methods]** By using the chemical library consisting of 1280 FDA-approved drugs, we evaluated the growth inhibition rate against three choriocarcinoma cell lines (JAR, JEG-3 and BeWo) and the xenograft mouse models. The inhibition rate was determined by z-scoring based on the value from MTS assay in vitro. **[Results]** In the primary screening of uniformly treatment as 10 μ M concentration, 51 drugs were selected ($z > 2$) and in the second screening, they were narrowed to 14 drugs which showed over 80% inhibition. In the third screening, we identified 5 drugs which significantly worked in low concentration (2.5 μ M) and they did not affect normal trophoblasts. Based on the result of safety assessment in vivo, vorinostat, the histone deacetylase inhibitor, was selected as promising candidates. RNAseq reveal that vorinostat down-regulate *GPX4*, *NRF2* and *SLC3A2* expressions which related to the ferroptosis pathway. The amount of their protein also decreased in a dose-dependent manner in choriocarcinoma cell lines. In vivo experiment, vorinostat significantly reduced tumor growth by more than 50%, and protein expressions of *GPX4* and *NRF2* were also decreased in vorinostat-treated tumor tissues. The expression of those proteins also confirmed in human choriocarcinoma tissue. **[Conclusion]** Our study demonstrated the feasibility that vorinostat or agents inducing ferroptosis are novel therapeutic strategy in choriocarcinoma patients.

ISP-15-6

Primary pulmonary choriocarcinoma diagnosed by histopathologic and genetic examination Odai Tamami, Ohno Haruko, Nakamura Reiko, Tsukada Takafumi, Oshima Noriko, Wakana Kimio, Miyasaka Naoyuki Tokyo Medical and Dental University **Introduction :** Non-gestational choriocarcinoma is rare. When the tumor is found in the lung, to determine whether it is primary or metastatic pulmonary cancer is sometimes difficult. We herein present a case of primary pulmonary choriocarcinoma di-

agnosed by histopathologic examination and cancer genomic profiling test. **Case :** A 46-year-old female (gravida 1, para 1), was referred to our hospital due to a solitary lung tumor. It was located in the right lower lobe and 20 mm in diameter. A whole-body positron emission tomography/computed tomography (PET/CT) showed faint 18F-fluorodeoxyglucose accumulation within the tumor, but no other hotspot was found. She underwent thoracoscopic right lower lobectomy. Histopathological examination revealed that the tumor was choriocarcinoma mainly composed of multinucleated syncytial-like trophoblastic cells with strong beta-hCG immunostaining. Although the pathological finding prompted us to examine reproductive organs, no abnormal finding was found. Serum free beta-hCG level was 0.1 ng/ml one month after the surgery. To determine the primary origin of the tumor, a multi-gene panel testing for the rare cancer was conducted. Epidermal growth factor receptor V774M gene mutation, a rare but lung cancer specific missense mutation, was detected. Thus, she was diagnosed stage IA2 primary pulmonary choriocarcinoma and no recurrence or metastasis was observed until six months after the surgery. Cancer genomic information could support the diagnosis of the primary origin in rare cancer.

ISP-15-7

A case of primary peritoneal choriocarcinoma of gestational origin Yamauchi Kota¹, Sato Yukiyasu¹, Sakurai Azusa¹, Akamatsu Yoshimasa¹, Harada Yuriko¹, Harada Ryusuke¹, Mori Yoko¹, Usui Hirokazu², Goto Masaki¹ Takamatsu Red Cross Hospital¹, Chiba University²

Peritoneum is a rare site for the primary extrauterine choriocarcinoma to develop. While it is straightforward to ascribe tubal choriocarcinoma to gestational origin, primary peritoneal choriocarcinoma could even be gestational or non-gestational origin. We here describe a case of primary peritoneal choriocarcinoma that was successfully diagnosed as gestational origin using multiplex short tandem repeat (STR) polymorphism analysis. Case is a 46-year-old woman with history of two artificial abortions at the ages of 20 and 43, who presented with acute abdomen. Although she had taken oral contraception, urine hCG test proved positive. Computed tomography revealed left adnexal mass with hemorrhagic ascites. Emergency laparotomy was performed under the suspicion of ruptured left tubal pregnancy, revealing walnut-sized hemorrhagic tumor on the surface of left mesosalpinx and apparently intact left ovary and fallopian tube. The tumor resection in combination with left salpingo-oophorectomy was executed. Pathological diagnosis of the resected tumor was choriocarcinoma. DNA analysis using STR polymorphism revealed that tumor was androgenic/homozygous XX gestational choriocarcinoma. Since FIGO prognostic score was calculated to be 12 (high-risk), multi-agent chemotherapeutic regimen EMA/CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, and oncovin) was selected, leading to steady decrease of serum hCG level.

ISP-15-8

Potentially lethal gynecological disorder : A rare case of septic shock in a woman with a hydatidiform mole Yoshimoto Yuki, Murata Tsuyoshi, Shibano Yoshiaki, Nakamura Souichi, Yamauchi Ryuuji Shirakawa Kosei General Hospital Although hydatidiform moles are relatively common, they can be fatal (especially after 10 weeks of gestation) because of massive bleeding or a thyroid storm. Other potentially lethal conditions in women with hydatidiform moles should be elucidated. Hydatidiform moles rarely occur concomitantly with septic conditions, according to the literature. Herein, we present a case of septic shock associated with a hydatidiform mole. A 30-year-old

multiparous woman with a history of Basedow disease was referred to a general internal medicine doctor due to fever lasting 3 days. Blood cultures were positive (gram-negative rods), indicating infection. Amenorrhea for 10 weeks and vaginal bleeding led to a positive pregnancy test, which led to a gynecological consultation. Transvaginal ultrasonography revealed a 100-mm swollen uterus with intrauterine vesicular pattern. Laboratory tests revealed human chorionic gonadotropin (994,000 mIU/mL) and mild hyperthyroidism. Computed tomography detected no other possible infectious site or mole metastasis in the body. Antibiotics (tazobactam, piperacillin) were administered, and dilation and curettage (D&C) was planned. However, her blood pressure suddenly plummeted to 69/45 mmHg, which was stabilized using noradrenalin and albumin. The uterine content was naturally extracted at this juncture, and her vital signs gradually stabilized. D&C was performed twice. She was pathologically diagnosed with a complete hydatidiform mole. Bacterial culture of the intrauterine content detected *E. coli* infection, leading to the diagnosis of septic shock associated with the hydatidiform mole. Antibiotics were administered for 8 days. She was discharged 11 days after hospitalization. Thus, a hydatidiform mole can cause septic shock-a lethal condition.

ISP-16-1

Exploration of the tools to predict chemotherapy-related severe adverse events in the very elderly gynecologic cancer patients Okuma Yuki, Sugimura Kodai, Sato Mikiko, Matsuda Erina, Katoh Kanoko, Kobayashi Osamu, Nakajima Takahiro, Kawakami Kaori, Ikeda Yuji, Komatsu Atsushi, Chishima Fumihisa, Kawana Kei *Nihon University*

[Objective] Assessing the feasibility of giving chemotherapy to elderly patients is an essential issue because risks of severe adverse events (SAEs) could outweigh the benefits of the chemotherapy among vulnerable elderly cancer patients. Therefore, practical tools to predict SAEs in elderly gynecologic cancer are required. Performance Status (PS), comprehensive geriatric assessment 7 (CGA7), and Geriatric Nutrition Risk Index (GNRI) is widely used for general health assessment of elderly patients. This study aimed to assess the usability of those health assessment tools to predict chemotherapy-related SAE in very elderly gynecologic cancer patients. **[Methods]** Gynecological cancer patients older than 75 years who received chemotherapy treatment in our hospital were investigated. Patient background, the incidence of SAE, PS, CGA7, and GNRI were retrospectively evaluated. SAE was defined as an adverse event that caused hospitalization or chemotherapy discontinuation. **[Results]** Thirty-three patients with a mean age of 79.8 years (76~89 yrs) were studied. SAE occurred in 14 (42.4%) patients. The incidence of SAE was associated with low GNRI (defined as <92, $p=0.03$ by Fisher's exact test). Moreover, 100% of the patients with the combination of low GNRI and positive CGA developed SAE. On the other hand, positive CGA7, poor PS alone, or a combination of PS and GNRI did not relate to SAE. **[Conclusion]** Our data suggested that assessing the feasibility of chemotherapy by the combination of low GNRI and positive CGA7 could contribute to developing the treatment plans for very elderly gynecologic patients.

ISP-16-2

Thrombopoietin : a novel candidate diagnostic biomarker for ovarian cancer Murakami Isao¹, Kurahashi Takashi², Kajiwara Hiroshi³, Tanaka Kyoko¹, Mikami Mikio⁴ *Toho University Ohashi Medical Center¹, Saitama National Hospital², Department of Pathology, Tokai University³, Tokai University⁴*

[Objective] Cancer antigen 125 (CA125) is a serum marker that is clinically used for ovarian cancer and is elevated in the major-

ity of ovarian cancer cases. However, false positive CA125 results are common. Thrombocytosis is a frequent preoperative finding in ovarian cancer and may be a marker of aggressive tumors. To assess the diagnostic relevance of serum thrombopoietin (TPO) levels, we compared preoperative serum TPO levels in patients with cervical cancer, endometrial cancer, ovarian cancer, and benign gynecological tumors. **[Methods]** We carried out a retrospective cohort study using the medical and histopathological records of 335 cancer cases from 2016 to 2018. **[Results]** This study included 24, 39, 34, 3, and 235 cases with cervical cancer, endometrial cancer, ovarian cancer, recurrent ovarian cancer, and benign gynecological tumors, respectively. Preoperative serum TPO levels of the malignant cases (median, 0.81 ; range, 0.2-5.32) were significantly higher compared with those of benign cases (median, 0.51 ; range, 0.2-3.67) ($p<0.001$). Preoperative serum TPO levels were significantly higher in stage III-IV and recurrent ovarian cancer cases than levels in stage I-II ovarian cancer cases ($p<0.001$). In contrast, there was no significant difference in serum TPO levels between stages in endometrial and cervical cancer cases. Notably, preoperative serum TPO levels were correlated with CA125 in all cancer cases ($p=0.022$). **[Conclusion]** Preoperative serum TPO levels correlated with ovarian cancer staging and recurrence. These data suggest that preoperative serum TPO level is a candidate diagnostic biomarker for ovarian cancer.

ISP-16-3

Pelvic lymph node squamous cell carcinoma of unknown primary treated surgically and CCRT : A case report Saito Hikaru¹, Kobayashi Masayuki¹, Nakayama Kentaro², Orita Takeshi¹, Nonomura Yuki², Yamashita Hitomi², Sawada Kiyoka², Fukushima Ruriko², Ishibashi Tomoka², Ishikawa Masako², Sato Seiya², Kyo Satoru² *Hamada Medical Center¹, Shimane University Hospital²*

Squamous cell carcinoma of unknown primary origin with pelvic lymph node metastases is extremely rare. We report this rare condition in a 38-year-old gravida 2, para 2, who presented with left lower extremity edema and left lower abdominal pain. Computed tomography (CT) revealed a left pelvic lymph node. Tumor markers (SCC ; 23.5ng/ml and CEA ; 21.2ng/ml) were elevated, which suggested squamous cell carcinoma metastasized to lymph node. The primary lesion was not identified on PET-CT and endoscopy did not reveal evidence of gastrointestinal or urinary cancer ; therefore, she was referred to our department. Cervical cytology results were reported as NILM, colposcopy findings were normal, and HPV testing, as well as endometrial cytology showed negative. Fine needle aspiration biopsy of left pelvic lymph node lesions was performed under transvaginal ultrasonography. Immunohistochemical analysis showed cells with immunopositivity for AE1/AE3, CK5/6, p40, and p16 and immunonegativity for CK7, CK20 ; therefore, we suspected HPV-related squamous cell carcinoma with lymph node metastasis. For the purpose of definitive diagnosis and treatment, simple total hysterectomy, bilateral adnexectomy and left pelvic lymph node dissection were performed. Postoperative histopathological evaluation showed no evidence of uterine or bilateral adnexal malignancy ; however, the left pelvic lymph nodes showed squamous cell carcinoma, and the patient was diagnosed with squamous cell carcinoma of unknown primary origin metastasized to lymph node. In view of p16 immunopositivity, the patient received CCRT (external irradiation 50.4Gy + weekly CDDP 7 course) based on the treatment of cervical cancer. Currently, no recurrence is observed 2 months after treatment.

ISP-16-4

Genetic panel tests for patients with gynecologic cancer at our hospital : A retrospective study Koh Iemasa¹, Nakamoto Kosuke¹, Morioka Hirohiko¹, Oomori Yuriko¹, Teraoka Yuko¹, Nosaka Suguru¹, Tomono Katsuyuki¹, Sekine Masaki¹, Yamazaki Tomomi¹, Mukai Yurika¹, Hinoi Takao², Kudo Yoshiki¹ *Hiroshima University¹, Department of Genetic Medicine, Hiroshima University²*

[**Objective**] FoundationOne CDx (FICDx) and OncoGuide NCC Oncopanel tests were approved by insurance companies in June 2019 as these tests that can simultaneously analyze changes in multiple cancer-related genes. Gene panel tests are now conducted in clinical practice. However, the number of gene panel tests for patients with gynecologic cancer performed in Japan remains few, and their usefulness and limitations have not been fully investigated. [**Methods**] This study retrospectively analyzed changes in cancer-related genes and treatment implementation in patients with gynecologic cancer who underwent a genetic panel test at our hospital between November 2019 and September 2021. [**Results**] The gene panel tests were performed for 51 patients, with FICDx in 40 cases (71.4%). The cancer types were ovarian cancer (20 patients), endometrial cancer (14 patients), uterine carcinosarcoma (5 patients), uterine sarcoma (8 patients), and cervical cancer (6 patients). The most frequent cancer-related genetic changes were *TP53* mutation (67%), *PIK3CA* mutation (37%), and *PTEN* mutation (20%). Twenty-six patients (51%) were eligible for clinical trials, of whom only 1 was able to reach the treatment stage, thus accounting for 2% of the total. Disease worsened in five patients, and two died ; thus, these were unable to receive treatment. [**Conclusion**] Genetic panel test results in gynecologic cancer cases revealed a relatively large number of genetic changes, although only few cases reached the treatment stage. Modifying treatment based on genetic alterations is important, and genetic panel testing should be performed at the appropriate time to maximize the use of treatment opportunities.

ISP-16-5

Significance of zinc supplementation during chemotherapy for gynecological malignancy Yanazume Shintaro, Ushiwaka Takashi, Yorouki Honami, Onigahara Motohisa, Fukuda Mika, Mizuno Mika, Togami Shinichi, Kamio Masaki, Kobayashi Hiroaki *Kagoshima University*

[**Objective**] Typical essential trace element of zinc deficiency causes taste disturbance, dermatitis, hair loss, anemia, stomatitis, immunocompetence, and osteoporosis. The efficacy of zinc supplementation for symptoms of gynecological malignancy, including taste alteration associated with zinc deficiency has not been understood. To define the significance of zinc supplementation for zinc deficiency during chemotherapy for gynecologic malignancies. [**Methods**] Twenty-eight patients suspected of zinc deficiency before chemotherapy were prospectively evaluated. Gustatory test, serum zinc, blood count, and biochemical examinations were made pre-chemotherapy at three and six week intervals. Patients with serum zinc levels <70 µg were prescribed oral zinc acetate hydrate (167.8 mg/d) for three weeks. The primary outcome was efficacy of zinc supplementation, the secondary outcomes were zinc deficiency rates and adverse effects of the zinc supplement. [**Results**] Fifteen (mean serum zinc level : 67.4 ± 6.2 µg/dl) out of 28 patients were administered zinc supplementation pre-chemotherapy, and subsequent serum zinc levels reached 83.2 ± 15.3 µg/dl in three weeks. Factors associated with chemotherapy (vs. chemoradiation, $P=0.041$) and taxane + platinum ($P=0.048$) were significant risk factors for decreasing zinc levels following chemotherapy. Although patients that required zinc supplementation showed de-

creased serum zinc levels after chemotherapy and tended to experience taste alteration (sour : $P=0.041$), zinc supplementation for zinc deficiency during chemotherapy did not alter taste perception. [**Conclusion**] Zinc supplementation promptly increased serum levels without major complications and may prevent an alteration in taste perception.

ISP-16-6

Activities of daily living measurements may be useful for estimating the quality of life in patients with gynecologic cancer receiving chemotherapy Irie Kyohei¹, Nakamura Keiichiro¹, Haruma Tomoko², Okamoto Kazuhiro¹, Matsuoka Hirofumi¹, Ida Naoyuki¹, Ogawa Chikako¹, Masuyama Hisashi¹ *Okayama University¹, Okayama Saiseikai General Hospital²*

[**Objective**] The purpose of this observational study was to investigate the correlation between the factors affecting activities of daily living (ADL) and quality of life (QOL) scores in patients with gynecologic cancer (GC) receiving either three or six cycles of chemotherapy. [**Methods**] ADL factors, including the sensory nerve conduction velocity (SNCV), the amplitude of the sensory nerve action potential (SNAP), performance on the 10 m Walk Test (10mWT), and grip strength (GS) were measured, and QOL scores were determined from responses on the Short Form-36 (SF-36) questionnaire among 28 patients with GC receiving chemotherapy. Statistically significant correlations were determined using χ^2 tests. [**Results**] Compared with pretreatment baseline values, the social functioning (SF) and three role/social component summary (RCS) component scores were significantly reduced in patients who received six cycles of chemotherapy based on the SF-36 questionnaire ($P=0.003$ and $P=0.017$, respectively). Therefore, the 10mWT was significantly correlated with the SF and 3RCS after six cycles of chemotherapy when divided by the respective pretreatment baseline score (SF : $R=0.754$, $R^2=0.569$, $P=0.005$; and 3RCS : $R=0.703$, $R^2=0.495$, $P=0.011$, respectively). [**Conclusion**] The introduction of ADL measurements, especially 10mWT may be suitable for QOL evaluation and useful for estimating the QOL in patients with GC receiving chemotherapy.

ISP-16-7

Comprehensive metabolomic analyses reveal novel potential therapeutic approaches in gynecologic cancers Shigeta Shogo¹, Shimada Muneaki¹, Shibuya Yusuke¹, Li Bin², Minato Takamichi¹, Minato Junko¹, Ishibashi Masumi¹, Nagai Tomoyuki¹, Tokunaga Hideki¹, Yaegashi Nobuo^{1,2} *Tohoku University Hospital¹, Advanced Research Center for Innovations in Next-Generation Medicine, Tohoku University²*

[**Objective**] Plasma metabolites have received focused research attention as potential biomarkers for early detection and precision cancer medicine. This study aims to unveil metabolomic signatures of major gynecologic malignancies by comprehensive analysis. [**Methods**] Preoperatively collected plasma from patients with uterine cervical cancer, endometrial cancer, or ovarian cancer were analyzed. Plasma samples from matched healthy cohort members were also examined as controls. Metabolites were absolutely quantified using an MxP[®] Quant 500 Kit, which simultaneously determines concentrations of up to 630 metabolites. [**Results**] Principal component analysis and orthogonal partial least squares discriminant analysis revealed evident metabolite differences between each cancer type and its matched healthy control. Subsequent statistical analyses identified 60, 33, and 197 metabolites that were significantly increased or decreased in cervical cancer, endometrial cancer, and ovarian cancer, respectively. Cluster analysis and pathway analysis indicated unique metabolite signatures, with elements in common among the cancers, and elements unique to each cancer type.

We calculated 232 metabolic parameters in ovarian cancer patients, and found indoleamine 2,3-dioxygenase (IDO) activity significantly increased in this patient population. Ovarian cancer patients also presented elevated kynurenine/tryptophan (Kyn/Trp) ratios, which reflect IDO activity, and are associated with worse prognosis than lower Kyn/Trp ratios. **[Conclusion]** The current analyses indicate that plasma metabolomic profiling in gynecologic cancers offers the potential to contribute to multiple aspects of gynecologic cancer therapy. As one example, IDO activity, which plays an important role in tryptophan catabolism, is a potent prognostic indicator, and a therapeutic target in ovarian cancer.

ISP-17-1

Whole-Exome Sequencing of cancer of unknown primary
Sawada Kiyoka, Nakayama Kentaro, Kanno Kousuke, Makihara Kan, Fukushima Ruriko, Yamashita Hitomi, Ishibashi Tomoka, Ishikawa Masako, Sato Seiya, Iida Koji, Kyo Satoru *Shimane University*

[Objective] Cancer of unknown primary (CUP) is defined as a tumor in which the primary origin cannot be identified during the pretreatment evaluation period, despite a thorough enough search. There is no established standard treatment. Therefore, we performed whole-exome sequencing for one case of CUP to evaluate the usefulness of NGS. **[Methods]** A 79-year-old woman received medical checkup, wherein multiple lymphadenopathy of the para-aorta was found on a MRI and abnormal accumulation on the lymph nodes on a PET-CT. After 6 months, the lymphadenopathy progressed. Laparoscopic biopsy was performed to examine the tissue type. Histologically, it was diagnosed as serous adenocarcinoma, while the immunohistochemical analysis suggested the possibility of gynecologic cancer. Therefore, we performed a surgery, wherein no primary lesion was found in the sample, leading the diagnosed of CUP and metastasis of the para-aortic lymph nodes. She received six cycles of carboplatin and paclitaxel. Whole-exome sequencing was performed on genomic DNA, and the protein expression levels of CD8, PD-L1, and PD-1 were evaluated using immunohistochemical analysis. **[Results]** *TP53* mutation was identified as an actionable variant. No recommended treatment based on the gene mutation was found. Immunohistochemical analysis revealed that the patient was positive for CD8, PD-1, and PD-L1 expression. **[Conclusion]** In this case, we were not able to find an appropriate treatment based on the gene mutation, but a high infiltration of T cells into the tumor and PD-1/PD-L1 expression were thought to be potential biomarkers for indicating a response to immune checkpoint inhibitors.

ISP-17-2

Clinical availability and characteristics of multi-gene panel testing for recurrent gynecologic cancers
Kitazawa Shoko¹, Chiyoda Tatsuyuki¹, Nakamura Kohei², Sakai Kensuke¹, Yoshihama Tomoko¹, Nishio Hiroshi¹, Banno Kouji¹, Iwata Takashi¹, Yamagami Wataru¹, Nishihara Hiroshi², Tanaka Mamoru¹, Aoki Daisuke¹ *Keio University¹, Genomics Unit, Keio Cancer Center, Keio University²*

[Objective] Multigene panel testing has been approved in Japan. This study aims to determine its potential availability and utility in a gynecologic oncology clinical setting. **[Methods]** We analyzed characteristics of gynecologic cancer patients who underwent gene panel testing between November 2019 and August 2021, using FoundationOne CDx[®] or NCC Oncopanel[®]. **[Results]** We analyzed 56 cases, comprising 21 patients with cervical cancer, 7 with endometrial cancer, 24 with ovarian cancer, and 4 with sarcoma. Druggable alternations were found in 35 cases (62.5%) : 66.7% of cervical cancer, 85.7% of endometrial

cancer, 50.0% of ovarian cancer and 75.0% of sarcoma. The most common druggable alternations were *PIK3CA* alternation (n=12), followed by TMB-H (n=8). TMB-H cases included four cervical cancer (three squamous and one adenosquamous), three endometrial cancer (one each of endometrioid, serous, and clear cell) and one endometrial stromal sarcoma case. Ten patients (17.9%) received molecular-targeted therapy according to their gene aberrations. Of the 35 patients with druggable alternations, 10 received treatment, 5 had not had a recurrent tumor, 7 did not undergo any recommended treatment, 10 died or their condition worsened before obtaining the test results, and the remaining 3 refused treatment. **[Conclusion]** Druggable alternations were identified in many cases, which allowed 17.9% of the patients to receive treatment. TMB-H observed in various histologic subtypes of cervical or endometrial cancer could be considered a therapeutic immune biomarker.

ISP-17-3

Kampo medicines (Juzentaihoto, Hochuekkito, Shosaikoto) may prolong the survival of transgenic mice bearing lens epithelial tumors through the activation of distinct innate immunity
Nakamura Takafumi *Kawasaki Medical School*

[Objective] We previously reported *a* T3 mice that produced lens epithelial tumors by SV40 T antigens. We have been studying that these Kampo medicines (Juzentaihoto, Hochuekkito and Shosaikoto) might modulate the innate immunity, and that these Kampo medicines might prolong the survival of *a* T3 mice. **[Methods]** In first study, the *a* T3 mice were mated with the *a* /IL-1 β mice, which were expressing IL-1 β in lens cells. The *a* T3 β mice were produced in order to study an effect of local inflammation for cancer development. The *a* T3 β tumors progressed much faster than *a* T3. Tumor associated macrophages (TAM) in *a* T3 β mice was much more recruited than *a* T3. Both *a* T3 and *a* T3 β mice were fed the baits, containing each different Kampo medicines, Juzentaihoto, Hochuekkito, Shosaikoto. **[Results]** Oral administration of each Kampo medicines tended to increase TAM in *a* T3 and prolonged the survival of *a* T3 as compared with the untreated control. However, only Shosaikoto could make *a* T3 β mice prolong the survival comparing the other baits. **[Methods]** In second study, the *a* T3 mice were mated with IL-2 receptor γ chain-deficient mice, producing NK cells-deficient *a* T3 (*a* T3IL-2R γ KO) mice. The *a* T3IL-2R γ KO mice were fed the baits, containing each different Kampo medicines, Juzentaihoto, Hochuekkito, and the survival rate of these mice was compared with the untreated control. **[Results]** Interestingly, Juzentaihoto made *a* T3IL-2R γ KO mice prolong the survival but Hochuekkito could not. **[Conclusion]** These results suggested that Shosaikoto was the Kampo medicines that could regulate a local inflammation, and that Hochuekkito specially could affect NK cells. Three Kampo medicines may enhance the local tumor immunity in different manner.

ISP-17-4

Accuracy of FDG-PET/CT evaluating lymph node metastasis in gynecologic malignancies
Nakamoto Tomoko, Watanabe Toshiaki, Shimoji Yuko, Arakaki Yoshihisa, Taira Yusuke, Kudaka Wataru, Aoki Yoichi *University of the Ryukyus*

[Objective] To assess the diagnostic accuracy of PET/CT using ¹⁸F-fluorodeoxyglucose (FDG) in detecting lymph node (LN) metastasis in patients with gynecologic cancers, and identify the factors which influence false-positive rate of FDG-PET/CT. **[Methods]** From January 2016 to December 2020, 70 patients with gynecologic malignancies who were evaluated by FDG-PET/CT prior to lymphadenectomy or LN removal were included in this retrospective study. The data including patient

characteristics, diagnosis, stage, short axis diameter of LN, maximum standardized uptake value (SUV max), recent white blood cell (WBC) count, glucose level, C-reactive protein, and the pathological diagnoses were collected by chart review. The factors which influence false-positive rate were analysed by logistic regression model, with $p > 0.05$ as significant. **[Results]** The median age was 51.5 (range, 24-78) years, and the median body mass index was 25.5 (range 15.7-47.8). Thirty four patients had cervical cancers, 28 endometrial cancers, 4 uterine sarcomas, 3 ovarian cancers, and 1 vulvar cancer. Median short axis diameter of enlarged LNs was 7.5 (range, 5-43) mm, and median SUV max was 6.4 (range, 2.9-25.7). Of 34 patients with abnormal FDG uptake, 25 were pathologically proven true-positives, and 9 were false-positives. Sensitivity was 75.8% (25/33), and specificity was 75.7% (28/37). Only WBC counts $\geq 9000/\mu\text{L}$ was a significant factor for false-positive by multivariate analysis (odds ratio 11.8, 95%CI : 1.52-143.1, $p=0.018$). **[Conclusion]** Nine of 70 patients revealed false-positives for LN metastasis by FDG-PET/CT. WBC counts $\geq 9000/\mu\text{L}$ was the significant factor which influence false-positive of LN metastasis by FDG-PET/CT.

ISP-17-5

Elucidate the mechanism of lymphedema from the analysis of lymphatic function and morphology before and after pelvic lymphadenectomy using indocyanine green fluorescence lymphangiography Hirai Mitsuko, Hirayama Takashi, Fujihara Risa, Yoshida Emiko, Fujino Kazunari, Terao Yasuhisa, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] It is said that lymphedema develops in 20-40% of patients after pelvic lymphadenectomy in gynecological surgery. Several risk factors have been shown, but many patients develop lymphedema without them. We therefore presume innate lymphatic function and morphology contribute to the development of lymphedema. In this study, to elucidate the mechanism of lymphedema from the aspect of lymphatic function, we evaluate the changes in the lymphatic vessels before and after surgery using indocyanine green (ICG) fluorescence lymphangiography. **[Methods]** From November 2019, we started the study as a specified clinical trial. We performed ICG fluorescence lymphangiography preoperatively and 1.3.9 months after operation, respectively, to who given consent before pelvic lymphadenectomy. In addition to physical findings, we analyzed systematic changes which can only be assessed by lymphangiography. **[Results]** By the present, we have performed the test on 11 patients including 4 cervical cancer, 6 corpus cancer and 1 fallopian tube cancer. So far, we have obtained the following three new findings. (1) If a patient already has lymphedema preoperatively, there is no improvement after lymphadenectomy; (2) Lymphedema that was present at one month after surgery may improve over time; and (3) Though the lymphangiography pointed out the lymphedema without subjective symptoms, lymphedema may become apparent later. **[Conclusion]** The results of the intermediate analysis to the present show significant findings that innate lymphatic vessel function and morphology may be involved in the development of lymphedema. The final evaluation will be made at the time of 30 cases registered for this study.

ISP-17-6

Our Experience of Preoperative Prediction of Uterine Sarcoma Using Magnetic Resonance Imaging (MRI) for 4.5 Years and Its Limitations on Clinical Use Oka Yasuko, Nakade Kyohei *Komatsu Municipal Hospital*

[Objective] Preoperative prediction of uterine sarcoma is difficult. We previously presented the finding that a tumor with high tumor-to-subcutaneous fat signal intensity ratio on MRI T2 weighted imaging (TFSIR) and low ADC is highly suspected of

sarcoma. This time, we report our experience of preoperative prediction of uterine sarcoma using this method for 4.5 years. **[Methods]** The materials are 144 uterine tumors which performed MRI preoperatively and confirmed the pathological diagnosis in our hospital for recent 4.5 years. Both TFSIR and ADC had calculated for all tumors. The tumors with both positive parameters are predicted as sarcomas. After the operations, the preoperative predictions were matched to the pathological results. The sensitivity, specificity, positive predictive rate and negative predictive rate of this preoperative prediction method were calculated. **[Results]** Among 144 uterine tumors, 7 tumors were predicted as sarcomas and 5 of those tumors were indeed sarcomas. Thus 2 false positive case resulted. The other 137 tumors were predicted as benign tumors and 136 of those tumors were indeed benign tumors. Thus 1 false negative case resulted. The sensitivity of this method is 83%, the specificity is 99%, the positive predictive rate is 71% and the negative predictive rate is 99%. **[Conclusion]** Preoperative prediction of uterine sarcoma is possible using conventional MRI. However, we have to be careful for false positive cases especially in cases which the patient wishes to remain fertile.

ISP-17-7

Palliative chemotherapy (BEP Regime) with good response—Rare malignant steroid cell tumour of the ovaries with lung & liver secondaries in a female patient Weng Kong Aprof Dr Eugene Leong *Taylors University School of Medicine, Sri Kota Specialist Medical Centre, Klinik Pakar Wanita Imperial NewLife-Precious Obstetrics & Gynaecology, Malaysia*

Objective : To discuss about a rare malignant steroid cell tumour of the ovaries FIGO Stage 4 and palliative BEP Regime (Bleomycin, Etoposide & Cisplatin). **Methods :** A 50 year old multiparous lady came for a 2nd. opinion in May 2021. 1st. operated in 2019 - pelvic clearance with disseminated disease (liver & lungs) in another Tertiary Centre. Histopathology confirmed rare malignant steroid cell tumour of the ovaries with elevated serum testosterone. In 2019 - no further treatment was given. May 2021 - She has no pre-morbid illness with good normal functional status. Patient and family counselled fully. Pros and Cons. Leave alone option given. They decided for palliative chemotherapy. Pre-chemotherapy - lung function & cardiac tests done. Cyclical 21 day BEP regime with GCSF support was done eventfully. **Results :** She responded well. Required symptomatic abdominal peritoneal tapping on a few occasions (5 to 7 litres). Oxygen saturation (room air) 97 to 99%. There is no palpable masses, jaundice, stigmata of liver disease, can walk, talk, shop & socialise normally with good bowel & urinary functioning. Serum testosterone 7.9 nmol/L (normal 0.1 to 1.4). Peritoneal tap cytology - malignant cells seen initially to no atypical cells seen now. PET CT scan done. **Conclusion :** Palliative BEP regime in this selected FIGO Stage 4 setting with full counselling with good family support is possible and helpful (28.8.2021 V1). Patient and family is happy. Further tests soon.

ISP-18-1

The presence of an attendant during germline BRCA testing as an important indicator of the patients' psychological status Okamoto Kazuhiro, Nakamura Keiichi, Irie Kyohei, Matsuoka Hirofumi, Ida Naoyuki, Ogawa Chikako, Masuyama Hisashi *Okayama University Hospital*

[Objective] Oncologists are facing an increased demand for germline BRCA (gBRCA) testing following recommendations prescribed by global authorities on ovarian cancer. Research so far has focused on the impact of gBRCA testing on patients' psychological status, and has ignored whether the presence of an attendant during gBRCA impacts patients' psychological status.

This study aims to clarify the association between the presence of attendants and psychological status (distress, anxiety, and depression) of patients with advanced ovarian cancer undergoing gBRCA testing. **[Methods]** We examined the psychological status (distress, anxiety, and depression) of 17 patients with advanced ovarian cancer before and after gBRCA testing using the Quick Inventory of Depressive Symptomatology (QIDS-J) questionnaire. Statistically significant correlations were determined using Student's *t*-test, Mann-Whitney U test, and Pearson's χ^2 test. **[Results]** Patients were more prone to nocturnal insomnia before gBRCA testing than after the test ($p=0.087$). Patients accompanied by attendants were found to feel more sadness than those who were unaccompanied whether before or after gBRCA testing ($p=0.020$ and $p=0.082$). Furthermore, in cases where patients were accompanied by their husbands, they tended to feel deeper sadness than unaccompanied patients both before and after gBRCA testing ($p=0.061$ and $p=0.091$). In addition, before gBRCA testing, unaccompanied patients tended to develop fatigue and require more energy/effort to start or finish their daily activities, than accompanied patients ($p=0.073$). **[Conclusion]** It is preferable to request family members to accompany patients undergoing gBRCA testing, as it helps patients share their thoughts and feelings with their loved ones.

ISP-18-2

A case report of multilocus inherited neoplasia alleles syndrome (MINAS) with simultaneous Lynch syndrome and HBOC Ueda Mako¹, Tsubamoto Hiroshi¹, Takimoto Yumi¹, Ueda Tomoko¹, Inoue Kayo¹, Mimura Shiho², Kamihigashi Mariko¹, Tanaka Hiroyuki¹, Sawai Hideaki¹, Shibahara Hiroaki¹ *Hyogo College of Medicine¹, Kinki Central Hospital²*

[Introduction] Once a patient is diagnosed with a hereditary tumor and the family health care begins, they are often unaware of the possibility of other hereditary tumors. However, simultaneous pathological variants of hereditary oncogenes and develop multiple overlapping hereditary tumors was reported. A 2018 report by Whitworth J et al, who proposed MINAS, reported that up to 3% had MINAS in patients with a history of multiple malignancies. A 22-years-old woman (client) went to see our hospital because her mother had history of colorectal, endometrial, and ovarian cancer with pathological *MSH6* variant. Her father died of pancreatic cancer at the age of 45. The client was diagnosed with Lynch syndrome and regular surveillance for Lynch syndrome has been conducted for 9 years. At her age of 31, her paternal aunt developed breast cancer and a pathological variant of *BRCA2* was diagnosed. Then, the client was found to have the same variant. **[Conclusion]** In the treatment of patients with hereditary tumors, MINAS should be kept in mind. Though MINAS is not associated with severe morbidity, an appropriate surveillance should be planned for the simultaneous hereditary cancer. In addition, the era of routine cancer genomic profiling will increase the incidental finding of MINAS.

ISP-18-3

Assessment of Advanced care planning for recurrent/advanced gynecologic cancer patients with ostomy construction Ohno Ayumi, Nishio Hiroshi, Yokota Megumi, Tanimoto Satoko, Shiina Miki, Tanaka Ikumo, Sugawara Yo, Nakamura Masaru, Tanaka Mamoru, Aoki Daisuke *Keio University*

[Objective] The decision-making-process on end-of-life care such as hospice referral or code status assessment is called as advanced care planning (ACP). The Society of Gynecologic Oncology recommended early PCP for all the patients with recurrent or advanced gynecologic malignancy. They occasionally suffer from malignant bowel obstruction (MBO) and MBO related therapies especially ostomy (colostomy or ileostomy) con-

struction may alter the timing of ACP decisions. We report the prognosis after ostomy construction and their ACP decisions. **[Methods]** All patients treated at our institution for the diagnosis of gynecologic cancer from 2015 to 2021 were reviewed. Among these patients, we selected and reviewed medical records of patients with palliative ostomy construction. **[Results]** A total of 37 cases with palliative ostomy construction were identified, 13 (35%) were cervical cancer, 3 (8%) were endometrial cancer, 21 (57%) were ovarian or primary peritoneal cancer. Percentages of inpatient palliative care unit enrollment were 78% (29/37), which was consistent with previous report. Median time from the ostomy construction to hospital discharge was 23 (8-299) days, and to hospice referral was 79 (24-497) days and to death was 152 (59-608) days. Eight patients (17%) died at our institution and the duration of palliative care unit enrollment of these patients was longer than the patients with hospice referral (mean, 68 vs 151 days). **[Conclusion]** Among ostomy constructed patients, the time from diagnosis to palliative care enrollment was longer for those who descended in hospital than patients with hospice transfer. Early PCP should be considered to ostomy constructed patients.

ISP-18-4

Palliative care for patients with gynecologic cancer Shimomai Wakiko, Komazaki Hiromi, Tanabe Hiroshi, Onishi Junki, Kato Sayako, Tomita Keisuke, Saito Motoaki, Takano Hirokuni, Yamada Kyosuke, Okamoto Aikou *The Jikei University*

[Objective] It is important for patients and physicians to understand the end of life. The aim of this study is to present an overview of palliative care for patients with gynecologic cancer and the last lesion site. **[Methods]** We investigated patients who died of gynecologic cancer (endometrial cancer : EC, cervical cancer : CC, ovarian cancer : OC), and had CT scans within six months to die. Patient background, the last lesion site, and treatment for palliative care were retrospectively reviewed from medical records. **[Results]** A total of 220 cases (EC/CC/OC : 26/79/115) were enrolled. About the last lesion site, there were 96 residual or recurrent of primary sites (EC/CC/OC : 10 (38%) / 49 (62%) / 37 (32%)), 144 peritoneal dissemination (EC/CC/OC : 16 (61%) / 38 (48%) / 90 (78%)), 145 lymph node metastases (EC/CC/OC : 17 (65%) / 55 (69%) / 73 (63%)), 30 pleural dissemination (EC/CC/OC : 1 (3%) / 10 (12%) / 19 (16%)), 124 distant metastasis (EC/CC/OC : 16 (61%) / 43 (54%) / 65 (56%)). About the treatment for palliative care, aspiration of ascites for 53 cases (EC/CC/OC : 5 (19%) / 4 (5%) / 44 (38%)), aspiration of chest fluid for 24 (EC/CC/OC : 1 (3%) / 5 (6%) / 18 (15%)), insertion of nasogastric or intestinal tube for 40 (EC/CC/OC : 3 (11%) / 16 (20%) / 21 (18%)), percutaneous nephrostomy or ureteral stent insertion for 39 (EC/CC/OC : 2 (7%) / 29 (36%) / 8 (6%)), the use of opioid for 181 (EC/CC/OC : 23 (88%) / 66 (83%) / 92 (80%)) were done. **[Conclusion]** A percutaneous nephrostomy or ureteral stent insertion was common in CC, because of frequently residual or recurrent from primary sites. In the case of OC, aspiration of ascites was often done due to peritoneal dissemination. By the primary site, there was characteristic treatment for palliative care associated with the last lesion site.

ISP-18-5

A retrospective study of preoperative imaging findings in 18 cases of struma ovarii pathologically diagnosed after surgery at our hospital Tamura Nami, Murakami Keisuke, Ozaki Rie, Ochiai Asako, Kawasaki Yu, Ikuma Shinichiro, Okada Yukiko, Kitade Mari, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] 95% of Struma ovarii are benign, but is often over-treated because of the difficulty to distinguish from malignancy. In this study, our aim is to evaluate the current situation of the preoperative diagnosis and the chosen surgical procedure, and to improve preoperative diagnostic accuracy by retrospectively reviewing the imaging findings. **[Methods]** We retrospectively reviewed the clinical course and imaging characteristics of 18 cases of struma ovarii operated at our hospital from 2015-2021. **[Results]** The preoperative diagnosis was malignant in six cases, borderline malignant in one case and benign in 11 cases. No case was diagnosed as struma ovarii. Seven cases had a desire for childbearing and four patients who was suspected of borderline or malignant tumor was performed an abdominal salpingo-oophorectomy. In patients without a desire for childbearing, laparoscopic surgery was chosen in only 45% of cases whose preoperative diagnosis was benign. CA125, CA19-9 and CEA were all normal. On MRI, 54% of the cases had enhanced solid components which is characteristic in malignant tumors, but no diffusion restriction was observed in 89% of the cases. 60% of the patients who underwent PET showed increased accumulation. 67% of the cases which CT was taken for systemic search for malignancy, showed a high attenuation lesion cyst reflecting the thyroid tissue. **[Conclusion]** The possibility of struma ovarii should be kept in mind in women of reproductive age whose MRI findings show stained-glass pattern and has low tumor markers. Plain CT might be useful in differentiating them.

ISP-18-6

Laparoscopic Ovarian Cystectomy after Ovarian Transposition : A Case Report Aoyagi Yoko, Kai Kentaro, Nishida Masakazu, Nasu Kaei, Kawano Yasushi *Oita University*

Introduction : Ovarian transposition is used for reproductive-age women with cervical cancer who undergo a radical hysterectomy for the protection of their ovaries from radiation injury. However, ovary sparing can pose a risk of future tumor development. **Case :** A 43-year-old nulligravida Japanese woman was referred to our department for bilateral ovarian tumors incidentally identified at a medical check-up. Her past medical history was significant for abdominal radical hysterectomy and bilateral ovarian transposition at age 30 for stage Ib1 cervical squamous cell carcinoma (FIGO 1994, pT1b1N0M0) ; both ovaries were moved to the retroperitoneal cavity at paracolic gutters with intact vascular pedicles, fixed with silk thread, and marked with clips. Postoperative irradiation was waived because the pathological examination revealed low-risk cervical squamous cell carcinoma. The 5-year follow-up examination and contrast-enhanced CT demonstrated no evidence of disease. At our department, CT and MRI showed bilateral 6-mm-diameter ovarian tumors. Tumor markers for epithelial ovarian cancer were negative. We performed a laparoscopic ovarian cystectomy for a pathological examination and relief of the mass effect. Although anatomical and fibrotic changes caused by the first surgery made it difficult to explore the ovarian tumors in the retroperitoneal space, the clips on the ovarian surface helped us remove the cyst. The postoperative course was uneventful. The pathological diagnosis was serous cystadenoma. **Conclusion :** Ovarian transposition is performed to prevent early menopause in reproductive-age patients. Marking of the ovarian surface with clips is useful for potential subsequent ovarian surgery.

ISP-18-7

Rectosigmoid resection in recurrent cases of ovarian mucinous cystadenoma Matsuoka Ayumu, Tate Shinichi, Otsuka Satoyo, Habu Yuji, Nakamura Natsuko, Nishikimi Kyoko, Usui

Hirokazu, Shozu Makio *Chiba University Hospital*

Introduction : Rectosigmoid resection can contribute complete surgery for recurrent ovarian cancer. Even for recurrent cases of benign ovarian tumors, rectosigmoid resection may be required. **Case 1 :** A 54-year-old woman has a history of total abdominal hysterectomy for leiomyoma at age 40 years and left salpingo-oophorectomy for mucinous cystadenoma adhered to the pelvis at age 53 years. She was referred to our institution with recurrence tumor and abdominal fullness. Recurrent tumor removal including lower anterior resection of rectum was performed. **Case 2 :** A 56-year-old woman with a history of myomectomy at age 37 years. She was referred to our institution with ovarian mucinous cystadenoma at age 55 years. She was performed total abdominal hysterectomy and bilateral salpingo-oophorectomy due to adhesions. Six months later, a cystic tumor perforating from the vaginal stump was found in the pelvis. Recurrent tumor removal including Hartmann's procedure was performed. **Case 3 :** A 61-year-old has a history of total abdominal hysterectomy for leiomyoma at age 40 years. Left salpingo-oophorectomy for ovarian mucinous cystadenoma was performed at age 58 years. Twenty-five months later, laparotomy was performed for the recurrent tumor in the pelvis, but the tumor could not be removed due to adhesions. She was referred to our institution with recurrence of ovarian mucinous cystadenoma and tumor removal including Hartmann's procedure was performed. None of these cases had relapsed 17 months, 4 months, or 2 months after surgery, respectively. **Conclusion :** Rectosigmoid resection may be necessary to complete removal in recurrent cases with mucinous cystadenoma adhered to the pelvis.

ISP-18-8

Successful complete resection of growing teratoma syndrome in the anterior abdominal wall in combination with repair using tensor fasciae latae flap Iwai Miho¹, Yoriki Kaori¹, Aoyama Kouhei¹, Tarumi Yosuke¹, Kataoka Hisashi¹, Kokabu Tetsuya¹, Numajiri Toshiaki², Mori Taisuke¹ *University Hospital, Kyoto Prefectural University of Medicine¹, Department of Plastic and Reconstructive Surgery, University Hospital, Kyoto Prefectural University of Medicine²*

Introduction Growing teratoma syndrome (GTS) is the progression of mature teratoma during systemic chemotherapy for germ cell tumors. We report a case of successful treatment of GTS in the anterior abdominal wall in combination with repair using a myocutaneous flap. **Case** A 23-year-old woman presented to the emergency department with right lower abdominal pain. Ultrasonography and computed tomography revealed a right 9cm ovarian mass that was suspected to be mature teratoma with torsion. She underwent emergency laparoscopic-assisted ovarian cystectomy. Histopathological findings revealed immature teratoma Grade I. Postoperative α -fetoprotein (AFP) increased, and the mass in the anterior abdominal wall was observed. She underwent laparoscopic right salpingo-oophorectomy, excision of multiple peritoneal nodules, and biopsy of abdominal wall mass. All of these were diagnosed as metastatic immature teratoma. Three courses of chemotherapy (bleomycin-etoposide-cisplatin) were administered. Although post-chemotherapy AFP normalized, the residual tumor in the abdominal wall grew to 8.7 cm. Complete removal of the chemotherapy-resistant disease was necessary. The residual tumor including both rectus abdominis muscles was excised, and the anterior abdominal wall was repaired using a right tensor fasciae latae musculocutaneous flap. Histopathologically, the residual tumors were identified as mature teratoma with, no immature elements, resulting in GTS. Follow-up after eight months since the last surgery revealed that the patient was disease free. **Conclusion** The presence of residual disease at initial

surgery is the risk factor for GTS. Repair using a myocutaneous flap contributed to complete removal of GTS in the abdominal wall, which might result in preserving fertility.

ISP-18-9

Checkpoint-Inhibition in Gynecological Cancer : Hope or Hype? Pietzner Klaus Charité-Universitätsmedizin Berlin, Germany

The rise of checkpoint-inhibitors revolutionized immunology in the past decade. The evolution of three generations of agents, from anti-CTLA4, to anti-PD1, to anti-PD-L1-inhibitors translated into unheard-of efficacy in the clinical setting. Prior to this development cancer entities like malignant melanoma or non-small-cell-lung-cancer did not benefit from classic cytotoxic chemotherapy. The fact that these clinically challenging cancer types responded to this novel immunotherapy, created a huge hype for checkpoint-inhibition. The hope was, that this success could be transferred to gynecological malignancies. However, the first results in front-line ovarian cancer could not live up to the hype, with two large negative front-line studies. The remaining hope for immunotherapy in ovarian cancer now lies on the recurrent setting. Here, the MEDIOLA trial showed very promising results for a very innovative chemotherapy-free combination of PARP- and checkpoint-inhibitors. In a BRCA-positive cohort, this combination achieved response rates that were reminiscent of the sensational effect of checkpoint-inhibition in other cancer entities. These results encourage the selection of patients with damaged DNA-repair such as BRCA-mutation for the treatment with immuno-therapeutic agents. The hypothesis behind this thought being, that these patients will have a higher mutational burden and will produce more neo-antigens, therefore boosting the efficacy of any t-cell based immunotherapy. The same school of thought was behind the design of the GARNET trial, that investigated the use of dostarlimab, an anti-PD1-inhibitor in mismatch-repair (MMR) deficient endometrial cancer. Dostarlimab monotherapy was able to achieve a respectable overall response rate of 42.3% in this population. A combination of Pembrolizumab and Lenvatinib was able to demonstrate a comparable efficacy independent of MMR status in a similar population in the KEYNOTE-775 study. Both studies led to approvals in Europe and resulted in the availability of multiple immune-therapeutic options for patients with endometrial cancer. The latest break-through for checkpoint-inhibition was demonstrated in front-line cervical cancer, where the results of the KEYNOTE-826 trial showed an overall survival benefit of 7.9 months for a combination with pembrolizumab. **Conclusion** : While checkpoint-inhibition seems to be ineffective in front-line ovarian cancer, there might still be a chance in recurrent disease, with the selection of more immunogenic patients. In the meantime immunotherapy has secured itself a fixed place in the management of endometrial cancer and is about to change the therapeutic landscape in cervical cancer.

ISP-19-1

Establishment of a novel mouse model of adenomyosis using mechanical induction Mohammed Elsherbini Elshal, Koga Kaori, Maki Eiko, Hiraoka Takehiro, Satake Erina, Izumi Gentaro, Hirata Tetsuya, Harada Miyuki, Hirota Yasushi, Hiraike Osamu, Osuga Yutaka The University of Tokyo Hospital

[Objective] The purpose of this study was to establish a novel mouse model of adenomyosis. **[Methods]** The uterine horns of mice were exposed, and the uterine wall was punctured using a 30G needle at a frequency of 100 punctures/1cm. Mice were sacrificed on day14 (D14) or day65 (D65) (n=3). The uterus was stained, lesions were detected and counted, and their volumes

were measured. Cell proliferation and fibrosis were assessed by Ki67 and Masson's Trichrome staining, and blood vessels were detected by CD31 immunostaining. Four mice were mated and sacrificed on postpartum day3. **[Results]** The number of lesions was not different between D14 and D65. The overall volume of the lesion was larger in D65 than in D14 (D14 : 34.5 ± 6.1, D65 : 231.5 ± 64.6 mm³/lesion, mean ± SEM, p < 0.0001). The volume of the stroma was larger in D65 (D14 : 15.8 ± 2.9, D65 : 131.0 ± 37.9, p < 0.0001). The proportion of Ki67 positive cells in epithelia was higher in D14 (D14 : 15.3 ± 5.0%, D65 : 2.6 ± 1.3, p < 0.05), while those in stroma was higher in D65 (D14 : 0.5 ± 0.4%, D65 : 6.3 ± 1.6%, p < 0.01). The area of fibrosis in the stroma was higher in D65 (D14 : 0.007 ± 0.004, D65 : 5.1 ± 1.01, p < 0.01). Blood-vessel density in lesions was higher in D65 (D14 : 0.06 ± 0.01%, D65 : 0.1 ± 0.01%, p < 0.05). The number of lesions was equivalent between the non-pregnant and the pregnant group. **[Conclusion]** The mouse model of adenomyosis established in this study showed similar progression to human lesions and continued after pregnancy. This model can be applied to evaluate the pathogenesis of this disease and the mechanism by which adenomyosis affects perinatal outcome.

ISP-19-2

Unkeito, a Traditional Japanese Kampo Medicine, Improves Follicular Development by Upregulating FSH Receptor Expression Yoshita Sayako¹, Osuka Satoko¹, Sonehara Reina¹, Miyake Natsuki¹, Murakami Mayuko¹, Muraoka Ayako¹, Nakanishi Natsuki¹, Nakamura Tomoko¹, Goto Maki¹, Kajiyama Hiroaki¹, Shimizu Tomofumi², Matsumoto Chinami² Nagoya University¹, Kampo Research Group 3, Tsumura Kampo Research Laboratories, Tsumura & Co.²

[Objective] Unkeito, a traditional medicine composed of 12 crude drugs, has been used to treat menstrual disorders and infertility in Asian countries ; however, the underlying mechanism is unclear. Thus, we investigated the effect of Unkeito administration on ovarian follicle development and steroidogenesis using polycystic ovary syndrome (PCOS) model rats with cycle disorder and rat granulosa cells (GCs). **[Methods]** Prenatal dihydrotestosterone-treated Wistar rat PCOS models were generated. Model rats were fed a normal (control) or 3% Unkeito (UKT) diet. Hormonal profiles and ovarian samples were evaluated. Primary GC cultures of normal or model rats were treated with human chorionic gonadotropin (mimicking high luteinizing hormone status), follicle stimulating hormone (FSH), and Unkeito. Progesterone levels were evaluated in the supernatant ; expression of FSH receptor (Fshr), bone morphogenetic protein (Bmp), and genes encoding steroid hormone synthase was quantified. **[Results]** Number of preovulatory follicles ; *Fshr*, *Bmp2*, and *Bmp6* mRNA expression in ovaries ; and *Fshr* protein levels significantly increased. Serum progesterone levels were higher in the UKT group than the control group. Treating model rat GCs with Unkeito significantly increased expression of *Fshr*, *Bmp2*, and *Bmp6* mRNA and *Fshr* protein levels. Treating normal GCs with Unkeito significantly increased *Fshr*, *Star*, and *Cyp11a1* expression and progesterone concentration in the supernatant. **[Conclusion]** Higher *Fshr* expression in GCs treated with Unkeito increased the number of preovulatory follicles in Unkeito-fed, PCOS model rats. Unkeito treatment increased the expression of *Star*, *Cyp11a1*, and *Bmp* in GCs. These findings may explain the effect of Unkeito administration on ovarian follicle development and steroidogenesis.

ISP-19-3

Temporal relationship between alterations in the gut microbiome and the development of polycystic ovary syndrome-like phenotypes in prenatally androgenized female mice

Kusamoto Akari, Harada Miyuki, Kunitomi Chisato, Koike Hiroshi, Tanaka Tsurugi, Kaku Tetsuaki, Hiraike Osamu, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] It has been recently recognized that prenatal androgen exposure is involved in the development of polycystic ovary syndrome (PCOS) in adulthood. In addition, the gut microbiome in adult patients and rodents with PCOS differs from that of healthy individuals. Thus, we wondered whether prenatal androgen exposure induces gut microbial dysbiosis early in life and is associated with the development of PCOS in later life. To test this hypothesis, we studied temporal changes in PCOS phenotypes and gut microbiome using prenatally androgenized (PNA) mouse model. **[Methods]** The PCOS phenotype and gut microbiome of control or PNA female offspring were examined from 4 to 16 weeks of age. The PCOS-like reproductive phenotype was identified by estrous cyclicity, ovarian histology, and serum testosterone levels; and the metabolic phenotype was determined by body weight, the size of visceral adipocytes, insulin tolerance testing, and fasting blood glucose levels. **[Results]** PNA offspring showed a reproductive phenotype from 6 weeks and a metabolic phenotype from 12 weeks. The α -diversity of gut microbiome of the PNA group was higher at 8 weeks and lower at 12 and 16 weeks, and the β -diversity differed from controls at 8 weeks. However, a significant difference in the composition of gut microbiota between the PNA and control groups was already apparent at 4 weeks. **[Conclusion]** Abnormalities in the gut microbiome appear as early as or even before PCOS-like phenotypes develop in PNA mice. Thus, the gut microbiome in early life is a potential target for the prevention of PCOS in later life.

ISP-19-4

Activated Treg cells are suppressed in the endometrium of women with endometriosis Fujii Maya, Tanaka Yukiko, Okimura Hiroyuki, Sugahara Takuya, Maeda Eiko, Kataoka Hisashi, Ito Fumitake, Koshiha Akemi, N Khan Khaleque, Kusuki Izumi, Mori Taisuke, Kitawaki Jo *Kyoto Prefectural University of Medicine*

[Objective] We previously demonstrated that an enhanced inflammatory response caused by reduced activated Treg cells (aTregs), the pure suppressive type, could be involved in the progression of endometriosis. This study aimed to understand how different Treg subpopulations fluctuate in tandem with the menstrual cycle in women with and without endometriosis. **[Methods]** We enrolled 72 Japanese women (20-45 years), having regular menstruation, with (N=39) and without (N=33) endometriosis. Peripheral blood (PB), peritoneal fluid (PF), normal endometrium (NE), eutopic endometrium with endometriosis (EE), and ovarian endometrioma (OE) were sampled from patients who underwent surgery. Treg cell fractions in human CD4⁺ cells were examined by flow cytometry. **[Results]** The main outcome measure was local differences in Treg distribution between women with and those without endometriosis during the menstrual cycle. The proportion of aTregs during the ovulatory phase was higher in the NE than in the EE ($P < 0.05$). In the OE, the aTregs proportion was higher during the proliferative phase than during the secretory phase ($P < 0.05$). The expression of chemokines (CCL2/CCL17/CCL22) was higher in the OE than in the endometrium ($P < 0.01/0.05/0.05$). CCL2 expression was higher in the secretory phase ($P < 0.05$) and CCL17 ($P < 0.01$) and CCL22 ($P < 0.01$) expression was higher in the ovulatory phase than in the other phases. **[Conclusion]** Patients with endometriosis have disturbances in the immune system during each phase of the menstrual cycle. These disturbances may be involved in endometriosis pathophysiology.

ISP-19-5

Molecular background of retinoic acid receptor expression in the endometriotic cells Azuma Yukihiko, Taniguchi Fuminori, Nagata Hiroki, Wada Ikumi, Nakaso Takaya, Ikebuchi Ai, Moriyama Maako, Yamane Emiko, Sato Eri, Harada Tasuku *Totomi University*

[Objective] As a first step assessing the role of retinoic acids in the endometriotic lesions, we challenged to demonstrate retinoic acid receptor (RAR) gene expression in the human endometriotic cells. **[Methods]** Stromal cells were prepared from the endometriotic tissues (n=7). RAR gene expression was evaluated using RT-PCR. Primer sets for RARs were prepared using cDNA and genomic sequences in UCSF genome browser. To test RAR function, cell proliferations were evaluated in the presence of all-trans retinoic acid (ATRA) and selective RAR modulators (SRARMs). **[Results]** **Demonstration of multiple RARs in endometriotic cells** 1) Expression of a wild-type and a splice variant RAR α mRNAs were demonstrated. The variant predicted a truncated molecule without DNA binding domain. 2) Expression of a wild-type and a splice variant RAR β mRNAs were demonstrated. The variant predicted a truncated molecule without transactivation domain at the N-terminal. 3) Expression of a wild-type and a splice variant RAR γ mRNAs were demonstrated. The variant predicted a molecule with distinct transactivation domain at the N-terminal. **Effect of ATRA and SRARMs on cell proliferation** 1) The cell proliferation rate was decreased and Ki-67 expression was downregulated in the presence of ATRA. 2) Among SRARMs tested, a selective RAR γ modulator tended to decrease the cell proliferation. **[Conclusion]** We demonstrated the molecular background of RAR expression in the endometriotic cells for the first time. The finding suggested multiple function of RARs in the endometriotic lesions.

ISP-19-6

A low-nutrient environment may promote endometriosis through the peroxisome proliferator-activated receptor-gamma coactivator 1-alpha mediated pathway Shimura Koki, Kataoka Hisashi, Fujii Maya, Ogawa Kanae, Tarumi Yosuke, Okimura Hiroyuki, Takaoka Osamu, Koshiha Akemi, Khan Khaleque, Kusuki Izumi, Mori Taisuke *Kyoto Prefectural University of Medicine*

[Objective] The development of endometriosis is regulated by the microenvironment. Low-nutrient status, one of the microenvironments, is known to be involved in the pathogenesis of cancer, however, its significance in endometriosis is obscure. Here, we investigated the effect of a low-nutrient microenvironment on endometriosis. **[Methods]** Stromal cells (SCs) from ovarian endometrioma (OESCs) or normal endometrium without endometriosis (NESCs) were isolated and cultured. OESCs and NESCs proliferation under the low-nutrient condition was measured. Expression of exacerbating factors in endometriosis under the low-nutrient condition was examined at the mRNA and protein levels. **[Results]** OESCs showed higher proliferation than NESCs under the low-nutrient condition ($P < 0.05$). Furthermore, in OESCs, the low-nutrient conditions upregulated mRNA expression of vascular endothelial growth factor (VEGF), interleukin-6 and -8, aromatase, BCL2, and peroxisome proliferator-activated receptor-gamma coactivator-1 α (PGC-1 α) ($P < 0.05$ versus control for each) and downregulated that of BAX ($P < 0.05$ versus control) and induced transcription of the aromatase promoters P13 and P11 and exon II. Western blotting revealed elevated VEGF and PGC-1 α expression under the low-nutrient condition in OESCs. All changes in response to the nutrient deprivation coincided with the elevated expression of PGC-1 α , which was reduced at the mRNA level upon rescue of

the nutrient status ($P < 0.05$ versus pre-rescue). **[Conclusion]** The low-nutrient microenvironment exacerbated endometriosis by promoting cell proliferation, angiogenesis, inflammation, anti-apoptosis, and local estrogen production, which could potentially be attributed to PGC-1 α -mediated metabolic mechanisms.

ISP-19-7

Low-frequency electroacupuncture at bilateral Guilai (ST 29) and Sanyinjiao (SP 9) activates sympathetic nerves in brown adipose tissue in polycystic ovary syndrome-like rats Gao Hongru, Tong Xiaoyu, Hu Wei, Wang Yicong, Li Kunyu, Xu Xiaoqing, Shi Jiemei, Pei Zhenle, Lu Wenhan, Chen Yuning, Zhang Ruonan, Feng Yi *Department of Integrative Medicine and Neurobiology, School of Basic Medical Sciences, Fudan University, China*

[Objective] Low-frequency electroacupuncture (EA) has been shown to ameliorate obesity and reproductive dysfunctions in patients with polycystic ovary syndrome (PCOS), and further explorations in PCOS-like rats showed that EA could affect white adipose tissue (WAT). However, the function and neuro-modulation of brown adipose tissue (BAT) in PCOS and after EA treatment have remained unknown. **[Methods]** The present study focused on the role of BAT in PCOS-like rats and its relationship with EA, and it characterized the three-dimensional (3D) innervation of BAT associated with activation molecules. **[Results]** First, dihydrotestosterone-induced PCOS-like rats showed both obvious weight gain and reproductive dysfunction, similar to what is seen in high-fat diet-induced obesity rats except for the absence of reproductive dysfunction. We found that the body weight gain was mainly caused by an increase in WAT, but surprisingly we also observed the an abnormal decrease in BAT. Because both the lipid metabolism and reproductive disorders could be improved with bilateral EA at "Guilai" (ST 29) and "Sanyinjiao" (SP 9), especially the restoration of BAT, we further investigated the neuromodulation and in BAT and identified the sympathetic marker tyrosine hydroxylase as one of the key factors of sympathetic nerves. We used tissue clearing and 3D high-resolution imaging technology to show that crooked or dispersed sympathetic nerves, were reconstructed and associated with the activation of BAT and are likely to be the functional target for EA treatment. **[Conclusion]** Taken together, the results of our study highlight the significant role of BAT and its sympathetic innervations in PCOS and in EA therapy.

ISP-19-8

Endoplasmic reticulum stress-induced Notch signaling disturbs cumulus-oocyte complex expansion in PCOS Koike Hiroshi, Harada Miyuki, Kunitomi Chisato, Kusamoto Akari, Tanaka Tsurugi, Urata Yoko, Hirota Yasushi, Hiraike Osamu, Koga Kaori, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] Recent studies suggest that Notch signaling pathway plays an important role in various ovarian physiology and pathology. PCOS presents many symptoms including ovarian dysfunction which is caused by local factors in follicular microenvironment, including endoplasmic reticulum (ER) stress. In the present study, we investigate the association between Notch signaling and ER stress in the pathophysiology of PCOS. **[Methods]** The expression of Notch signaling in the ovary of PCOS patients was examined by immunohistochemistry and quantitative RT-PCR (qPCR). To evaluate the contribution of ER stress to Notch signaling, primary cultured human granulosa cells (GCs) were treated with an ER stress inducer, inhibitor or siRNA, and were assayed by qPCR and Western blotting. Involvement of ER stress and Notch signaling on cumulus-oocyte complex (COC) expansion was examined in cultured murine

COCs. **[Results]** The expression of Notch2 and Hey2, a transcription factor activated by Notch 2 signaling, were up-regulated in GCs from PCOS patients. In cultured human GCs, Notch signaling was induced by tunicamycin (an ER stress inducer) treatment and was inhibited by TUDCA (an ER stress inhibitor) or knockdown of ATF4 (a transcription factor induced by ER stress). In cultured murine COCs, COC expansion was hyper-activated by tunicamycin treatment and was inhibited by DAPT (a Notch signaling inhibitor). **[Conclusion]** This study revealed that ER stress-induced Notch signaling disturbs COC expansion and Notch signaling inhibition improved this disturbance, indicating that ER stress-induced Notch signaling contributes to ovulatory dysfunction in PCOS pathophysiology.

ISP-19-9

Comparison of the effect of combined oral contraceptive pills and medroxyprogesterone acetate on the recovery of ovulation in women with polycystic ovary syndrome Ju Yi Young¹, Han Soo Jin^{1,2}, Kim Hoon^{1,2}, Kim Sung Woo^{1,2}, Ku Seung Yup^{1,2}, Suh Chang Suk^{1,2} *Seoul National University Hospital, Korea¹, Seoul National University College of Medicine, Korea²*

[Objective] Both oral contraceptive pills (OCPs) and cyclic medroxyprogesterone acetate (MPA) are effectively used for the regulation of menstrual abnormalities in women with anovulatory polycystic ovary syndrome (PCOS). However, data comparing the effects of the two medications on the recovery of ovulation after treatment are few. We aimed to evaluate the chance of ovulation recovery after treatment with the two medications in women with anovulatory PCOS. **[Methods]** A retrospective study was conducted in anovulatory PCOS patients who were treated with OCPs or cyclic MPA from January 2016 to March 2019. After the initial treatment for 2-6 months, ovulation was determined using serum progesterone and/or basal body temperature. **[Results]** Of a total of 256 women with anovulatory PCOS, 128 women used OCPs and the other 128 women used cyclic MPA for 2-6 months. Recovery of ovulation was revealed in 18.0% of women (n=23) after MPA treatment and 21.9% (n=28) after OCPs treatment. The adjusted odds ratio of recovery of ovulation in MPA users was 1.02 (95% CI, 0.92-1.13) after inverse-probability-weighted analysis-covariate balancing propensity score. **[Conclusion]** Women with anovulatory PCOS experienced a comparable chance of ovulation recovery after treatment with OCPs and MPA. Treatment with cyclic MPA for patients with contraindications to OCPs may achieve a similar effect on ovulation recovery.

ISP-20-1

Differential gene expression in decidualized human endometrial stromal cells induced by different stimulations Tanaka Yumiko, Tamura Isao, Fujimura Taishi, Shirafuta Yuichiro, Mihara Yumiko, Maekawa Ryo, Taketani Toshiaki, Tamura Hiroshi, Sugino Norihiro *Yamaguchi University Hospital*

[Objective] In the study for decidualization of endometrial stromal cells (ESCs) in the human endometrium, decidualization of can be induced by several biochemical stimuli in vitro, such as cAMP and medroxy-progesterone acetate (MPA). However, little information is available about whether decidualized cells induced by different stimuli are identical, and if different, how different they are. In this study, we investigated gene expression profiles among the decidualized ESCs induced by different stimuli. Furthermore, we searched which stimulus induces biological changes that are characteristics of decidualization in vivo. **[Methods]** ESCs were cultured under four types of stimulation protocols: cAMP, MPA, cAMP+MPA, and estradiol+MPA (E+MPA). Gene expression profiles were analyzed by RNA-

sequence. Differentially expressed genes (DEGs) compared to the control were extracted in each group, and similar and different cellular functions among the four groups were examined by Gene-ontology and IPA analysis. **[Results]** Any stimulations altered the expression of thousands of genes. Common altered cellular functions were associated with cellular morphology, metabolisms and proliferation. cAMP-used stimulation (cAMP and cAMP+MPA) showed quite different transcriptome profiles from stimulations without-cAMP (MPA and E+MPA), which were associated with angiogenesis, inflammation, immune system, and embryo implantation whereas they were not altered by stimulations without-cAMP. On the other hand, MPA-used stimulation (MPA and E+MPA) activated insulin signaling whereas cAMP-stimulation did not. By utilizing the published single-cell RNA-sequence data of human endometrium, our results suggested that cAMP+MPA-induced decidualization was the closest to the in vivo decidualization. **[Conclusion]** There is much difference in cellular profiles among decidualized cells induced by different decidualization stimuli.

ISP-20-2

Inflammatory cytokines activate HIF-1 α and epithelial-mesenchymal transition-inducing factors in immortalized endometrial glandular cells Hashimoto Yoshiko, Tsubokura Hiroaki, Nakao Tomoko, Murata Hiromi, Okada Hidetaka *Kansai Medical University*

[Objective] The endometrium is a tissue that undergoes repeated proliferation and shedding throughout the menstrual cycle. The partial pressure of oxygen in the endometrium is highly variable, thus mandating the investigation of the involvement of hypoxia-inducible factors (HIFs) in endometrial tissue. On the other hand, there are various phenomena that cannot be explained by the classical dogma that "HIF activation=hypoxia," and one of the key words is inflammation. The purpose of this study is to demonstrate the interrelationship between intrauterine oxygenation, HIF, and inflammation, and to analyze their effects on the differentiation and function of endometrial cells. **[Methods]** Immortalized endometrial glandular cell line EM-E6/E7/TERT was used for the experiments. Western blot analysis was performed to examine the effects of inflammatory cytokines and hypoxia on HIF activation. Additionally, we assessed genome-wide gene-expression patterns via RNA-Seq to determine the effects of inflammatory cytokines and hypoxia. **[Results]** Treatment with inflammatory cytokines induced HIF-1 α protein accumulation and hypoxia increased HIF-1 α and HIF-2 α protein accumulation in EM-E6/E7/TERT cells. RNA-Seq showed that administration of inflammatory cytokines and hypoxia increased expression of epithelial-mesenchymal transition-inducing factors. **[Conclusion]** Epithelial-mesenchymal transition is thought to play an important role during implantation. It has also been observed that HIF induces epithelial-mesenchymal transition-inducing factors in other cells. In this study, we found that HIF and epithelial-mesenchymal transition-inducing factors were induced by inflammatory cytokines and hypoxia in EM-E6/E7/TERT cells. This result suggests that HIF and epithelial-mesenchymal transition-inducing factors induced by chronic endometritis may affect implantation function.

ISP-20-3

Uterine epithelial LIF receptors are critical to implantation chamber formation and blastocyst attachment Fukui Yamato, Hirota Yasushi, Hiraoka Takehiro, Kaku Tetsuaki, Ishizawa Chihiro, Iida Rei, Hirata Tomoyuki, Akaeda Shun, Matsu Mitsunori, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] The formation of an implantation chamber com-

posed of a uterine crypt, an implantation-competent blastocyst, and uterine glands is a critical step in mouse blastocyst implantation. Leukemia inhibitory factor (LIF) activates signal transducer and activator of transcription 3 (STAT3) via uterine LIF receptors (LIFRs), permitting successful blastocyst implantation. Recently, we revealed that both epithelial and stromal STAT3 are essential for blastocyst attachment although they have different roles. However, the roles of epithelial and stromal LIFR in blastocyst implantation remain unclear. This study aimed to clarify their roles. **[Methods]** Mice with deletion of LIFR in the epithelium (EKO mice) and in the strom (SKO mice) were generated by crossing LIFR-floxed mice with LTF-Cre and AMHR2-Cre mice, respectively. Reproductive phenotypes of EKO and SKO mice were evaluated. **[Results]** Fertility and blastocyst implantation in SKO mice were normal despite stromal STAT3 inactivation. In contrast, EKO mice had blastocyst attachment failure and failed to form the implantation chambers with epithelial inactivation of STAT3. In addition, normal responsiveness to ovarian hormones was observed in the peri-implantation uteri of the EKO mice. **[Conclusion]** These findings indicate that the epithelial LIFR-STAT3 pathway initiates the formation of implantation chambers, leading to complete blastocyst attachment, and that stromal STAT3, but not stromal LIFR, controls blastocyst attachment. Since LIFR is expressed in the luminal epithelium of the human endometrium in the secretory phase and the endometrial expression of LIFR is decreased in infertile women, endometrial LIFR may also play a role in human fertility.

ISP-20-4

Analysis of the effect of preceding endometrial decidualization on endometrial regeneration and decidualization in the next cycle Murakami Keisuke, Ochiai Asako, Kitade Mari, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] It is well known that endometrial decidualization is important for the acquisition of embryo receptivity, but its effect on endometrial regeneration in the next cycle is not clarified yet. In this study, we analyzed the effect of endometrial decidualization on subsequent cycle of endometrial regeneration and decidualization. **[Methods]** Endometrial biopsies were obtained with consent from 13 women of reproductive age who underwent laparoscopic ovarian cystectomy at our hospital. Endometrial stromal cell cultures were treated with or without decidualization stimulation (0.5mM 8-bromoadenosine cAMP and 1 μ M medroxyprogesterone acetate), and cloning efficiency, re-decidualization ability after passaging, the effect for cloning efficiency of neighboring cells in co-culture were compared between group D (decidualized cultures) and group U (undecidualized cultures). **[Results]** The cloning efficiency was significantly higher in group D (D, 0.8 (0.2-2.5) ; U, 0.1 (0-1.4) ; $p=0.005$). There was no significant difference in the expression of decidualization markers (PRL and 11 β HSD1) between the groups during the process of re-decidualization after passaging. Analysis of paracrine effect by co-culture of group D and U showed that the cloning efficiency of group D seeded on dish was significantly higher when co-cultured with group D (insert : D, 1.4 (0.5-4.2) ; U, 0.8 (0.2-3.4) ; Medium, 0.5 (0.1-1.0), $p=0.002$). The cloning efficiency of group U was significantly higher when co-cultured with group D (insert : D, 1.1 (0.4-2.9) ; U, 0.4 (0.3-2.1) ; Medium, 0.2 (0.1-0.9), $p=0.001$). **[Conclusion]** Endometrial decidualization should promote endometrial regeneration in the next cycle by enhancing cells' own clonogenicity and paracrine effect on neighboring cells.

ISP-20-5

Investigation of inflammatory signaling pathways in decidualized human endometrial stromal cells Ichikawa Go¹, Negishi Yasuyuki^{1,2}, Takizawa Ayako¹, Yamada Mayu¹, Harigane Eika¹, Watanabe Asako¹, Tsunoda Youhei¹, Shinmura Hiroki¹, Kurashina Ryuhei¹, Ichikawa Tomoko¹, Matsushima Takashi¹, Suzuki Shunji¹ *Nippon Medical School¹, Department of Microbiology and Immunology, Nippon Medical School²*

[Objective] Appropriate inflammation is necessary for implantation and invasion of trophoblastic tissue in the mother during early pregnancy. Interleukin (IL) -1 β and IL-18 are representative proinflammatory cytokines produced by inflammasomes. Nevertheless, the mechanisms involving the expression of IL-1 β and IL-18 that are recruited in the process of implantation remain unclear. **[Methods]** Decidualization of the human endometrial stromal cells (HESCs) was induced by the addition of cAMP and progesterone on days 1, 3, 5, and 7 in vitro. The mRNA levels of IL-1 β , IL-18, ACS, caspase-1, and the NLRP3 inflammasome were measured in LPS-stimulated d-HESCs by real-time polymerase chain reaction. **[Results]** IL-1 β mRNA was enhanced in the early phase (1 h) after LPS addition. Contrarily, IL-18 mRNA was increased in the late phase (24 h) after LPS addition. There were no time dependencies for ASC and caspase-1 mRNA expression; however, NLRP3 mRNA was enhanced in the middle phase (2-4 h) following LPS treatment. **[Conclusion]** We found a difference in the expression peaks between IL-1 β and IL-18 mRNA levels. These results might indicate differential roles of IL-1 β and IL-18 in the decidua during early pregnancy.

ISP-20-6

Physiological microvascular blood flow profile of the endometrium during menstrual cycle described using superb-microvascular imaging Mitao Hiroshi, Yoshizato Toshiyuki, Fukagawa Mayumi, Fujita Tomoyuki, Horinouchi Takashi, Ushijima Kimio *Kurume University Hospital*

[Objective] To describe the physiological changes of endometrial blood flow on the menstrual cycle using superb microvascular imaging (SMI). **[Methods]** The subjects were 16 women (median, 32.5 years old) having regular menstrual cycles, cared for at our clinic between 2020 and 2021. The uterus was delineated at the sagittal section using transvaginal ultrasonography, incorporated with SMI. The day of ovulation was estimated by ultrasonography and/or urinary LH. For each subject, observations were performed within one day of ovulation (OV) and at 5-7 days after ovulation (Day 5-7), covering a total of 40 cycles. The images were recorded, and still images during the systolic phase were retrieved. Endometrial blood flow was evaluated by the depth and density of vascular signals. Depth was categorized as follows: signals only on the basal layer of the endometrium (grade I), reaching up to half the endometrium (II), and covering the whole endometrium (III). Density was determined by the number of vascular signals per 1cm. **[Results]** There was good agreement about vascular depth grading between the two examiners (kappa index, 0.616). The reproducibility of parameters in different cycles was analyzed in 5 cases. In all cycles, vascular depth was found to decrease, from OV to Day 5-7. No differences were noted, however, in vascular density between periods. There was a correlation between vascular depth grading and endometrial thickness. **[Conclusion]** Microvascular endometrial flow was related to endometrial thickness and decreased from the ovulatory to the implantation phase, possibly reflecting the localized hormonal circumstances of endometrial tissues, from ovulation to implantation.

ISP-20-7

Prostacyclin synthase is expressed in the pregnant endometrium under the control of miRNAs Ichikawa Ryoko, Yoshizawa Hikari, Owaki Akiko, Miyamura Hironori, Nomura Hiroyuki, Nishio Eiji, Nishizawa Haruki, Fujii Takuma *Fujita Health University*

[Background] Prostacyclin synthase (PTGIS) is an enzyme that uses PGH₂ as a substrate to produce PGI₂; a prostaglandin with vasodilatory and platelet aggregation inhibitory properties. We reported elevated highly expression of miRNAs (miR-508-5p, -4450, -765) in non-pregnant endometrium compared with pregnant one, and elevated mRNA expression of their target, PTGIS, in pregnant endometrium. **[Objective]** To compare the expression of PTGIS in pregnant and non-pregnant endometrial tissues using immunohistochemistry. **[Methods]** Patients who underwent endometrial curettage or hysterectomy for treatment, 18 pregnancies (miscarriages, ectopic pregnancies), and 14 non-pregnant women (uterine fibroids, endometrial polyps, etc.) were included in the study. Patient consents were obtained in writing. Endometrial tissues were examined by immunohistochemistry for PTGIS, and the localization and expression of PTGIS were compared in pregnant and non-pregnant women. The staining level for PTGIS in endometrium was evaluated by scoring the epithelium and stroma separately from 0 to 3+. **[Results]** In non-pregnant endometrial tissue, the median PTGIS immunohistochemistry staining score was 0 for epithelium and 1+ for stroma, while in pregnant endometrial tissue, the median PTGIS immunohistochemistry staining score was 1+ for epithelium and 2+ for stroma. A two-tailed Mann-Whitney U test comparing the PTGIS staining scores of the two groups showed that the staining scores in the endometrial stroma were significantly higher in the pregnant group than in the non-pregnant group. (p < 0.05). **[Conclusion]** Immunohistochemical study showed that PTGIS was significantly expressed in the endometrial stroma of pregnant patients compared with non-pregnant patients.

ISP-21-1

Effects of the estrogen milieu on hypothalamic oxytocin gene expression and serum oxytocin levels in female rats Kamada Shuhei, Minato Saki, Yanagihara Rie, Taniguchi Yuka, Kawakita Takako, Yamamoto Yuri, Yoshida Kanako, Kato Takeshi, Irahara Minoru, Iwasa Takeshi *Tokushima University*

[Objective] Oxytocin (OT) and its receptor (OTR) play various roles in the central and peripheral regulation of appetite and body weight. Previously, we have shown that the administration of OT markedly decreased appetite and body weight gain in ovariectomized (OVX) obese rats. In addition, recent studies have shown that the endogenous OT system is also affected by endogenous or exogenous estrogen. **[Methods]** Firstly, we examined the effects of ovariectomy on hypothalamic OT gene expression and serum OT levels in female rats. Secondly, we investigated the effects of chronic estrogen administration on these factors in OVX rats to assess the underlying causes of ovariectomy-induced changes. Thirdly, we evaluated the effects of acute estrogen administration in OVX rats to confirm the direct effects of estrogen in rats with similar body weights. **[Results]** Ovariectomy decreased rats' hypothalamic OT/OTR mRNA and serum OT levels, but did not affect their visceral fat OTR mRNA levels. The chronic administration of estradiol (E2) abrogated these ovariectomy-induced changes: i.e., it increased the rats' hypothalamic OT/OTR mRNA and serum OT levels, and may be associated with reductions in food intake and body weight gain. In addition, acute E2 administration increased the rats' hypothalamic OTR mRNA and serum OT levels, but did not affect their hypothalamic OT mRNA levels. **[Conclusion]** OT might be a target hormone to pursue subsequent interven-

tions of menopause for menopause-induced metabolic disorders.

ISP-21-2

Effects of serotonin on Human Sperm Functions Omote Maya, Hasegawa Akiko, Sugiyama Yukiko, Wakimoto Yu, Shibahara Hiroaki *Hyogo College of Medicine*

[Objective] The World Health Organization Manual of Laboratory Medicine reports that male factors, including sperm dysfunction, account for approximately 50% of infertility cases. We believe that serotonin [5-hydroxytryptamine (5-HT)] is a promising candidate to improve the success rate of assisted reproductive technology and intrauterine insemination. 5-HT regulates the functions of dopamine and noradrenaline in the central nervous system and intestinal tract. In reproductive organs, it regulates the formation of germ cells and the synthesis and secretion of hormones. Fourteen types of 5-HT receptors have been found, mainly in the central nervous system. This study aimed to investigate whether serotonin (5-HT) is involved in human sperm functions. **[Methods]** First, we investigated the effect of 5-HT on sperm motility and then detected the type of 5-HT receptors. Sperm parameters such as sperm motility rate, linear velocity, curvilinear velocity, mean velocity, linearity, straightness, head amplitude, and head frequency were evaluated using a computer-aided sperm analyzer-SMAS (Sperm Motility Analysis System). Localization of 5-HT receptors were evaluated by immunofluorescent staining with a specific anti-5-HT antibody. **[Results]** No significant difference was noted in the motility of swim-up sperm under the time course and concentration change in addition of 5-HT. We detected 5-HT1B, 5-HT2A, 5-HT3A, 5-HT4, 5-HT5A, 5-HT6, and 5-HT7 receptors in human sperm and observed a significant decrease in sperm motility with the addition of 5-HT2A, 5-HT4, and 5-HT6 receptor antagonists. **[Conclusion]** This indicated that these receptors affect sperm motility. Based on these findings, 5-HT may have some functional role in human sperm.

ISP-21-3

Effect of ethanol on gonadotropin action in the primary culture system of rat ovarian granulosa cells Kasahara Yuta, Kishi Hiroshi, Mori Yusuke, Hidaka Miwa, Sato Takuma, Shiraishi Eriko, Kusahara Atsuko, Okamoto Aikou *The Jikei University*

[Objective] Although ethanol affects human ovarian function, the detail of its mechanism is still unclear. To clarify the effect of ethanol on follicle development and sex steroid hormone secretion, we investigated the mechanism using a primary culture system of rat granulosa cell. **[Methods]** A primary culture system using ovarian granulosa cells obtained from immature female rats treated with diethylstilbestrol was used. FSH/hCG alone or FSH/hCG and ethanol were added to this system and their effects were analyzed for (1) Measurement of mRNA centered on the *Lhcgr* gene and genes related to sex steroid hormone synthesis (2) Sex steroid hormone assay in the culture media (3) cAMP assay. **[Results]** Addition of ethanol enhanced each change as follows, as compared with the case of FSH/hCG alone. (1) Both *Lhcgr* and *Cyp19a1* mRNA expressions increased in FSH. When adding hCG alone, the expression of *Lhcgr* decreased strongly. (2) Regarding FSH, the E2 concentration in the culture media increased, and no enhancement of hormone secretion was observed in hCG. (3) For both FSH and hCG addition, cAMP concentration increased by 2.4 folds and 1.6 folds, respectively. Although ethanol also enhanced hCG-induced cAMP production, unlike FSH, it didn't enhance *Lhcgr* and *Cyp19a1* expression. **[Conclusion]** Ethanol enhanced FSH-induced various changes associated with follicle development, hormone synthesis and the mechanism involved the cAMP pathway. These dif-

ferences between FSH and hCG may be due to differentiation of granulosa cells, and it was speculated that the effects of ethanol differed depending on the stage of follicle development.

ISP-21-4

Time-restricted feeding impairs fertility competence in female mice Konishi Nafuko¹, Kurokawa Mayu¹, Kurihara Yasushi¹, Tahara Mie¹, Hamuro Akihiro¹, Misugi Takuya¹, Nakano Akemi¹, Tachibana Daisuke¹, Morimoto Yoshiharu², Sumi Toshiyuki¹, Koyama Masayasu³ *Osaka City University¹, HORAC Grand Front Osaka Clinic², Ishikiriseiki Hospital³*

[Objective] The aim of this study is to evaluate the effects of time-restricted food access on fertility competence in female mice. **[Methods]** Six-week-old C57BL/6J female mice were raised in the following four groups. We fed Normal chow (N) or moderate fat chow (F), and classified into Ad libitum (AL) group which could access food anytime and time restriction (TR) group which could access food in 8 hours in active phase. After 11 weeks, the mice were superovulated, and oocytes were collected and fertilized in vitro. **[Results]** The TR groups showed a rapid increase in caloric intake after feeding regardless of the type of food, and increasing in blood insulin levels causes increasing in the expression of circadian genes in the liver. Blood total cholesterol, HDL, number of antral follicles, number of oocytes retrieved, and number of morphologically normal oocytes increased in group F ($p < 0.05$). In the N-TR group, the ratio of total cholesterol to HDL was higher than in the other three groups ($p < 0.05$), blastocyst formation rate was lower than in the other three groups ($p < 0.05$), and reactive oxygen species (ROS) in the oocyte cytoplasm increased compared to the N-AL and F-AL groups ($p < 0.01$). **[Conclusion]** Time restriction of regular diet intake results in lower number of developing follicles, increased reactive oxygen species in oocytes, lower blastocyst development rate, increased number of apoptosis-related genes, and increased number of atretic follicles.

ISP-21-5

Analysis of the Sperm-Immobilization Phenomenon by Sperm-Immobilizing Antibodies Using CASA Honda Haruka, Wakimoto Yu, Omote Maya, Takeda Kazuya, Hasegawa Akiko, Shibahara Hiroaki *The Hospital of Hyogo College of Medicine*

[Objective] When the sperm-immobilization test (SIT) is performed using sera with sperm-immobilizing antibodies, the shaking phenomenon can be observed, in which the tail oscillates in concentric circles while the sperm head is fixed. Here, we analyzed the phenomenon of sperm-immobilization over time using computer-aided sperm analysis (CASA). **[Methods]** SIT-negative patient (group I) and SIT-positive patient (group II) were compared obtaining informed consent. Semen was donated by volunteer males with normal semen without anti-sperm antibodies. SIT was performed using these sera and sperm, and sperm motility parameters were analyzed using CASA until the sperm were completely immobilized. **[Results]** In group I, all parameters decreased gradually and linearly with time. In group II, the sperm negative correlation with SI50 value (50% sperm immobilization values) in group II. The ALH (amplitude of lateral head displacement) and BCF (beat cross frequency), which are indicator of sperm head oscillation, showed a transient increase in comparison with the previous value just before sperm immobilization. Similarly, VAP (average path velocity), VSL (straight line velocity), and VCL (curvilinear velocity), which are indicators of sperm motility velocity, showed a transient increase in comparison with the previous value. **[Conclusion]** We found that the sperm-immobilization phenomenon did not show a gradual decrease in mobility, but a transient lateral bending of the sperm head and faster velocity

just before immobilization. This is consistent with the phenomenon observed under the microscope, where ALH and BCF are indicators of sperm head oscillation. The time until sperm-immobilization also correlated with the SI50 value.

ISP-21-6

Characterization of spontaneously-occurring self-reactive antibody to sperm in mice Chen Yuekun, Hasegawa Akiko, Honda Haruka, Takeda Kazuya, Wakimoto Yu, Shibahara Hiroaki *Hyogo College of Medicine*

[Objective] It has been reported that anti-sperm antibodies detected in humans possibly cause infertility. The mechanism of antibody production and the corresponding antigen are still unknown. Previously, we established a monoclonal antibody (named Ts3) reactive to sperm from an aged male mouse without any immunization. This study aims to identify the target molecule of Ts3 that is reactive to self-antigen. **[Methods]** To examine the localization of the corresponding antigen, mouse sperm were collected from the epididymis for immunofluorescent staining. Male reproductive organs such as testis, cauda and caput epididymis, and vas deferens were used for immunohistochemical staining. The sperm proteins were extracted and two-dimensional electrophoresis (2D-PAGE) was conducted, followed by western blot analysis. Positive spots were subjected to mass spectrometry (MS). Sperm immobilization testing of Ts3 was carried out to determine influences on sperm motility. **[Results]** Ts3 reacted to the midpiece and principal piece of mouse sperm. The corresponding antigen was localized in the testis, caput and cauda epididymis and vas deferens. The molecular weight of the antigen to Ts3 was detected around 37 kDa, while the reactive molecule was identified as outer dense fiber protein 2 (ODF2) by MS. The sperm immobilization value was greater than 2, suggesting that Ts3 had harmful effects on sperm motility. **[Conclusion]** This study showed that Ts3 recognized ODF 2 as a targeted antigen and had an inhibitory effect on sperm motility. Therefore, ODF2 might be a pathogenic antigen in human male infertility.

ISP-21-7

Ultra-fine bubbles synthesized using carbon monoxide transmit the signals for embryonic differentiation Hirakawa Toyofumi¹, Hata Kenichiro², Tachibana Katsuro³, Miyamoto Shingo¹ *Fukuoka University Hospital¹, Department of Maternal-Fetal Biology, National Center for Child Health and Development², Department of Anatomy, Fukuoka University³*

[Objective] *In vitro* differentiation of embryo, which is highly recognized in assisted reproductive technologies (ART), is regulated by antioxidants. Carbon monoxide (CO), one of the gaseous signaling molecules, plays pivotal roles as an antioxidant in biological processes. The ultra-fine bubbles synthesized using these gaseous molecules have been utilized to elaborately transfer the signals between cells. In this study, we investigated the effect of CO-UFB on *in vitro* differentiation of mouse embryo. **[Methods]** In total, 1 mL KSOM medium with CO-UFB (CO-UFB-KSOM) was produced using the super high-speed vibration bubbling system. The size and number of UFB were estimated using the laser nanoparticle analysis system. The transfer rate of blastocyst from embryo was evaluated through visual confirmation. In culture condition, one hundred cells were evaluated using single-cell RNA sequencing. Each transcriptome was analyzed using machine learning to identify the gene clusters associated with embryonic differentiation. **[Results]** The main size of UFB was found to be distributed between 50 to 300 nm. The number of UFB ranged from $1.90 \times 10^9 \pm 1.13 \times 10^9$ / mL. Each transfer rate of blastocyst in KSOM or CO-UFB-KSOM was 75 or 94%, thereby indicating that CO-UFB induced

in vitro differentiation of embryo. In the comprehensive analysis, upregulation of antioxidant and antiapoptotic gene clusters was observed in CO-UFB-KSOM. **[Conclusion]** CO-UFB exhibits extreme antioxidant and antiapoptotic activities, thereby resulting in *in vitro* differentiation of embryo. The medium with CO-UFB can be utilized to improve the pregnancy rate in women treated with ART.

ISP-22-1

Efficacy of intrauterine infusion of granulocyte-colony stimulating factor in patients with thin endometrium or recurrent implantation failure Kawasaki Akiko *University of Tsukuba*

[Objective] The purpose of this study was to investigate the effect of intrauterine infusion of granulocyte-colony stimulating factor (G-CSF) on reproductive outcomes in patients with thin endometrium or recurrent implantation failure. **[Methods]** This was a one-arm, retrospective study in a university hospital. The study group included 29 patients with repeated implantation failure or thin endometrium undergoing IVF-ET. A total of 300 µg of G-CSF were infused just before decidualization of the endometrium with hCG or progesterone administration in embryo transfer cycles. Pregnancy outcomes and the increase in endometrial thickness after G-CSF infusion were evaluated. **[Results]** The mean age of the study group was 38.7 ± 4.30 years. Nineteen cases had thin endometrium, 5 cases had recurrent implantation failure, and 5 cases had both. The serum hCG-positive rate, pregnancy rate, and live birth rate after G-CSF infusion therapy were 48.3%, 17.2%, and 13.8%, respectively. Endometrial thickness before and after G-CSF infusion was 7.25 ± 1.39 mm and 7.61 ± 1.91 mm, respectively; there was no significant difference ($p=0.21$). There were no adverse events with the therapy during this study. **[Conclusion]** The present results suggest that intrauterine G-CSF infusion therapy has a possibility to improve pregnancy outcomes for patients with a poor prognosis for IVF-ET. However, an increase in endometrial thickness is not apparently related to the mechanism of the G-CSF effect.

ISP-22-2

The maternal risk factors for placenta accreta spectrum in cases conceived after frozen-thawed embryo transfer on hormone replacement cycle Fujita Tomoyuki¹, Yoshizato Toshiyuki¹, Mitao Hiroshi¹, Shimomura Takuya², Kuramoto Takeshi³, Fukagawa Mayumi¹, Ushijima Kimio¹ *Kurume University Hospital¹, St. Mary's Hospital², Kuramoto Women's Clinic³*

[Objective] Assisted reproductive technology (ART), especially frozen-thawed embryo transfer (FET) on hormone replacement cycle (HRC) is a known risk factor for placenta accreta spectrum (PAS). This study aimed to clarify the risk factors in pregnancies conceived after FET on HRC for PAS. **[Methods]** Among 14,020 cases cared for in two tertiary perinatal centers from 2010 to 2021, there were 305 cases of PAS and 494 cases conceived after FET on HRC. PAS was diagnosed in cases 1) with pathological findings of placenta increta/percreta, 2) requiring manual evacuation of the placenta after delivery, or 3) retained placental tissue. Among cases conceived after FET on HRC, 60 cases with PAS and 124 cases without PAS were selected. Maternal clinical background and parameters on ART were retrieved from medical records taken from two hospitals and ART facilities, respectively. Multivariate logistic regression models were used for case-control comparisons. Adjustment factors were a history of uterine surgeries including cesarean section, endometrial curettage and endometrial polypectomy, endometrial thickness (EmT) measured by transvaginal ultrasonography at ET, indications for ART and the presence of endometriosis/adenomyosis, autoimmune disease and placenta

previa. **[Results]** PAS was associated with the number of previous uterine surgeries of ≥ 2 (adjusted odds ratio [OR], 3.74; 95% confidence interval [CI], 1.26-11.00) and EmT of < 8.3 mm at ET (adjusted OR, 2.38; 95% CI, 1.03-5.50). **[Conclusion]** Repetitive uterine surgeries and thin endometrial thickness at ET were considered risk factors for PAS in cases conceived after FET on HRC.

ISP-22-3

Additional data on endometrial and myometrial blood flow along with uterine cavity volume at the time of embryo transfer will allow more accurate prediction of embryo transfer outcomes Komiya Shinnosuke^{1,2}, Nakao Tomoko¹, Asai Yoshiko², Inoue Tomoko², Morimoto Yoshiharu², Okada Hidetaka¹ *Kansai Medical University¹, HORAC Grand Front Osaka Clinic²*
[Objective] Conventional transvaginal ultrasonography evaluates endometrial status subjectively based on echo brightness. This study was conducted to validate the hypothesis that more accurate prediction of embryo implantation outcome is possible by using three-dimensional power Doppler (3D-PD) voxel data to quantify blood-flow data in the endometrium and nearby myometrium. **[Methods]** Patients were scheduled for their first hormone replacement cycle frozen-thawed single blastocyst transfer between April 2018 and March 2019. They had no apparent uterine or endometrial abnormalities. The 3D-PD data on the day of embryo transfer and the fertility prognosis of 181 patients were followed. Receiver operating characteristic (ROC) analyses were performed and compared by a conventional model using two-dimensional (2D) data and a new model using 2D plus 3D-PD data. DeLong's test was used to compare the area under the curve (AUC) of both ROCs. **[Results]** When the objective variable was live birth, AUCs for the conventional and new models were 0.83 (95% CI : 0.77-0.89) and 0.87 (95% CI : 0.82-0.92), respectively ($p=0.02$). The threshold of the new model was 0.56, and sensitivity, specificity, positive predictive value and negative predictive value at the threshold point were 0.76, 0.80, 0.85 and 0.69, respectively. **[Conclusion]** Although it is known that endometrial thickness affects embryo implantation outcomes, this study demonstrates that additional data on blood flow in the uterus and nearby myometrium, along with uterine cavity volume, could improve the prediction of embryo implantation outcomes.

ISP-22-4

Endometriosis fertility index and pregnancy outcomes of assisted reproductive technology Takahashi Kyoko, Takehara Isao, Nakamura Fumihiro, Nakai Nanako, Matsukawa Jun, Matsuo Koki, Nagase Satoru *Yamagata University*
[Objective] Endometriotic infertility is associated with poorer pregnancy outcomes of assisted reproductive technology (ART). The r-ASRM classification is often used to classify the severity of endometriosis, but it does not correlate with postoperative pregnancy outcomes. In contrast, the endometriosis fertility index (EFI) could predict pregnancy outcomes of non-ART after endometriosis surgery. However, there are few reports about EFI and postoperative pregnancy outcomes of ART, and the correlation remains controversial. Therefore, we investigated the relationship between EFI and pregnancy outcomes of ART at our institution. **[Methods]** The study included oocyte retrieval cycles of endometriotic infertility performed in our institution from January 2017 to December 2020. Subjects with a history of previous endometriosis surgery underwent 84 cycles and those without underwent 80 cycles. The patients' background, surgical findings, and pregnancy outcomes were extracted from the medical records and analyzed retrospectively. Pregnancy was defined as the result of all fresh and frozen-thawed embryo

transfers that used the embryos obtained in that oocyte retrieval cycle. **[Results]** In the 84 cycles in patients with a history of surgery, the EFI score of the cycles that resulted in pregnancy was significantly higher than that of the cycle without pregnancy (5 vs 4, $p=0.031$). None of the EFI categories, such as Least Function score, r-ASRM score, age at surgery, duration of infertility, and pregnancy history, correlated with pregnancy outcomes. **[Conclusion]** In our data, a significant correlation was found between the EFI and ART pregnancy outcomes. The EFI could be useful in predicting pregnancy outcomes of ART.

ISP-22-5

Two novel pregnancy outcome predictors related to serum human chorionic gonadotropin levels Takehara Isao, Kaneko Hiromu, Nakamura Fumihiro, Nakai Nanako, Takahashi Kyoko, Matsukawa Jun, Matsuo Koki, Nagase Satoru *Yamagata University*
[Objective] In assisted reproductive technology, serum human chorionic gonadotropin (hCG) levels in the first trimester have been reported as predictors of pregnancy outcomes. In this study, we examined: 1) serum hCG levels upon gestational sac (GS) visibility on day 21 and 2) daily hCG level changes between 4 and 5 weeks of gestation (defined as "A-hCG"). **[Methods]** The study included 501 pregnancies (217 were fresh embryo transfers and 284 were frozen embryo transfers) treated at our institution from January 2012 to December 2020. Multiple pregnancies were excluded from analysis. We measured serum hCG levels upon GS visibility on day 21 and calculated "A-hCG" by dividing the value reflecting the change in serum hCG levels between 4 and 5 weeks of gestation by the value representing the duration between these time periods. Significant differences were defined at $p < 0.05$. **[Results]** 1) Serum hCG levels upon GS visibility on day 21 of gestation were significantly higher in the fresh embryo transfer livebirth group ($p=0.01$), with a cutoff of 2,798 mIU/mL. However, no correlation was observed between serum hCG levels and the presence or absence of a livebirth ($p=0.945$) in the frozen embryo transfer group. 2) "A-hCG" was significantly higher in the livebirth group for both fresh and frozen embryo transfers ($p < 0.01$). **[Conclusion]** The findings of the present study suggest the usefulness of two novel indicators for predicting pregnancy outcomes: serum hCG levels with confirmed GS and daily changes in hCG ("A-hCG") levels.

ISP-22-6

Innovative controlled ovarian stimulation (COS) method for severe polycystic ovary syndrome (PCOS) without ovarian hyperstimulation syndrome (OHSS) and higher oocyte quality Tanaka Atsushi¹, Yanagihara Yasuho², Ohno Motoharu³, Nagayoshi Motoi¹, Itakura Atsuo² *Saint Mother Hospital¹, Juntendo University², Juntendo University Urayasu Hospital³*
[Objective] We developed an innovative controlled ovarian stimulation method for severe PCOS cases without OHSS, higher oocyte quality and optimal number of oocytes using an aromatase inhibitor (Letrozole). **[Methods]** 34 severe PCOS patients who had over 20 antral follicles in both ovaries, over 10 mg/ml of anti-Mullerian hormone (AMH). From the third day of the period, 2.5mg or 5mg of Letrozole and 150iu of FSH/HMG were administered every day until the day of trigger administration. When the leading follicle reached 18mm in diameter, the injection of 0.25mg of GnRH antagonist started and continued until the day of the trigger shot. Estradiol (E2), luteinizing hormone (LH) and progesterone (P) were measured every day. After confirmation that the largest follicle was 22-24 mm in diameter and E2 level was less than 500-700pg/ml, 5000iu of HCG was administered as trigger and oocyte pickup was performed 37 hours later under general anesthesia with Propofol. All em-

bryos were cryopreserved after IVF or ICSI. 5mg of Letrozole, 0.5mg of Cabergoline and 0.25mg of GnRH antagonist were administered just after the oocyte retrieval for five days consecutively. **[Results]** 1. Clinical pregnancy rate/frozen ET and miscarriage rate : 52.4% (11/21), 18.2% (2/11) 2. Cryopreservation rate : 85.3% (29/34) 3. OHSS (moderate or severe cases) : 0% (0/34), (mild) : 8.8% (8/34) 4. Days between oocyte pickup and menstruation start : 7.04 **[Conclusion]** This newly developed controlled ovarian stimulation with consecutively used Letrozole for severe PCOS cases seems to be a possible first line treatment for severe PCOS though no clinical data is available yet.

ISP-22-7

A modified GnRH antagonist method in combination with aromatase inhibitors and cabergoline : Safe and effective ovarian stimulation to rescue PCOS and prevent OHSS Yanagihara Yasuho^{1,2}, Tanaka Atsushi¹, Nagayoshi Motoi¹, Ohno Motoharu³, Yamaguchi Takashi¹, Itakura Atsuo² *Saint Mother Hospital¹, Juntendo University², Juntendo University Urayasu Hospital³, Takasaki ART Clinic⁴*

[Objective] To establish a modified controlled ovarian stimulation (COS) protocol for polycystic ovary syndrome (PCOS) that does not cause ovarian hyper stimulation syndrome (OHSS) while maintaining egg quality. **[Methods]** This study is a retrospective cohort study of reproductive medicine at our hospital. Forty-five PCOS patients received the modified COS and seventy-five transfer cycles completed, the results were compared to 130 PCOS patients treated with conventional methods. The key point of the modified COS is to reduce rapid estradiol (E2) levels by using letrozole before oocyte pickup and to administer a combination of cabergoline + letrozole + GnRH antagonist for 5 days after oocyte pick up. ART clinical outcome, embryonic development and hormone levels of 175 PCOS patients treated with four different COS at our hospital were analyzed. **[Results]** After applying the modified COS we found that the average number of cryopreserved blastocysts was 6.13. No clinically problematic OHSS and higher clinical outcomes than in conventional methods were observed. Average days between oocyte pickup and menstruation was 5.24. Clinical pregnancy rate and miscarriage rate were 48.0% and 19.4%. Clinical pregnancy rate at one trial were 72.3%. **[Conclusion]** The promising this modified COS eliminated the incidence of OHSS in PCOS patients. This modified COS can significantly reduce the financial, physical and mental burdens by improving clinical outcomes and eliminating OHSS.

ISP-22-8

The association between lesion type and clinical outcomes of ART in infertile women with symptomatic adenomyosis Matsumura Asako, Kitajima Michio, Kajimura Itsuki, Matsumoto Kanako, Harada Ayumi, Miyashita Noriko, Kitajima Yuriko, Miura Kiyonori *Nagasaki University Hospital*

[Objective] The appropriate combinations of surgery, medication, and ART may lead to successful treatment in adenomyosis associated infertility. The different types of adenomyosis may relate to clinical course of treatment. In this study, we evaluated association between type of adenomyotic lesion and outcomes of ART. **[Methods]** Infertile women with adenomyosis who treated by ART from April 2018 to July 2021 were included. According to MRI, we classified adenomyosis into four groups : 1) adenomyosis occupied intrinsic layer of myometrium with disruption of junctional zone (JCZ) (type I), 2) adenomyosis occupied extrinsic layer of myometrium by serosal invasion without JCZ disruption (type E-a), 3) extrinsic lesion with JCZ involvement (type E-b), and 4) adenomyosis diffusely occupy myometrium

(type D). The difference in clinical course and treatment outcomes in ART according to the lesion type were compared. **[Results]** Twenty-six treatment cycles in 17 cases were evaluated. The lesion type of adenomyosis were classified as I in four, E-a in six, E-b in five, and D in seven cases. Morphologically competent blastocysts were obtained in 16 cycles (2.8 per cycle). Clinical pregnancy was achieved in six cases by frozen-thaw embryo transfer with GnRH-a and on-going pregnancy was confirmed in two cases with E-a and woman with E-b had surgery before ART. Two cases with I and one case with E-a failed to miscarriage. **[Conclusion]** Frozen/thaw embryo transfer conjoined with surgery and/or medical treatment is effective in women with adenomyosis associated infertility, however, the type of adenomyotic lesion may differently contribute to the treatment success.

ISP-22-9

Efficacy of intrauterine infusion of granulocyte-colony stimulating factor in patients with thin endometrium or recurrent implantation failure Mori Yuki¹, Kawasaki Akiko¹, Itagaki Hiroya¹, Ijiri Hiroko¹, Hasegawa Yuko², Kita Naoki², Wada Atsushi², Ishiwata Isamu³, Kono Itoe¹, Shima Minami¹, Teruya Hiromi¹, Satoh Toyomi¹ *University of Tsukuba¹, Tsukuba Gakuen Hospital², Ishiwata Obstetrics and Gynecology Hospital³*

[Objective] The purpose of this study was to investigate the effect of intrauterine infusion of granulocyte-colony stimulating factor (G-CSF) on reproductive outcomes in patients with thin endometrium or recurrent implantation failure. **[Methods]** This was a one-arm, retrospective study in a university hospital. The study group included 29 patients with repeated implantation failure or thin endometrium undergoing IVF-ET. A total of 300 µg of G-CSF were infused just before decidualization of the endometrium with hCG or progesterone administration in embryo transfer cycles. Pregnancy outcomes and the increase in endometrial thickness after G-CSF infusion were evaluated. **[Results]** The mean age of the study group was 38.7 ± 4.30 years. Nineteen cases had thin endometrium, 5 cases had recurrent implantation failure, and 5 cases had both. The serum hCG-positive rate, pregnancy rate, and live birth rate after G-CSF infusion therapy were 48.3%, 17.2%, and 13.8%, respectively. Endometrial thickness before and after G-CSF infusion was 7.25 ± 1.39 mm and 7.61 ± 1.91 mm, respectively ; there was no significant difference (p=0.21) . There were no adverse events with the therapy during this study. **[Conclusion]** The present results suggest that intrauterine G-CSF infusion therapy has a possibility to improve pregnancy outcomes for patients with a poor prognosis for IVF-ET. However, an increase in endometrial thickness is not apparently related to the mechanism of the G-CSF effect.

ISP-22-10

Association between quantitative evaluation of blastocyst morphology based on estimated cell number of trophoctoderm and continued pregnancy rate Kimura Hiroko, Utsuno Hiroki, Hamatani Toshio, Miyazaki Kotaro, Kamijo Shintaro, Mizuguchi Yuki, Uchida Sayaka, Yamada Mitsutoshi, Uchida Hiroshi, Maruyama Tetsuo, Aoki Daisuke, Tanaka Mamoru *Keio University Hospital*

[Objective] The Gardner classification is commonly used to evaluate the morphology of blastocysts. However, its classification is qualitative and may be inadequate to determine the order of transfer. In this study, we estimated the number of trophoctoderm (TE) cells in blastocysts in order to develop a quantitative morphological index, and examined its relation to the continued pregnancy rate. **[Methods]** We analyzed 328 day5 blastocysts from 167 couples who underwent vitrified-warmed embryo

transfer at our institute. At 116 ± 2 hours after insemination, we took the images of blastocysts with an expansion stage ≥ 3 , and measured their surface and mean area per TE cell. The estimated number of TE cells (ETC) was calculated by dividing blastocyst surface area by the mean area of ≥ 5 TE cells. A multivariate analysis for patient age, blastocyst diameter, Gardner classification was used to evaluate the effect of ETC on continued pregnancy beyond 12 weeks' gestation. **[Results]** The median of female age and ETC were 38 years (27-46) and 76 (29-186) respectively. The multivariate analysis showed ETC was significantly associated with continued pregnancy ($P < 0.001$) independent of female age and blastocyst grades according to Gardner classification. In the group with ETC less than 60, the continued pregnancy rate was 0% (0/65), while continued pregnancy rate consistently increased with ETC, up to 44.4% in the group with ETC over 120. **[Conclusion]** ETC is a promising index for predicting pregnancy success. The quantitative characteristics of ETC would help decide the order of blastocyst transfer.

ISP-23-1

Impact of assisted reproductive technologies on the maternal pregnant complications and offsprings congenital deformities Chiang Hsin-Ju¹, Yang Yao-Hsun², Sung Pei-Hsun³ *Kaohsiung Chang Gung Memorial Hospital, Taiwan¹, Department for Traditional Chinese Medicine, Health Information and Epidemiology Laboratory, Chang Gung Memorial Hospital, Chiayi, Taiwan², Division of Cardiology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan³*

[Objective] In those couples receiving assisted reproductive technologies (ART), there are still many concerns about maternal and offspring's health owing to high-concentrated hormone exposure. The aim of this study is to investigate the influence of ART on the maternal pregnancy and offspring's health. **[Methods]** Nationwide database were utilized for the study. From 2004 to 2019, a total of 13,778 infertile women aged between 18-45 years undergoing ART were retrospectively collected. After matching pregnant age in a 1 : 2 ratio, there are 13,765 infertile women treated with ART and 27,530 women with normal pregnancy. Baseline data and follow-up outcomes were compared with the independent *t* and Chi-square tests. **[Results]** Women treated with ART had significantly higher prevalence of hyperlipidemia (6.0% vs. 4.4% ; $p < 0.0001$) but similar rates of hypertension and diabetes compared with normal pregnant counterparts. As compared to normal pregnant women, the infertile women had notably higher incidence of miscarriage (16.0% vs. 11.4% ; $p < 0.0001$) and rate of live birth (92.5% vs. 90.9% ; $p < 0.0001$), mainly attributing to higher average number of pregnancy and delivery in the infertile population. As to offspring's outcomes, the children delivered from infertile mothers who received ART had significantly higher incidence of overall congenital deformities (30.5% vs. 27.5% ; $p < 0.0001$), including congenital heart defects (14.7% vs. 13.3% ; $p < 0.0001$) and endocrine/metabolic disturbance (22.0% vs. 19.1% ; $p < 0.0001$), but had similar incidence for urogenital deformities, diabetes, congenital heart block as well as neurologic defects between groups. **[Conclusion]** ART-associated healthy concerns from pregnant complications to offspring's congenital disorder remain existing, suggesting further long-term follow-up.

ISP-23-2

Universal Screening for COVID-19 as applied to IVF-ET Horibe Yu, Nakabayashi Akira, Toma Chihiro, Shimoji Kanoko, Murata Shuko, Hashimoto Tomomi, Kanno Toshiyuki, Motohashi Takashi, Akizawa Yoshika, Funamoto Hiroshi, Kumakiri Jun, Tabata Tsutomu *Tokyo Women's Medical Uni-*

versity

[Objective] With the spread of COVID-19 in Japan, it was necessary for IVF-ET to implement measures to minimize infection risk during treatment. At our hospital in Tokyo, COVID-19 PCR testing was instituted for all patients undergoing IVF-ET. In addition for controlled ovarian stimulation, we recommended home self-injection to reduce their need for hospital visits. **[Methods]** To determine the effectiveness of these measures, we reviewed data on numbers of PCR tests performed, the rate of positive results, rate of home self-injection, and numbers of IVF-ET cycles conducted before and after these measures had been implemented. **[Results]** PCR testing was performed in all 202 IVF-ET cycles, with zero cases testing positive for infection. Of the 93 oocyte retrieval cycles performed, 80 cycles utilized home self-injection. Exceptions were made where few injections were required, and there was resistance to self-injection from patients themselves. The number of oocyte retrieval/embryo transfer cycles prior-to and post measures were 62/58, and 94/108, respectively. **[Conclusion]** The fact that our hospital implemented PCR testing for nosocomial infection as a prerequisite to hospitalization for all patients made it easier generally to gain their understanding. Also, by reducing the number of hCG injections at night, we were able to allow emergency room staff to allocate more resources onto COVID-19 related duties. Moreover, as the volume of IVF-ET cycles actually increased, we concluded that our COVID-19 measures were welcomed by patients in general.

ISP-23-3

Analysis of fertility preservation for cancer patients : a single-institution experience Yamamoto Koyo¹, Takiuchi Tsuyoshi², Honda Hidemine¹, Ito Futa¹, Handa Mika¹, Takahashi Naoko¹, Miyake Tatsuya¹, Kimura Tadashi¹ *Osaka University¹, Clinical Genomics, Osaka University²*

[Objective] Advances in cancer treatment have dramatically improved the survival rate of child, adolescent and young adult cancer patients, therefore their fertility preservation has become deep concern. We have provided counseling and treatment regarding fertility preservation for cancer patients since gonadal dysfunction could be caused by cancer treatment. We report our experience of fertility preservation in our institute. **[Methods]** Sixty-eight female and 24 male cancer patients visited our reproductive medical center with their hope of fertility preservation between April 2018 and August 2021. We retrospectively analyzed their characteristics and outcomes. **[Results]** In females, the primary diseases were : breast cancer in 20 patients, ovarian cancer (including borderline malignant tumors) in 17 patients, hematopoietic tumors in 13 patients. In males, the primary disease was hematopoietic tumors in 10 patients. Twenty-nine females and 6 males did not proceed to actual practice. In females, 9 patients underwent embryo cryopreservation (median 51 days from initial visit to the treatment), 26 patients chose oocyte cryopreservation (median 29 days), and 4 patients underwent ovarian cryopreservation (median 23 days). In males, there were 16 patients with ejaculated sperm cryopreservation (median 1 day) and 2 patients with testicular sperm extraction (median 15 days). All of the patients preserving fertility have survived. Two out of 3 female patients who underwent embryo transfer after embryo cryopreservation had live-birth. **[Conclusion]** Providing appropriate information, treatment, and continuous follow-up be important for cancer patients who desire fertility preservation. Further experience is needed to clarify the efficiency and safety of fertility preservation.

ISP-23-4

Relationship between ovarian weight and ovarian reserveOgino Nana *The Hospital of Hyogo College of Medicine*

[Objective] Ovarian tissue cryopreservation (OTC) is a fertility preservation method for the adolescent and adult (AYA) cancer patients. Chemotherapy not only injures ovarian tissue but also affects ovarian volume. The purpose of this study was to investigate the relationship between ovarian volume and ovarian reserve after chemotherapy and compare the histopathological study of follicular density at each developmental stage. **[Methods]** OTC after chemotherapy was performed in 10 patients from June 2020 to September 2021 at our hospital. We search the correlation between serum AMH level and ovarian volume. Follicles were classified each developing stages and the density was calculated, and the correlation with serum AMH levels was examined. **[Results]** Serum AMH level was positively correlated with ovarian volume ($r=0.85$). In the evaluation of follicles at each developmental stage, serum AMH was negatively correlated with primordial follicle density ($r=-0.42$), positively correlated with transitional follicle density ($r=0.59$), not correlated with primary follicle density ($r=0.12$), and positively correlated with secondary follicle density ($r=0.56$). **[Conclusion]** It has been reported that AMH is produced by granulosa cells of developing follicles and is positively correlated with the number of primordial follicles. However, in our study, the serum AMH level did not correlate positively with the number of primordial follicles after chemotherapy, which may reflect the result of increased recruitment due to burnout of primordial follicles. In addition, ovarian volume and serum AMH level were positively correlated even after chemotherapy. Since ovarian toxicity differs depending on the drug used and the cumulative dose of chemotherapy, it needs individualized studies with more cases.

ISP-23-5

The role of anti-Mullerian hormone (AMH) and women age in predicting chemical pregnancy outcome of infertile patients underwent IVF-ICSI treatment Ariffianto Adi¹, Widad Shofwal¹, Fauzia Meydita¹, Setiawan Syahru Agung² *Universitas Gadjah Mada, Yogyakarta, Indonesia¹, Taipei Medical University, Taiwan (Republic of China)²*

[Objective] To determine and design an alternative scoring system for patients who will undergo IVF-ICSI procedures. **[Methods]** A retrospective study was conducted to observe the pregnancy outcomes among 108 women who received IVF-ICSI treatment in a tertiary hospital in Yogyakarta, Indonesia, from January 2018 to April 2021. Women with polycystic ovarian syndrome, endometriosis, cancer or age over 44 years old are excluded. **[Results]** The mean AMH levels of patients who were not pregnant were significantly lower than those who were pregnant (2.025 ng/ml vs 2.590 ng/ml, $p=0.047$). Moreover, patients with favourable AMH levels ($>1.8\text{ng/ml}$) and younger age (<36 years old) had a significantly higher probability of obtaining positive biochemical pregnancy test results (OR=3.35, 95%CI=1.141-9.861, and OR=2.82, 95%CI=1.055-7.576, respectively). Multivariate analysis showed that AMH levels independently contributed to the pregnancy outcome of the IVF-ICSI procedure (OR=3.249, 95%CI=1.087-9.707). Based on the univariate logistic regression of AMH levels and the women's age, we combined these two parameters into a scoring system to stratify further the patients who would undergo the IVF-ICSI procedure. According to the scoring results (0=less-likely, 1=moderately-likely, and 2=most-likely), each score had a pregnancy percentage of 4.0%, 20.0% and 36.4%, respectively. Every increase in one level scoring has a 2.96 probability of getting pregnant (95%CI=1.41-6.21). **[Conclusion]** AMH scoring based on AMH levels and women's age can stratify IVF-ICSI outcomes

so that in the future, it has the potential to assist clinicians in guiding patients who will carry out IVF-ICSI.

ISP-23-6

Laparoscopic vaginoplasty procedure using pull-down technique of peritoneal flaps and uterine strand support in patients with Mayer-Rokitansky-Küster-Hauser syndrome : Kisu modification Kisu Iori^{1,2}, Tokuoka Asahi¹, Yamaguchi Keigo¹, Tanaka Kunio¹, Semba Hiroshi¹, Nakamura Kanako¹, Matsuda Kiyoko¹, Hirao Nobumaru¹ *Tachikawa Hospital¹, Keio University²*

[Objective] To demonstrate a novel laparoscopic vaginoplasty procedure, known as the Kisu modification, in patients with Mayer-Rokitansky-Küster-Hauser syndrome (MRKHS). **[Methods]** Ten patients with MRKHS (mean age : 22.9 ± 6.8 years, mean postoperative follow-up period : 18.4 ± 4.0 months) underwent laparoscopic vaginoplasty with the Kisu modification. After vaginal dissection into the potential vaginal space, the supravaginal and Douglas pouch peritoneum were laparoscopically detached from the bladder and rectum, respectively, creating anterior and posterior peritoneal flaps. The apex of the neovagina was opened via a transverse incision below the uterine strand. A longitudinal incision was also made in the middle of the uterine strand, dividing it bilaterally. The anterior and posterior peritoneal flaps were pulled down and sutured to the neovaginal introitus. The supravaginal and suprapectal peritoneum were sutured at approximately 10 cm to create the neovaginal vault. The bilateral incised uterine strands were sutured to the lateral aspects of the neovaginal apex for structural support in the pelvis to prevent a neovaginal prolapse. **[Results]** The mean neovaginal length at discharge and one year after surgery was 10.4 ± 0.2 cm and 9.9 ± 1.1 cm, respectively, indicating anatomical success. No obliteration, granulation tissue formation at the neovaginal apex, and neovaginal prolapse were recorded. All five patients who attempted sexual intercourse were satisfied with the sexual activity, indicating functional success. Patients who were not sexually active maintained an adequate length and width of the neovagina. **[Conclusion]** The Kisu modification of the laparoscopic vaginoplasty procedure is an effective approach for neovagina creation, both anatomically and functionally, in patients with MRKHS.

ISP-23-7

Intraoperative findings of TCR and postoperative ART outcomes in patients with implantation failure due to endometrial polyps Ikuma Shinichiro, Okada Yukiko, Ozaki Rie, Murakami Keisuke, Matsumura Yuko, Ochiai Asako, Kawasaki Yu, Kitamura Eri, Takeuchi Shiori, Kitade Mari, Itakura Atsuo *Juntendo University*

[Objective] The aim of this study was to compare the ART (assisted reproductive technology) outcomes after TCR (transcervical resection) for endometrial polyps to examine which clinical backgrounds contribute to pregnancy. **[Methods]** From 2014 to 2019, 39 patients who underwent TCR and ART for implantation failure due to endometrial polyps were classified into two groups (pregnant group : 23 cases, non-pregnant group : 16 cases) according to whether they had a pregnancy. The study items were the cumulative pregnancy rate and the comparison of patient backgrounds, intraoperative findings and ART results between the two groups. **[Results]** The cumulative pregnancy rate in the pregnancy group was 62.6% at 1 year postoperatively and 90.5% at 2 years postoperatively. In the comparison of patient backgrounds, age (pregnant group : 37.9 ± 3.7 (mean \pm SD) years, non-pregnant group : 40.3 ± 2.7 years) was significantly lower in the pregnant group ($p=0.04$), but AMH (4.4 ± 3.1 ng/ml, 3.0 ± 1.8 ng/ml) and duration of infertility (3.5 ± 2.4 years,

4.6 ± 3.2 years) were no significant differences. In the comparison of intraoperative findings, there were no significant differences in the maximum diameter of endometrial polyps (7.1 ± 3.3 mm and 9.0 ± 5.7 mm) and the number of polyps (6.9 ± 5.6 and 5.8 ± 5.3). Endometrial polyps were more frequently associated with chronic endometritis in the pregnancy group: 19 (82.6%) and 7 (46.7%) ($p=0.02$). The ART results showed that the number of follicles punctured during oocyte retrieval (11.2 ± 6.9, 7.3 ± 6.1) and the number of oocytes retrieved (6.1 ± 3.4, 3.7 ± 3.7) were significantly higher in the pregnancy group ($p=0.01$). **[Conclusion]** To improve postoperative ART outcomes, endometrial polyps with chronic endometritis should be aggressively treated with TCR.

ISP-23-8

Retrospective survey of female subfertile patients with systemic lupus erythematosus visited to reproduction unit in our hospital Honda Hidemine, Takiuchi Tsuyoshi, Yamamoto Koyo, Ito Futa, Handa Mika, Takahashi Naoko, Miyake Tatsuya, Kimura Tadashi *Osaka University Hospital*

[Objective] Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects women of reproductive age, and diseases itself or treatment may cause infertility. We reviewed patients who diagnosed as infertile complicated with SLE and treated in our reproductive unit. **[Methods]** We retrospectively reviewed characteristics and outcomes of women with SLE who visited to our reproductive unit for fertility treatment from 2021 to 2021. **[Results]** There were 24 women with SLE, of whom 22 patients proceeded to treatment. The mean age was 34.9 years (range, 22-41 years). Seven patients (29.1%) complicated with lupus nephritis and 6 patients (25.0%) with antiphospholipid syndrome (APS). Five patients (20.8%) had received cisplatin, 4 patients (16.7%) had received cyclophosphamide. Eleven patients was evaluated for AMH after treatment for SLE in the acute phase (median 1.14ng/ml, range 0.01-13.2ng/ml). One patient was evaluated for Anti-Müllerian Hormone (AMH) before and after treatment for SLE in the acute phase, such as high-dose corticosteroid pulses and mycophenolic acid mofetil. Her AMH level dropped from 4.02 ng/ml to 2.07 ng/ml in 36 months. Five patients (20.8%) were diagnosed as primary ovarian insufficiency. On obstetrical outcome, 10 pregnancies (41.6%) were confirmed, of which six pregnancies (25.0%) were achieved by IVF-ET program. Three cases (30%) had ended in miscarriage, 1 case (10%) delivered preterm, and the others (60%) had normal course. **[Conclusion]** Poor ovarian reserve was found in SLE patients and a significant number of POI patients were observed. Appropriate evaluation and treatment of infertility is important for SLE patients.

ISP-23-9

Preoperative differential diagnosis between obstructed hemivagina and ipsilateral renal anomaly and Wunderlich syndrome using magnetic resonance imaging Kamada Yasuhiko, Okamoto Ryota, Kashino Chiaki, Kubo Kotaro, Hasegawa Toru, Mitsui Takashi, Masuyama Hisashi *Okayama University Hospital*

[Objective] Periodic lower abdominal pain with pelvic hematoma in adolescent girls, also referred to as menstrual molimina, suggests a vaginal septum or defect. Magnetic resonance imaging (MRI) provides important information in a variety of conditions; however, it is particularly useful for diagnosis of sexually differentiated diseases (DSDs). Vaginal hematoma in obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome and cervical hematoma occurs in Wunderlich syndrome and is only diagnosed based on histopathological examination of the resected septum. However, few studies have reported preopera-

tive diagnosis. **[Methods]** We retrospectively analyzed the clinical records of 16 patients with DSDs accompanied by menstrual molimina treated at our hospital between 2010 and 2020. MRI was used for differential diagnosis. **[Results]** The study included nine patients with vaginal defects, two with imperforate hymen (IH), three with OHVIRA, and two with Wunderlich syndrome. Cervical glands showed hyperintense signals on T2-weighted (T2WI) MRI sequences. Among patients with vaginal defects, four had a dilated cervix with hyperintense signals within the hematoma wall. Five patients were diagnosed with cervical atresia. The upper part of the hematoma wall showed hyperintense signals on T2WI MRI, with a clearly distinguishable boundary between the dilated cervix and the vagina in patients with IH. On T2WI MRI, the lower part of the hematoma showed hypo- and hyperintense signals in OHVIRA and Wunderlich syndrome, respectively. **[Conclusion]** Cervical gland hyperintensity on T2WI MRI is a useful sign for preoperative diagnosis of pelvic hematoma in adolescent girls and facilitates differential diagnosis between OHVIRA and Wunderlich syndrome.

ISP-23-10

Study of mullerian anomalies in private hospital and reproductive outcome Barnwal Kavita *Samarpan Hospital, India*

The prevalence of congenital anomalies of female genital tract is not clear. This study was done to know the incidence of uterine abnormalities and their reproductive outcome. This is a retrospective study done between March 2019 to February 2021 at Samarpan Hospital. All cases with anomalies were studied with USG (TAS and TVS), MRI and Laparohysteroscopy. The septate uterus is the most common finding. Agenesis of uterus and vagina was rare and associated with worst prognosis. Reproductive outcome of unicornuate and didelphys was poor while that of septate and bicornuate uteri was better. Mullerian anomalies are uncommon but important cause of infertility and recurrent pregnancy losses. Their timely detection, surgical management and modern ART can improve reproductive outcome in certain number of cases.

ISP-23-11

Fitz-Hugh-Curtis syndrome a silent offender : 2 cases Rizvi Suboohi *FOGSI, India*

INTRODUCTION : It is an eye opener to witness a seemingly harmless looking pelvic infection causing so much havoc inside in the form of fine adhesions in the pelvis and in perihepatic region. Chlamydia, Gonorrhoea are more common. Also seen with Tuberculosis. **CASE PRESENTATION :** Case 1 : 23yrs nullipara female, wanted second opinion for primary Infertility, Dysmenorrhea. Examination : BMI increased. P/S : Cervical erosion P/V : Decreased uterine mobility TVS : Bulky ovaries close to uterus, multi-follicular appearance. Antibiotic course for PID and metformin 2 cycles. Dysmenorrhea not relieved Abdominal Scan : Fatty liver, polycystic ovaries. MRI : Polycystic ovaries. Laparoscopy : Multiple fine adhesions in pelvis, approach to uterus, ovaries difficult. Doxycycline and Metroglol x 14days. PCR-TB of EB positive, ATT Case 2 : 28-year female with subfertility, H/o Right side rupture ectopic, tubectomy. Anxious to conceive. On Examination : Average built and height, P/S cream discharge P/V restricted mobility Uterus. Day 2 TVS : Left ovary polycystic, Right ovary normal. HSG : Left tube patent, arcuate uterus. Treatment : Antibiotics, OCP 2 cycles. Ovulation induction 50mg CC. UPT positive, 8 days overdue. TVS : Thick endometrium small hypoechoic shadow in left ovary. Probability Ovarian ectopic. Did not return back. Came in emergency after 48 hours, suspected ruptured ectopic. Emergency Laparoscopy : Ruptured ectopic. Left tube adherent to

ovaries Perihepatic fine adhesions seen. **DISCUSSION** : Pelvic infections can cause serious problems in young females, it is important to treat both the partners. Adolescent should be educated to adopt safe sexual practices.

ISP-24-1

Estimation of the number of zygotes required for a live birth assuming PGT-A implementation Mariya Tasuku^{1,2}, Endo Toshiaki¹, Saito Tsuyoshi¹, Kurahashi Hiroki² *Sapporo Medical University Hospital¹, Division of Molecular Genetics, Institute for Comprehensive Medical Science, Fujita Health University²*
[Objective] In genetic counseling for PGT-A, many patients ask about the number of eggs required to obtain a live birth, but there is no reliable data to refer to. In this study, based on the available literature, we examined the number of zygotes required to obtain a live birth after PGT-A-based embryo selection, stratified by maternal age. **[Methods]** The parameters used in the calculations were collected from literature or open databases. To compare with the embryo transfer without PGT-A, we used the Japanese Society of Obstetrics and Gynecology database about ART. **[Results]** In the euploid embryo transfer with PGT-A, the live birth rate after embryo transfer exceeded 50% in all age groups, a marked increase compared to controls without PGT-A. However, the euploid rate of the blastocyst decreases significantly with maternal age. In estimates, the required number of zygotes for at least one live birth was 11.1 at age 40 with PGT-A and further increased to 29.7 at age 43. Notably, even in either age group, there was only a little difference in the rate of live births per zygote in the estimation between the PGT-A and non-PGT-A groups. **[Conclusion]** It was clear that PGT-A markedly reduced the miscarriage rate per embryo transfer. However, the number of zygotes required for live birth is extremely high in advanced maternal age, and the use of PGT-A does not provide significant improvement. It is necessary to provide correct information to patients through the further accumulation of clinical data.

ISP-24-2

Clinical outcomes of endometrial receptivity analysis for recurrent implantation failure patients following chronic endometritis examination ; a retrospective study in our hospital Ito Futa, Takiuchi Tsuyoshi, Honda Hidemine, Yamamoto Koyo, Handa Mika, Takahashi Naoko, Miyake Tatsuya, Kimura Tadashi *Osaka University*
[Objective] Recently, several studies have found that chronic endometritis (CE) and asynchronous window of implantation (WOI) identified by endometrial receptivity analysis (ERA) could be the etiologies of recurrent implantation failure (RIF), however there are few reports about effect of CE on asynchronous WOI. We report clinical outcomes of the RIF patients who underwent ERA following CE examination in our hospital. **[Methods]** The study population consisted of women with RIF who underwent ERA following CE examination between October 2018 and June 2021 in our hospital. RIF was defined as two or more failed in vitro attempts. Subjects were divided into two groups as follows : patients without CE (non-CE group) and patients successfully treated for CE (cured-CE group). Patients underwent an endometrial biopsy 5 days after progesterone administration (P+5) in an HRT cycle and ERA diagnosis of receptive or non-receptive is informed. We evaluated the results of ERA, pregnancy rate and their characters. **[Results]** Thirteen patients underwent ERA following CE : 5 in cured-CE group and 8 in non-CE group. In cured-CE group and non-CE group, the rates of receptive were 20.0% and 0%, respectively ($p=0.19$) ; the rates of post-receptive were 60.0% and 50.0% ($p=0.72$) and the rates of pre-receptive were 20.0% and 12.5% ($p=$

0.71). Twelve patients underwent hormone replacement treatment-frozen embryo transfer (HRT-FET) and there were no significant differences in pregnancy rate at the first HRT-FET (50% vs 37.5%, $p=0.68$). **[Conclusion]** There were no significant differences in ERA results and pregnancy rates between cured-CE and non-CE group.

ISP-24-3

Retrospective analysis of chronic endometritis in infertile women who underwent hysteroscopic surgery Ochiai Asako, Murakami Keisuke, Takeuchi Shiori, Kitamura Eri, Kawasaki Yu, Ozaki Rie, Ikuma Shinichiro, Okada Yukiko, Kitade Mari, Itakura Atsuo *Juntendo University Hospital, Juntendo University*
[Objective] Chronic endometritis (CE) is one of the endometrial factors of recurrent pregnancy loss (RPL) and recurrent implantation failure (RIF). Office hysteroscopy can help diagnose CE with visualization of mucosal edema, endometrial hyperemia, and micropolyps. However, hysteroscopic findings do not always accompany histological identification of plasma cells in the endometrial stroma, which is the gold standard for the diagnosis of CE. The prevalence of CE in each hysteroscopic finding is unknown. Herein, we analyzed the prevalence of CE in different hysteroscopic findings among infertile women who underwent hysteroscopic surgery. **[Methods]** This retrospective study was performed in one university hospital in Japan. Ninety-eight infertile patients who underwent hysteroscopic surgery between April 2017 and March 2020 were evaluated. CE was histologically diagnosed by the presence of plasma cells (CD138 immunostaining) in the endometrial stroma. **[Results]** Of the 98 infertile women who underwent hysteroscopic surgery, 50 (51.0%) were diagnosed with CE histologically. Patient age, pregnancy history, and past history of RPL and RIF were not significantly different between the CE+ group and CE- group. Prevalence of CE was 88.9% ($n=8/9$) in Asherman's syndrome, 50.0% (4/8) in submucosal myoma, 50.0% (2/4) in septate uterus, and 48.9% (44/90) in endometrial polyps. In the CE+ group, the presence rate of five or more endometrial polyps and endometrial hyperemia were significantly higher than in CE- group ($p=0.007$ and $p=0.026$, respectively). **[Conclusion]** The presence of CE should be histologically evaluated in infertile women who undergo hysteroscopic surgery due to a relatively high prevalence of CE in this population.

ISP-24-4

Possible association of anti-beta2-glycoprotein I/HLA-DR complex antibody with systemic hypercoagulation in patients with recurrent pregnancy loss (RPL) Matsumi Hirotaka *MATSUMI Ladies Clinic Mita, Tokyo*
[Objective] Recurrent pregnancy loss (RPL) is one of clinical manifestations of antiphospholipid syndrome (APS). However, in more than half of patients with RPL, the cause is never determined. Recently, autoantibody against $\beta 2$ -glycoprotein I ($\beta 2$ GPI) complexed with HLA class II molecules ($\beta 2$ GPI/HLA-DR) has been reported to be a novel autoantibody related to APS. The present study aimed to explore the association of anti- $\beta 2$ GPI/HLA-DR antibody with coagulation-related biomarkers in women with RPL. **[Methods]** Serum levels of conventional antiphospholipid antibodies (aPLs), including IgG/IgM anticardiolipin antibodies, anti- $\beta 2$ GPI antibody, and lupus anticoagulant were measured in 23 women with history of RPL along with that of one miscarriage (the RPL group). To evaluate coagulation status, serum levels of TAT, AT3 and D-dimer were also measured. **[Results]** Conventional aPL antibodies were detected in 7/22 (31.8%), whereas anti- $\beta 2$ GPI/HLA-DR antibody was positive in 4/23 (17.3%). There were two women showing dou-

ble positive for aPLs and anti- β 2GPI/HLA-DR antibody. Elevation of TAT concentration was detected in 13/20 (65%) in the women with the RPL group. Interestingly serum levels of TAT were commonly high in the women positive for anti- β 2GPI/HLA-DR antibody implying that coagulation pathway was activated in those women. A woman with anti- β 2GPI/HLA-DR antibody positive was pregnant without pharmacological intervention, resulting in miscarriage. **[Conclusion]** In some group of women with RPL, anti- β 2GPI/HLA-DR antibody might be associated with systemic hypercoagulation, which is reflected by a coagulation marker of TAT.

ISP-24-5

Role of MMP-2 and periostin in patients with recurrent pregnancy loss Ozawa Fumiko¹, Goto Shinobu^{1,2}, Yoshihara Hiroyuki^{1,2}, Kitaori Tamao^{1,2}, Ozaki Yasuhiko^{1,2,3}, Sugiura-Ogasawara Mayumi^{1,2} *Research Center for Recurrent Pregnancy Loss, Nagoya City University Hospital¹, Nagoya City University Hospital², Nagoya City University West Medical Center³*

[Objective] MMP-2 (matrix metalloproteinases -2), which degrade protein of extracellular matrix, is important for forming placenta in early pregnancy. Periostin, cell adhesion protein that allows the maintenance of cancer stem cells and upregulated MMP-2 expression by inhibiting MMP-2 binding to the cell surface or by its degradation. In this study, we investigated the expression and the localization of MMP-2 and periostin in decidua of patients with recurrent pregnancy loss (RPL). **[Methods]** With informed consent, decidual tissues were collected from idiopathic RPL patients with normal fetal chromosome (NC) and with abnormal fetal chromosome (AC). The expression and the localization of MMP-2 and periostin was investigated using western blotting and fluorescence immunohistochemistry. **[Results]** The expression of MMP-2 in decidua and villi was confirmed by western blotting. Periostin is known to have 4 spliced isoforms within the C-terminal domain. The expression of all isoforms in decidua and mainly the short isoform in villi was confirmed by western blotting. The staining of MMP-2 and periostin was observed in the stroma cell of decidua, epithelium and stroma cell of villi. Stainability of MMP-2 was observed at HLA-G (+) site in decidua. **[Conclusion]** These results suggested that the expression of MMP-2 was expressed at the implantation site and regulation of MMP-2 may be controlled by periostin.

ISP-24-6

Autoantibody against beta 2-glycoprotein I/HLA-DR complexes (a beta 2GPI/HLA-DR) in infertility Ono Yosuke¹, Takimoto Kanako¹, Nakatani Makiko¹, Ota Hajime¹, Fukushi Yoshiyuki¹, Wada Shinichiro¹, Yamada Hideto² *Teine Keijinkai Hospital¹, Center for Recurrent Pregnancy Loss, Teine Keijinkai Hospital²*

[Objective] a β 2GPI/HLA-DR is involved in the pathophysiology of recurrent pregnancy loss. This study aimed to evaluate a β 2GPI/HLA-DR in infertility. **[Methods]** This prospective cohort study was approved by IRB, and written informed consent was obtained from participants. We measured serum levels of a β 2GPI/HLA-DR (normal <73.3U) in 154 infertile women, and compared background, and risk factors for infertility between women with (A) and without a β 2GPI/HLA-DR (B). **[Results]** Of the 154 patients, 14.9% (23) tested positive, and 95.7% (22/23) of them had secondary infertility. There was no difference in patient background between A (n=23) and B (n=131) groups. In A group, infertility due to tubal factors accounted for the highest percentage of 43.5%, which tended to be higher than that of B (27.4%, P=0.083). The frequency of endometriosis was higher in A group compared with B (39.1% vs 18.3%, P=0.026).

Women with endometriosis tested more frequently for a β 2GPI/HLA-DR, and the titer was higher than women without endometriosis (median 40.6U vs 15.5U ; P<0.001). The frequency of recurrent implantation failure (RIF ; implantation failure after 3 or more embryo transfers) in A group was higher than in B group (women with RIF / women with ART ; 50.0%, 7/14 vs. 16.8%, 16/95 ; P=0.012). Of the 154 patients, 14.9% (23) had RIF, of which 30.4% (7/23) tested positive for a β 2GPI/HLA-DR. **[Conclusion]** We for the first time demonstrated the positive rate of a β 2GPI/HLA-DR in infertile women and their clinical characteristics. a β 2GPI/HLA-DR may be associated with the pathophysiology of infertility, especially with endometriosis and RIF.

ISP-24-7

Reproductive tract microbiota changes during the menstrual cycle and association with vitro fertilization outcome Fukuoka Mio¹, Yamada Mitsutoshi^{1,3}, Sasabe Junpei², Miyado Kenji³, Akashi Kazuhiro¹, Saito Saki¹, Kamijo Shintaro¹, Aoki Daisuke¹, Tanaka Mamoru¹ *Keio University¹, Department of Pharmacology, Keio University², Department of Molecular Endocrinology, National Center for Child Health and Development³*

[Objective] Symbiotic microbiota in reproductive tract is reported to be present and involved in embryo development of model organisms. We aimed to clarify the changes of microbiota in the human reproductive tract during the menstrual cycle and the differences depending on the *in vitro* fertilization (IVF) outcome. **[Methods]** Twenty subjects (eight in the successful pregnancy group (S-group ; mean \pm standard deviation 35.5 \pm 2.8 years) defined as gestational sac detected on ultrasound at 5 weeks' gestation ; twelve in the unsuccessful pregnancy group (U-group ; 35.5 \pm 2.7 years)) were included in the study. Vaginal and intrauterine samples were collected during each menstrual cycle of IVF and frozen embryo transfer. Genomic DNA extracted from microbiota was analyzed by next-generation sequencing from the genus to the species levels. **[Results]** The vaginal samples (N=23) showed changes in microbiota during the menstrual cycle and significantly higher percentage of *Lactobacillus* spp. compared to the intrauterine samples (N=16). However, there was no significant difference in the ratio of *Lactobacillus* spp. between the S and U-groups. *Gardnerella vaginalis*, *Bacteroides* spp., and *Prevotella* spp., which are known to associate with bacterial vaginosis, were not detected in either the vagina or intrauterine samples. *L. crispatus*, *L. gasseri*, and *L. ultunensis* were significantly abundant in the intrauterine samples of the S-group, while *L. jensenii* was abundant in the U-group. **[Conclusion]** The dominance of *Lactobacillus* spp. increased during the menstrual cycle, while it did not associate with the successful pregnancy. Our results suggest a correlation between species-level microbiome profiling and IVF outcomes.

ISP-24-8

Impact of Body Composition on Recurrent Pregnancy Loss : towards the future preconception care Kirino Satoe¹, Eto Eriko¹, Yokohata Satomi¹, Mitoma Tomohiro¹, Mishima Sakurako², Oohira Akiko², Tani Kazumasa², Maki Jota², Hayata Kei², Nakatsuka Mikiya³, Masuyama Hisashi¹ *Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama University¹, Okayama University Hospital², Graduate School of Health Sciences, Okayama University³*

[Objective] After regular assessments, 50% of RPL causes usually remain unexplained. The aim of this study was to evaluate the impact of body composition on Recurrent Pregnancy Loss (RPL) prognosis. **[Methods]** Sixty RPL patients in our hospital between September 2014 and September 2015 were included in our study. Their body compositions were evaluated with Bio-

electrical Impedance Analysis scale at their initial assessment, including indexes such as %Fat Mass (FM), Fat Mass (FM), Fat Free Mass (FFM), and Total Body Water (TBW). Thirty-five got pregnant within one year follow-up, resulting in seven miscarriages before 24 gestational weeks and twenty-eight pregnancies beyond 24 gestational weeks. Using our medical records, we made a retrospective analysis on the association between each body composition index and RPL outcomes in the following year after the initial treatment plans were decided. **[Results]** The miscarriage group had a significant tendency with high volume FFM, while there were no significant differences in age, BMI, %FM, FM, and TBW. **[Conclusion]** This is the first study that investigated the correlation between body composition and RPL among Japanese women. Our study indicated that each body composition index can have a different impact on RPL prognosis. We will continue this analysis with more eligible cases.

ISP-24-9

Comparison of the histopathology of chronic endometritis with the findings of hysteroscopy performed immediately after menstruation Sawai Yudai¹, Mitsui Takashi¹, Okamoto Ryota¹, Kashino Chiaki¹, Kubo Kotaro¹, Kamada Yasuhiko¹, Nakatsuka Mikiya², Masuyama Hisashi¹ *Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences¹, Health Sciences, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences²*

[Objective] Chronic endometritis (CE) is associated with infertility and recurrent miscarriage. Diagnosis of CE is made by endometrial histopathology during the implantation window. Diagnosis of CE by hysteroscopy (HFS) during the proliferative phase has been reported, but not established. In this study, we compared the histopathology of CE with the findings of HFS in the proliferative phase. **[Methods]** A total of 73 patients who underwent HFS and endometrial histopathological assessment from January 2018 to March 2021 were included. Endometrial histopathology was assessed in the middle of the implantation window; CE was diagnosed when one or more CD138-positive cells were found by immunohistochemical staining, while HFS was performed within 7 days from the end of menstruation. The presence or absence of characteristic findings of CE (micropolyps and/or hyperemic endometrium) was evaluated. **[Results]** Of 73 patients, 43 (58.9%) experienced infertility, 34 (46.6%) experienced recurrent miscarriage, and 4 (5.5%) experienced both; HFS showed CE-related characteristic findings in 27 patients (37.0%), micropolyps in 12 (16.4%), hyperemic endometrium in 22 (30.1%), and both in 7 (9.6%). Five of 28 patients (17.8%) without HFS-related findings were diagnosed with CE, compared with 6 of 12 (50.0%) diagnosed with micropolyps and 11 of 22 (50.0%) diagnosed with hyperemic endometrium ($p=0.06$ and $p=0.03$, respectively). Seven of nine patients (77.8%) who were suspected for infertility due to implantation failure and were treated with doxycycline in our hospital achieved a successful pregnancy. **[Conclusion]** HFS performed during the proliferative phase might be useful for the diagnosis of CE.

ISP-24-10

Association between antinuclear antibodies and pregnancy outcome in patients with recurrent pregnancy loss Yoshihara Hiroyuki, Goto Shinobu, Kitaori Tamao, Suzumori Nobuhiro, Sato Takeshi, Sugiura Mayumi *Nagoya City University*
[Objective] Although an association between antiphospholipid antibodies and recurrent pregnancy loss (RPL) has been established, the possibility that antinuclear antibodies (ANA) may be involved in RPL remains controversial. We therefore con-

ducted the present study to evaluate whether ANA affects subsequent live births in patients with RPL. **[Methods]** All were seen in our hospital from 2006 to December 2019. The following pre-pregnancy tests ruled out uterine malformations, and antiphospholipid syndrome, an abnormal chromosome in either partner. Since some unexplained patients wished for medication, such patients were also excluded from the analysis. Thus, the present study included 798 patients with a history of two or more pregnancy losses and the next pregnancy. ANAs were measured by indirect immunofluorescence on Hep-2 cell slides. **[Results]** The rate of ANA-positive patients was 39.0% (390/1000) when the 1:40 dilution result was positive. With a 1:160 dilution, it was 3.50% (35/1000). With the use of the 1:40 dilution, Analyzing only live births and euploid miscarriage, live birth rates were 92.4% (220/238) for the ANA-positive group and 92.0% (346/376) for the ANA-negative group. Subgroup analyses were performed for each pattern on immunofluorescence staining, but there was no significant difference in the live birth rate between the two groups. **[Conclusion]** We examined whether ANA predict the next pregnancy prognosis for 798 patients with RPL, however, we found no predictive value of ANA. ANA is a biomarker for autoimmune diseases screening such as SLE, but it does not seem to be a biomarker for prognosis of pregnancy in patients with RPL.

ISP-24-11

Abnormal ciliogenesis in decidual stromal cells in recurrent miscarriage Hassan Esraa *Nagoya City University*

[Objective] To know the difference between normal pregnancy and recurrent miscarriage (RM) at the cellular level focusing on primary cilia and TGF- β signaling. **[Methods]** The decidual tissues of 8 patients with unexplained RM and 7 pregnant controls who underwent an artificial abortion were used. Immunohistochemistry was performed using antibodies against primary cilia, extravillous trophoblasts (EVTs), macrophages, uterine Natural Killer (uNK) cells, decidual stromal cells, and the activation of TGF- β , and CREB signaling in the decidua of early pregnancy was studied. **[Results]** The density of decidual stromal cells, but not EVT, macrophages, or uNK cells, was found to be significantly higher in the decidua of patients with RM compared to healthy controls. The percentage of ciliated decidual stromal cells was significantly decreased in RM decidua compared to healthy control decidua. There was no difference in the primary ciliary length on decidual stromal cells between RM and healthy controls. Regarding TGF- β signaling, p-Smad2 in these cells was diminished significantly in patients with RM, and 86% and 80% of cilia were detected in p-Smad2-positive decidual stromal cells, meaning that most of the TGF- β -activated decidual stromal cells of both RM patients and healthy controls have primary cilia. As for the activation of transcriptional factor CREB, no difference was found between RM patients and healthy controls. **[Conclusion]** Abnormal primary cilia on decidual stromal cells may be one of the explanatory factors of unknown RM. The inactivation of TGF- β signaling may lead to abnormal ciliogenesis in the decidua.

ISP-25-1

Preterm premature rupture of membranes secondary to amniocentesis for diagnosis and subsequent evaluation of intra-amniotic infection or inflammation Nakagawa Takuya¹, Tsumura Keisuke², Yoshitake Kaoruko², Gondo Kanako², Ookuma Kana², Tsuda Satoko², Oshima Yuko², So Kunio², Ono Takeshi², Kozuma Yutaka², Nomiya Makoto² *Takagi Hospital¹, Saga Hospital²*

[Objective] This study aimed to examine the incidence, associated factors, and their effects of preterm premature rupture of

membranes (PPROM) secondary to amniocentesis for diagnosis and subsequent evaluation of intra-amniotic infection or inflammation. **[Methods]** Among singleton pregnancies with preterm labor, cervical insufficiency and maternal fever were managed in hospital from June 2014 to March 2019, including cases of amniocentesis for intra-amniotic infection or inflammation. Cases with persistent genital bleeding and other were excluded; PPRM secondary to amniocentesis was identified by time elapsed after amniocentesis and the number of occurrences per day. Clinical data were compared with and without PPRM secondary to amniocentesis, to exclude the effects of intra-amniotic inflammation; the same analysis was performed in cases with intra-amniotic inflammation only. **[Results]** 118 were finally analyzed (28 cases underwent serial amniocentesis). PPRM secondary to amniocentesis could be defined as occurring within 24 hours and was seen in 4 cases (3.4%). All four of them were associated with intra-amniotic inflammation; none was associated with serial amniocentesis. In the 44 cases with intra-amniotic inflammation, no significant association was found between PPRM secondary to amniocentesis and preterm birth within 2 or 7 days after amniocentesis. **[Conclusion]** Frequency of PPRM secondary to amniocentesis for diagnosis of intra-amniotic infection or inflammation was 3.4%; PPRM secondary to amniocentesis was associated with intra-amniotic inflammation and not with preterm birth within 2 and 7 days. There was no increased frequency of PPRM secondary to amniocentesis for subsequent evaluation of intra-amniotic infection or inflammation.

ISP-25-2

Accuracy of prenatal factors such as amniotic fluid findings for diagnosis of fetal inflammatory syndrome Ohkuma Kana, Kozuma Yutaka, Yoshitake Kaoruko, Gondo Kanako, Ikeda Masazumi, Tsuda Satoko, Oshima Yuko, So Kunio, Ono Takeshi, Tsumura Keisuke, Nomiya Makoto *Saga Hospital*
[Objective] Prenatal factors such as amniotic fluid IL-6 levels show good diagnostic accuracy for FIRS. **[Methods]** We investigated 232 women with singleton pregnancies, who underwent amniocentesis for evaluation of intra-amniotic inflammation or infection at 22+0 to 36+6 weeks' gestation and delivered within 24 hours at our hospital between August 2014 and March 2020. We excluded women who underwent amniocentesis after onset of labor. Spearman's rank correlation coefficient was used to confirm the correlation between amniotic fluid interleukin (IL)-6 and umbilical cord blood IL-6 levels, and the area under the curve (AUC) and cut-off value of amniotic fluid IL-6 for diagnosis of FIRS were calculated using the receiver operating characteristic curve. Multivariate logistic analysis and stepwise variable section were used to determine the factors associated with FIRS and the diagnostic system of the estimating equation. **[Results]** Finally, we analyzed data of 160 patients. The correlation coefficient for the association between amniotic fluid IL-6 and umbilical cord blood IL-6 levels was 0.69 ($P=0.0001$). The amniotic fluid IL-6 cut-off value for diagnosis of FIRS was ≥ 15.5 ng/mL (AUC=0.93, sensitivity and specificity 80% and 90%, respectively). Multivariate logistic analysis showed that amniotic fluid IL-6 levels ≥ 15.5 ng/mL, gestational age at amniocentesis, and microbial invasion of the amniotic cavity (MIAC) were independently associated with FIRS, and the AUC of the estimating equation combining the three factors was 0.94. **[Conclusion]** Prenatal factors such as amniotic fluid IL-6 levels show good diagnostic accuracy for FIRS.

ISP-25-3

Intra-amniotic inflammation with maternal inflammatory response including histological chorioamnionitis Gondo Kanako,

Tsumura Keisuke, Ikeda Masazumi, Yoshitake Kaoruko, Ookuma Kana, Tsuda Satoko, Oshima Yuko, So Kunio, Ono Takeshi, Kozuma Yutaka, Nomiya Makoto *Saga Hospital*
[Objective] Maternal inflammatory response (MIR) including histological chorioamnionitis is defined as the infiltration of neutrophils into the subchorionic fibrin, chorion, and amnion. This study aimed to determine the relationship between MIR and the degree of intra-amniotic inflammation and presence of microorganisms in the amniotic fluid. **[Methods]** From August 2014 to April 2020, patients with preterm delivery with intra-amniotic inflammation or infection confirmed by transabdominal amniocentesis within 24 hours before labor were included. Cases with intra-amniotic inflammation or infection were already confirmed before final amniocentesis and others were excluded. **[Results]** After exclusion, 57 cases were included in the analysis. Positive amniotic fluid culture was confirmed to be an independently associated factor for MIR using logistic regression analysis. Minimum amniotic fluid IL-6 levels for MIR in positive and negative bacterial cultures of amniotic fluid were 5.0 ng/mL and 13.1 ng/mL, respectively. The frequency of MIR at each minimum amniotic fluid IL-6 level (or higher) and the proportion of stages 2/3 among cases with MIR were higher in cases with positive bacterial cultures of amniotic fluid than in cases with negative cultures (92% (23/25) and 50% (8/16), respectively, $p=0.007$), (83% and 38%, respectively, $p=0.03$). **[Conclusion]** Expression of MIR is generally weaker in intra-amniotic inflammation with negative bacterial culture of amniotic fluid rather than in culture-positive cases, whereas there may be cases where no association with MIR was found.

ISP-25-4

Effect of maternal steroid and antimicrobial administration on amniotic fluid interleukin-6 Ikeda Masazumi, Yoshitake Kaoruko, Gondo Kanako, Okuma Kana, Tsuda Satoko, Oshima Yuko, So Kunio, Ono Takeshi, Kozuma Yutaka, Tsumura Keisuke, Nomiya Makoto *Saga Hospital*
[Objective] This study aimed to determine the effects of maternally administered drugs (steroids and antimicrobials) on intra-amniotic inflammation (IAI). **[Methods]** From August 2014 to April 2020, we retrospectively reviewed singleton patients with PPRM between 22 weeks and 33 weeks 6 days of gestation who underwent amniocentesis at the time of diagnosis. We excluded patients who delivered less than 5 days after the first amniocentesis, those who did not receive steroids and antimicrobials, and those who did not receive SBT/ABPC+AZM for intra-amniotic infection. Patients were classified into group A (with IAI and positive bacterial culture), group B (with IAI and negative bacterial culture), and group C (without IAI and negative bacterial culture), according to the results of the initial amniotic fluid interleukin (IL)-6 detection. Changes in amniotic fluid IL-6 levels before and 6 days after maternal drug administration and rate of change in IL-6 levels were compared among the three groups. **[Results]** In the final analysis of 23 patients, group A (6 patients), group B (4 patients), and group C (13 patients) all showed a decrease in amniotic fluid IL-6 levels, with P values of 0.03, 0.13, and 0.006, respectively, while the median rates of change were -0.93, -0.55, and -0.52, respectively. The rate of change in group A was significantly greater than those in groups B and C, with p values of 0.048 and 0.008, respectively. **[Conclusion]** Our results suggest the usefulness of SBT/ABPC+AZM in the treatment of intra-amniotic inflammation with microbial invasion of the amniotic cavity.

ISP-25-5

Amnion epithelial cells can potentiate the proliferation in cases with preterm premature rupture of membrane

(pPROM) and bulging fetal membranes Matsuzaka Yu, Mogami Haruta, Yasuda Eriko, Inohaya Asako, Takakura Masahito, Ueda Yusuke, Kawamura Yosuke, Chigusa Yoshitsugu, Mandai Masaki *Kyoto University*

[Objective] pPROM is a major cause of preterm birth that leads to severe perinatal morbidity and mortality. The aim of this study was to find whether the amniotic membrane has capability to protect itself from damages causing pPROM. **[Methods]** Tissue preparations of human amnion were collected from patients with cesarean birth between 23 to 25 weeks of gestation. Six cases with pPROM or bulging fetal membranes (stressed membrane group) and six cases of control (non-reassuring fetal status or hypertensive disorder of pregnancy) were compared. Specimens with severe epithelial necrosis were excluded. This study was approved by the ethics committee in our institute. **[Results]** In the stressed membrane group, shedding and necrotic changes of amnion epithelial cells were prominent whereas these findings were not observed in control (54.0% and 18.3%, respectively, $p=0.021$). At placental amnion, the rate of ki67 positive cells was significantly higher in the stressed membrane group than that in control ($0.23 \pm 0.09\%$ and $0.84 \pm 0.24\%$, respectively, $p=0.036$). At reflected amnion, the rate of Ki67+ cells tended to be higher in stressed fetal membranes than that in control ($0.45 \pm 0.25\%$ and $0.064 \pm 0.042\%$, respectively, $p=0.062$). There were no significant differences in the rate of ki67 positive cells between placental and reflected amnion. Cleaved caspase-3 positive cells were not observed in either group. **[Conclusion]** In pPROM and budging fetal membranes, proliferation of amnion epithelial cells was stimulated. This might be a recovery reaction from various stresses to fetal membranes, although further studies are needed.

ISP-25-6

The role of prostaglandins in the healing of fetal membranes Takakura Masahito, Mogami Haruta, Matsuzaka Yu, Yasuda Eriko, Inohaya Asako, Ueda Yusuke, Kawamura Yosuke, Chigusa Yoshitsugu, Mandai Masaki *Kyoto University*

[Objective] Preterm prelabor rupture of membrane (pPROM) is associated with preterm deliveries. However, spontaneous sealing of the ruptured fetal membranes are sometimes observed. Prostaglandins (PGs) are involved in the wound healing process, such that PGE2 promote tissue regeneration of colon and liver. In addition to uterine contraction and cervical ripening, we hypothesized PGs might also be involved in the healing of fetal membranes. Here, the roles of PGs in the healing of fetal membranes were investigated. **[Methods]** Fetal membranes of pregnant C57/BL6 mice were punctured with a sterile 20-gauge needle by laparotomy under general anesthesia on 15 dpc. In each uterus, half of gestational sacs were punctured and half were not. Gestational sacs were collected at 24 hours after rupture of membrane and histologically analyzed. The differential gene expression between ruptured and intact site of fetal membrane was analyzed by qPCR. **[Results]** The expression of *COX2* mRNA, a rate-limiting enzyme of PGs, was significantly upregulated in ruptured site than that in intact site ($x2.49$, $n=12$, $p<0.05$). In immunofluorescence, *COX2* was expressed in the ruptured site of amnion mesenchymal cells, whereas it was not in the intact site. mRNA levels of prostaglandin E2 synthase (*PTGES*) was not upregulated ($x1.46$, $n=12$, $p=0.17$), whereas prostaglandin I2 synthase (*PTGIS*) was significantly upregulated ($x2.63$, $n=10$, $p=0.02$) in ruptured site. **[Conclusion]** Prostaglandin synthesis seems to be promoted in the ruptured site of fetal membranes, which might be involved in the wound healing of fetal membranes.

ISP-25-7

Medroxyprogesterone acetate has anti-inflammatory effects on human amnion Teraoka Yuko¹, Konishi Haruhisa², Sugimoto Jun¹, Koh Iemasa¹, Kudo Yoshiki¹ *Hiroshima University¹, Miyoshi Central Hospital²*

[Objective] We generated dentally infected mice with *Porphyromonas gingivalis* (*P.g.*), a periodontal pathogen, and reported its usefulness as a model of chronic inflammation and preterm birth. Treatment of these *P.g.*-infected mice with natural progesterone (P4) improved the shortened gestational period and suppressed inflammatory cytokines in the fetal membrane which was the main part of inflammation. The relationship between the anti-inflammatory effects of progesterone in fetal membranes and its associated effects on preventing preterm birth remains unclear. In this study, we investigated the anti-inflammatory effects of natural progesterone (P4) and medroxyprogesterone acetate (MPA) in *P.g.*-LPS stimulated primary human amniotic mesenchymal cells (hAMC). **[Methods]** Amniotic membranes were obtained from the placenta of cesarean section with the consent of the patients. The hAMC were isolated and pretreated with P4 or MPA for 12 hours. After stimulation with *P.g.*-LPS, gene expression of inflammatory cytokines and COX-2 was measured by real-time RT-PCR. **[Results]** The *P.g.*-LPS stimulation induced gene expression of IL-1 β , IL-6, TNF α and COX2 in hAMC. Even though P4 had little effect on *P.g.*-LPS stimulation, MPA treatment significantly decreased the inflammatory cytokine expressions. **[Conclusion]** MPA showed anti-inflammatory effects on hAMC, suggesting that it may be effective in preventing preterm birth induced by inflammation of the amnion. Further analysis of anti-inflammatory effects of MPA in hAMC may improve our understanding of the mechanism of human preterm birth.

ISP-25-8

Examination of the usefulness of therapeutic cervical cerclage in maternal transport Minamoto Toshiko¹, Hara Tomomi¹, Nonomura Yuki¹, Kanasaki Haruhiko¹, Kyo Satoru¹, Kurioka Hiroko² *Shimane University¹, Shimane Prefectural Central Hospital²*

[Objective] The difficulty of the cerclage is high in cervical shortening (≤ 25 mm) and prolapsed membranes at maternal transport, and may be lead to premature rupture of membranes or labor. We considered whether cerclage for short cervix and prolapsed membranes at maternal transport contributed to the prolongation of the pregnancy period regardless of the past premature birth. **[Methods]** We focused on singleton pregnancies between Jan 2008 and May 2018. The number intended for prolapsed membranes and short cervix (25 mm or less) in 20-25 weeks in this study. We intended for 33 cases that we excluded the cases CRP1.0 or more at first visit, multiple birth, premature rupture of membranes, cases that had already been cerclaged. All statistical analyses were conducted using SPSS, the threshold for statistical significance set at $p<0.05$. **[Results]** The average weeks of delivery in the cerclage group was 38.3 weeks, that in the non-cerclage group was 29.7 weeks, and the cerclage group showed a significant prolongation. Birth weight was 2993 g in the cerclage group and 1641 g in the non-cerclage group, which were significantly heavier. **[Conclusion]** There are few report investigating the usefulness of therapeutic cervical cerclage for cases of cervical shortening at maternal transport, including regardless of the past premature birth. In addition, it is difficult to make a rigorous diagnosis of the presence of chorioamnionitis at first visit. This study suggests the usefulness of therapeutic cervical cerclage even in such urgent situations.

ISP-25-9

Rate of spontaneous preterm delivery between gestational diabetes and normal pregnancy Boriboonhirunsarn Dittakarn, Tanpong Sirikul *Siriraj Hospital, Mahidol University, Thailand*
[Objective] To compare the rate of spontaneous preterm delivery between GDM and normal pregnancy. Pregnancy outcomes and associated risk factors for spontaneous preterm delivery were evaluated. **[Methods]** A retrospective cohort study was conducted in 120 GDM and 480 normal pregnant women. All women received GDM screening with 50-g GCT and 100-g OGTT at first visit and repeated at 24-28 weeks. Data was retrieved from medical records, including baseline and obstetric characteristics, preterm risks, GDM risks, and pregnancy outcomes. Spontaneous preterm birth was defined as delivery before 37 completed weeks of gestation that had been preceded by spontaneous labor. **[Results]** GDM women were more likely to be 30 years ($p=0.032$), and have previous GDM ($p=0.013$). Incidence of overall preterm delivery was significantly higher in GDM women (17.5% vs. 8.5%, $p=0.004$) as well as incidence of spontaneous preterm delivery (15.8% vs. 7.1%, $p=0.004$). GDM women had less gestational weight gain ($p<0.001$) and were less likely to have excessive weight gain ($p=0.002$). GDM women were more likely to deliver LGA ($p=0.02$) and macrosomic infants ($p=0.027$). Neonatal hypoglycemia was significantly more common among GDM ($p=0.013$). Multivariate analysis showed that, after adjusting for potential confounders, previous preterm birth and GDM independently increased risk of spontaneous preterm delivery (adjusted OR 2.56, 95%CI 1.13-5.79, $p=0.024$ and adjusted OR 2.15, 95%CI 1.2-3.84, $p=0.010$, respectively). **[Conclusion]** GDM and previous preterm birth significantly increased the risk of spontaneous preterm delivery. GDM also increased the risk of LGA, macrosomia, and neonatal hypoglycemia.

ISP-25-10

Absolute Quantification of 16S Ribosomal DNA in Amniotic Fluid Can Help Determine the Termination of Pregnancy Urushiyama Daichi¹, Miyata Kohei¹, Kiyoshima Chihiro¹, Izuchi Daisuke¹, Fukagawa Satoshi¹, Sanui Ayako¹, Kurakazu Masamitsu¹, Nomiyama Makoto², Hata Kenichiro³, Miyamoto Shingo¹ *Fukuoka University Hospital¹, Saga Hospital², Department of Maternal-Fetal Biology, National Center for Child Health and Development³*

[Objective] Intra-amniotic infection (IAI) can be diagnosed by amniocentesis and eradicated using antibiotics. However, currently, there are no appropriate methods of managing IAI. This study aimed to evaluate the amounts of bacteria in amniotic fluid (AF) by assessing the copy number of 16S ribosomal DNA (c16S) to clarify the association with perinatal outcomes and provide a deadline for pregnancy termination. **[Methods]** Overall, 69 women who had preterm labor underwent amniocentesis owing to suspected IAI before 34 weeks of gestation at one of two hospitals during 2011-2020. The c16S in 1 mL of AF was measured using droplet digital PCR. IAIs were identified as Grade 3 (G3), 1-2 (G1-2), and 0 (G0) depending on c16S, $\geq 10^6$, 10^4 - 10^6 , and $<10^4$ copies/mL, respectively. A case-control study was performed in G3 ($n=30$), G1-2 ($n=22$) and G0 ($n=17$). **[Results]** All cases were not clinical chorioamnionitis, and antibiotic administration was started after amniocentesis in all cases. The number of patients who delivered within 24 and 48 hours after amniocentesis were G3 : 21, 25 (70%, 83%), G1-2 : 14, 19 (64%, 84%), and G0 : 3, 6 (18%, 35%), respectively. The cases of historical CAM (Stage III, Blanc's classification) and funisitis were G3 : 25, 24 (83%, 80%), G1-2 : 6, 10 (27%, 45%), and G0 : 0, 1 (0%, 6%), respectively. G3 was significantly higher than G0 in all items (max $P=0.003$) and G1-2 in histological diagnosis (CAM

Stage III : $P<0.001$, Funisitis : $P=0.017$). **[Conclusion]** In G3 IAI, early termination of pregnancy would be desirable since prolonged pregnancy was hopeless.

ISP-25-11

Association between Maternal Serum C-Reactive Protein in Early Pregnancy and Spontaneous Preterm Delivery Kyaw Ei M, San Cherry *Shan State, University of Medicine, Taunggyi, Myanmar*

[Objective] -To determine the serum C-reactive protein level of pregnant women of less than 22 weeks gestation -To identify the preterm delivery rate among the study population -To find out the association between maternal serum C-reactive protein in early pregnancy and spontaneous preterm delivery **[Methods]** - This study is a hospital based prospective study and study period was one year that was carried out in antenatal outpatient clinic of Central Women's Hospital. All singleton pregnancies of less than 22 weeks gestation with no history of medical diseases and no past history of preterm deliveries were measured serum CRP level for one time during their antenatal visit. And they were followed up throughout their pregnancies until delivery, noted the gestational age at delivery and occurrence of preterm delivery was assessed. Prematurity was assessed by Ballard Score under the supervision of Paediatrician. **[Results]** -Out of 234 women, eight women had preterm deliveries (3.4%) and 226 women had term deliveries (96.6%). Among 201 women whose CRP level ≤ 6 , there were 5 women who delivered preterm. Among women of CRP >6 mg/L, there were 3 women who delivered preterm ($p=0.087$). **[Conclusion]** -When compared the CRP levels between term deliveries and preterm deliveries, the mean CRP value was not significantly different. Therefore it cannot be used as a biochemical marker for prediction of preterm delivery. Moreover, it cannot be further used as help in making decision for time of delivery and the management strategies to improve the maternal and fetal outcomes.

ISP-25-12

Development of novel therapeutic agents for preterm labor using glycosaminoglycan chain-remodeled urinary trypsin inhibitor Kodama Tomoe¹, Tanaka Kanji¹, Tanaka Seigo², Ito Asami¹, Yokoyama Yoshihito¹ *Hirosaki University Hospital¹, Mutsu General Hospital²*

[Objective] Urinary trypsin inhibitor (UTI), which is derived from fetal urine and found in large quantities in the amniotic fluid, is known to inhibit inflammation of the cervix, ripening, and uterine contraction by decreasing various proteases and cytokines. In this study, we first clarify the role of glycosaminoglycans in the anti-inflammatory effects of UTI using a series of remodeled glycosaminoglycan (GAG) chains of UTI and then identify the glycan structures that contribute to its more potent anti-inflammatory effects. In the future, we aim to develop new drugs for preterm birth that are more effective than natural UTIs. **[Methods]** GAG chain-remodeled UTIs were prepared according to previously reported methods. Patients who consented to participate in the research were included, and cervix tissue (1 cm²) was collected from residual specimens obtained from a total hysterectomy. Cervical fibroblasts were isolated from the specimens and cultured. Next, lipopolysaccharide (LPS) was added to the cervical fibroblast culture system and used as an inflammation model. The expression of cytokines involved in cervical ripening (IL-8) and receptors involved in the signal transduction of LPS-stimulated inflammation (toll-like receptor 4 (TLR4)) were measured using an enzyme-linked immunosorbent assay and quantitative real-time polymerase chain reaction. **[Results]** GAG chain-remodeled UTIs showed greater anti-inflammatory effects than natural UTIs. **[Conclusion]** The gly-

can moiety may be important for the anti-inflammatory effect of UTI. We report the details of this study with a discussion of the literature.

ISP-25-13

Pregnancy is a State of Balance between Two Opposing Interactive Forces, Mechanisms, and Systems : A Hypothesis Hegazy Ali *Portiuncula University Hospital, Ireland*

[Objective] The mechanisms responsible for maintaining pregnancy and initiating parturition have not been fully elucidated in any species. Failures in understanding uterine functions during pregnancy are a major shortcoming of modern healthcare. **[Methods]** 1. This study investigated the current evidence-based literature and research that may support our proposed hypothesis. 2. A 40-second 3D animation was developed in conjunction with a Houston-based medical company to support this hypothesis. **[Results]** and **[Conclusion]** Uterine mechanotransduction has functional and molecular components, wherein the uterine wall tension (UWT) is the functional component and intrinsic myometrial cell character (IMCC) is the molecular component. IMCC enables the uterus to control its functions both autonomically and intrinsically, secondary to changes in tension, where high tension induces relaxation and low tension induces contraction. UWT is created and maintained by a complex interaction among the gestational sac, uterus, and cervix, for which the primary function is to maintain the UWT. An exponential increase in UWT throughout pregnancy induces the inhibitory system, which is the main system that maintains pregnancy through a stretch-dependent mechanism, in addition to direct myometrial relaxants. Contractions of the complex uterine system § lead to the development of two forces in opposite directions, creating the direct and indirect uterine cervical interaction (DIDUCI). DIDUCI makes the cervix loses its strength through TYVU pattern formation and transforms into the lower uterine segment where the U pattern initiates labor. There is evidence-based support for the hypothesis which might be the first step in uncovering the mystery of human parturition.

ISP-26-1

Low-dose aspirin therapy improves perinatal outcomes and is associated with placental pathology Tomimori Kayo¹, Satou Yuuichiro², Obata Shizuka¹, Osawa Ayako¹, Yoshimoto Nozomi¹, Muraoka Junsuke¹, Matsuzawa Satoshi¹, Kodama Yuki¹, Katsuragi Shinji¹ *University of Miyazaki Hospital¹, Division of Pathology, University of Miyazaki Hospital²*

[Objective] Hypertensive disorders of pregnancy is an important perinatal disease that can cause serious problems for both infant and mother. Low-dose aspirin (LDA) has been used to prevent preeclampsia, but it is unclear how LDA improves the maternal-placental circulation. The aim of this study was to investigate the effects of LDA based on clinicopathological analysis of placental tissue. **[Methods]** Perinatal outcomes and pathology of the placenta were analyzed in patients with a history of preeclampsia (n=27, 2011-2021) in a single center. Of these patients, 10 were treated with LDA (LDA group) and 17 were treated without LDA (control group). Perinatal outcomes and pathological findings were compared between the two groups. **[Results]** The frequencies of preeclampsia and emergency Cesarean section were significantly lower, and the median pregnancy period and birth weight were significantly higher in the LDA group (all p<0.05). Histopathologically, the LDA group had a lower incidence of decidual thrombosis (p<0.05). **[Conclusion]** LDA improved perinatal outcomes of patients with a history of preeclampsia. The lower incidence of decidual thrombosis with LDA treatment suggests a mechanism in which LDA has an effect on preeclampsia.

ISP-26-2

Inhibitory Effect of Magnesium Sulfate on Vascular Endothelial Damage in preeclampsia Moriuchi Kaori¹, Kawasaki Kaoru¹, Ueda Akihiko², Mogami Haruta², Mandai Masaki², Matsumura Noriomi¹ *Kindai University Hospital¹, Kyoto University Hospital²*

[Objective] The etiology of preeclampsia is still not completely clarified, but it is speculated that increased oxidative stress leads to vascular endothelial dysfunction and maternal organ damage. Magnesium Sulfate (MgSO₄) is generally used to prevent and treat seizure for 48 hours in cases of preeclampsia. The purpose of this study was to investigate whether long-term administration of MgSO₄ alleviates vascular endothelial dysfunction in preeclampsia. **[Methods]** We use MgSO₄ not only for patients with hypertensive disorder of pregnancy with severe blood pressure (conventional indication) but also for patients with organ damage regardless of blood pressure level (novel indication) from diagnose till at least 24 hours postpartum. We retrospectively investigated the blood coagulation function (the level of fibrinogen and platelets) and perinatal outcome of 34 cases treated with MgSO₄ for novel indication from 2013 to 2021. **[Results]** Median gestational age at diagnosis of preeclampsia was 30 (25-33) weeks. The level of fibrinogen and platelets were increased after MgSO₄ administration in 28 cases (82.3%) and 28 cases (82.3%), respectively. The median gestational age at delivery was 33 (27-35) weeks. Median duration of expectant management under MgSO₄ administration was 8 (5-16) days. 20 cases (58.8%) were able to maintain pregnancy for more than 7 days. The breakdown of indications for delivery were maternal complication (15 cases), non-reassuring fetal status (13 cases) and attainment of 37 weeks' gestation (1 case). **[Conclusion]** In preeclampsia, MgSO₄ may improve blood coagulation function and contribute to good pregnancy outcome.

ISP-26-3

Early prediction of hypertensive disorders of pregnancy using advanced machine learning Nagayasu Yoko, Yano Keiko, Fukunishi Tomomi, Natsuyama Koichiro, Masuda Yuki, Takaki Yumika, Nunode Misa, Sawada Masami, Sugimoto Atsuko, Fujita Daisuke, Ohmichi Masahide *Osaka Medical and Pharmaceutical University*

[Objective] The aim of this study is to establish effective models to predict hypertensive disorders of pregnancy (HDP). **[Methods]** The data were collected from perinatal records of all deliveries at our institute between January 2014 and August 2021. We classified the deliveries after 22 gestational weeks into the following outcomes : (1) no HDP or (2) HDP. While evaluating them, we selected 54 variables as risk factors during the first trimester. Based on a machine learning (ML) -driven selection method, 12 variables were selected. We constructed three models : the logistic regression (LR) model, the random forest (RF) model and the convolutional neural network (CNN) model. **[Results]** 3,346 deliveries were eligible during the period (including 237 cases of HDP). A total of 2,510 and 836 cases were included in the training and testing sets respectively. Of the three models, the best model was the CNN model, with an accuracy of 82% and an AUC of 0.80. The RF model had an accuracy of 79% and an AUC of 0.78. Finally, the LR model had an accuracy of 74% and an AUC of 0.72. In the RF model, the importance score was highest for hypertension complications, second for pre-existing HDP and third for BMI. **[Conclusion]** We employed ML models that achieved high accuracy in predicting HDP in the first trimester. Advanced ML models are able to include many different factors, allowing the risk of HDP to be analyzed based on the complex factors of early pregnancy.

ISP-26-4

The expression alteration of placental inflammatory factor according to onset period in preeclampsia Kim Seung-Chul, Jo Hyun-Bin, Kim In-Hye, Kang Seung-Wan, Lee Sul *Pusan National University College of Medicine, Korea*

[Objective] To investigate whether the serum concentration of calprotectin, tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) in preeclampsia (PE) are changed depending on the onset-period. **[Methods]** The concentration of calprotectin, TNF- α and IL-6 were measured in serum of preeclampsia and normotensive pregnancy. The levels of these inflammatory factors in serum were measured using enzyme-linked immunosorbent assay (ELISA). ANOVA test was used to compare among early onset PE, late onset PE and normotensive pregnancy. **[Results]** The concentration of calprotectin was statistically significant between normotensive pregnancy and early onset PE ($p < 0.05$). TNF- α was also statistically significant alteration between normotensive pregnancy and PE group. IL-6 was statistically significant between normotensive pregnancy and late-onset preeclampsia instead. **[Conclusion]** There results seems to be a difference in the inflammatory factors expressed according to the onset period of preeclampsia, and it can be inferred that these alterations interlocked with each other are also related to the severity of preeclampsia according to the onset period.

ISP-26-5

The relationship between the placental hemodynamics evaluated by 3D vocal power Doppler and placental histological analysis in the pregnant women with normal and preeclampsia Sakuragi Toshihide, Shibata Eiji, Kinjo Yasuyuki, Yoshino Kiyoshi *University of Occupational and Environmental Health*

[Background] Pre-eclampsia (PE) are mainly caused by uterine placental perfusion disturbance due to uterine spiral artery remodeling disorder, but it is difficult to accurately detect blood remodeling disorder from the spiral artery to the intervillous space. **[Objective]** We investigated whether vascularization index (VI), flow index (FI), and vascularization flow index (VFI) correlate with the pathological structure of placenta and whether there was any difference in VI, FI, VFI and placental pathological structure between Normal group and PE group. **[Methods]** 55 pregnant women (Normal group : n=27, PE group : n=28) underwent for VI, FI, and VFI at four locations on the placenta in the second and third trimesters. Two HE-stained specimens of post-partum placenta were prepared. We randomly selected two of these locations and used Image J, the open source image package, to quantify intervillous blood vessels (IBV), intervillous spaces (IS) and intervillous blood vessels + intervillous spaces (IBV+IS) per unit placenta and analyze their correlation with VI, FI, and VFI. **[Results]** There was no positive correlation between VI, FI, or VFI and IBV, IS, IBV+IS. There were no significant differences in VI, FI, and VFI between the normal and PE groups, but there were significant differences in IBV, IS, IBV+IS in the PE group compared to the normal group. **[Conclusion]** Placental hemodynamics measured by VI, FI, and VFI did not positively correlate with placental morphology at the third trimester. VI, FI, and VFI at the third trimester did not differ between the normal and PE groups, suggesting that they may reflect placental circulatory insufficiency.

ISP-26-6

Comparison of two management for preeclampsia and superimposed preeclampsia : a single center analysis Sakai Atsuhiko, Kamura Shunsuke, Hachisuga Nobutaka, Sugitani Maiko, Hara Emiko, Kido Saki, Fujita Yasuyuki, Kato Kiyoko *Kyushu University Hospital*

[Objective] Although advancement of maternal and neonatal care has improved their prognosis, hypertensive disorders of pregnancy is still a leading cause of maternal and neonatal morbidity and mortality. Therefore, evidence to establish a better management for the disorder is in need. We evaluated pregnancy outcome in patients with preeclampsia (PE) and superimposed preeclampsia (SPE) which were distinctly managed by two strategies. **[Methods]** A retrospective analysis was performed on women with PE or SPE treated at Kyushu university hospital from January 2018 to March 2019 (Period 1 : P1) and from October 2019 to March 2021 (Period 2 : P2). During P1, antihypertensive therapy was started when blood pressure was higher than 160/110mmHg, and pregnancies with severe PE/SPE beyond 34 weeks of gestation were terminated without exception. On the other hand, during P2, antihypertensive drugs were administered when blood pressure was higher than 140/90 mmHg and attempted to extend gestation until 37 weeks of gestation. Maternal and neonatal outcomes were analyzed and compared between two periods. **[Results]** Forty five and 70 cases of PE or SPE were managed during P1 and P2, respectively. Background of the mothers was similar between two groups. Compared with P1, gestational week of delivery was significantly higher in P2. Birth weight of the newborns tended to be larger, and duration of neonatal intensive care unit admission was significantly shorter in the newborns during P2. **[Conclusion]** Aggressive antihypertensive therapy with cautious observation for PE/SPE can extend pregnancy duration, and may benefit the babies born from hypertensive mothers.

ISP-26-7

Maternal deaths due to stroke related to pre-eclampsia significantly associated with delayed intensive observation : The nationwide maternal death analysis Nishimura Yoko², Hasegawa Junichi², Tanaka Hiroaki², Nakata Masahiko², Katsuragi Shinji², Nakamura Masamitsu^{1,2}, Sekizawa Akihiko², Murakoshi Takeshi², Ishiwata Isamu², Kinoshita Katsuyuki², Ikeda Tomoaki² *St. Marianna University¹, The Japan Association of Obstetricians and Gynecologists and the Maternal Death Exploratory Committee (JMDEC) Obstetrics and Gynecology²*

[Objective] To clarify characteristics and recurrent preventive measures of clinical practice in maternal deaths due to stroke related to pre-eclampsia in Japan. **[Methods]** Descriptive study based on the maternal death registration system established by the Japan Association of Obstetricians and Gynecologists and the Maternal Death Exploratory Committee was attempted, in pregnant women died between 2010 and 2020 throughout Japan. Causes related to obstetric medical practice of maternal deaths suffered with stroke and pre-eclampsia were analyzed. **[Results]** In analyzed 477 maternal deaths, 70 (15%) were deaths associated with stroke. 36 cases were associated with pre-eclampsia, of these 20 cases were complicated with HELLP syndrome. 25 cases had pre-eclampsia from outpatients' management (PE outpatient onset group) and 11 cases did after onset of labor (PE labor onset group). 16% (4/25) of cases in outpatient onset group and 36% (4/11) of cases in labor onset group were difficult to save life because of immediate onset of stroke. However, 84% (21/25) of cases in PE outpatients onset group were not admitted to the hospital even occurrence of severe preeclampsia, and 52% (13/25) of them were not taken blood test immediately, resulting in delayed diagnosis of HELLP syndrome. **[Conclusion]** Maternal deaths due to stroke related to pre-eclampsia was significantly associated with delayed admission and point of care blood test in pregnant women suffered severe pre-eclampsia during outpatients' management. For the prevention of stroke due to coagulopathy related to pre-eclampsia, pregnant women should immediately be under the intensive observation with blood test when diagnosis of severe

pre-eclampsia was made.

ISP-26-8

Single-cell transcriptome and T cell receptor analysis revealed the diversity and phenotypic characteristics of decidual CD4+ T cells in normal pregnancies and preeclampsia Tsuda Sayaka, Morita Keiko, Shima Tomoko, Nakashima Akitoshi, Saito Shigeru *University of Toyama*

[Objective] The balance between regulatory T cells (Treg) and conventional T cells (Tconv) is important to maintain allogenic pregnancies. Our objective is to describe the phenotypic characteristics of decidual CD4+ T cells during normal pregnancies and preeclampsia. **[Methods]** Decidual lymphocytes were collected from patients of early gestation (n=2), late gestation (n=2) and early onset preeclampsia (n=1). CD4+ T cells were sorted, and single-cell mRNA derived cDNA were amplified by BD Rhapsody single-cell Analysis System. Targeted T cell response related genes and T cell receptor (TCR) genes were analyzed. **[Results]** 14,603 cells in total and 4553 genes were analyzed. Eleven clusters were identified, 1) four cytotoxic T cell (CTL) like clusters, 2) three naïve clusters, 3) one Treg cluster and three other clusters. Clonally expanded clonotypes were mainly in CTL and Treg clusters. Expanded clones were hardly overlapped between each cluster. CCL4 was up-regulated in expanded clonotypes. The analysis of differentiations status of each cell revealed that expression levels of CCL4 and its receptor, CCR5, were increased as cells differentiate. When gene expressions were compared, CD69 which is the T cell activation marker was down-regulated in most clusters in late gestation than early gestation. Immediate stress response related genes were up-regulated in most clusters in preeclampsia than late gestation. **[Conclusion]** Distinct expanded clonotypes between Treg and CTL like clusters suggest that they recognize different antigens. TCR stimuli and CCL4-CCR5 axis are probably part of the drivers of phenotypic differentiation. Both Treg and CTL like clusters were activated by acute immunogenic stress in preeclampsia.

ISP-26-9

In-utero exposure to preeclampsia induces fetal brain inflammation and neuropsychiatric disorders of the offspring in mice Katoh Yoshihisa¹, Iriyama Takayuki¹, Ichinose Mari¹, Sayama Seisuke¹, Inaoka Naoko¹, Seyama Takahiro¹, Toshimitsu Masatake¹, Kumasawa Keiichi¹, Nagamatsu Takeshi¹, Fujii Tomoyuki², Osuga Yutaka¹ *The University of Tokyo¹, Sanno Hospital, Tokyo²*

[Objective] Although accumulating epidemiological evidence has shown neuropsychiatric disorders including autism develop in the offspring born to mothers with preeclampsia (PE), no animal study has examined its causal relationship. Recently, much attention has been paid to the involvement of intrauterine fetal brain inflammation in the future development of neuropsychiatric disorders. Using PE mouse model, current study aimed to investigate whether maternal PE affects the development of brain disorders in the offspring and its underlying pathophysiology by focusing on fetal brain inflammation. **[Methods]** In the offspring from PE model mice induced by continuous infusion of angiotensinII (n=31) and PBS-administered mice (n=22), 11 behavioral tests to investigate the development and higher brain function were conducted. Quantitative RT-PCR was performed on the whole brain of fetuses from these mice to examine inflammatory cytokine expression (PE : n=35, PBS : n=28). **[Results]** Elevated plus maze test revealed the male offspring from PE mice was more likely to feel anxiety. Moreover, the offspring from PE mice showed more anxiety in open field test. The offspring from PE mice displayed behavioural phenotype of autism

represented by decreased active interaction time in social interaction test. Quantitative RT-PCR revealed mRNA expression of IL6, IL1 β , and TNF- α was significantly enhanced in the fetal brain from PE mice. **[Conclusion]** Current animal study implies that maternal PE could lead to neuropsychiatric disorders such as mood disorder and autism in the offspring, which supports the epidemiological evidence. Enhanced inflammation in the fetal brain might be the key factor in its pathophysiology.

ISP-26-10

Production of Endothelin-1 via the placental (pro) renin receptor in preeclampsia mice models Mishima Sakurako, Mitsui Takashi, Mitoma Tomohiro, Yokohata Satomi, Oohira Akiko, Tani Kazumasa, Maki Jota, Kirino Satoe, Eto Eriko, Hayata Kei, Masuyama Hisashi *Okayama University*

[Objective] Particular focus has been paid to the role of the (pro) renin receptor (PRR) in the pathology of preeclampsia (PE). We examined the production of endothelin-1 (ET-1) via placental PRR in preeclampsia mice models. **[Methods]** ICR female mice were pair-housed with ICR male mice. The presence of a vaginal plug was designated as 0.5 days postcoitum (dpc). At 14.5 dpc, we performed the Reduced Uterine Perfusion Pressure (RUPP) operation : we made a midabdominal incision and ligated the uterine artery. The blood pressures of the mice were measured at 15.5 dpc and 18.5 dpc by the tail-cuff method. At 18.5 dpc, the blood, urine, and placentas were collected. The fetus and placenta were weighed. We evaluated placental hypoxia by quantitative polymerase chain reaction (PCR) using hypoxia-inducible factor-1 α (HIF-1 α) as an index. We also evaluated the expression of PRR, transforming growth factor- β 1 (TGF- β 1), and ET-1 in the placenta by quantitative PCR and Western blotting. The concentration of ET-1 in the blood plasma was assessed by enzyme-linked immunosorbent assay. **[Results]** The blood pressure significantly increased, the proteinuria tended to increase, and the fetal and placental weights became significantly less in the PE model mice. The expressions of HIF-1 α , PRR, TGF- β 1, and ET-1 significantly increased in the placentas of the PE model mice. The concentration of ET-1 in the blood plasma of PE model mice significantly increased. **[Conclusion]** In PE model mice that underwent the RUPP procedure, placental hypoxia increased the expression of PRR, suggesting that ET-1 was increased by intracellular signaling of PRR.

ISP-27-1

Plasmapheresis for pregnant women with Coagulation factor XI deficiency : A case report Saito Yuya, Kumagai Yusaku, Hamada Hirota, Iwama Noriyuki, Tadakawa Mari, Hoshiai Tetsuro, Saito Masatoshi, Yaegashi Nobuo *Tohoku University Hospital*

[Introduction] Coagulation factor XI (fXI) deficiency is a rare disorder with an estimated incidence of 0.0001%. As fXI concentrates are not available in Japan, administration of fresh frozen plasma (FFP) is used as a primary treatment. Considering its rarity, the optimal management of this disease during pregnancy has not been established. Herein, we report a pregnant patient with fXI deficiency who underwent plasmapheresis during the perinatal period. **[Case report]** A 35-year-old woman, treated with prednisolone and immunosuppressive drugs for Mixed Connective Tissue Disease, became pregnant by frozen-thawed embryo transfer. Prolonged activated partial thromboplastin time was detected in her first visit to our clinic. Further blood tests revealed lack of fXI and positive for fXI inhibitor. She was diagnosed as fXI deficiency, and received FFP administration, however, increase of fXI was not to be demonstrated. Termination of the pregnancy was required due to worsening maternal nephritis at 30 weeks gestation. To elimi-

nate the fXI inhibitor, three courses of plasma exchange therapy were performed before delivery, following with planned C-section along with FFP transfusion at 30 weeks and 6 days of gestation. The measured intraoperative blood loss including amniotic fluid was 1225g, and the mother followed a good course. Unfortunately, the infant was diagnosed as periventricular leukomalacia with MRI at 2 months after his birth. **[Conclusion]** Clinical evidence for the perinatal management of pregnant women with fXI deficiency in our country is lacking, thus, treatment against this condition remains challenging. Our case report highlights a conservative treatment strategy combined with plasmapheresis and FFP administration.

ISP-27-2

A case of complete maternal recovery after prolonged cardiac arrest due to uterine rupture Yasuda Ayumi, Tanaka Satomi, Sugawara Mayu, Kido Yuka, Kasahara Taro, Akiba Junya, Murase Yoshiko, Yata Shotaro, Kaneda Hiroshi, Tanaka Toshitaka *Juntendo University Shizuoka Hospital*

Introduction : In-hospital occurrence of maternal cardiac arrest has been reported to be 29-83%. After cardiac arrest, the survival rate decreases by 7-10% every minute. We experienced a case in which cardiac arrest occurred due to massive bleeding because of uterine rupture but recovered without serious complications by continuing cardiopulmonary resuscitation (CPR) over 30 minutes. **Case :** A 26-year-old woman, gravid 2, para 1, showed continuous postpartum hemorrhage with cervical laceration after vaginal delivery. Despite sutured cervical laceration, she was transferred to our hospital due to consciousness disorder by continuous genital bleeding of over 3000g. Upon arrival, her vital signs were as follows : consciousness, JCS 300 ; blood pressure, unmeasurable ; heart rate, 128 beats per minute. Blood test : Hb 1.6g/dL, Fibrinogen 62mg/dL. She urgently underwent a massive transfusion protocol, tracheal intubation, mechanical ventilation and infusion of noradrenaline. We decided to suture the cervical laceration under general anesthesia. However, during operation, we changed to abdominal hysterectomy because uterine rupture was strongly suspected. During hysterectomy, cardiac arrest occurred one hour after the start of operation with total blood loss of 9000g. She achieved return of spontaneous circulation, requiring chest compressions over 30 minutes and 12 mg of adrenaline infusion. After surgery, 24-hour hypothermia therapy was performed in intensive care unit, and consciousness improved the day after rewarming. She was discharged on 18th postoperative day. **Conclusion :** There are no clear criteria for the CPR duration of maternal cardiac arrest but continuing accurate resuscitation can help lifesaving without sequelae.

ISP-27-3

A case of gestational diabetes mellitus diagnosed as type 1 diabetes after delivery Satomi Yukine, Hara Emiko, Kamura Shunsuke, Hachisuga Nobutaka, Sakai Atsuhiko, Sugitani Maiko, Kido Saki, Fujita Yasuyuki, Kato Kiyoko *Kyushu University Hospital*

Gestational diabetes mellitus (GDM) is known as impaired glucose tolerance due to the effects of human placental lactogen and other factors. In some cases of GDM, abnormal glucose tolerance may become apparent during pregnancy, leading to the diagnosis of type 1 diabetes. We report a case of GDM diagnosed with type 1 diabetes after delivery. The patient was a 30-year-old primipara with a family history of type 2 diabetes. At 28 weeks of gestation, she underwent a 75g OGTT, and was diagnosed with GDM. HbA1c was 5.5%, the anti-glutamic acid decarboxylase (GAD) antibody was negative, and immunoreactive insulin was 20.7 μ U/mL. Insulin therapy was started at 34 weeks

of gestation due to poor glycemic control. She was admitted to a hospital at 39 weeks of gestation. Her blood glucose was 180 mg/dl, which was considered difficult to control, and she was transferred to our hospital. On admission, continuous intravenous insulin was initiated, after which the baby was vaginally delivered. The insulin dose was increased to 3 U/min and the blood glucose was 175-200 mg/dl during delivery. The anti-GAD antibody was positive and C-peptide was 0.02 ng/dl, leading to the diagnosis of type 1 diabetes developed during pregnancy. Cases diagnosed and managed as poorly-controlled GDM may have a rapid onset of type 1 diabetes, and it can be difficult to distinguish each other. Type 1 diabetes should be diagnosed early by measuring islet-related antibodies and evaluating insulin secretion capacity in case of poor glycemic control.

ISP-27-4

Ninjin-yoei-tou, influences hemoglobin recovery during preoperative autologous blood donation for cesarean section Yoshida Tomohiro¹, Misugi Takuya¹, Suekane Tomoki¹, Nakai Kensaku¹, Kurihara Yasushi¹, Tahara Mie¹, Hamuro Akihiro¹, Nakano Akemi¹, Tachibana Daisuke¹, Sumi Toshiyuki¹, Koyama Masayasu² *Osaka City University¹, Ishikiriseiki Hospital²*

[Objective] Ninjin-yoei-tou (NYT) is well known as a treatment for anemia, though little is known about the efficacy for pregnant women. In this study, we retrospectively examined the effect of NYT in pregnant women who underwent autologous blood donation. **[Methods]** Between January 2016 and December 2020, pregnant women who underwent cesarean section for placenta previa were selected for the study. Autologous blood donation was performed in case of hemoglobin level was above 10.0 g/dl every seven days until one week before cesarean section. All patients donated 300 ml each time. All patients began daily oral iron medication (100mg/day) at the day of first donation until the day before cesarean section. Group A consisted of women who took oral iron medication only. Group B consisted of women treated with NYT (7.5g/day) in addition to oral iron medication. To evaluate the effect of NYT, hemoglobin (Hb), hematocrit (Ht) and red blood cell (RBC) levels were measured after 7 days of donation (next opportunity of donation). **[Results]** NYT was administered to 28 of 74 patients. At the 7 days after autologous donation, Hb level was reduced by 0.4 g/dl as compared to day of blood donation in group A, whereas Hb level was reduced by 0.1 g/dl in group B with significant difference ($p=0.017$). Similar results were obtained for RBC and Ht. **[Conclusion]** NYT is useful for treatment of anemia during preoperative autologous donation for cesarean section.

ISP-27-5

A case of chronic active Epstein-Barr virus-associated secondary hemophagocytic lymphohistiocytosis in pregnancy Takahashi Masaya, Koizumi Akari, Oguma Kyoko, Ishii Sumire, Ichiyama Takuhiko, Ohno Motoharu, Takamizu Ai, Okumura Toshiyuki, Ujihira Takafumi, Yoshida Koyo, Makino Shintaro *Juntendo University Urayasu Hospital*

Background : Secondary hemophagocytic lymphohistiocytosis (sHLH) is a rare and fatal disease that causes cytokine storms. Unfortunately, this condition can occur even during pregnancy and threaten both maternal and fetal life. Given that delayed diagnosis and treatment can be fatal, early diagnosis with immediate therapeutic interventions is essential. **Case presentation :** A 23-year-old nulliparous woman at 26 weeks of gestation presented with continuous fever, coughing, and sore throat. She visited a general physician but was immediately transferred to our hospital due to her critical status. Upon arrival at our hospital, her temperature was 38°C, and laboratory findings indicated cytopenia (neutrophil count, 779/ μ L ; hemoglobin level, 10.2 g/

dL ; platelet count, 29,000/ μ L), elevated ferritin level (1,308 ng/mL), and elevated soluble IL-2 receptor level (11,200 U/mL). Computed tomography showed marked splenomegaly. A bone marrow examination revealed hemophagocytosis, and blood examination showed plasma Epstein-Barr virus (EBV) DNA quantitation of 8.9×10^7 copies/ μ g DNA. The monoclonal proliferation in EBV-infected T-cells was confirmed by Southern blotting, and the patient was diagnosed with chronic active EBV (CAEBV) -associated sHLH and T-cell lymphoproliferative disease. Immediately after admission, the patient's condition deteriorated, and she developed shock and disseminated intravascular coagulation, requiring endotracheal intubation along with methylprednisolone pulse and etoposide therapy. She was treated with chemotherapies. Although the patient recovered, she delivered a stillborn baby. The patient is scheduled to receive bone marrow transplantation. **Conclusions :** sHLH, which may cause maternal and fetal death, needs to be carefully considered in critically ill pregnant women, especially those who present with continuous fever and cytopenia.

ISP-27-6

Case report of fourteen pregnant women with syphilis Kubota Iroha, Deguchi Masashi, Tanimura Kenji, Shi Yutoku, Uchida Akiko, Shirakawa Tokuro, Imafuku Hitomi, Terai Yoshito *Kobe University Hospital*

[Objective] The prevalence of syphilis in women of childbearing age and pregnant women with syphilis have increased worldwide in recent years. Here, we report 14 pregnant women with syphilis from 2015 to 2020. **[Methods]** Twenty four million units of penicillin G (PCG) daily are administered intravenously for 2-3 weeks in pregnant women with untreated syphilis basically. When the rapid plasma reagin (RPR) titers at 3 months after treatment decreased by a quarter in card tests or by half in automated tests compared with the RPR titers before treatments, the syphilotherapies were considered effective. The workup for congenital syphilis was performed in their newborns. **[Results]** Nine of 14 case were late latent and four were early latent syphilis. Another one was secondary syphilis. Twelve cases didn't have any typical symptoms of syphilis at the time of diagnosis, of which five cases had some histories of eruption or genital ulcer. One early latent case without any prenatal care had delivered a stillbirth of congenital syphilis with saddle nose and hepatosplenomegaly at 29 gestational weeks. Remaining 13 were treated with penicillin. Although the treatments were not considered effective in 3 of 13 cases, none of 13 had congenital syphilis of their newborns. **[Conclusion]** Most of the pregnant women with untreated syphilis were difficult to determine the timing of transmission. Therefore, they should be treated as late syphilis. PCG 24 million units daily for 3 weeks may be effective on late syphilis.

ISP-27-7

Management of pregnancy as an opportunity for transition of follow-up for the women with adult congenital heart disease Hyodo Hironobu, Kou Sain, Ijuin Takashi, Shibakawa Miki, Nitta Satoshi, Iwasa Kanami, Sue Fusako, Mizuno Yoshiaki, Hikosaka Chikako, Funakura Midori, Imada Shinya, Kugu Koji *Tokyo Metropolitan Bokutoh Hospital*

[Objective] Medical or surgical management has been improved which has brought better prognosis of congenital heart disease. The follow-up care for adults has been still being established and some of the women with the disease were not under the proper follow-up care before or during pregnancy. Most of them had, however, an uneventful pregnancy course. Pregnant women necessarily medical care, thus pregnancy can be an opportunity for the arrangement of medical care for women's lives

after childbirth. **[Methods]** The medical records of pregnancy in the adult congenital heart disease women that managed at our hospital from 2014 to 2020 were reviewed. The care of the disease before, during and after pregnancy was investigated. **[Results]** 85 cases and 110 pregnancies were identified. All of them were in NYHA I and VSD was the most major disease. 43 cases were in under regular follow-ups. Cardiac evaluation was done during and after the delivery. Follow-up care were recommended and referred to the specialized institute to 11 cases. **[Conclusion]** It is still being discussed how often the women with adult congenital heart disease women may need regular medical care. As they need the care anyhow and anyway, pregnancy can be a good opportunity to arrange that.

ISP-27-8

Changes in unfractionated heparin requirements over time during pregnancy Kido Saki, Kamura Shunsuke, Nakahara Kazushige, Hachisuga Nobutaka, Sakai Atsuhiko, Sugitani Maiko, Hara Emiko, Fujita Yasuyuki, Kato Kiyoko *Kyushu University Hospital*

[Objective] Although pregnant women with a high risk of thrombosis sometimes need long-term continuous intravenous administration of unfractionated heparin, the change in heparin dose during pregnancy remains unknown. The aim of this study was to examine the changes in unfractionated heparin requirements during pregnancy. **[Methods]** This retrospective observational study performed between April 2012 and September 2021 included pregnant women who received continuous intravenous unfractionated heparin for 4 weeks or longer. The dose of unfractionated heparin was adjusted according to the target activated partial thromboplastin time, and the daily dose (units/kg/day) was observed for each week. The gestational week at which the heparin requirement changed (inflection point) was mathematically calculated. **[Results]** Nineteen pregnancies in 18 women were analyzed. Continuous heparin administration was indicated in 11 pregnancies with deep vein thrombosis (DVT), 7 pregnancies after the Fontan procedure, and 1 pregnancy after mechanical valve replacement. Six pregnancies with DVT had a thrombophilia (Antithrombin III deficiency, protein S/C deficiency, or beta-thalassemia). Heparin requirements increased in all pregnancies until the second trimester, and it tended to decrease in the third trimester. The inflection point was calculated to be 27 weeks of gestation. After 34 weeks of gestation, heparin requirements decreased in all pregnancies and at term, became equal to early pregnancy levels. **[Conclusion]** The requirement for continuous intravenous administration of unfractionated heparin in pregnant women increases in the second trimester of pregnancy and tends to decrease in the third trimester.

ISP-27-9

Autoantibody against beta2-glycoprotein I/HLA-DR complexes is involved in adverse obstetric events Tanimura Kenji, Sasagawa Yuuki, Deguchi Masashi, Saito Shigeru, Tsuda Sayaka, Nagamatsu Takeshi, Fujii Tomoyuki, Nakatsuka Mikiya, Kobashi Gen, Arase Hisashi, Yamada Hideto *AMED BIRTHDAY*

[Objective] We have reported that autoantibody against β 2-glycoprotein I/HLA-DR complexes ($\alpha\beta$ 2GPI/HLA-DR) is associated with the pathology of recurrent pregnancy loss (RPL) [*Arthritis Rheumatol*, 2020] as well as antiphospholipid syndrome [*Blood*, 2015]. This multicenter study aimed to evaluate whether $\alpha\beta$ 2GPI/HLA-DR is involved in adverse obstetric events, including RPL, FGR, HPD, and preterm delivery before 34 gestational weeks (PD<34GW) by both prospective cross-sectional and cohort studies. **[Methods]** These studies were ap-

proved by IRB, and written informed consent was obtained from all participants. In the cross-sectional study, from August 2019 to June 2021, serum β 2GPI/HLA-DR levels (normal < 73.3U) were measured in 293 women with RPL, 66 with FGR, 73 with HDP, and 36 with PD < 34GW by flow cytometry analysis. In the prospective cohort study, from August 2019 to June 2021, 398 pregnant women received a β 2GPI/HLA-DR measurements before 20 GW and subsequent pregnancy outcomes were assessed. The outcomes were compared between 38 women with positive tests for a β 2GPI/HLA-DR and 360 women with negative tests. **[Results]** In the cross-sectional study, positive rates for a β 2 GPI/HLA-DR in women with each adverse event were as follows: RPL, 20% (57/293); unexplained RPL, 19% (31/163); FGR, 17% (11/66); HDP, 16% (12/73); and PD < 34GW, 8% (3/36). In the prospective cohort study, the proportion of women achieving normal term deliveries in the a β 2GPI/HLA-DR-positive group was significantly lower than those in the negative group (66% vs 82%, $p < 0.05$). **[Conclusion]** Our prospective studies for the first time demonstrated that a β 2GPI/HLA-DR might be involved in the pathophysiology of adverse obstetric events.

ISP-28-1

A case of pregnancy after radical trachelectomy: successful trans-vaginal cerclage in early pregnancy for extremely residual short cervix Tsuji Saori, Miyake Tatsuya, Honda Hidemine, Yamamoto Koyo, Ito Futa, Handa Mika, Takiuchi Tsuyoshi, Mimura Kazuya, Kimura Toshihiro, Sawada Kenjiro, Endo Masayuki, Kimura Tadashi *Osaka University*

Radical trachelectomy (RT) is a fertility-preserving treatment for cervical cancer. However, it is not easy to accomplish live-birth, especially in a case with postoperative thin endometrium, cervical stenosis, or shortened residual cervix. We experienced a case of ongoing pregnancy after RT, who underwent vaginal cerclage for extremely residual short cervix. The patient was 36-year-old, trigravida uniparous female, who underwent RT for stage IBI cervical cancer and cervical dilation for postoperative cervical stenosis, during which her prophylactic cerclage was removed. Since she didn't conceive by artificial insemination, we started in-vitro fertilization and embryo transfer (ET) at three years post operation. The uterine neo-cervix was stenotic, the length of residual uterine cavity was short (35mm), and endometrium was thin. We treated chronic endometritis by antibiotics, and adjusted the timing of ET by Endometrial Receptivity Analysis. At five years postoperatively, she conceived by fifth ET under hormonal replacement cycles. Although we had planned to perform trans-abdominal cerclage at 12 weeks of gestation, her residual cervix progressively being shorter at eight weeks of gestation. Because residual cervix was too short to place trans-abdominal cerclage, we underwent trans-vaginal cerclage with cervical traction at nine weeks of gestation. We continued intramuscular injection and trans-vaginal administration of progesterone and administration of lactoferrin to prevent miscarriage and preterm birth. The residual cervix was further shortened (8mm) at 14 weeks of gestation, therefore, we started tocolysis with oral nifedipine. Between 14-22 weeks of gestation, the residual cervical length had not changed and she achieved an ongoing pregnancy.

ISP-28-2

A retrospective study of ultrasonographic findings and accuracy diagnosis of cervical benign polypoid lesions during pregnancy Yokomine Masato, Tetsuo Aki, Horinouchi Takashi, Yoshizato Toshiyuki, Ushijima Kimio *Kurume University Hospital*

[Objective] It is vital to determine anatomical origins of cervi-

cal benign polypoid lesions (polyp) during pregnancy located within the canal or protruding from the endocervix, for prediction of obstetrical outcomes, including abortion and preterm delivery. We aimed to analyze retrospectively, transvaginal ultrasonographic characteristics of cervical polyps. **[Methods]** Subjects were 18 pregnant women with cervical polyp who underwent ultrasonographic imaging and pathological diagnoses after resection: 6 cases with cervical polyp and 12 cases with non-cervical polyp (decidual 11, endometrial 1). Ultrasound examinations were made at 10-14 weeks gestation using B-mode in all cases, color Doppler, and/or bidirectional power Doppler (BPD) in 17 cases, and superb-microvascular imaging (SMI) in 7 cases randomly. Cervical polyp origin was determined by whether or not the polyp and/or Doppler signals on the polyp were visible beyond the cervical canal by ultrasound. Diagnostic accuracy was retrospectively analyzed. **[Results]** Color Doppler, BPD and SMI demonstrated two linear Doppler signals running parallel in the cervical canal, implying feeding artery and vein of the polyp. When all examinations were combined, 88.8% (16/18) had correct diagnosis. In only B-mode, four cases couldn't be diagnosed correctly, of which two cases could be diagnosed with color Doppler and SMI respectively. It was impossible to diagnose cases in which only B mode was performed and cases in which blood flow was not observed even with SMI. **[Conclusion]** Identification of cervical polyp origin during pregnancy can be possible by combining B-mode and Doppler images including color Doppler, BPD and SMI.

ISP-28-3

Pregnancy in a patient with caudal regression syndrome following urethral reconstruction surgery Shigenobu Yuki *Jichi Medical University*

Caudal regression syndrome (CRS) is rare congenital malformation, which is characterized by abnormal development of the lower end of the spine and complicated with neurodevelopmental disorders of vesico-rectal functions and the lower extremities. We report the case of a woman with CRS who became pregnant and gave birth following urethral reconstruction surgery. A 25-year-old primigravida woman with CRS became pregnant naturally and was referred to our department. She had undergone urethral reconstruction in our institute at 14 years old. Emergency cesarean section (CS) was performed at 30+5 weeks of gestation due to severe preeclampsia. This is the first report of a woman with CRS who became pregnant and gave birth following urethral reconstruction surgery. CRS may readily induce early-onset PE due to the increased abdominal pressure. In addition, CS should be paid attention to following urethral reconstruction surgery. The urethral reconstruction may increase sexual behavior in women with CRS, and so obstetricians may encounter pregnancies more frequently. More cases need to be accumulated.

ISP-28-4

A case report of pregnancy complicated by threatened preterm birth after undifferentiated sarcoma treatment Imaizumi Karin¹, Yasuda Shun¹, Kato Asami¹, Miura Hideki¹, Isogami Hirotaka¹, Fukuda Toma¹, Murata Tsuyoshi¹, Kanno Aya¹, Yamaguchi Akiko¹, Fujimori Keiya¹, Jimbo Masatoshi¹, Nishigori Hidekazu² *Fukushima Medical University Hospital¹, Fukushima Medical Center for Children and Women, Fukushima Medical University Hospital²*

[Background] With significant developments in cancer therapies, the childhood cancer survival rate has improved in recent decades. The number of patients experiencing pregnancy after childhood cancer treatment has also, therefore, increased. However, there is a risk of adverse outcomes during pregnancy

among childhood cancer survivors. Recent studies have proposed that childhood cancer survivors are at high risk of preterm delivery, preeclampsia, caesarean section, and prolonged delivery. However, there is no consensus regarding these topics. Here, we report a case of pregnancy after undifferentiated sarcoma treatment with preterm birth. **[Case]** The patient was a 25-year-old primigravida woman. When she was 15 years old, she developed undifferentiated sarcoma in the left vulva. Treatment included surgery, followed by multi-agent chemotherapy and radiotherapy for a year. There was no recurrence for 8 years after the treatment. She conceived naturally and her pregnancy was managed at a nearby maternity clinic. The pregnancy progressed without any particular problems. Because of her medical history, she was referred to our institution. At 30 weeks of gestation, her cervix was found to be dilated to 4 cm; thus, she was hospitalized, and tocolytics were administered. She had a spontaneous rupture of the membrane at 36 weeks and 4 days of gestation, and her baby was born through vaginal delivery. **[Conclusion]** Childhood cancer survivors should be provided with adequate information about the possible adverse effects of cancer treatment before pregnancy and delivery. These patients may require extra vigilance during pregnancy.

ISP-28-5

A case of colon cancer in pregnancy presenting as liver metastases Wu Mengjia, Otsuka Koji, Mori Hikaru, Suzuki Masaya, Hosokawa Mayu, Takesawa Ami, Yasuda Koya, Mitani Takahiro, Kadooka Mizuho, Suemitsu Tokumasa, Otsuka Isao, Furusawa Yoshiaki *Kameda Medical Center*

Introduction : Colorectal cancer is the 2nd most common type of cancer in females in Japan but is uncommon in pregnancy. Diagnosis is often difficult and delayed due to the overlapping of symptoms with that of pregnancy and the limitations placed on potential diagnostic imaging and testing. **Case :** A 40-years-old woman (G5P1) was referred from a local hospital in the 32nd gestational week after persistent right upper quadrant abdominal pain prompted an ultrasound that showed multiple lesions in the liver. Contrast-enhanced ultrasound and colonic biopsy confirmed the diagnosis of colon cancer with liver metastasis. After weighing the potential risks of starting chemotherapy during pregnancy against the benefits of prolonging the gestational age of the fetus, she was delivered at 34 weeks by cesarean section after receiving antenatal corticosteroids. Left hemicolectomy was performed right after delivery of the fetus to prevent bowel obstruction during chemotherapy. Pathology was consistent with adenocarcinoma of the transverse colon. Patient started chemotherapy on postoperative day 8 and is continuing with treatment on an outpatient basis. **Discussion :** Diagnosis of colorectal cancer is uncommon in pregnancy and there is currently no report within Japan of colorectal cancer first presenting as liver metastases in pregnancy. Diagnostic algorithms are not yet well established and clinicians are also often hesitant to obtain the necessary testing because of concern for the fetus. Even in pregnancy, tests to rule out gastrointestinal tumors should be considered in the presence of liver lesions that are highly suggestive of malignancy.

ISP-28-6

A case of mitochondrial disease diagnosed after pregnancy Okimura Hiroyuki, Otani Masahiro, Tarumi Yosuke, Tanaka Yukiko, Maeda Eiko, Mabuchi Aki, Yoriki Kaori, Waratani Miyoko, Mori Taisuke *Kyoto Prefectural University of Medicine*
[Introduction] Mitochondrial disease exhibits various symptoms because of heteroplasm. Therefore, sometimes this condition remains undiagnosed even in adulthood. However, diagnosis of patients with mitochondrial disease is important for the

management of current and future medical conditions. Here, we present a case of mitochondrial disease diagnosed after pregnancy. **[Case presentation]** A 28-year-old primigravida woman was referred to our hospital for threatened premature delivery at 28 weeks of gestation. She had a history of Wolff-Parkinson-White syndrome at 6 years old and sensorineural hearing loss at 16 years old. Her mother had a history of diabetes mellitus, cardiac failure, and deafness, and her grandmother had a history of diabetes mellitus. She was admitted to our hospital and received magnesium sulfate. At 31 weeks and 1 day of gestation, she developed ptosis. At 31 weeks and 4 days of gestation, she developed dyspnea, and blood exam showed increased brain natriuretic peptide. Chest X-ray revealed pleural effusion, and cardiac ultrasound showed reduced fractional shortening. Her condition was diagnosed as acute heart failure, and a cesarean section was performed under general anesthesia at 31 weeks and 5 days of gestation. Postoperative administration of furosemide improved her condition, and she was discharged 14 days after delivery. She underwent genetic testing, and m.3243A>G in the *MTTL1* gene was detected. **[Conclusion]** Pregnancy complications such as premature birth and heart failure led to the diagnosis of mitochondrial disease. Early diagnosis of mitochondrial disease in pregnant women with certain conditions or family history is crucial for managing the disease.

ISP-28-7

Immune-mediated necrotizing myopathy occurred during pregnancy : a case report Oride Tadashi, Nakamura Koji, Kakuda Mamoru, Toda Aska, Miyake Tatsuya, Hiramatsu Kosuke, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University Hospital*

Background : Immune-mediated necrotizing myopathy (IMNM) is a subset of idiopathic inflammatory myopathy (IIM) characterized by acute and severe proximal weakness, and myofiber necrosis with minimal inflammatory cell infiltrate on muscle biopsy. Although pregnancy complicating IMNM has been rarely reported, IIM is known to be associated with pregnancy loss, preterm labor, fetal growth restriction. **Case presentation :** Here we present a 27-year-old primipara, naturally pregnant woman without any medical history who was affected by new-onset IMNM during her pregnancy. She developed muscle weakness and severe pain in her both proximal lower extremities at 12 weeks of gestation. Four weeks later, her symptoms became worse and she was referred to our hospital for further investigation. Laboratory studies showed extraordinarily high serum creatine kinase (CK : 16729IU/L) and negative myositis-associated antibodies. The immunostaining pattern of her muscle biopsy was compatible with IMNM. Three course of corticosteroid pulse therapy was initiated at 18 weeks of gestation followed by oral corticosteroid therapy. Additional Tacrolimus was subscribed at 22 weeks of gestation. Her symptoms gradually improved and she was discharged at 26 weeks of gestation. At 32 weeks of gestation, her disease is well controlled. **Conclusion :** We should be aware that autoimmune myopathy including IMNM can develop during pregnancy and consider consultation with a rheumatologist when the patient awares severe and continuous myalgia and weakness. Since pregnancy outcome largely depends on the disease activity, prompt diagnosis and subsequent treatment is critical to optimize disease control.

ISP-28-8

Prognosis of pregnant woman requiring Chlorpromazine to treat hyperemesis gravidarum Nonomura Yuki, Minamoto Toshiko, Hara Tomomi, Kanasaki Haruhiko, Kyo Satoru *Shimane University Hospital*

[Objective] Hyperemesis gravidarum affects about 0.5% of pregnant women and can lead to complications such as multiple organ failure without proper treatment. We examined the characteristics of pregnant women who require treatment with chlorpromazine for hyperemesis gravidarum. **[Methods]** We included the 104 pregnant women diagnosed with hyperemesis gravidarum from October 2016 to September 2021. We examined the need for postpartum care in the group with and without chlorpromazine and the length of the period spent on a hospital due to hyperemesis gravidarum. **[Results]** In the chlorpromazine-using group, the psychiatric consultation rate and the Edinburgh postpartum depression scale were significantly higher ($p=0.003$). There was no significant difference in hospital stay between the group with and without chlorpromazine, but it tended to be shorter. **[Conclusion]** Patients who require chlorpromazine to treat hyperemesis gravidarum may have mental illness or psychological factors behind the onset of hyperemesis gravidarum. It is necessary to pay particular attention to such patients and follow them mentally. In addition, such patients should be treated with the possibility of strong symptoms of hyperemesis gravidarum in mind.

ISP-28-9

Maternal mental health ; current status and future directions

Hirota Chika, Nao Seiichiro, Ueki Ken *Shiso Municipal Hospital*

[Objective] Perinatal mental health problem is a significant health concern. The mental healthcare program to improve maternal health has started since April 2018 in Japan. The purpose of this report is to describe mental disorders and the risk factors for mental disorders in women with depressive symptoms assessed with the Edinburgh Postnatal Depression Scale (EPDS) during the first trimester and postpartum to compare them with pregnant women without depressive symptoms. **[Methods]** All the pregnant women visited our hospital answered the EPDS questionnaire at the first trimester, and 5 days, 2 weeks and 1 month postpartum. EPDS score of 13 or higher was considered to be screen-positive and these women were further assessed. Screen-negative pregnant women were chosen as controls. The screen-positive women received the intervention by public health nurses. **[Results]** The prevalence of depression during pregnancy in this area was revealed. The factors related to the maternal mental health were evaluated. The EPDS scores were significantly lower after the intervention. **[Conclusion]** The results indicate that our intervention program may reduce the maternal concern and improve their mental health.

ISP-29-1

Acute coagulopathy and fetal death in pregnant women with COVID-19

Sagara Akihito, Yamaguchi Munekage, Sakisaka Sanayo, Yoshimura Saori, Koderia Chisato, Ohba Takashi, Kondoh Eiji *Kumamoto University*

Acute coagulopathy, specific pathological changes in the placenta, and an increased risk of fetal death have been reported in pregnant women with COVID-19; however, the association between coagulopathy and fetal death remains unknown. We report two cases of stillbirth in pregnant women with COVID-19 who showed acute coagulopathy and whose placentas showed characteristic pathological findings due to SARS-CoV-2 infection. **Case 1 :** A 28-year-old pregnant woman (gravida 3, para 2) who had undergone two cesarean sections had a fever of 39 degrees and was positive for SARS-CoV-2 at 26 weeks of gestation. She showed thrombocytopenia on day 7. Coagulopathy progressed and her fetus died on day 9. She underwent a cesarean section after blood transfusion and her coagulability improved thereafter. **Case 2 :** A 35-year-old pregnant woman (gravida 3, para 2) with no symptoms was positive for SARS-CoV-2 at 20

weeks of gestation. She also presented with thrombocytopenia on day 5. Her fetus was dead, and she vaginally delivered a still-born baby on day 9. Her coagulability returned to normal thereafter. Placental histology in both cases showed intervillous infiltration of histiocytes, necrosis of trophoblasts, and intervillous fibrin deposition, which were consistent with previously reported pathological findings related to SARS-CoV-2. In the management of pregnant women with COVID-19, thrombocytopenia may be a predictive marker of fetal death following coagulopathy and placental inflammatory changes due to SARS-CoV-2 infection. Maternal platelets, as well as fetal status, should be evaluated at least once after testing positive with SARS-CoV-2, even if the clinical symptoms are mild.

ISP-29-2

Bimodal abnormalities of blood tests in pregnant women infected with SARS-Cov2 novel coronavirus

Matsunaga Asami, Kawakami Kaori, Katoh Kanoko, Tanaka Yuria, Kobayashi Osamu, Nakajima Takahiro, Ikeda Yuji, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] The clinical features, symptoms, and time course of blood test in pregnant woman with SARS-Cov2 novel coronavirus (COVID-19) are not well known. Coagulopathy and liver dysfunction observed in COVID-19 infection should be distinguished from HELLP syndrome. We examined the trends in blood test results of pregnant women infected with COVID-19. **[Methods]** A retrospective study was conducted on 16 pregnant women with COVID-19 who were admitted to our hospital for treatment in 2021. Patient background, severity of infection, treatment, and time course in the sick days of blood tests were reviewed. **[Results]** The median week of admission was 30 weeks of gestation, and 56% of the patients had household infection. The severity of new COVID-19 infections was mild to moderate I in 62.5%, moderate II in 31%, and severe in 6% respectively. 37.5% of cases needed oxygen administration, and one case required endotracheal intubation management. The median number of days with the highest oxygen demand was day7. All patients had thrombocytopenia and high D-dimer levels, those values were the worst between day6 and day8. 87% of patients had hepatic dysfunction, which were exacerbated between day10 and day11. The appearance of coagulopathy occurs significantly earlier than that of hepatic dysfunction. **[Conclusion]** Pregnant women infected with COVID-19 often develop coagulopathy on about day7, and liver dysfunction about day10, both of which are transient and reversible. The phase shift between coagulopathy and liver dysfunction was important for the differential diagnosis of HELLP syndrome.

ISP-29-3

Novel profiles of pulmonary functions on COVID-19 in pregnancy : a new perspective

Komatsu Naoto¹, Furuya Kichiro¹, Tanaka Yoshitomo¹, Takemoto Yuki¹, Yamashita Saya¹, Chang Yangsil¹, Tsubouchi Hiroaki¹, Shikado Kayoko¹, Yokoi Takeshi², Ogita Kazuhide¹ *Rinku General Medical Center¹, Kaizuka City Hospital²*

[Objective] With the emergence of SARS-CoV-2 epidemic, many pregnant women have been also infected. We have found that some of those suffered from prolonged symptoms of cough and dyspnea. Furthermore, many of those who were without hypoxemia could be classified as "mild" or "intermediate I" using the Japanese criteria for severity despite of the symptoms. **[Methods]** Our study focused on the characteristics of maternal respiratory functions using spirometry for COVID-19 in pregnancy twice upon their easing isolation and one-month postpartum check-up on outpatient clinic. **[Results]** During the observa-

tional period from May to September 2021, forty-one COVID-19 pregnant women were transferred to our hospital and isolated and 39 patients were included in the study. Of the 39 patients studied, 28 (71.8%) were in the third trimester. Of the 28 patients quarantined in the third trimester, 23 underwent a spirometry after the completion of their isolation period. 15 (65.2%) patients showed the restrictive lung disorders from spirometry on easing isolation. Of the 28 pregnant women isolated in the third trimester of pregnancy, 20 (71%) were not in demand for oxygen. 15 of the 20 patients without oxygen demand underwent respiratory function tests and 7 (46.7%) presented with restrictive disorder. **[Conclusion]** Our findings conclude that pregnant women suffered from COVID-19 in the third trimester of pregnancy sometimes develop restrictive lung impairment. Our findings showed that restrictive lung disease can occur in nearly half of the cases without oxygen demand.

ISP-29-4

Single-center retrospective study for change of perinatal situation in COVID-19 pandemic Kamoshida Tsukuru, Horibe Yu, Inoue Momo, Suzuki Masato, Suzuki Takashi, Suzuki Yuto, Kanazawa Junko, Abe Yuki, Kuramoto Goro, Masaoka Naoki, Kakogawa Jyun, Tabata Tsutomu *Tokyo Women's Medical University Hospital*

[Objective] By COVID-19 pandemic, perinatal situation has been dramatically changed. Measures against COVID-19 infection control is strongly required as perinatal center of university hospital in Tokyo. Here we show measures and change in single-center retrospective study. **[Methods]** We performed a single-center retrospective study, groups were divided into two which were a year before and after first Emergency Statement in Japan. Age, experience of infertility, number of pregnancy, weeks of delivery, rate of caesarean section, threatened premature labor (PTL), birth weight, amount of bleeding at delivery, perinatal compilation, Apgar score, number of perinatal transport and Edinburgh Postnatal Depression Scale were statistically analyzed. **[Results]** As a result, no significant difference was found. Number of birth was decreased in proportion to birth rate in Japan by 757 to 673. As our measures against COVID-19, SARS-CoV-2 polymerase chain reaction (PCR) testing is conducted for patients at aged 36 weeks of pregnancy and triage before admission. 100% patients underwent PCR testing, and positive rate was 0% except patients who underwent perinatal transport (include patient with PCR positive), was triage positive and correspond to close contact to patient with COVID-19 positive. **[Conclusion]** Patient's acceptance for PCR testing was favorable. And our measures and result may reflect to feasibility of safe delivery in COVID-19 pandemic. As long as extinction of COVID-19 is obscure, role as Perinatal Medical Center would become more significant.

ISP-29-5

Association between serious psychological distress and loneliness during the COVID-19 pandemic in pregnant women Yoshimi Kana^{1,2}, Kai Sayaka¹, Takeda Takashi¹ *Research Institute of Traditional Asian Medicine, Kindai University¹, Psychiatry, Hannan Hospital²*

[Objective] Coronavirus disease 2019 (COVID-19) has caused a global pandemic and put a great deal of stress on many people. Pregnant women are especially vulnerable to stress. Actions to prevent COVID-19 has also reduced social interactions, which has increased social isolation and loneliness. Such situations and emotions can increase perceived stress, cause psychological distress, and increase the risk of mental illness, such as depression. This study examined the association between serious psychological distress (SPD) and loneliness during the COVID-19 pan-

dem in pregnant Japanese women. **[Methods]** An internet survey of 1022 pregnant women in Japan was conducted between June 1 and July 21, 2021. The 6-item Kessler Psychological Distress Scale, 3-item Revised UCLA Loneliness Scale, and Fear of COVID-19 Scale were used as measurement tools. The prevalence of SPD was defined as a K6 score of ≥ 13 . **[Results]** The prevalence of SPD was 16.5%. Multivariate analysis revealed that the risk factors for SPD were younger age (odds ratio [OR] 1.05; 95% confidence interval [CI] 1.01 to 1.10; $p=0.020$), history of abortion or miscarriages (OR 1.56; 95% CI 1.04 to 2.36; $p=0.034$), unemployment (OR 1.67; 95% CI 1.14 to 2.45; $p=0.008$), fear of COVID-19 (OR, 1.12; 95% CI, 1.08 to 1.17; $p<0.001$), and loneliness (OR 1.53; 95% CI 1.38 to 1.70; $p<0.001$). **[Conclusion]** Pregnant women in Japan showed a high prevalence of SPD. Younger age, unemployment, history of abortion or miscarriages, fear of COVID-19, and loneliness were independently associated with SPD.

ISP-29-6

Changes in Anxiety and Stress Among Pregnant Women During the First Wave of the COVID-19 Pandemic: Content Analysis of a Japanese Social Question-and-Answer Website Shirabe Ritsuko¹, Kiuchi Takahiro² *Department of Health Communication, Graduate School of Medicine, The University of Tokyo¹, Department of Health Communication, School of Public Health, The University of Tokyo²*

[Objective] The changing pattern of anxiety and stress experienced by pregnant women during the COVID-19 pandemic is unknown. We aimed to examine the sources of anxiety and stress in pregnant women in Japan during the COVID-19 pandemic. **[Methods]** We performed content analysis of 1000 questions posted on the largest social website in Japan (Yahoo! Chiebukuro) from January 1 to May 25, 2020 (end date of the national state of emergency). The Gwet AC1 coefficient was used to verify interrater reliability. **[Results]** A total 12 categories were identified. Throughout the study period, anxiety related to going outdoors appeared most frequent, followed by anxiety regarding employment and infection among family and friends. Following the declaration of the state of national emergency at the peak of the infection, infection-related anxiety decreased, whereas anxiety about social support and mood disorders increased. Stress regarding relationships appeared frequent throughout the pandemic. **[Conclusion]** The sources of anxiety and stress in pregnant women in Japan changed during the pandemic. Our results suggest the need for rapid communications in the early phase of a pandemic as well as long-term psychosocial support to provide optimal support to pregnant women in Japan. Health care professionals should understand the changing pattern of requirements among pregnant women.

ISP-29-7

Impact of COVID-19 on behaviour change of pregnant women Kondo Akane, Hayashi Aki, Tachibana Ayaka, Morine Mikio, Hinokio Kenji, Maeda Kazuhisa *Prenatal Medical Center, Shikoku Medical Center for Children and Adults*

[Objective] The COVID-19 pandemic has impacted on maternity care, supports and women's mental health in the world. We focused on this effect on psychological aspects of pregnant women. This survey was done to understand the impact of the COVID-19 pandemic on behaviour change of pregnant women during pregnancy, birthing at a local prenatal medical center. **[Methods]** We conducted a web-based Questionnaire survey on the impact of COVID-19 on post-delivery women at outpatient from December 2020 to September 2021. The survey included closed and open-ended questions to assess women's perceptions and satisfaction with their antenatal care. The participants were

women who delivered healthy term baby via normal delivery (n=257) or planned caesarean section (n=94). We excluded women who had severe complication with mother or fetus. **[Results]** 351 post-delivery women completed the survey. Women reported that they experienced good delivery even under restrictions implemented in the maternity services limited their face-to-face interactions with healthcare professionals and meant their partners could not attend labour or support them in the postpartum period in the maternity setting. They had stronger connection with ward midwives since they were the closest supporter for them. **[Conclusion]** Our findings indicate pregnant women had less face-to-face, couple-based antenatal care as a result of the restrictions implemented in response to the COVID-19 pandemic, potentially intensifies pregnancy specific stress. However, they had good relationship with ward midwives through labour and they seem more confident regarding management themselves and also infants compared to before COVID-19.

ISP-30-1

Magnetic resonance imaging is useful for evaluating the bleeding risk of placenta previa accurately Kato Masaya^{1,2}, Tanaka Satomi², Yasuda Ayumi², Segawa Masafumi², Makino Yuya², Ito Saki², Ishida Yuri², Murase Yoshiko², Yata Shotaro², Kaneda Hiroshi², Tanaka Toshitaka² *Juntendo University Hospital, Juntendo University¹, Juntendo University Shizuoka Hospital²*

[Objective] One of the most serious complications of placenta previa (PP) is massive bleeding during cesarean section (CS). This study aimed to evaluate the bleeding risk using prenatal MRI. **[Methods]** A retrospective cohort study was conducted. We dealt with 14192 deliveries between January 2014 and March 2020 in our hospital and the 97 patients were diagnosed as PP. The distance from short side placental edge to the internal cervical os (PI), cervical length (CxL) and placental height (PH) were measured with MRI. The patients without MRI or patients of placenta accrete (n=4), multiple pregnancy (n=2), myoma (n=2), preterm birth less than 35 weeks (n=1) were excluded from this study. 57 patients were researched and analyzed statistically. **[Results]** The PP patients were categorized as total PP (N=38, 66.7%) or Marginal/Partial PP (N=19, 33.3%). The median bleeding amount during CS was 1510 ml (interquartile range=1170 - 2000 ml). There was stronger correlation between PI and bleeding amount in that of MRI (R=0.48945, p=0.0001) than that of 30-32w US (R=0.43377, p=0.0016) or 35-37 w US (R=0.40702, p=0.0101). Moreover, there was stronger correlation in PI x PH (R=0.5056, p<0.0001) than that of only PI. There was little correlation between bleeding amount and CxL or PH. **[Conclusion]** The measurement of PI and PI x PH using prenatal MRI could be useful for evaluating the bleeding risk of placenta previa accurately.

ISP-30-2

The volume of posterior cervical varicose correlates intraoperative blood loss in placenta previa Kamiya Akio¹, Yamada Takahiro², Yoshida Aya¹, Oku Kaede¹, Nishibata Shuhei¹, Morikawa Mamoru¹, Okada Hidetaka¹ *Kansai Medical University¹, School of Public Health, Kyoto University²*

[Objective] To analyze whether the volume of posterior cervical varicoses (pCV) which is often observed in placenta previa attached to the posterior wall of the uterus is associated with blood loss (BL) during cesarean section. **[Methods]** This is a retrospective study at a tertiary facility in Japan. The cases of singleton pregnancy with placenta previa who were scanned with MRI prenatally and had a cesarean section at our institution between April 2012 and March 2021 were included. We used magnetic resonance imaging to quantify the volume of the pCV and

calculated the sum of the product of the areas of the pCV region in each sagittal section and the slice width as the approximate Volume of pCV (aVpCV) in posterior placenta previa. Pearson's correlation coefficient was used to determine the relationship between aVpCV and BL during cesarean section was evaluated. The ROC curve was used to determine the appropriate cut-off value of aVpCV to predict massive intraoperative bleeding (>2500mL). **[Results]** The ln (aVpCV) was weakly correlated with intraoperative bleeding. (r=0.30, p<.01) ln (aVpCV) range was 0.27 to 2.38. The area under the curve was 0.66. With an ln (aVpCV) cutoff value of 1.67, the sensitivity and specificity were 60.0% and 78.1%, respectively, with a positive predictive value of 30.0% and a negative predictive value of 92.6%. **[Conclusion]** Large pCV could be the risk of intraoperative massive hemorrhage in patients with posterior placenta previa. The quantification of pCV could be helpful to predict massive intraoperative bleeding.

ISP-30-3

Recurrent incarcerated gravid uterus with placenta previa : a case report Kobayashi Mariya¹, Hiramatsu Kosuke¹, Taniguchi Mariko², Kakuda Mamoru¹, Toda Aska¹, Nakamura Koji¹, Miyake Tatsuya¹, Mimura Kazuya¹, Kimura Toshihiro¹, Endo Masayuki¹, Tsutsui Tateki², Kimura Tadashi¹ *Osaka University¹, Japan Community Health Care Organization Osaka Hospital²*

Incarcerated gravid uterus (IGU) is a rare obstetric complication and IGU with placenta previa (PP) has not been reported. A 38-year-old patient, gravida 2, para 1, had experienced a cesarean section (CS) in her previous pregnancy due to IGU caused by severe adhesion between posterior uterus and pelvic cavity. Three years after her last delivery, she conceived naturally, although her uterus was still retroverted. In 1st trimester, the anterior lower uterine wall appeared to become cephalad to the fundus, which is posterior-caudal and we feared recurrence of IGU. In 2nd trimester, ultrasound showed the placenta at the anterior uterine wall, however, due to the extension and severe anterior displacement of cervix behind the pubic symphysis, the anatomical relationship between the placenta and the internal os was unclear. We performed preoperative MRI at 19, 30 and 33 weeks of gestation (WG), which showed PP with recurrent IGU. Fortunately, she had no symptoms. CS was performed at 35+3 WG. Vertical supraumbilical skin incision revealed extremely retroverted uterus. The uterus was incised vertically to avoid injuring the placenta and cervix by confirming placental position with intraoperative ultrasound. A healthy female infant with pelvic presentation was delivered (2520 g, Apgar 8/9). After delivery of the placenta, active bleeding was observed, which was successfully controlled using an intrauterine balloon. It took 162 minutes and blood loss was 1230 mL. In this case, anatomic relationships were severely distorted due to recurrent IGU with PP, however, repeated imaging evaluations with MRI and ultrasound provided a safe CS.

ISP-30-4

The characteristics of ultrasound findings during surgery in cases with placental placenta previa accreta spectrum disorders using Doppler microvascular imaging Horinouchi Takashi, Yoshizato Toshiyuki, Muto Megumi, Sakamoto Yoshitaka, Yokomine Masato, Kawakami Kosuke, Ushijima Kimio *Kurume University Hospital*

[Objective] To test the feasibility of intraoperative ultrasonographic diagnosis of placenta accreta spectrum disorders (PPAS) using Doppler microvascular imaging. **[Methods]** Subjected were 4 cases with suspected PPAS based on the conventional findings of transabdominal ultrasonography and MRI in

our hospital between 2019 and 2021. In all cases, the pathological findings of the placenta were confirmed after cesarean hysterectomy. There were 3 cases with PPAS and one case without PAS. The hypothetical four criteria for PPAS were #1, absence of Doppler signals on myometrium, #2, between the myometrium and placenta and #3, projecting into the placenta from myometrium (i.e., jet flows from the spiral arteries), and #4, presence of tortuous flow signals attaching to the myometrium (i.e., dilated villous vessels). The relationship between above-mentioned findings and the final diagnosis of PPAS were retrospectively analyzed. **[Results]** The surgery was performed at 36-37 weeks of gestation. In 3 cases with PPAS, all 4 criteria were observed in 1 case and two criteria (#2 and #3) were met in 2 cases. However, no above-mentioned criteria were visible in a case without PPAS. **[Conclusion]** The absence of Doppler signals between myometrium and placenta implying decidua and jet flows from the spiral arteries were the direct and reliable findings for the diagnosis of PPAS on the intraoperative survey of microvascular flow profiles of myometrium, decidua and placenta.

ISP-30-5

Placenta previa and percreta in a case with previous Cesarean section : A longitudinal observation of chorionic/placental tissue and lower uterine segment Muto Megumi, Horinouchi Takashi, Yoshizato Toshiyuki, Sakamoto Yoshitaka, Yokomine Masato, Ushijima Kimio *Kurume University Hospital* We report a case of pregnancy with abnormally invasive placenta (AIP) and placenta previa in which ultrasonographic observation of myometrium and placenta was made, longitudinally, early in the first trimester. A 38-year-old Japanese pregnant woman having had three Cesarean deliveries was referred to our hospital at 7 weeks gestation due to suspected Cesarean scar pregnancy. Ultrasonography revealed that the gestational sac was located near, but not on, or within the niche. Myometrial residual thickness (RMT) was 4.6 mm. At 8 weeks gestation, chorionic villi invaded the niche. Despite the possible risk of AIP, the patient was determined to continue her pregnancy. RMT became thinner as gestation progressed. At 22 weeks gestation, the placenta was located on the internal os and the area of the posterior lower uterine segment, measuring 3 cm in diameter with myometrial tissue no longer visible, leading to the diagnosis of placental previa and percreta. Cesarean hysterectomy was performed at 34 weeks gestation and the pathological findings confirmed placenta percreta. This case revealed an "unique" placental development in which chorionic villi invaded the niche early in the first trimester, anchored on the niche with the myometrium being stretched and further migrated to the direction of the internal os with advance in gestation, forming AIP and placenta previa.

ISP-30-6

New ultrasonographic risk assessment of uterine scar dehiscence in pregnancy after cesarean section Kawakami Kosuke^{1,2}, Yoshizato Toshiyuki², Kurokawa Yusuke^{1,2}, Okura Naofumi¹, Ushijima Kimio² *National Hospital Organization Kokura Medical Center¹, Kurume University²* **[Objective]** To make qualitative and quantitative ultrasonographic assessments of the risk of uterine scar dehiscence in pregnancy after cesarean section. **[Methods]** The subjects were 31 cases of normal singleton pregnancy delivered by elective cesarean sections at our hospital between 2020 and 2021. Qualitative and quantitative evaluations of the lower uterine segments were longitudinally made at 16-21, 22-27 and 28-33 weeks of gestation. The subjects were divided into low-risk (19 cases) and high-risk (12 cases) groups depending on gross find-

ings of the lower uterine segments at cesarean sections and comparisons were made between the groups. **[Results]** The lower uterine segments changed from V-shape to U-shape and thin shape as gestation progressed, and this trend was more prominent in the high-risk group, occurring mostly at 22-27 weeks of gestation. At 22-27 weeks, myometrial thickness in the high-risk group (2.2 mm, 2.1 to 2.5 mm [median, range]) was less than in the low-risk group (3.8 mm, 2.9 to 4.9 mm) (P=0.0030). Marked changes were observed in myometrial thickness from 16-21 to 22-27 weeks in the high-risk group (1.2 mm, 0.6 to 1.8 mm) compared with those in the low-risk group (-0.3 mm, -1.7 to 1.0 mm) (P=0.021). In the high-risk group, the thinning areas of lower uterine segments moved cephalad by 22-27 weeks, compared with 28-33 weeks in the low-risk group. **[Conclusion]** The morphological changes and actual thinning of the lower uterine segments were prominent in the second trimester in cases considered at-risk for uterine scar dehiscence.

ISP-31-1

Analysis of RPOC (retained products of conception) in our hospital : a case report Nishizawa Miki, Kido Koichiro, Kosaka Takashi, Onodera Takako, Hashimoto Kei, Nakagawa Ipeei, Koike Ryoko, Kihira Chikara, Hiraike Haruko, Sasamori Yukifumi, Ryo Eiji, Nagasaka Kazunori *Teikyo University Hospital*

OBJECTIVE : The purpose of this study was to explore the risk factors characteristics of RPOC (retained products of conception) that needed interventions for late postpartum hemorrhage. **METHOD :** We retrospectively reviewed 14 cases of RPOC experienced at our hospital over seven years. **RESULT :** The mean age of the patients was 32 years (23-43 years), and only one of them became pregnant by ART (artificial reproductive technology). The mean number of weeks of delivery was 38.6 weeks (33-41 weeks) : 2 by cesarean section and one after miscarriage surgery. The indications for cesarean section were both pregnancies after enucleation of fibroids, one of which was suspected of having placenta accreta on imaging during pregnancy. Hence, an interventional radiology (IVR) team was on call at the time of the cesarean section. The average day of bleeding in cases with active postpartum hemorrhage was 19.4 days, but after miscarriage surgery, bleeding occurred several months later. Contrast-enhanced computed tomography (CT) was used to make the diagnosis in most cases. Most of the patients underwent IVR, but two patients underwent TCR (transcervical resection) without IVR. **CONCLUSION :** RPOC can occur in patients with no particular risk, and it is necessary to seek the cooperation of other departments such as radiology for treatment. However, it is challenging to predict RPOC in advance, and it is essential to establish a smooth treatment system after diagnosis.

ISP-31-2

A retrospective outcome after management of retained products of conception Tomonaga Chiharu, Hasegawa Yuri, Kajimura Itsuki, Harada Ayumi, Matsumoto Kanako, Kitajima Yuriko, Kitajima Michio, Miura Kiyonori *Nagasaki University* **[Objective]** To examine the outcome of retained products of conception (RPOC), we investigated the clinical findings between the expectant and interventional management groups for RPOC in our hospital. **[Methods]** We reviewed clinical records of patients who were diagnosed RPOC between January 2016 and June 2021, retrospectively. As clinical findings, maximum diameter of interventional management groups for RPOC. **[Results]** There were 37 cases with RPOC treated during the study period. Pregnancy after artificial reproductive technology were observed in 11 cases (29.7%). Bleeding was observed in 27 cases (73.0%) prior to the diagnosis of RPOC. The average of maxi-

mum diameter of RPOC was 32.9mm, and 30 cases (81.1%) showed hypervascularity within RPOC by ultrasound examination. The expectant management was performed in 13 cases (35.1%), and then spontaneous disappearance of RPOC was confirmed in the 8 cases (61.5%, 8/13). Interventional managements were selected in 24 cases (64.9%), and uterine artery embolization in 19 cases (79.1%, 19/24). We compared clinical findings between 13 cases of observation groups and 24 cases of intervention group as p -value < 0.05 in significant difference. There was no significant difference in maximum diameter of RPOC (36.1mm vs 27.1mm, $p=0.07$), but there were significant differences in presence of bleeding events (91.7% vs 46.1%, $P=0.002$) and hypervascularity of RPOC (87.5% vs 61.5%, $p=0.007$). **[Conclusion]** Therapeutic intervention was necessary for RPOC with bleeding events and/or hypervascularity of RPOC.

ISP-31-3

Subchorionic hematoma promotes epithelial-mesenchymal transition of amniotic epithelial cells Yasuda Eriko, Mogami Haruta, Matsuzaka Yu, Inohaya Asako, Takakura Masahito, Ueda Yusuke, Kawamura Yosuke, Chigusa Yoshitsugu, Mandai Masaki *Kyoto University*

[Objective] Subchorionic hematoma (SCH) is a risk of preterm prelabor rupture of membranes, which lead to poor perinatal prognosis. Here, we investigated the changes of the amnion epithelium by intrauterine hematoma. **[Methods]** We compared 9 cases of SCH and 7 cases of control (the median of gestational age at delivery was 26.2 and 25.3 weeks, respectively). The indication of caesarean section in the control group was HELLP syndrome and fetal distress. **[Results]** In the SCH group, necrosis and shedding of epithelial cells were observed in almost all cases. Iron-laden macrophages were increased in the amnion and chorion of the SCH group. In immunofluorescence, the expression of E-cadherin in amniotic epithelial cells was seen in both groups. Remarkably, the expression of vimentin in epithelial layer of amnion was enhanced in the SCH group compared to control by immunofluorescence (78.2% vs 46.3%, $P=0.003$). At the same time, the expression of α -smooth muscle actin was increased in both epithelial (77.5% vs 33.5%, $P=0.019$) and mesenchymal cells of amnion (86.1% vs 57.5%, $P=0.035$). **[Conclusion]** Subchorionic hematoma stimulated epithelial-mesenchymal transition of amnion, which further led to myofibroblast change of amnion cells. This EMT in amnion might be activated by iron-laden macrophages.

ISP-31-4

Quantification the size of SCH (subchorionic hematoma) causing perinatal complications Yoshihara Tatsuya, Okuda Yasuhiko, Yoshino Osamu, Sasatsu Satoko, Ohgi Maki, Ogasahara Eriko, Hirata Syuuji *University of Yamanashi Hospital*

[Objective] Large SCH is known to be a risk factor for obstetric complications including miscarriage, preterm labor, preterm PROM and placental abruption. But there is no index of what SCH size is considered high-risk. We quantified SCH ultrasonographically with multiple ways to find the optimal method related to obstetric complications. **[Methods]** Clinical data of 93 women diagnosed SCH (pregnancy 6-20W) in our hospital in 2019-2020 were collected. SCHs were evaluated in two ways. **Method 1** : SCH area size relative to the gestational sac (GS) or amniotic cavity size. **Method 2** : SCH contact length relative to the GS or amniotic cavity circumference, were measured. These parameters and subsequent obstetrics complications were examined retrospectively. **[Results]** By all measures, the larger the size of the SCH, the significantly higher the rate of obstetric complications. **Method 1** : The complication rate was significantly

higher for those with a larger area of SCH occupancy ($p=0.02$), and from the cut-off using the ROC curve, 25% or more was considered a high-risk group. **Method 2** : The longer the SCH is in contact with the GS circumference, the more complications ($p<0.01$), and the cut-off was 30% of GS circumference. **[Conclusion]** SCH with larger size may cause obstetrics complications. Especially, the longer the contact distance of the SCH to the GS circumference, the greater the obstetrics risks were suggested.

ISP-31-5

Umbilical cord ulcer with congenital fetal duodenal obstruction : A case report Aimoto Noritoshi, Nishida Tomomi, Nishida Kohei, Omae Ayano, Hirata Tomoko, Saijo Masayuki, Kawai Sayaka, Nakayama Tomoko, Seki Noriko, Odaka Koji, Mizutani Yasushi *Japanese Red Cross Society Himeji Hospital*

[Introduction] Umbilical cord ulcer is a complication of congenital upper gastrointestinal obstruction, which is caused by cord hemorrhage that is associated with high rates of perinatal mortality. We report a case of fetal anemia caused by hemorrhage from an umbilical ulcer associated with congenital duodenal obstruction in the fetus. **[Case]** A 31-year-old primipara was suspected with fetal duodenal obstruction after the triple bubble sign was identified. At a gestational age of 31 weeks and 0 days, cervical shortening and frequent uterine contractions occurred : therefore, intravenous administration of ritodrine hydrochloride was started with steroids. On the next day, the fetal heartbeat decreased and fetal dysfunction was diagnosed. A high volume of bloody amniotic fluid was observed intraoperatively, and the arterial wall of the umbilical cord was partially exposed and disrupted. The diagnosis was fetal anemia due to umbilical cord ulceration and hemorrhage. A neonate weighing 1,643 g with an Apgar score of 3/4 and Hb 6.6 was delivered who received a postnatal blood transfusion, underwent radical duodenal closure on day 4, and was discharged on day 76 after stabilization. **[Conclusion]** Umbilical cord ulcers are rare and have been associated with congenital upper gastrointestinal obstructions. They cannot be diagnosed before any bleeding occurs : upon bleeding, rapid deterioration and perinatal mortality can occur. We did not diagnose our patient preoperatively. Blood transfusion was required due to fetal anemia to prevent perinatal mortality.

ISP-31-6

3D vocal power Doppler sonography predicts the reduced placental glycocalyx expressed on maternal side of syncytiotrophoblast Kondo Emi, Shibata Eiji, Sakuragi Toshihide, Uchimura Takayuki, Murakami Midori, Kinjo Yasuyuki, Yoshino Kiyoshi *University of Occupational and Environmental Health*

[Objective] Placental glycocalyx (P-GCX) expresses on the maternal side of syncytiotrophoblast (STB), and may contribute to maintain the normal blood flow in the intra-villus space (IVS), but underline mechanisms of circulation control in IVS are not well-known. We asked if the reduced expression of P-GCX is related to the placental circulation insufficiency (PCI) in IVS, and if 3D vocal power Doppler sonography (3D-VPDS) can predict the P-GCX expression before delivery. **[Methods]** Subjects were 64 pregnant women complicated by preeclampsia (PE : $n=28$) and unaffected PE (UPE : $n=36$). Flow index (FI) was measured was assessed by 3D-VPDS, maternal plasma levels of sFlt-1, PlGF, and sEng just before delivery. P-GCX was analyzed by immunohistochemistry using the antibody for syndecan-1 which is the main component of GCX, and was semi-quantified by the specific scoring criteria. We assessed differences of FI, sFlt-1, PlGF, and sEng values between two groups, and the relationship

between FI values and P-GCX expressions in all cases. **[Results]** There were no significant differences in background characteristics between two groups. Significant decreased levels of P-GCX ($p=0.03$), and PIGF ($p=0.01$), and increased levels of sFlt-1 ($p<0.001$) and sEng ($p<0.001$) were seen in PE group. However, FI values were not different between two groups ($p=0.546$). In all cases, P-GCX expression was positively related to FI level ($r=0.42$, $p<0.001$) and negatively related to maternal systolic blood pressure ($r=0.34$, $p=0.006$). **[Conclusion]** P-GCX potentially regulates the blood flow in IVS. FI value predicts the severity of PE and the reduced P-GCX expressed on the maternal side of STB.

ISP-31-7

The challenge of establishing human trophectoderm stem cells using a CDX2 reporter line Io Shingo^{1,2,3}, Kondoh Eiji¹, Mandai Masaki³ *Kosaka Women's Hospital¹, Department of Life Science Frontiers, Center for iPS Cell Research & Application, Kyoto University², Kyoto University³, Kumamoto University⁴*
[Objective] Trophectoderm is a founder cell of the placenta. It has not yet been reported to be maintained and cultured as human trophectoderm. We expect that there will be counterpart cells in humans to the mouse polar trophoblast stem cells. This study aims to generate the *in vitro* trophectoderm stem cells. **[Methods]** To generate trophectoderm from human naive pluripotent stem cells (naive trophectoderm), we tried chemically induced differentiation. To monitor trophectoderm maintenance, we created a CDX2 : GFP knock-in reporter line by CRISPR-Cas 9-mediated heterologous recombination. After acquiring CDX2-positive cells at Day 3, the medium was switched due to establish trophectoderm stem cells. Cells re-cultured in medium of various combinations were evaluated by flow cytometry. **[Results]** Naive Trophectoderm is induced rapidly and efficiently by BMP4 and inhibition of MEK, Nodal and JAK/STAT signaling. Naive trophectoderm exhibited high transcriptome correlation with trophectoderm in humans and cynomolgus monkey, and immunocytochemistry demonstrated the expression of CDX2 and GATA3. Flow cytometry showed that naive trophectoderm expressed ITGA6, not HLA-ABC. The expression of C19 MC microRNAs in naive trophectoderm was as high as in choriocarcinoma cell-lines. *ELF5* promoters was hypomethylated in naive trophectoderm. Consequently, we confirmed that naive trophectoderm met trophoblast criteria. CDX2-positive cells continued to express GFP after 7 days by re-culturing in Nodal inhibitor, Wnt activator and lysophosphatidic acid. **[Conclusion]** The combination of compounds to maintain as trophectoderm stem cells is beginning to be discovered. The human trophectoderm stem cells can be valuable tools for investigating the early development of human placenta, modeling diseases, and reproductive medicine.

ISP-32-1

Neurological damage and partial recovery after massive fetal brain hemorrhage : a case report Yamanishi Hiroko¹, Obata Shizuka¹, Osawa Ayako¹, Yoshimoto Nozomi¹, Muraoka Junsuke¹, Matsuzawa Satoshi¹, Urabe Hirotohi², Katsuragi Shinji¹ *University of Miyazaki Hospital¹, IKIME no MORI LADIES CLINIC²*

[Objective] Fetal brain hemorrhage is a rare complication during pregnancy. The major causes are maternal external injury, vitamin K deficiency, and fetal thrombocytopenia or anomaly. We present a case of fetal brain hemorrhage that occurred at 24 weeks of gestation, in which we followed the clinical course in utero. **[Case]** A 26-year-old mother lost body weight of 15 kg in 16 weeks due to an eating disorder without intake of vitamin K. She was transferred to a tertiary center at 24 weeks of gestation

for decreased FHR variability. Fetal brain hemorrhage of grade 4 was found, and a maternal blood test showed PIVKA-2 1026 mAU/ml (<40 mAU/ml, normal). Fetal heart rate variability became zero with late decelerations 12h after admission, but became minimal a week later and moderate in three weeks. Ultrasonography did not show any breathing movements, muscle tones, or fetal movements just after brain hemorrhage, and rigid flexor posturing of the upper limbs with extensor posturing of the lower limbs like decorticate rigidity were observed. However, three weeks after onset of brain hemorrhage, fetal tongue movement was seen. **[Conclusion]** The fetus had extensive neurological damage, including to the autonomic nerve and cerebrum, with slight recovery of cranial nerves. **[Discussion]** FHR patterns and ultrasonography findings indicated temporary and prolonged damage to various neurological regions and the neurotransmission system in the acute and subacute phases in a fetus after brain hemorrhage.

ISP-32-2

Recognition of Fetal Facial Expressions using Deep Learning of Artificial Intelligence Miyagi Yasunari^{1,2}, Hata Toshiyuki³, Miyake Takahito^{1,3} *Miyake Ohfuku Clinic¹, Department of Artificial Intelligence, Medical Data Labo², Miyake Clinic³*
[Objective] The development of the artificial intelligence (AI) classifier to recognize fetal facial expressions that are considered being related to the brain development of fetuses. **[Methods]** Images of fetal faces with sonography obtained from outpatient pregnant women with a singleton fetus were enrolled in routine conventional practice from 19 to 38 weeks of gestation from January 1, 2020, to September 30, 2020. The images were classified into eight categories, such as eye blinking, mouthing, neutral face, scowling, smiling, sucking, tongue expulsion, and yawning. The category in which the number of fetuses was less than eight was eliminated before preparation. Next, we create an original deep learning artificial intelligence classifier with the data. **[Results]** The number of fetuses/images in the rated categories were 34/213, 91/536, 62/460, 16/74, 10/45, 8/28, 16/101 and 237/1457 for eye blinking, neutral face, mouthing, scowling, smiling, tongue expulsion, yawning and all, respectively. The accuracy of the AI fetal facial expression for the entire test data set was 0.996. The accuracy/sensitivity/specificity values were 0.996/0.964/1.00, 1.00/1.00/1.00, 0.996/1.00/0.994, 1.00/1.00/1.00, 1.00/1.00/1.00, 1.00/1.00/1.00 and 1.00/1.00/1.00 for blinking, mouthing, neutral face, scowling, smiling, tongue expulsion and yawning, respectively. F1 score, area under ROC curve, markedness and matthews correlation coefficient were over 0.96 in all categories. **[Conclusion]** The AI classifier has the potential to objectively classify fetal facial expressions. Artificial intelligence can advance fetal brain development research using ultrasound.

ISP-32-3

Maternal magnesium deficiency during pregnancy induces salt sensitive hypertension in the offspring Kumagai Asako, Ueki Norikazu, Takeda Satoru, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] Micronutrient deficiency during pregnancy affects not only the pregnancy complications, but also the health of the offspring in their adulthood. Magnesium (Mg) deficiency is one of the common deficiencies during pregnancy. We have reported that Mg deficiency develops salt sensitive hypertension (SSH) via activating renal NaCl cotransporter in DBA/2J mice which possesses genetically low catechol-O-methyltransferase (COMT) activity, an enzyme that metabolizes catechol including hydroxyestradiol, a catechol estrogen. COMT deficiency is also related with pregnancy complications such as preeclampsia

and gestational diabetes mellitus. In this study, we hypothesized that maternal Mg deficiency might affect the development of SSH in offspring via lowering their COMT activity. **[Methods]** 8-12 weeks old female DBA/2J mice were fed either normal (0.1% Mg) or Mg deficient (0.03% Mg) diet and were mated with normal-diet-fed male mice. The maternal diet was changed to normal diet after delivery. Offspring was fed with either normal (0.6% NaCl) or high salt (8% NaCl) diet after 7 weeks of age and systolic blood pressure was measured every week. The mice were sacrificed at 12 weeks of age and kidney was removed for the analysis of COMT activity. **[Results]** In both male and female offspring, SSH was developed only in the group whose mother was fed Mg deficient diet. In the SSH developed group, water retention was higher, kidney weight was heavier and COMT activity was lower. **[Conclusion]** Offspring who was born from Mg deficient mother are more prone to develop SSH possibly due to the innate lower COMT activity.

ISP-32-4

Maternal oxygen administration during NRFS did not improve umbilical artery (UA) gas measures and neonatal outcomes

Goda Mayuko, Arakaki Tatsuya, Takita Hiroko, Tokunaka Mayumi, Hamada Shoko, Matsuoka Ryu, Sekizawa Akihiko *Showa University*

[Objective] To clarify whether maternal oxygenation during non-reassuring fetus status (NRFS) improves umbilical artery (UA) gas measures and neonatal outcomes. **[Methods]** Term singleton pregnancies that required operative vaginal deliveries or emergency cesarean sections due to NRFS from January 2018 through September 2021 in our hospital were enrolled in this study. Congenital anomaly and chromosomal abnormalities were excluded. In our hospital, conventional oxygen administration during NRFS has been discontinued since April 2020, when the COVID-19 became a pandemic, to prevent the generation of aerosols. The patients were divided into two groups: oxygen group that was supplied oxygen (10L/min by facemask) and room air group that was not. Umbilical artery (UA) gas measures and neonatal outcomes were compared between oxygen and room air group. **[Results]** Of the 250 patients included in the study, 140 (56%) were in oxygen group and 110 (44%) in room air group. There were no differences in background factors in oxygen and room air group, maternal age over 35 years (68.5% vs. 59.1%), gestational age at delivery (39w5d vs. 39w4d) and the percentage of Light-for-date (12.1% vs. 5.5%). Comparing oxygen and room air group, umbilical artery pH < 7.2 (12.8% vs. 14.5%: p=0.69), Apgar score < 7 at 5min (8.5% vs. 13.6%: p=0.16), administration to NICU (12.1% vs. 19%: p=0.12), respiratory failure requiring CPAP or oxygenation (5.7% vs. 2.7%: p=0.25). **[Conclusion]** Oxygen administration during NRFS did not improve the umbilical artery (UA) gas measures and neonatal outcomes.

ISP-32-5

Sustained postnatal acidemia may be a key factor for the development of impaired neurodevelopment in infants born at periviable gestational ages

Ariyoshi Yu, Seyama Takahiro, Iriyama Takayuki, Kanatani Ayumi, Yoshikawa Midori, Akiba Naoya, Fujii Tatsuya, Toshimitsu Masatake, Sayama Seisuke, Kumasawa Keiichi, Nagamatsu Takeshi, Osuga Yutaka *The University of Tokyo Hospital*

[Objective] Survival rate as well as neurodevelopmental prognosis of infants born at periviable gestational ages have improved with advance in perinatal medicine. We aimed to evaluate the perinatal clinical factors associated with neurodevelopmental prognosis in periviable infants. **[Methods]** This is a retrospective cohort study of periviable infants born at 22-25

weeks of gestation at our institution between 2011 to 2020. The developmental quotient (DQ) score, corrected at 1.5 years old, over 85 was judged as normal neurodevelopment. Maternal and neonatal clinical factors were compared between the normal and subnormal neurodevelopment groups. **[Results]** Among 58 periviable newborns, thirty-four infants followed at 1.5 years old were included in the analysis. The survival rates in periviable newborns were 83%, 86%, 93%, and 93% at 22, 23, 24, and 25 weeks, respectively. The percentage of normal DQ was 19/34 (55%). Infants with subnormal DQ had lower birth weight (565 g vs 629g, p=0.01), lower Apgar Score at 1 minute (2 vs 4, p=0.04) and 5 minutes (6 vs 7, p=0.01), and lower arterial pH measured after birth (7.163 vs 7.342, p<0.01), as compared with those with normal DQ. There was no difference in other factors, including gestational age at birth, umbilical artery pH, and the frequency of histopathological chorioamnionitis, between the two groups. **[Conclusion]** Our study results suggest that poor responsiveness to resuscitation, leading to sustained acidemia after birth, might be associated with the impaired neurodevelopment in periviable infants.

ISP-32-6

Postnatal oxygenation promotes anatomical closure of the ductus arteriosus by basic fibroblast growth factor-mediated intimal thickening

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[Objective] Closure of the ductus arteriosus (DA) is critical for transition from fetal to neonatal circulation. Although it is well recognized that postnatal acute oxygenation promotes functional DA closure, the role of raising oxygen tension in anatomical DA closure remains unknown. We aimed to investigate whether raising oxygen tension promotes tissue remodeling of the DA, i.e., intimal thickening. **[Methods]** DA smooth muscle cells (DASMCs) and aortic smooth muscle cells (ASMCs) isolated from rat fetuses on 21 days of gestation were cultured under hypoxic condition (pO₂ 20 mmHg) and then transferred to a normoxic condition (150 mmHg). Basic fibroblast growth factor (bFGF) in the culture supernatants was quantified using ELISA. The intimal thickening of the DA was quantified using Elastica van Gieson stained paraffin sections. Reactive oxygen species (ROS) was measured by the fluorogenic probe CellROX. **[Results]** An increase in oxygen tension significantly increased bFGF secretion in a time-dependent manner in DASMCs (4.0 ± 0.56-fold, n=8), but not in ASMCs. Oxygenation increased ROS in DASMCs, but not in ASMCs. Inhibition of mitochondria complex I using rotenone or complex II using TTFA reduced oxygen-induced bFGF production in DASMCs. Maternally-administered neutralization antibody against bFGF significantly attenuated postnatal intimal thickening (0.83 ± 0.04-fold, n=4) and DA closure in full-term infants. Administration of recombinant bFGF promoted DA intimal thickening and DA anatomical closure in preterm (20 days of gestation) infants in which intimal thickening is poorly formed. **[Conclusion]** Raising oxygen tension markedly increased intimal thickening of the DA by ROS-mediated bFGF production.

ISP-32-7

Association between obstetric and neonatal outcomes among sonographically—Assessed small for gestational age and appropriate for gestational age term fetus in low-risk pregnancies: A retrospective study

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[Methods] This is a retrospective-correlational study which is to compare the obstetric and neonatal outcomes of fetuses as-

essed with sonographic estimated fetal weight less than the 10th percentile and those with a sonographic estimated fetal weight between the 11th-90th percentile among term, low-risk pregnancies who delivered in a tertiary hospital. **[Results]** It shows that all maternal and fetal demographic characteristics have no relationship to the SEFW of the fetuses included in the study. It shows that there is a significant association between the SEFW of the fetuses included in the study and gestational age at delivery, actual birth weight, and weight appropriate for gestational age. It also shows that all parameters showing the neonatal outcome of fetuses are not related to the SEFW of the fetuses included in the study. There is a significant difference between the Sonographic Estimated Fetal Weight Versus Actual Birth Weight for both SGA and Appropriate for Gestational Age (AGA) groups. Serial sonographic assessment of fetal size can provide useful information about growth, with the possibility of improving the prediction of SGA fetuses, particularly those at risk for morbidity. **[Conclusion]** To better discriminate between growth-restricted fetuses and constitutionally small fetuses, it is, therefore, logical to adopt customized growth charts for the ultrasound to adjust for the characteristics of each mother, taking her ethnic origin and her height, weight and parity and set a growth and birthweight standard for each pregnancy against which actual growth can be assessed. **Key-words** : neonatal outcomes, sonographically-assessed small for gestational age.

ISP-33-1

An optimal timing of delivery in pregnancies complicated by fetal growth restriction Yoshimoto Akiko, Tanimura Kenji, Uchida Akiko, Shi Yutoku, Shirakawa Tokuro, Imafuku Hitomi, Deguchi Masashi, Terai Yoshito *Kobe University*

[Objective] Fetal growth restriction (FGR) can cause mortality and long-term sequelae. Because there are no established treatments for FGR, assessment of timely delivery is most crucial for the management of FGR. The aim of this study was to assess optimal cutoffs of gestational weeks (GW) at delivery and birth weight (BW) for poor prognosis in surviving children affected with FGR. **[Methods]** This retrospective study was approved by the IRB. From March 2011 to December 2019, 172 singleton fetuses with FGR were delivered in our hospital, and they were received the assessment of neurological outcomes at 1.5 years of adjusted-age. Subjects were divided into two groups : those with and without poor prognosis. Poor prognosis was defined as an overall developmental quotient (DQ) <70, retinopathy of prematurity (ROP) requiring vitreous surgery, chronic lung disease (CLD) requiring home oxygen therapy (HOT), epilepsy, or cerebral palsy. To determine optimal cutoffs of GW at delivery and BW, receiver operating characteristic (ROC) analysis was performed. **[Results]** During this study period, 13 (8%) cases had poor prognosis (an overall DQ<70, n=10 ; an overall DQ<70 and CLD requiring HOT, n=1 ; ROP requiring vitreous surgery, n=1 ; and epilepsy, n=1). ROC analyses revealed that a cutoff of GW at delivery and BW for the prediction of poor prognosis were determined to be 28 GW (AUC=0.92) and 652 g (AUC=0.93), respectively. **[Conclusion]** Delivery after 28 GW and BW beyond 650 g may be associated with good prognosis in children with FGR.

ISP-33-2

Risk factors of unfavorable short-term neonatal outcomes in severe FGR patients : a single-center retrospective study Hashiramoto Shin¹, Kanamine Chihiro¹, Doi Shoko¹, Nakano Yuko¹, Izumi Yuki¹, Oyama Takuma¹, Yamashita Kaoru¹, Heshiki Chiaki¹, Sunagawa Sorahiro¹, Nagai Yutaka¹, Sakumoto Kaoru¹, Aoki Yoichi² *Nanbu Child Medical Center¹, University of*

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[Objective] To evaluate the risk factors of unfavorable short-term neonatal outcomes (USNO) in severe fetal growth restriction (severe FGR ; birth weight below 3rd percentile) patients. **[Methods]** We reviewed 158 severe FGR patients who gave birth in our hospital during April 2013 to July 2021. We excluded multiple pregnancies and intrauterine fetal deaths. We defined USNO as either neonatal deaths (NND), intraventricular hemorrhages (IVH), or periventricular leukomalacias (PVL), all within 28 days after birth. We compared the perinatal characteristics (maternal complications, oligohydramnios, onset of FGR, gestational age, and birth weight) in patients with and without USNO. We compared categorical variables by χ^2 test and continuous variables by Mann-Whitney U test. **[Results]** Three NND (1.9%), 3 IVH (1.9%), and no PVL were observed. Patients with and without USNO had oligohydramnios in 2/23 cases (8.7%) and 4/135 cases (3.0%), respectively ($p=0.237$), and were late onset in 1/38 cases (2.7%) and early onset in 5/120 cases (4.2%), respectively ($p=0.654$). The median gestational age was 28 (range : 25-40) weeks and 36 (range : 24-41) weeks in patients with and without USNO, respectively ($p=0.062$). The median birth weights, standard deviations (SD), and percentiles (%ile) in patients with and without USNO are 821 g (range : 312~1922 g) and 1604 g (range : 297~2525 g) ($p=0.022$), -2.69 SD (range : -5.09~-2.01 SD) and -2.72 SD (range : -6.56~-1.89 SD) ($p=0.794$), 0.45% ile (range : 0~2.2% ile) and 0.3% ile (range : 0~2.9%ile) ($p=0.957$), respectively. **[Conclusion]** In severe FGR patients, birth weight was the risk factor for USNO and gestational weeks should be also considered.

ISP-33-3

Relationship between perinatal parameters and neurodevelopmental prognosis at three years old in fetal growth restriction affected by placental dysfunction Masaoka Shun, Yamamoto Yuka, Hirai Mitsuko, Masaoka Ryu, Kawata Misato, Ando Hitomi, Ueki Norikazu, Sei Kiguna, Takeda Jun, Itakura Atsuo *Juntendo University*

[Objective] Fetal growth restriction (FGR) affected by placental dysfunction may lead to poorer growth and developmental outcomes. Birth timing significantly affects their prognosis because no effective treatment for FGR in utero. Although prenatal parameters obtained from ultrasonography or cardiocardiography are important in determining, the criteria for the timing of birth regarding long term prognosis have not been established. Our objective was to clarify the relationships between prenatal parameters and postnatal prognosis in FGR cases. **[Methods]** Nineteen FGR cases followed at our institute from 2015 to 2018, were collected. Complicated with major malformations or chromosomal anomalies were excluded. Prenatal parameters (fetal growth and Doppler, onset of FGR and growth arrest) and postnatal parameters (neurodevelopmental evaluation, body size, growth hormone use) at three years old (3Y) were evaluated. **[Results]** Maternal background was 17 primiparous, ages 33.6 ± 2.7 , and 6 cases with hypertensive disorder. Neonatal outcome was birth weight ($-2.38 \pm 0.67SD$), and birth height ($-1.97 \pm 0.95SD$). There was a negative correlation between resistance index (RI) in umbilical arteries (UmA) and birth weight SD ($p=0.02$, $r=-0.50$). There was a significant positive correlation between onset of FGR and body height at 3Y ($P=0.02$, $r=0.57$). 84.2% of FGR cases caught up to the normal range at 3Y. As for neurodevelopmental outcome, none showed delay at this moment. **[Conclusion]** RI in UmA related to short term outcome as birth weight. Onset of FGR was a major determinant for the growth at 3Y, however it is difficult to predict neurodevelopmental prognosis prenatally.

ISP-33-4

Altered transmission of cardiac cycles in ductus venosus flow velocity wave of fetal growth restriction caused by placental insufficiency Seo Naomi¹, Tachibana Daisuke¹, Suemitsu Chiharu¹, Konishi Nafuko¹, Suekane Tomoki¹, Kurihara Yasushi¹, Tahara Mie¹, Hamuro Akihiro¹, Misugi Takuya¹, Nakano Akemi¹, Sumi Toshiyuki¹, Koyama Masayasu² *Osaka City University Hospital¹, Ishikiriseiki Hospital²*

[Objective] To investigate where the nadir between the systolic and the diastolic phases of ductus venosus flow velocity wave (DV-FVW) corresponds to in the cardiac cycle. **[Methods]** A cross-sectional study was performed in 60 normal and 20 FGR fetuses. The following time-related measurements were taken: IRT-systolic, the sum of each absolute value of the difference between the systolic time in DV and the time from the top of the second peak of ventricular inflow (A-wave) to the opening of the mitral valve and that between the diastolic time in DV and the time from the opening of the mitral valve to the top of A-wave; IRT-diastolic, the sum of each absolute value of the difference between the systolic time in DV and the time from the top of A-wave to the closing of the aortic valve and that between the diastolic time in DV and the time from the closing of the aortic valve to the top of A-wave. We compared them in both groups. **[Results]** In control group, IRT-systolic was significantly decreased than IRT-diastolic (median 28.0 and 76.7 respectively, $p < 0.001$). However, in FGR group they didn't show significant difference (median 41.0 and 53.1 respectively, $p=0.29$), there was no difference in IRT in both groups (median 48.9 and 47.0 respectively, $p=0.59$). **[Conclusion]** We demonstrated that the transmission of cardiac cycles to DV-FVW in FGR is altered when compared to that of normal fetuses. Time interval of DV-FVW would reflect the cardiac cycles as well as hemodynamic changes in FGR.

ISP-33-5

Clinical characteristics of fetal premature ventricular contractions Imaizumi Junki, Kaji Takashi, Shirakawa Aya, Yoshida Atsuko, Irahara Minoru, Iwasa Takeshi *Tokushima University*

[Objective] Extrasystoles are the most common arrhythmias in fetuses, and consist of premature atrial contractions (PAC) and premature ventricular contractions (PVC). The clinical characteristics of fetal PVC are poorly understood because PVC are rarely diagnosed in fetuses compared to PAC. Therefore, the aim of this study was to clarify the clinical differences between fetal PVC and PAC. **[Methods]** Fifty-four consecutive fetuses diagnosed with extrasystoles at our hospital between 2011 and 2020 were included in this retrospective study. PVC and PAC were diagnosed prenatally using a dual Doppler technique (hepatic vein and descending aorta) and M-mode echocardiography. Information on coexisting congenital heart diseases, progression to tachycardia and persistence of PAC and PVC was collected. **[Results]** Fifty-four extrasystole cases consisted of 13 fetuses with PVC and 41 fetuses with PAC. Ventricular aneurysm coexisted in 2 fetuses with PVC (2/13, 15%), no fetuses with PAC had coexisting heart diseases ($p=0.012$). The PAC progressed to a paroxysmal supraventricular tachycardia in 2 fetuses (2/41, 4.8%), although no PVC progressed to a tachycardia ($p=0.42$). PVC persisted until birth in 6/13 (46%), PAC persisted until birth in 4/41 (9.8%) ($p=0.008$). **[Conclusion]** It seems essential to distinguish fetal PVC from PAC because the clinical characteristics of fetal PVC was different from those of fetal PAC. Fetal PVC tend to persist until birth and coexist congenital heart diseases, such as ventricular aneurysm.

ISP-33-6

Association between placental circulation and prenatal survival after thoracoamniotic shunting in fetal hydrothorax Ozawa Katsusuke, Muromoto Jin, Sugibayashi Rika, Wada Seiji, Sago Haruhiko *Division of Fetal Medicine, National Center for Child Health and Development*

[Objective] To assess association between placental circulation and prenatal survival after thoracoamniotic shunting (TAS) in fetal hydrothorax. **[Methods]** This was a retrospective study using data collected prospectively. Fetuses who underwent TAS for hydrothorax between September 2018 and September 2021 were included. TAS was carried out for chylothorax with rapid accumulation after removal of pleural effusion by thoracocentesis. Primary outcome was fetal death (FD) or non-reassuring fetal status (NRFS) resulted in emergent delivery. Gestational age (GA) at first TAS and at birth, and umbilical venous flow volume (UVFV) before the first TAS, after the last TAS and before birth was collected. **[Results]** Twenty cases were included. UVFV before birth was not available in three cases, therefore 17 cases were analyzed. The median (range) of GA at the first TAS and at birth was 25+5 (21+2, 32+4) weeks and 33+2 (25+5, 38+3) weeks, respectively. Skin edema was observed in 16/17 (94%) cases. FD or NRFS was observed in 8/17 (47%) cases. UVFV before birth was lower in fetuses with FD or NRFS than those without it (24 ± 11 vs 80 ± 25 ml/min/kg, $p < 0.01$). UVFV before the first TAS and those after the last TAS were not different between two groups. In the FD or NRFS group, low UVFV (< 50 ml/min/kg) was seen at median of 30.5 (range: 27-34) weeks gestation. FD or NRFS happened within 3 weeks after demonstrating low UVFV. **[Conclusion]** Decreased placental circulation in third trimester could be associated with FD or NRFS after TAS for fetal hydrothorax.

ISP-33-7

Functional evaluation with intraventricular pressure difference in fetus with critical aortic stenosis Yamamoto Yuka, Masaoka Shun, Sei Kiguna, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] Critical aortic stenosis (CAS) shows a several clinical features depending on the pathological changes and cardiac function. Severe mitral regurgitation induces left atrial expansion, cardiac dysfunction and fetal hydrops. For better understanding fetal condition, we evaluated fetal cardiac function with intraventricular pressure difference (IVPD) and other cardiac functional parameters. **[Methods]** After basic evaluation of the fetus, we collected color M-mode image, which was analyzed with using MATLAB to obtain IVPD. Total IVPD was divided into basal and mid-apical IVPD. IVPD was converted to z-score from normalized data. Mitral valve (MV) flow pressure and inflow duration was also acquired. **[Results]** The case was evaluated from 28⁵ to 36⁵ weeks of gestation every other week. In right ventricle (RV), total IVPD was significantly increased as 6.19 to 4.47 z-score. Although mid-apical IVPD was normal range (1.39 to 0.43 z-score), basal IVPD was significantly increased as 5.31 to 4.11 z-score. In left ventricle (LV), total IVPD was significantly decreased as -0.43 to -3.54 z-score. Especially mid-apical IVPD in LV was significantly decreased as -3.09 to -5.21 z-score. MV regurgitation was not detected at the beginning then started to be seen as 197cm/s. MV inflow was significantly short although tricuspid valve inflow was normal. **[Conclusion]** The increased total IVPD accompanied by increased basal IVPD in RV was seen. Decreased cardiac function led increased end-diastolic pressure in LV which induced the increased RV circulation. In difficult cases with congenital heart disease to evaluate cardiac function, IVPD might be one of parameters to evaluate fetal cardiac function.

ISP-33-8

Sonographic assessment of fistulas in fetuses with imperforate anus Kaji Takashi, Imaizumi Junki, Shirakawa Aya, Yoshida Atsuko, Irahara Minoru, Iwasa Takeshi *Tokushima University*

[Objective] A fistula is one of key factors in defining appropriate treatment in neonates with imperforate anus (IA). However, no studies have focused on the assessment of fistulas in fetuses with IA. The aim of this study was to clarify the sonographic appearance of fetal fistulas in IA. **[Methods]** This study included three consecutive cases of IA in which fistulas were detected and localized prenatally and confirmed after birth at our hospital between 2017 and 2019. Fetal and neonatal sonographic images of the fistulas were investigated. The fetal fistulas were visualized using a 3-8 MHz linear transducer. **[Results]** Three cases consisted of two cases with a rectovestibular fistula and one case with an anocutaneous fistula. Gestational ages at diagnosis of the fistulas were 27, 30 and 37 weeks. Each fistula in the fetuses was demonstrated as a hyperechoic linear structure, although the fistulas in the neonates were visualized as a hypoechoic tubular tract between hyperechoic thin walls. The fetal fistulas were detected in the axial view of the fetal pelvis, then localized in the sagittal or coronal view which show the longitudinal aspect of the fistulas. **[Conclusion]** The fetal fistulas in IA were demonstrated as a hyperechoic linear structure using a linear transducer. The sagittal or coronal view of the fetal pelvis visualized the longitudinal aspect of the fistulas, leading to the localization of the fistulas.

ISP-34-1

Uterine rupture during medical induction for second trimester abortion : A case report and review of the literature Hayashida Harue, Mimura Kazuya, Kakuda Mamoru, Toda Aska, Nakamura Koji, Miyake Tatsuya, Hiramatsu Kosuke, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University Hospital*

[Objective] Prostaglandin E1 derivatives (gemeprost or misoprostole) is widely used for second trimester abortion. These drugs are safe and effective, but there is limited published experience of its use in women with prior cesarean sections (CS). We report a case of uterine rupture during her termination in the second trimester. **[Case]** A 42-year-old woman G3P2 with two prior CS was referred to our hospital at twenty weeks of gestation for her fetus with hypoplastic left heart syndrome. She opted termination of her pregnancy. At the 7th doses in a second day of gemeprost, her cervix was closed and membranes has not been ruptured. For pain relief, fentanyl was administered intravenously. Although there was no obvious change of her vital sign, she had mild abdominal pain persistently without intermittent peiods. With trans-abdominal ultrasound, her fetus was observed in the intra-abdominal space out of the uterus. She underwent immediate laparotomy and repair of ruptured uterus. **[Discussion]** According to our retrospective data and review of the literature, there were 2.2% (13/588) cases of uterine rupture during second trimester abortion with gemeprost. Among cases in which the number of prior CS was reported, there is no uterine rupture cases (0/191) among who experienced one CS. While, women with multiple prior CS had an increased risk of 5.6% (2/36). When performing a second trimester abortion with prior CS (especially two or more CS), careful labor monitoring is necessary, including periodic observation of the abdominal cavity by trans-abdominal ultrasound.

ISP-34-2

Anatomical identification of ischial spines applicable to intrapartum transperineal ultrasound based on magnetic resonance

imaging of pregnant women Yano Eriko¹, Iriyama Takayuki¹, Sayama Seisuke¹, Ichinose Mari¹, Toshimitsu Masatake¹, Seyama Takahiro¹, Sone Kenbun¹, Kumasawa Keiichi², Nagamatsu Takeshi¹, Kobayashi Koichi², Fujii Tomoyuki³, Osuga Yutaka¹ *The University of Tokyo Hospital¹, JCHO Tokyo Yamate Medical Center², Sanno Hospital³*

[Objective] Intrapartum transperineal ultrasound (ITU) is considered useful in evaluating labor progression. Angle of Progression (AoP) is regarded as most reliable parameters in assessing head descent : AoP of 110 to 120° is considered equivalent to AoP at station 0. However, the inability to detect ischial spines on ITU has been a shortcoming to its reliability. The current aimed to determine the anatomical location of ischial spines, which can be directly applied to ITU. **[Methods]** Based on magnetic resonance imaging (MRI) of 67 pregnant women at 33rd-34th weeks gestation (median [interquartile range : IQR]), we analyzed the angle between the pubis and the midpoint of ischial spines (midline symphysis-ischial spine angle : mSIA), which is theoretically equivalent to AoP at station 0 on ITU. Furthermore, we measured symphysis-ischial spine distance (SID), defined as the distance between the vertical plane passing the lower edge of the pubis and the plane that passes the ischial spines. **[Results]** By determining spatial coordinates of the upper and lower edge of the pubis and the midpoint of ischial spines and utilizing vector analysis, mSIA and SID were calculated as 109.6° [105.1-114.0] and 26.4 mm [19.8-30.7] (median, [IQR]), respectively. There was no correlation between mSIA or SID and maternal characteristics, including height. **[Conclusion]** We identified the anatomical position of ischial spines which can be applied as positional landmarks to assess station 0 on ITU images. Our result provided valuable evidence to enhance the reliability of ITU in assessing fetal head descent by considering the location of ischial spines.

ISP-34-3

Comparison of National Institute of Child Health and Human Development classification and computed cardiocography for fetal acidemia prediction using fetal heart rate monitoring during labor Shimaoka Ryuichi¹, Tohmatsu Akie², Shiga Tomomi², Takahashi Yuichiro¹, Morishige Ken-ichirou² *Gifu Prefectural General Medical Center¹, Gifu University Hospital²*

[Objective] To compare the prediction accuracy of the National Institute of Child Health and Human Development (NICHD) classification and computed cardiocography (cCTG) for fetal acidemia using fetal heart rate monitoring during labor. **[Methods]** This retrospective observational study analyzed fetal heart rate records for 30 minutes before delivery in 830 single-fetal vaginal deliveries after 37 weeks of gestation at two tertiary perinatal centers. All data were randomly divided into training and testing data at a ratio of 7 : 3. Predictive models of cord blood pH were developed using parameters based on the NICHD classification and cCTG parameters (including baseline, short/long-term variation, and bradycardia/tachycardia area). This study was approved by the Institutional Review Board at each institution. **[Results]** Fetal acidemia was observed in 26 cases. Of these, 10 cases received medical intervention. Medical intervention for nonreassuring fetal status was performed in 74 cases, but no acidemia was observed in 69 cases. Severe perineal lacerations were noted in 17 cases, 90% of which were associated with medical intervention. The area under the receiver operating characteristic curve (AUC) of the NICHD classification model for fetal acidemia prediction was 0.626 for training data and 0.427 for testing data and that of the cCTG model was 0.724 and 0.634, respectively. The AUC of the deep learning model using cCTG parameters was 0.879 and 0.712, respectively. **[Conclusion]** The prediction accuracy of the NICHD classification for fetal acidemia is low. The cCTG parameters may improve the

prediction accuracy and reduce the complications associated with unnecessary medical intervention.

ISP-34-4

Analysis of the relationship change in time interval between systolic and diastolic of ductus venosus with pH of umbilical artery in fetal growth restriction Suekane Tomoki¹, Tachibana Daisuke¹, Konishi Nafuko¹, Suemitsu Chiharu¹, Seo Naomi¹, Kurihara Yasushi¹, Tahara Mie¹, Hamuro Akihiro¹, Misugi Takuya¹, Nakano Akemi¹, Sumi Toshiyuki¹, Koyama Masayasu² *Osaka City University Hospital¹, Ishikiriseiki Hospital²*

[Objective] The aims of this study were to investigate whether the time interval analysis of flow velocity waveforms (FVW) of ductus venosus (DV) in fetal growth restriction (FGR) shows the correlation with pH of umbilical artery (UA-pH). **[Methods]** FGR is defined as estimated fetal weight <-2.0 SD. The data of DV-S/D were transformed as z-scores from the reference ranges which already establish by our previous reports. Time intervals between the last Doppler examination and delivery ranged within 4 days. We investigated gestational weeks of examination was divided into ≤28w+6 and >29w+0. Correlations between parameters (DV-S/D, DV-PI, TV-SD, MV-SD) and UA-pH were calculated using the Pearson's correlation coefficient and $P < 0.05$ was considered statistically significant. **[Results]** In this study, 31 FGR fetuses were evaluated. Both DV-S/D and DV-PI showed significant correlation with UA-pH. In addition, more significances were observed in FGR ≤28+6 gestational weeks ($r = -0.819$, $p < 0.001$ and $r = 0.726$, $p = 0.005$, for DV-PI and z-score of DV-S/D, respectively) than in FGR >28+6 gestational weeks ($r = -0.634$, $p = 0.007$ and $r = 0.635$, $p = 0.020$, for DV-PI and z-score of DV-S/D, respectively). On the other hand, TV-S/D and MV-S/D showed no significant correlation with UA-pH. **[Conclusion]** We showed that DV-S/D is a useful parameter in the management of FGR fetuses regarding the prediction of fetal acidemia as well as DV-PI. DV-S/D possibly is the one of predictive parameter for short term outcome of fetuses complicated with FGR.

ISP-34-5

Pregnant women with threatened preterm labor have a shorter delivery time in the multiparous, but not null-parous women Sugimura Kodai, Kawakami Kaori, Katoh Kanoko, Nakajima Takahiro, Ikeda Yuji, Komatsu Atsushi, Takeya Chiaki, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] Extremely short delivery time often carry the risk of maternal complications. Pregnant women with threatened preterm labor (TPL) may have a shorter delivery time than those with no symptom. Here we focused on delivery times comparing pregnant women with or without TPL. **[Methods]** Pregnant women who underwent vaginal delivery in our hospital from January to December 2020 were enrolled in the study. We set two groups : pregnant women with threatened preterm labor (TPL group) and with no symptom regarding TPL (Normal group). TPL was defined as regular contractions and cervical length shortening (<30mm) before 37 weeks. The delivery times of these cases were evaluated comparing obstetrical factors. **[Results]** Among 293 women, 78 cases have been diagnosed with TPL. There were no significant differences between two groups regarding patient background, birth weight, bleeding volume. TPL group was likely to take shorter delivery time than Normal group (509 ± 452 minutes versus 584 ± 491 minutes, $P = 0.067$). The delivery time in TPL groups was significantly shorter than Normal group (282 ± 244 minutes versus 379 ± 276 minutes, $P = 0.023$) when limited to multiparous women. In addition, there was a significant difference in delivery time in the 1-

parous women, but not in the 2- or more parous women. **[Conclusion]** In the case of pregnant women diagnosed as having TPL, attention should be paid to maternal complications such as precipitate labor, cervical laceration and flaccid hemorrhage during delivery. Careful observation of delivery is needed especially in the multiparous women.

ISP-34-6

A single-center experience of induced abortion in mid-trimester Arai Tomohiro, Ozawa Katsusuke, Muromoto Jin, Sugibayashi Rika, Wada Seiji, Sago Haruhiko *Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child Health and Development*

[Objective] Mid-trimester induced abortion was previously performed at private clinics in Japan. Recently, it is commonly performed at tertiary perinatal centers due to the need for safety. However, the outcomes of mid-trimester induced abortion have not been well investigated. We investigated the outcomes of mid-trimester induced abortion procedures at our center. **[Methods]** This retrospective study included women who experienced mid-trimester induced abortion at 12-21 weeks of gestation in our institute. All the procedures were conducted in the same manner : Laminaria-dilation was performed three times two days prior to the induction of abortion with PGE1-vaginal tablets every three hours. Maternal demographics, perinatal and puerperal outcomes were extracted from electronic medical records. **[Results]** Between January 2016 and July 2021, 321 women were included in this study. The median gestational age at delivery was 18+5 weeks (13+1 to 21+6 weeks). One hundred one cases (31.5%) involved intrauterine fetal death. One hundred seventy-eight cases (55.5%) were nulliparous and 20 had a history of cesarean section. All women aborted the fetuses vaginally. Two cases (0.6%) required vaginal surgical maneuvers during delivery. Three cases (0.9%) required blood transfusion after an abortion due to severe intrapartum/postpartum hemorrhage during admission. Ten cases (3.1%) were admitted within six weeks of discharge due to severe postpartum hemorrhage, three of which (0.9%) required vascular embolization of the uterine artery. **[Conclusion]** Life-threatening hemorrhage was not rare as a complication of mid-trimester induced abortion. Preparation for severe hemorrhage is required for its management.

ISP-34-7

Reduced intrapartum analgesic dosing might decrease frequency of caesarean section Kondo Yoshimi¹, Goto Shinobu¹, Ogasawara Sakura¹, Shinoda Miki², Sawada Yuuki¹, Kitaori Tamao¹, Suzumori Nobuhiro¹, Tanaka Motoshi², Sugiura Mayumi¹ *Nagoya City University Hospital¹, Department of Anesthesiology, Nagoya City University Hospital²*

[Objective] Neuraxial analgesia is key for maternal pain relief during labour. Various studies report optimal regimens and routes of anaesthesia. We examined drug dose reduction effects on pregnancy outcomes. **[Methods]** This prospective study included 125 pregnant women who underwent analgesia during labour beginning January 2021. Each patient underwent combined spinal epidural anaesthesia, dural puncture epidural anaesthesia, or standard epidural anaesthesia. Epidural labour analgesia was maintained using combined Programmed Intermittent Epidural Bolus (PIEB) and Patient Controlled Epidural Analgesia (PCEA) with levobupivacaine or fentanyl. Group A consisted of 64 women who received the standard regimen. Group B consisted of 61 women with revised analgesic dosing and schedules. For this group, PIEB interval was increased from 30 to 60 minutes ; PCEA lock-out time was increased from 10 to 15 minutes ; and PCEA bolus volume was reduced from 30 ml to 20 ml per hour. Frequencies of caesarean section, instrumental deliv-

ery, during of second stage of labour, and blood loss were compared between groups by Fisher's exact test and Mann-Whitney U test. **[Results]** The frequency of caesarean section was significantly higher in Group A compared with Group B (19.0% vs 3.3%, $P < 0.01$). No differences in the frequency of instrumental delivery (52.9% vs 55.9%), blood loss (553ml vs 543ml) and duration of second stage of labour (52min vs 70min) were found between the two groups. **[Conclusion]** Prolonged PIEB interval, prolonged PCA lock-out time, and reduced bolus size may decrease the frequency of caesarean section. Further study is required for confirmation.

ISP-35-1

A rare case of a pubic fracture immediate before vaginal delivery Miyagi Miki¹, Miyazaki Shoko¹, Oshiro Miya¹, Yoshiaki Ken¹, Inamine Morihiko¹, Uesato Tadakazu¹, Aoki Yoichi² *Okinaawa Red Cross Hospital¹, University of the Ryukyus Hospital²*
Herein, we report a rare case of a pubic fracture before delivery. A 38-year-old woman was admitted with premature rupture of the membranes at 39 weeks of gestation. During walking, pain in the right hip joint appeared without any apparent trigger, leading to limping. The following day, she delivered a 3086 g male infant vaginally. The labor course was uneventful, but the hip joint pain persisted. On the second puerperal day, her pain worsened and she was referred to an orthopedic surgeon. A pelvic X-ray revealed a right pubic fracture, which was thought to have occurred before delivery. Her bone mineral density was within normal range. A blood test showed a serum albumin of 2.8 g/dL and serum 25-hydroxyvitamin D of 15.2 ng/dL, which were slightly low. The tartrate-resistant acid phosphatase form 5b level was 490 mU/dL, which was higher than normal. Calcium, inorganic phosphorus, and undercarboxylated osteocalcin were at normal levels. She received conservative management with a sacroiliac brace, crutches, and a prescription for vitamin D. One month after delivery, the pain had improved. Nine weeks after delivery, a pelvic X-ray showed callus formation at the fracture site. The known risk factors for pelvic fractures around delivery include a narrow pelvis, a high birthweight newborn, increased lumbar lordosis, rapid vaginal delivery, and osteoporosis or osteopenia. In the case, no risk factors were identified. Pubic fractures can occur even in women with no risk factors. If pregnant or postpartum women have pelvic pain, imaging evaluation is necessary for accurate diagnosis.

ISP-35-2

Sudden onset pneumothorax in the intrapartum period Nakano Kazutoshi, Nishikawa Kyouhei, Fujita Yu, Ogawa Kenji, Yasukawa Hisayoshi, Akada Shinobu *Osaka Habikino Medical Center*

Background : Pneumothorax in pregnancy is rare, occurring in only 1 out of 10000 cases. Pneumothorax that develops during delivery may lead to hypoxemia, putting both the mother and the fetus at risk. We report a case of pneumothorax the developed during the peripartum period. **Case report :** A 24-year-old primigravid noted dyspnea and chest pain after the onset of labor. She was otherwise healthy, and had an unremarkable pregnancy course. Computed tomography imaging revealed multiple bullas at the apex of the left lung. The presence of a left pneumothorax warranted pleural drainage was performed. Delivery was performed by vacuum extraction due to a non-reassuring fetal status. The baby was a 3004 g girl with an Apgar score of 9 points (after both one and five minutes). The mother was managed up with oral tramadol hydrochloride for pain control. However, because her left remained collapsed, a bullectomy was performed four days after delivery. The chest tube was removed on the second postoperative day. The patient was discharged on

the third postoperative day or the eighth postpartum day. **Conclusion :** The presence of chest pain and dyspnea during pregnancy should alarm the physician of a possible pneumothorax. Maternal hypoxia is fatal to the fetus. To prevent such outcomes, it is vital to have an environment that allows rapid delivery, such as a cesarean section or vacuum extraction with the treatment of chest tube drainage.

ISP-35-3

A case of a prenatally diagnosed rare isolated agnathia-otocephaly complex for ex-utero intrapartum treatment (EXIT) Takesawa Ami¹, Suemitsu Tokumasa¹, Hosokawa Mayu¹, Mitani Takahiro¹, Kadooka Mizuho¹, Furusawa Yoshiaki¹, Dohi Satoshi² *Kameda Medical Center¹, Showa University Koto Toyosu Hospital²*

[Introduction] Agnathia-otocephaly complex is a rare congenital malformation due to first branch arch disorder and has been considered lethal if it is complicated with holoprosencephaly. However, nonlethal cases have been reported for the isolated agnathia-otocephaly complex. Therefore, the EXIT procedure is performed to treat cases until the airway can be evaluated and secured while on placental support ; thus, it would achieve a better long prognosis. **[Case]** A 37-year-old woman was referred for fetal craniofacial anomalies and polyhydramnios at 27 weeks of gestation. Our fetal ultrasounds showed agnathia, microstomia, and synotia, but not holoprosencephaly ; afterward, isolated agnathia-otocephaly was diagnosed prenatally. Microbubble testing and MRI detected the delayed, yet incomplete, fetal lung maturation. Emergency cesarean section with EXIT were performed due to clinical chorioamnionitis at 35 weeks of gestation, after obtaining the patient's express consent. Tracheostomy was almost completed during the EXIT for 16 minutes and accomplished for 4 minutes after delivery. Nevertheless, neonatal death occurred 12 hours after delivery due to acute respiratory distress syndrome and tension pneumothorax due to pulmonary hypoplasia. Even though spending little time with her baby, the patient could feel what being a mother feels like. **[Conclusion]** Prognosis of the isolated agnathia-otocephaly complex is challenging ; long surviving cases have recently been reported. Therefore, the EXIT procedure may be considered for airway management, expecting a better prognosis in isolated cases. Moreover, accurately evaluating fetal lung maturation is very challenging ; thus, careful consideration is required to indicate cases for EXIT.

ISP-35-4

Continuous simulation training and reduction of the decision-to-delivery interval for category-1 caesarean sections Kudo Rie, Hamada Hirotaka, Iwama Noriyuki, Tomita Hasumi, Kumagai Natsumi, Tagami Kazuma, Takahashi Sara, Hoshiai Tetsuro, Saito Masatoshi, Yaegashi Nobuo *Tohoku University Hospital*

[Objective] Category-1 cesarean section (C1CS) is a surgical procedure performed to life-threatening conditions of pregnant women or fetus. European/American obstetric guidelines recommend to keep the decision-to-delivery interval (DDI) within 30 minutes. We had been providing annual C1CS simulation training to the corresponding medical staffs since 2017, to offer stable C1CS in our hospital having heavy turnovers. The aim of this study was to examine the DDI of C1CS after the protocol was introduced. **[Methods]** All 83 C1CS cases from January 2017 to September 2021 at our hospital were included and clinical data were analyzed retrospectively. **[Results]** Indications for C1CS were non-reassuring fetal status (n=34, 41.0%) and antepartum hemorrhage (n=33, 51.8%). 27 cases (31.8%) had 5-min Apgar score less than 7 points and the median (range) of umbilical

artery blood gas pH was 7.262 (6.877-7.371). Neonatal resuscitation was required in 73 cases (85.9%), and 63 cases (74.1%) admitted to NICU. Number of cases that achieved DDI within 30 minutes were 81 (97.6%), where two cases (2.4%) took more than 30 minutes. DDI was significantly longer during weekday night-shift ($p=0.007$) and holiday night-shift ($p=0.004$), compared to weekday daytime. DDI was significantly shortened after 2018 compared to 2017 ($p<0.05$). There was no significant correlation between DDI and corresponding physician's years of practice. **[Conclusion]** DDI was significantly shortened after induction of CICS protocol and maintained throughout 5 years. Continuous simulation training presumably contributes to guarantee the quality of CICS, and regular provision of simulation training is required to offer safe and rapid CICS.

ISP-35-5

Analysis of maternal zinc intake during pregnancy association with perinatal prognosis Maruyama Yojiro¹, Masuda Ayako², Terao Junna¹, Tanaka Motoki¹, Kuki Saki¹, Seo Eimi¹, Oguma Kyoko¹, Ito Yosuke¹, Kasahara Hanako¹, Hamamura Kensuke¹, Matsuoka Shozo¹, Ogishima Daiki¹ *Juntendo University Nerima Hospital¹, Hodaka Hospital²*

[Objective] The relationship between zinc and growth in the pediatric field has been clarified, and zinc supplementation has been established as a treatment for short stature. On the other hand, there are few reports on maternal zinc intake during pregnancy. This survey examined Maternal zinc intake during pregnancy by using BDHQ questionnaire. **[Methods]** The BDHQ questionnaires were conducted from August 2018 to October 2019, regarding dietary content during pregnancy of Japanese women. After extracting the nutrients ingested, the relationship between zinc intake and perinatal complications was statistically analyzed. **[Results]** 309 consented patients who answered. There were 195 normal term deliveries. Zinc intake was classified into two groups: less than 7mg/day (less than group) and more than 7mg/day (or more group). the birth weight (3069.69 ± 31.45 vs 2976.57 ± 31.61 , p value <0.05) was significantly lower in the lesser group. EPDS (3.95 ± 0.24 vs 4.78 ± 0.31 , p value <0.05) was significantly higher in the lesser group. **[Conclusion]** the relationship between postpartum depression and malnutrition is reported. This survey suggest that Zinc content may affect EPDS as well. And Zinc intake may affect birth weight same as in the pediatric field. Cheking blood test of zinc in pregnancy and zinc supplementation can be considered in the future.

ISP-35-6

Attitude changes toward prenatal testing among women with twin pregnancies after the introduction of non-invasive prenatal testing: a single-center study in Japan Ogawa Masanobu^{1,3}, Hasuo Yasuyuki^{1,2}, Taura Yumiko^{1,2}, Tsunematsu Ryouyuke⁴ *Clinical Research Institute, Kyushu Medical Center¹, Kyushu Medical Center², Clinical Genetics and Medicine, Kyushu University Hospital³, Kagoshima Medical Center⁴*

[Objective] This study aimed to evaluate changes in prenatal testing among women with twin pregnancies before and after the introduction of non-invasive prenatal testing (NIPT). To date, no consensus on prenatal testing for twin pregnancies has been reached in Japan. **[Methods]** Women pregnant with twins who requested prenatal testing at Kyushu Medical Center from 2005 to 2018 were included in this study. Genetic counseling was provided to all participants. Their chosen methods of testing were collected and classified as invasive diagnosis (ID), non-invasive screening (NIS), and no test requested (NR). Parity, chorionicity, and methods of conception were assessed as attributes. The study period was divided into three terms according to testing availability in our center. **[Results]** After NIPT was

introduced in our center, the use of ID methods decreased and eventually disappeared while NIS came to the forefront. NR was also the preferred choice of women with twin pregnancies before the introduction of NIPT and decreased but did not disappear after introducing NIPT. Women with twin pregnancies who underwent assisted reproduction initially showed hesitation to undergo testing but showed a strong preference for NIS after the introduction of NIPT. Differences in choice according to parity, chorionicity, and methods of conception were found before the introduction of NIPT but disappeared after introducing NIPT. **[Conclusion]** Increasing information about NIPT has apparently influenced the attitudes of women with twin pregnancies to prenatal testing in Japan. In particular, those who conceive through assisted reproductive technologies exhibited a strong preference for NIPT.

ISP-35-7

Use of cerebroplacental ratio (CPR) in prediction of adverse perinatal outcome in low-risk term pregnancies in a tertiary hospital (prospective study) Pacheco Maria Josefa B, Cayabyab Grace P *Rizal Medical Center, Philippines*

Cerebroplacental Ratio (CPR) is an obstetric ultrasound tool used as a predictor of adverse pregnancy outcome. The CPR is computed by dividing Pulsatility Index of the Middle Cerebral Artery (MCA-PI) over the Umbilical Artery (UMA-PI). An abnormal CPR reflects redistribution of cardiac output to the cerebral circulation (brain sparing effect). Recently, it has been suggested that the use of Doppler ultrasound in pregnancies with normal-sized fetuses at term is able to identify those at risk of subclinical placental impairment. **[Objective]** To investigate the potential clinical use of CPR for prediction of adverse perinatal outcomes in low-risk term pregnancies. **[Methods]** This Prospective study was conducted in a tertiary hospital and involved 143 low-risk pregnant women from which CPR was computed. Subjects were categorized into 2 groups (CPR <10 th=15 and >10 th percentile=128). They were followed-up for the actual date of delivery to correlate with perinatal outcomes. **[Results]** There is no significant difference of patient's CPR in terms of their demographic profile and manner of delivery. Patients with CPR <10 th percentile had a significant higher percentage of <7 APGAR score at 1 minute (20% versus 3.91%), NICU admission (26.67% versus 5.47%) and complication (20% versus 2.34%). This study also revealed that a normal CPR proved to be a very good predictor of normal outcome, as demonstrated by a high Specificity of $>90\%$. **[Conclusion]** Cerebroplacental ratio is a promising tool in detecting adverse perinatal outcome in low-risk term pregnancies. **Keywords:** Cerebroplacental Ratio, Low-Risk Pregnancy, Perinatal Outcome.

ISP-35-8

Pregnancy outcome of external cephalic version in singleton pregnancy with breech presentation at term Mishra Rajesh Kumar, Vardhan Shakti *Military Hospital, Amritsar, India*

[Objective] To evaluate maternal and neonatal outcome of external cephalic version in singleton pregnancies with breech presentation in third trimester. **[Methods]** A prospective observational study was carried out at a tertiary care hospital over a period of 2 years. This study included a total of 130 uncomplicated cases of breech presentation who fulfilled the inclusion criteria. External cephalic version was carried out after 36 weeks of period of gestation in primigravida and after 37 weeks in multigravida women. These patients were followed up till delivery and data was collected and analysed regarding the mode of delivery, maternal and fetal outcome. **[Results]** External Cephalic Version was successful in 82 patients with a success rate

of 63%. Out of them, vaginal delivery could be achieved in 62 cases (75.6%) and LSCS was done for rest of the 20 cases. The success rate was higher in multigravida ladies compared to primigravida ladies. No major procedure related adverse event was noticed in our study. **[Conclusion]** External cephalic version is a very safe and easy procedure which can reduce the rate of cesarean delivery in singleton pregnancies with breech presentation. The results of our study are in favour of wider practice of this procedure in selected cases.

ISP-35-9

Delivery intervention and prognosis of infants with trisomy 18 at our hospital Isogami Hirotsuka¹, Yasuda Shun¹, Kato Asami¹, Miura Hideki¹, Imaizumi Karin¹, Fukuda Toma¹, Yamaguchi Akiko¹, Fujimori Keiya¹, Jimbo Masatoshi², Nishigori Hidekazu² *Fukushima Medical University¹, Fukushima Medical Center for Children and Women, Fukushima Medical University²*

[Objective] Infants born with trisomy 18 have several complications including cardiac malformations, and the one-year survival rate in Japan is estimated to be approximately 10%. Recently, intensive care treatment in the neonatal period has improved the prognosis and allowed for home care of these patients. Delivery via Cesarean section is presented as an option to families of fetuses with trisomy 18. **[Methods]** In this study, we investigated if Cesarean delivery was desired by families of fetuses with trisomy 18 over the past 10 years at our hospital as well as the prognosis of the neonates. **[Results]** Twenty-two fetuses with trisomy 18 were delivered after 22 weeks gestation, of which 10 were delivered via Cesarean section, of which 3 cases of Cesarean sections were performed due to a non-reassuring fetal status. All three patients delivered via Cesarean section were successfully transferred to home care after being treated in the neonatal intensive care unit. Nine patients with trisomy 18 were delivered vaginally without wishing to apply for Cesarean delivery with fetal rescue, including four live births. None of these patients were able to be transferred to home care; they all died in the hospital. **[Conclusion]** Although the data regarding patients with trisomy 18 who are delivered via Cesarean section are limited, these results suggest that a Cesarean delivery may contribute to the patient's prognosis and allow for the transition to home care.

ISP-36-1

Transarterial embolization for post-partum hemorrhage : A retrospective study of predictive factor in failure cases Koizumi Akari, Ijichi Kouji, Mizukami Natsuko, Makino Yuya, Ishii Sumire, Takahashi Masaya, Takamizu Ai, Ujihira Takafumi, Yoshida Koyo, Makino Shintaro *Juntendo University Urayasu Hospital*

[Objective] Transarterial Embolization (TAE) is the standard treatment for postpartum hemorrhage (PPH). However, in rare cases, clinical failure may occur. We evaluated the results of TAE for PPH and analyzed causes of failure cases. **[Methods]** A retrospective analysis of 43 patients who underwent TAE for PPH was performed at our hospital between July 2012 and July 2021. We used clinical data on maternal characteristics, blood loss to TAE, time to TAE, blood transfusion to TAE, plasma fibrinogen levels, obstetric disseminated intravascular coagulation (DIC) and causes of bleeding. Patients were divided into success and failure groups depending on whether hysterectomy or surgical hemostasis was required after TAE. **[Results]** Specific diagnoses included uterine atony (n=9), abnormal placentation (n=8), vaginal or cervical laceration (n=8), retained placenta (n=5), pseudoaneurysm (n=4). The overall success rate for TAE was 79% (34/43 patients). There was no difference be-

tween the two groups in blood loss to TAE, time to TAE, blood transfusion to TAE, plasma fibrinogen level, and obstetrical DIC, but abnormal placentation was significantly higher in the failure group (p=0.02). **[Conclusion]** When PPH occurs, abnormal placentation can cause uncontrolled bleeding even in TAE. In such cases, the preparation of additional hemostatic methods other than TAE should be carefully considered.

ISP-36-2

The efficacy of transarterial embolization for postpartum hemorrhage complicated with disseminated intravascular coagulation : a single-center experience Tanaka Yuya, Ochiai Daigo, Abe Yushi, Tanaka Yuka, Takeda Masato, Tamai Junko, Hamuro Asuka, Hasegawa Keita, Ikenoue Satoru, Kasuga Yoshifumi, Aoki Daisuke, Tanaka Mamoru *Keio University Hospital*

[Objective] The efficacy of transarterial embolization (TAE) for postpartum hemorrhage (PPH) complicated by disseminated intravascular coagulation (DIC) remains controversial. In this study, we investigated the efficacy of TAE for PPH complicated by DIC. **[Methods]** A database review was conducted to identify patients treated with TAE for PPH at our hospital. The diagnostic criteria for DIC were based on the obstetrical DIC score. **[Results]** TAE was performed in 41 patients. The typical causes of PPH included uterine atony, placenta previa, and amniotic fluid embolism (DIC-type). Gelatin sponge, N-butyl-2-cyanoacrylate, and coil were used as embolic agents in 34, 7, and 2 cases, respectively. The mean obstetrical DIC score was 7.9 (range : 0-24), and the number of cases with a score of ≥ 8 or ≥ 13 was 19 (46.3%) and 9 (22.0%), respectively. Hemodynamic stability was achieved in all cases, but five patients (12.2%) later required additional procedures such as re-embolization. Hemodynamic stability rate was comparable between patients with or without DIC diagnosed using any criteria. In the early stages of DIC, the complete hemostasis rate was comparable between patients with and without DIC. However, the complete hemostasis rate of patients with the obstetrical DIC score ≥ 13 (66.7%) was significantly lower than those with <13 (93.8%). **[Conclusion]** TAE is an effective treatment for PPH complicated by DIC. However, additional procedures may be required for complete hemostasis in cases with DIC score ≥ 13 .

ISP-36-3

Transcatheter arterial embolization is effective in the management of postpartum hemorrhage Iura Ayaka, Masunaga Aya, Kikuchi Tomomi, Kanno Motoko, Ichijo Risa, Okawa Tomomi, Takano Mizuki, Tsukamoto Kanako, Kobayashi Ori, Tamura Kazuya, Umezawa Satoshi *Musashino Red Cross Hospital*

[Objective] Postpartum hemorrhage is an obstetric emergency, and it can lead to maternal death. Appropriate assessment and management of the hemorrhage is critically needed. Securing hemostasis is important when managing hemodynamically unstable patients, and the meaning of interventional radiology (IR) in achieving hemostasis has been demonstrated. **[Methods]** In the period from 12/26/2013 to 7/15/2021, 77 patients required 82 emergent transcatheter arterial embolization (TAE) procedures in our hospital's department of obstetrics and gynecology, with no fatalities. Fifty-six cases associated with postpartum hemorrhage received TAE, and we assess the cases retrospectively. **[Results]** Fifty-six cases associated with postpartum hemorrhage received a combination of embolic agents, such as gelatin sponge and/or 25% N-butyl-2-cyanoacrylate, for embolization. Most of these patients underwent dynamic contrast-enhanced computed tomography before the procedure, and extravasation was revealed. Indications for TAE were atonic postpartum hem-

orrhage, retained products of conception, pseudoaneurysm, hematoma, and placental abruption. Regarding hematomas, vaginal hematomas, vulval hematomas, and retroperitoneal hematomas were recorded. All cases received TAE procedures were resuscitated and treated successfully by a multidisciplinary team. In this study, 53% of the patients who needed TAE procedures for hemostasis arrived via emergency maternal transport. For the maternal transport, obstetricians and emergency physicians collaborate to manage an initial response, and interventional radiologist supported to hemostasis as needed. **[Conclusion]** Our report shows that prompt diagnosis and effective management of postpartum hemorrhage via TAE can improve patient outcomes. Collaboration among obstetricians, emergency physicians, and interventional radiologists is important in the management of postpartum hemorrhage.

ISP-36-4

ART is an independent risk factor for postpartum hemorrhage, especially in vaginal birth Yamamura Akitoshi, Okuda Akiko, Asai Mayu, Mizuta Yuka, Takaori Aya, Kawai Eri, Kojima Machiko, Yamamoto Aya, Kozono Yuuki, Sekiyama Kentaro, Yoshioka Yumiko, Higuchi Toshihiro *Tazuke Fokufai Foundation, Medical Research Institute, Kitano Hospital*

[Objective] Although the incidence of fatal obstetric hemorrhage is decreasing, it remains the major cause of maternal death. In cases of high-risk pregnancy, measures such as autologous blood storage can be taken beforehand. However, we sometimes experience unexpected bleeding, which leads to delayed treatment. Therefore, we need to find unknown risk factors. **[Methods]** We retrospectively analyzed the risk of postpartum hemorrhage (PPH) in 2,957 pregnant women, including 419 pregnancies achieved by assisted reproductive technology (ART group), who delivered in our hospital from 2017 to 2020. PPH was defined as hemorrhage exceeding the 90th percentile of blood loss per the mode of delivery and number of fetuses (bleeding exceeding 800 ml for a single and 1,600 ml for twins in vaginal delivery, and intraoperative bleeding exceeding 1,500 ml for a single and 2,300 ml for twins in cesarean section). **[Results]** Multivariate logistic regression analysis identified pregnancy with ART, non-pregnant maternal BMI, morbidly adherent placenta, placenta previa, twin pregnancy, previous uterine surgery, and vaginal delivery as independent risk factors for PPH. When we matched by propensity score for the mode of delivery, the odds of PPH were 15.94 times greater for vaginal delivery in the ART group. **[Conclusion]** Pregnancy with ART is an independent risk factor for PPH and should be addressed before delivery. In addition, attention should be given to patients who have established ART pregnancies, especially in cases of vaginal birth.

ISP-36-5

Evaluation of risk factors for massive postpartum hemorrhage due to retained products of conception Kurakazu Mariko, Kurakazu Masamitsu, Miyata Kohei, Yotsumoto Fusanori, Miyamoto Shingo *Fukuoka University Hospital*

[Objective] Retained products of conception (RPOC) can occur massive postpartum hemorrhage (PPH). It is the leading cause of maternal morbidity and mortality. We evaluated the risk factors for massive PPH due to RPOC. **[Methods]** This retrospective study included 56 patients with RPOC. Cases with blood transfusion therapy were considered as massive PPH in this study. We divided the patients into two groups based on the occurrence of massive PPH. We studied the background characteristics of the patients and assessed the effects of massive PPH, controlling for potential confounders using logistic regression models. **[Results]** Among 56 patients, five patients had massive

PPH and 51 patients did not. Logistic regression analysis showed that RPOC was associated with increased risk of 2nd trimester miscarriage (crude OR (cOR), 11.25 ; 95% confidence interval (CI), 1.58-100.27), time of diagnosis of RPOC (cOR, 12.73 ; 95% CI, 1.67-263.40), maximum length of RPOC (cOR, 36.0 ; 95% CI, 4.35-785.60), ultrasound vascularity score of 2 or more (cOR, 8.00 ; 95% CI, 1.08-163.04). The multivariable analysis showed that the maximum length of RPOC was the only significant risk factor for massive PPH (adjusted odds ratio (aOR), 16.43 ; 95% CI, 1.26-540.37), independent of 2nd-trimester miscarriage (aOR, 7.56 ; 95% CI, 0.36-231.70), time of diagnosis of RPOC (aOR, 4.49 ; 95% CI, 0.17-77.87), and ultrasound vascularity score of 2 or more (aOR, 2.01 ; 95% CI, 0.11-57.28). **[Conclusion]** Measuring the maximum length of RPOC, an important predictive factor for massive PPH, may be contributory to making treatment strategies in patients with RPOC.

ISP-36-6

Deep learning approach for the prediction of postpartum hemorrhage in vaginal birth Akazawa Munetoshi¹, Hashimoto Kazunori¹, Noda Katsuhiko², Yoshida Kaname² *Tokyo Women's Medical University Medical Center East¹, SIOS, SIOS Technology Inc²*

[Objective] Postpartum bleeding is a major cause of maternal morbidity. Clinical prediction of postpartum bleeding remains difficult, especially for vaginal delivery. We studied a deep learning model for predicting postpartum bleeding. **[Methods]** We included women who underwent vaginal birth at our hospital. Twenty-five clinical variables, including maternal age, height/weight, and pregnancy, were used to predict postpartum bleeding, which is defined as over 1000 mL of blood loss. After applying ensemble learning of five machine learning classifiers : logistic regression, support vector machine, random forest, boosting tree, and decision tree, we constructed a deep learning model consisting of a two-layer neural network. Using the k-fold cross-validation, we evaluated the area under the curve of the receiver operating characteristic (AUC) and the accuracy of the performance. We also used a boosted tree to assess the importance of the characteristics of each variable. **[Results]** A total of 4,960 patients were enrolled in the study, including 128 patients (2.5%) with blood loss greater than 1000 mL. A deep learning model predicted postpartum bleeding with an AUC of 0.679 and an accuracy of 0.744. Important variables of the prediction were considered to be fetal weight, maternal weight at birth, and age. **[Conclusion]** The size of the dataset and the number of variables included were small to improve the performance of the deep learning model. Further research is needed to analyze the appropriate variables and prepare big data such as millions of cases.

ISP-37-1

The correlation between amniotic fluid biochemical marker of fetal heart failure and staging of twin-twin transfusion syndrome in recipient fetuses Murata Susumu, Sekiya Aya, Okabe Mayuko, Shiroshita Amon, Mihara Yumiko, Maekawa Ryo, Sugino Norihiro *Yamaguchi University Hospital*

[Objective] This study investigated that myocardial performance index (MPI) in fetal echocardiography and amniotic fluid biochemical marker (natriuretic peptide precursor : NT-pro BNP) in recipients who underwent fetoscopic laser photocoagulation (FLP) for twin-twin transfusion syndrome (TTTS). In addition, we examined whether these two parameters were related to cardiac status in recipient fetuses. **[Methods]** For the patients who underwent FLP under diagnosis of TTTS stage from 1 to 4. MPI were measured in recipients using dual-gate Doppler method immediately before FLP, and NT-pro BNP in

the amniotic fluid from recipients at the time of FLP. **[Results]** Twenty-five cases were included in this study. There were 21 cases of TTTS stage from 1 to 3 donor with normal Doppler blood flow in the recipients (group A), 4 cases of stage 3 recipients, and stage 4 with abnormal Doppler blood flow in recipients (group B). There were no significant differences in the median left and right MPI of the recipients between the two groups. The median NT-pro BNP/total protein ratio (ng/g) was significantly higher in group B 3,773 (1,846-6,450) than that in group A 1,385 (153-3,105) ($p=0.039$). **[Conclusion]** A heart failure marker of NT-pro BNP/total protein ratio in TTTS recipients were higher in the group with abnormal Doppler blood flow than in the group without abnormal Doppler blood flow. This result suggested that classification of TTTS may reflect the heart failure in recipient fetuses. Measurement of NT-pro BNP may also have certain clinical importance.

ISP-37-2

Two cases of monochorionic-diamniotic twins with different phenotypes Murakami Toru, Hasegawa Yuri, Abe Yukiko, Hisamoto Nami, Matsumura Asako, Miyashita Noriko, Shigetomi Noriko, Tomonaga Chiharu, Abe Shuhei, Harada Ayumi, Miura Kiyonori *Nagasaki University Hospital*

[Introduction] We report two cases of monochorionic-diamniotic (MD) twin pregnancies with morphological abnormalities for only one of the fetuses. **[Case 1]** A 29-year-old woman (primipara) was referred to our hospital, carrying MD twins. Fetus A was diagnosed cystic hygroma at 15weeks' gestation, single umbilical artery, and selective fetal growth restriction (FGR) (-1.6~-3.0SD) at 22weeks' gestation. Fetus B showed no anomalies. An elective cesarean section was performed at 37 weeks' gestation. Birth weights were 1,560g and 2,154g, respectively. Both neonates were female, with Apgar scores of 8/9 (at 1/5min). Neonate A had ASD and VSD. Postnatal cord blood chromosomal analysis showed 46, XX karyotype in both neonates. **[Case 2]** A 33-year-old woman (one para) was referred to our hospital, carrying MD twins. Fetus A presented an abdominal cyst at 17weeks' gestation, followed by the diagnosis as omphalocele. This fetus also had spina bifida, left renal aplasia, single umbilical artery, and an unclear urogenital region, suggesting OEIS complex. Fetus B showed FGR (-1.6~-3.0SD) at 30 weeks' gestation, without any anomalies. An elective cesarean section was performed at 35weeks' gestation. Neonate A weighing 2,378g, with Apgar scores of 3/3, had immature external genitalia and the sex was indeterminate. Neonate B weighing 1,690g was female, with Apgar scores of 8/9. Neonate A died due to respiratory failure 8 hours after birth. Postnatal cord blood chromosomal analysis showed 46, XX karyotype in both neonates. **[Conclusion]** To analyze the cause of discordant phenotypes, we are investigating methylation analysis using DNAs derived from the cord blood of the twins.

ISP-37-3

Antepartum MD-twin score predicts the neurological prognosis of monochorionic diamniotic twins Nagashima Yoko, Matsuzawa Satoshi, Obata Shizuka, Osawa Ayako, Yoshimoto Nozomi, Muraoka Junsuke, Kaneko Masatoki, Katsuragi Shinji, Sameshima Hiroshi *University of Miyazaki Hospital*

[Objective] The goal of the study was to evaluate the monochorionic diamniotic (MD) -twin score, which includes the fetal heart rate pattern and ultrasonography findings, as a predictor of the neurological prognosis of neonates. **[Methods]** A retrospective study was conducted on 204 MD twin babies born between 2009 and 2019 at one center. The MD-twin score is defined on a 5-point scale based on : 1) weight difference $\geq 25\%$, 2) poly- or oligohydramnios, 3) hydrops fetalis, 4) marginal umbilical

cord insertion, and 5) non-reassuring fetal heart rate pattern. If the score reaches 3 points after 26 gestational weeks, the babies are delivered after informed consent is obtained. The MD-twin score, gestational weeks of delivery, birth weight, and prognosis of the baby (intrauterine death, neonatal death, cerebral palsy, mental retardation) were analyzed. **[Results]** Information was collected for 134 live births. Of these births, the number (%) of infants with poor prognoses were 4/18 (22.2%) and 5/116 (4.3%) in cases with MD-twin scores of 3 and 0-2, respectively ($p<0.05$). In the cases with MD-twin scores of 3, body weight difference, umbilical cord insertion, and a non-reassuring fetal heart rate pattern were positive in 2 cases, and weight difference, poly- or oligohydramnios, and umbilical cord insertion were positive in other 2 cases. **[Conclusion]** Infants born with an MD-twin score of 3 are more likely to have a poor neurological prognosis than those with an MD-twin score of 0-2 at birth.

ISP-37-4

The effect of delayed absorbable monofilament suture in cervical cerclage with twin pregnancy Ando Hitomi, Takeda Jun, Kawata Misato, Takahashi Mayu, Masaoka Ryu, Masaoka Shun, Ueki Norikazu, Sei Kiguna, Yamamoto Yuka, Itakura Tsuo *Juntendo University Hospital, Juntendo University*

[Objective] Cervical cerclage using absorbable monofilament is highly effective in preventing preterm birth for singleton pregnancy with cervical incompetency because it may avoid infection and immune response. The study was aimed to clarify the effect of preventing preterm birth by using absorbable monofilament for twin pregnancy. **[Methods]** At our institution, we perform therapeutic cervical cerclage using absorbent monofilament for cases of shortened cervical canal during the second trimester of pregnancy. Medical charts of the pregnant women with therapeutic cervical cerclage were reviewed from January 2013 to December 2020. The outcomes of twin pregnancy were compared with those of singleton pregnancy. Primary outcome was considered as pregnancy continued more than 34 weeks of gestation. **[Results]** Five and 59 patients were found with cervical cerclage in twin pregnancy and singleton pregnancy in the study period, respectively. However, the fetal membrane re-bulging toward the vagina, and the case end up with preterm birth. The rate of pregnancy last more than 34 weeks of gestation were 80.0% and 81.4% in twin and singleton pregnancy, respectively. One case had the thread slipped off from the cervix 8 days after the surgery, thus cervical cerclage was re-performed using Teflon tape with the method of Shirodkar. **[Conclusion]** We found that therapeutic cervical cerclage using absorbable monofilament thread have the potential to prevent preterm birth for twin pregnancy as well as singleton pregnancy.

ISP-37-5

Antepartum BNP is useful for predicting the development of postpartum heart failure in twin pregnancies Machi Maya, Arakaki Tatsuya, Odaki Chihiro, Yasui Osamu, Matsushita Tomomi, Takita Hiroko, Tokunaka Mayumi, Hamada Shoko, Matsuoka Ryu, Sekizawa Akihiko *Showa University*

[Objective] To investigate the usefulness of prepartum maternal BNP as a predictive marker for the development of postpartum heart failure in twin pregnancies. **[Methods]** Twin pregnancies in our hospital from September 2018 to September 2021 were enrolled in the study. The patients were divided into two groups : a heart failure (HF) group that developed heart failure after delivery and a normal (N) group that did not. Presence of hypertensive disorders of pregnancy (HDP), prenatal BNP level and ejection fraction (EF) were retrospectively compared with the development of postpartum heart failure. BNP sampling and transthoracic echocardiography (TTE) were performed just be-

fore delivery. Heart failure was defined as any of the following: hypoxemia, decreased urine output, pleural effusion, or pulmonary edema, and required treatment (oxygen, diuretics, carperitide or serum albumin). **[Results]** There were 99 twin pregnancies, of which 10 (10.1%) developed heart failure after delivery. In 66 cases (66.7%) prenatal BNP was measured and in 39 cases (39.3%) TTE was performed. The HDP complication rate in HF and N groups was 50.0% vs. 6.5%, respectively ($p < 0.05$), antepartum BNP level was 138.8 vs. 34.2 pg/mL ($p < 0.05$) and the EF was 55.0% vs. 62.8% ($p < 0.05$). With BNP cut-off value of 100 pg/mL, the sensitivity was 50.0%, the specificity 96.4%, the positive predictive value 71.4%, and the negative predictive value 91.5% for prediction of postpartum heart failure in twin pregnancies. **[Conclusion]** Antepartum BNP levels and the EF has the potential to be a predictive marker for the subsequent development of heart failure after delivery in twin pregnancies.

ISP-37-6

Time trends in maternal and child health indicators for each gestational week in multiple pregnancies: A population-based study in Japan Hayata Eijiro, Nakata Masahiko, Nagasaki Sumito, Takano Mayumi, Sakuma Junya, Kotaki Hikari, Shimabukuro Makiko, Maemura Toshimitsu, Morita Mineto *Toho University*

[Objective] Multiple pregnancies pose a high risk of morbidity and mortality in both mothers and infants: thus, obtaining reliable information based on large population is essential to improve management. **[Methods]** Based on the information obtained from the official government database of Japan, we calculated the maternal and child health indicators (perinatal mortality rate, stillbirth rate, and early neonatal mortality rate) for each gestational week in multiple pregnancies and analyzed the changes over time. Since more than 95% of multiple pregnancies lead to twin births, the indicators obtained were considered to be representative of twin pregnancies. **[Results]** The maternal and child health indicators in multiple pregnancies (twin pregnancies) were lowest at around 37 weeks of gestation and lower than those of single pregnancies at approximately 36 weeks of gestation. This may be because most multiple pregnancies were managed in large-scale medical institutions. In twin infants, the perinatal mortality and stillbirth rates of the second twins were approximately twice as high as those of the first-born twins, but the early neonatal mortality rates of both twins were almost the same. If one fetus died in utero during pregnancy, it may have been counted as a stillbirth of the second twin when the other fetus was born. **[Conclusion]** Since the data in the government database are accumulated and published continuously, the indicators can be calculated in the future using the method presented in this study. Further, our findings may be useful for policymaking related to managing multiple pregnancies.

ISP-37-7

Ovulation Induction-associated Twin Pregnancy with a Fetus and Coexistent Complete Hydatidiform Mole Pan Chen-Yu¹, Huang Sing-Ying¹, Huang Kuan-Ju¹, Wu Chin-Rui², Chang Wen-Chun¹, Shih Jin-Chung¹, Sheu Bor-Ching¹ *National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan¹, National Taiwan University Hospital Hsin-Chu Branch, Taiwan²*

Complete hydatidiform mole with a coexistent fetus is rare. Medication ovulation induction the increased incidence of multiple pregnancies which increased the incidence of complete hydatidiform mole in a patient with infertility. **Cases:** Two cases of complete hydatidiform mole with a coexistent fetus. One was

a 36-year-old woman who became pregnant with embryo transfer. No remarkable maternal complication except intermittent vaginal bleeding was noted and finally, a live premature baby was delivered at GA 24+6 weeks. The other one was 29-year-old woman who became pregnant with drugs of ovulation induction. Maternal complication has been noted since at GA 4 weeks and therapeutic dilation and curettage was performed at GA 10 weeks. The Postmolar gestational trophoblastic neoplasia occurred afterwards and condition became stable after the chemotherapy regimen of MTX-FA. **Diagnosis:** Complete hydatidiform mole with a coexistent fetus **Outcome:** Two cases both achieved complete remission after follow up for 5 months **Lessions:** We suggest the continuation of pregnancy in the patient with a complete hydatidiform mole with a coexistent fetus but should notice potential complications. **Abbreviations:** GA=gestational age, MTX-FA= methotrexate and folic acid, HM=hydatidiform mole, CHM= complete hydatidiform mole, PHM= partial hydatidiform mole, HMCF= Hydatidiform mole with a coexistent fetus, CHMCF= complete hydatidiform mole with a coexistent fetus, GTN= gestational trophoblastic neoplasia, NST = non-stress testing **Keywords:** complete hydatidiform mole with a coexistent fetus, infertility, postmolar gestational trophoblastic neoplasia, Taiwanese.

ISP-37-8

Grand multiparity in developed country: a retrospective cohort study on specific religion community and literatures review Tanaka Yoshitomo¹, Furuya Kiichiro¹, Komatsu Naoto¹, Takemoto Yuki¹, Yamashita Saya¹, Chang Yangsil¹, Tsubouchi Hiroaki¹, Shikado Kayoko¹, Yokoi Takeshi², Ogita Kazuhide¹ *Rinku General Medical Center¹, Kaizuka City Hospital²*

[Objective] There has been limited information about perinatal outcomes on multiparity in developed country. Our objectives of study were to: 1) retrospectively investigate the perinatal outcomes on developed country using special community with valuing of multiparity but without specific lifestyles, and 2) compare the differences of perinatal outcomes between primiparous advanced maternal age (AMA) and the candidates of our study. **[Methods]** It was retrospective single-cohort study on multiparity who delivered at our hospital from 2013 to 2021. Grand multiparity was defined as the pregnant women who have given birth five or more, but not including miscarriage. Subject of our study and clinical information were collected selected from medical charts of our hospital. **[Results]** Almost research candidates were Japanese. The range of age was from 25 to 41 years old. Pregnancy complications included as follows: HDP (n=20, 14.2%), GDM (n=9, 6.4%), FGR (n=6, 4.3%), and preterm delivery (n=9, 6.4%), others (19%). The IUFD was not found in this subject. The mean blood loss at delivery was 425 ± 485g. 82% of patients (n=116) underwent vaginal delivery. Induction of labor was performed in 39 patients. HDP, GDM, preterm birth, induction of labor, caesarean section, and massive blood loss were increased in primiparous AMA comparing with aged multiparity. **[Conclusion]** We showed the effects of multiparity on perinatal outcomes in developed country. Our results were different from previous evidence from developing country, contributing to understand the effect of parity and aged pregnancy.

ISP-38-1

The Intraperitoneal injection could optimize Engraftment and Survival in the Murine model of In Utero Mesenchymal Stem Cell Transplantation Hasegawa Akihiro^{1,2}, Samura Osamu¹, Sago Haruhiko³, Okamoto Aikou¹ *The Jikei University Hospital¹, Center for Regenerative Medicine, National Center for Child Health and Development², Center for Maternal-Fetal, Neonatal and Reproductive Medicine, National Center for Child*

*Health and Development*³

[Objective] In utero transplantation (IUT) has been proposed as a strategy for the prenatal treatment of congenital disease. Most of the studies regards IUT have used hematopoietic stem cells, but it is not currently possible to differentiate from induced Pluripotent Stem Cells (iPSC) and Embryonic Stem Cells (ESC). Mesenchymal stem cells, on the other hand, can be cultured and expanded more easily than hematopoietic stem cells, and can be an option for resources for in utero transplantation. In this study, we investigated whether mesenchymal stem cells can be viable as a resource for in utero transplantation and the optimal route of transplantation. **[Methods]** IUT using human MSC derived from human ESC was performed in 11.5-14.5 days old fetal mice. We compare the 3 clinically applicable routes of injection (intraperitoneal [i.p.], intrahepatic [i.h.] and intravenous [i.v.]), and assessed fetal survival and short donor cell engraftment in the murine model of IUT with hMSC. **[Results]** The survival rate was 35/156 in the intraperitoneal group and 12/60 in the intrahepatic group without significance (22.6% vs. 20.0%, $p=0.696$). All fetal mice in the intravenous group died in utero. In both the intraperitoneal and intrahepatic transplantation groups, engraftment was confirmed histologically, and immune tolerance for hMSC could be induced in mice. **[Conclusion]** hMSC can be viable as a resource for in utero transplantation. In addition to it, considering the direct invasiveness of the organ, i.p. route might be a more appropriate route for IUT using hMSC, although survival rates are not a significant difference.

ISP-38-2

Validation study of immune tolerance induction by allogeneic cell transplantation during fetal period Harada Aya *Department of Clinical Application, CiRA, Kyoto University*

[Objective] Fetal mesenchymal stem cell (MSC) transplantation is known to have potentials as a treatment for some genetic diseases. One of the advantages is that exposure to the allogeneic cells during fetal period enable patients to induce donor cell-specific immune tolerance. Publication by Medawar's group in 1953 has been referred as the basis of induction of immunotolerance, but there reported more negative arguments than supportive evidence. The impacts of fetal MSC transplantation on immune system are important issue for future clinical application. **[Methods]** (1) Splenocytes or bone marrow-derived MSCs from Balb/c mice were transplanted to E14 embryos of C57/B6 mice. The transplanted mice were then had Balb/c-derived skin transplantation and the days to the rejection were counted. Mixed lymphocyte reaction (MLR) were also performed. (2) The infiltration of CD8+ T cells were compared 48 hours after the intramuscular MSC injection between the 8-week-aged mice with and without previous immunization by fetal MSC transplantation. **[Results]** (1) No mice showed the engraftment of the transplanted skin, but MLR showed a decrease in cell division index in mice those had splenocyte transplantation during fetal period. Mice with fetal MSC transplantation had a comparable cell division index with non-transplanted mice. (2) T cells were aggregated around the cell-transplanted area in the TA muscles of mice with fetal MSC transplantation, but not in mice without fetal MSC transplantation. **[Conclusion]** Two experiments did not provide supporting evidence that fetal cell transplantation induces immune tolerance. There might be some cell fractions among splenocytes that lowered immune response.

ISP-38-3

Promotion of the Uterine Contraction by Microbial Signaling ; Quorum Sensing Miyata Kohei, Urushiyama Daichi, Kiyoshima Chihiro, Izuchi Daisuke, Fukagawa Satoshi, Sanui

Ayako, Kurakazu Masamitsu, Miyamoto Shingo *Fukuoka University*

[Objective] When and why "labor" has been occurred are unclear. It may regulate by several system, however, recent studies indicate that microbial biology have few but certain contribution to initiation of labor. We focused on the microbial signaling, quorum sensing, whether it related to the labor. **[Methods]** Vaginal secretion of 180 pregnant who were under emergency condition including threatened premature labor were harvested. Clinical information had been obtained from clinical record. To assess the Autoinducer-2 concentration (AI-2conc) as quorum sensing activity, strain BB-170, *Vibrio Campbelli* strain which is able to emit light under Autoinducer-2-enriched condition, was used as biosensor. Cells were assayed the luminescence after 4 hours incubation in 30 degrees Celsius. For contraction assay, human uterine smooth muscle cells were purchased from Lonza and cultured on FLECS plate (Forcyte biotechnologies, Inc.) which was able to measure the length of single cell. Mann-Whitney's U test and correlation test were used for statistical analysis. **[Results]** There was no correlation between AI-2conc and maternal age or gestational weeks. AI-2 conc was higher in vaginal secretion of term pregnant in labor ($p=0.0013$). The interval of uterine contraction was only correlated negatively to AI-2conc ($p=0.0486$), however other outcomes and clinical findings did not have correlation with statistical significance. Adding Autoinducer-2 into culture medium promote smooth cell contraction directly. **[Conclusion]** These data indicated that quorum sensing promoted the uterine contraction directly and did not have correlation with infection signs or complications. Auto inducers suggested as a novel and naive uterine contraction substance.

ISP-38-4

High-mobility group box1 peptide ameliorates bronchopulmonary dysplasia via suppressing inflammation and fibrosis in a mouse model Hara Takeya¹, Masuda Tatsuo², Endo Masayuki^{1,2}, Tomimatsu Takuji¹, Kimura Tadashi¹ *Osaka University¹, Department of Children's and Women's Health, Osaka University², StemRIM Institute of Regeneration-Inducing Medicine, Osaka University³*

[Objective] Bronchopulmonary dysplasia (BPD) is a chronic lung disease that typically affects infants delivered at a gestational age of <30 weeks. Although surfactant replacement therapies and gentle ventilation are common strategies for preventing BPD-related lung injury, they have limited efficacy. Relatively new approaches using mesenchymal stem cells (MSCs) have shown promise as potential curative therapies. Previously, we showed that high mobility group box 1 (HMGB1), released from injured tissue, induced regeneration through activating platelet-derived growth factor receptor alpha-positive bone-marrow MSCs. Our another work also identified and synthesized a critical domain in HMGB1 that induces regeneration. In this study, we tested whether the HMGB1 peptide can ameliorate BPD-related lung injury. **[Methods]** We used a well-characterized mouse BPD model created with a hyperoxic chamber. Briefly, normoxic mouse pups were kept in room air, and hyperoxic mouse pups were raised in hyperoxic chambers (90% O₂) from birth until postnatal day 14. Pups were administered with either HMGB1 peptide or saline on Postnatal 4, 8 and 12. Mice were sacrificed at P14 for detailed evaluations. **[Results]** HMGB1 peptide significantly rescued BPD-related decreases in body weight and survival. The treatment also restored alveolar structure via suppressing inflammation and fibrosis in the lung. Single-cell RNA-sequencing of the lung further showed that the peptide significantly suppressed a hyperoxia-induced inflammatory signature in macrophages and fibrotic signature in fibroblasts. These changes in the transcrip-

tome were also confirmed at the protein level. **[Conclusion]** Our data show that treatment with the HMGB1 peptide suppressed inflammation and fibrosis, thus preventing BPD progression.

ISP-38-5

BMP antagonist Gremlin1 contributes to cortical development, motor coordination and fear responses Ichinose Mari^{1,2}, Iriyama Takayuki¹, Sayama Seisuke¹, Osuga Yutaka¹ *The University of Tokyo¹, Precision Medicine, South Australian Health and Medical Research Institute, Australia²*

[Objective] Aberrant bone morphogenetic protein (BMP) signaling is associated with neurodevelopmental disorders in hereditary syndromes and increases susceptibility to exogenous perinatal brain injury, including hypoxic ischemic brain injury. However, the detailed mechanism by which the endogenous modulators of BMP signaling regulate the maturation of the developing brain remains unknown. We aimed to clarify the role of BMP signaling in the development of fetal brain by focusing on the endogenous BMP antagonist, Gremlin1. **[Methods]** Lineage tracing of Gremlin1-expressing cells in the fetal brain was examined by administration of tamoxifen to pregnant Gremlin1 creERT ; Rosa26LSLTdTomato mice at 13.5 days post coitum, followed by collection of embryos later in gestation. The function of Gremlin1 was assessed with neural stem/progenitor cell (NSPC) culture. We generated Emx1-cre mediated Gremlin1 conditional knockout mice (cKO) in which Gremlin1 was deleted exclusively in the cortex. **[Results]** Gremlin1 was expressed in the deep cortical layers during the embryonic period and dramatically decreased after birth. Our bulk mRNAseq analysis of Gremlin1 positive vs negative cells and publicly available human single cell RNAseq data suggested that Gremlin1 was expressed in committed glutamatergic neurons. Gremlin1 induced neural differentiation and increased proliferation of NSPC via antagonism of BMP in vitro. cKO showed significantly thinner cortex than littermate controls. Behavioral tests revealed cKO have impaired motor coordination and reduced sensitivity to fear stimuli. **[Conclusion]** Gremlin1 plays crucial roles in cortical formation and its depletion causes behavioral abnormalities in mice. Gremlin1 may be a key molecule to delineate the pathophysiology of neurodevelopmental disorders acquired perinatally.

ISP-39-1

Withdrawn

ISP-39-2

Improved obstetric management and initial treatment for maternal emergency in primary obstetric facilities reduced direct causes of maternal death in Japan Hasegawa Junichi^{1,2}, Sekizawa Akihiko², Tanaka Hiroaki², Katsuragi Shinji², Nishimura Yoko^{1,2}, Nakamura Masamitsu^{1,2}, Nakata Masahiko², Ikeda Tomoaki² *St. Marianna University¹, The Japan Association of Obstetricians and Gynecologists and the Maternal Death Exploratory Committee (JMDEC) Obstetrics and Gynecology²*

[Objective] To clarify whether maternal deaths in Japan could be reducing in recent decade. **[Methods]** Descriptive study based on the maternal death registration system established by the Japan Association of Obstetricians and Gynecologists and the Maternal Death Exploratory Committee (JMDEC) was attempted, in women died during pregnancy or within 42 days after delivery between 2010 and 2020 throughout Japan. Causes of maternal deaths related to obstetric medical practice were analyzed. **[Results]** Maternal deaths in Japan were gradually reduced, ranging from 45 cases in 2010 to 29 cases in 2020. Among all maternal deaths, frequency of direct obstetric causes, especially deaths due to obstetric haemorrhage declined from 29%

(2010) to 7% (2020) ($p < 0.001$). Since half of deliveries in Japan managed in primary obstetric facilities including private clinic and obstetric hospital, half of pregnant women resulted in maternal death had initial symptoms associated with death at the primary facilities. However, in recent cases resulted in maternal deaths, initial cardiopulmonary arrest was unlikely to occur before or during maternal transport to tertiary hospital. Duration from decision to arrival at the tertiary hospital was significantly reduced. **[Conclusion]** It is considered that reduction of direct obstetric maternal deaths is mainly due to initial basic life support and early decision of maternal transport when maternal emergency occurs in the primary obstetric facilities. We believe the activities of the JMDEC including annual recommendations and simulation programs are improving the medical practices of obstetric care providers especially primary obstetric facilities throughout Japan.

ISP-39-3

The impact of maternal pre-pregnancy body mass index on behavior problems and resilience of offspring aged 6-7 years old in Japan : Results from A-CHILD study Terada Shuhei *Department of Global Health Promotion, Tokyo Medical and Dental University*

[Objective] To investigate the association of maternal pre-pregnancy overweight or obesity with behavior problems and resilience among children aged 6-7 years in Japan. **[Methods]** A retrospective cohort study was conducted using data from the Adachi Child Health Impact of Living Difficulty (A-CHILD) study, a population-based study in 2017 and 2019 including 8711 first-grade students in public elementary schools in Adachi, Tokyo, Japan (response rate=84.7%). Strengths and Difficulties Questionnaire (SDQ) and resilience score were assessed by caregivers via questionnaire. Pre-pregnancy body mass index (BMI) (underweight : BMI < 18.5 ; overweight : 25 ≤ BMI < 30 ; obesity : BMI ≥ 30) was reported based on the mother and child health handbook. Ordinal logistic regression was used for SDQ and regression analysis was used for resilience to adjust for covariates. **[Results]** Of the 7328 valid respondents, 17.5% and 14.0% were in clinical and borderline range of total difficulties score, respectively. Maternal pre-pregnancy overweight and obesity were significantly associated with higher levels of total difficulties in their offspring after adjusting for covariates (odds ratio [OR] = 1.53 ; 95% confidence interval [CI] : 1.25 to 1.89 and OR = 2.16 ; 95% CI : 1.49 to 3.15, respectively). Maternal obesity was also associated with lower resilience of offspring (coefficient -3.24 ; 95% CI : -6.38 to -0.11). **[Conclusion]** Children whose mothers were overweight or obese prior to pregnancy had increased risk of behavioral problems and lower resilience. Controlling maternal weight to an appropriate BMI range before pregnancy may be important for both prevention of behavioral problems and promotion of resilience in the offspring.

ISP-39-4

A prefectural-wide study of unbooked labour in Miyagi : the impact of COVID-19 pandemic Tagami Kazuma, Hamada Hirotaka, Takahashi Sara, Kudo Rie, Kumagai Natsumi, Tomita Hasumi, Iwama Noriyuki, Hoshiai Tetsuro, Saito Masatoshi, Yaegashi Nobuo *Tohoku University Hospital*

[Objective] Pregnant women without adequate antenatal visits, who will proceed to unbooked labour (UL, so called "jump-in labour"), carry socio-economic and medical risks. COVID-19 pandemic had caused massive impacts on medicals and socio-economics. Our facility has been accumulating clinical data and questionnaires of UL cases in Miyagi since 2015. This study aimed to evaluate socio-economic backgrounds of unbooked

mothers and perinatal outcomes of the UL before/after the COVID-19 pandemic. **[Methods]** UL cases were defined as mothers whose antenatal visit were twice or fewer in this case series study. Medical and socioeconomic data were collected from clinical records and questionnaires, and were analyzed retrospectively. All 184 cases reported in Miyagi from January 2015 to September 2021 were included in this study, and divided into two groups : "pre-COVID-19" (delivery before March 2020, n=145), and "post-COVID-19" (after April 2020, n=39). **[Results]** UL proportion on total deliveries in Miyagi were 0.167% and 0.168% in pre- and post-COVID-19, respectively. Main findings were as follows (described as pre- vs post-COVID-19) : age under 20 (15.9% : 15.4%), age over 35 (17.2% : 20.5%), married (21.7% : 28.2%), preeclampsia (10.3% : 5.3%), C-section (20.6% : 12.5%), low birth weight infants (25.7% : 21.6%), and poverty (60% : 39.3%). **[Conclusion]** Following the COVID-19 pandemic, trend towards decrease in poverty was observed in UL mothers, presumably reflecting the socio-economic changes. The proportion of UL has yet to be increased, however, potentially could in the future due to characteristic alterations in pregnant women. Strategies to deal with jump-in labour is required, thus, continuous accumulation study is necessary, leading to enrich support systems for unbooked mothers.

ISP-39-5

Perineal repair hands-on seminar for junior residents using a handmade simulation model : a novel approach for obstetrician and gynecology education and recruitment under the COVID-19 crisis Hamada Hirota, Tomita Hasumi, Takahashi Sara, Tachibana Masahito, Saito Masatoshi, Yaegashi Nobuo *Tohoku University Hospital*

[Objective] Shortage of obstetricians and gynecologists (OB/GYNs) comprises a major concern worldwide and in Tohoku area as well. OB/GYNs recruitment is identified as a top priority, however, there are fewer recruitment opportunities provided to junior residents (JR) due to the COVID-19 pandemic. Perineal repair is a basic skill required for OBGYNs, however, JR have less chance to train. To solve these two issues, we developed a perineal repair hands-on seminar using "Einstein", a handmade simulation model. **[Methods]** JR from affiliated hospitals of our facility were recruited to a one-day hands-on seminar held by our department. Trainees were evaluated the pre-/post-lecture suturing according to the Operative Performance Rating System (OPRS) by the trainers. Web-based survey using 5 point linear Likert scales were distributed via e-mail QR. OPRS -scores and survey answers were compared using paired t-test and Mann-Whitney U-test, respectively, and p-values under 0.05 was considered significant. **[Results]** Among the participants (n=8), there was a significant improvement in both technical skills (OPRS score 52% : 79%, $p<0.05$), and self-confidence scale (survey score 1.9 : 4.3, $p<0.05$) after the seminar. 88% of JR "agreed" or "strongly agreed" that the seminar was enjoyable. Importantly, the rate of JR that answered "Very interested in the OB/GYN" showed trends towards increase after the seminar (25% : 50%). **[Conclusion]** This pilot project demonstrates that a casual hands-on seminar for JR improves technical skills, self-confidence, and interest towards OB/GYNs. Under the COVID-19 crisis, we believe that hands-on seminars play important roles to provide JR with both opportunities for skill-training and recruitment to OB/GYNs.

ISP-39-6

Development and effectiveness of an online Japanese version of mindfulness-based childbirth and parenting program for pregnant women : Single-group pre-post pilot study Tanke Ayumi *The University of Tokyo*

[Objective] The non-pharmacological approaches to improve mental health for pregnant women are needed increasingly for public health. Mindfulness-based intervention has been one of the promising approaches. This study aimed to 1) develop an online Japanese short version of the Mindfulness-based childbirth and parenting (MBCP) and 2) investigate its effectiveness to improve mindfulness, self-esteem, well-being, sense of coherence, and decrease depression, stress, anxiety, and fear of childbirth. **[Methods]** A single-group pre-post pilot study was conducted in Japan from February to October 2021. Thirty-two healthy pregnant women in 16-34 gestational weeks participated in a four weekly online short MBCP program (99.2% attendance), which included psychoeducation based on mindfulness practice and the physiological process of pregnancy and childbirth. They self-reported mindfulness, self-esteem, well-being, sense of coherence, depression, stress, anxiety, and fear of childbirth at pre- and post-test (100% response). **[Results]** Comparing pre- and post-intervention with paired t-test, the results showed a significant improvement in perceived stress, fear of childbirth, mindfulness, self-esteem, and well-being. No significant effects were observed in this low-risk population in perinatal depression, anxiety, and sense of coherence. **[Conclusion]** Newly developed short version of MBCP program significantly improved perceived stress, fear of childbirth, mindfulness, self-esteem, and well-being for pregnant women. Further study is needed to clarify the effectiveness of implementation with a larger sample size among the various pregnant population.

ISP-40-1

Does the experience of the first assistant affect organ injuries in laparoscopic hysterectomy for benign diseases? Tsuzuki Yoko, Kojima Kazushi, Matsumoto Sachiko, Ono Yosuke, Takimoto Kanako, Nakatani Makiko, Ota Hajime, Nakajima Ayako, Fukushi Yoshiyuki, Wada Shinichiro, Yamada Hideto, Fujino Takafumi *Teine Keijinkai Hospital*

[Objective] This study sought to explore whether the experience level of the first assistant surgeon influences perioperative organ injuries (ureteral, bladder, and intestinal injuries) in patients undergoing total laparoscopic hysterectomy (TLH) for benign diseases. We defined an experienced surgeon as a surgeon certified by the Skill Qualification Committee of the Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy or a surgeon with equivalent surgical skills. **[Methods]** We reviewed our surgical registry database of TLH for benign indications between 2014 and 2020 and only selected cases performed by an experienced primary surgeon. Patients were divided into two groups based on the experience level of the first assistant. Inverse probability of treatment weighting by propensity score, which was adjusted for patient and procedure characteristics, was used to examine differences in perioperative organ injuries according to the experience level of the first assistant. **[Results]** Among 1,682 patients who underwent TLH, 18 organ injuries were found (0.83%). In the propensity score inverse probability of treatment weighting models, less experience of the first assistant had no significant impact on the occurrence of perioperative organ injuries ($p=0.348$). **[Conclusion]** In TLH for benign indications at our hospital, given an experienced primary surgeon, the inclusion of a less experienced first assistant does not negatively affect the occurrence of perioperative organ injuries.

ISP-40-2

Clinical study on the effectiveness of laparoscopic circular ligament fusion in pelvic organ prolapse Kakinuma Toshiyuki, Kagimoto Masataka, Kaneko Ayaka, Kakinuma Kaoru, Yanagida Kaoru, Oowada Michitaka *International Uni-*

versity of Health and Welfare Hospital

[Objective] Laparoscopic sacrocolpopexy is widely used for pelvic organ prolapse (POP), which has been covered by the Japanese National Health Insurance (NHI) since 2014. However, FDA warning regarding mesh-related complication of this procedure prompted consideration of alternative autologous repair methods. Laparoscopic sacrocolpopexy, developed by Shull et al. in 2000, was introduced in our hospital in 2017. It has since shown limitations on effective repair in severe POP, attributed to a longer vaginal canal and the hyperextension of the uterosacral ligament. We conducted clinical evaluation of an intraoperative method involving the fixation of the vaginal stump to the circular ligament. **[Methods]** Thirty-three patients who underwent surgery for POP during January 2017 to May 2021 were enrolled. Sixteen cases of laparoscopic sacrocolpopexy (Shull group) and seven cases of circular ligament fusion (circular ligament group) were assessed clinically. **[Results]** Mean age, number of births, and body mass index were not significantly different between the groups. Mean operation time and mean blood loss volume were 157.8 ± 48.3 min and 123.8 ± 153.5 mL in the Shull group and 135.0 ± 28.1 min and 107.3 mL in the round ligament group, respectively. No perioperative complications occurred in either group. Recurrence was observed in three patients (18.8%) in the Shull group but not in the round ligament group. **[Conclusion]** Similar to the conventional Shull technique, the circular ligament fusion method can be safely performed in POP, suggesting its effectiveness in POP management.

ISP-40-3

Risk factors for abscess development in endometrioma cases presenting with an acute abdomen Kaseki Hanako, Ichikawa Masao, Toyoshima Masafumi, Shiraishi Tatsunori, Sakata Akiko, Matsuda Shigeru, Shirai Yuka, Nakao Kimihiko, Akira Shigeo, Suzuki Shunji *Nippon Medical School Hospital*
[Objective] The purpose of this study was to assess the potential risk factors for abscess development in endometrioma cases presenting with an acute abdomen. **[Methods]** A total of 51 patients who underwent emergency surgery for acute abdomen with endometrioma at our hospital between April 2011 and August 2021 were included in this study. Based on the endometrioma content during surgery, the patients were divided into Infected group (n=22) and Non-infected group (n=29). A number of characteristics and postoperative outcomes were analyzed. **[Results]** The Infected group was significantly older ($p=0.03$), had a history of endometriosis surgery ($p=0.04$), and had more transvaginal manipulation within three months ($p=0.01$). The body temperature on the day of admission was also significantly higher in the Infected group ($p=0.007$), and the CRP on the day of admission/preoperative and WBC on the day of admission were also significantly higher in the Infected group ($p<0.0001/p=0.018$ and $p=0.016$). Preoperative imaging showed significant tumor wall thickening ($p<0.0001$) and enhanced contrast effect ($p=0.0017$) in the Infected group. **[Conclusion]** Cases leading to endometrioma infection were characterized by course and imaging. If an infection is superimposed on the acute abdomen, immediate surgical intervention required.

ISP-40-4

Preoperative MRI classification of adenomyosis and surgical findings of total laparoscopic hysterectomy Fukushima Ai, Kitajima Michio, Kajimura Itsuki, Matsumoto Kanako, Harada Ayumi, Kitajima Yuriko, Miura Kiyonori *Nagasaki University Hospital*
[Objective] We evaluated the effects of type of adenomyosis on surgical outcomes. **[Methods]** We retrospectively reviewed the medical records, preoperative MRI images, and surgical records

of women who underwent total laparoscopic hysterectomy for adenomyosis at our hospital from September 2016 to September 2021. According to MRI findings, we classified adenomyosis into four groups: 1) adenomyosis occupied intrinsic layer of myometrium with disruption of junctional zone (JCZ) (type I), 2) adenomyosis occupied extrinsic layer of myometrium by serosal invasion without JCZ disruption (type E-a), 3) extrinsic lesion with JCZ involvement (type E-b), and 4) adenomyosis diffusely occupy anterior and posterior myometrium (type D). The difference in surgical findings were compared. **[Results]** Nineteen women were enrolled. The preoperative MRI classification of adenomyosis was type I in 5 cases, type E-a in 3 cases, type E-b in 4 cases, and type D in 7 cases. The mean operative time and mean blood loss in Type I, E-a, E-b, and D were 205 minutes and 86 grams, 277 minutes and 61 grams, 277 minutes and 275 grams and 206 minutes and 200 grams, respectively. One case with E-a and two cases with E-b showed complete obliteration of Douglas pouch. Four cases with E-a or E-b were complicated with ovarian endometriomas. **[Conclusion]** Extrinsic occupation of adenomyosis may complicate with severe adhesion caused by deep endometriosis and endometriomas that result in increased operating time and blood loss. The evaluation of characteristics of adenomyosis by MRI before surgery is important to perform surgical treatment safety.

ISP-40-5

Lessons learned from Danish experience: How did they recover from the HPV vaccine crisis? Akaba Hiroki¹, Haruyama Rei², Fujita Noriko² *Immunization, Vaccine and Biologicals, World Health Organization¹, Bureau of International Health Cooperation, National Center for Global Health and Medicine²*

[Objective] HPV vaccine crisis has been continuing in Japan for over eight years, while several countries, such as Denmark, Ireland and Colombia, successfully recovered from it. Taking a case in Denmark as an example, this study aimed to seek measures that may be applied in Japan to recover from the crisis. **[Methods]** A literature review was conducted to investigate the determinants of HPV vaccine recovery in Denmark. PubMed with additional hand search was conducted. **[Results]** The main reason for the recovery was an information campaign called "Stop HPV", that was launched in May 2017 led by Danish Authority. This campaign boosted the vaccine uptake from 49.6% to 109.2% of the pre-crisis period in about two years. The success of this campaign was underpinned by well-planned communication strategy, which used social media (Facebook[®]) as a key communication method targeting mothers of girls aged 10-14 years. "Heart-brain communication" method, including both personal stories (heart) and scientific evidence (brain), was used for communication. Providing personal stories created more positive dialogues on social media than just scientific evidence, which led to raising awareness and knowledge about HPV vaccination among the target population. **[Conclusion]** Denmark has recovered from the HPV vaccine crisis mainly due to the information campaign led by the Danish Authority. The success of the campaign was attributed to social media strategy with meticulous planning. Further research is needed to assess whether Danish strategy is applicable in Japanese setting.

ISP-40-6

Trocar-site hernia following laparoscopic salpingo-oophorectomy: an initial case report after 40 years of experience at a single center Ota Kuniaki, Katakura Masafumi, Nakaoka Kentaro, Maemura Toshimitsu, Katagiri Yukiko, Morita Mineto *Toho University Omori Medical Center*
[Background] Trocar site hernia (TSH) is a unique complication that causes severe small bowel obstruction and requires

emergency surgery. Its use has mainly been reported with respect to gastrointestinal laparoscopy, such as for cholecystectomy. Contrastingly, there have been few reports on gynecologic laparoscopy because common laparoscopic surgeries, such as laparoscopic salpingo-oophorectomy, are considered low risk due to shorter operative times. **[Case Presentation]** A 41-year-old woman who had undergone laparoscopic salpingo-oophorectomy 5 days previously presented with the following features of intestinal obstruction: persistent abdominal pain, vomiting, and inability to pass stool or flatus. A computed tomography scan of her abdomen demonstrated a collapsed small bowel loop that was protruding through the lateral 12-mm port. Emergency surgery confirmed the diagnosis of TSH. The herniated bowel loop was gently replaced onto the pelvic floor and the patient did not require bowel resection. After the surgical procedure, the fascial defect at the lateral port site was closed using 2-0 Vicryl sutures. On the tenth postoperative day, the patient was discharged with no symptom recurrence. **[Conclusion]** In 40 years of experience, despite the patient did not have common risk factors such as obesity, older age, wound infection, diabetes, and prolonged operative time, this was our first encounter with TSH. Greater attention should be paid to the possibility of TSH to ensure the prevention severe problems through early detection and treatment.

ISP-40-7

A retrospective study of parasitic myoma and disseminated peritoneal leiomyoma following laparoscopic myomectomy Takeuchi Shiori, Okada Yukiko, Murakami Keisuke, Ikuma Shinichiro, Ozaki Rie, Kawasaki Yu, Ochiai Asako, Kitamura Eri, Kitade Mari, Itakura Atsuo *Juntendo University Hospital, Juntendo University*

[Objective] Parasitic myoma (PM) and disseminated peritoneal leiomyoma (DPL) are ectopic leiomyomas caused by open morcellation during laparoscopic myomectomy (LM). In this study, we retrospectively examined PM/DPL that were surgically treated in our department to investigate the characteristics. Furthermore, we analyzed the intraabdominal findings of patients who underwent LM at our department and then underwent laparoscopic surgery again in order to evaluate the risk factors for the development of PM/DPL. **[Methods]** We studied the patient background and surgical findings of 25 PM/DPL cases operated from 2008 to 2020. In addition, we retrospectively evaluated the incidence of PM/DPL and risk factors in 71 patients who underwent laparoscopic surgery after LM at our hospital. **[Results]** 22 [y1] cases (88%) had a history of LM and all had open morcellation. The median (range) number of lesions was 3 (1-170), with 4 cases (16%) having more than 10 lesions. On the other hand, analysis of intra-abdominal findings in post LM patients showed PM/DPL in 12 (16.9%) of 71 cases. The group with postoperative PM/DPL had significantly heavier enucleated myoma weight than the control group, and all patients underwent open morcellation with a motorized morcellator. There was no PM/DPL in the cases of in-bag morcellation. [y2] Furthermore, uterine myoma at the time of first LM were more strongly expressed in progesterone receptor in patients with later PM/DPL than in those without. **[Conclusion]** In addition to thorough intra-abdominal lavage and observation, specimen collection by in-bag morcellation is useful in preventing the development of PM/DPL.

ISP-40-8

Changes in sexual function and vaginal topography using 3-Dimensional transperineal ultrasound in stress-incontinent women treated with Er : YAG vaginal laser Chang Chieh-Yu¹, Wu Pei-Chi², Loo Zi-Xi³, Ling Kun-Lin¹, Liu Yi-Ying⁴, Wu

Ching-Hu¹, Long Cheng-Yu¹ *Kaohsiung Medical University Hospital, Taiwan¹, National Taiwan University Hospital, Taiwan², Kaohsiung Municipal Ta-Ton Hospital, Taiwan³, Kaohsiung Municipal Siaogang Hospital, Taiwan⁴*

[Objective] To assess the changes in sexual function and vaginal topography using 3-D transperineal ultrasound in stress-incontinent women treated with Er : YAG vaginal laser. **[Methods]** Two hundred and twenty women with stress urinary incontinence (SUI) treated with Er : YAG laser were recruited. Assessment before and 6 months after the treatment included vaginal topography using 3-D transperineal ultrasound and sexual function using female sexual function index questionnaire (FSFI). **[Results]** A total of 50 women with complete data showed that the symptomatic improvement was noted in 37 (74%) women. In the vaginal topography, the width and the cross-sectional area of vagina both decreased significantly after treatment. Nearly all of the domains of FSFI improved significantly after the vaginal laser treatment, except sexual desire. **[Conclusion]** 3-D transperineal ultrasound can be used to conduct vaginal topography. After Er : YAG vaginal laser treatment, decreased width and cross-sectional area in proximal, middle, and distal vagina were found in women with SUI. Besides, nearly all domains of FSFI improved after treatment, except sexual desire. It appears to have positive correlation between the objective ultrasound findings and subjective questionnaire outcomes.

ISP-40-9

Successful Pull-through Vaginoplasty For Distal Vaginal Agenesis : A Case Report Moya Mohanna L *Veterans Memorial Medical Center, Philippines*

Distal vaginal agenesis is a rare malformation of the vagina, resulting in genital outflow tract obstruction. Thorough history taking and physical examination, supplemented by diagnostic imaging are essential to arriving at an accurate diagnosis and an appropriate management plan. We are presented with an amenorrheic, 13-year old patient who complained of pelvic pain. Perineal inspection revealed a pink dimple at the area of the introitus, with an intact hymenal fringe, and no vaginal opening. Magnetic Resonance Imaging of the genitourinary tract and transrectal with transperineal ultrasound showed presence of hematometra and hematocolpos, consistent with distal vaginal agenesis. She underwent Pull-through vaginoplasty, excision of vaginal septum, with evacuation of hematocolpometra. An innovative vaginal stent, using a 10mL syringe barrel, pierced with holes was left in-situ to keep the vagina patent, as well as to allow drainage of blood during the healing process. The patient tolerated the procedure well and was able to achieve regular menstrual flow following surgery.

ISP-41-1

The relationship between bone mineral density and ovarian function in perimenopausal women with endometriosis Uehara Mari¹, Hiraike Osamu¹, Hirano Mana², Koga Kaori¹, Osuga Yutaka¹ *The University of Tokyo Hospital¹, Mitsui Memorial Hospital²*

[Objective] The most detrimental factor that negatively affects on osteoporosis is an inevitable decrease of estrogen levels due to the decrease of ovarian reserve in women. Previous studies have shown that endometriosis and its surgical treatment reduces ovarian reserve. Therefore, we hypothesized that bone metabolism of patients with endometriosis might be negatively affected. This study included perimenopausal women aged 40 to 50 suffering from endometriosis and we aimed to investigate the correlation between changes in bone mineral density (BMD) and endocrinological data. **[Methods]** In this prospective study, we

evaluated 207 patients who visited our hospital between December 2015 and December 2020. We included patients aged 40 to 50 with a clinical history of ovarian endometriosis. During this study period, BMD judged by dual energy X-ray absorptiometry at lumbar (L2-L4) and blood sampling of these participants were annually examined. **[Results]** There was a negative correlation between follicle-stimulating hormone and BMD ($p < 0.001$), and a positive correlation between anti-Müllerian hormone and BMD ($p = 0.005$). A multivariate analysis revealed that the annual rate of change in BMD correlated with TSH levels alone ($p = 0.022$). Patients with higher TSH exhibited a higher rate of decreased BMD. **[Conclusion]** In perimenopausal women with endometriosis, decreased ovarian reserve was positively correlated with decreased BMD and elevated TSH levels increased the risk of BMD loss, indicating that the analysis of ovarian reserve and TSH levels could be useful to predict the risk of osteoporosis. These findings may help manage osteoporosis in women at their 40's.

ISP-41-2

The Effects of Three-year Hormone Replacement Therapy, Alendronate, Tibolone, Raloxifene, and Denosumab on Bone Mineral Density in Postmenopausal Women Yang Hoe-Saeng¹, Kim Mi-Woon² *Dongguk University Gyeongju Hospital, Korea¹, Dongguk University Gyeongju Hospital Anesthesiology, Korea²*
[Objective] To evaluate the effects of three-year hormone replacement therapy, tibolone, alendronate, raloxifene and denosumab on bone mineral density (BMD) in postmenopausal women. **[Methods]** We studied 351 postmenopausal women who had visited the menopausal clinic of Dongguk university hospital between October 2016 and September 2019. **[Results]** The BMD of the femoral neck increased significantly in the alendronate group by 6.4, 7.8, and 7.1% at 1, 2, and 3 years after treatment initiation, respectively. It increased in the EPT group by 3.5 and 3.4% at 1 and 2 years after, respectively. It increased in the tibolone group by 2.5 and 2.2% at 1 and 2 years after, respectively. It increased by 2.8% in the raloxifene group at 2 years after. It increased in the denosumab group by 3.8, 4.1 and 5.8% at 1, 2 and 3 years after, respectively. The BMD of the lumbar spine increased significantly in the denosumab group by 5.8, 7.8 and 9.4 at 1, 2, and 3 years after treatment initiation, respectively. It increased in the alendronate group by 3.3, 5.2, and 5.1% at 1, 2, and 3 years after, respectively. It increased by 1.3% in the EPT group at 1 year after. It increased by 1.8% in the raloxifene group at 1 year after. **[Conclusion]** These findings suggest that alendronate is most effective in improving the BMD levels of the femoral neck. And denosumab is the most effective in improving the BMD levels of the lumbar spine.

ISP-41-3

Correlations of androstenediol with reproductive hormones and cortisol according to stages during the menopausal transition Kawakita Takako¹, Yasui Toshiyuki¹, Matsui Sumika², Yoshida Kanako¹, Iwasa Takeshi¹ *Tokushima University¹, Tokushima Red Cross Hospital²*
[Objective] Associations of androstenediol, which has both androgenic and estrogenic activities, with circulating reproductive hormones and stress hormone in women during the menopausal transition may be different depending on the menopausal stage. The aim of this study was to determine the changes in circulating androstenediol during the menopausal transition in Japanese women and the associations of androstenediol with estrogen, androgen and cortisol for each stage of the menopausal transition. **[Methods]** We divided the 104 subjects into 6 stages by menstrual regularity and follicle-stimulating hormone level. Levels of dehydroepiandrosterone sulfate (DHEAS), estradiol,

estrone, testosterone (T), free T, androstenedione and cortisol were measured. Serum androstenediol concentration was measured by using liquid chromatography mass spectrometry. **[Results]** There were no significant differences in androstenediol levels among the 6 stages. Levels of DHEA-S and testosterone showed significant and positive correlations with androstenediol in all stages. Estradiol levels showed negative correlations with androstenediol levels in the late menopausal transition and very early postmenopause ($r = -0.452$, $p = 0.052$ and $r = 0.617$, $p = 0.006$, respectively). Cortisol levels showed significant and positive correlations with androstenediol levels in the mid and late reproductive stages ($r = 0.719$, $p = 0.003$ and $r = 0.808$, $p < 0.001$, respectively). **[Conclusion]** The strength of the present study is a measurement of androstenediol by using highly sensitive and high specific LC-MS/MS. The associations of androstenediol with estradiol and cortisol were different depending on the stage of the menopausal transition. Androstenediol may play a compensatory role for estrogen deficiency from late menopausal transition to very early postmenopause.

ISP-41-4

Effects of oral estradiol/drospirenone on reducing work productivity impairment: prospective cohort study Ikeda Yumie^{1,2}, Egawa Miho², Ohsuga Takuma², Mandai Masaki² *Department of Health Informatics, School of Public Health, Kyoto University¹, Kyoto University²*
[Objective] Estradiol/drospirenone (EE/DRSP) is known to be effective for dysmenorrhea and premenstrual syndrome (PMS). We examined the effect of EE/DRSP on work productivity impairment for patients with dysmenorrhea and PMS. **[Methods]** The patients who started EE/DRSP at 26 gynecological clinics were recruited between December 2019 and June 2021. Participants completed the app-based questionnaire including 4-point menstrual pain score, premenstrual symptoms screening tool (PSST) at the start of EE/DRSP, then a Work Productivity and Activity Impairment (WPAI) once every two weeks for 3 months. Severe dysmenorrhea was defined as a maximum score of 4. Moderate to severe PMS was identified by PSST. The changes in work impairment over time after starting EE/DRSP was observed, for participants with severe dysmenorrhea and PMS. **[Results]** Among 165 participants in paid work with a median age of 27 (18-46) years, 83 had severe dysmenorrhea and 125 had moderate to severe PMS. For those with severe dysmenorrhea, the mean (standard deviation) overall work impairment was 0.52 (0.3) at the start of the EE/DRSP, 0.25 (0.26) after 1 month, 0.27 (0.3) after 2 months and 0.21 (0.26) after 3 months. For those with moderate to severe PMS, they were 0.52 (0.29) at the start of EE/DRSP, 0.27 (± 0.26) at 1 month, 0.25 (± 0.25) at 2 months, and 0.20 (0.23) at 3 months. **[Conclusion]** For women with severe dysmenorrhea and PMS, the work impairment showed rapid improvement after starting EE/DRSP.

ISP-41-5

Botox injection enabled a woman with severe vaginismus to tolerate penile penetration without any pain, which made her husband to successfully ejaculate in vagina: A case report Murata Kanako, Sekiguchi Yuki, Nakamura Ryoko *Department of Female Sexual Dysfunction, Women's Clinic LUNA Yokohama*
[Objective] Vaginismus is defined as "Recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with sexual intercourse". Japanese females with vaginismus are conventionally treated by physical therapy and psychotherapy, but they consume a great deal of time and the number of patients who can be cured by those treatment is low. In addition, we rush to treat for patients who wish to get pregnant. This time we report the experience with a

patient with severe vaginismus, whose husband could ejaculate of semen into her vagina fifty days after Botox injection to treat vaginismus. **[Methods]** A 34-year-old woman visited us with complains of unconsummated marriage and she had desire to get pregnant. She was unable to tolerate gynecological examination. She was diagnosed with severe vaginismus (Lamont grade 4). She scarcely got better with physical therapy. We administered vaginal Botox injections to her. Just after the operation, we progressively dilated her vagina and her husband continued to dilate her vagina with dilator almost every day. **[Results]** It took forty-four days to insert his whole penis, and finally he was able to ejaculate in her vagina without pain fifty days after Botox injection. **[Conclusion]** This case suggests that Botox injection has possibility to treat severe vaginismus in a short time and enables women and their partners to have proper sexual intercourse, which leads women to get pregnant if they wish. We need more experience of Botox injection under anesthesia to vaginismus and further investigation.

ISP-41-6

Maternal bone metabolism, bone mineral density and bone microstructure at one month after delivery Miyashita Noriko, Kitajima Yuriko, Shigetomi Noriko, Tomonaga Chiharu, Matsumoto Kanako, Hasegawa Yuri, Kitajima Michio, Miura Kiyonori *Nagasaki University Hospital*

[Objective] During pregnancy and lactation, maternal bone metabolism is strongly affected to meet fetal or neonatal demands for calcium intake. But the detailed mechanism in maternal bone loss during pregnancy and lactation is unknown. The objective of this study was to evaluate maternal bone density, bone metabolism and bone microstructure at one month after delivery. **[Methods]** We prospectively recruited breast-feeding women over 20 years old with non-pregnant BMI less than 25 from April 2021 to August 2021. We excluded women with diseases and/or medications affect bone metabolism. We performed medical interview, blood examination, dual-energy x-ray absorptiometry (DXA) and high-resolution peripheral quantitative computed tomography (HR-pQCT) at one month after delivery. **[Results]** Eleven women were included. Mean age was 30.5 ± 4.0 years old. Mean non-pregnant BMI was 20.7 ± 1.8 . Mean serum TRACP-5b was 54.0 ± 115.5 mU/dL and mean serum total PINP was 70.5 ± 13.6 ng/mL, which indicates exaggerated bone turn-over. Mean serum 25-OH Vitamin D was 10.7 ± 1.9 ng/mL, which indicates vitamin D deficiency in all participated women. Mean lumbar spine Z-score was -0.59 (range : -3.2 to 1.7) and mean total femur Z-score was 0.12 (range : -1.4 to 3.2). One woman was diagnosed as primary osteoporosis. HR-pQCT didn't show significant difference comparing to those of age-matched non-pregnant and non-breast-feeding women. **[Conclusion]** At one month after delivery, bone turn-over was exacerbated in breast-feeding women though bone mineral density and bone microstructure did not reach distinct alteration. Primary osteoporosis can be found in healthy asymptomatic woman one month after delivery.

ISP-41-7

A retrospective study on the method of discontinuation of HRT and risk factors for relapse of perimenopausal symptoms Shimizu Yuri, Kobayashi Osamu, Katoh Kanako, Nakajima Takahiro, Kawakami Kaori, Ikeda Yuji, Komatsu Atsushi, Sato Mikiko, Chishima Fumihisa, Kawana Kei *Nihon University Itabashi Hospital*

[Objective] HRT is a standard treatment with perimenopausal symptoms. There is no obvious recommendation on the method of its discontinuation in Japan. Here we investigated the differences between the abrupt vs. tapering of medication and the

risk in relapse of perimenopausal symptoms. **[Methods]** Total of 45 cases that women discontinuation of HRT (28 of successfully quitted HRT and 17 of relapse perimenopausal symptoms) were examined in this study. The risk factors for relapse were evaluated with clinical characteristics (method of discontinuation, age, HRT duration, method of prescription, and adaptations etc.). **[Results]** In this study, relapse rate was 20% (9/45) and all cases relapsed within 12 months of the end of HRT. There was no difference in the rate between the abrupt (n=11) and tapering (n=30) discontinuation groups. No difference was also shown in the time to relapse between the two groups. No difference of relapse rate was shown in other factors (age at which HRT was started, HRT duration, method of prescription, and adaptations) between the successfully quitted or relapse. Interestingly, the relapse rate was much higher in the group of HRT combined with Kampo medicine than HRT alone ($p < 0.01$). **[Conclusion]** In this study, the time to relapse was found to be within 12 months. The combination with Kampo medicine was a risk factor for relapse. It may suggest that patients with concomitant use of Kampo medicine are more likely to relapse due to more severe symptoms.

ISP-41-8

Trabecular bone score (TBS) measurement is useful for assessing bone quality in postmenopausal women Tanimoto Satoko¹, Yokota Megumi¹, Nishio Hiroshi¹, Iwata Takashi¹, Shiina Miki¹, Tanaka Ikumo¹, Sugawara Yo¹, Ohno Ayumi¹, Deshimaru Ryota², Tanaka Mamoru¹, Aoki Daisuke¹ *Keio University¹, Tokyo SAISEIKAI Central Hospital²*

[Objective] Osteoporosis increases the risk of fracture due to a decrease in bone strength, which consists of decrease in bone density and deterioration of bone quality. Bone quality index trabecular bone score (TBS), which can be easily collected from DXA data, is considered to be a good method of assessing bone quality, but there are few reports about its availability. The purpose of this study is to evaluate the usefulness of TBS. **[Methods]** We retrospectively analyzed 108 postmenopausal patients who underwent DXA measurement at our hospital between 2016 and 2021. 36 patients with bone destruction (12 fractures and 24 osteoarthritis) (group A) were compared with the remaining 72 patients (group B). TBS iNspire[®] software was used to calculate the TBS of L2-4 from DXA data. Patient data such as age, BMI, and use of anti-bone resorption drugs were also extracted. Statistical analysis was performed by Mann-Whitney U test and Spearman's rank correlation coefficient. **[Results]** The median age at measurement was 61 (45-80) years and mean value of BMI was 20.6 ± 3.2 Kg/m², with no significant difference in age and BMI between these groups ($p = 0.51$). TBS was significantly lower in group A comparing with group B ($p = 0.01$). The mean value group A of TBS was 1.28 ± 0.61 , group B was 1.32 ± 0.52 , and however we found there was no significant difference in BMD between these groups ($p = 0.81$). We found no correlation between BMI and TBS, however and patients with bisphosphonate use significantly reduced their TBS following their drug use ($p < 0.01$). **[Conclusion]** TBS measurement is useful in assessing bone quality in postmenopausal women.

ISP-41-9

A survey of clinical practice patterns in the management of vaginal agenesis Imafuku Hitomi, Deguchi Masashi, Shi Yutoku, Uchida Akiko, Nagamata Satoshi, Yamasaki Yui, Tanimura Kenji, Terai Yoshito *Kobe University*

[Objective] To document current practices in the management of vaginal agenesis, we did case survey. **[Methods]** Institutions for gynecologic trainees in Kinki were invited to participate in a

questionnaire -based case survey dealing with management of women who diagnosed with vaginal agenesis between 2015 and 2019. **[Results]** Responses were obtained from 72 institutions out of 101 (71.2%). A total of 36 cases from 10 institutions were included in the study. The median age at diagnosis was 16.5 years (range 14-43 years). Twenty-three women underwent surgical construction of an artificial vagina at the age of 17 to 44 years (median 19 years), 4 are considering surgery, and 5 adapt dilation ; mainly the Frank technique. Another 4 lost to follow-up just after diagnosis. Of 23 cases with vaginoplasty, 14 underwent the Davydov procedure, and 8 women underwent the modified McIndoe's method using artificial dermis. The length of neovagina just after surgery ranged from 3 to 10 cm. In follow-up, the length of neovagina changed to 1-10 cm within 5-71 months, and median shorting length after surgery was 1 cm (range 0-4cm). Two had re-constriction of neovagina and one had prolapsus of neovagina. Thirteen cases have sexual intercourse after surgery. **[Conclusion]** Ninety-two percent of women with diagnosed with vaginal aplasia wished vaginal construction, including non-surgical and surgical methods. The neovagina after surgical construction is generally kept the enough length for sexual intercourse.

ISP-41-10

A case of "occult" Sheehan's syndrome caused acute adrenal insufficiency after second delivery Funatsu Eriko, Miyake Tatsuya, Ito Futa, Handa Mika, Nakamura Koji, Toda Aska, Hiramatsu Kosuke, Takiuchi Tsuyoshi, Mimura Kazuya, Kimura Toshihiro, Endo Masayuki, Kimura Tadashi *Osaka University Hospital*

<introduction> sheehan's syndrome sometime become fatal, but is difficult to diagnose. We experienced a case of "occult" Sheehan's syndrome, which couldn't diagnose even with usual examination and suddenly caused severe adrenal insufficiency after following delivery. **<Case>** The patient was 38-year-old, multiparous female, who had a sudden cardiopulmonary arrest caused by uterine rupture and massive intraabdominal hemorrhage at her second birth. She had amenorrhea after delivery, but her gonadotropin level was normal range. She conceived by frozen embryo transfer at hormone replacement cycle. At 32 weeks of gestation, she delivered by caesarian section after preterm premature rupture of membrane. Next day, she lost her consciousness for two days due to hypoglycemia and hyponatremia hypoglycemia, and hyponatremia, which caused by adrenal insufficiency in response to delivery stress. She recovered by intensive care and cortisol medication. After a month, even though her gonadotropin and anterior pituitary hormone levels became normal again, pituitary dysfunction couldn't be diagnosed until by CRH, TRH, and GnRH stimulation. **<Discussion>** From 2011 to 2020, four patients were diagnosed with Sheehan's syndrome in our hospital. All patients had menstrual abnormalities and needed reproductive assist to conceive her a next baby. Even if her cortisol level is normal, hypogonadism and amenorrhea may be the first sign to diagnose "occult" Sheehan's syndrome. In "occult" Sheehan's syndrome patients, adrenal insufficiency may occur anytime she experiences physical stress. More detailed examination, including pituitary stimulation test is needed for the prior intrapartum massive hemorrhage patients with symptoms such as amenorrhea to save her life.

HS-1-1 子宮内膜症マウスモデルを用いた発癌の検討

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【目的】卵巣子宮内膜症性嚢胞 (OEM) は約 0.7% が癌化し, 子宮内膜症関連卵巣癌 (EAOC) を発症するが, その過程は不明な点が多い。OEM 発癌研究においては, OEM 上皮が嚢胞内面にわずかしこ残存していないため実験に用いにくく, EAOC 動物モデルも存在しないという問題点がある。そこで本研究では, OEM マウスモデルでの発癌の検討を行った。【方法】既報の子宮内膜症マウスモデルを基にし, C57BL/6 マウス (ドナー) 子宮を摘出し小片を作製し, 別の同系マウス (レシピエント) の腹腔および卵巣に縫合固定して移植する (Control)。またドナーにミューラー管上皮特異的に Pten のみノックアウト (KO) (iPD) もしくは Pten と Arid1a のダブル KO (iPAD) を誘導可能な同系の遺伝子改変マウスを用いた。【成績】いずれのマウスをドナーとした場合も移植後 2 週間後には腹腔, 卵巣に Pax8 陽性の単層の子宮内膜上皮に裏打ちされた嚢胞病変が 100% 形成され, OEM が形成されたと判断した。そこで移植 2 週間後に KO を誘導し, 4 週後に安楽死させ嚢胞病変を摘出したところ, iPD ドナーの嚢胞上皮は軽度核異型を伴い重層化した上皮が裏打ちしており, 異型子宮内膜症に相当する所見と考えられた。iPAD ドナーの嚢胞上皮では, 核異型と重層化, 篩状構造を示す領域を認め, 癌化と判断した。また同部は免疫染色で Pten と Arid1a の発現消失が確認された。【結論】本法の OEM 形成は正所性子宮内膜の移植という子宮内膜症発症メカニズムを模倣しており, その癌化は OEM 発癌マウスモデルになりうる。このマウスモデルにより Arid1a 機能喪失が OEM 発癌に重要であることが示唆され, EAOC 発癌過程の解明や治療法開発に貢献しうると考える。

HS-1-2 患者由来がんモデルを用いた難治性婦人科悪性腫瘍の個別化医療の構築

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【目的】がん医療において手術検体を用いて遺伝子情報に基づく個別化治療が始まっている。手術前に胸水や腹水貯留を認める症例は予後不良であり手術自体が困難な場合がある。PDX (Patient-Derived Xenografts) は患者の検体を免疫不全マウスに移植し患者由来がんモデルを作成する方法であり, 個別化医療への活用が期待されている。今回, 腹水と手術で摘出した腫瘍を用いてそれぞれの PDX を作成し元の腫瘍との類似性を確認することで, 手術適応でない患者に対しても遺伝子情報に基づいた治療を行うことを目的とする。【方法】当院で 2021 年 1 月～2021 年 9 月の間に婦人科悪性腫瘍に対して手術が施行された腹水貯留のある患者 10 症例に対して, それぞれの PDX を作成した。生着症例において組織型や遺伝子解析を行い, 元の腫瘍との比較を行った。【成績】10 症例の癌腫の割合は, 卵巣癌 8 例, 子宮体癌 1 例, 子宮肉腫 1 例であり, 腫瘍の生着率は 5 症例 (50%), 腹水の生着率は 2 例 (20%) だった。そのうち, 腫瘍と腹水の両方から PDX が作成できた症例は子宮体癌 (endometrioid carcinoma) と卵巣癌 (clear cell carcinoma) の 2 例だった。それぞれの生着腫瘍と元の腫瘍とを HE 染色と免疫染色による病理組織標本の作製と次世代シーケンサーでの遺伝子解析を行いほぼ近似していることを確認した。【結論】腹水, 腫瘍から作製した患者由来がんモデルは元の腫瘍と組織学的特徴や遺伝子変異を再現しており, 術前に腹水貯留を認めるような進行婦人科悪性腫瘍の症例において, 腹水検体が手術検体の代替となる可能性があることが示唆された。今後さらに症例数を増やし検討する必要がある。

HS-1-3 子宮体部 Mesonephric-like Adenocarcinoma は類内膜癌と混同される傾向があり, 頻繁な KRAS 変異を伴う

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【目的】子宮体部 mesonephric-like adenocarcinoma (MLA) は, WHO2020 分類において新たな組織型として採用された。頸部中腎管癌に組織形態が類似し, 免疫組織化学的には GATA3 や TTF-1 の発現が特徴とされ, また KRAS 変異も診断上の指標となっている。しかし, そのいずれに重きを置くべきか, 診断基準は確立されていない。我々は明確な基準を設けた免疫組織化学的パネルを用いて, MLA の抽出を試みた。【方法】子宮体癌 533 例に対して GATA3, TTF-1, estrogen receptor, p53 の免疫組織化学を行った。MLA の criteria は TTF-1 または GATA3 がびまん性に陽性 (>50%), p53 が正常発現, estrogen receptor が陰性とした。抽出された MLA の KRAS 変異 (codon 12, 13, 61) を direct sequencing にて検出した。【成績】子宮体癌 533 例で上記 criteria を満たした 10 例について形態学的に MLA として矛盾しないことを確認した。MLA は類内膜癌 G1 から 4 例 (4/326, 1.2%), G2 から 3 例 (3/88, 3.4%), G3 から 3 例 (3/60, 5%) 抽出され, 他組織型 (漿液性癌や明細胞癌など, 0/59) からは抽出されなかった。MLA は類内膜癌 G1/2 に比して, リンパ管侵襲や深い筋層浸潤と有意に相関し, 無増悪生存期間および全生存期間が短かった。KRAS 変異は MLA の 70% と高頻度にみられた。【結論】MLA は子宮体癌の約 1% とされているが, 本研究では類内膜癌, 特に G2/3 の 3-5% にみられた。MLA は類内膜癌と混同される傾向にあり, 不良な転帰をとるので, 免疫組織化学的パネルによる鑑別が重要である。また高頻度な KRAS 変異を伴うため, KRAS を標的として薬剤が有望な治療戦略となりえる。

HS-1-4 子宮体癌症例におけるミスマッチ修復 (MMR) 遺伝子の生殖細胞系列病的変異の頻度とがん組織中の MMR たん白質発現欠失との関連

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【目的】本邦子宮体癌症例において、生殖細胞系列の MMR 遺伝子変異 (Lynch 症候群) の頻度や、変異陽性症例の臨床病理学的特徴、さらに MMR 遺伝子変異陰性かつ腫瘍組織での MMR 蛋白発現欠失がみられる症例 (非 Lynch 症候群の dMMR 体癌) の臨床病理学的特徴については報告が少なく、本邦症例の特徴を明らかにすることを目的とした。【方法】当院 IRB の承認 (2015-278, 2017-331) のもと、2011-2018 年に当院で子宮体癌 (特殊組織型も含む) と診断された 444 例を対象とした。末梢血検体より DNA を抽出し、生殖細胞系列の *MLH1*, *MSH2*, *MSH6*, *PMS2* 遺伝子の全エクソン領域 (*PMS2* は exon 10-15 を除外) に対してターゲットシーケンスを施行した。また 444 例のうち、腫瘍組織を得られた症例に対して MMR 蛋白 (*PMS2*, *MSH6*) に対する免疫染色を実施した。【成績】444 例のうち MMR 遺伝子に病的変異もつ Lynch 症候群症例は 16 例 (3.6%) で、*MSH6* 9 例、*MLH1* 3 例、*MSH2* 3 例、*PMS2* 1 例であった。16 例の年齢中央値は 55 歳 (28-77 歳)、組織型は類内膜癌 (Grade1, Grade2) が 8 例、漿液性癌が 6 例、癌肉腫が 1 例、脱分化癌が 1 例であった。Stage は I 期 10 例、III 期 4 例、IV 期 2 例であった。原病死は癌肉腫の 1 例のみで予後良好であった。免疫染色が実施された 167 例のうち、48 例 (28.7%) が *PMS2* あるいは *MSH6* の蛋白発現欠失を示した。そのうち非 Lynch 症候群の dMMR 体癌 44 例は Lynch 症候群症例と比べて類内膜癌 Grade3 の割合が有意に多かった。【結論】子宮体癌における Lynch 症候群及び dMMR 体癌の頻度については既報の再現性を確認できた。臨床病理学的特徴についても、Lynch 症候群は TypeII の頻度が高く、非 Lynch 症候群の dMMR 体癌は、類内膜癌 Grade3 の頻度が高いことが示された。

HS-1-5 子宮頸癌放射線治療後残存・再発に対する子宮摘出術の有用性と安全性の検討

信州大

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【目的】子宮頸癌では、同時化学放射線療法 (CCRT) /放射線療法 (RT) 後の照射野内残存・再発の予後は極めて不良であり、治療方針に一定の見解がない。我々は、摘出可能症例には積極的に子宮摘出術を行っており、今回その効果と安全性の検討を行なった。【方法】当院で 2007 年 4 月~2020 年 6 月に、子宮頸癌 CCRT/RT 後の照射野内残存・再発例に対して、同意を得て子宮摘出術を行なった 11 症例を対象とし、診療録より後方視的に検討した。【成績】遠隔転移例や、骨盤壁側の側方再発型は適応外とした。手術時年齢は 36~67 歳 (中央値 51 歳)、CCRT/RT 時の進行期は IIB 期 6 例、III 期 4 例、IV 期 1 例、組織型は扁平上皮癌 10 例、胃型粘液性癌 1 例であり、病変残存が 6 例で再発が 5 例であった。子宮全摘術は単純 4 例、広汎 6 例、超広汎 1 例であり、7 例にリンパ節郭清、2 例に他臓器合併切除が併施された。全例で腫瘍は完全切除され、我々の適用基準は適切であると考えられた。8 例 (73%) が生存中で、うち 7 例 (64%) が無病生存中 (観察期間 24~162 か月、中央値 77 か月) であり、死亡 3 例中 1 例は無病生存中の他病死であった。術中出血量 70~3200g (中央値 1000g) で 5 例に輸血を要した。重篤な術後合併症では尿管・膀胱・直腸の瘻形成を 2 例に認め、いずれも術後病理診断で傍組織浸潤を認めた症例であった。その他、腸閉塞 3 例、手術部位感染 5 例、尿路感染症 2 例、神経因性膀胱を 3 例に認めたが、手術関連死は認めなかった。【結論】CCRT/RT 後の照射野内残存・再発例に対する子宮摘出術は、膀胱腔瘻などの合併症のリスクが高いが、適切な適用基準下で施行することで、予後の改善や根治性を望める有効な治療法であると考えられた。

HS-1-6 本邦における RRSO の現状とオカルト癌に対する対応について

日本遺伝性乳癌卵巣癌総合診療制度機構 (JOHBOC)

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【目的】一般社団法人日本遺伝性乳癌卵巣癌総合診療制度機構 (JOHBOC) の登録事業により、本邦におけるリスク低減卵管卵巣摘出術 (RRSO) の現状と、その後のオカルト癌に対する治療方法について調査した。【方法】2019 年までに JOHBOC のデータベースに登録された情報を用い、RRSO を施行された 212 人について解析をした。更に、術後、異常所見を認めた症例に関して 2 次調査を行い、その後の治療経過も分析した。なお、本研究は筆頭演者施設の臨床試験部会で承認され実施した。【成績】遺伝性乳癌卵巣癌症候群 (HBOC) のデータベース登録患者数は 3969 人で、乳癌発症と未発症は、それぞれ 3274 人/695 人で、卵巣癌家族歴は 667 人に認めた。*BRCA1/2* 遺伝学的検査で、*BRCA1* 遺伝子病的パリアント (*BRCA1*), *BRCA2* 遺伝子病的パリアント (*BRCA2*), 両者の病的パリアントは、それぞれ 564 人/352 人/6 人であった。RRSO は中央値 47 歳 (34-78) で施行され、*BRCA1* が 117 人、*BRCA2* が 82 人、両者が 3 人、その他 10 人に行われ、*BRCA1* で 40 歳未満の施行は 15 例 (7.1%)、*BRCA2* で 45 歳未満は、24 例 (11%) であった。術後、オカルト癌が 7 例で、STIC は 4 例の登録があり、オカルト癌 5 例 (*BRCA1* 4 例、*BRCA2* 1 例) と STIC 4 例 (*BRCA1* 2 例、*BRCA2* 2 例) の 2 次調査を行った。全例、SEE-FIM Protocol にて確認され、オカルト癌は 5 例中 4 例に追加手術が施行され、5 例とも化学療法が施行されていた。STIC では 4 例中 1 例に化学療法のみ施行されていた。全例、その後も現在、生存を確認している。【結論】RRSO 後のオカルト癌に対する対応は、本邦を含め、一定の見解はない。症例の蓄積により、卵巣癌予防のために RRSO の推奨とオカルト癌に対する治療方針の一助になると思われる。

HS-2-1 原因不明の不妊症を対象とした静注免疫グロブリンの二重盲検群間比較試験

免疫グロブリン不妊症研究グループ

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【目的】原因不明の難治性不妊症に対するエビデンスのある治療法はない。本研究では、妊娠初期の静注免疫グロブリン (IVIG) の有効性を調べた。【方法】二重盲検ランダム化プラセボ対照群間比較試験 (RCT) により、原発性習慣流産で、4 回以上の自然流産歴かつ 1 回以上の染色体正常流産の経験があり、リスク因子不明または同定されたリスク因子に対する治療をして染色体正常の流産をした方、かつ年齢 42 歳未満の不妊症女性を対象とした。胎嚢が確認された後、妊娠 4-6 週にプラセボ (P)、ないし 400 mg/kg IVIG を 5 日間投与した。妊娠 22 週時点での妊娠継続、および生産を本研究のアウトカムとした。投与した全妊娠からなる intention-to-treat (ITT) と胎児染色体異常妊娠を除いた modified-ITT の群をそれぞれ解析した。【成績】ITT において、IVIG 50 人は P 49 人に比べて妊娠継続率 (Mantel-Haenszel chi-squared test $p=0.007$) と生産率 ($p=0.022$) が有意に高かった。Modified-ITT では、IVIG 47 人は P 38 人に比べて妊娠継続率 ($p=0.057$) と生産率 ($p=0.133$) が高い傾向にあった。ITT では、IVIG は P に比べて有意に早産と SGA が多く出生体重が低かったが、HDP には差がなかった。妊娠 4-5 週に投与した症例では、IVIG は P に比べて妊娠継続率 (ITT $p=0.0007$; modified-ITT $p=0.004$) と生産率 ($p=0.0034$; $p=0.0191$) が有意に高かった。しかし、妊娠 6 週に投与した症例では、これらの効果は認められなかった。【結論】RCT によって、妊娠初期の IVIG は、流産歴 4 回以上の原因不明の不妊症に有効であることを初めて明らかにした。特に妊娠 4-5 週に投与した場合に効果が認められた。

HS-2-2 コラゲナーゼ処理を行ったマウス卵巣組織培養と卵胞発育の評価

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【目的】近年、妊孕性温存を目的として卵巣自家移植および組織培養が検討されている。特に微小残存病変の再移植を回避するために、卵巣組織培養において新たな培養法の考案が期待されている。卵巣組織培養において、酸素の供給および培養液の浸潤は培養成績に大きな影響をもたらす。従来方法では培養液の循環を十分に達成することができず、4 日以上培養は不可能であった。今回我々は、マウス卵巣組織をコラゲナーゼ処理した後、メッシュ上で培養し、経時的に卵胞発育を評価した。【方法】1 週齢マウス卵巣を摘出し、コラゲナーゼ処理した後、培養皿にメッシュを設置し、その上でマウス卵巣組織を培養した。培養 0 日、3 日、6 日、9 日に卵巣を回収して HE 染色を行い、顕微鏡下にそれぞれの卵胞発育を観察した。培養液は α -MEM を基本とし 5% FCS、Vit.C、抗生剤、ITS を加えたものを使用し、培養液は 3 日に 1 回交換した。【成績】培養 0 日の卵巣組織は、原始卵胞のみからなり、発育卵胞を認めなかった。培養 3 日では初期発育卵胞の出現を観察した。培養 6 日では顆粒膜細胞数の増加を確認した。卵胞腔を有する成熟卵胞は認めなかった。培養 9 日ではより多くの発育卵胞の増加を確認した。【結論】コラゲナーゼ処理後、メッシュを用いたマウス卵巣組織培養を行い、胞状卵胞に至る以前において、良好な卵胞発育を誘導することに成功した。理由は、気相の環境と培養液中の有効成分の組織への浸透が改善された効果と考えられる。この方法により、初期卵胞の培養効率が向上し、成熟卵胞の十分な数の獲得が期待されることから早発卵巣不全や卵巣組織凍結を必要とするがん生殖医療への応用が期待できる。

HS-2-3 排卵周期とホルモン補充周期の融解胚移植における周産期合併症と出生児先天異常の発症頻度の比較

加藤レディスクリニック

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【目的】本邦における ART 出生児の約 8 割は融解胚移植の妊娠であり、自然周期と比べ、ホルモン補充 (HR) 周期が多いが、HR 周期では周産期合併症のリスクを上昇させる可能性が指摘されている。今回当院における排卵周期と HR 周期の融解胚移植において、周産期合併症と出生児先天異常の影響を調査する目的で検討を行った。【方法】2017 年 1 月-2019 年 12 月までに単一融解胚移植を行い、単胎生児を出産した 8,261 周期を排卵周期 [自然周期 (N 群: $n=6,774$) + レトロゾール周期 (L 群: $n=978$)] と HR 周期 (H 群: $n=509$) にそれぞれ分類し、周産期合併症 (帝王切開、早産、前期破水、妊娠高血圧症候群、妊娠糖尿病、前置/低置胎盤、癒着胎盤、常位胎盤早期剝離)、低出生体重児、出生児先天異常の発症頻度を比較検討した。【成績】分娩時年齢は N 群: 37.9 ± 3.6 歳, L 群: 36.6 ± 3.7 , H 群: 37.7 ± 4.3 歳であった。癒着胎盤、早産、帝王切開 [N 群, L 群, H 群 (%)] はそれぞれ H 群で有意に高かった (0.2, 0.1, 2.8, $P < 0.0001$; 4.3, 3.7, 8.5, $P < 0.0001$; 33.3, 26.0, 43.3, $P < 0.0001$) が、その他の周産期合併症、低出生体重児、出生児先天異常には有意差を認めなかった。【結論】HR 周期の融解胚移植は先天異常に影響を及ぼさない一方で、癒着胎盤や早産、帝王切開が高率となる結果であった。周産期観点からは、融解胚移植において HR 周期より排卵周期での移植を検討することが重要と思われる。

HS-2-4 VCD 閉経マウスモデルを用いた子宮周囲脂肪細胞面積の検討

浜松医大

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【目的】従来の閉経マウスモデルは卵巣摘出によるものである。今回我々は VCD (4-vinylcyclohexene diepoxide) 投与によって、選択的に原始卵胞・一次卵胞を閉鎖させて閉経させる VCD マウスモデルを用いて、閉経が子宮周囲脂肪細胞面積に及ぼす影響を検討した。このモデルは自然閉経と同様のホルモン動態を持つ点と閉経移行期を持つ点から、自然閉経に最も近いモデルと言われている。卵巣摘出モデルで確認されている閉経後の脂肪細胞肥大化を当モデルでも検討した。【方法】B6C3F1 雌マウスに3週齢より植物由来エストロゲンフリー餌を与え、4週齢より VCD 群は VCD (160 mg/kg/day)、コントロール群は sesame oil を20日間連日腹腔内投与した。16週齢時に陰腔診にて VCD 群の閉経を確認した。閉経後12週、16週、20週の三期にかけて、安楽死させたマウスより子宮周囲脂肪組織を採取した。脂肪組織から病理組織切片を作成し、画像解析ソフト WinRoof2018 を用いて脂肪細胞面積を測定し、二群間で比較した。【成績】三期とも二群間で飼育中の体重と摂餌量、組織採取時の子宮周囲脂肪組織重量に有意差はなかった。閉経後16週での子宮周囲脂肪細胞面積において、VCD 群 (n=5) で中央値 1087.2 (826.8-1664.1) μm^2 、コントロール群 (n=5) で 593.5 (472.8-716.6) μm^2 であり、VCD 群で有意に面積が大きかった (p=0.0317)。【結論】VCD 投与による閉経マウスモデルにおいても、閉経後16週時点で子宮周囲脂肪細胞の肥大化を確認できた。

HS-2-5 骨盤臓器脱患者における安静臥位での骨盤底のたわみ (sagging) に関する MRI を用いた検討

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【目的】一般に骨盤底筋の弛緩は、骨盤臓器脱 (POP) の発症に関与することが知られているものの、POP 患者の骨盤底のたわみ (sagging) を詳細に検討した報告は少ない。MRI を用い、POP 症例の安静臥位における骨盤底のたわみを骨盤底障害のない経産婦と比較したので報告する。【方法】POP-Q stage 3, 4 の POP 症例 188 例 (POP 群) および明らかな骨盤底障害のない経産婦 90 例 (対照群) を対象とし、安静臥位での MRI 上の Pubococcygeal line (PCL) (恥骨下縁と最下尾骨関節を結ぶ直線)、H line (恥骨下縁と肛門直腸角を結ぶ直線)、M line (PCL から H-line 後側端に引く垂線) を後方視的に測定し比較した。p 値 < 0.05 を統計的に有意とみなした。【成績】POP 群と対照群で、年齢、身長、BMI に有意差を認めなかった。PCL、H-line、M-line の長さ [mm (SD)] はそれぞれ (POP 群 vs. 対照群)、PCL : 98.7 (9.7) vs. 96.1 (7.5), p=0.046, H-Line : 62.3 (8.1) vs. 51.1 (6.0), p<0.0001, M-Line : 24.8 (7.3) vs. 9.3 (6.7), p<0.0001 であった。【結論】腹圧下の H line と M line は POP で延長すると言われているが、安静臥位でもそれぞれ有意に延長していた。POP 患者の骨盤底は潜在的に損傷・弛緩があり、安静臥位の MRI でもその状態が観察可能であった。一方、PCL は恥骨-尾骨関節を結ぶ基線であり、骨間の線のため群間差はないと考えていたが、本研究では有意差を認めた。この理由として、PCL の片端である尾骨関節は可動性を有し、骨盤底筋の一つである恥骨尾骨筋の付着部でもあるため、PCL も骨盤底障害の有無によって変動すると推察された。POP 群における PCL の有意な延長は、恥骨尾骨筋のたわみを反映していると考えられる。

HS-3-1 妊娠糖尿病診断時のインスリン抵抗性/分泌能の病態とインスリン治療との関連

国立長崎医療センター

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【目的】妊娠糖尿病 (GDM) の病態には、インスリン抵抗性とインスリン分泌能低下が関連している。これらのインスリン動態の違いとインスリン治療との関連について検討した。【方法】妊娠 24~32 週の GDM 診断症例のうち、診断時耐糖能検査 (OGTT) 時にインスリンを測定した症例を対象に後方視的に検討した。Homeostasis model assessment insulin resistance (HOMA-IR) ≥ 1.74 (GTT 正常群 75 パーセントイル) をインスリン抵抗性亢進、Insulinogenic index (IGI) < 0.4 をインスリン分泌能低下と定義し、インスリン抵抗性 (IR) 群、インスリン分泌能低下 (LIS) 群、混合群、正常群に分類した。各群のインスリン治療の頻度と周産期予後について比較検討した。【成績】対象は 287 例 (34 歳、非妊時 BMI 23.5) で、そのうち IR 群 92 例 (32%)、LIS 群 72 例 (25%)、混合群 13 例 (5%)、および正常群 110 例 (38%) であった。非妊時肥満妊婦では IR 群が最も多く (57%)、一方、やせ (BMI < 18.5) では LIS 群が 45% を占めていた。インスリン導入例は 141 例 (49.1%) あり、IR 群、LIS 群、および混合群のインスリン治療の割合は、各々 61%、49%、および 100% で、正常群 (34%) に比べ有意に高頻度であった。周産期予後 (帝王切開率、出生体重 z スコア、Heavy-for-dates 児の頻度) には、各群間で差を認めなかった。【結論】日本人 GDM 妊婦のインスリン抵抗性/分泌能の異常には、インスリン抵抗性過剰、インスリン分泌能低下、および両者の混合群が存在する。これらの異常を示す妊婦は、いずれの病態にも当てはまらない GDM 妊婦 (正常型) に比べてインスリン治療導入の頻度が高く、特に混合型はその頻度は少ないものの最重症であることを明らかにした。

HS-3-2 重症胎児発育不全の前方視的コホート研究 長期予後の検討

重症胎児発育不全の前方視的コホート研究班

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【目的】早産期の胎児発育不全 (FGR) 児は、短期的のみならず長期的な生命および神経学的予後についてもハイリスクであると認識されている。しかし、本邦における FGR 症例の長期予後とそれに関連する因子の研究は未だ限定的である。本研究では早産期の重症 FGR の前方視的コホート研究として、修正 1.5 歳時点での予後と関連因子を明らかにすることを目的とした。【方法】2014 年から 3 年間に、周産期母子医療センター 25 施設で、妊娠 22 週以降 28 週未満に診断された FGR (推定体重 < 2.0SD) 単胎 223 例を対象とした。修正 1.5 歳時点の予後不良を死亡、新版 K 式 DQ < 70、脳性麻痺、両側難聴、失明の複合有害転帰とした。長期的な生命・神経学的予後に影響する先天異常と予後不明の症例は除外した。母体背景、診断時の胎児心拍数異常、超音波因子等の周産期因子と複合有害転帰の関連についてロジスティック解析を行い、関連因子を抽出した。各施設の倫理委員会と妊婦の同意を得た。【成績】登録された 229 例中、除外後の 155 例にて解析した。予後不良は 37 例 (23.9%) であり、死亡は 13 例、DQ < 70 は 17 例、脳性麻痺は 7 例であった。両側難聴、失明は認めなかった。関連のあったのは、在胎週数のみであり、粗オッズ比 (95% 信頼区間) は 0.77 (0.67-0.89)、 $P < 0.01$ であった。【結論】早産期の FGR 児の予後改善をする可能性のある因子は、現状在胎週数のみであり、可能な限りの妊娠継続を目指した管理が望ましいと考えられる。

HS-3-3 妊娠 36 週以降の双胎妊娠における、妊娠高血圧症候群の関連因子の検討

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【目的】妊娠 36 週以降の双胎妊娠における妊娠高血圧症候群 (HDP) の関連因子を明らかにする。【方法】2016 年から 5 年間に妊娠 34 週以前から当院で妊娠管理を行い、妊娠 36 週以降に分娩となった双胎妊娠を対象とした後方視的コホート研究である。一絨毛膜性合併症、胎児手術症例、一羊膜双胎、既知の胎児異常、双胎一児死亡、妊娠 36 週未満の HDP 発症は除外した。評価項目は妊娠中および産褥期 HDP の頻度とした。35 歳以上、初産、体外受精、妊娠中の喫煙、非妊時の BMI ≥ 25 kg/m²、HDP 既往、膜性、妊娠糖尿病、妊娠蛋白尿 (定性 $\geq 2+$ または定量 ≥ 300 mg/日)、妊娠 36 週の母体血液検査値 (血小板、AST、ALT、フィブリノゲン、アンチトロンビン [AT]) のうち、単変量ロジスティック回帰分析で $P < 0.05$ である因子の HDP に対する調整オッズ比 (95% 信頼区間) を多変量ロジスティック回帰分析で算出した。単変量解析で $P < 0.05$ であった血液検査値は ROC 曲線で算出したカットオフを元に名義変数として多変量解析に導入した。【成績】対象 368 例から 70 例を除外した 298 例における HDP の頻度は 22% (66 例) であった。単変量解析において初産、妊娠蛋白尿、AT が HDP と有意に関連し、AT のカットオフは 90% であった。HDP の独立した関連因子は妊娠蛋白尿と AT < 90% であり、調整オッズ比はそれぞれ 4.65 (1.36-17.2)、4.01 (1.91-9.24) であった。妊娠蛋白尿陽性妊婦と妊娠蛋白尿陰性かつ AT $\geq 90\%$ の妊婦における HDP の頻度はそれぞれ 70%、7.8% であった。【結論】妊娠 36 週以降の双胎における HDP 発症予測に、妊娠蛋白尿および妊娠 36 週の AT が有用である可能性がある。

HS-3-4 ART 妊娠は産後の異常出血のリスク因子となる可能性がある

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【目的】産後の異常出血 (PPH: postpartum hemorrhage) は妊産婦死亡を引き起こしうる。これまで指摘されてきた既知のリスクをもたない妊婦においても、突然 PPH に至ることはまれではない。今後の分娩管理における注意点を見直し PPH の減少につなげるため PPH のリスク因子を検討した。【方法】2017~2019 年に当院で妊娠 37 週以降に頭位単胎経陰分娩に至った 555 例を対象として、後方視的に分娩時異常出血に関連したリスク因子について解析した。なお、分娩時異常出血量は、800 mL 以上とした (PPH 群)。【成績】1) PPH 症例は、86 例 (15.5%) であった。2) 単変量解析では、非妊時 BMI の増加 [25.4 Kg (20.3-34.8); $p=0.006$]、子宮内手術歴 (子宮内容除去術、子宮鏡下手術) 有 [23.3%; $p=0.017$]、ART 妊娠 [31.4%; $p < .001$]、妊娠中鉄剤投与 [27.9%; $p=0.01$]、前期破水 [41.9%; $p=0.044$]、分娩誘発 [26.7%; $p=0.014$]、出生体重 [3199g (1990-4320); $p < .001$]・児頭頭圍 [34cm (30-36.5); $p < .001$]・胎盤重量 [595g (370-882); $p < .001$] が大きいこと、低置胎盤 [2.3% $p=0.014$]、分娩第 3 期遅延 [8min (1-69) $p < .001$]、胎盤用手剥離 [9.3%; $p < .001$]、弛緩出血 [50%; $p < .001$] において有意に出血が多かった。3) 多変量解析では、ART 妊娠 [OR: 5.0, 95% CI: 2.7-9.3; $p < .001$]、低置胎盤 [OR: 25.6, 95% CI: 2.0-313.8; $p=0.01$] が独立したリスク因子だった。【結論】ART 妊娠は PPH のリスク因子として産婦人科診療ガイドラインには示されていないが、近年、PPH との関連を示唆する文献が散見される。ART 妊娠が増える現在、ART 妊娠の分娩管理において、PPH のリスクになり得ることを念頭に置いた対応が必要であると考えられた。

HS-3-5 当院における分娩後の産道血腫に対する治療戦略の検討

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【目的】経陰分娩後にみられる産道血腫は時に後腹膜腔に進展し、止血方法の選択に難渋する場合がある。当科で経験した産道血腫症例について、出血点となる責任血管を画像診断により同定し、適切な止血のアプローチ法を検討した。【方法】2016年1月～2021年8月に当院に搬送された産道血腫33症例を対象とし、血腫の責任血管、大きさ、位置、止血のアプローチ法(経陰、開腹、子宮動脈塞栓術)について後方視的に検討した。【成績】責任血管は内陰部動脈12例(36.4%)、腔動脈12例(36.4%)、子宮動脈枝1例(3.03%)、子宮動脈下行枝および腔動脈1例(3.03%)であった。血腫の大きさは内陰部動脈8.3±1.8cm, 腔動脈10.2±5.2cm, 子宮動脈枝11cmであった。内陰部動脈由来の12例のうち、6例(50%)が尿生殖隔膜より下方、3例(25%)が骨盤隔膜より下方に形成していた。腔動脈由来の12例のうち、9例(75%)が骨盤隔膜より上方に形成しており、そのうち2例が後腹膜腔に達していた。子宮動脈枝の血腫は骨盤隔膜より上方に形成していた。内陰部動脈の血腫は全例経陰的止血術が可能であった。腔動脈由来の12例のうち8例(66.7%)は経陰的止血術が可能であった。4例(33.3%)は子宮動脈塞栓術(TAE)により止血が行われ、そのうち1例は開腹術を必要とした。子宮動脈枝の血腫は経陰的止血術が可能であったが、子宮動脈下行枝および腔動脈の血腫に対してはTAEを施行した。【結論】内陰部動脈の血腫は経陰的止血術が全例可能であり、腔動脈や子宮動脈の血腫は多くは経陰的止血術が可能であったが、TAEまたは開腹術が必要な症例も認められた。血腫の責任血管を同定することで、適切な止血のアプローチ法の選択が可能であると思われた。

HS-3-6 栄養膜細胞から分泌されるナノ粒子の同定: BeWo細胞を用いた解析

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【目的】胎盤栄養膜細胞から分泌されるエクソソームには、胎盤特異的microRNA(miRNA)が含まれており、胎盤発達、妊娠維持に重要な役割を担っている。近年エクソソームとは異なり、小胞構造を持たない小さな粒子(ナノ粒子)の分泌が報告された。今回、栄養膜細胞株BeWoを用いて、栄養膜細胞由来ナノ粒子の同定と特徴付けを行ったので報告する。【方法】エクソソームの超遠心分離法に従いBeWo培養上清からエクソソームを分離した後、さらに上清を超遠心してペレットAを採取した。ペレットAをナノ粒子解析システムおよび電子顕微鏡により構造解析を行った。さらに、構成蛋白(ナノ粒子マーカー: AGO2, エクソソームマーカー: FLOT1)のWestern blot解析, 含有する胎盤特異的miRNA(miR-517a-3pなど)のPCR解析を行った。【成績】構造解析から、エクソソームは円形～楕円形の小胞構造(粒子径約80nm)、ペレットAは不定型、毛玉状の粒子構造(粒子径約40nm)を呈していた。Western blot解析から、エクソソームはAGO2陰性、FLOT1陽性、ペレットAはAGO2陽性、FLOT1陰性であった。以上よりペレットAはエクソソームと異なるナノ粒子であった。PCR解析から、ペレットAの胎盤特異的miRNA含有量は、エクソソームと比較して有意に高値を示した。【結論】はじめて栄養膜細胞由来ナノ粒子を同定した。ナノ粒子はエクソソームと比較してより多くの胎盤特異的miRNAを含有しており、胎盤母体間のコミュニケーションの主体はエクソソームではなく、ナノ粒子である可能性が示唆された。

P-1-1 CIN2 病変部における CD4 陽性細胞の浸潤密度は HPV 型と独立した予後予測因子である

慶應義塾大

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【目的】Cervical intraepithelial neoplasia (CIN) の病因はヒトパピローマウイルス (HPV) 感染で、排除に宿主免疫が関与する。今回 CIN2 病変の免疫細胞浸潤が予後と関連するか検討した。【方法】2012 年から 2014 年に初診で CIN2 と診断し、HPV 型判定を行った 115 例を対象とした。観察中に細胞診・組織診が正常化し、1 年以上持続した場合を消失とし、CIN3 への進行を進展とした。HPV 型と CIN2 の予後の相関を Log-Rank 検定で検討した。免疫細胞 (CD3, CD4, CD8, CD20, CD163, Foxp3 陽性細胞) は、まず消失・進展の各群 10 例を選び、狙い組織診検体を用いて免疫組織化学で同定した。次に解析ソフト Tissue Studio を用い、間質を除く CIN2 病変部の平均浸潤密度を計測し、Mann-Whitney U 検定で 2 群間で浸潤密度に有意差が出た免疫細胞を選択した。選択した免疫細胞について 115 例で後向きコホート研究を行い、浸潤密度が予後予測因子として有用か検討した。【成績】観察中に 115 例中 37 例が消失し、23 例が進展した。HPV16 型が検出されなかった 77 例では、HPV16 型陽性の 38 例に比べ有意に 5 年累積消失率が高かった (58.7% vs 30.5%)。進展群・消失群 2 群間で浸潤密度に差を認めた免疫細胞は CD4 陽性細胞 (CD4+) のみであった ($P=0.023$)。115 例の検討では CD4+ の浸潤密度が 27 個/mm² 以上の 77 例での 5 年累積消失率は 57.0% であったが、27 個/mm² 未満の 38 例は 39.0% で、CD4+ の浸潤密度が高い症例で消失率が高かった ($P<0.001$)。多変量解析で HPV 型と CD4+ 浸潤密度は病変消失の独立した予後因子であった。【結論】CIN2 病変部の CD4+ の浸潤密度が高い症例では病変消失の可能性が高く、CD4+ の浸潤密度は予後予測因子として有用であると考えられた。

P-1-2 同一症例の分葉状頸管腺過形成と胃型粘液性癌と全エクソーム配列による解析

信州大

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【目的】一部の分葉状頸管腺過形成 (LEGH) は子宮頸部胃型粘液性癌 (GAS) の前駆病変となる可能性があるが、その遺伝学的な発癌過程は不明である。GAS の全ゲノム/エクソーム解析やがん遺伝子パネルの変異解析結果から、TP53, KRAS, CDKN2A などの変異が比較的多いことが報告されている。一方で、癌化過程を検討する上では、同一症例の LEGH と GAS 部分の遺伝子変異を比較検討する必要があるが、これまでに報告がない。そこで今回、検討を行った。【方法】患者の同意を得て手術された LEGH を伴う GAS 症例のうち、LEGH 部分と GAS 部分の両方を含む新鮮凍結組織が採取できた 1 例から、LEGH 部分と GAS 部分を laser microdissection で採取し DNA を抽出した。正常筋層部分の DNA を対照として、全エクソーム配列による体細胞変異解析を行った。【成績】アミノ酸置換を伴う変異は LEGH62 カ所、GAS125 カ所に認めた。両者に共通する変異が 6 か所認められたことから、両者は同一起源と考えられるが、両者が分枝してから時間が経過していると考えられた。両者に共通する pathogenic 変異は GNAS (c.2531G>A, p.R844H) のみで、膵癌や大腸癌での報告が多い変異であった。LEGH には他に pathogenic 変異はなく、GAS の pathogenic 変異は GNAS の同じアミノ酸部位の変異 (c.2530C>T, p.R844C) が追加されているのみであった。【結論】本例の LEGH と GAS は同じ pathogenic 変異を共有しており、同一起源と考えられた。本例では GNAS が Driver 変異と考えられるが、LEGH から GAS への進行で他の Pathogenic 変異の追加はなく、Epigenetic な変化が癌化に関連している可能性が示唆された。今後、さらに症例の集積が必要である。

P-1-3 子宮頸癌放射線感受性とフェロトーシス制御因子との関連について

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【目的】子宮頸癌治療において手術療法以外で主軸となるのは、放射線治療である。個々の癌の放射線感受性は予後を決定し得る因子である。鉄関連細胞死であるフェロトーシスは、放射線によっても誘導されることがわかっており、フェロトーシスに関わる因子の中で子宮頸癌の放射線感受性に関わる因子を同定することを試みた。【方法】放射線治療後に腫瘍が残存したために子宮摘出を行った症例で、摘出子宮の腫瘍におけるフェロトーシス制御因子の発現を見ることで、放射線によるフェロトーシス誘導への抵抗性に関わる因子を見つける。また、子宮頸部腺癌と扁平上皮癌では明らかに放射線感受性に違いがある。両者の手術検体におけるフェロトーシス制御因子の発現の違いを見ることで、放射線によるフェロトーシス誘導に関わる因子を特定する。【成績】フェロトーシス制御因子の一つであるシスチントランスポーター xCT の発現とその制御因子である CD44 の発現は子宮頸癌の予後と関連することを先行研究で示している。その機序として、細胞内抗酸化物質であるグルタチオンの生成の制御が挙げられ、放射線による細胞内活性酸素種の処理にも関わると考えられる。【結論】フェロトーシス制御因子から放射線感受性を予測できれば、治療方針の決定に役立つと考えられ、また、フェロトーシス誘導剤であるソラフェニブやアルテスナイトなどは既に臨床で使用されており、放射線増感剤として早期に治療に役立てられる可能性もある。

P-1-4 糖鎖アレイを用いた HPV と結合するコンセンサス構造の探索

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【目的】ウイルスの宿主細胞への感染は、宿主細胞表面受容体への吸着に始まり細胞質内へ侵入していくステップを経る。インフルエンザのように特異性の高い糖鎖受容体構造が見出されているものもあるが、ヒトパピローマウイルス (HPV) は特異性の低い糖鎖受容体との吸着から始まる多段階機構により侵入するとされ、糖鎖受容体としてヘパラン硫酸プロテオグリカンが知られている。臨床応用として易感染性患者選別を考えた場合、“細胞顔つき”として他の特定糖鎖構造が見いだせれば有益と考えられるが、HPV と結合しやすい糖鎖構造の網羅的な検討報告は見られない。そのため、HPV に結合しやすいコンセンサス構造を糖鎖アレイを用い同定することを目的として測定を行った。【方法】HPV16 型 L1 タンパク質、HPV18 型 L1 タンパク質、インフルエンザ A 型のヘマグルチニン (HA) タンパク質、Concanavalin A (ConA) レクチンの 4 種類を検体として、300 種類の糖鎖アレイパネルを用い、検体と固定糖鎖との結合を測定した。測定値は検体ごとのアレイパネルに Positive Control を置き、その相対値として算出した。【成績】測定値は 4 サンプルの Positive Control 平均値で補正した。コントロール検体のインフルエンザ HA タンパク質や ConA レクチン結果を基に Positive Control 平均値の 10% を測定値基準として糖鎖構造を抽出した場合、HPV16 型では 8 種類、HPV18 型では 7 種類の糖鎖構造が同定された。しかしながら、HPV16 型および HPV18 型のいずれの同定糖鎖にもコンセンサス構造は認めなかった。【結論】HPV との結合において既知のヘパラン硫酸と並ぶ候補構造の同定できなかったが、各々同定された構造における真偽は今後の検討課題とした。

P-1-5 子宮頸癌患者由来オルガノイドの樹立方法の検討

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【目的】子宮頸癌は早期癌では生命予後は良好であるものの、円錐切除後妊娠では流早産の増加などの臨床的課題がある。細胞モデルに用いられる細胞株も限られ、また heterogeneity が保持される 3D オルガノイド培養の報告はほとんどない。そこで本研究では子宮頸癌患者由来オルガノイド (CxPDO) の樹立方法を確立することを目的とした。【方法】子宮頸癌患者の生検検体又は手術検体の一部を細断し、酵素処理で単離した細胞を Matrigel に包埋した。無血清培地に各種の増殖因子を添加し、5% CO₂ インキュベーターにて 37°C で培養した。CxPDO の増殖はオルガノイド形成速度及び ATP assay にて確認した。ホルマリン固定パラフィン包埋切片を作成して患者腫瘍との組織学的な相同性を検討した。【成績】13 検体中 9 検体 (樹立率 69%) で CxPDO が樹立された。組織型では非扁平上皮癌 (non-SCC) 4 例中 3 例、扁平上皮癌 (SCC) 9 例中 6 例で樹立でき、いずれも患者腫瘍の形態的特徴を模倣していた。増殖因子の組成は、初期 6 検体で使用した組成 A の樹立率は 50% で、non-SCC は放射線治療後の生検検体 1 例を除く 2 例中 2 例、SCC では 3 例中 1 例のみ CxPDO が樹立された。そこで組成を検討し、組成 B において SCC の増殖は、オルガノイド形成速度・ATP 産生量ともに有意に改善し、non-SCC では組成 A の増殖と同程度だった。以降の 7 例は組成 B で培養し、non-SCC 1 例中 1 例、SCC 6 例中 5 例で CxPDO が樹立された (樹立率 86%)。【結論】組成 B を用いることで SCC を含め CxPDO の樹立率が改善した。CxPDO は、新規の局所治療方法の開発や患者毎の薬剤スクリーニングへ応用可能な細胞モデルになると期待される。

P-1-6 子宮頸癌に対するホウ素中性子補足療法 (BNCT: Boron Neutron Capture Therapy) の効果

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【目的】ホウ素中性子補足療法 (BNCT: Boron Neutron Capture Therapy) は、中性子とホウ素の核反応を利用したもので、正常細胞にほとんど損傷を与えず、がん細胞を選択的に破壊する治療法で、初発・単発がんのみならず、再発・転移性がんにも効果が期待される。脳神経外科領域や頭頸部癌、悪性黒色腫では臨床応用されてきているが、婦人科癌における BNCT の研究は少ない。今回、子宮頸癌に対する BNCT の効果に関する研究を行った。【方法】子宮頸癌細胞株 (C4-1, SiHa, SKG-II, Hela) にホウ素化合物 (BPA: boronophenylalanine) を暴露し、その暴露濃度・時間ごとの各細胞株のホウ素濃度を測定した。SiHa, Hela 細胞に 10ppm の BPA を 3 時間暴露したのちに中性子を照射し、colony forming assay を用いて BNCT の効果を検討した。4 種類の細胞株の皮下腫瘍モデルを作成し、BPA 24mg/kg を腹腔内投与後の皮下腫瘍および各臓器、血液のホウ素濃度を測定した。【成績】上記の全子宮頸癌細胞株において BPA の暴露によりホウ素の取り込みを確認できた。ホウ素の取り込みは BPA の濃度に依存していたが暴露時間による変化はみられなかった。BPA 暴露後の SiHa および Hela 細胞に中性子を照射することで colony の減少がみられ、その効果を確認できた。皮下腫瘍モデルマウスへの BPA の投与により、腫瘍のホウ素濃度は BNCT の治療効果が期待できる十分量であった。また各臓器のホウ素濃度は低値であった。【結論】子宮頸癌に対しての BPA 投与後に中性子を照射する BNCT は期待できる治療の一つである。

P-1-7 子宮頸部すりガラス細胞癌におけるがん関連遺伝子変異の特徴

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【目的】子宮頸部すりガラス細胞癌(GCC)は、本邦での年間新規報告数が20例前後の極めて希な組織型である。予後不良な症例が多いものの分子生物学的な特徴は明らかではない。本研究では、細胞株を用いてGCCにおける遺伝子異常の特徴を検討した。【方法】GCC細胞株は、当科で樹立したHU-6、入手可能な細胞株であるTOM-2、HOKUGを用いた。HU-6は31歳のGCC症例の腫瘍検体から樹立し、患者腫瘍との相同性は組織学的及び遺伝子変異解析にて検討した。160のがん関連遺伝子を次世代シーケンサーにて解析し(GeneRead Human Comprehensive Cancer Panel, Qiagen)、GCCの3細胞株に共通する遺伝子異常を検討した。【成績】HU-6と患者腫瘍は組織学的に類似し、遺伝子変異は共通していた。HPV遺伝子型解析では、HU-6とTOM-2で18型、HOKUGで58型が検出された。GCCの3細胞株には、扁平上皮癌に多い*Noch1*及び予後不良な腺癌に多い*TP53*に加え、相同組み換え修復関連遺伝子(*ATM*, *BRCA2*, *FANCA*, *BRIPI*)、SWI/SNF経路の遺伝子(*PBRM1*, *EZH2*)を含む26がん関連遺伝子に共通するSNVsを認めた。さらに、HU-6では*KRAS*(G12C)変異に加え*Myc*の増幅を認めた。またHOKUGでは複数の遺伝子の欠失を、TOM-2では*SMO*, *AR*の変異と*STK11*の欠失を認めた。【結論】相同組み換え修復関連遺伝子の異常を共通して認め、PARP阻害薬がGCCに有効である可能性が示唆された。また*KRAS*(G12C)変異を認めるGCCでは*KRAS*阻害薬が有効である可能性が考えられた。

P-2-1 Molecular mapping法によるHSIL誘発HPV型の同定

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【目的】子宮頸部擦過細胞検体を用いた解析では、癌症例であっても複数のHPVが検出される多重型HPV感染症例が一部に存在する。先行研究において、我々は子宮頸癌や腔上皮内腫瘍(VaIN)中には単一のHPVしか存在しないことを明らかにした。本研究では多重型感染HSIL症例やHPV陰性例における真の責任HPVを明らかにすることにより、HSILの原因としてのHPVを再評価する。【方法】細胞診検体と組織診検体を有するCIN3:77例、CIN2:41例のうち、細胞診検体による分析では、多重HPV陽性の症例92例、単独HPV陽性25例、HPV陰性例1例であった。これらについてMolecular Mapping法でHPVを解析した。Molecular Mapping法:ホルマリン包埋切片の目的組織の部位のみを切り出してDNA抽出を行い、uniplex E6/E7 PCR法によりHPV型判定を行った。【成績】108例の病変から単一のHPVが検出された。ほとんどはハイリスク型であったが、ハイリスク候補型も検出された。1例のCIN3症例からローリスク型のHPV6が検出されたが、病理標本の再評価により、Papillary immature metaplasiaに修正された。液状細胞診HPV検査で検出されなかったHPVが検出された症例が、多重型感染92例中35例、単独型感染25例中7例、細胞診陰性1例みられた。高頻度のHPVはHPV16, 52, 18であり、ハイリスク候補型であるHPV26, 34, 53, 66, 69, 73, 82も検出された。【結論】Molecular mapping法解析により、病原性HPV型を明らかにすることは、真の癌誘発HPVを明らかにするうえで重要と思われる。高リスク型と認定されていないHPV型が7タイプHSIL症例から検出できたことより、これらハイリスク候補型の意義について再評価する必要があると考えられた。

P-2-2 子宮頸癌検診における細胞診・HPV併用検診の検証とHPV単独検診の解析

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【目的】子宮頸癌検診における細胞診・HPV併用検診(HPV併用)の有用性は多数報告されているが、偽陽性増加と費用対効果の課題が指摘されている。当院データより、HPV併用の効率的運用とHPV単独検診の有用性について解析した。【方法】2008年4月より2019年12月までの検診症例86,242例を対象とした。HPV検査は同意のもと希望者5510例に施行した。年代別に細胞診陽性率、細胞診陰性例でのHPV陽性率を分析し、HPV陽性例では型分析を行った。細胞診陰性・HPV陽性例では可能な限り、コルボスコピー検査と生検を実施し、CINの頻度とその年代別分布を解析した。さらに2010年から2018年におけるHPV併用でHPV陰性例における細胞診異常の頻度を分析した。【成績】細胞診陰性例でのHPV陽性率は11.2%であった。年代別では20代15.5%、30代14.1%で両年代間に有意差は認めなかった。細胞診陰性・HPV陽性例において精査できた症例の54.0%がCINと診断された。年齢別に精査できたCIN17例と非CIN108例を分析し、20-39歳と40歳以降を比較検討した結果、20-39歳で有意にCINの頻度が高かった。HPV併用でHPV陰性例のうち1.0%が細胞診陽性であり、HPV単独検診の細胞診異常を見逃す率は低いと考えられた。【結論】細胞診陰性・HPV陽性例での年代別比較検討で20代と30代で有意差がみられないことから、20代での一過性感染の可能性は低く、20代からのHPV検査が望ましいと思われた。HPV併用においては年代別CINの検出率から、20-39歳でのみHPV検査併用し、40歳以降は細胞診のみ行うことがより効率的な検診方法であると思われた。また、HPV単独検診の細胞診異常を見逃す率は1.0%と低く、頸癌検診の選択肢となることが示唆された。

P-2-3 HPV 検査の有用性を検証するコホート研究におけるアルゴリズム遵守状況の検討

子宮頸がん検診における細胞診と HPV 検査併用の有用性に関する研究研究班
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【目的】HPV 検査を用いた検診の有用性を検証するため, 細胞診単独検診を受診する対照群と HPV 検査と細胞診を併用で実施する介入群を比較/評価する「子宮頸がん検診における細胞診と HPV 検査併用の有用性に関する研究」が進行中である。今回, 本研究における初年度登録以降の参加者の追跡管理状況について検討した。【方法】対照群では, 検診陰性者に 2 年後の検診, ASC-US には HPV 検査によるトリアージ, ASC-US より高位の細胞診異常 (>ASC-US) には直ちにコロボ診/組織診の実施を指定している。また介入群では NILM/HPV 陰性には 2 年後の検診, NILM/HPV 陽性 (リスク保持者) と ASC-US/HPV 陰性には 12 か月後の細胞診, ASC-US/HPV 陽性と >ASC-US には直ちに組織診の実施を指定している。収集データより, 指定された精密検査の受診および検診陰性者の次の検診の受診の遵守状況を検討した。【成績】初回検診は 25,074 人 (対照群 13,845 人, 介入群 11,229 人) が受診し, 両群ともに検診陰性者の 2 年後の検診受診率は約 30% であった。介入群の直ちに組織診の対象者の遵守割合は 95% 以上であったが, 12 か月後の細胞診の適時の受診率は 15~20% と低く, 対象者の 40% 以上が 6 か月未満の時期に何らかの検査を受けていた。【結論】要精検者は, 直近の精密検査を推奨された場合に比して 12 か月後の場合は遵守が困難であることが明らかとなった。HPV 検診で増加するリスク保持者の精検受診率の高低は, HPV 検診そのものの成否につながる。HPV 検診を考慮する際は, これらの運用に十分な配慮が必要である。

P-2-4 HPV 検査併用子宮頸がん検診の成果と課題

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【目的】HPV 検査併用子宮頸がん検診が導入された場合の成果と課題について検討する。【方法】S 市では, HPV 検査併用検診を 2011 年度から導入している。2011 年-2019 年にかけての結果から, HPV 検査併用検診における成果と問題点について検討した。【成績】検診結果は, 細胞診-/HPV- 87.6%, 細胞診-/HPV+ 7.3%, ASC-US/HPV- 0.7%, ASC-US/HPV+ 0.6%, LSIL 以上 3.7% であった。細胞診-/HPV+ の 1 年後の検診で 57.9% が精密検査の対象となり, 少なくとも 19.2% に CIN, 4% は CIN 2 以上の病変であった。40 歳未満の受診者数が 1.3 倍に増加したこともあり, 導入後数年で併用検診以外も含めた検診による CIN3 以上の発見数も 3.5 倍増加した。しかし, 細胞診-/HPV+ の 1 年後の受診率は, 42.6% に過ぎなかった。S 県では, 現在 30-44 歳の HPV 検査の無料化事業を行っており, 確実な受診勧奨を行っているが, 細胞診-/HPV+ の 1 年後の受診率は, 60.6% であった。また, HPV 単独検診では見逃される細胞診+/HPV- は併用検診の 0.82% であった。その 62.5% に病変を認めたが, CIN2 以上の子宮頸部高度病変は全体の 0.1% (35/35,525 例) であった。しかし, 子宮体痛や子宮肉腫も 4 例含まれていた。【結論】HPV 検診を導入した場合は 1 年後の再受診対象者の管理のための適切な管理システムが重要である。また, HPV 単独検診で見逃される高度病変症例が少数ではあるが存在することを考慮の上で, 年齢を含めたアルゴリズムを検討する必要がある。

P-2-5 HPV ワクチンの接種率を上げるために積極的勧奨再開に加えて必要な啓発活動とは~高 1 女子と高 1 の娘をもつ母親を対象とした全国アンケート調査結果

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【目的】HPV ワクチンの接種率は 2013 年に急激に低下して以降 1% 未満で推移し, ここ数年回復の兆候を認めるが, まだ積極的勧奨中止前の約 70% には到底及ばない。積極的勧奨が再開したとしてもすぐに接種率が戻る可能性は低く, 現行の啓発活動の問題点と接種率向上のための有効な啓発手段は何かを把握することが効果的な啓発活動のために重要である。今回我々は日本の現状についてアンケート調査を行った。【方法】全国の高校 1 年生女子と高 1 女子の母親を対象として, 第三者調査会社を介したウェブアンケート調査を実施した (調査期間: 2020 年 8 月 20-24 日)。高 1 女子 473 名, 母親 326 名が接種有無を回答し, うち詳細調査に同意した 490 名 (高 1 女子 245 名, 母親 245 名) を対象に HPV ワクチンについての意識調査を行った。【成績】高 1 女子の HPV ワクチン接種率は 14.4% だった。未接種の主な理由は高 1 女子・母親ともに副反応や安全性に対する懸念であり, 特に母親には過去の副反応報道の影響が大きかった。また, 接種意向に最も貢献する情報は高 1 女子・母親ともに「HPV の感染率」だった。対象者が HPV ワクチンに関する情報提供を希望する媒体は, 高 1 女子は学校 (41.2%), SNS (29.7%), 医療機関 (28.8%), テレビ (28.2%), 母親はテレビ (39.9%), 医療機関 (37.5%), 自治体の DM (32.7%) の順に多かった。【結論】本調査結果より, HPV ワクチンの情報だけでなく HPV 感染の正確な知識を伝えること, そして自治体からの通知に加えて, 学校や医療機関, SNS, テレビを通じた情報提供が効果的であると考えられた。HPV ワクチン接種への不安は根強く, 多方面からの積極的かつ丁寧な情報提供を進めていく必要がある。

P-2-6 HPV ワクチンの副反応の実態

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【目的】HPV ワクチンは、持続的な疼痛を理由に積極的勧奨が中止された。疾病・障害認定審査会は、予防接種と疾病との因果関係を審議している。我々は、この審議結果を調査し、他の定期接種ワクチンと比較し、HPV ワクチンによる副反応を否定できない症例について検討した。【方法】定期予防接種であるDPT-IPV, IPV, DPT, Polio, Measles, Rubella, Japanese encephalitis, BCG, Influenza, Haemophilus influenza type b, Pneumococcal conjugate vaccine, Pneumococcal polysaccharide vaccine, HPV, Chickenpox, Hepatitis B virusについて解析した。解析期間は2004年から2018年とした。副反応患者数は分科会で副反応と認定された人数を集計した。接種者数は公開されているデータから調査した。HPV ワクチンの場合、2009年からの任意接種と定期接種の合計接種者数とした。【成績】副反応発症率は、10万人接種あたり、BCG 2.7人、HPV 0.8人、その他のワクチンは0.3人以下であった。HPV ワクチンの副反応は28人で、1人に局所の疼痛、27人に多様な複数の症状の組み合わせ(頭痛、脱力、慢性疼痛、微熱、神経不全麻痺、しびれ、筋力低下、倦怠感、不眠、めまいなど)が認められた。【結論】HPV ワクチンの副反応発症率はBCGよりも低く、その他のワクチンとほぼ同様であった。HPV ワクチンの副反応の特徴とされた多彩な症状は副反応であるという科学的事実はないとWHOは指摘する。HPV ワクチンの副反応とされたものの多くはCRPS, POTS, ISRRであった可能性がある。政府によるHPV 感染予防ワクチン接種の勧奨再開が必要である。

P-2-7 わが国のデータによる細胞診による子宮頸がん検診でのASC-US症例へのHPV トリアージの妥当性の検討

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【目的】わが国の地域保健健康増進事業での子宮頸がん検診の手法は子宮頸部細胞診であり、細胞診陰性(NILM)は2年後の検診、細胞診陽性(NILM以外の判定)は要精密検査の対象とする。ASC-USは要精密検査の約半数を占め、精密検査として①直ちにコルポ診・組織診②HPV 検査によるトリアージ③半年ごとに細胞診を繰り返す、の3つの選択肢があるが、①は侵襲が大きく③は2年間の実施・管理が困難である。現在②ではHPV (-)の場合1年後の細胞診実施とされているが、HPV (-)からの子宮頸がんやCervical Intraepithelial Neoplasia (CIN) 3の発症は僅かとされる。そこでASC-USへのHPV トリアージによるHPV (-)のCIN3以上の発症率をNILMと比較することを目的とした。【方法】2013年4月から2018年4月までに子宮頸がん検診および精密検査とそれらの判定・診断の実施施設において2回以上の子宮頸がん検診または精密検査の結果の把握ができた25,798人を対象とした。この期間の初回の細胞診の判定区分別(NILM, ASC-US/HPV (不明), ASC-US/HPV (-), ASC-US/HPV (+), >ASC-US)に2年間のCIN3以上の累積発症率を算出し、コックス比例ハザードモデルを用いて、初回検査結果NILMに対する累積発症のハザード比(HR)を年齢を調整して推計した。【成績】CIN3以上発生のHRはASC-US/HPV (+)で0.8(95%信頼区間:0.3-2.1), ASC-US/HPV (-)で0.2(0.1-0.7)であった。【結論】ASC-US/HPV (-)の2年間でのCIN3以上の発症はNILMより有意に低く、ASC-USに対してHPV トリアージを実施し、HPV (-)であれば2年後の検診に戻すことができると考えられ、本研究は受診者への負担軽減と検診を運用しやすくするためのアルゴリズムの設定の基礎資料になる。

P-2-8 現実になった HPV ワクチン積極的勧奨差し控えの弊害

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【目的】本邦でHPV ワクチンは2013年に積極的勧奨が差し控えられた。本研究は、積極的勧奨差し控えの影響を検証することを目的とした。【方法】24自治体(人口約1315万人)における1989~2000年度生まれの20歳時子宮頸がん検診での細胞診異常率(未受診者は21歳)を解析した。【成績】導入前世代(1989~1993年度生まれ)の各生まれ年度のASC-US以上の20歳時子宮頸部細胞診異常率は2.2%(120/5383), 3.1%(166/5389), 3.2%(211/6573), 4.3%(291/6825), 3.9%(312/7911)と明らかな増加傾向にあった。接種世代(1994~1999年度生まれ, 接種率:62.1~71.7%)は3.5%(250/7096), 3.6%(227/6379), 3.8%(267/6972), 3.6%(249/6925), 4.1%(288/6983), 3.9%(240/6099)と緩やかな増加傾向にあったが、この世代の生まれ年度ごとの細胞診異常率の対数近似曲線は導入前世代の近似曲線より明らかに下方に移動しており、HPV ワクチンの有効性が示唆された。一方、停止世代(2000年度生まれ, 接種率:10.2%)の細胞診異常率は5.0%(61/1211)であり、接種世代の対数近似から予測される率よりも高く、導入前世代の対数近似から推測される率と同等であった。【結論】停止世代の細胞診異常率の増加が観察された。HPV ワクチンの積極的勧奨差し控えの弊害と言える。積極的勧奨再開とともに、停止世代の女性へのキャッチアップ接種や定期的な子宮頸がん検診受診を強く推奨する必要がある。

P-2-9 健診機関における HPV 検査単独法による子宮頸がん検診への準備状況

公益財団法人東京都予防医学協会保健会館クリニック¹、国際医療福祉大三田病院予防医学センター²、こころとからだの元氣プラザ³、畿央大学大学院健康科学研究科健康科学研究科⁴、沖縄徳洲会千葉徳洲会病院⁵、木口一成¹、久布白兼行¹、齊藤英子²、大村峯夫³、小田瑞恵³、植田政嗣⁴、佐々木寛⁵

【目的】わが国の子宮頸がん検診の手法は地域保健健康増進事業（住民検診）では細胞診単独が選定され、「職域におけるがん検診マニュアル」も同様である。2019年度版「有効性評価に基づく子宮頸がん検診ガイドライン」では HPV 検査単独法も実施推奨になり、この方法は運用状況が効果に大きく影響するので、がん検診の一翼を担う健診機関での準備状況を調査した。【方法】日本人間ドック学会に所属する 1739 施設を対象に 2020 年 12 月～4 か月間、HPV 検査実施の有無と、「HPV 検査単独法・細胞診トリアージ→HPV 陽性かつ細胞診陰性者への 12 か月後の細胞診（追跡精検）」を想定した精度管理準備状況についてアンケートを実施した。項目は、①HPV 検査時の説明書の作成・配布、②HPV 陽性者へのトリアージの自施設実施と受診勧奨、未受診者への再受診勧奨、③トリアージ陽性者への追跡精検、受診勧奨、未受診者への再受診勧奨、④医師採取液状検体法での実施等である。【成績】1739 施設中 245 施設が回答し、子宮頸がん検診実施は 212 施設であった。住民検診、個人、職域の委託元に対して、医師採取 HPV 検査単独法実施の施設はそれぞれ 11.8%、24.9%、0-30% であった。精度管理準備状況は各項目について、現時点で実施可能な施設は 6～20% 程度、実現の可能性ありを加えると全て 50% 程度であった。【結論】すでに HPV 検査実施の施設がある一方で全体的には精度管理の準備は十分ではなかったが、いずれの項目も実現の可能性があると判明した。健診機関の特徴を生かし、委託元や精密検査実施機関との連携体制の定量化により、精度管理を兼ね備えた HPV 検査単独法検診の大規模での実現の可能性が示唆された。

P-3-1 術後早期に肩甲骨転移を認めた子宮頸癌 IB2 期の 1 例

京都桂病院

水津 愛、岩見州一郎、下地 彩、宗万紀子、家村洋子

子宮頸癌は時に骨転移をきたしうが、脊椎と骨盤骨への転移が主であり、遠位への転移は稀である。今回子宮頸癌 IB2 期に対し広汎子宮全摘術後早期に右肩甲骨転移を認めた症例を経験したので報告する。症例は 80 歳、4 妊 2 産。不正出血を主訴に当院紹介受診。子宮頸部は 4cm 大に腫大し、生検の病理組織所見は扁平上皮癌であった。子宮頸癌 IB2 期の診断で、腹式広汎子宮全摘、両側付属器切除、骨盤内リンパ節郭清術を施行した。病理組織所見で左閉鎖リンパ節転移を認めたため、術後化学放射線療法を検討していたが、術後 1 か月余りより右肩痛が出現した。整形外科に相談の上、対症療法で経過観察としていたが、疼痛改善乏しく、また SCC7.9ng/mL と高値を認めたため、CT 施行したところ、右肩甲骨に骨破壊を伴う腫瘍を認め、子宮頸癌肩甲骨転移が疑われた。生検で子宮標本と類似する扁平上皮癌を確認し、子宮頸癌肩甲骨転移と診断した。疼痛コントロール目的に放射線治療施行後、現在化学療法（ベパシズマブ+バクリタキセル+カルボプラチン）、抗 RANKL 抗体投与を施行しており、腫瘍縮小を確認、他部位への転移所見は認めていない。子宮頸癌の遠隔転移は頻度が低く、そのうち骨転移は 2-16% とされている。50% が腰椎、30% が骨盤への転移であり、遠位への転移は頻度が低く、肩甲骨転移についての報告は非常に稀である。骨転移診断後の生存期間中央値は 22～32 週であり、手術や化学療法、放射線治療が症状改善及び生存期間延長に寄与する。本症例でも放射線治療で疼痛緩和後、化学療法に臨んでいる。子宮頸癌肩甲骨転移をきたした 1 例を経験した。稀ではあるが、遠位骨への転移の可能性も念頭に置いて精査を行う必要がある。

P-3-2 両側に粗大な骨盤リンパ節転移と深部静脈血栓症をみとめ、下肢痛を呈した子宮頸部微小浸潤癌の 1 例

湘南鎌倉総合病院

青柳 遼、井上裕美、渋谷菜里、松本愛世、柴崎 聡、渡邊零美、鶴澤芳枝、大沼一也、福田貴則、木幡 豊

子宮頸部微小浸潤癌の骨盤リンパ節転移の頻度は少なく、またその多くが顕微鏡的な転移である。【症例】38 歳。1 経妊 0 経産。子宮頸部細胞診で HSIL と診断され当院へ紹介された。狙い組織診で子宮頸部高度異形成と診断された。子宮頸部円錐切除術を勧めたが、直ちに手術は希望されず、3 か月後の手術を予定した。手術予定日の 2 週間前に下肢痛を主訴に当院受診され、造影 CT 検査で約 13cm に及ぶ右大腿深部静脈血栓と右側約 5cm、左側約 3cm の骨盤リンパ節腫大を指摘された。再度頸部狙い組織診を行ったが高度異形成の診断であった。MRI 検査上も子宮頸部に異常所見はみとめなかった。悪性リンパ腫など子宮頸部以外に原発巣が存在する可能性を考慮し、CT ガイド下骨盤リンパ節生検を行ったところ p16 陽性の低分化な癌腫という診断であった。そのため子宮頸部が原発である可能性を考え、子宮頸部円錐切除術をおこなった。病理診断は子宮頸部非角化型扁平上皮癌であった。間質浸潤の深さは 1.4mm であり、リンパ管侵襲をわずかにみとめた。骨盤リンパ節腫大は子宮頸癌のリンパ節転移と考えられた。その後同時化学放射線療法を行い、現在経過観察中である。【結語】一般的に子宮頸癌は病勢が進行し、骨盤リンパ節転移を呈することが多い。しかしながら本症例のように微小浸潤癌であっても、粗大なリンパ節転移をきたすことがある。そのため子宮頸部の狙い組織診の結果が異形成や微小浸潤癌であっても、粗大な骨盤リンパ節腫大を認めた場合は原発巣の検索をしつつ、子宮頸癌のリンパ節転移の可能性も考え子宮頸部円錐切除を行い、詳細な病理学的検索が必要であると考える。

P-3-3 TC療法中に15年前の胃癌が骨髄腫腫症として再発した子宮頸癌の一例

宮崎県立宮崎病院¹, 宮崎県立宮崎病院病理²

今村紘子¹, 永谷優華¹, 愛甲 碧¹, 脇山 英¹, 安藤伶旺¹, 村上真友¹, 甲斐いづみ¹, 村上孟司¹, 高村一紘¹, 阿萬 紫², 谷口秀一¹, 嶋本富博¹

多くの癌腫において治療後5年以内の再発が多く、10年後以降はさらに再発率は低下し観察期間も終了していることが多い。症例は68歳、5妊2産。54歳時に胃癌に対し胃全摘手術を受け、再発なく経過していた。水腎症、子宮腫瘍を指摘され当科を初診した。子宮頸部の生検は扁平上皮癌で、仙骨転移を伴う子宮頸癌IVB期(cT3bN1M1)と診断し、同時化学放射線療法(CCRT)を行った。腫瘍マーカーのSCC、CEAは低下し腫瘍も縮小していたが傍子宮結合織浸潤等が残存しCCRT後約1か月半後よりTC療法を5回行った。SCCはTC療法開始後も低下していたがCEAはTC療法2回目頃より上昇傾向にあった。治療中、2回の造影CT検査で新規病変を指摘できず内診でも局所病変の増大はなかった。TC療法5回目day13に血小板減少に加え、ALP、Ca上昇を認め、その後の精査で胸椎から仙椎、頭蓋骨の多発骨転移と診断した。TC療法5回目day63で血小板数5万/μlに低下し骨髄検査を施行したところ、骨髄は低形成で異型を伴う上皮細胞を認め、腺癌の骨髄転移の所見であった。胃癌既往があることより15年前に治療した胃癌の骨髄転移と診断した。当院腫瘍内科でS1内服による加療を開始したがDICを併発し胃癌による腫瘍死となった。悪性腫瘍の治療成績の向上により複数の悪性腫瘍を発症することも稀ではない。今回、子宮頸癌の治療中に治療したと思われていた胃癌が骨髄腫腫症として再発した1例を経験した。化学療法中の他臓器腫瘍の再発を含め文献的考察を加え報告する。

P-3-4 G-CSF産生子宮頸部扁平上皮癌の1例

愛媛大附属病院

中野志保, 宇佐美知香, 松元 隆, 山内雄策, 西野由衣, 恩地裕史, 加藤宏章, 安岡稔晃, 森本明美, 藤岡 徹, 松原圭一, 杉山 隆

【緒言】G-CSFを産生する悪性腫瘍は様々な臓器で報告されているが、肺癌などに多いとされ、婦人科疾患では稀である。G-CSF産生腫瘍は原発臓器に関わらず低分化や未分化な癌に多く、予後不良とされる。今回、白血球増多の精査中にG-CSF産生腫瘍と診断された子宮頸癌の1例を経験したので報告する。【症例】53歳。健康診断にて白血球数高値を指摘され血液内科で精査中であった。不正性器出血の症状を認め前医の婦人科を受診したところ、子宮頸部に径5cm大の腫瘍を指摘され、子宮頸癌疑いで当院に紹介された。子宮頸部の腫瘍の組織検査結果は扁平上皮癌であり、内診および画像所見より子宮頸癌IB3期(FIGO2018)と診断した。FDG-PETを施行したところ、全身の骨にびまん性の高度FDG集積を認め、骨髄増殖性疾患の可能性が指摘された。骨髄穿刺を行った結果、白血病やリンパ腫は否定的であったが、血中G-CSFが高値であり、G-CSF産生腫瘍が疑われた。子宮頸癌に対して広汎子宮全摘及び両側付属器摘出術を施行し、摘出組織での免疫組織染色の結果、G-CSF陽性でありG-CSF産生子宮頸癌と診断された。術後速やかに白血球数は正常化し、再発リスク分類で中リスクであり術後補助療法を施行した。【考察】一般的に予後不良とされるG-CSF産生腫瘍であるが、子宮頸癌の症例報告においても同様であり、早期症例であっても死亡例が多く、急速な経過をたどる症例の報告もある。したがって、白血球増多を認める子宮頸癌の場合、速やかに診断し治療する必要があると考えられる。本症例では、現在のところ再発徴候は認めないが、注意深く経過観察する必要があると思われる。

P-3-5 生体腎移植後に子宮頸部小細胞神経内分泌癌を発症した一例

宮崎県立宮崎病院

永谷優華, 今村紘子, 脇山 英, 安藤伶旺, 村上真友, 愛甲 碧, 甲斐いづみ, 村上孟司, 高村一紘, 阿萬 紫, 谷口秀一, 嶋本富博

免疫抑制剤使用中は悪性腫瘍の発症率が上昇するとされている。症例は42歳、0妊0産。40歳時に生体腎移植後、当院外科で経過観察中であった。不正性器出血を主訴に近医を受診し、子宮頸部擦過細胞診がadenocarcinomaの診断であった。前医受診後より経口摂取不良となり、当院外科に入院、点滴加療を開始し入院中に当科を紹介受診した。子宮頸部からの病理組織学的検査結果は小細胞神経内分泌癌および扁平上皮癌であり、免疫組織化学検査でp16がびまん性に陽性であった。精査の結果、肝転移、胸膜播種、多発リンパ節転移を伴う子宮頸癌IVB期(cT3bN1M1)と診断し化学療法を行う方針で当科へ転科した。腎機能低下のため抗癌剤の選択を検討しつつ、入院時より認めていた腫瘍性SIADHと考えられる高度な低Na血症の治療を行っていたところ、急速な病状の進行があり、癌性疼痛が増悪した。肝転移病変が数日単位で増大しており、それに伴う疼痛コントロールが不良となった。同時に子宮頸部病変の増大、性器出血も増量し輸血を要する状態であった。さらに腎機能障害、PSの低下も進行したため、化学療法による治療自体が困難な状況となった。疼痛コントロール、低Na血症の治療を行うも、全身状態はその後急速に悪化し、化学療法を施行できずに死亡に至った。子宮頸部小細胞神経内分泌癌は非常に進行が早く予後不良である。今回、免疫抑制剤を使用しHPV関連腫瘍と思われる子宮頸癌を発症し、さらに予後不良とされる小細胞神経内分泌癌であったことから極めて不良な経過を辿った1例を経験したので文献的考察を加え報告する。

P-3-6 イリノテカン・ネダプラチンによる術前化学療法を施行した IB2 期子宮頸癌合併妊娠の 1 例

信州大附属病院¹, 諏訪赤十字病院²

品川真奈花¹, 小原久典¹, 遠藤瑞穂¹, 吉池奏人², 井田耕一¹, 山田 靖¹, 布施谷千穂¹, 菊地範彦¹, 宮本 強¹, 塩沢丹里¹

妊娠継続希望の子宮頸癌合併妊娠の管理方針に、一定の見解や推奨は示されていない。我々は、これまで術前化学療法(NAC)を積極的に行い、妊娠期間の延長を図ってきた。化学療法は主にパクリタキセル・カルボプラチン(TC)療法を用いてきたが、妊娠中にイリノテカン・ネダプラチン(CPT/N)療法を施行した報告は無い。今回、IB2期子宮頸癌合併妊娠に対してCPT/N療法を行った1例を経験したので報告する。症例は1妊0産の33歳女性で、妊娠初期に子宮頸部に約3cmの腫瘤を指摘された。組織診断は扁平上皮癌であり、妊娠8週に当院に紹介となった。MRIで子宮頸部に長径29mmの腫瘤を認め、CTで子宮外病変は指摘できず、子宮頸癌IB2期合併妊娠と診断された。本人と夫は強い妊娠継続希望であり、インフォームドコンセント後、妊娠14週からNAC施行の方針となり、初回TC療法後にカルボプラチンアレルギーを発症したため、CPT/N療法に変更した。Grade3以上の母体有害事象はなく、妊娠30週より2SDの胎児発育不全を認めたが発育停止はなかった。MRI上では子宮頸癌病変は不明瞭化した。3コース施行後に肉眼上増大傾向が疑われたため、妊娠33週3日に選択的帝王切開術、広汎子宮全摘術を施行した。術後経過は良好であった。病理診断で腫瘍径は長径35mm、間質浸潤5mmでIB2期(yT1b1N0M0)であり、術後補助治療は行わず現在まで再発はない。児は男児でApgar Score 8/9点、出生体重1495g(-1.85SD)、身長37.4cm(-2.37SD)とSFD児であったが、発育と発達は順調である。子宮頸癌合併妊娠に対するNACとしてCPT/N療法はTC療法の代替レジメンの選択肢となり得ると考えられた。

P-3-7 子宮頸がん IIIB 期にて化学放射線療法後、経過良好であった症例で、約 19 年後に見られた悪性腹膜中皮腫の 1 例

JCHO 熊本総合病院¹, 熊本大², 熊本労災病院³

東矢俊光¹, 西村朗甫², 今村裕子², 値賀正彦³, 田山親吾², 近藤英治²

【目的】婦人科がん患者での長期生存例が増えるに従い、二次腫瘍がみられる患者が散見されるようになってきている。こうした二次腫瘍の中で悪性腹膜中皮腫は極めて稀である。【症例】50歳代、G1P2。約19年前に子宮頸がんIIIB期にて化学放射線療法を受け、その後の経過は良好であった。約4年前の職場検診でCA125が44.6u/mlとやや高く、CTを撮ったところ、著変なく、経過観察となっていた。約6か月前に腹痛、嘔吐・下痢などの症状が出現し、CTにて胸腹水があり、PETにて腹膜、腸間膜に軽度集積が見られた。胸腔内には異常集積は見られなかった。約3か月前にイレウスになり、当院に入院となった。イレウス管にて改善傾向はあったが、約2か月前に診断も兼ねて試験開腹したところ、がん性腹膜炎で癒着が著明であった。腹膜の腫瘍部分を生検して終了した。組織検査の結果、悪性腹膜中皮腫であった。術後約2か月頃に永眠された。その診断には画像診断は決定的ではなかった。組織検査が最も重要で信頼のおける検査であった。HE染色のほかに免疫染色ではcalretinin, CK 5/6, D2-40, WTI, いずれも陽性であった。Desmin, CD146, p40, いずれも陰性であった。FISH法による遺伝子検査ではホモ接合型欠失が見られた。【結論】文献的には同様の報告は少なく、稀ではあるが、Cancer survivorにおいても、諸検査を行い、二次腫瘍の発生も念頭に置いておくことが必要であろう。

P-3-8 再発子宮頸部小細胞癌に対して同時化学放射線療法が著効した 1 例

市立柏原病院

内倉慧二郎, 山内 真, 野田拓也, 栗津祐一郎, 南野成則, 今井健至, 笠井真理, 福田武史, 市村友季, 安井智代, 角 俊幸

子宮頸部小細胞癌は稀な腫瘍であり、予後が悪く、治療戦略が確立されていない。当科では、子宮頸部小細胞癌に対する化学療法は、他の小細胞癌に対する治療と同様にCPT-11+CDDP療法を行っている。今回我々は再発子宮頸部小細胞癌に対して同時化学放射線療法が著効した1例を経験したので報告する。症例は31歳女性、1妊1産、既往歴なし。不正性器出血を主訴に近医を受診したところ子宮頸部腫瘍を指摘されたため、精査加療目的に当院に紹介となった。子宮頸部組織診は非角化型扁平上皮癌であり、MRIではT2強調画像で高信号の拡散制限を伴う30mm大の子宮頸部腫瘍を認めた。CTでは遠隔転移を認めなかった。FIGO stage IB1疑いの子宮頸癌として、広汎子宮全摘術、両側付属器摘出術を施行した。術後病理検査の結果は小細胞神経内分泌癌で、腫瘍辺縁部に非角化型扁平上皮癌を認めた。診断はFIGO stage IIA1 cervical small cell carcinoma, pT2a1N0M0であった。術後補助化学療法としてCPT-11+CDDP療法を3コース施行し、残存病変は認めなかった。初回治療終了から3か月後に骨盤内と腔に多発再発を認めたが、遠隔転移は認めなかった。同時化学放射線療法を行ったところ、骨盤内と腔内の腫瘍は消失した。その後照射野外に骨転移を認め、現在はTC+Bev療法を行っている。

P-4-1 近年当科で経験した子宮がん検診を契機に見えられた子宮頸部悪性腫瘍についての小考察～子宮頸部未分化胚細胞腫瘍、子宮頸部神経内分泌性大細胞癌、子宮頸部癌肉腫症例を中心に

倉敷成人病健診センター¹、倉敷成人病センター²
植田敏弘¹、安藤正明²

【緒言】COVID19 感染拡大により癌検診受診者が前年度比2割減であったと報道されている。そのような状況下で、今回我々は、2019年8月から2021年8月までに、非常に稀な子宮頸部未分化胚細胞腫瘍(Dysgerminoma)および子宮頸部神経内分泌性大細胞癌(LCNEC)、子宮頸部癌肉腫を含む複数の子宮頸部悪性腫瘍を経験したので、若干の知見を加えて報告する。【症例1】46歳、G1P1、月経不順。主訴は不正出血。子宮腔部前唇の非典型的な肉眼的腫瘍および経腔超音波検査(VS)での低エコー域を認めた。検診時細胞診 other malignant tumor、臨床診断はDysgerminoma 1b期であった。【症例2】44歳、G4P2、月経整。主訴はなし。子宮口周辺の乳頭状且つ易出血性病変およびVSでの不均一エコー域を認めた。検診時細胞診はAdenocarcinoma、臨床診断はLCNEC 1b期であった。【症例3】54歳、G3P3、月経不順。主訴は血性帯下。子宮口より突出した脆弱且つ易出血性ポリープを認めた。検診時細胞診は other malignant tumor、臨床診断は子宮頸部より発育した癌肉腫 1b期であった。【結語】短期間に非常に稀なDysgerminomaを含む複数の子宮頸部悪性腫瘍を経験したので報告した。コロナ禍に伴う検診・受診控えの影響とは言い切れないが、稀な疾患が続いたことには驚かされた。改めて子宮がん検診受診啓蒙の大切さを認識した。また、マクロの癌とは言え、検診時のVSがMRI所見や術後病理所見に一致していたことより、検診時のVSの重要性が提示できた。今回は示せなかったがHPV18型陽性が診断の手掛かりになった頸部腺癌症例もあり、有効と思われる手段を組み合わせることで、更なる早期発見に繋がる工夫をしていきたい。

P-4-2 子宮頸癌 IVB 期に対する全身化学療法中に発症した肝類洞閉塞症候群の1例

帝京大病院

寺島豪志、一瀬隆行、小阪 俊、小野寺貴子、竹原洗平、八木慶太、小池良子、高橋ゆう子、西田晴香、平池春子、梁 栄治、長阪一憲

【緒言】肝類洞閉塞症候群(sinusoidal obstruction syndrome: SOS)は、肝中心静脈ないし小葉下静脈の非血栓性閉塞あるいは狭窄により、肝に高度のうっ血状態を招く病態である。造血幹細胞移植前処置に含まれる大量化学療法、全身放射線照射、免疫抑制剤などが原因とされるが、稀な疾患である。我々の知る限りでは婦人科癌に対する化学療法中に発症したSOSの報告はない。今回、進行子宮頸癌に対する長期間の抗癌剤投与が原因で発症したSOSの1例を経験したので報告する。【症例】49歳、未産。異常子宮出血と下腹部痛を主訴に前医を受診した。胸腹部CTにて肺転移と骨盤リンパ節腫大を認めたため、当院を受診した。子宮頸部組織診にて神経内分泌癌を伴う腺癌を認めたことから、子宮頸癌 stage IVB と診断し、化学療法を行う方針とした。EP(Etoposide Cisplatin)療法を施行した。2サイクル施行後、傍大動脈から左頸部リンパ節の増大と肝転移巣の新出を認めたことからPDと判断し、TP+BEV(Paclitaxel, Cisplatin, Bevacizumab)療法に変更した。転移巣は縮小したがCRとならず、計13サイクル施行した。13サイクル後16日目に発熱、上腹部痛、肝胆道系酵素の上昇を認めた。腹部CTで肝左葉の血流低下と肝静脈狭小化を認め、抗癌剤に起因するSOSと診断された。デフィプロチドナトリウムを投与したが全身状態は悪化し、26日目に脳出血・多臓器不全にて死亡した。【結論】進行子宮頸癌に対するTP+BEV療法の奏効率は高く、長期継続投与を行う場合がある。近年SOS発症リスクと関連のある遺伝子変異がいくつか報告されており、抗癌剤長期継続投与の場合は慎重な全身管理とともに、遺伝学的なリスク評価が求められると考えた。

P-4-3 嘔吐、食思不振を契機に診断された子宮頸癌の1例

県立広島病院

伊勢田佑鼓、白山裕子、松島彩子、加藤俊平、浦山彩子、相馬 晶、中島祐美子、三好博史

【緒言】子宮頸癌の転移経路はリンパ行性転移が多く、後腹膜臓器への転移の報告はまれである。子宮頸癌の後腹膜臓器への転移を認めた症例を経験したので報告する。【症例】65歳。5日前からの嘔吐、食思不振を主訴に前医を受診した。血液検査で腎機能障害を認め、当院泌尿器科を紹介受診となったが、CT検査で子宮頸部腫瘍を認めたため、当科紹介受診となった。コルポスコピーでは子宮腔部に異型血管を伴う腫瘍を認め、腔壁上1/3まで浸潤を認めた。子宮頸部組織診は扁平上皮癌であった。腫瘍マーカーはSCC 121.1 ng/mL、CA19-9 74 U/mL、CA125 52 U/mLであった。MRI検査では子宮頸部に18×21×19mm大の腫瘍を認めた。CT検査では両側外腸骨、内腸骨、鼠径部、腹部大動脈周囲、左鎖骨上窩リンパ節の腫大、腹腔内、骨盤内の腹膜播種に加えて、臍鉤部から下十二指腸角に腫瘍影を認めた。また著明な胃の拡張があり嘔吐の原因になっていると考えられた。十二指腸癌、臍癌、あるいは子宮頸癌の転移が疑われたため、上部消化管内視鏡検査を行った。下十二指腸角付近に壁外からの圧迫による狭窄を認めたが、粘膜面に異常所見はなかった。EUS-FNAで生検を試みたが組織量が少なく評価はできなかった。十二指腸の狭窄により、経口摂取が困難であったため腹腔鏡下胃空腸吻合術施行し、その際に大網の播種性病変を摘出した。病理組織検査は扁平上皮癌であった。以上より子宮頸癌の十二指腸壁外への転移と診断した。【結語】多量の嘔吐を契機に子宮頸癌 IVB 期と診断した症例であった。画像検査、上部消化管内視鏡検査では診断に至らなかったが、腹腔鏡下での生検が治療方針の決定に有用であった。

P-4-4 子宮頸癌の加療後に小腸腔瘻を発生し外科的治療が有効であった一例

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今村裕子^{1,2}, 島田清史郎^{1,2}, 値賀正彦¹

【緒言】婦人科悪性腫瘍に対する放射線治療後に、腔瘻を形成する頻度は1~5%とされる。外科的な瘻孔の閉鎖は、手術や放射線治療による膀胱や腸管との高度な癒着や、組織血流の低下から非常に困難であり、治療方針に苦慮する場合がある。今回われわれは、子宮頸癌 IIB 期の腔断端再発に対する放射線治療後9年で小腸腔瘻を発生し、外科的治療が症状の改善に有効であった一例を経験したため報告する。【症例】症例は73歳3妊2産女性である。子宮頸癌 IIB 期の診断でX年に広汎子宮全摘出術が施行され、X+1年に腔断端再発のため放射線治療が行われた。X+9年に大腸癌 IVA 期の診断で結腸右半切除術が施行され、術後3か月で尿漏れの訴えならびに発熱がみられたため、精査目的に入院となった。既往より膀胱消化管瘻が疑われ、膀胱造影が施行されたが異常は認められなかった。当科の診察で、外陰部糜爛ならびに腔内に黄色調の消化液と思われる液体貯留が少量みられ、小腸腔瘻が疑われた。肉眼的に瘻孔部は明らかではなかったため、自然閉鎖を期待し、絶食管理とした。しかし、消化液の排泄が持続したため、上部消化管内視鏡カメラを経腔的に挿入し観察すると、腔断端に1cmほどの瘻孔が認められた。さらに小腸造影にて、腔と癒着している小腸の口側と肛門側が確認された。症状改善を目的に外科で開腹術が施行され、骨盤底との癒着部を迂回するように小腸吻合術が施行された。術後は経腔的な小腸液の排出はなくなり、術後11日目に退院の運びとなった。【結語】放射線治療後に腔瘻がみられた場合には、自然閉鎖を待つだけでなく、他科と連携し最適な治療法を検討することが患者のQOLの向上に繋がると考えられる。

P-4-5 子宮頸部扁平上皮癌の術前診断で広汎子宮全摘術後に子宮頸部癌肉腫と診断された1例

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伊藤 翼^{1,2}, 加藤顕人², 角倉 仁^{1,2}, 青山 真², 工藤一弥²

【緒言】子宮頸部癌肉腫はまれな疾患であり、一般的に予後不良である。今回、術前診断で子宮頸部扁平上皮癌と診断され、広汎子宮全摘術後に子宮頸部癌肉腫の診断に至った1例を経験したので文献的考察を加えて報告する。【症例】45歳、1妊1産。前医を不正性器出血で受診し、子宮頸部細胞診がClassV、扁平上皮癌であり、加療目的で当科に紹介受診となった。コルボスコピーでは腔内に外向性に発育する易出血性の腫瘍がみられ、生検による組織診では低分化扁平上皮癌と診断された。腫瘍マーカーの上昇はみられず、CT検査で明らかなリンパ節転移および遠隔転移はみられなかった。MRI検査では最大径6cm大の子宮頸部に限局する外行性腫瘍がみられ、左傍子宮組織の浸潤が疑われることから子宮頸部扁平上皮癌 IIB 期として広汎子宮全摘術を施行した。摘出標本病理組織検査では低分化扁平上皮癌および大型核を含む肉腫成分がみられており、子宮頸部癌肉腫 IB3 期の診断であった。再発中リスク群であること、組織型が癌肉腫であることから術後補助療法を施行する方針とし、Paclitaxel/Carboplatin (TC) 療法を施行した。治療後、再発なく経過観察中である。【結論】子宮頸部癌肉腫の56%の症例は術後病理組織検査で初めて診断されると報告があり、初期診断が困難である。一般的には子宮頸部癌肉腫の予後は不良だが、完全摘出できた症例については予後良好との報告があり、本症例は適切に治療を行うことができた。

P-4-6 妊娠中に先行化学療法を行った子宮頸癌の1例—当科の過去の症例と比較して—

琉球大学病院
友寄江梨佳, 仲本朋子, 金城淑乃, 渡部俊陽, 高江洲朋子, 下地裕子, 新垣精久, 平良祐介, 久高 亘, 金城忠嗣,
銘苅桂子, 青木陽一

【緒言】ESMO2018ガイドラインでは、妊娠22週以降に診断された子宮頸癌 IB 期に対して、妊娠中の化学療法も選択肢としている。今回妊娠22週の子宮頸癌 IB2 期症例に対し、化学療法後に生児を得た症例を経験したので、当科の過去の子宮頸癌合併妊娠例との比較を交え報告する。【症例】31歳1妊0産。妊娠初期の頸部細胞診で ASC-H を指摘され妊娠19週に紹介。腔拡大鏡で子宮腔部全周性に W2 病変、MRI で頸部前唇に長径2cmの腫瘍影を認めたが、浸潤の深さは不明であり妊娠22週で診断的円錐切除術を施行。腫瘍長径17mmで体部側の切除断端陽性、遺残病巣を認め子宮頸癌 IB2 期 (FIGO 2018) と診断。妊娠継続の希望強く、妊娠25週よりパクリタキセル、カルボプラチン療法を開始し計3コース施行。経過中に胎児の異常や母体の有害事象を認めなかった。妊娠35週4日に帝王切開+広汎子宮全摘術を施行。男児2479g Apgar7/7、奇形や貧血など新生児合併症を認めず、深い間質浸潤を伴う2cm大の遺残病巣を認めたため、術後補助化学療法を継続している。2006~2020年に当科で治療した子宮頸癌合併妊娠は計16例で、診断時の妊娠週数中央値は14(範囲:7-38)週。IB1期以上の12例では、妊娠中の広汎子宮頸部摘出術(妊娠16, 17, 19週)3例と正期産直前に診断された1例を除く8例中4例は妊娠中断し広汎子宮全摘術、残る4例は診断から最大10週(範囲:1-10)の待機期間の後に妊娠28~35週で帝王切開+広汎子宮全摘術を施行し、現在全例が無病生存中である。【結語】本症例では妊娠中に化学療法を施行し癌治療の遅延なく妊娠を継続できた。妊娠中の化学療法は選択肢の一つとなるが、症例ごとの慎重な検討が必要である。

P-4-7 トラスツマブが著効した HER2 陽性再発子宮頸癌の一例

福井大附属病院

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【緒言】乳癌の2割程度がHER2陽性であり、治療として抗HER2療法であるトラスツマブが有効である。乳癌以外にもさまざまな臓器のがんでHER2遺伝子異常が認められている。子宮頸癌では1-2%でHER2遺伝子異常を認めることが報告されているが抗HER2療法の効果はまだ明らかになっていない。【症例】40歳代、既往歴なし。X-3年に子宮頸癌の診断で広汎子宮全摘術および両側付属器摘出術を施行した。病理組織診断は子宮頸部原発の漿液性癌で、pT2bN1であり、後療法として同時化学放射線療法を行った。X-2年に頸部および縦隔に多発リンパ節転移再発を認め、以降化学療法を施行していたが、X-1年よりリンパ節転移巣が再び増大し、癌性リンパ管症とそれに伴う胸水貯留、癌性腹膜炎の状態となった。その間に初発時の手術標本で遺伝子パネル検査 (Foundation One CDx) を施行したところ、ERBB2 amplification が判明した。また、手術標本における免疫染色においてもHER2陽性 (IHC法3+) を認め、本人より強い治療の希望があり、トラスツマブ+PTXの併用療法を開始した。治療開始直後より癌性リンパ管症による呼吸苦の症状は改善し、胸水の減少を認めた。さらに治療開始前はCA125: 2444.6U/mlであったが、1コース後には1129.0U/ml、3コース後には576.8U/mlまで低下を認めた。その後8か月間 stable disease で治療を継続できた。【結語】子宮頸部原発の漿液性癌は非常に稀な腫瘍で進行が速く、標準治療に効果がないことが多い。今回がん遺伝子パネル検査を通してHER2陽性と判明し、抗HER2療法であるトラスツマブが有効であった症例を経験した。症例に応じて慎重な検討が必要ではあるが、がん遺伝子パネル検査を通して有効な治療薬が見つかる可能性がある。

P-4-8 子宮頸部原発胎児型横紋筋肉腫の一例

札幌医大附属病院

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【目的】横紋筋肉腫は、小児悪性腫瘍の5~10%を占め、小児軟部組織肉腫の中では最多の疾患である。原発巣として多い部位は頸頭部、続いて泌尿生殖系であり、組織型は胎児型が半数を占める。今回我々は、子宮頸部原発胎児型横紋筋肉腫の一例を経験したので文献的考察を行う。【方法】症例は未就学女児、腔に増大傾向の腫瘤があり、性器出血を認め近医婦人科受診した。腹部超音波検査で子宮から腔にかけて充満する充実性の7cm大の腫瘤を認め、腔内に子宮鏡を挿入して生検したところ横紋筋肉腫の診断となった。当院小児科受診し、ビンクリスチン+アクトキノマイシンD+シクロフォスファミド+イリノテカン (VAC12/VI) 療法を施行後、手術的に当科紹介となった。【成績】治療後のMRI T2強調画像にて41×19mmのモザイク型腫瘍を認めた。入院から4か月後、準広汎子宮全摘術+両側卵管切除術+骨盤リンパ節生検+右卵巢凍結施行した。病理検査では子宮頸部原発胎児型横紋筋肉腫、Stage IA (ypT1a ypN0 yM0)、JRS-III low risk B、断端陰性の診断となり術後化学療法が施行されて無病生存中である。【結論】本症例は生命予後を優先して根治治療を行ったが、将来的な生殖医療技術の発達に期待して卵巣凍結などを施行した。腫瘍の完全切除を達成した場合の5年生存率は低リスク群で80%を超える。再発した場合の5年生存率は50%程であり、治療後は腔部子宮鏡やCTで慎重経過観察を予定している。

P-5-1 高齢化地域に位置する当科における過去7年間の子宮体部悪性腫瘍に関する検討

京都府立医大附属北部医療センター

山下 優, 渡邊亜矢, 菅原拓也, 黒星晴夫

【目的】当院が位置する京都府丹後医療圏は2021年1月時点で高齢化率が38.0%と全国の28.8%と比較して非常に高く、当科を受診する70歳以上の高齢子宮癌患者も多い。今回当科での子宮体部悪性腫瘍患者に対する年齢による治療選択の差異について比較検討した。【方法】2014年4月から2021年9月までに当院で治療した子宮体部悪性腫瘍症例47例に対し、発症時年齢70歳で二分し後方的に比較検討した。【成績】高齢群でstage II 症例が多かった (p=0.013) が、他 stage や組織型、再発リスクは差を認めなかった。基礎疾患罹患率も差を認めなかった。手術方法に関して、高齢群にも標準術式 (拡大子宮全摘術、または広汎子宮全摘術) を施行しており、年齢による差を認めなかった。術後化学療法に関して、再発中リスク以上の群で高齢群の化学療法未施行率に有意差を認めた (p=0.029) が、再発高リスク群のみでは有意差を認めなかった。化学療法減量率、合併症、再発率等についても差を認めなかった。【結論】当院では高齢子宮癌患者に対しても標準術式を施行しており、合併症率も2群間での差は認めなかった。術後化学療法もQOLを損なわずに施行可能であった。京丹後地域は日本有数の健康長寿地域で、当院で行っている丹後生き生き長寿研究でも報告がある通り、国際老年学会が提唱している「Fit」の高齢者が多いことも一因と考える。ただし、2019年3月以前と2019年4月以降では当科における婦人科悪性腫瘍の患者数に大きな差があり、今後生存率や再発率について引き続き集積・解析を継続予定である。

P-5-2 当院における子宮体癌 I 期症例の後方視的解析～特に後腹膜リンパ節郭清実施省略症例に関する検討～

愛媛大

森本明美, 松元 隆, 西野由衣, 山内雄策, 恩地裕史, 加藤宏章, 安岡稔晃, 宇佐美知香, 松原裕子, 藤岡 徹, 松原圭一, 杉山 隆

【目的】子宮体癌の再発リスクを術前に正確に診断する手法が確立されていない現状では、術後補助療法選択のため後腹膜リンパ節郭清（以下、LN 郭清）が推奨されている。しかしながら子宮体癌症例は、高齢・肥満を含めた合併症併存例が多く、LN 郭清実施の判断は術前の再発リスクのみでは決定できないのが、現実である。そこで、当院における子宮体癌 I 期手術症例に対する LN 郭清省略症例を解析し、治療戦略を検討することとした。【方法】2014 年から 2019 年、当院において手術を施行した子宮体癌 I 期 285 例（IA 期 216 例・IB 期 69 例）を后方視的に解析した。【成績】[手術時年齢・中央値] I 期全体：60 歳/IA 期：56.5 歳/IB 期：67 歳。[LN 郭清率] I 期全体：13.0% (37 例) /IA 期：11.1% (24 例) /IB 期：18.8% (13 例)。IA・IB 期別で差はなかったが、悪性度別では有意差が認められた ($P=0.0004$)。また、IB 期のみの検討で、高齢・精神疾患など様々な合併症の有無が LN 郭清の実施に影響していたが、なかでも循環器疾患合併例では有意に省略されていた ($P=0.049$)。[再発率] I 期全体：2.8% (8 例) /IA 期：1.9% (4 例) /IB 期：5.8% (4 例)。[生存解析] 無増悪・全生存期間を、I 期亜分類別・悪性度別・脈管侵襲有無別・LN 郭清実施有無別・術後補助化学療法実施有無別と比較検討し、有意差が認められたのは、IA 期と IB 期別の無増悪生存期間 ($P=0.016$) および悪性度別の全生存期間 ($P=0.011$) であった。【結論】当院では合併症が併存する子宮体癌症例が多く、LN 郭清省略の選択を迫られる頻度が高い。特に子宮体癌 IB 期を疑う症例では、悪性度と予後を鑑みて LN 郭清を検討する必要があると考える。

P-5-3 子宮体癌における傍大動脈リンパ節郭清の有無での転帰の違い

天理よろづ相談所病院

山村 幸

【目的】子宮体癌の再発中・高リスク群に対する傍大動脈リンパ節郭清（PAN）は治療的意義があるとする報告が複数存在するが、統一した見解は未だに得られていない。そこで、再発中・高リスクと考えられる子宮体癌に対して骨盤リンパ節（PEN）郭清を施行した症例と、PEN/PAN 郭清まで施行した症例でのリンパ節転移率、再発率について検討することを目的として本検討を行った。【方法】2008 年 1 月から 2019 年 12 月までに当院で再発中・高リスク群と診断した子宮体癌の症例を対象とし、PEN のみ郭清した群と、PEN/PAN 郭清を施行した群を比較し、リンパ節転移率、再発率、生存率について后方視的に検討した。【成績】2008 年 1 月から 2019 年 12 月までで子宮体癌と診断された症例は 308 例であった。そのうち再発中・高リスク群の子宮体癌症例は 163 例であった。PEN 郭清を施行した症例は 69 例で、PEN/PAN 郭清を施行した症例は 46 例であった。リンパ節転移は PEN 郭清群で 14 例（20%）、PEN/PAN 郭清群で 18 例（39%）認めた。リンパ節転移陽性例の中で術前に転移が疑われていたのはそれぞれ 6 例、4 例のみであった。再発は PEN 郭清群では 69 例中 14 例（20.3%）、PEN/PAN 郭清群では 46 例中 8 例（17.4%）であった。PEN 郭清群で再発した 4 例中 3 例は PAN 再発であった。【結論】再発中・高リスクの子宮体癌に対して PEN 郭清を行った群と PEN/PAN 郭清群とは再発率に有意差は認めなかった。

P-5-4 子宮体癌における ICG 蛍光法のみを用いたセンチネルリンパ節生検：当院における初期成績

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【目的】子宮体癌におけるセンチネルリンパ節（SLN）は、トレーサーの種類や投与部位などプロトコルが確立していない。インドシアニングリーン（ICG）を子宮頸管に注入する簡便な蛍光法だけで SLN 同定が可能かどうかを検討した。【方法】同一術者の早期子宮体癌 12 例に対して、術中に ICG を子宮頸管 3 時と 9 時方向の浅部（2-3mm）と深部（25mm）にそれぞれ 5mg ずつ注入した。SLN 同定には開腹手術（6 例）で蛍光造影カメラ SPY-PHI を、ロボット支援手術（6 例）では Firefly mode を使用した。摘出した SLN は迅速病理組織診（凍結標本 2mm スライス）で転移の有無を確認し、転移の有無にかかわらず全症例に骨盤リンパ節のバックアップ郭清を行った。なお、本研究は倫理委員会の承認の下で患者の同意を得て行われた。【成績】ICG 注入後 20-30 分で全ての症例で骨盤の SLN 同定が可能であった（両側 11 例、片側のみ 1 例）。SLN 転移陽性は 1 例認め、そのリンパ節径は 1cm 程度であったが、2mm を超えるマクロ転移であった。陰性的中率・特異度ともに 100% で、SLN 陽性例では SLN 領域外の骨盤リンパ節への転移は認めなかった。1 症例あたりの SLN の個数（範囲）は 4 個（1-8）で、摘出した SLN（のべ 50 個）の部位は主に外腸骨節（24 個）と閉鎖節領域（8 個）であった。また SLN 生検に起因する合併症は見られなかった。【結論】当科の初期成績からは術中に子宮頸部に ICG を投与する蛍光法だけで骨盤 SLN の同定は可能であると考えられた。ただし、まだ症例数が少なく今後も継続的な症例集積が必要である。また術者間・施設間の再現性についても今後検討が必要である。

P-5-5 子宮体癌におけるセンチネルリンパ節 (SLN) の術中迅速診断に基づくナビゲーション手術の前方視的研究

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【目的】子宮体癌症例において SLN ナビゲーション手術の有用性を前方視的に検討する。【方法】対象はリンパ節転移スコア (Am J Obstet Gynecol 2003, Gynecol Oncol 2007, Gynecol Oncol 2013) で 0 または 1 点と診断された子宮体癌患者。SLN の同定には Tc99m フチン酸-ガンマブロープ及びインドシアニングリーン-Photo dynamic eye を、術中診断には Tissue rinse liquid-based cytology (TRLBC) 法を用いた。SLN 腫瘍細胞陰性の場合は系統的リンパ節郭清を省略した。永久標本で肉眼/微小転移の場合に転移陽性と定義した。サンプルサイズはリンパ浮腫非発生率で算出した。閾値非発生率 92%, 期待非発生率 97% に設定, α エラー 0.05, 検出力 0.9 で 178 例と計算した。【成績】試験登録 180 例における lymph node status の最終診断は陽性 13 例, 陰性 162 例 (同定失敗 5 例) であった。SLN の同定は両側成功 154 例, 片側成功 21 例, 失敗 5 例であった。失敗例のうち 1 例はバックアップのリンパ節摘出により肉眼転移が確認された。系統的リンパ節郭清を併用した症例は 37 例であった。TRLBC 法の感度は 100%, 特異度 98% であった。追跡期間中央値は 27 か月 (6-57 か月) で, 再発は 4 例のうち 2 例は SLN 転移陰性のため郭清を省略したがリンパ節再発はない。リンパ浮腫発生は 6 例でこちらは全例が系統的郭清 (SLN 転移陽性) を受けていた。【結論】リンパ節転移スコア 0-1 点の体癌に対し SLN ナビゲーション手術は実臨床で安全に実施できる可能性がある。

P-5-6 術前診断 IA 期相当, 類内膜癌 G1/G2 の子宮体癌における骨盤リンパ節郭清の検討

信州大

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【目的】当科での子宮体癌に対する郭清リンパ節は骨盤リンパ節 (PEN) と傍大動脈リンパ節を基本としており, IA 期相当で類内膜癌 G1/G2 に対してはリンパ節郭清術を省略していた。しかし, 2016 年以降は上記の症例でも MRI で筋層浸潤ありまたは腫瘍径 ≥ 2 cm の場合は PEN 郭清を施行している。そこで, その治療成績および意義について検討した。【方法】術前評価で子宮体癌 IA 期相当, 類内膜癌 G1/G2, 筋層浸潤ありもしくは腫瘍径 ≥ 2 cm の症例で, PEN 郭清なしの 41 例 (A 群) と 2016 年以降の PEN 郭清ありの 34 例 (B 群) を診療録から後方視的に検討した。【成績】手術方法は A 群が全例開腹術であり, B 群は開腹術 11 例, 腹腔鏡下手術 14 例, ロボット支援下手術 9 例であった。術後病理診断で G1/G2 以外の組織型は A 群に 3 例 (癌肉腫 1 例, 混合癌 2 例), B 群に 2 例 (G3 1 例, 癌肉腫 1 例) を認め, A 群/B 群の pT1b 以上はそれぞれ, pT1b 3/6 例, pT2b 2/2 例であった。これらと脈管侵襲の所見から, A 群では 12 例が術後補助化学療法 (AC) の対象となり, 8 例で完遂された。B 群は 14 例が AC の対象で, 8 例で完遂され 3 例が施行中である。B 群で PEN 転移を 3 例 (8.8%) に認めたが, 他のリスク因子から, 全例が PEN 転移の有無にかかわらず AC の対象であった。A 群の 3 例 (7.3%) に再発 (肺転移 2 例, 陰転移 1 例) を認めたが, リンパ節再発はなく, うち担瘤生存は 1 例 (観察期間 94 か月) のみで, 両群とも他の全例が無病生存中である。【結論】以前の当科基準でのリンパ節郭清省略例には約 1 割の PEN 転移例が含まれる可能性が示された。一方, 予後改善や AC 対象例の選出という点では, PEN 郭清追加の意義は限定的と考えられた。

P-5-7 婦人科高度肥満症例の子宮全摘に対する手術方法の選択についての検討

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【目的】高度肥満症例の場合, 腹腔鏡下子宮全摘術 (TLH) または開腹単純子宮全摘術 (TAH) のいずれを選択するかについては一定の見解はない。TLH は TAH と比較し創部離開, 疼痛, 輸血率は有意に少ないとされるが手技的に難度が高い。一方, TAH では手技的難度は相対的に低く手術時間を短縮でき, 術中呼吸管理のしやすさなどの利点もある。今回, 当院での高度肥満子宮全摘症例を検討し, 安全面に配慮し, 術者の技術的側面も含めどのような条件で TLH と TAH とを選択すべきかを検討した。【方法】2018-2021 年に BMI 35 kg/m^2 以上の高度肥満患者に対し, TLH もしくは TAH を行った 15 例を対象とした。年齢は 39 歳-75 歳 (中央値 47 歳), 身長は $139\text{cm}-164\text{cm}$ (中央値 160cm), BMI : $35-47 \text{ kg/m}^2$ (中央値 37 kg/m^2)。疾患は子宮筋腫 6 例, 子宮腺筋症 2 例, 異型内膜増殖症と子宮体癌 6 例であった。良性では原則的に TLH を選択し, 悪性では BMI 40 kg/m^2 未満に TLH, BMI 40 kg/m^2 以上で TAH を選択した。合併症を含めた手術成績について検討した。【成績】15 症例のうち, TLH は 8 例, TAH が 7 例であった。BMI 40 kg/m^2 未満の TLH は順調に施行しえた。患者身長も手術成績に影響を与え, BMI 40 kg/m^2 以上でも 160cm 以上の症例では TLH を完遂しえた。合併症は TAH にて創部離開が 1 例, TLH では 2 例で開腹移行した。【結論】高度肥満は TLH の難易度上昇に繋がるが, BMI 40 kg/m^2 未満, 身長 160cm 以上であれば開腹移行なく施行でき, 今後の術式決定における当科施設基準と考える。また悪性腫瘍では早期に手術が必要だが, BMI が最大 47 であっても術後合併症なく安全に手術が出来たことから同様の症例でも減量のために時期を遅らせる必要はないことが示唆された。

P-5-8 BMI43の高度肥満に対して腹腔鏡下子宮全摘術を行った1例

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【緒言】肥満症例では皮下脂肪が厚くトロッカー挿入に難渋する、血管や尿管・神経を同定しにくい、鉗子操作が制限されるといった要因で手術の難易度が上がるほか、長時間手術による褥瘡や血栓症、頭低位による換気不全などの周術期合併症のリスクも高い。今回我々はBMI43の高度肥満に対する腹腔鏡下子宮全摘術を行ったので、周術期の工夫点について文献的考察を加えて報告する。【症例】50歳, G1P1. 糖尿病, 高血圧症, 甲状腺機能低下症, 円錐切除術(46歳, 49歳)の既往歴あり。不正出血があり、子宮内膜細胞診で擬陽性であったため、吸引組織診を行ったところ異型内膜増殖症の診断であった。腹腔鏡下子宮全摘術の方針とした。術前に減量指導を行い、血糖コントロール目的に手術5日前に入院した。手術時は陰圧式固定具(マジックベッド)上で碎石位とした。腹部が平坦になるように粘着性弾力包帯(エラステックス・S)で側腹部の皮下脂肪を対側肩甲に固定した。臍部を直視下に小開腹シカメラポート, 12°の骨盤高位とし、気腹圧10mmHg, タイヤモンド型に5mm カフ付き操作用ポートを配置した。子宮・付属器を摘出して腔式に回収した。腔断端の縫合の際に、鉗子での腔断端の把持が困難であったため、腔断端は経腔的に縫合した。手術時間は4時間43分、出血量は250gであった。経過著変なく5日目に退院した。摘出標本の病理診断は子宮内膜異型増殖症であった。【結語】本症例では粘着性弾力包帯で皮膚を固定することで通常のポート挿入が可能であった。手術手技に関する工夫に加え、肥満患者は高血圧や糖尿病などを有することが多いため、周術期を通して全身状態を細かく把握し、合併症を予防する必要がある。

P-5-9 低リスク子宮体癌に対する後腹膜リンパ節生検の妥当性を検証する

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【目的】子宮体癌治療ガイドライン(2018年版)によると、術前に再発低リスク子宮体癌と想定される症例の一部では、骨盤及び傍大動脈リンパ節郭清の省略が考慮される(グレードC1)。当科では、当該症例に対して子宮全摘、両側付属器切除術に加え、後腹膜リンパ節生検を10年来行ってきた。このたび再発低リスク子宮体癌と想定される症例に対する後腹膜リンパ節生検の妥当性を検証したので報告する。【方法】2011年1月から2021年1月までに、術前に子宮体部類内膜癌G1/2及びFIGO IA期と診断され、当科で後腹膜リンパ節生検(傍大動脈リンパ節を含む)を行った301例を対象とした。年齢、手術進行期、術後病理組織型、再発率、死亡率、再発形式、全生存率、無増悪生存率等について検討した。【成績】年齢中央値は55歳(18-86歳)、摘出リンパ節個数中央値は4個(1-25個)、手術進行期はIA期237例、IB期38例、II期11例、IIIA期11例、IIIB期2例、IIIC1期2例であった。病理組織型は、類内膜癌G1/2 288例、G3 6例、漿液性癌1例、癌肉腫1例、混合癌5例であった。術後upgrade, upstageした症例は其々4.3%, 21.3%であった。術中迅速病理検査を246例に施行し、迅速結果は全例陰性であったが、永久標本でリンパ節転移を2例(0.7%)に認めた。これらの症例に対しては二期的に系統的郭清を行い、再発は認めていない。尿管侵襲を64例(21.3%)、腹水細胞診陽性を28例(9.3%)に認めた。術後補助療法を19例(6.3%)に行い、術後再発は15例(4.9%)に認められ、その内リンパ節再発は4例であった。原病死は5例(1.7%)で、5年全生存率、5年無増悪生存率は其々97.8%, 95%であった。【結論】後腹膜リンパ節生検を行った症例の予後は良好であった。

P-5-10 当院における傍大動脈リンパ節郭清症例の検討

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子宮体癌症例に対する傍大動脈リンパ節郭清(以下PAND)については、正確な手術進行期決定のための診断的意義は確立しているものの、治療的意義については確立していない。PAND自体が非常に侵襲の高い手術であることは周知の事実であり、現在JCOG1412試験でリンパ節転移リスクを有する子宮体癌に対するPANDの治療的意義について臨床試験中である。【目的】当院での子宮体癌PAND症例からPANDを省略できる条件を検討した。【方法】当院で2018年から2021年にPANDを施行した子宮体癌症例について後方視的に検討した。症例はいずれも術前推定IB期以上、もしくは推定IA期で病理組織型がII型と診断されていた。【成績】PAND症例のうち病理組織診断で傍大動脈リンパ節転移を認めたものは19%であり、その半数は術前のCT画像診断で傍大動脈リンパ節や骨盤リンパ節への転移が疑われていた。術前推定I期の症例で傍大動脈リンパ節の転移を認めた例は5.8%で、その組織型は類内膜癌G3であった。傍大動脈リンパ節転移を認めた症例の病理組織型はI型29%, II型71%であった。また、傍大動脈リンパ節転移を認めたすべての症例で腫瘍径が30mmを超えていた。【結論】術前推定I期かつ病理組織型I型G1/G2の子宮体癌はPANDを省略できる可能性が示唆された。術後合併症により後療法が遅れる場合も散見されたため、PANDの適応については再考の余地があるものと考えられた。

P-6-1 当院で免疫チェックポイント阻害剤を投与した6症例

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【目的】2018年12月, 高頻度マイクロサテライト不安定性 (MSI-H) を有する固形癌に対して免疫チェックポイント阻害剤であるペムプロリズマブが保険収載された。MSI-H 症例は全固形癌の中で子宮体癌に最も多いと報告されている。そこで当科における MSI 検査やペムプロリズマブ投与の現状, 免疫関連有害事象 (immune-related Adverse Events : irAE) の発症について調査した。【方法】2018 から 2021 年に, 当科で化学療法後に増悪し MSI 検査を実施した婦人科癌患者を対象とした。【成績】MSI 検査提出数は 65 例, 内訳は卵巣癌 24 例 (36.9%), 子宮体癌 21 例 (32.3%), 子宮頸癌 18 例 (27.7%), 外陰癌 1 例 (1.5%), 子宮癌肉腫 1 例 (1.5%) であった。陽性例は 7 例 (10.8%), 内訳は子宮体癌が 6/21 例 (28.6%), 卵巣癌が 1/24 例 (4.2%) であり, 陽性 7 例中 6 例でペムプロリズマブが投与され, 残り 1 例は使用中のレジメンが奏功しているため未投与である。投与直前の化学療法コース数の中央値は 3 コース (幅 1-6) であった。奏功は 4/6 例 (66.7%) であり, 無増悪生存期間の中央値は 17.5 か月 (幅 3-28) であった。投与コース数の中央値は 15 コース (幅 3-39) であり, 使用継続中は 3 例, 一時中止・再開は 1 例, 中止は 2 例であった。3/6 例 (50%) で irAE を発症しており, Grade2 が 1 例 (甲状腺機能亢進症), Grade3 が 2 例 (自己免疫性髄膜炎, 自己免疫性肝炎) であった。【結論】MSI-H 症例は子宮体癌で有意に多く, ペムプロリズマブ使用例では半数以上が奏功した。セカンドライン以降の化学療法の有効性が低い子宮体癌においては特にペムプロリズマブは有効な治療となり得るため, MSI 検査は重要である。投与に際しては重篤な irAE の発症も稀ではないため注意が必要である。

P-6-2 Pembrolizumab 使用後に蛋白漏出性胃腸症を発症した MSI-high 子宮体癌の 1 例

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がん化学療法後に増悪した進行・再発の高頻度マイクロサテライト不安定性 (MSI-high) を有する固形癌に対して, Pembrolizumab が保険適用となって以降, 多数の婦人科悪性腫瘍症例にも使用されている。今回, MSI-high の子宮体癌に対して Pembrolizumab を投与後, 蛋白漏出性胃腸症を発症し治療に難渋した 1 例を経験したので報告する。症例は 66 歳, 子宮体癌 IIIC 1 期 (類内膜癌 G1)。腹式単純子宮全摘術, 両側付属器摘出術, 骨盤リンパ節郭清術を施行後, Paclitaxel+Doxorubicin+Carboplatin 療法を 6 コース行った。その後多発リンパ節転移を認め, 同時化学放射線療法 (CCRT) を行った。再度多発リンパ節転移を認め, Paclitaxel+Carboplatin 療法, MPA 療法, 再度の CCRT を行うも徐々に治療抵抗性となった。MSI-high であったため, 術後 3 年 7 か月より Pembrolizumab 投与を開始したが, 22 コース投与した時点で蛋白漏出性胃腸症を発症し投与中止とした。この際の効果判定では CR が得られていた。発症から半年頃より全身性浮腫, 腹水などが増強した。ステロイド, 抗 TNF α 抗体製剤を投与したが改善なく, 胸水貯留, 肺水腫が出現した。病状は難治性で急激に呼吸状態が悪化し, 蛋白漏出性胃腸症の発症から 9 か月 (術後 6 年 2 か月) で死亡した。Pembrolizumab は治療抵抗性再発症例に対する効果が比較的長期間得られるとする報告がある一方で, 免疫関連有害事象も多数報告されている。有害事象の増加も予測され, 今後も症例の蓄積と検討が必要である。

P-6-3 当院における婦人科がんに対する MSI 検査と Pembrolizumab 使用症例の検討

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【目的】2018 年よりマイクロサテライト不安定性 (MSI) 検査及び MSI-High を有する固形癌に対し, 免疫チェックポイント阻害薬抗 PD-1 抗体 Pembrolizumab が保険適用となり, 新たな治療選択肢として期待される。当院で婦人科がん症例において施行された MSI 検査の結果と, Pembrolizumab を投与した症例について報告する。【方法】2019 年 5 月から 2021 年 9 月まで当院で進行・再発婦人科がんと診断された症例のうち, MSI 検査が施行された 20 症例について, その結果及び MSI-High 症例に対する Pembrolizumab の治療成績について検討した。【成績】MSI 検査を施行した 20 症例の内訳は子宮体癌 10 例, 卵巣癌 4 例, 子宮頸癌 4 例, 子宮平滑筋肉腫 2 例, 重複癌 (子宮体癌, 卵巣癌) 1 例であった。そのうち MSI-High は 4 例 (20%) であり, その内訳は子宮体癌 3 例, 重複癌 1 例で, 組織型はすべてが類内膜癌であった。MSI-High 4 例中の子宮体癌 3 例に対し Pembrolizumab が投与された。その結果 CR 1 例, PR 1 例であり, 残り 1 例は効果判定前である。CR の 1 例は明らかな有害事象もなく現在まで Pembrolizumab 9 サイクル投与されている。PR の 1 例は Pembrolizumab 17 サイクルの時点で血糖値上昇と肝障害が発現し休薬している。【結論】MSI-High 症例は重複癌も含めいずれも組織型は類内膜癌であった。少数例の検討ではあるが MSI-High 症例での Pembrolizumab の有効性が確認された。以上より今後も子宮体癌を中心に積極的な MSI 検査の検索を継続していく予定である。

P-6-4 学療法抵抗性進行・再発子宮体癌に対するペムプロリズマブの使用経験

高知大

氏原悠介, 松浦拓也, 泉谷知明, 樋口やよい, 谷口佳代, 前田長正

【緒言】ペムプロリズマブ (Pembro) は、2018年に標準治療困難な高頻度マイクロサテライト不安定性を有する固形癌 (MSI-High 固形癌) への適用が承認された。当院で Pembro を使用した化学療法抵抗性の MSI-High 子宮体癌 3例について報告する。【症例】症例 1: 49歳, IIIC2期相当。子宮傍組織浸潤が強く NAC (TC療法, AP療法) を行ったが PD となり, Pembro を開始した。3コース後の評価は PD であり, 治療終了2か月後に原癌死となった。症例 2: 35歳, 体癌 IIIC2期と頸癌 IB1期の重複癌症例。根治術後 TC療法 6コース施行したが, 終了後3か月に多発リンパ節転移で再発。TP-Bev療法で一時 PR となったが 12コースで PD となり, Pembro に変更した。3コースで PR となり, 有害事象なく継続している。症例 3: 43歳, IIIC2期, シェーグレン症候群合併。NAC (TC療法) 後に根治術を行ったが, 閉鎖リンパ節転移巣を摘出できなかった。術後 TC療法, AP療法を行ったが PD となり, Pembro に変更した。3コース後の CT で閉鎖リンパ節は著明に縮小しており PR と判断した。自己免疫関連副作用 (irAE) として, 1コース後に皮疹と右顔面神経麻痺, 2コース後に気管支喘息を認めしたが, 関連診療科との連携によりいずれの症状もコントロールでき, Pembro 継続中である。【結語】化学療法抵抗性の体癌 3例中 2例で奏効が得られた。体癌は他の固形癌と比べ MSI-High の割合が高く, Pembro の効果が期待できる。さらに体癌の標準治療が少ないことを考慮すると, 進行例では早期に MSI 検査を検討すべきと考える。

P-6-5 pembrolizumab が奏効した再発子宮体癌の 2 症例

横浜市南部病院

辻 圭太, 川野藍子, 宮田杏衣, 吉岡俊輝, 松尾知世, 内田絵梨, 上西園幸子, 藤原夏奈, 長谷川良実, 中村朋美, 荒田与志子, 遠藤方哉

【緒言】高頻度マイクロサテライト不安定性 (MSI-High) を有する難治性固形腫瘍に対して免疫チェックポイント阻害薬 pembrolizumab が保険収載された。再発子宮体癌に対して pembrolizumab が奏効した 2 症例を報告する。【症例 1】症例は 73歳, X 年子宮体癌に対して準広汎子宮全摘出術, 両側付属器切除, 骨盤・傍大動脈リンパ節郭清術を施行した。病理組織診断は子宮体部混合癌, 傍組織浸潤および卵巣転移あり, Stage IIIB (FIGO 2008), pT3bN0M0 の診断となった。術後補助化学療法として PTX/CBDCA 6 サイクルを施行, CR にて治療を終了した。X+1 年に左骨盤腹膜に播種病変の再発を認め ADR/CDDP 3 サイクルを施行も増大を認め PD と判断した。MSI-high の結果から pembrolizumab による治療を開始, 13 サイクルを施行し PR を維持している。【症例 2】症例は 42歳, X 年に子宮体癌に対して腹腔鏡下子宮全摘出術, 両側付属器摘出術を施行した。病理組織診断は子宮体部類内膜癌, 頸部間質浸潤あり, Stage II (FIGO 2008), pT2NXM0 の結果となった。PTX/CBDCA 5 サイクルを施行するも両側骨盤リンパ節転移が出現し骨盤・傍大動脈リンパ節郭清を施行した。X+1 年右肺転移に対して胸腔鏡下右肺中葉部分切除を施行した。X+2 年 縦郭リンパ節および肺右上葉に転移を認め, 縦郭リンパ節に 52Gy を照射, その後 MSI-high の結果から pembrolizumab による治療を開始した。甲状腺炎が出現し休薬, 治療を行った後 Pembrolizumab の投与を再開, 5 サイクルを施行し CR を維持している。【結語】再発子宮体癌において従来の薬物療法では十分な奏効は得られていない。pembrolizumab は特有な有害事象に留意が必要であるが有効な薬剤として期待される。

P-6-6 包括的がんゲノムプロファイリング (CGP) を契機に Lynch 症候群と診断し, pembrolizumab により長期 PR を得た若年子宮体癌の一例

兵庫医大病院

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CGP を契機として遺伝性腫瘍と診断され, 適切な治療が実施されることは少なくない。【症例】34歳, 0 妊 0 産, 既往歴はなし。家族歴は父方祖父が 70 歳代で前立腺癌。32 歳頃より少量の性器出血を自覚しており, 34 歳時に帯下の悪臭と下腿浮腫のため前医に緊急入院した。腔内を占拠する約 10cm 大の腫瘍を認め, コントロール不良の性器出血のため Hb 4.9g/dl と高度貧血を認め当科に転院となった。緊急対応として子宮動脈塞栓術を行い止血した。MRI 検査では子宮頸部から腔入口に至る約 10cm 大の腫瘍を認め, 子宮内膜の junctional zone は保たれていた。CT 検査では傍大動脈リンパ節腫大と多発肺結節を認めた。腫瘍生検で「低分化腺癌」と診断した。子宮頸部腺癌 IVB 期と診断し子宮摘出を目的として術前化学療法 (PTX 60 mg/m² day 1, 8, 15; CDDP 75 mg/m² day 2, TACE) を行ったところ初回治療中に DVT が進行したため抗凝固療法を開始し, CCRT followed by TC に治療を変更した。TC 療法終了 1 か月後に再燃し FoundationOne 検査を施行したところ, MSI-high, TMB 64 Muts/Mb, MSH2mt が検出され, 生殖細胞系列検査で Lynch 症候群と診断した。免疫チェックポイント製剤治療待機中に原発腫瘍感染による敗血症を発生し ICU 入院となった (治療不適)。抗生剤治療等により全身状態が改善したため pembrolizumab による治療を開始したところ, 腫瘍径は 5.6 cm から 2.5 cm に縮小し, 以後約 2 年間維持している。腫瘍縮小後の MRI 検査では子宮体下部から頸部にかけて腫瘍を認め, Lynch 症候群に特徴的な子宮体下部に発生する若年子宮体癌と診断を変更した。

P-6-7 MSI-High 婦人科がん4例に対するペムプロリズマブの使用経験

弘前大

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【目的】標準治療が困難になった MSI-High を有する固形癌に対し、ペムプロリズマブが保険承認された。当科におけるペムプロリズマブの使用症例について報告する。【症例】2019年4月～2021年9月に56例に対しMSI検査を行い、MSI-High5例中4例に対しペムプロリズマブを使用した。＜症例1＞子宮体癌IA期(類内膜癌)、術後8か月で腔断端に再発し腫瘍摘出後TC療法を行なった。その後右鎖骨上窩・腔断端に再発を認め放射線療法を施行したがPDとなりペムプロリズマブを開始した。治療中、甲状腺機能低下症を認めたが継続可能だった。1年10か月投与しgrade3の好中球減少発現のため中止した。現在CRである。＜症例2＞子宮体癌IIIA期(明細胞癌)で術後TC療法を施行した。右内腸骨節周辺に再発し放射線療法、ラステット投与したが、PDとなりペムプロリズマブを開始した。現在2年経過しSDを維持している。＜症例3＞子宮体癌IVB期(類内膜癌G2)に対し術後TC療法を施行したが鎖骨上窩、肺、腔の多発転移を認めAP療法に変更した。しかしPDとなりペムプロリズマブを開始した。現在4か月経過している。＜症例4＞23年前に卵巣癌(類内膜癌)の手術既往があり、腔断端、直腸に浸潤する腫瘍を認め、腫瘍摘出及び腸管合併切除術を行った。Endometriosis-associated intestinal tumor (EAIT, 類内膜癌)として術後2nd lineまで化学療法を行っていたがPDとなりペムプロリズマブを開始した。2クール行ったがPDとなり、全身状態が悪化したため中止としBSCとなった。【結語】抗瘤剤以外の治療の選択が困難になったMSI-High症例においてペムプロリズマブは大きな福音である。当科症例の有害事象は制御可能であった。

P-6-8 ペムプロリズマブ投与終了後に長期無増悪生存期間を得られている再発子宮体癌の1例

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ペムプロリズマブはMSI-High (microsatellite instability-high) 固形癌において無増悪生存期間の中央値は4.1か月、子宮体癌における奏効率は57.1%と報告されており、MSI-High 子宮体癌において有力な治療薬である。今回、我々は、子宮体癌術後再発、多発肺転移に対してペムプロリズマブを6回投与終了後、無治療で14か月無増悪を維持している症例を経験した。症例は、73歳で合併症に糖尿病及び双極性障害がある。子宮体癌の診断で手術(子宮全摘、両側付属器摘出及び骨盤内リンパ節郭清)を行い、術後診断は子宮体癌IB期、pT1bN0M0 (Endometrioid carcinoma G1)であった。追加治療なしで経過観察としていたが、術後8か月で多発肺転移を認めた。化学療法(カルボプラチン及びパクリタキセル)を行ったが、9コース終了後にPD (progressive disease)となった。MSI-Highであったため、ペムプロリズマブを投与したところ6コース終了時点でPR (partial response)であった。味覚障害による食欲不振や糖尿病が増悪し糖尿病性ケトアシドーシスを起こしたことなどから、本人が治療継続を望まなかったため、ペムプロリズマブを投与終了した。その後、投与終了後16か月経過した現在まで、無増悪状態を維持している。ペムプロリズマブ投与終了後の長期無増悪生存の報告はほとんどないため、若干の文献的考察を交えて報告する。

P-7-1 腎移植後の子宮体癌の2例

亀田総合病院

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腎移植後は免疫抑制剤の服用により免疫機能が低下し、ウイルス感染の増加やDNA修復の低下が生じ、癌発生リスクが3-5倍に増加する。婦人科領域ではHPV感染による子宮頸癌の発生リスク増加が知られているが、子宮体癌のリスクについては議論がある。われわれは腎移植後に発生した子宮体癌の2例を経験したので報告する。症例1は52歳0妊で、7年前に生体腎移植(右腸骨窩)を受け、タクロリムス(T)、ミコフェノール酸モフェチル(M)、プレドニンを内服していた。不正性器出血により受診し、内膜生検で高異型度腺癌を、PET/CTで骨盤リンパ節に加え、左腸骨・恥骨に集積を認めた。腹式単純子宮全摘、両側付属器摘出、左骨盤リンパ節摘出を施行した。病理所見は明細胞癌で、卵巣・骨盤リンパ節転移を認め、IIIC1期と診断した。術後は自宅近くの施設へ転院したが、骨転移が明らかとなり、腹膜播種も出現・増悪し5か月後に原病死した。症例2は62歳2妊2産で、6年前に生体腎移植を受け、M、Tを内服していた。血尿を訴え前医を受診し、精査で子宮体癌と診断され当科へ紹介となった。内膜生検で漿液性癌を、PET/CTで骨盤～傍大動脈領域に多発リンパ節転移を認めた。IIIC2期以上と診断し、術前化学療法としてパクリタキセル・カルボプラチン(TC)療法を6サイクル施行後リンパ節は縮小し、腹式単純子宮全摘、両側付属器摘出を施行した。術後3か月よりCA125が再上昇し、5か月で多発リンパ節再発を画像検査で認めたため、TC療法を再開したが奏功せず、治療開始22か月で原病死した。2例とも痛家族歴はなく、高異型度癌が転移を伴った状態で診断されており、長期にわたる免疫抑制状態が癌発生・進展に関与した可能性がある。

P-7-2 子宮体癌再発に対する AP 療法中に低 Na 血症をきたした 2 例

JCHO 大阪病院

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シスプラチンによる低 Na 血症は稀な合併症である。子宮体癌再発に対する AP 療法中に低 Na 血症をきたした症例を経験したので報告する。【症例 1】72 歳, 未経妊。(X-1)年 3 月 29 日子宮体癌に対して単純子宮全摘出術, 両側付属器摘出術, 骨盤内リンパ節郭清を施行。Endometrioid carcinoma, G1, pT1apN0M0 の結果であった。同年 11 月に転移性肺腫瘍が疑われ, 同月から X 年 4 月にかけて TC 療法を 6 コース施行。肺転移病変は一旦縮小を認めたが, 9 月には再び増悪を認め, AP 療法の方針となった。1 コース目投与翌日より嘔気・嘔吐のため経口摂取困難となり, 尿量も低下した。投与 3 日目に意識障害を来し, 精査にて低 Na 血症が原因と考えられた。【症例 2】69 歳, 2 経妊, 2 経産。(Y-3)年 8 月 24 日に子宮体癌と腹膜播種に対して単純子宮全摘出術, 両側付属器摘出術, 大網生検を施行。Serous carcinoma, pT4bNxM1b の結果であった。術後化学療法として(Y-3)年 9 月から同年 10 月にかけて TC 療法を 3 コース施行。翌月に IDS として大網部分切除術, 骨盤内リンパ節郭清, 傍大動脈リンパ節郭清を施行し, 摘出検体には残存腫瘍を認めなかった。同年 12 月から翌年 1 月にかけて TC 療法をさらに 3 コース施行し, 以後再発なく経過していた。(Y-1)年 11 月の造影 CT にて腹膜播種再発所見を認め, 同年 12 月から Y 年 3 月にかけて TC 療法を 6 コース施行。腹膜播種病変は一旦縮小を認めたが, 同年 6 月には再度増悪を認め, AP 療法の方針となった。1 コース目投与 3 日目より嘔気が出現, 投与 5 日目には食事摂取不良となり, 投与 6 日目の血液検査にて低 Na 血症を認めた。いずれの症例もシスプラチンによる薬剤性 SIADH が低 Na 血症の主な原因と考えられ, 考察を加えて報告する。

P-7-3 KRAS G12D 変異を伴う子宮体部中腎様腺癌の 1 例

大阪赤十字病院

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【緒言】中腎癌は中腎管遺残により子宮頸部に発生するまれな腫瘍である。近年, 中腎様構造を模倣した腫瘍が子宮や卵巣などに発生することが報告され, 中腎様癌として 2020 年の WHO 分類で新たに項目が設けられた。中腎様癌はまれで診断が難しく悪性度の高い稀な腫瘍で, ER/PR 陰性, GATA3/TTF-1 陽性, KRAS 変異などを特徴とする。今回我々は KRAS G12D 変異を伴う子宮体部中腎様癌を経験したため報告する。【症例】症例は 63 歳の未経産の女性で, 下腹部痛を主訴に当院を受診した。MRI と CT 検査から血流豊富な 6cm 大の子宮筋層腫瘍を認め, 子宮悪性腫瘍を疑い腹式単純子宮全摘術及び両側付属器切除術を施行した。子宮筋層腫瘍は白色腫瘍で, 右卵巣にも 3cm 大の多房性嚢胞を認めた。組織病理学的検査で, 子宮筋層腫瘍は異型細胞の胞巣状, 癒合腺管状増殖を認め中腎様癌と診断した。免疫組織化学的検査では, ER/PR (-), CD10 (+), TTF-1 (+) であり, 卵巣腫瘍も同様であった。中腎様癌に一致する所見であった。以上より子宮体部中腎様癌 IIIA 期と診断した。術後化学療法として TC 療法を行ったが, 術後 27 か月で多発肺転移再発に至った。初回化学療法に抵抗性と判断し, がん遺伝子パネル検査を行ったところ, KRAS G12D 変異をみとめた。これは既報からも子宮体部中腎様癌の裏付けとなる所見であった。【結語】子宮体部中腎様癌の 1 例を経験した。子宮体部中腎様癌は稀な腫瘍であるが近年報告が増えており, その特徴をこれまでの報告と合わせて考察する。

P-7-4 子宮体癌に対して Pembrolizumab 投与中に COVID-19 肺炎に感染し全身症状が遷延した一症例

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子宮体癌に対し免疫チェックポイント阻害薬である pembrolizumab を投与中の患者が COVID-19 に感染後, 肺炎が遷延したので報告する。症例は 48 歳 2 産。子宮体癌 IVB 期に対し手術と術後化学療法を施行したが増悪した。マイクロサテライト不安定性検査陽性のため pembrolizumab を投与したところ, 完全奏効となった。20 サイクル目 day15 に上気道炎症状と発熱を認め, PCR 検査で COVID-19 と診断された。自宅療養していたが, 発熱が持続し, day48 には 40°C を超える発熱と全身のリンパ節腫大を自覚した。Pembrolizumab の免疫関有害事象や腫瘍の再発を疑ったが, 来院時の CT で頸部リンパ節腫脹および COVID-19 肺炎に特徴的な上葉主体の多発性スリガラス陰影と, 下葉末梢側の線状影を認め, pembrolizumab による免疫賦活状態が COVID-19 肺炎の遷延をきたしたと考えた。全身症状が遷延していたため, 入院とし dexamethasone を投与した。投与後は速やかに解熱し, 入院 10 日目に退院となった。退院後の CT でリンパ節はいずれも縮小していた。退院 17 日目に pembrolizumab 投与を再開し, 以後症状の再燃や子宮体癌の増悪なく経過している。COVID-19 肺炎の本態はウイルス感染を契機とした自己免疫による肺胞の傷害である。免疫チェックポイント阻害薬投与は免疫細胞の活性化をきたすことから, COVID 肺炎を増悪させる可能性がある。Pembrolizumab 投与患者に COVID-19 肺炎が判明した場合は早期のステロイド投与が有効である可能性が示唆された。

P-7-5 子宮体部原発の骨外性骨肉腫 (extraskelatal osteosarcoma, ESOS) の一例

大分県立病院

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【緒言】骨外性骨肉腫 (ESOS) は骨肉腫の4%ほどの頻度とされるまれな疾患である。中でも子宮体部原発の症例は希少で、一例を経験したため報告する。【症例】76歳、4妊3産。増悪する貧血に対する精査目的で前医を受診し、胸腹部骨盤部造影CT検査を施行された。子宮体部筋層内の後壁に長径14cmで内部の吸収値が不均一な腫瘤を認め、婦人科疾患を疑われ当科を紹介受診した。骨盤造影MRI検査で、大部分は出血の信号強度だが拡散制限と造影効果を伴う充実部を認める腫瘍性病変を子宮筋層内に認めた。腫瘍マーカーはCA125が176U/ml, LDHが295U/Lと高値で、CEA, CA19-9は基準値範囲内であった。変性した子宮筋腫または子宮肉腫を疑い、腹式単純子宮全摘出術、両側付属器摘出術を施行した。病理組織所見で核異型の強い、淡好酸性物質を伴う多角形・紡錘形細胞が束状・充実性に増殖する像と腫瘍性類骨の所見を認めた。免疫染色と併せて他の肉腫への分化や上皮性腫瘍の所見は認めなかった。切除断端は陰性であった。骨軟部腫瘍におけるAJCC第8版に基づきESOS (T1N0M0)と診断し、追加治療は行わない方針とした。術後6か月まで再発なく経過している。【考察】上皮性腫瘍性分を認めず、免疫染色と併せて他の肉腫成分を否定でき、原発となりうる病巣を認めなかったことから、子宮原発のESOSと診断し得た。ESOSは治療法が確立されておらず手術での完全手術例できた症例以外は予後不良である。完全手術に対する補助療法は確立していないため、本症例では術後治療は施行しなかった。

P-7-6 子宮体癌術後の難治性乳糜腹水に苦慮した一例

東京女子医大東医療センター

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【目的】乳糜腹水は腹部手術の比較的稀な術後合併症として知られている。子宮体癌術後6か月に渡り入院加療を要した難治性乳糜腹水の一例を経験した。【方法】症例は84歳、子宮体癌の診断にて+単純子宮全摘術+両側付属器切除術+大網切除術+骨盤部～傍大動脈リンパ節郭清術を施行し残存腫瘍なく切除可能であった。組織型は漿液性癌であり、摘出した70個のリンパ節のうち左総腸骨節2個に転移を認めた。手術進行期は日産婦新進行期分類でIIIC1期であった。術後22日目に術後補助化学療法としてパクリタキセル・カルボプラチン併用療法を開始した。術後30日目より腹部膨満感が出現し、穿刺にて肉眼的乳糜腹水の貯留を認めた。利尿薬、脂肪制限食、オクトレオチド皮下注、CARTにて保存的に加療したが腹水の改善はみられなかった。本人・ご家族と相談し、術後107日目の4コース目で術後化学療法終了とした。以降も腹水改善せず、リンパ管造影や手術療法が検討された。術後126日目に開腹リンパ漏閉鎖術を施行した。しかし、術後4日目に腹水の再貯留を認めたため、当院より他院放射線治療科へ紹介し、術後143日目と146日目にリンパ管造影・塞栓術を施行した。両側鼠経リンパ節を穿刺しヨード化ケシ油脂肪酸エチルエステル注射液 (リピオドール®)にて漏出部位確認後、20%NBCA (NBCA:リピオドール®=1:4)にて塞栓を行った。【成績】リンパ管造影施行後は腹水の再貯留を認めず、腹水は残存するものの保存的に加療可能と考えられた。術後166日目にリハビリ転院となった。【結論】難治性乳糜腹水に関する症例報告に挙がる複数の治療法を試みたなかで、最終的にリンパ管造影・塞栓術が最も著効した症例であった。

P-7-7 当院における20歳代で発症した子宮体癌の臨床的検討

宮崎大附属病院

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【緒言】近年子宮体癌は増加傾向にあるが、20歳代の発症は0.5%前後であり稀である。当院で2011年以降に治療した子宮体癌のうち20歳代で治療を行った3症例について報告する。【症例】症例1:25歳。BMI18.3。診断の4年前から過多月経、月経不順あり。内膜全面搔爬で子宮内膜異型増殖症と類内膜癌G1の診断であり手術を施行した。術後病理診断では卵巣転移を認め子宮体癌IIIA期(類内膜癌G1, pT3aN0M0)だった。TC療法を6コース行い、術後40か月で再発なく経過している。症例2:27歳。BMI35.6。診断の2年前から過多月経あり。内膜組織診は類内膜癌G2であり手術を行った。子宮体癌IB期(類内膜癌G3, pT1bN0M0)の診断でTC療法を6コース施行した。術後10か月に肺門部、縦郭リンパ節転移、肺転移で再発しAP療法を施行したもので術後17か月で原癌死となった。病理診断を再度検討したところ類内膜癌G1と未分化癌の混合癌だった。症例3:25歳。BMI43.2。2年前から過多月経があり、内膜細胞診で類内膜癌G1であり、骨盤部MRIで子宮筋層浸潤を認めず子宮内膜全面搔爬を施行したところ類内膜癌G2の診断となった。術前に行った腹部CTでそれまで認めていなかったダグラス窩腫瘍、腹腔内結節を認め手術を施行した。子宮体癌IVB期(類内膜癌, G3, pT4N0M1, 大網転移)であり、AP療法を6コース施行した。術後6か月で再発なく経過している。【結語】20歳代の子宮体癌は一般的に予後良好とされているが、当院で経験した症例のように進行癌、予後不良癌もあり、治療方針の検討は慎重に行うべきである。

P-7-8 子宮鏡検査および子宮内膜掻爬術で診断できなかった子宮体癌の一例

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子宮内膜細胞診による子宮体癌のスクリーニングは感度が80%を超えるが、疑陽性・陽性の場合にはより感度の高い子宮内膜組織診により診断を確定する。今回、子宮内膜細胞診で繰り返し異常を認めたが、子宮鏡検査、子宮内膜掻爬術により術前に原発巣を特定できなかった子宮体癌の一例を経験したので報告する。症例は64歳、5妊2産、44歳時に子宮頸癌IA期に対して円錐切除術を施行されていた。腹部の違和感を感じたため近医を受診し、子宮内膜細胞診が疑陽性であったため当科を紹介受診した。子宮内膜肥厚は無く、子宮内膜組織診は陰性であった。子宮鏡検査では表面平滑な粘膜炎下筋腫を認めたため切除したが、悪性を疑う腫瘍は無かった。子宮内膜全面掻爬術も行い、病理組織診断は平滑筋腫、悪性所見は無かった。3か月後に再検した子宮内膜細胞診は陽性、adenocarcinomaを認めたが、組織診では悪性所見が無かった。婦人科腫瘍、転移性腫瘍の双方を疑い、造影CT、MRI、PETを行ったが原発巣を同定できなかった。全腹腔鏡下準広汎子宮全摘術、両側付属器摘出術、大網切除術、虫垂切除術を施行した。摘出標本に肉眼的に同定できる腫瘍を認めなかったが、病理組織診断で子宮内膜に局限した8mmの類内膜癌G2を認め子宮体癌IA期と診断した。早期の子宮体癌では子宮鏡検査や子宮内膜掻爬で原発巣を同定できないことがある。繰り返し子宮内膜細胞診異常を呈する場合、組織診が陰性であっても慎重にフォローするか、症例によっては手術による診断も考慮される。

P-7-9 子宮体癌術後補助化学療法中に発熱性好中球減少症を疑ったが重症COVID-19であった一例

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【緒言】発熱性好中球減少症(FN: Febrile neutropenia)は重篤な感染症に発展しうるため化学療法中に発熱した場合には必ず鑑別する。今回化学療法中に発熱をきたし、まずFNを考えたが重症新型コロナウイルス感染症(COVID-19)であった症例を経験した。【症例】55歳子宮体癌IIIC2期、紫液性癌pT3aN1M0に拡大子宮全摘術、両側付属器切除、骨盤リンパ節郭清、傍大動脈リンパ節郭清を行った後に術後補助化学療法としてTC療法を行っていた。2型糖尿病とBrinkman Index 500の喫煙歴があった。新型コロナウイルスワクチン1回目の接種を終え、TC療法4サイクルを行い2日目に発熱の症状が出現、8日目に呼吸困難の症状があり救急搬送された。FNによる肺炎を疑ったがCOVID-19等温拡散増幅法で陽性であり、PCR検査も陽性であった。尿培養、血液培養は陰性で喀痰培養検査も気道系常在細菌叢と考えられた。感染経路は不明、CT検査では両側肺野にスリガラス影があった。COVID-19によるウイルス性肺炎と診断した。侵襲的換気が必要と判断し、気管内挿管し、ICUで加療した。ヘパリンNaの持続投与、メチルプレドニゾロン2mg/kg/dayの投与を行った。入院15日目にICUを退室、入院18日目に新型コロナウイルスPCR検査陰性化を確認し、抜管、一般病棟へ転棟した。リハビリを行い、room airでSpO₂ 95%前後まで改善し、入院32日目に退院した。【考察】化学療法中に発熱をきたした場合、重篤化するFNをまず考え対応することが重要である。しかしながら、本症例のように発熱者はCOVID-19であることがあり、かつ担癌患者では重症化しうる。今後は化学療法中の発熱患者ではCOVID-19の可能性も念頭に置き、診療にあたる必要がある。

P-8-1 Female to male transgenderの若年発症の子宮体癌の一例

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【緒言】Female to male transgender(以下FTM)とは性自認は男性で、身体の性は女性である人物のことである。Transgenderの診断は、精神科医が性自認を確定し、産婦人科医、泌尿器科医が診察、画像診断、染色体検査やホルモン検査を行い、生物学的性を確定し、状況により形成外科医と協力し、手術加療を行うこともあり、各科連携が不可欠である。しかし本邦ではその後のケアにおいて、精神科医のみでホルモン療法が行われていることがある。FTMの子宮体癌の一例を経験したため報告する。【症例】30歳、FTMと23歳で診断。28歳時から近医精神科クリニックでテストステロン製剤の投与を行っていた。不正性器出血があったにも関わらず、婦人科を受診していなかった。下腹部痛を主訴に前医受診し、巨大卵巣腫瘍と子宮内膜肥厚を指摘され、当院に紹介受診となった。MRI検査では右卵巣に壁に不整な結節影を伴う19cm大の多房性病変があり、子宮内膜は肥厚し、筋層浸潤を疑う所見であった。子宮内膜組織診で類内膜癌G2の診断となった。CT検査ではリンパ節腫大と腹膜播種を認めた。腹痛があり早期手術が必要な状態であったため開腹手術を施行した。多数の腹腔内播種病変を認め、播種病変は一部残存した。病理組織診で子宮体部に類内膜癌G3を認め、部分的に前立腺への分化を示唆する所見があった。両側卵巣、大網、骨盤腹膜、傍大動脈リンパ節に腺癌の転移を認め、子宮体癌IVB期、pT3aN2M1の診断であった。【結語】アンドロゲン投与により子宮体癌を発症した1例を報告した。FTMのケアに対しては精神科医だけでなく産婦人科医も協力して診療に当たる必要がある。

P-8-2 子宮体癌に合併した血栓症症例の検討

医科歯科大

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【目的】婦人科悪性腫瘍の中で、卵巣癌は癌関連血栓症の発症リスクが高いことはよく知られているが、子宮体癌に合併した血栓症の発症に関するまとまった報告は少ない。今回、子宮体癌症例における血栓症の臨床的特徴について後方視的に検討した。【方法】2016年1月から2020年12月までに当院で子宮体癌と診断された患者のうち、追跡可能な134例の診療録を後方視的に検討した。【成績】134例中7例(5.2%)に血栓症を認めた。深部静脈血栓症(DVT)のみ2例、肺血栓塞栓症(PE)のみ1例、その他4例ではそれらの併発や心室内血栓など多様な病態を呈した。血栓症のない群と血栓症群の血栓リスク因子(年齢、BMI、生活習慣病、喫煙)、組織型、腫瘍径、初回治療前のD-dimerと腫瘍マーカーに有意差は認めなかった。血栓症群でIV期の割合が高かった。血栓症群では、病期はI期3例、III期2例、IV期2例だった。I期の3例はいずれも類内膜癌 grade 3であり、IV期2例は漿液性癌であった。血栓症の発症時期は、初回治療前2例、術後2週間以内3例、術後化学療法中1例で、1例はbest supportive careを行っていた。初回治療前の2例はいずれもIII期の進行癌だった。術後発症の3例はいずれも類内膜癌 grade 3であり、2例は骨盤内および傍大動脈リンパ節郭清が施行された。また術後発症3例のうち2例は麻痺性イレウスや肺炎で加療中であった。【結論】進行癌や、早期癌でも悪性度の高い癌、侵襲の高い手術、術後合併症による全身状態の悪化やADLの低下が血栓リスクとなる可能性が示唆された。

P-8-3 腎機能障害を伴った骨盤リンパ嚢胞に対しリンパ管塞栓術が有用だった一例

山形大附属病院

伊藤泰史, 清野 学, 堀川翔太, 榎 宏論, 太田 剛, 永瀬 智

【はじめに】骨盤リンパ嚢胞は骨盤リンパ節郭清術による合併症のひとつであり、大きさや部位によっては骨盤内臓器を圧迫することがある。さらにリンパ嚢胞による臓器障害ため、穿刺などの医療介入を必要とする場合がある。今回、骨盤リンパ嚢胞によって腎機能障害を来した子宮体癌術後症例に対してリンパ管塞栓術が奏功した症例を経験したので報告する。【症例】68歳女性、2妊2産。不正性器出血を主訴に前医で精査を行い、子宮体癌が疑われ当科へ紹介受診された。子宮体癌IA期の診断で腹式単純子宮全摘術、両側付属器摘出術、大網切除術、骨盤リンパ節郭清術、傍大動脈リンパ節郭清術を施行した。術後2か月で下腹部痛が出現し、超音波検査で径15cmの骨盤リンパ嚢胞を認めた。リンパ嚢胞の圧排による両側水腎症と腎機能低下(Crea 7.62 mg/dl)を認め加療のため入院となった。症状緩和と腎機能改善を目的に経腔的嚢胞穿刺およびPig tailカテーテル留置を行ったことで腎機能は改善したが、リンパ液漏出が持続した。リンパ節シンチグラフィーで左外腸骨領域のリンパ節漏出と診断され、計2回のリンパ管塞栓術を施行した。術後、リンパ液漏出減少と腎機能の悪化がないことを確認して退院となった。現在、径10cmのリンパ嚢胞の残存はあるものの、増大なく無症状で経過している。【結語】リンパ管塞栓術は難治性のリンパ嚢胞に対する治療のひとつとして有用であると考えられた。

P-8-4 腹腔鏡下膈上部切断術・仙骨腔固定術後に発症した子宮体癌の1例

岐阜大附属病院

齋竹健彰, 竹中基記, 森重健一郎

【緒言】骨盤内臓器脱に対する腹腔鏡下仙骨腔固定術(LSC:Laparoscopic sacrocolpopexy)はメッシュ固定のため頸部を残すのが一般的で、摘出子宮体部から体癌が発覚する報告や、術後子宮頸癌を発症する報告は散見されるが、LSC術後に子宮体癌を発生した報告はほとんどない。LSC施行後に発症した子宮体癌の1例を経験したので報告する。【症例】74歳、4妊2産。70歳時に近医で骨盤臓器脱に対し、腹腔鏡下仙骨腔固定術、左付属器・右卵管切除術を施行されたが、頸部断端に腫瘍を指摘、頸部・腔部細胞診から頸部腺癌の疑いで当科へ紹介。経腔超音波検査で頸部から発生するΦ32mm大の腫瘍を指摘。造影MRIで残存した体部から発生した腫瘍を認め、筋層浸潤は1/2以上。造影CTから遠隔転移やリンパ節転移は否定的で、体癌IB期と診断、子宮体癌根治術を施行。【手術】頸部は後腹膜腔に存在。腫瘍は直腸の右側にあり、直腸、右尿管など周辺臓器とのマージンを確保し、子宮頸部・残存子宮体部・メッシュ、右卵巣を一塊として摘出。骨盤内及び傍大動脈リンパ節郭清を施行。また、術前に指摘されなかったが、腸間膜リンパ節にΦ20mm大の腫大を指摘し生検。大網を部分切除。手術時間8時間36分、出血量2000g。術後腸閉塞を発症したが絶食食管理で改善、術後24日目に退院。術後病理結果で子宮体癌IVB期(腸間膜リンパ節転移)と診断、現在術後補助化学療法中。【結語】LSCにおいてメッシュ固定のため子宮頸部を残すことは妥当と考えられるが、切開ラインには留意する必要がある。体癌根治術は完遂できたが、LSC後の手術はメッシュ挿入による炎症のため剥離操作に難渋する。また、LSC術後の婦人科検診の必要性を再認識した。

P-8-5 乳癌とともに診断され、急速に進行した子宮体部大細胞性神経内分泌癌の一例

筑面市立病院

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【緒言】子宮体部大細胞性神経内分泌癌 large cell neuroendocrine carcinoma (LCNEC) は子宮体癌の1%未満と非常に稀な腫瘍である。今回我々は乳癌とともに診断され、急速に進行したLCNECの一例を経験したため報告する。【症例】69歳、2経妊2経産で糖尿病と高血圧の既往歴を認めた。腰痛を主訴に当院内科受診、CT検査で右乳腺腫大、骨盤内腫瘍、多発リンパ節腫大、肺転移の診断となり外科ならびに当科紹介。右乳腺腫大は乳癌の診断となりアロマターゼ阻害剤を内服開始。MRI検査で子宮体部筋層は腫瘍に置換され、子宮体癌や子宮肉腫が疑われた。また子宮内膜組織診では synaptophysin 陽性のため神経内分泌細胞への分化を示す腫瘍を認め手術の方針。腹式単純子宮全摘術、両側付属器摘出術、また子宮後壁側の腫瘍が虫垂や直腸に浸潤しており虫垂切除術、低位前方切除術を施行。最終病理診断では免疫組織学的に synaptophysin 陽性を示すLCNECの成分とGrade3相当の類内膜癌成分が混在し、子宮体部原発のLCNECと診断。リンパ管・脈管侵襲陽性であり、右卵巣や直腸や虫垂に転移を認め、手術進行期分類pT4N1M1, stageIVB期と診断。本人の希望もあり術後3週間で化学療法(TC療法)開始。しかしTC療法2コース目直前に全身状態悪化のため救急搬送。CT検査にて腰椎や腸腰筋への転移、下大静脈への腫瘍浸潤を認め、緩和医療の方針となるも術後3か月で永眠された。【結語】子宮原発LCNECは予後不良とされ、現時点で標準的な治療は確立されていない。今後、標準的な治療の確立にむけ、更なる症例の蓄積が必要であると考えられる。

P-8-6 子宮留膿腫で発見された子宮体部の Mesonephric-like carcinosarcoma の一例

音羽病院

野溝万吏, 福谷優貴, 瀬尾晃司, 下園寛子, 矢野阿壽加, 伊藤美幸, 藤井 剛, 堀 隆夫, 佐川典正

今回、発症部位、病理組織像、臨床病態ともに非定型である子宮体部の Mesonephric-like carcinosarcoma を経験したので報告する。78歳女性、2妊2産、閉経50歳、高血圧内服治療中。血尿を主訴に当院泌尿器科を受診し、画像検査で骨盤内腫瘍を指摘され当科紹介初診となった。子宮体部内腔は20cm大まで著明に拡張し、子宮頸部内子宮口付近から子宮頸管内にかけて不整形腫瘍を認めた。頸部腫瘍のため子宮留膿腫を呈している状態であり、全麻下に子宮内膜生検と子宮留膿腫内にドレーンを留置した。病理組織診断では、adenocarcinoma cervical typeであった。ドレーン留置後の画像検査では、子宮頸部前壁を置換するような不整形腫瘍は8cm大で間質浸潤と傍子宮組織浸潤を疑われた。子宮頸部腺癌IIB期の診断で、広汎子宮全摘術、両側付属器切除術、骨盤リンパ節郭清術を行った。摘出標本の病理検査結果は、腫瘍は子宮体下部から内頸部にかけて広がり、深い筋層浸潤を伴っていた。立方上皮が増殖する腺状部分、円柱上皮増殖の管状部分、細胞核比率の高い細胞が充実性に増殖する部分、紡錘形細胞が束状に増殖して肉腫様形態を示す部分が混在しており、一部の腺腔には濃縮した好酸性分泌物が認められ、組織像は子宮頸部の中腎癌が疑われた。HPV関連癌とするには所見が弱く、子宮頸部上皮内腺癌の像が見られないことから、積極的に子宮頸部原発の腺癌を示唆する所見は認めなかった。以上より、最終的には子宮体下部発生 of mesonephric-like carcinosarcoma と診断であったが非定型的な組織型で報告も少なく、エビデンスの高い化学療法がないことなどから追加治療行わず経過観察とした。

P-8-7 子宮体癌に対する腹腔鏡下手術時に偶発的に認めた腹膜中皮腫の1例

産業医大病院

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【緒言】中皮腫は胸膜や腹膜の中皮細胞から発生する稀な悪性腫瘍であり、悪性度は様々である。その中で高分化型乳頭状中皮腫 (well-differentiated papillary mesothelioma: 以下 WDPM) は低悪性度中皮腫の一亜型で腹膜発症が多い。生殖可能時期の女性に多く、石綿暴露との関連は低い。低悪性度ゆえにほとんどが無症状で外科手術の際に偶然発見され、診断されることが多い。今回、我々は子宮体癌に対して腹腔鏡下子宮全摘術を施行した際に点在する腹膜病変を認め、腹腔鏡下に切除し、病理診断で WDPM と診断した症例を経験した。現在 WDPM について無治療経過観察の状態であり、その場合の予後について考察を交えて報告する。【症例】46歳G0P0の女性。術前診断で子宮体癌1A期と診断し、腹腔鏡下単純子宮全摘術を施行した。術中所見として右後腹膜に結節様病変が点在しており、一部を生検した。術後診断は子宮体癌1A期, Endometrioid Carcinoma, pT1a, N0 M0で、腹膜病変の結果は Well differentiated papillary mesothelioma の診断であった。【結語】本症例のような腹膜病変に偶然遭遇した場合、術式判断には術中迅速組織診が重要であり、腹膜ごと合併切除する必要がある。WDPM は多くが無症候性の低悪性度病変であるが、高悪性度病変に転化した報告がある。そのため、術中迅速組織診による対応が重要で、病変が限局的であれば完全切除を試みる必要がある。びまん性に存在すると広範囲な腹膜切除は腹腔鏡下手術では困難であるため、開腹術へ移行すべきか、慎重な判断を行う必要がある。あるいは残存する病変に関しては、診断後は悪性化しないかを慎重に経過観察する必要がある。

P-8-8 歌舞伎症候群に発生した子宮内膜異型増殖症の1例

宮崎大

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【はじめに】歌舞伎症候群（以下本症）は先天性奇形症候群であり特異顔貌、骨格異常、皮膚紋理異常、精神発達遅延、低身長との5主徴とし、本症での悪性腫瘍の増加は指摘されていない。今回本症に子宮内膜異型増殖症を合併した症例を経験したので報告する。【症例】25歳女性、身長140.1cm、体重71.5kg、BMI 36.4と低身長、高度肥満を認めた。既往歴として生後1か月で口蓋裂と先天性股関節脱臼を指摘、その後当院小児科で本症の診断に至り外来で定期管理されていた。0経妊0経産、初経は12歳、以後22歳までは月経整であった。その後、1年程度の無月経の後に約3か月出血が持続し近医を受診した。超音波断層検査で子宮内膜肥厚と双角子宮を認め、Hb 7.7 g/dlと貧血を認め当科に紹介となった。初診時、子宮内膜肥厚は26mmに肥厚、さらに内膜から連続する外子宮口から突出するポリープを認めた。MRI検査でも同所見を認めたが筋層浸潤等の悪性を疑わせる所見はなかった。エストラジオール 21.4 pg/ml、腫瘍マーカーはCA125 42.2 IU/mlと軽度上昇を認めた。腔腔は狭く内膜細胞診は不可、ポリープ生検では内膜腺組織を認め悪性所見はなかった。以後出血が持続し輸血も要するため子宮摘出を行った。摘出標本では子宮内膜から発生するポリープを認め、子宮内膜およびポリープの全体に子宮内膜異型増殖症の所見を認めた。【考察】本症では過去に急性リンパ性白血病等の悪性腫瘍の合併は報告されているが、婦人科腫瘍の合併の報告はない。当症例では高度肥満を伴いそのため若年で子宮内膜異型増殖症を発症したと思われるが、本症との関連性について症例の集積と検討は必要と思われる。

P-9-1 腹腔内コミュニケーションに注目した卵巢癌腹膜播種における Notch シグナルの新規機能：腫瘍内不均一性と薬剤抵抗性への関与

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【目的】我々はこれまで微小環境間の細胞間クロストークに着目し、腹膜播種形成・維持の機序を探究してきた。今回腹膜中皮細胞 (mesothelial cells: MC) による癌細胞の Notch シグナル活性化が引き起こす腫瘍内不均一性と、これに伴う薬剤抵抗性獲得の新規メカニズムについて報告する。【方法】Notch 活性化をリアルタイムに可視化するため、Hes1 を標的としたゲノム編集技術を用いたレポーター卵巢癌細胞株を使用し、フローサイトリーにより Notch シグナル活性化癌細胞の可塑性を検証した。また MC との相互作用により生じた Notch 活性化癌細胞と非活性化癌細胞を分離回収し、メタボローム解析、RNA-seq により網羅的解析を行った。さらに MC と相互作用する癌細胞の薬剤抵抗性検討の為、癌細胞の Notch 活性化を発光で検出する Dual Luciferase assay を行った。【成績】MC との相互作用により、卵巢癌細胞のうち 5.63% の細胞で不均一な Notch 活性化が見られた。この Notch 活性化細胞を単独で培養すると、2日後には 76.3% の細胞が Notch 非活性化となった。MC と相互作用した Notch 活性化癌細胞では非活性化細胞と比べて、8.06 倍 ($p=0.057$) 多く還元型グルタチオンを保有しており、さらにグルタチオン代謝に関わるトランスポーター SLC7A11 の発現が上昇 (1.59 倍, $p=0.094$) した。シスプラチンにより卵巢癌細胞における Notch 活性化が上昇 (9.65 倍, $p<0.01$) し、この活性化はグルタチオン代謝阻害によって抑制された。【結論】卵巢癌腹膜播種において MC と相互作用した卵巢癌細胞の一部で Notch シグナルが活性化し、腫瘍内不均一性を誘導した。またこの活性化は代謝変容を介して薬剤抵抗性に寄与することが明らかとなった。

P-9-2 卵巢癌希少組織型患者由来ゼノグラフトモデルを用いたニラパリブの抗腫瘍効果の検討

北海道大

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【目的】PARP 阻害薬の一つであるニラパリブは、DNA 相同組み換え修復欠損を有する腫瘍に対して合成致死機序による抗腫瘍効果を示す。卵巢癌では高異型度漿液性癌及び類内膜癌を対象に有効性が示されたものの、その他の希少組織型に対する有効性は十分に検討されていない。本研究では、patient-derived xenograft (PDX) モデルを用いて卵巢癌希少組織型におけるニラパリブの有効性を検討した。【方法】患者組織検体を NOG マウスの皮下に移植し、PDX の樹立を試みた。ニラパリブの有効性バイオマーカー検索のため、患者腫瘍を用いて ARID1A 及び SLFN11 の発現レベルを免疫組織化学法で、癌関連遺伝子異常を次世代シーケンサーにて検討した。PDX モデルを用いてカルボプラチン (CBDCA) とニラパリブの腫瘍増殖抑制効果を評価した。【成績】明細胞癌 3 例、癌肉腫 1 例、神経内分泌癌を伴う腺癌 1 例、明細胞癌を伴う未分化癌 1 例の計 6 例の PDX を樹立した。組織学的に PDX 腫瘍は患者腫瘍を模倣していた。癌肉腫、神経内分泌癌を伴う腺癌、明細胞癌の 1 例の計 3 例で SLFN11 が陽性で、このうち癌肉腫と明細胞癌では ARID1A の欠損を認めた。BRCA1/2 の病的変異は癌肉腫でのみ認められた。癌肉腫の PDX では CBDCA とニラパリブともに有意な腫瘍増殖抑制効果がみられた。一方で SLFN11 が陽性であった神経内分泌癌を伴う腺癌と明細胞癌では CBDCA では腫瘍増殖が抑制されたが、ニラパリブでは抑制されなかった。他の PDX 検体では CBDCA、ニラパリブともに腫瘍増殖が抑制されなかった。【結論】SLFN11 の発現と BRCA1/2 の遺伝子異常の組み合わせは卵巢癌におけるニラパリブの有効性を予測するバイオマーカーである可能性が示唆された。

P-9-3 グルタチオン代謝経路阻害剤と paclitaxel の併用による細胞死誘導機構に関する検討

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【目的】がん細胞薬剤抵抗性機序として抗瘤剤が誘導する活性酸素 (ROS) を抗酸化物質であるグルタチオン (GSH) が抑制して apoptosis を阻害する機序がある。スルファサラジン (SAS) は, GSH 産生阻害作用を持ち, 非 apoptosis 性細胞死である ferroptosis を誘導する。卵巣明細胞癌細胞株において SAS と paclitaxel (PTX) の併用による細胞死誘導機構を検討した。【方法】明細胞癌細胞株 (TOV21G, RMG-1, HAC-2, ES-2) を用いた。明細胞癌細胞株に PTX, SAS の単剤または PTX と SAS を併用投与し, 1) 細胞増殖能, 2) ROS 産生, 3) apoptosis 誘導を検討した。4) ferroptosis 阻害剤 (ferrostatin-1) を用いて細胞増殖能に対する影響を検討した。5) GSH 代謝経路関連蛋白の発現を検討した。6) PTX と SAS 併用による抗腫瘍効果を RMG-1 の異種移植モデルで検討した。【成績】明細胞癌細胞株では HAC-2 を除いたすべての細胞株で PTX と SAS の併用投与はそれぞれの単剤投与と比較して 1) 細胞増殖能を抑制し, 2) ROS の産生が増加し, 3) apoptosis 誘導を増強した。4) ES-2 のみ PTX と SAS の併用投与による細胞増殖抑制効果が ferrostatin-1 で解除された。5) HAC-2 では他の細胞株に比較してシスタチオンガンマリアーゼ (CGL) 発現が上昇しており, ES-2 では他の細胞株に比較してグルタチオンペルオキシダーゼ (GPx4) の発現が低下していた。6) PTX と SAS の併用投与によってそれぞれの単剤投与と比較して抗腫瘍効果の増強を認めた。【結論】明細胞癌細胞株では CGL が高発現であると SAS の細胞死誘導効果が低下する。SAS と PTX の併用投与で誘導される細胞死の主たる機序は apoptosis であるが, GPx4 が低下していると ferroptosis も誘導されることが明らかとなった。

P-9-4 上皮性卵巣癌の転移浸潤における NGFR/CD271 発現の臨床予後および分子生物学的役割に関する検討

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【目的】神経成長受容体 NGFR は CD271 としても知られている細胞表面分子であり, 神経細胞や粘膜上皮の基底層などの正常組織の他, 悪性黒色腫, 食道癌, 神経膠腫などにおいても重要な役割を果たしていることが報告されている。今回我々は卵巣癌における NGFR の発現及び予後との相関, 遊走・浸潤能, 増殖能への関与を探究した。【方法】卵巣癌組織および細胞株における NGFR の発現を qPCR・イムノブロット・FCM 法により評価した。データベースを用い NGFR 発現と予後との相関を調査した。また卵巣癌細胞株を用い, NGFR に対する siRNA を導入し, 遊走・浸潤能, 及び増殖能への寄与を解析した。さらにプロテオーム解析により NGFR 発現と相関している分子の探索を行い, 卵巣癌進展における NGFR の生物学的意義を検討した。【成績】NGFR の発現は臨床検体では全例, 細胞株では 2 株 (ES2, NOE) に確認された。これら 2 株はいずれも高浸潤能及びマウス個体内にて高増殖能を示す株であった。データベースを用いた解析により, NGFR 発現と予後不良とに相関を見出した。卵巣癌細胞株において, siRNA を用いて NGFR の発現を減少させた結果, 遊走・浸潤能が有意に減少しており (遊走: 0.75 倍, $p < 0.01$, 浸潤: 0.68 倍, $p < 0.01$), 増殖能の減少も認められた (0.66 倍, $p < 0.02$)。またプロテオーム解析の結果, NGFR は癌細胞の転移・浸潤, 細胞骨格の形成, 増殖に関わる分子 (myosin, Rho ファミリー蛋白質, CDK 等) に有意に影響していることが確認された。【結論】NGFR は卵巣癌の遊走・浸潤能に寄与していることが明らかになり, 更に予後との相関, 細胞増殖能への影響も認められ, この分子が卵巣癌の悪性化に関与していることが示唆された。

P-9-5 卵巣明細胞癌細胞株における選択的 LAT1 阻害剤による細胞増殖抑制効果

広島大

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【目的】卵巣癌のうち卵巣明細胞癌は化学療法に抵抗性であることが多く予後不良であり, 新規治療戦略の開発が求められている。本研究では癌増殖に関わるとされる L-type amino acid transporter1 (LAT1) に着目し, LAT1 選択的阻害剤 (JPH203) を用いて, 卵巣明細胞癌に対する細胞増殖抑制効果を明らかにすることを目的とした。【方法】LAT1 の発現を確認した卵巣明細胞癌細胞株 (JHOC9) に対して JPH203 を添加・培養し, Incucyte zoom[®] を用いて 72 時間後までの細胞増殖の動態を観察した。次いで JPH203 を添加した JHOC9 からタンパクを抽出し mTOR1 pathway (4EBP1, P70S6K) の動態をウェスタンブロットにて確認した。【成績】JHOC9 において JPH203 の添加により, 濃度依存的に細胞増殖の抑制を確認した。また, JHOC9 において JPH203 添加による mTOR1 pathway のリン酸化の抑制を認めた。【結論】JHOC9 における JPH203 による細胞増殖抑制には mTOR1 pathway の抑制によるタンパク合成阻害が関与している可能性が示唆された。

P-9-6 Carbonyl reductase 1 は EIF シグナルを介して卵巣癌細胞増殖を抑制する

弘前大

門ノ沢結花, 横山美奈子, 横山良仁

【目的】卵巣癌細胞での Carbonyl reductase 1 (以下 CBRI) 蛋白質の高発現が, 癌細胞の増殖・転移を抑制することが報告されている。しかしその機序は不明な点が多い。ヒト CBRI 蛋白質を恒常的に過剰発現する細胞 (hCBRI 過剰発現株) を作成し CBRI の作用機序を解明する。【方法】卵巣癌細胞株 (OVCAR-3, SKOV-3) に hCBRI をコードする遺伝子領域を有するプラスミドベクター (pCMV6-AC-GFP-hCBRI) を transfection し G418 で選別し hCBRI 過剰発現株を分離した。hCBRI 過剰発現株, Mock 細胞の腫瘍増殖速度を比較した。hCBRI 過剰発現株の腫瘍増殖が抑制された場合, その細胞内シグナル伝達の変動を調べるために蛋白質を抽出し LC-MS/MS でプロテオーム解析した後, 同定された蛋白質に関してパスウェイ解析およびネットワーク解析を行った。【成績】hCBRI 過剰発現株 (OVCAR-3 では 2 種類, SKOV-3 では 4 種類), Mock 細胞 (OVCAR-3 では 3 種類, SKOV-3 では 3 種類) を作成した。どちらも野生型をコントロールとした。いずれの細胞株でも, hCBRI 過剰発現株は有意に細胞増殖が抑制された ($p < 0.05$)。さらに OVCAR-3 では CBRI 蛋白質発現量と細胞増殖曲線係数との逆相関を認め, この株についてネットワーク解析およびパスウェイ解析を行った。腫瘍制御に関するシグナル変動を複数認め, 中でも EIF2 シグナルの変動が大きかった。【結論】今回, 卵巣癌細胞内で CBRI 過剰発現により複数の腫瘍制御に関わるシグナルが変動していることが判明し CBRI が腫瘍増殖抑制にいくつかの経路を介して関与している可能性が示唆された。CBRI 蛋白質の腫瘍抑制機序について文献学的に考察する。

P-9-7 シスプラチン誘導性の急性腎障害による血中インドキシル硫酸の亢進と卵巣癌病態の促進~Mas 受容体に焦点を当てて~

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【目的】近年の研究から化学療法が癌の転移を促進することが示唆されている。化学療法は急性腎障害 (AKI) にも関連付けられている。腎機能が低下すると尿毒症物質インドキシル硫酸 (IS) が血中に蓄積するが, 薬剤性 AKI による血中 IS への影響や, IS による卵巣癌進行への影響は不明である。卵巣癌進行へのレニン-アンジオテンシン系 (RAS) の寄与が明らかとなっているが, 他方, 腎組織では IS による RAS 活性化が知られている。そこで『IS が RAS 活性化, 特に RAS 抑制分子である Mas 受容体 (R) の阻害を介して卵巣癌を進行させる』と仮説立て, 実験を行った。【方法】SKOV3 細胞を用い, 各種遺伝子の発現解析, 細胞増殖・遊走・浸潤アッセイを, 芳香族炭化水素受容体 (AhR) 発現のノックダウン条件下, アンジオテンシン (Ang) (1-7) 存在下などで行った。シスプラチン腎症モデルマウス及び対照マウスの血中 IS を測定した。卵巣癌同所移植モデルマウスに IS または生理食塩水を 1 か月間投与した後, 腫瘍増殖の観察を行った。【成績】IS で刺激した SKOV3 細胞において, MasR および E-cadherin 発現の減少, Slug および Zeb2 発現の増加, および, 増殖・遊走・浸潤の促進が観察された。それらは AhR 発現のノックダウン, または Ang (1-7) 刺激により抑制された。シスプラチン腎症モデルマウスで血中 IS の亢進が観察された。卵巣癌同所移植モデルマウスの IS 投与群で腫瘍増殖の促進が観察され, また, 腫瘍が広範囲に拡散していた。【結論】薬剤性 AKI による腎機能低下で亢進した血中 IS によって, MasR 発現の減少を介した RAS 活性化が起こり, 卵巣癌の進行が促進される可能性がある。また, RAS 活性化による卵巣癌進行は Ang (1-7) で抑制できる可能性がある。

P-10-1 侵入性及び圧排性浸潤を伴う粘液性卵巣癌と高異型度漿液性卵巣癌の比較

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【目的】侵入性浸潤を伴う粘液性卵巣癌 (Mucinous carcinoma with infiltrative invasion : MCI), 圧排性浸潤を伴う粘液性卵巣癌 (Mucinous carcinoma with expansile invasion : MCE), 高異型度漿液性卵巣癌 (High-grade serous carcinoma : HGSC) の臨床病理学的因子及び予後を比較すること。【方法】1984 年から 2019 年の間に粘液性卵巣癌 (Mucinous carcinoma : MC) 及び HGSC と診断された症例を抽出し, MCI, MCE, HGSC の臨床病理学的因子と予後を後方視的に比較した。【成績】MCI は 27 症例, MCE は 25 症例, HGSC は 219 症例であった。MC は HGSC と比較して, 全 FIGO 病期において無増悪生存期間 (progression-free survival : PFS, $p < 0.01$) 及び全生存期間 (overall survival : OS, $p < 0.01$) が良好であったが, 多変量解析では PFS と OS に有意差はなかった。MCI と HGSC の間には, 全 FIGO 病期において PFS, OS ともに有意差はなかったが, FIGO 病期 II-IV 期においては MCI の方が PFS ($p < 0.01$), OS ($p < 0.01$) ともに有意に予後不良であった。単変量解析においても, MCI は HGSC と比較して PFS (hazard ratio [HR] 2.83, $p < 0.01$), OS (HR 3.83, $p < 0.01$) において予後不良因子であった。HGSC と比較して, MCE は PFS ($p < 0.01$), OS ($p < 0.01$) ともに予後良好であった。多変量解析においても, MCE は HGSC と比較して PFS (HR 0.17, $p < 0.01$), OS (HR 0.18, $p = 0.03$) において予後良好因子であった。【結論】HGSC の予後と比較して, HGSC の予後は浸潤形態と FIGO 病期で異なっていた。これらの関係を考慮して, 今後更なる検討をしていくことが望ましい。

P-10-2 卵巣明細胞癌の Grading system の構築

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【目的】卵巣明細胞癌の Grading system の構築及び Grading と背景にある遺伝子変化を調査すること【方法】卵巣明細胞患者の組織スライドを再検鏡し, 卵巣明細胞癌の形態変化に着目し, 10% の充実部または線維芽細胞の増生を伴いつつ浸潤または索状構造を有する症例をまとめて High grade とし, その他の症例を Low grade の 2 つに分類した. 遺伝検索は FFPE 検体を用いて Oncomine tumor mutation load assay を用いた. 【成績】全体で 126 名おり, 39 症例を High grade に 87 症例を Low grade にそれぞれ分類した. 年齢, 進行期, 初回手術の残存腫瘍を有する症例数などの背景に両群間に有意な差がなかった. High Grade 群の無増悪生存期間 ($p < 0.01$) 及び全生存期間 ($p < 0.01$) は不良であった. 多変量解析で無増悪生存期間 (ハザード比 3.26, $p < 0.01$) 及び全生存期間 (ハザード比 4.48, $p < 0.01$) に対して予後不良因子であることを示した. 平均遺伝子変異量は, 全体で 19.24 (3.3-106) Mutation/Mb であり, High grade 群は 29.2 (2.5-106) Mutation/Mb で Low grade 群で 4.18 (3.3-6.7) Mutation/Mb であった. ARIAD1A と PIK3CA の mutation は, High grade 群及び low grade 群で ARIAD1A の mutation は 6/9 例 (66%) と 2/6 例 (33%), PIK3CA の mutation は 2/9 例と 1/6 例に見られた. 【結論】予後を推定する Grading system として役に立つ可能性がある. 今後も症例を蓄積し検討する必要がある.

P-10-3 当院における卵巣癌に対する新規腫瘍マーカーである TFPI2 測定の検討

大阪警察病院

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【目的】本邦における卵巣癌の罹患数・死亡数は共に増加傾向にあり, 婦人科悪性腫瘍の中では最も死亡数が多い疾患である. その中でも, 卵巣明細胞癌は本邦での発生頻度が欧米に比べて有意に高く, 他の組織型と比較して抗癌剤抵抗性で予後不良例が多いとされている. この度, 卵巣明細胞癌の早期診断や治療効果判定や経過観察に有用な新規の腫瘍マーカーとして TFPI2 が 2021 年 4 月に保険収載された. TFPI2 は胎盤に特異的に発現するプロテアーゼインヒビターとして報告された蛋白質である. 既存の卵巣癌マーカーである CA125 では, 卵巣癌全般と子宮内膜症性嚢胞との鑑別が困難であったが, TFPI2 は卵巣明細胞癌と子宮内膜症性嚢胞の間に測定値に有意差が認められ, 高い明細胞癌鑑別性能を示すことが報告されている. さらに, それぞれ単独では 50% 程度に留まる早期卵巣明細胞癌検出率が, CA125 と TFPI2 の同時測定によって陽性率が 90% にも向上するとの報告もあり, 早期の卵巣明細胞癌検出の感度向上に期待されている. 【方法】当院においても 2021 年 8 月から卵巣癌が疑われる症例および卵巣子宮内膜症性嚢胞の症例に対しての TFPI2 測定を開始した. 【成績】抄録提出の時点で測定した 7 例中で 2 例に陽性を確認した. 両症例ともに術後に卵巣癌の診断がなされているが, うち一例は明細胞癌であり, もう一例は漿液粘液性癌の組織型であった. 2 例ともに CA125 も同様にカットオフ値以上であったが, 明細胞癌は CA125 と比較して TFPI2 の上昇率が高く, 一方で漿液粘液性癌は CA125 の上昇率が高かった. 【結論】学会発表時にまで TFPI2 測定症例をさらに蓄積して検討していく予定である.

P-10-4 当院における進行卵巣癌症例に対する Predictive index の後方視的検討

順天堂大浦安病院

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【目的】進行卵巣癌において Primary debulking surgery (PDS) で optimal surgery が困難とされる症例では Neoadjuvant chemotherapy (NAC) 後 Interval debulking surgery (IDS) を行うことが推奨される. 近年腹腔内観察, 組織採取を目的に審査腹腔鏡も選択肢となっている. 審査腹腔鏡によりスコアリングされる Predictive index (PI) が, 8 点以上だと optimal surgery が困難で, 6 点以下なら容易と予測される. しかし他科連携の観点から, 施設により PI に準じた対応が困難な場合もあり, 実臨床での治療方針決定に PI が妥当であるかは議論の余地がある. 今回我々は当院における進行卵巣癌症例の診療録を用いて後方視的に PI の有用性を検討した. 【方法】2018 年 1 月から 2020 年 12 月に当院で手術を行った卵巣癌 III・IV 期の症例のうち, PDS を行った症例 (PDS 群) と NAC を行った症例 (NAC 群) を抽出し, PDS 群と NAC 群で試験開腹や審査腹腔鏡を施行した症例について, 術中所見による PI と optimal surgery の可否についての関連性を検討した. 【成績】対象症例は 38 例で, PDS 群は 14 例, NAC 群は 24 例であった. Optimal surgery 達成例は PDS 群と NAC 群でそれぞれ 9 例 (64%), 12 例 (55%) で有意差は認めなかった. NAC 群で試験開腹や審査腹腔鏡を行った症例は 5 例で, PI 中央値は 6 点であった. PDS 群の PI 中央値は 1 点であった. PDS で optimal surgery を達成できなかった 3 例の PI 中央値は 2 点であった. 【結論】当院における進行卵巣癌症例について術中所見から PI の有用性を検討した. PI 6 点でも optimal surgery が困難な症例もあり, その可否には他科との連携が非常に重要である. 今後症例を蓄積し, 審査腹腔鏡と PI のさらなる検討が必要である.

P-10-5 進行虫垂癌と卵巣癌における鑑別の要点

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【緒言】原発性虫垂癌の頻度は1.2人/10万人, 大腸癌手術例の0.2%と報告され, 非常にまれである。急性虫垂炎として虫垂切除後に診断される症例や, 卵巣転移, 腹膜播種で発症する報告が多く, 術前診断が難しい。今回, 卵巣腫瘍として手術し, 永久病理で虫垂癌と診断された症例を経験したので鑑別の要点を考察する。【症例1】37歳。腹痛精査で15cm大の両側多房性嚢胞性卵巣腫瘍を認めた。腹式単純子宮全摘(TAH), 両側付属器切除(BSO), 大網部分切除(pOm)に加え, 術中に虫垂腫大を認め虫垂切除術, 腸間膜リンパ節サンプリングを追加。永久病理で虫垂原発のadenocarcinomaと子宮付属器転移, 腹膜播種を認めた。【症例2】66歳。食欲低下で受診し, 画像検査で大腸イレウス, 癌性腹膜炎, 両側卵巣腫瘍, 5cm大の両側卵巣腫大を認めた。術中では腹腔内多発播種あり, 虫垂に硬結を触知し虫垂切除術を施行。術後病理で虫垂原発Goblet cell adenocarcinomaと診断され, 同様の像を両側卵巣, 子宮, S状結腸に認めた。【症例3】45歳。不正出血精査のMRIで両側卵巣腫瘍を認めた。PET-CTでは両側卵巣のみに軽度のFDG集積を認めた。TAH, BSO, pOm施行し, 迅速病理で印環細胞癌。回盲部は一塊となり虫垂に硬結を触れ, 回盲部切除を施行。病理結果では, 虫垂原発のGoblet cell adenocarcinomaと診断。子宮, 両側付属器, 大網に同様の像を認めた。【考察】虫垂は卵巣に隣接し, 虫垂癌は早期に卵巣に転移し, あたかも原発性卵巣癌の像を呈する。PET-CTではFDG集積を来さないと報告され, 腫瘍マーカーも含めて特徴的所見に乏しく, 術前の鑑別は難しい。両側卵巣腫瘍では虫垂癌の可能性の念頭におき注意して手術する必要がある。

P-10-6 新規卵巣明細胞癌特異的腫瘍マーカーTFPI2の診断性能

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【目的】卵巣明細胞癌(Clear cell carcinoma: CCC)は, 化学療法に対して治療抵抗性で予後不良であるため, 早期発見が求められる。CA125が卵巣癌の腫瘍マーカーとして広く用いられているが, CCCでは上昇しない場合が多く, CCCに特異的な腫瘍マーカーが必要である。我々はCCC細胞株の培養上清を用いてプロテオーム解析を行い, Tissue Factor Pathway Inhibitor 2(TFPI2)をCCC特異的マーカーとして同定した。今回は術前診断におけるTFPI2の診断性能の検証を行った。【方法】国内5施設の医療機関において, 外科的治療を必要とする卵巣腫瘍患者から術前に血清サンプルを採取した。CCC69例, 非明細胞上皮性卵巣癌(non-CCC EOCs)140例, 卵巣境界悪性腫瘍(BOT)65例, 良性卵巣腫瘍77例におけるTFPI2とCA125の診断性能を比較した。【成績】CCC群の血清TFPI2値(mean±SD, 508.2±812.0 pg/mL)は, 良性腫瘍群(154.7±46.5), BOT群(181±95.5), non-CCC EOCs群(265.4±289.1)よりも有意に高値であった。また, TFPI2はCCCの診断特異度が高かった(79.5%)。TFPI2とCA125の診断性能をROC曲線で比較すると, Stage II-IV期のCCC群とBOT+non-CCC EOCs群の鑑別(AUC 0.815 for TFPI2 vs 0.505 for CA125), Stage II-IV期のCCC群と良性子宮内膜症群の鑑別(AUC 0.957 for TFPI2 vs 0.748 for CA125), いずれにおいてもTFPI2はCA125より優れた診断性能を有していた。またCCC群とBOT+non-CCC EOCs群の診断では, TFPI2とCA125のカットオフ値を併用することで診断感度が43.5%から71.0%に向上した。【結論】この臨床試験により, TFPI2が術前にCCCを予測する特異的なバイオマーカーであることが実証された。

P-10-7 当院における卵巣明細胞癌の診療経過の集計

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【目的】当院で診療した卵巣明細胞癌症例の臨床経過を集計した。【方法】1998年から2020年に治療を開始した卵巣明細胞癌176人の診療経過を集計した。臨床病期は現行の規約にて集計した。【成績】対象患者群の初回治療開始時年齢中央値は56歳, 全患者の観察期間中央値は60.9月であった。進行期はI期99人(56.3%), II期29人(16.5%), III期38人(21.6%), IV期10人(5.7%)であった。各病期の2年/5年無病生存割合はI期90.7%/89.4%, II期82.4%/78.3%, III期41.7%/35.3%, IV期45.0%/33.8%で, 2年/5年全生存割合はI期95.8%/94.5%, II期96.4%/76.1%, III期70.0%/42.9%, IV期64.3%/48.2%であった。I期およびII期では, 開腹時に腹水細胞診陽性あるいは自然破綻の有無で予後に有意差が認められた。III期およびIV期では, 手術時に粗大な遺残病変(1cm以上)の有無で予後に有意差が認められた。再発は49人で確認された。初再発部位は腹腔内29人, 領域リンパ節14人, 遠位リンパ節12人, 遠隔臓器16人(重複あり)であった。再発後死亡が確認されたのは36人で, 1人は腫瘍随伴病態による死亡であった。初再発確認後の生存期間の中央値は322日で, 1年時/2年時/3年時生存割合は56.2%/29.4%/17.3%であった。【結論】これまでの報告と同じく, 当院で経験した卵巣明細胞癌においても早期症例の比率が高く, 進行期症例や再発症例では予後が不良であった。腹膜播種やリンパ節再発が多く, 初回手術に際しては可及的減量手術が重要である。

P-11-1 婦人科悪性腫瘍に対する AP 療法による末梢神経障害の評価

愛知医大

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【目的】近年、婦人科悪性腫瘍に対する化学療法の進歩に伴い、患者の予後は大きく改善した。一方、抗がん剤の副作用によりがん患者の QOL が低下し、中長期的に日常生活に支障をきたす症例が存在する。抗がん剤の副作用である末梢神経障害はその原因の一つであり、患者の QOL を悪化させるが、その自覚症状と末梢神経障害に対する生理学的検査による客観的な評価と有効かつ明瞭な対処法は確立されていない。今回、婦人科悪性腫瘍に対して AP 療法施行患者において、末梢神経障害に対する問診と客観的な生理学的評価により、障害の発症時期、部位および障害の種類と程度を評価した。【方法】当院で AP 療法を施行した子宮体癌患者 2 例につき、初回 AP 療法前と 3, 6 クール後に (1) 患者の末梢神経障害に対する問診 (神経障害性疼痛重傷度評価表) と、(2) 筋電図/電位誘発電位検査装置を用いて、正中神経 (MN)、尺骨神経 (UN)、後脛骨神経 (TN)、腓骨神経 (SN) の運動神経および感覚神経の伝導速度 (m/sec) と振幅 (μ V) を測定することにより、末梢神経障害を評価した。【成績】2 症例ともに、(1) 問診表による評価では手足の軽度の感覚障害を認め、(2) AP 療法を 6 クール施行による運動神経に有意な変化を認めず、感覚神経において電動速度と振幅の低下を認めた。(症例 1) SN: 58→49→53m/sec, MN: 35→23→26 μ V, UN: 23→16→17 μ V, SM: 9→6→5 μ V, (症例 2) MN: 53→46→49m/sec, UN: 50→43→47m/sec, MN: 39→32→22 μ V, UN: 33→32→16 μ V 【結論】AP 療法による末梢神経障害は治療開始早期より感覚神経が優位に障害され、髄鞘変性・軸索障害型の神経障害を呈する可能性が示唆された。また、その評価法として問診と生理学的検査は有用であると考えられた。

P-11-2 標準的化学療法が困難と考えられるハイリスク卵巣癌症例に対する weekly PC 療法の安全性と有効性

自治医大

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【目的】卵巣癌の標準化学療法には key drug であるパクリタキセルとカルボプラチンが用いられる。両剤の毎週投与 (W-PC) は状態不良の患者や高齢者に対して用いられることが多いが、どの程度の患者まで許容されるかは不明である。今回、化学療法の施行そのものがハイリスクである症例においてパクリタキセルとカルボプラチン毎週投与の安全性と有効性を評価した。【方法】対象は 2008 年 1 月から 2016 年 12 月までに当院で W-PC 療法を行った卵巣癌患者で、①80 歳以上、②performance status (PS) 3 以上、③重篤な合併症がある、の中に 1 つ以上該当する症例を選択した。パクリタキセル 60mg/m² とカルボプラチン AUC2 を day1, 8, 15 に投与し、28 日周期を原則とした。診療録より後方視的に検討し、腫瘍縮小効果は RECIST-ver1.1, 有害事象は NCI-CTCAEv4.0 を用いて評価した。【成績】症例は 31 例で、Grade3 以上の好中球減少、貧血、血小板減少はそれぞれ 18 例 (58%)、5 例 (16%)、1 例 (3%) に認めた。奏効率は 48% (15/31) で疾患制御率は 65% (20/31) だった。5 年無増悪生存率は 15% で、5 年生存率も 15% だった。9 例で 40 か月以上の生存期間を示した。PS2 以下、腫瘍縮小効果が CR/PR, 6 サイクル以上施行が予後良好な因子だった。多変量解析では、6 サイクル以上施行のみが、独立した予後良好因子だった (vs. ≤ 5 ; $p=0.002$)。【結論】W-PC は 80 歳以上、PS3 以上、重篤な合併症を有するなどの卵巣癌患者に対して十分に許容可能な安全性と、若干の有効性を示した。特に、W-PC6 サイクル以上継続できた症例では生存期間の延長が期待できる。W-PC は、全身状態が不良で化学療法の施行を躊躇してしまうような症例における選択肢の一つとして有用である。

P-11-3 カルボプラチンアレルギーを呈した卵巣癌における他のプラチナ製剤変更とステロイド前日追加投薬の安全性についての検討

静岡赤十字病院

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【目的】分子標的薬の登場で、卵巣癌のプラチナ製剤投与は治療戦略の鍵となっているが、その際に問題となるのが、薬剤過敏性反応 (HSR) である。脱感作療法は再発率が 33% と高い上に複雑であるため、当院では他のプラチナ製剤に変更とステロイド 4mg を前日追加投薬とするステロイドロングプロトコールを実施してきた。その安全性について検討する。【方法】当院において、2012 年 1 月 1 日から 2021 年 9 月 6 日までにカルボプラチンに対して HSR を起こした上皮性卵巣癌、卵管癌、腹膜癌を対象とした。HSR を起こすまでの投与回数、grade、またプラチナ変更後にステロイドロングプロトコールを使用した症例における、その後の HSR の有無について後方視的に検討した。【成績】2012 年 1 月から 2021 年 9 月までにおいてカルボプラチンを投与された上皮性卵巣癌、卵管癌、腹膜癌 109 症例中、16 症例 (14.6%) に HSR を認めた。1st レジメンで HSR を起こしたのは 4 例 (0.03%)、再発治療中の症例は 12 例 (11.0%) であった。HSR は grade2 が 8 例、grade3 が 4 例、grade 4 が 4 例であった。カルボプラチン投与量の中央値は 4360mg (2010~11040mg)、レジメン使用数の中央値は 10 回 (3~21 回) であった。ネダプラチンに変更した症例は 6 例、シスプラチンに変更した症例は 5 例であった。ステロイドロングプロトコールを実施した症例はネダプラチンで 6 例、シスプラチンで 3 例であり、いずれも HSR は認めなかった。【結論】カルボプラチンの HSR において、他のプラチナ製剤への変更に加えてステロイド前日追加投薬は安全な方法と考えられる。

P-11-4 治療前好中球リンパ球比は進行卵巣癌における初回治療時のペバシズマブの治療予測因子になる

千葉大附属病院

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【目的】肺癌や大腸癌ではペバシズマブ (Bev) の治療予測因子として、治療前好中球リンパ球比 (pretreatment peripheral neutrophil-lymphocyte ratio : NLR) が報告されている。NLR が卵巣がん初回治療時の Bev の治療予測因子になるか検討した。【方法】2008年から2017年までに治療がおこなわれたIII/IV期卵巣がん306例を対象とした。無増悪生存期間 (PFS) を用いて、Bevの保険適応 (2014年1月) 前後での期間とNLRの関係を明らかにした (前期: 112例, 後期 194例)。【成績】全体でのNLRの中央値は4.5であった。前期ではBevの使用は0/149 (0%)であったのに対し、後期では149/194 (77%)で有意に高かった ($p < 0.001$)。後期でのPFSは33.1か月で、前期での24.6か月と比較し有意に延長していた ($p = 0.019$)。Cox比例ハザード解析の結果、全症例では、Bev (HR : 0.75 (CI : 0.56-1.00), $p = 0.049$) で有意な予測因子となった。NLRが4.5以下の群では、Bev (HR : 0.61 (CI : 0.42 - 0.91), $p = 0.014$) はより有意な因子となった一方で、NLRが4.5以上の群では、Bev (HR : 0.87 (CI : 0.77 - 1.71), $p = 0.5$) は有意な因子とならなかった。【結論】治療前のNLRはBevの治療予測因子となる可能性が示唆された。

P-11-5 進行・再発卵巣癌・腹膜癌・卵管癌に対するペバシズマブの有効性と安全性

大阪市大

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【目的】ペバシズマブを用いて治療を行った卵巣癌, 腹膜癌, 卵管癌患者を対象に安全性と有効性について報告する。【方法】2014年4月から2021年8月までにペバシズマブを投与した卵巣癌, 腹膜癌, 卵管癌患者137例を対象に患者背景, 安全性, 有効性に関して後方視的に検討した。発表にあたり, 患者の個人情報とプライバシーの保護に配慮し, 本人から書面にて同意を得た。【成績】71例が初回治療患者, 66例が再発治療患者だった。初回治療患者は卵巣癌61例, 腹膜癌8例, 卵管癌2例で, 組織型は漿液性癌51例, 明細胞癌7例, 類内膜癌7例, 粘液性癌1例, その他5例だった。評価可能病変を有する56例の治療効果はCR30例 (53.6%), PR19例 (33.9%), SD5例 (8.9%), PD2例 (3.6%) だった。再発患者は卵巣癌62例, 腹膜癌3例, 卵管癌1例で, 組織型は漿液性癌40例, 明細胞癌12例, 類内膜癌5例, 粘液性癌4例, その他5例。化学療法のレジメンはTC (パクリタキセル, カルボプラチン) 47例, DC (ドセタキセル, カルボプラチン) 7例, リボソーマルドキソルピジン3例, ゲムシタピン2例, CPT-11+CDDP (塩酸イリノテカン, シスプラチン) 7例, 治療効果はCR26例 (39.3%), PR17例 (25.8%), SD14例 (21.2%), PD9例 (13.6%) だった。ペバシズマブに特徴的なGrade3以上の有害事象は, Grade3の蛋白尿12例 (18.2%), Grade4の小腸穿孔3例 (4.5%) だった。【結論】ペバシズマブを併用した治療は良好な治療効果が得られており, ペバシズマブは安全かつ有効に使用できる。

P-11-6 当院における進行卵巣がんに対するPAOLA レジメン施行例の検討

JCHO 徳山中央病院

平林 啓, 中川達史, 樫部真央子, 高木遥香, 平田博子, 澁谷文恵, 山縣芳明, 沼 文隆

【目的】進行卵巣がんに対するPAOLA レジメン施行例の臨床経過について検討する【方法】2021.3月以降, 進行卵巣がんではmyChoice CDx 後, PAOLA レジメンを施行した3例に対し, 治療効果・有害事象等臨床経過について検討した【成績】myChoice CDx を施行した卵巣癌・卵管癌は現在まで6例で進行期はIII期3例, IV期3例, 組織型は高異型度漿液性腺癌 (HGS) 5例, 癌肉腫1例であった。HRD陽性は3例 (50%) で2例はBRCA1変異陽性, 1例は野生型であり全例HGSであった。HRP例のGIスコアは32, 32, 17であり, 治療前CA125 (U/ml) の平均値はHRD群で1024, HRP群で184であった。HRD群3例の初回治療はいずれも両側付属器摘出 (+腹膜生検, 大網切除) であり肉眼的残存病変を認めた。術後TC療法後にTC+BEV療法5サイクル追加, PET/CTにて遺残や再発病変がないことを確認しオラパリブ600mg/日でPAOLA レジメンを開始。現在, PAOLA開始後3, 4, 6か月経過しているがCA125値も基準値以下で新規病変の出現を認めていない。オラパリブの有害事象対策として, 開始時には制吐剤を併用したが2例は1か月で投与中止, 1例のみ投与継続中である。貧血はG1: 1例, G2: 2例に認めたが輸血症例はなかった。疲労感, 貧血のためオラパリブ投与3か月から2例で400mg/日への減量を要したが投与継続中である。TC+BEV療法時より2例で降圧剤を内服していたが, 併用による更なる血圧上昇や蛋白尿の増悪は認めていない。【結論】症例も少なく観察期間も短い, 現在のところオラパリブとペバシズマブ併用による有害事象の増加は認めていない。症例を蓄積し治療効果についても検討していきたい。

P-12-1 妊娠 36 週に発見された IIIC 期上皮性卵巣悪性腫瘍合併妊娠の 1 例

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妊娠中に発見される卵巣悪性腫瘍の頻度は、1/10000-50000 分娩と非常に稀である。今回妊娠 36 週に判明した卵巣悪性腫瘍合併妊娠の 1 例を経験したので報告する。症例は 44 歳、3 妊 0 産、IVF-ET で妊娠成立した。前医で妊婦健診を行い、妊娠合併症なく経過していたが、妊娠 35 週の血液検査で LDH 上昇 (827 IU/L) を認め、partial HELLP 症候群が疑われ妊娠 36 週 4 日に当院へ紹介となった。超音波検査で右季肋部に 16cm 大の充実性腫瘍、胸腹水、および Douglas 窩腫瘍を認めた。妊娠 37 週 4 日に胸水 820ml を採取したが、悪性細胞は認めなかった。MRI・CT 検査結果より右卵巣由来の悪性腫瘍を疑い、妊娠 37 週 4 日に選択的帝王切開術とともに一次的腫瘍減量手術を行った。帝王切開術により 3100g の男児を Apgar score 8/9 で娩出した。右卵巣は 16cm 大に腫大し、子宮漿膜表面、Douglas 窩腹膜、右肝表面、左側腹部壁側腹膜に播種を疑う腫瘤を認めた。子宮漿膜表面の播種病変の術中迅速病理診断では腺癌の結果であり、最大径 3cm 大までの腹膜播種を含め肉眼的完全切除を達成した。摘出標本の最終診断は Endometrioid carcinoma, IIIC 期 (pT3cNXM0) であった。術後補助化学療法として TC 初回投与時に過敏性反応を認めたため、DC+Bevacizumab 療法に変更し 6 コース行った。HRD (相同組換え修復異常) 検査陽性で、現在 Bevacizumab+Olaparib 併用/維持療法中であり、術後 9 か月再発なく経過している。妊娠中の卵巣癌合併は非常に稀であり、診断自体が困難かつ標準治療が確立していないのが現状である。妊娠週数、組織型、進行期などを踏まえ、患者・家族への十分な病状説明のもと、分娩時期やその様式、原発巣の治療方針を個々に検討する必要がある。

P-12-2 付属器腫瘍と術前診断した腸管外原発 GIST の一例

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【はじめに】骨盤内充実性腫瘍の多くは卵巣由来であり、婦人科臓器由来であることを念頭に婦人科医による外科治療を行うことが多い。【症例】72 歳 2 妊 2 産、急性腹症のため急患センターを受診し、白血球数、LDH、CK の上昇を指摘された。CT 及び骨盤部 MRI では子宮右後方に 9cm 大の充実性、一部嚢胞性の腫瘍と血性腹水を疑う所見を認めた。腹痛及び血液データ異常は抗菌薬投与後改善した。腹水は消失したが腫瘍サイズに変化なく、付属器腫瘍の術前診断で開腹術を施行した。腫瘍は子宮後面から広間膜右側に癒着し、右卵管と一塊となって腫大しており、一部回腸に癒着していた。術中の肉眼所見からは右卵巣腫瘍と判断した。腫瘍を剝離した際に、回腸粘膜炎までの穿孔を生じた。術中迅速病理診断は異型を伴い、悪性を否定できない間葉系腫瘍であり、腫瘍残存が疑われた右広間膜も含めて単純子宮全摘術及び両側付属器摘出術と、穿孔部位の回腸部分切除・吻合術、大網部分切除術を施行した。術後病理診断では、c-kit、DOG-1 陽性の異型紡錘形細胞からなる充実性腫瘍であり、Modified-Fletcher 分類で high risk GIST と診断された。右卵管近傍に卵巣組織を認めたこと、穿孔した回腸に腫瘍組織を認めないこと、剝離後摘出した広間膜にも結節状の同様の病変を認めたことから、腹膜発生腸管外 GIST と診断した。術後経過は良好であり、後療法としてイマチニブ療法施行中である。【結語】子宮広間膜から右付属器に広く癒着し、術前及び術中にも右付属器腫瘍と判断していた腹膜原発腸管外 GIST 症例を経験した。

P-12-3 手術困難な進行卵巣癌に対してオラパリブ+ベバシズマブ併用維持療法で腫瘍縮小を得た 1 例

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【緒言】2020 年 12 月にオラパリブとベバシズマブの併用維持療法が HRD 陽性であり、初回化学療法が奏功した進行卵巣癌において本邦で承認された。今回、初回化学療法が奏功したが手術困難と考えられた症例にオラパリブとベバシズマブの併用維持療法を施行しさらなる腫瘍縮小を得た 1 例を経験したため報告する。【症例】70 歳、女性。家族歴として母に乳癌既往あり。腹部膨満感を主訴として受診した。MRI で一部石灰化を伴う嚢胞部と充実部が混在した骨盤内を占拠する病変を認め、CT では肝転移と腹水を認めた。審査腹腔鏡施行し、腫瘍は卵巣由来であり、腹腔内には多数の播種巣を認めた。腹膜生検結果は High grade serous carcinoma であり、卵巣癌 IVB 期と診断した。パクリタキセル+カルボプラチン+ベバシズマブを 6 コース施行したのち CT 再検した。原発巣、播種巣ともに縮小を認めたが、完全切除が困難を予想された。化学療法の副作用による全身状態不良で円滑に手術に移行できない状態であった。HRD 陽性であり、オラパリブ+ベバシズマブ併用維持療法を施行する方針とした。現在、併用療法開始後 10 か月経過しているが原発巣、播種巣ともさらに縮小傾向であり治療継続できている。【考察】本症例では IDS が施行できず、腫瘍が残存した状態でも奏功を得られている。オラパリブとベバシズマブの併用維持療法で腫瘍残存しているが PS や合併症等の理由で手術困難な症例に対しても長期に病勢コントロールが得られる可能性がある。

P-12-4 子宮頸癌 IVB 期に対するペムプロリズマブ療法中に劇症型 1 型糖尿病を発症した 1 例

金沢大附属病院

加戸太陸, 小幡武司, 水本泰成, 齊藤実穂, 松本多圭夫, 岩垂純平, 中村充宏, 藤原 浩

【緒言】今回、化学療法抵抗性子宮頸癌に対するペムプロリズマブ療法中に劇症型 1 型糖尿病を発症した 1 例を経験したので報告する。【症例】54 歳女性。子宮頸部扁平上皮癌 IVB 期と診断し、初回治療として TP 療法を開始したが、3 クール終了後に原発、転移病変共に増悪を認めた。MSI-high であったため、ペムプロリズマブ 200mg3 週間毎投与に変更したところ、原発、転移病変共に縮小傾向となった。本人同意の下で 12 クール目から 400mg6 週間毎投与に変更したが、その 3 週間後に倦怠感、口渇、多飲、嘔吐が出現し、自宅で体動困難となったため、当院に救急搬送された。随時血糖 1159mg/dl, HbA1c 8.3% と高値で、元来糖尿病の既往はなく、ペムプロリズマブ投与以降に糖尿病症状が出現し、1 週間前後でケトアシドーシスに至っている経過から、irAE による劇症型 1 型糖尿病と診断された。インスリン療法によって良好な血糖コントロールが得られているため、糖尿病発症 2 か月後からペムプロリズマブ療法を再開している。【考察】ペムプロリズマブ単独投与による 1 型糖尿病発症頻度は 0.24%、劇症型 1 型糖尿病発症頻度は 0.03% と極めて稀だが、軽症・中等症の時点で 1 型糖尿病と診断することが重要であるため、高血糖症状を自覚したらすぐに受診するように指導しておく必要がある。また本症例では経過からペムプロリズマブ 1 回投与量の増量と劇症型 1 型糖尿病発症との関係が疑われた。インスリン治療によって血糖コントロールが改善するまではペムプロリズマブの休薬が推奨されているが、具体的な再開可能基準や再開後推奨投与量等は示されており、糖尿病専門医との相談の上、慎重に検討する必要がある。

P-12-5 卵巣線維肉腫の 1 例

大分県立病院

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【緒言】卵巣線維肉腫は悪性性索間質性腫瘍の一つであり、悪性卵巣腫瘍中 0.1% 未満と極めて稀な疾患である。今回、卵巣原発の線維肉腫を経験したため報告し、文献の考察を加えた。【症例】62 歳 3 妊 2 産。下腹部の膨隆を主訴に近医を受診し、骨盤内腫瘍を指摘され当科を紹介受診した。経陰超音波断層法にて多房性で充実部を伴う 15cm 大の卵巣腫瘍を認めた。腫瘍マーカーの CA19-9 は 52.3U/mL, CA-125 は 216.2U/mL と上昇していた。CT 検査及び MRI 検査で多量の腹水を伴う悪性卵巣腫瘍を疑い、開腹術を施行した。大量の血性腹水を認め、卵巣腫瘍は右卵巣由来であった。後腹膜腔に進展しており、S 状結腸間膜、回盲部、子宮と強固に癒着していた。腹腔内に播種結節を認めなかった。右付属器を術中迅速病理組織診に提出し、間質系由来の境界悪性以上の卵巣腫瘍と診断した。腹式単純子宮全摘出術・両側付属器摘出術・虫垂切除術・大網部分切除術を施行し、腫瘍が浸潤していた S 状結腸間膜は外科応援のもと摘出した。肉眼的残存腫瘍はなく、optimal surgery であった。術後病理組織診で右卵巣腫瘍において、核異型を伴い、核分裂像を 17MF/10HRF 程度認め、細胞密度が高く壊死を伴う部分と、細胞密度の低い線維腫を呈する組織像が見られ、卵巣原発線維肉腫と診断した。S 状結腸間膜にも浸潤を認め、腹水細胞診は陰性だった。以上より卵巣線維肉腫 IIB 期 (pT2bNXMX) とした。現在、術後化学療法を施行している。【考察】卵巣線維肉腫は悪性の経過をたどる非常に稀な疾患であり、十分なエビデンスの集積がなく治療法は確立していない。本症例では上皮性卵巣腫瘍に準じて治療選択したが、今後の治療法のさらなる検討が望まれる。

P-12-6 Sister Mary Joseph's nodule を呈した婦人科悪性腫瘍の 4 症例

国立大阪南医療センター

島津結美

【目的】Sister Mary Joseph's nodule (SMJN) はかなり稀な転移性臍部分腫瘍の総称で、消化器癌に次いで婦人科癌が多いとされ、原発巣の病因にかかわらず予後不良であり 2 年生存率はわずか 13.5% との報告もある。今回我々は SMJN を 4 例経験したので報告する。【症例 1】77 歳、子宮癌肉腫で SMJN あり、腹式単純子宮全摘出術+両側付属器摘出術+大網部分切除術+臍腫瘍摘出術を施行した (complete pT4M1)。術後補助療法施行前に癌性腹膜炎の急性増悪を認め、Best supportive care の方針となった。【症例 2】75 歳、子宮体部類内膜腺癌で SMJN あり、腹式単純子宮全摘出術+両側付属器摘出術+大網部分切除術+臍腫瘍摘出術を施行した (suboptimal pT3a)。精神的要因で通院困難となり術後補助療法は希望されず、現在経過観察中である。【症例 3】81 歳、卵巣高異型度漿液性癌で SMJN あり、Primary debulking surgery を施行した (suboptimal pT3c)。dose-dense PTX/CBDCA 療法 9 コース後に残存腫瘍に対し Secondary debulking surgery を実施した (complete)。術後 9 か月でプラチナ感受性再発を認め、PTX/CBDC 療法中である。【症例 4】53 歳、卵巣高異型度漿液性癌で SMJN 認め、Primary debulking surgery を施行した (complete pT3c)。術後補助療法として PTX/CBDCA 療法を実施している。【結語】SMJN は非常に予後不良であり進行癌であるため緩和医療となるケースが多いが、臍転移部を含めた外科切除で根治術ができれば予後改善につながるという報告もあり積極的治療の可否について、症例ごとに慎重に選択する必要がある。

P-12-7 若年性卵巣癌に対する妊孕性温存手術後に新規卵巣癌を発症した一例

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症例は、X年Y月、22歳時に両側卵巣内膜症性嚢胞に対して腹腔鏡下両側卵巣嚢腫核出術を施行した。病理診断で右卵巣嚢腫壁にはEndometrioid carcinoma grade1を認め、右卵巣癌と診断した。妊孕性温存手術を希望され、Y+1月に右付属器切除、骨盤内リンパ節郭清、大網部分切除を施行した。追加手術では癌の残存を認めず、Ic期（FIGO1988）、pT1cN0M0（UICC第7版）と診断した。術後補助化学療法としてTC療法（パクリタキセル+カルボプラチン）を2コース実施、X+5年（27歳）には自然妊娠し、帝王切開により生児を得ている。X+9年（31歳）に壁在結節を有する5cm大の骨盤内腫瘍が出現し、卵巣癌を疑い、腹式子宮全摘術および左付属器切除術を施行した。組織診断では左卵巣腫瘍はEndometrioid adenofibroma（境界悪性）を背景として類内膜癌が存在しており、新規発症の異時性重複癌と考え、左卵巣癌IA期（FIGO2014）、pT1aNxM0（UICC第8版）と診断した。相同組換え修復欠損（Homologous Recombination Deficiency：HRD）について検討したところ、右卵巣癌（X年手術）では陰性、左卵巣癌（X+9年手術）では解析不可であった。左卵巣癌術後には補助化学療法は実施せず、術後4か月明らかな再発は認めていない。早期卵巣癌の標準術式は腹式子宮全摘術、両側付属器切除術および腹膜リンパ節生検を含むStaging laparotomyであるが、若年女性においては一定の条件下で妊孕性温存手術を選択することがある。しかし、生殖可能年齢のうちに対側に新規卵巣癌を発症し再手術となった症例報告は少ないので文献的考察を加えて報告する。

P-12-8 ペムプロリズマブ投与中に心タンポナーデをきたした卵巣癌の1例

済生会福岡総合病院

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免疫チェックポイント阻害薬は抗がん剤や分子標的薬とは異なり、様々な免疫関連有害事象（irAE）を発症することがある。今回ペムプロリズマブ投与中に一過性の心嚢液貯留をきたし、心嚢穿刺を施行した1例を経験した。症例は39歳、未妊。卵巣明細胞癌IVB期で単純子宮全摘術、両側付属器摘出術、大網全全摘を施行。残存する多発リンパ節転移に対し術後ドセタキセル、カルボプラチン療法を開始し、4コース目よりペバシズマブを併用した。6コース後のCT検査でリンパ節の増大傾向があり、ゲムシタピン、ペバシズマブ療法に変更したが、リンパ節の増大と肺転移の出現がありPDと判断した。MSI検査が陽性でペムプロリズマブ投与を開始し、投与後腫瘍マーカーの低下と共に多発リンパ節は縮小し、肺転移は消失した。5コース目投与後、倦怠感、脱力を認めたため入院。入院後、体動時の呼吸困難が増悪し、画像検査で胸水と著明な心嚢液貯留を認めた。心タンポナーデの診断で心嚢穿刺を行い、1000mlの血性心嚢液を排出し、さらに胸腔穿刺で1000mlの血性胸水を排出した。心嚢液、胸水共に細胞診陽性であった。ドレナージ後、心嚢液、胸水の再貯留傾向なく、腫瘍マーカーは低下し、他の再発病変も縮小しているためペムプロリズマブ投与を継続した。irAE検査では甲状腺・副腎機能・神経学的検査は正常で、腫瘍が見かけ上いったん増大したのち縮小するPseudo-progressionを呈していたと思われる。ペムプロリズマブ投与時にはirAEの出現に留意するとともに、Pseudo-progressionと真の増悪を鑑別することが必要である。

P-12-9 再発卵巣癌に対するPARP阻害薬を用いた維持療法中の再発に対し放射線療法を行った3症例

関西医大

久松洋司, 北 正人, 横江巧也, 佛原悠介, 村田絃未, 岡田英孝

進行卵巣癌に対してPARP阻害薬を用いた維持療法が行われている。維持療法中に病勢の進行があれば治療方針の変更が原則ではあるが、緩徐に病勢が進行していても全身状態や症状に顕著な変化がない場合には、維持療法を継続すべきか他の治療法に変更すべきか判断に苦慮することがある。我々は維持療法中に緩徐な病勢の進行の場合にはPARP阻害薬に放射線療法を組み合わせることでそれぞれの治療法の長所を生かすことができるのではないかと考え、PARP阻害薬投与中の局所的な病勢進行症例に対して放射線療法を併用した症例を経験したので報告する。【症例1】50歳代、卵巣癌IIIC期。傍大動脈リンパ節（PAN）に再発がありTC2サイクル後PRであったためOlaparibを開始した。一時CRの治療効果を得たがPANが徐々に増大したため、Olaparibの服用を継続しIMRTを行い治療効果はPRだった。【症例2】70歳代、卵巣癌IIIC期。腹膜播種と頸部リンパ節転移がありTC+Bevacizumab3サイクル後PRであったためOlaparibを開始した。腹壁と縦隔リンパ節に新規病変が出現したためそれぞれにIMRTを行いPRであった。【症例3】40歳代、腹膜癌IVB期。頸部リンパ節転移に対してIMRT後、骨盤内（PEN）、PANに転移がありTC6サイクル後PRであったためOlaparibを開始した。その後PANの病変が再燃したためOlaparibを継続しながらIMRTを行った。その4か月後に前回の照射野外PANとPENとに再燃を認め、血液毒性を懸念し治療後1か月までOlaparibを休薬の上IMRTを行った。卵巣癌のみならず他領域の癌種でもPARP阻害薬と放射線療法との併用療法に関する報告は限られているが、婦人科領域でも維持療法の患者数増加に伴い必要性が増して行くことが予想される。

P-12-10 リスク低減卵管卵巣摘出術 (RRSO) 前の画像検査で指摘された孤発性閉鎖リンパ節転移を契機に診断に至った原発性腹膜癌の1例

都立駒込病院

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【背景】 遺伝性乳癌卵巣癌症候群 (HBOC) 患者における卵巣卵管腹膜癌は高異型度漿液性癌 (HGSC) が多いこと、RRSO時に漿液性卵管上皮内癌 (STIC) を認め、術後に原発性腹膜癌が発生する症例が1-4.9%程度存在することが知られている。【症例】 45歳女性。前医で40歳時に指摘された左乳房の治療後、卵巣癌の家族歴があり、BRCA遺伝子検査を施行したところ、BRCA1病的変異を指摘された。RRSO希望のため当科紹介受診した。CA125の上昇と造影MRI検査上左閉鎖リンパ節腫大を指摘された。下部内視鏡検査や造影CT検査で明らかな原発巣は認めなかった。前医CT検査で2年前より左閉鎖リンパ節腫大を認め、緩徐に増大傾向であった。腹式単純子宮全摘術、両側付属器摘出術及び左骨盤リンパ節生検を施行した。肉眼的に明らかな腹膜病変は認めなかった。病理検査で、左閉鎖リンパ節に腺癌を認め、免疫染色から卵巣卵管或いは腹膜由来のHGSCと考えられた。乳癌のリンパ節転移やendosalpingiosisを発生母地とした漿液性癌は否定的であり、左卵管采の一部上皮がp53陽性で、漿液性卵管上皮内癌(STIL)に相当する病変を認めた以外卵巣卵管に明らかな癌病変は指摘できなかった。腹膜癌IIIA1(ii)期と診断し、パクリタキセル+カルボプラチン(TC)療法を6コース施行した。【結論】 本症例は、孤発性閉鎖リンパ節転移を契機に原発性腹膜癌の診断に至った。転移リンパ節は緩徐に増大するものの明らかな原発巣を認めず、組織学的には卵巣卵管腹膜由来と考えられたが、STIC病変も認めない稀な症例を経験したため報告する。

P-13-1 再発卵巣癌に対する化学療法中に血球貪食症候群を発症した1例

富山大附属病院

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【緒言】 血球貪食症候群 (HPS) は網内系におけるマクロファージの増殖と血球貪食を著明に認め、臨床症状として発熱、汎血球減少、DIC、高フェリチン血症など感染・悪性腫瘍などの基礎疾患を背景とする二次性が発症の大半を占めるとされる。今回、進行卵巣癌に対する化学療法中に血球貪食症候群を発症した症例を経験したので報告する。【症例】 39歳女性。肝転移を伴う卵巣癌IVB期に対し腫瘍減量術および術後化学療法を施行した。cTC、Gem+CBDC A+Bev、リボソーマル化ドキシソルピシン、CPT11+CDDP、オラパリブ等の治療を経るも、肝転移病巣は増大し、有効な治療なくETP(75mg/日)内服開始とした。内服15日目に38.3℃の発熱、全身倦怠感のため受診した。Hb: 5.1g/dL、血小板: 1.1万/μL、CRP: 33.34mg/dLにて感染症を念頭に抗菌薬(TAZ/PIPC)開始、DICと診断し抗DIC治療を開始した。赤血球輸血により貧血の改善を認めたが血小板の回復は見られず、さらに第3病日に好中球減少(60/μL)出現し、ETPによる骨髄抑制を考えフィルグラスチムを開始、血小板輸血を継続したが、汎血球減少の改善を認めなかった。フェリチンの高値(8235ng/dL)も認めたため、HPSを疑い第7病日に骨髄穿刺を施行した。血球貪食像を認め、HPSと診断し、ステロイド投与(PSL1gを3日間のうち40mg/日継続)を開始した。その後速やかに血球回復を認め、第15病日に在宅看取りの希望にて自宅退院となった。【結語】 HPSに関連する悪性腫瘍の3%が固形腫瘍であり、卵巣癌合併は非常に稀なケースである。悪性腫瘍の化学療法中に遷延する汎血球減少を認めた場合はHPSを除外診断として念頭に置き骨髄穿刺、治療を進めていく必要があると考えられた。

P-13-2 denovoに発生したリンチ症候群の再発卵巣癌に対してペムプロリズマブが著効した一例

奈良県立医大附属病院

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【緒言】 リンチ症候群 (LS) はミスマッチ修復遺伝子の生殖細胞系列変異を原因とする常染色体優性遺伝性疾患である。LSの卵巣癌の累積生涯発生率は6.1~13.5%と、大腸癌、子宮体癌に続き頻度が高い。今回、我々はdenovoに発生したリンチ症候群の再発卵巣癌に対してペムプロリズマブが著効した一例を経験したので報告する。【症例】 35歳女性、0妊0産。背部痛を主訴に近医を受診、CTで左水腎症とで骨盤内腫瘍を指摘され当科に紹介された。MRIで6cm大の左卵巣腫瘍と骨盤内リンパ節の腫大を認めた。CA-125 419U/mL、CA19-9 219U/mLと高値であった。卵巣癌根治術、左尿管部分切除、左尿管新吻合を実施し、IIIA1(ii)期(pT2bN1bM0, endometrioid carcinoma G3)と診断した。術後、TCを行ったがPTXアレルギーのため、DCを2サイクル行った。CTで肝転移、播種病変による直腸浸潤、傍大動脈リンパ節転移などを認め、再発卵巣癌と診断し、PLD+Bevに変更した。3サイクルの投与を行うもPDと判定し、GEMに変更した。GEMの2サイクル目で輸血を要する下血が出現し、大腸内視鏡検査で直腸内に腫瘍が露出していた。がんパネル検査でMSI-Highが判明し、ペムプロリズマブ200mgを3週間毎の投与を開始した。1サイクル後より下血は改善した。3サイクルの投与後にCT検査で肝転移病変やリンパ節転移の縮小を確認し、7サイクル投与後に大腸内視鏡検査で腫瘍消失を確認した。再発から12か月経過したが増悪なく経過している。【結論】 再発卵巣癌は予後不良であるが、ペムプロリズマブが著効した一例を経験した。長期予後が見込める可能性があり、今後はLS関連腫瘍のサーベイランスも重要である。今後の症例の蓄積が待たれる。

P-13-3 腫瘍減量術と術後化学療法により神経症状の改善が見られた、抗 Yo 抗体陽性の傍腫瘍性神経症候群を伴う進行卵管癌の一例

熊本大学病院

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【緒言】傍腫瘍性神経症候群 (Paraneoplastic Neurological Syndrome ; PNS) は担瘤患者で自己免疫学的機序により惹起される神経障害である。抗 Yo 抗体による PNS は婦人科癌や乳癌で見られ、亜急性の小脳失調症状を呈する。治療は抗腫瘍療法や免疫療法が行われるが、一般に治療抵抗性であり神経学的予後は不良である。今回われわれは、可及的な腫瘍減量術と術後化学療法により神経症状の改善が見られた抗 Yo 抗体陽性の PNS を伴う進行卵管癌の一例を経験したので報告する。【症例】40 歳未妊女性。6 か月前からのめまいと 2 週間前からの進行する小脳失調症状のため神経内科に入院となった。頭蓋内に器質的異常はなく、免疫グロブリン静注療法・ステロイドパルス療法が施行されたが症状は進行し、入院 3 週間後には臥床状態、意思疎通困難となった。造影 CT で両側卵巣腫大と多発リンパ節腫大が見られ、血清 CA125 高値 (187U/mL)、抗 Yo 抗体陽性であったため、卵巣がんに伴う PNS が疑われ当科紹介となった。入院 1 か月後に開腹腫瘍減量術 (減量率 60%) が行われ、卵管癌 IVB 期 (組織型：高異型度漿液性癌) の診断で術後 TC 療法 (パクリタキセル+カルボプラチン) が施行された。3 コース後には残存病巣は著明に縮小し CA125 は基準値内に低下した。神経症状も改善し座位保持や意思疎通が可能となった。現在も TC 療法を継続中である。【結語】抗 Yo 抗体陽性の PNS では腫瘍の完全摘出後も症状の改善は乏しかったとの報告が散見されるが、今回、可及的な腫瘍減量術と術後化学療法により神経症状の改善が得られた症例を経験した。

P-13-4 小腸通過障害を呈した卵管絨毛癌の一例

青梅市立総合病院

栗原大地, 伊田 勉, 野間友梨子, 齋藤 緑, 小泉弥生子, 郡 悠介, 立花由理, 大吉裕子, 小野一郎, 陶守敬二郎

【緒言】卵管原発の絨毛癌は極めて稀であり、絨毛性疾患の中でも悪性度が高く、病初期から肺や肝臓、脳への血行性転移をきたしやすい。今回、術前の CT で小腸浸潤を疑い、小腸合併切除により腫瘍摘出を行った一例を経験したため報告する。【症例】41 歳、3 妊 2 産 経産分産歴が 2 回、自然流産が 1 回あった。月経周期は整で、不正性器出血はなかった。性交渉はあったが、明らかな妊娠歴は、16 年前の自然流産が最後だった。最終月経から 3 週 2 日、嘔気と下腹部痛を自覚し、妊娠反応陰性を確認後、近医を受診した。単純 CT で、子宮から連続する腫瘍が認められた。子宮筋腫の変性痛を疑われ経過観察となったが、症状が持続するため 9 日後に再受診した。血中 hCG は院内上限以上と高値を認め、造影 MRI では腫瘍は増大し、内部不均一で辺縁に強い造影効果を認めた。4 日後に当科紹介となり、初診時の血中 hCG 値は 76 万 mIU/ml で、造影 CT で腫瘍は 7cm と増大傾向を認めた。腫瘍と接する部分の腸管は拡張し、腫瘍による小腸イレウスが疑われた。骨盤外に遠隔転移を認めなかった。絨毛性疾患を疑い緊急入院とし、翌日にイレウス解除および診断確定目的に手術を施行した。腫瘍は左卵管に発生し、広範囲で小腸と接していた。剥離不可能な箇所を認めたため、左卵管切除術と小腸切除を併施した。残存腫瘍は認めなかった。病理診断で絨毛癌と診断され、小腸平滑筋層までの浸潤を認めた。術後より EMA-CT 療法を開始し、現在継続中である。【結論】小腸浸潤をきたした卵管原発の絨毛癌を経験した。hCG 異常高値を伴う卵管部腫瘍の評価には、異所性妊娠との鑑別や腫瘍増大、浸潤の評価において、繰り返しの画像検査が有用である。

P-13-5 ホルモン療法中のチョコレート嚢腫に卵巣癌を発症した 3 例

千葉大附属病院

大塚聡代, 楯 真一, 松岡 歩, 錦見恭子, 生水真紀夫

【緒言】チョコレート嚢腫に対して、保存的治療としてホルモン療法を行うことが多い。ホルモン療法によって、癌化を抑制できるかは不明である。今回、ホルモン療法中に卵巣癌を発症したチョコレート嚢腫の 3 例を経験したので報告する。【症例】症例①51 歳 47 歳から 8cm の右チョコレート嚢腫に対してジェノゲスト内服開始した。ジェノゲスト投与開始から 1 年 5 か月後には 4cm に縮小した。投与開始後 3 年 8 か月で左卵巣に 2cm の嚢胞が新出し、投与開始後 3 年 11 か月後で左卵巣嚢腫が 8cm に増大し、当科紹介。左卵巣に充実部分を認め、左卵巣癌の疑いで初回手術を施行したところ、Clear cell carcinoma, pT1cN0M0 であった。症例②37 歳 27 歳時に前医で 3cm の左チョコレート嚢腫を指摘され、経過観察していた。30 歳時に左チョコレート嚢腫は 4cm で、月経困難症が増悪し、低用量ピルの内服を開始した。内服開始 9 年後に腫瘍径は 5cm に増大し、充実部分を認めたため、当科に紹介。左卵巣癌の疑いで初回手術を施行したところ、左卵巣癌、Clear cell carcinoma, pT2N0M0 であった。症例③44 歳 42 歳時に前医で 2cm の右チョコレート嚢腫を指摘され、経過観察していた。1 年後に腫瘍径が 3cm に増大したため、ジェノゲストを内服開始した。内服開始 9 か月後に腫瘍径が 8cm に増大し内部に充実成分を認め、当科に紹介。右卵巣癌の疑いで初回手術を施行したところ、右卵巣癌、Clear cell carcinoma, pT1cN0M0 であった。【結語】ホルモン療法中にもチョコレート嚢腫から卵巣癌を発症する可能性がある。ホルモン療法中に発症した卵巣癌は早期発見できる可能性が高いと考える。

P-13-6 ゲムシタピン、ベバシズマブが奏功した卵巢低異型度漿液性癌の文献的考察を交えた症例報告

近畿大病院

佐藤華子, 小谷泰史, 松村謙臣

【緒言】低異型度漿液性癌は化学療法抵抗性であり、高異型度漿液性癌と比較すると確立した治療法がないのが現状である。ゲムシタピン、ベバシズマブが奏功した自験例と文献的考察を交えて報告する。【症例】初発は28歳、G0P0の未経産婦。卵巢腫瘍に対して、右付属器摘出+大網部分切除術を施行した。術後病理組織は浸潤性腹膜インプラントを伴う漿液性境界悪性腫瘍 IIIA 期の診断であり、今後の加療目的で当院に紹介となった。術後 TC 療法を3コース施行した (GnRHa 併用)。化学療法終了後 (術後4か月後) には左卵巢に再発を認め、根治手術として単純子宮全摘+左付属器摘出+大網全摘+骨盤内・傍大動脈リンパ節郭清術を施行した。術後病理組織は漿液性癌、pT3cN0M0であった。プラチナ抵抗性再発であり、DG 療法を開始したが、ドキシソルビシン塩酸塩初回投与時にアナフィラキシー症状を認め中止し、ノギテカンへ変更し3コース施行した。無病期間5年3か月が経過したが、CTで腹腔内播種を認め、再々発の診断となった。腹腔鏡下生検術を施行した病理組織は低異型度漿液性癌の診断であった。再発難治例であり Foundation one を提出し、NF1 や TP53 遺伝子変異を認めたが、MSI は陰性であり、治療には繋がらなかった。その後再度補助化学療法を検討したが、増大傾向を示す石灰化腫瘍と、それに伴うサブイレウスを認めたことから、再度手術の方針とした。腫瘍は小腸と強固に癒着しており、複数ある再発腫瘍のうちメインの腫瘍のみの摘出となった。術後ゲムシタピン、ベバシズマブを開始し、画像上サイズは横ばいだが、CA125 はピーク時145から17まで低下、正常化しており、一定の効果を認めている。

P-13-7 当院で経験した卵管上皮由来の Wolff 管腫瘍の1症例

西神戸医療センター

鈴木裕紀子, 森上聡子, 夏山貴博, 小菊 愛, 登村信之, 近田恵里, 佐原裕美子

【緒言】Wolff 管腫瘍は1973年に初めて報告された腫瘍であるが、現在まで90例弱の報告しかない非常に稀な腫瘍である。ほとんどの Wolff 管腫瘍は良性の経過をたどるとされているが、一部で転移や再発症例もあり、治療方針に一定の見解はない。今回我々は左卵管上皮由来の Wolff 管腫瘍の1症例を経験したので、画像や術中の特徴的な所見、文献的考察も加えて報告する。【症例】患者は41歳1経妊0経産の女性。突然の下腹部痛を主訴に当院救急外来を受診した。骨盤造影 CT 検査で左付属器捻転が疑われ当科紹介となった。疼痛は一旦軽減したが、骨盤 MRI で左付属器の充実性腫瘍の可能性が高いと判断し、後日腹腔鏡手術を施行した。術中初見は左卵管から発生する鶏卵大の充実性腫瘍であり、術中迅速病理診断は Wolff 管腫瘍もしくはカルチノイド腫瘍であったが確定診断には至らなかった。最終術式を左付属器、右卵管、大網切除術とした。最終病理診断では子宮間膜由来の Wolff 管腫瘍で、腹水細胞診は陰性であった。外来にてフォローしているが現在に至るまで再発の兆候はない。【結語】今回我々は左卵管上皮由来の Wolff 管腫瘍の1症例を経験した。Wolff 管腫瘍は稀な腫瘍であり、治療方針に一定の見解はない。また、画像診断や腫瘍マーカー、術中所見などから Wolff 管腫瘍と診断することも難しい。ほとんどの症例は良性の経過をたどるが、最近では再発や転移を来す症例報告が増えており11%が再発するという報告もある。本症例は未婚で未経産であり、妊孕能温存を希望されたため子宮と右卵巢は温存している。今後も注意深い経過観察が必要と考える。

P-13-8 プラチナアレルギー再発卵巢癌患者に、長期間リボソーム化ドキシソルビシンを投与することで病状が安定し、その後の脾摘により完全寛解が得られた1例

市立奈良病院

原田直哉, 延原一郎, 春田典子, 東浦友美, 藤井 肇, 山尾佳穂

【緒言】ドキシソルビシンでは心毒性から添付文章上の限界総投与量が500mg/m²とされ、同じアントラサイクリン系のリボソーム化ドキシソルビシン (PLD) も総投与量に関しては慎重にならざるをえない。今回、カルボプラチンにアナフィラキシーを起こしたため、レジメンを変更せざるをえなかったにもかかわらず、PLDの長期間投与で病状が安定し、その後の手術とあわせて完全寛解 (CR) が得られた再発卵巢癌患者について報告する。【症例】41歳、初回手術は子宮内膜症による広範囲の癒着と痛性腹膜炎のため、子宮、両側付属器、大網のみの切除となった (suboptimal, pT3cNxM0)。高異型度漿液性癌でシスプラチンの腹腔内投与と TC 療法9コースで CR となった。3年後に CA125 が上昇し、PET-CT で脾臓後面での再発を認め、TC を再開するも3コース目にアナフィラキシーを起し、以降、PLD9コースで CR となった。無治療とした8か月後に CA125 の再上昇があり PLD を再開した。直ちに CA125 は低下し、CT でも病変を確認できなくなったが、前回 PLD 中止により CA125 が上昇したことから、2年間投与を継続した。総投与量は1212.5mg/m²となったが、左室駆出率を含め心機能は保たれていた。投与継続中に CA125 が再上昇 (134U/mL) し、PET-CT にて脾臓内での単発の再発であったため、脾臓の摘出を行った。術後、ドセタキセルによる維持化学療法を3コース行い、2年を経過した現在、無治療で CR を維持している。【結語】初発は11年前であり、まだベバシズマブや PARP 阻害薬が導入されておらず、現在なら初回から異なった治療法となったであろうが、プラチナアレルギー再発卵巢癌症例に対して、心機能を評価しながらの PLD 長期投与は有用であったと考えている。

P-13-9 腹腔鏡下手術後に悪性腫瘍の診断に至った卵巣腫瘍の1例

山口県立総合医療センター

西本裕喜, 三輪一郎郎, 今川天美, 高崎ひとみ, 大谷恵子, 浅田裕美, 讃井裕美, 佐世正勝, 中村康彦

【緒言】腹腔鏡下手術は近年増加傾向にあり、良性卵巣腫瘍に対しては腹腔鏡下手術が第一選択とされる。しかし、良性腫瘍の診断で腹腔鏡下手術が行われ、術後に境界悪性または悪性腫瘍と診断される症例が存在する。今回我々は、術前診断が良性卵巣腫瘍であり、腹腔鏡下手術後に悪性腫瘍の診断に至った症例を経験したので報告する。【症例】72歳、女性。左下腹部痛を主訴に前医を受診し、25mm大の左卵巣腫瘍を認めたため、精査加療目的に当院紹介受診となった。MRI検査で線維腫または莢膜細胞腫が疑われた。腫瘍マーカーの上昇はなく、腫瘍径も小さいので経過観察の方針とした。約1年後のMRI検査で左卵巣腫瘍は37mm大に増大するも、明らかな悪性所見は認めず、腫瘍マーカーの上昇も認めなかったが、患者および家族が手術を希望したため、腹腔鏡下左付属器切除術を施行した。術後病理検査で卵巣漿液性腺癌と診断されたため、初回手術より約1か月後にStaging laparotomy（子宮全摘術+右付属器切除術+大網切除術+骨盤内・傍大動脈リンパ節郭清術）を施行した。悪性腫瘍の残存や転移は認めなかったため、卵巣癌IA期と診断した。術後3か月経過しているが再発は認めていない。【結論】卵巣腫瘍の手術では、術後に境界悪性または悪性腫瘍と診断される可能性があることを十分に説明したうえで術式を決定することが重要である。また、術中に悪性を疑う所見があれば、術中迅速病理検査や術式変更を考慮する必要がある。

P-14-1 術前診断で卵巣癌との鑑別が困難であった腹膜中皮腫の1例

市立岸和田市民病院

田坂玲子

腹膜中皮腫は悪性中皮腫の10-20%を占め、予後不良な疾患である。今回我々は卵巣癌との鑑別が困難であった腹膜中皮腫の1例を経験したので報告する。症例は40歳代女性。急激な腹部膨満を主訴に前医受診。CT・超音波検査にて骨盤内腫瘍・多量の腹水を認めたため当科紹介。腹水細胞診は陽性で腺癌疑い、骨盤MRIで子宮背側に13cm大の充実性腫瘤を認め、胸腹部CTでOmental cake、広範な腹膜播種像を認め、うち横隔膜下病変は横隔膜を超えて胸腔内に浸潤・腫瘤形成が見られた。同部位以外の胸部病変は認めず、卵巣癌疑いで試験開腹術を施行した。術中所見で骨盤内腫瘍は子宮・右付属器・直腸・S状結腸を含む周囲臓器と一塊となっており左卵巣が確認できなかったため、卵巣癌疑いで一期的摘出は困難と判断し、大網腫瘍の生検に止めた。術後6日目に病理結果が判明し二相性中皮腫の診断であったため当院腫瘍内科へ紹介。ペメトレキセド・カルボプラチン療法5コース施行時点でSDを維持していたが、手術治療希望にて他院へ転院された。腹膜中皮腫は約20%で腫瘤形成型であり、女性では卵巣癌との鑑別が問題となる。腹水中のヒアルロン酸や腹水細胞診が診断に有用なこともあるが、術前細胞診での正診率は12.5%と低く、精度向上のためセルブロック作成・免疫染色が勧められている。悪性中皮腫は石棉暴露から30-40年の歳月を経て発症するが、1960年代の石棉輸入量の増加した時期を反映し近年急増している。石棉が完全使用禁止となったのは2004年で石棉関連健康被害は今後も当面増加が予想されており、粘稠度の高い腹水貯留を伴う癌性腹膜炎像を見た際の鑑別診断として中皮腫も念頭に置く必要があると考える。

P-14-2 卵巣癌に対する遺伝子パネル検査でリンチ症候群が疑われた1例

大分大

西田正和, 須奈家栄, 甲斐健太郎, 青柳陽子, 河野康志

【目的】がんゲノム医療とは、多数の遺伝子を同時に調べ、遺伝子変異に対し、臓器縦断的に治療を行う医療である。今回、標準治療後の治療薬探索のため、遺伝子パネル検査 (FoundationOne[®] CDx がんゲノムプロファイル検査) を行ったところ、MLH1の遺伝子異常を指摘され、リンチ症候群を疑われた症例を経験した。【症例】58歳、3妊2産、家族歴に特記事項なし。卵巣癌 (類内膜癌) 1c (b) 期の診断で、一次最大腫瘍減量術後TC療法を行い、2年1か月無病生存していたが、直腸RS領域に再発を認めた。二次最大腫瘍減量術後にTC療法を6コース施行し、完全寛解となった。さらにその5年後、肺転移を指摘され、再度TC療法中に遺伝子パネル検査を希望され当院を紹介された。がんゲノムレポートではMLH1 c.1897G>Aという結果で、「当該変異はスプライシング異常を引き起こすことが予想され、機能欠失変異である可能性が高く、遺伝カウンセリングを推奨する」とのコメントであった。クライアントにリンチ症候群の可能性について説明し、MSHの免疫染色を行ったところ、MSH1、2の発現が認められリンチ症候群は考えにくいとのコメントであった。【考察】遺伝子パネル検査の普及に伴い、予想外に遺伝性の腫瘍が指摘されることを経験する。今回、家族歴はなくMSIもstableであったが、遺伝子パネル検査ではMSH1遺伝子の異常を指摘された。今回、germ lineの検査による確定診断はつけていないが、免疫染色でリンチ症候群の可能性は低いと結論付けた。しかしクライアントに対して消化管の検査は意識して受けるよう指導を行った。遺伝子パネル検査の普及により類似の症例が増えていくことも考慮しておく必要がある。

P-14-3 腹腔鏡下子宮全摘術・リスク低減卵管切除術後1年後に発症した卵巣原発 high-grade serous carcinoma の1例

岐阜市民病院

桑山太郎, 山本和重, 豊木 廣, 平工由香, 柴田万祐子, 谷垣佳子, 尹 麗梅, 相京晋輔, 栗原万友香, 林 佳奈, 釣餌咲希

【緒言】一部の上皮性卵巣癌の発生母地が卵管采の上皮細胞を起源とするメカニズムが示唆されており、良性疾患の子宮全摘術の際に卵管切除を行うことで卵巣癌の発症予防につながる可能性が期待されるが、その有効性を示した報告は乏しい。今回我々は、腹腔鏡下子宮全摘術・リスク低減卵管切除術を行い、術後1年で発症した卵巣原発 high-grade serous carcinoma を経験したため報告する。【症例】初診時45歳。1経妊1経産。20XX年12月に過多月経主訴に受診した。画像検査で多発子宮筋腫を認め、過多月経の原因と考えられた。術前偽閉経療法の後に、腹腔鏡下子宮全摘術を行う方針とした。また、卵巣癌予防のための両側卵管切除術についても説明を行い書面で同意を得た。20XX+1年9月に腹腔鏡手術を行い、術後病理結果は良性の子宮筋腫の像で、切除した卵管にも悪性像は認めず一旦終診となった。20XX+2年8月に腹部膨満のため内科受診となり、CTで右卵巣腫大・腹水貯留・腹腔内播種病変を認め、卵巣癌の疑いのため再診となった。腹水細胞診で腺癌の所見を認めたため、卵巣癌もしくは腹膜癌の疑いで術前化学療法を行ったが、20XX+2年11月に癒着性イレウスを発症したため緊急手術を行った。手術は外科医師により癒着剝離を行った後に両側の卵巣と大網の切除を行った。術後病理結果は右卵巣原発の high-grade serous carcinoma の所見で大網にも2cmを超える播種結節を認め、卵巣癌 IIIC 期と診断し術後補助化学療法を行った。また、BRCA は陰性であった。【結語】リスク低減卵管切除術により卵巣癌発症のリスクを低下させる可能性があるが、卵巣温存症例では常に卵巣癌発症を念頭においたフォローが必要であると考えられる。

P-14-4 術後5年以上経過した後に晩期再発をきたした卵巣明細胞癌の2例

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卵巣癌の再発の95%は4年以内に発生し、5年以上の無病生存期間後の晩期再発は稀である。今回、術後5年以上経過した後に卵巣明細胞癌の再発と診断した症例を経験したため報告する。【症例①】57歳、0妊0産。10年前に卵巣癌に対して手術療法を施行した。明細胞癌 IIc 期であり、術後 TC 療法を7コース施行した。術後7年の時点では再発所見は認めなかったが、以降は自己判断にて定期受診を中断していた。術後10年目に多発脳梗塞による右不全麻痺を発症した。CTにて腹腔内腫瘍と腹水貯留を認め、腹水のセルブロックにて卵巣明細胞癌再発と診断した。腫瘍随伴性高カルシウム血症ならびに Trousseau 症候群を認め、加療を行ったが、入院15日目に突然の呼吸困難、意識レベルの低下、血圧低下を認め、肺梗塞、DICにて死亡した。【症例②】55歳、2妊2産。5年前に卵巣癌に対して手術療法を施行した。IC1期であり、TC 療法を4コース施行した。術後6年目のフォロー目的のCTにて肺右下葉に腫瘍を認めた。原発性肺癌が疑われ胸腔鏡下肺葉切除が施行されたが、術後の組織学的検索で卵巣明細胞癌の再発と診断した。術後 TC 療法を3コース施行し、現在はオラパリブにて維持療法を行っている。TC 療法終了後2か月経過しているが、再発徴候は認めていない。卵巣癌は腹膜播種やリンパ節転移という再発形態が多いが、今回のように、原発性肺癌を疑うような肺結節や、不全麻痺を契機に発見される場合等、多様な再発形態を取ることもある。また、初回治療後5年以上経過した後の晩期再発も稀ではあるが起りうるため、典型的な再発形態にとらわれずに、常に再発の可能性を念頭に置いて、長期的なフォローアップが必要と考えられる。

P-14-5 子宮頸部細胞診で adenocarcinoma を繰り返し指摘され、腹腔鏡下手術により卵管癌および漿液性子宮内膜上皮腺癌 (SEIC) と診断された1例

市立貝塚病院

廣瀬陸人, 市川冬輝, 倉橋寛樹, 菊池香織, 黒田実紗子, 甲村奈緒子, 田中あすか, 小笹勝巳, 増田公美, 横井 猛

【緒言】子宮頸部細胞診 (CC, cervical cytology) で異常を認める場合組織診や画像診断による精査が必要だが、CC 以外の異常を認めない場合に治療を行うべきかどうかのコンセンサスは確立されていない。今回 CC で adenocarcinoma を繰り返し指摘され、腹腔鏡下子宮全摘を施行した結果卵管癌および漿液性子宮内膜上皮腺癌 (SEIC) と診断された1例を経験したので報告する。【症例】58歳2妊2産、X-3年CCでadenocarcinomaを指摘。MRI、コルボスコピー下生検や子宮内膜全面搔把を行うも異常所見を認めなかった。診断目的に手術を提示したが、セカンドオピニオンの結果も踏まえ経過観察を行う方針とした。CCを繰り返し施行した結果adenocarcinomaを再度指摘され手術を希望された。X年1月腹腔鏡下子宮全摘、両側付属器切除を施行した。病理組織学的診断は卵管癌 High grade serous carcinoma, IC3期およびSEICだった。追加治療として Staging laparotomy を施行しリンパ節転移を認めなかった。術後補助化学療法として TC 療法を3サイクル施行した【考察】CCで悪性腫瘍を疑うも精査で異常を認めず診断的手術で卵管癌およびSEICと診断された症例を経験した。当院で2016年4月～2021年3月の間に組織学的に卵巣癌・卵管癌・腹膜癌と診断された103例のうち術前のCCで腺細胞系異常を指摘されたのは6例(5.8%)あった。文献的には卵巣癌のCC陽性率は15.7%、子宮内膜細胞診の陽性率は25.6%と報告されている。CCで腺細胞系異常が指摘され組織診や画像診断で異常所見を認めない場合、稀ではあるが付属器悪性腫瘍を鑑別に挙げ、場合によっては診断的手術による検索が考慮される。

P-14-6 腹腔鏡下仙骨腔固定術後に卵管癌が判明した1例

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【緒言】骨盤臓器脱に対する腹腔鏡下仙骨腔固定術(LSC)は増加している。今回LSCの際に切除した卵管から偶発的に漿液性癌が判明した一例を報告する。【症例】62歳, 5妊3産, 50歳閉経, 特記すべき既往歴, 家族歴はない。下垂感, 尿失禁を主訴に前医受診。骨盤臓器脱POP-QstageIIIの診断で保存的治療を行っていたが, ベッサリーによる性器出血, 膿性帯下を認め, LSC(子宮腔上部切断, 両側卵管切除)を施行した。術前の経陰超音波とCTでは異常を認めていなかった。腹腔鏡所見では両側付属器に腫瘍性病変は認めなかった。術後病理組織診断で片側卵管に2mm大のHGSCを認めた。術後の造影CT, FDGPET/MRIではリンパ節腫大や遠隔転移の所見はなかった。卵管癌不完全手術後に対し, LSC後80日にステーピング手術(両側卵巣摘出+子宮頸部摘出+大網切除+骨盤・傍大動脈リンパ節生検+メッシュ除去術)を施行した。子宮頸部と膀胱間のメッシュの癒着が強固であったため膀胱を損傷したが, 縫合修復し手術を完遂した。骨盤臓器脱に対してはshull法を追加した。摘出した全ての組織には腫瘍の所見を認めず, 最終診断は卵管癌IA期, HGSCであった。術後補助化学療法としてTC療法を施行中で, 再発徴候は認めない。【考察】良性疾患に対する子宮摘出時に卵管切除を追加するケースが増加しているが, 偶発的に摘出卵管からがんが発見される可能性を考慮する必要がある。特に, LSC後は癒着により追加手術を行う際他臓器損傷リスクがあり, 慎重な対応が求められる。

P-14-7 プラチナ抵抗性再発卵巣癌に対してプラチナ製剤を再投与し奏功した2症例

岡山大病院

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【緒言】進行卵巣癌はプラチナ製剤を含む多剤併用療法に当初効果を認めても, 多くはプラチナ抵抗性となり治療に難渋する。今回, プラチナ抵抗性再発卵巣癌に対しプラチナ製剤を再投与し奏功した2症例を経験したので報告する。【症例1】73歳女性。卵巣癌IVB期 High grade serous carcinoma (HGSC)に対し tri-PTX+CBDC (TC)療法を開始した。膀胱転移があり, 今後のQOLを鑑み, Interval debulking surgery (IDS)は施行せずTC療法8コースを施行した。2か月後再発し, プラチナ抵抗性再発として単剤療法を10か月間施行した。全身状態良好のため, 再度プラチナ製剤を含む weekly DTX+NDP療法を行った。CA125の推移やCTより奏功と判断し, ニラパリブ内服維持療法へと移行した。【症例2】44歳女性。卵巣癌IVA期HGSC, BRCA1病的バリエーションの症例に対しPTXアレルギーのため, GEM+CBDC (GC)療法を施行した。5コース終了後, IDSを施行し, 8コース施行後, 維持療法としてオラパリブ内服を開始したが, GC終了後3か月で再発した。プラチナ抵抗性再発として単剤療法を5か月間施行した後, 全身状態良好であり weekly CBDC療法を開始した。4コースで終了となったがCA125値とCTにて腫瘍制御を確認できた。【考察】プラチナ抵抗性再発卵巣癌にプラチナ製剤を再投与し奏功した。文献的考察でもプラチナ抵抗性再発にプラチナ製剤の再投与が奏功した報告は散見される。2例目はBRCA1病的バリエーション陽性例であり, プラチナ製剤の再投与が奏功した一因になる可能性がある。【結語】標準治療終了後に全身状態が良好であればプラチナ製剤の再投与を試みることは一考に値する。

P-14-8 膣と膀胱に転移を来した原発性腹膜癌肉腫の1例

神戸市立医療センター西市民病院

田辺昌平

原発性腹膜癌肉腫は過去に40例しか報告が無い極めて稀な疾患である。今回我々は原発性腹膜癌肉腫が膣と膀胱に転移を来した初の症例を報告する。患者は51歳の女性で妊娠歴はG0P0, 既往歴にリウマチ関節があった。腹水貯留のため前医から当院に紹介され, 腹水細胞診で腺癌を認めた。MRIではomental cakeを, CTでは膣と膀胱に腫瘍性病変を認めた。当院受診から9日目に審査腹腔鏡を行い, 大網が腫瘍に置換されている状態を認めた。大網と膣を生検して癌肉腫を認め, 腹膜原発癌肉腫と診断した。TC療法を開始したが治療は奏功せず, 腸閉塞が進行した。当院受診から50日目に腸閉塞解除を目的として小腸部分切除術+子宮摘出術+両側付属器摘出術を施行したが手術終了時に血圧が低下した。そのまま全身状態が悪化し, 当院受診から51日目に原病死した。病理解剖を行うと, 膣尾部の病変は膀胱の皮膜から浸潤しており, 病理所見から癌肉腫と診断された。子宮と両側付属器には病変をみとめなかった。よって, 腹膜原発癌肉腫による膣と膀胱転移と診断した。すでに多発転移を来している原発性腹膜癌肉腫の症例は, 抗癌剤にも治療抵抗性を示し, 急速に進行して予後不良だった。

P-14-9 子宮内膜症, 異型子宮内膜症, 類内膜癌を同時に認めた腹膜癌の1例

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【目的】今回我々は子宮内膜症, 異型子宮内膜症, 類内膜癌を同時に認めた腹膜癌の1例を経験したため報告する。【症例】49歳女性, 4妊3産。42歳時に子宮腺筋症と子宮内膜症に対し腹式単純子宮全摘術, 左付属器摘出術, 右卵管摘出術を施行した。術後よりジェノゲストの内服を開始しフォローしていたが, ジェノゲスト開始9か月後より通院は自己中断された。49歳時に下腹部痛にて受診, 入院管理となる。血清クレアチニンの上昇とMRI検査にて左水腎症, 骨盤内に右卵巣腫瘍を疑う単胞性嚢胞性腫瘍, 骨盤内左側に分葉上腫瘍, 左骨盤リンパ節腫大を認めた。希少部位子宮内膜症の悪性転化を疑い, 腫瘍摘出術の方針とした。腫瘍は後腹膜腔から発生し, 左尿管を巻き込むように発育していた。右卵巣腫瘍摘出, 左後腹膜内腫瘍摘出, 左骨盤リンパ節摘出を行い手術終了した。病理検査は日本病理学会コンサルテーションシステムにてEndometrioid carcinoma, well differentiated in endometriosis, retroperitoneumと診断され, 術後はパクリタキセル, カルボプラチン, ペバシズマブにて現在も化学療法中である。BRCA1/2遺伝学的検査では陰性だった。【結論】子宮内膜症術後7年後に後腹膜に類内膜癌を認めた症例を経験した。今回の手術検体では子宮内膜症, 異型子宮内膜症, 類内膜癌を認め, 子宮内膜症から異型内膜症を経て類内膜癌への進展を示唆する過程を同一検体で認められた。今後は遺伝学的検討を行い発生過程のより詳細な背景を明らかにする。

P-15-1 当科にて腹腔内器具遺残の有無を確認するために施行した術後腹部レントゲン画像の検討

高の原中央病院

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【目的】腹腔内に手術器具やガーゼの遺残の有無を確認するために, 術後の腹部Xp撮影を行うことは有用である。しかし石灰化した構造物や過去の手術のクリップなどを認めることがあり, その鑑別に苦慮することがある。今回我々は術後に撮影した腹部Xp画像を検証し, その効果的な方法について検討したので報告する。【方法】2019年1月より2021年6月までの間に当科でおこなった897例(腹腔鏡下手術819例, 開腹, 腔式手術78例)に対して, 術後腹部Xp撮影を行い, 腹腔内の手術器具やガーゼ遺残の有無を確認した。【成績】897例中, 破損も含めた金属製の手術器具やガーゼの遺残を認めたものはなかった。静脈結石を254例に認め, 造影剤の遺残は69例に認めた。静脈結石以外の微小な石灰化した構造物は, 78例に認めた。過去の手術によるクリップ等の構造物を11例に認めた。1例に術中バイポーラー鉗子の破損(金属製ではないパーツ)を認め, 腹腔内を検索したが発見できず, 術中Xpを撮影するも発見できなかった症例を経験した。【結論】今回の検討で, 手術を行った897例中, 金属製の手術器具やガーゼの遺残はなかったが, 微小な石灰化した構造物が手術器具の破損の一部かどうか迷う症例を経験した。入院時の腹部Xp撮影があれば鑑別が可能と思われるが, 特に挙児希望のある女性に対しては可能な限りXp撮影を減らしたい。そのための方針として①腹腔内に針やガーゼの挿入がなかった場合は術後Xp撮影を省略する。②腹部手術の既往歴のある症例は入院時に腹部Xp撮影をする。③破損しやすい手術器具は術直前にビデオ撮影しておく。これらの方法により, 安全を担保しながらXp撮影を可能な限り減らせるのではないかと考える。

P-15-2 多施設共同研究による内視鏡手術データベース構築について

Gyne-storage JAPAN

竹中 慎, 小池勇輝, 小田嶋俊, 島田佳苗, 太田 創, 小林光紗, 長船綾子, 大木規義, 松本光司, 田部 宏

【目的】手術は低侵襲化が進み高度な手技習得が必要になる一方, 産婦人科医は不足している。各医師は医療の質の担保をしつつ増加した仕事量をこなす必要がある。この課題を解決するため, 2020年9月より術者情報や臨床データなどを組み合わせた手術データベース「Gyne-storage JAPAN」の構築を開始した。データベースの利活用で創出されたプロダクトにより, 産婦人科医は効率的な手術手技の習得が可能となることが期待される。【方法】アカデミアを中心に全国45施設に協力依頼し, 単純子宮全摘出術, 子宮筋腫摘出術, 卵巣腫瘍摘出術, 仙骨腔固定術, 子宮悪性腫瘍手術の6術式, 腹腔鏡だけでなくロボット支援下手術も含めて手術動画を収集した。また手術時間, 出血量などの「手術データ」, 筋腫サイズなどの「臨床データ」, 医師年数, 技術認定医有無など「術者プロフィール」, MRIなどの「医療画像データ」を収集し, 体外情報にモザイク処理を行い, 各術式の工程情報のアノテーションも行った。【成績】合計733症例(単純子宮全摘出術502例, 子宮筋腫摘出術15例, 卵巣腫瘍摘出術15例, 仙骨腔固定術17例, 子宮悪性腫瘍手術143例, そのうちロボット支援下手術146例)のデータベースを構築した。また全例に体外モザイク処理を行い, 200症例に手術工程情報を付加した。【結論】今後はデータベースを活かし, 人工知能を用いた術中の臓器認識や手術工程認識などの情報支援内視鏡外科手術システムの開発を進める。また研究機関, 学会, 医療機器開発企業など, 様々な部門でデータベースの利活用が行われて, 手術教育, データ解析研究, 医療機器開発が進み, 世界に向けて様々なプロダクトが発信されることを目指す。

P-15-3 サージカルスモーク中のヒトコロナウイルス RNA の検出についてのモデル実験

関西医大附属病院

横江巧也, 北 正人, 久松洋司, 岡田英孝

【目的】手術器具から発生するガス状の副産物は、総称して「サージカルスモーク」と呼ばれ、ウイルスを患者から手術チームに伝播させる危険性がある。婦人科手術では子宮頸部円錐切除や、腹腔鏡手術の経腔搬出の際に問題になり得る。しかし、手術の煙による SARS-CoV-2 感染のリスクを評価するための十分な根拠は存在しない。モデル実験を用いて、サージカルスモーク中のヒトコロナウイルス RNA の存在と感染性を示し、手術用マスクによるウイルスの除去効果を評価した。【方法】Human coronavirus 229E を感染させた培養細胞塊に対し、電気メスと超音波メスによる切開を施行した。サージカルスモークを吸引し液体に吸着させ、PCR によりウイルス RNA を定量、プラークアッセイにより感染性を判定した。さらに、手術用マスクによるウイルス RNA をろ過する能力を評価した。【成績】このモデルでは、切開対象に含まれるウイルス RNA の $1/10^6 \sim 1/10^2$ が、採取したサージカルスモーク中から検出された。電気メスの煙のウイルス量は、4 日間の培養で $1/10^2$ に減量、超音波メスのそれでは 200 倍に増加した。また、手術用マスクでサージカルスモークをろ過することで、ウイルス RNA の量を 99.80% 以上減少した。【結論】外科手術の煙にヒトコロナウイルスは存在し、その感染力は細胞変性を起こすことができない程度にまで低下した。電気メスの熱はウイルスを不安定化させる可能性、超音波メスでは感染力を持つウイルスが飛散し、感染防御を要する可能性が示唆された。モデル実験において、サージカルスモーク経由の SARS-CoV-2 を含むコロナウイルスの感染防御には、通常の手術用マスクで十分な防御効果が得られると考えられた。

P-15-4 SDGs を考慮した吊り上げ単孔式腹腔鏡手術

京都桂病院¹, 大阪赤十字病院²岩見州一郎¹, 下地 彩¹, 宗方紀子¹, 家村洋子¹, 水津 愛¹, 中川江里子²

SDGs は持続可能な開発目標である。2015 年の国連サミットにおいて採択され、2030 年までに誰ひとり取り残さない社会の実現を目指し、17 のゴールと 169 のターゲットから構成されている。最近、医療分野でも SDGs への取り組みが散見されるようになってきている。当科では、患者の健康だけでなく、環境や教育への取り組みも重要視しており、可能な症例に対しては脊椎麻酔下吊り上げ法で環境に配慮した単孔式腹腔鏡手術を行っているので紹介する。近年の腹腔鏡は高価な機器や多くの単回使用品が必要であり、高コストで医療廃棄物が多い。環境に優しい手術をしようとすると開腹手術などに逆戻りすると思われがちだが、工夫すれば低侵襲かつエコロジックな手術は可能である。腹腔鏡での環境に対する懸念は、温室効果ガス排出と医療廃棄物増加である。CO₂ の温室効果は周知の事実であるが、吸入麻酔薬はそれ以上に温室効果が強いとの報告がある。トロッカーやエネルギーデバイスの殆どは単回使用で医療廃棄物増加に繋がる。当科では、症例を選択して脊椎麻酔下吊り上げ単孔式腹腔鏡手術を行っているが、温室効果ガスの排泄はなく、単回使用品はスマートリトラクター[®] (トッパ製) のみと医療廃棄物は気腹法に比べ大幅に減らすことが可能である。術前に手術法だけでなく麻酔法・使用機器まで検討することが重要で、その結果、低侵襲かつエコロジックな手術が出来る。術後フィードバックも重要で、これらを繰り返し行うことで新しい方法が生まれる場合もあり、それらは SDGs に掲げられている教育の一環である。全症例で本術式を行うことは難しいであろうが、癒着が軽度な良性子宮・付属器疾患などでは可能であると考えられる。

P-15-5 Plus One Seminar 2021 ③~ICT を駆使し実現できた 10 大学での遠隔腹腔鏡教育トレーニング~

岡山大病院

久保光太郎, 入江恭平, 松岡敬典, 依田尚之, 岡本和浩, 櫻野千明, 牧 尉太, 光井 崇, 長谷川徹, 衛藤英理子, 早田 桂, 増山 寿

【目的】腹腔鏡手術の習熟には、ドライボックスによるトレーニングが必須である。より多くの若い先生に腹腔鏡に興味を持ってもらうために教育セミナーを定期的に行ってきた。しかし、近年のコロナ禍の影響で遠隔地から多数の先生を招いてのセミナー開催が難しくなっていた。今回我々は、ICT (Information and Communication Technology) を駆使して 10 大学合同でドライボックスを用いた腹腔鏡セミナーを施行した。【方法】学生・初期研修医を対象にして当大学より 10 大学へ遠隔配信を行い、腹腔鏡教育トレーニングを実施した。各大学にはそれぞれ指導医となる窓口教員の先生を事前に依頼し、各大学に配置したドライボックスで種々のタスクを行ってもらった。各大学のボックスに設置したカメラから画像を受け取り、それぞれのドライボックス画像をリアルタイムで観察しながら各大学とコミュニケーションを取って指導を行った。【成績】33 名の参加者がセミナー修了後にアンケートに回答した。15 名が学生、18 名が初期研修医であった。5 段階評価で満足度は平均 4.7、難易度設定は 2.9 と、適度な難易度で満足度は高い結果となった。80 分のセミナーであったが、時間もちょうど良いと 93.9% が回答した。問題点としては、ドライボックスの画像を通信する必要があったため、実際に操作している画面と若干のタイムラグが生じたことが挙げられた。【結論】ICT を駆使することで、遠隔地とコミュニケーションを図りながら人の流れを最小限に抑えてドライボックストレーニングを実施できた。この経験は今後も移動が難しい遠隔の他大学の交流などにも応用でき、より教育の裾野を広げることが可能となると考えられた。

P-15-6 リクルートはゴールではなくスタートである～WIND（北海道大学産婦人科）の次なる一手～

北海道大

井平 圭, 金野陽輔, 加藤達矢, 渡利英道

【背景】北海道大学産婦人科は2008年に法人化され、現在は一般社団法人WINDとして北海道の女性医療を守るために若手医師のリクルートと教育に力を注いできた。初期臨床研修における再必修化を受け、リクルートにアウトカムを求めずに必修科としての責任を果たそうと取り組んできた結果、産婦人科の魅力が学生や研修医に伝わり、ここ数年は専攻医登録数が安定して推移している。一方で、自身の成長に行き詰まりを感じる専攻医、種々の理由により休職が必要になる専攻医が存在する。【目的】WINDにリクルートした専攻医に対し、よりよい研修を提供するために、精神的なフォローも含む包括的な関りを行う。【方法】若手医師を中心としたコミュニティを設立し、日常抱える不安や悩みを共有する場を提供した。また、専攻医が現在の研修をどう評価しているかを明らかにするためにWINDに所属する専攻医にアンケート調査を実施した。アンケート調査は無記名とし、google formを用いた。【成績】専攻医アンケートの回収率は85.7%（18/21例）であった。ほとんどの専攻医は自身の研修に満足感を感じていたが、6割が自身の成長に不安を感じたことがあると回答した。また、3割の専攻医は、治療方針などの相談を上司にしにくいと感じたことがあると回答し、若手中心のコミュニティは精神的な支えになる可能性があるという回答したのは全体の8割であった。【結論】浮かび上がった研修の問題点を、実際の改善に導くまでの方法や手段には課題が残るが、若手医師を中心としたコミュニティは、個人が抱える問題点を共有することで成長を促し精神的な支えになる可能性が示唆された。

P-15-7 布製骨盤内モデル作製のススメ～腹腔鏡手術習得と複雑な骨盤内構造の深い理解のために～

福岡徳洲会病院

峰松麻里, 大西義孝, 廣田智子, 夏秋伸平, 宮川 孝

【目的】当院では2019年より腹腔鏡手術を開始することとなり、これまでと違う視点で骨盤内構造を理解する必要に迫られた。腹腔鏡のカメラから見る景色は新鮮で、角度・接近度合いなど、これまで腹式手術・腔式手術から見てきた景色とは違うもののように感じた。臓器（子宮・膀胱・尿管・直腸）・血管・靭帯・神経・腹膜の三次元的な構造の理解が非常に困難であったことや、少ない症例から複雑な骨盤内構造を理解する必要があったことより、解剖学の教科書・アトラス・手術動画・webセミナー等を参考に骨盤内モデルを作製することとした。【方法】洗面器を骨盤底に見立て、フェルト・綿・スポンジ・毛糸・マジックテープなどを材料とし、それぞれ細かく色分けし、作製した。腹膜の存在が骨盤内の理解を一層困難にしていると考え、透ける布を腹膜とし、臓器に沿わせるように固定した。理解を深めるために時に腹膜を切開し、交換可能とした。【成績】教科書やアトラス、手術動画の振り返りには時間を要したが、一から各臓器を作製して見直していくことで知識が定着した。また、安い費用で材料を揃えることができ、作製は家事的な合間に自宅でもできることも利点と思われる。骨盤内モデルの作製には約1か月を要した。【結論】一から骨盤内モデルを作製することで、尿管・血管・神経の走行、靭帯付着部位など、自身の理解の中で曖昧であった部分を発見でき、何度も振り返り見直すことができた。今後はこの骨盤内モデルを利用して、腹腔鏡手術を習得していくことが目標である。

P-16-1 当院における遺伝性乳癌卵巣癌症候群の現状と課題

三重大附属病院

金 美希, 金田倫子, 砂田希美, 手石方康宏, 北村亜紗, 岡本幸太, 吉田健太, 鳥谷部邦明, 近藤英司, 池田智明

【目的】遺伝性乳癌卵巣癌症候群（Hereditary Breast and Ovarian Cancer：HBOC）において、リスク低減卵管卵巣摘出術（risk reducing bilateral salpingo-oophorectomy：RRSO）は卵巣癌リスクを軽減する最も有効な予防法である。HBOC診療の保険拡大に伴い、RRSO目的の紹介患者が増加している。今回、当科におけるHBOC症例の臨床背景と課題を検討した。【方法】当科で2019年10月～2021年9月にHBOC診療を受けた14例を、診療録より臨床情報を後方視的に抽出した。【成績】当科受診時年齢は中央値44歳（37-66歳）、BRCA1変異が6例、BRCA2変異が8例で、乳癌発症が13例、うち両側乳癌既往4例、乳癌未発症者は1例であった。家族歴は乳癌、卵巣癌、前立腺癌、膵臓癌のいずれかが13例にみられた。RRSO施行例は7例、うち乳癌未発症者で自費診療が1例、腹腔鏡下子宮上部切断術+仙骨腔固定術、腹腔鏡下子宮全摘術施行が各1例、4例は手術予定である。未施行2例は更年期障害の懸念による延期と、乳癌の再燃の治療優先であった。遺伝カウンセリングからRRSOまでの期間の中央値は4か月（2-15か月）で、最長はRRSO保険取載まで延期した症例であった。RRSO手術時年齢は中央値49歳（38-66歳）、手術時間は中央値117分（77-324分）、出血量は全例少量であった。摘出標本には全例病変なく、腹水細胞診は陰性であった。術後から退院までの日数は中央値4日（3-5日）であった。【結論】本検討ではRRSOは安全に施行できた。一方で、RRSO施行時の年齢が高いこと、同時手術の保険適応、乳癌未発症者の自費診療、術後の卵巣欠落症状が課題と考えられた。当科では今後HBOC外来を開設予定であり、他職種チームと患者支援を行っていく。

P-16-2 遺伝性乳癌卵巣癌症候群に対する当院での腹腔鏡下リスク低減卵巣卵管摘出術 (RRSO) の5例

神戸大学大学院医学研究科産科婦人科学分野

鷲尾佳一, 矢野陽子, 加地崇裕, 山中啓太郎, 安積麻帆, 笹川勇樹, 西本昌司, 長又哲史, 山崎友維, 寺井義人

【緒言】遺伝性乳癌卵巣癌症候群 (Hereditary Breast and Ovarian cancer Syndrome: 以下 HBOC) は BRCA1/2 遺伝子変異による遺伝性疾患である。卵巣癌発症リスクは BRCA1 で 44%, BRCA2 で 17% とされている。未発症卵巣癌に対する有効なサーベイランスは確立されておらず、予防的切除によって罹患率・死亡率を低下させることが知られている。当院で経験した腹腔鏡下リスク低減卵巣卵管摘出術 (Risk Reducing Salpingo-Oophorectomy: 以下 RRSO) について報告する。【対象】年齢は 42-62 歳、乳癌既往で BRCA 遺伝子変異を認めた 5 例 (BRCA1 変異 2 例, BRCA2 変異 3 例) 【方法】術前に全例で遺伝カウンセリングを行い, MRI にて卵巣の腫瘍性病変の有無など評価をおこなった。手術では腹腔内を視察後に腹水細胞診を採取した。付属器は尿管の走行を確認後に卵巣提索を卵巣より 2cm 以上マージンをとって切断, 子宮側には卵管や卵巣固有韧带が残存しないよう切断した。摘出臓器は回収袋に入れ細切などせずに摘出した。SEE-FIM プロトコールに則り病変の有無を評価した。【結果】手術時間, 出血量の平均値はそれぞれ 118.4 分, 10ml で合併症は認めなかった。病理診断では全例で悪性所見を認めなかった。【考察】本検討では全例低侵襲手術で対応でき合併症の発生なく安全に実施することが可能であった。一方で RRSO 後, 数%に腹膜癌を発症する可能性が示唆されているが有効なサーベイランスは確立されておらず, 今後さらなる検討が必要と考える。

日本語
ポスター
6日(土)

P-16-3 生殖細胞系列のがん関連遺伝子 84 種類を一括検査する遺伝性腫瘍マルチ遺伝子パネル検査の実施報告

兵庫医大

澤井英明, 鏑本浩志, 上田真子, 田中宏幸, 磯野路善, 井上佳代, 上田友子, 柴原浩章

【目的】2019 年にがんゲノムプロファイリング検査が保険適用され, 抗がん薬物療法はがん関連遺伝子の病的バリエーションにもとづく投与という新しい時代を迎えた。当院ではがんゲノム医療拠点病院に認定されたのを契機に, がんの治療や予防, 早期発見に役立つ目的で, 生殖細胞系列のがん関連遺伝子 84 種類を一括検査する遺伝性腫瘍マルチ遺伝子パネル検査を自費の研究検査として導入した。【方法】2020 年 4 月より, 対象は①がんの既往歴や家族歴がある人と②がんゲノムプロファイリング検査で腫瘍組織にがん関連遺伝子の病的バリエーションが検出された人とした。該当者には遺伝カウンセリングを行って IC を得た上で採血し, 米国 Invitae 社に送付した。約 3 週間後に結果報告を受けて, その後の診療に反映した。【成績】2021 年 9 月まで 1 年 6 か月間に遺伝性腫瘍マルチ遺伝子パネル検査を 25 名に実施した。①既往歴・家族歴の適応が 18 名で, 乳がん卵巣がん 11 名, 子宮内膜がん 2 名, 乳がん卵巣がん+子宮内膜がん 3 名, 網膜芽細胞腫が 1 名, 若年性ポリポーシスが 1 名であった。乳がん卵巣がん 11 名のうち 1 名で SDHB 遺伝子の病的バリエーションを認めた。②がんゲノムプロファイリング検査の結果による適応は 7 名で, BAP1 陽性 (中皮腫) 2 名, BRCA1 陽性 (乳がん・子宮内膜がん) 1 名, MLH1・PTEN 陽性 (子宮内膜がん) 1 名, MLH1 陽性 (乳がん) 1 名, MSH2・APC・BRCA1 陽性 (子宮内膜がん) 1 名, PTEN 陽性 (子宮内膜がん) 1 名であった。BRCA1 陽性の乳がん・子宮内膜がんの 1 名に BRCA1 の病的バリエーションが検出された。【結論】生殖細胞系列の遺伝性がん関連遺伝子パネル検査は, その後の診療に有用であるが, 病的バリエーションがみつからないことの方が多い。

P-16-4 当院における遺伝性乳癌卵巣癌症候群に対するリスク低減卵巣卵管摘出術の経験

東北大病院

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【目的】遺伝性乳癌卵巣癌症候群 (HBOC) は一般集団と比較し卵巣癌発症のリスクが高い。しかし, 卵巣癌の有効なサーベイランス法はなく, リスク低減卵巣卵管摘出術 (RRSO) が確実な予防法として国内外のガイドラインで推奨されている。当院における HBOC に対する RRSO の現状とその課題について検討した。【方法】HBOC と診断され 2020 年 8 月~2021 年 10 月に RRSO または卵巣サーベイランス目的に当科 HBOC 外来を受診した 39 名のうち, 14 例が RRSO を施行, 10 例が今後 RRSO 予定, 15 名がサーベイランスを希望した。RRSO を施行した 14 例の患者背景, 手術成績, 病理学的所見について検討した。【成績】RRSO を施行した 14 例の平均年齢は 50.9 歳, 2 名は 30 歳代であった。BRCA1/2 病的バリエーションはそれぞれ 10 例 (71.4%) / 4 例 (28.6%), 乳癌既往症が 13 例 (92.8%), 閉経後が 11 例 (78.6%), 経産婦が 11 例 (78.6%), 卵巣癌家族歴ありが 4 例 (28.6%) だった。RRSO は腹腔鏡下手術で行い, 全例において術中出血量は少量で周術期合併症は認めなかった。子宮全摘術は子宮腺筋症を合併していた 1 例に施行した。病理組織学的検査では全例において STIC やオカルト癌は認めず腹水細胞診は陰性であった。術後に腹膜癌の発症した症例は認めなかった。【結論】RRSO は腹腔鏡下手術にて安全に施行可能であった。当院の RRSO 施行例は, 平均年齢がガイドラインの推奨年齢より高く, 閉経後の割合が高かった。閉経前女性では外科的閉経による身体的影響への不安が RRSO の障壁となっている可能性があり, 術後の長期的なヘルスケアについての検討が必要と考えられた。

P-16-5 当院における腹腔鏡下リスク低減卵管卵巣摘出術の現状と課題

高知大附属病院

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【緒言】 遺伝性乳癌卵巣癌症候群 (HBOC) における卵巣癌の一次予防として最も有効な対策は、リスク低減卵管卵巣摘出術 (RRSO) である。当院では、2017年にRRSOを開始した。全例腹腔鏡手術で実施している。【目的】 当院の腹腔鏡下RRSOの現状を解析し、今後の課題を考察する。【方法】 対象は2017年6月から2021年10月までにRRSOを希望した23例で、診療録より情報を収集した。なお、RRSOはNCCNガイドラインに則って行っている。【成績】 RRSOを実施したのは19症例で、自費診療2例、保険診療17例であった。RRSOを中止した症例は4例で、3例が術前PET-CTで乳癌再発を発見したためであった。実施例は全例乳癌既発症例で、平均年齢53.2歳(44-68歳)、有経3例、閉経16例、BRCA1病的バリエーション陽性者6例、BRCA2 13例であった。子宮摘出併施4例、リスク低減対側乳房切除術(CRRM)併施2例、子宮全摘・CRRM2例、乳癌治療目的の乳房切除併施2例であった。いずれも病理診断で付属器に潜在癌やserous tubal intraepithelial carcinoma (STIC)は認めなかった。術後は6か月毎に腹腔鏡サルーベイランスとして経膈超音波検査と血中CA125測定を行っており、現在のところ腹腔鏡発症例はない。【結論】 RRSO導入当初、術前PET-CTの必要性は検討課題だったが、3例に乳癌再発を認めたことから、乳癌既発症例では必要と考える。また、術後の腹腔鏡サルーベイランスの方法について明確なエビデンスはなく、今後その有用性についての評価が必要と考える。

P-16-6 当院における遺伝性乳癌卵巣癌症候群患者へのリスク低減卵管卵巣摘出術の現状と今後の課題

弘前大附属病院

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【目的】 遺伝性乳癌卵巣癌症候群 (hereditary breast and ovarian cancer: HBOC) はBRCA1あるいはBRCA2の生殖細胞系列の病的バリエーションに起因する乳癌および卵巣癌をはじめとするがんの易罹患性症候群である。2020年4月よりBRCA病的バリエーションが確認された乳癌患者ではリスク低減卵管卵巣摘出術 (risk reducing salpingo-oophorectomy: RRSO) が保険適用となった。それに伴い当院では2021年4月よりRRSOを導入し同年8月までに4症例を経験した。当院におけるRRSOの現状および今後の課題について報告する。【方法】 当院でRRSOを施行した4症例を対象としカルテベースの後方視的検討を行った。【成績】 術前には産婦人科担当医が患者本人、家族に遺伝カウンセリングを施行している。RRSOを施行した4症例の内訳は以下の通りである。HBOC診断時の平均年齢は40.7歳(35-56歳)、全例がBRCA1の病的バリエーションであった。RRSO施行時の平均年齢は41.7歳(36-56歳)、平均手術時間は60分(51-71分)、出血量は全例で少量のみで、手術合併症は認めず術後2日目に退院となっていた。摘出標本はSEE-FIMに基づいて細切し、HE染色とp53免疫染色により病理診断を施行した。全例で悪性所見は認めなかった。術後は腹腔鏡のサルーベイランスとして半年毎の経膈超音波検査、CA125の測定を行う方針となっている。【結論】 今後、当院乳腺外科でのリスク低減乳房切除術が導入となる見込みであり、RRSOとの同時手術も検討する。また術後は腹腔鏡のサルーベイランスだけでなく卵巣欠落症状をはじめとした女性ヘルスケアの観点からの継続的なサポート、手術による喪失感や子孫への影響の不安感などの心理的なサポートの整備も課題となる。

P-16-7 遺伝学的検査の保険収載に伴うBRCA遺伝子検査の動向とその課題

大阪大

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【目的】 遺伝性乳癌卵巣癌症候群 (HBOC) 診療の一部保険収載により、リスク低減卵管卵巣摘出術 (RRSO) の一部のみならず、卵巣癌既往者については保険診療で全例HBOCかどうかを診断可能となった。保険収載後の当院でのBRCA遺伝子検査率とRRSOの適応および件数を検討した。【方法】 2020年4月~2021年6月のRRSOの件数および適応と同期間に当院通院中の卵巣癌症例のうち2018年1月以降に当院で初回治療を受けた症例について、BRCA1/2遺伝子検査の有無、病期、組織型、HBOC関連癌既往歴・家族歴を診療録より抽出した。【成績】 RRSOは13件、通院中の卵巣癌症例は170例であった。組織型は漿液性腺癌80例、類内膜腺癌25例、明細胞腺癌38例、粘液性癌10例その他17例で、このうちgBRCA遺伝子検査を受けたのは40例であった。gBRCA遺伝子検査を受けていない症例中、検査を提案したが希望なし6例、Mychoice診断システムにてtBRCA遺伝子変異陰性16例、がんゲノム検査受検症例が6例であった。gBRCA、tBRCA共に評価されていない症例は90例であった。gBRCA変異が判明した症例のうち60%が遺伝子診療部にて血縁者に遺伝カウンセリングが行われた。【結論】 gBRCA遺伝子検査症例の65%はコンパニオン診断であった。HBOC診断目的で受検した症例のうち75%は漿液性腺癌、HBOC関連癌の既往・家族歴有り40%であった。一方で明細胞腺癌の89%は遺伝子検査を受けなかった。病期、組織型、既往歴・家族歴により主治医の検査推奨に差があることが推測された。またRRSOは全例乳癌既往症例で、BRCA遺伝子検査の保険収載に伴い血縁者に未発症変異保有が判明する機会が増加しているが、私費でのRRSOは増加しておらず、手術費用の影響が示唆された。

P-17-1 子宮体癌に対する免疫療法における新たな標的の検索～マルチカラーフローサイトメトリーによる腫瘍浸潤リンパ球の解析～

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【目的】チェックポイント分子である CTLA-4 (cytotoxic T-lymphocyte-associated protein 4) は疲弊 CD8⁺T 細胞や免疫寛容を誘導する制御性 T 細胞 (regulatory T cell : T_{reg}) において発現し, メラノーマ等で免疫療法の標的になっている。子宮体癌における抗 CTLA-4 抗体療法の可能性を探るため CD8⁺T 細胞および T_{reg} における PD-1 と CTLA-4 の発現を検討した。【方法】2019 年 2 月から 2021 年 4 月に子宮摘出術を施行した類内膜癌 I-II 期 16 例 (G1-2 : 13 例, G3 : 3 例), III-IV 期 9 例 (G1-2 : 4 例, G3 : 5 例), 漿液性癌 3 例から PBMC と腫瘍浸潤リンパ球 (tumor-infiltrating lymphocyte : TILs) を回収した。CD8⁺T 細胞, effector T_{reg} (eT_{reg} : CD4⁺CD45RA⁺Foxp3⁺) における PD-1, CTLA-4 の発現をマルチカラーフローサイトメトリーにより評価し PBMC と TIL の比較を行った。(Mann-Whitney U test) 【成績】CD8⁺T 細胞における PD-1, CTLA-4 の発現は, PBMC で 0.27 (0.073-3.8) %, 0.66 (0.10-4.4) %, TIL では類内膜癌 I-II 期で 15 (2.2-77) %, 0.55 (0.095-2.2) %, III-IV 期で 25 (1.8-57) %, 0.42 (0.059-4.4) %, 漿液性癌で 36 (25-53) %, 1.3 (1.0-2.2) % であり, CD8⁺T 細胞における PD-1 発現は TIL で有意に上昇した (p<0.0001)。eT_{reg} における PD-1, CTLA-4 の発現は, PBMC で 0.15 (0-1.6) %, 0.25 (0-1.5) %, TIL では類内膜癌 I-II 期で 17 (1.4-52) %, 18 (11-29) %, III-IV 期で 17 (5.2-61) %, 16 (4.9-39) %, 漿液性癌で 18 (9.4-40) %, 32 (21-44) % であり, eT_{reg} における PD-1, CTLA-4 発現は TIL で有意に上昇した (p<0.0001)。【結論】子宮体癌では腫瘍に浸潤する T_{reg} において CTLA-4 が高発現しており, T_{reg} が抗 CTLA-4 抗体療法の標的となる可能性がある。

P-17-2 子宮体癌の腫瘍マーカーとしてのヒト精巣上体蛋白 4 (HE4) の有用性の検討

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【目的】HE4 は 2017 年 4 月より卵巣癌の腫瘍マーカーとして保険適応となり, 糖質抗原 125 (CA125) に比べ婦人科良性疾病や月経の影響を受けにくいといわれており, それらを組み合わせる計算する卵巣悪性腫瘍推定値 (ROMA) は感度 0.775 特異度 0.855 と精度が高く良悪性の鑑別に有用とされている。子宮体癌に対して HE4 を測定しその有用性を検討した。【方法】当院で 2018 年 1 月から 2020 年 12 月までに子宮体癌に対して手術を行った全 227 症例のうち, 術前に HE4 測定を行った 72 例に対してその診断有用性を後方視的に検討した。HE4 のカットオフ値には参考基準値である閉経前 70pmol/L, 閉経後 140 pmol/L を使用し, ROMA のカットオフ値には基準値である閉経前 7.4%, 閉経後 25.3% を使用した。【成績】患者年齢は平均 56.9 (33-78) 歳, 閉経後が 48 例 (66.7%), ステージ I が 55 例, II が 1 例, III が 11 例, IV が 5 例であった。組織型は類内膜癌 G1 が 33 例, G2 が 10 例, G3 が 8 例, 癌肉腫が 5 例, 明細胞癌が 2 例, 漿液性癌が 2 例, 混合癌が 4 例, その他 8 例であった。卵管癌の合併を 1 例認めた。ステージ I および II の症例で HE4, CA125, ROMA の陽性率は 16%, 25%, 38%, ステージ III および IV の症例では 31%, 50%, 71% であった。CA125 陰性で HE4 陽性が 6 例 (8.3%), ROMA 陽性が 31 例 (43.1%) であった。【結論】子宮体癌の腫瘍マーカーとして HE4 は CA125 に相補的であり ROMA は子宮体癌の診断補助に有用である可能性が示唆された。

P-17-3 免疫染色検査によって dMMR と判定された子宮体癌の予後解析

弘前大

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【目的】dMMR (mismatch repair deficient) とは DNA 複製の際に生じるミスマッチを修復する機能が低下している状態である。dMMR はマイクロサテライト不安定性を引き起こし腫瘍発生に関与すると考えられている。また, dMMR を示す子宮内膜癌症例は無増悪生存期間 (progression-free survival : PFS) が不良である傾向が示唆されているが一定の見解には至っていない。今回我々は IHC 検査で判定した dMMR が子宮体癌の予後因子となるか後方視的に検討した。【方法】2017 年 8 月から 2021 年 3 月に当院で子宮体癌と診断され, かつ IHC 検査を行った 71 例を解析対象とした。MLH1, MSH2, MSH6, PMS2 に対する免疫染色を行い, 1 つ以上のタンパク質発現が消失している場合を dMMR と判定した。71 例の再発もしくは再燃の有無と観察期間を明らかとし, PFS に対して dMMR がリスク因子となるか解析した。【成績】対象者 71 名の平均年齢は 55.7 ± 10.5 歳, 観察期間は平均 14.6 ± 5.5 か月, 病期の内訳は I 期 57 名 (81.4%), II 期 1 名 (1.4%), III 期 6 名 (8.6%), IV 期 6 名 (8.6%) であった。71 名中 9 名 (I 期 5 名, IV 期 3 名) が再発もしくは再燃した。PFS の平均値は 9.5 ± 3.9 か月であった。dMMR と判定されたのは 21 名 (29.6%) であり, そのうち 3 名 (I 期 2 名, IV 期 1 名) が再発・再燃していた。COX 回帰分析では IHC 検査で判定した dMMR は PFS を変化させる有意なリスク因子ではなかった (OR : 1.196, 95% CI : 0.286-5.008, P=0.807)。【結論】今回の解析では IHC 検査によって判定された dMMR は再発・再燃の有意なリスク因子ではなかったが観察期間が短く, かつ対象者が少数であるため十分な解析ができてきない可能性もある。今後も症例を増やし調査を継続する方針である。

P-17-4 子宮体癌における E-cadherin, N-cadherin の発現と予後との相関

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【目的】当院子宮体癌症例において EMT (epithelial-mesenchymal transition) マーカーの発現と予後の相関を検討する。【方法】1989年から2017年の間当院で子宮全摘術および両側付属器切除術を施行した症例を後方視的に検討した。E-cadherin と N-cadherin の発現は免疫組織化学染色を用いて E score, N score として評価し, 各 cadherin の発現と臨床病理学的因子, 予後との関連を統計学的に検討した。【成績】子宮体癌 485 症例につき E-cadherin の発現は 327 例 (67.4%, N-cadherin の発現は 311 例 (64.1%) でみられた。N score - E score が ≥ 2 となる症例は 110 例 (22.6%) であった。E-cadherin の発現低下は卵巣転移および遠隔転移と有意な相関があり (p -value, 卵巣転移: 0.025 遠隔転移: < 0.01), N-cadherin の発現は FIGO stage, 頸部間質浸潤の有無, 卵巣転移, 腹水細胞診陽性, 後療法の有無と有意に相関があった (p -value, FIGO stage: < 0.01 cervical stromal invasion: 0.015 ovarian metastasis: 0.029 distant metastasis: < 0.01 peritoneal cytology: 0.014 adjuvant therapy: < 0.01). 多変量解析を行った結果では, E-cadherin の減弱および N-cadherin の発現は予後予測因子とはなり得なかったが, N score - E score が ≥ 2 となる症例は有意に予後が増悪することが示された (PFS; HR 1.60, 95% CI: 1.05-2.44, $p = 0.028$, OS; HR 1.86, 95% CI: 1.06-3.23, $p = 0.028$). 【結論】本検討により子宮体癌において EMT が進行度, 遠隔転移と相関している可能性, E-cadherin, N-cadherin の評価の組み合わせにより予後予測因子となりうる可能性が示された。

P-17-5 子宮体癌におけるリンチ症候群のユニバーサルスクリーニングの有効性

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【目的】リンチ症候群 (LS) は大腸癌や子宮内膜/卵巣/消化器/尿路臓器癌などの発症リスクの高まる常染色体優性遺伝性腫瘍である。子宮体癌患者から LS を診断することは, 後続癌の早期診断・血縁者にも遺伝学的評価や予防医療の機会を提供する。家族歴・既往歴からの LS の拾いあげには限界があり, 大腸癌ではユニバーサルスクリーニングが定着しつつある。子宮体癌において LS のユニバーサルスクリーニング方法を確立することを目的とした。【方法】当院において 2019/10-2021/2 の期間に子宮体癌と診断され, 当該研究に対する同意を得た 116 名が対象となった。手術検体組織の MLH1, MSH2, MSH6, PMS2 蛋白に対する免疫組織化学 (IHC) を行い, ミスマッチ修復 (MMR) 機能欠損腫瘍を拾いあげた。IHC 陰性症例を LS 疑い症例として, 遺伝カウンセリングを行い, MMR 遺伝学的検査・MSI 検査・MSH1 遺伝子プロモーター領域のメチル化分析を施行した。【成績】EC は 100 症例, IHC 陰性は 19 例で, MMR 遺伝学的検査・MSI 検査の対象となった。MMR 遺伝学的検査の結果, MSH2 と MSH6 の病的バリエントを 1 例ずつ認め, 2 例が LS と確定した。MSH6 の VUS を 2 例認め, PMS2 の良性バリエントを 1 例認め, 14 例は変異を認めなかった。MSI-H は 16 例 (84.2%) に認めた。MLH1 のメチル化は 11 例 (57.9%) に認めた。【結論】EC における LS のユニバーサルスクリーニング方法は, まず IHC を用いて絞り込みを行うことが有用であった。EC の約 2% に LS 患者を認めた。

P-18-1 当院における包括的ゲノムプロファイリング検査の現状

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【目的】包括的ゲノムプロファイリング検査 (CGP) が保険適用となり, 約 2 年が経過した。当院はがんゲノム医療連携病院の認定と同時にがんゲノム医療センターを設置し, CGP を開始した。現状を報告する。【方法】直近 2 年間に検出中核拠点病院のエキスパートパネル (EP) で検討された全症例を対象として, 検査種別, 出検から EP レポート返却までの Turnaround time (TAT), druggable 変異の検出率, 結果に基づく治療の実施率を検討した。【成績】FoundationOne CDx に 55 例, FoundationOne liquid CDx に 2 例, NCC オンコパネルに 2 例を出検した。内訳は脳腫瘍 2, 頭頸部 1, 胸腺 2, 胸膜 1, 消化器 15, 肝胆膵 9, 骨軟部 7, 泌尿器 3, 婦人科 19 例であった。59 例中, 解析不能が 3 例, EP 前の死亡が 1 例あり, 残る 55 例の TAT は中央値 37 日 (22-63) であった。druggable 変異を認めたのは 25 例 (42.4%) であり, うち 5 例 (8.5%) で治療が実施された。治療に至らなかった理由として最も多かったのは治験実施施設へのアクセス (5 例) であった。婦人科癌 19 例症例の内訳は頸癌 2 例, 体癌 5 例, 体部肉腫 6 例, 卵巣癌 6 例であり, druggable 変異を認めた 7 例 (36.8%) のうち 3 例 (15.8%) が「遺伝子パネル検査による遺伝子プロファイリングに基づく複数の分子標的治療に関する患者申出療養」(受け皿試験) に参加した。【結論】地方の施設では治験へのアクセスが課題である。今後, 受け皿試験のさらなる拡充が望まれる。

P-18-2 卵巣癌 I 期・II 期における germline BRCA 検査の実際

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【目的】遺伝性乳癌卵巣癌症候群診断を目的として、すべての上皮性卵巣癌患者は BRCA 検査を受けることが推奨されている。本邦でも 2020 年 4 月より卵巣癌患者に対して、遺伝性乳癌卵巣癌症候群診断を目的とした germline BRCA 検査が保険適用となった。I-II 期卵巣癌患者では BRCA 検査は治療方針に影響しないことから、情報提供や患者のニーズの実際が進行例と異なる可能性も考えられる。今回、当院の I-II 期卵巣癌患者における BRCA 検査の実態について検討した。【方法】2020 年 4 月から 2021 年 9 月に、当院で治療を行った上皮性卵巣癌 I 期, II 期の患者を対象とし、BRCA 検査の情報提供や検査実施の実際について後方視的に検討した。【成績】対象は 8 例で、年齢中央値は 56.5 歳 (48-79 歳)、乳癌・卵巣癌の家族歴を有する症例はいなかった。組織型は類内膜癌 4 例, 明細胞癌 2 例, 高異型度漿液性癌 2 例だった。進行期は IA 期 1 例, IC1 期 3 例, IIA 期 1 例, IIB 期 2 例だった。全例に BRCA 検査の説明が行われ、5 例が germline BRCA 検査を希望した。そのうち類内膜癌 II 期の 1 例に BRCA1 の変異を認め、今後遺伝カウンセリングを予定している。【結論】I-II 期卵巣癌患者においても、germline BRCA 検査に対するニーズは高かった。適切な情報提供とカウンセリング体制の元で、BRCA 検査を受ける機会を提供することが重要と考えられた。

P-18-3 リスク低減卵管卵巣摘出術 (RRSO) 後に腹膜癌を発症した BRCA1 病的バリエント保持者の一例

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【緒言】BRCA1/2 病的バリエント保持者に対するリスク低減卵管卵巣摘出術 (以下 RRSO: Risk reducing salpingo-oophorectomy) が、本邦でも徐々に普及している。RRSO 施行後にも原発性腹膜癌発生リスクがあるとされているが、今回 RRSO 術後 5 年で腹膜癌を発症した一例を経験したため報告する。【症例】48 歳 2 妊 2 産, 米国人。実母が若年性乳癌・大腸癌罹患歴あり, 米国で BRCA1 病的バリエントを認めたため、41 歳でリスク低減乳房全摘出術, 43 歳で RRSO を施行された。X-1 年 11 月頃より下痢と便秘を繰り返し、嘔気と腹痛症状を認めた。X 年 2 月に当院消化器内科を受診し、上部・下部消化管内視鏡は異常なく、CA125 高値 (5134 U/ml)、CT で骨盤内腫瘍を認め、当科紹介となった。少量の腹水を認め、多発する腹膜播種が疑われた。腹水細胞診は classIII であり、審査腹腔鏡を行った。術中腹水細胞診は classV で、腹膜播種病変を生検し高異型度漿液性癌の診断となった。術後、パクリタキセル・カルボプラチン (TC) 療法を開始し、腫瘍は順調に退縮し、CA 125 32.4 U/ml に低下した。今後、IDS (interval debulking surgery) を行い、TC (+Bevacizumab) 療法を術後に数コース追加したのち、Olaparib 維持療法への移行を検討している。【結論】BRCA1/2 病的バリエント保持者では、RRSO 後でも腹膜癌の発症を留意すべきであるが、推奨しうるサーベイランス方法の確立などは、依然として検討課題である。本症例も、プラチナ感受性卵巣癌に準じた治療を行ってきたが、IDS 以降の経過詳細と、これまでの報告例に関する考察を併せて報告する。

P-18-4 当科におけるがんゲノム医療の現状

国立四国がんセンター

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【目的】2019 年 6 月 1 日より『標準治療がない、または終了する見込みである固形がん患者』に対するがん遺伝子パネル検査の保険診療が開始された。当科での現状を報告する。【方法】2019 年 6 月から 2021 年 6 月までの 2 年間に当科でがん遺伝子パネル検査を施行した 38 例について検討した。【成績】①癌腫：子宮頸癌 5 例, 子宮体癌 11 例, 平滑筋肉腫 2 例, 卵巣・卵管・腹膜癌 16 例, 原発不明癌 3 例, その他 1 例。②パネル検査：FoundationOne CDx 27 例, NCC オンコパネル 4 例, Guardant 360 自費検査 4 例, 先進医療 3 例。③MSI-High は 0 例, 生殖細胞系列バリエントの可能性が 9 例で示唆された。④治験・治療に結び付いた件数：患者申出療養 1 例 (2.6%)。第 1 相試験を 8 例, 第 2 相試験を 5 例で提示できたが、地理的理由, PS の悪化, 効果の見込みがない等の理由で参加できなかった。④検査数と転帰：2019 年 7 例, 2020 年 18 例, 2021 年は上半期で 13 例と増加傾向である。前半 1 年間は 15 例中 11 例死亡, 出検から死亡までの中央値は 3 か月, 結果開示前の死亡が 2 例あった。後半 1 年は 23 例中 5 例死亡, 出検から死亡までの中央値は 4 か月だが、前半に比べると標準治療の終了が見込まれる比較的早い段階で出検していた。【結論】治療・治験を提示できた症例は 14 例 (36.8%) あったが、治療に結び付いたものは 1 例 (2.6%) と低かった。出検のタイミングは徐々に早くなっており、標準治療終了が見込まれる患者に提示できる選択肢として今後も症例の増加が見込まれる。

P-18-5 卵巣癌患者に対する遺伝学的検査の意義

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【目的】生殖細胞系列のBRCA1/2 (g BRCA1/2) 遺伝学的検査と腫瘍組織のBRCA1/2 (t BRCA1/2)・相同組み換え修復欠損(HRD)検査、所謂 myChoice 診断システム(myChoice 診断)の臨床的有用性や課題を明らかにする。【方法】当院で gBRCA1/2 遺伝学的検査、myChoice 診断を行った卵巣癌患者を後方視的に検討した。【成績】① 初発進行癌 50 例中、gBRCA1/2 検査は 35 例、myChoice 診断は 15 例に施行され、高異型度漿液性癌 (HGSC) 28 例/明細胞癌 7 例/類内腺癌 6 例/その他 9 例であった。gBRCA1/2 の病的バリエーション陽性(GM+)は 9 例(20%)、myChoice 診断は 5 例(30%)が陽性で、1 例に tBRCA1 病的バリエーション陽性(TM+)を認めた。再発卵巣癌 19 例中、gBRCA1/2 検査は 14 例、myChoice 診断は 5 例に施行され、GM+は 2 例(14%)、myChoice 診断は 1 例(20%)が陽性であった。② GM+、myChoice 診断陽性例は全例 HGSC で、化学療法が著効し PARP 阻害剤の投与、または投与予定である。③ GM+・TM+11 例中、2 例に乳癌の既往・併発を認め、4 例に乳癌・卵巣癌等の家族歴を認めた。GM+・TM+全例に遺伝カウンセリングが案内され、8 例(80%)に実施された。【結論】GM+率は本邦の多施設共同試験結果と同程度であった。GM+・myChoice 診断陽性全例が PARP 阻害剤の投与適応となり、コンパニオン診断としての意義が確認された。また、GM+・TM+患者の遺伝カウンセリングの実施率も高頻度であった。

P-18-6 当院における再発卵巣癌の myChoice 診断システム™ (myChoice) についての取り組み

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【目的】卵巣癌の治療は分子標的薬とコンパニオン診断の発展に伴い急速な変化を遂げている。コンパニオン診断が保険収載され治療の選択肢が増加し、多様化している。myChoice は、ゲノム不安定性及び腫瘍における BRCA1/2 遺伝子の病的変異の有無により相同組換え修復欠損(HRD)の有無を評価する包括的な検査で、その再発卵巣癌症例に対する取り組みについて報告する。【方法】2021年4月～9月に再発卵巣癌症例に対し myChoice を施行し、判定不能1例を除く14例を、HRDをA群10例と homologous recombination proficient (HRP) をB群4例に分類し、遺伝子検査結果、組織型、治療方針、予後等について検討した。【成績】年齢中央値 67 歳、進行期は I 期 1 例、II 期 1 例、III 期 11 例、IV 期 1 例。A 群の病的変異は、BRCA1 3 例と BRCA2 1 例、臨床的意義不明のバリエーション 2 例だった。高異型度漿液性癌 (HGSC) は 9 例 (90%)、PFI は中央値 22 か月 (10-50)、検査前のレジメン数は中央値 4 回 (3-9)。PARP 阻害薬を使用した 9 例中、1 例は貧血休業中に痛死 (DOD 76M)、PD3 例、有害事象 (骨髄抑制、吐き気、食思不振、腎機能低下、倦怠感など) で減量・休業で治療判定未が 5 例で、OS は中央値 43 か月 (26-182) であった。一方 B 群の内、HGSC は 3 例 (75%) であった。PFI は中央値 20.5 か月 (13-32)、検査前の化学治療歴は中央値 4 回 (3-6) 回、OS の中央値 32 か月 (30-59) であった。【結論】HRD の有無で PFI、組織型、レジメン数に明らかな差はないが、OS は A 群で長かった。A 群の 9 割で PARP 阻害薬を使用した。PD 症例や有害事象で休業している症例も多く、今後長期の経過観察とさらなる症例の積み重ねが必要であると考えられた。

P-18-7 婦人科悪性腫瘍に対するがん遺伝子パネル検査：運用の現状と課題

京都大附属病院

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【目的】2019年に保険収載されたがん遺伝子パネル検査(以下パネル検査)は、標準治療不応例が適応となる。治療抵抗性の機構には Innate Resistance (IR: 初回治療以降全ての治療に不応)と、Acquired Resistance (AR: 治療の途中で抵抗性を獲得)がある。今回我々はこの抵抗性獲得機構の観点からパネル検査の役割を検討した。【方法】2019年12月から2021年8月に当科でパネル検査を施行した婦人科悪性腫瘍 42 症例(卵巣癌: OV18 例、子宮体癌: UC14 例、子宮肉腫: US5 例、子宮頸癌: CX5 例)について、臨床背景、パネル検査の結果、その後の治療経過と予後を後方視的に検討した。【成績】IR 12 例(OV5 例、UC4 例、US2 例、CX1 例)、AR30 例(OV13 例、UC10 例、US3 例、CX4 例)であった。Actionable mutation は全例に認め、エキスパートパネル(エキパネ)にて推奨治療ありとされたものは IR: 4/12 例(33.3%)、AR: 8/30 例(26.7%)であった(IR/AR: OV: 1/2、計 3 例、UC2/3、計 5 例、US1/1、計 2 例、CX0/2、計 2 例)。実際にエキパネ推奨治療を施行できたのは IR: 3/12 例(25%)、AR: 3/30 例(10%)で、IR がやや多い傾向にあった。治療後 4 か月時点の評価で PR であるものは IR で 1/3 例、AR では 0/3 例で、1 例の PR 以外は全例 PD で中止となっていた。パネル検査申し込み 6 か月後の生存率を比較したところ、AR の 65% に対して IR は 30% と低い傾向にあり、特に Performance Status (PS) が申し込み時に 2 以上であった 3 例は 5 か月以内に全例原病死となっていた。【結論】IR にも AR とほぼ同率に、エキパネ推奨の治療が存在しうる。初回治療の最中に抵抗性が危惧される症例にパネル検査を検討する際は、急速に病状が進行しうるため、PS に留意しつつ早めの対応を心がけるべきである。

P-18-8 当院で施行した HRD 検査の組織型をふまえての検討

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【目的】HRD 検査は進行卵巣癌の初回化学療法後の維持療法、および再発卵巣癌における治療にあたり、PARP 阻害剤使用の有無について重要な指標とされる。BRCA1/2 遺伝子は相同組換え修復に関与し、その病的バリエーションは HRD を引き起こすとされているが、それ以外にも HRD は様々な原因で生じるとされている。BRCA1/2 遺伝子は漿液性癌での発現率が高く、HRD 検査についても同様かについて後方視的に検討した。【方法】当院で加療した術後化学療法後の維持療法を投与している進行卵巣癌および腹膜癌 Stage III/IV 期症例と、3 つ以上の化学療法歴のある再発卵巣癌症例を対象とした。14 症例に HRD 検査を行い、組織型、HRD および tBRCA 陽性率、ゲノムの不安定スコアについて検討した。【成績】年齢中央値は 62 歳 (42-85)、全症例で PS0。家族歴に第 2 度近親者が乳癌および卵巣癌の既往を 3 例に認めた。HRD 陽性を 7 例 (53.8%) に認め、6 例 (46.2%) が陰性であり、tBRCA 陽性は 1 例 (7.7%) 認め、(解析不可を 1 例認めた)、ゲノムの不安定スコア中央値は 43 (22-71) であった。組織型の内訳は漿液性癌が 9 例、類内膜癌が 1 例、明細胞癌が 1 例、粘液性癌が 1 例、卵巣癌肉腫が 2 例であった。漿液性癌の HRD 陽性率は 55.6%、ゲノムの不安定スコアは 44.2 ± 19.3 、それ以外の組織型の陽性率は 40%、スコアは 46.3 ± 21.8 と差を認めなかった。【結論】当院で HRD 検査を施行した症例の検討を行った。卵巣癌肉腫などの稀少な組織型についても HRD 陽性の症例を認め、現在 Olaparib と Bevacizumab の併用維持療法を行い、再発を認めていない。組織型が特殊な症例においても、HRD 検査を勧めることが示唆されるも、さらなる症例の蓄積が必要と考えられる。

P-18-9 当院で myChoice 診断システムを実施した患者背景・検査結果

兵庫県立がんセンター
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【目的】卵巣癌の初回治療におけるコンパニオン診断として相同組換え修復欠損 (HRD) と腫瘍 BRCA 変異 (tBRCAm) を調べる myChoice 診断システムを実施した。当院での結果をまとめ、考察する。【方法】当院で初回治療時に検査を受けた全例を対象とした。2021 年 9 月 30 日をデータカットオフとし、患者背景と検査結果を統計処理した。連続変数を中央値 (最小-最大) で示す。【成績】32 例が検査を受けた。診断時の年齢は 63 (34-83) 歳であった。診断は卵巣癌が 23 例 (71.9%)、卵管癌が 5 例 (15.6%)、原発性腹膜癌が 4 例 (12.5%) であった。進行期 (FIGO) は III 期が 16 例 (50%)、IV 期が 16 例 (50%) であった。組織型は高異型度漿液性癌が 23 例 (71.9%)、類内膜癌が 3 例 (9.3%)、明細胞癌が 1 例 (3.1%)、癌肉腫が 2 例 (6.2%)、確定困難が 3 例 (9.3%) であった。検体採取方法は開腹手術が 11 例 (34.4%)、腹腔鏡下手術が 18 例 (56.2%)、針生検が 3 例 (9.4%) であった。全例で検査結果を得られた。tBRCAm を 13 例 (40.6%) に認めた。ゲノム不安定 (GI) スコアが 42 以上であったのは 20 例 (62.5%) であった。全症例の GI スコアは 58.0 (2-81) であった。tBRCAm の全例が GI スコア 42 以上であった。【結論】III 期以上の卵巣癌の全例に検査を実施し、tBRCAm の陽性率ならびに HRD の陽性率は想定よりも高かった。

P-18-10 進行卵巣癌に対する HRD 検査と BRACA analysis の実施状況ならびに検査施行時期について

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【目的】近年、卵巣癌に対する維持療法として PARP 阻害薬の有用性が示されつつある。同時に、HRD (homologous recombination deficiency) の有無が PARP 阻害薬の適応を判断する上で重要となる。今回、当院での進行卵巣癌に対する HRD 検査と BRACA analysis の実施状況などにつき報告する。【方法】対象は進行卵巣癌に対して HRD 検査を行った 14 例である。HRD 検査ならびに BRACA analysis の結果、組織型、施行タイミングを検討した。【成績】14 例のうち HRD 陽性が 6 例、陰性が 6 例、検査不能が 2 例であった。陽性であった症例の組織型は高異型度漿液性癌が 4 例、奇形腫の悪性転化が 1 例、混合型が 1 例であった。陽性であった症例のうち tBRCA 陽性のものが 3 例あり、そのうちの 1 例に BRACA analysis を施行した。検査のタイミングとしては、HRD 検査が導入された後に発症した卵巣癌症例においては PDS 後もしくは NAC+IDS 後の補助化学療法の 1-3 コース目までに検査を提出しているものがほとんどであった。また、HRD 検査が導入される前に初回治療が終了していた症例については再発時に検査を提出しているものが多く、HRD 検査に先立って BRACA analysis 検査に提出している症例が 4 例あったが、いずれも gBRCA に病的バリエーションを認めなかった。【結論】当院での進行卵巣癌に対する HRD 検査結果は海外の文献における頻度と大きな相違を認めなかった。手術療法後の補助化学療法の早い段階で HRD 検査へ提出している症例が多くみられ、維持療法を選択するうえで一つの重要な判断材料となっている。HRD 検査ならびに BRACA analysis を実施する適切な時期などについては定まったものはなく、今後もさらなる症例の蓄積が必要である。

P-19-1 当院の myChoice™ 診断システムの臨床実装

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【目的】近年、卵巣癌・腹膜癌の治療は、遺伝子パネル検査や、BRACAnalysis[®], myChoice™ 診断システムといったコンパニオン診断の登場により目覚ましい進歩を遂げている。2021年より保険収載された myChoice™ 診断システムの当院における実装について報告する。【方法】2021年3月～2021年9月の期間に、当院で myChoice™ 診断システムを行った卵巣癌・腹膜癌12例を対象とし、その検査結果と提案した治療について後方視的に検討した。【成績】12例中の内訳は、卵巣癌10例(83%)、腹膜癌2例(17%)であった。平均年齢は58.9歳、組織型は high-grade serous carcinoma 10例(83%)、clear cell carcinoma 1例(8%)、low-grade serous carcinoma 1例(8%)であった。HRD陽性が5例(42%)認められ、GI score (ゲノム不安定性の状態スコア)のみ陽性が3例、GI score および腫瘍組織の BRCA 遺伝子変異がともに陽性が2例(17%)であった。HRD陽性の5例中3例で維持療法として PARP 阻害薬を投与し、2例にも今後 PARP 阻害薬を使用することを検討している。【結論】当院で myChoice™ 診断システムを施行した症例で、HRD陽性の症例は42%(12例中5例)であった。卵巣癌・腹膜癌における更なる治療結果向上には積極的なコンパニオン診断を行っていくことが望まれる。

P-19-2 卵巣癌 III/IV 期に対する myChoice™ 診断システムによる HRD 診断と臨床経過に関する検討

宮崎大附属病院

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【目的】進行卵巣癌ではその約50%に相同組換え修復欠損(以下 HRD)を認める。また、myChoice™ 診断システムによる HRD 検査が2021年1月に保健収載されことにより、HRD 検査陽性(スコア42以上)は、進行卵巣癌の初回治療の維持療法に PARP 阻害薬を使用する必要条件となった。今回の HRD 検査スコアが臨床経過にどのような影響があるかを検討した。【方法】2021年に当院で卵巣癌 III/IV 期に対して初回治療を行ない、HRD 検査を施行した10症例を検討対象とした。【成績】年齢39～74(中央値61)、病期は III 期6例、IV 期4例、組織型は HGSC(High grade serous carcinoma)9例、EM(Endometrioid carcinoma)1例であった。初回手術は PDS2 例のみであり、7例は病期確定のための試験開腹術を行い、1例のみ腹水細胞診後の NAC+IDS を行なった。HRD陽性は6例であり、tBRCA は3例で陽性であった。IDSを行なった8例中 HRD スコアが63以上の症例では NAC+IDS で CR が得られた。逆に HRD スコア53以下の症例では IDS での suboptimal が5例中4例に認められた。【結論】myChoice™ 診断システムによる HRD 検査では、スコアが高い症例に初回化学療法が有効な症例が多くなる傾向を認めた。HRD スコアが低い症例では、プラチナを含む NAC 後の IDS でも suboptimal になることが多く、optimal surgery でも再発までの期間が短いことが示唆される。

P-19-3 当院における初発進行卵巣がん患者に対する HRD 検査の現状

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【目的】2020年12月、相同組み換え修復欠損(HRD)を有する卵巣がんに対して、初回化学療法後の維持療法としてベバシズマブとオラパリブによる併用維持療法が承認された。それに伴い、コンパニオン診断である myChoice 診断システム(HRD 検査)も保険適用され普及してきた。当院で HRD 検査が施行可能となった2021年6月以降の検査状況について報告する。【方法】2021年6-9月にかけて HRD 検査を実施した初発進行卵巣がん症例を対象とし、患者背景、検査陽性率(HRD, tBRCA), GIS 値, 検体採取時期などを後方視的に調査した。【成績】対象期間内に、22例(III期13例, IV期9例)に HRD 検査を実施した。HRD陽性は12例(55%)、HRD陰性は8例(36%)、解析不可能は2例(9%)だった。HRD陽性かつ tBRCA陽性は4例(18%)で、全例に対し gBRCA1/2 遺伝子検査について説明したが、2例は検査を希望しなかった。検査を希望した2例中、1例は gBRCA2 陽性、1例は検査準備中である。組織型は漿液性が18例(うち HRD陽性は61%)、明細胞が3例(すべて HRD陰性)、類内膜が1例(HRD陽性)だった。漿液性癌における HRD陽性例の年齢は、HRD陰性例に比較して有意に低かった(58 vs 72, p=0.03)。また、年齢と GIS 値には負の相関を認めた(r=-0.48)。提出した検体は、PDS 検体が10例、NAC開始前の生検組織が8例、NAC後の IDS 検体が4例だった。解析不可能だったのは、NAC後の IDS 検体が1例、他院での NAC 開始前の生検組織が1例だった。【結論】当院における初発進行卵巣がん症例の HRD陽性率は55%であった。今後症例数の蓄積により、本邦における組織型別の HRD陽性率などが明らかとなることに期待したい。

P-19-4 がん遺伝子パネル検査の現状と課題

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【目的】「がん遺伝子パネル検査」は標準治療終了後のがん患者の治療選択肢を拡大することを目的として2019年6月に保険適用された。厚生労働省の調査では、2020年8月時点で8.1% (607人/7,467人)の患者が「がん遺伝子パネル検査」に基づく治療を受けている。本研究は当院での「がん遺伝子パネル検査」の現状を調査することを目的とした。【方法】2019年より「がん遺伝子パネル検査」を実施した、標準治療終了後の婦人科がん患者38例(卵巣がん:18例, 腹膜癌:1例, 子宮体癌:9例, 子宮頸癌:5例, 肉腫:5例, 外陰癌:1例)を後方視的に検討した。【成績】FoundationOne®CDxがんゲノムプロファイルを用いた「がん遺伝子パネル検査」を行い、全ての症例において何らかの遺伝子変異が検出された。検査に基づく治療が提示された症例は5例(13%)であり、子宮癌肉腫でCDK12遺伝子変異、子宮体癌(漿液性癌+類内膜癌)と卵巣がん(明細胞癌)でBRCA1遺伝子変異、子宮体癌(漿液性癌)と子宮頸部腺癌(粘液性癌)でERBB2遺伝子変異が確認された。5例中、2例は標準治療施行中であり、1例は当院で対象となる治験に参加しておらず治療を断念、1例は治療待機中に原病死した。ERBB2遺伝子変異が認められた子宮頸部腺癌症例に対してトラスツズマブが投与されたものの、奏効しなかった。【結論】「がん遺伝子パネル検査」を実施した38例のうち、検査に基づく治療を行った症例は1例(2%)であり、奏効を得られなかった。現状治療に結びつく症例は限られており、検査のメリットを最大限享受できていない状況が示された。更なる治療適応拡大に向けた前臨床研究、臨床研究が望まれる。

P-19-5 当科におけるがんゲノム遺伝子パネル検査の有用性の検討

名古屋市大

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標準治療がない、または局所進行もしくは転移が認められ標準治療が終了となった固形がん患者に対して行う「がん遺伝子パネル検査」が2019年に保険収載され、再発以降の癌患者に対する治療選択肢の可能性が広がった。2019年11月から2021年8月に当科でがんゲノム遺伝子パネル検査を行った婦人科悪性腫瘍19例について、院内の倫理委員会の審査を経て診療録を用いて詳細を検討した。年齢は中央値60歳(46-79歳)で、子宮頸癌3例、子宮体癌5例(うち1例は卵巣癌との重複癌)、卵巣癌8例、外陰癌1例、子宮内膜間質肉腫1例、原発不明癌(子宮頸癌として治療)1例であった。出検したパネル検査の種類は、18例がFoundation One CDx®, 1例がNCC オンコパネル®であった。パネル検査前に施行した化学療法レジメン数の中央値は3レジメンであった。エキスパートパネルの結果から、治療につながる保険診療もしくは臨床試験のある遺伝子変異を認めた症例は11例にのぼった。そのうち3例は臨床試験の適格基準を満たさず、2例は遠方のため治療を受けず、1例は実施中の化学療法を継続した。実際に変異に基づいた治療を施行できたのは5例(26%)であった。3例は免疫チェックポイント阻害剤、1例はプラチナ製剤を使用しその後PARP阻害薬、1例はFGFR阻害剤の投与を受けた。5例のうち1例はニボルマブ投与にてPRとなり、PFS10か月以上と経過良好であった。26%が実際に治療施行できたことは開始前の予測を上回っており、パネル検査の臨床的有用性が確認できた。適切な時期に提案することが必須であると考えた。

P-19-6 当院における遺伝学的検査成績に関する現況報告とその課題

帝京大病院

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【目的】婦人科腫瘍に対する遺伝学的検査に基づいた治療方針決定が一般的となった。当院で施行した遺伝子学的検査の現状について検討する。【方法】当院ではゲノム診療外来を開設しており、認定遺伝カウンセラー®とともに総合的なケアを行っている。当院で施行されたBRCA遺伝学的検査、MSI検査、HRD検査の検査数およびその陽性率、陽性者の治療経過・転帰について、後方視的に検討し考察を行った。【成績】2019年4月から2021年9月までに34例のBRCA遺伝学的検査が施行された。コンパニオン診断目的は32例、遺伝性乳癌卵巣癌症候群(HBOC)を疑い受検したのは2例であった。8例(23.5%)で病的変異が陽性であった。陽性者は卵巣癌6例、腹膜癌1例(いずれも漿液性癌)、乳癌1例であり、年齢中央値は55.5歳であった。陽性者のうち1例はHBOCでRRSOを施行し、5例はOlaparib維持療法が導入された。2例は初回療法中のため今後導入が検討される。8例の陽性者は全員生存しているが(無病増悪期間(PFS)中央値20か月)、陰性であった26例のPFS中央値は15か月であった(p=0.22)。MSI検査数は14例で、4例(28.6%)が陽性であった。陽性者の3例にPembrolizumabが導入された。陽性者には遺伝カウンセリングが導入されているが、Lynch症候群の確定診断まで希望される患者はいなかった。HRD検査数は4例で、2例(50%)が陽性であり、Olaparib+Bevacizumab療法やNiraparibの導入を検討している。【結論】積極的に遺伝学的検査を施行していくことは重要であるが、検査が陰性となった場合の治療成績や、検査の持つ意義について遺伝カウンセリングを含めた十分な説明を事前に行い、癌患者の心理的な面を含めたケアが求められる。

P-19-7 当科におけるがん遺伝子パネル検査の実際

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【目的】近年、悪性腫瘍に対する個別化医療の進歩はめざましく、がんゲノム医療の治験も世界中で行われている。本邦でもがん遺伝子パネル検査が2019年6月に保険収載され、婦人科領域においてもがんゲノム医療が本格的に始まっておりその実情を知ることは重要である。【方法】当科では既存の治療に抵抗性の婦人科悪性腫瘍に対してがん遺伝子パネル検査の一つであるFoundationOneCDxがんゲノムプロファイル検査を施行しているが、今回、2019年6月から2021年10月までに当科で施行したFoundationOneCDxがんゲノムプロファイル検査の実際について診療録をもとに後方視的に検討したので報告する。【成績】症例数は13例、疾患の内訳は卵巣癌7例、卵巣癌肉腫1例、子宮体癌1例、子宮肉腫2例、子宮癌肉腫1例、子宮頸癌1例であった。そのうち推奨薬ありは7例、推奨薬なしは5例、患者死亡により検査のみで推奨薬の有無について検討されなかったものが1例であった。推奨薬あり7例のうち5例は卵巣癌、卵巣癌肉腫であり、PARP阻害剤、Pembrolizumab、EGFR阻害剤が推奨され、2例は子宮癌肉腫、子宮肉腫でLDK12、FGFR、CDK274、METに対する推奨治験あるいは患者申し出療養が提案されていた。然しながら推奨薬あり7例のうち実際に治療開始されたものは1例のみであり、3例は状態悪化で治療されず、3例は今後使用考慮されるが使用時期は未定である。【結論】現在の体制では検査時期や使用するタイミングによっては、患者の状態悪化で推奨薬を使用できない場合があることが示唆された。【結論】今後、がん医療のいっそうの個別化が進むにつれ、患者ごとにより効率のよい治療が提供できる体制が望まれる。

P-19-8 婦人科がん患者にFoundationOne CDxを実施した場合の薬剤到達率の検討

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【目的】本院では2018年6月に包括的ゲノムプロファイリング (CGP) が倫理承認され、2019年11月から保険診療で実施した。これまでに実施した婦人科がん患者についてその現状を検討する。【方法】2019年11月から2年間にCGPを実施した婦人科がん患者について、現時点での臨床試験や治験状況を考慮した薬剤到達率を検討した。【成績】実施数53名。年齢中央値61歳(36-81歳)。原発部位は、卵巣・卵管・腹膜18名、子宮体部15名、子宮頸部17名、その他3名。組織型は上皮性癌48名、肉腫5名。実施した検査は全例FoundationOne CDx (F1)であった。得られた結果から薬剤へのアクセス可能な遺伝子変化は、PIK3CA/PIK3RI 15名 (JRCTs051190006)、相同組み換え修復遺伝子4名 (子宮体癌3名、原発不明癌1名)、MSI/TMB-high 11名 (MSI-high 3名、MS stable/TMB-high 8例 [子宮頸癌5名、POLE陽性子宮体癌2名、卵巣癌1名])、ERBB2増幅2名 (子宮体癌1名、子宮頸部胃型粘液性癌1名)。当科で実施しているトランスレーショナルリサーチ以外に、F1検査によって保険適応薬や治験薬に到達できるのは25% (53名中13名)と推定された。【結論】CGP開始当初と比較して遺伝子変化に基づく治験が増加しており、以前は対象外であった患者もアクセス可能となっていると思われた。

P-19-9 当院における遺伝カウンセリングの変遷

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【目的】本施設では2003年より遺伝カウンセリングを専門とする中央診療施設を設立し、遺伝カウンセリングを継続してきた。初期にはカウンセリングの対象はほとんどが周産期であった。2019年にがんゲノム検査が保険適応となり、遺伝カウンセリングの対象として腫瘍関連のクライアントが増えてくることが想定される。そこで、どのような変遷が見られるのかを検討した。【方法】2003年～2020年3月末に本施設で遺伝カウンセリングを行った症例を対象とした。年次ごとに、遺伝カウンセリングを行った初診件数と、疾患群を検討した。また、がんゲノム検査を含めた腫瘍関連遺伝学的検査を行った症例のうち、どのくらいの症例で遺伝カウンセリングを行っているかを検討した。【成績】当初年間2例しかなかった遺伝カウンセリング件数は、2020年度には年間130～140例程度で推移している。2020年度の内訳は周産期が98例であるのに対し、腫瘍は15例である。遺伝性腫瘍の遺伝カウンセリングはがんゲノム検査の影響で増加傾向があるが、著明に増加しているわけではない。40例のがんパネル検査の結果、生殖細胞系列変異の可能性があり、開示対象と判断された例が10例あったが、実際に遺伝カウンセリングを行った症例は5例で、遺伝カウンセリングを希望しなかった症例は4例であった。我々は、原則としてがん関連遺伝学的検査時に認定遺伝カウンセラーが同席しているが、主治医からは、同席してほしいという意見が多い。【結論】遺伝カウンセリングの実施件数は確実に増加している。現時点で遺伝性腫瘍に関する遺伝カウンセリングの割合は、全体の10%程度であるが、今後増加してゆくと思われる。

P-20-1 BMP 経路は婦人科癌の新たな治療標的となり得る

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【目的】BMPs (bone morphogenetic proteins) は TGF β ファミリーのリガンドで、胚発生や骨リモデリングに不可欠である。近年、BMP 経路は血管新生や EMT (epithelial-mesenchymal transition) を誘導しがんの進展に寄与することが示唆されているが、婦人科癌に於ける働きは明らかでない。婦人科癌の中でも卵巣癌の腹膜播種や子宮体部の癌肉腫発生に EMT は重要な役割を担う。従って、卵巣癌と子宮体癌に於ける BMP 経路の役割を EMT の観点からも明らかにすることを目的とし、本研究を施行した。【方法】TCGA を含むデータベースを用いて、卵巣・子宮体癌検体の BMP リガンドと受容体の遺伝子発現、変異と予後との関連について解析した。次に、卵巣・子宮体癌細胞株を BMP リガンドで刺激し、細胞増殖・幹細胞性・細胞遊走・浸潤をそれぞれ MTS・スフェア形成・スクラッチ・細胞浸潤アッセイで評価した。また、EMT 転写因子と関連タンパクの発現を各リアルタイム PCR とウエスタンブロット法・細胞免疫染色で解析した。最後に、卵巣癌 SKOV3 細胞株同所移植モデルマウスを用いて、新規 BMP 阻害薬 RK783 の効果を評価した。【成績】卵巣・子宮体癌検体では、高頻度で BMP リガンドと受容体の mRNA 高発現を認めた。また、子宮体癌では他がん種と比較し BMP1 型受容体である ACVRI に高頻度に変異を認め、約半数は活性化型変異であった。更に、卵巣癌では BMP2, 子宮体癌では BMP7 高発現が予後不良と相関した。次に、細胞株を用いた実験では、BMP2 は c-KIT を誘導し細胞増殖と幹細胞性を促進し、SLUG 誘導により EMT を促進し細胞遊走を増強した。更に、マウスモデルで RK783 は有意な腫瘍縮小効果を示した。【結論】卵巣・子宮体癌で BMP 経路は腫瘍促進的に働き、BMP 阻害薬は有望な分子標的薬である。

P-20-2 絨毛癌の免疫微小環境の解明～NK 細胞抑制型受容体に着目して

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【目的】絨毛細胞では古典的 HLA-class I 抗原の HLA-A, -B 抗原を発現していない。絨毛癌細胞でも同様であるため、T 細胞の攻撃を回避し NK 細胞が免疫の中心を担っていると予測される。今回我々は、絨毛癌における NK 細胞を中心とした免疫微小環境について検討した。【方法】同意を得て採取した絨毛癌 4 例と子宮内膜癌 3 例において、腫瘍検体に浸潤するリンパ球と術前の末梢血単球細胞より抽出したリンパ球を FCM を用いて解析した。次に、絨毛癌 (妊娠性 13 例, 非妊娠性 4 例) の腫瘍検体を用いて腫瘍内浸潤 NK 細胞と NK 細胞抑制型受容体の発現を免疫組織学的染色で検討し、腫瘍細胞の染色強度と陽性細胞の分布割合から計算する H score を用いて評価した。さらに、絨毛癌細胞株 3 種と正常絨毛細胞株 (HTR8) を用いた RT-PCR で NK 細胞抑制型受容体の mRNA 発現を調べた。【成績】絨毛癌の腫瘍内では、NK 細胞/CD8 陽性 T 細胞比率が末梢血よりも有意に上昇しており (p=0.0232), 子宮内膜癌と比較しても有意に高かった (p=0.0176)。免疫染色では絨毛癌では全例で NK 細胞が腫瘍に浸潤していた。絨毛癌組織での免疫染色では、H-score が 100 以上となる症例が PD-L1 は 17 例中 14 例, HLA-G では 15 例中 8 例と多く認めた。さらに PD-L1 は化学療法実施前が実施後より、また治療例が死亡例より有意に発現が高かった (p=0.004, p=0.0207)。RT-PCR では、PD-L1 では mRNA 発現が各絨毛癌細胞株において HTR8 より高発現であった。【結論】今回の検討から、絨毛癌の免疫環境においては NK 細胞が重要である可能性が示唆された。また絨毛癌では NK 細胞抑制型受容体、特に PD-L1 が高発現しており、NK 細胞抑制性シグナルの解除が絨毛癌治療につながる可能性がある。

P-20-3 巨大子宮頸部筋腫に対し全腹腔鏡下子宮摘出術を実施した 1 例—頸部筋腫の半核出は術野展開に対する有効性の検討

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【目的】子宮頸部筋腫は、約 1-2% と比較まれな疾患である。子宮筋腫全体が腫大することで子宮動脈や尿管の解剖学的変位を来すことが多く、子宮全摘術は手技的に困難である。巨大子宮頸部筋腫に対し、全腹腔鏡下子宮筋腫摘出術を実施した 1 例を経験したので報告する。【方法】41 歳 0 経妊 0 経産。過多月経にて手術目的に紹介となった。経陰診察では外子宮口が観察でき、骨盤造影 MRI では頸管左側から外側に発育する 10*7 cm の子宮頸部筋腫を含め、多発子宮筋腫を認めた。術前に GnRH アゴニストを 5 回投与し、全腹腔鏡下子宮摘出術施行の方針となった。子宮頸部筋腫は外側発育のため、子宮マニピュレーターは容易に留置でき、子宮動脈本幹を同定・結紮し、尿管を子宮動脈交叉部まで同定した。傍子宮結合織を処理するに、両側卵管間膜、卵巣固有韌帯、広間膜後葉を処理したのち両側基韧带及びその頭側を結紮した。その間を焼灼切断しつつ、基韧带の処理を試みたが、左側は子宮頸部筋腫のため難渋した。頸部筋腫を子宮頸部から剝離するように基韧带側の筋腫のカプセルを切開し、筋腫を半核出した。傍子宮結合織を外子宮口レベルまで処理し、型の通り頸部筋腫と子宮体部を一塊にして摘出した。【成績】手術時間 3 時間 57 分、出血 50 ml、検体重量 944 g であった。術中・術後合併症は無かった。【結論】巨大子宮頸部筋腫に対し、全腹腔鏡下子宮摘出術を施行した症例を経験した。子宮頸部筋腫は解剖学的問題において他部位に比べ子宮全摘術は操作に難渋することが多く、子宮動脈本幹の処理、尿管の同定は手術合併症の回避に有効であり、頸部筋腫の核出・半核出により術野展開や基韧带処理が容易となることが示唆される。

P-20-4 子宮内膜症モデルマウスにおける血管内皮グリコカリックスの障害

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【目的】子宮内膜症は腹腔内に慢性的な炎症を起こすことが知られており、近年では炎症性疾患としての側面が注目されている。全身性炎症性疾患では血管内皮障害およびグリコカリックスの障害が起こり、その構成成分の1つであるヒアルロン酸の血中濃度が上昇することが報告されている。本研究は子宮内膜症マウスモデルと対照群のマウスを用い、血清ヒアルロン酸濃度を計測することで、子宮内膜症モデルマウスにおけるグリコカリックス障害の可能性について検討することが目的である。

【方法】1mm程度に細切したドナーマウスの子宮片をレシビエントマウスの腸間膜や腹腔内の脂肪組織内に移植し内膜症性病変を発症させた子宮内膜症モデルマウスと、偽手術のみの対照群マウスを用い、ELISA法により血清中のヒアルロン酸濃度を計測し、比較検討した。【成績】子宮内膜症モデルマウス群 (n=15) と対照群 (n=5) では血清ヒアルロン酸濃度は 9.12 ± 2.91 vs. 5.11 ± 1.53 ng/ml ($p < 0.05$) と、子宮内膜症モデルマウス群で有意に高かった。【結論】子宮内膜症モデルマウスを用いた本実験系では、子宮内膜症の発症により血清ヒアルロン酸濃度が上昇することがわかった。この結果により、子宮内膜症は腹腔内の炎症のみにとどまらず、血管内皮のグリコカリックスの傷害も引き起こす可能性が示唆された。

P-20-5 骨髄移植とともに骨髄間葉系間質細胞を投与されたマウスは子宮内膜症の発育を抑える

札幌医大附属病院

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【目的】免疫調整能を持つ骨髄間葉系間質細胞 (MSC) が慢性炎症性疾患の性格を持つ子宮内膜症の病態へ与える影響を検討することを目的として以下の実験を行った。【方法】a) 培養した MSC を子宮内膜症モデルマウスへ投与した。MSC のかわりに溶媒を投与したものをコントロールとして比較する。投与 60 日後に病変のサイズを計測し、病変内に投与した MSC が存在するかどうかを調べるため免疫蛍光染色を行った。b) 培養した MSC をマウスの骨髄へ生着させることを期待して、骨髄移植と同時に MSC を投与した。骨髄移植単独のものをコントロールとした。移植 30 日後に子宮内膜症誘発手術を行い、術後 60 日目に a) と同様に病変を観察した。c) 骨髄移植に MSC 投与を併用することで MSC が体内へ生着したかどうか確認するためフローサイトメトリーを行った。さらに、MSC 投与による骨髄の環境変化を調べるため、移植後 30 日目に骨髄細胞における様々なサイトカインの発現量を qRT-PCR で比較した。【成績】a) 病変のサイズに変化はなく、投与した MSC も確認できなかった。b) 骨髄移植に MSC 投与を併用したマウスでは、コントロールマウスに比べて病変は有意に縮小した ($P < 0.000001$)。c) 骨髄移植に MSC 投与を併用したマウスは、コントロールマウスと比較して、骨髄細胞中の TNF- α および CXCR4 mRNA の発現量が低下していた。【結論】MSC は直接的には子宮内膜症の病態に影響を与えないであろうことがわかった。しかし、骨髄移植時に MSC 投与を併用すると、MSC は生着しないがマウスの骨髄環境に変化をきたし、そのマウスでは子宮内膜症病変の発育が抑制されることがわかった。

P-20-6 子宮筋腫の局所増殖におけるマクロファージ活性化に関する免疫組織学的研究

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【目的】子宮筋腫は均一に増殖する良性腫瘍である。我々は栄養血管の破綻による出血壊死部と通常筋腫部の境界領域にマクロファージが混在する局所増殖巣の存在を報告している。今回は増殖巣の形成機序を明らかにするために増殖巣および辺縁組織に存在する活性化マクロファージの関与について検索した。【方法】材料：閉経前の直径約 5cm の出血巣を有する通常型壁内筋腫 6 症例を用いた。観察は、HE 染色および免疫染色に Ki-67, CD34, VEGF, bFGF, CD68 抗体を用い、さらに M1M Φ に CD68-iNOS, M2M Φ に CD206 を加え、アポトーシスの観察には p53 と TUNEL 法を行った。観察部位：出血壊死巣部 (a), 壊死辺縁部 (b), 局所増殖巣 (c), 通常筋腫部 (d) とした。【成績】1. 局所増殖巣 (c)：長紡錘形の筋腫細胞は bFGF 陽性を示し約 2mm の幅で集束していた。Ki-67 と CD-34 陽性細胞の密度は通常筋腫部の約 4 倍である。iNOS：CD206 陽性は 1：1 同程度であった。なお、p53, TUNEL は陰性であった。2. 出血壊死辺縁部 (b)：p53 および TUNEL 陽性細胞が高頻度に認められ、iNOS：CD206 は 1：3 と CD206 が多数存在した。CD206 は VEGF 陽性であった。3. 出血壊死部 (a)：細胞密度は乏しく硝子様変性を認め、壊死細胞と TUNEL 陽性細胞が点在した。CD206：iNOS は 1：1 であり、p53 は陰性であった。【結論】1. 出血壊死辺縁部における多数の CD68 陽性細胞の存在は、出血により障害を受けた筋腫細胞が p53 により誘導されたアポトーシス細胞を貪食するため出現したと考える。2. 出血壊死辺縁周囲に高密度に分布する M2M Φ は VEGF を産生し、さらに増殖巣の筋腫細胞自身が bFGF を産生することにより腫瘍血管の新生を促し局所増殖巣が形成されるものとする。

P-21-1 急性腹症で診断された卵管捻転の4症例

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【はじめに】婦人科急性腹症の原因として、異所性妊娠、卵巣腫瘍の茎捻転や破裂、骨盤腹膜炎などがあるが、卵管捻転は稀である。当院で4年間に経験した4症例の卵管捻転について報告する。【症例1】25歳、G0。急性腹症で紹介となった。経陰超音波、MRI検査で4×6.5cm大の傍卵巣嚢腫茎捻転が疑われ、腹腔鏡下手術を施行した。孤立性左卵管水腫の捻転で、左卵管を摘出した。【症例2】20歳、性交経験なし。発達障害、知的障害、精神科の病院に入院管理中。急性腹症で紹介となった。経腹超音波、CT検査で骨盤内に2つの腫瘤を認めた。卵巣腫瘍の茎捻転を疑い、腹腔鏡下手術を施行した。左卵巣嚢腫と左卵管水腫がそれぞれ捻転しており、左付属器を摘出した。【症例3】32歳、G0。急性腹症で紹介となった。経陰超音波、CT検査にて9×7cm大の卵巣嚢腫捻転が疑われ、腹腔鏡下手術を施行した。孤立性左卵管捻転で、左卵管を摘出した。骨盤内、肝周囲にクラミジア感染と思われる癒着を認めた。【症例4】17歳、性交経験なし。急性腹症で紹介となった。経腹超音波、MRI検査で右卵管水腫の茎捻転が疑われ、腹腔鏡下手術を施行した。孤立性右卵管捻転で、右卵管を摘出した。【結語】卵管捻転は150万例に1例程度の稀な疾患と報告されているが、もっと頻度は多く一度な遭遇する疾患かもしれない。術前に卵管捻転を疑った場合の術式の選択について考える必要がある。

P-21-2 子宮マニピュレーターのバルーン拡張により子宮筋層が損傷し、仮性動脈瘤を生じた一例

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【緒言】子宮マニピュレーター挿入による合併症として子宮穿孔や他臓器損傷が知られているが、バルーン拡張による子宮破裂や仮性動脈瘤の形成は稀である。今回我々は子宮マニピュレーター使用により子宮筋層の損傷をきたし、術後仮性動脈瘤を生じた一例を報告する。【症例】62歳、1妊1産。38歳で卵管閉塞を指摘、今回術前に発見されたヒラメ静脈血栓のためエドキサパンを内服していた。右傍卵巣嚢胞にたいし子宮マニピュレーターの挿入(バルーン注入液は約3ml)し腹腔鏡下両側付属器摘出術を行った。術中に子宮穿孔は認めず、術後より少量性器出血は持続していたが貧血進行なく、子宮内貯留も少量であったため術後3日目に退院した。退院後も出血は持続し、術後13日目に塊状の出血を認め来院した。造影CTの動脈相では子宮内腔に造影増強を示す7mmの結節状腫瘤を認め仮性動脈瘤と診断した。貧血進行もあり緊急で腹腔鏡下子宮全摘術を行った。子宮内腔の後壁には約3cmの縦走する内膜および筋層の裂傷を認め、同部位に血腫が付着しており血管が露出していた。損傷の形状から子宮マニピュレーターのバルーン拡張による子宮筋層の裂傷部位に仮性動脈瘤が形成されたと考えた。【結論】本症例は加齢により子宮内腔が委縮、筋層の伸展性が低下したためバルーン拡張により損傷したと考えられる。子宮マニピュレーターは腹腔鏡手術において有用な器具であるが、高齢者や子宮内癒着、炎症などにより子宮筋層の伸展性低下が想定される場合は子宮筋層の損傷に注意すべきである。また術中に子宮穿孔を認めなかった場合も不正出血が持続する際は、仮性動脈瘤を念頭に精査を行う必要がある。

P-21-3 卵巣癌術後の腔断端離開に対し腹直筋皮弁が有効であった一例

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【緒言】子宮摘出後の腔断端離開は稀であるが重篤な合併症である。腔外に腸管が脱出し穿孔、絞扼、壊死を起し重篤になることもある。今回卵巣癌術後の腔断端離開に対し、腹直筋による有茎皮弁で修復した症例について報告する。【症例】患者は、62歳、3妊2産、併存症はない。初回治療として卵巣癌IVA期に対し卵巣癌基本術式を施行した。術後は術後3か月間の性交渉禁止を指導していた。術後38日目に下部消化管精査目的に下剤を内服中に急激な下腹部痛を認め当科受診。腔鏡診で腔断端離開、小腸脱出を認め、緊急手術を実施した。開腹時すでに腸管は腹腔内に還納されており、腸管壊死は認めなかった。腔断端は高度に黒色壊死しており、再縫合は困難と判断した。腔断端の壊死組織のデブリードマンを行い、当院形成外科の協力の下、腹直筋の有茎筋弁をプロペラ皮弁として腔断端離開部位を補強し、閉鎖した。術後は感染徴候を認めることなく経過良好であり術後8日目に退院となった。【考察】今回、直視下で臓器損傷や腸管壊死がないことを確認したあとに修復を行うこととなった。これまでの症例報告では大多数が腔断端の再縫合が可能なものが多く、断端の再縫合かつ骨盤底腹膜を追加で縫合することで断端の閉鎖を行っている。また大網を有する場合は大網での腔断端補強も考慮されている。今症例では大網切除後かつ腔断端の再縫合が困難な症例であり、腹直筋による有茎皮弁での修復を行うこととなった。このような腔断端の再縫合が困難な症例には有茎皮弁での腔断端の閉鎖も有効と考える。

P-21-4 当院でのペバシズマブ使用後に穿孔を来した症例の検討

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【目的】進行・再発卵巣癌や子宮頸癌の治療において、ペバシズマブ（以下 BEV）を使用する機会は多い。重篤な合併症の1つとして、消化管穿孔（0.9%）があげられる。今回我々は、BEV 使用後比較的早期に腸管穿孔・膀胱穿孔をきたした症例をそれぞれ1例経験したため、BEV 使用例で穿孔をきたした症例について後方視的に検討した。【方法】2014年1月から2021年8月に、自院で BEV を使用した143例（年齢30-85歳、中央値57歳）を検討。【成績】症例①腹膜癌に対して、術前化学療法として TC（パクリタキセル+カルボプラチン）2コース、BEV1コース施行後、day12に腹痛・炎症反応の上昇を認め、小腸穿孔が疑われ穿孔部閉鎖術施行した。症例②子宮頸癌再発に対して、TP（パクリタキセル+シスプラチン）+BEV1コース施行し、day5に下腹部痛出現し受診。CTで膀胱破裂を認め、CTガイド下ドレーナージや尿管ステント留置術を行い、全身状態が改善したところで両側尿管皮膚瘻造設術を施行した。上記2例を含め、当院で BEV を使用中に穿孔あるいは穿孔疑いで投与を中止した症例は10例、そのうち外科的治療を行なった症例は4例であった。手術により穿孔部位が判明した症例は2例、穿孔部位が不明であった症例は2例であった。【結論】消化管穿孔の発症時期に関しては、GOG-2018試験では2-6回目の投与で発症している症例が40症例中37例との報告がある。今回の結果からは1回目の投与でも、消化管穿孔をきたす可能性があることが示唆された。BEV 使用例に関しては、投与回数が少ない症例であっても腹痛を生じた症例では穿孔の可能性を念頭に置き、経過をフォローしていく必要がある。

P-21-5 カルボプラチンによる過敏性反応発症後のプラチナ製剤再投与に関する後方視的検討

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【目的】カルボプラチンは婦人科悪性腫瘍患者の予後改善に大きく寄与しており、過敏性反応 HSR により再投与を断念することは感受性患者にとって非常に大きな痛手となる。当院では HSR の重症度によらず同一薬の再投与は行わず、他のプラチナ製剤へ変更し、必要に応じて脱感作療法を行う方針としている。【方法】2010年から2021までの期間に当院において治療を受けた婦人科悪性腫瘍患者の中で、カルボプラチンによる HSR が発生した30人を対象とし、HSR 発生までの投与回数、発生後のプラチナ製剤投与の試みと2回目の HSR 発生状況を調査した。【成績】カルボプラチンによる HSR が発生した28人において、HSR 発生までの投与回数は、6回以下が4人（14.3%）、7-12回が15人（53.6%）、13-18回が7人（25%）、19回以上が2人（7.1%）であった。このうち19人でシスプラチン脱感作療法、7人でシスプラチンの通常投与、1人でネダプラチンの通常投与によるプラチナ再投与を試み、24/27人（89%）において原疾患の寛解か病勢進行まで継続可能であった（2-25サイクル、平均7サイクル）。しかし、シスプラチン脱感作療法2人とシスプラチン通常投与1人の計3人で、4、5、7サイクル目に再び重篤な HSR が発生した。この3人のうち1人では更にネダプラチンの通常投与を試み病勢進行まで2サイクル継続可能であり、他の1例はプラチナ製剤の再々投与を行わなかった。【結論】HSR 発生後のプラチナ製剤再投与は成功率が高く、厳重な経過観察のもとで試みる価値があると思われる。一方、2回目の HSR は重篤であり、心肺停止にも対応可能な体制で臨む必要があると思われる。

P-21-6 医師業務負担軽減のための診療科データベースの構築

埼玉県立がんセンター

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【目的】各種学会年次報告や研究等のために診療科治療台帳を作成しておくことは有用である。一方で、入力項目が増えれば増えるほど医師の業務量は増え、また、人為的ミスによりデータの正確性が損なわれる可能性がある。本検討では、IT 技術を駆使して医師の業務負担を軽減しつつ、正確な入力支援が行えるデータベースの構築を目的とした。【方法】データベース構築ソフトとして FileMaker Pro 19 (Clarif) を用いた。DWH (データウェアハウス) として、診療 DWH Lites (NEC) を用いた。入力支援のために、NEXT Stage ER (TXP Medical) のテキスト解析 AI を利用した。また、治療台帳等作成に係るアンケートを医師に対して行った。【成績】医師が台帳入力に費やす時間は医師一人あたり約4時間/月であった(n=7)。特に負担を感じている入力作業としては病理検査結果項目が多かった。一方、DWH を利用することで、入退院履歴、手術関連項目(術式、手術時間、出血量、術者等)、化学療法関連項目(実施レジメン、実施薬剤、投与量、PARP 阻害剤投与歴等)、予後(受診歴)は自動で入力することが可能となった。また、テキスト解析 AI により、既往歴や服薬歴などの初診時入力項目は入力誤差(揺らぎ)によらず正規化・構造化して入力することが可能となった。さらに、定型化された病理レポートについては、テキスト解析により組織型やリスク因子、リンパ節転移個数などを自動で入力することが可能となった。【結論】IT 技術を駆使した正確なデータベースを構築することで、医師の業務負担が軽減され、その分医師が臨床や研究により専念できる環境が構築できるものと考えられた。

P-21-7 がん医療の方針選択に苦慮した進行婦人科がんの2例

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【緒言】進行婦人科がんに対して、集学的治療で積極的に制がんを試みることは一般的であるが、今回我々は、病的肥満のために婦人科検査に難渋し、進行子宮がんを診断するもがん医療の方針選択に苦慮した症例を経験したため報告する。【症例】症例1: 45歳, 未妊。BMI 38, 婦人科受診歴なし。腰痛を主訴に前医受診, 画像検査で骨盤内腫瘍と多臓器に転移性腫瘍を疑う所見を認めた。腋窩リンパ節生検で扁平上皮癌を認めたため, 子宮原発腫瘍を疑い精査したところ子宮の扁平上皮癌を確認した。化学療法を施行したが, 程なくして全身状態悪化し医療機関初診から約3か月で死亡した。症例2: 49歳, 1産婦。BMI 57, 分娩後婦人科受診歴なし。腹部膨満感と呼吸困難感のため救急搬送され来院。初診時CTで大量の胸腹水貯留と骨盤内腫瘍を認め, 婦人科悪性腫瘍が疑われた。子宮腔部生検で類内膜癌を認め, 子宮体部原発腫瘍を疑ったが, 婦人科腫瘍診断のための一般的な検査は病的肥満と全身状態不良のため施行できなかった。末期腎不全に伴う全身状態不良のためBSCの方針となり, 医療機関初診から19日目に死亡した。【考察】婦人科領域では診断時に手術不能な進行がん症例も抗がん薬物治療や放射線治療など治療介入できることは珍しくない。初診時からbest supportive careを選択せざるを得ない症例は比較的稀である。壮年期でありながら身体の状態からは標準治療を行うには困難性がある場合や高齢者においては, 症例毎に適切なアセスメントとプランニングのもとにがん医療提供することが肝要になると思われる。

P-21-8 子宮悪性腫瘍手術における腔切開時の腔分泌物細胞診の検討

自治医大さいたま医療センター

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【目的】子宮頸癌に対するランダム化比較試験で腹腔鏡下手術は開腹より有意に再発が多いことが示された。一因として、腫瘍の腹腔内露出、細胞濾出が指摘されている。今回、子宮悪性腫瘍手術の腔切開時の腔分泌の細胞診に対する検討を行った。【方法】子宮頸癌9例、子宮体癌40例の手術症例に対して、腔切開時の腔分泌物細胞診を行い、腫瘍細胞の有無について検討した。【成績】子宮頸癌9例は腹腔鏡・開腹に限らず、全例細胞診陽性だった。子宮体癌は24例が腹腔鏡、16例が開腹で手術され、腹腔鏡症例の50.0%が、開腹症例の94.4%が腔分泌細胞診陽性であった。【結論】腹腔鏡、開腹を問わず、腔管切開時は高率に腔分泌物細胞診が陽性であった。この結果から、腔管切開時に腫瘍細胞が腹腔内に散布されると推察した。そのため子宮悪性腫瘍手術では、腔管切開前後に洗浄・腫瘍のisolationをすることが必要と考える。

P-21-9 子宮筋腫の逃げ込み療法に対する GnRH antagonist 製剤の新しい投与方法について

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【目的】Pre-menopauseの子宮筋腫症例に対して、GnRH antagonist 製剤を用いた、いわゆる逃げ込み療法にGnRH antagonist 製剤を用いた際の副作用を軽減できる新しい投与方法を開発した。【方法】研究開始に当たり当院の倫理委員会に対してプロトコールをすべて公開し、審議に諮り許可を得た。各症例には十分なインフォームドコンセントを行い同意を得た。48歳以上で貧血などの臨床症状を伴い、手術を希望しない26例を対象とした。GnRH antagonist 製剤40mg/dayを4週間連続投与した後、1-2日間隔の間欠的投与方法に切り替え6か月間投与した。投与前後の血中FSH, estradiol値, hot flush (HF, VASスケールで評価)および骨吸収マーカー(血中NTx)の変化につき検討した。【成績】FSH: $20.4 \pm 9.2 \rightarrow 3.0 \pm 0.6$ mIU/ml, estradiol: $37.3 \pm 17.5 \rightarrow 17.1 \pm 5.3$ pg/mlと、いずれも有意に低下した($p < 0.01$)。HFのVAS値は $5.5 \pm 2.4 \rightarrow 6.3 \pm 2.9$ と有意の変化は認められなかった。NTx値も $39.5 \pm 18.2 \rightarrow 40.7 \pm 20.1$ nmolBCE/lと著変はなかった。6か月の治療後に閉経となったと考えられた症例は7例(26.9%)であった。【結論】子宮筋腫の逃げ込み療法にGnRH antagonist 製剤を用いる際は、副作用を軽減できる間隔を空けた投与方法が有用であると考えられた。

P-22-1 術後リンパ嚢胞が直腸穿孔をきたした1例

京都桂病院

下地 彩, 宗万紀子, 家村洋子, 水津 愛, 岩見州一郎

婦人科悪性腫瘍に対して行われる後腹膜リンパ節郭清術の合併症として術後リンパ嚢胞が知られている。リンパ嚢胞が尿管を圧迫し尿管狭窄を来すことは報告にあるが、直腸穿孔を起こした症例はこれまでに報告がない。今回骨盤内リンパ節郭清後のリンパ嚢胞が直腸穿孔をきたした1例を経験したため報告する。症例は83歳女性、2妊2産。不正出血を主訴に当院紹介受診、子宮内腔に5cmの嚢胞性病変と骨盤内に充実性腫瘍をみとめた。子宮体癌・卵巣癌合併を疑い、腹式単純子宮全摘術/両側付属器切除術/骨盤内・傍大動脈リンパ節郭清術/大網部分切除術を施行した。術後早期から左骨盤内リンパ嚢胞をみとめた。病理組織診断は左卵巣癌、high-grade serous carcinoma, IIIC期, pT2b, pN1b, M0であり、術後化学療法(パクリタキセル・カルボプラチン・ペバシズマブ)を施行した。徐々にリンパ嚢胞が増大し尿管狭窄をきたし尿管ステントを留置した。化学療法5回目終了後に発熱を訴え受診し、リンパ嚢胞の増大と感染が疑われた。抗生剤加療するも徐々に下痢が増悪し、便に黄色粘調な液体の混入があり、精査にてリンパ嚢胞の直腸穿孔が判明した。ミノマイシンによるリンパ嚢胞癒着術や腸穿孔部位への大腸カメラ下クリッピング術を試みるも奏功しなかった。当初は感染兆候なく徐々に食事摂取を開始したが、穿孔部を介したリンパ嚢胞感染を来し、人工肛門増設を要した。約3か月に及ぶドレナージ術で現在徐々にリンパ嚢胞は縮小傾向にある。術後リンパ嚢胞が直腸穿孔をきたした1例を経験した。稀ではあるが、術後リンパ嚢胞の急速な増大がみられる場合は腸穿孔のリスクも鑑み対応にあたるのが肝要である。

P-22-2 MRI検査・FDG-PET検査で悪性を疑う所見を認め、術前に悪性外陰腫瘍と考えた結節性筋膜炎の一例

岡山大病院

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結節性筋膜炎は皮下に発症する良性の病変であり、上肢、頸部、体幹部に好発し、外陰では世界的にも十数例の症例報告があるのみである。今回、外陰部に発生した結節性筋膜炎の一例を経験したので文献的考察を踏まえて報告する。患者は49歳、3妊2産、2か月前より比較的急速に増大する外陰部腫瘍を主訴に前医を受診され、外陰部腫瘍の診断にて当院に紹介となった。診察にて右大陰唇上方に鶏卵大の可動性良好で圧痛のない腫瘍を認めた。腫瘍マーカーの上昇は認めなかった。骨盤造影MRI検査では右側の外陰部皮下に3cm大の腫瘍を認め、内部は不均一な信号強度で拡散制限を伴い、リング状の濃染を示し、内部壊死を伴った悪性腫瘍が疑われた。FDG-PET検査では同部位に異常集積を認めた。転移を疑う所見はなかった。皮下腫瘍であり、生検は行わず、診断目的に腫瘍摘出術を施行した。摘出組織の剖面は白色で一部出血を伴い、組織学的に比較的均一な紡錘形細胞が束状に増殖し、細胞間の粘液、赤血球漏出を伴っていた。異型核分裂像はみられなかった。各種免疫染色から鑑別疾患の除外を行い、結節性筋膜炎と診断した。結節性筋膜炎は、数週から数か月で急速に増大する原因不明の反応性病変とされていたが、本疾患に特異的とされるMYH9-USP6融合遺伝子が同定され、単クローン性増殖を示す良性的腫瘍性病変であることが報告されている。病歴や画像検査では悪性腫瘍との鑑別、術前診断は困難と考える。典型的でない皮下腫瘍に対しては、腫瘍摘出により確定診断を行い、治療方針を検討する必要がある。

P-22-3 当院における排膿散及湯(TJ-122)著効症例の検討

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排膿散及湯は日本でつくられた漢方薬である。西洋医学的病名は皮膚化膿症、癰、癤、面疔などだが、漢方という腫物は化膿巣に止まらず良性、悪性腫瘍までを含む。筆者は実臨床において月経や妊娠に関連した皮膚トラブルのみならず、乳腺炎、開腹手術後、がんサバイバーの血栓後症候群、口内炎などに対し排膿散及湯が奏効した症例を数多く経験している。今回は、著効した症例を検討する。症例1は57歳バルトリン腺腫瘍。近医で穿刺排膿されたが疼痛、腫脹が治まらず受診した。局所は超鶏卵大に腫脹していたが、排膿散及湯と桂枝茯苓丸(TJ-25)を内服し2週後に自壊して疼痛は消失し、4週後に腫脹は消失した。症例2は64歳原発性腹膜癌IIIC期の骨盤リンパ嚢胞感染。骨盤リンパ節転移に対する開腹手術後に60mmの嚢胞が出現し、半年後に発熱と下腹部腫瘍が生じた。排膿散及湯を内服後3週で発熱はなく、嚢胞は30mmに縮小し腫瘍は触れなくなった。9週後嚢胞は消失した。症例3は52歳子宮頸癌IB1期の広汎子宮全摘術後に生じた骨盤リンパ嚢胞。術後4週に発熱と腹部膨満を訴えた。CTで肝周囲まで達する腹水と140mmの被包化した骨盤嚢胞を認めた。排膿散及湯と同時に、かえる腹で下腿浮腫も顕著であり防己黃耆湯(TJ-20)を併用した。10日で腹水は消失し骨盤嚢胞は60mmに縮小した。7週内服し、骨盤嚢胞は消失した。排膿散及湯は抗炎症作用を有し、単独または駆瘀血剤や利水剤などと併用して産婦人科疾患に広く応用可能と考える。特別な漢方医学的随証はなく、体力如何にかかわらず用いることが出来る。副作用も少なく、安全かつ有用な漢方薬である。

P-22-4 腹腔鏡下手術の術後上腹部痛と肩の痛みに対する予防的治療に関する前向き RCT 比較試験

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【目的】腹腔鏡下手術術後の上腹部痛と肩の痛みは創部痛以上に不快に感じることがあり、術後の肩の痛みを発症する頻度は30~85%との報告がある。腹腔鏡下手術後の上腹部痛と肩の痛みを軽減させるために、術中に術後腹腔内のCO₂を軽減させる工夫をし、術後胸部X線画像にて術直後のfree airを確認すると共に術後の痛みを評価した。【方法】対象は、2015年から2020年までの、当科で施行した良性疾患に対する予定腹腔鏡下手術症例とし、循環器・呼吸器疾患を有する患者や術中開腹術へ変更となった症例は除外した。本研究はRandomized Controlled Trialで、A群：手術終了時にTrendelenburg positionにし、麻酔科医により60cmH₂Oの圧で肺を加圧する、B群：手術終了時に15-20ml/kgの生理食塩水を腹腔内に注入する、C群：A群とB群の手技を両方行う、D群：コントロール、に割り付けた。評価項目は手術内容、出血量、手術時間、手術当日および術後1~4日目の肩・臍部・上腹部の疼痛の程度、free airの有無とした。【成績】症例はA群：45人、B群：41人、C群：42人、D群：47人であった。D群と比較して、B群で手術当日と術後3日目の上腹部痛が有意に低く(p<0.0001, p<0.034)、また術後4日目の肩の痛みもB群が有意に低かった(p<0.001)。術直後のfree airは、あり：136人、なし：33人であった。手術当日と術後4日目の肩の痛みが、free airなし群と比較してあり群で有意に高かった(p<0.001, p<0.001)。【結論】術後の疼痛にfree airが関与しており、手術終了時の腹腔内への生理食塩水注入が、術後の疼痛軽減に有用である可能性が示された。文献学的考察をふまえ、本研究の結果を報告する。

P-22-5 婦人科悪性腫瘍の化学療法施行中に治療関連骨髄異形成症候群を発症した3症例

手稲溪仁会病院

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【緒言】近年、集学的治療の発展により婦人科悪性腫瘍患者の長期生存例が増加している。一方で、治療関連二次性血液疾患の発症が散見され新たな問題となっている。しかし、その発症の契機について明確ではない。今回、化学療法施行中に治療関連骨髄異形成症候群(t-MDS)を発症した3症例を報告する。【症例】症例1は65歳、子宮頸癌、扁平上皮癌、進行期IVB期。CCRT後、4か月で再発し、TC療法22コース、Bev5コース、CPT11/CBDCA療法5コースを施行した。初回治療から5年6か月で末梢血に骨髄球出現と好塩基球の割合増多を認め、骨髄検査でt-MDSの診断となった。症例2は55歳、子宮体癌、類内膜癌G1、進行期IVB期。初回根治手術とTC療法6コース後7か月で再発し、TC療法25コース、陰断端再発腫瘍へRTを施行した。初回治療から3年10か月で遷延する血小板減少を認め、骨髄検査を施行し、t-MDSの診断となった。症例3は83歳、子宮頸癌、扁平上皮癌、進行期IVB期。CCRT後1年8か月で再発し、TC療法5コース、CPT11/NED療法12コース、CPT11/CBDCA療法5コース施行した。初回治療から7年2か月で急激な貧血進行のため骨髄検査を施行し赤芽球癆の診断となった。9か月後には末梢血に芽球検出あり異形成も伴うことからt-MDSと考えられた。【結論】長期化する化学療法や放射線治療により遷延する骨髄機能抑制を経験することがある。その場合、二次性骨髄としての血液疾患の発症を念頭におき、速やかに血液内科と連携をとり骨髄検査等を施行することが必要であると考えられる。

P-22-6 当院における妊孕性温存手術後の癒着因子の抽出とアウトカム

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【目的】腹部手術における術後癒着形成は、腸閉塞や不妊、慢性的な腹痛などを引き起こす他に、再手術時に腸管損傷のリスクを高める。女性は生涯において男性よりも手術を受ける回数が多いため、わたしたちは手術をするうえで癒着防止に努めなければならない。今回自施設で2ndルック可能であった手術を振り返ることで、癒着因子や影響を考察し報告する。【方法】当院にて妊孕性温存手術後に帝王切開した8症例、もしくは子宮体癌手術を施行し、追加で腹腔鏡下傍大動脈リンパ節郭清術を施行した2症例について、癒着因子の抽出を行った。項目として、子宮内膜症の有無・術者の経験・手術時の腹膜欠損面積・子宮の切開部評価・縫合糸・癒着防止剤・術後の炎症反応を挙げて統計学的評価を行った。【成績】10例中2例が癒着を認めており、いずれも子宮体癌術後であった。一方、腹腔鏡下子宮筋腫核出術や腹腔鏡下リンパ節郭清術後の症例においては癒着を認めなかった。術中の出血や術者の経験、腹膜欠損面積、癒着防止剤による有意な差異は認めなかった。【結論】癒着のリスク因子として、緊急手術、骨盤手術、下部消化管手術、60歳未満などが報告されている。今回の検討では、比較的血量が多い子宮筋腫核出術において癒着を認めず、陰断端以外に縫合操作を加えていない子宮全摘後の症例で癒着を認めた。術後の炎症反応なども相せず、リスク因子の抽出は困難であった。しかし、妊孕性温存術式において、癒着症例を認めなかったのは、癒着防止剤や手術操作の工夫によるものと思われた。

P-22-7 良性疾患に対するロボット支援下子宮全摘術 (RAH) と腹腔鏡下子宮全摘術 (TLH) の比較検討

三重大附属病院

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【目的】2018年4月に良性疾患に対するロボット支援下子宮全摘術 (RAH) が保険収載され, その症例数は着実に増加傾向にある。その一方で腹腔鏡下子宮全摘術 (TLH) との棲み分けには議論の余地がある。【方法】2015年~2020年までに行った TLH 291 例, 2017年 (校費負担)~2021年9月までに行った RAH 139 例を対象とした。適応疾患名は, 子宮筋腫・子宮腺筋症・CIN2/3とした。検討項目は, 患者背景 (年齢・BMI・既往開腹術) および周術期結果 (総手術時間・腹腔鏡操作またはコンソール時間・出血量・摘出標本重量・合併症) を後方視的に検討した。【成績】2群間の患者背景は, BMI ($p=0.461$), 既往開腹術 ($p=0.093$) と差はなかった。併存術式として, 卵巣腫瘍摘出術 (全摘・核出) は TLH 群で多かった ($p=0.001$)。総手術時間の中央値は 185 分程度で有意差はない ($p=0.979$) が, 腹腔鏡操作時間 (中央値 166 分) と比較して, コンソール時間 (中央値 130 分) は有意に短かった ($p<0.001$)。出血量も中央値は 2 群ともに 3ml であったが, RAH 群で有意に少なかった ($p=0.01$)。摘出標本重量は, TLH 群で 222g, RAH 群で 172g と, TLH 群が有意に重かった ($p<0.001$)。Clavien-Dindo 分類 grade2 以上の合併症は, TLH 群で 15 例, RAH 群で 3 例と有意差はなかった ($p=0.113$)。【結論】ロボット手術は導入して間もないため, 子宮重量の大きなものや卵巣腫瘍摘出術が必要なものは TLH 群に振り分けられ, 実際の手術操作の時間にも差がでた。一方で, コンソールまでの時間が必要であり, 習熟することで総手術時間を短縮することは可能である。

P-22-8 S 状結腸への穿孔を認めた卵巣成熟嚢胞性奇形腫に対し腹腔鏡補助下に手術を施行した 1 例

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卵巣成熟嚢胞性奇形腫の結腸への穿通は本邦においてこれまで 12 例の文献的報告を認めるのみで極めてまれである。今回われわれは, 卵巣成熟嚢胞性奇形腫の S 状結腸穿孔に対して腹腔鏡補助下に手術を実施した 1 例を経験したのでこれを報告する。症例は, 25 歳, 2 任 0 産の女性で, 2 週間持続する発熱の精査目的に当院へ入院となった。CT で骨盤内に遊離ガスを伴った石灰化を伴う嚢胞を認め, 血液検査にて高度の炎症を認めたため, 成熟嚢胞性奇形腫の腸管穿孔が疑われた。下部消化管内視鏡検査を行い, S 状結腸に穿孔部位が確認できたため, 腹腔鏡補助下に手術を行った。病理診断は, 良性腫瘍である成熟嚢胞性奇形腫の S 状結腸への穿孔であった。成熟嚢胞性奇形腫が微小破綻し, その炎症により S 状結腸への癒着を生じた後に S 状結腸穿孔を生じたものと考えられた。良性腫瘍と考えられ, 消化器症状に乏しい場合であっても, 消化管穿孔の可能性を念頭において検査, 治療を開始する必要があると考えられた。

P-22-9 肥満症に対する腹腔鏡下手術の術後合併症に関する検討

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【目的】肥満症は深部静脈血栓症や術後感染症の増加など周術期合併症のリスク因子のひとつであるほか, 手術の施行にも困難を伴う。今回, 当院で実施した肥満症例に対する腹腔鏡下手術成績をもとに, 肥満症例に対する腹腔鏡下手術の安全性を検討した。【方法】2019年10月~2021年3月の間に, 当院で施行した予定腹腔鏡下手術 218 例を対象とした。Body Mass Index (BMI) 30.0 未満の群 (非肥満群) と 30.0 以上の群 (肥満群) の 2 群に分け, 手術時間, 出血量, 術後 1 日目の白血球数, c-reactive protein (CRP) 値, 術後感染症の有無を比較した。術後感染症は, 術後感染症のために入院期間延長を要した症例, 再入院となった症例と定義した。統計解析は χ^2 検定を行った。【成績】対象症例の内訳は, 非肥満群 203 例 (BMI 平均 22.8), 肥満群 15 例 (BMI 平均 34.7) であった。術式は子宮全摘術 112 例 (非肥満群 102 例/肥満群 10 例), 卵巣腫瘍摘出術 69 例 (66 例/3 例), 筋腫核出術 15 例 (15 例/0 例), 仙骨腔固定術 16 例 (14 例/2 例), その他 6 例 (6 例/0 例) であった。手術時間平均値は非肥満群 151.1 分, 肥満群 174.0 分 ($p=0.21$), 出血量平均値非肥満群 42.2ml, 肥満群 78.7ml ($p=0.26$) には有意差は認めなかった。術後 1 日目の WBC 平均値は非肥満群 8342/ μ l, 肥満群 10053/ μ l ($p=0.02$), CRP 平均値は非肥満群 1.54 (mg/dl), 肥満群 2.34 (mg/dl) ($p=0.03$) であり, いずれも肥満群が有意に高かった。しかし術後感染症は, 非肥満群 3 例, 肥満群 1 例であり, 両群に有意差を認めなかった ($p=0.81$)。【結論】BMI30.0 以上の肥満症例においても, 手術時間の延長や出血量の増加, 術後感染症はじめ周術期合併症の増加を認めず, 腹腔鏡下手術を安全に施行できていると考える。

P-23-1 腹腔鏡下手術により診断し得た子宮ミュラー管嚢胞の一例

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【緒言】子宮の嚢胞性腫瘍は全子宮腫瘍の0.35%であり、中でもミュラー管由来の子宮嚢胞は非常に稀とされている。今回我々は、左卵巣腫瘍の術前診断であったが、腹腔鏡下手術後の病理検査にて子宮ミュラー管嚢胞と診断した一例を経験したので報告する。【症例】50歳、0妊0産。前医で卵巣腫大を指摘され、手術的に当科紹介となった。内診で付属器は触知しなかったが、経陰超音波検査では左付属器腫瘍と思われる所見を認めた。MRIでは子宮前方に8cm大の単房性嚢胞性腫瘍を認め、左卵巣と連続しているように見えたため左卵巣腫瘍が疑われた。左卵巣腫瘍の診断に対して腹腔鏡下左付属器切除術の方針となった。術中所見では、子宮底部から有茎性に発育する嚢胞性腫瘍を認め、両側付属器は正常所見であり、嚢腫と付属器に連続性はなかった。茎を切断し摘出した。術後病理診断はMullerian cystで悪性所見はなかった。【考察】子宮の嚢胞性腫瘍は先天性と後天性に分けられ、先天性はウォルフ管由来とミュラー管由来に、後天性のものは子宮筋腫の嚢胞性変性、嚢胞性筋筋症、頸部貯留嚢胞、漿膜嚢胞に分類される。子宮のミュラー管嚢胞は非常に稀であり、術前に診断することは通常不可能である。腹腔鏡下手術は嚢胞の診断と切除を同時に行うための低侵襲治療として有用であると思われた。

P-23-2 婦人科悪性腫瘍におけるリンパ節転移の術前評価に対するFDG-PET/CTの有用性

聖マリアンナ医大病院

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【目的】婦人科悪性腫瘍におけるリンパ節転移の治療前評価は、治療方針を左右させる重要な情報となる。婦人科悪性腫瘍初回治療前のリンパ節転移の有無を判断するためのFDG-PET/CT (PETCT) の有用性について、知見を得る。【方法】2014～2021年に婦人科悪性腫瘍で術前にPETCTを行い、その後当院で系統的リンパ節郭清(LAN)を行った症例を対象に、PETCTと通常行われるCTのリンパ節転移の評価、摘出されたリンパ節の組織診断の結果を比較検討する。なお、本研究は当院臨床試験部会で承認され実施した(承認番号:5366)。【成績】PETCT後にLANを行った症例は20例で、子宮頸癌15例、体癌4例、卵巣癌1例であった。全例骨盤内のLANが行われ、摘出リンパ節数の中央値は38個(17～56個)であった。PETCTでリンパ節転移が疑われたのは20例中6例で、そのうち3例で組織学的にリンパ節転移を認めた。一方リンパ節転移が疑われなかった14例のうち、2例で組織学的に転移を認めた。PETCTの感度は60%、特異度は80%であった。通常のCTで短径10mm以上のリンパ節を確認できないが、PETCTでLAN領域にFDGの集積を認めた症例は15例中1例あったが、組織学的には陰性であった。一方、CTで短径10mm以上のリンパ節腫大を認めた症例は5例で、全例がPETCTでもリンパ節転移が疑われたが、組織学的に陽性だったのは3例であった。【結論】婦人科悪性腫瘍の術前検査の際、リンパ節転移の判断についてPETCTは有用な情報となる可能性があるが、最終的な判断はPETCTの精度を考慮し、ヘリカルCT等の他のモダリティも合わせて判断する必要がある。

P-23-3 高齢(65歳以上)婦人科がん薬物治療患者を対象とした高齢者総合機能評価(Geriatric Assessment:GA)に関する前向き観察研究

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【目的】2019年「高齢患者のがん薬物療法ガイドライン」が発刊されたが、婦人科対象の研究が非常に乏しくかつ海外のデータである。目的は、婦人科高齢がん薬物療法の治療方針を個別化するため、新たなGAを確立することである。【方法】当院にて2020年7月～2021年6月までに65歳以上の婦人科がん薬物治療を予定し本研究の同意を得た89名を対象とした。GAにはGeriatric8(G8)とmini-COG(認知症スクリーニング)を用いた。G8は2分程度、mini-COGは3分程度の間診で簡便に使用できるGAのツールである。担当医が施行した薬物療法のレジメならびにdoseを変えなしに3サイクル完遂できたものを「成功」、途中で減量したあるいは初めから減量し3サイクル完遂できたものを「条件付き成功」、それ以外を「失敗」とした。【成績】G8(17点満点)点数が15-17点、11-14点、7-10点はそれぞれ40人(44.9%)、37人(41.6%)、12人(13.5%)であった。mini-COG(5点満点)点数が5、4、3、1-2点はそれぞれ57人(64%)、17人(19.1%)、10人(11.2%)、5人(5.6%)であり0点はいなかった。G8×mini-COG(満点85点)の点数としたところ、64-85点が46人(51.7%)、46-63点が26人(29.2%)、45点以下が17人(19.1%)であった。それぞれの群の化学療法の完遂度は、成功率が76.1%、61.5%、29.4%であり点数の高い群で低い群で有意な差を認めた。【結論】婦人科高齢がん薬物療法を施行する際にGAを行うことは、治療完遂度の推定に役立ち有用であることが示唆された。今後更なる症例の検討が必要である。

P-23-4 難治性癌性腹水を呈した婦人科癌に対して腹水濾過濃縮再静注法 (CART) を施行した 25 例の検討

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【目的】進行婦人科癌において難治性癌性腹水はコントロール困難な症状の1つである。腹部膨満感や息切れ等を呈し患者のQOLを低下させるだけでなく、低蛋白血症や血管内脱水を認める症例も多い。近年、患者から穿刺排液した腹水を濾過し、濃縮し血管内に再静注する腹水濾過再静注法 (cell-free and concentrated ascites reinfusion therapy ; CART) がQOL改善や低蛋白血症の予防に有効とされるようになった。今回、当院で腹水に対しCARTを施行した婦人科癌25症例につき、その有効性と安全性を後方視的に検討した。【方法】対象は2015年から2021年まで当院でCARTを施行した進行婦人科癌25症例である。CART施行総回数は62回であった。これらの臨床データを診療録により各種パラメータを抽出し後方視的に検討した。検討事項は、PS、自覚症状の変化、血液生化学検査値、体温変化とした。【成績】患者の平均年齢は58歳であり、卵巣癌が21例、子宮体癌1例、子宮肉腫1例、腹膜癌2例であった。CART施行時に18例が治療中、緩和ケア44例、一人当たりの平均CART回数は2.44回であった。CART療法前後において腹部膨満感やPSは改善し、血清アルブミン (前2.53g/dl, 後2.60g/dl) も維持された。一方、CART前後で体温は有意に上昇したものの (前36.63℃, 後37.14℃, $p<0.0001$)、CART施行による感染や循環動態の悪化等の有害事象は認めなかった。【結論】CART療法はPSの維持や症状の緩和、血清アルブミン値の維持に寄与することが示唆された。また、本療法実施による明らかな有害事象はなく、比較的安全に実施可能であった。本療法実施により化学療法を継続しえた症例も複数あり、予後の改善に寄与する可能性が示唆された。

P-23-5 病的肥満患者に対する化学療法の安全性に関する後方視的研究

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【目的】米国臨床腫瘍学会 (ASCO) の肥満者に対する化学療法ガイドラインは実体重換算の薬剤投与を推奨しているが、本邦では高度肥満者の診療経験に乏しく治療に苦慮する。そこで病的肥満者への適切な化学療法のあり方を検討する目的で、当科での病的肥満者への抗腫瘍剤投与量や有害事象について後方視的に解析した。【方法】2018年4月から2021年7月に当科でパクリタキセル/カルボプラチン併用療法を施行した患者のうち、Body Mass Index (BMI) 40kg/m²以上の6症例を対象とした。6例の平均年齢42歳、平均BMI47kg/m²であり、4例が子宮体癌、2例が卵巣腹膜癌であった。1例を除く全例が補助化学療法であった。実際投与量を実体重・理想体重・推算糸球体濾過量 (eGFR) 換算した薬剤量を踏まえて検討し、有害事象や予後について調査した。【成績】実体重換算薬剤投与した4名中、同量で完遂したのは2名で、2名は発熱性好中球減少症のため投与量を減量した。2名は初回から薬剤量を減量した。重篤な有害事象はなかったが骨髄抑制が軽度であり投与量不足の可能性も考えられた。治療後4名が無病生存し、子宮体がんIIIA期の1例が担癌生存、腹膜癌IIIC期の1例が原病死した。【結論】重篤な有害事象を呈した2名はBMI50kg/m²以上であり、極端な病的肥満者では実体重換算の薬剤投与が不適切な可能性がある。BMI40kg/m²台であれば安全に実体重換算量投与が可能であったため、根拠のない減量は回避すべきである。だが、心不全など有害事象が重篤化しうる合併症を持つ患者には慎重な投与量にならざるを得なかった。我が国でも高度肥満者が増加しつつあり、臨床経験を蓄積し病的肥満者への安全な治療を検討していく必要がある。

P-23-6 髄腔内化学療法が有効であった子宮頸癌原発癌性髄膜炎の1例

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【緒言】癌性髄膜炎は固形癌の約10%に認めるが、婦人科癌原発は非常に稀である。確立した治療法はなく予後不良であり、症状緩和が治療の主体となる。今回、癌性髄膜炎を発症した子宮頸癌症例に対し、メソトレキセート (MTX) 髄腔内投与が有効であった1例を経験したので報告する。【症例】55歳女性、2妊2産、閉経52歳。不正性器出血および右下腿浮腫を主訴に前医を受診し、子宮頸癌を疑われ当院紹介となった。全身リンパ節転移を認め、子宮頸癌4B期 (Endometrioid adenocarcinoma) と診断し、X年4月-7月CCRTおよび追加化学療法を行った。X年7月中旬から頭痛を認めていたが頭部MRIで脳転移は認めず、7月末CTで腹腔内病変縮小、頸部～腋下行リンパ節やや増大認めた。同時期より頭痛、嘔吐増悪し、全身状態不良のため8月初旬に入院となった。入院時CA19-9の著明な上昇を認め、頭部MRI再検し癌性髄膜炎疑い、髄液細胞診adenocarcinomaを認め、癌性髄膜炎と診断した。頭蓋内圧亢進症状に対しグリセリンやステロイド点滴行ったが効果は一時的であったため、他院にてCSFリザーバーを留置し、当院転院後MTX5mg 髄腔内投与 (2回/週) と適宜髄液ドレナージを行った。MTX3回施行後より症状改善認め、髄液中の異形細胞は消失した。その後も症状再燃なく、終日傾眠傾向ではあるものの短時間の会話や少量の経口摂取可能となり、療養型病院へ転院となった。【結語】子宮頸癌原発癌性髄膜炎に対し、CSFリザーバーを用いた髄腔内化学療法や髄液ドレナージを行い終末期の患者QOL改善に有用であった。頭蓋内圧亢進症状や神経症状を認める場合には癌性髄膜炎を疑い、早期診断および早期治療行うことが重要である。

P-23-7 進行・再発婦人科癌患者の腸閉塞に対する緩和的治療に関する検討

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【背景】婦人科癌の終末期患者は、骨盤内腫瘍や腹膜播種に起因した腸閉塞を併発することが多い。しかしながら処置内容の選択基準はなく、担当医の裁量によるのが現状である。【目的】婦人科癌終末期患者の背景・治療法を後方視的に検討することにより外科的手術療法の意義、適応について明らかにする。【方法】2011年1月～2021年5月の標準治療終了後に骨盤内再発・再燃し、腸閉塞を発症した患者を手術療法群（手術群）とイレウス管挿入群（イレウス管群）に分け、臨床的背景、処置後の状態変化、予後について後方視的に検討した。なお、本研究は当院臨床試験部会で承認され実施した。（承認番号：5449）【成績】対象は56例で、原疾患は子宮頸癌18例、子宮体癌9例、卵巣癌・腹膜癌・卵管癌（以下卵巣癌）29例で、手術群が25例、イレウス管群が31例であった。処置後に経口摂取が可能だったのは手術群100%、イレウス管群58%であった。処置後、経口摂取可能までの期間の中央値は手術群 vs イレウス管群で5日（2-16日）vs 20日（6-47日）と有意差を認め、（ $p < 0.001$ ）処置後の経口摂取可能期間は、手術群が有意に長かった。（ $p = 0.0461$ ）。また、手術群では17例（68%）、イレウス管群では15例（48.3%）が化学療法の再開が可能であった。手術群で閉塞性黄疸を合併した2症例は予後不良かつ術後も食思不振継続した。【結論】終末期腸閉塞で手術を行った婦人科癌患者は、全例で経口摂取可能となり、かつ経口摂取可能となるまでの日数が短かったことから、手術適応は適切に評価されていたと考えられた。手術可能と評価される終末期腸閉塞の患者に対しては、積極的な手術加療がQOL改善に寄与する可能性が考えられた。

P-23-8 当院での婦人科悪性腫瘍の悪性腸閉塞症に対するPTEGの使用経験

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【緒言】癌性腹膜炎による悪性消化管閉塞（malignant bowel obstruction：以下MBO）の管理には、外科的治療と内科的治療がある。頻回の嘔吐を来す場合、経鼻胃管留置による減圧は症状緩和を期待できるが、長期間の留置は患者のQOLを下げる。経皮経食道の胃管挿入術（percutaneous trans-esophageal gastro-tubing：以下PTEG）は、鼻腔の不快感や整容面など経鼻胃管の短所を解消する。【目的】当院での婦人科悪性疾患のMBO例に対するPTEG留置例をまとめ、その有用性とMBOの管理を検討する。【方法】2015年4月から2021年9月までの当院で入院加療を受けた婦人科癌患者でMBOを発症し治療を受けた症例を抽出し、PTEG造設例の詳細を後方視的に検討、有用性や合併症を評価する。【結果】MBO症例は19例（60.6±8.6歳）、15例が卵巣癌及び腹膜癌であった。7例（59.9±7.0歳）に対しPTEGが造設され、うち5例が在宅療養に移行した。PTEG造設後から死亡までの日数は平均42.0±16.5日、在宅療養出来た日数は平均20.3±20.5日であった。合併症として挿入部からの出血が3例、管の閉塞が2例見られた。造設を検討されたが、施行に至らなかった3例は、病勢進行によるDIC、先に留置したイレウス管で十分な症状緩和が得られなかったことが理由であった。【考察】MBOは、単一の方法や薬剤による治療に対応することは難しく、手術・薬物治療・減圧治療の組み合わせが必要である。PTEGは予後が2月以上見込めることがガイドラインにおける推奨の条件だが、当院では余命のより短い例でも留置を行い、在宅療養へとつなげていた。【結語】PTEGは患者の希望や予後予測をふまえ適切なタイミングで導入されれば、在宅療養の一助となるMBOの治療選択肢である。

P-23-9 化学療法が奏功し、ADLが著明に改善した原発不明癌の1症例

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【緒言】原発不明癌は未だ症例数も少ない上、治療に難渋するケースが多くある。今回、原発不明癌で化学療法が奏功し、ADLが著明に改善した1例を経験したため報告する。【症例】33歳、女性、腰痛を主訴に当院へ救急搬送となり、整形外科入院。MRIで脊椎に腫瘍性病変を認め、疼痛のため臥位は可能であったが、座位、歩行困難であった。PET-CTで多発骨病変、骨盤内、左鎖骨上、左頸部リンパ節、右肺の結節影、右肺門部リンパ節への集積を認め、原発巣の検索を開始。骨髄穿刺は、正常骨髄。上部、下部内視鏡を施行されたが腫瘍性病変は認めず。乳腺エコーで乳腺腫瘍は否定的。頸部左副神経リンパ節生検を行い、低分化腺癌の所見を認め免疫染色でCK7, BerEP4, p16陽性の結果であった。経膈エコーで子宮、付属器に腫瘍性病変なく、子宮頸部細胞診がAGCの結果であったが、副神経リンパ節生検の組織像とは異なる像であった。原発不明癌としての化学療法が望ましいと判断し当科へ転科。Th12～L3の骨転移部へ緩和照射を施行したのち化学療法を開始した。パクリタキセル、カルボプラチンを開始したが、アレルギーのためレジメン変更。ゲムシタピン、シスプラチンへ変更し、4コース終了後のPET-CTでCR。癌性疼痛消失し、歩行可能となり、現在も同治療継続中である。【考察および結語】原発不明癌は悪性腫瘍の5%前後とされており、一般的に予後不良である。原発巣がのちに発見された症例は7.6%と低く、原発巣同定まで12か月を要したという報告もある。今回の症例のように若年女性の原発不明癌は原発巣検索に時間をかけ続けるより、早期治療介入が望ましいと思われた。

P-24-1 自然周期・低刺激周期を基本とする大規模 ART 施設の臨床成績～2019 ART オンライン登録より～

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 小林 保¹、加藤恵一¹

【目的】当院は卵胞の選択的成長機構を重要視し、単に発育卵胞数を増やす目的の誘発刺激は行わず、自然周期とクロミフェン周期を採卵周期の基本とし、単一胚移植を全例に徹底している。高刺激・過排卵・複数胚移植が効率的とされるなか、自験例に基づき培われた当院 ART は特殊とも言える。2019年のART成績を報告する。【方法】対象：2019年1月～12月に当院でARTを施行された症例。方法：ARTオンライン登録より当院症例を抽出し、臨床成績を算出した。【成績】採卵周期（n=20,239平均年齢39.5歳）の刺激方法の内訳は、自然11.8%、クロミフェン単独77.2%、その他11.0%であり、回収卵子数の平均は、自然1.2個、クロミフェン単独2.1個、その他4.0個であった。卵子獲得/周期は全年齢で91.2%、39歳以下で92.5%、受精卵発生/周期は75.9%、79.9%であった。分割胚移植での生産率は21.5%（890/4,134）、胚盤胞移植での生産率は30.0%（2,899/9,668）であった。39歳以下に絞ると、分割胚移植での生産率は28.9%（767/2,651）、胚盤胞移植での生産率は42.9%（1,942/4,532）であった。【結論】本会に報告してきた例年の成績と同等であった。適切な診療、技術クオリティがあれば、回収卵子数や移植胚数に頼ったARTにこだわる必要はないと考える。最新の海外からのメタアナリシスでも低刺激周期の有効性が示されており、本邦の全国統計において低刺激周期での成績が芳しくない理由は、刺激方法の個別化により卵巣機能低下症例に低刺激が選択されていることによる母集団バイアスや、施設間の技量の差が根底にあると考えられる。2019年の全国統計公表を待ち、比較検討を行いたい。

P-24-2 PPOS法における経口プロゲステロン製剤に関する検討

ミズクリニックメイワン
 今中聖悟、橋本平嗣、小林 浩

【目的】体外受精法における卵巣刺激において、PPOS法（progesterin-primed ovarian stimulation）が従来のGnRHアゴニスト法やアンタゴニスト法にならび、その有効性が注目されている。PPOS法に用いる経口プロゲステロン製剤に関しては、複数の製剤や投与量が報告されているが、至適製剤ならびに至適用量については一定の見解はない。当院ではメドロキシプロゲステロン酢酸エステルを用いたPPOS法を行っているが、その用量について検討したため報告する。【方法】当院で2020年6月1日から2021年8月31日までに行った、PPOS法での体外受精の卵巣刺激39周期について検討した。メドロキシプロゲステロン酢酸エステル10mg/日の周期（以下A周期）、5mg/日の周期（以下B周期）が25周期であった。今回早発LHサージ率（採卵決定日LH>15mIU/mLと今回は定義する）、排卵率、採卵周期キャンセル率、採卵数、成熟率などについて検討した。【成績】A周期B周期ともに早発LHサージ率、排卵率は0%であったが、A周期において卵巣刺激に対する反応不良のため16%（4/25周期）が途中キャンセルとなった。【結論】排卵抑制のためには、メドロキシプロゲステロン酢酸エステル5mg/dayで十分な効果を得ることができると考えられる。臨床妊娠率、出産率、周産期合併症などの周産期予後について今後症例を蓄積し、検討を進めたい。

P-24-3 子宮内膜症合併患者に対するDienogest併用排卵誘発法（PPOS）を施行し出産に至った症例の妊娠・出産予後

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【目的】従来、子宮内膜症治療とART治療の同時並行は不可能と考えられてきた。しかし、我々は近年多数報告されている黄体ホルモン併用排卵誘発法（PPOS）にDienogestを用いることで、持続的な子宮内膜症治療とARTの両立を行い、排卵誘発法の有効性について論文報告をしてきた。これまで同方法を用いた分娩に関する予後報告は少なく、Dienogest併用PPOSにより凍結胚を獲得し、移植後、妊娠・分娩となった96症例の患者の予後について後方的に検証した。【方法】当院にて同意が得られART治療を行なった患者を対象とした。Dienogest内服群（Study群）はART治療開始前より内服継続、HMG連日投与による過排卵誘発を施行し、採卵後は全胚凍結とした。Control群は同期間に当院にて他の排卵誘発法を用い採卵、胚移植を行って妊娠・分娩に至った群（N=1081）とした。統計的検討としてunpaired t-test、Mann-Whitney U test及びChi-square testを用い、P<0.05を有意差ありとし検討を行った。【成績】患者背景はAMH、基礎FSH値、BMIに有意差は認めなかった。また子宮内膜症手術歴・子宮腺筋症についてはStudy群が有意に多いという背景差は認められた。分娩予後については平均分娩週数（S群38.1w±2.1 vs. C群38.6w±2.2, P=0.07）、出生体重（S群2952g±592 vs. C群3011g±497, P=0.272）と有意差はなく、分娩方法、妊娠中の合併症の有無、児の先天奇形発生率においても両群間での有意差は認めなかった。【結論】Dienogest内服継続でのARTは子宮内膜症治療継続し、良好胚の獲得が可能な治療方法である。今回の検討では凍結胚移植後の出生した児の予後についても、他の誘発法と比較し良好であった。今後も症例を増やし検証を行いたい。

P-24-4 当科における遺伝子組換えヒト絨毛性ゴナドトロピン使用の成績

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【目的】体外受精施行症例における遺伝子組換えヒト絨毛性ゴナドトロピン(以下 hCG)の使用成績を明らかにすること。【方法】当科にて2020年7月から2021年5月までに体外受精の卵成熟目的として遺伝子組換え hCG (オビドレル®皮下注シリンジ)を使用した145例(r-hCG群)と2019年1月から2021年3月までに尿由来 hCGを使用した146例(u-hCG群)を対象に、診療録を後方視的に検討した。当院では2019年7月以降は原則として r-hCG を使用し、それ以前の症例や患者自身が希望した症例には u-hCG を使用している。【成績】r-hCG群と u-hCG群の間で年齢(39.2 vs 40.0歳; $p=0.14$)、FSH基礎値(12.7 vs 11.0 mIU/mL; $p=0.66$)、抗ミュラー管ホルモン値(1.35 vs 1.55 ng/mL; $p=0.55$)、調節卵巣刺激を施行した割合(46.9 vs 41.8%; $p=0.41$)、総HMG投与量(1103 vs 1010 IU; $p=0.50$)、採卵前エストロゲン値(1303.5 vs 1197.8 pg/mL; $p=0.82$)、多嚢胞性卵巣症候群の割合(4.1 vs 3.4%; $p=0.77$)の背景に有意差はなかった。両群における採卵数(5.3 vs 4.8個; $p=0.63$)、卵成熟率(85.4 vs 83.7%; $p=0.79$)、受精率(55.2 vs 58.3%; $p=0.56$)、卵変性率(4.5 vs 6.5%; $p=0.28$)、良好胚盤胞数(0.75 vs 0.73個; $p=0.70$)、凍結卵数(1.4 vs 1.3個; $p=0.85$)に有意差はみられず、採卵キャンセル率(4.8 vs 6.2%; $p=0.80$)、卵巣過剰刺激症候群の割合(2.8 vs 2.7%; $p=1.0$)も同等であった。【結論】体外受精の卵成熟目的の使用とした遺伝子組換え hCG は尿由来 hCG と同等の成績である。

P-24-5 高齢患者におけるトリガー日の卵胞径と卵子獲得率の検討

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【目的】トリガーのタイミングは卵細胞成熟完了時に一致させなければ未熟や過熟の問題が生じ、特に卵巣予備能低下患者においては採卵決定の判断は重要である。アンタゴニスト法は様々な患者に適しているが、大小不同の卵胞発育が見られ、最適なトリガー日の判断に苦慮することがある。高齢不妊患者において、年齢とトリガー日の卵胞径がARTの治療成績に及ぼす影響について後方視的に検討した。【方法】2016年1月~2021年8月においてPCO除外の35歳以上のうちアンタゴニスト法 hCG トリガーを行った154例を対象とした。35-36歳, 37-39歳, 40歳以上の各年齢群における卵子獲得のあった卵胞のトリガー日卵胞径を12mm未満, 12-19mm, 19mmより大きい卵胞の3群に分類しその割合と成績を比較検討した。【成績】卵子獲得のあったトリガー日の卵胞径は全年齢群において12-19mmの割合が最も多くどの年齢群も70%前後であった。40歳以上では19mmより大きい卵胞よりも12mm未満での卵子獲得率が有意に高く、他の年齢群との比較では12mm未満の卵子獲得率は高い傾向があり、19mmを超える卵胞では有意に低かった。また獲得卵子1個あたりのE2値は40歳以上群で受精率と相関がみられた。【結論】全年齢群において、トリガー日の卵胞径は12-19mmで最も卵子獲得が多かったが、40歳以上では19mmを超える卵胞からの卵子獲得率は低く、12mm未満の小卵胞径での卵子獲得率が高かった。40歳以上の患者では、小卵胞径でのトリガー決定や採卵時の小卵胞穿刺も考慮されることが示唆された。

P-24-6 Poor ovarian responder に対する全胚凍結周期における PPOS 法と GnRH antagonist 法の有用性及び費用対効果の比較検討

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【目的】本研究は Poor ovarian responder (POR) に対する Progestin-primed ovarian stimulation (PPOS) 法の有用性及び費用対効果を明らかにすることを目的とした。【方法】2019年1月から2020年6月にBologna criteriaで診断したPORのうち、PPOS法またはGnRH antagonist法(GA)で卵巣刺激・採卵を行った全胚凍結症例を対象とし、ART成績及び費用対効果を比較検討した。高度乏精子症、無精子症は除外した。PPOSは月経2~3日目よりジドロゲステロン20mg/日とゴナドトロピン(Gn)を併用し、GAは月経2~3日目よりGnを投与し、主席卵胞径16mm以上あるいは14mm以上かつ血清E2 250 pg/mL以上でGnRH antagonist 0.25mg/日を開始し、各々採卵の35時間前にトリガーを行った。卵巣刺激費用は排卵誘発剤及び排卵抑制剤の患者負担費用の合計とした。【成績】対象となったPPOS群は60周期、GA群は27周期であり、両群間の年齢、BMI、血清AMH値に有意差は認めなかった。PPOS群、GA群の採卵決定時の血清LHが15 mIU/mL以上であった確率は0%、11.1% ($p=0.0009$)であった。採卵数はPPOS群で優位に多かったが、凍結率や胚盤胞到達率、着床率、臨床妊娠率に有意差を認めなかった。周期当たりの卵巣刺激費用は48,062±27,880円、58,742±23,966円 ($p=0.71$)、卵子1個獲得当たりの卵巣刺激費用は8,382±20,794円、17,429±30,864円 ($p=0.001$)であった。【結論】PORにおいて、PPOSはGAとほぼ同等のART成績を示し、GAよりも優位にLHサージを抑制できることが示唆された。また、卵子獲得に対する費用対効果においてもPPOSで高く、PPOS法はPORにとって身体的及び経済的に有用な卵巣刺激方法であることが示唆された。

P-24-7 Drilling 効果による多嚢胞性卵巣 (PCO) 患者の卵子回収率

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【目的】採卵周期において、発育卵胞数に比して採卵数が極端に少ない場合があり、説明に苦慮する。ただし、このような症例のうち、とくに多嚢胞性卵巣 (PCO) の場合で、次回の採卵において回収率 (可視卵胞に対する採卵数の割合) が増加することを経験する。今回、後ろ向きコホート研究によって、その傾向の解析を試みた。【方法】PCO と診断され 2017 年 1 月から 2021 年 6 月に当院で採卵を行い、回収率が 50% 未満の患者様を対象とした。ただし初回の採卵日から 2 回目の採卵周期の生理開始日までが 180 日を超えた症例は除外した。卵巣刺激は PPOS (Progesterin-Primed Ovarian Stimulation) により行った。そして、初回採卵時と 2 回目採卵時の回収率を比較した。【成績】初回採卵時の平均年齢 (SD) は、32.3 歳 (4.09) であった ($n=9$)。投与した総 HMG 量の平均は、初回採卵時より 2 回目の方が増加していたが、有意な差は見られなかった ($P=0.144$)。平均回収率 (SD) は、初回採卵時 31.9% (13.2) から 2 回目採卵は 66.9% (27.8) となり、有意な増加が見られた ($P=0.005$)。【結論】回収率が 50% 未満の PCO 患者群は、採卵を経験することで回収率が有意に増加することが明らかになった。この drilling 効果は、採卵による卵巣への物理刺激により Hippo シグナルを抑制した可能性が考えられる。

P-24-8 卵巣機能低下症例に対するレトロゾールの効果について

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【目的】レトロゾールは安全で有効な排卵誘発効果が報告されているが、卵巣機能低下症例に対する効果に関しては報告が少ない。IVF 治療における卵巣機能低下症例への卵巣刺激としてレトロゾールの効果を検証した。【方法】対象は 2019 年 8 月から 2021 年 8 月までの期間、当院で採卵手術を施行した症例のうち、AMH < 1.0 の卵巣機能低下症例を対象とした。Antagonist (39 周期), クロミフェン (CC) (35 周期), レトロゾール (35 周期) の 3 群で、患者背景, IVF 治療成績を比較した。【成績】antagonist, CC, レトロゾールで、年齢の平均値 40.2, 40.1, 41.3 歳, AMH の中央値 0.6, 0.34, 0.5 ng/ml, 刺激開始前の FSH 平均値 8.1, 10.3, 8.6 IU/mL に有意な差を認めなかった。採卵前の内膜厚は 9.6, 7.4, 7.4 mm と, antagonist で有意に厚いものの, CC とレトロゾールに差を認めなかった。採卵キャンセル率 2.6, 8.6, 5.7%, 卵子が得られた周期の割合 92, 77, 83% で 3 群に有意差なく, 1 周期あたりの平均採卵数は 3.7, 1.3, 1.6 個, 正常受精卵数は 2.3, 0.96, 1.1 個と, antagonist で有意に多かったが, CC とレトロゾールでは有意差はなかった。胚盤胞到達率は 61, 50, 47% と 3 群で同等, 移植ができた胚盤胞 (計 31 個) で移植あたりの臨床的妊娠率を比較すると, 31 (5/16), 25 (2/8), 0 (0/7) % でレトロゾールでは妊娠率を認めなかったが, 3 群で有意差はなかった。【結論】卵巣機能低下症例に対するレトロゾールの治療成績は, antagonist 法には劣るが, CC と同等の治療成績であった。

P-24-9 高年不妊女性の調節卵巣刺激におけるレトロゾール併用 Progesterin-primed ovarian stimulation 法の有用性

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【目的】近年、調節卵巣刺激にプロゲステロン製剤の排卵抑制を組み合わせた排卵誘発プロトコル (Progesterin-primed ovarian stimulation : PPOS) の有用性が近年注目されている。レトロゾール併用の PPOS 法が高年女性に対して好適であるかについて検討した。【方法】2020 年 5 月~2021 年 9 月までに、採卵時年齢が 40 歳以上の女性を対象に行ったレトロゾール併用の PPOS 法 75 周期 (P 群) と GnRH アンタゴニスト法 45 周期 (A 群) を後方視的に比較した。両群ともに採卵周期の月経 3 日目より、レトロゾール 2.5mg × 5 日間を併用し、ゴナドトロピン (FSH/hMG) 製剤による調節卵巣刺激を行った。P 群は投与開始と同時にジドロゲステロン 20mg/day を採卵決定日まで内服し、A 群は主席卵胞径が 14mm を超えた時点からセトロリクス酢酸塩 0.25mg を採卵決定日まで連日投与した。卵子成熟誘起は GnRH アゴニスト and/or HCG 投与を使用し、受精卵はガードナー分類で BB 以上および AC, CA に到達した胚盤胞を凍結した。【成績】P 群は A 群と比べて (P 群 vs A 群 : mean ± SE), 年齢が有意に高く (42.1 ± 0.2 歳 vs 41.3 ± 0.2 歳, $p=0.008$), AMH (2.1 ± 0.2ng/ml vs 2.4 ± 0.3ng/ml) に有意差を認めなかった。採卵決定日の LH 値に有意差を認めず、同日の E2 値は P 群で有意に低値であった (944.7 ± 99.0 pg/ml vs 1432.8 ± 166.9pg/m, $p=0.007$)。P 群は A 群と比べてゴナドトロピン製剤の総投与量は有意に少なかった (1010.7 ± 96.6 IU vs 1633.5 ± 126.3 IU, $p=0.0000006$) が、採卵数 (4.5 ± 0.5 個 vs 5.8 ± 0.7 個), 受精卵数 (3.1 ± 0.4 個 vs 3.6 ± 0.5 個) に有意差を認めなかった。【結論】レトロゾール併用の PPOS 法は、高年不妊女性に対して積極的に適応できる卵巣刺激法であると考えられた。

P-25-1 凍結融解初期胚の移植時期に関する解析

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初期胚は移植後、子宮内膜の蠕動で卵管付近に移動し卵管因子の修飾を受けるとされる。当院では凍結融解初期胚をP4値の上昇が少なく子宮内膜の蠕動が活発な排卵翌日に移植している。【目的】凍結融解初期胚を排卵翌日に移植した際の予後を検討する。【方法】2008年5月から2020年7月の間に当院にて採卵、移植を行った40歳未満の自然周期およびレトロゾール周期症例の凍結融解初期胚移植後の血中 β hCG陽性率(≥ 20 ng/mL)、胎嚢出現率、出産率、血中P4値を検討した。対照として同時期の新鮮初期胚移植症例と比較検討した。本研究に関してインフォームドコンセントを得ている。【成績】40歳未満の凍結融解初期胚(Day2胚)移植周期は381(自然周期89, レトロゾール周期292)で、新鮮初期胚移植周期は1522(自然周期609, レトロゾール周期913)であった。凍結融解初期胚移植後の血中 β hCG陽性率(≥ 20 ng/mL)は42.8%、胎嚢出現率36.7%、出産率29.1%、P4値は 3.7 ± 1.9 ng/mLであった。対照とした新鮮初期胚移植(採卵2日後に移植)の血中 β hCG陽性率(≥ 20 ng/mL)は39.3%、胎嚢出現率35.3%、出産率27.2%、P4値は 5.5 ± 3.3 ng/mLであった。血中P4値のみ有意差を認め、他の因子には有意差を認めなかった。また、凍結Day3胚を排卵翌日に移植した結果を同時期の新鮮初期胚移植(採卵3日後移植)と検討したと同様の結果を得た。【結論】40歳未満の自然周期およびレトロゾール周期の採卵による凍結融解初期胚(Day2胚, Day3胚)を排卵翌日に移植しても、新鮮初期胚移植と比較し、血中 β hCG陽性率(≥ 20 ng/mL)、胎嚢出現率、出産率に有意な差を認めなかった。凍結初期胚に関して子宮内膜の蠕動がみられる排卵翌日の移植が有効であることが示された。

P-25-2 凍結融解胚移植の際の内膜調整法別(ホルモン補充周期つまりHRC周期と自然周期)の妊娠成績比較検討

徐クリニック

徐 東舜

【目的】凍結融解胚移植の際の内膜調整法別移植の成績に関してはいずれが優れているかはいまだ明確ではない。そこで今回我々は後方視的に両者の胚移植での成績を比較検討した。【方法】2016年1月から2021年6月までに3BB以上のSETを行った凍結融解胚移植1444症例を対象とした。内訳はHRC周期792症例、自然周期652周期で、それぞれの妊娠率、着床率、流産率などを比較検討した。【成績】卵胞発育不良や内膜発育不良などによる移植キャンセル率は1.2% vs 5.0%で自然周期が有意に高かった。不妊原因別では排卵因子が21.7% vs 5.7%で有意にHRC周期が高かった。背景では既往移植回数は 1.3 ± 1.7 vs 1.5 ± 1.9 と自然周期で有意に多かった。妊娠率、着床率では妊娠率は47.0% vs 53.2%と自然周期で有意に高かった。不妊要因別の妊娠率に両者の差は認めなかった。流産率は19.4% vs 17.3%で有意ではないがHRC周期が高い傾向にあった。年齢別(29歳以下, 30~34歳, 35~39歳, 40歳以上)のHRC周期、自然周期の妊娠率は、50.0% vs 61.8%, 52.2% vs 57.4%, 47.0% vs 53.9%, 37.6% vs 43.3%いずれの年齢別でも自然周期が有意ではないが高い傾向にあった。流産率の年齢別は29歳以下では24.1% vs 14.3%, 40歳以上では32.2% vs 18.2%とHRC周期が有意ではないが高い傾向にあった。【結論】凍結融解胚移植の際の内膜調節は可能な限り自然周期にするのが望ましい。

P-25-3 凍結融解胚移植における子宮内膜パターンと妊娠分娩転帰-1947周期の検討より

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【目的】子宮内膜パターンと妊娠分娩転帰の関連性については、これまで様々な検討がなされているが、一定の見解を得ていない。今回、凍結融解胚移植における子宮内膜パターンと妊娠分娩転帰を検討した。【方法】2012年から2019年までに単一施設でホルモン補充周期下に単一胚盤胞を凍結融解胚移植した35歳以下の症例を対象とした。経陰超音波断層法で子宮内膜厚7mm以上を目安として胚移植日を決定し、その時点の子宮内膜像を記録した。子宮内膜のLeaf pattern 中央の線状エコーに注目し、3つのパターンに分類した(Lf:線状エコーが連続, Partial Lf(P-Lf):線状エコーが一部断裂, Non-Lf:線状エコーが不明瞭)。1947周期に対して胚grade毎の子宮内膜パターンと妊娠率、出生率、流産率を後方視的に解析、検討した。【成績】子宮内膜パターンの内訳はLf 522例, P-Lf 913例, Non-Lf 62例であった。全周期において、Lf, P-Lf, Non-Lfの妊娠率はそれぞれ70.3%, 57.8%, 29.0% ($p < 0.01$)、出生率は55.6%, 45.0%, 16.1%であった ($p < 0.01$)。流産率はそれぞれ21.0%, 22.1%, 44.4%であった (LfとP-Lf: $p > 0.05$)。胚grade毎の検討では、全ての胚gradeにおいてNon-LfはLfよりも妊娠率が低く ($p < 0.05$)、出生率は良好胚盤胞で低かったが ($p < 0.05$)、流産率は全ての胚gradeで有意差がなかった。また、Non-LfはP-Lfよりも妊娠率、出生率が低い傾向があった。【結論】今回の検討では、胚移植決定日の超音波断層法で子宮内膜パターンがNon-Lfを呈する症例では妊娠率、出生率が低いことから移植に適していない可能性が示唆される。今後、子宮内膜パターンを改善する因子を見つけ、妊娠分娩転帰を改善するための検討が必要である。

P-25-4 グレードCCの胚盤胞を2胚移植のために凍結保存しておく意義はあるか？

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【目的】 Gardner 分類 CC 胚の単一胚移植 (SET) ではほとんど妊娠成立しないため、当院では主に2胚移植 (DET) に用いる。一方で、BB 以上の形態良好胚に BB 未満の形態不良胚を併せた DET では妊娠率が低下するとの報告が散見される。今回は CC 胚を併せて DET を実施した症例の妊娠予後を調査し、CC 胚を凍結保存しておく意義について検討した。【方法】当院における 2016 年 1 月から 2020 年 12 月までの凍結融解胚移植症例を対象とした。媒精あるいは顕微授精後 5、6 日目に BL3 以降で凍結保存した胚を用いた。2胚移植は 35 歳以上あるいは 2 回以上続けて妊娠不成立の症例のみで実施した。BB 以上の high grade (H) 群、CC 胚を除く BB 未満の low grade (L) 群、および CC 胚の poor grade (P) 群に分類し、CC 胚を併せた DET (CC-DET) 症例を胚の組み合わせで HP 群、LP 群、および PP 群に分類した。【成績】SET 症例は 1168 周期、DET 症例は 376 周期で、そのうち CC-DET 症例は 117 周期であった。SET 症例より CC-DET 症例は高年であった (36.3 歳 vs 37.8 歳: $p < 0.001$)。臨床的妊娠率は SET 症例ではそれぞれ 36.3% (352/971), 14.6% (23/158), および 0% (0/36) で、CC-DET 症例ではそれぞれ 28.1% (18/64), 26.7% (12/45), および 12.5% (1/8) であり、CC 胚を併せたことによる臨床的妊娠率のオッズ比 (95%CI) はそれぞれ 0.69 (0.39-1.21), 2.13 (0.96-4.73), および 15.8 (0.59-426.03) であった。また、流産も含めた双胎妊娠は H 群の 1 例、HP 群の 5 例、および LP 群の 6 例であった。【結論】CC 胚を併せることによる妊娠率の有意な低下は認めなかった。BB 未満の形態不良胚との DET では CC 胚が妊娠率向上に寄与する可能性が示唆され、CC 胚の凍結保存意義はあると考えられた。

P-25-5 当院における凍結胚を使用した2段階胚移植の治療成績について

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大越千弘¹、菅沼亮太¹、高橋俊文²、藤森敬也¹

【目的】2段階胚移植は implantation window を拡げ着床率を高める可能性があり、反復着床不全 repeated implantation failure RIF に対する治療となり得る。これまで2胚移植 double embryo transfer DET と比較し多胎率は変わらないものの臨床妊娠率、生児獲得率を上昇させると報告されているが、その多くは新鮮胚移植で検討であり、凍結胚移植における有効性は報告されていない。近年日本では凍結胚移植が主流であり、日本産科婦人科学会の ART 登録施設からの報告では 2019 年には凍結胚移植での出生児数が 89.4% となっている。その現状をふまえ、当院での凍結胚を使用した2段階胚移植の成績について、同時期に DET を行った群と比較し検討を行った。【方法】2018 年 1 月から 2021 年 6 月の間に2段階胚移植または DET を行った RIF 症例を対象とした。2段階胚移植群 (A 群) では黄体ホルモン補充開始 3 日後に初期胚、5 日後に胚盤胞の凍結胚移植を行った。DET 群 (B 群) では初期胚 2 個もしくは胚盤胞 2 個を移植した。【成績】対象症例は A 群が 137 周期、B 群が 173 周期だった。平均年齢や受精方法、不妊の原因、妊娠既往の有無に関しては両群間で差を認めなかったが、A 群で既往移植回数が多かった。臨床妊娠率、流産率、多胎率、生児獲得率は A 群で 23.3% (32 例)、31.2% (10 例)、15.6% (5 例)、11.7% (16 例)、B 群で 22.5% (39 例)、30.7% (12 例)、17.9% (7 例)、13.3% (23 例) であり、いずれも 2 群間で有意差を認めなかった。現時点で妊娠継続症例は両群とも 4 例だった。【結論】凍結胚を使用した2段階胚移植と DET において今回の比較ではその治療成績に有意な差を認めなかった。今後さらに症例数を増やして検討を行っていききたい。

P-25-6 新鮮胚移植後妊娠と凍結融解胚移植後妊娠における妊娠第 1 三半期での血小板数の相違

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【目的】新鮮胚移植 (新鮮 ET) 後妊娠と比較し凍結融解胚移植 (凍結 ET) 後妊娠では児の平均出生体重が重いことが知られている。近年、妊娠第 1 三半期の血小板数と出生体重に正の相関があることが報告された。新鮮 ET と凍結 ET との違いによる児の出生体重差の要因を解明するために、妊娠第 1 三半期における血小板数が関連するかどうかにつき検討した。【方法】2020 年度に当院で出生し、多胎妊娠、妊娠高血圧症候群、妊娠糖尿病、早産を除いた、新鮮 ET 後妊娠 13 例と凍結 ET 後妊娠 76 例につき、妊娠第 1 三半期における血小板数を比較した。【成績】新鮮 ET 後妊娠、凍結 ET 後妊娠、それぞれの平均母体年齢は 36.9 ± 4.4 歳、 38.1 ± 3.9 歳、平均分娩時週数は 39.4 ± 0.6 週、 39.0 ± 0.6 週、平均出生体重は 2940.6 ± 228.5 g、 3031.0 ± 348.6 g ($p=0.2$) であった。妊娠第 1 三半期における平均血小板数は、新鮮 ET 後妊娠で 21.7 ± 5.4 万、凍結 ET 後妊娠で 24.6 ± 4.4 万であり、凍結 ET 後妊娠で有意に高かった ($p=0.02$)。【結論】胎盤形成時の母体らせん動脈リモデリングにおいて、母体血管内の血小板がらせん動脈内の絨毛膜外栄養膜細胞に沈着することで、絨毛膜外栄養膜細胞の母体血管への浸潤移動が誘導されるという説がある。本検討では新鮮 ET 後妊娠と凍結 ET 後妊娠とで児の平均出生体重の有意差を認めなかったが、妊娠第 1 三半期における血小板数に有意差を認め、血小板数が胎盤形成を介して出生体重に関連している可能性が示唆された。

P-25-7 当院 IVF-ET における慢性子宮内膜炎の取り扱いと妊娠率の検討

山梨大

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【目的】慢性子宮内膜炎 (CE) は妊娠率を低下させるとされ, 反復着床不全の原因として注目されているが, 診断基準は一定しておらず文献により異なる。当院では既報のうち, 増殖期子宮内膜組織の CD138 免疫染色で内膜間質の形質細胞が 5 個/10HPF 以上で CE 陽性と診断する基準を採用し, CE に対する治療を実施している。今回は 2 回以上胚移植をしても妊娠が成立しなかった症例に対して CE 検査を行い, その結果や治療歴およびその後の胚移植における妊娠予後について検討した。【方法】2019 年 7 月から 2021 年 8 月までに当院で CE 検査を行い, その後も胚移植を施行した 43 症例を対象とした。CE 陰性を A 群, CE 陽性でドキシサイクリン内服加療にて改善した症例を B 群, 再検査で CE 陽性でありシプロフロキサシンおよびメトロニダゾール内服加療にて改善した症例を C 群, 再々検査でも CE 陽性であった症例を D 群に分類した。D 群は間質に形質細胞の存在する内膜を物理的に剝離し改善する目的で黄体期に子宮内膜を 8 方向キュレットした。【成績】各群はそれぞれ, 19 例, 8 例, 6 例, および 10 例であった。年齢や妊娠分娩歴に差はなかった。CE 検査加療後の初回胚移植での臨床的妊娠率はそれぞれ 36.8% (7/19), 50.0% (4/8), 50.0% (3/6), および 60.0% (6/10) であった。また, 累積妊娠率はそれぞれ 47.4% (9/19), 62.5% (5/8), 50.0% (3/6), および 70.0% (7/10) であった。いずれも各群間で有意差を認めなかった。【結論】子宮内膜間質の形質細胞が 5 個/10HPF 以上で CE 陽性と判断し加療することで, CE 陰性の症例と同等の妊娠率に改善しえた。また, いずれの治療段階で CE が改善した場合でも, 同様に妊娠率を改善しうる可能性が示唆された。

P-25-8 人工知能を用いた新しい自動胚評価システムは有用か

桜十字渋谷パースクリニック

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【目的】胚評価法の新しいソフトウェアツールである iDA スコア[®]は, 人工知能を用いた自動胚評価システムである。今回単一凍結胚盤胞移植において iDA スコアが妊娠予想に有用か検討した。また, iDA スコアに影響する因子を検討した。【方法】2018 年 9 月~2021 年 9 月に当院で卵巣刺激後採卵を行い, 胚盤胞となった 223 症例 980 個の胚を対象とし後方的に解析した。タイムラプス観察には Embryo Scope+[™] (Vitrolife) を用い, iDAScore ver.1.0 により, 各胚盤胞を 1 から 9.9 までスコアリングした。妊娠成立の有無と iDA スコアで ROC 曲線を作成し AUC を求めた。また, 患者背景, KID スコア, iDA スコアを単変量解析で比較し, さらに多変量解析にて妊娠成立の有無に関連する因子を検討した。また, 採卵時の卵の成熟段階と iDA スコアを多重比較し, 受精方法により Mann-Whitney 検定を用いて iDA スコアを比較した。【成績】単一凍結胚盤胞移植を行なった 318 個の胚を対象に ROC 解析を行った。iDA スコアの妊娠予測は AUC が 0.6 であり, 弱い正の相関関係を認めた。多変量解析を行なったところ, 年齢と iDA スコアが有意に妊娠と関係していた。凍結保存した 980 個の胚盤胞を対象に解析したところ, 採卵時の胚の成熟段階については MII 卵, MI 卵由来の胚盤胞は GV 卵より iDA スコアが有意に高値であった。また, 受精方法に関しては, 媒精法で受精した胚盤胞は顕微受精と比較すると iDA スコアが有意に高値であった。【結論】単一凍結胚盤胞移植において iDA スコアは妊娠予想に有用である可能性がある。採卵時の卵の成熟段階や受精方法は iDA スコアに影響している可能性がある。今後は症例を増やして検討する必要がある。

P-25-9 反復着床不全例に対する子宮内フローラ検査の有用性の検討

岩手医大

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【目的】反復着床不全 (RIF) の原因として, 多くは受精卵の染色体異常であるが, 一部に子宮内膜側の異常があることも知られている。慢性子宮内膜炎 (CE) は無症状であるが, 着床を阻害する報告が多数あり, 子宮内フローラ検査にて原因菌を推定することが可能となった。今回反復着床不成功患者に対し, 子宮内フローラ検査を行い, その有効性, 妊娠転帰に関し検討した。【方法】対象は当院で 2020 年 6 月~2021 年 9 月までに子宮内フローラ検査を行った患者 38 名とした。患者背景, 子宮内における乳酸桿菌の割合, CE 原因菌の有無, 検査後の胚移植結果, 妊娠転帰を後方視的に検討した。【成績】患者平均女性年齢 37.0 ± 3.7 歳, 既往移植回数 3.1 ± 1.7 回であった。子宮内乳酸桿菌割合の正常 (乳酸桿菌 90% 以上) 症例が 13 例, 異常症例が 25 例 (65.8%) であった。CE 検査の結果は陰性 31 例, 陽性 7 例であった。子宮内フローラ異常群に対し, 同定された菌に対し感受性のある抗菌薬で治療を行い, ラクトバチルス錠による加療を行った。検査介入後の移植施行は 35 例だった。再度ホルモン補充 (HRT) 周期による凍結融解胚移植を施行し, 子宮内フローラ異常群で移植 23 例中着床 17 例 (73.9%), 初期流産 4 例 (23.5%) であった。また子宮内フローラ正常群で移植 12 例中着床 8 例 (66.7%), 初期流産 2 例 (25%) であった。【結論】子宮内フローラ異常群に適切な治療を行った場合, 子宮内フローラ正常群よりも妊娠率の改善を認めることから, RIF 患者には積極的に子宮内フローラ検査を行うことで, 妊娠率の改善が望まれると考えられた。今後子宮内環境と子宮内膜症などの不妊原因, 細菌性陰炎, 切迫流産等の関連についても検討を行いたい。

P-26-1 当院における TESE-ICSI の治療成績と周産期予後の検討

徳島大病院

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【目的】無精子症および射精障害に対して精巣内精子採取術 (TESE) が行われているが、周産期予後を含む報告は少ない。TESE 実施あたりの治療成績と周産期予後について、無精子症の原因別に検討することを目的とした。【方法】2008年12月から2020年12月の間に当院で TESE を施行した 109 例の原因別治療成績と、分娩に至った 43 例について周産期予後を検討した。【成績】対象とした症例のうち、TESE による精子回収率は非閉塞性無精子症で 25% (14/56)、閉塞性無精子症で 94% (33/35)、射精障害で 94% (17/18) であった。受精率はそれぞれ 36% (59/160)、49% (269/546)、42% (147/342) で、非閉塞性は閉塞性と比較して有意に低かった ($p < 0.01$)。移植あたりの妊娠率はそれぞれ 42% (8/19)、48% (38/78)、36% (17/47)、移植あたりの生産率はそれぞれ 31% (6/19)、32% (25/78)、25% (12/47)、移植あたりの流産率はそれぞれ 5% (1/19)、11% (9/78)、10% (5/47) で、いずれも群間で差を認めなかった。出産に至った 43 例のうち 15 例に周産期合併症を認めた。内訳は、非閉塞性無精子症で FGR が 1 例、閉塞性無精子症で HDP、GDM、絨毛膜羊膜炎、切迫早産、早産 (重複あり) が 9 例、射精障害で FGR、羊水過少、胎盤位置異常、HDP、GDM、絨毛膜羊膜炎、早産 (重複あり) が 5 例であった。【結論】非閉塞性無精子症では精子の回収率は低く、受精率も閉塞性無精子症と比較すると低い結果であった。しかし、受精した場合には他の原因と同等の治療成績が得られていた。また、TESE-ICSI による妊娠では周産期合併症の発症率が高い傾向であり、慎重な周産期管理が必要と思われる。

P-26-2 頭蓋咽頭腫術後に汎下垂体機能低下症となり生殖補助医療にて妊娠・出産に至った 1 症例

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【緒言】汎下垂体機能低下症の女性は不妊治療における妊娠・分娩の達成率が低く、流産リスクが高いことが知られている。今回術後汎下垂体機能低下症で ART による生児を獲得した症例を報告する。【症例】症例は 27 歳女性、22 歳時に両耳側半音が出現し、精査の結果頭蓋咽頭腫と診断され腫瘍全摘出術により汎下垂体機能低下症となり下垂体ホルモン補充およびカウフマン療法を開始。26 歳時に結婚を機に当院へ紹介。超音波検査で子宮は正常大、両側付属器は小さめ、血液検査で PRL : 15.5, LH < 0.1, FSH < 0.1, TSH : 0.63, FT3 : 2.62, FT4 : 0.66, AMH : 0.64 とゴナドトロピンと AMH の低下を認めた。まずはクロミフェン (CC), hMG による卵巣刺激とタイミング療法から開始した。計 4 クール目で day20 に卵胞発育し排卵を認めたが妊娠せず ART を希望し CC, hMG による調節卵巣刺激を開始し (総量 5400 単位) day23 に採卵、採卵数 16 個、cIVF で 15 個受精、胚盤胞 5 個を凍結、ホルモン補充下に内膜厚確認し day5 のガードナー分類 5AA の胚を移植し妊娠成立。ホルモン補充を継続し胎児発育良好で HFD にて 40 週 4 日に陣痛誘発。子宮口 4cm 開大時遷延性徐脈を 2 回認め胎児機能不全の適応で緊急帝王切開を施行、4118g の男児を出産した。調節卵巣刺激に時間や量は要したがホルモン補充により妊娠中の大きなトラブルはなく出産に至った。【考察】下垂体機能低下症患者では基礎分泌が不足するため卵胞の発育までに一定期間を要し今回の症例でも相当量の hMG を要した。AMH は低かったが若い患者であり hMG を十分使用することで採卵数を確保することができたと思われた。

P-26-3 ヒト胚盤胞における Na^+/K^+ -ATPase isoform の発現と胚発育挙動の検討大館市立総合病院¹, 秋田大²平川威夫¹, 後藤真由美², 高橋和政², 富樫嘉津恵², 白澤弘光², 佐藤 亘², 熊澤由紀代², 寺田幸弘²

【目的】哺乳動物胚の胞胚腔拡張時には栄養外胚葉細胞の基底側にある Na^+/K^+ -ATPase (NAKA) による Na^+ イオンの胞胚腔への取り込みが生ずるとされている。NAKA の α および β サブユニットには種々の isoform が知られており、マウス胚盤胞では $\alpha 1$ と $\beta 1$ が胞胚腔拡張に関与すると報告されているが、ヒト胚での検討はない。本研究はヒト胚盤胞における NAKA isoform の発現とヒト胚の発育挙動との関連を明らかにし、日常の ART でタイムラプス下観察される胞胚腔拡張のメカニズムを検討した。【方法】本学部および日本産婦人科学会の倫理委員会の承認のもと、患者の個別同意を得た上で、当施設の体外受精で得られたヒト余剰凍結胚盤胞 ($n=20$) を対象とした。融解後、タイムラプスにて胚の直径を 20 分ごとに 24 時間計測し、その変化率から胚盤胞の拡張速度を求めた。観察後、RNA を抽出し RT-qPCR で各 isoform mRNA の発現解析を行った。また、蛍光免疫染色で isoform 構成タンパクの局在を観察した。【成績】ヒト胚盤胞では NAKA $\alpha 1$, $\beta 1$, $\beta 3$ の mRNA 発現を認めた。観察終了時にハッチングしていた胚では $\beta 3$ mRNA 発現量が有意に上昇していた。各 isoform の mRNA 発現量と胚盤胞の拡張速度との間には有意な関係を認めなかった。 $\alpha 1$ および $\beta 3$ 構成タンパクは基底膜側に、 $\beta 1$ 構成タンパクは細胞間に局在していた。【結論】ヒト胚盤胞における NAKA α および β サブユニットの各 isoform の mRNA 発現および構成タンパクの局在を確認した。ヒト胚盤胞の拡張には NAKA isoform のうち $\alpha 1$ と $\beta 3$ 、特に $\beta 3$ が関与していると考えられた。また、 $\beta 1$ はこれらと相違する部位に局在し、ヒト由来細胞の知見と同様に細胞間の tight junction の形成に関与していると考えられた。

P-26-4 過去16年間のART周期中に発生した卵巣過剰刺激症候群の後方視的検討

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【目的】近年、我が国では卵巣刺激方法の変遷や新鮮胚移植周期の減少を背景に卵巣過剰刺激症候群 (Ovarian hyperstimulation syndrome; OHSS) の発生率は年々減少傾向となっている。今回、過去16年間に当院で治療を行ったOHSSについて後方視的に検討した。【方法】2006年4月から2021年9月までの16年間に当院で入院管理した生殖補助医療 (Assisted reproductive technology; ART) 周期に発症したOHSSの発生率の変遷や重症度などについて検討した。また、新鮮胚移植群と全胚凍結群の発症背景を比較した。【成績】対象症例は32例で、中等症17例、重症15例であった。このうち自施設でのART症例は23例で、当院での採卵周期当たりのOHSS発生率は2006年~2016年まで0.32~1.9%で推移していたが、2017年以降は発生していない。対象32症例の卵巣刺激方法は、GnRH agonist法7例、GnRH antagonist法2例、PPOS法2例、クロミフェン+hMG法1例であった。トリガーは、hCGが29例、hCGとGnRH agonistの併用が3例であった。新鮮胚移植群が19例、全胚凍結群が13例であった。両群間の年齢、BMI、血清AMH値、ゴナドトロピン投与量、血清peak E2値に有意差を認めなかったが、採卵数に有意差を認めた (新鮮胚移植群 8.3 ± 3.5 個、全胚凍結群 17 ± 10.1 個 $p=0.002$)。【結論】OHSS発症の全例でトリガーにhCGが使用されており、約70%が新鮮胚移植症例で、OHSSの主要なハイリスク因子が発症の背景に存在していた。また、新鮮胚移植群における採卵数は、全胚凍結群と比較して採卵数が優位に少なかったことから、全胚凍結を前提とした周期では新鮮胚移植周期よりもOHSSを回避しながらより多くの獲得卵子数が許容されることが示唆された。

P-26-5 抗糖化食品ヒシエキスは終末糖化産物を低下し、高齢者ART生産率を著しく増加する：前方視的無作為試験

ウィメンズクリニック神野

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【目的】終末糖化産物 (AGE) は、加齢、糖尿病、不妊を含むインスリン抵抗性関連疾患の主要な原因である。ヒシ科植物エキスはAGE形成抑制と分解をする。倫理委員会承認、説明と同意のうえ、前方視的無作為試験 (UMIN000017758) で、ヒシエキス投与によりAGEを低下し、高齢者ART成績を改善することを試みた。【方法】38-42歳、1-3回目ARTの64例を、前方視的無作為にヒシエキス (プレグナサポート、林兼産業) 投与/非投与群 (対照群) に振り分けた。第1周期は一般不妊治療をし、第2周期はカウフマンとGnRHa開始とし、第3周期にlong法でARTを施行した。非妊娠例には凍結胚移植を続けた。投与前・後の血清AGE、OGTT等の変化と、卵胞液AGEを両群で比較した。【成績】ヒシエキス群32例と対照群31例 (1例drop out) の累積生産率は、47% vs. 16% ($p<0.01$; RR, 4.6; 95%CI, 1.4-15.0), ETあたり生産率は、28%/47 ET vs. 10%/49 ET ($p<0.05$; RR, 3.4; 95%CI, 1.1-10.4) と、ともにヒシ群で有意に高かった。年齢、day 3 FSH, AMH, ヒシエキス有無のうち、ヒシエキスのみが累積生産率と相関した ($p<0.05$; OR, 5.1; 95%CI, 1.4-18.3, logistic)。ヒシエキス投与は、卵・胚発育能と自然周期での内膜着床能を有意に増加し、血清と卵胞液AGEを有意に低下した。AGEと受精、胚発育、着床の指標には有意な相関を認めた。【結論】ヒシエキスは、血清と卵胞液AGEを低下し、卵・胚発育能と内膜着床能を増加し、よって高齢者ART生産率を著しく増加した。AGE低下による新しい不妊治療法が示された。ヒシエキスは、糖尿病、高血圧などのインスリン抵抗性関連疾患の治療にも応用が期待される。

P-26-6 ヒト6日目胚盤胞径は栄養外胚葉構成細胞の遺伝学的均一性を反映する

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【目的】胚盤胞の拡張は、着床前胚染色体異数性検査 (PGT-A) を受けていない胚では妊娠の独立した予測因子であるが、PGT-Aで正倍性が確認された胚では予測因子ではないことが報告されている。一方で、異数性胚についても速度は遅いものの十分に拡張することが報告されている。胚盤胞の膨張 (内径) が妊娠の独立した予測因子となるのはなぜか検討した。【方法】本研究は、当該施設および日本産科婦人科学会倫理委員会の承認のもと実施した。研究利用へ個別同意の得られた、培養6日目で内径160 μ m以上に達した顕微授精由来余剰胚盤胞103個について解析を行った。患者および胚の特性 (年齢、精液所見、胚盤胞の形態評価、PGT-A結果) と胚盤胞の内径との関連を解析した。【成績】euploid胚盤胞 (187.6 \pm 10.9 μ m, n=23) とaneuploid胚盤胞 (184.0 \pm 14.2 μ m, n=31) の内径に有意な差は認められなかった。mosaic胚盤胞 (178.6 \pm 11.8 μ m, n=49) の内径は、euploid胚盤胞の内径よりも有意に小さかった ($P<0.01$)。胚盤胞の内径と患者の特徴や胚盤胞の形態的なグレードとの間には、有意な関連および差は認められなかった。多変量解析の結果、胚盤胞内径は遺伝的mosaic胚盤胞を予測できる独立した因子であった (調整オッズ比: 0.95, 95%CI: 0.92-0.99, $P<0.01$)。【結論】Mosaic胚盤胞はeuploid胚盤胞に比べ妊娠率が低率であることが報告されている。胚盤胞の内径は栄養外胚葉の遺伝学的均一性を反映し、その結果妊娠の予測因子となることが示唆された。

P-26-7 TESE-ICSI 受精卵に対するタイムラプスイメージングを用いた胚発生過程の検討

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【目的】非閉塞性無精子症のため MD-TESE で得られた精子で ICSI を行った卵子を、タイムラプスイメージング (TI) を用いて観察を行い、初期の胚発生過程について検討を行った。【方法】2016 年 6 月から 2021 年 6 月に、MD-TESE で得られた凍結保存精子で ICSI を行った 44 症例 80 周期のうち、TI で観察した 10 症例 13 周期 89 胚 (T 群) を、射出精子で ICSI を行った 14 症例 15 周期 64 胚 (E 群) と比較した。T 群を、融解時運動精子を用いた胚 (TN 群 31 個) と、不動のためペントキシフィリン添加後に運動を認めた精子を用いた胚 (TP 群 59 個) に分け、前核出現時間 (T1)・消失時間 (T2)、第 1 分割 (T3)、第 2 分割 (T4)、前核径、Direct cleavage 等の異常分割、良好胚率、胚盤胞到達率等について検討した。【成績】TN 群、TP 群、E 群の T1/T2/T3/T4 (min) はそれぞれ 695/1522/1847/2897, 644/1629/1970/2538, 482/1433/1614/2262 であり、TN 群と TP 群に差を認めなかった。E 群と比較して TN 群では T2-T3 に、TP 群では T1, T2 に延長を認めた。受精率は 16%, 30%, 69% 良好胚率は 13%, 29%, 45%, 胚盤胞到達率は 3%, 20%, 39%, TN 群、TP 群は E 群より不良であり、TN 群は TP 群より良好であった。異常分割率に差を認めなかった。2PN 胚のみでは第 1 分割率は全群ほぼ 100% で、第 2 分割率は 100%, 79%, 98% と差を認めなかった。2PN あたりの良好胚率は 37%, 25%, 61% であった。TP 群では前核の輪郭が不明瞭なものがあり、分割率は低く、良好胚は得られなかった。雄性/雌性前核径(μm)は、25/22, 26/22, 27/24 で差はなかった。【結論】正常受精確認後は T 群と E 群では前核径や分割率、分割速度に差がないことより、T 群では前核形成までの問題が推測される。その原因として卵子活性化障害等が考えられ、今後、人為的活性化の効果についても検討したい。

P-26-8 初期子宮体癌内膜搔爬後の子宮内膜菲薄に伴う妊孕性低下への PRP 療法の有効性

産婦人科 PRP 研究会

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【目的】子宮体癌 IA 期および子宮内膜異型増殖症の診断と MPA 療法の効果判定目的に繰り返し行われる子宮内膜全面搔爬は子宮内膜を菲薄化させ治療後の妊孕性が低下することが知られている。PRP (Plate Rich Plasma: 多血小板血漿) 療法は再生医療の一つでさまざまなサイトカインを含み、子宮内投与により菲薄化した子宮内膜の増殖促進、炎症抑制による着床環境の改善が期待されている。本研究では PRP が子宮内膜搔爬術後の菲薄化内膜の再生を促し妊孕性を改善させるか検討した。【方法】産婦人科 PRP 研究会では凍結胚移植予定の反復着床不全患者 (主に排卵期子宮内膜 7mm 以下の内膜菲薄化患者) を対象に移植周期 10 日目と 12 日目に PRP 子宮内投与を行い内膜厚増加量や妊娠率を調査している。同研究会データベースから子宮体癌 IA 期等で子宮内膜搔爬既往のある患者 28 名を抽出し PRP 投与前 (Day 10) の子宮内膜厚、PRP 投与後 (移植決定時) の子宮内膜厚および妊娠率を後方視的に追跡した。【成績】PRP により投与前子宮内膜厚 $6.61 \pm 1.82\text{mm}$ が投与後 $7.75 \pm 1.79\text{mm}$ と増加し、過去の平均排卵期子宮内膜厚 $6.96 \pm 2.24\text{mm}$ より有意に増加した。胚移植 26 例中 9 例 (34.6%) に生化学妊娠が確認され 4 例 (15.3%) に臨床的妊娠が確認された。生化学妊娠 9 例中 6 例は初めての陽性反応であった。子宮内膜厚が増加しない症例でも妊娠成立例が見られた。【結論】子宮体癌 IA 期等で内膜搔爬後の内膜菲薄化患者において PRP が子宮内膜厚増加と妊娠率上昇をもたらすことが確認された。また内膜厚と妊娠率は必ずしも一致せず、内膜肥厚以外にも PRP による血漿中成長因子や炎症抑制サイトカインなど着床環境改善因子が妊娠成立に寄与する可能性が示唆された。

P-27-1 新しい精子計測装置 LensHooke[®]による客観的な精子の評価とその臨床的有用性の検討医科歯科大¹, 国立成育医療研究センター周産期母性診療センター不妊診療科²山室采佳¹, 辰巳嵩征^{1,2}, 齊藤和毅¹, 岩原由樹¹, 石川智則¹, 宮坂尚幸¹

【目的】精液検査は一般的に Makler chamber (MC) を用いて目視で評価することが多いが、施設間や検者間によって結果にばらつきが生じうる。最近、新しい精子計測装置である LensHooke[®] (LH) が開発され、従来の精子計測装置では出来なかった精子の形態評価も可能となった。しかし、LH は使用経験が未だ少ないため、LH と MC を用いて得られた結果を比較して、LH が臨床的に有用であるかを検討した。【方法】2021 年 6 月から 9 月に当院に精液検査のため受診した男性患者 27 例を対象とした。(検討 1) 同一検体の精子濃度、運動率、奇形率を LH と MC でそれぞれ 3 回ずつ測定した結果の平均値を比較した。(検討 2) LH と MC それぞれで測定した同一検体の 3 回の測定値の分散を比較した。【成績】(検討 1) Pearson の相関係数 r を算出したところ、LH と MC の測定値は精子濃度 ($r=0.94$)、運動率 ($r=0.74$) において強い正の相関が、奇形率 ($r=0.41$) において正の相関が見られた。(検討 2) 2-way Repeated Measures ANOVA の結果、いずれにおいても複数回測定値の分散に有意差を認めなかった。【結論】一般臨床で用いられる MC と比較したところ、LH は精子濃度、運動率、奇形率について測定値に大きな差は見られず、再現性も変わらなかった。LH は MC を用いた目視法と比べ熟練を必要とせず、誰が測定しても同一の方法・基準で測定が行われるため臨床上有用である。LH を用いることで、現在施設間・検者間で異なっている精液検査の方法や基準が統一され、精液の評価が標準化されることが望まれる。

P-27-2 当院での心疾患合併妊娠の年齢と妊娠方法の比較検討

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【目的】先天性心疾患を持つ女性に月経異常が多いことは知られている。心疾患を持つ女性の妊娠時年齢と生殖医療の介入率を検討した。【方法】2010年1月～2021年10月までに当院で分娩管理をした心疾患合併妊娠1029例を対象とし、先天性心疾患(チアノーゼ性・非チアノーゼ性)と後天性心疾患に分類し、また、チアノーゼ性心疾患は、両大動脈右室起始症術後、大血管転位症術後、ファロー四徴症術後、フォンタン術後に分類した。各群において妊娠時年齢と生殖医療の介入の有無、種類を診療録から後方視的に検討した。【成績】先天性心疾患を持つ女性は後天性心疾患と比較して、妊娠時年齢が有意に低かった(30.8±4.9歳 vs 32.4±4.8歳, $p<0.05$)。チアノーゼ性心疾患と非チアノーゼ性心疾患、また、チアノーゼ性心疾患の疾患別の比較では、妊娠時年齢に差を認めなかった。先天性心疾患を持つ女性の10.6%、後天性心疾患の18.2%において、生殖医療の介入があった。そのうち、先天性心疾患を持つ女性の3.0%、後天性心疾患の10.8%は、ARTによる妊娠であった。わが国における年齢別ART率との比較では、先天性心疾患を持つ女性は同等であったが、35歳以上の後天性心疾患を持つ女性では高率であった。【結論】先天性心疾患を持つ女性の妊娠時年齢が比較的低いことは以前より指摘されており、今回の検討でも同様の結果であった。生殖医療の介入率は、先天性心疾患を持つ女性のほうが低く、年齢要因が考えられた。35歳以上の後天性心疾患を持つ女性では、ART率が一般に比べて高く、その要因は今回の検討からは明らかではなかった。

P-27-3 当院における早発卵巣不全患者に対する不妊治療の後方視的検討

京都大附属病院

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【目的】早発卵巣不全とは40歳未満で無月経となる状態である。早発卵巣不全の患者でも無月経となった時点では原始卵胞が残存していると考えられたため、これらの卵胞を发育させて高度生殖医療に供することで妊娠を目指すことが可能である。今回の解析では、早発閉経患者が卵胞发育を認める条件を探索し、また全く卵胞发育を確認できなかった症例を抽出することで治療介入の終了を考慮する条件を明らかにすることを目的とした。【方法】倫理委員会の承認を得て、2011年1月1日から2021年3月31日の間に当院で早発卵巣不全に対する不妊治療を開始した30例を抽出し、後方視的に検討した。【成績】早発卵巣不全の原因は特発性が最も多く(67%)、続いて悪性腫瘍治療などによる医原性が多かった(23%)。卵胞发育を20例(67%)に認め、妊娠成立5例(17%)、生児獲得3例(10%)であった。卵胞发育群と非发育群で比較すると、卵胞发育群で、無月経となつてから治療を開始するまでの期間が有意に短かった(34.8 vs 87.5か月, $p=0.0045$)。また卵胞发育群では、治療開始から平均11.3か月(2.5-20.1か月:95%CI)に初回卵胞发育を認め、90%が18か月までに初回卵胞の发育を認めた。2回以上卵胞发育を認めた症例では、卵胞发育ごとの間隔は平均5.2か月(3.7-6.7か月:95%CI)であり、95%の症例で12か月以内に次の卵胞发育を認めた。【結論】早発閉経例において生児希望があれば不妊治療はなるべく早期に開始すべきであること、また全く卵胞发育を認めない症例における治療介入期間は18か月としてもよいことが示唆された。

P-27-4 慢性子宮内膜炎に対する抗菌薬治療効果の検討

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【目的】不妊症や不育症の患者において、慢性子宮内膜炎(Chronic endometritis; CE)の抗菌薬治療による高い治癒率や妊娠率の改善が報告されているが未だ一定の見解はない。本研究では抗菌薬治療による妊娠率への影響について検討することを目的とした。【方法】2017年8月から2019年10月までに、CE検索目的で子宮内膜組織診を実施した不妊症患者を対象とした。組織診でCD138免疫染色陽性の形質細胞が20視野中に5個以上でCE、5個未満で正常とした。CE診断後抗菌薬治療を行い、再検査で正常となった症例を治癒群、治療後もCEであった症例を非治癒群、初回検査時に正常と診断された症例を陰性群とした。本研究は当院の倫理委員会の承認の下に行った。【成績】対象患者は年齢 36.1 ± 4.3 歳、BMI 21.7 ± 3.6 kg/m²、AMH 3.48 ± 4.00 ng/mlであり、症例数(移植回数)は244(522)例(治癒群38[99]例、非治癒群100[185]例、陰性群103[238]例)であった。治癒群における抗菌薬の平均投与回数は 2.2 ± 0.9 回であった。治癒時の使用抗菌薬の内訳はメトロニダゾール+クラリスロマイシン6例、テトラサイクリン塩酸塩12例、ミノマイシン塩酸塩7例、ドキシサイクリン塩酸塩7例、メトロニダゾール+シプロキサシン5例であった。臨床妊娠率(症例数別/移植数別)は全体で38.0%/17.8%、治癒群42.1%/16.7%、非治癒群35.0%/19.1%、陰性群39.4%/17.2%であり、3群間に有意差を認めなかった。【結論】治癒群の妊娠率は陰性群とほぼ同等であった。一方、非治癒群の妊娠率も治癒群・陰性群とほぼ同等であることから、CEが非治癒の場合でも抗菌薬治療が妊娠率の改善へ寄与している可能性が示唆された。

P-27-5 当院における43歳以上の高齢者に対する不妊治療とその成績

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【目的】女性の結婚年齢の高齢化に伴い不妊治療の開始年齢も上昇している。卵巣機能の加齢変化などにより妊孕性の低下は否めないが、当院では43歳以上の高齢者に対してもインフォームドコンセントのもと、ARTを含めた不妊治療を実施している。今回43歳以上の高齢者に対する不妊治療成績を解析し、適正な治療法について明らかにしようとした。【方法】当院では高齢者も希望者にはタイミング法ないし人工授精から治療を開始し、必要によりARTにステップアップする方針で治療を行った。2019年8月から2020年12月までに実施した43歳以上の女性に対する不妊治療成績を、人工授精、新鮮胚移植、凍結融解胚移植にわけて妊娠予後を解析した。【成績】人工授精平均年齢45.1歳で129回の実施で1例が妊娠・分娩した(0.8%)。新鮮胚移植平均年齢45.1歳では22回の実施で1例が妊娠した(4.6%)。凍結融解胚移植平均年齢44.5歳では256回実施で20例が妊娠し(7.8%)、9例が分娩に至った(3.5%)。最高齢は48歳時の採卵で49歳での分娩であった。AMHは胎嚢確認症例で平均1.72、分娩症例で1.23であった。【結論】43歳以上の高齢者に対する不妊治療成績は、42歳以下に対して著しく低下することが確認された。特に人工授精では良好な成績は期待できず、ART希望者には早々にステップアップすることが望ましい。体外受精においては一定の割合で妊娠・出産に至るものもあり、正確な情報を提供し患者にあった治療方法を提示、選択していくことは可と考える。

P-27-6 CD138免疫染色と子宮内microbiotaのcombined testに子宮内pH測定を加えた慢性子宮内膜炎の病態整理

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【目的】慢性子宮内膜炎の診断法としては子宮内膜のCD138免疫染色や子宮内microbiotaが行われているが、未だ確定的ではない。今回91例に対し、その両検査を同時に施行するcombined testを実施した。また、我々はESHRE2020やASRM2021で正常子宮内pHは6.0前後で弱酸性であることを報告しており、今回子宮内pH測定を加えて慢性子宮内膜炎(CE)の病態を整理した。【方法】当院を受診した反復着床不全と不育症例の合計91例(中央値38歳)に対してCD138の免疫染色とmicrobiota検査(16S rRNA)を同時に実施した。面積当たりの全陽性細胞を数えて、 <5.15 個/10xmm²(Liu法, 2019)。また乳酸菌 $\geq 90\%$ を陰性(正常)として、4グループに分けた。CD138陽性+乳酸菌 $<90\%$ をグループ(I)、CD138陽性+乳酸菌 $\geq 90\%$ をグループ(II)、CD138陰性+乳酸菌 $<90\%$ をグループ(III)、CD138陰性+乳酸菌 $\geq 90\%$ をグループ(IV)として比率を求めた。医療用生体内pH測定器を用いて、各グループの子宮底のpHを測定した。【成績】91例のうち細菌性CE(I)症例は20%、非細菌性CE症例(II)は18%、評価困難症例(III)は24%、CEの無い症例(IV)は38%だった。各グループの子宮内pH(mean)は(I)は6.59、(II)は6.04、(III)は6.25、(IV)は6.06だった。多重比較ではpHは(I) $>$ (IV)($p < 0.01$)だった。また(III)の22例のうち、(I)のpHのmean+SD以上だったのが6例で、(IV)のmean-SD以下だったのが5例だった。【結論】非細菌性CE(II)の頻度が高い事が明らかになった。細菌性CE(I)ではpHが上昇しており、(III)のうちpHが高い症例はdybiosis、pHが低い症例はMolinaら(2021)が指摘する検体採取の際のcontaminationの可能性が否定できない。combined test+pH測定から新発見が得られた。

P-27-7 ヨード剤を使用した子宮卵管造影前の甲状腺機能がその後の妊娠転機に与える影響に関する検討

琉球大

仲村理恵、山田久子、大石杉子、宮城真帆、赤嶺こずえ、銘苅桂子、青木陽一

【目的】子宮卵管造影(HSG)で使用するヨード剤(ヨード化ケシ油脂脂肪酸エチルエステル)は甲状腺機能に影響する因子として知られており、HSG前後でTSH値が変動する。HSG前の甲状腺機能に応じた内分泌内科介入の有無が妊娠・流産率へ与える影響について検討した。【方法】2018年4月~2021年3月の期間に、不妊検査としてHSGを施行した症例で、HSG前に甲状腺機能検査を施行した182例を対象とした。HSG時に全例でヨード剤を使用した。原則として、TSH ≥ 2.5 mIU/lの場合、HSG前に内分泌内科へ紹介し、甲状腺自己抗体検査や超音波検査、レボチロキシン内服を検討する方針である。【成績】HSG前のTSH値正常(正常群131例)、TSH ≥ 2.5 mIU/lでHSG前に内分泌内科に紹介した群(介入群25例)、TSH ≥ 2.5 mIU/lだが、内分泌内科に紹介せずにHSGが施行された群(非介入群26例)の3群に分類し検討した。検査時年齢は、非介入群で有意に高齢であった($P=0.006$)。不妊期間、抗ミューラー管ホルモン値、造影剤使用量、観察期間は3群で有意差を認めなかった。3群の妊娠率は、正常群38.9%(54/131例)、介入群56.0%(14/25例)、非介入群30.8%(8/26例)と介入群で妊娠率が高い傾向にあったが3群間に有意差は認めなかった($P=0.167$)。3群の流産率は、正常群3.05%(4/131例)、介入群0%(0/25例)、非介入群11.5%(3/26例)と非介入群で流産率が高い傾向にあったが3群間に有意差は認めなかった($P=0.116$)。初期流産を除く妊娠・分娩に至った全症例で新生児甲状腺異常は認めなかった。【結論】TSH ≥ 2.5 mIU/l症例において、HSG前からの内分泌内科介入が妊娠・流産率へ与える影響については、さらなる多数例での検討が必要である。

P-27-8 当院の不妊症における腹腔鏡下子宮内膜症性嚢胞摘出術後の治療予後

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【目的】子宮内膜症嚢胞を有する不妊症に対する腹腔鏡下卵巣嚢腫摘出術後の問題点として手術による卵巣予備能低下や不妊治療中の再発が挙げられる。不妊治療中には調節卵巣刺激法により高濃度のエストロゲンに暴露される症例もあるため、再発に留意しながら早期の妊娠成立を目指すことが必要である。今回腹腔鏡下子宮内膜症性嚢胞摘出術後の不妊治療の予後と再発について検討した。【方法】2015年4月～2020年8月の間に当院リプロダクションセンターで腹腔鏡下子宮内膜症性嚢胞摘出術を施行し、術後1年以上不妊治療を施行した21例を対象とした。妊娠群と非妊娠群に分類し、術中の内膜症所見、不妊治療内容、転帰について後方視的に検討した。【成績】21例のうち妊娠は14例(66.7%)に成立した。術後再発は4例(19%)であり、全例非妊娠群であった。妊娠群14例と非妊娠群7例において年齢、腫瘍径、Re-ASRMscore、不妊要因に有意差はなかった。不妊治療法は妊娠群と非妊娠群でそれぞれ自然周期+タイミング療法 or 人工授精; 8例/1例, 排卵誘発+タイミング or 人工授精; 2例/0例, 体外受精移植 (IVF-ET); 4例/3例であり、非妊娠群ではIVF-ETが多い傾向があった。術後から妊娠までの期間は 11.1 ± 5.2 (2-28) か月、術後から再発までの期間は 44.3 ± 6.3 (34-65) か月であった。再発症例のうち2例が再手術となり、2例は高齢及び反復IVF-ET不成功の要因で不妊治療を終了しジェノゲスト療法で経過観察中である。【結論】術後の累積妊娠率は66.7%と良好な成績であり、術後の積極的な不妊治療による妊娠成立は再発率を低下させると考えられた。一方で非妊娠群では再発、IVF-ET症例が多く、長期化する不妊治療は再発のリスク因子と考えられた。

P-27-9 不妊治療中に慢性子宮内膜炎と診断され精査の結果結核性子宮内膜炎と判明した一例

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【緒言】反復着床不全のため慢性子宮内膜炎を疑い、精査の結果結核性子宮内膜炎と判明した1例を経験したので報告する。【症例】34歳、未経妊。フィリピン出身、日本在住で家族歴に結核あり(のちに判明)。前医にて体外受精後、凍結融解胚移植を3回施行するも反復着床不全となり、慢性子宮内膜炎の検索目的に子宮内膜のCD138免疫染色検査が施行された。その結果、CD138陽性と内膜間質に多発する小型の類上皮細胞肉芽種の診断であり、精査加療目的に当科紹介となった。当科で提出した病理検査ではZiehl-Neelsen染色陰性で抗酸菌の存在は証明できなかったが、子宮内容物の抗酸菌培養検査でMycobacterium tuberculosis陽性であり結核性子宮内膜炎の診断に至った。喀痰培養や全身CTでは活動性結核はなく、潜在性結核感染症として治療開始となった。呼吸器内科と併診し、isoniazid (INH), rifampicin (REP), pyrazinamide (PZA), ethambutol (EB)の4剤併用療法が選択された。現在治療中であり、6か月の治療期間終了後に不妊治療再開を予定している。【結論】不妊症の検査として行われる子宮内膜検査を契機として発見された性器結核の1例を報告する。性器結核は肺外結核の中でも稀であり日常診療で遭遇する事は非常に少ないが、不妊の原因となり得る事を考慮すべきである。

P-27-10 NKp46の発現率が妊娠率に影響を及ぼすかの検討

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【目的】子宮NK (uNK) 細胞は妊娠の成立、維持に重要な役割を果たしている。NK細胞表面に発現する活性化受容体の一つであるNKp46は、NK細胞の細胞傷害性とサイトカイン産生に関与していると考えられている。我々は不育症・着床不全などの生殖異常患者NK細胞においてNKp46発現が低下することを報告してきた。今回、妊娠の予測マーカーとしてuNK細胞におけるNKp46の発現率が有効であるか否かを明らかにすることを目的に以下の検討を行った。【方法】本学倫理委員会の承認と患者への説明と同意のもと、生殖異常を有する患者(n=81)より黄体中期に子宮内膜を採取した。uNK細胞浮遊液を作成のうえ、uNK細胞におけるNKp46発現をフローサイトメトリーにて測定し、その後の一年間のフォローアップで妊娠が成立した群(n=68)と妊娠が成立しなかった群(n=13)とに分け、NKp46発現率につき検討した。【成績】NKp46⁺ uNK細胞のカットオフ値を82.9%とすると、感度は45.6%および、特異度は92.3%であった(AUC:0.63)。またNKp46^{bright} NK細胞のカットオフ値を60.5%とすると、感度は52.9%、特異度は92.3%であった(AUC:0.71)。【結論】NKp46受容体はその発現強度の違いにより、生殖において異なる役割を果たすことを報告してきた。NKp46のうち、NKp46^{bright} uNK細胞はサイトカイン産生性のNK細胞であり、今回の検討からNKp46^{bright} 細胞発現が低下することにより、妊娠が成立しがたい状況となっている可能性が示唆された。

P-28-1 子宮内膜幹細胞マーカー SUSD2/W5C5 を用いた子宮内膜症病変における幹細胞様細胞の同定と細胞特性の解析

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【目的】子宮内膜症（内膜症）の病因仮説として、移植説や化生説に加えて、近年、内膜症細胞の由来が子宮内膜の幹細胞であるとする内膜症幹細胞説が提唱されている。同説を検証する一環として、内膜症病巣における子宮内膜幹細胞の表面抗原 SUSD2/W5C5（以下、W5C5）を有する細胞の存在とその幹細胞特性の有無を明らかにすることを目的とした。【方法】内膜症性卵巣嚢胞組織（対象者 32 名、平均 35.7±7.8 歳）から機械的分散および酵素処理により内膜症間質細胞を分離し、フローサイトメトリーで W5C5 を含む細胞表面抗原の解析を行った。内膜症組織から W5C5 陽性および陰性細胞（W5C5⁺および W5C5⁻）を分離した後、コロニー形成試験と分化誘導実験により自己複製能と多分化能をそれぞれ評価した。また抗 W5C5 抗体による内膜症組織の免疫染色を行った。【成績】分離した内膜症間質細胞の 28.2±9.5% は W5C5⁺であった。W5C5⁺のコロニー形成能は W5C5⁻に比して有意に高く（0.89% vs 0.30%, $p < 0.05$ ）、W5C5⁺は軟骨・骨・脂肪・筋細胞への多分化能も有したが、W5C5⁻では認めなかった。免疫染色では、血管周囲に存在する内膜間質マーカー CD10 陽性細胞の多くが W5C5 を共発現していたが、腺上皮とその近傍には W5C5⁺は認められなかった。【結論】内膜症間質にも、正所性内膜と同様の W5C5 陽性細胞が存在し幹細胞特性である自己複製能と多分化能を有していた。正所性内膜由来の W5C5 陽性細胞が、幹細胞様の細胞として内膜症間質成分の発生・進展に寄与している可能性が示唆された。

P-28-2 子宮内膜症初期病変の腹膜浸潤におけるテネイシンの役割

鳥取大

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【目的】子宮内膜症モデルマウスの腹膜組織における遺伝子発現スクリーニングにより、初期病変の腹膜への接着・浸潤過程に関わる因子を同定し、その役割を解明することを目的とした。【方法】自然周期の 7 週齢 BALB マウスを用いて子宮内膜症モデルマウスを作製した。病変辺縁から径 2mm までの腹膜組織を病変周囲腹膜 (n=4)、病変から離れた腹膜組織を対照とした (n=4)。子宮移植後 3 日の腹膜組織から抽出した total RNA より cDNA を得た。PCR アレイ (RT² Profiler PCR Array™) を用いて、84 種の接着・浸潤関連遺伝子発現をスクリーニングした。発現増強のあった遺伝子群は RT-PCR で再検証した (n=10)。さらに、ヒト腹膜細胞 (HMrSV5) を下層に、子宮内膜症患者の子宮内膜間質細胞を上層に播種する共培養システムを構築した。細胞浸潤への siRNA 導入による遺伝子発現抑制効果をみた。目的遺伝子のノックアウトマウスを作製し、子宮内膜症病変の腹膜や周囲臓器への接着について比較した。【成績】子宮内膜症初期病変周囲の腹膜組織において、テネイシン C 遺伝子の著明な発現増強を認めた。その他、インテグリンやセレクチンなどの細胞接着因子の発現増強がみられた。野生型マウスに比して、テネイシン C ノックアウトマウスでは接着した子宮内膜症病変数が約 60% 減少し、浮遊した子宮片数の増加がみられた。浸潤アッセイにおいて、テネイシン C-siRNA 導入群では対照に比して、ヒト子宮内膜間質細胞の浸潤細胞の割合が約 20% 減少した。【結論】テネイシン C は、子宮内膜症の発生初期段階における細胞接着・浸潤のキーファクターであることが示唆された。

P-28-3 子宮内膜症間質細胞と細胞老化の特性

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【目的】子宮内膜症と酸化ストレスや炎症性サイトカインの関与を示唆する報告は多い。酸化ストレスは炎症性表現型 (SASP) を特徴とする細胞老化を誘導する。近年、様々な疾患で“Senotherapy”の効果が報告されている。我々は卵巣子宮内膜症間質細胞と老化の関係を検証した。【方法】卵巣子宮内膜症なし正所性子宮内膜間質細胞 (n-euESC)、卵巣子宮内膜症あり正所性子宮内膜間質細胞 (e-euESC)、および卵巣子宮内膜症間質細胞 (ecESC) を手術検体から初代培養した。X-Gal 染色および免疫細胞化学染色により、各細胞の老化マーカー (SA-β-gal, p16^{INK4a}, LaminB1, IL-6) を比較した。Senolytic drug (アジスロマイシンおよびナビトクラックス) を用いて細胞生存率分析を行った。【成績】SA-β-Gal 陽性細胞の割合は ecESC で高かった (n-euESC: 26.3±21.0%, e-euESC: 31.9±21.6%, ecESC: 64.5±15.0%; $P < 0.001$)。p16^{INK4a} と IL-6 の発現は ecESC で高く (p16^{INK4a}: n-euESC 65.4±34.9%, e-euESC 64.1±42.4%, ecESC 87.0±18.4%; $P < 0.01$, IL-6: n-euESC 74.8±39.0%, e-euESC 90.2±26.0%, ecESC 98.0±8.6%; $P < 0.05$)。LaminB1 は低かった (n-euESC 80.1±19.0%, e-euESC 72.7±42.3%, ecESC 45.2±35.0%; $P < 0.01$)。また、アジスロマイシン 50μM (A) およびナビトクラックス 1μM (N) を添加すると、ecESC において有意に細胞数が減少した (A: 45.7±16.2%; $P < 0.01$, N: 63.0±23.9%; $P < 0.001$)。一方、n-euESC では差がなかった (A: 7.3±53.0%, N: 26.7±34.6%)。【結論】卵巣子宮内膜症間質細胞は老化マーカー・SASP を呈し、老化細胞の特性を持つ可能性が示唆された。Senotherapy が子宮内膜症の新たな治療戦略となる可能性がある。

P-28-4 血清 miRNA による卵巣子宮内膜症性嚢胞核出術後の卵巣予備能の予測モデル

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【目的】卵巣子宮内膜症性嚢胞核出術では術後に卵巣予備能の低下が問題である。術後の卵巣予備能の予測因子となりうるバイオマーカーを探索する目的で血清 miRNA 網羅的遺伝子発現解析を行った。【方法】当該施設の倫理委員会の承認の下、同意書を取得した。先行 RCT 研究にて卵巣子宮内膜症性嚢胞核出術前後の合計 4 か月間、ジェノゲスト 2mg/日を内服した患者を対象にした。手術後は卵巣予備能を示す血清 AMH 値が総じて低下したが、術後 1 年までの検討で AMH 値が回復してくる患者(良好群)と低下したまま回復しない患者(不良群)に分けられた。良好群(n=4)と不良群(n=4)に対して血清 miRNA 網羅的遺伝子発現解析を行った。【成績】miRNA sequence により 925 個の miRNA が患者血清から検出された。RPM (reads per million mapped reads) >100 であった 276 個を解析対象とし、術後 1 年の時点で良好群において発現上昇した 15 個、発現低下した 7 個、合計 22 個の miRNA を抽出した ($P < 0.05$)。術後 2 か月 (内服終了時点) から術後 1 年の各 miRNA の変化率を比較し、良好群で発現が上昇、かつ、不良群で発現が低下する miR-140-3p 及び miR-629-5p が AMH の回復と関連する傾向を有する miRNA として抽出された。両群の平均変化率は miR-140-3p 及び miR-629-5p において良好群、不良群でそれぞれ 1.32 : 0.54, 1.22 : 0.57 であった。【結論】患者血清を用いた miRNA 網羅的遺伝子発現解析により術後の卵巣予備能を予測するバイオマーカーとして 2 種の miRNA が検出された。これらの血清 miRNA を用いて、術前の miRNA 発現量から術後の卵巣予備能を予測出来るモデルの確立を目指す。

P-28-5 子宮内膜症における腹水中 NK 細胞受容体の発現強度の解析

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【目的】子宮内膜症における腹水中 NK 細胞の活性化受容体と、抑制性受容体の共発現およびサイトカイン産生につき検討した。【方法】子宮内膜症手術患者(子宮内膜症群: n=13)、子宮内膜症のない良性疾患手術患者(対照群: n=12)を対象とした。すべての腹腔内操作開始前に腹水を採取し、NK 細胞 (CD56⁺細胞) における活性化受容体 (CD16, NKp46, NKG2C, NKG2D), 抑制性受容体 (CD158a, NKG2A) 発現, サイトカイン (TNF- α , IFN- γ , IL-4, IL-10, TGF- β) につき、フローサイトメトリーを用いて測定した。さらに、月経困難症の程度を評価し NK 細胞の受容体発現, 細胞内サイトカイン産生につき相関分析を行った。【成績】子宮内膜症群の CD16⁺/CD56^{dim} NK 細胞および CD56^{dim}/NKp46⁺ NK 細胞は対照群に比して低値であった。さらに、月経痛の程度と CD16⁺/NKp46⁺ NK 細胞との間に正の相関を認めた ($\rho = 0.69$, $p < 0.01$)。活性化受容体 NKG2C と NKp46 との共発現は、NKp46⁺/NKG2C⁺ NK 細胞が子宮内膜症群で有意な低下を認め ($p < 0.05$)。発現強度も加味すると NKp46^{dim}/NKG2C^{dim} NK 細胞, NKp46^{bright}/NKG2C⁺ NK 細胞, NKp46^{bright}/NKG2C^{bright} NK 細胞, NKp46^{bright}/NKG2C^{dim} NK 細胞が子宮内膜症で有意に低下した ($p < 0.01$)。一方、抑制性受容体 NKG2A と NKp46 との共発現は NKp46⁺/NKG2A⁺ NK 細胞が対照群に比して高値であった。発現強度も加味すると NKp46^{dim}/NKG2A^{dim} NK 細胞は子宮内膜症群で有意に高値であった ($p < 0.05$)。NK 細胞内サイトカインは両群間に差を認めず、月経痛との関連も認めなかった。【結論】子宮内膜症患者の腹水中 NK 細胞では受容体の発現強度の違いにより細胞傷害性が異なるだけでなく、月経困難症の程度と表面抗原の発現とも関連が示唆された。

P-28-6 子宮内膜症に対する P2X4 受容体拮抗薬の効果

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【目的】P2X4 受容体は細胞外 ATP によって活性化される P2X 受容体のサブタイプであり、脊髄後角に存在するミクログリアに発現がみられ神経障害性疼痛に関与する。P2X4 受容体は卵巣やマクロファージを含む全身の組織にも広く発現することが知られている。近年、子宮内膜症による慢性疼痛の原因として神経障害性疼痛がの関連が報告されている。本研究では、P2X4 受容体の子宮内膜症病変形成における役割を知り、P2X4 受容体阻害薬 (NC-2600SD) の治療薬としての可能性を検討することを目的とした。【方法】8 週齢の BALB/c マウスから卵巣を摘出し、吉草酸エストラジオールを投与した。ドナーマウスから子宮を摘出し、細切してレシピエントマウスの腹腔内に移植することで、子宮内膜症モデルマウスを作成した。NC-2600SD を 2 週間経口投与した。モデルマウスに対してホットプレートテストによる行動試験を行った後に、腹腔内の子宮内膜症病変および子宮を採取した。子宮内膜症様病変に対する RT-PCR を施行し、内膜症病変における遺伝子発現をみた。【成績】ホットプレートテストによる行動試験の結果、NC-2600SD 投与群において疼痛緩和が認められたが、病変組織および子宮の総重量は変化しなかった。子宮内膜症病変組織では薬剤投与群において、IL-33 の発現が減少した。【結論】子宮内膜症モデルマウスへの NC-2600SD 投与により、疼痛刺激に対する過敏性が抑制された。病変組織内の IL-33 の関与が示唆された。

P-28-7 Leucine rich α -2 glycoprotein (LRG) の子宮内膜症における有用性の検討～新規診断マーカーになりうるか～

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【目的】子宮内膜症は月経困難症や不妊症など女性の QOL を著しく低下させる。異所性に生着した子宮内膜が子宮内膜症と画像的に診断されるには約 10 年を要し、診断時はすでに非可逆的な癒着や線維化をきたすことが多い。そこで我々は、心筋線維化に関与している leucine rich α -2 glycoprotein (LRG) に着目し、子宮内膜症診断の新規血清マーカーとなり得るかを探索することとした。これにより子宮内膜症に早期介入し、重症な不妊症などの QOL 低下を防ぐことを目指している。【方法】当施設倫理委員会承認のもと、2020 年 3 月から 2021 年 9 月に当院でチョコレート嚢胞摘出術を施行した患者(内膜症群)、卵巣腫瘍摘出術を施行した患者(良性群)、子宮内膜症や卵巣腫瘍を合併していない ART 施行した患者(コントロール群)のうち、同意を得られた 25 名(内膜症群: 11 名, 良性群: 4 名, コントロール群: 10 名)を対象に血清 LRG 濃度を測定した。【成績】各群の術前 LRG 濃度中央値は、内膜症群: 38.43 μ g/mL [24.93-60.90], 良性群: 29.24 μ g/mL [24.83-46.02], コントロール群: 29.16 μ g/mL [21.63-37.39] であり、内膜症群で LRG 濃度が高い傾向にあった。多重比較を行ったところ、内膜症群とコントロール群で有意差を認めた。また内膜症群と良性群で、術前と術後 1 か月の LRG 濃度で符号付き順位と検定を行ったが、有意差は認めなかった。【結論】内膜症群における LRG 濃度が、コントロール群に比べて LRG 濃度が有意に高いことが確認できた。LRG が子宮内膜症の新規血清マーカーの候補となることを示すことができた。今後、更なる症例の集積、および、術後の経時的な LRG 濃度の変化についてもデータを集積し、解析を進める予定である。

P-29-1 卵巣内膜症性嚢胞合併不妊症症例に対する腹腔鏡補助下腔式エタノール固定術と腹腔鏡下内膜症性嚢胞核出術の比較検討

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【目的】卵巣内膜症性嚢胞に対する手術療法の妊孕性を向上させるため、標準手術として嚢胞核出術が行われることが多い。嚢胞核出術は正常卵巣組織が損傷され、卵巣予備能の指標である AMH の低下・排卵誘発に対する反応の減弱や採卵数の減少を引き起こすことが指摘されている。当科では卵巣内膜症性嚢胞を有する不妊症症例に対して、正常卵巣組織の損失が少ないことが示唆されている腹腔鏡補助下腔式エタノール固定術 (Ethanol Sclerotherapy; EST) を行っている。今回 EST と嚢胞核出術の臨床成績について比較検討した。【方法】2000 年から 2021 年の間に、当科で卵巣内膜症性嚢胞を有した不妊症症例で腹腔鏡下手術を行った 136 例(嚢胞核出術 46 例, EST90 例)を対象とし、術後の不妊治療成績および再発の有無等につき後方視的に検討した。【成績】手術時年齢(核出: 33.0 \pm 4.2 歳, EST: 32.5 歳 \pm 3.5 歳), 不妊期間(核出: 3.3 \pm 2.6 年, EST: 3.3 \pm 2.4 年)に有意な差を認めなかった。嚢胞最大径(核出: 45.7 \pm 21.9mm, EST: 54.6 \pm 18.0mm p <0.05), 血清 CA125 値(核出: 37.9 \pm 28.5IU/mL, EST: 64.4 \pm 63.7IU/mL p <0.01)はいずれも EST で有意に大きくなった。累積妊娠率は ART 未施行症例・施行症例いずれも差を認めなかった。術後の累積再発率は、EST で有意に高くなった。調節卵巣刺激をロング法で行う ART を施行した症例では、総 FSH 投与量(核出: 2322 \pm 1158IU, EST: 1747 \pm 690 p <0.01)は嚢胞核出術で有意に多くなったが、採卵数に有意な差はなかった(核出: 6.8 \pm 5.8 個, EST: 5.3 \pm 3.8 個)。【結論】EST は再発率が高いものの卵巣機能への影響が少ない可能性があり、内膜症性嚢胞を有する不妊症症例に対し有効な治療である可能性が示唆された。

P-29-2 40 歳以上の子宮内膜症に対する薬物療法について

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【目的】子宮内膜症は再燃する可能性が強いため、閉経期周辺までの薬物療法が必要となることが多い。40 歳以上の場合は血栓症などの合併症が懸念されるため、LEP 製剤以外の薬物療法となる。本研究では患者の QOL からみた場合、どのような薬物療法が有益であるかを検討した。【方法】腹腔鏡手術により子宮内膜症と診断され、薬物療法が必要な 40 歳以上の患者 33 例を対象とした。いずれも子宮には器質的な疾患を合併していない症例で、手術後 5 年以上経過しており、それまでは LEP 製剤を内服していた。A: dienogest (D) 2mg/day を投与した群 (22 例), および B: GnRH antagonist (G) 40mg/day を投与した群 (18 例) に分け、治療開始後 3 か月の時点での下腹痛の改善度、不正子宮出血の出現頻度、投与中の血中 estradiol 値の変動につき比較検討した。G の投与法は最初の 2 週間は連日投与とし、それ以後は 2-3 日間隔で投与した。【成績】観察期間中の下腹痛は、両群ともに改善していた。A 群では 22 例中 6 例 (27.3%) に不正子宮出血が出現したが、B 群では 1 例も出現しなかった。血中 estradiol 値は 49.8 \pm 23.4 vs. 25.6 \pm 11.0pg/ml と B 群で有意に低下していた (p <0.01)。卵巣欠落症状は両群とも発生しなかった。【結論】40 歳以降の子宮内膜症に対しては D のみではなく G の間隔を空けた投与方法も有用である。不正子宮出血が予防可能であることから、この方法は患者の QOL を損ねることがない有用な方法であると考えられた。

P-29-3 若年チョコレート嚢胞に対しLEP+アルコール固定が有効であった1症例

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【はじめに】子宮内膜症は性成熟期の女性の5~10%が罹患していると言われており、若年女性に発生することは比較的にめまるとされているが、慢性的な骨盤痛を認める10代女性では腹腔鏡で50~70%に子宮内膜症を認めたとの報告もある。今回我々は、骨盤痛のない若年症例に対し卵巣チョコレート嚢胞のう胞アルコール固定術とLEPを使用し良好な経過を得た1症例を経験したので報告する。【症例】16歳、未婚、未妊。身長158cm、体重66kg、初経10歳、月経困難などの症状は認めなかった。半年前からの腹部腫瘤感を主訴に近医を受診する。卵巣のう腫を指摘され当科へ紹介となる。MRIで右卵巣に15×10cm大のチョコレート嚢胞と、子宮周囲に漿液性嚢胞を多数認めた。腫瘤による圧迫感が強く手術の方針となった。嚢胞が大きかったが若年であるため、腹腔鏡下アルコール固定術を施行した。腹壁にヘモジデリン沈着がみられた。両側の付属器周囲はフィルム状の癒着で覆われており、漿液性嚢胞を多数認めた。左卵管は盲端となっていた。R-ASRM分類IV期であった。画像と腹腔鏡所見から子宮奇形は認めなかった。術後にLEPを開始し3年半が経過した。右卵巣は3cm程度に縮小し、漿液性嚢胞の消退も認めている。【結論】若年者の子宮内膜症に対しアルコール固定術とLEPは有効であると考えられた。

P-29-4 当院における稀少部位子宮内膜症の検討

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【目的】稀少部位子宮内膜症は臓器ごとに多様な症状が出現し、婦人科以外の科が初診になることも少なくない。症状と月経周期に関連があることが特徴的であるが、診断方法、管理方針は確立されておらず、婦人科と各科の連携が必要とされる。当院での症例を後方視的に調査し、現状と今後の課題について検討した。【方法】対象は2011年4月から2021年3月に当院で管理された稀少部位子宮内膜症症例である。診療録をもとに、患者背景、診断契機・方法、初診の科、婦人科受診の有無、治療内容について検討した。【成績】稀少部位子宮内膜症は10例(回腸4例、胸腔3例、虫垂1例、膀胱1例、臍部1例)で平均年齢は40歳であった。回腸3例は腸閉塞を契機に診断、1例は婦人科手術時の腸管切除で診断された。胸腔2例は月経に伴う気胸を契機に診断、1例は婦人科手術の術前検査で気胸の診断、手術時に横隔膜に内膜症病変を認め診断された。虫垂と膀胱は婦人科手術時に切除され組織学的に診断された。臍部は月経に伴う疼痛を訴え、手術で摘出され組織学的に診断された。初診は婦人科が5例でいずれも関連する科に紹介された。初診が婦人科以外であった5例のうち4例は婦人科に紹介された。手術が8例に施行され、ホルモン療法が5例に施行された。治療後に再発が疑われた症例は臍部の1例で、婦人科受診がない症例であった。【結論】月経と関連する症状がなく、偶発的に診断された症例が4例あり無症候性の稀少部位子宮内膜症患者が多く存在する可能性が示唆された。10例中9例が婦人科と各科で連携し、手術療法とホルモン療法で再発なく管理されていた。稀少部位子宮内膜症には婦人科と各科の連携した医療が重要である。

P-29-5 当院で胸腔子宮内膜症が疑われた14例の検討

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【背景】胸腔子宮内膜症は稀少部位子宮内膜症に分類される稀な疾患であり、その背景や臨床経過は多彩であることから、管理法は確立されていない。胸部症状の出現は性成熟期女性の生活の質を著しく低下させる。今回、当院で経験した胸腔子宮内膜症について文献的考察を加え、報告する。【対象と方法】2007年から2021年までの14年間に当院で胸腔子宮内膜症と診断した症例もしくは疑い症例を抽出した。胸腔病変に対する治療を行ったのは14例で、それらの背景、臨床経過について後方視的に比較検討した。【結果】対象の14例中、12例は当院および近医外科で気胸、血胸に対して胸腔鏡手術を施行された。そのうち実際に組織学的に子宮内膜症を診断しえたのは2例であったが、全例に肺実質、横隔膜に存在するblueberry spotや横隔膜の小孔を認め、臨床的に胸腔子宮内膜症と診断した。婦人科診察を行って骨盤内子宮内膜症の存在が疑われたのは6例であった。また、術前・術後に子宮内膜症に対するホルモン療法(GnRHアナログ製剤、低用量ピル、ジエノゲスト)を行ったのは6例で、子宮内膜症の治療中にもかかわらず気胸を再発したのは1例であった。【考察】胸腔子宮内膜症の発症は月経周期のいずれの時期においても出現すると考えられ、呼吸苦を主訴とした内科受診を介した症例が多かった。また、ホルモン療法に対する心理的抵抗があり、投薬を希望されない症例も見受けられたものの、ホルモン療法は胸腔子宮内膜症による血気胸の再発、予防に寄与すると考えられた。性成熟期女性の呼吸器症状、胸部痛に対しては胸腔子宮内膜症を鑑別に挙げ、他科と連携して適切な管理を行うことが望ましいと考えられた。

P-29-6 子宮内膜症に対するジェノゲスト治療中の不正性器出血のリスク因子の検討

高知大附属病院

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【目的】子宮内膜症治療にジェノゲスト (DNG) を用いる際、その代表的な副作用として不正性器出血がある。DNG を長期間投与することで不正性器出血は改善することが多いが、症状が持続する症例では治療満足度が低下する可能性や、その程度によっては治療継続が困難となる場合もある。今回、DNG 使用中の不正性器出血の有無やその持続期間と症例の背景について後方視的に検討した。【方法】2008年8月から2021年1月で、当院において子宮内膜症に対してDNGで6か月以上治療した87例を対象とした。対象を、A群：DNG内服開始から6か月以内で不正性器出血を認めなかった症例(n=26)、B群：6か月以内には不正性器出血を認めたが、その後出血が消失した症例(n=33)、C群：6か月以降にも不正性器出血が持続した症例(n=28)に群別化した。それぞれの群の患者背景(年齢, BMI, DNG開始前の子宮内膜症に対する手術療法の有無)、血中エストラジオール値(E2値)について検討した。本臨床研究は高知大学IRBの承認を得ている。【成績】A群とB群の比較では、BMI, 血中E2値, その他患者背景に有意差は認めなかった。B群とC群の比較では、BMI等に有意差はなかったがC群で有意に血中E2値が高かった(20.26 vs 64.06, $p < 0.001$)。A群とC群の比較では、BMIがC群で有意に高く(22.21 vs 24.98, $p = 0.03$)、血中E2値はC群で有意に高値だった(20.04 vs 64.06, $p = 0.01$)。【結論】本検討から、DNG使用時の不正性器出血の出現、持続はBMIや血中E2値と関連している可能性が示唆された。患者の体格の評価とDNG治療中の血中E2値測定は、不正性器出血のリスク評価、治療の継続性、患者の治療満足度上昇に寄与する可能性が示された。

P-29-7 帝王切開術後の子宮瘢痕部に発生した希少部位子宮内膜症に対し保存的治療が奏功した1例

聖マリア病院

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【目的】帝王切開後の希少部位子宮内膜症として腹壁瘢痕部からの発生報告は散見されるが、子宮切開創部からの発生報告は0.8%と稀である。今回我々は帝王切開術後5年経過した子宮切開創から発生したと考えられる子宮内膜症の1例を経験したので報告する。【症例】45歳, G1P1, 37歳時に帝王切開術の既往がある。近医で過多月経、子宮筋腫に対し定期的に経過観察されていた。3年前から子宮頸部前壁に2cm大の血腫様腫瘍を認め、その後6cm大まで増大してきたため、LEP製剤が投与された。しかし、縮小傾向を認めなかったため当院紹介となった。内診では子宮頸部の腫大と圧痛を認め、経陰超音波断層法では、子宮頸部前壁に6cm大のチョコレート様腫瘍を認めた。腫瘍マーカーはCA125 43.0 U/mL, CA19-9 33.2 U/mLとCA125が高値であった。骨盤MRI検査では子宮体～頸部移行部前壁右側主体に長径52mm大の血腫様腫瘍を認め、帝王切開瘢痕部に希少部位子宮内膜症が嚢胞を形成していると考えられた。そのほか子宮体部に小結節が散見され子宮筋腫を認めたが、両側卵巣には異常所見は認めなかった。保存的治療としてGnRHアゴニスト療法を開始し、6コース後には1cm以下まで縮小し子宮筋層の不連続を認めた。その後、ジェノゲストを1年6か月投与したが再増大を認めていない。【結論】帝王切開の子宮切開創から発生したと考えられる子宮内膜症に対し、薬物療法が奏功した症例を経験した。帝王切開は希少部位子宮内膜症のリスク因子の1つであり、子宮切開創部に嚢胞性腫瘍を認めた場合、本疾患を念頭に置いた診断と治療が必要であると考える。

P-29-8 回盲部子宮内膜症により絞扼性腸閉塞をきたした1例

自衛隊札幌病院

三宅太郎, 高崎和樹, 海士洋平, 濱口大志

【緒言】子宮内膜症は、子宮内膜組織が子宮外に異所性に増殖する疾患で、腸管子宮内膜症はそのうち約10%に認められるとされるが、小腸での発生は稀である。今回、下腹部痛で当院を受診し、絞扼性腸閉塞の診断で回盲部切除術後に、回盲部子宮内膜症と診断された症例を経験したので報告する。【症例】44歳, 2妊1産。既往歴として、7年前に左チョコレート嚢胞に対して左付属器切除術を施行されたが、その後のフォローを自己中断していた。下腹部痛を主訴に当院を受診した。受診時、左下腹部に強い圧痛を認め、腹膜刺激症状を認めた。造影CTでは、回盲部に腫瘍陰影とその口側小腸の拡張を認めたため、回盲部の閉塞が疑われた。経陰超音波検査では、子宮や右卵巣の腫大を認めず、腹水貯留も認めなかった。大腸内視鏡では回盲末端部に隆起を認め生検を施行したが正常な回腸粘膜のみ認めた。イレウス管を挿入して減圧を図るも、症状改善を認めず、入院6日目に試験開腹術を施行した。回盲部に硬結を伴う絞扼性癒着を認めたため、閉塞部と判断して、回盲部切除術を施行した。右卵巣に2cmのチョコレート嚢胞を認めた他、腹腔内に明らかな異常所見を認めなかった。術後経過は良好で、入院11日目に退院となった。病理組織では、硬結を認めた回盲部の筋層から粘膜下組織に子宮内膜組織が島状に分布しており、回盲部子宮内膜症と診断された。術後から再発予防のためディナゲスト内服を開始した。現在も継続中である。【結語】絞扼性腸閉塞を発症後に、回盲部子宮内膜症と診断された症例を経験した。術前の診断は困難であるが、既往歴など臨床経過を踏まえて、本疾患の可能性を考慮することが肝要である。

P-30-1 当院で経験したNIPTの判定保留3症例

広島赤十字・原爆病院

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無侵襲的出生前遺伝学的検査(NIPT)が広く認知されてきているが、全体の0.3%に判定保留という結果が発生すると言われる。当院で2020年4月1日から2021年3月31日の間に行った295件のNIPTのうち、3件(1%)で判定保留という結果を認めたため、詳細を含めて報告する。1例目は36歳、2妊1産、6.5cm大の子宮筋腫合併妊娠であった。妊娠11週に行った1回目のNIPTで判定保留、妊娠13週に行った2回目のNIPTで陰性となった。妊娠28週に羊水過少症、子宮内胎児発育不全、臍帯血流異常で緊急帝王切開での分娩となったが児に明らかな異常は認めなかった。2例目は37歳、2妊1産、合併症なし、妊娠15週で行った1回目のNIPTで判定保留、妊娠16週に行った2回目のNIPTでも判定保留であったため妊娠17週に羊水検査を実施、正常核型と診断した。妊娠38週で経陰分娩となり、胎盤のFISH検査で21トリソミーの胎盤モザイクを認めた。3例目は40歳、3妊2産、合併症なし、妊娠11週で行ったNIPTで判定保留となり、21番染色体のduplicationが存在する可能性が示唆された。妊娠16週に羊水マイクロアレイ検査を行ったところ21番染色体のduplicationは認めなかった。分娩経過に問題はなかった。このようにNIPTは、頻度は少ないがある一定の確率で判定保留という結果が発生する。その際には個々の症例に応じた適切なカウンセリングと追加検査が必要となるため、対応可能な施設でのNIPTの実施が望ましいと考えられた。

P-30-2 エピジェネティクス関連疾患を高効率にゲノム診断可能なターゲットDNAメチル化シーケンス法の基盤確立

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【目的】臨床診断や配列ベースの遺伝子検査では診断困難な疾患は一定数存在し、近年遺伝子プロモーター領域をはじめとするDNAメチル化情報の補完がゲノム診断率を向上させる可能性が示された。しかし、既存のDNAメチル化シーケンス法(DMS)は標的領域が約300万箇所までゲノム領域全体を対象としているため非効率的でシーケンス費用の上昇に寄与するため、疾患と関連する遺伝子領域に絞った高効率なTargeted DMS(T-DMS)の確立が望まれている。本研究の目的は、エピジェネティクス関連疾患を対象とした高効率なT-DMSの基盤を確立することである。【方法】T-DMSの標的領域は、全遺伝子プロモーター領域(37,661箇所)とエピジェネティクス関連疾患に関連する既知のDNAメチル化領域(3,643箇所)のみとした(全標的領域の約25%)。T-DMSの実用性を評価するため、非疾患群の末梢血から採取したDNA(8検体)を用いて、パイサルファイトシーケンスによりデータを取得・解析した。【成績】T-DMSにより標的領域の99%を解析することが可能であった。T-DMSの解析可能なデータの割合を示すマッピング率の中央値は76%(範囲75-77%)、解析データ精度の指標であるカバレッジの中央値は84(範囲54-106)、標的領域のデータ取得の効率を示すオンターゲット率の中央値は97%(範囲95-98%)であった。【結論】今回我々の確立したT-DMSでは、全標的領域の約25%に標的領域を絞り高効率に解析を行うことが可能であった。これにより、シーケンス費用を従来の約1/4に下げることが可能となると考えられた。

P-30-3 胎児超音波所見を理由にNIPTを受検した妊婦に対する母体年齢の影響の検討

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【目的】母体血胎児染色体検査(NIPT)の受検理由は母体高年が最も多いが、前児染色体異数性、胎児超音波異常所見などがある。胎児超音波異常所見を適応としてNIPTを受検した症例について母体年齢の影響を含めて検討することを目的とした。【方法】2013年4月から2021年7月までに当院にて遺伝カウンセリングを施行し、その後NIPTを実施した妊婦のうち、受検理由が胎児超音波異常所見であった症例について、母体年齢により2群に分けて、受検時妊娠週数、超音波所見、検査結果、児の出生週数、出生児体重について後方視的に比較検討した。【成績】NIPT受検者は8698人で、胎児超音波所見を適応として受検したのは76人(0.87%)であった。母体年齢34歳以下(I群)は41人、35歳以上(II群)は35例で、平均年齢はI群31.2歳、II群38.2歳であった。超音波所見はI群では頸部浮腫92.7%、鼻骨低形成2.4%、羊水異常2.4%、II群では頸部浮腫91.4%、鼻骨低形成2.9%、臍帯ヘルニア2.9%、トリソミー疑い2.9%であった。NIPT陽性はI群4.9%(2例)、II群14.3%(5例)であった。I群では2例とも羊水染色体検査で21トリソミー確定診断となり、II群では21トリソミー2例と18トリソミー1例は確定診断に至ったが、他は自然産産となった。検査後の転帰が判明している22週以降に出生した児(I群24例、II群23例)について、出生週数、出生時体重は両群に明らかな差は認められなかったが、I群では1例に新生児死亡(13、18、21トリソミー以外の染色体異常)を認めた。【結論】妊娠初期に胎児超音波検査で頸部浮腫等の所見を認めた妊婦については、年齢が高いと羊水を含めた胎児染色体検査をより考慮されることが示唆された。

P-30-4 妊娠初期における18トリソミーの診断—NIPTと超音波の役割

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【目的】妊娠初期における18トリソミーの診断に際しての、NIPTと超音波のそれぞれの役割を明らかにする。【方法】当院で、2016年1月から2021年8月までの間に、妊娠初期に超音波検査を行った後に、染色体検査によって最終的に18トリソミーと確定診断した胎児55例について、診断に至った経緯、超音波検査所見、妊娠転帰について検討した。【成績】妊娠初期に超音波検査を行ったきっかけは、本人の希望6例、浮腫またはNT肥厚指摘45例、NIPT陽性6例(NT肥厚との重複2例)であった。ほぼ全てのケースでストロベリーサイン、手関節拘縮、心奇形、単一臍帯動脈、臍輪部形成の遅延などといった特徴的な複数の超音波所見が見られていたが、所見に乏しいケースも6例存在した。典型的所見に乏しいケースでは、血清マーカー検査を加えたコンバインド検査としての評価が診断に役立った。確定診断は、32例が絨毛生検、11例が羊水穿刺、13例が流産後絨毛で行われた。6例が子宮内胎児死亡、48例が人工妊娠中絶、1例が妊娠継続し41週で出産した。【結論】妊娠初期における18トリソミーの診断において、超音波検査の役割は大きく、必ずしも陽性的中率が高いといえないNIPTの結果を捕捉することが可能となる。複数の顕著な異常超音波所見が存在する際には、羊水穿刺以外の方法によるより迅速な判断が可能となる。一方で、NIPT陽性であっても超音波所見の乏しいケースでは、慎重な扱いが必要とされる。

P-30-5 当院の出生前確定検査における検査方法選択の現状

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【目的】マイクロアレイ染色体検査法(SNPアレイ法)は、G-band法で解析できない染色体微細構造異常を検出できる。一方、均衡型構造異常は検出できず、意義不明バリエーション検出時の対応では留意が必要である。当院で行った出生前確定検査のうちSNPアレイ法とG-band法の症例背景を検討した。【方法】2019年1月から2021年3月までに当院で妊娠22週以前に確定検査(絨毛検査・羊水検査)を施行した患者のうち、SNPアレイ法を用いた症例(S群)の検査施行理由や検査週数をまとめた。またS群とG-band法を用いた症例(G群)を比較した。【成績】対象は127症例、そのうちS群が9例(7%)、G群が118例(93%)、平均検査週数は両群とも16.5週であった。S群の検査施行理由は、妊娠歴・家族歴1例、NIPT判定保留1例、NIPT15トリソミー疑い(他無認可施設で実施)1例、超音波検査で先天性心疾患が疑われた症例が6例だった。また、超音波所見で検査した6症例中3症例はNIPT陰性確認の後に超音波所見を理由にSNPアレイを施行していた。一方、G群の検査施行理由は妊娠歴・家族歴9.3%、NIPT結果14.4%、超音波所見16.9%、コンバインド検査結果8.5%、クアトロ検査結果8.5%、その他42.4%であった。【結論】SNPアレイ法は形態異常を理由とした確定検査で利用されることが多い一方、G-band法は21/18/13トリソミーを想定して選択されることが多かった。出生前確定検査における遺伝学的検査の方法は、胎児形態情報を加味して遺伝カウンセリングを実施し、クライエントの検査目的に沿って選択することが重要と思われた。

P-30-6 当院における出生前検査外来開設の影響について

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【目的】当院は過疎地域の周産期センターでありNIPTの認可は受けていない。出生前検査への関心が高まり、当院では従来のクアトロ検査と羊水検査に加え、2017年7月から1st trimester scanを開始した。さらに2021年5月には出生前検査外来を新規開設し、検査会社所属の臨床遺伝専門医、超音波専門医の医師の指導の元、コンバインド検査を新規導入し、臨床遺伝科と連携し遺伝カウンセリング体制も充実させたため、従来と比較し現状を報告する。【方法】2016年から2017年6月をクアトロ検査と羊水検査のみの第一期、2017年7月から2021年4月を1st trimester scan開始後の第二期、2021年5月から9月を出生前検査外来開設後の第三期とし、出生前検査内容を後方的に検討した。【成績】各検査の年平均施行数は、クアトロ検査は第一期12件、第二期6.8件、第三期4.8件と減少し、1st trimester scanは第二期27.7件、コンバインド検査は第三期36件で、非確定検査の合計としては第一期12件、第二期34.5件、第三期40.8件と増加を認めた。羊水検査は第一期15.2件、第二期11.5件、第三期7.2件と減少し、非確定検査未施行の羊水検査の割合は第一期73.9%、第二期59.1%、第三期0%と明らかな減少を認めた。なお、羊水検査施行理由は高齢妊娠が全期間で68.6%と最も多かった。【結論】第一期から第三期にかけて非確定検査の診療体制拡充とともに実施数が増加し、これまで当院診療圏で対応しかねていた検査ニーズに応えた結果と考える。また、非確定検査の実施数増加に反して羊水検査の実施数は減少しており、遺伝カウンセリングおよび検査実施の体制が整ってきたことが示唆される。今後は受診者の満足度調査も行い追って報告したい。

P-30-7 当院における絨毛採取症例 36 例の検討

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【目的】当院における絨毛穿刺 (CVS) 症例を後方視的に検討すること。【方法】当院の診療記録から CVS 症例を抽出し、その適応、採取方法 (経腹か経陰か)、転帰等について検討した。【成績】2010 年 1 月から 2021 年 10 月までにのべ 36 例で施行されていた。母体年齢 (中央値) は 34 歳 (25~40)、妊娠週数は (中央値) 11 週 5 日 (9.6~18.3)、のべ 36 例中 8 人 (計 16 例) が検討期間内に 2 回 CVS 施行されていた。適応は神経筋疾患 16 例、先天代謝異常症 7 例、染色体疾患 6 例、中枢神経疾患 3 例、骨系統疾患 2 例、先天奇形 1 例で、採取方法は経腹が 22 例、経陰が 14 例だった。検体取量が得られないなどの失敗例は 3 症例認められ、1 例は経腹から経陰法に変更し採取成功。他の 2 例は同一クライアントで経腹・経陰いずれも検体が得られず、羊水検査によって検査完遂した。全 36 例中 CVS が原因で IUID や流産に至った症例は無かった。2010 年から 2016 年までの 18 例 (前半) と 2017 年から 2021 年までの 18 例 (後半) で比較すると、適応としては前半では神経筋疾患が 11 例 (61%) を占め、後半では 5 例 (27%) だった。また、前半では経腹法が 16 例 (89%) で、後半では 6 例 (33%) と最近では経陰法を選択することが多くなっていった。【結論】当院における 2010 年から現在までの CVS 症例 36 例を後方視的に検討した。開始当初は経腹法が大部分だったが、経陰法の割合が増える傾向が認められた。CVS により診断が得られない失敗例は 3 例あり、流産や IUID に至った症例は無かった。前児既往疾患による保因者診断例が複数人で認められ、最近では神経筋疾患を適応とする症例が減少していた。最近では多彩な適応から遺伝子検査を要する例が増しており、今後 CVS のニーズが増すことが示唆された。

P-30-8 超音波検査での胎児精査に適した週数の検討

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【目的】胎児発生過程に左大動脈弓が退化し右大動脈弓が残存すると「左動脈管, RAA, 左鎖骨下動脈起始異常」となる。このような胎児では流出路より頭側の気管周囲の構造評価が必要になり、週数に応じて超音波検査による評価がどのように変化するか検討する。【方法】当院に紹介を受けた上記先天性疾患児の超音波検査による精査で週数により要した時間と評価項目の精度を後方視的に調査し、胎児精査に適した週数を検討した。【成績】30 週以降、週数が進むにつれて胎児精査に要する時間は延長傾向を認めた。また、評価不能項目が増加した。特に 36 週以降では胎児超音波検査の精度が低下し、3VTV 断面付近の描出が約 50% と困難な状況で、母体肥満傾向ではこの傾向が強まった。母体の体位変換、時間間隔をあけての再検、color mode 仕様で描出率は 90% まで上昇した。【結論】母体体位変換、color mode 使用、時間をあげ、観察者を変えての検査が有効であった。30 週以前での実施が望ましく、評価不能項目が最小となったのは 22 週から 24 週となった。超音波機器の性能向上に伴いより早い週数での胎児構造評価が可能となり、30 週に比べ、18-20 週での実施の重要性が増していると思われる。

P-30-9 一般集団における出生前検査について知識についての調査研究

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【目的】妊娠年齢の高年齢化と共に出生前検査への関心が高まっているが、一般市民がどのような意識や知識を持っているかの客観的データはない。そこで、出生前検査に関する知識の普及度を把握する目的で調査を行った。【方法】20~59 歳の全国の男女を対象に、基本属性 (年齢など)、出生前検査の知識等についての 60 問からなる WEB 調査を実施した。男性 (男)、妊娠期女性 (妊女)、一般女性 (般女) に分類したうえで、妊娠既往がある女性またはパートナーが妊娠既往のある男性を妊娠既往群 (S 群)、それ以外を非妊娠既往群 (NS 群) として比較した。【成績】調査対象は 2995 人 (各群: S 男 574 人, NS 男 461 人, S 妊女 589 人, NS 妊女 383 人, S 般女 589 人, NS 般女 349 人) である。出生前検査をそれぞれ知っているかという問いに対して、精密超音波、クアトロ、NIPT、羊水検査ともに「よく知っている」「目的などおおよそ知っている」がどの分類でも S 群で有意に高い一方、遺伝カウンセリングも含め、どの出生前検査も「全く知らない」との回答がすべての群で 50-70% あった。妊娠既往がある者に対して、出生前検査を受けなかったことに対してどう思うかという間に、「受ければよかった」という回答が 14.6% 得られた。【結論】妊娠既往群でも出生前検査を全く知らない者が 50-70% を占め、出生前検査についての知識や情報が妊婦やそのパートナーにおいて不足している状況が判明した。出生前検査は自発的な意思によって選択されるものだが、出生前検査を認知し内容を理解していなければ選択することもできない。今後は妊婦やパートナーはもとより、一般市民にとっても出生前検査を含めた生殖の一般的な知識の教育の重要性が示唆された。

P-30-10 形態・発育異常を認められた胎児の転帰に関する検討

長崎大

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【目的】胎児形態・発育異常と遺伝学的検査との関連について検討した。【対象と方法】2019年1月から2021年8月までの間、nuchal translucency (NT) 肥厚, 胎児ヒグローマ, 胎児水腫, あるいは胎児発育不全 (FGR) を指摘され当科を受診した妊婦を対象とし, 染色体検査の有無, 染色体異常の有無, および妊娠転帰について検討した。【結果】胎児形態異常のため当科を受診した43例 (NT 肥厚15例, 胎児ヒグローマ21例, 胎児水腫6例) の平均年齢は33.9歳であった。受診した妊娠週数の平均値は妊娠13.5週であった。NT 肥厚15例のうち, 染色体検査を受検したのは9例 (60%) で2例がNIPT, 7例が羊水染色体検査を選択した。NIPT2例は陰性であり, 染色体検査を受けた7例のうち4例に染色体異常が認められた (21トリソミー, 18トリソミー, 同腕染色体, 重複染色体それぞれ1例)。NIPT陰性2例, 染色体正常核型の2例および21トリソミーと診断された1例は妊娠を継続した。胎児ヒグローマを認めた21例のうち, 染色体検査を受検したのは15例 (71%) であった。染色体異常を4例に認め, 全てが21トリソミーであった。染色体正常核型の10例と2絨毛膜2羊膜性双胎のII児が21トリソミーであった1例, 染色体検査を受検しなかった2例は妊娠を継続した。胎児水腫を認めた6例のうち染色体検査を受検した1例 (17%) は21トリソミーで, 4例は子宮内胎児死亡した。また, FGRに形態異常を認めた9例のうち7例 (77.8%) に染色体異常が認められた。原因不明のFGR21例のうち1例 (4.8%) に胎盤限局性モザイク (CPM) が認められた。【結論】胎児形態・発育異常と染色体異常との関連が確認され, 遺伝カウンセリングの重要性が示唆された。

P-31-1 NIPTで21・18・13番染色体以外のトリソミーが指摘された症例の転帰

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【目的】学会認定外施設で実施させているNIPTで, 21・18・13番染色体以外のトリソミー陽性と判定された症例について, これに続く検査選択ならびに管理について検討する。【方法】2019年8月から2021年7月までの間に, 学会認定を受けていない医療機関でNIPTを受けた結果, 21・18・13番染色体以外のトリソミー陽性と判定された8例について, 検査施設でのその後の対応や当院で行った羊水検査結果について検討した。【成績】8例の内訳は, 7トリソミーが3例, 6番, 10番, 15番, 16番, 20番のトリソミーがそれぞれ1例であった。全例で羊水穿刺し, SNPマイクロアレイ検査を行った結果, トリソミーやモザイクが存在した症例はなかった。6トリソミーおよび16トリソミー陽性例において, 母親由来の片親性ダイソミーが確認された。また, 7トリソミー陽性の1例において, 他の染色体の均衡型転座と部分欠失が判明した。【結論】NIPTの結果で常染色体トリソミー陽性と判定されている症例では, 胎盤性モザイクの存在や片親性ダイソミーに起因する問題, 常染色体劣性遺伝疾患の発症の可能性など, 複雑な問題に対応することが必要である。

P-31-2 胎児超音波計測値による21トリソミーの予測に関する検討

長野県立こども病院

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【目的】21トリソミーは先天性心疾患や消化管疾患を合併する場合や, 出生後に筋緊張低下や哺乳困難を来す場合があり, 高次医療機関での周産期管理が望ましい。しかし, 出生後に初めて21トリソミーが疑われ, 新生児搬送となる症例もあり, 胎児期に21トリソミーを予測できることが望まれる。胎児21トリソミーでは長管骨が短縮することが知られており, 超音波計測値から21トリソミーの予測が出来ないか検討した。【方法】2015年1月から2020年12月の期間に当院で分娩となった21トリソミーの単胎40症例をT21群とした。T21症例の3rd trimester以降に児頭大横径 (BPD), 頭囲 (HC), 推定体重 (EFW), 大腿骨長 (FL), 上腕骨長 (HL) が計測されている妊娠28~37週のデータを用いて検討した。T21症例の計測週数とEFWが近い (妊娠週数 \pm 1週, EFW \pm 0.5SD) 単胎症例, かつ21トリソミーのリスクが高いとされる高齢妊娠 (35歳以上) の症例をcontrolとした。T21症例1例につき3例のcontrolを抽出し, control群120症例とした。T21群, control群の各計測値と, 週数を考慮する必要のないように各計測値の比について統計学的に検討した。【成績】control群と比較し, T21群ではBPD, HC, EFWに有意な差は認めなかったが, FL, HLは有意に短縮していた ($P < 0.05$)。EFW/HL比のROC曲線下面積 (AUC) は0.63であった。BPD/HL比はBPD/FL比に対して有意差をもってAUCが大きかった (0.87 vs 0.74)。BPD/HL比, HC/HL比のAUCに有意差を認めなかった (0.87 vs 0.85)。BPD/HL比が1.696より大きい場合にT21となる感度81.7%, 特異度85.0%であった。【結論】3rd trimester以降のBPD/HL比が胎児21トリソミーの予測に有用な可能性がある。

P-31-3 周産期における管理方法の違いによる18トリソミー児の予後

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【目的】18トリソミー (T18) は極めて予後不良なため、積極的な医療介入が控えられてきた。しかし、近年では積極的な管理による生存期間の延長が報告されている。当院では両親の希望に沿ってT18に対する管理方法を決定している。当院で管理したT18の管理方法、生命予後、治療内容について検証する。【方法】2005年から2021年に当院で管理した、T18の胎児診断例を対象とした後方視的研究である。多胎、中絶、転院、妊娠22週未満の胎児死亡は除外した。妊娠中および出生後のそれぞれにおいて、十分なカウンセリングのもと両親の管理方針に関する希望を確認した。特に胎児適応の帝王切開を含む管理を妊娠中の積極的管理とし、出生後の挿管や外科的手術を含む管理を新生児の積極的管理とした。妊娠中の積極的管理例と待機的管理例における生産率を算出した。また生産児に対して積極的管理例と待機的管理例の生存期間と在宅ケア移行率についてそれぞれ検討した。【成績】対象116例のうち35例を除外した81例で検討した。妊娠中積極的管理21例、待機的管理60例における生産率は、それぞれ86% (19例)、50% (30例)であった。生産児49例のうち17例が新生児期の積極的管理を希望され、3例に心臓外科手術を、8例に消化器外科手術を施行した。生存期間の中央値は積極的管理例で347日 (18-3907)、待機的管理例で9.5日 (1-4870)であった。在宅ケアに移行できた児はそれぞれ11例 (58%)、10例 (33%)であった。【結論】T18の積極的管理例では、待機的管理例に比べ生産率が高く、生存期間が長かった。T18児に対する治療選択の上での客観的データとなるが、個々の医療介入のT18児の予後への影響についてはさらなる検証が望まれる。

P-31-4 当院で胎児診断された18トリソミー症例の現状

新潟大病院

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【目的】18トリソミーの多くは胎児診断されるが、その後の周産期管理に関する一定の方針がなく、当院では、症例毎に対応を検討している。今回、当院で18トリソミーと胎児診断された症例の現状を明らかにすることを目的とした。【方法】2007年1月から2021年9月の間に当院で羊水染色体検査(AC)にて胎児診断された18トリソミー56症例について、診断の契機、診断後の経過、分娩様式、児の予後につき診療録より後方視的に検討した。【成績】母体年齢は中央値37歳 (23-45歳)であり、ACの適応は胎児超音波での形態異常指摘が44例 (78.6%)と最多であった。全体の21例 (37.5%)が過去3年の症例であり、そのうち無侵襲的出生前遺伝学的検査 (NIPT) 陽性からの診断例が28.6% (6例)を占めていた。22週以前に診断された25例のうち、14例は紹介元に逆紹介、11例は当院での妊娠管理となった。妊娠22週以降に診断された31例のうち、6例は紹介元で、25例は当院で妊娠管理を行った。当院で管理された25例のうち、子宮内胎児死亡6例 (24.0%)を除いた19例の分娩様式は、経膈分娩8例 (42.1%)、帝王切開11例 (57.9%) (母体適応3例、胎児適応8例)で、分娩週数の中央値は38週 (28-43週)であった。出生後1か月以上の生存例は14例あり、6症例で在宅移行が可能であった。【結論】子宮内胎児死亡及び早期新生児死亡症例の割合は依然として高いものの、合併症の程度によっては長期生存が得られる症例もあり、今後も症例毎に周産期管理を検討していく必要がある。

P-31-5 当院で出生した13トリソミー症候群の臨床経過

都立多摩総合医療センター

遠藤美香, 松田美奈子, 本多 泉, 馬場慎司, 中村浩敬, 谷口義実, 光山 聡

【目的】13トリソミー症候群は予後不良な染色体異常症である。超音波所見は様々で複数奇形を認めることもあれば、奇形を認めずに出生後に判明することもある。本症候群を疑い両親に情報提供する際、予後の多様性から苦慮する場面が多い。今回、当院で経験した12例について妊娠分娩経過、出生前診断の有無、児の転帰について検討した。【方法】2012年5月から2021年1月までに診断した13トリソミー症候群12症例を対象とし、診療録を用いて後方視的に解析した。【成績】9年間で13トリソミー症候群と診断された例は12例で、超音波所見から疑った症例は3例、遺伝カウンセリングで情報提供し出生前診断をされたのは2例だった。子宮内胎児発育不全を4例、頭部・顔面異常を9例、心血管異常を7例で認めた。その他様々な多発奇形を契機に疑う症例が多いが、一方で子宮内胎児発育不全のみと考えていた症例も2例あった。妊娠転帰は出生8例、死産3例、人工流産1例だった。分娩方法は子宮内胎児死亡3例、人工流産1例、自宅分娩となった1例の5例が経膈分娩、7例が帝王切開で、そのうち胎児機能不全での胎児適応が3例だった。5例で積極的な蘇生が行われ、24時間以内、1か月以上6か月未満、1年以上の生存がそれぞれ3例、2例、3例だった。3例で在宅療養へ移行し、現在も2例 (6歳5か月、4歳7か月) が生存している。【結論】13トリソミー症候群の多くは胎児死亡や新生児死亡だったが、中には長期生存例も存在した。積極的に医学的介入を行った場合の児の予後を予測することは困難だが、長期生存し在宅療養へ移行できる症例もあるため、新生児科と連携しつつ経時的に両親へカウンセリングを行うことが重要である。

P-31-6 当科における Cystic hygroma の検討

NTT 東日本札幌病院

寺本瑞絵, 安宅真名美, 古来愛香, 田淵雄大, 二瓶岳人

【目的】Cystic hygroma (CH) は、リンパ管の合流異常によって発生する胎児頸部の腫大であり、妊娠初期～中期の超音波検査にて発見され、染色体疾患が多いことが知られている。当科で診断された CH 症例について検討し報告する。【方法】当科において 2019 年 1 月～2021 年 10 月までに診断された CH 症例 13 例について、臨床的背景、妊娠転機、染色体核型、胎児奇形の有無などを後方視的に検討した。【成績】母体平均年齢は 34.7 歳 (25～48 歳)、妊娠/分娩平均回数は 2.08/0.56。頸部肥厚を指摘されたのは妊娠 8～13 週であり、CH 診断の中央値は妊娠 12 週であった。全例に遺伝カウンセリングが提案され、1 例を除いた 12 例に遺伝カウンセリングが施行された。染色体検査を行った 9 例のうち、T21 を 1 例、T13 を 1 例、45, X を 1 例に認めた。残り 6 例は正常核型であったが、3 例に先天性疾患 (致死性骨系統疾患 1 例、内臓錯位・多発心奇形 1 例、横隔膜ヘルニアの 1 例を含む) を認めた。胎児水腫を 5 例に認め、一方 CH の消失を 3 例に認めた。妊娠転機は妊娠中断が 5 例、子宮内胎児死亡が 3 例、新生児早期死亡が 2 例、CH が消失し正常児を得た症例が 3 例であった。【結論】CH は NT 肥厚に比べ、予後不良であることが知られており、当院においても 76.9% で不良な転機に至った。染色体が正常核型であっても多発奇形を認めることがある一方、CH が消失し生命予後の良好な症例も見受けられた。CH 所見を認めた場合には、個別に検討し、正確な情報を患者・家族へ提供することが重要であることが再確認された。

P-31-7 羊水中胎児細胞染色体 14 トリソミーモザイクと児血液は由来不明環状染色体モザイクのため説明に苦慮した一例

岩手医大附属病院

細見信悟, 馬場 長, 小山理恵, 岩動ちず子, 羽場 巖, 川村花恵, 寺田 幸

【緒言】羊水染色体検査では 14 トリソミーモザイクと判定され、児の血液染色体検査で由来不明の過剰な環状染色体モザイクであった一例を経験したので報告する。【症例】38 歳、2 妊 1 産。前医で妊娠 28 週に胎児腸管拡張、羊水過多のため精査紹介となった。入院後の検査で胎児十二指腸閉鎖の診断となり、羊水染色体検査の G 分染法にて mos 47, XX+14 [2] /46, XX [13] と診断された。妊娠 37 週 3 日より管理目的で入院。37 週 6 日に遷延性一過性徐脈を認め緊急帝王切開をとった。出生児は女児、出生体重 2700g。Apgar score 9/9 点 (1 分値/5 分値)、明らかな外発奇形と心奇形を認めなかった。生後 1 日、十二指腸閉鎖の Windsock 膜様狭窄合併に対しダイヤモンド吻合を行った。生後 2 日、児の末梢血染色体検査では mos 47, XX, +r [9] /46, XX [21] と過剰な由来不明環状染色体 (+r) を認めた。SKY 検査でも +r の由来は不明であった。また、遺伝カウンセリングを希望せず小児科にてフォロー中である。【考察】環状染色体によるトリソミーは、断片を失った染色体が正常の染色体に置き換わり断片は過剰環状染色体 (+r) となると考えられている。環状染色体が小さく重要な遺伝子を含まない場合は表現型正常のことがある。児と家族支援するにあたって環状染色体の由来と構造を知ることが重要である。【結語】(1) 羊水胎児染色体検査の児血液染色体検査の解離を知った。(2) 14 トリソミーモザイクや環状染色体モザイクの病状説明に苦慮した症例であった。

P-31-8 巨大な臍帯嚢胞を伴う 18 トリソミー児の分娩に際して、臍帯切断に苦慮した一例

鹿児島大病院

鮫島浩継, 濱島雅代, 萬呼帆波, 永井さより, 濱田朋紀, 太崎友紀子, 小林裕明

症例は 33 歳、G3P2、妊娠 25 週の経腹超音波検査で臍帯嚢胞と診断された。臍帯嚢胞は膀胱と交通がみられ、尿膜管由来の臍帯嚢胞と考えられた。胎児発育不全、心室中隔欠損、揺り椅子状足底などもみられたことから羊水染色体検査を実施、18 トリソミーと診断した。臍帯嚢胞は増大傾向で浮腫もみられ、妊娠 36 週の時点で病変部臍帯長約 50cm、最大短径は約 8cm、胎盤側の正常臍帯は約 5cm であった。経陰分娩、帝王切開のいずれの場合でも臍帯切断が困難と予想され、対応を事前に検討した。妊娠 37 週 1 日に陣痛誘発を行い、1796g の男児を頭位で娩出した。胎児心拍異常は分娩直前の変動一過性徐脈のみで、娩出直後に第一啼泣がみられた。膣入口部まで脱出した臍帯は約 5cm 径であり切断困難であった。母体腹部から子宮底を圧排し、正常臍帯部が膣内にまで下降するのを待って、臍帯を切断した。臍帯遅延結紮法を参考に臍帯切断まで児は母体の腹上の高さ以下で保持し、出生から約 2 分後に臍帯切断した。Apgar スコアは 2 分値で 4 点、5 分値は 7 点であった。マスク換気、CPAP を行ったが、生後 1 時間以降は呼吸も安定し、呼吸補助なく一晩母児同床で経過した。臍帯は 1 生日目に一時的に臍部で切断し、30 生日目に臍下部を小切開し尿膜管を結紮した。無呼吸発作とうっ血性心不全による呼吸不全への人工呼吸管理、動脈管開存と肺高血流への肺動脈絞扼術と動脈管結紮術を経て、81 生日目に呼吸管理下に自宅退院となった。臍帯嚢胞は病理所見で上皮を認めず尿膜管開存に伴う臍帯仮性嚢胞と診断した。巨大な臍帯嚢胞を伴う 18 トリソミー児の分娩管理に関して考察する。

P-31-9 当院で管理した18トリソミー 33症例の検討

静岡県立こども病院

河村隆一, 南波美沙, 増井好穂, 竹原 啓, 加茂亜希, 新谷光央, 西口富三

【目的】18トリソミーは予後不良な染色体異常疾患であるが、18トリソミー児への周産期管理は多様化してきており、積極的管理により長期生存が可能となる症例が報告されている。当院では症例ごとに関連診療科によるカンファレンスを行い、家族の選択を考慮した上で、治療およびサポートを行っている。当院において周産期管理を行った18トリソミーについて検討したので報告する。【方法】2010年から2020年で当院で胎児期および新生児期に出生前遺伝学的検査を行い18トリソミーと診断された33症例を対象とした。出生前診断の有無、在胎週数、出生体重等の妊娠転帰、出生児への治療介入、予後について後方視的に検討を行った。【結果】検討した33例中、出生前診断されたものは25例(76%)で、8例(24%)は出生後の診断であった。全例にFGRを認め、心疾患は1例を除く32例に合併し、子宮内胎児死亡を2例に認めた。平均在胎週数は35週2日、平均出生体重は1488gであった。分娩様式は帝王切開術17例(緊急帝王切開7例、選択的帝王切開10例)で16例が経陰分娩であった。積極的な治療を希望し挿管等の呼吸管理を行った症例は3例あり、心臓手術を行った症例はなかった。生後28日以内の新生児死亡は25例で、1か月以上の生存は8例。退院し自宅療養に移行できたものは5例であった。平均生存期間は26日であり、2例は現在も生存し治療を継続している。【結論】当院において、積極的な治療を行い、長期生存を得られている症例は2例であった。18トリソミーは症例ごとの多様性を重視した周産期管理が必要であり、今後も症例を蓄積し、周産期管理の向上を目指したい。

P-32-1 妊娠26週胎児CTで臨床診断した骨形成不全症II型の一例

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【緒言】骨形成不全症は全身の骨脆弱性に加え、結合組織症状を示す先天性骨系統疾患であり、発症頻度は2~3万例に1例である。妊婦健診で大腿骨短縮を認め26週に胎児CT施行、骨形成不全II型と診断、予後の情報提供を行い看取りの方針となった一例を報告する。【症例】41歳、1経産、自然妊娠。子宮筋腫核出術後、妊娠糖尿病、妊娠12週より当院妊娠管理。20、24週健診時に大腿骨頭長測定不可、26週再診時に超音波検査で四肢短縮の他、頭蓋骨圧迫による変形があり骨系統疾患を考え、胎児CT施行、VR画像・MIP画像を合成した。長管骨の屈曲・短縮、多発肋骨骨折、胸郭低形成を認め、骨形成不全症II型の診断に至った。予後の情報提供、周産期致死型のため看取りの方針とした。35週早期破水のため緊急帝王切開術施行、男児、1258g、呼吸不全のため出生後35分死亡確認。児のレントゲン撮影、臍帯血より遺伝子検査提出、COL1A2のヘテロ接合突然変異を認め確定診断に至った。【考察】骨系統疾患の出生前診断には超音波やCTが用いられる。超音波は被曝なく安全な検査であるが、CTの方が骨形態の変化や骨化の程度まで捉え、骨疾患に対する診断能力が高い。児への被曝影響が少ない妊娠28週以降で推奨されるが、放射線被曝による先天異常のしきい値は50mGy以上である。当院のCTの被曝量は26.5mGyであったため、診断目的に26週に胎児CTを行った。早期診断し、家族へ情報提供を行うことで、ショックから否認、悲しみ、適応までの時間を確保でき、35週破水による緊急帝王切開術にもかかわらず、家族立ち会いのもと看取りができた。【結語】早期に診断し予後を受容する時間の確保のため26週胎児CTは有用であった。

P-32-2 胎児骨格異常を示し診断に苦慮した胎児一過性型副甲状腺機能亢進症の1例

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【緒言】子宮内の骨化不全・骨脆弱性を示す胎児例の大部分は、骨形成不全症または低ホスファターゼ症である。今回我々は胎児超音波検査で四肢短縮、胸郭低形成、羊水過多を認め、骨形成不全症を疑っていたものの出生後一過性副甲状腺機能亢進症と診断した1症例につき報告する。【症例】30歳2妊0産、自然妊娠成立し、他院で妊娠管理をされていたが、妊娠28週頃より血圧の上昇を認めた。胎児超音波検査でFGRは認めないものの、四肢短縮、胸郭低形成、羊水過多を認め、また子宮収縮があり、頸管長の短縮を認めたため入院となり、子宮収縮抑制を行っていた。胎児は、骨系統疾患の可能性があり、精査および新生児管理の必要性から当院に妊娠30週2日紹介受診となった。胎児ヘリカルCTにて軽症型骨形成不全症が疑われた。妊娠32週6日心窩部痛、頭痛の訴えあり、肝酵素の上昇を認め、また血圧の上昇傾向あり、子宮収縮抑制困難となり、妊娠33週0日緊急帝王切開術を施行した。1588g女児、Apgar score: 6/8で娩出した。児は出生後単純X線検査で副甲状腺機能亢進症が疑われ、PTHを測定したところ742pg/ml(正常: 10-65pg/ml)と高値を認めたが、生後70日目で164pg/mlと低下しつつある。副甲状腺機能亢進症の遺伝子パネル検査を行ったところ、TRPV6遺伝子にc.1168C>T(Arg390Cys)のヘテロ接合性でバリエーションを認めた。【考察】一過性副甲状腺機能亢進症はTRPV6の両アリルの変異で生じる常染色体劣性遺伝の疾患と考えられている。しかし、本症例では片アリルの異常しか証明できていない。発症機転として、片アリル異常による優性阻害効果がありうるのか、通常の検査では見つからない稀な変異があるのか検討中である。

P-32-3 胎児期に疑い出生後早期に診断に至った矢状縫合早期癒合症の1例

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【緒言】頭蓋縫合早期癒合症は頭蓋縫合が胎児期に早期癒合してしまうために、機能的に脳の発育が妨げられ、また整容的にも頭蓋の変形を来す疾患である。先天奇形の中でも頻度が高い疾患であり、頭蓋冠のみの早期癒合である非症候群性が大部分を占めるが、診断は容易ではない。今回、胎児期に矢状縫合早期癒合症を疑い、出生後早期に診断に至った症例を経験したので報告する。【症例】25歳、1妊0産。前医にて妊娠30週頃より頭蓋骨の形態異常を指摘され、妊娠34週で当院紹介となった。胎児超音波検査で頭蓋冠の輪郭は不整形、児頭大横径は85.2mm (-0.2SD)、児頭周囲長は325.3mm (3.1SD)であり、横幅が狭く前後径が長い舟状頭蓋が想定され、矢状縫合早期癒合症を疑った。長管骨の発育は正常範囲内であり、四肢、中枢神経系、心臓に明らかな奇形を認めなかった。妊娠35週のMRIでは舟状頭蓋を認めるものの、その他、特記すべき所見を認めなかった。胎児発育は良好で、妊娠39週1日に経陰分娩にて出生した。児は3196gの男児でApgar scoreは1分値9点、5分値9点であった。児頭は舟状頭蓋で大泉門、小泉門は触知困難であったが、その他、明らかな奇形を認めなかった。日齢4に施行した3DCTで矢状縫合の癒合を認め、矢状縫合早期癒合症と診断された。今後は経過観察目的に小児脳神経外科へ紹介予定である。【結語】頭蓋縫合早期癒合症は認知度が低く、特に非症候群性は出生後でも診断が困難なため発見が遅れることが多い。胎児超音波検査にて頭蓋骨の輪郭不整を認める場合には本疾患の可能性も念頭に入れ、出生後早期に適切な管理へと繋げることが重要である。

P-32-4 骨系統疾患の鑑別に超音波検査と両親のALP測定が有用であった骨形成不全症の1例

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【緒言】骨形成不全症は全身性の骨脆弱による易骨折、進行性の骨変形に加えて、様々な程度の結合組織症状(骨外症状)を呈する先天性疾患である。低ホスファターゼ血症を鑑別に挙げ、胎児診断が得られた1例を経験したので報告する。【症例】30歳4妊3産、妊娠20週に妊婦健診を初めて受診し、大腿骨の短縮を認めた。胎児超音波断層法で大腿骨の変形、全肢型の長管骨短縮(大腿骨-3.1SD, 上腕骨-2.9SD, 脛骨-3.1SD, 腓骨-3.3SD)、児頭大横径の計測時の胎児頭蓋の変形を認めた。妊娠27週で胎児CT検査を施行し、頭蓋骨の非薄化・大腿骨の短縮を主体とした骨形成不全と上下肢の短縮を認めた。低ホスファターゼ血症を鑑別にあげたが、両親の血清ALPは低値を認めなかった。ベル型胸郭を認めず、骨形成不全症(I型またはIV型)が疑われた。産道におけるストレスを避けるために、妊娠37週に選択的帝王切開術で出生した。出生した児は両側大腿骨の骨幹部骨折を認め、両側性難聴・青色強膜を認めたことから骨形成不全症IV型と診断した。【結論】骨系統疾患が疑われる場合には、胎児超音波断層法に加えて両親のALP測定が鑑別の一助となり得る。

P-32-5 胎児左下腿短縮と足関節以遠の骨化欠損に対する母児周産期管理の経験

瀬戸病院

川邊絢香, 篠塚憲男, 木村周平, 林 崇, 瀬戸理玄, 瀬戸 裕

【緒言】胎児の形態異常の出生前診断は時に妊婦や家族のメンタルヘルスに負の影響をもたらすことがある。今回、妊娠中期に胎児左下腿短縮等の診断後母体に適応障害を合併した症例を経験したので報告する。【症例】25歳G2P0。自然妊娠し初期から妊婦健診を施行されており、妊娠24週に胎児下腿欠損を疑われ、帰省先である当院に紹介された。胎児精密超音波検査で、左下腿には右側の半分程度の長さしかない腓骨と脛骨を認め、足趾骨はみられず下腿先端に組織塊を認めるのみであった。羊膜索症候群は否定的でその他に明らかな異常はなく、3D-CT検査により骨系統疾患を否定した。児の生命予後等は問題ないと判断した。母体は胎児診断後に希死念慮を生じて精神科を受診しカウンセリングを継続した。高次医療機関への転院も検討したが、本人や家族と相談を重ね、当院の産科医、新生児科医、助産師の他、精神科医、自宅・帰省先それぞれの地域行政と、カンファランスを行いつつ、当院での分娩に備えた。36週に陣痛発来し胎児機能不全のため吸引分娩で2656gの男児(Apgar score8/9)を出産した。胎児診断と同様の体表所見を認め、現在小児整形外科に通院中である。【結論】左下腿短縮に関して精査し繰り返し丁寧に説明しながら妊婦のメンタルヘルスケアを重視して周産期管理を行った。精神科と周産期センターをともに有する病院は限られており、当院は産科開業病院である。妊婦や家族の分娩満足度ひいてはボンディング形成につながるのであれば、本症例のような周産期管理も一つの選択肢と考える。

P-32-6 胎児超音波にて屈曲肢骨異形成症を疑い、胎盤絨毛の遺伝子検査で診断確定した一例

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【症例】35歳、2妊0産。自然妊娠成立し、近医にて妊娠初期に cystic hygroma を指摘され羊水染色体検査を施行された。結果は正常核型であったが、その後長骨の短縮を認め当院へ紹介となった。超音波検査にて屈曲像を伴う下肢優位の長骨の短縮及び胸郭低形成などの特徴的な所見を認め、屈曲肢骨異形成症 (CD) を第一に考えた。ご夫婦の希望により、妊娠20週6日に人工妊娠中絶となった。児は男児であったが、尿道下裂を認めた。出生後の外表所見及び単純X線写真でも下肢に特徴的な高度の屈曲像を認め、CDを支持する所見であった。出生後の胎盤絨毛より提出した遺伝子検査にて、SOX9の機能低下に関連するフレームシフトバリエーションを認め、遺伝学的にもCDと診断された。ご夫婦には、表現型に加えて遺伝学的にもCDと診断されたこと、CDはほぼ全例が点突然変異であり経験的な次児再発リスクは上昇しないこと、今回の経過をもって次回妊娠時にNIPTや羊水検査などで特別に出生前診断を勧める根拠は乏しいことを説明した。【考察】骨系統疾患は稀なものを含めると多くの疾患が含まれ、次回妊娠を見据えた情報提供を行う際には正確な診断が求められることがある。CDは出生10万あたり1人前後と骨系統疾患の中では時折みられる疾患である。SOX9のヘテロ接合による機能喪失が原因とされているが、通常の染色体検査での診断は不可能である。本症例は胎児の表現型からCDを強く疑い、出生前から鑑別診断を絞り込むことによって出生後に適切な遺伝子検査を行い、診断を確定することが出来た。妊娠中・出生後の検査方法・目的を整理し、適切な情報提供を基にした方針決定が重要である。

P-32-7 妊娠経過に伴う母体血中アルカリホスファターゼ (ALP) の推移

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高橋雄一郎¹、渡邊 淳²、室月 淳³、松井雅子⁴、上妻友隆⁵、堤 誠司⁶、佐藤秀平⁷、佐世正勝⁸、澤井英明⁸

【目的】我々は妊娠中のALP測定が、周産期型低ホスファターゼ症 (HPP) の診断補助になる可能性を報告してきた (Takahashi et al 2017 JSCC 妊婦 <123 U/L, 夫 <165, 少なくとも一つを満たすと陽性的中率 82%)。一方でALP値の妊婦の正常値は未だ確立していない。HPPの胎児診断は生後早期からの酵素補充療法の導入が可能となり、意義が高い。今回、既存のJ法及び、本邦で2021年4月に全国で導入されるIFCC法とで正常値の確立を行った。【方法】2018年までの2年間に6施設による前方視多施設、企業委託研究で、正常単胎妊娠の12週から2週間毎に合計280検体を採取し、J法、I法で測定した。J法ではアイソザイムを測定、骨型ALP (BAP) 濃度も測定した。【成績】J-ALPでは12、20、28、36週ではそれぞれmean 131 (SD±29) U/L, 151 (29), 197 (44), 316 (65) でI-ALPでは46 (11), 54 (10), 74 (15), 130 (25) であった。また妊娠20週まではJ値=I値×2.84で既存の成人のものと同じであったが、妊娠38週では係数は2.55まで低下していた。アイソザイムは妊娠20週から胎盤由来の活性上昇が確認された。BAPは妊娠36週9.4µg/Lで有意な上昇が見られた (12, 20, 28週7.37, 7.36, 7.75)。【結論】正常妊婦におけるALP活性の正常値、アイソザイムの推移を確立した。妊娠20週未満では成人の基準値を使用できると考えられるが、それ以降では本研究の結果を利用できる。今後、HPPの胎児診断補助のためにIFCC法でもcut-off値の確立を目指していく予定である。

P-33-1 妊娠早期に診断された胎児心構築異常の2例：妊娠13-14週のHDlive Flow所見

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【緒言】妊娠早期に診断した胎児心構築異常2例を経験したので、妊娠13-14週のHDlive Flow所見について報告する。【症例1】37歳、初妊婦。妊娠13週6日、逆行性の大動脈血流が認められた。HDlive Flow (Voluson E10 BT20, GE Healthcare, Zipf, Austria)でaortic kinkingが著明で、蛇行も疑われた。妊娠20週の胎児スクリーニング時に、心嚢液、胸水、腹水と、胎児心エコーで僧帽弁閉鎖、大動脈弁閉鎖、三尖弁逆流を認めた。HDlive Flowでは、逆行性の大動脈血流、動脈管瘤、螺旋状の大動脈蛇行、aortic kinkingが立体的に明瞭に描出された。妊娠21週4日、両親の希望により387gの男児を死産した。外見上の異常はなく、病理解剖、染色体検査は行われなかった。【症例2】33歳、初妊婦。妊娠14週、color Doppler with STICによるMultiplanar viewで肺動脈の左側に左上大静脈遺残 (PLSVC)、narrowing isthmusを伴った大動脈が描出された。HDlive Flowで右上大静脈、narrowing isthmusを伴った大動脈、肺動脈、PLSVCが立体的に認められた。また、Preductal 'shelf'も推察された。妊娠中期および後期のスクリーニングでnarrowing isthmus、PLSVCが確認された。妊娠40週6日、2586gの女児をAS 8/9、臍帯動脈血pH 7.288で出産した。新生児の心エコーで胎児大動脈縮窄症 (CoA) (isthmus diameter = 2.4 mm) およびPLSVCと診断された。上肢、下肢の血圧差はなく、PG E1投与不要のため経過観察となり、生後の経過は良好である。【結語】我々の知る限り、CoAおよびPLSVCの例、および僧帽弁閉鎖、大動脈弁閉鎖を伴った大動脈蛇行およびaortic kinkingの例の、妊娠15週以前でのHDlive Flow所見の最初の報告である。

P-33-2 当院における総肺静脈還流異常症2症例の経験

下関総合病院

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【緒言】総肺静脈還流異常症(TAPVC)は先天性心疾患の0.3~2%と非常に頻度が低く、かつ胎児診断が困難とされる疾患である。当院で2019年度に2例のTAPVCを経験した。症例1は胎児超音波スクリーニングで異常は指摘されず、出生後に呼吸障害を呈したことで診断された。この際にはカラードブラで両側肺静脈の左房への還流を確認する方法(方法1)でスクリーニングを行っていたが出生前診断はできなかった。症例1の経験から四腔断面像における下行大動脈と左房後壁の最短距離を計測する方法(方法2)を追加した。症例2は方法2を追加したことで胎児診断に至った。今回、TAPVCでの方法2の有用性について報告する。【症例】症例1:妊娠25週時にスクリーニング検査施行し異常は認めなかった。妊娠39週経産分娩で出生。出生7分後もSpO₂70%台で推移した。酸素投与で改善なく小児科医師の超音波検査でTAPVCと診断され高次施設へ新生児搬送となった。症例2:妊娠24週時にスクリーニング検査施行し異常は認めなかった。妊娠34週時に再度方法2を追加して検査を行ったところ、下行大動脈と左房後壁の最短距離が6.4mmと長く、スクリーニング異常が指摘された。精査でTAPVCの胎児診断となり、小児循環器外科手術可能な施設へ紹介。同院にて出生し同様の診断であった。【考察】当院ではこれまで方法1を用いてTAPVCのスクリーニングを行っていた。しかし症例1を経験し方法2を追加した。症例2では方法2を追加したことでTAPVCの検出が可能であった。診断率の低いTAPVCのスクリーニングには、複数の方法を用いた出生前スクリーニングが望ましいと考えられた。

P-33-3 鹿児島県における先天性心疾患の出生前診断に関する現状と今後の課題鹿児島大病院¹, 静岡県立こども病院²新谷光央^{1,2}, 折田有史¹, 濱田朋紀¹, 太崎友紀子¹, 小林裕明¹

【目的】出生前診断率の低い先天性心疾患(Congenital heart disease; CHD)を把握し、胎児心臓スクリーニング検査の課題を明らかにすること。【方法】対象は2015年4月から2021年3月に、当科にて胎児診断された心臓構築異常219例と、当院NICUへ新生児搬送された後に診断された心臓構築異常44例。このうち染色体異常等の全身疾患を除外した孤発性かつ重症度分類レベル3以上のCHDのみを各々より抽出し、出生前診断群と出生後診断群として出生前診断率を算出した。【成績】対象期間に県内で発生した重症CHDの出生前診断あるいは出生後管理は全例当院で行われており、出生前診断群109例、出生後診断群20例であった。前者の内訳はCoA/CoA complex/IAA 22例, RAI/LAI 21例, DORV 13例, HLHS/Critical AS 12例, dTGA 7例, Ebstein anomaly/Dysplastic TV 7例, PAVSD 6例, PAIVS/Critical PS 5例, TA 5例, APV 2例, PTA 2例, DILV 2例, TAPVC 1例, ccTGA 1例, 上記以外のSV 1例, Shone complex 1例, AORPA+APW 1例であった。後者はdTGA 5例, DORV 4例, PAIVS 3例, CoA/CoA complex/IAA 3例, PAVSD 2例, DILV 2例, TAPVC 2例, HLHS 1例, Ebstein anomaly 1例, ccTGA 1例, RAI 1例, AORPA 1例であった。出生前診断率下位はTAPVC(33%), ccTGA(50%), DILV(50%), AORPA(50%), dTGA(58%), PAIVS(62.5%)の順であった。【結論】従来どおりTAPVCの出生前診断率が低く引き続き今後の課題であるが、4CVで異常に気付く可能性がある疾患が下位を多く占めたことは注目すべき点である。心室壁構造に注目したスクリーニングに加え、カラードブラ使用による房室弁流入・逆流の有無の確認も診断率向上には重要であると考えられた。

P-33-4 胎児期に診断された心臓腫瘍の臨床経過

長野県立こども病院

小松 登, 横山由佳, 山田 諭, 寺尾美代子, 高木紀美代, 吉田志朗

【目的】胎児の心臓腫瘍は稀であり、胎児期に診断された心臓腫瘍の臨床経過は不明な点が多い。今回、当院で診断した心臓腫瘍の臨床経過について検討した。【方法】2012年4月から2021年3月まで、当院で心臓腫瘍と診断した8症例を対象とした。【結果】1例は初診時より胎児水腫を合併しており、19週で胎児死亡となった。生児を得た7例で多発性腫瘍は4例、単発性腫瘍は3例であった。多発例はすべて胎児期には横紋筋腫が疑われていたが、出生後に結節性硬化症と診断された。多発例では腫瘍は心房、心室、中隔、流出路など複数個所に認められ、長径3~20mmであった。単発例は胎児期に1例が横紋筋腫、2例は線維腫が疑われ、生後に結節性硬化症と診断された例は認められなかった。線維腫は2例とも長径30mm以上と大きく、一例は左室を占拠し出生後に左室で体循環を維持できず、PGE1の投与、経カテーテル式心房中隔裂開術、肺動脈絞扼術、動脈管ステント術を行った後に腫瘍切除術、心房中隔欠損閉鎖術、肺動脈形成術が施行された。もう一例は左室壁から外向性に発育しており、循環動態に影響は与えていないため経過観察となった。【結論】多発性の心臓腫瘍は全て、出生後に結節性硬化症と診断された。結節性硬化症の確定診断は出生後に行うことになるが、胎児期に心臓に多発する腫瘍を認めた場合は結節性硬化症の可能性が高いと考えられる。今回、単発性の心臓腫瘍で結節性硬化症と診断された例は認められなかったが、発生部位や大きさによっては循環動態に影響し、出生後に外科的治療を要することがある。

P-33-5 診断に苦慮した胎児卵円孔早期閉鎖の一例

国立四国こどもとおとなの医療センター

林 亜紀, 森根幹生, 立花綾香, 近藤朱音, 檜尾健二, 前田和寿

【緒言】胎児卵円孔早期閉鎖(PCFO)では右房から左房へ流れる血流が減少し、左室流入血流が減少することで左室の成長障害を来す。出生後は左室の前・後負荷が増大するため適応障害が生じ、チアノーゼや多呼吸、新生児遷延性肺高血圧症(PPHN)を呈する場合がある。今回、胎児期に単純型大動脈縮窄症(simple CoA)との鑑別に苦慮したPCFOの症例を報告する。【症例】35歳, 2妊1産。自然妊娠し、前医にて妊娠管理されていた。妊娠36週の胎児超音波検査で心構築異常が疑われ、妊娠37週に当院紹介となった。初診時の胎児超音波検査では左房・左室の狭小化、左右のアンバランス(三尖弁輪径/僧帽弁輪径(TVD/MVD)=2.2)、細い大動脈弓、大動脈弓の逆流波、左房側に大きく突出する心房中隔瘤を認めた。鑑別診断としてsimple CoAが挙げられた。左心拍出量の低下(LV CO=57.3mL/min/kg)を認めたため、分娩誘発を行い、妊娠38週0日3204g(0.48SD)の女児を経産分娩にて出産した。出生後、チアノーゼや呼吸障害は認めなかった。左心低形成症候群(HLHS)様血行動態は認めないも、大動脈弓の狭小化を認め、CoAの可能性が考慮されPG製剤の投与を開始した。その後、PG製剤を漸減・中止し、左室・大動脈弓も正常化したためCoAは否定された。【考察】PCFOの胎児診断はCoAやAS、HLHSが鑑別にあげられる。当院でこれまで経験したPCFO症例5例の妊娠・出生後経過および文献的考察を加えて報告する。

P-33-6 抗不整脈薬投与による母体の副作用のため治療に苦慮した胎児頻脈性不整脈の2例

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【緒言】胎児頻脈性不整脈に対する経胎盤の抗不整脈薬投与による母体副作用は78%にみられる。今回、抗不整脈薬による母体副作用を認め、治療に苦慮した胎児頻脈性不整脈の2例を報告する。【症例1】37歳, 5妊1産。妊娠30週5日に胎児頻脈、胎児水腫を認め当院受診。心房400bpm, 心室200bpmの2:1伝導の心房粗動(AFL)と診断し、母体へdigoxinとsotalolの投与を開始した。6日後、胎児AFLは持続するも母体に洞性徐脈が出現したためflecainide単剤に変更。AFLは改善せず、妊娠32週4日にdigoxinを再開し頻脈は改善したが、2:1伝導は継続。母体に洞不全症候群を認め投薬を中止。妊娠33週4日、胎児頻脈の再燃のためflecainideのみ再開。その後、母体副作用を認めず、胎児頻脈及び胎児水腫が改善。2:1伝導のみ持続したが妊娠37週2日に洞調律に復帰。妊娠37週4日、帝王切開にて3133gの男児を臍帯動脈血pH7.34で娩出した。出生後も児は洞調律で経過している。【症例2】37歳, 2妊1産。妊娠24週6日に胎児頻脈、胎児水腫を認め当院受診。見心拍は230bpmであり、shortVAの上室性頻拍と診断し、母体へdigoxinとsotalolの投与を開始。妊娠25週1日に見心拍は130bpmと70bpmを繰り返すようになった。妊娠25週2日、母体のジゴキシン中毒のためsotalol単剤へ変更。児に期外収縮を伴う徐脈を持続的に認め、妊娠26週0日に投薬を中止した。その後は洞調律に復帰し、妊娠37週、帝王切開にて3289gの女児を臍帯動脈血pH7.26で娩出した。出生後も児は洞調律で経過している。【考察】胎児頻脈性不整脈の治療では、母体への抗不整脈薬の投与が必要であるが、母児の循環動態を慎重に把握し治療薬を選択していく必要がある。

P-33-7 当院で経験した胎児頻脈性不整脈の3例

名古屋第一赤十字病院

寺沢直浩, 伊藤由美子, 手塚敦子, 齋藤 愛, 坂堂美央子, 廣村勝彦, 津田弘之, 安藤智子, 水野公雄

【緒言】胎児不整脈疾患は胎児の1~2%に見られ、なかでも胎児頻脈性不整脈は、進行すると胎児心不全、胎児水腫より、胎児・新生児死亡になりうる。今回、我々は様々な経過を経て胎児頻脈性不整脈と診断された3例を報告する。【症例1】31歳, 2経妊1経産。前医で妊娠23週6日より切迫早産の診断でリトドリン錠定期内服開始。妊娠26週0日の健診時に200bpm以上の胎児頻脈を認め当院紹介受診し管理入院となった。リトドリン錠内服中止後も頻脈発作を認め、short VA typeの上室性頻拍と診断されジゴキシン開始。胎児頻脈継続のためソタコール併用し胎児頻脈は消失した。その後妊娠37週4日に分娩誘発し経産分娩となった。児は日齢3日に頻脈発作が出現し発作性上室性期外収縮の診断となった。【症例2】32歳, 2経妊1経産。前医より切迫早産でリトドリン錠定期内服管理されていたが妊娠28週2日より管理目的のため当院入院となった。その後頸管短縮進行しリトドリン点滴開始。妊娠33週2日のドップラー施行時に220bpmの胎児頻脈を認めた。超音波検査で2:1伝導の心房細動を認めリトドリン点滴中止。その後は頻脈発作と自然軽快を繰り返した。妊娠35週5日に分娩誘発し経産分娩となった。児は、心奇形・不整脈いづれも認めなかった。【症例3】38歳, 1経妊0経産。妊娠33週5日の妊婦健診時に超音波検査で胸水・腹水・皮下浮腫、220bpmの胎児頻脈を認め、1:1伝導の上室性頻脈を疑われた。胎児水腫、持続性胎児頻脈のため同日緊急帝王切開を施行した。児はWPW症候群の診断で日齢93日にカテーテルアブレーションを施行された。【結語】胎児不整脈は適切な診断・周産期管理が、妊娠継続の判断に重要である。

P-33-8 心室中隔欠損症の胎児診断の現状および意義について：手術症例からの検討

徳島大

中川奉宇, 加地 剛, 今泉絢貴, 白河 綾, 吉田あつ子, 苛原 稔, 岩佐 武

【目的】心室中隔欠損症（VSD）は生後早期に治療が必要なことは稀で、手術を要しないことも多いため、胎児診断の意義は不明である。今回、手術を要した症例から VSD 胎児診断の現状および意義について検討した。【方法】2011年～2020年に当院で手術を行った VSD 単独症例（心内・心外の合併異常がない）72例を対象とし後方視的に検討した。【成績】72例のうち、胎児診断されていた（胎児診断群）のは14例、出生後に診断されていた（生後診断群）のが58例であり、胎児診断率は19%であった。胎児診断率は2011～2015年の13%（6/46）から2016～2020年は31%（8/26）に上昇していたが有意差はなかった。VSDの部位は、胎児診断群は全例が膜様部であった。一方、生後診断群は膜様部40例、漏斗部15例、筋性部3例であり、漏斗部欠損は生後診断群に有意に多かった（ $p=0.03$ ）。VSDの大きさや手術時年齢は、二群間に差を認めなかった。生後診断群のVSD診断時期は、生後1か月までが52例（90%）、2か月以降が3例（2か月、3か月、4か月が各1例）、不明が3例であった。VSDの診断契機は心雑音49例（84%）、呼吸不全8例、心内膜炎1例であった。【結論】手術を要したVSDにおいて、胎児診断率は約20%を占めた。一方、胎児診断されていなかった症例の多くは生後早期に心雑音を契機に診断されていたが、発症後まで診断が遅れた症例もあり、胎児診断に一定の意義があることが示唆された。胎児診断率の向上には、膜様部に加え漏斗部欠損の検出が重要と考えられた。

P-33-9 当院における妊娠22週未満に施行した胎児心エコー症例の検討

JCHO九州病院

川上剛史, 大塚慶太郎, 進本かれん, 松本裕佳, 池之上李都子, 安東明子, 魚住友信, 東條伸平, 愛甲悠希代, 西村和泉, 河野善明

【目的】超音波診断装置の性能の向上により妊娠22週未満で胎児異常が発見されることも少なくない。妊娠22週未満であるために妊娠継続に関して意思決定を支援する必要がある慎重な対応を要する。当院において妊娠22週未満に胎児心エコーを施行した症例の転帰を検討したので報告する。【方法】2012年12月から2021年9月において妊娠22週未満に施行された胎児心エコーで形態異常が確認された21例を診療録より後方視的に検討した。【成績】胎児心エコー施行時の妊娠週数は19.8週であった。21例中19例に心奇形、2例に心外奇形（横隔膜ヘルニア1例、先天性肺気道奇形1例）を認めた。心奇形の内訳は単心室10例（総肺静脈還流異常合併は3例）、Ebstein奇形5例、ファロー四徴症2例、心筋症1例、逆位1例であった。21例中11例が妊娠帰結を、10例が妊娠継続を選択した。妊娠帰結を選択した11例の内訳は単心室5例（総肺静脈還流異常合併は3例）、Ebstein奇形3例、ファロー四徴症1例、心筋症1例、横隔膜ヘルニア1例であった。妊娠継続を選択した10例は子宮内胎児死亡を2例に認めたが、8例（80%）が生産となった。【結論】妊娠22週未満に胎児心エコーを施行した症例は心臓の位置異常や単心室・Ebstein奇形など特徴のある四腔断面像を呈する疾患が多く、妊娠帰結を選択した症例には重症例が多くみられた。一方、妊娠継続を選択した症例の多くは生産に到達したが、現病の進行による子宮内胎児死亡も念頭に置く必要がある。予測される変化を情報提供し、患者家族の心情や意思決定に寄り添っていかなければならない。

P-33-10 当院において出生後に診断された先天性心疾患症例の検討

JA 旭川厚生病院

今田芽紀, 杉山沙織, 山田和佳, 三坂琴美, 中嶋えりか, 野崎綾子, 小田切哲二, 吉田俊明, 光部兼六郎

【目的】先天性心疾患の中には、生直後に循環動態が急激に悪化してしまう症例もあり、胎児期の診断が児の予後改善に寄与している。当院では出生前の胎児スクリーニング検査として、妊娠20週と妊娠30週に計2回、全例に超音波検査を行っている。今後さらに胎児診断率向上させるため、当院において出生後に診断された先天性心疾患症例を検討した。【方法】2017年1月から2020年12月までに当院で分娩となった妊婦のうち、外来および入院中に胎児スクリーニング検査を行ったものを対象とした。出生後に児が先天性心疾患と診断された症例について、胎児診断、出生後診断、および新生児治療の有無を診療録を用いて後方視的に検討を行った。【成績】出生後診断された症例は2017年2例、2018年5例、2019年3例、2020年5例であり、いずれもスクリーニングでは正常とされていた。内訳はASD3例、VSD9例、ASD+VSD1例、PVC1例、心筋緻密化障害が1例であった。新生児治療を要した症例はなかった。【考察】ASD、VSD等の比較的軽症の疾患がスクリーニングで見逃ししやすい傾向にあった。当院のスクリーニング項目では、心房・心室中隔欠損の確認は必須ではないことが原因の一つと考えられた。4 chamber viewや流出路の断面でカラードプラを用いた検査を行うことで、正診率を上げることができると可能性がある。【結論】今回の検討では、出生後治療を要する先天性心疾患は認めなかったが、今後も検査の精度や診断率の向上を目指し、さらに症例を増やし検討を行っていく。

P-33-11 秋田県における胎児先天性心疾患の出生前診断に関する検討

秋田大附属病院

小野寺洋平, 藤嶋明子, 亀山沙恵子, 三浦広志, 寺田幸弘

【目的】先天性心疾患 (congenital heart defect : CHD) の出生前診断は、適切な分娩施設の選択や出生後の速やかな治療が可能とする。CHD のほとんどは超音波検査を通して診断されるが、その診断方法において一定の見解はない。秋田県における CHD の出生前診断状況を調査し、胎児診断成績ならびに周産期成績の向上に向けた実地調査を本検討の目的とした。【方法】2016年1月から2020年12月にかけて、CHD 管理を主たる目的に当院小児科に新生児入院を要した症例を対象とした。胎児期の CHD 指摘の有無、胎児期の CHD 指摘時の妊娠週数、新生児搬送の有無、疾患名について、診療録を用いて後方視的に検討した。【成績】対象は45例だった。胎児期に CHD を指摘されていたのは21例 (46.7%) だった。CHD を指摘された平均週数は29.5 (±4.7) 週だった。22例 (48.9%) が新生児搬送されていた。CHD の内訳はファロー四徴症7例が最も多く、大動脈縮窄6例、肺動脈閉鎖+心室中隔欠損6例、両大血管右室起始症4例、房室中隔欠損症3例と続いた。以上5疾患における胎児期 CHD 指摘率はそれぞれ、71.4%、16.7%、33.3%、25.0%、66.7% だった。【結論】半数ほどの症例が出生後に CHD を指摘され、新生児搬送されていた。出生前診断されたものは、妊娠末期に異常を指摘されたものが多かった。また、出生前診断は疾患ごとに成績が異なることが示された。本検討を踏まえ、系統立った胎児超音波検査の導入が必要であると考えられた。地域の事情に合致した検査方法を検討し、周産期成績の向上につなげていきたい。

P-34-1 胎児超音波検査で閉鎖部位診断が困難であった1例

宮崎大附属病院

中村希実, 松澤聡史, 長島陽子, 河野猛嗣, 富森馨予, 吉本 望, 山田直史, 児玉由紀, 桂木真司

【緒言】先天性小腸閉鎖症・狹窄症は新生児外科疾患では直腸肛門異常について多い疾患である。部位としてもっとも多いのは遠位回腸と言われている。今回、胎児超音波検査で閉鎖部位診断が困難であった遠位回腸閉鎖症例を経験したので報告する。【症例】26歳。既往歴なし。3妊1産。第一子は帝王切開で娩出。自然妊娠で妊娠成立し、妊娠34週の妊婦健診で消化管拡張を指摘され精密目的に当院へ紹介された。胎児超音波検査で胃と連続性のある拡張した腸管を認め、十二指腸/上部消化管の狹窄症が疑われた。しかし multiple bubble sign も認め、羊水過多がないことから遠位腸管閉塞も疑われた。既往帝王切開のため妊娠39週で帝王切開術で分娩した。新生児は出生体重3090g, Apgar score 8/9点。腹部膨満あり、十二指腸造影で十二指腸や空調の拡張なく、注腸検査で micro colon を認めた。回腸閉鎖の診断で同日緊急手術となった。腸間膜裂孔を認め、その裂孔に回腸が嵌入し7cm程度拡張していた。拡張腸管切除+腸管吻合術を施行した。【考察】胎児期に腸間膜裂孔ヘルニアと遠位回腸閉鎖をきたした症例であった。ヘルニア部口側の拡張した腸管が胃に隣接し、かつ、拡張腸管と胃が同等のエコー輝度を呈していたため、十二指腸拡張を想起し、診断が困難であったと考えられた。【結論】胎児腸管閉塞性疾患の診断では胎児超音波検査で隣接して見える拡張した腸管が必ずしも連続した腸管腔ではない事を考慮すべきである。

P-34-2 先天性食道閉鎖の胎児超音波診断における esophageal pouch と間接所見について

徳島大

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【目的】先天性食道閉鎖 (EA) は羊水過多、胃泡が小さいもしくは欠如 (以下胃泡小)、合併奇形の3つの間接所見によりスクリーニングされ、esophageal pouch (以下 pouch) が描出できれば胎児診断となる。しかしながら、pouch の描出に至らず出生することも多い。今回、当院の EA の胎児超音波所見について検討した。【方法】2010年から2021年8月までに当院で出生した EA 15例 (C型14例, A型1例) において、pouch の描出および間接所見 (羊水過多、胃泡小、合併奇形) の有無について後方視的に検討した。【成績】15例中、pouch が描出されていたのは6例 (40%) であった。間接所見は、羊水過多12例 (80%)、胃泡小11例 (73%) で認め、合併異常も10例 (67%) あり心疾患9例、鎖肛3例などであった。全例で少なくとも1つ以上の間接所見があり、3つすべてを認めたのは6例 (40%)、2つが6例 (40%)、1つが3例 (20%) であった。一方 pouch が描出された6例と pouch が描出されていなかった9例で間接所見の有無をみると、羊水過多 (83%, 78%)、胃泡小・欠 (100%, 56%)、合併異常 (83%, 67%)、羊水過多かつ胃泡小 (83%, 44%) であった。いずれの所見も pouch が描出された群で多かったが、有意差はなかった。【結論】pouch が描出され EA の胎児診断がされていたのは40%のみであった。一方で間接所見は全ての症例で認め、約80%の症例で2つ以上認めた。間接所見を2つ以上認めた場合に、pouch の描出を繰り返し試みることで EA の胎児診断が向上する可能性がある。

P-34-3 先天性両側横隔膜ヘルニアの1例

筑波大附属病院

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【緒言】先天性横隔膜ヘルニア (CDH) は、左側が患側である場合が90%を占め、両側 CDH は1%未満とまれであり、予後不良である。今回、胎児診断された先天性両側 CDH の1例を経験したので報告する。【症例】30歳, 2妊1産。妊娠21週に胎児多発奇形を指摘され、妊娠23週に前医紹介受診。羊水検査施行され正常核型であった。妊娠29週に当院へ紹介となり、胎児超音波検査では、左横隔膜ヘルニア、臍帯ヘルニア、右水腎症、羊水過多を認めた。胎児心臓超音波検査では Fallot 四徴症の診断であった。妊娠33週、切迫早産のため塩酸リトドリンの持続投与、胎児肺成熟目的にベタメタゾンを投与した。妊娠34週、胎児 MRI を施行し、両側横隔膜ヘルニアの診断であった。L/T比0.13、両側 CDH であること、心疾患合併であることから、予後不良と考えられた。妊娠35週、切迫症状増悪のため羊水を2L除去し、妊娠36週1日予定帝王切開術にて、2644gの女児を出産した。児は出生直後に挿管管理、その後高頻度オシレーション (high frequency oscillation : HFO)、一酸化窒素 (NO) による呼吸管理を行われたが、アシドーシスが進行し、日齢3に新生児死亡となった。剖検の結果、両側の CDH で肝・胃・脾の脱出があり、重度の肺低形成に Fallot 四徴症合併を認めた。【考察】CDH の予後は近年改善傾向であるものの、両側 CDH は依然として予後不良である。両側 CDH の問題点としては、胎児診断が難しいとされること、合併奇形が多いこと、胎児肺低形成評価法などがある。先天性両側 CDH について文献的考察を加えて報告する。

P-34-4 妊娠後期に発症したと考えられる胎児胸部異所性腎の一例

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【緒言】胸部異所性腎は稀な病態であり、出生前診断の報告は少ない。今回、妊娠後期に発症したと考えられる胸部異所性腎の1例について報告する。【症例】35歳, 1妊0産。生殖補助医療により妊娠が成立した。既往症としてクローン病を合併していた。妊娠25週時には両側腎臓を正常の位置に確認した。妊娠35週時の胎児超音波検査で右腎の胸腔内への偏移が疑われた。その後複数回の超音波検査で胸部異所性腎を疑い、妊娠38週時に胎児 MRI 検査を施行した。MRI 検査では右胸腔内に腎臓とともに消化管の一部が脱出しており、先天性右横隔膜ヘルニア疑いの診断であった。出生後の小児外科的治療のため、総合産科センターへ紹介した。同院で妊娠38週5日に選択的帝王切開術で分娩した。児は、3,051gの女児で Apgar score 8/9(1分/5分)、臍帯動脈血 pH 7.14 であった。出生後は気管挿管の上で人工呼吸器管理を受け、日齢1に右横隔膜ヘルニア修復術を施行された。【考察】異所性腎は1/10,000人の頻度で認められ、胸部異所性腎はその1%とされる。胸部 X 線検査や CT 検査で偶発的に発見されることが多く、胎児診断での報告は少ない。胸部異所性腎の発生には横隔膜異常を合併することが多いとされる。本症例では発症の時期が妊娠後期であったが、出生前診断に至ることができたため、出生時の対応を適切に行うことができた。【結語】今回、妊娠後期に発症したと考えられる胸部異所性腎を経験した。出生直後に手術を要する疾患の識別のためにも、いずれの妊娠週数においても臓器の確認を行う重要性を改めて実感した。

P-34-5 剖検により先天性肺リンパ管拡張症が判明した超早産児の一例

宮崎大

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【緒言】先天性肺リンパ管拡張症 (Pulmonary lymphangiectasia ; PL) は先天的な肺リンパ管拡張を特徴とし、肺胞拡張障害をきたして重篤な呼吸不全となる予後不良な疾患である。今回、超早産で出生し診断と治療に難渋した先天性肺リンパ管拡張症の一例を報告する。【症例】早産児, 超低出生体重児 (在胎23週2日, 610g, 男児)。母体は30歳, 4妊1産。胎児超音波検査では形態学的異常は認めなかった。妊娠23週1日に胎胞形成を認め、23週2日に経膈分娩で出生した。母体羊水、血液検査では子宮内感染を疑う所見はなく、臍帯血及び新生児の培養検査で細菌・真菌は陰性であった。出生早期は呼吸窮迫症候群のため人工肺サーファクタント気管内投与後、人工呼吸管理を行った。日齢15より CRP 上昇を認め、各種抗菌薬を使用するも呼吸状態が悪化した。日齢29の気管内分泌物からウレアプラズマが培養され、アジスロマイシン水和物を開始した。CRP は1.0mg/dl まで低下したが、呼吸不全は持続し日齢44に死亡した。病理解剖では左右の肺リンパ管がびまん性に拡張し、PL の所見を呈していた。【考察】剖検例での先天性 PL の頻度は0.5-1%と報告され、その病態や治療法は明らかでないのが現状である。出生直後から重篤な呼吸不全を呈し、集中的な治療にもかかわらず早期に死亡する重症例や、乳児期発症後に改善した症例の報告が散見される。本症例は、出生後2週間は順調に経過したが、感染を契機に呼吸不全を呈し、死亡に至った。本疾患認知度の向上、病態解明、治療法などの課題があり、症例集積が必要である。

P-34-6 妊娠中に胎児胎便性腹膜炎と診断され、出生後に手術加療を要した1例

三重大附属病院

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【緒言】胎児胎便性腹膜炎は診断および管理方針について一致した見解がない。胎児腹水および腸管拡張から妊娠中に診断を行い、分娩後に手術を要した胎便性腹膜炎症例を経験した。【症例】31歳未経産、妊娠29週4日に胎児腸管拡張、腹水、羊水過多を指摘された。経腹壁超音波断層像、胎児MRI検査で小腸の拡張と腹腔内に石灰化を伴う腫瘤、腹水を認め、胎便性腹膜炎と診断した。胎児腹水は増加傾向なく羊水過多は改善傾向で、妊娠37週4日に陣痛発来し経陰分娩に至った。児体重は3044gの男児で、Apgar scoreは6/8、臍帯動脈血液ガス分析の結果はpH7.156、BE-11.6であった。児は腹部膨満およびこれに伴う呼吸障害を認め、小腸部分切除と人工肛門造設術を行った。小腸は周囲の臓器と強固に癒着し、多発型の小腸閉鎖であった。また、閉鎖部の周囲に小腸穿孔を想起させる1cm大の膿瘍の遺残様腫瘤を認め、内部は黄色泥状であった。【考察】胎便性腹膜炎の原因として捻転、腸閉鎖、胎便性腸閉塞などが挙げられる。本症例では小腸穿孔の原因は不明だが、漏出した胎便による腹膜刺激が腹水を発生させたと考えられる。また癒着による小腸閉鎖が腹部膨満を招き、呼吸状態を悪化させた可能性も考慮される。MRIによるメコニウム仮性嚢胞の指摘は、出生後に手術を要するリスクが増大すると報告されており、分娩時には小児科だけでなく小児外科にもバックアップを依頼することが重要である。【結語】妊娠29週で胎便性腹膜炎と診断し、出生後速やかに手術を行い、治療できた症例を経験した。診断時の所見および妊娠管理中の胎児状態変化に注意し、分娩後の手術を考慮し多職種と連携を取ることは極めて重要である。

P-34-7 先天性横隔膜ヘルニアの出生前診断と出生児の予後について

琉球大

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【目的】出生前先天性横隔膜ヘルニア (congenital diaphragmatic hernia: 以下 CDH) の診断と重症度予測の正診率を検討すること、生存児の合併症について調査すること。【方法】2009年から2021年までに当院でCDHと診断された37例を後方視的に検討した。出生後の重症度予測は、肺胸郭断面面積比 (以下 LT 比) と肝脱出の有無で分類した。LT 比 \geq 0.08かつ肝脱出なしをA群、LT 比 \geq 0.08かつ肝脱出ありをB群、LT 比 $<$ 0.08かつ肝脱出なしをC群、LT 比 $<$ 0.08かつ肝脱出ありをD群とした。またCDH生存児の合併症を調査することとした。分娩は原則経陰分娩としている。【成績】出生前にCDHと診断された症例からIUFD1例、死産1例、横隔膜弛緩症3例、重症度分類されていない2例を除く30例中、A群が16例(53.3%)、B群が8例(26.7%)、C群は0例、D群が6例(20%)であった。出生前の90日以内の死亡症例が5例(16.7%)あり、A群が3例、B群が2例であった。A、B群で死亡した5例は、Cornelia de Lange 症候群、脊髄膜瘤、腸回転異常、大血管転位症、多発奇形の合併例であった。A群の1例、B群の1例、D群の2例の計4例(13.3%)にECMOを要した。A群の1例、B群の3例、D群の全例、計10例(33.3%)に在宅酸素療法を要したCDHの生存例24例(80%)のうち、CDH再発4例、発達障害3例、停留精巣5例(男児16例)、漏斗胸3例、胸郭変形3例、胃食道逆流症2例を認めた。【結論】重症度が高いと考えられたD群では死亡症例がなかったが、呼吸状態の予測は可能であった。軽症と予測されたA、B群から死亡例があり、CDH以外の合併奇形を加味した予測が重要である。さらに、生存児の54%にCDH特有の慢性合併症を認め、児は長期的な経過観察が必要である。

P-34-8 超音波による左心低形成症候群に伴う肺リンパ管拡張症のリスク予測

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【目的】心房間交通が狭小化した左心低形成症候群では左房内圧の上昇により二次性に肺リンパ管拡張症を来すことがある。最重症で予後不良な病態だが胎児超音波による肺実質の評価は困難である。一方、心房間交通狭小化の程度と肺動静脈の超音波所見の関連についての報告は散見されるものの、それら超音波所見と肺リンパ管拡張との関係は明らかではない。肺リンパ管拡張と肺動静脈の超音波所見との関連および肺病変を有する群の超音波の特徴を明らかにすることを目的とした。【方法】当院で2016年以降に胎児期から管理した左心低形成症候群とその関連疾患を対象とし後方視的に検討した。肺リンパ管拡張は胎児MRIでnutmeg lung (NL) と呼ばれる肺門部から胸膜表面まで伸びる線状のT2高信号の所見が明らかに認められるものとした。超音波所見は肺静脈ドブラ波形の逆行性 (reverse) と順行性 (forward) の velocity time integral 比 (PV-VTI R/F) と、肺動脈の経母体酸素投与前と投与中の pulsatility index の変化率 (PA-PI, %) とした。両項目をNLの有無で比較し、またNLを予測する両項目の閾値を検討した。検定はMann-Whitney U検定を用い $p < 0.05$ を有意とした。【成績】対象は23例 (NLあり3例, NLなし20例) で、NLの有無により超音波の両項目 (PV-VTI R/F $p=0.009$, PA-PI $p=0.007$) で有意差を認めた。またNLを予測する値はPV-VTI R/F が0.40以上、PA-PIが5%以下であった。【結論】NLと肺動静脈の超音波所見とに関連を認め、心房間交通狭小化の特徴を有していた。

P-34-9 1st trimester に指摘された胎児腹部嚢胞が原因と考えられる先天性横隔膜ヘルニアの1例

群馬県立小児医療センター

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【緒言】先天性横隔膜ヘルニア (congenital diaphragmatic hernia: CDH) は、妊娠9~10週において胸腹膜孔の閉鎖不全によって起こる。今回、我々は1st trimester に指摘された胎児腹部嚢胞が原因と考えられる先天性横隔膜ヘルニアの1例を経験したため報告する。【症例】31歳、2妊1産、妊娠11週で胎児腹腔内に嚢胞を認め、当科紹介となった。超音波検査で胎児左横隔膜直下に上腹部を占拠する1cm大の嚢胞を認めた。当初は低輝度な単純嚢胞であったが、妊娠23週より内部に隔壁を認めるようになった。大きさは1~2cmで推移し、児の発育とともに相対的に縮小し、妊娠32週以降は同定困難となった。また、妊娠25週頃より腹部臓器(脾、胃、肝左葉、脾弯曲部結腸)が頭側に挙上し、心臓が右方に偏位した。MRIでも同様の所見を認め、CDHまたは横隔膜挙上症を疑った。妊娠38週6日に2648gの男児を経産分娩した。出生後、目を追うごとに胸腔に腸管が嵌入していく像が認められ、左CDHと診断した。日齢11に手術を行い、左胸腔へ嵌入していた脾、肝、横行結腸を腹腔内に還納し、CDHを修復した。【考察】1st trimester に指摘された孤立性の胎児腹部嚢胞は自然消失することが多い。本症例でも、妊娠11週で胎児左横隔膜直下に指摘された腹部嚢胞は妊娠経過とともに相対的に縮小し、同定困難となった。一方、妊娠25週頃より胎児腹部臓器の頭側への挙上と心臓の右方偏位を認め、出生後にCDHと診断された。胎児腹部嚢胞が指摘された時期と位置から、この腹部嚢胞が胸腹膜孔閉鎖を阻害してCDH発症の原因と考えられる。

P-35-1 腎盂尿管移行部狭窄における腎瘻造設の予測因子についての後方視的検討

順天堂大順天堂医院

精きぐな, 山本祐華, 竹田 純, 植木典和, 安東 瞳, 正岡 駿, 川田美里, 正岡 龍, 平井みつ子, 板倉敦夫

【目的】腎盂尿管移行部狭窄 (ureteropelvic junction obstruction: UPJO) は2000人に1人の発生率とされ、水腎症あるいは腎盂拡張で胎児期に発見されることが多い。出生前から進行する腎機能障害に対する早期治療開始のため胎児診断が有用な疾患の一つであるが、腎機能保護のため腎瘻造設を必要とする重症例の予測因子は明らかでない。当院において診断されたUPJO症例について、その予測因子を検討した。【方法】2016年1月から2021年10月までの間、当院において診療を受けたUPJOの症例のうち、出生後の経過を追跡できた10例を対象とした。異常指摘週数、患側、初診時と分娩直前の腎盂前後径、在胎中および新生児期の水腎症 grade 最大値、腎瘻造設の有無と時期を集積した。水腎症 grade は Society of Fetal Urology 分類に従い Grade1~4 (G1~4) とした。また初診時と分娩直前の腎盂前後径の変化率を指摘週数で除した指数 (C) で比較した。【成績】指摘週数は 28 ± 5 週であった。10例中患側右が1、左が9例であった。10例中5例で腎瘻造設を要し、うち3例は新生児期に施行された。水腎症の grade は在胎中から新生児期にかけて全例 G3 または 4 と変化を認めず、腎瘻造設の有無に明らかな差異を認めなかった。腎瘻造設を行った5例と行わない5例で $C=7.57 \pm 6.89$, 0.99 ± 1.22 と、腎瘻造設を行った群で大きい傾向を認めた。新生児期に腎瘻造設を行った3例と残り7例では、 $C=11.76 \pm 5.27$, 1.08 ± 1.26 と造設群で大きい傾向を認めた。【結論】UPJOは妊娠中期に指摘されることが多いが、指摘時期が早くかつ腎盂前後径が増大し続ける場合、出生後早期に腎瘻造設が必要となる。

P-35-2 仙尾部奇形腫に伴う心拍出量増加と羊水過多を認めたが、正期産まで妊娠継続し得た一例

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【緒言】仙尾部奇形腫 (SCT) は新生児に発生する比較的稀な腫瘍である。しばしば胎児期に腫瘍部からの多量出血や、巨大な腫瘍の血流分配から高拍出性心不全を来すことがある。今回、本疾患に心拍出量増加とそれに伴う羊水過多を合併したが、正期産まで管理可能であった症例を経験したので報告する。【症例】41歳、G3P1。既往歴、第一子の経過に特記事項なし。自然妊娠し妊娠初期からの健診にて近医で管理されていた。21週の健診の際に仙部の脊髄髄膜瘤が疑われ当院紹介となった。超音波検査上、内部が不均一で豊富な血流を伴う腫瘤を認め、SCTと診断した。当院外来通院にてフォローを行い、母体の頸管短縮のため34週より入院管理となった。Combined cardiac output (CCO) の上昇並びにAFI>40cmの著明な羊水過多を認めた。また、MCA-PSVは33.9cm/sec (0.95MoM)であったが、比較的状态は安定していた。その後37週6日で選択的帝王切開を行い3720gの女児を分娩した。児はAps7/8、出血量は羊水込みで2290mlであった。児は心エコーにて右心系の容量負荷を認めたが、出生時BNPは30.2pg/mLで、明らかな高拍出性心不全を認めなかった。Altermann2型のSCTとして日齢1に腫瘍摘出術を施行。術後下肢運動は良好であったが、膀胱直腸障害が認められた。問欠的導尿を導入後、日齢66にて退院し、外来フォローとなった。【考察】本症例では、巨大なSCTへの血流分配に伴う心拍出量増加と羊水過多を認めたが、腔水症をきたしておらず心不全には至っていないと考えられた為、妊娠を継続し正期産に至った。本疾患のように血流豊富な腫瘍を胎児に認めた場合、CCOやMSA-PSVの測定が高拍出性心不全の評価に有用な可能性がある。

P-35-3 出生前診断された胎児上眼瞼腫瘍の一例

名古屋市立大病院

大谷綾乃, 鈴森伸宏, 野村佳美, 小笠原桜, 吉原紘行, 伴野千尋, 澤田祐季, 後藤志信, 北折珠央, 杉浦真弓

【緒言】上眼瞼腫瘍には血管腫や静脈性リンパ管腫の報告が多い。血管腫は新生児期から乳児期、静脈性リンパ管腫は小児期に発症することが多く、胎児期に認めたと報告は稀である。今回、胎児期に診断された左上眼瞼腫瘍を経験したので報告する。【症例】33歳、1妊0産、既往歴は特記事項なし。妊娠初期より近医で妊婦健診され、妊娠24週の胎児超音波所見で前額部膨隆が指摘され、妊娠31週にやや増大傾向あり精査目的で当科紹介受診。胎児超音波所見にて血流がなく内部均一で低輝度の約3cm大の胎児左上眼瞼腫瘍を認めた。妊娠33週3日、胎児精査のための単純MRI検査を実施。左上眼瞼腫瘍は静脈奇形もしくは静脈性リンパ管腫の疑いで夫婦と相談し腫瘍破裂のリスクから分娩は帝王切開術の方針とした。妊娠38週2日、帝王切開術にて児娩出。児は2874gの女児で、Apgar score7点(1分)/9点(5分)。左上眼瞼に弾性硬の1cm大の腫瘍を認め、その他に左右膝関節や左腰部、肛門周囲等に最大8mm大の多発血管腫を認めた。精査目的にNICU管理となり、頭部超音波所見で脳室拡大と脳出血を認めた。頭部MRI所見で、脳出血後の水頭症のため髄液シャント術が施行され、経過良好にて日齢42に退院。現時点では左上眼瞼腫瘍や全身の血管腫は著明な増大はみられていない。【考察】胎児期に診断された左上眼瞼腫瘍の症例を経験した。静脈奇形もしくは静脈性リンパ管腫が疑われ、出生後に全身に多発血管腫と脳出血の所見を認めており、オスラー病等の血管奇形を特徴とする全身性疾患の可能性があり、現在経過観察中である。

P-35-4 3次元超音波断層法が出生前診断の一助となった胎児後腹膜腔・大腿部リンパ管腫の1例

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山下 薫, 屋比久彩, 喜舎場千裕, 金嶺ひろ, 土井生子, 中野裕子, 泉 有紀, 大山拓真, 平敷千晶, 砂川空広, 長井 裕, 佐久本薫

リンパ管腫はその多くが胎児期に発生するとされる。前頸部や腋窩が好発部位であるが、稀に腹腔内や後腹膜腔に発生する。今回、出生前診断した後腹膜腔から大腿部に発生した胎児リンパ管腫の1例を報告する。症例は35歳、6妊3産。自然妊娠成立後、近医で妊婦健診を受けていた。増大傾向を認める胎児腹部の嚢胞性腫瘍を指摘され、妊娠26週に当科紹介受診となる。当科での超音波断層法では、胎児の両側腎盂の軽度拡張に加え、腹部の右腎下方から骨盤内にかけて血流の乏しい多房性嚢胞を認めた。両側臍動脈(側臍靭帯)の走行より、最も左側の嚢胞が正中から左側に圧排された膀胱と考えられ、3次元超音波断層法(3DUS)では、右臍動脈と右外腸骨動脈との間、および右外腸骨動脈の外側に嚢胞を認めた。また、右鼠径部から右大腿部にかけて浮腫状の所見を認めた。さらに、3DUSのsilhouette/inversionモードでは複数の嚢胞の位置関係の把握、特に一部が膀胱より低位に存在していることが確認できた。tomographic ultrasound imaging (TUI) モードでは腫瘍が脊椎の前方に沿う様に存在しており、これらの嚢胞が腹腔内ではなく後腹膜腔内に存在すると考えられた。以上より、後腹膜腔から右大腿部にかけての胎児リンパ管腫を疑った。妊娠31週に胎児MRIを施行し、超音波断層法同様の診断を得た。妊娠経過は良好で、妊娠38週に既往帝王切開の適応で選択的帝王切開を施行した。児は3214g、Apgar score:8(1分)/9(5分)で出生した。出生後の診察より、胎児診断同様の診断となった。退院後は自宅近くの地域周産期母子医療センターで経過観察の方針となった。胎児腹腔内の嚢胞性疾患の出生前診断に3DUSが有用だった症例と考える。

P-35-5 胎児・新生児溶血性疾患のリスクが低い不規則抗体が複数陽性となり胎児貧血を来した一例

豊岡病院

今竹ひかる, 大月美輝, 山田 香, 濱田航平, 門元辰樹, 上林翔大, 住友理浩

【緒言】不規則抗体が複数陽性の場合の周産期子後については不明な点が多いが、今回、胎児貧血を来した胎児輸血を要した症例を経験したので報告する。【症例】34歳、G3P2。第2子分娩時に産道裂傷による出血のため輸血を行った。今回、自然妊娠成立し当院を受診した。妊娠10週時の血液検査で不規則抗体陽性であった。妊娠22週までは抗Fyb抗体価2倍であったが、妊娠29週時に抗Fyb抗体弱陽性、抗Jkb抗体価1倍となった。超音波パルスドプラ法にて胎児中大脳動脈最高血流速度(MCA-PSV)は<1.5MoMで推移した。妊娠31週時に抗Fyb抗体価16倍、抗Jkb抗体価64倍となり、MCA-PSV 1.91MoMと上昇を認めたため胎児貧血の精査加療目的に他院へ紹介した。胎児採血でHb10.1g/dlと貧血あり妊娠33週4日に胎児輸血を行った。以後、当院で妊婦健診継続し、MCA-PSVは異常なく経過したが、入院にて慎重に経過観察を行った。妊娠37週から分娩誘発を行い妊娠37週3日に経陰分娩となった。出生児は貧血なく、日齢1に採取した直接クームス試験は陽性であった。貧血や黄疸の出現なく経過し、産褥5日目に母児同時退院となった。【考察】抗Fyb抗体と抗Jkb抗体はいずれも胎児・新生児溶血性疾患の原因となる可能性は低いものと認識されているが、本症例では妊娠中に各々の抗体価が上昇し胎児貧血を認めた。抗D抗体と不規則抗体が陽性であると抗D抗体のみが陽性の場合と比較して重症胎児・新生児溶血性疾患のリスクが上昇するという報告もあり、文献的な報告はないもののリスクが低いとされている抗体も複数陽性になる場合には胎児・溶血性疾患の発症リスクが高くなる可能性があり、慎重な管理が必要であると考えられた。

P-35-6 胎児期に後頸部腫瘍として発見された先天性乳幼児線維肉腫の一例

宮崎大附属病院

川口涼大, 松澤聡史, 児玉由紀, 桂木真司, 鮫島 浩

【緒言】先天性乳幼児線維肉腫は小児軟部肉腫のうち約7%と比較的まれな疾患で、通常生後1年未満の乳児に発症する。最近では胎児診断の進歩により胎児期の発症を認める例も増加してきた。今回、胎児期に後頸部腫瘍として発見された先天性乳幼児線維肉腫の一例を経験したので文献的考察を含めて報告する。【症例】母体は27歳、3妊2産。妊娠22週の健診で胎児の後頸部に腫瘍を指摘された。妊娠24週で当科初診し、経腹超音波断層法検査で胎児胸水と後頸部から背部にかけて7.5×5.1cm大の腫瘍を認め腫瘍に0.5~1cm大の多数の小嚢胞を認めた。胎児MRI検査で腫瘍は頸椎から上部胸椎を巻き込んでおり、一部が後縦郭へ張り出す所見も認めた。その後、胎児胸水量の増加、胎児水腫の進行を認め妊娠28週6日に子宮内胎児死亡を確認した。妊娠29週2日に児娩出となり、児は男児、1040gであった。腫瘍の病理組織像ならびにETV6-NTRK3融合遺伝子が検出されたことから、腫瘍は先天性乳幼児線維肉腫と診断された。【考察】先天性乳幼児線維肉腫は成人期発症の線維肉腫と比較して一般的に予後良好とされるが、胎児期発症例は予後不良である。本症例では腫瘍の発症時期が早く、急速に増大したことならびに腫瘍内出血をきたしたことから胎内死亡に至ったと考えられる。【結語】出生前に後頸部腫瘍として発見される先天性乳幼児線維肉腫の症例はまれである。本症例のように、腫瘍増大に伴い児の状態が悪化する可能性を念頭に入れた周産期管理が必要であると考えられた。

P-35-7 出生前診断しえたDD双胎、低出生体重児の尿道下裂の一例

榊原記念病院

井澤美穂, 前田佳紀, 中尾真大, 鈴木 僚, 堀内 縁, 吉田 純

【緒言】性分化異常(Disorder of Sex Development:以後DSD)は、4500出生に1人程度と稀な疾患であるが、その中で尿道下裂は150-300人に1人である。尿道下裂は正常出生体重児と比較し、低出生体重児に多いことが分かっています。更に胎児発育不全症、早産、双胎(MD>DD)に比較的多く合併し、最近では増加傾向といわれています。また超音波機器の精度向上で出生前に超音波で診断できる場合もある。今回産婦人科・小児循環器科の当院で尿道下裂を出生前検査(超音波)で疑った1例を経験したので報告します。【症例1】29歳G1P0、自然妊娠でDD双胎。初期より当院で妊娠管理。先進児の推定体重はAGAで経過するも、後続児-1.2SD前後で経過、GROWTHは認めていました。両児ともに男児との診断をされていたが、36週の超音波検査で後続児の外生殖器異常が疑われた。ご夫婦に対しDSDガイドライン通りに『外生殖器の成熟が遅れています。性別に関しては出生後に検査をして判断させてください。』と説明。37週1日帝王切開で分娩。第1子2620g、男児、Apgar 8/9、第2子出生2248g、Apgar 8/9。第2子の外生殖器は矮小陰茎、尿道下裂が疑われた。その他の全身状態は良好で排尿も確認された。出生前より相談していた総合小児病院の新生児専門医と連携をとり、退院後の受診予定となった。退院後、専門医の受診し染色体検査:46,XY、男児、二分陰囊、尿道下裂と診断され、今後加療予定となった。【結語】文献的考察を交えて考察します。

P-35-8 多脾症を合併したIniencephalyの一例

大分大附属病院

佐藤祐輔, 衛藤 聡, 西田欣広, 河野康志

【緒言】後頭孔脳脱出症(以下、Iniencephaly)は神経管閉鎖障害の1つとされ、後頭骨の欠如、頸椎の形態異常、頸部後屈といった特徴的な所見を持つ。多くは出生後早期に死亡するため予後不良な疾患だが、妊娠中の診断に難渋し出生後に初めて診断される場合もある。今回、胎児MRIで多脾症をはじめとした多発奇形が疑われ、出生後にIniencephalyと診断した症例を経験した。【症例】35歳、3妊1産。新鮮凍結胚移植で妊娠後、当院で妊婦健診を開始された。妊娠17週に脊髄の屈曲および頸部浮腫を認め、羊水検査を施行し正常女児核型だった。妊娠32週に切迫早産で入院。胎児MRIで後頸部浮腫、横隔膜ヘルニア、多脾症などの多発奇形が疑われた。予後について十分説明した上で妊娠37週2日に選択的帝王切開術を施行した。児は2,216g、女児、Apgar score1分1点、5分1点、臍動脈血pH7.308だった。自発呼吸を認めず、出生2時間後に死亡した。Autopsy imagingで後頭骨の欠如、頸椎の形態異常を認め、特徴的な外見からIniencephalyの診断に至った。【考察】Iniencephalyの発症率は0.1~10/10,000人と報告されるが、その原因は未だ明らかでない。多脾症は先天性心疾患との合併が多いが、Iniencephalyとの合併は我々の検索する限りでは1例の報告のみであり、多彩な合併奇形を示す疾患概念の理解が必要と思われる。【結語】Iniencephalyの多くは出生後早期に致死的な経過を辿る。出生前診断した際は適切な情報提供とカウンセリングが肝要である。

P-35-9 羊水過多を呈した ABCC9 ミスセンス変異のある Cantu 症候群の一例

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Cantu 症候群(多毛性骨軟骨異形成)は、胎児期過成長、羊水過多、多毛、特徴的顔貌などを呈する奇形症候群の一つである。ATP 感受性 K チャネルの異常が原因であり、責任遺伝子として ABCC9, KCNJ8 の変異が同定されている。今回、原因不明の羊水過多に対して羊水除去を行い、羊水検査結果より Cantu 症候群を鑑別に挙げ管理を行った症例を経験したため報告する。症例は 32 歳、1 回経産婦。妊娠 22 週より羊水過多を認め、妊娠 27 週に精査目的に当科紹介となった。AFI32 と羊水過多を認め、胎児推定体重が 1151g(+0.9SD)と過成長傾向であった。また頸管長 21mm と短縮しており入院管理とした。妊娠糖尿病を認めたが血糖管理が良好にも関わらず羊水過多は改善しなかった。児は経腹超音波検査で明らかな構造異常は認めなかったが、胎児推定尿量が多く Bartter 症候群も疑った。妊娠 30 週に羊水過多による腹部緊満感増強のため 1500ml の羊水を除去し、検査へ提出した。羊水染色体は正常核型であり、羊水中アルドステロンは低値、Cl は正常値であった。妊娠 32 週以降には心拡大も認めたことから Cantu 症候群も鑑別に挙げて管理を行った。妊娠 33 週 4 日に既往帝王切後妊娠、子宮収縮抑制困難のため緊急帝王切開術を行い、2437g の女児を娩出した。児は心拡大、動脈管閉存症、多毛などを認め、奇形症候群として遺伝子解析を依頼し ABCC9 ミスセンス変異による Cantu 症候群と診断された。Cantu 症候群は近年認識された疾患であり胎児診断が難しいとされるが、羊水過多、心拡大、胎児過成長を呈する症例では本疾患も鑑別にあげる必要がある。

P-35-10 胎児過成長、羊水過多を呈し、出生後に Cantu 症候群と診断された児の 1 例

苫小牧市立病院

三國史嵩, 山田恭子, 宮城正太, 島畑顕治, 佐藤 修, 藤本俊郎

【緒言】Cantu 症候群は先天性多毛、特異的顔貌、心血管異常などを伴い、胎児期には過成長、羊水過多を呈する稀な疾患である。ATP 感受性 K チャネルの機能異常が原因とされ、責任遺伝子の ABCC9 と KCNJ8 の変異が同定されている。今回、原因不明の過成長、羊水過多を呈した児が出生後に遺伝子検査で Cantu 症候群と診断された症例を経験したので報告する。【症例】41 歳、3 妊 2 産。他院で凍結胚移植により妊娠に至り、妊娠 11 週 0 日に当院紹介初診となった。妊娠 26 週 4 日に胎児推定体重が 1195g(+1.70SD)、AFI が 25.6 と胎児過成長と羊水過多を認めた。妊娠 28 週 0 日に子宮収縮を認めたため、切迫早産と診断し管理入院とした。妊娠 29 週 5 日に AFI50.8 と著明な羊水過多を認め、母体の呼吸困難感の増強、切迫早産徴候の悪化を認めたため、妊娠 32 週までに計 2 回、2800mL の羊水除去を施行した。胎児過成長、羊水過多の原因として糖代謝異常などの母体合併症は否定的で、児に明らかな構造異常も認めなかった。妊娠 36 週 3 日に前期破水し、陣発、経陰分娩に至った。児は出生体重 4226g (+4.57SD) の巨大児で、全身多毛を認めた。出生後、動脈管閉存が遷延したため、日齢 5 に動脈管結紮術を施行した。胎児期の羊水過多、巨大児、全身多毛、動脈管閉存症を認めたことから Cantu 症候群を疑い、遺伝子検査を行った結果、ABCC9 遺伝子に新規のミスセンス変異 (c.1276T>C : p.Trp426Arg) を認めたため、Cantu 症候群の診断に至った。【結語】原因不明の胎児過成長、羊水過多を認めた場合には稀ではあるが Cantu 症候群を疑い、早産となる可能性や出生後の児の循環管理が必要となる可能性があるため、高次医療機関での周産期管理が望ましい。

P-35-11 二絨毛膜三羊膜品胎において三児全員が Bardet-Biedl syndrome であった症例

さいたま赤十字病院

久保田未唯, 道崎 護, 土屋 雅, 植村朝子, 伊藤朋子, 石田博美, 岡本修平, 高橋泰洋, 宮本純孝, 中村 学

【緒言】Bardet-Biedl syndrome (BBS) は肥満、知能障害、網膜色素変性症、慢性腎障害、性腺機能低下症、多指症・合指症を特徴とする常染色体劣性遺伝病であり、原因遺伝子は BBS 遺伝子と同定されている。今回、二絨毛膜三羊膜品胎(DT 品胎)において、三児全員が BBS であった症例を経験したので報告する。【症例】32 歳、1 妊 0 産、自然妊娠成立後、DT 品胎と診断され、妊娠 15 週で当院紹介。切迫早産のため妊娠 27 週から入院管理とし、妊娠 34 週 5 日で選択的帝王切開術を施行した。妊娠中のスクリーニング検査では三児とも異常所見なく、胎児発育不全は認めなかった。胎盤病理検査では II-III 児が一絨毛膜二羊膜であり、DT 品胎として矛盾しない所見であった。I 児 2198g, II 児 2128g, III 児 2110g で出生、全員男児であった。出生後、三児とも両下肢多指症と I 児は左上肢多指症、II・III 児は右上肢多指症を認めた。NICU 入院後の精査で、軸後性多指(肢)症と両側腎低形成の診断であった。NICU 退院後、10 か月の時点で遺伝科を受診し、染色体検査では異常なし、遺伝子検査で BBS2 に 2 つのバリエントを認め、BBS の診断となった。現在 1 歳 1 か月の時点で肥満と腎機能障害を認めるが、眼疾患は認めず、発達検査でも問題なく経過している。【結語】BBS は稀な疾患であり、同胞発生の報告は少なく、非常に珍しい症例を経験した。今回胎児超音波でに多指(肢)を診断することはできなかったが、多胎は奇形率が上昇することを念頭に置き、詳細なスクリーニング検査を心がけることが重要であると改めて感じた。

P-36-1 妊娠初期血中ビタミンD値と妊娠中の母体体重増加に関する研究

足立病院

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【目的】令和3年3月厚生労働省は「妊娠前から始める妊産婦のための食生活指針」へ指針改定した。妊娠期における望ましい体重増加量については、「妊娠中の体重増加指導の目安」(令和3年3月日本産科婦人科学会)を参考として提示。また、妊婦の食事摂取基準(日本人の食事摂取基準2020年版)ではビタミンD摂取量が7 μ g/日から8.5 μ g/日に改定された。妊娠初期のビタミンD値と妊娠中の母体体重増加との関連に関する多数症例での報告は少なく、定まった見解に至っていない。今回、当院症例での検討を行ったので報告する。【方法】2017年9月から1年間に、書面で同意の得られた当院分娩予定の単胎妊娠妊婦に対し定期の妊娠初期血液検査時に25-ヒドロキシビタミンD(25(OH)D)を化学発光酵素免疫測定法により測定。妊娠初期(第1三半期)に25(OH)D値を測定し、当院で単胎出生した1027例を解析対象とした。【成績】1027例の妊娠初期(第1三半期)25(OH)D値は14.70 \pm 4.74 ng/mLで、ビタミンD充足率は0.68%。妊娠中の母体体重増加は、10.43 \pm 3.48 kgであった。妊娠中の母体体重増加と妊娠初期25(OH)D値と単回帰分析では有意な相関は認めなかった。年齢、分娩回数、妊娠期間、妊娠前母体体重を交絡因子とした重回帰分析においても両者に有意な相関は認めず、媒介分析を用いた評価も有意ではなかった。【結論】今回の検討は、解析対象集団がビタミンD充足率の極めて低い日本の妊婦であるが、妊娠初期の25(OH)D値と妊娠中の母体体重増加との有意な関連を認めなかった。

P-36-2 平均血小板容積(MPV)は妊娠合併症の予測マーカーになり得るか

杏林大

田嶋 敦, 松島実穂, 尾坂 真, 戸田友美, 岡 愛子, 佐藤泰紀, 谷垣伸治, 小林陽一

【目的】平均血小板容積(MPV: Mean Platelet Volume)は血小板の活性化の指標のひとつとされ、様々な疾患マーカーとされている。周産期領域でも妊娠糖尿病(GDM)、妊娠高血圧症候群(HDP)、在胎不調過小児(SGA)等との関連が報告されている。しかし妊娠中のMPVの推移については明らかにされておらず、妊娠中のMPV値によって妊娠合併症が予測出来るかについては不明である。今回、当院で管理した妊娠各時期のMPV値が妊娠合併症(GDM, HDP, SGA)を予測可能かについて検討した。【方法】2018年4月から2020年3月に当院において妊娠初期から周産期管理を行った単胎妊婦、678例を対象とした。妊娠初期(14週未満)、中期(26週前後)、後期(36週前後)産後(出産後5日以内)でのMPV値と妊娠合併症の有無を検討した。【成績】MPVの平均値は初期、中期、後期、産後でそれぞれ8.1fL(95%信頼区間8.04-8.16)、8.1fL(8.04-8.16)、8.6fL(8.52-8.69)、8.4fL(8.33-8.47)であった。初期の90%タイル以上群ではSGAがオッズ比3.10(95%信頼区間1.26-7.61)、HDPが3.27(1.33-8.07)であった。中期では75%タイル以上群、90%タイル以上群でGDMがオッズ比1.50(1.01-2.24)、1.78(1.04-3.06)、HDPがオッズ比2.73(1.24-5.99)、4.08(1.71-9.76)であった。後期と産後は90%タイル以上群でHDPがオッズ比4.40(1.72-11.2)、2.66(1.03-6.87)であった。【結論】妊娠初期からMPV値が高値の場合はHDPを発症しやすく、中期に高値の場合はGDMの発症も高率である事が明らかとなった。MPVは妊娠合併症の発症予測マーカーになり得る可能性が示唆された。

P-36-3 Diamond ring signを用いた分娩予定日決定法とその意義について

エルム女性クリニック

佐藤秀平

【目的】分娩予定日決定法の精度を高める方法として、高解像経陰超音波機器を用いて、妊娠5週5日から6週2日周辺での所見であるDiamond ring sign(DRS)とその近似所見を用いた予定日決定法に基づき、自然陣痛が発来した時期を検討した。【方法】対象は2017年以降当院を妊娠にて受診した妊婦。検者は1名、GE社製Voluson P8およびIC9-RS経陰プローブにて、胎囊、胎芽、卵黄嚢を十分な拡大率で観察し、特に胎芽サイズが小さい時期で拍動を伴って観察される胎芽が、卵黄嚢と共に指輪の形で観察できるDRSに注目した。先行する人工授精と体外受精における症例で得られたデータの平均より、1mm前後を5週5日、2mm前後を6週0日、3mm前後を6週2日とした。さらに胎芽が米胚芽様の形態(rice grain sign以下RGS)である場合4mmは6週3日、5mmは6週4日とした。2018年1月から2020年12月までに当院で出生した720例の症例のうち、里帰り、合併症、骨盤位などでの予定帝王切開となった症例を除き、当院で初期にDRSかRGSを確認できた530例を検討対象とした。妊娠41週に入った場合は入院で観察した。分娩誘発の希望の有無を確認し、希望がない場合は自然陣痛発来を待機した。分娩に至った時期を3日間の移動平均として検討した。【成績】DRSかRGSで分娩予定日決定法では自然に陣痛で分娩に至った時期は40週0日が最も多く(移動平均30人)、36週台は1名、37週台が28名、38週台が128名、39週台が184名、40週台が144名、41週0~2日まで31名、41週3-4日まで7名、41週5-6日まで4名、42週0日は3名であった。【結論】分娩予定日の正確な評価は、予定日超過、FGRの評価、選択的帝王切開の時期決定などの方針に非常に重要な根拠となる。予定日決定における問題点も含め考察を加える。

P-36-4 分子状水素と妊娠中の免疫寛容状態に関する検討

名古屋大附属病院

青木智英子, 飯谷友佳子, 中村紀友喜, 牛田貴文, 今井健史, 小林知子, 小谷友美, 梶山広明

【目的】昨年、早産患者では呼気中水素濃度が低いことを当研究室より報告した。しかし、妊婦における分子状水素の産生や早産との関連についてはまだ解明されていない点も多い。そこで、妊婦における分子状水素の産生と免疫細胞に与える影響について検討した。【方法】①妊娠 37-38 週予定帝王切開患者の呼気中水素濃度測定と糞便の 16srRNA 解析を施行した(N=16)。②健常人の CD3 陽性細胞を MACS を用いて分離した。培養液中に分子状水素を添加し 24 時間培養後、RNASequence を行った(N=3)。③②の結果より、細胞外フラックスアナライザーを用いて妊娠中期の末梢血単核球細胞(PBMC)の脂肪酸利用率を測定した。また、PBMCの Total ROS とミトコンドリア特異的 ROS の産生、ミトコンドリア量を比較した。細胞死を評価するために培養液の LDH assay を行った(N=6-8)。【成績】①呼気中水素高値群では、Clostridiales 目 Lachnospiraceae 科が多い傾向であった(p=0.093)。②分子状水素添加群において FC>1.2 は 749 遺伝子、FC<0.83 は 694 遺伝子であった。③脂肪酸利用率は Control 群と比較し、分子状水素添加群で有意に上昇していた(p=0.040)。Total ROS、ミトコンドリア特異的 ROS も分子状水素添加群で有意に上昇していた。(p=0.043 および p=0.029)。Total ROS については、培養液中水素濃度 0~1ppm で濃度依存性を認めた。ミトコンドリア量、培養液中の LDH は両群間で差を認めなかった(p=0.472 および p=0.612)。【結論】上記結果より、分子状水素は妊娠中の免疫細胞に作用することで免疫寛容状態の維持に関与している可能性がある。

P-36-5 血清 PIGF 値は分娩転機の前測に有用である

三重大附属病院

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【目的】分娩転機を予測する指標として、胎盤予備能を反映するバイオマーカーである胎盤増殖因子(以下 PIGF)に着目し、陣痛発来時に測定した血清 PIGF 値と胎児心拍数(以下 FHR)モニタリング所見との関連を検証した。【方法】妊娠 35~42 週の単胎妊娠で、陣痛発来のため、入院となった 35 例を対象とした。入院時に血清 PIGF 値を測定し、分娩転機により経膈分娩(以下 VD)群、帝王切開(以下 CS)群に分けて、FHR モニタリング所見について比較・検討した。【成績】VD 群は 26 例、CS 群は分娩停止の適応で CS となった 2 例を除いた 7 例で解析を行った。血清 PIGF 値は VD 群が 157 ± 106 pg/ml、CS 群が 74 ± 62 pg/ml で、VD 群で有意に高かった(p=0.03)。また、血清 PIGF 値と分娩中の FHR 波形 5 段階分類における波形レベル 3 以上の割合との間に負の相関を認めた(r=-0.42)。【結論】陣痛発来時に測定した血清 PIGF 値は、分娩中の FHR 波形 5 段階分類と相関し、胎児適応による帝王切開の前測に有用である可能性が示唆された。

P-36-6 妊娠中の葉酸サプリメント摂取状況と血清葉酸値ならびに母児への影響についての検討

三重大

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【目的】日本は、欧米と異なり穀物への葉酸添加がなく、妊婦の葉酸不足が報告されている。葉酸は、様々な細胞発育に関与しているため、その影響、特に胎児発育に着目し、葉酸サプリメントの摂取との関係について評価することを目的とした。【方法】倫理委員会承認後、当院の妊婦を対象として研究を実施した。妊娠 24-29 週で登録し、登録時と分娩時の母体血清ならびに臍帯血清を保存し、葉酸値を測定した。葉酸サプリメントの摂取状況・種類、食事での葉酸摂取状況は質問紙を用いて聴取した。葉酸サプリメント摂取状況によって 3 群(未摂取群、妊娠第 1 三半期での中止群、継続群)に分け、母体・臍帯血の血清葉酸値、出生体重について群間比較を行った。また、血清葉酸値と出生体重、母体ヘモグロビン値との相関について検討した。【成績】妊婦 191 例:未摂取群(n=29)、中止群(n=51)、継続群(n=111)を解析し、3 群間で母体背景に有意差は認めなかった。出生体重については 3 群間で有意な差は認めなかった。出生体重と登録時、分娩時、臍帯血のそれぞれの血清葉酸値の相関は認めなかった。妊娠後期のヘモグロビン値と血清葉酸値は弱い正の相関があった。【結論】葉酸サプリメント摂取状況や血清葉酸値と出生体重との相関を認めなかった。出生体重は様々な要因が関与しており、日本における妊婦の栄養状態は良いため、葉酸のみでは、出生体重へ影響として表現されないのかもしれない。葉酸は、脳神経発達にも関与しており、出生した児に対する神経学的影響も、今後は調査が必要である。

P-36-7 メタゲノム解析を用いた喫煙妊婦の口腔内細菌叢の検討～Oral Microbiome Prospective Unicenter Cohort Study of Mother and Children～

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【目的】口腔内細菌叢(OM)のdysbiosisは様々な疾患に与える影響が報告され, 周産期領域では早産や妊娠高血圧症候群などのリスク上昇と関連がある。また口腔内細菌叢は喫煙により変化することが知られているが, 喫煙妊婦における報告は少ない。本研究の目的は, 母子のOM及び健康に関するコホート研究(OMPU-CS)に参加した妊婦より, 喫煙妊婦および受動喫煙妊婦のOMに対する影響を検討することである。【方法】対象はOMPU-CSに参加した妊婦を, 喫煙曝露群(喫煙妊婦群, 受動喫煙妊婦群)と非曝露群(非喫煙群)に分け(1:2), 出産年齢と唾液採取の妊娠週数をマッチングさせて, それぞれのOMの α 多様性(菌種の多様性), β 多様性(菌種の多様性の相違度)について比較検討した。なお本研究は当院研究倫理委員会の承認を取得し, 対象者には説明同意を得ている。【成績】喫煙群9例と非喫煙群16例では, α 多様性(observed OTU, shannon index)で有意差を認めなかった($P=0.777, 0.571$)が, β 多様性(unweighted unifrac distance)で有意差を認めた($P=0.001$)。喫煙曝露群21例と非喫煙群40例では, α 多様性において有意差を認めなかった($P=0.732, 0.659$)が, β 多様性で有意差を認めた($P=0.002$)。受動喫煙群18例と非喫煙群34例では, α 多様性で有意差を認めなかった($P=0.637, P=0.787$)が, β 多様性において有意差を認めた($P=0.002$)。【結論】喫煙妊婦や受動喫煙妊婦は, 非喫煙群と比較して α 多様性で有意差を認めなかったが, β 多様性で有意差を認めた。今後はこれらの妊婦のOMが妊娠合併症・妊娠転帰にどのような影響を与えるのかについて検討していく。

P-36-8 ラット妊娠子宮筋に対するプロゲステロンによる non-genomic action の作用機序の検討

関西医大

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【目的】ラット妊娠子宮筋収縮に対するプロゲステロン(P_4)の即時性作用である non-genomic action を検討したところ, P_4 の濃度 $5 \times 10^{-7}M$ より子宮収縮作用を認め, 濃度依存的に増強したが, $10^{-6}M$ 以上の濃度では収縮は抑制された。また, オキシトシン誘導収縮に対しては濃度依存的に増強作用を示し, さらに濃くなると抑制作用を示すが, 高濃度塩化カリウム(High-KCL)誘導収縮に対しては濃度依存的に抑制作用を示すのみであった。この P_4 の収縮および抑制作用は核内プロゲステロン受容体を介した機序ではないことを報告した。今回, P_4 の non-genomic action (即時性作用)の作用機序について追加検討した。【方法】妊娠20日目のラット妊娠子宮筋を用いて, 細胞外カルシウムイオン(Ca^{2+})の有無ならびに電位依存性 Ca^{2+} チャネル(VDCC)遮断薬による P_4 の収縮作用への効果, およびVDCC刺激薬による P_4 の抑制作用への効果を検討した。なお, 本研究は本学実験動物委員会の承認を得て行った。【成績】 Ca^{2+} 入りまたは Ca^{2+} なしの栄養液下に, P_4 を濃度 $5 \times 10^{-6}M$ で投与したところ, Ca^{2+} なしの栄養液下では子宮収縮作用は認めなかった。そこで, VDCC遮断薬VerapamilおよびNifedipineで処理後に, P_4 を濃度 $5 \times 10^{-6}M$ を投与したところ, 子宮収縮作用を認めなかった。一方, High-KCL誘導収縮は P_4 によって抑制されるが, そこに, VDCC刺激薬FPL64176を投与すると, 強直性収縮の回復を認めた。【結論】ラット妊娠子宮筋収縮に対して Ca^{2+} なしの栄養液下や, VDCC遮断薬処理後は P_4 の収縮作用は認めなかったこと, P_4 によって減弱したHigh-KCL誘導収縮はVDCC刺激薬で回復したことから, P_4 の non-genomic action (即時性作用)にVDCCの関与が示唆された。

P-37-1 やせ妊婦の妊娠前BMIは周産期予後に影響する

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【目的】肥満はBMIに応じて肥満1.4度に分類されており, 肥満度に応じて妊娠中の体重増加の目安が異なっている。一方やせはBMI18.5未満と定義され, 細分類はされていない。やせの妊婦を妊娠前BMIで分類し, 周産期の転機に差があるかを検討した。【方法】2009年10月から2020年6月に当院で単体分娩し, 妊娠前のBMI<18.5であった妊婦を対象とした。対象の妊婦を妊娠前BMI(16未満, 16-17未満, 17-18.5未満)で分類し, 妊娠前のBMIが, 母体背景(年齢, 妊娠中の体重増加, ARTの有無)周産期の転機(早産, 出生体重, LFD, 胎盤重量, 分娩方法)に影響するかX検定, ロジスティック回帰分析, 線形回帰分析を行い評価した。【成績】対象となった妊婦は1610人であった。BMI16未満74人, BMI16-17 261人, BMI17-18.5 1275人であった。それぞれの群で分娩時妊娠週数, 切迫早産, 早産, 分娩方法, 妊娠中の体重増加に差はなかった。児の出生体重の中央値は2688g, 2766g, 2846gとBMIの低い群で児の出生体重が低く, 低出生体重児, SGA児, LFD児がBMIの低い群で優位に多かった。【結論】やせの妊婦において, BMIがより低い群では低出生体重児, LFDが多かった。生殖年齢の女性に対し, 妊娠前からの適正な体重指導が求められる。

P-37-2 健常妊婦における血清 PIGF 値と母体因子および周産期予後との関連に関する解析

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【目的】近年、血管新生因子 PIGF とその阻害分子である sFlt-1 の比 (sFlt-1/PIGF 比) が妊娠高血圧腎症の発症予測マーカーとなることが示された。一方、健常妊婦においても、妊娠中期の血清 PIGF 値が母体の長期的な心血管疾患の発症リスク予測に有用であるとの報告がある。主に海外の報告において、血清 PIGF 値が母体年齢、非妊時 BMI、人種、喫煙歴、分娩回数、母体栄養、糖尿病などの基礎疾患、といった母体因子の影響を受ける可能性が示唆されており、妊娠期または産後の疾患予測マーカーとして血清 PIGF 値を使用する際にはこれらの因子の影響を考慮する必要がある。本研究では、日本人健常妊婦を対象とし、妊娠中期・後期の血清 PIGF 値に影響を与える母体因子、および妊娠中期・後期の血清 PIGF 値と周産期予後との関係について明らかにすることを目的とした。【方法】本学出生前コホートに参加した妊婦のうち、日本人の健常単胎妊婦 90 名を対象とした。妊娠中期と後期に採取した母体血を用い、ELISA 法にて血清 PIGF 値を測定した。血清 PIGF 値と母体因子および周産期予後との関連について線形回帰分析を用いて解析した。【成績】予備的解析において、非妊時 BMI > 23 kg/m² の妊婦では血清 PIGF 値が低い傾向がみられ、この結果は既報と一致していた。他の母体因子についても解析を進めている。【結論】血清 PIGF 値は複数の母体因子の影響を受けると考えられる。疾患予測マーカーとしての結果解釈においてそれらの要因を考慮することは、よりの確かな個々の病態理解に役立つと考えられる。

P-37-3 分娩時のサージカルマスク着用が与える周産期アウトカムへの影響についての後方視的コホート研究

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【目的】新型コロナウイルス感染症に対する感染拡大予防策として、当院ではサージカルマスクの着用 (以下マスク分娩) のもと分娩管理を行った。本研究の目的はマスク分娩の周産期予後への影響を明らかにすることである。【方法】2019年4月7日から2021年4月7日に当院で経陰分娩を行った1822例中多胎妊娠とIUIDを除く1127例を対象とした。マスク分娩開始前後1年ずつをA群(マスク不使用群487件)、B群(マスク使用群640件)とし以下の項目につき検討を行った。母体背景: 年齢、BMI、既往、妊娠分娩歴、妊娠様式、産科的合併症、後期血液検査、分娩成績: 分娩週数、分娩様式、総出血量、分娩時間、分娩時異常、酸素投与・臨床的絨毛膜羊膜炎の有無、新生児成績: 体重、性別、アプガースコア、臍帯動脈血液ガス分析、胎盤臍帯異常、羊水混濁、NICU入院率。統計学的検討は傾向スコアマッチングにより母体背景の影響を除外した後各種統計学的解析 (Fisherの正確確率検定、Student-t検定、Wilcoxonの順位和検定他) を行い群間で周産期予後を比較した。【成績】分娩成績: A群に比しB群で分娩第I、II期の延長 ($p=0.0431$, $p=0.005$)、羊水混濁率 ($p=0.0012$)、微弱陣痛率 ($p=0.0005$) の低下を有意に認めた。新生児成績: A群に比しB群で有意にHFD率が上昇 ($p<0.0001$) し、UApO₂は低下 (中央値/23mmHg: 21mmHg, $p=0.0256$)、UApCO₂<32mmHg率はB群で有意に低下した ($6.85\% \pm 2.29\%$, $p=0.0369$)。一方、NICU入院率やアプガースコア、UApHには有意差を認めなかった。【結論】マスク分娩は分娩時間の延長や児のわずかな酸素分圧の低下を引き起こす可能性が示唆されたが母体、新生児における周産期予後への大きな影響を認めず、感染予防策としてのマスク分娩は安全に行えることが示唆された。

P-37-4 レルミナ内服中に妊娠維持・継続した一例

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【緒言】GnRH アゴニストのレルミナは、妊婦又は妊娠している可能性のある患者、授乳中の患者に対しての投与が禁忌であり、これまでレルミナ内服中の妊娠継続の報告はない。今回、多発子宮筋腫に対して子宮全摘術を計画していた患者が、レルミナ内服中に妊娠判明し、手術中止となった一例を経験した。【症例】41歳、3妊0産 (人工流産2回)。X年2月に多発性子宮筋腫に対し手術を希望し当院受診した。挙児希望なく、4か月後の子宮全摘術を計画し、それまでレルミナ錠40mg/dayを内服することとした。月経開始後内服開始とした。その間、コロナ禍ということもあり子宮の診察は行われなかった。6月、術前の超音波検査で子宮内に胎児 (心拍有り) を確認した。この時点で妊娠20週5日相当であった。最終月経は1月末であり、妊娠初期の性器出血を月経と考えレルミナを内服開始し、悪阻をレルミナの副作用と考えていたことが分かった。胎児発育、形態ともに異常を認めず、妊娠継続の方針とした。妊娠38週に妊娠高血圧症候群が出現し、分娩誘発したが、妊娠38週6日で帝王切開となった。児は2736gの男児で形態異常は認めなかった。【結語】レルミナ内服中に妊娠維持継続した稀な症例を報告した。レルミナの動物実験では、着床後胚死亡率の増加及び生存胎児数の減少が報告されている。本症例では、初回診察時は妊娠反応陰性が推定され、初期の性器出血 (推定5週) を契機に内服開始し、悪阻を副作用と考えられていた。また、コロナ禍という状況もあって妊娠確認が遅れた。

P-37-5 妊娠中の食事と母児の細菌叢に関する検討

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【目的】新生児・乳児期の腸内細菌叢は、炎症性腸疾患、アレルギーなど様々な疾患に関連するとされるが、妊娠中の食事、母体の細菌叢状態が児の腸内細菌叢形成に与える影響は明らかでない。【方法】対象は同意が得られた合併症のない健常妊婦と新生児29組58名、妊娠32週に簡易型自記式食事歴法質問票(BDHQ)による食事調査、腸内細菌検査、尿検査、妊娠35週に腔内細菌検査をおこない、出生直後に児の尿検査、生後1か月で腸内細菌検査を施行した。細菌叢は次世代シーケンサーにて解析、食事パターンはBDHQの因子分析を用い検討した。【成績】分娩時年齢は35歳(30, 36)、非妊時BMIは20.5 kg/m² (18.8, 21.7)(中央値, 四分位範囲)、全症例が経陰分娩であった。母体の食事パターンと細菌叢の関連では「緑黄色野菜、果物類、芋類の摂取が多い」と腸内のLachnospiraceae-Ruminococcus属占有率に負の相関($r=-0.469$, $p=0.01$)、「肉類、油脂類が多く菓子類が少ない」と腸内のFaecalibacterium属に正の相関($r=0.448$, $p=0.01$)、「豆類、卵類、魚介類が多い」と腔内のLactobacillaceae科に正の相関を認めた($r=0.513$, $p=0.004$)。消化管内の腐敗物質量を示す尿中インドキシル硫酸値は母児間で正の相関を認めた($r=0.348$, $p=0.08$)。抗菌薬の使用なく完全母乳栄養の15組の母児においては、腸内環境を良好にするBifidobacterium属の占有率に正の相関を認めた($r=0.607$, $p=0.02$)。【結論】妊娠中の食事内容と母体の細菌叢には相関があり、抗菌薬の不使用、経陰分娩、母乳栄養の条件下で、良好な腸内環境が児へ引き継がれることが示唆された。

P-37-6 分娩後貧血に対するカルボキシマルトース第二鉄投与の有効性の検討

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【目的】鉄欠乏性貧血は体内の鉄需要と供給のバランスが崩れて発症する。妊娠中は必要な鉄量が増加し、鉄欠乏性貧血を合併しやすい。さらに分娩時出血により鉄欠乏性貧血が進行する。分娩後の鉄欠乏性貧血は母乳哺育や産後うつと関連することも知られているため早期改善が望まれる。鉄欠乏性貧血の第一選択は経口鉄剤投与である。今回我々は分娩後鉄欠乏性貧血に対する高用量静注鉄剤の有効性について後方視的に経口鉄剤投与と比較検討した。【方法】2019年から2021年に当院で分娩した妊婦において、高用量カルボキシマルトース第二鉄静注もしくはクエン酸第一鉄経口投与された患者を対象に後方視的検討を実施した。主要評価項目は退院時の血中ヘモグロビン濃度の変化量とした。副次的評価項目は分娩から退院までの日数、輸血の有無、エジンバラ産後うつ病質問票のスコアとした。【成績】現在データを解析中である。【結論】高用量カルボキシマルトース第二鉄静注は経口鉄剤投与と比較して早期の貧血改善効果が期待される可能性がある。

P-37-7 子宮収縮時の子宮動脈血流波形、オキシトシン誘発症例の収縮時とプロスタグランジン誘発症例の収縮時の比較

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【目的】オキシトシン(OXY)、プロスタグランジンF2 α (PGF)による母体子宮動脈血管抵抗に及ぼす影響、薬剤投与によって生じる血管抵抗の差を検討する。【方法】母体・胎児共に合併症のない正期産期を対象とした。陣痛促進薬投与の適応としては、予定日超過、微弱陣痛、社会的適応とし、同一症例を対象に、経時的に測定を行った。子宮口開大度によって3群に分類した。①子宮口2~6cm(潜伏期)、②子宮口6~10cm(活動期)、③10cm~児娩出(分娩第二期)までとし、それぞれの期間で算出された左右子宮動脈PI・RI値について平均値を算出した。サンプルサイズは、各15症例ずつで合計30症例とした。子宮動脈血流PI・RIをOXY群とPGF群の2群間で比較検討し、子宮動脈血流RIと臍帯動脈血pHとの関連についても検討した。【成績】PIに関して、OXY群とPGF群の2群間において分娩進行度による3つの時期においていずれも有意差を認めなかった。OXY群においてRI、PI共に活動期で子宮動脈血管抵抗が最も上昇している傾向を示した。しかし、PGF群ではPIにおいて同様の傾向を認めたが、RIでは分娩第二期で最も上昇していた。子宮動脈血流RIと臍帯動脈血pHとの関連についてそれぞれの子宮口開大度においてRIとpHとの間に相関が認められなかった。【結論】OXYとPGFにおける子宮動脈のPI、RIに差を認めなかった。子宮動脈血流への薬剤の差異による影響はないと考えられた。

P-38-1 胎生期低栄養環境と生後の Catch-up growth が起こす脂肪組織の遺伝子発現変化の検討：Developmental Origins of Metaflammation

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【目的】胎生期低栄養環境を経験し授乳期に Catch-up growth を経験するとメタボリックシンドローム (MS) を発症するハイリスク群となる。近年、MS 発症における脂肪の慢性炎症が注目され Metaflammation (MF) と呼ばれている。今回、マウスモデルを用い脂肪組織の遺伝子発現の網羅的な解析を行った。【方法】妊娠マウスを自由摂餌群 (NN 群) と摂餌制限群 (UN 群) に分け、授乳匹数調整を行い catch-up growth を促した。産生仔に高脂肪餌を与え、Vehicle (Veh) または二次胆汁酸 (Tauroursodeoxycholic acid : TU) を投与した。16 週齢の精巣周囲脂肪組織のマイクロアレイ、エンリッチメント解析、定量 PCR、Mφ 特異的 F4/80 染色を行った。【成績】16 週齢産生仔の体重・脂肪重量ともに、NN 群と比較して UN 群では有意に増加し、TU 投与により有意に改善した ($p < 0.05$)。エンリッチメント解析では、UN 環境の有無 (NN-Veh vs UN-Veh) と TU 投与の有無 (UN-Veh vs UN-TU) それぞれ Gene Ontology (GO) を同定したが、両者に共通した 4GO は全て炎症関連であり、MF 増悪への関連が考えられた。4GO に含まれる遺伝子群の発現は、UN 環境と TU 投与により相反する増減を認めた。Mφ 数は UN 群で増加し TU 投与により減少した。【結論】胎生期低栄養環境および catch-up growth による慢性炎症が、DOM (Developmental Origins of MF) における遺伝子発現変化の一端となることが明らかになった。

P-38-2 低出生体重とレジスチン SNP-420 G/G 遺伝子型の組み合わせは将来の 2 型糖尿病発症に関連する

愛媛大

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【目的】最近、我々は日本の一般住民コホート研究において低出生体重児が肥満をきたすと 2 型糖尿病発症リスクが高い事を報告した。しかし、その機序については十分には解明されていない。今回、低出生体重と 2 型糖尿病疾患感受性遺伝子リスクアレルが将来の糖尿病発症に及ぼす影響を明らかにすることを目的とした。【方法】一般住民 1,174 名を低出生体重 (2,500g 未満) の有無と現在の糖尿病の有無で 4 群に分け、臨床的特徴および既知の 20 個の 2 型糖尿病感受性遺伝子との関連について解析を行った。【成績】低出生体重かつ糖尿病を発症している群では肥満の割合が高かった。さらに、2 型糖尿病感受性遺伝子において、インスリン抵抗性や肥満に関連するレジスチン遺伝子 (RETN) の SNP-420 G/G 型を有する頻度が高かった。次に、低出生体重とレジスチンのリスクアレルを持つ SNP-420 G/G 型の有無で 4 群に分けて解析を行った結果、低出生体重かつレジスチン SNP-420 G/G 型の群では、年齢、性別で調整後も、血中レジスチンが高値であり、インスリン抵抗性の指標である HOMA-IR の悪化を認めた。また多変量ロジスティック回帰分析では、低出生体重かつレジスチン SNP-420 G/G 型の群は、出生体重 2,500g 以上かつレジスチン SNP-420 C/C 型または C/G 型の群 (reference) と比較し、年齢と性別で調整後も高率に糖尿病を発症していた (オッズ比 6.7, 95% 信頼区間: 2.3-18.1)。【結論】低出生体重児がレジスチン SNP-420 G/G 型を有する場合、将来糖尿病を発症するリスクが高く、若年期からの介入の対象になる可能性がある。

P-38-3 血糖と胎動の関連性～持続血糖測定器と FMAM レコーダーによる長時間持続的な同時測定～

帝京大

八木慶太, 梁 栄治, 世永由里子, 鎌田英男, 長阪一憲

【目的】血糖と胎動の関連については一定の見解に至っていない。近年血糖の持続的な測定が簡便に行えるようになった。また FMAM レコーダーを用いて長時間の胎動測定も可能となった。今回長時間の血糖と胎動を同時に測定し、その関連について検討した。【方法】当院で妊娠・分娩管理を行ったボランティア妊婦 15 名を対象とした。妊娠 28～33 週を前半、34～39 週を後半とし、原則として週に 1 回、昼食前 1 時間～食後 3 時間の測定を行った。血糖は FreeStyle リブレ[®] を使用し 15 分おきの間質液中のグルコース濃度、胎動は FMAM レコーダーを使用し gross movement の占有割合を 15 分ごとの平均値として測定した。測定結果から以下の 2 項目について検討した。①血糖値と胎動占有割合の関連を単回帰分析した。②血糖値の上昇・下降それぞれに対して胎動占有割合の増減によって 4 群に分け、例数の差の有無をカイ二乗検定した。【成績】計 56 回 (前半 35 回, 後半 21 回) の胎動記録が解析可能であった。①前半では血糖と胎動占有割合は正の相関 ($p = 0.0006$)、後半は相関無し ($p = 0.8778$)、全体では正の相関 ($p = 0.0148$) を示した。②前半は血糖上昇に伴い胎動占有割合が増加したものは 87 回、減少したものは 76 回。血糖下降に伴い増加したものは 108 回、減少したものは 71 回となり例数に差を認めなかった ($p = 0.1940$)。同様に後半は 64 回, 41 回, 64 回, 49 回 ($p = 0.5177$) で、全体では 151 回, 117 回, 172 回, 120 回 ($p = 0.4784$) でともに差を認めなかった。【結論】血糖と胎動占有割合は特に前半でわずかに正の相関を示した。一方血糖の変化は胎動占有割合の増減に影響しなかった。妊娠 30 週前後では、母体からの胎児血糖値変化が胎動に影響を与えている可能性がある。

P-38-4 リトドリン塩酸塩の点滴投与が胎動に及ぼす影響について—Fetal movement acceleration measurement recorder (FMAM recorder) を用いて—

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【目的】母体に投与される薬剤の胎動に及ぼす影響についての報告はほとんどない。自宅で夜間の胎動を測定可能な胎動計 (FMAM recorder) を用いてリトドリン塩酸塩内服薬の影響を検討した結果, 日中の内服は夜間の胎動に影響しないことが報告されている。今回は, 内服薬と比較し, 高い血中濃度が一定に保たれるリトドリン塩酸塩注射液の点滴投与の影響を検討した。【方法】胎動測定および胎動占有割合の算出: FMAM recorder により妊娠 28 週以降, 原則として週に 1 回, 夜間・就寝中の胎動を記録した。母体動センサーに信号がなく, 胎動センサーのみに信号がある場合を胎動陽性と判定した。一晩当たり 4 時間以上記録できたものを採用し, 10 秒毎のエポックに分割し, 全区画の中で胎動陽性である区間の頻度 (占有割合) を算出した。対象: 2010 年 4 月から 2021 年 4 月までに当院, 産婦人科で分娩した単胎妊婦 407 例のうち, 胎児発育不全, 胎児奇形, 精神科領域の薬を服用, リトドリン塩酸塩内服治療を行ったものを除外したリトドリン点滴投与群 (50~200 μ g/min) 22 例と非投与群 160 例を対象とした。胎動占有割合の比較: 妊娠週数を, 前期 (妊娠 28 週から 31 週) と後期 (妊娠 32 週以降) に分け, それぞれ投与群と非投与群の間で, 胎動占有割合を比較した。解析方法: t 検定を用い, $p < 0.05$ を有意差ありとした。【成績】胎動占有割合は, 前期では投与群 14.70 \pm 1.56%, 非投与群 17.13 \pm 0.44% ($p=0.203$), 後期では投与群 18.70 \pm 1.20%, 非投与群 12.83 \pm 0.27% ($p < 0.001$) であった。【結論】胎動占有割合は, 後期において投与群で有意に高く, 妊娠 32 週以降のリトドリンの点滴投与が胎動を増加させることが示唆された。

P-38-5 急激に胎児胸腹水を発症し, 出生後に全身型若年性黄色肉芽腫と診断された一例

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【緒言】若年性黄色肉芽腫 (juvenile xanthogranuloma; JXG) は小児期発症の非ランゲルハンス細胞性組織球症で, 皮膚病変が主体の場合は治療を要さないことが多いが, 皮膚以外の臓器に病変が多発する全身型の場合は化学療法を要することもある。今回我々は, 突然胎児胸腹水を認め出生後に JXG と診断された一例を経験したため報告する。【症例】30 歳 1 妊 0 産 [合併症] 家族性高コレステロール血症 [現病歴] 自然妊娠後, 当院で妊娠 19 週から妊婦健診し 31 週までは特記すべき異常を認めなかったが, 33 週 0 日に胎児胸腹水を認めたため管理入院となった。胸腹水に加え胎児心拍の低下が散発したため, 33 週 6 日で緊急帝王切開となった。母体は術後 7 日に退院となった。児は男児, 2,169 g, Apgar score 4/8, UA pH 7.239。皮下浮腫を認め, 無呼吸のため気管内挿管となり, 血小板数 1.1 万, フィブリノーゲン 70 μ g/ml と凝固異常を認め, DIC の診断で輸血を行った。出生時に顔面や胸部などに皮疹を認め, 皮疹の病理検査では上皮へのリンパ球の浸潤がみられ, 免疫染色では CD68 陽性, CD1a と S100 は陰性であった。臨床所見と病理所見から, JXG と診断された。循環不全に対して開始したステロイドが JXG にも奏功し, ヒドロコルチゾン 1mg/kg の内服を継続した。生後 4 か月で退院となり外来で経過観察中である。【考察】JXG は出生後に皮膚病変を契機に診断されることが殆どで, 胎児診断は困難と思われる。本症例では突然に胸腹水が出現し, 感染症や血液型不適合, 胎児形態異常などは認めず, 原因は不明であった。原因不明の胎児腔水症が発生した際は新生児治療を要する場合もあるため, 対応可能な施設での周産期管理が重要と考えられた。

P-38-6 出生前ステロイド投与が胎児脳に与える影響の検討

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【目的】34 週未満の早産には出生前ステロイド投与 (ACS: antenatal corticosteroid) が推奨されている。他方, 近年, 動物モデルや疫学調査で児の神経発達への悪影響の報告が散見される。本研究では, 脳障害マーカー S100B を用いて, ACS の影響を検討した。【方法】2012 年~2020 年に当院で妊娠 34 週未満早産となった 285 例に, 後方視的研究を行った。多胎, 胎児疾患, 臍帯血使用不可の症例は除外した。ACS 非実施群と, 実施群 (Betamethasone, 12mg \times 2 日間完遂) の臍帯静脈血 S100B 濃度を ELISA 法で測定した。解析にはマン・ホイットニー U 検定および, 分娩週数, 性別, small for gestational age (SGA) を共変量とした重回帰分析を用いた。【成績】ACS 非実施群 ($n=27$), 実施群 ($n=65$), 以下の背景に差を認めなかった: 年齢, 初産, 妊娠高血圧症候群, 硫酸マグネシウム投与, 帝王切開, SGA, 臍帯動脈血 pH $<$ 7.2, 組織学的絨毛膜羊膜炎の有無, 分娩週数, 児の性別, 出生体重。ACS 実施群で S100B は低値であった [中央値 (min-max)]: 1.05 (0.58-4.0) vs 0.84 (0.23-2.2) ng/ml, $p < 0.001$]。重回帰分析では, 分娩週数 ($p=0.035$) と ACS 実施 ($p < 0.001$) はそれぞれ S100B 低値と関連していた。また, 投与後 7 日以上経過して出生した児では, 有意差は認めなかった。【結論】早産児では ACS 投与により臍帯血 S100B 濃度の低下を認め, 脳障害予防に寄与していることが示唆された。

P-38-7 Fetal HQ を用いた新しい胎児心機能評価の検討

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【目的】Fetal HQ は Speckle-Tracking 法を用いて胎児心室壁の運動を解析する方法である。Speckle-Tracking 法は心臓の動画の中で、基準となる超音波画像上の小斑点 (speckle) をフレームごとに追跡する技術である。Fetal HQ を用いることで左右心室壁の Sphericity index や Fractional shortening, Fractional area change など自動的に測定することができる。また、左室を心基部から心尖部まで 24 の segment に分割し、Simpson 法を用いることで stroke volume を簡便に測定することができる。本研究の目的は Fetal HQ で測定できる項目と、胎児心機能の評価に用いられてきた項目における相関関係の有無を評価することである。【方法】正常単胎胎児を対象とし、4-chamber view の B-mode 画像を数秒間記録し解析を行った。22 名の胎児で計 30 回の超音波検査および解析を行った。Fetal HQ で解析した項目は左右心室の Sphericity index・Fractional shortening・Fractional area change・Global strain, 左室心拍出量 (LCO, Stroke Volume×Heart rate), ejection fraction (EF), 心機能の評価項目として左右 Cardiac output, Tei index, 静脈管 PI 値, 下大静脈 preload index, UV flow volume を測定し、それぞれの項目に対して Pearson の相関係数を求めた。【成績】Fetal HQ で解析した LCO と従来法にない超音波検査で求めた LCO に相関関係が認められた (相関係数=0.636 P=0.00154)。【結論】Fetal HQ は 4-chamber view を記録するのみで解析が可能であり、従来の超音波検査よりも簡便である。Fetal HQ は胎児心機能の評価に有用である可能性がある。

P-38-8 AI による 3D 超音波データセットを用いた CRL の自動計測法の開発に向けた基礎的検討

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【目的】正しい CRL の計測は正中矢状断面で行うことが求められる。しかしながら 2D 経陰超音波検査では正中矢状断面が得られないこともあり、その計測には苦慮することも少なくない。3D 超音波データセットから AI により正中矢状断面を構築しさらに CRL を自動計測するシステムの開発に資するデータの集積が本研究の目的である。【方法】最終月経または胚移植日から決定され従来の CRL 計測により確認された妊娠 8 週から妊娠 11 週の胎児 82 例 (教師データ 68, テストデータ 14 例) を対象とした。胎児全体の 3D ボリュームデータを取得したのち 3D ボリュームから胎児領域を抽出し (深層学習), 胎児領域の最遠点を検出し CRL 計測ポイントとした (ロジック)。1) 2D で計測された CRL 値 (2DCRL) と 3D ボリュームから得られた CRL 計測値 (3DCRL)。2) AI で計測された CRL 値 (AICRL) と 2D で計測された CRL 値について回帰式および相関の有無を評価した。本研究は施設内倫理委員会の承認を得て書面による同意を得て行った。【成績】全ての 3D ボリュームデータから胎児矢状断 CRL 計測断面が得られた。1) $3D=0.792+0.985*2D$, $r^2=0.986$, $r=0.992$ ($p<0.001$) であり 2DCRL と 3DCRL には強い相関が認められた。2) $3D=-1.447+1.032*2D$, $r^2=0.879$, $r=0.938$ ($p<0.001$) であり 2DCRL と AICRL には強い相関が認められた。【結論】3D 超音波を用いることで CRL 計測断面が得られることが示された。さらに AI による自動 CRL 計測は従来の CRL 計測と同等の精度であることが示された。以上のことから 3D 超音波データセットを用い AI により全ての胎児において正確な CRL が自動で計測可能となることが示唆された。

P-39-1 Population-based study における臍帯動脈血ガス pH 7.0 未満の検討

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【目的】新生児低体温療法は、中等症から重症の低酸素性虚血性脳症 (hypoxic-ischemic encephalopathy : HIE) に対して死亡率改善効果、生存児の神経学的後遺症軽減効果があるといわれている。今回、本県の臍帯動脈血ガス (UA) pH 7.0 未満の背景と推移、低体温療法の効果について調べる。【方法】本県では 1998 年以降、周産期死亡と脳障害ハイリスク症例を登録して原因分析を行っている。1998-2020 年の総出生数 227,278 例のうち、脳障害ハイリスク症例登録数は 490 例あり、このうち在胎 36 週以降の UA pH 7.0 未満の登録症例は 48 例であった。当院では 2016 年から 2015CoSTR の低体温療法のエントリー基準を使用し新生児低体温療法を行っており、本治療の適応となる県内の出生児は当院で受け入れている。UApH 7.0 未満のうち 10 例に低体温療法を行った。先天異常 1 例を除く 47 例を対象とし、低体温療法導入前後での周産期因子、新生児予後を検討した。本研究は当大学「医の倫理委員会」の承認を得て行った。【成績】UApH 7.0 未満症例は、低体温療法導入前 30 例 (前群)、導入後 17 例 (後群) であり、発生頻度は前群 1.7 例/年、後群 3.4/年であった。後群に初産婦が多かった。原因となった周産期合併症は、常位胎盤早期剝離 16 例、子宮内感染 6 例、臍帯脱出 2 例、malpractice 4 例、原因不明 6 例であった。後群 17 例中低体温療法を施行したのは 10 例であった。退院時頭部 MRI で HIE の所見を認めたのは前群 17 例 (56.7%)、後群 4 例 (23.5%) であった ($p=0.02$)。【結論】UApH 7.0 未満の症例 47 例のうち 10 例に低体温療法を施行した。導入後では頭部 MRI 所見が有意に改善していた。低体温療法導入は新生児の短期予後改善に寄与している。

P-39-2 絨毛膜羊膜炎による児の脳容積および脳障害への影響：先進的ニューロイメージング技術を用いた検討

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【目的】絨毛膜羊膜炎(CAM)を発症した母から生まれた児は、神経発達障害や精神疾患のリスクが高いことが知られている。今回我々は、在胎34週未満の早産児の修正満期頭部MRI画像をもとに先進的ニューロイメージング技術を用いて、CAMによる児の脳容積および脳障害への影響を検討した。【方法】2010~2018年に当院で出生した在胎34週未満の早産児304例から、双胎、胎児奇形、妊娠高血圧症候群、子宮内胎児発育不全、明らかな脳障害症例を除外した58症例(CAM群[n=20]と非CAM群[n=38])を対象とした。Voxel-based morphometry (VBM) および Infant FreeSurfer を用いてCAMによる局所脳容積の変化を評価した。またKidokoro脳障害スコアを用いてCAMによる粗大な脳構造変化および脳障害レベルを評価し、修正1.5歳での発達指数(DQ)を用いて神経学的予後を評価した。【成績】VBMでは、白質(CAM:139.1±8.0ml, 非CAM:144.2±12.2ml)・灰白質(176.8±22.8ml vs. 172.1±23.2ml)の脳容積は2群間で有意差を認めなかった。Infant FreeSurferでは、両側淡蒼球(左:p=0.045, 右:p=0.044,)、両側側坐核(左:p=0.005, 右:p=0.044)においてCAM群で有意な容積の減少を認めた。Kidokoro脳障害スコア(CAM:4, 非CAM:4)、1.5歳DQ(92.6±10.7 vs. 90.4±15.1)では2群間に有意差を認めなかった。【結論】今回先進的ニューロイメージング技術および脳障害スコアを用いて、CAMによる早産児の脳への影響を詳細に検討した。本検討ではCAMにより、粗大な脳構造変化やDQへの影響は少ない一方、淡蒼球・側坐核における脳容積の減少を認め、早産児の将来的な自閉症スペクトラム障害や統合失調症のリスク上昇との関連が示唆された。

P-39-3 後期早産期の前置胎盤合併妊婦から出生した新生児の呼吸適応への影響

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【目的】早産児の帝王切開分娩は、新生児の呼吸器系の有害な転帰につながる危険因子である。本邦では前置胎盤を合併した妊娠は緊急の出血等のリスクを避けるために、妊娠38週までに選択的帝王切開術が行われている。本研究の目的は、前置胎盤が後期早産期の帝王切開分娩で生まれた児の呼吸器症状に及ぼす影響を評価することである。【方法】後期早産児の単胎帝王切開分娩について後方視的に解析した。前置胎盤を適応とした帝王切開術(前置胎盤群)とその他の適応での帝王切開分娩(Control群:胎児発育不全, 妊娠高血圧症候群, 骨盤位や既往帝王切開後妊娠の前期破水など)の間で、出生児に対する酸素投与や人工呼吸器管理を必要とする新生児呼吸器疾患の有病率と、出生前母体ステロイド投与率を比較した。【成績】対象は後期早産期の単胎の帝王切開分娩99例で、前置胎盤群が29例、残りの70例をControl群とした。新生児呼吸器疾患の有病率は、前置胎盤群で38%、Control群で34%であったが、統計的に有意ではなかった。出生前母体ステロイド投与率は、前置胎盤群(38%)がControl群(17%)よりも有意に高かった(p<0.001)。【結論】後期早産児の帝王切開分娩では、前置胎盤の妊娠では他の適応症に比べて出生前母体ステロイド投与の頻度が有意に高かったにもかかわらず、新生児の呼吸障害を十分に防ぐことはできなかった。妊娠34週以前に管理入院された前置胎盤合併妊娠は多くが出生前ステロイド投与を行い、妊娠34週以降まで妊娠継続されることがある。そのため、妊娠34週以降の複数ケールの出生前母体ステロイド投与の再検討の余地がある。

P-39-4 妊娠高血圧症候群の母から産まれた早産児における拡散テンソル画像を用いた脳白質統合性の評価

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【目的】MRI拡散テンソル画像(diffusion tensor imaging:DTI)は、生体内の水分子の拡散の方向や大きさを定量化することが可能であり、拡散方向の指標である異方性比率(fractional anisotropy:FA)は脳白質統合性評価に有用である。早産児において、母の妊娠高血圧症候群(hypertensive disorders of pregnancy:HDP)が出生後の児のFA値に与える影響を評価した。【方法】2014年から2020年に当院で出生した在胎34週未満の早産児のうち、修正40週前後(37~42週)でDTIを撮影した症例うち、双胎、先天異常、臍帯動脈血液ガスpH<7.1、撮影条件不良の症例を除外した69例を対象とした(HDP群:16例, non-HDP群:53例)。DTIを元にFA画像を作成し、tract-based spatial statistics (TBSS)を用いて全脳における両群のFA値の比較を行った。【成績】対象症例は分娩週数29.9±2.8週、出生体重1288±461g、DTI撮影時週数38.8±1.4週であった。HDP群で男児が多かったが(p<0.05)、両群で分娩週数、出生体重、DTI撮影時週数、絨毛膜羊膜炎(Chorioamnionitis:CAM)の頻度に差を認めなかった。TBSSの結果、単変量および多変量解析(共変量:在胎週数、DTI撮影時週数、児性別、CAM)ともに、両群でFA値に有意差のある領域は認めなかった。CAMを伴わない男児症例のみで実施したサブ解析でも有意差のある領域は認めなかった。【結論】修正40週前後に実施したDTIでは、2群間でFA値に有意差のある領域は認めなかった。本研究の結果から、母のHDPが児の脳白質統合性へ与える影響は少ないと考えられた。

P-39-5 妊娠糖尿病母体の新生児予後とその関連臨床因子についての検討

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【目的】妊娠中に妊娠糖尿病 (GDM) を適切に診断する目的は周産期合併症の予防である。今回、我々は正期産 GDM 母体の新生児合併症の頻度とその関連臨床因子を検討した。【方法】対象は2015年から2019年に当院で周産期管理を行ったGDM単胎正期産症例で、新生児合併症とその関連因子について後方視的に検討した。新生児合併症は、低血糖、呼吸障害、新生児黄疸、large-for-gestational age (LGA) および NICU 入院とし、前述の合併症を一つでも認めるものを新生児合併症陽性とした。それぞれの合併症頻度と、種々の臨床因子 (年齢、初産婦、非妊時肥満、インスリン治療、分娩前 HbA1c 値、帝王切開など) との関連について検討した。【成績】対象症例は393例で、低血糖 26例 (6.6%)、呼吸障害 8例 (2.0%)、高ビリルビン血症 39例 (9.9%)、LGA12例 (3%)、NICU 入院 49例 (12.4%) で、いずれかを認めた新生児合併症陽性は 95例 (24%) であった。呼吸障害は初産婦に多く ($p < 0.01$)、新生児黄疸は初産婦 ($p < 0.001$)、肥満 ($p < 0.05$)、妊娠中のインスリン投与 ($p < 0.05$) で、NICU 入院は、35歳未満 ($p < 0.01$)、初産婦 ($p < 0.001$) で有意に高かった。新生児合併症陽性は、初産婦 ($p < 0.005$)、肥満 ($p < 0.05$)、35歳未満 ($p < 0.05$) で高頻度であった。低血糖、LGA と関連する臨床因子は特定できなかった。また、分娩前の HbA1c 値はいずれの新生児合併症との関連を認めなかった。【結論】単胎正期産の GDM 症例の 4分の1に何らかの新生児合併症を認めた。初産婦、非妊時肥満、母体年齢がそのリスク因子として抽出された。分娩前の HbA1c 値は新生児合併症の予測因子とはならなかった。

P-39-6 帝王切開後の新生児血糖値と帝王切開前の母体血糖値の症例対照研究

音羽病院

瀬尾晃司

【目的】新生児の血糖が 48 mg/dL 以下の場合、発達障害の原因となるという報告がある。また治療には新生児の入院が必要であり、医療費も増加するため、予防が必須な疾患である。予定帝王切開には様々な合併症があるが、その一つに新生児低血糖がある。母体術前血糖と出生後児血糖の相関の研究は少ない。【方法】2018年5月から2019年3月に当院で施行された予定帝王切開 27例について、出棟直前の母体血糖と、出生直後の児血糖及び出生後3時間の児血糖、新生児が低血糖に対して点滴治療を要したかどうかの相関を調べた。【成績】出生直後の児血糖と出棟直前の母体血糖は相関関数 $r=0.406$ とよく相関していた。一方、低血糖に対する点滴治療を要さなかった児の出生後3時間の児血糖と、出棟直前の母体血糖は相関関数 $r=0.130$ とほぼ相関していなかった。【結論】予定帝王切開において、出生直後の児血糖と出棟直前の母体血糖はよく相関し、出棟直前の母体血糖が十分であれば、治療を要する新生児低血糖となることはほとんどないことがわかった。ブドウ糖を含む術前輸液が出生児の血糖を改善することは知られているが、術前ブドウ糖輸液の投与時間や量についてはエビデンスに乏しい。また麻酔後低血圧を予防するエビデンスのあるボルベンを使用する施設が増加しているが、ボルベンはグルコースを含まないため、使用施設での新生児低血糖増加が懸念される。今後は本研究を基に RCT をデザインし、予定帝王切開前の術前ブドウ糖輸液の適切な投与時間や量について調べていく予定である。

P-39-7 胎動減少の自覚が早期発見につながった fetomaternal hemorrhage の一例

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【緒言】母胎間輸血症候群 (fetomaternal hemorrhage : FMH) は 9000 例に 1 例でありながら胎児死亡の 15% が関連していると言われる疾患である。今回は胎動減少の自覚が FMH の早期発見に有用であった 1 例を報告する。【症例】症例は G1P0、既往歴は特になし、自然妊娠成立し前医で管理されていた。妊娠経過に特に問題は指摘されていなかったが、34w1d 胎動減少の自覚があり前医受診。精査加療目的で当院に搬送となった。当院搬送後経腹エコーで中大脳動脈の収縮期最高速度 (MCV-PSV) は 92cm/s と明らかに上昇し、CTG では sinusoidal pattern を呈し胎児貧血が疑われた。緊急帝王切開を施行し、児は体重 1264g、Apgar1 分値 1 点、5 分値 5 点であり Hb28g/dl と高度貧血を認めた。【考察】FMH では胎動減少・消失が胎児死亡に先立つ事例が相当数報告されている。胎動減少・消失を迅速に知覚するための方法として胎動カウントがあげられるが、胎動カウントが胎児死亡を減少させるとの明確なエビデンスはない。本症例では胎動カウントを行っていなかったが、前医で胎動減少・消失が危険なサインであると教示されていた。そのため早い段階で受診したことで FMH の早期発見につながったと考えられた。【結論】胎動減少・消失は FMH を早期に発見するための重要な症状であり、体動チェックアプリなどを用いて地道に啓蒙していくことが重要であると考えられた。

P-39-8 妊婦健診時の胎児心拍陣痛図異常で帝王切開になった母時間輸血症候群の一例

大分大附属病院

栗山 周, 山田知徳, 衛藤 聡, 井上尚実, 西田欣広, 河野康志

【緒言】母児間輸血症候群は、胎児血が胎盤を通して母体血に移行することで胎児貧血を来す疾患で、その多くは特発性である。新生児貧血は様々な原因によって生じるが、今回母児間輸血症候群の診断に至った症例を経験したので報告する。【症例】31歳、1妊0産、人工受精で妊娠成立後、近医で妊娠管理を行い、特記なく経過していた。妊娠37週0日の妊婦健診時の胎児心拍数陣痛図で軽度変動一過性徐脈を散見したため、NRFS疑いで当院へ緊急搬送となった。入院時無痛性の子宮収縮に伴い軽度～高度変動一過性徐脈を認め、NRFS疑いで同日緊急帝王切開となった。児は2,418g, female, Apgar score 5/5, 臍帯動脈血 pH 7.30であった。児は全身チアノーゼ、呼吸障害のためNICU管理となり、Hb 4.0g/dLと重症新生児貧血を認めた。母体血のHbF 5.1%と著明な上昇を認め、母児間輸血症候群による貧血と診断した。【考察】本症例では、バルボウイルス B19を含めた感染症検査は陰性で、胎盤病理では直径10mm程度の絨毛血管腫および臍帯の一部が単一臍帯動脈の診断であったが、新生児貧血の原因とはなり難いものであり、特発性の母児間輸血症候群と診断した。今回、軽度の胎児心拍数陣痛図異常で帝王切開した症例において偶発的に母児間輸血症候群を認めた症例を経験した。

P-40-1 メチルドパ内服による薬剤性温式自己抗体陽性が疑われた妊婦の2例

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【緒言】自己免疫性溶血性貧血(以下 AIHA)は、赤血球膜上の抗原と反応する自己抗体が産生され血管外溶血を来す疾患である。そのうち一部の薬剤により赤血球のRh抗原に対する自己抗体が産生される薬剤性 AIHA の存在が報告されている。薬剤性も非薬剤性関わらず重篤な疾患であり、厳重な管理が必要となる。今回当院において、メチルドパの内服により温式抗体が産生されたことが疑われる症例を経験したので報告する。【症例1】43歳女性、G2P1。前医にて凍結融解胚移植にて妊娠成立し、当院紹介受診となった。高血圧合併妊娠にてメチルドパの内服を開始した。妊娠12週での妊娠初期の採血にて温式抗体陽性を指摘、明らかな溶血所見なくメチルドパによる薬剤性温式抗体を疑った。13週からメチルドパ中止にて妊娠管理を継続。23週の時点で温式抗体陰性を確認した。【症例2】39歳女性、G3P2。妊娠高血圧症既往。妊娠反応陽性にて当院受診。高血圧合併妊娠にてメチルドパを内服。妊娠11週での妊婦健診の初期検査にて温式抗体陽性。明らかな溶血所見なくメチルドパによる薬剤性温式抗体を疑った。メチルドパを中止し妊娠管理を継続。26週の時点で温式抗体陰性を確認した。【考察】温式 AIHA における汎凝集素抗体の存在は、供血の交差適合試験を困難にする。輸血により溶血を加速することが報告されており、出血リスクの高い周産期患者にとっては致命的である。一方薬剤性である場合、多くが薬剤中止後数週間まで自己抗体が消失すると言われている。妊娠高血圧症候群に対し広く使用されているメチルドパを投与により温式抗体が出現することを周知し、使用する際は定期的な不規則抗体スクリーニングを行うことが推奨される。

P-40-2 慢性骨髄性白血病合併母体に対し妊娠中ニロチニブによる治療を行い正期産生児を得た症例

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【緒言】慢性骨髄性白血病(CML)の第一治療薬はBcr-Abl蛋白を標的とするチロシンキナーゼ阻害薬(TKI)で特殊な状況を除き中止されない。日本血液学会造血器腫瘍診療ガイドライン2018ではTKIは胎児毒性があり治療中女性が妊娠を希望する場合は、厳格な治療条件達成を得た上で休薬を検討するとされている。今回我々は中止条件に合致せず予定外の妊娠をし、本邦では妊娠中使用報告がないニロチニブでの治療を行い生児を得た症例を経験した。【症例】30歳代、初産婦。X年前にCMLと診断されイマチニブ無効でダサチニブでの治療中だがコンプライアンス不良から分子遺伝学的に深い奏功は得られず分子遺伝学的大奏功(MMR)で経過していた。予定外妊娠となり妊娠6週時にダサチニブを自己中断し妊娠管理のため通院先血液内科から当科へ紹介となった。母児リスクを十分説明したが強い妊娠継続希望があり妊娠11週から妊娠18週まで有益性投与であるインターフェロン α を投与したが無効でMMRを失いCML再発に至った。その時点でも妊娠継続希望強くTKI再開を決定しEuropean Leukemia Net Database opinionを参考にニロチニブを開始した。ニロチニブは有効でMMRを維持でき34週時に中止した。妊娠33週から子宮内胎児発育不全を認め妊娠36週時に妊娠高血圧腎症を発症し妊娠37週時に選択的帝王切開術にて分娩に至った。分娩後ニロチニブ再開されMMRを維持している。臍帯血ニロチニブ濃度1.16 ng/mLと胎児移行を認めたが汎血球減少等は認めなかった。【結語】CML合併女性が妊娠を希望する場合、TKI中止条件を得た計画妊娠が第一だが、諸外国を含めた最新の動向に基づいた治療を行い母体に重篤な合併症を来さず生児を得た。

P-40-3 妊娠高血圧症候群を併発した後天性血友病 A 合併妊娠の 1 例

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【緒言】後天性血友病は100~400万人に1人程度に発症し悪性腫瘍や自己免疫疾患罹患患者の他に妊娠分娩に関連して第VIII因子への自己抗体が産生される稀な疾患である。後天性血友病の治療中妊娠出産した報告例は極めて稀である。今回我々は前回の妊娠分娩を契機に発症した後天性血友病治療中の患者に対して、他科と連携し周産期管理を行った例を経験したので報告する。【症例】37歳で2妊1産である。第1子を帝王切開で分娩した2か月後、両下肢痛や紫斑などを契機に後天性血友病 A と診断された。血液腫瘍内科で治療中に妊娠と診断されたため紹介となった。血液腫瘍内科と連携し自己抗体量をモニタリングし妊娠を継続した。胎児の発育は25週頃まで-1.5SD前後で推移したが27週頃から妊娠高血圧症候群を発症し、胎児発育停止傾向が認められたため妊娠28週5日より管理入院とした。血友病に関連した症状や検査所見は特に異常なかった。妊娠29週2日に胎児機能不全の診断で帝王切開術を施行した。児は667g, 女児, Aps8/8 (1/5分), pH7.205, BE-4.9であった。分娩後母体は問題なく経過し第6病日退院した。新生児は原因不明のAPTT延長を認めたものの自己抗体は検出されず経過し日齢96日に退院となった。【考察】後天性血友病合併妊娠は極めて稀であり、他科との連携を強化しながら慎重に妊娠や周産期管理をおこなっていく必要があると考えられた。

P-40-4 特発性血小板減少性紫斑病の診断が第2子出産時に von Willebrand 病 2B 型となり、その後卵巣出血で多量血性腹水を呈した 1 例

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von Willebrand 病は von Willebrand 因子 (以下 VWF) の質的・量的異常をきたす遺伝性出血性疾患であり、本邦の患者数は約1500人の稀な疾患である。VWF は血小板を内皮下結合組織へ粘着させる機能と血漿中の血液凝固第VIII因子を安定化させる機能をもつ。von Willebrand 病は量的減少の1型・質的異常の2型・完全欠損の3型に分類され、主に常染色体優性遺伝で、1型が8割以上を占め、血小板減少を呈するのは2B型のみである。患者は幼少期より特発性血小板減少性紫斑病の診断で加療されていたが、血小板数は2~16万/ μ Lと不安定であった。第1子を自然妊娠し当院で周産期管理を行ったが、免疫グロブリン療法に反応せず血小板は2万/ μ Lであり、分娩進行中に胎児機能不全となり血小板輸血後に緊急帝王切開分娩となった。第1子に血小板減少は認めなかった。6年後に第2子を自然妊娠し、血小板輸血後に選択的帝王切開術を行った。第2子は出生直後より血小板減少を認めたが治療抵抗性であり、精査の結果 von Willebrand 病 2B 型の診断に至った。同時期に患者も von Willebrand 病 2B 型と診断された。診断2年後に肝下面まで及ぶ血性腹水を伴う卵巣出血を認め入院した。血小板数は3.2万/ μ Lであり全身状態は安定していたことから、血小板輸血・赤血球輸血・血液凝固第VIII因子製剤投与を行い、手術は行わず保存的加療した。von Willebrand 病 2B 型は稀な疾患であり血小板減少を呈することから特発性血小板減少性紫斑病と診断されるとの報告がある。治療抵抗性の血小板減少を認め、家族歴がある場合は本疾患を疑う必要がある。周産期管理や出血症状に対しては血小板輸血や血液凝固第VIII因子製剤投与を含めた慎重な管理が必要である。

P-40-5 血友病保因者の出血傾向；分娩時に凝固因子製剤の補充を行った血友病 A 確定保因者妊婦の出産

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【緒言】近年、凝固因子活性値が低い血友病保因者の存在が明らかになっている。今回、分娩時に凝固因子製剤の補充が必要であった症例を経験したので報告する。【症例】29歳、血友病 A 確定保因者の初妊婦。妊娠初期の第VIII因子活性値が25%、その後55%まで上昇。34週5日、前期破水を認め、凝固第VIII因子製剤を予防的に投与し、同日緊急帝王切開を行った。出生した児は軽症血友病 A であったが、母子ともに異常出血は認めなかった。【結語】保因者の分娩では産後出血が多いという報告や、分娩時の血友病新生児の頭蓋内出血の報告があるが、我々が2011年に行ったアンケート調査では、確定保因者12名中6名は、自身が血友病の子どもを出産するまで、保因者であることを知らされていなかった。妊婦も産科医も血友病患児が生まれるかもしれないというリスクを認識せずに分娩に臨んでいる事が稀ではないという事を示しており、分娩時の頭蓋内出血のリスクを減らせない一因となっていると考える。また2018年に行った別の調査では、約4割の保因者が出血症状を認めた際に血友病の家族歴があることを告げないまま医療機関を受診しており、保因者の出血に対して、適切な診断・治療が行われていないことが多々あると推察される。今回我々は「エキスパートの意見に基づく血友病周産期管理指針2017年版」に基づき、血友病専門医、産科医、新生児科医が連携し、適切な分娩管理を行う事ができた。保因者を適切に支援していくためには、妊娠・分娩管理だけでなく、保因者告知、保因者診断、出血傾向への対応などにおいても、血友病専門医と産婦人科医との適切な連携が必要である。

P-40-6 妊娠を契機に診断された成人型先天性血栓性血小板減少性紫斑病の一例

福井大附属病院

白藤 文, 川村裕士, 中森あかり, 加藤将人, 藤田将行, 清水可奈子, 高橋 望, 宮崎有美子, 玉村千代, 品川明子, 折坂 誠, 吉田好雄

【緒言】先天性血栓性血小板減少性紫斑病 (TTP) は、von Willebrand 因子を特異的に切断する酵素である ADAMTS13 の遺伝子変異に起因する極めて稀な血栓性疾患である。今回、妊娠を契機に先天性 TTP と診断された 1 例について報告する。【症例】26 歳 1 妊 0 産。6 歳時に特発性血小板減少性紫斑病 (ITP) の治療歴あり。妊娠 30 週 1 日に血小板数の低下を認め、妊娠 30 週 1 日に当院へ搬送。血液内科と連携し、ITP の増悪を疑ってステロイド治療を開始したが改善認めなかった。その後肝機能異常、溶血性貧血、蛋白尿、心窩部痛が出現し、経過から HELLP 症候群を含む妊娠関連の血栓性微小血管症と診断した。これ以上の妊娠継続は危険と判断し、妊娠 30 週 5 日、帝王切開術により妊娠婦結とした。術後に輸血を行い、術後 3 日目までは血小板数は 8 万/μL 前後で推移したが、術後 4 日目に再び血小板数が 2.3 万/μL と低下し、溶血所見の増悪も認めた。ADAMTS13 活性 13%、抗 ADAMTS13 抗体陰性であったため TTP は否定し、腎機能障害も進行したため臨床的に atypical HUS と診断し血漿交換を行った。血漿交換後、一旦病状は改善したがすぐに増悪した。増悪時の FFP 投与前に ADAMTS13 活性を再検査すると 4% と著減しており、先天性 TTP が疑われた。患者の ADAMTS13 遺伝子変異を確認し先天性 TTP の診断に至った。現在第 2 子妊娠中であり、妊娠 33 週まで問題なく経過している。【考察】先天性 TTP では幼少期に ITP と誤診されている例がある。ITP 合併妊婦が妊娠中に急激な血小板数低下に加え溶血を認めた場合、先天性 TTP を疑って ADAMTS13 活性を評価する必要がある。FFP を投与すると ADAMTS13 活性の低下が評価できなくなるため、輸血前の検査が必須である。

P-40-7 特発性血小板減少性紫斑病合併妊娠における妊娠中の血小板数の推移

山形大附属病院

日根早貴, 深瀬実加, 伊藤友理, 渡邊真理子, 渡邊憲和, 山内敬子, 永瀬 智

【目的】特発性血小板減少性紫斑病 (idiopathic thrombocytopenic purpura ; ITP) は、血小板数が 10 万/μl 以下に減少する良性的血液疾患である。一般的に、妊婦では妊娠週数が進むに従って血小板数が減少するが、ITP 合併妊娠における血小板数の妊娠中の推移は明らかにされていない。そこで、当院での ITP 合併妊婦における血小板の推移を検討した。【方法】2011 年 6 月から 2021 年 4 月までの期間に当院で周産期管理を行った妊婦のうち、ITP を合併した症例を対象とした。対象症例の診療録を後方視的に調査し、各症例の妊娠中の血小板数の推移を検討した。【成績】対象期間中の ITP 合併妊娠は 22 名で分娩は 36 例であった。36 例のうち、十分な情報を取得できなかった 8 例を除いた 28 例について検討した。ITP の発症時期は妊娠前が 22 例 (79%)、妊娠中が 6 例 (21%) であった。12 例 (43%) で ITP に対する妊娠中の治療を要した。子宮内胎児死亡の 2 例を除いた 26 例で検討すると、血小板数が最も低かった時期は妊娠初期が 2 例 (8%)、中期が 7 例 (27%)、後期が 17 例 (65%) であった。妊娠初期、中期に血小板数が最低値となった 10 例のうち、7 例 (70%) では ITP の治療を行っていなかったが後期の血小板数の方が高かった。対象期間中に 2 回分娩した 6 症例 (12 分娩) のうち 5 症例 (80%) で、1 回目と 2 回目の妊娠の妊娠後期の血小板数の差が 1 万/μl 以内であった。【結論】ITP 合併妊娠では、正常妊娠とは異なる血小板の推移をたどることがあり、無治療でも血小板が増加する場合があった。また ITP 合併の経産婦においては前回妊娠時の後期の血小板数により次回妊娠における後期の血小板数が予測できる可能性がある。

P-41-1 腹腔鏡下切除術を施行した副角妊娠の 1 例

大阪総合病院

綿重直樹, 竹内茂人, 森 琴子, 百々裕子, 辻 誠, 東理映子, 南 元人, 菅谷 健

【緒言】副角妊娠は、全妊娠の 76000~150000 例に 1 例と極めて稀な疾患である。術前診断は困難とされ、手術時に初めて副角妊娠と診断されることも多い。今回、超音波検査と MRI 検査で術前に副角妊娠と診断し、腹腔鏡下摘出術を施行した症例を経験したので報告する。【症例】33 歳、G2P1 29 歳時、超音波検査、子宮卵管造影検査にて単角子宮 (右卵管疎通性あり) の疑いで、MRI 検査を行い AFS 分類 IIC (単角子宮、副角内腔なし) と診断した。自然周期/人工授精 (右卵巣より排卵) にて妊娠し、正常経産分娩した。今回、自然周期/タイミング療法 (左卵巣より排卵) にて妊娠成立するも、妊娠 5 週 (血中 hCG 8351.6mIU/mL)、超音波検査で子宮内に胎嚢を確認できず子宮左側に胎嚢を認め、MRI 検査でも同様な所見で副角妊娠と診断し、腹腔鏡下手術を施行した。【考察】不妊治療で単角子宮の疑いがあれば、MRI などで子宮奇形分類することにより異所性妊娠の場合、早期に異所性妊娠部位を診断し、未破裂の状態与安全に腹腔鏡下手術を施行できると思われた。

P-41-2 妊娠期に急速に増大した子宮腔部尖圭コンジローマの1例

近畿大奈良病院¹, 近畿大奈良病院病理²西岡和弘¹, 山本皇之祐¹, 橋口康弘¹, 岸本佐知子¹, 若狭朋子², 大井豪一¹

症例 25 歳。既往歴・家族歴に特記事項なし。妊娠 25 週に子宮頸癌合併妊娠のため当院紹介受診した。前医細胞診では扁平上皮癌、組織診では扁平上皮癌であった。内診では子宮頸部前唇に約 25mm 大の乳頭様腫瘤を認めた。当院病理医の組織診断では尖圭コンジローマであった。当院で再度組織診を施行すると同様に尖圭コンジローマであった。その後尖圭コンジローマは 2 週間で約 5cm 大にまで増大した。易出血性であり緊急帝王切開の可能性の否定できなかったため妊娠 27 週 5 日に周産期 3 次医療機関 A に紹介となった。医療機関 A でも尖圭コンジローマの診断であった。その後著明な増大傾向を認めなかったため、妊娠 30 週 5 日に当院逆紹介となった。妊娠 38 週 1 日で予定帝王切開とした。児は 3158g 男児 Ap9/10 であった。子宮頸部全周性にカリフラワー状の約 6cm 大の腫瘤を認めた。易出血性の出血のためこの時のコンジローマ切除術は断念した。産褥 1 か月では子宮腔部全周性に約 3cm 大の鶏冠状の腫瘤を認め、帝王切開時よりコンジローマは縮小していた。子宮頸部細胞診は L-SIL であった。産褥 2 か月に子宮腔部コンジローマ切除術を施行した。5mm のマージンを取り全周性に浅く切除した。術後 2 か月の子宮頸部細胞診は NILM であり、6 か月ごとの子宮頸部細胞診は NILM であり、術後 1 年 6 か月経過しているが再発を認めていない。

P-41-3 子宮頸部筋腫合併妊娠の一例

桑名市総合医療センター

脇坂太貴, 榎原康平, 大阪 優, 二村 涼, 前川剛輝, 千田時弘, 平田 徹

子宮筋腫合併妊娠に出会うことは臨床では珍しくはなく、多くは特別な対応が管理が必要なものが多い。今回、巨大子宮頸部筋腫により、妊娠・分娩管理に苦慮した子宮頸部筋腫合併妊娠を経験したので報告する。症例は、35 歳、2 妊 1 産、既往歴は特になかった。1 人目は自然妊娠成立され筋腫合併妊娠として対応、無痛分娩で経膈分娩に至っている。今回も自然妊娠成立され前医で妊娠管理されていたが子宮頸部筋腫が前妊娠時より増大しており、診断と分娩管理目的で紹介となった。頸部筋腫の腫瘍径は 8cm あり、腔鏡診では筋腫に圧排されて外子宮口が視認できなかった。病理学的検査では、擦過細胞診は経過を通じて NILM であり、組織診でも悪性所見は認めなかった。児の発育は AGA で推移していたが、筋腫は 10cm まで増大を認め、それに伴い筋腫表面が裂け出血を繰り返し、切迫早産として入院管理とした。カンファレンスでは経膈分娩は不可能と判断し、妊娠 37 週 5 日で選択的帝王切開術予定としたが、妊娠 36 週 2 日に陣痛発来を認め、緊急帝王切開術の運びとした。産褥経過は良好で術後 5 日目に退院となっている。子宮筋腫合併妊娠の報告は散見されるが、子宮頸部筋腫合併妊娠となると報告はかなり少なくなる。文献学的考察だけではなく経過中の豊富な画像を交えて本例を報告する。

P-41-4 子宮底部横切開で娩出を要した子宮腺筋症術後妊娠の1例

宮崎県立宮崎病院

高村一紘, 村上真友, 脇山 英, 安藤伶旺, 永谷優華, 愛甲 碧, 甲斐いづみ, 村上孟司, 今村絃子, 谷口秀一, 嶋本富博

子宮腺筋症は、30 代を好発年齢とし月経痛や過多月経などの症状により、QOL を損なう疾患である。晩婚化、出産年齢の上昇傾向にある昨今において、子宮腺筋症に対し、将来の妊娠に備え、病変を摘出する子宮温存手術が行われつつある。症状緩和が得られ QOL 改善に寄与する一方で、妊娠時の子宮破裂や癒着胎盤などの周産期リスクが問題である。子宮腺筋症術後妊娠の周産期予後についての報告は散見されるが、管理や手術の実情については不明な点が多い。今回、帝王切開時に子宮底部横切開で娩出を要した子宮腺筋症術後妊娠を経験したので報告する。31 歳、G3P0。28 歳時に月経痛、性交痛、過多月経を伴う子宮腺筋症に対し手術が施行された。病変部位は前壁で核出重量は 90g であった。その後、自然妊娠し、切迫早産で妊娠 26 週から総合周産期センターで入院管理され、転居のため妊娠 27 週に当院に母体搬送となった。入院時の MRI 検査で癒着胎盤の所見はなかった。妊娠 32 週 6 日に、切迫子宮破裂の診断で緊急帝王切開術を施行した。児は 1936g の女児で、アプガースコア 1 分後 8 点 5 分後 8 点、臍帯血 pH7.325 であった。開腹時、子宮筋層に非薄化はなかったが、視野の中央に子宮底部、左付属器、左円靭帯を認め、子宮体部下節を同定できず、子宮底部横切開で児を娩出した。MRI 画像や手術記録から、腺筋症を摘出し縫合した部位は妊娠中に伸展しないため、子宮が高度に偏在していたと考えられた。子宮腺筋症術後妊娠では、摘出した腺筋症の病変部位によって通常の子宮体部下節で切開ができない可能性を念頭に置く必要がある。

P-41-5 当院における子宮奇形合併妊娠の後方視的検討

防衛医大病院

西谷想子, 岩橋秀樹, 鈴木理絵, 石橋弘樹, 伊藤 翼, 岸本直久, 角倉 仁, 大塚由花, 垣本壮一郎, 宮本守員, 笹 秀典, 高野政志

【目的】子宮奇形合併妊娠は産科合併症の頻度が高く、早期の診断と慎重な妊娠管理および分娩様式の選択が重要とされる。今回我々は当院で経験した子宮奇形合併妊娠の臨床経過について後方視的に検討したので報告する。【方法】2008年1月から2020年12月までの間に、当院で22週0日以降に分娩となった単胎妊婦を対象とし、子宮奇形合併妊娠例をA群、正常子宮妊娠例をB群と分類し、妊娠分娩予後について比較した。また、A群の各症例の分娩管理とその転機について検討した。【成績】対象は5219例あり、A群が28例(0.5%)、B群が5191例(B群99.5%)だった。子宮奇形の分類は双角子宮が22例(82.1%)、重複子宮が4例(10.7%)、単角子宮が2例(7.1%)だった。早産は8例vs873例(28.6%vs16.8%, $p=0.10$)、死産は2例vs46例(7.1%vs0.8%, $p=0.02$)だった。分娩様式が帝王切開術は24例vs2126例(85.7%vs40.6%, $p<0.01$)、分娩時出血の中央値は525ml vs 438ml ($p=0.26$)だった。A群の中で、経膈分娩を予定していた11例のうち、7例(NRFS4例、分娩停止2例、妊娠高血圧症1例)が緊急帝王切開術となり、2例(NRFS1例、微弱陣痛1例)が吸引分娩、2例(26週IUFDI1例を含む)が正常経膈分娩であった。また、選択的帝王切開術を行った17例の適応は、既往帝王切開後妊娠8例(28.6%)、胎位異常7例(25.0%)、既往子宮手術後妊娠1例(3.6%)、子宮奇形を理由とした選択的帝王切開術が1例(3.6%)だった。【結論】子宮奇形合併妊娠では胎位異常が多く、死亡率も高いことが示唆された。帝王切開率が高く、経膈分娩の成功率が低いことを考慮した周産期管理が必要と考えられた。

P-41-6 子宮奇形の症例における周産期予後の検討

聖隷浜松病院

今野寛子, 清水陽彦, 清水由実, 伊賀健太郎, 鈴木貴士, 塩島 聡, 安達 博, 村越 毅

【目的】当院における子宮奇形合併妊娠の周産期予後について検討する。【方法】2013年~2020年に当院で妊娠12週以降に分娩した単胎妊娠12023例について、子宮奇形合併妊娠症例と合併していない症例にわけ、母体背景と周産期予後について後方視的に検討した。【成績】子宮奇形合併妊娠は49例で全体の0.4%に認められた。両群間で母体の背景には有意差は認めなかった。高次生殖医療による妊娠率は3例(6.1%)、1135例(9.5%)と有意差は認めなかった($p=0.111$)。既往の流産回数にも有意差は認めなかった($p=0.157$)。分娩週数、分娩時の出血量、胎盤の重量、胎児の体重、身長、Apgarスコア、臍帯動脈pHなどに有意差は認めなかった。帝王切開率は34例(69.4%)、4455例(37.2%)と子宮奇形合併妊娠で有意に多かった($p<0.001$)。胎位異常は15例(30.6%)、593例(5%)と子宮奇形合併妊娠で有意に多かった($p<0.001$)。【結論】子宮奇形合併妊娠では、これまでの報告と同様、胎位異常とそれによる帝王切開が多いという結果であった。子宮奇形は流早産や分娩時出血量増加の原因となるとする報告もあるが、今回の検討では分娩週数や分娩時の出血量には有意差を認めず、児の周産期予後にも有意差を認めなかった。

P-41-7 巨大子宮筋腫合併妊娠から見た、妊娠中に注意すべき子宮筋腫とは

自治医大さいたま医療センター

石黒 彩, 桑田知之, 伴 操, 柴田あずさ, 牧野佑子, 牛嶋順子, 近澤研郎, 堀内 功, 高木健次郎

【緒言】子宮筋腫合併妊娠はハイリスク妊娠として知られている。その位置、大きさによって妊娠中の核出が考慮されたり、分娩方法が制限される。妊娠中増大例もあり、注意深く管理すべき疾患である。今回2症例の巨大子宮筋腫合併妊娠を経験した。それらの経過から、妊娠中に注意すべき項目について知見を得た。【目的】2症例の巨大子宮筋腫合併妊娠を経験した。それらの経過から妊娠中の変化に着目し、妊娠初期の段階で注意すべき項目について検討した。【成績】1例目は、初期に10cmの筋腫が体下部にあった32歳の初産婦である。20週には筋腫は21cmとなり、胎児発育は-1.8SDだが発育していた。妊娠中の筋腫核出も考慮したが、無症状であることと核出による胎児への影響が大きいため断念し、妊娠継続とした。子宮底長は50cmまで増大し、35週にIABO留置下cesarean hysterectomyを行なった。児は2096gの男児であった。2例目は初期に12cmの筋腫が底部に有茎性であった37歳の初産婦である。21週に筋腫は15cmとなり、筋腫変性痛で入院管理した。39週に筋腫は17cmであったが2764gの女児を経膈分娩した。【結論】2症例から、筋腫の位置により妊娠中の筋腫増大のスピード、有痛症状等に違いがあることがわかった。子宮動脈流入部と胎囊の間に筋腫があると、妊娠中の増大速度は大きくなり、子宮動脈流入部から離れた位置にあり、有茎性など血流不足が推定される筋腫では、変性痛が見られる可能性が示唆された。本検討では、巨大筋腫であったことが症状の違いを際立たせた可能性がある。2症例以外の経過も加えて報告するが、今後、より多数例の検討が必要と考えられる。

P-41-8 当院における筋腫核出術と周産期予後の検討

大阪医科薬科大

村上 暉, 恒遠啓示, 夏山幸一郎, 増田ゆうき, 吉田篤史, 上田尚子, 宮本隣輔, 寺田信一, 中村奈津穂, 古形祐平, 藤田太輔, 大道正英

【目的】近年、拳児を希望する年齢が高くなり、子宮筋腫に対する手術治療として妊孕性温存を希望して筋腫核出術を行う女性が増えている。筋腫核出後の妊娠率や周産期予後を包括的に検討した報告は少ない。筋腫核出術、不妊治療、周産期管理を一貫して行える当院で、筋腫核出術後の妊娠率や周産期予後を後方視的に検討した。【方法】2016年から2021年の5年間に当院で筋腫核出術を行った症例に対し、妊娠率や周産期予後を後方視的に検討した。【成績】2016年から2021年の5年間に、当院で筋腫核出術を行ったのは144症例であった。そのうち、現時点で68症例が既婚者であり（未産は55症例）、周産期予後が追跡できたのは25症例で、14症例では生児を得ていた（A群）。A群のうち、不妊治療を行ったのは9症例であった。分娩様式は1例のみ経陰分娩であり、その他は帝王切開であった。子宮破裂や癒着胎盤は認めず、妊娠症例全てで安全に周産期管理を行えた。不妊治療を行うも妊娠に至らない症例を11症例認めた（B群）。A群とB群を比較すると、手術時に核出された筋腫の大きさ、個数、内膜損傷の有無、開腹手術・腹腔鏡下手術の術式などに差はなかったが、A群と比べてB群では年齢が高かった（平均年齢：A群34.5歳 VSB群41.0歳）。【結論】当院で追跡できた症例の生児獲得率は56%（14/25症例）と概ね良好な結果であった。一方で筋腫核出を行っても高齢の場合には、不妊治療を施行しても生児を獲得できない症例を認めた。今後も、子宮筋腫に対する筋腫核出術の適応は個別に検討していく必要がある。

P-41-9 びまん性平滑筋腫核出術後に2度自然妊娠し生児を得た1例

金沢大附属病院

曾根香穂, 鏡 京介, 竹田初美, 細野 隆, 中山みどり, 松岡 歩, 折坂俊介, 山崎玲奈, 藤原 浩

【緒言】びまん性平滑筋腫は無数の小筋腫が子宮頸部以外の筋層にびまん性に増生する稀な病態である。小筋腫は往々にして100個を超える。20代から30代の女性に好発するため妊孕性温存が可能な管理方法が求められる。今回、びまん性平滑筋腫核出術後に2回自然妊娠し、2回ともに生児を得た症例を経験したので報告する。【症例】37歳、G2P1。30歳時にびまん性平滑筋腫のため当院で筋腫核出術を施行し、内膜近傍まで子宮を切開して169個の筋腫を核出した。術後10か月で自然妊娠に至った。妊娠中、切迫早産の併発などなく、妊娠37週に帝王切開術で生児を得ることができた。子宮体部左側壁は菲薄化し、子宮筋層は全体的に不均一な厚みを呈していた。胎盤は手動的に容易に剝離でき、癒着や遺残なく娩出した。児は2800g、Apgar score9/10であり、児に特記すべき異常はなく発育は良好である。産後1か月後の診察では筋層の菲薄化は認めなかった。今回、筋腫核出後5年半後に2度目の自然妊娠に至った。周産期管理目的に当院を紹介受診した。妊娠10週に性器出血があり、絨毛膜下血腫を認めた。妊娠13週から1回目の妊娠時にはなかった腹痛、性器出血、子宮収縮があり慎重に管理している。妊娠25週の時点で児の発育は良好である。妊娠30週にMRI検査を行い、帝王切開術での娩出を予定している。【考察】びまん性平滑筋腫の術後に2度生児を得た1例を経験した。1度目の妊娠経過に問題はなかったが、核出術後5年半後の2度目の妊娠では切迫早産となり管理に難渋した。びまん性平滑筋腫の核出術後は早期の妊娠が望ましいと考える。核出術後の子宮筋層の厚さは不均一であり、子宮破裂に注意する必要がある。

P-41-10 子宮腺筋症核出術後の周産期予後

自治医大附属病院

成見莉紗, 高橋宏典, 杉山瑞穂, 大橋麻衣, 藤本揚子, 小古山学, 鈴木寛正, 馬場洋介, 種市明代, 薄井里英, 大口昭英, 藤原寛行

【目的】子宮腺筋症核出術後の妊娠例が増加している。筋腫核出術と異なり、正常筋層も合併切除するので、腺筋症核出術後妊娠においては子宮破裂を合併する頻度が高いと報告されている。当院における腺筋症核出術後妊娠の周産期予後について検討した。【方法】2011-2020年に当院で周産期管理した腺筋症核出術後妊娠19例を対象とした。当院における管理方針として、子宮破裂や切迫早産の可能性を考慮して、妊娠28週には管理入院とし、積極的な子宮収縮抑制を行い、35-36週に選択的帝王切開術を施行した。この条件下で妊娠経過、周産期予後について後方視的に検討した。【成績】母体年齢は中央値37（IQR：34.5-40）歳、手術から妊娠まで中央値12（IQR：7-14）か月、ART妊娠は13例（68.4%）だった。点滴による子宮収縮抑制が必要だったのは12例（63.2%）であった。分娩週数は中央値35（IQR：34-35）週、34週未満での分娩は3例（15.8%）で、いずれも子宮収縮抑制困難例だった。子宮破裂は認めなかった。帝王切開時、腹腔内癒着は11例（57.9%）、子宮筋層菲薄化は2例（10.5%）でそれぞれ観察された。術中出血は中央値820（IQR：600-1118）mlであった。固着胎盤は3例（15.8%）で認められ、いずれも腺筋症核出部位と胎盤付着部位が一致していた。【結論】腺筋症核出術後妊娠は積極的な子宮収縮抑制薬使用など慎重な管理を行うことで概ね良好な周産期予後が得られることがわかった。帝王切開時には腹腔内癒着に注意が必要で、腺筋症核出部位と胎盤付着部位が一致する場合は固着胎盤の発生に留意すべきであることが示唆された。一方で、様々な腺筋症核出方法が存在するため、術式別に周産期予後を追跡するべきかもしれない。

P-42-1 妊娠中にリツキシマブを使用した多発血管炎性肉芽腫症合併妊娠の一例

浜松医大附属病院

加藤貴史, 成味 恵, 小田智昭, 松本雅子, 幸村友季子, 磯村直美, 田村直顕, 内田季之, 鈴木一有, 伊東宏晃

【緒言】多発血管炎性肉芽腫症 (granulomatosis with polyangiitis; GPA) 合併妊娠は稀であり, 原病治療的に妊娠中にリツキシマブ (RIT) を使用した報告は過去にない。今回, 妊娠を契機に現病が増悪し, 寛解導入療法に RIT を併用することで原病の病勢を制御し, 生児を得た症例を経験したので報告する。【症例】24 歳 3 経妊 1 経産, 15 歳時に GPA と診断された。初回妊娠時は原病の増悪なく分娩に至り, その後自然流産し, プレドニゾロン (PSL) のみの維持療法中に自然妊娠した。妊娠 4 週から PSL 内服困難となり, 妊娠 8 週に発熱・血痰が出現した。血液検査上抗好中球細胞質抗体値の上昇等と, CT 検査上両肺に多発する結節影を認め, GPA の再燃・増悪と診断された。ステロイドパルス療法により解熱したが, 病勢制御不十分のため, 免疫抑制療法の追加が必要であると判断された。そこで胎児毒性の観点から RIT を選択し, 375mg/m²/週投与を妊娠 16 週から 4 回施行したところ病勢を制御でき, PSL のみの維持療法へ移行できた。また, 胎児発育は全妊娠期を通して良好であった。妊娠 29 週時に発熱と前期破水から子宮内感染が疑われ緊急帝王切開となった。発熱は肺感染によるものと診断され, 抗菌薬投与後に解熱, 退院した。児は RIT の主な副作用である白血球数減少を認めることなく, 日齢 60 で退院した。【結語】妊娠中の GPA 増悪に対し RIT を投与し, 病勢制御に成功し, 児への副作用なく経過した GPA 合併妊娠を経験した。妊娠中の GPA 増悪に対する治療法確立へ向けて, 症例蓄積が待たれる。

P-42-2 ループス腹膜炎が疑われた全身性エリテマトーデス合併妊娠の 1 例

新潟大病院

為我井加菜, 須田一暁, 山脇 芳, 島 英里, 五日市美奈, 生野寿史, 西島浩二, 榎本隆之

【目的】妊娠中の腹水の増悪は妊娠高血圧腎症と関連し, 妊娠終結後に改善することが多い。今回我々は, 妊娠高血圧腎症を呈し, 腹水を合併した全身性エリテマトーデス (Systemic lupus erythematosus, SLE) 合併妊娠症例において, 妊娠終結後に腹水が増悪し, ループス腹膜炎が疑われた 1 例を経験したので報告する。【症例】33 歳, 3 妊 0 産 (自然流産 2 回)。SLE, 抗リン脂質抗体陽性のためプレドニゾロン (5mg/日), タクロリムス (3mg/日), アスピリン (100mg/日) の内服治療を行っていたが, 自然妊娠が成立し, 血栓症の予防強化のためヘパリンカルシウムの皮下注射を開始した。妊娠 29 週時に高血圧と尿蛋白を認め, 妊娠高血圧腎症の管理目的に入院した。入院時に軽度腎機能障害および補体価の低下を認めた。妊娠 30 週より母体腹水と嘔気・下痢症状が出現した。その後, 腎機能障害が進行したため妊娠高血圧腎症の増悪と判断し, 妊娠 30 週 3 日に緊急帝王切開術を施行した (女児, 1156g: Light for date, Apgar score: 1 分値 7 点/5 分値 8 点)。術中に 900ml の腹水を認め, 術後は利尿目的にアルブミンを投与した。胸水は認めなかった。術後 4 日目より腹壁切開創部から多量の腹水排出を認め (最大 3980ml/日), 術後 6 日目まで改善せず, SLE 増悪に伴うループス腹膜炎が疑われた。副腎皮質ステロイドホルモンによる治療を強化したところ, 腹水は著明に改善し, 尿蛋白および腎機能の改善を認めた。内科へ転科後, 自宅退院となった。【結論】SLE 合併妊娠における腹水の増悪は, 急性増悪に伴うループス腹膜炎を念頭に置く必要がある。

P-42-3 精神疾患合併妊娠における周産期管理および周産期予後に関する検討

日本大板橋病院

谷口博美, 加藤果野子, 田中ゆりあ, 小林 理, 松永麻美, 中島隆広, 川上香織, 池田悠至, 小松篤史, 佐藤美紀子, 千島史尚, 川名 敬

【目的】精神疾患合併妊娠は, 産科的および新生児リスクが増大することから, 2016 年よりハイリスク妊娠に位置付けられているが, それら患者の周産期管理に関する報告は少ない。本研究では, 精神疾患合併妊婦の周産期リスクを評価することを目的とした。【方法】当院において, 2018 年 1 月から 2021 年 8 月に分娩した精神疾患合併妊婦 126 名, および, 2020 年に分娩した精神疾患非合併妊婦 617 名を対象とした。精神疾患合併妊婦と非合併妊婦において, 産科的合併症の有無, 分娩方法, 分娩時出血の多寡, 母処置の有無, 胎数, Apgar スコア, NICU 入院の有無, および, 児の出生体重・身長・頭囲を, 統計学的に解析し, 周産期リスク評価を行った。【成績】精神疾患合併妊婦では妊娠糖尿病の合併率が高く, 精神疾患非合併妊婦が 15% であるのに対し, 精神疾患合併妊婦では 23% であった (P=0.018)。また, 妊娠高血圧症合併も, 精神疾患合併妊婦で高い傾向にあった。周産期リスク評価においては, 児の NICU 入院率が, 精神疾患非合併妊婦で 47% であるのに対し, 精神疾患合併妊婦では 58% と高値であった (P=0.053)。さらに妊娠糖尿病を合併した精神疾患合併妊婦の場合は, NICU 入院率が 72% に上昇した。母体の分娩時リスク, および, 児の出生体重・身長・頭囲などへの影響はなかった。【結論】精神疾患合併妊婦は, 非合併妊婦に比し, 有意に妊娠糖尿病合併率が高く, さらに産科的合併症のリスクおよび児の NICU 入院率が高くなる傾向があった。精神疾患合併妊婦で, 妊娠糖尿病がある場合は, 妊娠糖尿病管理を行うことが周産期予後の改善につながると考えられた。

P-42-4 精神疾患合併妊婦の医学的・社会的リスクに関する検討

琉球大学病院

小崎三鶴, 銘苅桂子, 大木悠司, 屋良奈七, 金城淑乃, 知念行子, 金城忠嗣, 青木陽一

【目的】精神疾患合併妊婦は妊娠中から分娩、育児期間を通して医学的・社会的支援を要する症例が多く、多職種が関わった連携を必要とされる。当院における精神疾患合併妊婦の医学的・社会的リスクについて検討する。【方法】2020年10月から2021年9月の期間で、当院で妊娠分娩管理を行った精神疾患合併妊婦41例を対象に、疾患背景、分娩予後、地域連携介入の有無について診療録から後方視的に検討した。地域連携は、産科医・助産師・精神科医・小児科医・心理士などが関わり、必要な症例については地域と共に養育環境などの確認や訪問調整を行った。【成績】精神疾患の内訳は、統合失調症10例、うつ病8例、パニック障害7例、不安神経症6例、その他10例であった。妊娠中の産科合併症は18例(43.9%)；切迫早産10例、GDM5例、HDP3例に認め、うち5例(12.2%)が早産となった。精神状態に関して、妊娠中増悪を13例(31.7%)に認め、9例(22.0%)が精神科入院を要した。産後増悪を5例(12.2%)に認め、1例は産後2か月時に抑うつ状態悪化に伴う投身行為を行い、救急病院へ搬送となった。妊娠中の抗精神病薬内服を32例(78.0%)に認め、19例(46.3%)は2剤以上の多剤内服患者であった。妊娠中および産後から訪問看護導入となった症例は15例(36.6%)あり、地域への情報提供を行なったものが19例(46.3%)であった。9例(22.0%)は妊娠中に要保護児童対策地域協議会を行い、4例(9.8%)；全例一時保護同意ありが分娩後に乳児院へ退院となった。【結論】精神疾患合併妊婦は妊娠中から産後にかけて精神状態の増悪を約44%に認め、約83%に社会的支援を要するため、医学的・社会的ハイリスクに対する多職種の連携が重要である。

P-42-5 妊娠糖尿病におけるエジンバラ産後うつ病質問表の有用性に関する検討

国立長崎医療センター

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【目的】産科合併症を有するハイリスク妊婦は通常の妊婦に比して不安が多いと推測される。中でも妊娠糖尿病(GDM)を有する妊婦では産後うつが増加するという報告がある一方で否定的な報告もあり評価が一致していない。そこで当科におけるGDM妊婦のエジンバラ産後うつ病質問表(EPDS)の有用性について検討した。【方法】2019年1月から2020年12月までに当科で分娩した35週以上の単胎分娩のうち、GDM妊婦(G群)と合併症のないローリスク妊婦(C群)を後方視的に抽出し妊娠中のEPDSのスコアを比較検討した。【成績】G群は148例(年齢:34.5±4.6, 非妊時BMI25.4±6.1), C群は186例(年齢:32.2±5.2, 非妊時BMI21.9±3.9)で、G群は年齢、非妊時BMIともに有意に高かった。EPDSスコアは両群間で有意差はなく(G群:4.20±4.1 vs C群:3.40±3.4, P=0.092)。産後うつの疑いとされるEPDS9点以上はG群20例(13.4%), C群18例(9.6%)であった(P=0.30)。GDM診断時期に注目し、GDM診断後にEPDSを実施したG群(n=90)と、妊娠24週以降にEPDSを実施したC群(n=161)の比較では、EPDSスコアはG群:4.40±4.4 vs C群:3.42±3.4(P=0.052)、9点以上はG群16例(17.8%), C群は15例(9.3%)であった(P=0.10;オッズ比0.51[95%信頼区間0.24-1.10])。【結論】GDM妊婦は、有意差はないもののEPDSスコアが高く9点以上の異常症例の割合が高い傾向にあり、EPDSの有用性が示唆された。

P-42-6 当院における5年間の統合失調症合併妊娠の検討

東邦大医療センター大森病院

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【目的】統合失調症に対する新規の向精神薬による治療や早期受療による長期入院治療の減少および心理社会的支援の普及などにより日常生活レベルが向上し、その合併妊娠は増加傾向にある。当院での統合失調症合併妊娠における周産期予後を検討した。【方法】当院の2017年1月から2021年9月の約5年間の統合失調症合併妊娠について後方視的に検討した。【成績】対象期間中の総分娩数は4,007例の中で、精神疾患合併症例は200例(5.0%)であった。そのうち統合失調症は23例(11.5%)であった。母体の平均年齢は34.3±5.24歳であった。妊娠前に入院治療歴があった症例は9例(39.1%)、妊娠成立時に内服加療を行っていた症例は8例(34.7%)であった。妊娠中に精神症状が増悪し入院加療となったのは3例(13.0%)であった。早産分娩は妊娠高血圧腎症となった1例(4.3%)のみであった。分娩後は16例(79.5%)が断乳していた。分娩後に精神症状が増悪し医療保護入院が必要となったのは6例(26.0%)であった。妊娠から分娩後の期間で9例(39.1%)が入院加療を必要とし、5例(55.5%)が服薬を中断していた。また当院では精神疾患合併症例は全例で妊娠期間中から地域保健所と連携をとっており、分娩後に医療保護入院を必要とした6例中2例は速やかに児童相談所の介入となった。【結論】周産期は精神疾患の増悪、再燃するリスクが高く、本研究でも39%が症状の増悪、再燃のため入院管理が必要であった。統合失調症では服薬中断等による増悪の可能性もあり、精神科を含めた密接な管理の必要性があると思われた。

P-42-7 筋強直性ジストロフィー合併、一絨毛膜二羊膜性双胎のため胎児の病態評価に難渋した一例

金沢大附属病院

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【緒言】筋強直性ジストロフィー合併妊娠は児罹患による羊水過多や早産、母体の横紋筋融解症等が報告されている。今回一絨毛膜二羊膜性双胎のリスクも併存し、複数のリスク因子によることで妊娠経過中の所見から胎児の病態評価が困難だった症例を経験したので報告する。【症例】32歳1妊0産。自然妊娠し前医で一絨毛膜二羊膜性双胎と診断された。妊娠22週から子宮頸管長短縮を認め塩酸リトドリン内服を開始された。切迫早産加療目的に妊娠23週6日に当院紹介となり入院となった。入院後の検査で塩酸リトドリンによる横紋筋融解症を認め、さらに筋強直性ジストロフィーの家族歴が判明し、自身も筋力低下を認めたことから同疾患を疑い脳神経内科受診とした。妊娠中のため侵襲的な検査は控えられたが、身体所見と臨床症状より同疾患の臨床診断に至った。妊娠33週頃には1児のFGRとVSDを認めた。妊娠36週0日には1児の羊水最大深度13mmの羊水過少や、MCA-PSVが107.1cm/秒(>1.5MoM)であり胎児貧血が疑われ、NSTはVDが散発していたことから胎児機能不全と判断して同日緊急帝王切開術を施行した。出生時の所見は、1児(1719g, Hb 9.3g/dl)、2児(2189g, Hb 22.8g/dl)とTAPSを認めた。さらに両児共に身体所見から21トリソミーを疑い、染色体検査で同診断に至った。【考察】本症例は筋強直性ジストロフィーと双胎妊娠を念頭に妊娠管理を行い、羊水過多やTTTSに注意したがTAPSが生じていた。また、1児のFGRとVSDは把握できていたが、出生時には21トリソミーの言及は困難だった。本症例のように疾患が重なることで胎児の病態評価が困難な症例もあるため、様々なリスクや疾患を想定し母児管理に携わる必要がある。

P-42-8 リトドリン塩酸塩による横紋筋融解症を契機に筋強直性ジストロフィー合併妊娠と診断された1例

砂川市立病院

佐藤元哉, 宇田智浩, 佐野友宇子, 櫻井愛美, 山下陽一郎, 津田加都哉

【緒言】筋強直性ジストロフィー(myotonic dystrophy; 以下DM)は、進行性の筋力低下を主症状とする常染色体優性遺伝の疾患である。妊娠中に増悪することがあり、流早産・胎児死亡・新生児死亡に至る可能性が高いため、周産期管理に注意を要する。今回リトドリン塩酸塩投与による横紋筋融解症と羊水過多を契機に発見されたDM合併妊婦の1例を経験したので報告する。【症例】35歳。G1P0。生殖補助医療にて妊娠成立し、妊娠26週時に頻回な子宮収縮、子宮頸管長短縮および羊水過多を認め、切迫早産の診断で入院管理となった。リトドリン塩酸塩点滴を開始したが、投与数時間後に上下肢の筋肉痛を認め、採血では筋酵素(CK)の異常高値を認めた。リトドリン塩酸塩による横紋筋融解症が疑われ、硫酸マグネシウム水和物点滴、ニフェジピン錠内服に変更したところ、CKは速やかに下降し筋肉痛も消失した。その後、子宮収縮抑制不良にてクレブテロール錠を追加投与したところ、心窩部痛・CKの再上昇を認め投与中止した。β刺激薬投与による急激な横紋筋融解症ならびに羊水過多からDMの存在を疑い、神経内科にて神経学的検査、遺伝子検査を施行され、後日DMと診断された。母体は周産期管理目的に高次医療機関へ搬送となり、妊娠31週時に前期破水および胎児機能不全のため緊急帝王切開術を施行された。児は1626gでApgar scoreは1/1(1分/5分)点であり、出生直後より挿管管理となった。【結語】リトドリン塩酸塩等のβ刺激薬投与による急激な横紋筋融解症と羊水過多がみられた場合には、原因の一つとしてDMの存在を念頭におく必要がある。

P-42-9 妊娠悪阻による意識障害から判明した低Na血症の1例

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【緒言】低ナトリウム血症は血中ナトリウム濃度が136mEq/L未満に低下することであり、溶質に対する水分の過剰が原因である。一般的な原因としては、利尿薬の使用、下痢、心不全、肝疾患、腎疾患、ADH不適合分泌症候群(SIADH)、水中毒などがある。今回、妊娠7週の妊婦が妊娠悪阻による食事摂取不良、水中毒を契機に低ナトリウム血症となり、意識障害を来した一例を経験したので、報告する。【症例】31歳、1妊0産。自然妊娠成立。妊娠6週頃に妊娠判明してから悪阻症状があり、食事はとれるが嘔吐する状態で、1日2リットル以上飲水を行っていた。妊娠7週に自宅内にて倒れているところを発見され、意識障害を主訴に救急搬送された。来院時、JCS:III-200 GCS:E1V1M3、四肢は除皮質硬直様で、左共同偏視を来している状態であった。血中Na濃度:112mEq/Lを認めた。肝逸脱酵素の上昇あり重症妊娠悪阻かと思われたが、大量の希釈尿、尿ケトン陰性からすると悪阻の所見とは合わない状態であった。飲水のエピソード、血清浸透圧低下、尿中Na低下、水制限によるNa濃度上昇から水中毒と診断された。入院当日より血中Na濃度補正を開始し、過補正に伴う橋中心性髄鞘崩壊症などの合併症もなく、Na濃度上昇を得てそれに伴い意識障害の改善を認めた。以降の妊娠経過は問題無く経過し、妊娠40週4日に自然頭位経陰分娩に至り、産褥経過も良好で自宅退院となった。【結語】一般的に妊娠初期の嘔気、嘔吐の持続後の意識障害はWernicke脳症発症を疑うが、妊娠中のWernicke脳症と低ナトリウム血症との鑑別は臨床症状の違いが少ないため困難である。妊娠悪阻と診断しても他の疾患の可能性について常に留意する必要がある。

P-43-1 妊娠中に発症した節外性NK/T細胞リンパ腫、鼻型：症例報告

自治医大

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【緒言】妊娠中に発症する悪性リンパ腫の約60%はホジキンリンパ腫で、成熟Natural killer/T (NK/T)細胞リンパ腫は稀である。さらに、成熟NK/T細胞リンパ腫の中で節外性NK/Tリンパ腫、鼻型(Extranodal NK/Tcell lymphoma: ENKL)合併妊娠の報告はない。今回、妊娠中にENKLを発症した症例を経験した。【症例】39歳、1妊0産、自然妊娠。Basedow病既往あり。妊娠20週頃から難聴と鼻閉感を自覚した。32週、両下肢に違和感が出現し、35週、両下肢脱力から歩行困難となり前医に入院した。複視、顔面筋力低下、聴力低下があり、頭頸部MRIで右鼻腔から上咽頭領域に3cm大の占拠性病変を認めため、妊娠36週0日に当院に転院した。末梢血液像異常はなかったが、上咽頭腫瘍と下肢運動障害からENKLの中枢神経浸潤が疑われ、精査治療目的に36週1日、妊娠を終結させた(全身麻酔下帝王切開、2,540g女児、Apgar 8/8)。鼻腔内に浸潤した腫瘍の生検からENKL(CD56陽性)と確定診断された。髄液からCD2、CD56陽性のリンパ腫細胞が多数検出され、髄腔浸潤も併せて確認された。術後4日目から化学療法(SMILE療法: DEX+MTX+IFM+L-Asp+ETP)と中枢神経浸潤に対する髄注療法(MTX+AraC+PSL)が開始された。下肢運動障害は改善し室内歩行可能になりSMILE療法2サイクル+髄注療法6サイクルにより完全奏効したが、その4週間後に髄腔内再発したため、自家末梢血幹細胞移植し化学療法を継続中である。【結語】ENKL合併妊娠の第1例目報告である。難聴や鼻閉感は妊婦の比較的commonな症状であるためENKLを早期から鑑別し挙げることは難しいが、これらの症状が強く出現したり随伴症状がある場合はENKLの可能性も考慮して精査を行うべきである。

P-43-2 当院における悪性腫瘍合併妊娠についての検討

徳島大

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【目的】悪性腫瘍合併妊娠は妊娠中から産後1年の間に悪性腫瘍を診断・治療された妊娠を指す。癌の治療に加え、妊娠・分娩管理や以降の妊孕性、胎児への影響など多数の問題がある。今回当院における悪性腫瘍合併妊娠の現状や問題点を検討した。【方法】2005年10月～2020年10月に当院で分娩管理した悪性腫瘍合併妊娠における癌の内訳・診断契機・周産期予後・腫瘍予後について検討した。【成績】悪性腫瘍合併妊娠は妊娠前診断3例、妊娠中期14例、産後診断4例の21例で、子宮頸癌8例、乳癌4例、卵巣癌2例、子宮体癌1例、また白血病など非婦人科癌6例であった。妊娠前診断の白血病2例はともに化学療法計画中での計画外妊娠のため中絶を選択したが、1例は妊孕性温存を行った上で追加治療を行った。妊娠期子宮頸癌は癌の精査中の妊娠や妊娠初期検査を契機に診断された例で、中絶や人工早産に至った。妊娠中期乳癌は全例自覚症状で発見され、中絶や37週までの分娩となった。また、そのうち1例が死亡していた。子宮体癌1例は自然早産の胎盤病理検査で偶発的に発見された。悪性腫瘍合併妊婦から出生した児に癌の転移や化学療法の影響は見られていないが、早産児については未熟児網膜症の治療や発達フォローを要している。【結論】当院の悪性腫瘍合併妊娠は妊娠中期癌を主とし、子宮頸癌や乳癌が多かった。これらは中絶や早産を要したが、腫瘍予後は概ね良好であった。妊娠前診断の癌は計画外妊娠の不利利益回避や妊孕性温存の検討のため十分なプレコンセプションケアが求められる。また妊娠中の乳房症状について乳癌の可能性を考慮することは重要である。

P-43-3 重症妊娠悪阻として治療開始された脳腫瘍合併妊娠の1例

飯塚病院

安部直希, 後藤麻木, 渡邊さや, 吉良さちの, 藤本茂樹, 林宗太郎, 小田美穂, 李 理華, 藤 庸子, 西山 哲, 江口冬樹, 辻岡 寛

脳腫瘍合併妊娠は非常にまれであり、少数の症例が報告されているのみである。今回我々は、妊娠初期に悪阻症状として紹介され、脳腫瘍が判明した症例を経験したので報告する。症例は23歳、1妊1産、自然妊娠。既往歴なく、妊娠前も頭痛等の症状は認めず、近医で妊娠管理をされていたが、妊娠12週頃から嘔気、嘔吐症状が出現し、次第に増悪傾向となり、妊娠14週0日に重症妊娠悪阻として当科紹介され、同日入院管理となった。安静、補液にて妊娠14週1日に症状はやや改善した。妊娠14週2日にJCS II-10、GCS E3V4M6の意識レベル低下があり、神経学的診察を行なったが、明らかな異常所見は認めなかった。ウェルニッケ脳症の可能性を疑い、補液を継続した。妊娠14週3日に数分間持続する痙攣発作を認め、瞳孔の左右差が出現しており、脳神経内科へコンサルト。頭部MRIを撮像し、左前頭部に6cm大の嚢胞、出血を伴う脳腫瘍があり、脳実質の圧排所見も認めていたため、脳神経外科より緊急開頭脳腫瘍摘出術が施行された。術後、嘔気症状は改善した。摘出病理は膠芽腫の診断。予後不良の腫瘍であり、早期の治療が必要である事を脳神経外科担当医から説明。患者が、治療に専念するため妊娠帰結を希望されたため、妊娠16週2日に人工妊娠中絶を行なった。その後早期に放射線治療、抗癌剤治療が開始され、現在フォロー中である。妊娠悪阻の症状は他疾患でも出現しやすい症状であり、随伴症状や身体所見などから他の疾患の鑑別を考える姿勢は必要と考える。

P-43-4 帝王切開の術前検査にて発見された肺癌合併妊娠の一例

名古屋第一赤十字病院

田中梨紗子, 手塚敦子, 伊藤由美子, 齋藤 愛, 坂堂美央子, 廣村勝彦, 津田弘之, 安藤智子, 水野公雄

【初めに】肺腺癌は非喫煙者の女性の肺癌患者の中でもっとも多く、比較的症候が出にくいと言われている。肺癌全体の5年生存率は3割程度と、予後が悪い腫瘍の一つである。今回我々は帝王切開の術前検査にて発見された stageIVA 期の肺癌合併妊娠を経験したので報告する。【症例】症例は39歳の女性、2妊1産。既往歴はなく1年前の検診では異常を指摘されていなかった。妊娠29週ごろより咳嗽が出現した。近医内科受診していたものの妊娠中のためレントゲンを含め画像精査は行われなかった。里帰り出産のため妊娠33週で当院受診された。既往帝王切開後妊娠のため妊娠38週で帝王切開を予定しており、術前検査のため妊娠34週で胸部単純レントゲン撮像したところ左全肺野透過性低下を認めた。胸部CTにて左主気管支を閉塞する巨大腫瘍と多発性に高度に腫大した縦隔リンパ節、大量胸水、対側肺には転移と思われる複数の小結節影、また胸腰椎にも融解像を認め肺癌 stageIV 期と考えられた。左胸腔内にドレーン留置の上、妊娠37週で緊急帝王切開術施行。胸水細胞診より肺腺癌を認め術後1日目に呼吸器内科に転科、術後3日目より抗がん剤投与が開始された。術後合併症、抗がん剤の有害事象認めず術後22日目で自宅退院となり、その後は外来通院で抗がん剤を継続しており再発なく経過している。【結語】生殖可能年齢において肺癌の罹患率は高くないが、肺癌は女性の部位別癌死亡率の第2位を占めている。内科医師は妊婦に対し画像精査をためらうことも多いが、若年妊婦であっても有症状時には適切な検査を行い、早期診断に繋げることが重要である。

P-43-5 視野障害を契機に診断し得た下垂体疾患合併妊娠の2例

三重大附属病院

平野志織, 真木晋太郎, 山口瑞希, 玉石雄也, 榎本尚助, 萩元美季, 高倉 翔, 真川祥一, 二井理文, 田中佳世, 田中博明, 池田智明

【緒言】下垂体疾患合併妊娠は腫大に伴う神経症状やホルモン分泌異常を引き起こし、慎重な管理が必要となる。今回、妊娠中の視野障害から診断に至り、分娩を終了した下垂体疾患合併妊娠の2例を経験したため報告する。【症例1】35歳、G2P1、自然妊娠。妊娠33週4日から視力低下を自覚しており、妊娠36週4日に右視力低下と両耳側上1/4盲が認められた。頭部MRIで下垂体腫瘍を認めホルモン過剰症状やホルモン基礎値の異常がないことから、非機能性下垂体腺腫が疑われた。妊娠37週5日に選択的帝王切開により分娩となった。術後に視障害が悪化したため、術後7日目に内視鏡下経鼻下垂体腫瘍摘出術を施行された。病理組織診断は下垂体腺腫であった。【症例2】31歳、G2P0、自然妊娠。妊娠7か月前に職場健診で高血圧を指摘されており、妊娠管理中自宅血圧は正常範囲内であった。妊娠30週から霧視と頭痛を自覚していた。妊娠35週3日に血圧が144/105mmHgと上昇し、頭痛増悪のため妊娠36週0日に当院に母体搬送となった。左後頭部に拍動性の頭痛があり、両耳側上1/4盲が認められた。頭部MRIで下垂体柄の腫大と下垂体後葉の信号不明瞭化を認め、リンパ球性下垂体炎が疑われた。妊娠36週1日に緊急帝王切開により分娩となった。術後1日目からPSLが開始され、視野障害と頭部MRI所見は改善した。【結語】頭痛、視力低下、視野障害などの症状を認める場合には、下垂体疾患も鑑別に入れることが重要であると考えられた。分娩管理や治療方針については一定の見解がなく、集学的な管理が求められる。

P-43-6 Plummer 病と妊娠一過性甲状腺機能亢進症により甲状腺クリーゼを発症した一例

広島赤十字・原爆病院

西本祐美, 甲斐一華, 児玉美穂, 中前里香子, 三春範夫, 伊達健二郎

日本における Plummer 病の頻度は甲状腺中毒症のうち0.15%~0.3%と稀である。また妊娠中は血中hCGが上昇し、特に8~10週頃には最高値を迎え、その影響で一過性に甲状腺機能が亢進する場合がある。今回我々は、Plummer 病に妊娠一過性甲状腺機能亢進症が加わり甲状腺クリーゼを発症したと考えられた一例を経験したので報告する。症例は42歳女性、3妊2産。妊娠7週3日に当院で妊娠を確認した時点で嘔気嘔吐などの症状を認め、制吐薬を処方されたが症状は改善しなかった。その後動悸や著明な倦怠感、傾眠傾向が出現し、妊娠11週3日の妊婦健診時の血液検査でFT-3 16.22 pg/mL、FT-4 6.14 pg/mL、TSH 0.005 μ IU/mLと甲状腺機能亢進を認め、加えて肝機能異常や黄疸、低K血症を認めた。超音波検査では甲状腺は正常大で実質に血流亢進は認めなかったが、左葉に15mm大の血流亢進を伴う腫瘍を認めた。TSH受容体抗体、抗TPO抗体、抗Tg抗体は陰性であった。各種検査から甲状腺クリーゼと診断し、その原因として未治療のPlummer 病があり、加えてhCGが最高値となる時期を迎えたことにより妊娠一過性甲状腺機能亢進症が発症の契機になった可能性があると考えた。ヒドロコルチゾンコハク酸エステル、ヨウ化カリウムを投与開始したところ全身状態は数日で改善し、適宜血液検査で甲状腺機能を確認しながら投薬を漸減・終了した。妊娠12週4日に施行したTcシンチグラムでは腫瘍への集積はやや弱いものの、既に治療介入後のPlummer 病としては矛盾しないと考えた。本人やご家族に各科からICを行い、妊娠14週1日に甲状腺左葉切除術を施行した。術後は甲状腺クリーゼの再発なく経過しており、その後の妊娠・分娩経過も併せて報告する。

P-43-7 Denosumab を使用し二児を得た腰椎骨巨細胞腫合併妊娠の一例

湘南藤沢徳洲会病院¹, 湘南鎌倉総合病院²

梶谷由真^{1,2}, 里吉雅恵¹, 水野 泉¹, 三川 猛¹, 福田貴則², 木幡 豊², 井上裕美², 橋口和生¹

骨巨細胞腫は悪性転化や再発, 転移を生じ得る腫瘍で膝周囲に好発する。脊椎発生は稀で妊娠中の報告は少なく, 外科切除以外の治療法は未確立である。前学術集会で我々は妊娠中に腰椎骨巨細胞腫の診断に至り, 手術不可のためやむを得ず禁忌薬である denosumab 投与により腫瘍縮小, 生児を得た一例を報告した。その後, 同症例が再度妊娠し再度 denosumab 投与を余儀なくされたが周産期異常なく生児を得た症例を経験した。2回の妊娠を比較し, 文献的考察も交え報告する。症例は37歳G4P3, 第4子を自然妊娠し22週時に第5腰椎骨巨細胞腫と診断された。早期治療を要したが, 宗教的理由で輸血拒否かつ妊娠中のため大量出血の危険がある外科切除は不可能であり, 十分な倫理的評価および患者の希望・同意のもと26週時に denosumab 120mg 投与された。直後より症状改善・腫瘍縮小し, 37週3日2400g女児(Apgar10/10)自然経陰分娩に至った。児は無症候性低Ca血症のためCa経口補充し, 生後11日目退院とした。分娩後 denosumab 定期投与のため避妊指導していたが第5子妊娠に至り, 判明後は投与中断したが血清マーカー上昇を認め23週時に denosumab 120mg 皮下注された。経過良好で38週4日2862g女児(Apgar8/9)自然経陰分娩に至った。母児ともに全身状態良好で産後4日目退院とした。第4子は生後1年2か月, 第5子は2か月現在ともに発達・発育に異常はない。腰椎骨巨細胞腫の診断後2回の分娩に至った症例を経験した。手術不可のため禁忌薬の denosumab をIRB承認下で使用し, 妊娠分娩産褥に異常はなく症状も抑制された。現在までの同様の報告はなく同一症例2回を経験であるが, 今後同様の症例に対し denosumab 使用の可能性が示唆された。

P-43-8 妊娠中に症候性水腎症を繰り返し, 治療に難渋した1例

大津赤十字病院

大谷遼子, 北村幸子, 恩地孝尚, 林真麻子, 松坂 直, 家村洋子, 中村彩加, 星本泰文, 金 共子, 藤田浩平

【緒言】無症候性水腎症は90%の妊婦に生じ, そのうち症候性水腎症は0.23%との報告がある。輸液, 抗生剤投与による保存的治療が第一選択だが, 20-30%程度に外科的治療を要する。今回, 妊娠中に症候性水腎症を反復し, 治療に難渋した1例を経験したため報告する。【症例】22歳, 1妊0産, 自然妊娠。妊娠19週1日より発熱を認め, 当院を受診, 細菌尿, 右水腎症を認め急性腎盂腎炎として保存的治療を行うも, 症状改善せず右尿管ステントを留置した。いったん症状改善するも23週3日に発熱と左背部痛が出現, 左水腎症を認め, 同日左尿管ステント留置を行った。28週2日に再度発熱, 左背部痛あり両側水腎症を認めた。保存的治療で改善なく, 28週3日に腰椎麻酔下にて左腎瘻造設を行った。右水腎症は術中には消失していた。36週1日に再度発熱し, 右水腎症を認めたが, 保存的治療で改善を認めた。38週4日に陣痛発来し, 同日正常経陰分娩に至った。産褥4日目に左腎瘻カテーテルを抜去し, 産褥5日目に母児ともに退院した。産褥15日目に右尿管ステントを抜去, その後水腎症の再発は認めていない。【考察】尿管ステントと腎瘻造設術の治療効果は水腎症治療で同等の効果と認めるが, 尿管ステントの石灰化による閉塞やステントの脱落により再治療を要するまでの期間が短く, 再々治療を要する頻度も高いとの報告がある。本症例でも, 左腎瘻造設後の左水腎症の再発は認めなかった。【結語】症候性水腎症では保存的治療が第一選択だが, 時には侵襲的な治療を要する。妊娠早期での水腎症の発症や尿管ステント留置後に水腎症が再発した場合は, 腎瘻造設も治療選択肢である。

P-43-9 創部感染との鑑別に苦慮した帝王切開創部に発症した壊疽性膿皮症の一例

奈良県立医大附属病院¹, 大阪暁明館病院²

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症例は35歳, 1妊0産。既往歴にうつ病があり, 家族歴に糖尿病と高血圧症が指摘されている。自然に妊娠が成立し, 妊娠36週3日に重症妊娠高血圧症・遅発型の診断となった。分娩誘発を開始したが妊娠36週5日に分娩停止の診断で帝王切開を施行した。術後5日目に創部が離開した。腹部造影CTでは膿瘍形成はなく, 術後創部感染を疑い創部洗浄とセファゾリン3g/日の投与を開始した。しかし治療に抵抗性であり, 徐々に創部に硬結, 水疱が出現し, 創上部の発赤が拡大した。その後抗菌薬を変更しても硬結が癒合して増悪傾向となり, さらに創部に潰瘍形成を認めた。創部の細菌培養は陰性であり, 病理組織検査は真皮全層性に好中球主体のびまん性炎症細胞浸潤を認める特徴的な所見であったことから, 壊疽性膿皮症を疑った。術後10日目から抗菌薬と並行しブレドニゾロン30mg/日の全身投与を開始したところ, 徐々に創部の肉芽組織が増殖し, 改善傾向となった。創部状態の外來管理が可能となった術後50日目で退院となり, 術後150日目に創部がほぼ上皮化したことからステロイド投与を終了した。壊疽性膿皮症は疼痛を伴う無菌性潰瘍を主徴とする好中球性皮膚症であり, 術後の創部合併症において感染治療が奏効しない場合は, 壊疽性膿皮症の可能性を考慮すべきである。

P-44-1 深部静脈血栓症の加療中にヘパリン起因性血小板減少症を発症し、アルガトロバン投与にて妊娠管理を行った1例

国立別府医療センター

広瀬奈津子, 大塚裕一郎, 新貝妙子, 大神靖也, 井ノ又裕介, 弓削乃利人, 穴見 愛

【緒言】ヘパリン起因性血小板減少症 (heparin induced thrombocytopenia, HIT) は、ヘパリンの投与中に免疫学的機序を介して血小板減少や血栓症をきたす、ヘパリンの重篤な副作用である。未分化ヘパリン投与と患者の2.7%にHITが出現したとの報告があるが、妊産婦はHITのリスクが低い(<0.1%)とされている。今回、妊娠中に発症した深部静脈血栓症 (deep vein thrombocytopenia, DVT) の加療中にHITを発症し、アルガトロバンに変更し妊娠継続・分娩に至った1症例を経験したので報告する。【症例】34歳, 1妊0産。自然妊娠が成立した。妊娠12週に左下肢のDVTを発症した。ヘパリンNaの持続静脈投与を開始した。妊娠18週、ヘパリンCaの皮下注射に変更したが、薬疹が出現したため、妊娠21週、ヘパリンNaの持続静脈投与を再開した。妊娠27週、38.8°Cの発熱を認め、血液検査で血小板数の低下とD-dimerの上昇を認めた。新たな血栓形成や感染症、HELLP症候群、またHIT発症などの可能性を考慮し精査を行い、HIT抗体陽性(1.5U/mL)を認め、HITと診断した。ヘパリンNaの持続静脈投与を中止し、妊娠28週よりアルガトロバンの持続静脈投与に変更した。その後アルガトロバンの投与にて治療域までAPTT延長を図り新規の血栓が出現することなくコントロール良好であった。妊娠37週に入り妊娠帰結の方針とし、誘発頭位経膈分娩に至った。アルガトロバンは胎盤移行性がある薬剤であるが出生後の児の血液検査で凝固系異常を認めなかった。【結語】ヘパリン投与中は妊婦であっても血栓症や血小板減少に注意を要し、HITが疑われる場合には速やかな対応が重要であることを実感した症例であった。

P-44-2 産褥期発症の深部静脈血栓症とD-dimerについて当院での検討

国立循環器病研究センター

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【目的】産褥期は深部静脈血栓症 (DVT) 発症の危険性が高い時期である。下肢の腫脹や疼痛などを契機として診断されることが多いが、無症状で肺血栓症を発症することもあるとされる。当院での産褥期発症のDVTにおいて、下肢症状の有無やD-dimerについて検討を行った。【方法】2013年5月から2021年9月の間に当院で分娩し、産褥6週間以内に下肢の血栓を疑う症状が出現した症例、D-dimerが自然低下しない症例、D-dimerが再上昇を認めた症例で下肢静脈超音波検査を施行した132例を対象とした。後方視的に下肢症状の有無、D-dimerの値、DVTの有無を検討した。【成績】132例中9例(6%)に新規発症のDVTを認めた。下肢症状があり超音波検査を施行した症例は10例で、うち4例(40%)でDVTを認めた。D-dimerの値で超音波検査を施行した122例では5例(4.0%)でDVTを認め、全例D-dimerが産後1週間で自然低下しない症例であった。この5例中3例は分娩後のVTEリスク分類が中間リスク、2例は低リスクであった。またD-dimerの値で超音波検査を施行し、DVTを認めた群と認めなかった群で、分娩直前のD-dimerの値、D-dimer最大値、またその上昇程度のいづれを比較しても有意差は認めなかった。下肢症状からの血栓の陽性的中率は44.4%、D-dimerの値での血栓の陽性的中率は4.0%であった。【結論】産褥期でのD-dimerのVTEの陽性的中率は低いことが示された。産褥期にD-dimerが高値である場合には、症状を確認し、注意深く理学所見を観察する必要がある。

P-44-3 帝王切開後の両肺動脈血栓症にPCPSと低体温療法が有効であった一例

春日部市立医療センター

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帝王切開後に両肺動脈血栓症にPercutaneous cardiopulmonary support : PCPS (経皮的心肺補助装置) と低体温療法が有効であった症例を経験したので文献的考察を加え報告する。症例: 30歳初産婦, 非妊時BMI38。骨盤位の適応にて妊娠37週帝王切開分娩となった。術後DVT予防目的にヘパリンの投与開始していた。手術終了約25時間後、いびき様の音を聞き訪室、床に腹臥位で横たわっているのを発見。脈拍触知されないうえ心マッサージ・アドレナリン投与と挿管人工呼吸を開始しCPRに成功した。肥満で帝王切開分娩後であること等から肺血栓症を第一に考え肺動脈造影CT撮影の予定としたが再度心停止。救命の為に診断よりもPCPS装着が先であると判断、カテーテル室へ移動しPCPS装着。人工呼吸器接続とPCPSにより循環動態は安定し、造影CT撮影、両肺動脈の主幹部にまたがる血栓の存在を確認した。また左大腿静脈血栓も認められた。術後出血を避ける為t-PAではなくウロキナーゼによる血栓溶解療法とヘパリン療法を選択。また脳保護目的に低体温療法を開始した。徐々にPCPS回転数落としても循環動態維持され、血栓症3日目、PCPS離脱、ウロキナーゼ投与終了し下大静脈フィルター設置した。6日目には人工呼吸器離脱。離脱直後は、会話はするが内容がかみ合わないことが多かったが徐々に回復した。肺動脈血栓症発症後35日目、独歩にて退院となった。脳機能は軽度の注意力低下またはごく軽度の短期記憶障害は残ったものの、夫の協力で育児可能なレベルまで回復した。

P-44-4 当院における VTE 合併妊婦の管理と治療における後方視的検討

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小林理沙

【目的】VTE（静脈血栓塞栓症）は、日本において以前は稀な疾患とされていたが、診断率の向上や、生活の欧米化によって増加している。当院で経験した周産期 VTE 合併症例について管理・治療、既往歴や背景等の関連性について後方視的に検討した。【方法】2016年1月から2021年8月までに当院で経験した17例の周産期 VTE 合併症例について、VTE 発症時期、治療経過、発症から治療終了までの凝固マーカーの推移、また既往歴や合併症、流産歴等を後方視的に検討した。【成績】VTE 発症時期は妊娠初期7例、妊娠中期4例、妊娠後期1例、産褥期5例であり、そのうち3例はPE合併を認めた。発症部位は、下肢14例と最も多く、内頸2例、外腸骨1例であった。VTEの既往は3例あり、血栓性素因は抗リン脂質抗体症候群2例、プロテインS低下1例で認めた。流産の既往は2例で認めた。治療は妊娠中ではヘパリンを使用し、産褥にワーファリンやDOACに切り替え治療を行った。治療期間は最短で6日間、血栓消失に要した期間は平均120日間、血栓が溶解せず現在も治療を継続している症例が2例であった。Dダイマーの中央値は7.4で、検査を行った16例全例で陽性となった。可溶性フィブリン（SF）はVTE発症早期から上昇する凝固マーカーであるが、61%で陽性であり、治療開始からすみやかに低下し12日目は87%が陰性化した。【結論】周産期に発症するVTEは妊娠初期と産褥期の2峰性に発症する傾向がみられた。妊娠初期にVTEを発症する誘因として妊娠悪阻が考えられ、悪阻の症状を有する妊婦に対してVTEの注意喚起を行うことで発症予防・早期治療介入が期待される。またSFは治療後の評価の簡便なマーカーとしての可能性が考えられた。

P-44-5 切迫流産に対する自宅療養中に深部静脈血栓症を発症した1例

青梅市立総合病院
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【緒言】切迫流産の患者に対して自宅安静を指示することは一般的に行われている。しかしながら自宅安静についてはその有効性は確立しておらず、妊娠予後を悪化させる可能性も指摘されている。今回、切迫流産に対する自宅療養中に深部静脈血栓症を発症した症例を経験した。切迫流産を管理する上で問題となる合併症と考えられたので報告する。【症例】35歳5妊1産（自然流産3回、帝王切開1回）。自然妊娠成立後、妊娠5週に性器出血と腹痛を認め切迫流産と診断した。自宅ではトイレ、シャワー以外は臥床していた。妊娠11週、左鼠径部痛と色調変化のため救急受診した。診察上、左下腿の色調変化、左鼠径部と膝窩の圧痛を認め、下肢超音波検査で左大腿静脈から左膝窩静脈までの血栓を認めた。Dダイマーは23 μ g/mlと上昇していた。深部静脈血栓症の診断で入院の上、未分画ヘパリン15000単位/日の持続静注を開始し、22000単位/日まで増量してAPTTは目標値に達した。11病日に皮下注射に切り替え24病日に自宅に退院した。治療開始後は血栓症の増悪は認めなかった。既往帝王切開後妊娠のため、選択的帝王切開の方針とした。妊娠36週5日に入院し、ヘパリンを持続静注に切り替えた。また造影CTで血栓がないことを確認し、下大静脈フィルターは留置しなかった。妊娠37週4日選択的帝王切開術を行った。術直後よりヘパリン10000単位/日持続静注を再開し、術後1日目からワルファリンを開始した。術後7日目にヘパリンを終了し退院、外来管理を継続している。【結語】切迫流産の外来管理中には、深部静脈血栓症の発症を念頭におき、安静の程度や深部静脈血栓症の徴候について、適切な指導と観察が必要である。

P-44-6 妊娠後期に発見されたアンチトロンビン欠乏症合併妊娠の一例

和歌山医療センター
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【緒言】アンチトロンビン（以下ATと略す）欠乏症は血栓性素因の一つであり、日本人でのAT欠乏症の頻度は0.15%とまれである。AT欠乏症合併妊娠では不育症・胎盤循環障害・妊娠高血圧腎症といった産科的合併症との関連が知られている。周術期に血栓症発症なく良好な転帰を得たAT欠乏症合併妊娠の1例を経験したので報告する。【症例】30代4妊0産（自然流産3回）既往歴：糖尿病 家族歴：特記なし 当院にてIVFにより妊娠成立。糖尿病合併妊娠のため血糖測定と食事療法を行い、児頭大きめ（+2.0SD程度）で推移していた他、妊娠経過は良好であった。妊娠後期（妊娠37週5日）の採血で尿酸高値（7.2mg/dL）とAT活性低値（45%）を認めた。Lo-HDPや難産といった合併症ハイリスクと考え、妊娠37週6日から入院し陣痛誘発を開始した。妊娠38週1日AT活性39%まで低下認め先天性AT欠乏症が疑われた。血栓症予防のためATIII製剤連日投与を開始。下肢静脈エコーにて血栓は認めず、弾性ストッキング着用と離床を促進した。妊娠38週5日、分娩停止と診断し緊急帝王切開を行った。術前のAT活性は82%であった。出生児は3110g、Apgar Score10/10、術中出血量（羊水込み）790gであった。術後1日目にAT活性72%と低下傾向認め、ATIII製剤単回投与と抗凝固療法を開始した。AT活性は術後2日目74.5%、術後6日目63%と低下傾向を示したため同日再度ATIII製剤を投与し、術後7日目にAT活性81.3%まで上昇、母児ともに全身状態良好で同日退院となった。【考察】本症例では不育症・不妊歴があり、AT欠乏症と関連していた可能性が示唆される。今後の血栓症発症を予防するためにも遺伝学的検査の検討や次回妊娠時の慎重なフォローが必要となる。

P-45-1 ART患者における不妊治療初診時と妊娠初期の不安が周産期予後に及ぼす影響について

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【目的】妊娠中の不安は周産期予後に関与する可能性が指摘され、早産や低出生体重児の割合増加が報告されている。一方、不妊治療患者は治療中から不安を抱えることも多いが、妊娠前の不安が周産期予後に及ぼす影響については明らかではない。今回、ART治療後妊娠女性について、不妊治療施設初診時と妊娠初期の不安が周産期予後に及ぼす影響について検討を行った。【方法】対象は2018年1月～2019年9月にT不妊治療施設で胚移植を行い分娩に至り、初診時および/または妊娠初期にHADS (Hospital Anxiety and Depression Scale) 質問紙に回答した女性で不安項目の合計が8点以上を不安ありとした。周産期予後は分娩施設からの調査票に基づき、後方視的に検討を行った。本研究はT施設の倫理委員会で承認を受けオプトアウトを行った。【成績】初診時不安ありは32/210人(15.2%)で、不安ありと不安なし群の比較において児体重・在胎週数・Apgar Score (5分)・早産率・HDP率・帝王切開率に差を認めなかった。一方、妊娠初期不安ありは90/634人(14.2%)で、不安あり群で早産率が高い傾向(14.4% vs 8.3%, $p=0.060$)を認めた。また、初診時・妊娠初期ともに不安ありは13/210(6.2%)で不安なし群との比較で周産期予後に差を認めなかった。【結論】今回の検討で妊娠初期不安と早産率はこれまでの報告と同様関連が示されたが、不妊治療初診時の不安と周産期予後には関連を認めなかった。初診時から継続的と考えられる不安も周産期予後と関連していなかった。妊娠成立後、新たに生じた不安が周産期予後に影響を及ぼす可能性が示唆された。

P-45-2 DVDを用いた受動的的心理教育がエジンバラ産後うつ病評価票スコアへ与える効果

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【目的】有効な産後うつ病発症予防策として対人関係療法や認知行動療法が報告されているが、専門技術と時間を要するため日常診療で全ての産褥婦に実施することは困難である。一方、映像視聴をはじめとする受動的的心理教育は簡便に施行でき、産後うつ病予防に有効であったとの報告もある。施行可能かつ有効な予防策確立を目指し、産後うつ病に関する受動的的心理教育を目的とした当院独自のDVDを作成した。このDVD視聴が産後一か月健診でのエジンバラ産後うつ病評価票(EPDS)スコアを低下させるかを検討した。【方法】本研究は後方視的二群間比較である。2018年1月～2021年2月に当院で分娩した褥婦699人を対象とし、DVD視聴のない2018年1月～2019年6月に分娩した褥婦を非視聴群、DVD視聴のある2019年11月～2021年2月に分娩した褥婦を視聴群とした。DVDは分娩後の入院中に褥婦が個別に視聴した。診療録より妊娠・分娩関連項目と産後一か月健診時のEPDSスコアを抽出した。傾向スコアマッチングを用いて二群の患者背景を調整し、EPDSスコアを比較した。【成績】非視聴群401例、視聴群298例。傾向スコアマッチングでの調整後(両群とも233例)の患者背景に二群間で有意差を認める項目はなかった。全例でのEPDSスコアの平均値(±SD)は、非視聴群4.96(±4.17)、視聴群4.67(±3.82)で、二群間に有意差はなかった(p 値=0.43)。サブグループ解析では、児に奇形のある褥婦において、非視聴群7.69(±5.57)、視聴群4.80(±4.20)で、有意に視聴群で低値であった(p 値=0.014)。【結論】DVDでの受動的的心理教育は簡便であり、児に奇形のある褥婦に対してはEPDSスコア改善に寄与する可能性が示唆された。

P-45-3 単科精神科病院における周産期症例の実態調査

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【目的】周産期メンタルヘルスケアにおいては、支援を要する妊産婦のスクリーニングと、多機関の連携が必要となる。産科医療機関や地域母子保健担当者は、必要に応じて精神科での評価を依頼する。一方精神科では、周産期症例に対応できる総合病院へ集約される傾向がある。単科精神科病院における周産期症例の実態を調査し、診療課題について検討した。【方法】2017年1月から2021年9月までに単科精神科病院2施設に受診した周産期症例のうち、初診例を対象とし、後方視的に診療録調査を行った。【成績】対象期間に受診した周産期症例は222例で、そのうち初診は115例であった。初診例の受診時期は産後が80例(69.6%)で、特に産後3か月から6か月に多かった。紹介元は行政機関、産科、他院精神科の順に多かった。診断は、うつ病、双極性障害、統合失調症、急性一過性精神病性障害、強迫性障害の順に多かった。42例(36.5%)が入院し、そのうち9例は母児同室とした。外来通院例のうち30例(26.1%)が自己中断していた。【結論】単科精神科病院における周産期初診例は、産科での健康診査が終了した以降の時期に多く受診していた。入院管理では単科精神科病院としては数少ない母児同室を整備し、育児能力の把握や精神ケアに利用した。また妊産婦が自由に意見交換する場を設け、多職種で妊産婦を支援するようにした。しかしながら通院自己中断例があり、行政機関と連携してフォローアップするなど、長期的な支援体制が課題である。

P-45-4 機械学習を用いた産後うつ予測ツールの構築

名古屋大附属病院

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【目的】産後うつは妊産婦の10~20%に発症するとされ、早期検出、早期介入が必要と考えられている。今回我々は、既存の周産期情報を用いた産後うつを予測する機械学習モデルを作成し、その有用性を検証することを目的とした。【方法】主にローリスク妊娠を管理する12施設において、2014年4月~2018年12月に分娩管理した妊産婦のうち、多胎、死産、データ欠損症例を除外した10013例を研究対象とした。まず、分娩日に基づいて訓練データ6930症例と検証データ3083症例に割り当てた。次に、訓練データを用いて1か月健診でのEPDS9点以上を予測する以下の3つの機械学習モデルを作成した：モデル1-妊娠初期に得られた母体背景(18変数)、モデル2-妊娠分娩関連因子を加えた退院時までには得られる項目(38変数)、モデル3-モデル2に加え2週間健診における乳房・睡眠・精神状態に関する問診(41変数)。さらに、検証データを用いて各モデルの予測精度(AUROC)を算出した。【成績】1か月健診でのEPDS9点以上は644/10013例(6.4%)であった。各モデルのAUROCは以下に示す結果であった：モデル1(0.53~0.64)、モデル2(0.57~0.63)、モデル3(0.64~0.70)。作成した3つのモデルの中で、2週間健診の情報を追加したモデル3のAUROCが最も高く、モデル1や2と比べ有意に予測精度が改善した(各々 $p < 0.01$, $p < 0.01$)。【結論】予測精度は海外における既報より低く、既存の周産期情報のみを用いた産後うつ予測ツール構築には限界があることが示唆された。一方で、2週間健診などの早期の心理的評価の実施が産後うつの早期検出に有用である可能性が示唆された。

P-45-5 新型コロナウイルス感染症の流行が妊産婦に与える精神的ストレスの解析

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【目的】新型コロナウイルス感染症の流行による妊産婦の精神的ストレスの悪化の報告があるが、流行の長期化および患者数の更なる増大による影響は検討されていない。本研究では新型コロナウイルス感染症の第3波以降の流行が妊産婦の精神的ストレスに与える影響を検討した。【方法】2019年5月から9月および2021年の同時期に当院で1か月健診を受診しエジンバラ産後うつ病質問票のスコア(EPDS)により評価した症例を対象とした。対象者のEPDS実数および9点以上および自傷因子にチェックのついた症例の割合、もしくはそのいずれかを満たす症例をハイリスク群としてその割合を比較した。【成績】対象となった症例は2019年の症例(流行前群)が359例、2021年の症例(流行後群)が347例であった。両群間で母体背景には差を認めなかった。EPDSは流行前が3(0-18)、流行後群が3(0-28)と両群間で差をみとめなかった($P=0.42$)。高値群の割合は流行前群で9.2%、流行後群で12.7%と増加傾向を認めたが有意差は認めなかった($P=0.15$, 95%CI 0.43-1.12)。自傷因子にチェックのついた症例は高値群の割合は流行前群で6.4%、流行後群で5.5%と有意差は認めなかった($P=0.64$, 95%CI 0.63-2.21)。EPDS高値または自傷因子にチェックのついたハイリスクは高値群の割合は流行前群で11.7%、流行後群で13.5%と増加傾向を認めたが有意差は認めなかった($P=0.85$, 95%CI 0.54-1.32)。【結論】新型コロナウイルス感染症の流行による妊産婦の精神的ストレスは結果的には有意な差は得られなかったが、コロナ窩でより点数が高い傾向を認めた。EPDS高値のハイリスク妊婦に対してはより適切なケアが必要である。

P-45-6 当院における周産期メンタルヘルス外来の取り組みと要支援妊婦の拾い上げについて

仙台赤十字病院

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【目的】当院は常勤の精神科医師は不在であったが、他院精神科医師の応援を得て2017年より周産期メンタルヘルス外来を開設した。その現状について検討し支援を要する妊婦のサポートや今後の診療体制の拡充に繋げることを目的とした。【方法】2017年9月から2021年9月に周産期メンタルヘルス外来を受診した妊産婦を対象に診療録から後方視的に調査した。【成績】上記の期間に周産期メンタルヘルス外来を受診した妊産婦は55例であり分娩時年齢の中央値は32歳(19-41歳)、初産は29例であった。精神疾患既往歴があったのは15例であり、パニック障害や適応障害が多かった。エジンバラ産後うつ病質問票の中央値は10点であり、一般的に産後うつの可能性が高いといわれている9点を上回っていた。また28例で医療ソーシャルワーカー(MSW)の介入があり、飛び込み分娩や支援不足による育児不安、家族関係の悪化を主訴とする症例が多く、産後も地域の保健師などによる継続的な行政介入が必要となる例も少なくなかった。臨床心理士の介入があったのは44例であり、外来開設直後は問診票などから産科医師や助産師が要支援と判断した症例が多かったが、2020年以降では本人希望による臨床心理士のカウンセリングを経て受診につながる症例が増加していた。【結論】精神科受診の必要性を判断する手段の一つとして、臨床心理士の介入により、リスク因子の少ない見過ごされてしまう要支援妊婦を積極的に拾い上げることができた。要支援妊婦には精神科医師による治療だけでなく臨床心理士やMSWなど、行政機関も含めた多方向からの介入が必要となるため、多職種との情報共有や連携を強化することが重要であると考えられる。

P-45-7 産後うつとリン酸エタノールアミンの関連に関する検討

福島県立医大

菅野重矢, 山口明子, 小宮ひろみ, 藤森敬也

【目的】産後うつが発症するメカニズムはいまだ明らかではない。また、産後うつのスクリーニング検査としてエジンバラ産後うつ病質問票 (EPDS) が使われているが、早期発見のためのバイオマーカー開発が期待される。リン酸エタノールアミン (PEA) は脳内に多く存在するリン酸アナンタミドから生成される物質である。大うつ病性障害で低値を示すことが報告されているが、これまで産後うつに関する報告はない。さらに、産後うつとの関連が研究されている CRP は、PEA と結合することが知られている。本研究は、産後うつ疑い産婦の PEA と血清高感度 CRP (Hs-CRP) の変化及び PEA と Hs-CRP の関連を明らかにすることを目的とした。【方法】本院で分娩管理を行った産婦 197 名を対象とし、産褥 40 日目の EPDS の点数が 9 点以上を産後うつ疑い (A 群)、9 点未満を非産後うつ (B 群) とした。産褥 5 日目と 40 日目に PEA と Hs-CRP を測定し、t 検定を行った。【成績】A 群は 19 症例 (9.6%) であった。初産婦、有職者、児の出生体重が低い産婦の割合が A 群で有意に高かった。PEA 値は産後 5 日目で A 群 $1.51 \pm 1.25 \mu\text{M}$ 、B 群 $1.22 \pm 0.90 \mu\text{M}$ 、産後 40 日目で A 群 $1.96 \pm 1.55 \mu\text{M}$ 、B 群 $1.63 \pm 0.98 \mu\text{M}$ で両群に有意差を認めなかった。しかし EPDS の点数が高い症例では PEA が低値となる傾向を認めた。Hs-CRP は産後 5 日目と 40 日目において A 群、B 群に有意差を認めなかった。また EPDS 値と PEA、Hs-CRP について相関関係を認めず、PEA と Hs-CRP も相関関係を認めなかった。【結論】本研究は産褥期 PEA の変化を検討した最初の報告である。EPDS において区分点を 8/9 点とした場合、PEA の変化を認めなかった。しかし、EPDS が高い産婦において PEA が低値となる傾向を認めさらなる検討が必要である。

P-45-8 当院で過去 15 年間に経験した精神疾患合併妊娠：ソーシャルワーカー介入の観点からの検討

東海大

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【目的】精神疾患合併妊娠は近年増加傾向にある。当院では以前より産科・小児科と精神科、ソーシャルワーカー (MSW) での合同カンファレンスを定期的実施し、精神疾患合併患者や社会的ハイリスク患者の情報共有を行っている。今回、MSW 介入の観点から自験例を検討した。【方法】2006 年 4 月から 2021 年 9 月までに当院で分娩した 315 例の精神疾患合併妊娠を対象とした。精神疾患の分類 (ICD-10 による)、MSW 介入の有無と介入回数、児童相談所介入の有無、分娩時妊娠週数、分娩形式につき後方視的に検討した (施設内研究倫理委員会承認)。【成績】症例数は 315 例 (全分娩数の 4.1%) で年度毎に分娩数に対する割合は増加傾向を示した ($R^2=0.58$)。また、MSW の介入件数は 104 件 (33.0%) であり、うち介入率は発達障害 (F8) : 7/7 例 (100%)、統合失調症 (F2) : 22/46 例 (47.8%)、気分障害 (F3) : 41/103 例 (39.8%) と多かった。MSW が介入している特徴として、早産 (OR 2.58, 95%CI : 1.2-4.5, $P=0.014$)、児童相談所介入 (OR 29.2, 95%CI : 3.5-240.8, $P=0.002$)、2010 年以降 (OR 2.62, 95%CI : 1.51-4.53, $P=0.001$) であった。児童相談所介入症例 12 例のうち、11 例は MSW の介入があった。また、精神疾患の産後増悪により死亡した症例は 2 例であり、これらでは MSW の介入はなかった。【結論】MSW 介入症例は近年増加傾向であった。また、児童相談所介入例の多くは MSW との連携が取れており、行政との円滑な連携ができた。一方で、精神疾患の産後増悪は母体死亡に繋がるリスクがあると認識され、該当症例をいかに事前に察知し、MSW の持つ調整援助・問題解決機能につなげていくかが今後の課題の一つと考えられた。

P-45-9 周産期におけるストレス関連症状および産褥精神障害と自律神経活動の客観的評価との関連

弘前大

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【目的】近年心拍変動の周波数スペクトル解析により、自律神経活動の定量化が行われている。今回、妊婦及び褥婦において自律神経活動の測定を行いストレス関連症状や産褥精神障害との関連を検討した。【方法】自律神経活動の測定はハートリズムスキャナー (米国 BIOCROM 社) を用いた。対象は 2020 年 8 月~2021 年 9 月の間に当科で分娩した妊婦 97 名で、分娩開始前・分娩数日後、産褥 1 か月健診時の自律神経活動測定と Visual Analog Scale (VAS) によるストレス関連症状 (疲労感・肩こり・ほてり・頭痛・頭重感・不安感・憂鬱・イライラ感) の問診及びエジンバラ産後うつ病質問票 (EPDS)、赤ちゃんへの気持ち質問票 (ボンディング) を用い検討した。【成績】妊婦の年齢の中央値は 34 歳であり、初産婦は 46 名、経産婦は 51 名であった。自律神経活動は周波数により交感神経系を反映する SNS index と副交感神経系を反映する PNS index が算出され、値が高いほど各神経系の活動が高いとされる。ストレス関連症状では、妊娠中の疲労感と SNS index との間に正の相関、PNS index との間に負の相関を認めた。産褥精神障害に関して、分娩数日後では EPDS と SNS index の間で正の相関、PNS index との間で負の相関を認めた。分娩数日後のボンディングや産褥 1 か月の EPDS およびボンディングと自律神経活動測定値との間には今回は相関を認めなかった。妊娠中及び産褥期のストレスに交感神経系の活動が関与している可能性が示唆された。【結論】産褥精神障害について、これまでは自己記入式の評価 (主観的評価) のみであったが、自律神経活動による客観的評価ができる可能性が示唆された。各種パラメーターについて統計学的解析を行い報告する。

P-45-10 新型コロナウイルス感染症によって生じた褥婦の心理的影響に対する検討

東北医科薬科大病院

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【目的】新型コロナウイルス感染症の拡大により面会制限が行われるようになり、妊娠中の両親学級や立ち合い分娩などができなくなり、妊娠中の指導の在り方に変化をきたし、妊娠中から様々な不安が見られたり、育児不安を訴える褥婦が多くみられるようになった。今回、産褥期に行われているエジンバラ産後うつ病質問票 (EPDS) を用いて、面会制限による褥婦の心理的变化を検討した【方法】2019年11月から2021年9月に当院で分娩した症例のうち、面会制限前の群 (Group1, N=24)、面会制限後の群 (Group2, N=95)、立ち合い分娩再開群 (Group3, N=17) を対象とし比較した。産褥4日目と2週間健診時、1か月健診時のEPDSの得点を後方視的に検討した。【成績】産褥4日目のEPDSはGroup1で 4.0 ± 3.96 点、Group2で 5.4 ± 4.43 点、Group3で 3.6 ± 3.48 点、2週間健診時のEPDSはGroup1で 3.5 ± 3.91 点、Group2で 4.6 ± 4.37 点、Group3で 3.9 ± 3.38 点、1か月健診時のEPDSはGroup1で 2.6 ± 3.2 点、Group2で 3.6 ± 3.86 点、Group3で 2.6 ± 2.5 点であった。また、Group1のEPDS9点以上の割合は産褥4日目で4%、2週間健診時で4%、1か月健診時で1%であり、Group2の各々は、20%、18%、10%、Group3の各々は2%、4%、0%とEPDS9点以上の割合はGroup2においてすべての検査時期で高く、また産褥4日目におけるEPDS9点以上の割合が高かった。【結論】面会制限後は産褥4日目のEPDSの得点が他2つの群よりも高値を示す傾向にあり、また9点以上の割合も高く、分娩直後の様々な不安に関して面会制限や社会的にも規制される生活が関連していると考えられた。今後も感染の状況を踏まえ、可能な限り育児中の不安感や孤独感の解消に取り組むことが重要と考えた。

P-45-11 精神疾患を合併した社会的ハイリスク妊婦に対し医療・行政間で連携し包括的ケアを行なった2例

弘前大附属病院

杉本里奈, 大石舞香, 横山美奈子, 伊東麻美, 田中幹二, 横山良仁

【緒言】精神疾患合併や社会的ハイリスク妊婦は児童虐待の要因ともなり、適切な介入が重要である。精神疾患合併社会的ハイリスク妊婦に対し、妊娠中～産褥期にかけて医療・行政間で連携支援を行なった症例について報告する。【症例1】24歳、4妊0産。20歳からうつ病、強迫性障害などの既往あるが加療なし。生活保護受給者で入籍予定なし。15週で初回妊健受診し胎児腹壁破裂指摘。24週切迫早産で緊急入院となるが精神状態悪化のため、精神科コンサルト。小児期逆境性体験。周産期うつ、強迫性障害など疑われたが内服加療拒否。多職種カンファにて医療・行政間で今後の包括的ケアについて情報共有した同夜に脱走。翌日帰院したものの入院同意得られず退院。38週帝王切開術施行。産褥は精神状態増悪なく、精神科受診および保健師による自宅訪問継続。子の父のサポートも加わり、現在精神状態は安定しフォロー継続中である。【症例2】43歳、6妊4産。統合失調症指摘あるも加療なし。子の父とは入籍予定なし。経済的事情で妊健は2度のみで複数医療機関とトラブル。家族のいる当地での分娩希望し33週首都圏より里帰りするも予約日に受診しないなどトラブルあり。38週当科紹介。39週自然分娩。最低限必要な住居、育児用品、サポート体制も確立されておらず多職種カンファを開催するも、攻撃的態度、虚言および早期退院希望あり退院。元々の居住地での産褥健診先を確保するも受診せず、サポート体制確立に難渋。【考察】精神疾患合併妊婦は時に急激な増悪あり、緊急アセスメント、早期精神科相談、行政への情報提供などの介入を要する。母児とも不幸な転機に至ることもあり多職種連携して取り組むべきである。

P-45-12 無痛分娩と周産期メンタルヘルスの関連性について

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【目的】当院は計画無痛分娩のため、夜間・休日は無痛分娩希望者に対応できない体制である。無痛分娩希望者が予定外に無痛分娩でなく分娩となった場合、産褥期のEPDS (Edinburgh Postnatal Depression Scale) は高値となり、周産期メンタルヘル스에影響を及ぼすと仮説し、希望外の分娩様式が周産期メンタルヘル스에及ぼす影響について検討した。【方法】2020年10月から半年の間に分娩を行った患者655人中、子宮内胎児死亡・予定帝王切開・多胎・早産を除外した488人を対象とした。分娩後EPDSを実施した診療録を調査し後方視的に検討した。EPDS9点以上を要支援者とした。【成績】要支援率は、A群 (無痛分娩希望・無痛経陰分娩) : 15%、B群 (無痛分娩希望・無痛分娩施行中に帝王切開) : 23%、C群 (無痛分娩希望・非無痛経陰分娩) : 11%、D群 (無痛分娩希望・非無痛分娩施行中に帝王切開) : 50%、E群 (無痛希望なし・非無痛経陰分娩) : 11%、F群 (無痛希望なし・非無痛分娩施行中に帝王切開) : 26% だった。無痛・非無痛関係なく分娩様式において、経陰分娩 : 12%・帝王切開 : 26% であり、分娩様式に関係なく、無痛分娩 : 16%・非無痛分娩 : 4% であった。ともにカイ二乗検定で有意差を認めた。【結論】希望通りの分娩が叶った群では要支援率は低く、分娩転帰が帝王切開になった群は、いずれも要支援率が高かった。無痛分娩希望者は、分娩様式に関わらず要支援率が高いため、無痛分娩後フォローは重要であり、分娩に対する振り返りの時間を設ける意味でも、2週間健診や1か月健診でフォローする体制が必要と思われる。

P-45-13 当院における緊急事態宣言前後の産褥メンタルヘルスの変化

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【目的】我々はCOVID-19の世界的流行を経験し、社会的制限下で様々なストレスにさらされているが、産褥の心理的負荷を評価した報告は少ない。コロナ禍において当院の妊産婦背景とエジンバラ産後うつ病自己評価票 (Edinburgh Postnatal Depression Scale: EPDS) の変化を検討した。【方法】2019年7月から2021年7月までに当院で分娩した単胎妊娠のうち、産褥健診でEPDSを評価した791名を対象とした。初回緊急事態宣言が発令された2020年4月7日を基準とし、2020年3月31日までをpreコロナ群 (P群)、4月1日以降をwithコロナ群 (W群) として2群に分け後方視的に検討した。EPDSは9点/30点以上を高得点者とした。【成績】P群596例、W群195例であり同月比較でP群に比べW群では分娩数は減少した。経産婦はP群50.2%、W群61.0%で有意に経産婦の割合が増加した ($p < 0.01$) が、母体年齢や妊娠合併症に有意差は認めなかった。EPDS高得点者はP群11.9%、W群12.8%であり有意差を認めなかったが、自傷についての問いである「質問10」が1点以上であった割合はP群5.5%、W群10.8%でありW群で有意に増加した ($p < 0.05$)。また経済的困窮や育児不安などで医療ソーシャルワーカー (MSW) が介入した割合はP群5.7%、W群9.2%と増加傾向を認めた。MSW介入妊婦はEPDS高得点者が25.0%、「質問10」1点以上の者が21.2%であり、介入を要さない妊婦と比較し有意に高値であった ($p < 0.01$)。【結論】COVID-19の流行に伴い当院の分娩数は減少したが、MSWの介入を要した妊婦の割合は増加していた。このような社会的ハイリスク妊婦はEPDS高得点・産後うつ病のリスクが高く、コロナ禍においてメンタルヘルスにリスクを有する割合が増加している可能性がある。

P-45-14 妊娠初期の鉄・亜鉛欠乏と周産期うつ症状との関連

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【目的】本邦の有経女性は鉄欠乏の頻度が高く、鉄欠乏性貧血には亜鉛欠乏の合併が多い。妊娠期の鉄欠乏性貧血は産後うつ病のリスク因子とされているが、貧血のない鉄欠乏や亜鉛欠乏と産後うつとの関連についての研究は少ない。今回、貧血のない鉄欠乏及び亜鉛欠乏と周産期のうつ症状の関連とを検討した。【方法】当院で妊娠初期から管理し2018年8月から2019年9月に分娩に至った症例のうち、早産、双胎、胎児奇形、精神疾患既往を除いた35例について、初期のHb・フェリチン・亜鉛と、妊娠中期と産後1か月のエジンバラ産後うつ病質問票 (EPDS) を解析した。貧血、鉄欠乏、亜鉛欠乏及び潜在性亜鉛欠乏の基準はそれぞれHb11g/dl未満、フェリチン30ng/ml未満、亜鉛60及び80 μ g/dl未満とした。【成績】Hb、フェリチン及び亜鉛の中央値はそれぞれ12.5 (12.0-13.0) g/dl, 35.5 (18.9-76.6) ng/ml, 72.0 (61.0-82.0) μ g/dlであった。35例中、貧血も鉄欠乏もない正常群は19例、貧血のない鉄欠乏群は13例で、貧血がない症例のうち41%に鉄欠乏を認めた。EPDSの点数は、正常群では中期は中央値4.0、平均値7.2、産後は中央値2.0、平均値5.6と中期から産後で変化なく、貧血のない鉄欠乏群では中期は中央値4.0、平均値3.3、産後は中央値5.0、平均値6.6と中期から産後で有意に上昇を認めた ($p < 0.05$)。亜鉛はフェリチンと弱い相関を認め (相関係数0.47)、亜鉛欠乏および潜在性亜鉛欠乏は35例中8例 (23%) および23例 (66%) だったが、いずれもEPDSとの関連は認めなかった。【結論】妊娠初期の貧血がない鉄欠乏、潜在性を含む亜鉛欠乏は比較的頻度が高く、初期に貧血のない鉄欠乏があると産後にうつ症状が悪化する可能性が示唆された。

P-46-1 D-dimer 高値が診断の一助となった妊娠後期発症の大動脈解離の一例

仙台市立病院

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【緒言】若年女性における大動脈解離の発症の約半数は、妊娠に合併するといわれており、妊娠に伴う循環血漿量の増大や心拍出量の増加に加え、エストロゲンの曝露による血管壁の脆弱化が原因と言われる。今回、D-dimerの上昇により急性大動脈解離を疑い、診断に至った妊婦の一例を経験したため報告する。【症例】37歳女性。身長170cm、体重74.3kg。妊娠歴: 1妊0産。既往歴: 気管支喘息、漏斗胸手術。X-1日 (妊娠35週0日) 11時頃自宅で家事をしている際に背部痛を自覚。15時に前医受診し、尿管結石の疑いとして鎮痛薬投与され入院となった。X日 (妊娠35週1日) にも症状改善なく、当院救急科へ搬送された。受診時にD-dimer 11 μ g/mlと上昇を認めたため腎梗塞の疑いとして造影CTを施行したところ、急性大動脈解離の診断となり、当院で緊急帝王切開を施行した。術後は降圧のみで経過良好であったが、今回の経緯及び体格所見よりMarfan症候群が疑われ、今後遺伝子検査を施行する方針である。【考察】妊婦の腰背部痛は約半数に認められる症状の一つであるが、中には母児の生命に関わる重篤な疾患が原因であることがある。妊娠中でも起こりうる致死疾患に大動脈解離があることを念頭に置き、診療にあたる必要がある。また妊婦におけるD-dimerの計測は血栓疾患の検索に有用となるか、文献的考察を交えて報告する。【結論】妊娠中に急性大動脈解離を合併した一例を経験した。D-dimerは妊娠経過に伴い上昇する傾向はあるが、妊娠中も血栓性疾患などのスクリーニングに有用であると考えられた。今後妊婦の血栓性疾患の検索にD-dimerを使用するにはカットオフ値を検討する必要がある。

P-46-2 急性心筋炎既往のある女性の妊娠出産の検討

国立循環器病研究センター

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【目的】急性心筋炎は心筋を主座としたウイルス感染や自己免疫機序で発症する炎症性疾患である。心筋炎既往妊娠の周産期経過に関する報告は少なく、今回我々は当院で妊娠管理をした18妊娠について検討した。【方法】過去に心筋炎と診断され、2006年～2021年に当院で妊娠管理をした11人、18妊娠を対象とし、診療録に基づき後方視的に検討を行った。【成績】心筋炎発症時の年齢中央値は22歳 [1-32歳] で、劇症型が5人 (45%) であった。原因は、ウイルス性が6人 (EBウイルス2人、コクサッキーウイルス1人、他3人)、好酸球性が3人、不明が6人であった。発症時の最低左室駆出率 (Ejection Fraction, 以下EF) の中央値は31%、劇症型では19%であった。妊娠時の年齢中央値は32.5歳で、心筋炎発症から妊娠までの期間の中央値は12.5年 [5-29年] であった。全症例が、妊娠開始時点のNYHA分類1度で、EFは正常範囲であった。3例は妊娠後期または産後にEFの軽度低下を認めたが、その後3例とも回復を認めた。この3例は妊娠前もしくは初期のEFが正常下限であった。分娩週数の中央値は39週で、心疾患を理由として早期分娩を図った症例はなかった。経陰分娩が13例、帝王切開での分娩が5例 (うち緊急が2例) であり、帝王切開術の適応は全て産科適応であった。児のアウトカムは良好であった。【結論】心筋炎の既往があり妊娠開始時点で心機能が正常範囲である女性では、妊娠出産経過で心血管合併症を認めなかったが、17%にEF軽度低下を認めた。これらは妊娠初期にEFが正常下限であり、心筋炎後心機能が正常に回復しても、妊娠直前または初期の心機能精査が重要であり、また注意深い周産期経過観察が必要と考える。

P-46-3 HCM合併妊娠とその1年後の予後について

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【目的】肥大型心筋症 (HCM) は心筋の異常肥大と拡張能低下を病態とし、左室流出路閉塞をきたすHOCMと閉塞を来さないHNCMに分かれる。妊娠の循環血漿量の増加により左室流出路の圧較差増大や心拍数増加により不整脈やうっ血性心不全のリスクが上昇すると言われているが、長期的な母体予後の報告は少ない。【方法】当院にて生児を得た16人 (HOCM9人、HNCM7人うち拡張相1人) の17妊娠 (HOCM9妊娠、HNCM8妊娠) を対象とし妊娠成立から産後1年までの母体死亡、心血管イベント (心不全、心原性失神またはICD作動、新規不整脈の発生) を後方視的に検討した。【成績】妊娠前ではβ遮断薬がHOCMで9/9例 (100%)、HNCM5/8例 (63%) で導入されていた。HOCMの6/9例 (66.6%) にMorrow術 (外科的心筋切除術) またはPTSMA (経皮的心室中隔アブレーション術) あるいは両方の非薬物療法が行われていた。妊娠中の心血管イベント (不整脈・心不全) 発生率はHOCMで非薬物療法が行われていた例では1/6例 (16%)、行われていない例では3/3例 (100%) であった。一方HNCMでは2/8例 (25%) であった。HOCMの2例では妊娠中または産直後に日持続性心室頻拍によりICD留置が行われた。産後1か月から産後1年では母体死亡、心血管イベントは観察されなかった。【結論】妊娠中にHOCMではより心血管イベントの発生頻度が多く、非薬物療法はその発生を軽減させる可能性がある。産後1年までの予後は比較的良好であるが、心機能や左室拡張障害、心筋の変化なども検討する必要性はある。

P-46-4 当院における僧帽弁形成術および僧帽弁生体弁置換術後妊娠の検討

国立循環器病研究センター

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【目的】僧帽弁逆流 (MR) に対する手術は主に弁形成術 (MVP) と人工弁置換術に分けられる。当院で経験したMVPおよび生体弁置換術 (MVR) 後妊娠について術式による心臓予後、産科予後に差がないかを検討した。【方法】2010年から2021年に分娩したMVP11例、MVR4例の心合併症、産科予後、長期弁機能予後について検討した。【成績】僧帽弁狭窄 (MS) を表す平均僧帽弁圧較差の中央値は妊娠前、初期がMVP 6.5 [2.3-12.0] mmHg, MVR 6.4 [4.0-12.0] mmHgと同等だったが、妊娠中期以降、MVPで7.5 [3.0-10.0] mmHg, MVRで13.5 [8.0-19.0] mmHgに増加した。分娩後1年でMVP 5.0 [1.4-17.0] mmHgまで回復し、MVRでは8.5 [6.0-10.5] mmHgとMSが残存した。左房容量の中央値は、妊娠前、初期でMVP 59.5 [41.0-162.0] ml, MVR 77.0 [65.0-89.0] mlだったが、分娩後1年ではそれぞれ91.0 [37.0-131.0] ml, 93.0 [69.0-131.0] mlと両者とも回復は不良だった。回復不良だった症例は中等度以上のMRが残存していた。妊娠中の心不全、不整脈の発症と、それらに起因する早産はMVP, MVRで0.0% vs. 25.0%, 9.1% vs. 25.0%, 0.0% vs. 25.0%だった。分娩後平均4.8年の観察期間で再手術率はMVP 27.3%, MVR 75.0%だった。【結論】心合併症や産科予後、弁の再手術率はMVRで多い傾向が見られた。MVRでは生体弁であってもMVPに比べて妊娠中、分娩後にもより注意を要する。

P-46-5 機械弁置換術後患者における妊娠中の治療量未分画ヘパリンによる抗凝固療法のプロトコールの検討

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【目的】機械弁置換術後患者の妊娠中の抗凝固療法は，国内で使用できる薬剤は限られており，また定まったプロトコールもない。通常，治療量未分画ヘパリン（UFH）を使用しモニタリングにはAPTTを用いるが，妊娠中は凝固因子の増加のためAPTTでの管理に苦慮する。我々は妊娠中の治療量UFHの管理を独自に作成したプロトコールで実施している。本研究では，APTTを用いたプロトコールを，凝固因子に左右されない抗Xa活性（ヘパリン血中濃度）を用いて検証する事を目的とした。【方法】対象は機械弁置換術後で妊娠中に治療量UFHを投与した5症例（僧帽弁置換術後3例，大動脈弁置換術後2例）である。症例は前向きに登録しAPTT測定後の残余検体を用い，抗Xa活性，VIII因子，VWF，アンチトロンビン（AT）活性を測定した。UFHは15単位/kg/時間で開始し，APTTを正常対照の2.0-3.0倍になるよう独自のノモグラムで調節し全妊娠期間UFHの持続点滴とした。AT活性値は70%以上を維持するようAT製剤を補充。分娩はヘパリン中止時間短縮のため予定帝王切開とした。【成績】VIII因子抗原量およびVWF抗原量は妊娠経過と共に増加した（トレンド検定， $p < 0.01$ ）。AT活性値は $78.2 \pm 11.0\%$ （mean \pm SD）。抗Xa活性は，概ね治療域（0.35-0.70 U/mL）内にあった。UFHの投与量は妊娠週数と共に増量したが，概ね30,000単位/日以内に留まった。また出血性，血栓性ともに重大なイベントは認めなかった。【結論】機械弁置換術後患者の妊娠中のAPTTによるUFHプロトコールを抗Xa活性を用いて検証した結果，概ね治療域内にある事が確認された。AT活性値を適切に維持する事は，ヘパリンの過剰投与を防ぐためにも重要である。

P-46-6 心疾患合併妊娠における，PGE2腔内留置製剤の使用経験

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【目的】分娩誘発の際，頸管未熟化例では従来，器械的な頸管拡張が行われているが，本邦でも腔内留置用のPGE2製剤が使用可能となり，当センターでは2020年6月から使用を開始した。PGE2 receptorは血管平滑筋や内皮細胞等に発現し，血圧に影響しうる。またPGE2は，血管壁のremodelingや血小板凝集に関与するとされ，これらの機序を介し母体の心機能に影響する可能性があるが，PGE2製剤の母体循環動態に与える影響はほとんど知られていない。本研究は，PGE2製剤による母体循環動態への影響を明らかにすることを目的とした。【方法】2020年6月～2021年6月に分娩誘発を行った心疾患合併妊娠28例を対象とした後方視的コホート研究を行った。PGE2製剤使用群=13例，非使用群=15例であり，両群間で介入を要した心血管イベントや血圧上昇の発生，分娩前後の心エコー，BNP値，体重の変化，分娩経過を比較検討した。【成績】非使用群で投薬を要した不整脈1例，表在性静脈血栓1例を認めた他，分娩～産後に介入を要した心血管イベントを認めなかった。介入を要した血圧上昇の発生に両群間で有意な差はなかった（PGE2群=5例（38.5%），非使用群=4例（20.7%）， $p=0.69$ ）。二元配置分散分析を行い，両群間の分娩前後での心エコー所見，BNP値，体重の変化を検討したが差はなかった。帝王切開率（PGE2群=38.5%，非使用群=13.3%， $p=0.20$ ）に有意な差を認めなかった。PGE2群では，6例（46.2%）で十分な頸管拡張が得られず，追加で機械的拡張を要した。【結論】PGE2製剤は心疾患合併妊娠の頸管熟化において，安全に使用できると考えられた。一方，使用経験は依然乏しく，さらに症例を蓄積して検討する必要があると考えた。

P-46-7 肥大型心筋症女性の妊娠中の心エコー変化と分娩後の長期予後について

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【目的】肥大型心筋症（HCM）の経過中に，肥大した心筋壁厚が非薄化し，左室収縮能低下（ $EF < 50\%$ ）と左室内腔の拡張を来たしたものを拡張相肥大型心筋症（D-HCM：dilated phase of HCM）という。予後不良と考えられているが，HCM合併妊娠において，妊娠中の負荷によりD-HCMへの移行を予測できるかどうかは不明である。今回，当院で経験したHCM合併妊娠の症例からD-HCMへの移行に関する予測因子がないかどうかを検討した。【方法】分娩後に一定の長期観察期間が得られた，1994年1月から2014年12月の間に当院で分娩したHCM合併妊娠のうち，妊娠初期-中期から当院で周産期管理を行い経過観察できた患者18名，分娩18例を対象とした。分娩後にD-HCMに移行した群（D-HCM群）7名と，移行しなかった群（non D-HCM群）11名について，心エコー所見や心血管イベント，妊娠転帰について後方視的に検討した。【成績】分娩後の経過観察期間はnon D-HCM群で11年7か月，D-HCM群で12年1か月で有意差はなかった（ $p=0.89$ ）。分娩時年齢，経産回数などの患者背景には有意差がなかった。妊娠中の心血管イベントとして，不整脈の新規出現・増悪や自覚症状の増悪は有意差がなかったが，D-HCM群では妊娠初期の左室拡張末期径（LVDd）が大きい傾向があり（42mm vs 48.5mm， $p=0.11$ ）。左室機能低下（ $EF < 50\%$ もしくは $FS < 25\%$ ）を来たした例が有意に多かった（0 vs 42.9%， $p=0.024$ ）。分娩週数や分娩様式，出生体重，早産，低アプガースコアなどの妊娠転帰は有意差を認めなかった。妊娠高血圧症候群や常位胎盤早期剝離はいずれも認めなかった。【結論】HCM合併妊娠において，妊娠中の心機能低下は将来的にD-HCMへ移行する予測因子である可能性が示唆された。

P-46-8 術後合併症を契機に判明し、重篤な転機を辿った母体基礎心疾患の2症例

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循環動態が目まぐるしく変化する妊娠後期の周産期管理において、潜在的な母体の基礎心疾患は、その後の経過に大きく影響することがある為、早期に把握する意義は大きい。それぞれ異なる母体の基礎心疾患に起因する重篤な緊急帝王切開術後合併症の2症例を経験したので報告する。【症例1】37歳の1回経産婦。過去に心雑音を指摘されたが、精査にて異常を認めず。妊娠35週にコントロール不良の重症妊娠高血圧腎症に対し、緊急帝王切開を行った。術後に難治性の呼吸不全を認め、心エコーにて高度の大動脈逆流を指摘され心原性呼吸不全と判明した。術後18日目、追精査した経食道エコーにて、大動脈2尖弁が判明した。【症例2】30歳の2回経産。過去2回の出産では特記異常なく、家族歴にも特記すべき申告はなかった。双胎妊娠に対し、塩酸リトドリンの持続点滴による切迫早産加療を行っていた。妊娠35週に前期破水となり、緊急帝王切開を実施。術半日後に急性呼吸不全となりICU管理。non sustained VTが頻発し、VF・心停止を認め、除細動により数十秒後に心拍再開。その後の家族歴の再聴取にて複数にペースメーカー留置者・QT延長が判明した。過去の心電図ではQT延長は認めていなかった。塩酸リトドリン中止後の心拍数減少がVFの起因となった可能性がある。産褥期に肺水腫が重症化する場合には心原性要因の精査として、早期の心エコー検査が望まれる。また日常生活に不整脈が潜在している可能性があり、妊婦健診時のスクリーニングとしての心電図検査の役割は大きい。

P-47-1 初発症状が失語であった、出産後に脳出血と診断した1例

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【緒言】妊娠/産褥期に発症する脳血管障害は、出血性疾患では脳出血、梗塞性疾患では動脈系が閉塞する脳梗塞、静脈系が閉塞する脳静脈洞血栓症が知られている。脳出血の原因としては、脳動脈瘤、妊娠高血圧症候群、HELLP症候群、もやもや病などが挙げられる。今回われわれは失語が初発症状であった、出産後に脳出血と診断した1例を経験したため、若干の文献的考察を加えて報告する。【症例】患者は32歳。1妊0産。既往歴に特記すべきものなし。前医にて妊娠確認され、妊娠22週0日、転居で当初初診。その後の妊娠経過は順調であり、妊娠41週0日陣痛発来で入院。その後順調に分娩経過。子宮口全開大後2時間10分の時点で、運動障害や嚥下障害を認めなかったが、発語がわずかであった。疼痛によるヒステリー発作を疑い、早期的分娩を目指す方針とし、微弱陣痛の適応でオキシトシンを使用し、発症から1時間35分で経陰分娩となった。児は2778gの女児であり、Apgar Score 8/9点であった。分娩終了後も発語なく、頭部CTを撮影し脳出血と診断。その後右麻痺が出現。同日当院脳神経外科で開頭血腫除去術を施行した。現在産褥1か月であり、失語/右麻痺は改善傾向であり、リハビリ継続中である。【考察】脳出血は妊婦の死亡原因の第2位であり、虚血例と比較し予後不良、基礎疾患を有する症例が多いという報告がみられる。本症例では基礎疾患はなく、妊娠/分娩経過中高血圧なく、分娩後の精査で脳動脈瘤や血管奇形を認めなかった。【結語】児娩出のタイミングや娩出方法など、診断時の分娩経過により個々の柔軟な対応が必要であり、早期に診断し治療を開始することが重要と考える。

P-47-2 異なる転機をたどった多発性硬化症 (MS) 合併妊娠1例と視神経脊髄炎類似疾患 (NMOsd) 合併妊娠1例

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自己免疫機序の関与が想定されている中枢神経系の炎症性脱髄性疾患として多発性硬化症 (MS: Multiple Sclerosis) はよく知られているが、一方で、視神経脊髄炎 (NMO: Neuromyelitis optica) はあまり知られていない。いずれも女性に好発する。従来は多発性硬化症の一亜型 (視神経型 MS) とされていた NMO だが、中枢神経系とくに視神経や脊髄への抗 AQP4 抗体 (抗 AQP4 抗体) の関与が判明し、さらに現在では抗 AQP4 抗体陰性例でも類似の病態をとるため、2015年に視神経脊髄炎類似疾患 (NMOsd: Neuromyelitis optica spectrum disorder) として提唱された。MS が時間的・空間的に病変が多発するのが特徴で症状は多岐にわたる。一方で、NMOsd では重度の視力低下・視野欠損・横断性脊髄障害 (脊髄レベルに一致した感覚障害、対麻痺、膀胱直腸障害など) がみられる。MS 合併妊娠は、妊娠中の年間再発率は低下し、産後3か月にもっとも再発リスクが高くなることはよく知られている。他方、NMOsd 合併妊娠は、MS とは特徴が異なる。妊娠への影響は大きく、流産や preeclampsia のリスクが高いと内科ガイドラインにおいても記載される。妊娠中の再発率について、最近の systematic review では妊娠中または直後の増悪が4割強に及ぶと指摘している。このたび、妊娠中に異なる転機をたどった MS 合併妊娠1例 (妊娠中の MS 増悪) と NMOsd 合併妊娠1例 (妊娠中と産後に視力異常でステロイドパルス療法を要した) を経験したので報告する。

P-47-3 妊産褥婦の睡眠時無呼吸に関する観察研究

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【目的】睡眠時無呼吸症候群 (sleep apnea syndrome, 以下 SAS) は、繰り返す呼吸停止による睡眠障害の一つで、妊婦は睡眠呼吸障害を起こしやすいと考えられ、妊娠第3期には悪化するともいわれ、様々な合併症と SAS の関連を示す報告もある。本邦ではデータは乏しい妊婦の SAS について、今回自宅でのスクリーニングを行い、頻度、症状との関連を検討した。【方法】当院で健診中の未成年、多胎や重篤な胎児異常を除き、文書で同意を得た妊婦を対象に、携帯用睡眠時無呼吸検査装置 PULSOX-Me30 を用い自宅で妊娠初期 (10 週台)、中期 (20 週台)、後期 (30 週台)、入院中に産褥の 3% 酸素飽和度低下回数 (3% ODI) を求め、異常とみなす 5 以上を示した場合、呼吸フローも測定する SAS-2100 による二次検査を行った。【成績】当院で分娩に至った妊婦で、初期の検査を 102 例に施行、平均値は開始時年齢 34.0 歳、BMI 22.6、児の体重 2910g、出生週数 38.6 週、3% ODI 異常は 4 例で GDM 合併が 1 例あった。異常例のうち 2 例は BMI 21 台で肥満との関連は明らかでなかった。産褥までの横断的追跡 59 例で、初期と後期の ODI 平均値は 2.10 と 2.04 で、明らかな悪化は認めなかった。中期までに二次検査になった 4 例のうち 1 例は中等度の SAS の診断となったが産後には改善していた。また初期 ODI からみた有病率は海外の報告と差がなかった。症例数が少ないが ODI 異常例に FGR や合併症の増加傾向は認められなかった。【結論】当科で行った妊婦の SAS スクリーニングの結果、海外と有病率は差がなく、異常例の合併症増加、肥満や HDP 等との関連は認めなかった。

P-47-4 Mendelson 症候群による急性呼吸窮迫症候群を認めた妊娠高血圧腎症について

大阪医科薬科大

夏山幸一郎、藤田太輔、小川範子、入江惇太、齊藤駿介、森田奈津子、布出実紗、永易洋子、澤田雅美、杉本敦子、大道正英

妊婦は誤嚥しやすいことが知られている。Mendelson 症候群は産婦人科医の Curtis Lester Mendelson が無痛分娩後に生じた重篤な誤嚥性肺炎を報告したことに由来する。今回我々は、Mendelson 症候群による急性呼吸窮迫症候群 (ARDS) を認めた妊娠高血圧腎症 (PE) の一例を経験したので報告する。患者は G1P0 で妊娠中期から軽度の呼吸苦を認めていた。妊娠 39 週 4 日で血圧 132/79mmHg、尿蛋白 1+、妊娠 39 週 5 日に陣痛発来し、硬膜外無痛分娩を行う際に急激な呼吸困難感の増悪、SpO2 80% 台 (マスク 10L) の低下を認め当院に母体搬送となった。当院到着時の血圧 143/94mmHg、心拍数 140bpm、呼吸数 30 回/分、SpO2 82% (マスク 10L)、JCS 1、胎児心拍数陣痛図は reactive であり、子宮口は 7cm 開大していた。母体の呼吸状態の急激な悪化のため、全身麻酔下での超緊急帝王切開を行った。児の出生体重は 3,200g、男児、Apgar Score 4/7、UmA-pH 7.170、BE -8mmol/L。胸部 CT で両肺背側に広範な浸潤影、すりガラス影を認め、これまでの臨床経過から Mendelson 症候群による ARDS と診断した。術後 1 日目に抜管し一般病棟に転棟した。血圧は 140/80mmHg、術後 4 日目の尿蛋白/クレアチニン比は 0.879 のため PE と診断した。術後肺水腫と誤嚥性肺炎は軽快し、術後 9 日目に退院となった。本症例は PE を背景とした肺水腫に、誤嚥性肺炎を発症し ARDS となったことが推察される。また無痛分娩中であったため局所麻酔中毒や血管内誤注入・中毒、全脊髄麻酔などの鑑別を要した。妊娠中の ARDS の母体死亡率は約 9% という報告もあり、その対応には集約的管理が重要である。

P-47-5 新型コロナウイルス感染症との鑑別を要した粟粒結核合併妊娠の 1 例

荏原病院

小島七瀬、本間 進、吉野佳子、幸本康雄

【緒言】粟粒結核は、結核菌が血行性に播種し、びまん性の粟粒大あるいはこれに近い大きさの結核散布巣を有する病態であり、妊婦の合併は極めて稀である。今回、我々は新型コロナウイルス感染症 (COVID-19) との鑑別を要した粟粒結核合併妊娠症例を経験したので報告する。【症例】34 歳、1 妊 0 産。既往歴：なし。妊娠経過に特記すべき異常は認めなかった。33 週 4 日微熱・咳嗽が出現し他院受診、上気道炎の診断にて投薬を受けたがその後も症状持続。35 週 3 日 38 度台の発熱増悪および呼吸困難感を認めたため当院救急外来を受診した。SAT94% と酸素化不良、COVID-19 を疑い入院管理としたが、入院後陣痛発来したため、同日緊急帝王切開術にて分娩となった。第 1 病日、入院時施行した SARS-CoV-2 PCR 検査陰性が判明、詳細な病歴聴取の結果、28 歳時に職場で結核患者と接触、QFT 検査陽性にて抗結核薬を予防投与されていた。臨床症状および病歴より結核感染症を考え CT 検査を施行。粟粒結核が疑われ、確定診断目的に喀痰・尿 PCR 検査を施行したところ陽性となり、粟粒結核の診断に至った。一時人工呼吸器管理が検討されるほど呼吸状態が悪化した。抗結核薬による治療が著効し速やかに症状は軽快、第 13 病日退院した。現在外来にて加療継続中である。【結語】今回我々は妊娠後期 COVID-19 を疑ったが粟粒結核の診断であった症例を経験した。妊婦が発熱と呼吸器症状を呈した場合、詳細な病歴聴取が極めて重要であり、結核感染症も鑑別に上げるべきである。

P-47-6 妊婦に紛れ込んでいた肺結核合併妊娠の一例

田川市立病院

瓜生泰恵, 吉田祥子, 椎名隆次, 藤田拓司

妊婦可能年齢層の新規結核患者数は約1万人に1人である。結核は感冒症状に類似しており、非常に厄介である。妊婦は被曝を考慮して画像検査が非積極的になるため、発見の遅れが問題となる。新生児感染や院内感染のリスクがあり、分娩取扱い可能な施設に限られるため、対応に難渋する。今回、通常の妊婦健診を行う中で、紛れ込んでいた肺結核合併妊娠を経験したので報告する。症例は28歳、3妊2産。自然妊娠が成立し、当院で妊婦健診を行った。妊娠35週に前胸部痛、妊娠38週に発熱および背部痛が出現した。呼吸器症状を認めず、尿路感染症と診断し、抗生剤で治療した。その後、症状は消失した。予定日超過で誘発分娩を予定したため、妊娠39週3日に術前検査を行ったところ、上肺野に異常陰影と胸水を認めた。胸部CT検査所見から肺結核を疑ったが、喀痰塗抹検査は陰性であった。肺結核を否定できなかったため母体搬送を依頼したが、COVID-19流行のため診療を制限している施設が多く、正産期であり、難渋した。妊娠39週4日に搬送先で頭位経陰促進分娩に至り、産褥管理は当院で行った。産褥5日目に喀痰および胃液のPCR検査の結果が陽性と判明し、肺結核と診断した。正産期の結核合併妊娠は、感染管理と分娩管理の両方を要し、受け入れ先を確保するのに苦渋するため、早期発見が大切である。結核は感冒様症状の他、胸背部痛や消化器症状が出現する。外来診療が多忙であると、感冒や胃腸炎として見過ごされている可能性がある。有症状時は胸部単純X線検査を撮影し、必要なら胸部CT検査を行うことが重要である。結核は昔の疾患ではない、通常診療の中に、結核が潜んでいることを忘れてはならない。

P-47-7 分娩時に肺結核を合併した妊婦の1例

産業医大病院

福元裕貴, 和田 環, 内村貴之, 金城泰幸, 村上 緑, 近藤恵美, 柴田英治, 吉野 潔

【背景】本邦の結核罹患率は人口10万対12.3と欧米と比較して高い割合で推移しており、若年層の新規患者が増加傾向にある。しかし結核合併妊婦の周産期管理についてはまとまった指針がなく、各医療機関で個別対応している。今回我々は、妊娠39週の活動性肺結核合併妊婦の症例を経験したので報告する。【症例】28歳、3妊2産、自然妊娠成立後、妊婦経過は順調であった。妊娠38週2日に38℃の発熱、排尿時痛、腰背部痛を認めた。腎盂腎炎を疑い抗菌薬投与を開始し解熱したが、妊娠39週2日に湿性咳嗽と前胸部痛が出現した。胸部単純X線検査で左上肺野に浸潤影と胸水貯留を認めた。胸部CT検査で左上葉にtree-in-bud appearanceを伴う小葉中心性粒状影、浸潤影および胸膜変化を伴う胸水貯留を認め、活動性肺結核、結核性胸膜炎が疑われた。喀痰抗酸菌検査で塗抹陰性であった。妊娠39週4日に陣痛発来し、活動性結核疑い妊婦の周産期管理目的に当院へ母体搬送となった。妊娠39週4日活動性結核疑いの適応でオキシトシンにて分娩誘発を開始し同日に経陰分娩に至った。児は速やかに個室でのクベース管理とした。胎盤および羊水の結核菌PCRは陰性であった。分娩後経過は良好であり当院到着から8時間後に前医へ転院した。前医で活動性結核・結核性胸膜炎と確定診断に至り、抗結核薬4剤で治療を開始した。児は潜在性結核疑いとしてイソニアジド単剤を開始した。【考察】結核妊婦の対応においては患者の治療に加え周囲への感染防止対策も重要となるが、稀であり非結核病床で対応する場合もある。今回、非結核病床において活動性結核妊婦の分娩を行い、児を含め周囲への感染なく分娩に至った症例を経験したため文献的考察も含めて報告する。

P-47-8 妊娠中に発症した原因不明の非心原性肺水腫の1例

ベルランド総合病院

清水優作, 松木貴子, 安井友紀, 仲尾有美, 清水亜麻, 松山佳奈子, 小和貴雄, 吉村明彦, 濱田真一, 宮武 崇, 山崎正人, 村田雄二

【緒言】妊娠中の呼吸困難は肺塞栓、肺水腫などを疑い迅速な診断と治療介入が重要である。今回、妊娠中に発症した原因不明の肺水腫の1例を経験したので報告する。【症例】33歳、初産婦。ICSI-ETにて妊娠成立。妊娠33週2日、早期前期破水のため入院となった。感染徴候は認めず、予防的抗菌薬投与とステロイド注射、硫酸マグネシウム持続投与を開始した。入院3日目に呼吸苦が出現しSpO₂低下と低酸素血症(PaO₂ 59.5mmHg)を認め、酸素投与を開始した。妊娠高血圧腎症の臨床所見は認めず、血中Mg濃度は4.2mg/dlであった。造影CTでは血栓症は認めず、両側胸水と肺水腫を認めた。心エコーで異常は認めなかった。硫酸マグネシウムを中止し、リザーバマスクを使用したが無効な酸素化は得られず、経鼻高流量酸素療法(NHFC)に変更した。その後陣痛発来し、陣痛促進を行った。CTGでは胎児心拍異常は認めなかったが、分娩停止の適応で緊急帝王切開術を行った。児は1844g(AFD)、Ap8/9、臍動脈血液ガスはpH 7.32、pCO₂ 45.6mmHg、pO₂ 17.7mmHg、BE -2.9mmol/Lであった。術後非侵襲的陽圧換気療法に変更し、酸素化の維持が可能となった。子宮内感染を認め、抗菌薬治療を開始した。心エコーで循環血液量を評価しながら積極的利尿を行い、産褥2日目に酸素中止し6日目に抗菌薬終了した。肺水腫かARDSかの鑑別に苦慮したが、経過より肺水腫と診断した。産褥10日目に退院となった。産褥30日後の心エコーでは異常なかった。【結語】肺水腫とARDSの鑑別が非常に難しく、他科との連携が必要であった。単一要因ではなく、子宮収縮抑制剤の使用や子宮内感染などの要因が重なり肺水腫を発症したと考えられた。

P-47-9 妊娠・産褥期の可逆性脳血管攣縮症候群 (RCVS) に併発した脳血管障害の検討当院で経験した RCVS22 例より

東海大八王子病院

橋山知明, 牧野田佳, 牧野田知奈美, 矢島優希, 重盛波留子, 泉 顕治, 間邊貴俊, 大岩一平, 橋山知紗, 西島義博, 村松俊成

【緒言】妊娠・産褥期の脳卒中は妊産婦の 0.008~0.03% に発症し, 妊産婦死亡の約 16% を占めている。妊娠関連の脳血管障害のうち約半数は脳内出血で, 脳血管の一過性可逆性分節状攣縮を伴う可逆性脳血管攣縮症候群 (reversible cerebral vasoconstriction syndrome; RCVS) の関与が考えられている。今回, 妊娠・産褥期に発症した RCVS22 例のうち 3 例に重篤な脳血管障害を認めたため後方視的に検討した。【結果】当院で診断された RCVS 22 例の平均年齢は 32.4 歳 (14-42 歳)。発症時期は, 妊娠中が 15 例 (14-37 週), 分娩時が 1 例 (38w4d), 産褥期が 6 例 (1-28 日)。22 例中, 18 例 (82%) は雷鳴頭痛が診断時の症状であった。22 例中 13 例に妊娠高血圧症候群を合併し, 2 例にてんかんの既往を認めた。1 例は RCVS 後に小脳および脳幹部梗塞を発症し, 1 例は分娩子癩を, 1 例は産褥子癩を発症した。頭部 MRA では全例で両側主幹脳動脈に多発性分節状の高度な攣縮や狭窄を認め, その大部分に著明な脳血流の低下を認めた。RCVS 発症後の follow up で頭部 MRA を施行すると, 多くは 3 か月以内に脳血管の攣縮や狭窄, 脳血流の改善を認めた。【結論】妊娠・産褥期の一過性頭痛 (雷鳴頭痛) を発症した場合には, RCVS を既に併発している可能性がある。速やかに頭部 MRA を施行し, 両側主幹脳動脈の多発性分節状の攣縮の有無を精査を行い, 続発する重篤な脳血管障害の予防や早期発見に繋げることが望ましいと考える。

P-48-1 同一コホート内で異なる検査試薬を用いた妊婦サイトメガロウイルス抗体スクリーニング

三重大附属病院¹, セントローズクリニック²

鳥谷部邦明¹, 北村亜紗¹, 萩元美季¹, 紀平正道², 池田智明¹

【目的】我々は県内において 2013 年より妊娠中のサイトメガロウイルス (CMV) 初感染妊婦の抽出を目的とした妊婦 CMV 抗体スクリーニングを前向きコホート研究として行っている。2018 年度まではコホート内の全施設のデータがデンカ社試薬によるものであった。しかし, 2019 年より一部の施設のデータがアボット社試薬によるものに変更された。さらには, 2020 年よりデンカ社試薬が改良され変更となった (変更前を旧試薬, 変更後を新試薬とする)。今回, コホート内で異なる検査試薬が使用されるようになった 2019~2020 年度の妊婦 CMV 抗体スクリーニング結果について報告する。【方法】倫理審査と患者同意を得て研究を行った。2019 年 4 月~2020 年 2 月は旧デンカ社試薬とアボット社試薬によるデータが使用された。2020 年 2 月~2021 年 3 月はアボット社試薬と新デンカ社試薬によるデータが使用された。妊娠初期に CMV IgG・IgM 抗体を検査し, IgG (+)・IgM (+) (旧デンカでは IgM 4 以上) の場合には初感染疑いと判定した。IgG (-) の場合には妊娠後期に抗体を再検した。IgG が陽転した場合に初感染と判定した。新生児尿 CMV DNA 検査により先天性 CMV 感染 (cCMV) を診断した。【成績】2019 年度の 5644 人のうち, 旧デンカ IgG (+)・IgM (+) の 31 例のうち cCMV が 2 例, アボット IgG (+)・IgM (+) の 33 人のうち cCMV が 1 例であった。IgG 陽転の 9 例のうち cCMV が 3 例であった。2020 年度の 5968 人のうち, アボット IgG (+)・IgM (+) の 36 例のうち cCMV が 0 例, 新デンカ IgG (+)・IgM (+) の 53 例のうち cCMV が 1 例であった。IgG 陽転の 1 例のうち cCMV は 0 例であった。【結論】我々のコホートでは異なる試薬が使用されるようになっても混乱なく妊婦 CMV 抗体スクリーニングが遂行できる。

P-48-2 COVID-19 流行後における妊婦のサイトメガロウイルス初感染の減少の可能性

三重大附属病院

北村亜紗, 鳥谷部邦明, 萩元美季, 池田智明

【目的】国内では COVID-19 流行の第 1 波が 2020 年 3~5 月に発来した。国民全体が新型コロナウイルス感染予防を行うことにより, 妊婦においてもインフルエンザウイルス等の新型コロナウイルス以外の病原体による接触・飛沫・空気感染のリスクも低減されていると考えられる。我々は 2013 年より妊婦のサイトメガロウイルス (CMV) 初感染を調査している。今回, 妊婦の CMV 初感染が 2020 年よりどのように変化しているのかを検討した。【方法】倫理審査と患者同意を得て前向きコホート研究を行った。2013~2019 年度までと同様に, 妊婦 CMV 抗体スクリーニングにより妊婦の CMV 初感染を同定した。妊娠初期 CMV IgG 陰性の場合には妊娠中の CMV 感染予防を指導し, 妊娠後期に CMV IgG を再検した。CMV IgG が陽転した場合に初感染と同定し, 新生児尿 CMV DNA 検査により先天性 CMV 感染を診断した。【成績】妊娠初期 CMV IgG 陰性妊婦における妊娠中の CMV IgG 陽転率/先天性 CMV 感染率はそれぞれ 2013 年度で 0.18%/0.18% (570 人中, 1 例/1 例), 2014 年度で 0.61%/0.35% (1148 人中, 7 例/4 例), 2015 年度で 1.50%/0.71% (1131 人中, 17 例/8 例), 2016 年度で 0.49%/0.16% (1233 人中, 6 例/2 例), 2017 年度で 0.41%/0.20% (1479 人中, 6 例/3 例), 2018 年度で 0.41%/0.14% (1462 人中, 6 例/2 例), 2019 年度で 0.77%/0.26% (1176 人中, 9 例/3 例) であり, 2013~2019 年度でまとめると 0.63%/0.28% (8199 人中, 52 例/23 例) であった。一方, 2020 年度は 0.11%/0% (919 人中, 1 例/0 例) であり, 妊娠中の CMV IgG 陽転率が低かった (Fisher's exact, $p < 0.05$)。【結論】COVID-19 流行後において妊婦の CMV 初感染が減少している可能性がある。

P-48-3 新生児聴覚スクリーニング Refer 児における先天性サイトメガロウイルス感染の検索

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【目的】我々は県内で妊婦サイトメガロウイルス (CMV) 抗体スクリーニングにより初感染妊婦を抽出し、その児において先天性 CMV 感染の検索を行ってきた。その一方で、妊婦抗体スクリーニングの有無や結果にかかわらず新生児聴覚スクリーニング Refer 児においても先天性感染の検索を行ってきた。今回、県内の Refer 児における先天性 CMV 感染の検索結果について報告する。【方法】倫理審査と患者同意を得て前向きコホート研究を行った。新生児聴覚スクリーニング Refer 児において新鮮尿を採取し、リアルタイム PCR 法により尿中の CMV DNA 検出を行った (大学病院中央検査部)。CMV DNA が検出された場合に先天性 CMV 感染児と診断した。【成績】2013 年～2021 年までに Refer 児 92 例で尿 CMV DNA 検出を行った。先天性 CMV 感染児は 4 例、非感染児は 88 例であった。先天性 CMV 感染児 4 例のみに難聴を認めた。みな CMV 初感染妊婦からの児であった。4 例のうち 1 例は耳奇形を認めた。一方、非感染児の 88 例のうち、少なくとも 24 例に難聴を認めた。難聴例には耳奇形、心奇形、それ以外の奇形や新生児仮死、等を認めた。【結論】妊婦 CMV 抗体スクリーニングと新生児聴覚スクリーニングを組み合わせることにより、難聴を認める初感染妊婦からの先天性 CMV 感染児の全例を同定できる可能性がある。

P-48-4 HIV 感染妊娠におけるコントロール不良例に関する検討

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【目的】HIV 母子感染予防対策は確立され、薬剤の発展とともに感染妊婦のウイルス量コントロールは良好になってきている。しかし少数だが、現在でもコントロール不良例は存在し続けている。今回コントロール不良例の背景を検討することで、現在の母子感染予防対策を再考する。【方法】cART が標準化された 2000 年以降分娩に至った 599 例のうち分娩前ウイルス量が 1000 コピー以上であった (不良例) 36 例を対象に、感染判明時期・投薬内容・母子感染の有無等を検討した。【成績】コントロール不良例は 6.0% (36/599) のみであったが、感染判明時期は妊娠前が 11.1%、今回妊娠時が 83.3%、分娩直前・不詳がそれぞれ 2.8% で、妊娠前例も認めた。国籍は外国籍が 66.7% を占め、今回妊娠時に感染判明した例のうち、妊娠中の感染判明時期は、妊娠初期に 12.5%、中期に 21.9%、後期に 40.6%、不明が 25.0% であった。抗 HIV 薬は 88.6% に投与されており、投与開始時期は妊娠前が 9.7%、妊娠初期が 6.5%、中期が 22.6%、後期が 51.6% であった。投与レジメンは近年ほぼ 100% 多剤併用療法が施行されているが、不良例では AZT 単剤のみを 35.5% で認めた。分娩前ウイルス量は 1 万以上が 38.9% を占め、母子感染は 1 例 (2.8%) で生じていた。【結論】母子感染予防対策によりウイルス量コントロールは確実に良好となっているが、不良例には妊娠前や妊娠初期に感染判明していた例も一定数含まれており、母子感染例も認めた。薬剤の発展に伴い治療コンプライアンスが良好であればウイルス量はコントロール可能となってきたため、今後妊娠早期に HIV 感染を判明させ、さらに治療コンプライアンスを保つことがさらなる母子感染予防につながると考えられた。

P-48-5 風疹低抗体価妊婦の産後風疹ワクチン接種状況～妊娠初期の感染性疾患スクリーニングが母子の長期健康保持増進に及ぼす影響に関する観察研究より～

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【目的】日本では数年毎に風疹が流行している。風疹低抗体価妊婦は産後風疹ワクチン接種が推奨されるが、実際の接種状況はどうか。産前の風疹ワクチン接種経験によって接種割合は変わるか。妊婦へのアンケート調査より、風疹低抗体価妊婦の産後風疹ワクチン接種状況を明らかにする。【方法】全国 23 施設の協力を得て 20 歳以上の妊婦を対象とし、妊娠中および産後 1 年後にアンケートを行い 2018 年 5 月～2021 年 10 月に得られた回答と、妊娠中および分娩後の診療録データを解析した。風疹抗体価 (HI 法) 16 倍以下を低抗体価とし、低抗体価妊婦の産後風疹ワクチン接種状況を調査した。【成績】有効回答数は 4331 人のうち 1333 人 (30.8%) が風疹低抗体価であった。低抗体価妊婦のうち産後 1 年のアンケートへの回答が得られたのは 436 人であり、産後に風疹ワクチン接種を「うけた」と回答したのは 257 人 (58.9%)、「うけていない」171 人 (39.2%)、「わからない」8 人 (1.8%) であった。妊娠前風疹ワクチン接種経験別に比較すると、妊娠前接種あり群では産後接種率 60.7%、妊娠前接種なしまたは不明群では産後接種率 54.2% であり有意差はなかった。【結論】産後風疹ワクチンを接種した風疹低抗体価妊婦は 6 割弱に留まった。産後接種をしなかった人の多くは妊娠前に風疹ワクチン接種歴がある人と予測していたが、接種歴なし又は不明と回答したにも関わらず産後に接種していない人が半数近く存在することが明らかになった。風疹ワクチン接種経験のない妊婦は産後ワクチン接種で抗体獲得の可能性が高い。医療者は風疹低抗体価妊婦、特にワクチン接種経験のない妊婦に対する産後ワクチン接種をより積極的に勧める必要がある。

P-48-6 妊娠中の風疹特異的 IgM 抗体陽性の臨床的意義

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【目的】風疹感染が疑われる妊婦への対応として、ベア血清 HI 抗体価測定および風疹特異的 IgM 抗体価測定が施行されている。しかしながら長期間 IgM 抗体が陽性を示す persistent IgM 抗体の存在のため、IgM 陽性例が直近の感染を示すとは言えない。本研究では、日本人妊婦における風疹 HI・IgM 抗体の保有状況を明らかにし、風疹 IgM 陽性妊婦の転帰および臨床的意義を調査することを目的とした。【方法】2007年1月から2020年12月までに当院で妊娠初期検査を施行した妊婦を対象とした。妊娠初期検査では、全例に風疹 HI・IgM 抗体価を測定した。EIA 法風疹 IgM 抗体価 >1.2 を陽性と定義し、IgM 陽性率および HI 抗体価毎の IgM 陽性率、IgM 陽性例の妊娠転帰・風疹感染の有無について後方視的に検討した。【成績】期間中に風疹抗体価を測定された妊婦は14965人で風疹 IgM 陽性者は186人(1.2%)だった。HI 抗体価毎の IgM 陽性率は、 $<8=0.3\%$ (2/775), $8=0.1\%$ (1/832), $16=0.5\%$ (8/1688), $32=0.9\%$ (30/3246), $64=1.4\%$ (51/3603), $128=1.5\%$ (44/2863), $256=2.4\%$ (33/1371), $512=2.8\%$ (15/534), $1024=2.1\%$ (1/48), $2048=25\%$ (1/4), $4096=0\%$ (0/1) であり、風疹 HI256倍以上における IgM 陽性率は50/1958(2.6%)だった。IgM 陽性者のうち、流産率は3.8% (7/186)、臨床的に直近の母体風疹感染と診断された例は1例のみ(0.5%)だった。当該症例は風疹 HI 抗体価2048倍、IgM 抗体価10であり妊娠初期に発熱を認め、妊娠初期に妊娠中絶を選択された。本研究期間に先天性風疹症候群の児の出生はなかった。【結論】風疹特異的 IgM 抗体陽性者は、ほぼ全て persistent IgM 抗体保有者だった。直近の感染評価は症状と問診、およびベア血清による評価が重要である。

P-48-7 新規トキソプラズマ IgG 抗体・IgM 抗体測定キット CLIA 法と従来法 (ELISA 法、CLEIA 法) との相関およびアビディティとの相関はあるか？

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【目的】トキソプラズマ (以下 T と略す) IgM 抗体陽性妊婦を分析し、現在臨床検査センターで主に使用されている3キット (ELISA 法、CLEIA 法、CLIA 法) の T-IgM 抗体・同 IgG 抗体値およびアビディティ値を比較検討し、各キットの特性を解析した。【方法】2019年4月~2021年3月の間に当院に、T-IgM 抗体陽性のため紹介された78例の妊婦を対象とした。各症例につき T-IgG 抗体のアビディティ (以下 AI) を測定した。【成績】T-IgG 抗体について、ELISA 法、CLEIA 法、CLIA 法全て上限値未満の78例の各キット間の指数近似式あるいは一次近似式と相関係数は各々、(CLEIA) $=27.3 \cdot \exp(0.018 \cdot \text{ELISA})$, $r=0.72$, (CLIA) $=5.88 \cdot \exp(0.019 \cdot \text{ELISA})$, $r=0.54$, (CLEIA) $=0.09 \cdot (\text{CLEIA}) + 53.1$, $r=0.49$ で、ELISA 法と CLIA 法とが最も相関係数が高値であった。T-IgM 抗体については、指数近似式あるいは一次近似式と相関係数は各々、(CLEIA) $=0.70 \cdot \exp(0.51 \cdot \text{ELISA})$, $r=0.94$, (CLIA) $=0.16 \cdot \exp(0.48 \cdot \text{ELISA})$, $r=0.90$, (CLIA) $=0.12 \cdot (\text{CLEIA}) + 0.28$, $r=0.92$ で、何れも相関が高く、T-IgM 抗体の CLIA 法は CLEIA 法の約12%となることが示された。アビディティ値と T-IgM 抗体との相関については、AI $=31.7 \cdot \exp(-0.23 \cdot \text{ELISA})$, $r=0.43$, AI $=20.5 \cdot \exp(-0.047 \cdot \text{CLEIA})$, $r=0.46$, AI $=21.6 \cdot \exp(-0.026 \cdot \text{CLIA})$, $r=0.54$ で、AI は T-IgM 抗体 (CLIA 法) と相関が高い傾向であった。【結論】T-IgG 抗体は3測定法で強い相関は認められず、換算式は作成できなかったが、T-IgM 抗体は CLIA 法が CLEIA 法の約12%となることが示された。アビディティは T-IgM 抗体 (CLIA 法) と相関が高い傾向であったが、症例の蓄積が必要である。また紹介例などでは、測定キットの確認が必要である。

P-49-1 飛び込み分娩後に梅毒感染が判明し、新生児死亡に至った1例

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【緒言】近年、若年・未受診妊婦における梅毒合併妊娠が問題視されている。今回、梅毒感染が判明した未受診・飛び込み妊婦の周産期経過について報告する。【症例】23歳, G3P0 (AA×2)。医療機関の受診歴はなく、最終月経より29週6日に5分間隔の腹痛及び性器出血を認め、当院に救急搬送となった。受診時には子宮口は全開大で、その30分後に児は娩出された。母体血液検査では、WBC (μL) /CRP (mg/dL) : 22060/15.1, RPR (R.U.) 25.7, TPHA (mU/ml) 63.9 と梅毒感染と診断された。児は1086g, 男児で Apgar score 1/3 (1分/5分)、臍帯動脈血 pH 7.270, BE -7.2 であった。胎盤病理所見は、臍帯及び絨毛に Treponema pallidum 抗体を認めた。出生児は手掌、足底に水疱を多数認め、著明な肝脾腫、貧血、血小板減少、凝固異常を認めた。PCG, γ グロブリンの投与、輸血及びGI療法等を行なったが、肝不全及び腎不全は不可逆的となり、日齢17に多臓器不全のため永眠された。【考察】母体が未治療の梅毒感染の場合には、40%の児が死産または新生児死亡を起こすと報告されている。超音波画像検査では、肝腫大、MCA-PSVの上昇、胎盤肥厚、羊水過多、胎児水腫などが特徴的な所見とされるが、これらは20週以降に見られることが多く、妊娠初期の血液検査を含めた早期診断が必要である。【結語】先天梅毒は妊娠中の治療で予防可能な疾患であり、未受診妊婦を減らすための更なる取り組みが必要である。

P-49-2 当院における梅毒合併妊娠の周産期的検討

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【目的】梅毒診断時のRPR定量値(自動化法)が低値(8.0RU以下)の場合、活動性と陳旧性の鑑別は困難な場合が多い。RPR定量値の推移と治療効果判定の関係から、活動性梅毒と陳旧性梅毒を鑑別することが可能か検討する。【方法】2012年4月から2021年10月までに活動性梅毒と診断され、当院で分娩した15例に関して後方視的研究を行った。診断時のRPR定量値が8RU以下の場合をlow RPR群、8RUより大きい場合をhigh RPR群と定義した。治療はRPRが治療開始前値の1/2未満(治療有効域)となるまで継続し、RPR定量値が分娩前に治療有効域まで低下した場合を治療有効群、低下しなかった場合を治療無効群と定義した。【成績】母体年齢は中央値25.4歳(17歳-37歳)であった。13例は無症候性で、1期梅毒、2期梅毒を1例ずつ認めた。2期梅毒の1例は未治療、自宅墜落産であり除外した。low RPR群5例中3例が治療無効、2例が治療有効で、治療期間は8~25週間であった。うち1例は12週間の治療で漸く治療有効と判断された。high RPR群9例中2例が治療無効、7例が治療有効で、治療期間は4~27週間であった。【考察】low RPR群治療無効の原因として、陳旧性梅毒、治療効果不良、コンプライアンス不良が考えられる。low RPR群は、活動性梅毒であっても治療開始後4週間のRPR定量値の推移評価では変化しない場合があった。low RPR群では活動性と陳旧性の見極めは非常に困難であり、治療開始早期の段階で陳旧性梅毒と判断し、経過観察することは活動性梅毒の見落としに繋がる場合がある。【結論】活動性梅毒の治療では経時的なRPR定量値の推移評価が重要である。low RPR群は長期の治療を行わなければ、活動性と陳旧性の判断が困難な場合がある。

P-49-3 B群溶血性レンサ球菌(GBS)の薬剤耐性からみた母子感染予防に用いる抗菌薬の有効性に関する検討

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【目的】腔内の常在菌であるB群溶血性レンサ球菌(GBS)は、産道感染により新生児感染症を発症する。これらの頻度は高くないが、発症すれば新生児死亡に至るため保菌妊婦には、分娩時に予防的抗菌療法が行われる。診療ガイドラインは、予防的抗菌療法の第一選択にアンピシリン(ABPC)、セファゾリン(CEZ)またβ-ラクタム系抗菌薬に過敏症を有する妊婦には、クリンダマイシン(CLDM)やエリスロマイシン(EM)を推奨している。しかし、近年、GBSの薬剤耐性化が問題視されているにも関わらず妊婦スクリーニングでは感受性試験が実施されていないことが多い。本研究は、妊婦の腔内より分離されたGBSの薬剤耐性を評価し、母子感染予防に用いる抗菌薬の有効性を検討した。【方法】2018年から3年間、絨毛膜羊膜炎を疑われ生殖器分泌物の培養検査を行った22週以降の妊婦を対象とした。ABPC、CEZ、CLDM、EM、イミペネム(IPM)に対する薬剤感受性試験は、米国臨床検査標準協議会が定めた微量液体希釈法に準じて評価した。【成績】62例の生殖器分泌物からGBSを検出した。これらは、ABPC、CEZ、IPMに対する薬剤耐性を認めなかったが、27.4%がCLDM、25.6%がEMに対する薬剤耐性を確認した。また、CLDM、EMに関する耐性率は3年間の年次推移に有意な変化を認めなかった。【結論】すべてのGBSにおいてABPCやCEZなどβ-ラクタム系抗菌薬に対する耐性は確認されず、GBSの母子感染予防に有効と考えられた。しかし、CLDM、EMは、20%を超える耐性化が確認され、β-ラクタム系抗菌薬に過敏症を有する妊婦のGBSスクリーニングは薬剤感受性試験を併用し有効な抗菌薬を選択する必要があると考えられた。

P-49-4 生児を得たりステリア菌による絨毛膜羊膜炎の一例

産業医大

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【緒言】リステリア感染症の多くは汚染された食品の経口摂取により発症し、妊娠中に母体が感染すると胎児死亡を含めた重篤な病態を引き起こすことが知られている。今回我々は妊娠26週で分娩となり生児を得たりステリア菌による絨毛膜羊膜炎の一例を経験したので報告する。【症例】33歳G3P1 IgA腎症に対して妊娠前よりPSL2.5mg/dayを隔日内服していた。自然妊娠成立後、妊娠経過は良好であった。妊娠22週時に発熱あり、内科受診時にCRP:1.3mg/dlを認めたが、内服加療なく自然軽快していた。妊娠26週1日に38℃の発熱、子宮収縮を自覚し前医受診、母体搬送となった。腔鏡診で破水、出血、悪臭を伴う帯下は認めず、子宮口は閉鎖していた。血液検査所見でWBC:15600/μl, Neutro:76%, CRP:5.63mg/dlであったが子宮圧痛は明らかでなく、US・CTGで胎児機能不全兆候を認めなかった。絨毛膜羊膜炎疑いの診断でABPC+GMを投与、子宮収縮は塩酸リトドリン100μg/minでtocolysis可能であり、胎児肺成熟目的にベタメタゾンの投与を行った。翌日子宮口は3cm開大し胎胞を形成、子宮収縮時にvariable decelerationを認めた。臨床的絨毛膜羊膜炎、胎児機能不全の診断で緊急帝王切開術を施行した。術後母体の発熱、WBC、CRPは改善し、術後5日目に退院した。児は1016g、男児、Ap:4/6で生後7分に挿管された。生後4日目に腸管穿孔のため緊急人工肛門増設術を施行され、以後の経過は概ね良好である。母体の胎盤組織培養、児の胃液培養からリステリア菌が検出されたが、児の血液培養は陰性であった。リステリア感染の原因となる食餌摂取歴は明らかでなかった。【結語】リステリアは通常の食生活でも感染する可能性があり、特に易感染状態の妊婦の発熱時には考慮する必要がある。

P-49-5 比較的徐脈を呈した *Mycoplasma hominis* による骨盤内感染症の2例

香川大

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【緒言】比較的徐脈とは、体温上昇に比して脈拍数の上昇が少ない状態のことを指す。Cunha らの定義では、体温 39°C で脈拍数 <110/分、体温 40°C で脈拍数 <130/分とされている。また、*Mycoplasma hominis* (*M. hominis*) は、細菌培養検査で分離されるまで時間を要するため、有効な抗菌薬投与開始が遅れたとの報告が散見される。そこで、今回我々は、比較的徐脈を呈した *M. hominis* による産褥熱と骨盤腹膜炎の2例を経験したので、文献的考察を交えて報告する。【症例】症例1: 39歳初産婦 妊娠41週分娩停止のため緊急帝王切開術を施行した。術後3日目に体温 39.3°C、脈拍数 82/分となり、産褥熱を認めた。同日採取した悪露から、*M. hominis* が術後6日目に検出された。抗菌薬をミノマイシンへ変更したところ速やかに下熱した。症例2: 35歳女性 卵巣のう腫破裂による骨盤腹膜炎のため、当院へ救急搬送となった。来院時、体温 39.1°C、脈拍数 103/分であった。同日、患側付属器摘出術を施行した。術後発熱は認めなかったが、麻痺性イレウスとなり、術後経過不良であった。術中採取した腹水から *M. hominis* が術後4日目に検出されたため、クリンダマイシンを追加したところ、軽快した。【考察】レジオネラ肺炎や腸チフスなどで比較的徐脈を呈すると報告されている。同じ細胞内寄生菌である *M. hominis* による感染症でも、比較的徐脈を呈する可能性は考えられる。【結語】比較的徐脈を呈する *M. hominis* 感染症の2例を経験した。産婦人科領域の感染症において、体温と脈拍を同時に観察することは、*M. hominis* に対して適切な抗菌薬を早期から投与することにつながる可能性が示唆された。

P-49-6 治療に難渋した結節性紅斑を伴う妊娠中の肉芽腫性乳腺炎の一例

旭川医大

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【目的】妊娠中の乳腺炎の報告は少なく、肉芽腫性乳腺炎の報告が数例認められるのみである。非妊時の肉芽腫性乳腺炎では起炎菌は *Corynebacterium kroppenstedtii* であり、結節性紅斑を伴う症例についても報告されている。妊娠中の乳腺炎の起炎菌と結節性紅斑の合併から肉芽腫性乳腺炎が疑われた1例を報告する。【症例】37歳4妊2産の経産婦で、双胎妊娠のため周産期管理目的に妊娠8週時に当院に紹介となった。妊娠経過は順調であったが、妊娠23週頃より左乳腺炎を自覚していた。妊娠24週の妊婦健診時に左乳房 AC 領域に径4cm大の発赤・腫脹と、超音波検査で同部位の液体貯留を認め、乳腺炎並びに膿瘍の形成が疑われた。乳腺外科に紹介し抗生剤内服、切開・ドレーン留置による排膿を行ったが、乳腺炎は遷延した。妊娠25週頃より両足底の紅斑と疼痛が出現し、結節性紅斑・足底筋膜炎の診断となったが、ステロイド外用で軽快した。結節性紅斑を伴った乳腺炎であることから肉芽腫性乳腺炎が疑われた。その後の切開排膿時の膿汁の細菌培養検査は肉芽腫性乳腺炎の起炎菌をターゲットとして提出し、肉芽腫性乳腺炎の起炎菌である *Corynebacterium kroppenstedtii* が検出された。妊娠31週から検出菌の感受性のあるエリスロマイシン内服を開始したが、乳腺炎は改善せず内服終了している。【考察】妊娠中の乳腺炎は稀であり、肉芽腫性乳腺炎も比較的稀な疾患である。起因菌の *Corynebacterium kroppenstedtii* は脂質好性で培養に時間を要し、検出が難しく治療に難渋する。妊娠中の乳腺炎では肉芽腫性乳腺炎を念頭におき、乳汁の培養検査に加え組織検査を行い診断する必要があると考えられる。

P-49-7 CD11c ミクログリアと髄鞘化に着目した周産期脳障害の病態解明

名古屋大

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【目的】胎児期に母体の炎症に暴露すると将来の精神疾患を含む脳障害のリスクとなる。近年、新しいミクログリアのサブセットとして、生後早期に活性化し髄鞘化の役割を担う CD11c 陽性ミクログリアが着目されている。本研究は、母体の炎症が児の CD11c ミクログリアや髄鞘化に及ぼす影響を検討した。【方法】妊娠17日目 CD1 マウスに LPS (50 μ g) を腹腔内投与し母体炎症モデルマウスを作成した。新生仔脳組織を回収し、磁気ビーズ分離法によりミクログリアを抽出した。RNA-Seq による網羅的遺伝子発現解析、FACS による CD11c 陽性ミクログリア数評価を行なった。髄鞘化について qRT-PCR 法および免疫染色法を用いて検討した。また、当院で出生した児の臍帯血および MRI を用いて、母体の絨毛膜羊膜炎と、臍帯血 IL-6、IL-17A 濃度、MRI における髄鞘化遅延の有無を検討した。【成績】日齢3ミクログリアは、LPS 群において IL-1 β 、CXCL1、CXCL10 の発現が有意に上昇した。日齢3ミクログリアにおける CD11c 陽性細胞の割合は LPS 群で有意に低下した。日齢8におけるミエリン関連タンパク質 (PLP、MBP) の mRNA 発現は LPS 群で有意に低下した。MRI では、CAM2 度以上を認めた場合に髄鞘化遅延を有する児の割合が有意に高く、CAM2 度以上を認めた患者の臍帯血サイトカイン (IL-6、IL-17A) は有意に上昇した。【結論】動物実験では、母体の炎症により児の CD11c ミクログリア数が減少し、髄鞘化遅延が起こることが示唆された。臨床においても、炎症を有する母体から出生した児の髄鞘化は遅延する割合が高いことが示され、CD11c ミクログリアは、母体炎症に起因した脳障害において、重要な役割を果たす可能性が示唆された。

P-50-1 当院で施行した子宮動脈塞栓術についての検討

ベルランド総合病院

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【目的】近年、子宮動脈塞栓術は分娩時異常出血において妊孕性温存が期待できる治療法として多くの施設で行われている。当院で施行した子宮動脈塞栓術の症例に関してその有効性について検討した。【方法】2016年1月～2021年9月までに当院で子宮動脈塞栓術を行った22症例を対象として後方視的に検討した。【成績】年齢の中央値は36歳(22-39歳)であり、12例(55%)で生殖補助医療を行っていた。分娩様式は経陰分娩が11例、帝王切開が10例、瘢痕部妊娠が1例であった。分娩後24時間以内に子宮動脈塞栓術を施行した症例は14例あり、診断の内訳は弛緩出血9例、前置胎盤2例、胎盤遺残1例、癒着胎盤1例、腔壁裂傷1例であった。平均出血量は3300mlで、11例で子宮腔内バルーンを先行して使用していた。また、分娩後24時間以降で子宮動脈塞栓術を施行した症例は7例あり、診断の内訳は、弛緩出血1例、胎盤ポリープもしくは胎盤遺残が6例であった。止血成功率は20例(91%)、止血が得られず子宮全摘となった症例は2例あり、内訳は羊水塞栓1例、産科DICによる再出血1例であった。合併症として4例で子宮内膜炎に対して抗菌薬加療を行い、うち1例で重篤な子宮内感染および筋腫壊死に対して子宮全摘を施行した。子宮全摘を必要とした症例の分娩様式はいずれも帝王切開であった。【結論】当院での検討において適切な適応で子宮動脈塞栓術を行った場合の止血成功率は非常に高く、子宮動脈塞栓術は安全かつ有用な治療法であることが示唆された。

P-50-2 当院で分娩後に子宮動脈塞栓術を必要とした症例の後方視的検討

東邦大医療センター佐倉病院

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【目的】妊産婦死亡における産科危機的出血は死亡要因の1位であり、その対処法としての子宮動脈塞栓術(uterine artery embolization; UAE)は迅速な止血、妊孕性温存、侵襲性の低さが利点である。今回当院で分娩後にUAEを要した症例を検討し、妊娠方法による発生率と分娩方法、産科危機的出血の要因及びUAEの転帰について検討した。【方法】2018年4月から2021年7月に当院で分娩、中期中絶後にUAEを施行した症例を後方視的に検討した。検定方法はカイ二乗検定で行い、 $p < 0.05$ を有意差ありとした。【成績】当院で分娩・中期中絶を施行した1101例のうち、UAEを施行例は11例(0.9%)であった。妊娠方法は自然妊娠5/951例(0.5%)、凍結融解胚妊娠6/150例(4.0%)であり、有意に凍結胚移植妊娠が高かった。分娩方法は帝王切開術4例、鉗子分娩2例、吸引分娩1例、自然頭位分娩2例、中期中絶2例であった。産科危機的出血の要因は自然妊娠では遺残胎盤2例、仮性動脈瘤3例、凍結胚移植後妊娠では遺残胎盤3例、仮性動脈瘤3例であった。11例のうち3例にUAEを先行してバルーンタンポナーデを施行した。UAE施行後の転帰は、9例はUAEのみで経過観察可能であったが、癒着胎盤1例、子宮内感染1例に子宮全摘術を施行した。【結論】遺残胎盤は生殖補助医療後の妊娠、仮性動脈瘤は子宮術後妊娠で発生率が高いとされている。今回の検討ではUAE施行症例が11例と症例数が少なく、妊娠方法と産科危機的出血の要因との因果関係は明らかでなかったが、凍結胚移植後妊娠ではUAEの適応症例が多い傾向が見られた。UAEは産科危機的出血の緊急処置として有効な手段であるが、子宮全摘に至る症例もあり、処置後の慎重な経過観察が必要である。

P-50-3 当院で過去5年に施行した分娩後出血に対する子宮動脈塞栓術(UAE)の検討

愛知医大病院

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【目的】妊産婦死亡の原因となる産科危機的出血に対する治療として、双手圧迫や子宮収縮薬の使用で止血困難な場合、バルーンタンポナーデ、子宮動脈塞栓(UAE)、子宮圧迫縫合術、子宮全摘術が行われる。当院では、比較的低侵襲で子宮温存可能なUAEを放射線科と連携し24時間体制で行っており、ハイブリッド手術室でUAEと手術を同時に行うことも可能となっている。また、出血量が多く循環動態不安定な症例に対しては救命救急科とも連携し治療を行っている。今回、当院で分娩後出血に対しUAEを施行した症例について臨床的に検討した。【方法】2016年1月から2021年8月までに当院で分娩後出血に対してUAEを施行した50症例を対象とし、患者背景、出血原因、転帰等について後方視的に検討した。【成績】1)対象期間にUAEを施行した症例における年齢の中央値は34歳(27-44歳)であった。2)分娩回数は初産婦(74%)で、分娩方法は経陰分娩(74%)が多かった。また、他院からの紹介が72%を占めていた。3)出血量の中央値は2067ml(150-8000ml)であり、27例で輸血が行われた。出血原因は胎盤遺残18例(36%)、弛緩出血15例(30%)、血腫6例(12%)、仮性動脈瘤4例(8%)、癒着胎盤4例(8%)、子宮不全破裂3例(6%)であった。4)穿通胎盤による子宮不全破裂の血流再開通症例、胎盤遺残の出血持続による症例の2例を除き、48例(96%)で重篤な合併症なく子宮温存が可能であった。【結論】コントロール不能な分娩後出血に対するUAEは、ほとんどの症例において子宮温存可能で、有効かつ安全な治療であることが示唆された。

P-50-4 分娩後異常出血に対するIVRの有効性及合併症および予後についての臨床的検討

山梨大

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【目的】分娩後異常出血では産科危機的出血に進展すると、内科的および外科的治療が奏功せず interventional radiology (IVR) を要することがある。しかしながら、IVRの有効性及合併症、予後についての報告は比較的少数であることから後方視的に検討した。【方法】2007年から2020年までに分娩後異常出血に対して当院で治療的IVRを施行した44例を対象とした。出血の原因、産科DICの有無、止血効果の有無、追加治療の有無、IVRの合併症および予後について検討した。【成績】初産婦が30例(68.2%)、ARTによる妊娠が19例(43.2%)、他院からの搬送が18例(40.9%)であった。出血の原因(重複あり)は癒着胎盤18例、弛緩出血15例、産道損傷13例、胎盤附着部異常7例、常位胎盤早期剥離4例、多胎4例、子宮筋腫3例、羊水塞栓1例であった。産科DIC(スコア8点以上)をきたした症例は25例(56.8%)であった。44例中、癒着胎盤の1例が止血困難で残存胎盤の緊急経頸管的切除術を要し、2例が再出血のため再度のIVRを要した。全例救命可能であり、経頸管的切除術を胎盤遺残7例に追加したが、子宮摘出術や産道裂傷再縫合術を施行した症例は認めなかった。止血困難の3例の共通点はARTによる妊娠、癒着胎盤、産科DICの症例であった。止血の有効性は93.2%であり、子宮壊死等の重篤な合併症は認めなかった。IVR後の9例における11妊娠を確認し、自然流産1例、分娩7例、妊娠中3例である。分娩例では3例が自己血輸血を要したが、同種血輸血やIVRは不要であった。【結論】産後異常出血に対するIVRの有効性及予後は比較的良好であると思われたが、特に癒着胎盤では止血困難症例が見られ、速やかに追加治療を行うことが肝要である。

P-50-5 蘇生的大動脈内バルーン遮断と子宮全摘術にて救命し得た産科危機的出血の2例

東海大付属病院

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【緒言】産科危機的出血症例では、両手圧迫などの止血操作や大量輸血を施行しても循環動態の維持が困難な場合がある。今回我々は、蘇生的大動脈内バルーン遮断(Resuscitative Endovascular Balloon Occlusion of the Aorta: REBOA)を併用しながら子宮全摘術を行い救命し得た2症例を経験したので報告する。【症例1】31歳, 1妊0産。妊娠38週2日。陣痛発来にて前医入院した。人工破膜後に意識消失し、胎児徐脈を認めたために緊急帝王切開が施行された。術中から子宮収縮不良が持続し、出血量が6,000ml以上となり当院へ搬送された。到着時のShock Index (SI) >1.5, JCSI100, Hb2.7g/dl, Fib38mg/dlであった。急速輸血を開始し、子宮両手圧迫や両側内腸骨動脈塞栓術等を施行したが反応に乏しく、REBOA併用で子宮全摘術を施行した。総出血量は12,000ml以上であった。【症例2】41歳, 6妊2産。妊娠37週5日、前医にて硬膜外カテーテル併用にて計画分娩となった。胎盤娩出後より、子宮口から噴射状の強出血を認めたために当院へ搬送された。到着時のSI>2.7, JCSI100, Hb2.4g/dl, Fib<35mg/dlであった。REBOA施行しながら急速輸血等を行うも止血を得られず、遮断を解除すると血圧を保つのが困難であった。REBOA併用で子宮全摘術を施行し救命した。総出血量は14,000ml以上であった。【結論】産科危機的出血の症例では、循環動態の改善を行いながら治療することが重要である。本症例の様に、両手圧迫などの止血操作や大量輸血への反応に乏しい場合には、REBOAを併用して治療を行うことが有用と考えられた。

P-51-1 胎盤内巨大血腫により胎児発育不全を来した一例

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【緒言】胎盤内血腫は、出生前超音波検査でしばしば認められるが、巨大血腫の場合は胎児発育不全(FGR)や子宮内胎児死亡(IUFD)等を起こし得ると報告されている。今回、FGRの原因が胎盤内巨大血腫と考えられた一例を経験したので報告する。【症例】29歳4妊0産(人工妊娠中絶3回)。前医妊婦健診中の超音波検査で胎盤内低エコー領域を指摘されていたが、Placental Cystの診断で経過観察とされていた。しかしながら、妊娠後期に低エコー域の拡大とFGRを認めたため妊娠36週で当院紹介となった。経腹超音波検査で児の推定体重は1676g(-3.0SD)、胎盤内に3cm×5cmの脱着膜側から絨毛膜下まで連続する低エコー域を認め、FGRの診断で入院管理とした。母体血液検査では、明らかなFGRの原因は認めなかった。妊娠37週2日胎児血流やbiophysical profile scoreに異常は認めなかったが、胎児心拍モニタリングで軽度の子宮収縮に伴い軽度変動一過性徐脈が散見されたため、胎盤機能不全を考えcontraction stress testを提示するも妊婦とご家族が帝王切開での分娩を強く希望された。妊娠37週3日帝王切開で分娩となり、出生時体重1713g、臍帯動脈血pH7.31, Apgarスコア1分値9点/5分値9点。新生児科入院時の検査では形態異常を認めなかった。病理所見では、胎盤14cm×13cmに対し、中央に7.0cm×3.5cmの巨大絨毛膜間血腫を認めた。血腫以外の胎盤組織や臍帯には異常所見は認められなかった。【結論】今回、胎盤内巨大血腫がFGRの原因と考えられた一例を経験した。胎盤内の低エコー領域はしばしば見られる所見であるが、稀に周産期予後が不良となる可能性があるため、その性状や経過に注意していく必要がある。

P-51-2 胎児頭蓋骨欠を伴う先天性皮膚欠損症 (Aplasia cutis congenita: ACC) と先天性横軸形成障害 (terminal transverse limb defect: TTLD) を合併した胎児発育不全 (FGR) の一例

帝京大病院

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【緒言】ACCは、皮膚の局所的または広範な欠損を特徴とする稀な先天性疾患群である。頭皮の欠損に加え、頭蓋骨や硬膜の欠損が認められることもある。また、多くの遺伝的症候群や先天性異常と関連していることがある。今回、胎児頭蓋骨欠損を伴うACCとTTLDを合併したFGRの妊娠管理を経験したので、報告をする。【症例】38歳、G2P1C1。第1子にFGRなし。既往歴と家族歴に特記なし。自然妊娠。妊娠9週0日のCRLは20.4mmで、妊娠8週6日相当であった。妊娠21週からBPD 50mm (-0.3SD)、AC 146mm (-1.3SD)、FL 27mm (-2.4SD)、EFBW 316g (-1.7SD)となり、非対称性FGRを認めた。妊娠28週に当院紹介され、BPD 67.8mm (-1.4SD)、AC 199mm (-2.3SD)、FL 39.6mm (-3.9SD)、EFBW 808g (-3.0SD)、胎盤臍帯に特記なし。TTLDを伴う非対称性FGRと判断した。妊娠38週にはBPD 84.1mm (-1.45SD)、AC 269mm (-1.9SD)、FL 52.4mm (-4.4SD)、EFBW 1773g (-3.2SD)となった。羊水は来院時よりMVP 2cm以上かつAFI 5から7で推移し、羊水過少傾向であった。胎位は頭位であったが新生児呼吸管理の可能性を考慮し、妊娠38週5日で予定帝王切開術を行った。Apgar1分8点、5分9点、出生体重1601g、臍帯動脈pH7.229の女児を出生した。呼吸障害は認めなかった。新生児所見は、出生前診断と同じく、裂手、裂足、合指を認めた。頭頂部頭皮と頭頂骨が6cmほど欠損し、大脳表面が透視でき、軟口蓋裂、舌小帯短縮、耳介異常、乳頭欠損、心房中隔欠損を認めた。【結語】出生前診断なく経陰分娩を選択した場合には、内診や機械分娩による脳損傷リスクがあったと考えられた。胎児期にTTLDを認めた際には、ACC合併による頭蓋骨欠損について評価が必要と考えられた。

P-51-3 胎児発育不全に対して羊水注入による胎児治療を施行した三例

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【緒言】胎児発育不全 (FGR) に対して、未だ根本的な治療法はない。今回、羊水過少を伴うFGRに人工羊水注入による胎児治療を施行した3例を経験したので報告する。なおいずれもインフォームド・コンセントを得て施行した。【症例】症例1. 34歳、妊1産0。妊娠24週。FGR。羊水過少の診断で紹介初診。児は461g (-2.3SD)で羊水腔を認めず、静脈管血流逆流を認めた。合計3回の人工羊水注入を施行した。人工羊水注入後、静脈管血流は順行性となり妊娠継続可能であったが、妊娠27週1日、繰り返す遷延一過性徐脈を認め、胎児機能不全の診断で帝王切開を施行した。児は594g、Apgar score 4/6 (1分値/5分値)で、日齢11まで人工呼吸管理を要した。症例2. 38歳、妊3産2。妊娠24週。高血圧合併妊娠とFGRで紹介初診。児は305g (-3.9SD)で、臍帯動脈血流途絶を認めた。2回の人工羊水注入を施行したが血流異常は持続した。妊娠27週3日、静脈管血流逆流を認め胎児機能不全の適応で帝王切開術を施行した。児は468g、Apgar score 1/7点 (1分値/5分値)で、日齢50まで気管挿管による呼吸管理を要した。症例3. 36歳、妊3産1。妊娠18週より82g (-4.1SD)のFGRを認め、羊水過少、臍帯動脈血流途絶を認めた。合計4回の人工羊水注入を施行したが、臍帯動脈血流途絶は持続した。妊娠29週3日、繰り返す高度変動一過性徐脈を認め、胎児機能不全の診断で帝王切開術を施行した。児は455g、Apgar score 1/6点 (1分値/5分値)で、1歳時点まで人工呼吸管理を継続している。【考察】羊水過少を伴うFGRに対する人工羊水注入は、臍帯圧迫の緩和による血流改善が期待でき妊娠期間の延長の可能性が期待できる。今後の経験と議論の蓄積が必要と考えられた。

P-51-4 妊娠前の痩せと妊娠中の体重増加の胎児発育への影響についての検討

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【目的】母体のやせや体重増加不良はSGAのリスク因子として問題となっており、やせや標準体型の妊婦の体重増加基準が従来より上方に修正された。今回、妊娠前の栄養状態や妊娠中の体重増加がSGAに与える影響を明らかにする目的で検討を行った。【方法】2017年6月～2021年7月まで当院で管理した単胎日本人妊婦を対象に、妊娠前BMIで3群に分類し (低体重群: BMI<18.5, 正常体重群: 18.5≤BMI<25, 肥満群: 30≤BMI), それぞれを妊娠中の体重増加量別に分け周産期予後と比較した。妊娠中の体重増加量は2021年に改訂された妊娠中の体重増加指導の目安 (低体重: 12-15kg, 正常体重: 10-13kg, 肥満: 7-10kg)を元に増加不十分, 適正増加, 増加過多に分類した。SGAを評価項目として妊娠前BMI分類, 体重増加分類の多変量解析を行った。【成績】1745例中, 低体重290例, 正常体重1310例, 肥満145例であった。低体重のうち増加不十分が258例 (89%), 適正増加27例 (9%), 増加過多5例 (2%)で, SGAは10% vs 0% vs 0%であった。正常体重のうち増加不十分が847例 (65%), 適正増加が363例 (28%), 増加過多が100例 (7%)で, SGAは8% vs 3% vs 3% (p<0.05)であった。肥満のうち増加不十分が68例 (47%), 適正増加が39例 (27%), 増加過多が38例 (26%)で, SGAは4% vs 0% vs 0%であった。多変量解析ではSGAの予後因子として体重増加分類の増加不十分 (p<0.05, OR 3.39, 95%CI 1.87-6.16)が抽出された。【結論】低体重群の約9割が妊娠中の体重増加が不良であり, 結果的に低体重群でSGAの発生が増加してはいたが, SGAの発生には妊娠前低BMIより妊娠中の体重増加不十分がより強く影響を与える可能性が考えられた。

P-51-5 タダラフィル投与母体より出生した児の新版K式発達検査を用いた長期発達予後評価

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【目的】子宮内胎児発育不全 (FGR) の胎内治療を目的としてホスホジエステラーゼ5阻害薬であるタダラフィルを用いた臨床試験を行っている。タダラフィルを投与した母体より出生した児の長期発達予後を評価した。【方法】2015年から2019年にFGR (胎児推定体重 \leq -1.5SD) に対してタダラフィルの経母体投与を行った症例における, 修正1.5歳, 3歳の新版K式発達検査の結果を後方視的に検討した。【成績】タダラフィル経母体投与を行った症例は55例であり, 在胎週数の中央値は37週 (IQR35-38) であり, 出生体重は1967g (1440-2361), Zスコアは-2.1 (-2.7~-1.5) であった。修正1.5歳時に発達検査が行われていたのは37例, 修正3歳時に行われていたのは17例であり, それぞれDQ値の中央値は1.5歳時で姿勢-運動: 89, 認知-適応: 91, 言語-社会: 93, 総領域: 89, 3歳時で姿勢-運動: 96, 認知-適応: 88, 言語-社会: 92, 総領域: 89であった。DQ70以下と判断されたのは1.5歳時で4例 (10.8%), 3歳時で3例 (17.6%), 70-85が8例 (21.6%) と5例 (29.4%), 85以上は25例 (67.6%) と9例 (52.9%) であった。【結論】タダラフィル投与母体から出生した児において, 神経発達は良好であると考えられた。現在プラセボ対照ランダム化比較試験を行っており, 前向きな検討を行っていく予定である。

日本語ポスター
6日(土)

P-51-6 当院でのLight For Dates児から考えるFGR管理について

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【目的】胎児発育不全 (FGR) の原因は多岐に渡り, 胎児の内的な異常だけでなく, 胎盤機能不全, 妊娠高血圧症候群 (HDP) や複数の病態が混在することもある。またその分娩においては帝王切開のリスクが上昇することが報告されている。今回我々は, 第1三半期より当院にて管理した妊娠について, 患者背景やスクリーニング超音波検査, HDP及び分娩週数と, Light For Dates (LFD) との関連, 分娩リスクについて後方視的に検討した。【方法】2018年4月から2021年3月に妊娠22週以降に当院で分娩を行った1843例のうち, 過期産10例, 双胎54例及び死産3例を除く, 1776例を対象とした。【成績】母体分娩時年齢 30 ± 5.6 歳, 分娩時在胎日齢 275.1 ± 10.2 日, 初産870例, 経産906例であった。LFDは138例で, そのうちHDPは24例, 早産は14例, HDPを発症し早産となったのは9例であった。LFDで, 既往帝王切開・子宮手術後妊娠, 骨盤位, 前置胎盤及び性器感染症を適応として帝王切開術を施行した10例を除いた128例では, 帝王切開率13.3%, 器械分娩+帝王切開率22.7%あった。AFDでは, 同様にして135例を除いた1323例のうち, 帝王切開率5.0%, 器械分娩+帝王切開率13.5%とともにLFDで有意に高かった ($P < 0.01$)。ロジスティック回帰分析にて, HDP, 体重増加不良, 低身長及び妊娠前低体重がLFDのリスク因子で, 妊娠34週以降のLFDでは, HDP及び初産が, 帝王切開のリスク因子と考えられた。妊娠20週付近での推定体重と妊娠30週付近での推定体重, 妊娠30週付近での推定体重と出生時体重に相関を認めた。妊娠20週付近での推定体重と出生時体重には相関を認めなかった。【結論】LFDが予測される場合には, HDP及び初産は帝王切開のリスクがあることを考慮して管理することが必要である。

P-51-7 当院におけるConfined placental mosaicism 4症例の臨床的特徴

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【緒言】Confined placental mosaicism (CPM) は絨毛検査の約2%で認める。絨毛検査以外が診断契機となったCPM4症例を報告する。【症例】症例1: 30歳2妊1産。妊娠18週より胎児発育不全 (FGR) を認めた。妊娠31週6日, 胎児機能不全にて緊急帝王切開術を施行, 792g, Apgar score4/8点, 臍帯動脈血液ガスpH7.251で出生。胎盤染色体検査47, XX, +16, 児染色体46, XX。生後修正1歳半, 新版K式全領域修正で97。小児科フォロー中。症例2: 37歳2妊1産。妊娠12週のNIPTで13trisomy (T13) 陽性, 初期超音波検査で異常所見なし, 羊水検査46, XXで妊娠継続。妊娠39週3日, 3398gで出生。間期核FISH法の胎盤解析で13番染色体3シグナル細胞が54%, 2シグナル細胞が46%。生後半年発達正常。症例3: 35歳3妊1産。妊娠18週よりFGRを認め, 羊水検査で46, XX。妊娠30週1日, 胎児機能不全にて緊急帝王切開術を施行, 587g, Apgar score1/3点, 臍帯動脈血液ガスpH7.101で出生。胎盤染色体検査47, XX, +15 [10] /46, XX [10]。現在生後修正1か月, GCU入院中。症例4: 37歳2妊1産。妊娠14週のNIPTでT13陽性, 初期超音波検査で異常所見なし, 羊水検査46, XXで妊娠継続。妊娠38週0日, 2402gで出生。間期核FISH法の胎盤解析で13番染色体3シグナル細胞が35%, 2シグナル細胞が65%。生後1か月発達正常。【考察】CPMの診断契機はNIPT偽陽性が2例, 重度のFGRが2例であった。T13のCPMは通常の妊娠分娩管理が可能であった。NIPT受検者の増加に伴い, 今後NIPT偽陽性がT13のCPMの診断契機になる例が増えると予想される。一方, T15とT16のCPMは重度のFGRが診断契機であった。-2SD以下のFGRの16%にCPMを認めるとの報告がある。CPMは染色体の種類やモザイクの割合で予後や管理が異なり, 適切な妊娠管理と情報提供が重要である。

P-52-1 国際的な定義による胎児発育不全の分類による周産期事象の検討

東邦大医療センター大森病院

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【目的】本邦では胎児発育不全は胎児体重基準値の-1.5SDを下回る場合に羊水過少や腹囲なども考慮し総合的に診断される。一方 ISUOG (International society of ultrasound of obstetrics and gynecology) における胎児発育不全の定義では大きさの評価に加えて超音波ドプラ法による評価を合わせることで FGR (fetal growth restriction) と SGA (Small for gestational age) を区別している。本研究の目的は当院で胎児発育不全と診断した児を ISUOG の基準で FGR 群と SGA 群に分けて周産期事象を検討することである。【方法】対象は 2019, 2020 年に当院で胎児発育不全と診断された児。診療録を元に後方視的に ISUOG での FGR の定義に沿って FGR 群と SGA 群に分けて統計学的に検討した。【成績】53 例の胎児発育不全と診断された児を Consensus definition に沿って 7 例の胎児奇形症例を除き分類したところ FGR 群は 31 例, SGA 群は 15 例であった。FGR 群と SGA 群で経産の有無, 妊娠方法, 妊娠前体重 (51.7/51.4 (以下%以外は平均値)), 分娩時年齢 (33.6/33.3) に両群に統計学的な差を認めなかった。一方で分娩週数 (34.7 週/38.9 週), 出生体重 (1665g/2374g), 胎盤重量 (384g/437g), 胎児適応での緊急帝王切開術 (35%/6%) に統計学的な差を認めた。Apgar score (1 分値 6.5/7.7, 5 分値 8.3/8.8), 臍帯動脈血 pH (7.31/7.31), 低血糖 (26%/6%), 未熟児貧血 (19%/3%), 呼吸窮迫症候群 (16%/3%), 壊死性腸炎 (3%/0%), 脳室内出血 (0%/0%), 慢性肺疾患 (0%/0%) には統計学的な差を認めなかった。【結論】胎児発育不全のなかでも FGR 群は SGA 群に比べて早産や緊急帝王切開術, 低出生体重児リスクが高く, ISUOG Consensus definition を用いた分類が有用と考えられる。

P-52-2 胎児発育不全における胎児構造異常の有無による児の予後の比較

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【目的】近年, 胎児発育不全 (Fetal growth restriction ; FGR) は, 構造異常の有無による分類が試みられている。しかし, FGR における胎児構造異常の有無と短期的予後の関連は報告によって異なり, 一定していない。本研究では, 当院で FGR として管理した症例を胎児構造異常の有無で比較し, 胎児構造異常の有無が日齢 28 時点の生命予後に影響するかを明らかにすることを目的とした。【方法】2014 年から 2020 年までに当院で妊娠 22 週以降の単胎分娩をした妊婦のうち, 妊婦健診時に一度でも FGR と診断された妊婦とその児を対象とした。対象症例について後方視的に診療録から情報を抽出し, 胎児構造異常を認めた群 (奇形群) と認めなかった群 (非奇形群) で, 日齢 28 時点での児の生存率および NICU 入院率を比較した。【成績】対象症例は, 奇形群が 23 例, 非奇形群が 55 例であった。分娩週数に有意差は認めず, 出生体重は 1592 g vs 2350 g で奇形群で有意に低かった ($p < 0.001$)。日齢 28 時点での児の生存率は 78.2% vs 96.3% で, 奇形群で有意に低かった ($p = 0.02$)。日齢 28 時点での NICU 入院率は 77.8% vs 9.4% で, 奇形群で有意に高かった ($p < 0.001$)。周産期死亡の原因を比較すると, 奇形群では構造異常の原因疾患自体が死因となっていたが, 非奇形群では児の未熟性に伴う疾患が死因となっていた。【結論】構造異常を伴う FGR の短期的な生命予後は, 構造異常を伴わない FGR と比較して不良であった。胎児構造異常の有無が胎児の生命予後予測において重要な因子となるため, FGR と診断した場合は超音波検査などによる入念な構造異常の検索が必要である。

P-52-3 正期産期の血流異常を認めない胎児発育不全の周産期予後

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【目的】妊娠 37 週に胎児血流異常を認めない胎児発育不全 (FGR) の周産期転帰を検証し, その周産期転帰を Appropriate for gestational age (AGA) の胎児と比較する。【方法】2018~2020 年に当院で正期産に分娩した単胎妊娠を対象にした後方視的研究である。妊娠中に診断された染色体異常や重篤な形態異常は除外した。妊娠 37 週にドプラ血流異常を認めない FGR について, その後の血流異常の有無および複合有害転帰 (陣痛発来前の胎児機能不全 : NRFS, NRFS による帝王切開, 胎児・新生児死亡) の発生割合を明らかにし, AGA と比較した。また, 分娩まで血流正常であった FGR (NDF), 妊娠 37 週以降で血流異常を認めた FGR (ADF) について, 複合有害転帰の発生率を算出した。胎児血流は, 臍帯・中大脳動脈および静脈管で評価した。臍帯動脈血流の $PI > 95\%$ tile, 中大脳動脈血流の $PI < 5\%$ tile, 静脈管の $PI > 95\%$ tile を血流異常とした。【成績】対象は 3615 例で, 胎児血流異常を認めない FGR は 105 例, AGA は 3510 例であった。FGR の在胎週数は中央値 39.6 週 (37-41.7 週), 出生体重は中央値 2374g (1684g-3050g) であった。複合有害転帰は, FGR は 2.9% (3 例), AGA は 1.5% (52 例) であった ($P = 0.219$)。また, NDF は 96 例 (91%), ADF は 9 例 (9%) で, 複合有害転帰は, それぞれ 2% (2 例) と 11% (1 例) であった。【結論】妊娠 37 週に血流異常を認めない FGR の周産期転帰は AGA と変わらないため, FGR を適応とした妊娠終結は必要ないと思われた。しかし, 9% が血流異常を認め, 有害転帰の発生率も上昇するため, 継続した胎児評価が望まれる。

P-52-4 重症胎児発育不全の前方視的コホート研究—短期予後の検討—

重症胎児発育不全の前方視的コホート研究班

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【目的】胎児発育不全 (FGR) 児の周産期管理法は未だ確立されていない。出生体重3%tile未満の重症SGA児を対象とした我々の後方視的研究では、在胎週数以外には羊水過少のみが短期予後因子であったが、胎児死亡例や血流データが欠如していた。本研究の目的は前方視的コホート研究で重症FGR児の短期予後因子を明らかにすることである。【方法】本邦25施設での多施設コホート研究で、妊娠22週以降28週未満に推定体重-2SD未満の単胎重症FGRを対象とし登録した。母体合併症により登録時に妊娠継続が困難な症例は除外し、母体合併症、妊娠合併症、胎児超音波所見(胎児推定体重(EFBW)、羊水量、血流所見等)、分娩時情報、新生児情報(出生体重、修正40週までの合併症等)などの各種データを収集し、主要評価項目は短期予後不良として解析した。短期予後不良は子宮内胎児死亡(FD)、修正40週までの死亡・3度以上脳室内出血(IVH)・脳室周囲白質軟化症(PVL)と定義した。【成績】2014年10月~2017年9月に233例が登録された。脱落9例、予後不明9例、データ不備1例を除外した214例中、生後判明した先天異常14例を除外した200例を解析対象とした。平均登録週数は25.7週、平均分娩週数は33.2週、平均出生体重1303gであった。短期予後不良はFD7例、死亡6例、IVH3例、PVL4例の計19例(9.5%)であった。短期予後不良に関連する登録時所見の調整オッズ比[95%信頼区間]は羊水過少(6.67[1.90-23.42]、 $P=0.003$)、EFBW-3SD未満(2.93[1.04-8.25]、 $P=0.042$)、臍帯動脈血流異常(2.66[0.84-8.42]、 $P=0.096$)であった。【結論】羊水過少に加え、EFBW-3SD未満がFGR児の新生児予後に関連していることが示唆された。

P-52-5 重症胎児発育不全の前方視的コホート研究～血流異常出現パターンの検討～

重症胎児発育不全の前方視的コホート研究班

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【目的】発育不全胎児における血流異常の出現パターンと時間経過を解析し、傾向を明らかにする。【方法】25施設による前方視的コホート研究である。2014年10月-2017年9月に、妊娠28週未満で推定胎児体重-2SD未満の単胎例を対象とした。臍帯動脈(UA)、中大脳動脈(MCA)、静脈管(DV)の血流波形を分娩まで週1回以上計測し、UAの拍動指数(PI)の>95%ileと拡張期途絶逆流、MCAのPI<5%ile、CPR(MCA-PI/UA-PI)<5%ile、DVのPI>95%ileとa波の逆流を異常のポイントとしてタイミングを同定し、出現順とインターバルを検討した。【成績】対象209例中、121例が人工早産、10例が自然早産、7例が胎児死亡となった。最も典型的な出現順はUA-PI↑、CPR↓、DV-PI↑、MCA-PI↑、UA途絶、UA逆流、DV逆流で、出現から分娩までの日数の中央値は各々、23.5、19、17、15、8、4、0.5であった。UA途絶から分娩までの日数の中央値は8日で、14日以上なのが39%あり最大値は51日であった。UA途絶逆流が先行しDV-PIが後で上昇するパターンは結果的に人工早産になる例でしか見られないが、DV-PI上昇が先行するパターンでは、以後正産期まで至るケースが相当数みられた(22%)。エントリー時点で複数の血流異常のあった例を除いた131例中、DV-PI↑がUA-PI↑やMCA-PI↓に先行したものが28例あったが、12例は最終的に正産期分娩となっており、うち10例ではUA-PI↑やMCA-PI↓が最後まで出現しなかった。【結論】FGRにおける血流異常出現に一定の傾向はあるが、典型から外れる場合も多い。UA途絶から長期妊娠継続可能な例があり、また、DV-PIの上昇はしばしば早期よりみられ、単独では病的意義が高くない。各血流異常を複合的に捉えることが管理に重要である。

P-52-6 重症胎児発育不全の前方視的コホート研究～妊娠36週以降の分娩に対する超音波予測因子の検討～

重症胎児発育不全の前方視的コホート研究班

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【目的】早産期の胎児発育不全(FGR)症例のうち早期に娩出が必要となる症例と正産期まで待機が可能な症例がある。重症胎児発育不全の前方視的コホート研究のサブ研究として、妊娠28週の重症FGR症例において妊娠36週以降の分娩の頻度および超音波予測因子について検討した。【方法】本邦25施設での多施設コホート研究で対象とした妊娠22週以降28週未満の推定体重(EFBW)が-2SD以下のFGR症例のうち、妊娠28週時点で胎児生存例を対象とした。主要評価項目は妊娠36週以降の分娩の割合であり、また母体背景および妊娠28週(±1週)の超音波計測値と予後との関連を検討した。妊娠28週未満の早産、先天疾患、胎児死亡、転帰不明は除外した。娩出基準は各施設の基準とした。年齢、EFBWのSD(0.5毎)、臍帯動脈PI値95%タイル以上(UAPI)、中大脳動脈PI値5%タイル未満(MCAPI)、中大脳動脈最高血流速度1.5MoM以上(MCA-PSV)、cerebroplacental ratio(CPR)(0.1毎)に関して予後に対する調整オッズ比を多変量ロジスティック解析にて算出した。【成績】232の登録例のうち157例が解析対象となった。妊娠36週以降の分娩は81例(51.6%)であった。関連のあった因子の調整オッズ比[95%CI値]はEFBW(-3.0SD以下)が3.43[1.34-8.78]($P<0.05$)、UAPIが0.23[0.09-0.58]($P<0.01$)であった。ROC曲線から求めたEFBW(SD)カットオフ値とその感度、特異度、AUCは2.63SD以上、68.0%、76.5%、0.726であった。【結論】妊娠28週の重症FGRの52%が妊娠36週以降の分娩に至り、特にEFBWが2.6SDより大きいこと、およびUAPIが正常の場合がその予測因子であった。

P-53-1 羊水過多症例に対する羊水除去術の有無による周産期予後の検討

長野県立こども病院

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【目的】羊水過多症に対して、母体症状の緩和などを期待して羊水除去術が行われる。一方、羊水除去術は子宮穿孔という侵襲を伴うため、様々な合併症のリスクを十分に説明した上で行うことが求められる。今回、当院での羊水過多症例において、羊水除去術の有無による周産期予後について検討を行った。【方法】2012年1月1日から2020年12月31日の間に当院で分娩となった羊水過多174例について、羊水除去術を行わなかった群(A群:112例)、1回のみ行った群(B群:33例)、2回以上行った群(C群:29例)の3群間で、臨床背景、羊水過多の診断週数・分娩週数・診断から分娩までの日数・分娩時出血量・分娩時間、切迫早産・前期破水・分娩誘発または促進・緊急帝王切開・病理学的絨毛膜羊膜炎・常位胎盤早期剝離の有無について χ^2 検定を用いて後方視的に検討した。【成績】C群はA群と比較して有意に、消化管閉鎖または胎便性腹膜炎の胎児診断となった症例が多かった($p<0.05$)。A群、B群、C群それぞれにおいて、診断週数は 30.0 ± 3.7 , 28.7 ± 3.2 , 26.9 ± 3.5 (平均値 \pm SD)、分娩週数は 37.9 ± 2.4 , 37.1 ± 2.7 , 35.9 ± 2.4 (平均値 \pm SD)であり、いずれもA群とC群間に有意差を認めた($p<0.001$)。切迫早産と診断された症例は、C群はA群と比較して有意に多かった($p<0.05$)。他の項目には各群間に有意差を認めなかった。【結論】複数回の羊水除去術を行った症例における合併症としては、切迫早産のみ発症頻度が高かった。羊水過多症を有する症例においては、切迫早産の管理を行いつつ羊水除去術を行うことは有益であると考えられる。

P-53-2 羊水過多における羊水量と原因疾患についての検討

静岡県立こども病院

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【目的】羊水過多を契機として胎児異常が見つかることがあるが、原因疾患は多岐に渡り、診断に苦慮する時もある。羊水過多の程度と胎児異常に関して後方視的に検討した。【方法】2010年9月~2021年9月に入院管理を要した羊水過多症例のうち、胎児異常を伴う単胎100例を対象とした。AFI値(最大値)で、24~30を軽度群、30~34.9を中等度群、35以上を重度群と分類した。【成績】重症度群は56例(56%)、中等度群32例(32%)、軽度群は12例(12%)であった。重症度群の原因疾患は、消化管閉鎖19例、顎形成異常などの嚥下障害によるものが10例、18trisomy 9例、骨系統疾患8例であった。このうちAFI50を超える羊水過多が3例あり、2例は顎形成異常、1例は骨系統疾患であった。中等度群では、18trisomy 9例で、横隔膜ヘルニア4例、胎児水腫4例であった。軽度群は18trisomy 3例で、消化管閉鎖2例、胎児水腫2例であった。羊水過多の程度と胎児異常の関連は認めなかったが、嚥下障害が重度群で多かった。妊娠転帰では、早産は重度群31例(55%)、中等度群15例(46.8%)、軽度群7例(58%)で、胎児適応によらない早産は、重度3例、中等度1例、軽度2例であり、羊水過多の程度と早産に関連は見られなかった。【結論】今回の検討では羊水過多の程度と原因疾患、妊娠転帰に関連を認めなかったが、嚥下障害によるものは重度群に多い事が分かった。超音波診断では、羊水過多の原因として消化管閉鎖や18trisomy、骨系統疾患は診断されることが多い一方で、嚥下障害は超音波で同定しにくく、出生直後に気道確保が困難となる形態的異常を伴う場合もある。羊水過多が重度の場合は、嚥下障害を伴う胎児異常に留意することが望ましいと考えられる。

P-53-3 当院における羊水過少例の検討

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【目的】羊水過少は遭遇することの多い産科異常であるが、その原因・母体合併症・胎児異常・周産期予後など不明な部分が多い。当院において管理した羊水過少症例を検討し、新生児予後に影響を与える因子を抽出する。【方法】例は2016年から2020年の5年間に当院で分娩となった症例のうち、AFP $<$ 2cmもしくはAFI $<$ 5cmを一度でも認めたものを対象とし、多胎は除外した。酸素不要の退院症例をA群、IUFDや死亡退院、在宅酸素を要した症例をB群とした。【成績】A群(n=15)とB群(n=7)において、両群で年齢、妊娠分娩回数、FGRやHDP合併、妊娠契機、分娩様式は差を認めなかった。A群ではHDP4例、CAOS1例、Trisomy211例、原因不明9例であった。うち3例は一度羊水過少を指摘されるもその後正常化した(1例はARB内服による医原性)。B群ではPotter症候群2例、CAOS2例が含まれており、A群に比して羊水過少診断時期や分娩週数が有意に早く、形態異常を合併する割合が高かった。一方でHDPやFGR、分娩様式は新生児予後に影響していなかった。【結論】A群では原因不明の羊水過少が多く、また一度羊水過少を指摘されても自然に羊水量が回復している症例もあり予後は良好であると考えられた。一方でB群ではCAOS及びPotter症候群が含まれており、早期に羊水過少の診断となり予後の悪化につながっていると考えられた。またHDPやFGRの存在よりも早期に羊水過少と診断され早産を余儀なくされる方が予後に与える影響が大きいと推測された。羊水過少症例ではその診断週数及び胎児形態異常の有無が予後に影響するため、特に診断週数が高い症例では胎児全身スクリーニングにより胎児形態異常の有無を精査する必要があると考えられた。

P-53-4 胎児炎症反応症候群を予測する新規羊水バイオマーカーの検討

滋賀医大附属病院

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【目的】胎児炎症反応症候群 (FIRS) は脳性麻痺や慢性肺疾患との関連が報告されているが、その発症を事前に予測することは困難である。既存の予測因子として IL-6 が報告されているが十分ではない。近年尿中 L 型脂肪酸結合蛋白 (L-FABP)、好中球ゼラチナーゼ結合性リポカイン (NGAL) は敗血症の急性腎障害のマーカーとして注目されており、我々は胎児尿である羊水中に存在するこれらのマーカーが FIRS を予測する新規羊水バイオマーカーの候補となりえるかを検証した。【方法】当院で管理した単胎妊婦症例を対象に、分娩時に羊水を採取し、分娩後の胎盤病理、臍帯血 IL-6 値から FIRS 群 (胎盤病理で絨毛膜羊膜炎と臍帯炎、または臍帯血 IL-6 ≥ 11 pg/mL) と non-FIRS 群に分類した。両群間で母体背景、羊水中 IL-6、L-FABP、NGAL を比較検討し、新生児の臨床転帰との関連を解析した。【成績】129 症例を解析した。FIRS 群 (27.9%, 36/129) と non-FIRS 群 (72.1%, 93/129) に分けられた。母体白血球数 (9600 vs 7950 μ L; $p=0.008$)、羊水中 IL-6 (22022 vs 2282 pg/mL; $p<0.001$)、NGAL (36050 vs 15600 μ g/gCr; $p=0.002$) において両群間で有意差を認め、多変量解析でも、母体白血球 (OR 3.69; $p=0.012$)、羊水中 IL-6 (OR 4.39; $p=0.005$)、NGAL (OR 3.74; $p=0.016$) が有用な予測因子であった。羊水中 L-FABP (132 vs 131 μ g/gCr; $p=0.677$) は両群間で有意差は認めなかったが、新生児の呼吸管理群 (296 vs 119 μ g/gCr; $p<0.001$) で有意に高値であった。【結論】母体白血球、羊水中 IL-6、NGAL は FIRS、羊水中 L-FABP は新生児の呼吸管理の有用な予測因子と考えられ、これらのマーカーを組み合わせることで FIRS を予測するマーカーとして活用できる可能性が示唆された。

P-53-5 慢性早剥羊水過少症候群 (CAOS) の新生児予後規定因子の解析

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【目的】慢性早剥羊水過少症候群 (CAOS) は長期持続する性器出血と時系列的な羊水過少を主な臨床症状とする病態を指す。平均分娩時期は 25-27 週と早く、新生児予後は必然的に不良となる。また羊水過少および血性羊水を呈することから胎児肺への影響は強く、新生児慢性肺疾患 (CLD) や肺高血圧症、dry lung syndrome は必発ともいえる。今回妊娠期間中に新生児予後を規定する因子があるか検討した。【方法】当院で管理し 2010 年から 2020 年に分娩に至った 17 症例について、分娩週数、児出生体重、肺高血圧症に対する一酸化窒素 (NO) 使用の有無、CLD、在宅酸素の有無、羊水量を解析した。【成績】分娩週数 (中央値および範囲) は 26 週 3 日 (23 週 2 日-37 週 0 日)、出生体重は 809g (562-1891g)、Z score は -0.42 (-2.05-2.12) であり、FGR (Z score < -1.5) は 2 例のみであった。娩出後一時的に NO を使用した新生児は 6 例 (35.3%) であり、羊水最大深度 (MVP) < 1 cm の期間が有意に長かった ($p=0.0016$, 5.33 日 vs 0.36 日) が、MVP < 2 cm の期間は有意差を認めなかった ($p=0.46$, 11.50 日 vs 7.36 日)。転院及び死亡した症例を除いた 12 例全例に修正週数 36 週で CLD を認め、うち 6 例で NICU 退院時に在宅酸素が導入されたが、1 歳半の時点では 1 例のみであった。【結論】CAOS は新生児の呼吸状態に影響を及ぼし、MVP < 1 cm の期間が長いほど肺高血圧が出現し一時的な NO の使用が必要となる可能性が示唆された。1 歳半で在宅酸素を離脱できるため、可能な限りの妊娠継続が望ましい。

P-54-1 臍帯過捻転により、Non-reassuring fetal status (NRFS) となり、緊急帝王切開が行われた 2 例の、妊娠中の NST 所見と分娩時の CTG Monitoring 所見、超音波所見、胎盤臍帯所見

明和病院

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【緒言】胎児が NRFS や死産となるのは、常位胎盤早期剥離と形態異常以外では臍帯の異常が多い。当院の連続 493 分娩例において、2 例の臍帯過捻転による緊急帝王切開 (CS) があったので、妊娠中の NST 所見と分娩時の CTG 所見、超音波所見、胎盤臍帯所見について報告する。【症例 1】19 歳、初産婦、37 週、前期破水で入院。同日、遷延性徐脈が出現し超緊急 CS を行い、臍帯過捻転を認めた。Umbilical coiling index (UCI: coils per centimeter, $0.5 \leq$) は、1.2 であった。3266g の女児。ApS: 1/4/5。Umb A の pH: 6.791。同日、H 大に新生児搬送した。胎盤病理検査で CAM III 度の所見を認めた。児は 11 日後に、軽快退院。病名は、①新生児遷延性肺高血圧症、②出血性肺浮腫であった。1 か月健診は当院で行い、経過に著変を認めなかった。【症例 2】23 歳、初産婦、39 週の外來での NST で、基線細変動減少と一過性徐脈を認め管理入院。翌日、CST Positive、超音波検査にて胎動を認めず、緊急 CS。2650g の女児。ApS: 4/7/9。Umb A の pH: 7.117。臍帯過捻転を認め、USI は 0.8 であった。母児の経過に著変を認めなかった。【考察】臍帯過捻転は出生時に診断されることが多いが、胎児に影響を与えない症例から、子宮内胎児死亡となる症例まで様々である。NRFS や死産となる臍帯因子のなかで、臍帯過捻転は 44.2% である。小児科と産婦人科があり、MFICU と NICU を持たない総合病院では、重症妊娠高血圧症候群がある常位胎盤早期剥離や、形態異常の児の妊娠管理をすることは少ないが、臍帯過捻転で NRFS となって急速遂娩を必要とすることは多い。【結論】通常の分娩取り扱い施設では、NRFS や胎内死亡の原因として、臍帯過捻転を常に念頭に置く必要がある。

P-54-2 臍帯動脈血栓により急性の胎児発育不全、胎児機能不全を来したと考えられた一例

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【緒言】臍帯動脈血栓により急性の胎児発育不全、胎児機能不全を来したと考えられた一例を経験した。【症例】33歳、1妊0産。自然妊娠で妊娠成立し、妊娠25週の健診時まで妊娠経過に異常を認めなかった。胎児推定体重は-0.1SD~0.2SDで推移し羊水量は正常であった。妊娠27週2日の妊婦健診で胎児推定体重809g(-1.8SD)と胎児発育不全を認め Amniotic Fluid Index 6cmと羊水量は減少していた。Biophysical Profile Scoreは10/10点であった。同日精査目的で紹介され、経腹超音波検査で右臍帯動脈の途絶を認めた。胎児心拍モニタリングで胎児心拍165~175bpmの頻脈、基線細変動減少、高度遅発一過性徐脈を認め、胎児機能不全と判断し同日緊急帝王切開を行った。児は男児であり、823g(-1.5SD)、アプガースコアは1分値6点、5分値7点、臍帯動脈血液ガス分析値はpH7.416、pCO₂27.9mmHg、pO₂28.5mmHg、BE-5.1mmol/Lであった。臍帯は黄緑色に変色し臍帯捻転を認めた。胎盤、臍帯病理では2本の臍帯動脈と1本の臍帯静脈を確認したが、臍帯動脈の1本に器質化を伴わない比較的新しい血栓を認め、臍帯動脈血栓による機能性単一臍帯動脈と判明した。【考察】2週間以内という短時間で臍帯動脈血栓により急速に胎児発育不全、胎児機能不全を来した一例であった。臍帯動脈血栓では胎盤因子による胎児発育不全より急速に胎児の状態が悪化する可能性がある。【結語】急性経過の胎児発育不全を認めた場合臍帯動脈血栓による機能性単一臍帯動脈が考慮され、急速に胎児機能不全となる可能性があるため注意深い管理が必要である。

P-54-3 分娩開始直前に臍帯卵膜付着および前置血管を診断し生児を得た2例

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【緒言】臍帯卵膜付着は、胎児発育不全や胎児・新生児死亡などに関連し、妊娠予後を左右しうる。前置血管は破水や分娩進行によって胎児血管が破綻すると胎児死亡のリスクが高く、分娩開始前に診断することが重要である。今回、分娩開始直前に臍帯卵膜付着および前置血管を診断し、胎児血管の破綻前に児を娩出し得た2例を報告する。【症例①】37歳3妊1産。IVF-ET妊娠成立。もやもや病合併妊娠のため妊娠初期に当科紹介。硬膜外無痛分娩の方針とし、妊娠38週3日より分娩誘発を開始した。妊娠39週1日の経腹超音波検査にて、B-modeでは指摘できなかったが、カラードプラ法で内子宮口と児頭の間に胎児血管を認め、前置血管と診断した。分娩誘発を中止し、緊急帝王切開術を施行した。児は2890g、Apgar Score 8/9点、臍帯動脈血pH7.342であり児の転帰は良好であった。【症例②】39歳4妊2産。自然妊娠成立。前医での妊婦健診で経過良好であった。妊娠34週4日に前期破水のため当院母体搬送となった。入院時の経腹超音波検査カラードプラ法にて内子宮口付近に胎児血管を認め、卵膜付着臍帯および前置血管を疑った。破水後であり胎児血管の破綻リスクが高く、緊急帝王切開術を施行した。児は2246g、Apgar Score 6/8点、臍帯動脈血pH7.334であり児の転帰は良好であった。いずれの症例も帝王切開時に子宮切開直下に胎児血管を認めており、破綻させないように慎重に操作を行った。【結論】臍帯付着部異常および前置血管は妊娠中期までの超音波検査によるスクリーニングが勧められている。B-modeのみでは診断困難な症例もあり、カラードプラ法を併用したスクリーニングが必要かもしれない。

P-54-4 Dual gate Doppler 法により計測した左室流出路と臍帯付着部の動脈波形の位相差は臍帯長と関連する

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【目的】臍帯長は分娩時の胎児機能不全に関連し、児の周産期予後に影響を与える可能性があるがその予測法は確立していない。今回妊娠中期にDual gate Doppler法により計測された左室流出路と臍帯付着部の動脈波形の位相差が、満期で出生した児の臍帯長と関連するか検討を行った。【方法】研究デザイン：前方視的研究。対象：妊娠36週から41週で出産した単胎妊娠で染色体異常症例を除外した。妊娠24週から妊娠26週にDual gate Doppler法を用い、左室流出(left ventricle outlet)と臍帯付着部(cord insertion)の二点にサンプルゲートを設定し、二点間の動脈波形の位相差(pulse transit time)をLI-PTTとして計測した。またその際に羊水量、胎児推定体重、umbilical coiling index(UCI)、臍帯の太さ、胎児心拍数も計測をした。LI-PTTと各パラメーターの関連をPearsonの積率相関係数から求めた。本研究は当院倫理委員会の承認のもと施行した。【成績】対象となった71例中3例が観察部位の正確な描出が困難であり、LI-PTTが計測不能であった。68例の観察においてLI-PTTの平均値は89.3msであった。LI-PTTと出生時の臍帯長のとの間に中等度の相関を認めた($r=0.51$, $p<0.01$)。LI-PTTとUCIの間に弱い相関を認めた($r=0.26$, $p=0.018$)。LI-PTTと、胎児心拍数、羊水量、胎児発育との間に有意な関連を認めなかった。【結論】妊娠中期の超音波による観察で出生時の臍帯長を予測できる可能性があるが、正確な予測のためには手技の習熟、LI-PTTと関連する他の因子との関連を考慮する必要がある。

P-54-5 前置血管の術前評価としてMRIが有用であった2症例

ベルランド総合病院

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【緒言】前置血管は通常は超音波検査で診断が可能であるが、臍帯血管の走行を立体的に把握することが困難な場合も多い。術前にMRIを実施することで卵膜上の臍帯血管の走行を把握し、安全に帝王切開を実施できた2症例について報告する。【症例1】30歳、初産婦。排卵誘発で妊娠成立。妊娠18週の中期スクリーニングで臍帯卵膜附着を確認し、妊娠21週の経陰超音波検査で内子宮口上に臍帯血管の走行あり、前置血管と診断した。妊娠32週にMRI撮影し、卵膜附着した臍帯血管が内子宮口を通して子宮前壁の胎盤に繋がっていることが確認できた。妊娠32週から管理入院し、ステロイド投与後に妊娠33週6日で選択的帝王切開術を実施し、1918gの男児をApgarスコア1分8点、5分9点で娩出した。【症例2】34歳、初産婦。IVF-ETで妊娠成立。妊娠24週に前置胎盤の疑いで当院紹介となり、経陰超音波検査で内子宮口付近に卵膜を走行する臍帯血管を認め、前置血管と診断した。妊娠31週にMRI撮影し、臍帯が子宮前壁側に卵膜附着し、頭尾側方向に分かれて卵膜上を走行した後に後壁の胎盤に到達していることが分かった。妊娠32週から管理入院し、ステロイド投与後に妊娠34週1日に選択的帝王切開を実施し、MRI所見を参考に子宮切開創の直下を走行している臍帯血管を破綻させることなく、2106gの女児をApgarスコア1分8点、5分9点で娩出した。【考察】超音波検査とMRIを組み合わせることで実際の臍帯血管の走行を正確に把握し、安全に児を娩出することができた。前置血管の補助診断としてMRIが有用である可能性が示唆された。

P-54-6 妊娠38週で子宮内胎児死亡となった臍帯動脈血栓症の一例

山形県立中央病院

福長健史, 高橋裕也, 丸山真弓, 小幡美由紀, 堤 誠司

【緒言】臍帯動脈血栓症の発症率は0.0025~0.045%と稀な疾患であり、胎児機能不全や胎児死亡の原因となりうる。今回、妊娠後期に臍帯動脈血栓症が原因で子宮内胎児死亡に至ったと考えられる一例を経験したので報告する。【症例】37歳、3妊1産、自然妊娠し前医を受診した。Rh(D)陰性のため妊娠12週から当院に紹介された。妊娠20週から羊水量は正常上限で経過し、妊娠28週で間接クームス試験陰性を確認して抗D免疫グロブリン投与を行った。妊娠30週から羊水過多を認めたが原因検索で明らかな異常なく、妊娠35週からは羊水量正常で経過した。妊娠38週3日の朝から胎動減少を自覚し、同日の妊婦健診で胎児心拍数陣痛図および胎児超音波で胎児心拍が確認できず、子宮内胎児死亡の診断で入院となった。入院時の血液検査では特記異常を認めず、間接クームス試験は陰性であった。翌日から子宮頸管拡張を開始したところ陣痛発来し、自然死産に至った。児は3,270gで明らかな外表奇形を認めず、臍帯は胎児側から20cm程が暗赤色に変色していた。胎盤には明らかな異常を認めなかった。死亡時画像診断では明らかな異常を認めず、胎盤の病理検査では臍帯動脈内に新鮮な血栓形成を認めた。児の剖検は希望されず、胎盤の遺伝子検査では染色体異常はなかった。産後に施行した血液検査では、母体に明らかな血栓性素因は認めなかった。【考察】臍帯動脈血栓症は臍帯血管血栓症の約10%を占める。臍帯血管血栓症の原因として臍帯過捻転や臍帯巻絡、臍帯結節などの機械的閉塞や母体の血栓性素因などの報告があるが、本症例はいずれも認めなかった。

P-54-7 臍帯動脈瘤による臍帯血流途絶によって子宮内胎児死亡に至ったと考えられる1例

JCHO 大阪病院

赤田 将, 谷口茉莉子, 森 禎人, 松村有起, 田中稔恵, 繁田直哉, 清原裕美子, 大八木知史, 筒井建紀

【緒言】臍帯動脈瘤は臍帯静脈の圧迫や臍帯の捻転によって胎児の低酸素血症、胎児死亡を引き起こしうる稀な疾患である。臍帯動脈瘤による臍帯血流途絶によって子宮内胎児死亡に至ったと考えられる1例を経験したので報告する。【症例】30歳女性、1妊0産。近医にて妊婦健診を実施し、妊娠35週より当院での周産期管理を開始した。前医、当院での胎児精密超音波検査で特記すべき所見を認めなかった。妊娠39週1日、陣痛発来し来院。陣痛開始した時点から胎動の減少を自覚していた。来院時の診察で胎児心拍は認めず子宮内胎児死亡の診断となった。経陰分娩で娩出し、児に明らかな形態異常はなかったが、臍帯動脈に約1.8cm大の動脈瘤を認め、病理学的検査で臍帯静脈の圧迫を認め診断に至った。【考察】子宮内胎児死亡の原因は多岐に渡り病理の検索においても特定できないことが多い。本症例では病理検査結果で臍帯動脈瘤形成部位の臍帯静脈が閉塞しており、臍帯血流途絶によって急性胎児死亡の原因となった可能性が考えられた。【結語】本症例は陣痛発来と同時に胎動減少が起きていることから臍帯因子を疑い、稀な疾患である臍帯動脈瘤を診断し得た貴重な一例である。また胎児死亡においてはグリーンフケアの観点を持って対応することも重要であり、原因検索はグリーンフケアの一助ともなると考える。

P-54-8 前置血管4例における周産期臨床像の検討

国立九州医療センター

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【目的】前置血管とは、臍帯卵膜付着や副胎盤などで羊膜と脱落膜の間を走行する臍帯血管が内子宮口周辺を通る状態を指す。全分娩の0.04%と稀な合併症ではあるが、前置血管の断裂は胎児からの出血となり、胎児機能不全や胎児死亡を来すため、分娩前診断の有無が周産期予後を左右する。2020年より当院で経験した前置血管4例の周産期臨床像について文献的考察を含め報告する。【症例】母体背景は平均年齢33歳。単胎3例(自然妊娠1例, 体外受精2例), 双胎1例(自然妊娠)であった。平均診断週数は妊娠30週で、経陰超音波断層法で内子宮口上に管腔構造を認め、カラドプラーで胎児血流を確認し前置血管と診断した。胎盤位置異常の合併は2例のみで、臍帯卵膜付着が1例、分葉胎盤間の卵膜上走行が2例であった。平均分娩週数は妊娠34週(31-37週)で、術中に血管走行を確認の上、破綻なく娩出した。児は1例で重症新生児仮死を来したが、全例で発達は良好であった。【結論】前置血管の発症リスク因子である体外受精、多胎妊娠、胎盤位置異常、胎盤構造異常、臍帯付着部異常を当院の4症例は有し、診察時に胎盤および臍帯付着部を確認することが前置血管を診断する契機となった。いずれも経陰超音波断層法にカラドプラーを併用して診断に至った。全症例で分娩前の診断で血管破綻なく娩出を行うことができ、児への致死的な影響は回避された。

P-54-9 分娩前に診断された前置血管の4例

大分県立病院

内田今日香, 豊福一輝, 藤内伸智, 守口文花, 神尊雅章, 前田裕美子, 小山尚子, 林下千宙, 後藤清美, 佐藤昌司

前置血管は分娩前に診断されなければ周産期死亡率は70~90%と報告されており妊娠中の診断が予後不良回避のためには必須である。今回分娩前に診断された前置血管4例を管理したので報告する。【症例1】34歳, 1妊0産, 妊娠16週前置血管と診断され妊娠29週4日管理入院となり妊娠34週1日, 選択的帝王切開術を施行した。児は2122g, Apgarスコアは7/1 8/5, 臍帯動脈血pHは7.40であった。【症例2】34歳, 4妊2産, 妊娠36週2日胎児発育不全, 臍帯卵膜付着の診断で紹介となった。胎児推定体重は-1.8SDで, FGRの診断で管理下分娩の方針とした。妊娠39週0日誘導分娩開始前に施行した経陰超音波カラドプラー法で内子宮口近くを走行する卵膜付着した血管像を認め前置血管と診断した。同日緊急帝王切開術を施行。児は2585g, Apgarスコア7/1 9/5, 臍帯動脈血pHは7.4であった。【症例3】26歳, 1妊0産, 妊娠26週, 前置血管と診断された。妊娠28週4日切迫早産で母体搬送となった。経陰超音波断層法で子宮頸管のfunnelingを認め、内子宮口に近接する卵膜付着した血管を認めた。児は頭位で卵膜付着した血管は児頭周囲にも存在した。妊娠36週0日に選択的帝王切開術を施行, 臍帯血管損傷回避のため子宮切開は子宮底部横切開を選択した。児は2690g, Apgarスコアは7/1 9/5, 臍帯動脈血pH7.28であった。【症例4】28歳, 1妊0産, 妊娠21週時, 前置血管を指摘され妊娠27週6日管理入院となり現在も妊娠継続中である。ワルトン膠質を欠く血管はB-modeのみでは同定困難な場合があり, 臍帯卵膜付着症例での前置血管除外診断の重要性と卵膜付着した血管は数, 位置も多様であることから子宮筋層切開部位も慎重に選択する必要性を再確認した。

P-55-1 Maternal floor infarction (MFI) と診断された血液型不適合妊娠の一例

産業医大病院

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【緒言】Maternal floor infarction (MFI) は病理学的に絨毛周囲の広範囲なフィブリン沈着を特徴とする。MFIはFGR, IUFDの原因となり、発生率はそれぞれ69%, 40%, 再発率は14%, 39%と報告されている。胎児の神経学的予後は約70%が不良であり、特に白質梗塞が多い。本症例は妊娠26週で胎児機能不全に対し緊急帝王切開術を施行し、胎盤の病理組織検査でMFIと診断された。文献的考察を加え報告する。【症例】30歳, 2妊1産, AB型RhD陰性, 前回妊娠時, 妊娠28週にIUFDの診断で帝王切開分娩。精査の血液検査でプロテインSの軽度低下を認め、今回妊娠初期から低用量アスピリンを内服していた。自然妊娠し、妊娠25週3日に前期破水の診断で同日当院に救急搬送となった。【経過】胎児超音波検査で児の推定体重は483g (-2.9SD, symmetrical FGR), AFIは8.78cmであった。胎児心拍数陣痛図でvariabilityは保たれていた。AB型RhD陰性に対し、抗D免疫グロブリン注射を投与した。妊娠26週0日, 胎児心拍数陣痛図で繰り返す遅発一過性徐脈を認めたため、胎児機能不全と診断し緊急帝王切開術を施行した。児は557g (SGA児), APGAR score 1分値4点, 5分値は挿管中, 臍帯動脈血pHは7.318であった。児はNICUで入院管理, 日齢170日目に退院となり, 神経学的予後は良好である。胎盤は肉眼的に白色梗塞を認め、胎盤重量は294g, 病理組織検査で絨毛周囲に広範囲なフィブリン沈着を認めMFIと診断した。【考察】今回, 分娩後の胎盤病理でMFIと診断した症例を経験した。本症例のように超早産域の重度FGRである場合, 原因が胎盤因子である可能性がある。次回妊娠のためにも胎盤病理検査を十分に行い, 病態を理解することが重要である。

P-55-2 Fetal vascular malperfusion と周産期臨床所見との関連

浜松医大附属病院

磯村直美, 谷口千津子, 加藤貴史, 小田智昭, 成味 恵, 松本雅子, 幸村友季子, 田村直顕, 内田季之, 鈴木一有, 伊東宏晃

【目的】Fetal vascular malperfusion (FVM) と子宮内胎児発育不全や子宮内胎児死亡との関連が報告されている。当院単胎症例でFVMの有無と胎盤肉眼所見・臨床所見について比較検討をしたので報告する。【方法】2015年から2020年の6年間当院分娩となった37週以降の単胎で胎盤病理組織学的検査に提出した症例を抽出し、FVM所見の有無を確認した。臨床所見(IUFD・羊水過少・妊娠高血圧症候群・胎児機能不全・緊急帝王切開術・臍帯巻絡)・胎盤肉眼所見(臍帯付着部異常・臍帯過捻転・臍帯径)新生児所見(Apgar score・挿管・SFD児)の項目についてFVM所見の有無との比較検討を行った。【成績】2015年から2020年で37週以降に分娩となった単胎症例4091例のうち、胎盤病理組織検査に提出した症例は589例であった。更にFVM症例は59例で10%を占めた。FVMあり/なしではIUFD2例/0例($p<0.01$)羊水過少1/13($p=1.00$)妊娠高血圧症候群7例/38例($p=0.09$)NRFS8例/70例($p=0.51$)緊急帝王切開術8例/126例($p=0.48$)臍帯巻絡13例/124例($p=0.73$)臍帯付着部異常は15例/40例($p<0.01$)臍帯過捻転2例/9例($p=0.22$)臍帯径8mm以下9例/82例($p=0.54$)SFD10例/28例($p<0.01$)APSI分値3以下5例/31例($p=0.21$)APS5分値7以下9例/62例($p=0.17$)新生児挿管症例10例/112例($p=1.00$)であった。【結論】FVMはこれまでの報告と同様にIUFD・臍帯付着部異常・SFD児と関連していることが示された。FVM所見のあった症例について児の発達予後を追跡する必要があると考えられる。妊婦健診などの日常診療で検出できるFVMのリスク因子について検討を進めていきたい。

P-55-3 胎児共存奇胎との鑑別に苦慮した間葉性異形成胎盤の一例

姫路赤十字病院

大前彩乃, 西田友美, 西田康平, 相本法慧, 平田智子, 西條昌之, 河合清日, 中山朋子, 関 典子, 小高見嗣, 水谷靖司

【緒言】間葉性異形成胎盤(placental mesenchymaldysplasia; PMD)は胎盤の嚢胞状変化を呈するまれな疾患であり、5000例に1例の頻度で発生すると報告されている。悪性所見を呈することはないが、合併症に胎児発育不全(FGR)やBeckwith-Wiedemann症候群(BWS)などがある。しばしば部分奇胎や胎児共存奇胎との鑑別が必要となる。今回我々は、胎児共存奇胎との鑑別が困難であり、胎盤病理で最終診断がついたPMDの1例を経験したため報告する。【症例】41歳、5経妊4経産。自然妊娠成立後、近医で妊婦健診を行われていたが、妊娠14週の超音波検査で胎盤に接する直径約40mmのびまん性陰影を認めたため、妊娠15週0日に当科を紹介受診された。当院初診時の超音波検査では胎児に異常所見はなかったが胎盤に小嚢胞の集簇を認めた。血中HCG β 77,605.4mIU/mlと特に高値ではなかった。胎児共存奇胎が疑われたが、夫婦は妊娠継続を希望され引き続き慎重に周産期管理を行った。経過中も胎児長頭蓋を認める程度で他に明らかな形態異常は指摘できなかった。妊娠22週3日の血中HCG β 60,258.7mIU/mlであったが、妊娠36週0日は血中HCG β 95,002mIU/mlと上昇傾向を認めた。全前置胎盤もあったため自己血貯血を行い、妊娠36週4日に選択的帝王切開術、腹式単純子宮全摘術を施行した。2224g(-1.0SD)の女児、Apgar Score 8点(1分値)/9点(5分値)であった。その後、胎盤病理所見よりPMDの診断となる。【結語】臨床経過上ではPMDと胎児共存奇胎の鑑別は困難であるが、PMDはFGRやBWSなどの合併症の報告があるものの、比較的良好的な母児の予後が期待されるため、無用な人工流産を防ぐためにも両者の鑑別は重要である。

P-55-4 産褥1か月健診で子宮内に胎盤遺残を疑い高輝度エコー領域を認めた症例の自然史

大阪母子医療センター

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【目的】産褥1か月健診の超音波検査で子宮内に胎盤遺残を疑う高輝度エコー像(遺残像)を認めた症例のその後の経過を明らかにする。【方法】2016年から2020年に当院の産褥1か月健診で遺残像を認めた症例を対象とした後方視研究である。フォローアップ情報欠損例は除外した。主要評価項目を1か月健診以降の異常性器出血の頻度、副次評価項目を複合有害事象(1か月健診以降の輸血、子宮内バルーン止血術、子宮内除去術、子宮動脈塞栓術、子宮摘出術)の頻度および遺残像の消失時期とした。また主要評価項目の有無による母体背景を比較した。統計学的検定はカイ二乗検定、Fisher正確確率検定、Mann-Whitney U検定を用い、有意水準は $P<0.05$ とした。【成績】対象期間中に産褥1か月健診を受けた8425例中、91例に遺残像を認めた。15例を除外し、76例における遺残像の厚みは中央値14.2(10.2-26.6mm)であった。9.2%(7例)に異常性器出血を認め、2.6%(2例)に複合有害事象を認めた。遺残像の消失時期は中央値84(37-717日)であった。異常性器出血を認めた群では認めなかった群に比べて、分娩時の胎盤用手剥離の頻度(71.4% vs. 18.8%, $P=0.007$)と遺残像にカラードブラ血流量を伴う頻度(57.1% vs. 15.9%, $P=0.025$)が高かった。【結論】産褥1か月健診で遺残像を認めた症例の異常性器出血の頻度は約9%であった。ほとんどの症例で遺残像は自然消失したが、その時期は様々であった。

P-55-5 待機療法で管理した retained products of conception の5例に関する検討

東京女子医大病院

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【目的】retained products of conception (RPOC) は分娩後あるいは流産後に子宮内に遺残した組織が器質化したものとされ、頻度は全分娩の1%程度と報告されている。RPOC の治療は待機療法か手術療法であるが、管理方針には一定の見解は得られていない。そのため治療方針は臨床症状、超音波検査による腫瘍径や血流の評価等により症例毎に検討され、血流が豊富なRPOC では無症状であっても早期に interventional radiology (IVR) 併用による子宮内容除去術や子宮鏡手術が行われることがある。今回、我々は待機療法で管理し得た RPOC 症例の臨床経過を検討し、管理方針について考察することを目的とした。【方法】2018年1月から2021年12月に経験した RPOC9 症例のうち待機療法で管理した5症例を対象とし、妊娠・分娩と RPOC の臨床経過について診療録から後方視的に検討した。4症例は IVR または手術療法を行った。【成績】検討期間中に待機療法で管理した RPOC 症例は5例であり、妊娠・分娩については22週未満が4症例(流産3例, 人工妊娠中絶1例), 22週以降の分娩が1例であった。診断時の hCG 値は 27-294mIU/ml で、超音波検査で子宮筋層に及ぶ豊富な血流像を認めたのは3例だった。全例で血流像の消失と hCG 値のカットオフ値未満を確認し、それぞれの診断からの期間は42-84日、42-84日であった。全例で RPOC は自然排出され(診断後14-301日)、排出期間が最長であった症例は22週以降の分娩症例であった。【結論】待機治療には大量出血のリスクがあるが、血流豊富な RPOC でも待機療法で管理し得るため、IVRなどで大量出血時に迅速に対応可能な施設であれば待機療法も考慮されると考えられた。今後さらなる症例の蓄積が望まれる。

P-55-6 胎児機能不全と診断した症例の胎盤病理の後方視的検討

高知大

堅田千晶, 渡邊理史, 前田長正

【目的】胎児機能不全の胎盤病理所見として、梗塞や虚血、炎症が報告されている。今回、当院で経験した、明らかな産科リスクを認めないものの分娩中胎児機能不全を生じて緊急帝王切開となった症例の胎盤病理を後方視的に検討した。【方法】2018年1月から2021年9月の間に、当院で胎児機能不全の診断で緊急帝王切開を施行した単胎かつ正常産症例の胎盤病理について検討した。臍帯因子のあるもの、妊娠高血圧症候群、妊娠糖尿病、常位胎盤早期剝離症例は除外した。【成績】対象症例は66例で、62例が胎盤病理検査を施行していた。胎盤病理で chorangiosis を認めたものが17例(27.4%)、炎症16例(25.8%)、梗塞10例(16.1%)、虚血7例(11.2%)であり、所見が合併したもの、つまり虚血と梗塞が2例(3.2%)、炎症と虚血が1例(1.6%)、炎症と chorangiosis が2例(3.2%)、また血腫などその他の所見を認めたのが2例(3.2%)、臍帯のみに炎症を認めたのが2例(3.2%)と多くの症例で胎盤病理の異常を認めた。一方、病理学的に有意な所見を認めなかったものが3例(4.8%)存在した。【結論】今回検討した95%の症例において、胎盤病理に炎症、梗塞、虚血、chorangiosisなどの所見を認めた。これらの胎盤所見に、分娩時のストレスが加わり胎児機能不全を発症したと考える。妊娠経過が順調であっても、分娩中に胎児機能不全となる症例では何らかの胎盤病理異常所見を有している可能性がある。

P-55-7 当院における RPOC による産科出血の7例について

三重大附属病院

福森史也, 榎本尚助, 山口瑞希, 萩元美季, 真川祥一, 高倉 翔, 真木晋太郎, 二井理文, 田中佳世, 田中博明, 池田智明

【目的】Retained Products Of Conception (以下 RPOC) は、流産・分娩後に胎盤や卵膜の一部が子宮腔内に残留することを指し、大量出血や子宮内感染を合併することがある。リスクファクターとして高年出産、生殖補助医療が指摘されており、近年増加していると考えられる。当院においても RPOC による出血が増えてきていると考えられ、本研究は RPOC の臨床的特徴を明らかにすることを目的とした。【方法】2021年4月から2021年9月までの期間中に、当院で経験した産科出血症例のうち RPOC, RPOC 疑いと診断され、出血をきたした7例について検討した。年齢、生殖医療の有無、分娩週数、出血時期、治療内容、輸血の有無、出血量の7項目について比較・検討を行った。【成績】生殖医療の有無について比較したところ、7例中6例が生殖補助医療により成立した妊娠であり、そのうちの5例がホルモン補充周期下胚盤胞移植であった。出血した時期については分娩直後より出血をした例が3例、分娩1~2週目が3例、分娩後30日目が1例あった。治療内容・輸血の有無についても、待機療法で RPOC が自然消失した例が2例、機械的圧迫法で止血を得られたのが1例、胎盤用手剝離を行った例が2例、機械的圧迫法で止血できず子宮動脈塞栓術、子宮全摘術を行ったものが2例であった。【結論】RPOC による出血について、出血するタイミングや持続日数は様々な経過をたどるとされており、当院で経験した症例においても様々であった。しかし、出血をきたした7例中6例が生殖補助医療による妊娠であった。今後、さらに生殖補助医療による妊娠が増加することにより RPOC で出血をきたす症例が増加する可能性がある。

P-55-8 RPOC (Retained products of conception) に対する子宮内バルーンタンポナーデの有用性

東海大付属病院

佐柄祐介, 重盛波留子, 網野ちひろ, 柏木寛史, 佐藤健二, 三上幹男, 石本人士

【目的】血流を有する RPOC の症例では UAE (uterine artery embolization) や TCR (transcervical resection) を施行する施設もある。ただし UAE 後の妊孕性の長期予後は不明であり、また TCR においても子宮内腔癒着の可能性があるとされ、妊孕性温存の観点からは待機療法が望ましいが、その際には大量出血のリスクは常に考えなければならない。血流の無い RPOC の多くは自然排出されるとの報告があり、近年当院では血流を有する RPOC 症例に対し、血流消失による自然排出を目的に子宮内バルーンタンポナーデを導入してきた。今回血流を有する RPOC に対する子宮内バルーンタンポナーデの有用性につき、後方視的に検討した。【方法】2019年8月～2021年10月までに当科で血流を有する RPOC に対して子宮内バルーンタンポナーデを実施した6例について後方視的に検討した。【成績】先行妊娠は、12週未満の中絶および流産4例(子宮内容除去術後3例、手動真空吸引法後1例)、正期産2例(2例とも経陰分娩)であった。診断時点は、子宮内容排出後17～53日(中央値37.5日)で、Gutenberg Classification では Group0 および1は認めず、Group2が3例、Group3が3例であった。使用したバルーンカテーテルは14Frが4例、20Frが1例、ミニメトロが1例であり、固定水の量は6cc～20ccであった。血流が消失するまでの期間は6時間～20時間であり、その後自然脱落するまでの期間は23～108日(中央値29.5日)であった。バルーン除去後からほとんどの症例で少量の出血を呈したが、輸血を必要とする症例は認めなかった。【結論】血流を有する RPOC に対する子宮内バルーンタンポナーデは、自然排出までの時間短縮と大出血を防げる可能性が示唆された。

P-55-9 当院における胎盤残留症例の転機に関する検討

静岡県立総合病院

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【目的】経陰分娩後に胎盤が残留し対応に苦慮するケースはしばしば遭遇する。胎盤用手剥離術は産後出血や子宮全摘術、子宮内感染、DIC の発症を増やすとされ、胎盤を子宮内に残す待機的対応の重要性は高いが、どのようなケースで行うべきかについては明確な基準はない。【方法】今回我々は2016年1月1日～2021年9月31日までに当院にて経陰分娩となった症例のうち、分娩第3期の積極的管理を行っても分娩第3期が30分以上と胎盤残留を認め、保存的対応を試みた36症例のうち、自然と胎盤娩出となったグループA、用手剥離術を行ったグループB、用手剥離術を行うも制御困難な出血に対し子宮動脈塞栓術を行ったグループC、子宮全摘術施行となったグループDについて分娩週数、分娩時出血量および分娩第3期に要した時間について後方視的に検討した。【成績】各グループの分娩週数はそれぞれ38週2日±2日、39週6日±1.2日、41週0日±2日、40週4日±4.5日と自然剥離群で有意に分娩週数が早い傾向があった。胎盤娩出までの出血量は740±285ml、2159±184ml、1760±611ml、2535±611mlで自然剥離群と用手剥離術群で有意差を認めた。分娩第3期に要した時間は各群271±507分、922±2052分、2881±4017分、168±142分と各群間で有意な差を認めなかった。自然剥離群では輸血を要した症例はなかったが、用手剥離術群では26症例中の14症例(53.8%)で輸血を必要とした。【結論】胎盤残留を認めた際に、比較的早い週数で出血量が許容できる症例に対しては、待機的管理により輸血のリスクを回避できる可能性がある。

P-56-1 子宮破裂から出血性ショックに至り、心停止をきたしたが、集学的治療で合併症なく救命できた一例

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母体心停止は2万人に1人と非常にまれであり、発症時に適切な集学的治療が必須である。今回我々は自然経陰分娩時の子宮破裂から出血性ショックに至り心停止をきたしたが、体外式膜型人工肺を含む集学的治療で合併症なく救命できた一例を経験したので報告する。症例は41歳4妊1産(1回自然経陰分娩)、自然妊娠後の妊娠経過は良好であり、妊娠40週4日に陣痛発来し前医に入院した。妊娠40週5日に微弱陣痛に対しオキシトシン点滴による陣痛促進後、分娩停止の診断でクリステレル児圧出法を併用し鉗子分娩で児を娩出した。分娩8分後に不穏症状、shock vital を認め、当院に搬送された。来院時はShock Index1.1のショックバイタルおよびDICを認め、急速輸血を開始し、腹部所見および画像検査より子宮破裂を疑い、緊急開腹止血術を施行した。開腹時、子宮右側後面に子宮動脈におよぶ約5cmの裂傷あり、同部位より強出血を認めていた。手術開始6分後に母体心停止に至り、以後心肺蘇生下に術操作を進め術開始22分後に子宮摘出し、術開始30分後に自己心拍が再開した。胸骨圧迫による肺損傷、急速輸血による肺水腫を認め、母体の酸素化が保たず体外式膜型人工肺を導入後止血確認し終刀とした。術後経過は良好であり、術後7日目に体外式膜型人工肺を離脱。術後9日目に人工呼吸器を離脱。術後21日目に自宅退院した。退院後、合併症なく経過良好である。DICは体外式膜型人工肺の相対禁忌とされるが、DICを伴う産後出血の症例で人工換気下に酸素化が保たれてない症例では集学的治療の管理下において選択肢の1つとなり得る。

P-56-2 卵管間質部妊娠により妊娠26週に子宮破裂後出血性ショックとなった母体を救命できた一例

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前田央祐¹、松澤聡史¹、中村希実¹、魏馨予¹、高橋典子¹、指宿昌一郎²、石山健次郎²、金丸勝弘³、桂木真司¹

【緒言】診断に苦慮した卵管間質部妊娠により、妊娠26週に完全子宮破裂を起こし母体ショックとなったが多科の医療連携により母体救命できた症例を経験できたので報告する。【症例】26歳経産婦(2回帝王切開歴)。妊娠6週で子宮右卵管角部に胎嚢の存在が疑われたが、腹痛なく経過し、低リスク妊娠として一次施設にて妊婦健診が施行された。妊娠26週5日に腹痛を自覚、救急搬送中に意識状態の低下、血圧の低下を認めた。当院へ受け入れ要請があり、子宮破裂や脳・心血管障害を念頭に各科に連絡し、救命救急センターへの受け入れ準備や輸血、緊急手術の準備を行った。当院到着後ショックインデックスの上昇も認めため、急速輸液システムで急速輸血を行った。胎児超音波検査では胎児心拍数20bpm以下であったが母体救命を優先し、出血源その他の鑑別目的に、頭部から骨盤部造影CTを施行した。腹部造影CTでは子宮右背側に造影剤の腹腔内流出を認めた。帝王切開歴からも子宮破裂を最も疑い緊急帝王切開術、血腫除去術の方針となった。手術搬入後の経腹超音波検査で胎児心拍停止を確認し、子宮内胎児死亡と判断した。術中、前回帝王切開の子宮切開部位は正常で、右側卵管角部に破裂を認め子宮破裂と診断した。児娩出後の出血の活動性は抑えられており、子宮は温存することができた。術後経過は良好であり、術後7日目に自宅退院となった。【結論】救急科をコマンダーとして、産婦人科、麻酔科が迅速な医療連携体制をとり適確な子宮破裂の診断と加療を行い母体救命に繋がった。また、妊娠初期において超音波検査での卵管間質部妊娠の診断は困難であり、疑わしい場合はMRIを含めた異所性妊娠の検索を行うべきである。

P-56-3 当院で15年間に経験した子宮破裂28症例の検討

日赤医療センター

降旗莉子、有馬香織、細川さつき、渡邊理子、山田学、笠井靖代、木戸道子、宮内彰人

【目的】子宮破裂は稀であるが、母児ともに重篤な状態に陥るため早期診断と高次医療施設での治療が求められる。当院で経験した症例からその臨床的特徴を検討する。【方法】2006年10月から2021年9月の当院での分娩および母体搬送症例のうち、子宮破裂症例について診療録より後方視的検討を行った。【成績】子宮破裂症例は28例で、うち子宮手術既往のある瘢痕子宮破裂23例、子宮手術既往のない非瘢痕子宮破裂5例であった。瘢痕子宮破裂の先行手術は帝王切開術13例、子宮筋腫核出術8例で、手術から妊娠まで1年未満であるのは各々1例、5例であった。帝王切開術後13例は、前回帝王切開の創部が逆T字切開である1例を除いた子宮下節横切開12例が妊娠37週以降の発症であり、うち9例は既往帝王切開後経陰分娩(trial of labor after cesarean; TOLAC)中に緊急帝王切開術の方針となり、6例が子宮破裂を疑う徴候である子宮収縮と関連のない腹部症状、胎児機能不全、母体のショックバイタルのうち少なくとも1つを呈していた。母体および胎児・新生児死亡はなく、全例で子宮の温存が可能であった。子宮筋腫核出術後8例は妊娠19-36週に発症し、7例が先述の徴候のうち少なくとも1つを呈し、5例は腹部超音波検査で腹腔内出血が確認された。胎児死亡は2例で、子宮全摘術を施行したのは1例であった。非瘢痕子宮破裂5例は全て分娩後の出血性ショックで当院へ搬送された症例であり、リスク因子として経産婦、子宮収縮薬の使用、器械分娩、クリステル胎児圧出法、硬膜外麻酔分娩、急速分娩が挙げられた。【結論】子宮手術既往のある妊婦では、妊娠初期から子宮破裂のリスクを念頭におき、早期診断と治療に繋げることが重要である。

P-56-4 診断が困難であった子宮破裂の1例

長崎大病院

松本加奈子、阿部由紀子、久本菜美、松村麻子、阿部修平、朝永千春、原田亜由美、長谷川ゆり、北島道夫、三浦清徳

【緒言】子宮破裂は稀であるが、その診断は困難であり、発症すると母児共に危機的状態に陥る疾患である。今回母児共に救命できた子宮破裂の1例を経験したので報告する。【症例】30歳、3G2P、2回の帝王切開既往あり、またHTLV-1ウィルスキャリアである。自然妊娠し、妊娠8週0日に前医で一絨毛膜二羊膜性双胎妊娠と診断された。今後の管理のため妊娠10週5日に当科を受診した。妊娠経過に問題なく、妊娠31週2日より管理入院した。入院後の妊娠経過は順調であった。妊娠37週5日での選択的帝王切開分娩を計画されていたが、その2日前の夜間に突然、強い腹痛が出現した。腹痛は持続的であるが腹部の板状硬や性器出血は認めなかった。バイタルサインは正常で、超音波検査で胎盤に異常所見はなく、胎児心拍はreassuring FHR patternであった。血液検査で有意な所見を認めず、尿路結石を疑い、アセトアミノフェン投与後に症状はやや改善したため、経過観察した。その4時間後に再び腹痛が増強し、頻回の子宮収縮が出現した。陣痛発来と診断し、緊急帝王切開を決定した。手術開始直前に左下腹部に部分的な膨隆を認めた。開腹すると、子宮左側で子宮漿膜が破綻し、直径10cmほど卵膜が露出し膨隆しており、完全子宮破裂と診断した。子宮筋層からの出血は認めなかった。慎重に子宮を切開し、破膜させ、児を娩出させた。両児ともに出生後の状態および母体の術後経過に問題なかった。【考察】完全子宮破裂の初発時の症状として、胎児心拍異常や母体の循環不全が挙げられるが、今回の症例ではそのいずれも認められなかった。子宮手術既往がある妊婦の急性腹症では、念頭に置くべき疾患であると考えられた。

P-56-5 子宮手術既往妊娠における子宮筋層評価の重要性 子宮筋腫核出後妊娠の穿通胎盤により自宅で出血死した症例聖路加国際病院
山中美智子, 百枝幹雄

【症例】41歳, 1妊0産の女性。夫は海外在住で独居であった。4年前に腹腔鏡補助下子宮筋腫および小さな腺筋症核出術(筋腫60個:1665g摘出)を他院で施行され、顕微授精・凍結胚移植で妊娠に至った。当院では妊娠10週から妊婦健診を行っていた。胎盤は子宮底部右方寄りに付着しており、特に問題なく経過していた。妊娠30週に癒着胎盤の有無・筋層の評価をするためにMRIを撮像したが、異常所見は確認されなかった。妊娠34週の健診時も特に著変なく、帝王切開分娩のための術前検査でも異常を認めていなかった。その健診から7日後に所轄警察署から自宅で死亡しているのが確認されたとの連絡があった。行政解剖の結果、腹腔内に2400mlの出血を認め、子宮底部右方に約2cm程度の亀裂があり、この部からの出血であったと考えられた。ここには胎盤が付着していたが、部分的に筋層が欠損しており、穿通胎盤の所見であった。児は2507gで週数相当の発育であり、外表奇形は認めなかった。穿通胎盤部分の血管破綻による腹腔内出血により死亡に至ったと考えられたが、救急要請すらできなかった理由は不明である。【結論】子宮手術既往妊娠で子宮筋層や胎盤付着異常の有無の評価を行う場合、妊娠後期ではすでに子宮筋が伸展されているため評価が困難となる可能性があり、早期に行う方が有用かもしれない。またこのような例で挙児希望がある際には、妊娠前の筋層の評価なども検討が必要と考えられた。

P-56-6 経膈分娩後の内側頸管裂傷に連続した不全子宮破裂症例日本赤十字社愛知医療センター名古屋第二病院
梶健太郎, 加藤紀子, 鈴木敬子, 河井啓一郎, 白石佳孝, 高木春菜, 新保暁子, 茶谷順也, 林和正, 山室理

症例は38歳2妊1産、既往歴や手術歴はなし。妊娠経過に問題はなく妊娠39週2日、前医で無痛分娩を開始し、胎児機能不全に対して子宮底圧迫法を併用した吸引分娩2回で児娩出に至った。胎盤は問題なく速やかに娩出されたが、胎盤娩出直後より出血量が増加した。子宮体部収縮は良好で触診上頸管の連続性は保たれており視診でも頸管断裂所見はなかった。頸管収縮不全による大量出血の診断でBakri®バルーンを留置した状態で当院へ搬送されたが、CT検査で子宮左側壁破裂を強く疑ったため、緊急開腹手術を行った。開腹所見では子宮漿膜は保たれており不全子宮破裂の状態であった。後腹膜血腫により傍子宮組織が極めて浮腫状で外科的止血操作が困難と判断した。閉腹し、動脈塞栓により子宮血流を減少させた上で再度開腹手術を行い、子宮全摘出により止血を得た。子宮は体下部から頸管にかけて長軸方向に6cm断裂していたが、頸管の下端2cmは全周性に保たれていた。止血が得られるまでに、濃厚赤血球32単位、新鮮凍結血漿28単位、濃厚血小板45単位、フィブリノゲン製剤10gの投与を要した。本症例では子宮漿膜まで断裂が及ばない不全子宮破裂であったこと、頸管下端に損傷がなくかつ頸管上部でも壁の完全断裂がなかったこと、無痛分娩により疼痛が緩和されていたことにより臨床診断に苦慮したと考えられる。分娩後異常出血の際に、触診・視診で明らかでない頸管断裂を認めず子宮収縮が良好な症例においては、本症例のような内側頸管裂傷や不全子宮破裂等の軟産道裂傷を考慮する必要がある。また、無痛分娩では疼痛緩和により自覚症状が乏しくなり発見の遅れにつながることに注意が必要である。

P-56-7 経腹超音波断層法およびMRIで診断した非癒痕子宮における不全子宮破裂の1例新潟大学医学総合病院¹, 新潟大学医学総合病院総合産科産期母子医療センター²
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【はじめに】子宮破裂は危機的出血を引き起こし、母児ともに重篤な状態に陥る。破裂の程度により、子宮全層が断裂する完全子宮破裂と子宮漿膜が保たれる不全子宮破裂に分類される。一般的に、癒痕子宮に発症することが多いが、非癒痕子宮にも稀ながら発症する。診断は、主に超音波検査やCTを用いるが、診断が困難な場合もあり、手術時に初めて発見されることもある。今回、経腹超音波断層法で疑い、MRIによって診断した非癒痕子宮の不全子宮破裂の1例を報告する。【症例】20歳代, 1妊0産。既往歴や合併症は特記事項なし。他院で妊娠41週、予定日超過のためオキシトシンによる分娩誘発を行った。胎児機能不全のため、子宮底圧迫法を併用した吸引分娩で出生となった(男児, 3274g, Apgar score: 1分値9点)。分娩時出血量1200ml, その後1時間半で1000mlと持続的な出血があり、ショックインデックスは1.5となった。ヘモグロビン4.9g/dL, フィブリノゲン119mg/dLであり、濃厚赤血球(RCC)と新鮮凍結血漿(FFP)を投与開始した。また、子宮内バルーンタンポナーデを挿入し、止血が得られた。バイタルサインは輸血療法に反応し安定した。CTを施行し、後腹膜血腫の診断ではあったが、出血原因は特定できなかった。止血後の全身状態は安定して経過し、RCC6単位とFFP8単位のみ使用し、追加の治療は不要だった。産褥1日目の経腹超音波断層法で後腹膜血腫は子宮内腔より連続する状態が疑われた。産褥4日目にMRIを施行し、子宮下部左側に約7cm程度の筋層断裂部を認めた。子宮漿膜は保たれ、不全子宮破裂と診断した。【まとめ】子宮破裂の診断には苦慮する場合があるが、超音波断層法およびMRIは診断に有用であった。

P-57-1 自然陣発後硬膜外分娩と計画硬膜外分娩の周産期帰結の比較検討

名古屋市立大病院¹, 名古屋市立大病院麻酔科²

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【目的】硬膜外麻酔による無痛分娩の需要が近年増えており、当院でも年々増加傾向にある。当院では妊婦の希望により自然陣痛発来後に硬膜外分娩を実施するか、計画による硬膜外分娩を実施するかを選択している。今回自然陣発後硬膜外分娩と計画硬膜外分娩において、周産期合併症や分娩様式などを検討することを目的とした。【方法】2019年11月から2021年5月までに当院で硬膜外分娩管理を行った妊婦308例の内、前期破水や妊娠高血圧症候群などを理由に硬膜外分娩を行った症例を除外した自然陣発後硬膜外分娩群（自然群）137例と計画硬膜外分娩群（計画群）105例の計242例を対象とした。年齢、入院期間、帝王切開率、器械分娩率、分娩時出血量、会陰および頸管裂傷の程度、臍動脈血pH値、アプガースコア1分値および5分値について自然群と計画群で、後方視的に比較検討した。【成績】自然群と計画群では入院期間（5日 vs 6日, $p < 0.01$ ）、帝王切開率（5.8% vs 21.9%, $p < 0.01$ ）、分娩時出血量（437g vs 606g, $p < 0.01$ ）で有意差を認めた。全242例のうち初産婦169例（69.8%）と経産婦73例（30.2%）で検討すると、初産婦では計画群が自然群よりも有意に帝王切開率が高く分娩時出血量も多かったが、経産婦ではすべての項目に有意差を認めなかった。帝王切開率は初産婦が有意に高かった。【結論】経産婦では帰結に有意差がないことから妊婦の希望を尊重する現状維持でよいことがわかった。一方、初産婦では計画硬膜外分娩のデメリットが明らかになったため、帰結の差についての情報提供をして方針を決定する必要があると思われた。

P-57-2 当院における無痛分娩の検討

岡山大病院

坂田周治郎, 谷 和祐, 三苦智裕, 横畑理美, 三島桜子, 大平安希子, 桐野智江, 牧 尉太, 衛藤英里子, 早田 桂, 増山 寿

【目的】当院では2004年より硬膜外無痛分娩を施行している。当院では本人希望、母体適応の患者は24時間体制で麻酔科医による硬膜外無痛麻酔を行う。当院における3年間の硬膜外無痛分娩症例における周産期転帰について検討した。【方法】正期産で分娩となった妊婦を対象とし、本人希望による無痛あり経陰分娩を無痛分娩群、無痛なし経陰分娩を非無痛分娩群として診療録を後方視的に検討した。選択的帝王切開、多胎妊娠、子宮内胎児死亡の症例は除外した。【成績】2018年1月から2020年12月までの総分娩数は1269例であった。除外例を除き無痛分娩群は142例、非無痛分娩群は643例であった。無痛分娩群では器械分娩19.7%（28/142例）、陣痛促進剤78%（111/142例）、出血量300ml（50-1800）、緊急帝王切開率5.3%（8/150例）であったのに対し、非無痛分娩群ではそれぞれ8.1%（52/643例）、51%（331/643例）、240ml（20-3130）、8.7%（62/710例）と無痛分娩群で有意に器械分娩率、陣痛促進剤が高く、出血量が多かった。無痛分娩群の初産婦、経産婦の分娩第2期遷延率はそれぞれ26%（25/98例）、18%（8/45例）であり、非無痛分娩群ではそれぞれ17%（62/367例）、10%（29/281例）と両群で有意差は認めなかった。新生児転帰も有意差を認めなかった。【結論】既存の報告では硬膜外無痛分娩により帝王切開率は増加しないが、器械分娩率・陣痛促進率は増加するとされている。本検討でも同様の結果となり、非無痛分娩群と比較して母児の予後や帝王切開率は大きく変わらなかった。麻酔科の協力を得て計画分娩にすることなく無痛分娩を行い、適切な時期に介入を行うことで帝王切開率を上昇させず、安全な無痛分娩を提供できていると考えられる。

P-57-3 当院の周産期センターによる無痛分娩の実態調査

昭和大江東豊洲病院

相澤利奈, 小松玲奈, 本多容子, 竹村有理, 高林綾乃, 小林裕貴, 河野春香, 山下有加, 西 健, 土肥 聡, 近藤哲郎, 大槻克文

【目的】当周産期センターでは、近年の妊産婦ニーズに答えるべく2018年より経産婦の無痛分娩を開始した。これまでの成果と問題点を明らかにすることを目的とした。【方法】2018年1月から2021年9月までの無痛分娩を対象とし、診療録より後方視的に検討した。なお、当院では、経産婦かつ日中の計画分娩のみを対象としている。無痛分娩206例（無痛群）、同期間の正期産の経産婦606例（非無痛群）において、分娩様式と母児予後を検討した。さらに、無痛群を経陰分娩例（無痛経陰群）と帝王切開分娩例（無痛帝王切群）に分類し、母体年齢、分娩週数、BMI、Bishop score、頸管拡張処置の有無、出生時体重などの周産期因子と分娩転帰との関連を検討した。統計学的検討はt検定、x²検定、Mann-WhitneyのU検定を用いた。【成績】経陰分娩は、無痛群：200/206例（97.1%）、非無痛群：594/606例（98.0%）。器械分娩は、無痛群：51/206例（24.8%）、非無痛群：21/606例（3.5%）。帝王切開分娩は、無痛群：6/206例（2.9%）、非無痛群：12/606例（1.9%）。器械分娩にのみ有意差を認めた（ $P < 0.05$ ）。Apgar score 5分値で7点以下は無痛群：2/206例（1%）、非無痛群：4/606例（0.6%）であった。また、無痛経陰群と無痛帝王切群において全周産期因子に有意差は認めなかった。無痛経陰群の分娩誘発時間1日以下（A群）192例、2日間（B群）8例で、Bishop score（A/B群）は入院時：3/2点、誘発開始時：4/2点とB群誘発開始時で有意に低かった（ $P < 0.05$ ）。【結論】当院では安全な無痛分娩が提供できていると考えられた。日中のみの計画無痛分娩を遂行するためには頸管熟化を十分にを行った上で、緊急時に対応できる体制を整えることが必要である。

P-57-4 無痛分娩における児頭回旋異常症例の周産期予後とその発生に寄与する因子の検討

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【目的】無痛分娩における分娩第二期回旋異常症例の周産期予後と、その発生に寄与する因子を明らかにすること。【方法】2018/9-2021/9に、妊娠34~41週に当院で無痛分娩した初産単胎妊娠を対象とした。分娩第二期回旋異常症例をCase、それ以外をControlとし、母体背景、分娩経過と麻酔方法を後方視的に比較した。また回旋異常に寄与する因子として、母体身長(145-155cm, 156-165cm, 166cm-175cm)、母体体重増加(≥13kg, <13kg)、新生児体重SD値、陣発有無、入院時Bishop Score(≥4点, <4点)、麻酔導入時児脊椎位置(4-8時, それ以外)、麻酔方法で多変量解析を行った。なお、回旋異常は経陰超音波検査で確定した。本検討は当院の倫理委員会の承認を得ている。【成績】無痛分娩は695例、初産は378例で、経陰分娩完遂は287例、帝王切開は91例で、Caseは62例、Controlは316例であった。母体背景で母体身長が低く(p=0.003)、分娩結果で産科手術分娩率がCaseで高かった(p=0.04)。麻酔方法により発生頻度に差を認めた。多変量解析で入院時Bishop scoreのみが抽出された(p値=0.04 OR18.1:95%CI 1.05-328.5)。【結論】初産無痛分娩における分娩第二期回旋異常は低身長妊婦に多く、麻酔方法の影響を受け、産科手術の頻度を上げた。頸管熟化の判断が、計画無痛分娩成功だけでなく回旋異常や産科手術回避に重要であると考えられた。

P-57-5 当院における硬膜外無痛分娩についての検討

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【目的】硬膜外無痛分娩では重篤な麻酔合併症が発生する可能性や、器械分娩の増加により出血量が多くなる傾向があるため、母体安全への提言2016で「無痛分娩を提供する施設では、器械分娩や分娩時異常出血、麻酔合併症などに適切に対応できる体制を整える」とされている。当院では2020年4月から24時間麻酔科医師と共同で行う硬膜外無痛分娩を導入した。今回、当院における硬膜外無痛分娩の安全性を検討した。【方法】2020年4月から2021年9月までの当院における選択的帝王切開を除外した310分娩のうち硬膜外無痛分娩を実施した58例(無痛群)と非実施の252例(対照群)について分娩転帰、出血量、輸血の有無、麻酔合併症の有無、Apgar score、臍帯動脈血pHを比較検討した。【成績】患者背景は、無痛群で年齢が高かった(p=0.003)が、初産婦の割合に有意差はなかった。無痛群で吸引分娩が多かった(p<0.001)が、緊急帝王切開率に有意差を認めなかった。出血量は無痛群で多かった(p=0.001)が、輸血を行った症例はなかった。麻酔合併症もなかった。低Apgar score、臍帯動脈血pH7.2未満の割合に有意差はなかった。【結論】硬膜外無痛分娩で吸引分娩率が上昇したが、帝王切開率、Apgar score、臍帯動脈血pHは変化しなかった。出血量は増加したが輸血を施行した症例はなく、麻酔合併症もなかった。安全に硬膜外無痛分娩を施行できていると考えられた。

P-57-6 無痛分娩麻酔導入直前の児背の位置は回旋異常予測に役立つか

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【目的】無痛分娩では器械分娩が増加することが知られており、要因として回旋異常がある。本研究の目的は、無痛分娩麻酔導入時の胎位により分娩第二期の回旋異常予測が可能かどうかを明らかにすること。【方法】2018年9月~2021年9月の無痛分娩症例を対象に後方視的に検討した。分娩第一期の麻酔導入直前に児背の位置(Bp)と児頭矢状縫合と小泉門の位置(PFp)を経腹超音波検査断層法で確認し、分娩第二期回旋異常の有無を以下の3条件下で比較した。検討1: Bpが母体3~5時または7~9時方向の症例をCase、9~3時をControl 検討2: Bpが母体5~7時方向の症例をCase、9~3時をControl 検討3: PFpが5~7時方向の症例をCase、9~3時をControl なお、回旋異常の診断は、全開大時の経陰超音波所見で母体正中線と矢状縫合がなす角度(Midline angle)が45度以上とした。【成績】それぞれの検討で計測完遂したのは検討1: 70症例、検討2: 57症例、検討3: 35症例であった。回旋異常の発生は、検討1: Case45例中11例、Control25例中2例で、両群に差を認めなかった。検討2: Case4例中3例、Control53例中8例で、Caseで回旋異常が多かった。(p=0.02) 検討3: Caseは6例中1例、Controlは29例中4例で、両群に差を認めなかった。【結論】無痛分娩導入前の児背の向きは、分娩第二期回旋異常の予測に役立つ、児背が母体背側に近いほど、回旋異常が起きやすいことがわかった。

P-57-7 初産無痛分娩において経陰完遂に寄与するものは何か？

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【目的】初産婦の無痛分娩時の分娩停止に寄与する因子を明らかにすること。【方法】2018/10~2021/10に、当院で管理した初産婦無痛分娩症例を対象とした。分娩停止症例のうち、帝王切開症例をCase、経陰分娩を完遂した症例をControlとし、以下の項目で比較検討した。なお、分娩停止の診断は、十分な陣痛が得られた上で分娩進行が2時間以上停滞している状態とした。母体背景としては母体年齢、身長、妊娠中の体重増加を、分娩因子としては分娩週数、陣痛発来の有無、計画入院の有無、Bishop score(入院前・入院時・誘発前)、頸管拡張処置の有無、回旋異常の有無、新生児因子：出生児体重SD値を検討した。【成績】対象は338例で、Caseは53例(18.4%)、Controlは285例(84.3%)あった。母体背景において2群に差は認めず、分娩因子ではcaseにおいて、計画分娩、Bishop score不良、頸管拡張処置で有意に多く、新生児体重が有意に大きかった。さらに母体身長、体重増加、入院時Bishop score、計画分娩の有無、新生児体重SD値を多変量解析した結果、入院時Bishop score(OR2.5, 95%CI 1.1-5.9)、新生児体重SD値(OR1.52, 95%CI 1.1-2.5)、計画有り(OR3.4, 95%CI 1.5-8.2)が抽出された。【結論】初産婦の無痛分娩では、児体重が大きくなるとも、頸管熟化不良や未陣発計画分娩症例で分娩進行が滞りやすいことが分かった。陣痛発来を待たない初産計画無痛分娩では、頸管熟化が経陰完遂の是非に寄与すると思われる。

P-57-8 硬膜外無痛分娩における分娩進行に影響を与える因子の検討

聖隷浜松病院

清水由実, 入駒慎吾, 清水陽彦, 伊賀健太郎, 今野寛子, 村越 毅

【目的】無痛分娩における麻酔法は硬膜外麻酔が一般的であり、当院でも第一選択である。麻酔導入後に分娩は遅延すると言われているが、日常臨床では時々麻酔導入後に急速に分娩が進行する症例も経験する。今回、硬膜外麻酔導入後に、急速な分娩進行が起こる場合に影響する因子について検証した。【方法】2017年1月から2020年12月の期間に、当院で硬膜外麻酔を使用し無痛分娩を行った妊娠37週以降の単胎妊娠585例を対象とした。当院では全例、陣痛発来後に硬膜外麻酔を導入するオンデマンドの無痛分娩を行っている。対象患者について診療録から、母体年齢、経産回数、分娩週数、麻酔導入決定時の痛みの強さ(以下NRS: Numerical Rating Scale)、麻酔導入直前の内診所見(子宮口開大、展退、児頭下降度)、麻酔薬投与時間、麻酔の効果が出現した時間(NRS<3となった時間)、子宮口が全開大した時間、分娩時間、麻酔導入時の促進剤使用の有無、麻酔導入後促進剤使用の有無、分娩様式、分娩転機、児の出生体重の各項目を抽出し、麻酔導入後から子宮口全開大するまでの時間をAF-time (Analgesia to full-dilatation time)とし、EZRを用いて重回帰分析を行った。【成績】AF-timeが30分以内、1時間以内であった症例の中で、分娩進行に影響を与えた因子はいずれもNRSのみであった。AF-timeが2時間以内であった症例で、分娩進行に影響を与えた因子はNRSに加え、麻酔導入後の促進剤使用の有無と、導入時の子宮口の開大度であった。【結論】硬膜外麻酔導入後に急速な分娩進行が起こる場合に最も影響を与える因子は、麻酔導入時の痛みの強さの程度であると言えた。急激な疼痛緩和に伴って急速な分娩進行がみられるため、硬膜外麻酔導入後の分娩管理に注意が必要である。

P-57-9 Breakthrough Pain が児頭嵌入前に2回出現した場合、無痛分娩における硬膜外カテーテルの再穿刺率は上昇する

聖隷浜松病院

清水陽彦, 入駒慎吾, 清水由実, 伊賀健太郎, 今野寛子, 村越 毅

【目的】無痛分娩管理でBreakthrough pain (BTP) が児頭嵌入前に出現した場合、硬膜外カテーテルの再穿刺をよく経験する。児頭嵌入前後で陣痛刺激の伝達位置が変化するため、カテーテルの麻酔効果が不十分な場合には、局所麻酔薬の総投与量が増え、副作用のリスクが上昇する。分娩終了まで有効なカテーテルとして使えるか判定する法則を見つけるため、BTP回数に応じた再穿刺率について検討した。【方法】当院の無痛分娩記録を用いた後ろ視的コホート研究を行った。対象は2019年1月から2020年12月の間に硬膜外無痛分娩を行った生児単胎妊娠の妊婦で、硬膜外麻酔以外の麻酔法や、児頭嵌入前に帝王切開、あるいは嵌入後に麻酔導入となった例を除外した。BTPはNumeric Rating Scaleの点数が一度3点未満になり、再度3点以上に上昇した痛みと定義した。麻酔維持期の再穿刺基準は、BTPが3回出現、もしくはレスキューで改善が不十分な場合としている。母児の情報、BTP数、陣痛促進や回旋異常の有無、分娩転機を抽出した。児頭嵌入前に出現したBTP数が2回以上の群とそうでない群で、カテーテルの再穿刺率について χ^2 検定を行った。【成績】無痛分娩を行った全556例うち、417例が対象となった。BTP数が2回未満の群で再穿刺となったのは389例中59例(15.2%)、2回以上の群では28例中11例(39.3%)で、有意に再穿刺となることが判明した(オッズ比3.60: 95%CI 1.45-8.64)。陣痛促進や回旋異常、母児の身体的特徴には差は認めなかった。【結論】児頭嵌入前にBTPが2回出現した群では、カテーテルの再穿刺が必要になる可能性を考慮した管理が推奨される。

P-57-10 分娩誘発における硬膜外麻酔併用無痛分娩が分娩経過に与える影響

慶應義塾大

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【目的】COVID-19 流行を受け当院では入院5日前以内のPCR検査が義務となり、対応の一環として経陰分娩予定者は全例計画分娩の方針としている。その結果、従来は困難であった分娩誘発下での無痛分娩の影響を背景が一致した集団で検討することが可能となった。今回我々は分娩誘発下で無痛分娩が分娩経過にどのような影響を与えるか検討した。【方法】対象は2021年1月1日～6月30日に当院で分娩誘発を実施した103例である。検討項目は母体年齢、分娩回数、非妊時BMI、妊娠中体重増加量、分娩週数、出生体重、分娩様式、分娩第1・2期所要時間、分娩時出血量、臍帯動脈血pH、Apgar score、NICU入院率とした。なお、分娩誘発にはオキシトシンを使用し、必要に応じてメトロイリントールや頸管拡張剤による分娩前処置を施行した。無痛分娩は硬膜外麻酔で行い、active phaseを確認後に導入した。【成績】無痛分娩が61例、非無痛分娩が42例であった。両群間で分娩回数、非妊時BMI、妊娠中体重増加量、分娩週数、出生体重、帝王切開率、分娩第1期所要時間、分娩時出血量に差はなかった。無痛分娩群は非無痛分娩群と比較し、母体年齢(35.4±3.9歳 vs 33.5±5.1歳, p<0.05)と吸引分娩率(24.6% vs 4.8%, p<0.05)が高く、分娩第2期が延長した(63±51分 vs 39±39分, p<0.05)。また、臍帯動脈血pHは無痛分娩群で低かったもの(7.28±0.06 vs 7.30±0.05, p<0.05)、pH 7.1未満症例、Apgar score 1・5分値、NICU入院率に両群で差はなかった。【結論】分娩誘発下での無痛分娩は分娩第2期遷延、吸引分娩率の上昇の原因となるが、出血量、Apgar ScoreやNICU入院率に差はなく、母児の周産期転帰に明らかな影響を与えないと考えられた。

P-58-1 双頭双角子宮の各副角に妊娠した二絨毛膜二羊膜性双胎の1例

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【緒言】子宮奇形は、胎生期におけるMüller管の発生異常癒合で生じ、不妊や流産の原因検索で発見されることが多い。正常子宮と比較し、不妊や流産、胎児発育不全、子宮破裂などの割合が高いとされる。今回我々は体外受精にて双頭双角子宮の各副角に妊娠した双胎の1例を経験したので報告する。【症例】37歳、1妊0産。前医にて重複子宮の指摘あり。反復妊娠不成功のため両側子宮に1個ずつ胚移植を行い、二絨毛膜二羊膜性双胎妊娠が成立した。妊娠10週2日に当科を紹介受診。両児は頭位であったが、徐々に長頭蓋が目立つようになった。大横径は-3SD前後であったが、頭囲や腹囲・大腿骨長は正常範囲で発育した。妊娠30週3日より管理入院を開始し、MRI検査や自己血貯血などを行い分娩に備えた。妊娠35週6日妊娠高血圧症候群のため緊急帝王切開術を施行した。第1子出生体重2146g、女児、Apgar score 8/9、臍帯動脈血pH 7.24であり、第2子出生体重1961g、女児、Apgar score 8/9、臍帯動脈血pH 7.254であった。児は早産・低出生体重児のためNICU入院となった。術中所見より重複子宮ではなく、双頭双角子宮と診断した。術中出血は2487ml(羊水量込み)であり、自己血輸血を行った。術後経過は良好であり、術後6日目に自宅退院となった。【考察】双頭双角子宮の双胎妊娠は報告数が少なく、管理方針は定まっていない。今回は30週という早い時期からの管理入院を開始して備えることで、結果的にさほど大きな経過異常なく妊娠を終結することができた。分娩方式や娩出時期の決定などは症例に応じて慎重に検討していく必要があるとともに、子宮奇形における妊娠のリスクを妊婦自身にも伝えていくことも重要と考えられた。

P-58-2 胎児鏡下レーザー手術後の羊膜索症候群を契機に発症した児のDIC：症例報告

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【背景】胎児鏡下レーザー手術(fetoscopic laser photocoagulation: FLP)後に注意すべき合併症に羊膜索症候群がある。Selective fetal growth restriction (sFGR)に対するFLP後に羊膜索が死亡児の臍帯とともに生存児の示指を強く絞扼したことで壊死し、DICを発症した例を報告する。【症例】39歳、2妊0産、自然妊娠、一絨毛膜二羊膜性双胎妊娠。妊娠17週、推定体重差45.4%でsFGR児の持続する臍帯動脈血流異常を認め、sFGR (type2)と診断しFLPを行った。翌日にsFGR児は死亡したが、生存児は順調に経過した。妊娠31週5日、胎動が減少し来院。ノンストレステストで基線細変動の減少と繰り返す遅発一過性徐脈を認めたため胎児機能不全と診断し、同日緊急帝王切開した(1,754g, Apgar score: 2/6点, UmA-pH: 7.265)。母体経過は順調で術後7日目に退院した。児は右第2-3指と左第2-4趾に羊膜索による絞扼輪を認めた。中でも右示指は羊膜索に加えて死亡児の臍帯も絡まり壊死していた。死亡児の臍帯は約30cm長で生存児の卵膜に卵膜付着していた。児に感染徴候はなかったが、高度の凝固障害(血小板: 6.7×10³/μL, FDP: 722 μg/mL, フィブリノゲン: <25 mg/dL)を認め、DICと診断した。DICはトロンボモデュリン製剤やアンチトロンピン製剤により1週間で改善した。右示指は生後9日目に自然脱落したが、他の指趾に明らかな機能障害は認めず、経過順調で生後57日目に退院した。【結論】児に基礎疾患と感染徴候とを認めなかったことから、右示指の壊死がDICの発症に関与し胎児機能不全を示した可能性が高い。また、生存児の右示指を絞扼した羊膜索は死亡児の臍帯を巻き込んでおり、これが強い絞扼につながったと推察された。

P-58-3 双胎間輸血症候群に対する胎児鏡下レーザー凝固術後の流早産に関連する因子の検討

大阪母子医療センター

山本瑠美子, 山本 亮, 山田拓馬, 川口晴菜, 林 周作, 石井桂介

【目的】胎児鏡下レーザー凝固術 (FLP) は双胎間輸血症候群 (TTTS) に対する根治療法であるが、流早産のリスクを上昇させる。本研究では周産期の早産に対するリスク因子を明らかにする。【方法】2011年1月～2020年12月に妊娠16週から妊娠26週未満にTTTSに対してFLPを施行した自験例を対象とした後方視的コホート研究で、三胎、一羊膜双胎、手術未完遂例は除外した。主要評価項目は術後4週以内の流早産の頻度で、副次評価項目は術後2週間以内の流早産、妊娠28週未満の早産、妊娠32週未満の早産の頻度とした。前方視的に記録した術前因子として早産既往、頸管縫縮術、子宮収縮抑制剤点滴、FLPの週数、Quintero分類、第2・三半期の子宮出血および絨毛膜下血腫、羊水量、胎盤位置、子宮頸管長 (CL)、瘤胎児性フィブリン (FN)、IGFBP1について、主要評価項目との関連をCox比例ハザードモデルでハザード比を算出した (model 1)。さらに手術時間、羊水除去量、羊水注入量、手術終了時の受血児の羊水量とCL等の術中因子に関しても同様に検討した (model 2)。【成績】解析対象は288例で、術後4週間以内の流早産は24例 (8.3%)、術後2週間以内、妊娠28週未満、妊娠32週未満の早産は各々14例 (4.9%)、46例 (16.0%)、98例 (34.0%)であった。主要評価項目に関連する因子は第2・三半期の出血のみであり、ハザード比8.04 (95%CI 2.01-32.22, $P < 0.01$)であった。【結論】FLP後約1割が4週間以内に流早産となった。特に第2・三半期に出血を認めた症例はハイリスクである。

P-58-4 双胎間輸血症候群またはsIUGRで胎児鏡下胎盤吻合血管レーザー凝固術を受けた児における先天性心疾患の検討

国立成育医療研究センター胎児診療科

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【目的】一絨毛膜二羊膜性双胎 (以下MD双胎) では先天性心疾患 (以下CHD) の罹患頻度が高いことが知られている。当院においてTTTSまたはsIUGRで胎児鏡下胎盤吻合血管レーザー凝固術 (以下FLP) を受けた児におけるCHD罹患の実態について明らかにする。【方法】当院においてTTTSまたはsIUGRの診断でFLPを施行し、出生後にCHDの診断が判明している症例を対象とし診療録より後方視的に検討した。出生後の診断が不明もしくは多発奇形は除外した。【成績】2003年2月から2020年12月までの対象は691例 (胎児1382名) で、FLP施行平均妊娠週数は20.5週、平均分娩週数は32.2週であった。TTTSのQuintero Stage分類、sIUGRの内訳はTTTS 657例 (Stage I 147例, Stage III 104例, Stage III 348例, Stage IV 58例)、sIUGR 34例であった。生存出生の割合は供血児536/691名 (77.6%)、受血児641/691名 (92.8%)であった。供血児におけるCHDの罹患は20/536名 (3.7%)であり、心室中隔欠損症5名 (0.9%) が最も多かった。受血児におけるCHDの罹患は51/641名 (8.0%)であり、右室流出路狭窄33名 (5.1%) が最も多かった。両児にCHDが診断されていた妊娠は4/691例 (0.6%)であった。【結論】TTTSまたはsIUGRに罹患したMD双胎におけるCHDの罹患頻度は高く、特に受血児における右室流出路狭窄の頻度が高い。FLP後は児のCHDに留意して管理することが肝要である。

P-58-5 妊娠後期における、双胎妊娠が母体腎機能に及ぼす影響～単胎妊娠と比較した retrospective study～

名古屋第一赤十字病院

筈田 章, 津田弘之, 伊藤由美子, 手塚敦子, 齋藤 愛, 坂堂美央子, 廣村勝彦, 安藤智子, 水野公雄

【目的】妊娠により母体腎は構造的、機能的变化を引き起こし、血清クレアチニン (Cre) 値は初期から中期にかけて低下するものの、妊娠後期から末期にかけて上昇することが知られている。これらの変化は単胎と双胎で異なる可能性があるがあまり検討されていない。今回、単胎・双胎の妊娠後期における母体腎機能について検討した。【方法】2019年1月1日から2021年6月30日の間に当院で出産した単胎・双胎を対象とした後方視的観察研究である。診療録よりデータを抽出し、分娩の1か月以内にBUN, Cre, eGFRの項目を含む血液検査を実施した合計1712例の患者を対象とした。本研究に際し、当院倫理委員会の承認を得た。【成績】対象症例中、単胎は1548例、多胎は164例 (うちMM双胎2例, MD双胎52例, DD双胎110例)であった。単胎と双胎の比較では、FGRの割合が双胎で有意に高かった ($p < 0.001$)。腎機能の比較では、多胎は単胎と比較して有意にCreが高く ($p < 0.001$)、eGFRが低く ($P < 0.001$)、腎機能障害の割合が高かった ($p = 0.001$)。双胎の膜性別での差は認めなかった。多変量ロジスティック解析上、多胎は母体腎機能障害の独立した関連因子であった (OR 3.36, $p < 0.001$)。腎機能障害を認めた双胎13例のうち、分娩後も腎機能低下が持続したものは2例で、ともに途中でフォロー中断されており、その後の腎予後は不明である。その他11例は産後1週間から1か月前後で腎機能は改善した。【結論】双胎妊娠は妊娠後期における腎機能低下の有意なリスクである可能性が示唆された。分娩後はほとんどの症例で腎機能は速やかに改善したが、一部には分娩後も腎機能低下が持続する症例もあるため、慎重な腎機能のフォローが必要である。

P-58-6 1児に全前脳胞症を合併した一絨毛膜二羊膜双胎の1例

JA 旭川厚生病院

山田和佳, 今田冨紀, 三坂琴美, 杉山沙織, 中嶋えりか, 野崎綾子, 小田切哲二, 吉田俊明, 光部兼六郎

【目的】全前脳胞症は前脳分割不全と顔面奇形を特徴とする先天性疾患である。約1万分娩に1例の有病率であるが、流産や胎内・新生児死亡率が高い予後不良の疾患である。一絨毛膜二羊膜双胎(MD)の1児の無分葉型全前脳胞症を出生前診断したが、妊娠継続し2児とも生児を得た症例を経験したので報告する。【方法】32歳, 1妊0産, 特記合併症なし。自然妊娠しMD双胎と診断した。妊娠17週に1児(以下「病児」)の全前脳胞症が疑われた。所見のない児(以下「健児」)側の羊水染色体検査を行い正常核型であった。病児はMRIにて全前脳胞症無分葉型と診断したが、顔面その他の奇形は認めなかった。病児の水頭症は増悪したが、頭囲以外は週数相当の発育であった。健児は妊娠33週より発育が鈍化し、妊娠35週1日時点で推定体重は1578g(-2.8SD)であり、ドプラ異常が出現した。胎児機能不全の診断で妊娠35週3日に病児の頭囲拡大のため帝王切開術で娩出した。健児は合併症なく生後52日目にNICUを退院した。病児は頭囲拡大やけいれん発症があり、複数回のV-Pシャント手術を要したが、最終的に病態は安定し、生後10か月目に自宅退院した。【成績】全前脳胞症児は胎内死亡の可能性もあるが、MD双胎では他児への影響も懸念される。今回は健児のselective IUGRの合併もあり、娩出時期の決定に苦慮した。無分葉型では新生児死亡の報告も多いが、本症例では顔面奇形などの合併症が少なく、予測よりも良好な転帰であった。【結論】MD双胎に合併した全前脳胞症では妊娠継続の判断や娩出時期、方法の決定において難しい判断を迫られる。最重症型でも自宅退院可能となる症例もあり、合併症などを考慮しながらの慎重な管理が望まれる。

P-58-7 一絨毛膜二羊膜双胎の一児胎児死亡後2か月後に母体DICを発症した一例

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死胎児症候群は子宮内の胎児が死亡後に母体DICを起こしうる病態である。一児胎内死亡後の母体DICは、直近で起こることが多いとされており、慎重な管理が求められる。今回我々は、一絨毛膜二羊膜双胎の一児の子宮内胎児死亡を確認後、8週間後に母体DICと診断した症例を経験したので報告する。症例は39歳, 2妊1産, IVF-ETにて妊娠成立し一絨毛膜二羊膜双胎と診断し外来管理していた。妊娠25週0日にTTTSの診断でFLPを施行したところ、翌日に供給児の子宮内胎児死亡を確認した。以後、入院管理とし血液検査を行ったが、母体DIC兆候は認めなかった。その後も問題を認めず、妊娠27週4日に退院とし外来管理とした。妊娠33週0日、母体の凝固系が急速に変動したため死胎児症候群の母体DICと診断し、妊娠33週0日に緊急帝王切開術を施行した。生存児は1938g, 女児, Apgar score 1分値5点, 5分値7点, 臍帯動脈血液ガスpH 7.290, BE -2.8mEq/Lであった。出血量1310g(羊水込)であり、輸血および抗DIC治療を施行した。その後母体のDICは改善傾向となり、経過良好のため術後7日目に退院した。児はNICU入室後、生後31日目に退院となった。今回、子宮内胎児死亡確認後、8週間後に母体DICを認めた。現在、一絨毛膜二羊膜双胎における一児死胎児症候群の管理については一定のコンセンサスはない。今回の症例のように、直後の母体DIC兆候が無くとも、長期間をあけての母体DIC発症も可能性があることを念頭に置いて管理する必要があると考えられた。

P-58-8 FGR児のみに臍帯過捻転、胎盤梗塞を呈したMD双胎の1例

JCHO 群馬中央病院

伊藤理廣, 安部和子, 矢崎 淳, 田村美樹, 堀口静恵, 太田克人

【目的】Selective FGRを呈したMD双胎でFGR児の臍帯過捻転を呈し、胎盤病理組織検査所見でFGR児の側のみに胎盤梗塞を認めた症例を経験したので報告する。【方法】症例は30台G1P0, 自然妊娠でMD双胎となった。合併症なし。妊娠初期より児発育に差を認めた為、双胎児間輸血症候群を警戒し厳重管理されていた。妊娠32週切迫早産で入院。入院以降第2児は超音波断層法で臍帯か捻転を呈し計測上発育は見られなかったため、NSTにて慎重管理した。妊娠36週で第2児の予想体重が-2.5SD以下のため、帝王切開施行し、第1児2338g, 第2児1706gであった。第1児の臍帯は浮腫状で第2児は辺縁付着で過捻転を呈し胎盤は第2児の側で梗塞性変化を認めた。【成績】当院で2020年1月から臍帯過捻転を認めた3例では全て子宮内胎児発育遅延を呈していた。胎盤病理所見では絨毛間フィブリンの高度の沈着を認めた。一方同時期にMD双胎の分娩は8例で、双胎児間輸血症候群を示した症例はなく、5例は第1児と第2児の出生時体重に差がほぼなかったが、3例では1児のみFGRであった。1児のみFGRであった中で、37週で分娩に至った例でも胎盤の病理所見でFGRの側に高度の絨毛間フィブリン沈着を認めた。30週で分娩に至った症例では胎盤病理上部位による所見の違いは確認されなかった。児体重に差がない群では胎盤所見に分布上の違いは認められなかった。【結論】MD双胎の同一胎盤上で、梗塞巣の分布が均一でなく、梗塞が存在する側の児でFGRや臍帯過捻転を示す場合があり、過捻転を呈する場合は血流の慎重な測定による管理と、梗塞の予防のために抗凝固療法を考慮する必要があるかもしれない。

P-58-9 性別の異なる一絨毛膜二羊膜双胎の一例

宮崎大附属病院

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【緒言】一絨毛膜双胎では双胎間の性別は通常同じであるが、性別が異なる一絨毛膜双胎が複数報告されている。我々も外性器の性別が異なる一絨毛膜二羊膜双胎を経験したので報告する。【症例】症例は33歳、2妊0産。自然流産2回。男性因子の不妊のため、不妊治療施設で精巣内精子採取・顕微授精を施行し、凍結胚2個を移植して妊娠成立した。妊娠8週に一絨毛膜二羊膜双胎と診断され、両児の発育は週数相当で認めていたが、一児の羊水過少、切迫早産兆候を認め妊娠22週に当院転院となった。当院入院後は、性器出血なく絨毛膜下血腫も次第に消失し、羊水量の改善を認めた。また、妊娠19週時に妊娠糖尿病と診断され、食事療法および強化インスリン療法を行い、血糖コントロールも良好であった。妊娠27週時の経腹超音波断層法で双胎間の外性器の表現型が異なるように認められ、その後の診察でも同様の所見が認められた。双胎間の体重差は軽度認めていたが、両児ともに発育は週数相当であり、羊水量の不均衡などの双胎児間輸血症候群を疑う所見なく経過した。妊娠37週4日に選択的帝王切開施行した。第1子は体重2020g (-2.0SD)、Apgar scoreは1分8点、5分10点で外性器の表現型は正常女性型であった。第2子は体重2786g (+0.2SD)、Apgar scoreは1分8点、5分9点で外性器の表現型は正常男性型であった。【結論】胎盤病理検査の結果では一絨毛膜二羊膜性であり、現在両児の染色体検査を提出中である。学会にては染色体検査の結果も踏まえ本例の解析結果を発表予定である。

P-58-10 当院で経験した一絨毛膜一羊膜双胎の一例

国立弘前病院

當麻絢子, 横山万智, 追切裕江, 横田 恵, 丹藤伴江

【背景】一絨毛膜一羊膜 (MM) 双胎は自然妊娠10000人に1人の割合で発生する頻度の低い双胎妊娠である。羊膜による両児間の隔壁がないため、臍帯相互巻絡などにより4~20%は胎児死亡に至り、妊娠30~36週でも4.5~8%と高い胎児死亡率が報告されている。他の種類の双胎よりも周産期リスクは高いが、症例数が少ないため管理や分娩時期に関して一定の見解はない。我々が経験したMM双胎の経過を、文献の考察を交え報告する。【症例】32歳、1経妊0経産。既往歴・家族歴に特記事項なし。自然妊娠後近医で正所性妊娠を確認された。最終月経より妊娠11週5日に近医よりMM双胎疑いで当院へ紹介された。両児間に羊膜が存在しないことを確認し、MM双胎の診断となった。20週以降は週1回の外来超音波を行い、27週以降は入院管理の上3回/日の胎児心拍数モニタリングを継続した。34週2日に選択的帝王切開術で分娩となった。兄は早産、低出生体重児として小児科入院となったが、両児間に大きな体重差はなく順調に発育して退院となった。【結語】既存報告を参考に管理を行い健児を得たMM双胎の一例を経験した。

P-58-11 当院における一絨毛膜一羊膜双胎に関する検討

京都第一赤十字病院

井村友紀, 西 茜, 藪本和也, 赤澤美保, 山田惇之, 川俣まり, 松本真理子, 安尾忠浩, 大久保智治

【目的】一絨毛膜一羊膜双胎 (MM 双胎) は双胎間輸血症候群や一児発育不全などのリスクに加え、臍帯相互巻絡という特殊な合併症が生じうること、他膜性に比べ予後不良であることが知られている。初期の膜性診断の正確さが求められるが、妊娠中期以降では膜性診断は困難であることが多い。当院で過去5年間に経験したMM双胎について、分娩転帰や診察時の超音波所見について後方視的に検討した。【方法】2016年1月から2020年12月までに当院で分娩した双胎妊娠のうち、双胎種別の分娩転帰やMM双胎に特徴的な超音波所見について後方視的に検討した。【成績】2016年1月~2020年12月までの全分娩数3469例のうち双胎は194例 (5.5%) で、二絨毛膜二羊膜双胎が109例 (3.1%)、一絨毛膜二羊膜双胎が83例 (2.3%)、MM双胎が2例 (0.05%) であった。MM双胎は2例とも自然妊娠であった。経腹超音波上、2例とも臍帯付着部間の距離は短く、臍帯相互巻絡を認め、1例では臍帯真結節も認めた。2例とも妊娠31~32週台に帝王切開での娩出となったが兄の神経学的予後に異常はなかった。双胎妊娠間で兄の周産期予後には大きな有意差はなかった。【結論】妊娠中期以降のMM双胎の診断の一助となる超音波所見について、臍帯付着部間の距離が短いこと、臍帯相互巻絡、臍帯真結節などが報告されているが、当院の症例でも同様であった。MM双胎は症例数自体が少なく、周産期センターである当院でも5年間で2例であった。今後も症例を蓄積し中期以降の超音波所見の有用性の検討や周産期予後の検討を行っていく予定である。

P-59-1 当院における妊婦健康診査未受診症例の検討

東邦大医療センター大森病院

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【目的】「未受診妊婦」の現状と問題点を明らかにすること。【方法】2016年1月～2021年9月の間に当院で分娩した未受診妊婦を対象とし、診療録を元に後方視的に臨床情報を検討し、未受診妊婦の定義は「妊婦健診を1回も受けずに分娩または入院に至った」「全妊娠経過を通じての妊婦健診受診回数が3回以下」「最終受診日から3か月以上の受診がない」とした。【成績】研究期間中の未受診妊婦の分娩件数は22例、全分娩に占める未受診率は0.44%であった。母体年齢は10代4例(18.2%)、20代12例(54.5%)、30代6人(27.3%)であった。未婚が16例(72.7%)、初産婦が13例(59.1%)であった。未受診理由は、妊娠の未自覚8例(36.4%)、経済的理由5例(22.7%)、他に社会的な孤立、多忙、複雑な家庭事情などがあつた。分娩週数の中央値は妊娠39週(24-42)、早産例は5例(22.7%)であった。墜落産3例、帝王切開3例であった。母体合併症は妊娠高血圧症候群3例、妊娠糖尿病2例、常位胎盤早期剝離1人であった。児のNICU入院は3例で、児の合併症は脳出血2例、脳室周囲白質軟化症1例であった。児の退院先は乳児院または特別養子縁組6例、自宅退院16例であった。【結論】これまで本邦で報告された未受診妊婦の頻度は0.2～0.5%とされており、当院で経験した頻度は同程度であった。未受診の理由は経済的理由と妊娠の未自覚が大半を占める現状は諸家の報告と同様だった。母体合併症に重篤な転帰をたどるものはいなかったが、早産例が2割と多く、未受診がハイリスクであることを示していた。医療機関と行政機関の連携は改善されつつあるが、一定数の未受診妊婦が存在することを認識し、さらなる社会への啓蒙と医療機関と行政機関の連携が求められると思われた。

P-59-2 適切な Interpregnancy care による周産期予後の改善を目指して

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【目的】Preconception care の概念が普及しつつあるが、先行妊娠後に介入を行い後続妊娠の予後、またその後の人生における疾患予防につながる Interpregnancy care はまだ普及していない。今回、その基盤となるエビデンス構築に向けて、Interpregnancy における Body mass index (BMI) の年間変化量と妊娠高血圧症候群 (HDP) や妊娠糖尿病 (GDM) を中心に後続妊娠の予後に及ぼす影響について明らかにすることを目的とした。【方法】周産母子医療センター (n=2) と一次施設 (n=12) において 2009-2019 年に2回の周産期管理を行った妊婦の臨床情報を後方視的に収集した。Interpregnancy における年間 BMI 変化量について、標準年間 BMI 変化量 (0.2 kg/m²/年) を基準として、後続妊娠での HDP と GDM の発症リスクについて多変量解析で検討した。【成績】高血圧などを除外した単胎妊娠 (n=1,746) の検討で、先行妊娠での HDP 発症例と非発症例で、それぞれ年間 BMI 増加量が 0.6 kg/m²/年、1.0 kg/m²/年を上回ると、後続妊娠での HDP 発症リスクが有意に増加した。糖尿病などを除外した単胎妊娠 (n=1,640) の検討で、先行妊娠での GDM 発症例は 68.6% (48/70) と再発率が高く、特に肥満合併の9割が再発した。先行妊娠で GDM 非発症の標準 BMI 女性では、年間 BMI 増加量が 0.6 kg/m²/年を超えるると GDM 発症リスクが有意に増加した。【結論】HDP および GDM は将来の心血管系疾患や糖尿病の発症リスクを高め、再発はそのリスクをさらに増加させる。今後、個々のリスクに応じて次の妊娠に向けた年間 BMI 変化量の目標値を設定し生活改善を行うことは、後続妊娠での HDP・GDM の発症予防となり、さらには将来の心血管系疾患の予防となることが期待される。

P-59-3 妊娠中の加熱式タバコの使用状況に関するインターネット調査

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【目的】本研究の目的は、インターネット調査データを分析し、妊婦において、近年日本で流行している加熱式タバコも含めた喫煙状況を明らかにすることである。【方法】対象は、COVID-19 による社会・健康格差評価研究 (The Japan COVID-19 and Society Internet Survey, JACSIS) に参加した男女のうち、2019年9月から2021年7月までに単胎分娩を1回行った女性 6,256 名とした。インターネット調査は2021年7月から8月に実施し、不正および矛盾回答を除外した 5,688 名を解析した。喫煙状況については妊娠初期と妊娠中期以降に分け、燃焼および加熱式タバコの1日における喫煙本数をそれぞれ質問し、どちらかを1日1本以上喫煙したと回答した場合を喫煙妊婦と定義した。また、喫煙妊婦を燃焼タバコのみ・加熱式タバコのみ・燃焼タバコと加熱式タバコの両方に分類し、年齢別の検討も行った。p<0.05 を統計学的に有意差ありとした。本研究は最終演者所属機関の倫理委員会承認されている (承認番号: 20084)。【成績】回答時年齢の中央値は 32 歳 (18-48)、初産婦の割合は 53.9% であった。妊娠初期もしくは妊娠中期以降の喫煙者は 5,688 名のうち 265 名 (4.6%) で、内訳は燃焼タバコのみが 127 名 (2.2%)、加熱式タバコのみが 102 名 (1.8%)、燃焼タバコと加熱式タバコの両方が 36 名 (0.6%) であった。妊娠中に加熱式タバコを使用している割合を年齢別に比較したところ、30-34 歳を基準とした場合、25 歳未満がその 5.8 倍 (p<0.001)、25-30 歳がその 1.6 倍 (p<0.05) といずれも有意に高かった。【結論】現在、日本での喫煙妊婦の約 1/2 は加熱式タバコを使用していた。また、加熱式タバコの使用率は若い世代で高かった。

P-59-4 全例計画分娩の方針が分娩時間帯に与える影響

慶應大病院

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【目的】当院は COVID-19 対応のため、病院方針として入院日 5 日以内の PCR 検査が必須となった。産科では、自然分娩の対応が困難となり全例計画分娩の方針で対応した。本検討では、全例計画分娩の方針が分娩時間帯に与える影響を検討することを目的とした。【方法】通常対応を行った 2019 年 4 月から 2020 年 3 月までの 664 分娩（通常群）と、全例計画分娩の 2020 年 4 月から 2021 年 9 月まで 817 分娩（計画群）の 2 群について、帝王切開も含む全ての児娩出時間を比較検討した。なお、分娩誘発症例では 7:00 からオキシトシン点滴を開始した。初めに、児娩出時間を平日は 8:30 から 4 時間ごと 6 区分、休日 を 1 区分とした計 7 区分に分け、Cochran-Armitage の傾向検定を用いて比較した。次に、全分娩例に対する平日 8:30-19:00 分娩例の割合をカイ二乗検定で比較した。【成績】分娩時平均年齢と初産婦の割合は 2 群間で同等であった。計画群は通常群と比較し、平日 20:30-8:30 および休日に分娩となった割合が有意に低率であった ($p<0.0001$)。また平日 8:30-19:00 に分娩となった割合は、通常群 (69.6%) に対し計画群 (86.2%) で有意に高率であった ($p<0.0001$)。なお、帝王切開率や出生児 Apgar score は 2 群間で同等だった。【結論】全例計画分娩の方針により、平日 8:30-19:00 に分娩となる割合が増加し、夜間・休日の分娩となる割合が減少した。COVID-19 対応による現場の負担増もあったなか、全例計画分娩の方針は労働緩和には好影響を与えた可能性が示唆された。

P-59-5 社会的ハイリスク妊婦の周産期予後の検討と当院の取り組み

音羽病院

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社会的ハイリスク妊婦とは「経済的・家庭的要因などにより子育て困難が予想される妊産婦」と定義され、妊娠中より養育上の支援が必要な状態であると言える。当院では以前より独自に考案したアセスメントシートを用いて妊娠初期に社会的ハイリスク妊婦を抽出し、対象妊婦のフォローを行政と共に重点的に行っている。今回この方法で抽出された社会的ハイリスク妊婦の周産期予後について検討した。【目的】社会的ハイリスク妊婦では周産期予後が非ハイリスク妊婦に比して悪化するかどうかを検討する。【方法】2021 年 3 月から 2021 年 6 月の期間において、当院で考案したアセスメントシートに沿って抽出した社会的ハイリスク妊婦 35 名と社会的ハイリスク因子を含まなかった妊婦（非社会的ハイリスク妊婦）64 名を対象に検討した。【成績】母体年齢、初産婦の割合、帝王切開術の割合、児体重、分娩時出血量では、両群間に有意差は認めなかった。また、低出生体重児の割合も両群間で有意差を認めなかった。児に関する因子として、出生後 1 か月までの 1 日当たりの体重増加は両群で有意差を認めなかった。母乳栄養率（人工乳との混合栄養含む）は、社会的ハイリスク群で 63.6%、正常妊婦群で 93.5% であった ($p=0.0002$)。さらに、社会的ハイリスク群の中で助産制度を利用しているのは経産婦で多い傾向にあった。また、社会的ハイリスク因子が 1 点の群と 4 点以上の群で周産期予後と比較したが有意差は認めなかった。【結論】社会的ハイリスク群では母乳栄養率が有意に低かった。また、社会的ハイリスク因子の数は周産期予後に影響を与えないと考えられた。今後、乳児期以降のリスクとアセスメントシートの有効性について検討したい。

P-59-6 当センターの“飛び込み無痛分娩”の現状

大阪はびきの医療センター

安川久吉, 小川憲二, 中野和俊, 西川恭平, 藤田由布, 赤田 忍

【目的】当センターでは 2013 年から硬膜外麻酔を用いた計画無痛分娩を実施している。無痛希望でない産婦が分娩途中から無痛分娩を希望される、いわゆる“飛び込み無痛分娩”を実施することがしばしばある。今回、飛び込み無痛分娩の現状について調査したので報告する。【方法】2017 年 1 月から 2020 年 12 月までの期間に PCA スマートポンプを用いた PCEA (Patient controlled epidural analgesia) を実施した産婦 303 例のうち、分娩の途中で硬膜外鎮痛を実施し経陰分娩できた産婦 25 例（以下飛び込み無痛群：A 群）と HDP など医学的適応を除いた希望のため計画的に硬膜外鎮痛を実施し経陰分娩できた産婦 246 例（以下計画無痛群：B 群）を対象とし、2 群間で年齢、初産率、妊娠週数、吸引分娩、総分娩時間、分娩第 2 期、出血量、出生体重、アプガースコア 1 分値、アプガースコア 5 分値、臍帯血 pH、新生児予後 (HFNC 以上の呼吸管理または感染治療を要した児の割合) について比較検討した。【成績】統計的に有意差があったのは、年齢 (A 群 28.52 ± 7.11 vs B 群 32.28 ± 4.52)、初産率 (A 群 24/25 vs B 群 115/246)、妊娠週数 (A 群 40 週 1 日 ± 5 日 vs B 群 38 週 5 日 ± 5 日)、分娩時間 (A 群 1159.72 ± 584.79 分 vs B 群 469.23 ± 335.70 分) であった。治療を要した新生児は A 群 5/25 (2 例感染, 3 例 HFNC) と B 群 26/246 (1 例感染, 残りは HFNC) で統計的有意差は認めなかった ($P=0.0788$)。【結論】飛び込み無痛群の方が、より若い年齢の産婦、初産婦が多く、分娩時間、特に分娩第 1 期が遅延していた。治療を要した新生児は飛び込み無痛群の方が多い傾向にあり、飛び込み無痛分娩は帝王切開を回避できる可能性はあるが、感染や胎児の well-being を十分評価した上で慎重に実施される必要がある。

P-59-7 妊婦の口腔ケアに対する意識調査

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【目的】妊婦の歯周病と早産や低出生体重児との関連が昨今着目されており、妊娠中歯科受診に対して助成が出る地域もある。本研究は歯科受診の助成がない当地区において、妊婦の口腔ケアに対する意識および受診動向の現状把握を行うことを目的とした。【方法】2021年6月から9月まで当院で分娩した褥婦341人にアンケートを配布し、以下の項目について調査した。①妊娠中の歯科口腔ケアに対して必要性を感じているか。②妊娠中の歯科健診の受診状況(受診した場合はその理由や回数、受診しなかった場合はその理由)。③妊娠経過および産後(分娩時の妊娠週数、出生児体重、産科合併症(前期破水、切迫早産入院歴))。【成績】97%から回答があり、歯科受診の必要性を感じている妊婦は88%であった。全体の46%が歯科健診を受診しており、受診した全妊婦のうち初産婦は84人(53%)、経産婦73人(46%)と初産経産婦間で有意な差は認められなかった(p=0.17)。また86人(55%)は妊娠以前より歯科受診歴があり、妊娠を契機に歯科健診を受診したのは70人(44%)であった。歯科受診していない妊婦の86%は補助が出れば受診したいとの結果を得た。歯科受診の有無で妊娠週数、出生児体重で有意差を認めなかった。調査対象全体で8%に切迫早産管理目的の入院歴があった。そのうちの歯科健診受診歴あり41%、なし59%であり、歯科健診受診なし群で有意差を認めなかった。【結論】妊娠中の口腔ケアの重要性については多くの妊婦が認識していた。一方で、歯科健診の受診率は初産経産ともに半数程度であり受診率の増加を図る必要がある。歯科健診の財政的補助は受診率の向上を増加させる可能性が示唆された。

P-59-8 行政主体の産後ケア事業における産婦人科医の関わり

福岡大

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【目的】近年、妊産婦のメンタルヘルスケアの重要性フォーカスされたこと、コミュニケーションの方法が変革したことにより社会的隔絶が容易に形成されるようになったことから、孤立する産褥婦を妊娠期からの切れ目のなく支援する社会システムが求められている。【方法】令和元年に改正された母子保健改正法により、行政による産後ケア事業の実施が努力義務となり、民間・行政による産後ケア施設の運営がより円滑になった。一方で、同法施行後2年が経過し、産後ケア事業における種々の問題点も明らかになってきた。地域の基幹病院の産婦人科医師が行政主体の産後ケア事業に関わることで、明らかとなった問題点を抽出した。【成績】当該産後ケア施設は特定妊婦を積極的に受け入れる指定施設であり、年間約15人程度の妊婦の受け入れを行っており、特定妊婦に相当する特殊利用者は8例であった。一方で、当院における育児支援を要する妊婦は年間64人であり、うち保健福祉センター介入事例は29例であったが、うち産後ケア事業利用者は2名であった。入所中の産褥婦および母子関係の評価と問題点抽出は困難であり、スタッフのスキル・人材不足が原因と考えられた。また、現行の事業形態では単独での経営的な維持は困難であった。【結論】特定妊婦にとって本事業は虐待や社会的孤立を防止するために有益であるが、需要と供給の不一致があり、利用件数が伸び悩んでいるのが実際である。社会的な問題点の多様性から評価と継続した支援の難易度が高く、スタッフの拡充と修練が課題となる。加えて、収益上継続困難となる恐れがあり、運営資金の調達がしばしば問題点となる。

P-59-9 当院に緊急入院した旅行者妊婦の転機について

沖縄県立南部医療センター・こども医療センター

喜舎場千裕, 山下 薫, 柱本 真, 金嶺ちひろ, 土井生子, 中野裕子, 泉 有紀, 大山拓真, 平敷千晶, 砂川空広, 長井 裕, 佐久本薫

【目的】本県は観光立県であり、国内外から多くの観光客が訪れる。当院は空港に近く、宿泊施設も多い地域に設置される総合産科産後ケアセンターであり、旅行者の緊急受診を受けることも多い。当院を救急受診し緊急入院した旅行者妊婦症例の臨床像について検討する。【方法】2015年4月から2021年9月までに当院の救急部を受診した旅行者妊婦の内、緊急入院を要した症例の臨床像について後方視的に検討した。【成績】対象症例は9例(訪日旅行者3例)であり、受診時の妊娠週数の中央値は27週であった。8例は初産婦、1例は経産婦であった。入院中に分娩となった症例は3例(24週、27週、28週)であり、2例は経産婦、1例は帝王切開術による分娩であった。出生児は長期のNICU管理を要し、修正週数35週~41週で転院となった。院外分娩で母児ともに救急搬送された症例が1例であった。切迫早産で当院に母体搬送となり子宮収縮抑制剤による治療を要するも、退院希望が強く産科医師が飛行機に同乗し転院となった症例が2例であった。また、全前置胎盤で警告出血があるにも関わらず自主退院し帰国した症例が1例であった。その他、合併症疾患の増悪で内科管理を要した1例や、高エネルギー外傷後に安静目的で入院した症例が1例あった。COVID-19感染症が流行し緊急事態宣言下であったが当県への旅行を敢行し、早産となった症例も認めた。全例、旅行中に入院する事態になることを全く想像していなかった。旅行先での長期入院や分娩は精神的、金銭的負担が大きく、また訪日旅行者では言語や文化の違いから適切なコミュニケーションに難渋した。【結論】妊娠中の旅行では切迫流早産で緊急入院や分娩に至る可能性があり、リスクに関して積極的な啓蒙が必要と思われた。

P-60-1 LSC 導入後 2 年の報告

JA 北信総合病院

今井 宗, 佐々ゆかり, 高野宏太, 倉石美紗子, 野池雅実, 長田亮介

【緒言】腹腔鏡下仙骨腔固定術 (laparoscopic sacrocolpopexy; 以下 LSC) は骨盤臓器脱に対する低侵襲で再発率の低い優れた手術として、欧米では標準的手術として広く行われてきた。本邦でも 2016 年に保険収載されて以降、全国的に普及している。さらに 2020 年 4 月からは、RSC (Robotic sacrocolpopexy) も保険適応となり、急速に普及しつつある。当院で 2019 年 6 月に LSC を導入し、2021 年 8 月までに、LSC 以外の骨盤臓器脱術後の再発を含む 50 例の LSC を経験したので、方法、成績、合併症、当院における適応や課題を踏まえて報告する。【手術方法】1. S 状結腸脂肪垂を吊り上げ、視野を展開し、2. 仙骨岬角を露出し、岬角 S1 前縦帯に針糸をかけ、3. 後腹膜を切開し、後腔壁を露出、4. 膀胱を下方へ Aa 点まで剥離し、前腔壁を露出、5. 子宮腔上部切開、6. 後腔壁の縫縮、7. メッシュを前腔壁と腔断端に固定、8. 岬角 S1 前縦帯にメッシュ上端を縫合固定、9. 腹膜開窓部を縫合閉鎖し、ドレーンを留置して終了。【成績】平均年齢：65.8 歳 (44~80)、平均 BMI：24.8kg/m² (19.7~25.5)、平均手術時間：142.2 分 (110~243)、出血量：少量、合併症：1 例で肺動脈塞栓症、同症例で大網膜瘍と腹壁癒痕ヘルニア、2 例で癒着性イレウス (いずれも保存的に軽快) 再発：なし【結語】LSC は効果が高く、低侵襲な手術であり、患者の満足度も高い。ただ、適応については、従来の NTR (Native Tissue Repair)、TVM (Tension-free Vaginal Mesh) と LSC を慎重に判断する必要がある。また、NTR や TVM 再発例に対しても、工夫をすることで、LSC で修復できることも多い。今後もさらにチームで検討工夫しながら、術式の標準化を目指したい。

P-60-2 LSC 導入による骨盤臓器脱治療の変化

JA 北信総合病院

長田亮介, 今井 宗, 佐々ゆかり, 高野宏太, 倉石美紗子, 野池雅実

【目的】腹腔鏡下手術の普及とともに LSC (Laparoscopic Sacrocolpopexy) を導入する施設が増えている。当院の骨盤臓器脱治療もベッサリーによる保存的治療と腔式手術 (Native Tissue Repair; NTR) で対応してきたが、2019 年に LSC を導入して治療方法の選択肢が広がった。LSC 導入による当院での骨盤臓器脱治療法の変化を検討し、今後の治療方法選択につき考察した。【方法】LSC 導入前の 2016 年 1 月から 2019 年 6 月と導入後の 2019 年 7 月から 2021 年 6 月に治療が開始された症例について治療方法と患者背景につき検討した。【成績】LSC 導入前の症例数は 108 例であった。治療方法の内訳は、ベッサリー自己脱着なし 20 例 (18.5%)、自己脱着あり 23 例 (21.3%)、腔式子宮全摘+腔壁形成 (Vaginal hysterectomy and colporrhaphy; VTH) 51 例 (47.2%)、その他の NTR (Manchester 手術、腔閉鎖等) 14 例 (13.0%) であった。LSC 導入後の症例数は 98 例であった。治療方法の内訳は、ベッサリー自己脱着なし 19 例 (19.4%)、自己脱着あり 9 例 (9.2%)、VTH 14 例 (14.3%)、その他の NTR 12 例 (12.2%)、LSC 44 例 (44.9%) であった。LSC 導入によってベッサリー自己脱着ありと VTH が減少したがベッサリー自己脱着なしとその他の NTR に変化はなかった。ベッサリー自己脱着と VTH において LSC 導入前後で合併症の合併率、年齢について有意な差はなかったが、VTH では、LSC 導入後に糖尿病の合併率が高まった。【結論】今回の検討からはベッサリー自己脱着、腔式子宮全摘+腔壁形成、LSC は競合する治療方法と考えられた。それぞれの患者が適切な治療を選択できるよう、合併症や患者の生活背景に配慮しつつ適切な治療方法を提供する必要がある。

P-60-3 骨盤臓器脱に対する腹腔鏡下仙骨腔固定術 (LSC) とロボット支援下仙骨腔固定術 (RSC) の手術成績の比較

国立京都医療センター

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【目的】当院では、2019 年 5 月より腹腔鏡下仙骨腔固定術 (LSC)、2020 年 5 月よりロボット支援下仙骨腔固定術 (RSC) を導入した。RSC 導入後は LSC を行っていない。今回、当院で行った LSC と RSC の手術成績について比較検討する。【方法】LSC 21 例と RSC 36 例について後方視的に検討した。LSC ではダイヤモンド型のトロカー配置で、RSC ではダ・ヴィンチ X システムを用いてロボットトロカー 4ヶ所+助手用トロカー 1ヶ所を配置し手術した。子宮上部切開後に前腔壁および子宮頸部前壁にガイネメッシュ®を留置するシングルメッシュ法を用いた。評価項目は年齢、BMI、POP-Q スコア、手術時間、術中出血量、術中・術後合併症、術後再発の有無、在院日数とした。術式間の比較には t 検定を用いた。【成績】LSC/RSC の順に年齢の中央値は 73 歳/72 歳、BMI の中央値は 23.5/24.1 であった。POP-Q スコアは、Stage III 以上が 7 例 (33%) / 12 例 (33%) であった。子宮摘出後症例は 1 例/4 例であり、腔閉鎖術後例は 0 例/1 例であった。手術時間の中央値は 209 分/229 分であり、両術式で有意な差は認めなかった。出血量は全症例で少量 (0-50ml) であった。在院日数の中央値はいずれも 6 日であった。RSC 症例のうち、1 例で術中膀胱損傷を認め、1 例でメッシュ背側の小腸陥陥による絞扼性イレウスを認めた。また術後に LSC の 1 例および RSC の 2 例で腹圧性尿失禁の顕在化を認めた。術後再発はいずれの群にも認めなかった。【結論】RSC において LSC と同様の良好な術後成績が確認された。

P-60-4 当院における女性泌尿器外来開設と骨盤 Cine MRI 検査の導入について—2 症例の検討から

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遠藤 拓¹、澤田紫乃¹、杉下陽堂³、五十嵐嵐^{1,2}、戸澤見子¹、長谷川潤一¹、鈴木 直¹

【目的】高齢化に伴う骨盤臓器脱患者および下部尿路症状が付随する患者の増加により、当院において女性泌尿器外来を新規開設した。骨盤臓器脱の診断は客観性が乏しく、症状の再現性が乏しいことが臨床的な課題であるが、適切な治療介入を行うためには骨盤臓器脱を確実に診断することが重要である。Cine MRI 検査は被曝せず造影剤不使用で軟部組織を高い解像度で描出でき、さらに偶発的に骨盤臓器脱以外の病変を発見できる利点があることから、当院における女性泌尿器外来の開設に伴い、診断精度の向上を目的に骨盤 cine MRI 検査を導入することとした。【方法】骨盤臓器脱を主訴として受診した患者 (n=2) を対象とした。患者から同意を得た上で、質問票を用い下部尿路症状を含めた基本情報を抽出し、膀胱内に尿を貯留させた状態で腹圧負荷と肛門収縮を指示し CineMRI 検査にて骨盤臓器脱の先進部と骨盤底筋を動的に評価した。【成績】症例①72歳2妊2産。主訴は子宮下垂感で受診。既往に子宮全摘出術があり、台上診で POP-Q3 度の陰道前壁脱と診断。女性下部尿路症状として尿意切迫感を認めた。Cine MRI 検査を施行し先進部が膀胱であることを動的に確認した。症例②78歳3妊3産。主訴は子宮下垂感と尿意切迫感で受診。台上診で膀胱瘤 POP-Q3 度の診断。Cine MRI 検査施行し膀胱瘤に加え子宮脱も併発していることを動的に確認した。【結論】Cine MRI 検査の導入により診断精度の向上が期待される。今後、骨盤臓器脱の臨床的、解剖学的研究の強力なツールなり得ることから症例数を増やし、前向き臨床研究として検査の有用性検証する。

P-60-5 LSC 術後にメッシュ感染を来した2例

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今回 LSC 術後に脊椎椎間板炎を来した症例と、後腹膜膿瘍を発症した症例を経験したため、文献報告例の検討を加えて報告する。症例1は74歳の女性で、骨盤臓器脱に対する腹腔鏡下仙骨陰固定術 (LSC) 術後4日目に発熱と腰痛が出現。抗菌薬投与で著明な改善を認めず、施行した MRI 検査で L5-S1 の脊椎椎間板炎と診断された。メッシュに沿って経腔的に発症した脊椎椎間板炎と診断し、腹腔鏡下メッシュ除去術を施行。術後は特に合併症無く現在まで感染および骨盤臓器脱の再発を認めない。症例2は64歳、LSC 術後11日目に発熱を認め12日目に術後感染の疑いで入院となった。CT・MRI 検査でメッシュに沿った膿瘍を認め、メッシュ感染の疑いで腹腔鏡下手術を施行。仙骨近傍のメッシュ前面に白苔の付着を認め、また子宮頸管組織も脆く、感染を疑う所見であった。経腔的メッシュ感染の診断で除去術を施行、現在まで感染および骨盤臓器脱の再発を認めない。

P-60-6 当科における腹腔鏡下仙骨陰固定術 (LSC) の治療成績—特にペッサリー療法中止からの手術例について—

公立安栗総合病院

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【目的】骨盤臓器脱 (POP) に対するペッサリー療法は広く臨床的に行われているが、その長期留置例などでは合併症からペッサリー抜去をせざるを得なくなり、POP による症状が持続または再燃する場合は次治療に苦慮することがある。近年、骨盤臓器脱 (POP) に対する腹腔鏡下仙骨陰固定術 (LSC) は普及しつつあり、当科でも 2018 年以降本術式にて治療を行ってきた。特にペッサリー療法既往からの手術症例について、ペッサリー中止理由、留置期間、術前の状態、手術手技、その成績、患者満足度について今後の課題を含めて報告する。【方法】2018 年 12 月から 2021 年 4 月まで当科でペッサリー療法中止後に LSC を施行した 29 例を対象として、ペッサリー中止理由、留置期間、術時間、手術手技、合併症、再発、患者満足度などについて後方視的に検討した。【成績】患者背景は平均年齢 68 歳 (59-85)、平均 BMI26 (17-36)。ペッサリー中止理由は炎症・帯下増量・出血 15 例、脱落 7 例、不快感 (下垂感・違和感) 5 例、疼痛 1 例、本人希望 1 例であった。術前 POPQ stage2 10 例、stage3 17 例、stage4 2 例であった。平均術時間 251 分 (181-351) で、術後の合併症は認められなかった。術後に麻痺性イレウス 1 例、臍周囲炎 1 例、下腸間膜動脈血栓症 1 例が見られた。術後 POPQ2 以上の再発は 1 例に、尿失禁は 2 例に見られた。術後 6 か月時点での患者満足度調査では、大変満足 15 例、満足 9 例、どちらともいえない 4 例、不満足 2 例であった。【結論】POP におけるペッサリー療法中止後の次治療としての LSC は問題ないものと思われたが、術時間の短縮などさらなる低侵襲化を図る必要があると考えられた。また、ペッサリー療法による腔壁の変化についても考察してみたい。

P-60-7 vNOTESによる腔断端仙骨子宮靱帯固定術の初期成績

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石塚貴紀, 齋藤研祐, 庄とも子, 吉村和晃

【目的】NOTES (Natural orifice transluminal endoscopic surgery) は自然孔を用いて内視鏡手術を施行する方法で、我々は骨盤臓器脱に対する Native tissue repair 手術に vaginal NOTES (vNOTES) を導入し、経腔的内視鏡下腔断端仙骨子宮靱帯固定術を行ったので初期成績を報告する。【方法】2020年10月から2021年9月の間に子宮脱を主体とするPOP-Q stageII以上の骨盤臓器脱18例に対して、経腔的内視鏡下子宮全摘術および腔断端仙骨子宮靱帯固定術を施行した。手術前後でPOP-Q scoreを記録し、Ba点、C点およびBp点について術前と術後1か月のscoreを比較した。手術の概要は、まず前後陰門蓋を開放してからvNOTESを開始し、腔式子宮全摘術と同様に基靱帯・円靱帯を処理する。さらに骨盤漏斗靱帯を処理して子宮・両側付属器を摘出する。次に仙骨子宮靱帯を同定し、その外側より後腹膜を切開し、尿管と骨盤神経叢を同定剥離する。仙骨子宮靱帯に遅延性吸収糸を左右それぞれ2針ずつかけ、V-Pathを取り外す。その後、前後陰壁に糸を通して腔断端をShull法に準じて縫合固定し閉鎖した。【成績】年齢：70.1±7.2歳、BMI：24.2±2.8kg/m²、手術時間：109.4±20.5分、気腹時間：60.3±18.1分、出血量：10-270(中央値60)gだった。周術期合併症は認めなかった。術前/術後のPOP-Qスコアは、Ba点1.8±1.7/-2.7±0.5cm、C点1.4±2.3/-5.1±0.9cm、Bp点-0.1±1.9/-2.8±0.5cmで、いずれも有意に改善した。【結論】経腔手術と腹腔鏡手術の融合とも言える本法は、腹式手術より低侵襲な腔式手術でありながら、鏡視下の操作によって確実な断端固定と尿管損傷など合併症の回避が可能である。今後も症例を重ね、長期成績の検討を要する。

P-60-8 アシストポートをなくしたロボット支援仙骨腔固定術 (RSC) の導入—3ポート式RSCへの術式変更—

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鈴木省治

【目的】米国が2000年に多孔式ロボット支援手術を承認し、この30年間に仙骨腔固定術は腹腔鏡手術 (LSC) からロボット支援手術 (RSC) へ発展した。LSCと比較すると、ダビンチを用いたRSCは触覚がないための合併症、手術時間、コストの増加などのデメリットがある。我々はアシストポートを含む4または5ポートのRSCから、アシストポートをなくした3ポート式RSCへ改良を試みたので、段階的導入手順を説明する。【方法】2020年5月から現在まで、3度以上の骨盤臓器脱50人を対象とした。最初は10mmフレキシブル(2D)スコープでポート配置は臍12mm、左12mm、右5mmの3ポート式LSCから、ロボット操作直前にポート配置を単純にトロッカー交換または12mmポートにダビンチ用トロッカーを重ねたダブルトロッカーへ変更し、腹腔内に針糸袋を挿入した後、ダビンチ用(3D)スコープでRSC縫合を開始し、RSC縫合の割合を徐々に増やした。次はポート配置は臍12mmと左右5mmおよびロボット操作直前に臍ダブルトロッカーと左右ダビンチ用トロッカーに変更を選択し、ダビンチ用(3D)スコープを使用したLSC剥離とRSC縫合に習熟した。最終的には10mmフレキシブル(2D)スコープおよび臍12mmと左右ダビンチ用トロッカーで術野を確保後、臍ダブルトロッカーに変更し全ての操作を3ポート式RSCで行った。【成績】10mmフレキシブル(2D)スコープも使用するLSC剥離・RSC縫合は適応範囲が広く、高度癒着や大きな子宮筋腫、視覚だけでは岬角剥離が難しい例も対処できた。全例で3ポート式RSCが可能であった。【結論】困難な症例でもLSCで補助することで、針糸袋挿入および臍ダブルトロッカーによりアシストポートをなくした3ポート式RSCは安全に導入できる。

P-60-9 岬角前面へのメッシュ固定が困難な骨盤臓器脱症例に対してLaparoscopic lateral suspensionを施行した6例

トヨタ記念病院

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【目的】骨盤臓器脱に対する手術療法として、近年、ゴールドスタンダードとなっているLaparoscopic sacrocolpopexy(LSC)では、岬角前面での前縦靱帯の露出とメッシュ固定が不可欠である。しかし、種々の要因により手術操作が困難な症例が一定の割合で存在する。腹腔鏡下側方メッシュ固定術(Laparoscopic lateral suspension: LLS)は、脆弱化した膀胱陰筋膜や直腸陰筋膜に固定したメッシュのアームを腹膜下に通し、前腹壁の筋膜に固定し側方へ牽引する術式で、LSCが困難な症例に対して施行可能な術式であるが、本邦での報告は少ない。【方法】これまでに当院でLSCの適応と考えられた骨盤臓器脱症例のうち、術前、術中にLLSに術式を変更した6例について、年齢、重症度、LLSへの術式変更理由、手術時間、周術期合併症の有無、術後経過につき後方視的に検討したので報告する。【成績】平均年齢は76.3歳で、重症度はPOP-Q stageIIIが5例、stageIIが1例であった。LLSへの術式変更理由としては、5例が岬角前面の総腸骨動静脈走行のため、1例が岬角前面からの出血のためであった。手術時間は平均3時間47分で、全例で周術期合併症はなく、術後平均4日(3-6日)で退院となった。術後の観察期間は平均5か月(2-13か月)で、現状、再発例はなく短期的予後は良好であった。【結論】LLSは岬角前面へのメッシュ固定が困難な骨盤臓器脱症例においてLSCに替わる術式である可能性が示された。

P-60-10 sacrospinous hysteropexy 施行症例の検討

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【目的】仙棘靱帯固定術は本邦で古くから腔断端脱に施行されている術式であるが、近年子宮頸部に固定した方法（sacrospinous hysteropexy）が施行されるようになり良好な成績が報告されている。当院は以前より骨盤臓器脱に対しメッシュ手術を主に施行しており現在も大半がTVMかLSCであるが、その中で様々な理由でNTRをすることもある。今回当院でsacrospinous hysteropexyを施行した症例を経験したので報告する。【方法】対象は2021年3月から2021年10月までに当院でsacrospinous hysteropexyを施行した7例。sacrospinous hysteropexyのみを施行した症例が3例、前腔形成術を併用した症例が2例、頸管切除を併用した症例が2例で、前壁形成症例は前方から仙棘靱帯へアプローチした。【成績】症例の平均年齢は68歳（46-78歳）であった。平均手術時間は46分、平均出血量は26gであった。Capio™を使用した症例が5例あった。【結論】sacrospinous hysteropexyは通常の後壁からのアプローチでは前壁下垂の再発例が多いとの報告があり、最近前壁からのアプローチが検討されているため前壁下垂のあった症例では前壁アプローチで施行し、さらに前壁形成術を追加した。また再発で頸管延長の報告もあるので頸管延長している症例では頸管切除も同時に施行した。TVMの経験から仙棘靱帯への穿刺は難度の高い手技ではなく、さらにCapio™を使用すれば容易であった。併用手術を施行しても短時間で施行でき、合併症も少ないことがわかった。手術適応患者が高齢化しており、侵襲が少ない手術として子宮脱に対してsacrospinous hysteropexyは有用でないかと示唆される。発表では術後の成績も含めて報告したい。

P-60-11 多発子宮筋腫合併膀胱瘤に対してロボット子宮全摘術（RSH）とロボット仙骨腔固定術（RSC）を併用した症例

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【目的】当院では骨盤臓器脱に対するRobot Sacrocolpopexy（RSC）を行う際に、あらかじめ上部靱帯をロボットで切断後、腔式に子宮摘出するRobot-assisted vaginal hysterectomy（RAVH）を併用している。メッシュを覆うために腹膜欠損が大きくなるようにRobot simple hysterectomy（RSH）ではなくRAVHを選択している。今回子宮が大きく（摘出子宮重量560g）、RAVHが困難だと考えRSHを初めて併用した。その経験と当院での工夫を報告する。【方法・成績】56歳5妊3産。1年前から残尿感の自覚あり受診し、膀胱瘤G3子宮脱G1を認め、手術の方針とした。同時に多発する子宮筋腫も併存しており、子宮が大きかったため、RSCにRSHを併用した。まず初めに肛門挙筋筋膜を露出し前腔壁はAa点-2.5cmまで剝離した。上部靱帯を切断し、尿管を確認。子宮動脈を結紮・切断後に子宮傍組織を処理。ロボット下に尿管を切断し、子宮は経腔回収した。腔断端もロボット下に連続往復縫合し、前後腔壁と岬角にダブルメッシュで固定した。腹膜は閉鎖しメッシュを被覆した。手術時間169分（コンソール時間147分）子宮重量560g出血量86mlであった。術後1日目より歩行を開始し、術後3日目に自宅退院とした。【結論】腹膜欠損部はRAVHに比べて広範囲となるため、メッシュを被覆させるのにやや難渋した。よって基本的にはRAVHの併用が相応しいと考える。ただし子宮が大きくRAVHが困難な症例には、RSHの併用も選択肢となりえると考えられた。

P-61-1 Premenstrual disorder 女性におけるQOLの検討

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【目的】PMS（月経前症候群）を含むpremenstrual disorders（PMDs）は、性成熟期女性の多くにみられ、QOLの低下や社会生活への影響があることが指摘されている。しかし、日本人におけるPMD患者に対する健康関連QOLの報告は少ない。特に、うつ病の一亜型として定義されるPMDD（月経前不快気分障害）や、既存する精神的・身体的疾患の月経前増悪であるPME（premenstrual exacerbation）について、前方視的記録による鑑別診断を行った上で、QOLの差異を検討したものはほとんどみられない。そこで今回、PMS、PMDD、PME女性のQOLについて比較検討を行なった。【方法】当院をPMS症状のため受診した女性のうち、前方視的症候評価表を用いて診断を確定でき、PMS、PMDD、PMEのいずれかに該当した33例（年齢35.6±8.3歳）を対象とした。診断名ごとに群分けを行い、初診時に行なった健康関連QOL（SF-36）の各下位尺度スコアを、比較検討した。【成績】各群の年齢には差は認めなかった。SF-36下位分類の平均値は、PMSおよびPMDD群では身体機能（PF）以外のすべてで、そしてPME群ではすべての項目で、国民標準値より低値であり、QOLが阻害されていた。各群間の比較では、PME群ではPMS群と比較してPF以外のすべてのSF-36下位尺度で有意に低く、またPMDD群との比較では日常役割機能・精神（RE）が有意に低値であった。【結論】PMD女性のQOLは低く、特にPMEにおいては、身体的にも精神的にもQOLが顕著に低下していることが明らかとなった。PMEの診断には詳細な問診と前方視的記録が必須であるため、初診時からPMEの可能性も念頭におき、正しく診断したうえで、治療にあたるのが重要であると考えられた。

P-61-2 当科での婦人科悪性腫瘍治療後のヘルスケアの現状

徳島大

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【目的】婦人科悪性腫瘍患者の30~40%は50歳未満の女性であり、患者の多くは両側卵巣摘出術を含む手術や化学療法、放射線療法などを受け、これらの治療により卵巣機能の廃絶を伴っている。当院で治療した婦人科悪性腫瘍患者のうち、治療により閉経をきたした症例に対する管理の現状と問題点を考察する。【方法】当院で婦人科悪性腫瘍治療後に閉経となった47例について、治療後の卵巣欠落症状、脂質異常の有無、骨塩量、治療法と問題点について検討した。【成績】診断の内訳は、子宮頸癌22例(扁平上皮癌11例、腺癌9例、腺扁平上皮癌1例、glassy cell carcinoma 1例)、子宮体癌12例(類内膜癌12例)、卵巣癌13例(類内膜癌4例、漿液性癌2例、明細胞癌2例、漿液性境界悪性腫瘍3例、粘液性境界悪性腫瘍2例)で、年齢中央値は47歳(31~56歳)、閉経年齢は39歳(20~51歳)であった。卵巣欠落症状についてはhot flashが34例と最も多く、続いて倦怠感、頭痛、不眠、不安などの症状を訴えた。脂質異常は13例に認め、骨密度は正常24例、骨量減少10例、骨粗鬆症3例であった。子宮頸癌と卵巣癌に対しては治療後早期からHRTを開始していたが、子宮体癌に対してはHRT開始が遅れる傾向にあった。HRTを施行している31例のうち、卵巣欠落症状のある25例中22例で症状の改善が見られた。骨量についてはHRT+ビタミンD併用群で有意に骨密度上昇効果を認めた。【結論】婦人科悪性腫瘍治療後に閉経をきたした患者についてはトータルヘルスケアの観点から十分なインフォームド Consentのもと積極的にHRTを導入していく必要がある。

P-61-3 子宮感染により汎発性腹膜炎と診断された高齢者3症例の検討

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【緒言】高齢女性の子宮感染の原因に子宮留膿腫が原因となり、稀に穿孔を起こすことで汎発性腹膜炎をきたすことが報告として散見される。今回、当院で様々な原因により子宮感染をきたし、全身治療を要した3症例を経験したので報告する。【症例】症例1は90歳、慢性心不全で通院中も家族と共に生活。急性腹症により搬送後、CTで子宮留膿腫および腹腔内遊離ガスを認め、婦人科で診察し子宮留膿腫による子宮穿孔を疑い子宮全摘術およびドレナージ術を施行した。術後に敗血症治療を行うも状態は改善せず、術後5日目に永眠となる。症例2は83歳、高血圧以外は持病なく家族と共に生活。2週間前より下腹部痛出現し近医で大腸内視鏡検査するも異常なくCT検査で子宮腫大を指摘。急性腹症で搬送後、子宮内腔とは交通性がない膿瘍の穿孔による腹膜炎が疑われ、子宮全摘術およびドレナージ術を施行。術後27日に全身状態が改善し退院となった。病理学的には原因が不明であった。症例3は79歳、高血圧、高コレステロール血症のみで独居により生活。1か月前より便通異常、尿量減少を自覚しその後下肢の浮腫と呼吸苦が出現。前医で腹部腫瘍を指摘され紹介受診。CTおよびMRI等で子宮膿瘍および直腸癌の診断となり入院後3日目に緊急で子宮全摘および直腸切除、人工肛門増設を施行。術中、直腸癌の子宮壁に癒着、穿孔している所見を認めたが病理学的には子宮筋腫の感染が膿瘍の原因として推測され、術後52日目に退院となる。【考察】子宮膿瘍および穿孔による汎発性腹膜炎は様々な原因により発症することが推測され、高齢者に発症するために予後に直結する可能性が極めて高い。可能な限り、婦人科的検診でのリスク抽出が重要と考えられる。

P-61-4 閉経後性器尿路症候群(Genito-urinary Syndrome of Menopause, GSM)にはエストロゲン含有クリーム製剤が有用である

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【目的】閉経期の女性は卵巣からのestrogen分泌が低下する結果、GSM(外陰部の乾燥に伴う搔痒感、性交痛など)を発症し、その結果QOLが低下する。今回このような女性に対する各種女性ホルモン製剤の効果を比較検討した。【方法】研究遂行に際して病院の倫理委員会に諮り許可を得た後、被験者に十分なインフォームド Consentを行い同意を得た。GSMを訴えた患者45例を対象とした。At randomにA群(22例):estrogen含有クリーム製剤(1g中にestradiol 0.6mg, ethinyl estradiol 0.2mg含有)を0.1g外陰部に塗布、およびB群(23例):estriol錠剤(1錠中にestriol 0.5mg含有)を1日1回それぞれ2週間自己投与させて、外陰部のかゆみ、乾燥度、性交時の疼痛を0-3の4段階に分けて評価した。患者には適宜白色ワセリンや性交時の潤滑ゼリーを使用するよう指導した。【成績】外陰部のかゆみ(A:2.9±0.2→0.4±0.1, B:2.8±0.3→0.7±0.4)、乾燥度(A:2.8±0.2→0.3±0.4, B:2.9±0.5→0.9±0.2)については、A群でやや良好であった。性交時疼痛については(A:2.9±0.4→0.3±0.2, B:2.9±0.3→1.1±0.5, p<0.05)とA群で有意に改善していた。B群では、自分で錠剤を入れるに、入れた錠剤がそのまま出てしまうという症例がみられた。薬剤投与による重篤な副作用は認められなかった。【結論】Estrogen含有クリーム製剤は外陰部乾燥、搔痒症および性交痛に悩むGSM患者のQOL改善に極めて有用であることが明らかとなった。

P-61-5 診療科横断的な対応が必要であった無月経アスリートの2例

長崎大病院

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【緒言】女性アスリートの三主徴をきたす若年アスリートは、無月経を契機に産婦人科を受診し、栄養指導やホルモン療法を行うことが多いが、競技に影響する合併症や心理的葛藤への対応に苦慮することも少なくない。今回、当院で管理が困難だったアスリートの2例を提示する。【症例1：自閉症スペクトラム障害】18歳、大学1年生。原発性無月経。1型糖尿病で小児期からインスリン療法を行っている。中学生から陸上部（長距離）で、大学入学に伴う転居のため当院へ紹介された。受診時のBMIは14.9とやせを認めた。陸上部の練習以外に自主練習を追加する「過活動」と「こだわり」が認められた。腰椎BMDは0.771g/cm³、Zスコア-2.9と骨粗鬆症を認めた。前医からホルモン補充療法を施行されており継続した。糖尿病は当院内科で管理されたがコントロールは不良だった。大学での新しい環境に馴染めず、精神科的ケアを提案したが拒否し休学した。【症例2：運動誘発性アナフィラキシー】23歳、実業団陸上部（長距離）所属。原発性無月経。仙骨疲労骨折で受診した整形外科から無月経の精査目的に当科へ紹介された。初診時の腰椎BMDは0.790g/cm³、Zスコア-2.8と骨粗鬆症を認めた。栄養士による栄養指導とホルモン補充療法を開始した。練習再開後、再び仙骨の疲労骨折をきたしたため、当院整形外科よりテリパラチドが開始された。疲労骨折を繰り返すことへのストレスと運動誘発性アナフィラキシーを発症したことからの引退を選択した。【まとめ】若年女性アスリートへの対応は、本人や周囲の理解だけでなく、診療科横断的な対応が求められる場合がある。アスリートの状況を把握し、包括的に対応する体制が重要と考えられた。

P-61-6 更年期女性の脂肪量指数とホットフラッシュは正に関係し、除脂肪量指数と不眠は負に関係する

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【目的】本研究は、更年期女性の体組成と身体・精神症状の関係について明らかにすることを目的とする。【方法】倫理委員会の承認を得て、当大学更年期外来の系統的健康・栄養教育プログラムに参加した40歳以上64歳未満の女性554名（平均年齢51.1歳）について、初診時の記録をもとに横断的検討を行った。脂肪量と除脂肪量を身長²の2乗で割ったものを脂肪量指数(FMI)、除脂肪量指数(LMI)として設定し、中央値で2群にそれぞれ分けた。更年期QOLスコア質問票の症状の項目、病院不安とうつ病尺度(HADS)、アテネ不眠尺度(AIS)のうち、差があるものを抽出した。更年期QOLスコア質問票の「顔があつくなる」という項目に対し週1回以上と回答した場合を「ホットフラッシュ(HF)あり」、AIS10以上を「不眠あり」と設定し、多重ロジスティック回帰分析を用いて、背景因子として考えられる年齢、閉経状態、HADS、運動の有無による調整を行って、それぞれに独立に関連する因子を同定した。【成績】(1)単変量解析でFMI群によって差がある症状はHFであった。背景因子を調整しても、FMI(kg/m²)がHFと独立に正の関連を示した(オッズ比[95%信頼区間]=1.08[1.02-1.15])。 (2)単変量解析でLMI群によって差がある症状は不眠であった。背景因子を調整しても、LMI(kg/m²)が不眠と独立に負の関連を示した(オッズ比[95%信頼区間]=0.72[0.55-0.94])。【結論】FMIはHFと正に、LMIは更年期女性の不眠と負に関連していた。更年期女性において、減量がHFの改善に、筋肉量の増加が不眠の改善につながる可能性が示唆された。

P-61-7 早発閉経に影響を与える因子の検討

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【目的】45歳未満での早発閉経は冠動脈疾患の罹患率が上昇すると報告されている。早発閉経に影響を与える因子を検討し、早発閉経の予測因子を明らかにする。【方法】2009年から2015年に地域住民対象のコホート研究に参加した自然閉経女性7,239人のうち、45歳未満で閉経した241人と、平均閉経年齢群(-1~+1SD)の5,651人を対象とした。自己記述式質問票を用いて初経年齢、20歳時の月経周期、最終学歴、婚姻歴、分娩歴、授乳歴、現在のBMI、喫煙状態を調査し、ロジスティック回帰分析、Kruskal-Wallis test、尤度比検定を用いて、2群を比較検討した。【成績】2群の平均閉経年齢は、45歳未満閉経群は41.2±2.9、平均閉経年齢群は50.8±1.8だった。45歳未満閉経群は、平均閉経年齢群と比較して、BMI<18.5(オッズ比1.7, 95% CI: 1.07-2.49)、最終学歴が小学または中学校(オッズ比1.83, 95% CI: 1.32-2.49)、20歳時の月経不順(オッズ比12.2, 95% CI: 1.68-63.1)、未婚(オッズ比2.51, 95% CI: 1.16-4.8)の割合が高かったが、喫煙や分娩歴、初経年齢、授乳歴は2群間で有意な差はなかった。尤度比検定において、最終学歴が小学または中学校、未婚、20歳時の月経不順、痩せの順で、早発閉経に与える影響が大きかった。【結論】早発閉経に影響を与える因子は最終学歴が小学または中学校であること、未婚、20歳時の月経不順、痩せの4つの因子で、早発閉経の予測因子となり得る可能性がある。

P-61-8 外科的閉経を来した婦人科がん患者に対する HRT の再発・予後への影響

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【目的】婦人科がん治療における外科的閉経は更年期症状、骨粗鬆症や心血管障害の発症リスクの上昇など様々な臓器に影響を与えることから術後にホルモン補充療法 (HRT) を行うことが多い。HRT はエストロゲン欠落症状・疾患などに効果があることは明らかであるが、一方で HRT のがん再発への影響が懸念される。当科ではがん術後ヘルスケア外来を開設し、外科的閉経後のホルモン補充療法 (HRT) などの管理・説明を個別に行っている。今回我々は外科的閉経を来した婦人科悪性腫瘍患者を対象とした HRT が再発率および無増悪生存期間 (PFS) に影響するかについて後方視的に検討した。【方法】有経婦人科がん患者で外科的閉経を来した卵巣がん (OC) 130 人 子宮体癌 (EC) 141 人 子宮頸がん (CC) 151 人を対象とし、HRT 施行率および HRT 後の再発率および PFS への影響を後方視的に検討した【成績】患者の平均閉経年齢は CC 41.8 歳, EC 43.9 歳, OC 44.1 歳であり 45 歳以下における HRT 施行率は CC 51.5%, EC 42.0%, OC 42.9% だった。再発率は CC I-II 期で non-HRT : 16%, HRT : 5.9% EC I-II 期で non-HRT : 4.9%, HRT : 3.7%, OC I-II 期で non-HRT : 8.7%, HRT (+) : 3.7% でありそれぞれのがん腫において統計学的有意差はなかった。III-IV 期も同様に有意差はなかった。また PFS においてもいずれのがん腫、進行期で有意差はなかった。【結論】従来の報告と同様、HRT 施行によるがん再発への影響はなかった。また当科における外科的閉経後の HRT 施行率は 2016 年までは 40% であったが、術後ヘルスケア外来開設後の 2017 年以降では 71% の施行率と増加しており、がん患者のヘルスケアの個別管理の重要性を再認識した。

P-61-9 当院の若年婦人科がんサバイバー患者における骨密度の実際

順天堂大練馬病院

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【目的】婦人科癌に対する治療は年々進歩し、婦人科癌サバイバーが増加している。とくに近年は閉経前に発症する婦人科癌が増加し、それに伴う外科的閉経患者でのサバイバーの増加が著しい。外科的閉経では卵巣摘出により、術後持続的な低エストロゲン状態に陥る。そのため骨密度の早期低下が予想され、卵巣温存手術やホルモン補充療法 (HRT) の重要性が示唆されている。今回我々は当院で手術した閉経前発症の婦人科癌患者を対象に原疾患や手術法、ならびに特定の患者背景の骨密度への影響と HRT 治療の現状や効果を明らかにするため後方視的に検討した。【方法】2010 年から 10 年間、当院で婦人科悪性腫瘍手術を施行し、現在無病生存が得られている手術当時 45 歳以下の未閉経患者 105 例を対象とした。治療当時の年齢, BMI, 原疾患, 卵巣摘出の有無, 血中エストロゲン値, 術後 HRT の有無などに関して抽出し、術後に行った腰椎・大腿骨頸部の骨密度との相関を検討した。【成績】対象患者は 105 例で、手術当時の年齢は 20 から 45 歳。子宮頸癌 36 例, 子宮体癌 (肉腫) 36 例, 卵巣癌 33 例で、卵巣温存例は 29 例, HRT 施行例は 18 例あった。原疾患の種類, 卵巣摘出の有無あるいは HRT 施行の有無では骨密度に有意差を認めなかった。しかし、卵巣摘出群の大腿骨において術後継続的に骨量が低下する傾向にあった。一方、手術時 BMI が 25 以上の場合、それ以下の症例に比して腰椎骨量が高かった。【結論】婦人科がん患者において外科的閉経患者はもちろん、卵巣温存症例や早期 HRT 開始症例でも骨量低下を認めることがある。また、患者背景によって腰椎、大腿骨各骨量の低下傾向が違うため、複数部位の骨評価を行い、対策する必要がある。

P-62-1 遺伝性出血性疾患を有する日本人女性における月経の負担と PBAC の妥当性に関する研究

PBAC Working Group

長尾 梓, 徳川多津子, 松尾陽子, 森下英理子, 福武勝幸, 西田恭治

【目的】過多月経の 2 割近くに先天性止血異常症 (WGBDs) が隠れていたという報告もある通り、明らかな過多月経でも WGBDs の診断までに年余にわたり時間がかかる、あるいは診断に至らないことが問題である。原因の一つが客観的指標に乏しいことで、海外では 1990 年に Pictorial blood-loss assessment chart (PBAC) という生理用品の染まりを点数化する客観的で簡便なシステムが開発されているが、現代の日本人における PBAC の適応妥当性については未検討である。よって、今回日本人 WGBDs における PBAC のカットオフ値を検討し、月経の負担を評価した。【方法】多施設共同研究。20~45 歳のフォンヴィレブランド病 (VWD) と血友病保因者、健康人 (対照) を対象にアンケートと 2 回分の PBAC 記載を依頼。婦人科疾患あり・過多月経治療中などは除外した。生理用品の長さ、夜用・厚手の使用率、コストも解析した。【成績】VWD 8 名, 保因者 23 名, 対照 71 名の PBAC を分析した。PBAC 点数の中央値/平均値はそれぞれ 185/214, 136/137, 134/139 点で、VWD で有意に高く (P 値<0.05)、VWD の診断に繋がる最適なカットオフは 171 点だった (ROC 分析, 感度 66%, 特異度 72%)。重回帰分析では、夜用と厚手の使用率が高いほどスコアが低い傾向だった。VWD で長め・夜用の使用率が高く、月経あたりのコストが有意に高かった。【結論】原著では 100 点以上を過多月経としており、日本人で同様に使用しても過小評価とはならない。ただ同時に夜用や厚手がスコアを低くする可能性を警告すべきである。また PBAC は VWD の診断補助となり、VWD では月経の負担が大きかった。

P-62-2 生理用ナプキンを通じた月経・月経量研究～月経量の実態と主観の関係～

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【目的】AUB (abnormal uterine bleeding) に関する FIGO System1 によれば, 経血量は患者主観で分類することとなった。我々は日本人女性における月経量の実測値 (重量法) と主観回答の関係を検証した。【方法】月経がある 18~49 歳女性 211 名に, 2019 年 9 月~12 月末の 2~3 月経期間, 日記形式の月経時ナプキン重量測定結果, 主観について Web にて回答を得, 月経量を測定結果から算出した。全ての項目に不備のなかった 167 名・497 周期を集計・解析対象とした。月経量の実測値は, 周期毎の月経量を 5 パーセントイル, 第 1 四分位, 第 3 四分位, 95 パーセントイルで区切り 5 区分で集計を行った。主観回答は「異常に少ない/少ない/ふつう/多い/異常に多い」の 5 段階で月経毎に回答を得て実測値との関係を比較した。研究者所属大学倫理審査委員会の承認を得, 自由意思で参加の同意を得た。【成績】月経量実測値は平均値 77.6g, 中央値 56.7g, 最大値 1398.7g, 最小値 3.1g であった。実測 5 区分の平均月経量は, それぞれ 10.2g/26.6g/60.3g/121.1g/343.8g であったのに対し, 主観回答 5 段階の平均月経量は, 25.7g/56.6g/80.0g/124.7g/160.1g であった。実測 5 区分と主観回答 5 段階の各水準が対応すると仮定し各周期を比較すると, 実測と主観水準の異なる周期は全体で 54%, その内 10% は 2 水準以上異なっていた。また, 月経量が多い第 3 四分位以上の群で少なく見積もっており, 異なる率が高かった。【結論】月経量の実測値と主観回答には差がみられ, 特に実際に月経量の多いものの方が主観では少なく捉えている傾向が認められた。区分の設定, 主観回答表現など議論の余地はあるが, 主観のみによる月経量判断は難しく示唆された。

P-62-3 帝王切開術後の排尿—腹圧性尿失禁のリスク要因の探索

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【目的】疫学的に, 帝王切開 (以下, CS) で出産しても腹圧性尿失禁 (以下, SUI) 発症のリスクは増大する。分娩様式を問わず, 分娩後に蓄尿量が急速に 600mL を越えることがあれば膀胱の平滑筋と神経の機能を損ない, 腹圧による排尿を強化する。本研究は, CS 後の膀胱過伸展について調べるために行った。【方法】2017 年 3 月以後に自施設の助産業務で使用した「排尿メモ」の偶々保管されていたものを対象とした。その他の医療情報は電子カルテを参照した。排尿の質的指標として, 術後の自排尿開始から 1 日以内の最大単回排尿量 (以下, VVmx) を Mann-Whitney U 検定で比較した。【成績】対象となった「排尿メモ」は 61 例あり, 褥婦の年齢は 23.0-41.8 歳, 出産歴は 0-2 回, CS 既往は 0-2 回だった。予定, 緊急 CS はそれぞれ 22, 39 例で, 術後の硬膜外和痛 (以下, POEDA) は 49 例に行われ, うち 36 例では POEDA 使用中に自排尿を開始していた。VVmx が 1000mL 超, 800mL 超 1000mL 以内, 600mL 超 800mL 以内の褥婦はこの順に 7, 6, 23 例あり, 蓄尿量の数字はさらに大きかったと見られる。予定 CS 例のうち, 経産群は初産群よりも VVmx が有意に大きかった (中央値はこの順に 700/550mL, $p < 0.044$)。初産例のうち, 緊急 CS 群は予定 CS 群よりも VVmx が大きい傾向があった (中央値はこの順に 725/550mL, $p = 0.069$)。緊急 CS 例のうち, POEDA 非実施群と実施群の VVmx には差異が見出されなかった (中央値はこの順に 725/700mL)。【結論】CS の後に膀胱過伸展は頻繁に生じている。出産歴と今回の経産試行は, VVmx を増大させる要因である可能性がある。後ろ向き調査では POEDA 実施群と非実施群で経産試行による侵襲の差が大きく, POEDA の影響の比較は難しいと思われる。

P-62-4 経産プローブカバー脱着時の飛沫防止対策

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【目的】経産プローブカバー脱着時に飛沫が散乱し経産超音波プローブや超音波操作板に細菌やウイルスが付着していることが報告されている。これを防止するために経産超音波プローブカバー回収カバーを作成し基礎的検討を行った。【方法】回収カバーの素材は, 経産プローブがすべり易いポリエチレン製剤を使用した。試行錯誤の結果, カバーの形状はピストル型が確実にプローブカバーを収納できることが判明した。プローブカバーに触れる部分は狭く, 全体として操作者の手首まで覆う形状とした。①作成した回収カバーをプローブに覆い, その上からプローブカバーを装着した。回収カバーを外し, プローブカバーが収納できるか検討した (N=20)。②回収カバーとプローブカバー装着後にプローブカバーの表面に腔分泌の粘度に類似した手洗いトレーニング用蛍光ローション (ニチオン製) を全体に塗布した。その後白紙の上 30cm の位置で, プローブを下向きにして回収バックを牽引しプローブカバーを回収した。白紙に滴下した蛍光溶液を, LED ランプを用い飛沫の散乱程度を測定した (N=8)。コントロールとして回収カバー使用せず同様の処置を行った (N=8)。【成績】試行 20 回ともすべてのプローブカバーは回収カバーに回収された。回収カバー装着群では全例で飛沫の散乱は確認されなかったが, コントロール群では 8 例中 7 例に飛沫の散乱が確認された。【結論】ピストル型回収カバーは, プローブカバーの飛沫を散乱させずに回収できることが示された。また介助者なく, 医師自身でプローブカバーを回収できる利点もある。本回収カバーは医療者の感染リスクを軽減し, 内診台周辺の感染対策に有効であると考えられた。

P-62-5 当院産婦人科による乳腺外来の現状

徳島大

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【目的】本邦の女性において乳がんは最も罹患率の高いがんである。女性ヘルスケアの観点から乳がん検診の受診率向上への取り組みは産婦人科医にとって重要な課題である。当科では産婦人科医による乳がん検診を実施しており、より多くの受診機会を提供することで確実な検診受診を目指している。当院の産婦人科医による乳がん検診の現状を把握し、今後の課題を明らかにすることを目的として各種臨床指標を後方視的に検討した。【方法】2021年1月から9月までの6か月間に当科の乳腺外来で検診を実施した52例を対象とした。対象の年齢は23~88歳(中央値55歳)であった。当科では原則としてマンモグラフィを事前に撮影した後に超音波検査を実施している。検査担当医は、日本乳がん検診精度管理中央機構の超音波検査担当医師B以上の資格を有する者としている。【成績】検診受診理由は、ホルモン補充療法に関連したスクリーニングが31例、月経困難症に対するホルモン療法中が4例、その他が17例であった。期間中にカテゴリー4以上の症例はなく、カテゴリー3で精査のため乳腺外科へ紹介した症例は5例であった。いずれも悪性疾患は認めず、線維腺腫など良性疾患であったものが3例、異常のなかった症例が2例であった。結果として要精密検査率は9.6%であった。【結論】当院ではHRTに関連したスクリーニングが多くを占めた。要精査率はマンモグラフィによる乳がん検診の平均(6.3%)よりも高かったが、許容値(11%以下)は満たしていた。乳腺外科との積極的な連携により精密検査などの対応は可能であった。

P-62-6 「母乳育児成功のための10カ条」と「赤ちゃんにやさしい病院」の周知度、および、妊娠・分娩時の処置について

吉野産婦人科医院

吉野和男

【目的】1990年8月1日にWHOとユニセフは母乳育児の保護・促進・支援の必要性を「イノチェンティ宣言」し、「母乳育児成功のための10カ条」を発表した。今回、その10カ条の周知度を調べるために、全国の分娩取り扱い施設にアンケート調査をした。【方法】「母乳育児成功のための10カ条」、「赤ちゃんにやさしい病院」についての質問を総合病院(NICUあり)、一般病院、診療所に分け、妊娠・分娩時の処置についての5つの質問を「赤ちゃんにやさしい病院」であるかどうかで統計学できに処理した。【成績】「母乳育児成功のための10カ条」をよく知っているのは70.6%であり、総合病院が84.4%で有意に高く、「赤ちゃんにやさしい病院」をよく知っているのは65.6%であり、病院の種類で有意差は認めなかった。乳頭・乳房ケア、乳管開通操作、パースプラン、分娩時の硬膜外麻酔、分娩促進について、「赤ちゃんにやさしい病院」は乳頭・乳房ケア、乳管開通操作、パースプランを施行している率が有意に高かったが、分娩時の硬膜外麻酔、分娩促進は有意差を認めなかった。【結論】「母乳育児成功のための10カ条」の周知度は比較的高かったが、「赤ちゃんにやさしい病院」が施行している妊娠・分娩時の処置は「赤ちゃんにやさしい病院」でない施設が施行している処置と大きな差は認められなかった。

P-62-7 免疫正常者に発症した、サイトメガロウイルス感染が原因であった骨盤内炎症性疾患(PID)の1例

愛仁会高槻病院

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【緒言】サイトメガロウイルス(CMV)が、免疫正常者の女性生殖器に感染した報告は稀である。免疫正常者にPIDを発症したCMV感染症の1例を報告する。【症例】45歳。未妊。免疫異常の既往や免疫抑制薬の使用歴なし。クラミジアによるPIDが軽快した5日後に発熱と下腹部痛を認めた。子宮と付属器周囲に圧痛を認め、PIDの再発と考え抗菌薬を1週間投与したが、症状は改善しなかった。白血球は症状に比して増加せず(8400/ μ L)、リンパ球比率は45%と高値であった。加えて、薬剤性と思われる軽度の肝障害があったことから、ウイルス疾患も鑑別に挙げた。精査の結果、CMVの血中IgM、IgGに加えて、腔分泌物のCMVのPCR検査でも陽性が判明した。振り返ると、初めのPIDが軽快した直後に数日間の咽頭痛と軽度の脾腫を認めており、伝染性単核球症の症状が存在していた。以上より、下腹部痛はCMVの性器感染が原因と診断、抗菌薬の投与を中止し、自然経過のみで1か月後に症状は消失した。【考察】CMVはPIDの原因になりうるとされているが、免疫正常者ではCMV感染の多くは無症状であり、下腹部痛からCMVの性器感染と診断することは困難である。ときにCMVは伝染性単核球症を発症するが、その症状もEBウイルスによるものより軽度とされ分りづらい。本症例では、クラミジアによるPIDが先行していたことが診断を更に困難にした。抗菌薬が奏功しないPIDでは、CMVなどのウイルス疾患の可能性にも目を向けるべきである。

P-62-8 家族性地中海熱 (FMF) の月経期骨盤痛に対して漢方薬で軽快した1症例

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【目的】家族性地中海熱 (FMF) は主に常染色体性遺伝の形式とされ MEFV 遺伝子の変異の下, 周期的に繰り返す発熱, 漿膜炎症状による腹・胸膜痛, 関節痛を生じる自己炎症性疾患である。この漿膜炎は月経期に増悪し易く, 難治性の月経困難症と診断され婦人科へ紹介されることが多いが治療にしばしば難渋する。今回 FMF 患者の月経期骨盤痛に対して漢方薬が奏効した症例を経験したので報告する。【症例】既に前医で遺伝学的に FMF と診断された 40 代前半の女性。主訴は月経期に付随する腹痛, 骨盤痛, 発熱であった。当院膠原病科でコルヒチン+カナキスマブ (ヒト型抗ヒト IL-1 β モノクローナル抗体) の標準治療を受けていたが, 月経期の骨盤痛悪化 (仙痛) に対して当科に対応依頼。受診時の痛みの NRS (Numeric Rating Scale) は毎回 9-10 であった。その都度応急的にアセトアミノフェンの内服・静注を使用するが, 効果は良い時でも NRS : 6-7 程度で持続は 3 時間程度であった。某日既述の標準+応急治療にもかかわらず仙痛が増悪したため, 証に基づき安中散を用いたところ痛みが軽快した。その後の周期でも月経期 NRS : 3-4 となり生活の質が向上した。なお標準治療により CRP 等の炎症反応はすべて negative であった。【考察】FMF の標準治療の中心はコルヒチンで 92% が奏効すると報告されている。本症例にも標準治療がなされており炎症反応は negative であったが, 症状増悪したバリエーションと思われた。本症例の奏効理由として安中散に含まれる延胡索の鎮静・鎮痛・鎮痙作用が非炎症性の仙痛緩和に寄与した可能性を考える。【結語】FMF の月経期骨盤痛に安中散が選択肢のひとつとなる可能性が示唆された。

P-62-9 当センターにおける女性尿道憩室の臨床的検討

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【目的】一般に尿道憩室 (UD) は成人女性の 0.02~6%, 傍尿道腫瘍性病変の 84% を占める。しかし疾患認知度が低いことに見逃され, 診断に時間を要することが多いとされる。我々の経験した UD 症例を検討した。【方法】対象は 2019 年 4 月から 2021 年 9 月までに UD と診断された 22 症例で, 患者背景, 初診時主訴, 内診所見, 検査, 診断までに要した時間, 治療方法について診療録により後ろ向きに調査した。【成績】年齢は中央値 41.5 歳 (18~80 歳)。主訴は繰り返す尿路感染症, 性交時痛, 様々な下部尿路症状, 腫瘍の圧痛, 下腹部痛, 下垂感, 膿の付着, 検診での指摘 (無症状) と多彩であった。多くの症例の内診所見で, 尿道部前腔壁に膨隆を認め, これを圧排すると外尿道口から膿あるいは尿の排出が確認できた。検査超音波・MRI での憩室の確認が有用であった。診断までに要した期間は平均 34.9 か月 (2 週間~15 年)。治療は 18 例が手術療法, 4 例は保存療法が選択されていた。【結論】UD の症状は多彩で, 古典的三徴 (dysuria, dyspareunia, dribbling) をすべて呈するものは認めず, 症状のみから UD の可能性を想定するのは難しいと思われた。UD の診断に内診時所見や検尿は必須だが, 超音波・MRI が最も有用性が高かった。また診断までに長時間を要した症例が多かったが, これは検者が UD を念頭に置き尿道腫瘍の触診と MRI あるいは超音波による画像診断を行うことで改善されると考えられる。UD の根治には手術療法が必要なことが多く, 早期診断と治療のために, 下部尿路症状や陰周囲の症状を有する患者では常に UD を念頭に置いて診療にあたるべきであろう。

P-63-1 当院の患者動態推移からみる新型コロナウイルス感染症パンデミックによる生殖医療への影響

加藤レディスクリニック

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【目的】新型コロナウイルス感染症 (COVID-19) のパンデミックは生殖医療にも大きな影響をもたらした。第 1 波時, 日本では 2021 年 4 月 1 日付で日本生殖医学会から不妊治療の延期を支持する声明が発出され, 時間的制約のある治療を担う生殖医療現場では様々な緊急対応を要した。本研究においては COVID-19 パンデミック渦中における患者動態の推移を調べ, 生殖医療への影響を検討した。【方法】2019 年 1 月から 2021 年 9 月において当院で行った採卵, 移植, 妊娠周期数を月毎に調査し, 関連学会のパンデミック中の生殖医療に関する声明発出時期もふまえ, パンデミック前後における治療周期数の変化を比較検討した。【成績】2020 年 4 月における当院の採卵周期数は, 前年の 6 割 (917/1,448), 移植周期数は 4 割 (377/1,122) まで低下した。一方で翌月には, 生殖医療の段階的な再開を認め, パンデミック中も生殖医療を継続することが重要と認識する声明が世界の関係学会から出され, 採卵・移植周期数のいずれにおいても急回復した。2020 年 7 月には前年比 9 割まで回復し, 以降は 2021 年 10 月現在, 目立った治療の差し控え傾向は見られなかった。なお, 2020 年 4 月から 2021 年 3 月の妊娠周期数は同前年比で 93.6% (4,201/4,556) であった。【結論】パンデミック初期には大幅に治療周期数が低下したが, その後速やかに生殖医療継続の重要性を強調する声明が発出され, 治療差し控えの傾向は短期的であったと考えられる。少子化が深刻化する中, パンデミックにおいても出生率を極力低下させず, また, 適齢期の女性が時期を逸さず安全に妊娠が目指せる環境を整えることが重要だと考えられる。

P-63-2 新型コロナウイルス感染症 (COVID-19) 流行による生殖医療の実態と不妊患者の行動・意識への影響

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【目的】COVID-19 流行により 2020 年 4 月日本生殖医学会から不妊治療の中止ないし延期の声明が発出され、不妊治療は不要不急で控えるべきかという議論が生じ、妊娠や妊活に対する不安が増大した。その後、COVID-19 長期化により、働き方など社会構造や行動変容、価値観の変化が起こる中、不妊治療への影響と生殖行動の実態を検討した。【方法】東京・福岡・京都の不妊治療 3 施設通院中の患者 768 名を対象に、書面説明同意の上、無記名式アンケート調査を実施した。質問は、年齢や不妊期間等の基本的項目、中断や継続等の治療への影響、通院や育児希望等の影響を含み、回答は選択式・自由記載で得た。また 3 施設の COVID-19 流行前 (2019 年) と流行・蔓延期 (2020 年～2021 年 8 月) の月別不妊治療周期数を比較検討した。【成績】通院差し控えを考えた人が第一波 2020 年 4 月は 19.7% に上ったが、同 11 月には 0.9% に減少した。治療継続理由は年齢が 79% を占め、中断理由は自分もしくは児への感染不安が多かった。治療周期数では、採卵数は第一波で特に京都と福岡で減少したがその後回復し、年間では、2020 年は前年よりも増加した (2019 年 1003 件, 2020 年 1176 件, $p=0.03$)。胚移植数は、第一波時に全国で減少し (2019 年 292 件/2 か月, 2020 年 198 件/2 か月)、その後回復傾向にあったが、第五波 2021 年 7-8 月で再び減少した (2019 年 318 件, 2020 年 368 件, 2021 年 255 件, $p=0.011$)。【結論】第一波で生じた不妊治療の差し控えは改善し、治療周期数も回復傾向にある。しかし妊娠に直結する移植周期は第五波で再び減少し、COVID-19 長期化の生殖医療への影響が危惧される。長期的視野に立った生殖医療の継続支援が必要である。

P-63-3 新型コロナウイルス感染症緊急事態宣言下における婦人科受診控えの現状～ホルモン補充療法治療と骨粗鬆症管理

獨協医大

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【目的】コロナウイルス感染症による緊急事態宣言下においては外出自粛を余儀なくされ、受診控え、身体活動の制限や自主的な服薬中断さらにフレイルの進行などが懸念された。その中で、大学病院婦人科外来のホルモン補充療法 (HRT) 患者と骨粗鬆症管理患者の受診実態を調査した。【方法】2019 年まで当科の中高年外来に継続的に通院中の患者で、2020 年 4 月以降未受診の HRT 施行者と骨粗鬆症管理者を対象に、年齢、治療内容、治療期間、重症度、通院の困難さ、合併症、受診の連絡の有無などについて後方視的に調査した。【成績】HRT 施行者群は 114 例中 2 例 (0.88%) が未受診となり、2 例とも 58 歳、E2 貼付剤単剤および E2 貼付剤+DYD の連続療法中で通院 30 分以上を要する方たちであった。骨粗鬆症管理者群では 491 例中未受診は 9 例 (1.83%) であった。9 例の平均年齢は 68.4 ± 12.4 (48-89) 歳。受診期間は平均 14.9 ± 8.1 (3-27) 年であり HRT 既往が 6 例あった。9 例中 8 例は骨量フォロー中であったが、1 例はデノスマブ治療中であった。9 例とも連絡なく、自宅と病院の通院 30 分以内が 4 例、30 分以上遠距離が 5 例であった。【結論】2020 年 4 月以降未受診は HRT 中 2 例で骨粗鬆症管理は 9 例であった。受診控えが懸念されたが約 98% が受診を継続していた。骨粗鬆症治療に関しては薬剤の種類により中止することで新規骨折を生じやすくなる。骨粗鬆症治療は健康寿命延伸につながる必要不可欠な治療であることを患者と家族に周知し治療継続することが重要である。

P-63-4 不妊専門クリニックにおける COVID-19 ワクチン接種の試み～不妊治療患者へのアンケート～

園田桃代 ART クリニック

園田桃代, 小柳良子

【目的】当院では、不妊治療目的にて当院通院中の女性、その配偶者にコロナワクチン接種を行ってきた。今回、接種 2 回目来院時にアンケートを行い集計。【方法】2021 年 7 月下旬から 10 月 6 日の期間に接種した 167 人。【成績】平均年齢 35.9 ± 4.0 歳。当院通院治療状況は、検査中: 5 例 (3.2%)・タイミング療法: 14 例 (9.0%)・AIH: 15 人 (9.7%)・ART: 95 例 (61.3%)・治療休月中: 26 例 (16.8%)。接種時期に関して、タイミング療法中では排卵前: 6/14 (42.9%)・排卵後: 3/14 (21.4%)・妊娠中: 5/14 (35.7%)。AIH では排卵前: 9/15 (60.0%)・AIH 施行後: 5/15 (33.3%)・妊娠中: 1/15 (6.7%)。ART では採卵前: 11/95 (11.6%)・採卵後: 8/95 (8.4%)・胚移植前: 34/95 (35.8%)・胚移植後: 7/95 (7.4%)・準備周期中: 21/95 (22.1%)・妊娠中: 14/95 (14.7%)。接種に対する不安は、なし 6 例 (3.6%)・あまりなし 38 例 (23.0%)・少しあり 86 例 (52.1%)・あり 35 例 (21.2%)。不安のあった症例においてどのような情報で安心を得られたかは、当院ワクチンセミナー参加: 7 例 (5.8%)・当院ブログ: 58 例 (47.9%)・当院医師や看護師に相談: 44 例 (36.4%)。接種時期を迷ったのは 73 例 (44.8%)、迷わなかったのは 90 例 (55.2%)。1 回目接種後の副反応は、あり 63.6%、腕の痛み 49.4%、倦怠感 10.5%、発熱 8.0%、頭痛 6.8%、筋肉痛 1.2%。【結論】不妊治療中の女性は接種を決断したものの 7 割で不安を感じているが、治療中どの時期においても接種をしており、不安軽減には実際に不妊治療を行っている、かかりつけ医からの情報提供や相談等による役割が大きいことが分かった。

P-63-5 不妊専門クリニックにおける COVID-19 ワクチン接種の試み～妊婦へのアンケート～

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小柳良子, 園田桃代

【目的】当院にて不妊治療中および治療後の妊婦に接種を行っていたが、保健所との協議により8月末より妊婦、配偶者に専用枠を設け接種を行ってきた。今回、接種2回来院時にアンケートを行い集計。【方法】2021年8月28日から10月6日の期間に接種した豊中市在住、里帰り分娩婦省中の妊婦139人。予約方法は本人が自治体妊婦専用窓口を介し当院接種枠を予約。【成績】平均年齢31.7歳。平均妊娠週数26.4週(12週未満3人, 12-21週37人, 23-36週90人, 37週以上6人)。接種に対する不安は、なし1例(0.7%)・あまりなし11例(7.9%)・少しあり82例(59.0%)・あり45例(32.4%)。不安に感じることは、児への影響78例(60.0%)・副反応64例(49.2%)。どのような情報で安心を得られたかは、かかりつけ医と相談:89例(70.1%)。接種時期を迷ったのは66例(48.2%)。接種を決断した理由は、もともと時期を問わず早く接種したかった16例(11.5%)・接種時期が妊娠中いつでも可能になったから44例(31.7%)・感染妊婦の報道104例(74.8%)。1回目接種後の副反応は、あり66.9%、腕の痛み52.5%、倦怠感8.6%、発熱8.6%、筋肉痛5.0%。接種予約が困難だったとの回答は39例で、その理由は、かかりつけ医が接種をしていない18例・妊娠中ということで予約不可10例(ワクチン接種病院5例・大規模接種会場5例)。【結論】妊婦は接種を決断したものの9割で不安を感じており、児への影響に関する不安が最も多かった。接種を決断した理由は感染妊婦の報道が最も多かったが、学会や公的機関からの接種時期に関する声明や見解も大きく影響しており、また不安軽減にはかかりつけ医の役割が大きいことが分かった。

P-63-6 新型コロナウイルス感染症対策下における働く女性の健康の課題(市民への意識調査から)

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【目的】新型コロナウイルス感染症の拡大防止対策下の地域住民の意識を調査し、コロナ禍で働く女性の健康やQOLに与えた影響を明らかにし、ポストコロナに向けた対策を考察する。【方法】令和2年10月下旬に中核市在住の18~75歳の男女1022人を対象に郵送法で、コロナ禍の日常生活と健康への影響に関するアンケート調査を実施した(回収率60%)。本研究は本学の倫理委員会の承認を得て実施した。【成績】1.「働く女性の出産と育児の支援策」への評価は100点満点で平均点が男性44.9点、女性48.0点、60点以上との評価は男女とも約2割。2.「家庭での子育てがしやすい」との認識は、男性25.0%、女性32.5%で有意差なし。3.「家族の世話で疲れた」は、男性4.5%、女性23.1%で女性が有意に高率。4.「心身の健康が保たれる」に対して、肯定的(「そう思う」と「どちらかというそう思う」の合計)は全体で、男性47.6%、女性46.9%で有意差なし。年代別では女性の就業率のM字カーブの底の30代前後で他世代の1/2に低下。5.「コロナ禍で医療機関への受診を控えた」は、男性30.4%、女性41.7%で、女性の方が高率、年代別では30代で高率。6.女性の「受療行動の抑制」は、世帯全体の取入に減少があると高率に認められた。(5%水準で有意)【結論】新型コロナウイルス感染症対策下で働く女性の出産と育児へさらなる支援策が必要との認識が、女性のみならず男性にも共有されている一方、家庭における負担感や女性は高い。心身の健康保持の認識率は、30代で低下し、医療機関への受診を控える率は女性の方が男性より高く、30代で高率となり、経済的な背景も推測される。その後の健康状態の検証と適切な受診方策の検討が重要である。

P-64-1 扁平上皮基底第1層のKi-67発現はLSIL進展予測因子として有用である

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【目的】子宮頸部の軽度扁平上皮内病変 low-grade squamous intraepithelial lesion (LSIL) は HPV 感染による感染性異型を指すが、高度扁平上皮内病変 high-grade squamous intraepithelial lesion (HSIL) 進展前の腫瘍性異型も同様の像を呈するため、簡便な鑑別方法が望まれている。今回、LSIL 症例を対象として、HSIL への進展と扁平上皮基底第1層での Ki-67 発現の関係を検討した。【方法】2015年に子宮頸部組織診で LSIL と診断された症例を対象として、免疫組織化学的手法を用いて LSIL 診断部位の Ki-67 染色を行い、基底第1層の Ki-67 発現を検討した。Ki-67 の発現割合で2群に分け、5年後の病変進行との関係を、ハイリスク HPV 感染状態とあわせて後方視的に評価した。【成績】LSIL 247 例のうち、5年後までの転機を確認できた136例が評価の対象となった。LSIL 136 例のうちハイリスク HPV 感染陽性は 67.6% (92/136) で、そのうち基底第1層の Ki-67 発現亢進群 29.3% (27/92) は発現亢進を認めなかった群 70.7% (65/92) と比較し、5年以内に HSIL 以上の病変へ進行し治療介入が必要となる割合が有意に高い (77.7% vs 23.0%) ことがわかった。一方、ハイリスク HPV 陰性は 32.4% (44/136) で、基底第1層の Ki-67 発現状態に関わらず、HSIL 以上の病変へ進行した症例は 4.5% (2/44) であった。【結論】子宮頸部 LSIL において、ハイリスク HPV 感染陽性での扁平上皮基底第1層の Ki-67 発現亢進は、HSIL 進行の予測因子となる可能性を示した。

P-64-2 子宮頸部異形成治療後の細胞診、HPV 検査についての検討

浜の町病院

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【目的】近年、若年女性の子宮頸部異形成 (CIN) が増加傾向にあり、治療方針の決定目的や治療後のフォローアップ目的の検査として HPV 検査が施行されている。CIN 治療後の HPV 検査についての報告は少ないため、治療後の細胞診と併用して HPV 検査を行った症例について検討を行うこととした。【方法】当院では CIN 2, 3 に対する治療として LEEP による子宮頸部円錐切除術もしくはレーザー蒸散術を施行しており、治療後 4~6 か月の時点で治療後検査を行っている。2020年4月から2021年8月までの期間に子宮頸部円錐切除術 (LEEP 法)、レーザー蒸散術を施行した CIN 2 または CIN 3 の症例のうち、治療後に細胞診と併せて HPV 検査を施行した 53 症例 (子宮頸部円錐切除術 36 症例、レーザー蒸散術 17 症例) について後方視的に検討を行った。【成績】子宮頸部円錐切除術後に細胞診異常を認めた患者は 1 人 (2.7%)、ハイリスク HPV 陽性患者は 7 人 (19%) であった。レーザー蒸散術後に細胞診異常を認めた患者は 1 人 (5.8%)、ハイリスク HPV 陽性患者は 2 人 (11%) であった。【結論】子宮頸部円錐切除術 (LEEP 法) についてもレーザー蒸散術についても、治療後のハイリスク HPV 陽性率は低かった。治療後 HPV 検査の長期的経過観察における有用性については今後異形成の再発率、再発時期に関するデータを集積して検討を加えてゆきたい。

P-64-3 子宮頸部上皮内腫瘍 (CIN) に対するタラポルフィンナトリウムを用いた光線力学療法 (Photodynamic therapy using Talaporfin sodium: TS-PDT) の臨床試験と今後の展望

浜松医大

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【目的】子宮頸癌はその前病変にあたる子宮頸部上皮内癌 (CIN3) を含めると 20 代及び 30 代の若年女性において罹患数は最も多い。CIN3 の治療法としては子宮頸部円錐切除術や PDT、子宮頸部蒸散術が挙げられる。PDT と円錐切除術の治療効果は同等であるにもかかわらず、使用される第1世代のポルフィマーナトリウムの副作用である光線過敏症のため普及しなかった。一方、肺癌や再発食道癌などに対し応用される TS-PDT で用いられるタラポルフィンナトリウム (TS) は第2世代の薬剤で代謝が早く光制限期間も短い特性を持つ。CIN に対する TS-PDT の治療効果及び有害事象について、以前行った臨床試験の結果を提示するとともに、保険適用を目指して医師主導治験を開始したので報告する。【方法】CIN を認め、頸部細胞診及び頸部組織診による病理所見が一致した症例を対象とした。TS 投与量は 40mg/m² とし、投与後 4 時間後にレーザー照射を行った。治療効果についての評価は治療後 3 か月と 6 か月において頸部細胞診及び組織診、コルポスコピーを用いて判定した。【成績】CIN2 及び CIN3 と診断された 9 例に対し TS-PDT を施行した。追跡できた 8 例において治療効果判定で CR であった。治療後 36-60 か月の追跡では再発は認めなかった。有害事象として下腹部痛を 6 例認めたが G2 以下であり重篤ではなかった。光線過敏症は TS 投与 14 日以降で 1 例のみに認められた。【結論】CIN に対する TS-PDT の有効性及び安全性が示唆された。同時期に他の施設で行われた臨床試験結果と併せ 2019 年より TS-PDT の有効性及び安全性を検討するため 4 施設において医師主導治験を開始している。

P-64-4 当院における HSIL/CIN2-3 に対する子宮頸部レーザー蒸散術の成績

筑波大附属病院

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【目的】近年の若年 CIN3 の増加に伴い, HSIL/CIN2-3 に対し様々な治療法が選択される。その中でレーザー蒸散術は比較的低侵襲で, 一定の有用性が認められる。今回当院における HSIL/CIN2-3 に対するレーザー蒸散術の成績について検討した。【方法】対象は 2014 年から 2019 年に組織診にて HSIL/CIN2-3 と診断され, 当院でレーザー蒸散術を行った 152 名である。手術時間, 周術期合併症, 病変の消失率, 再発率, 妊娠中の有害事象について後方視的に検討した。病変消失の判定は術後 6 か月までに細胞診で ASC-US 以下に改善した症例とした。再発の判定は一度 NILM となり, 再度 LSIL 以上になった症例とした。また 2019 年より婦人科専攻医の指導のもと後期研修医を中心に手術を行っている。婦人科専攻医と後期研修医での臨床経過, 予後を Fisher's exact test もしくは t 検定で比較した。【成績】症例は CIN2 53 名, CIN3 99 名, 婦人科専攻医 128 例, 後期研修医が 24 例であった。年齢中央値 32 (19-47) 歳, 婦人科専攻医群と後期研修医群で観察期間 23 (0-76), 20.5 (0-41) か月 ($p=0.34$), 手術時間中央値 18, 16.5 分 ($p=0.27$), 周術期合併症発生率 13.1, 16.7% ($p=0.53$), 病変消失率 91.4, 95.8% ($p=1.0$), 再発率 11.0% ($p=0.13$) であった。2 群間で手術時間, 合併症発生率, 病変消失率, 再発率について有意差を認めなかった。周術期合併症は後出血 18 名, 消毒による皮膚障害 1 名, 膣炎 1 名で重篤なものはなく, 術後妊娠例は 29 名 (19%) であり, 8 名に有害事象を認め, 内訳は 35 週早産 2 名, 35 週前期破水 1 名等で重篤なものはなかった。【結論】手術時間, 合併症, 病変消失率, 再発率など有意差を認めず, 後期研修医でも比較的安全に施行し得た。ただし, 婦人科専攻医の適切な指導の必要性を認識しておくべきである。

P-64-5 子宮頸部上皮内病変に対して蒸散術を行った症例における再発予後因子の検討

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【目的】子宮頸部上皮内病変 (CIN) に対し蒸散術が行われているが, 本術式の問題点として, 再発率が高いこと, 手術時に組織を採取しないため浸潤癌の可能性を完全には否定できないこと, が挙げられる。今回, 蒸散術の再発リスク因子および術後の浸潤癌の発症率を検討した。【方法】2015 年から 2019 年に CIN2 または CIN3 と診断され, 初回治療として CO2 レーザーを用いて蒸散術を行った 1469 例を対象とした。術後に組織診断で CIN2 以上の病変が検出された場合を再発, と定義した。年齢, 術前診断, 感染 HPV 型について, 再発と関連するか検討するとともに, 浸潤癌の発症率を調査した。【成績】術前診断の内訳は CIN2 : 877 例, CIN3 : 592 例, 観察期間の中央値は 23 (2-79) か月, 年齢は 36 (20-75) 歳であった。1469 例中 282 例 (19.2%) が再発し, 再発までの期間は中央値で 12 (2-75) か月, 病変別再発率は CIN2 が 17.2% (151/877), CIN3 が 22.1% (131/592) で, CIN3 の再発率が高かった ($P=0.019$)。術前に HPV タイピングが行われた CIN2 の 317 例と CIN3 の 201 例で検討したところ, CIN2 において HPV16 型陽性 118 例の再発率は 22.0% で, その他 209 例での 13.9% に比べて高かった ($P=0.023$) が, CIN3 では HPV 型は有意な予後因子ではなかった。年齢別では 50 歳未満と 50 歳以上の再発率はそれぞれ 19.6%, 18.8% で有意差はなかった。これまでに 18 例 (1.2%) が浸潤癌を発症し, 進行期は IA1 : 8 例, IB1 : 10 例であったが, 治療後の再発および死亡例は認めていない。【結論】CIN2/3 に対する蒸散術の再発高リスク因子は, CIN2 での HPV16 型感染および CIN3 であった。蒸散術後に浸潤癌が検出される症例も存在し, 術後の慎重な管理が必要である。

P-64-6 我が国における HPV ワクチンの直接予防効果と集団免疫効果 : MINT スタディ 10 年の軌跡

MINT スタディ

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【目的】HPV ワクチンの有効性を評価すること【方法】2012-2021 年に全国 24 施設で新規に子宮頸癌/CIN/AIS と診断された 16-39 歳の日本人女性をワクチン接種歴と共に登録し, ワクチンが予防できる HPV16/18 型の陽性率 (H16/18 率) を解析した ($n=6742$)。【成績】CIN2-3/AIS 患者の H16/18 率は, 接種群 ($n=169$) では非接種群 ($n=4295$) と比較して有意に低下していたが (28% vs. 47%, $P<0.0001$), 接種年齢によって大きな差が見られ [15 歳までの接種 ($n=36$) で 0%, 16-18 歳 ($n=23$) で 13%, 19-22 歳 ($n=14$) で 36%, 23 歳以上 ($n=91$) で 40%, $P \text{ trend}<0.0001$], 18 歳までとそれ以降の接種で有意差が見られた (5% vs. 39%, $P<0.0001$)。この中で初交年齢データが得られた症例において H16/18 率は初交前接種 ($n=16$) で 0%, 初交後 3 年以内の接種 ($n=8$) で 13%, 3 年以降の接種 ($n=15$) では 40% だった ($P \text{ trend}=0.003$)。なお, CIN2-3/AIS/頸癌患者の性交経験率は 14 歳までは 10% だが, それ以降は急激に上昇した (16 歳で 48%, 18 歳で 78%)。非接種者でも, 20-24 歳で診断された CIN1 の H16/18 率は 2012-2020 年の間に 36% から 10% に有意に低下した ($P \text{ trend}=0.03$)。同年齢の CIN2-3/AIS でも同様の傾向が見られた (63%→36%, $P \text{ trend}=0.07$)。この結果は, ワクチン接種率が高い 1994-1999 年生まれの若い世代では非接種者であっても他の世代の非接種者と比較して H16/18 率が有意に低いこと ($P=0.04$) による集団免疫効果と考えられた。【結論】ワクチン効果は接種年齢によって大きく異なり, 14 歳までの定期接種, 18 歳までのキャッチアップ接種が望ましい。非接種患者における H16/18 率低下は集団免疫効果を示唆する。我が国では初めてのエビデンスである。

P-64-7 妊孕性温存を必要としない CIN3 症例に対する子宮頸部円錐切除術後の頸管狭窄発症リスクに関する検討

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【目的】CIN3の標準療法である円錐切除術は、低侵襲であり妊孕性が温存されるため、妊娠を希望する若年症例に対しては最適な治療である。本術式の問題点として術後頸管狭窄があるが、発症例の多くは閉経後症例のため無症状で経過することが多く、臨床で問題となることは少ない。しかし、症状のない潜在的頸管狭窄例であっても、頸管側残存病変の浸潤癌への進展の覚知や子宮体癌の診断を困難にする場合があり注意が必要である。そのため、妊孕性温存を必要としない CIN3 症例では子宮全摘術が治療オプションとなる。ただし子宮全摘術は円錐切除術と比較し侵襲が大きくなるため、慎重に適応症例を選択する必要がある。今回、CIN3 症例に対する子宮全摘術の適応に関して、術後頸管狭窄の発症リスクという視点から後方視的検討を行った。【方法】2010年1月～2020年12月までの期間に当院で円錐切除術を施行した CIN3 症例のうち、手術時年齢が40歳以上であり円錐切除術を最終治療とした229例に対し、術後の頸管狭窄症の発症状況、患者の背景因子について検討した。【成績】全226症例中35例(15.2%)に(潜在的を含む)頸管狭窄を認めた。狭窄群は非狭窄群と比較し有意に手術時年齢が高く($p < 0.0001$)、既閉経例が多かった($p < 0.0001$)。多変量解析では「手術時年齢 ≥ 50 歳」と「手術時既閉経」が独立した術後頸管狭窄のリスク因子となった。【結論】妊孕性温存を必要としない CIN3 症例に対し子宮全摘術を考慮する場合、術後頸管狭窄の発症リスクという視点からは「既閉経例、あるいは50歳以上の未閉経例」を適応とすることが妥当と考えられた。

P-64-8 CIN に対するフェノール療法の臨床的検討

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【目的】子宮頸部上皮内腫瘍(CIN)の治療として円錐切除術が主流であるが、合併症として早産率の増加、頸管狭窄による有症状が課題である。フェノールは蛋白質を凝固させ強い腐食作用を示し、CINに対する非外科的治療として有用性が期待され、症例を集積してきた。その治療効果と予後因子について解析した。【方法】対象はCIN1-3の181例(CIN1:56例, CIN2:54例, CIN3:71例)であり、フェノール療法の治療回数、非治療率、再発率、予後因子を分析した。4週毎にフェノールを病変部に塗布し、コルポ診で効果を観察した。細胞診2回連続陰性とコルポ診正常で治療とした。再発は組織診でCIN1以上とした。フェノール塗布にて最終的に治癒しなかった例を非治療とした。予後因子としてはCINのgrade別に子宮腔部病変占拠率(1/3未満, 1/3-2/3未満, 2/3以上)、HPV陽性の有無、HPV型と治療回数を解析した。【成績】フェノール療法単独の治療率は87.3%(158/181)であり、12.7%(23/181)が非治療であった。再発率は5.1%(8/158)であった。非治療23例の内訳はCIN1:6例(26.1%)、CIN2:4例(17.4%)、CIN3:13例(56.5%)であった。CIN1, 2, 3の平均治療回数は5.6, 8.4, 11.8回であり、CIN1とCIN2, 3において有意差を認めた。CIN1-3において病変占拠率の高いほど有意に治療回数が増加した。HPVの有無およびHPV型と予後との関連性は認められなかった。【結論】フェノール療法の治療率は87.3%であり、非外科的治療として有用である。予後因子として、CINのgradeおよび病変占拠率が高いほど治療回数が有意に多くなった。CIN3における治療回数が増えること、さらに非治療率が高いことが課題である。

P-64-9 子宮頸部軽度異形成に対する凍結療法の効果

岐阜市民病院

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【目的】子宮頸部中等度・高度異形成に対する治療として本邦では現在円錐切除術またはレーザー照射が適応となっているが、海外では加えて子宮頸部への凍結療法も選択肢となっている。子宮頸部軽度異形成(CIN1)は自然治癒が期待できる病態であるため治療の推奨はされていないが、過去の報告ではLSILやASC-USに対して凍結療法を行い、その後良好な経過を報告されているものもある。今回はCIN1における凍結療法の効果を評価することを目的とした。【方法】当院では2019年以降、CIN1と診断された患者に、経過観察に加え液体窒素による凍結療法の選択肢を提示している。我々は今回、当院にて2019年9月から2021年2月まで希望に応じて外来にて子宮頸部への凍結療法を行った患者に関して、その後のフォローアップを後方視的に検討した。【成績】CIN1に対して凍結療法を行った患者は期間内に61人、うち6か月後の時点で未受診・転居のためフォローロストとなったのが4人、6か月までに細胞診にてNILMとなったのが34人(55%)であった。一方でその後の細胞診で進行が疑われ円錐切除を行ったのが2人、進行癌が判明した症例は認めなかった。なお施行した患者の多くが噴霧から数日間の水溶性帯下や性器出血を訴えたが、その他に重篤な合併症は認めなかった。【結論】今回の検討では、凍結療法後6か月の時点で改善を認めた症例もあり、特に重篤な合併症は認めなかったため、持続するCIN1の患者では選択肢として提案できるのではないかと考えられた。今後前方視的に検討を加え、その効果についてさらに検討したいと考えている。

P-64-10 子宮頸部円錐切除術にて偶発的に発見された子宮頸部海綿状血管腫の一例

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【緒言】子宮頸部に発生する海綿状血管腫は稀であるが、時に大量出血をきたし子宮全摘が必要となることもある。今回、子宮頸部海綿状血管腫の一例を経験したため文献学的考察を加え報告する。【症例】42歳、0経妊、挙児希望のため近医より不妊治療目的に当院へ紹介となった。初診時の陰鏡診では子宮頸部前唇が暗赤色にうっ血していた。また経膈超音波検査にて5cm大の子宮筋腫を認めたため、造影MRI検査をしたところ子宮頸部前唇にT1低信号、T2高信号、拡散強調画像高信号、ガドリニウムで造影されない25×15×23mmの腫瘤を認めた。子宮頸部細胞診はNILMであったが、MRI検査にて子宮頸部に腫瘤を認めたため子宮頸部組織診を行ったところ、CIN3の診断に至り、腫瘤の診断目的も兼ねて子宮頸部円錐切除術を施行した。術時の出血は少量であった。切除検体標本では、子宮頸部前唇に海綿状血管が集簇性に観察され、子宮頸部海綿状血管腫の診断に至った。また、異形成病変については上皮剝離にて評価困難であった。術後1か月後のMRIでは子宮頸部の腫瘤は消失していた。【考察】子宮頸部海綿状血管腫の報告例は少なく、報告されている症例の多くは妊娠中または分娩後の出血にて生検または子宮全摘を行い判明している。非妊娠例の報告が少ないのは、非妊娠時には多くが無症状で、妊娠により子宮血流が増加することで出血症状が出やすくなるのではと考えられる。今症例では挙児希望例であり、偶発的ではあるが妊娠前に血管腫に対する治療を行うことができ、妊娠時の出血リスクを避けることができた。

P-65-1 広汎子宮頸部摘出術の卵巣予備能に対する影響

名古屋大附属病院

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【目的】我々の先行研究において、広汎子宮頸部摘出術(radical trachelectomy: RT)後の生殖補助医療では卵巣刺激への反応性が低下することが明らかになった。その原因としてRTにより子宮体部から卵巣への血流が低下して卵巣予備能が低下するためではないかと考え、この仮説を実証するために当院の倫理委員会の承認のもと今回の前向き観察研究を行った。【方法】当院で2019年9月から2021年7月の間にRTを施行した子宮頸癌の患者9例において、血清抗ミュラー管ホルモン(AMH)値を①術前、②術後1か月、③術後6か月の計3回測定して解析した。【成績】患者は27歳から39歳(中央値33.8歳)で、組織型は6例が扁平上皮癌、3例が腺癌であった。術後補助化学療法を施行したのは2例であった。血清AMH値の平均値は術前は2.25ng/mL、術後1か月は1.78ng/mL、術後6か月は2.12ng/mLであった。血清AMH値の変化を解析すると、術後1か月で10%以上の低下が5例(55%)、10%以上の増加が2例(22%)、不変が2例(22%)であり、低下する傾向を認めた(paired testでp=0.08)。術前1か月で低下した5例のうち4例は上昇に転じた。しかしながら、術後6か月までにおける血清AMH値の推移は様々であり現在の症例数では一定の傾向を認めなかった。【結論】血清AMH値はRT後1か月で低下する傾向を認めた。一方で、RT後6か月では改善した症例が多かった。RT後の生殖補助医療において卵巣刺激の反応性は低下するが、卵巣予備能は必ずしも低下しない可能性が示唆された。詳細な傾向を明らかにするには更なる症例数の蓄積が必要である。

P-65-2 子宮頸部非扁平上皮癌に対する術後補助化学療法としてのドセタキセル/カルボプラチン(DC)併用療法の検討

がん研究会有明病院

小池 亮, 温泉川真由, 尾松公平, 伏木 淳, 阿部彰子, 尾身牧子, 谷川輝美, 青木洋一, 根津幸穂, 岡本三四郎, 野村秀高, 金尾祐之

【目的】当院では子宮頸部非扁平上皮癌に対する術後補助療法として化学療法を行ってきた。また、術後補助化学療法の標準レジメンは定まっていないが、Satoらが子宮頸部非扁平上皮癌の再発高リスク群患者に対しDC療法を施行した結果、2年無再発生存(RFS)率が80%と有効であったと報告しているため、以後、当院ではDC療法を行ってきた。DC療法の有効性を評価するために本研究を行った。【方法】当院で2007年から2021年に子宮頸部非扁平上皮癌IB-IIB期の診断で手術が行われ、術後補助化学療法としてDC療法を受けた157人の患者を対象とし後方視的に検討した。病理学的に4cm以上の腫瘤、1/2以上の頸部間質浸潤、脈管侵襲陽性であれば再発中リスク、骨盤リンパ節転移陽性、子宮頸部傍組織浸潤陽性であれば高リスクと定義した。ドセタキセル(60-70mg/m²)、カルボプラチン(AUC5-6)を3週間毎に6サイクル投与した。有効性の解析は3サイクル以上の症例を対象とし、主要評価項目は2年RFS率とした。【成績】有効性の検討症例は145例で中リスクは98例、高リスクは47例であった。高リスクの内訳は傍組織浸潤陽性が11例、骨盤リンパ節陽性が18例、傍組織浸潤陽性かつ骨盤リンパ節陽性が18例であった。中リスク、高リスク、骨盤リンパ節転移陽性の2年RFS率はそれぞれ94.7%(95%信頼区間[CI], 88.0%~97.8%)、80.1%(95%CI, 64.9%~89.7%)、82.6%(95%CI, 57.7%~94.3%)であった。【結論】子宮頸部非扁平上皮癌に対し手術療法を行った上での術後DC療法は、術後補助療法の一つとして有効である可能性が示唆された。

P-65-3 当院における子宮頸部腺癌の治療成績について

三重大附属病院

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【目的】子宮頸部腺癌は扁平上皮癌よりも予後不良であると報告されており放射線治療低感受性であることから手術や化学療法による集学的な治療が必要になると考えられる。現状、子宮頸部腺癌の明確な治療方針はなく扁平上皮癌に準ずることになっている。当院でも根治的手術療法を選択し、進行症例に化学療法や同時化学放射線療法を選択している。当院における子宮頸部腺癌の治療成績を後方視的に検討した。【方法】2016年から2020年までに子宮頸部腺癌の診断で根治的治療を施行したFIGO病期(2008)I-IV期34例を検討した。【成績】観察期間中央値は28か月(3-57か月)、FIGO病期(2008)I/II/III/IV期が24/2/2/5例、亜分類診断は通常型内頸部腺癌/粘液癌/その他が20/6/8例であった。治療方法は手術/同時化学放射線療法(CCRT)/放射線療法/放射線療法/化学療法(CT)が28/4/2/2例、術式は広汎子宮全摘術及び両側付属期切除術/広汎頸部切除術/円錐切除が32/1/1例施行され、傍組織浸潤0例、脈管侵襲8例、リンパ節転移陽性1例であった。開腹/腹腔鏡/ロボットが12/11/2例であった。術後治療はCCRT/CTが1/4例、再発が6例であった。再発形式は肺転移/腹膜播種増悪/子宮頸部再発/骨転移が2/2/1/1例であった。再発症例の病期はI/II/III/IV期が1/0/2/3人であった。術後の再発症例は1例であった。【結論】観察期間は短いが手術症例の予後は良好であり、進行症例は再発率が高く予後不良であることが示唆された。

日本語
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ポスター

P-65-4 当院の術前化学療法を施行した子宮頸部腺癌症例の予後に関する検討

静岡がんセンター

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【目的】当院では手術待機期間中にoperabilityが失われる可能性がある子宮頸部腺癌症例に対して術前化学療法(以下NAC)を行っているが、NACが予後に与える影響は不明である。当院の子宮頸部腺癌症例においてNACの有無による予後を比較検討することを目的とした。【方法】当院で2003年1月-2021年9月までに子宮頸部腺癌IB3-IIB, IIC1r期(FIGO2018)に対して広汎子宮全摘術を施行した73例を対象とした。NAC/非NAC群間で患者背景、無増悪生存期間、全生存期間を後方視的に比較検討した。【成績】NAC群24例(33%)、非NAC群49例(67%)、観察期間の中央値は52か月(2-183)であった。NAC群で治療開始前の腫瘍径が有意に大きく(中央値54 vs. 41mm, $p < 0.01$)、脈管侵襲が少なかった(62.5 vs. 87.5%, $p = 0.03$)。無増悪生存期間はNAC/非NAC群とも中央値未到達($p = 0.94$)。全生存期間はNAC群中央値89か月、非NAC群未到達($p = 0.46$)と有意差はなかった。【結論】当院の子宮頸部腺癌症例はNACの有無に関わらず予後に差はなかった。

P-65-5 CIN3合併妊娠・分娩例に対する子宮頸部円錐切除術に関する検討：術後子宮頸管狭窄のリスク因子と分娩後の待機的管理について

埼玉医大総合医療センター

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【目的】CIN3合併妊娠の分娩後の治療方針に関しては分娩後早期の円錐切除術が推奨されているが、その施行時期に関しては明確なコンセンサスはない。当院では術後の子宮頸管狭窄を回避する目的で、所見の進行が疑われなければ可能な限り月経再来まで手術待機する方針としている。今回CIN3合併妊娠・分娩例における術後頸管狭窄のリスク因子について検討を行った。【方法】当院において2004年9月から2021年8月までにCIN3と診断、妊娠中経過観察し分娩後に病変を再評価した160例について患者背景、分娩後の経過・治療内容等について後方視的に検討した。【成績】分娩時の平均年齢は32.0歳(19-44歳)であり、円錐切除は135例(84.4%)に施行された。術後頸管狭窄は9例(5.6%)に認められた。術後の最終病理診断で浸潤癌を5例(全例pT1a)に認めた。病変の減弱あるいは消失を認め手術を回避し得た症例は25例(15.6%)であった。術後頸管狭窄例と非狭窄例の比較では手術時年齢($p = 0.001$)、手術時の月経再開の有無($p < 0.001$)、分娩から手術までの期間($p < 0.001$)に有意差を認め、ロジスティック回帰分析を用いた多変量解析では、「手術時年齢(38歳以上)」と「手術時月経再開なし」が独立した術後子宮頸管狭窄のリスク因子となった(オッズ比: 5.43, 22.2)。【結論】CIN3合併妊娠・分娩例では、慎重な経過観察が可能であれば、月経再来まで手術を待機することは術後頸管狭窄のリスク低減の観点から一つの選択肢となり得る。しかし、月経再来までの待機的管理は病変進行のリスクを伴うという問題も存在する。

P-65-6 子宮頸部円錐切除後の頸管狭窄を予防するデバイスの開発

佐賀大
橋口真理子, 横山正俊

【目的】子宮頸部円錐切除術は子宮頸部病変に対する治療として広く行われている。その術後の合併症として子宮頸管狭窄に伴う月経困難症や子宮留血腫等は臨床的にもしばしば遭遇し、治療に苦慮する合併症である。我々は過去に高密度コラーゲン線維の新素材であるコラーゲンビトリゲル®を用いた複数の医療用デバイスを開発し、それらが創部の上皮化の促進と筋線維芽細胞の出現を抑制することを報告している。今回この特性を利用して頸管狭窄を予防するデバイスの作製に着想した。【方法】コラーゲンビトリゲル®を被覆したナイロン糸からなる複合糸を作成した。ウサギの子宮頸部を切除して円錐切除後の状態とし、切除後の頸管内に、コラーゲンビトリゲル®を留置した群、ナイロン糸のみ留置した群、無処置群を準備し、21日後に子宮を摘出した。肉眼的な頸管狭窄の有無や組織学的な変化を分析した。【成績】円錐切除後、ナイロン糸のみ留置群と無処置群では、頸管が狭窄しその子宮側が拡張傾向を示し、嚢胞状になっていた。一方でコラーゲンビトリゲル®留置群では、嚢胞性の拡張は見られなかった。組織学的には、コラーゲンビトリゲル®留置群では、他の2群に比べて再生した子宮頸部間質内に筋線維芽細胞の出現が少なく、線維化が抑制されていた。【結論】コラーゲンビトリゲル®を用いたデバイスは、円錐切除術後の頸管狭窄を予防する効果がある。今後、実用可能な至適形状の検討および長期的な効果等について検討する予定である。

P-65-7 治療的円錐切除術後妊娠の早産リスク

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【目的】円錐切除術後に妊娠、出産に至った症例における早産リスクとその関連因子について検討することを目的とした。【方法】2011年1月から9年間で当院で治療的円錐切除術を実施し、その後妊娠、出産に至った単体妊娠症例の周産期予後について後方視的に検討した。母体および円切術要因(年齢、非妊時肥満度、切除機器、切除検体のサイズ、手術時間、出血量、手術から妊娠までの期間、妊娠20週の子宮頸管長等)と早産との関連について検討した。【成績】治療的円錐切除術実施件数は273件で、そのうち円切後出産に至った64例を対象とした。早産は14例(22%)であり、そのうち10例(71.4%)は破水(pPROM)が先行した早産であった。頸管長短縮のために緊急縫縮術を8例に施行し、そのうち半数の4例が早産となったが、3例はpPROMが先行した早産であった。正期産群と比較して、妊娠20週での頸管長が早産リスク因子として抽出されたが、他には有意なリスク因子を認めなかった。子宮頸管縫縮術実施症例を除外した解析、およびpPROMをアウトカムとした解析でも同様の結果であった。【結論】円錐切除術後妊娠の20%が早産の転機をとり、その多くはpPROMが先行した早産であった。妊娠20週の頸管長が早産予測因子となる可能性が示唆された。

P-65-8 CCRTにおけるシスプラチン投与時のショートハイドレーション安全性の評価

大阪国際がんセンター
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【目的】子宮頸癌に対する放射線同時化学療法でのCDDP投与時は、腎毒性回避のために大量補液が必要とされる。近年CDDP含有レジメンのショートハイドレーション法(以下、SH法)の有用性が報告されており、2015年に日本肺癌学会より「シスプラチン投与におけるショートハイドレーション法の手引き」が発行されSH法が進められている。今回子宮頸癌に対し放射線同時化学療法においてSH法を導入し安全性を検討した。【方法】2020年1月末日にSH法を導入し、1コース目は通常法で、2コース目よりSH法を開始した。SH法導入開始時~2021年9月でCDDP投与を全て終えた患者を対象とし、完遂率と血清クレアチニン値について後方視的に検討した。【成績】SH法を導入したのは60例、全275コースが施行された。患者背景は年齢25-74歳(中央値45歳)、術後adjuvant照射/根治照射が18/42例、組織型は扁平上皮癌/腺癌/腺扁平上皮癌/低分化癌で50(内1例腺癌)/7/2/1例、Stage(FIGO2018)はIB1/IB2/IIA1/IIA2/IIB/IIB1/IIB2/IVAで14/7/1/1/4/2/3/22/4/2例であった。SH法を中止したのは1/60例(1.7%)であり、grade2(CTCAE ver.4)の腎機能障害を認めため以降は通常法とした。この1例以外にgrade1以上の腎機能障害は生じなかった。経口補液不十分により輸液追加となったのは15/275コース(5.5%)で、経口補水液の味の好みや嘔気による飲水不良が原因であった。利尿薬が必要であったのは5/275コース(1.8%)であった。【結論】通常法に比して腎機能障害発生率は高くなく、SH法は安全性に問題ないと思われる。SH法により入院期間短縮やルート確保時間短縮が見込まれ、患者負担が軽減されることより今後積極的に導入が勧められる。

P-65-9 分葉状頸管腺過形成 (LEGH)・胃幽門腺化生 91 例の臨床経過に関する検討

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【目的】子宮頸部の分葉状頸管腺過形成 (LEGH) や胃幽門腺化生 (PGM) の一部から胃型粘液性癌が発生することが知られている。しかし、LEGH, PGM の自然史については不明点が多い。今回われわれは、LEGH, PGM を有する症例の臨床経過について後方視的に検討した。【方法】対象は 1998 年 9 月～2021 年 7 月に当院で子宮全摘出術を行い病理組織学的に診断した LEGH 46 例, PGM 11 例, さらに子宮頸部細胞診(黄色調粘液を有する頸管腺細胞の存在), HIK1083 ラテックス凝集検査, 経膈超音波検査あるいは MRI 検査(内子宮口付近に存在する小嚢胞集簇病変の有無)から診断した clinical LEGH 18 例, clinical PGM 16 例の計 91 例である。悪性が疑われたり, 他に適応がある場合には手術を行い, それ以外の症例は経膈超音波検査と内子宮口を含む内頸部から採取した細胞診(直接塗沫法)で 3～6 か月毎に follow-up を行った。本研究は当院の倫理委員会で承認を受けている。【成績】初診時年齢は 30～86 歳(中央値 53 歳), 初診から 3 か月以内の手術が 33 例, follow-up 期間は初診から 3 年以上が 26 例(うち 8 例は 5～10 年, 5 例は 10 年以上)であった。LEGH に関連した腺癌が 9 例 (AIS 7 例, 胃型粘液性癌 2 例) 認められ, これは LEGH (clinical LEGH を含む) の 14% に相当した。いずれの症例も 50 歳以上で, AIS の 4 例は follow-up 中(初診から最長 4 年 3 か月後)に診断された。PGM に関連した癌は認められなかった。【結論】LEGH の 14% に LEGH 関連 AIS/腺癌が認められた。LEGH から発生する癌を早期に捉えるのに, 内子宮口を含む内頸部から採取した細胞診が有用であった。

P-66-1 腹式広汎子宮全摘術後の尿道カテーテル留置期間短縮による在院日数の変化と安全性の評価

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【目的】腹式広汎子宮全摘術後の尿道カテーテル留置期間短縮クリニカルパス適用による術後在院日数の変化と安全性についての評価を目的とした。【方法】当院で 2016 年 1 月 1 日から 2021 年 1 月 31 日までの期間に, 子宮頸癌の診断で腹式広汎子宮全摘術を行った 43 例について後方視的に検討した。術後在院日数, 退院時の自己導尿導入割合, 術後 30, 90 日の自己導尿継続割合, 術後合併症について, 術後 7 日目抜去群(標準群)と 4 日目抜去群(短縮群)で比較した。【成績】2018 年 12 月 31 日まで術後 7 日目に尿道カテーテルを抜去するパスが適用され, 2019 年 1 月 1 日以降は術後 4 日目抜去のパスが適用された。症例は標準群 26 例, 短縮群 17 例で, 年齢の平均値はそれぞれ 53.1 歳 (33-71), 49.2 歳 (34-71) だった。術後在院日数の平均値は標準群 16.2 日 (9-50), 短縮群 10.9 日 (7-16) だった。退院時の自己導尿導入割合は標準群 9 例 (34.6%), 短縮群 10 例 (58.8%), 自己導尿継続割合は標準群で術後 30 日 9 例 (34.6%), 90 日 6 例 (23.1%), 短縮群で術後 30 日 9 例 (52.9%), 90 日 5 例 (29.4%) であった。術後合併症は標準群で尿路感染症 5 例 (19.2%), イレウス (11.5%), 骨盤内感染 1 例 (3.8%), 深部静脈血栓症/肺塞栓症 1 例 (3.8%), 短縮群では尿路感染症 2 例 (11.8%) のみであった。在宅自己導尿管理期間中の尿路感染症は, いずれの群においても認めなかった。【結論】尿道カテーテル留置期間短縮後, 術後合併症は減少し, 術後退院までの日数は短縮した。退院時の自己導尿率は増加したが, 経過とともに自己導尿率は低下しており, 外来管理期間中に尿路感染症の発症は認めず, 安全性は高いと考えられた。

P-66-2 子宮頸癌の骨盤リンパ節転移と治療法が予後に及ぼす影響～新 IIIC1 期に対する最良の治療は何か?～

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【目的】FIGO 分類, 日産婦分類の改訂により, 骨盤リンパ節転移のある子宮頸がんは up-stage された。しかし, 骨盤リンパ節転移のある症例(新 IIIC1 期)の最適な治療法は明らかでない。本研究は, 子宮頸癌の骨盤リンパ節転移の有無および治療法と, 予後との関係を明らかにすることが目的である。【方法】2013 年 1 月～2021 年 3 月に当院で初回治療を行った子宮頸癌のうち, 旧分類 IA2 期～IIIB 期(神経内分泌癌は除外)を対象とし, 年齢, 病理組織型, リンパ節転移の有無, 治療法, 無再発生存期間 (RFS), 全生存期間 (OS) について後方視的に検討した。【成績】検討対象となった 210 例の年齢中央値は 55.5 歳 (25～97 歳) で, 観察期間中央値は 30 か月 (1～102 か月), 扁平上皮癌が 136 例 (65%), 腺癌が 58 例 (28%), 腺扁平上皮癌が 16 例 (8%) であった。骨盤リンパ節転移を有する症例(新 IIIC1 期に相当)は 61 例 (29%) あり, そのうち手術療法を主体とした症例は 38 例 (62%), 放射線療法を主体とした症例は 23 例 (38%) であった。手術療法主体症例と放射線療法主体症例の間で RFS, OS 共に有意差はなかった ($p=0.58, 0.54$)。新 IIIC1 期に相当する 61 例のうち, T 分類に着目すると, T2N1 症例 (31 例) のうち, 放射線療法を施行した群 (15 例) の方が, 放射線療法を施行しなかった群 (16 例) よりも有意に RFS が延長した ($p=0.032$)。T2N1 症例で再発した 9 例全例で骨盤内再発を認め, 8 例 (89%) は放射線療法が施行されていなかった。新 IIIC1 期相当の症例で, 放射線療法が施行された場合, 扁平上皮癌と非扁平上皮癌間で, RFS に差はなかった ($p=0.22$)。【結論】骨盤リンパ節転移を有する症例, 特に T2 症例では, 局所再発制御のために放射線療法を加えることが非常に重要である。

P-66-3 広汎子宮全摘術実施症例における FIGO2018 進行期分類 IIIC1 期の臨床病理学的検討

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【目的】子宮頸癌 IIIC1p 期 (FIGO2018 進行期分類) における臨床病理学的特徴を検証する 【方法】2013年1月から2017年12月までに広汎子宮全摘術を行った子宮頸癌 IB-IIIB 期 (FIGO2008) 97 例を対象とし、後方視的検討を行った。【成績】IB-IIIB 期 (FIGO2008) を再検討した結果、30 例 (30.9%) が IIIC1p 期 (FIGO2018) へ再分類された。特に IIB 期 (FIGO2008) では、12/18 例 (66.7%) が IIIC1p 期 (FIGO2018) へ分類された。SCC 18 例, non-SCC 12 例であった。IIIC1p 期 (FIGO2018) の 5y-PFS/OS は IB-IIIB 期 (FIGO2018) と比較し、有意に予後不良であった (5y-PFS 76.7% vs 92.3%, OS 80.0% vs 92.9%)。IIIC1p 期 (FIGO2018) 症例のみの検討では、組織型別 5y-PFS/OS は、SCC に比して non-SCC で予後不良の傾向 (5y-PFS 83.3% vs 66.7%, OS 83.3% vs 75.0%) を認めたが、有意差は認めなかった。また、リンパ節単独転移に比して複数転移では、予後不良の傾向 (5y-PFS 84.6% vs 70.5%, OS 84.6% vs 76.4%) を認めたが、有意差を認めなかった。深い頸部間質浸潤陽性率、脈管侵襲陽性例は、IB-IIIB 期と比して IIIC1p 期のほうが有意に高かった (83.3% vs 64.2%, 80.0% vs 38.8%)。【結論】広汎子宮全摘術を行った IB-IIIB 期 (FIGO2008) 症例の病理組織診断に基づいて、子宮頸癌進行期分類 (FIGO2018) IIIC1p 期の臨床病理学的特徴を示した。IIIC1p 期症例における組織型、転移陽性リンパ節個数別の検討については、症例数を追加しさらなる検討を行いたい。

P-66-4 子宮頸癌 FIGO2018 変更後の予後についての検討

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【目的】子宮頸癌は FIGO2018 へ変更となり、腫瘍径、リンパ節転移の要素が新たに進行期分類に組み込まれた。今回我々は、変更された進行期分類の予後について後方視的に検討した。【方法】施設内倫理委員会の承認を得て、2007年4月1日から2020年4月30日までに、当院で初回治療を行った子宮頸癌 730 症例 (FIGO2018 I 期: 276 例 II 期: 122 例 III 期: 251 例 IV 期: 81 例) のうち、IB1 期から IVB 期に対し、初回治療として手術療法 (298 例), CCRT (231 例), RT (73 例) を施行した症例を対象とし後方視的に検討した。【成績】FIGO2018 Stage の序列順と相関し予後不良であった。(Kaplan-Meier method log-rank test $P=0.009$)。しかし IB2 期, IB3 期に対し、IIA1 期は予後良好であり、IIIB 期は IIIC1 期より予後が不良であった。IB1 期から IIB 期の予後因子の検討では、年齢, 初回治療, 組織型に有意差はなく、腫瘍径 2cm 以上 4cm 未満 (HR 2.96 95%CI 1.23-7.13, $P=0.015$), 4cm 以上 (HR 3.46 95%CI 1.34-8.89) と腫瘍径が予後不良因子であった。FIGOIII 期の予後因子の検討では、年齢, 初回治療, 組織型, 腫瘍径に有意差はなく、傍大動脈リンパ節転移 (HR 23.04 95%CI 2.59-204.62 $P=0.005$), 水腎症あり (HR 3.51 95%CI 1.47-8.41 $P=0.005$) が予後不良因子であった。【結論】IIA1 期は腫瘍径によっては IB 2 期, IB3 期より予後が良好な可能性がある。水腎症を伴う III 期は水腎症を伴わない III 期より予後不良であった。IIA 期の腫瘍径, III 期の水腎症有無は予後因子になる可能性があり、今後さらなる検討が必要である。

P-66-5 高齢者に対する広汎子宮全摘術は安全か?

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【目的】本邦では子宮頸癌 IB1 期から IIB 期において、手術療法あるいは放射線療法が選択されている。今後の更なる高齢化の進行および健康寿命の延長に伴い、高齢者に対する根治術の必要性の高まりも予測される。当院での高齢者の子宮頸癌に対する広汎子宮全摘術の安全性を検討した。【方法】2011年1月から2020年12月の間に、当院で子宮頸癌に対する広汎子宮全摘術(少なくとも片側は神経温存術式)を実施した、65歳以上の13例の成績を診療録よりデータを抽出し、「人を対象とする生命科学・医学系研究に関する倫理指針」に従い、後方視的に検討した。【成績】年齢の中央値(範囲)は71(65-75)歳であった。Stage は IB1 7 例, IB2 1 例, IIA 3 例, IIB 2 例であった。組織型は扁平上皮癌 9 例, 腺癌 2 例, 神経内分泌腫瘍 1 例であった。術中出血量の中央値(範囲)は 1,100 (115-2,779) ml で、自己血以外に輸血は 4 名 (31%) に必要であった。50ml 以下の残尿に要した日数の中央値(範囲)は 22 (7-117) 日であった。排尿困難以外の術後合併症として、左大腿筋力低下 1 例, 尿路感染 1 例を認めた。手術による入院期間の中央値(範囲)は 14 (13-22) 日であった。術後補助療法として化学療法が 6 例 (46%)、同時化学放射線療法が 2 例 (15%) に実施された。下肢リンパ浮腫 (II 期晩期以上) を 1 例 (8%) に認めた。術後 3 年以上経過している 8 名の生存率は 100% であった。【結論】65 歳以上の高齢者に対する広汎子宮全摘術も安全に実施することが可能である。

P-66-6 子宮頸癌における傍大動脈リンパ節郭清の意義は

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【目的】治療的意義を目的にした傍大動脈リンパ節郭清 (PALA) は、生存への寄与が明らかではない。一方で骨盤リンパ節転移陽性例、IIB期症例や bulky な原発巣をもつ症例では考慮してもよいとされている。当院では術中病理診断で骨盤リンパ節転移陽性であった症例 PALA を施行している。今回我々は PALA の意義について後方視的に検討した。【方法】施設内倫理委員会承認を得て、2007年4月1日から2020年4月30日までに、当院で初回治療を行った子宮頸癌 730 症例 (FIGO2018 I期: 276例 II期: 122例 III期: 251例 IV期: 81例) のうち、広汎子宮全摘出術 (RH) および PALA を施行した症例を対象とし、傍大動脈リンパ節転移のリスク因子 (腫瘍径、傍組織浸潤、組織型、年齢)、および PALA の治療意義を検討した。【成績】RH を施行した 266 例中、骨盤リンパ節転移を認めた症例は 99 例であった。そのうち PALA は 81 例に施行し、傍大動脈リンパ節転移は 26 例に認めた。傍大動脈リンパ節転移は、骨盤リンパ節多発転移症例に多く (OR 1.95 95%CI 1.37-2.80, $P < 0.001$)、腫瘍径 (2cm 以上 4cm 未満 $P=0.414$, 4cm 以上 $P=0.711$)、傍組織浸潤 ($P=0.265$)、組織型 (SCCorNon-SCC $P=0.599$) は影響がなかった。傍大動脈リンパ節の転移の有無を Propensity Score にて因子を補正し、Kaplan-Meier method log-rank test にて検討した。傍大動脈リンパ節転移陽性例、傍大動脈リンパ節転移陰性例に PALA を施行しても、予後に差を認めなかった ($P=0.577$)。【結論】子宮頸癌における傍大動脈リンパ節転移のリスク因子は骨盤リンパ節多発転移であった。

P-66-7 当院における広汎子宮頸部摘出術後妊娠に対する検討

岐阜大付属病院

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【目的】妊娠性温存を希望する浸潤子宮頸癌症例に対する手術方法として広汎子宮頸部摘出術があり、女性の晩婚化、妊娠・出産年齢の高年齢化などの社会背景が重なり症例数が増加している。今回我々は本術式による妊娠への影響について検討する。【方法】2010年1月~2021年6月において、当院にて本術式を完遂した 20 例について早産群・満期産群、妊娠成立群・非成立群に分けて後方視的に比較検討した。【成績】年齢は中央値 34.5 歳 (26-40 歳)、観察期間の中央値は 49 か月 (2-144 か月)、既婚 9 例・未婚 11 例、未経産 17 例、FIGO2018 ; 1A1 期 2 例・1A2 期 6 例・1B1 期 12 例、組織型 ; 扁平上皮癌 16 例・腺癌 4 例であった。合併症は術中尿管損傷 1 例・術後頸管狭窄 1 例であったが、現在再発症例は 1 例も認めていない。20 症例中 10 症例が術後妊娠を計画し 6 症例で 8 妊娠成立し、生児 6 人を獲得した。生児 6 人の妊娠契機は、自然妊娠 2 例、AIH 1 例、IVF-ET 3 例であった。分娩週数はそれぞれ 26 週, 33 週, 36 週がそれぞれ 1 症例, 37 週が 3 症例であり、うち 2 症例に前期破水を認めた。【結論】早産 3 症例と満期産 3 症例、および妊娠成立群 6 症例と非成立群 4 症例について文献的考察を踏まえて比較検討した結果、術後残存頸管長短縮による流早産への影響を認めしたが、妊娠成立に影響する因子は検出されなかった。広汎子宮頸部摘出術後妊娠の管理上の問題点として、子宮内感染リスクが高く前期破水になりやすい点や、手術により頸管長が短縮しているため早期の子宮収縮を誘発しやすい点があげられる。

P-66-8 陽圧下経腔内視鏡からみた骨盤解剖 : endopelvic fascia 上の神経の走行を視覚化する

関西医大

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【目的】広汎子宮全摘術において膜構造を中心とした神経、血管の骨盤解剖の理解が重要である。今回当院で広汎子宮全摘術時に行なっている経腔内視鏡から見えてきた endopelvic fascia を中心とした神経、血管の骨盤解剖についての動画を供覧させていただく。【方法】腔内視鏡は腔口にデバイスを設置し腔内を密閉したのちに送気、陽圧化することで腔および後腹膜腔内を拡張、可視化するものである。子宮摘出に際し腹腔側から子宮上部靭帯、子宮周囲腹膜切開、子宮動脈切断、膀胱子宮靭帯前層切断、尿管分離、基靭帯血管、仙骨子宮靭帯を実施し経腔内視鏡を用いて腔側から腔壁切開、カフ縫合形成による腫瘍密閉、傍腔組織 (腔動静脈) および子宮頸部を全周性に剝離し腔側腔を展開することで、子宮頸部は骨盤壁に繋がる靭帯群 (膀胱腔中隔、膀胱子宮靭帯後層、子宮直腸靭帯、Denonvilliers 筋膜) で全周性に支持され、これらは経腔内視鏡では扇状の Paracervical endopelvic fascia として観察される。【成績】腔側から光源を照らし腹腔側から骨盤底を観察すると膀胱子宮靭帯後層や基靭帯が endopelvic fascia の上に乗った神経、血管の組織の束として観察することができ骨盤解剖の理解が深まる。endopelvic fascia のみで繋がった子宮はより可動性が得られるため子宮を十分に頭側へ牽引でき骨盤内臓神経叢 (子宮枝) をより選択的に切除することができる。【結論】経腔内視鏡を用いることで詳細な腔壁浸潤評価と腔カフ形成およびカフを破綻させない子宮摘出が可能となるだけでなく腔側・腹腔側両方からみた子宮頸部の靭帯・血管・神経の立体的な解剖を可視化し、安全な神経温存手術を可能にする。

P-66-9 子宮頸癌 IB1 期に対しての鏡視下（ロボットを含む）広汎子宮全摘術の検討

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【目的】子宮頸癌 IB1 期における鏡視下広汎子宮全摘術の実施妥当性を検討する。【方法】2007 年 1 月より 2018 年 12 月の間に当院で治療を行った子宮頸癌 787 例のうち、初回治療として広汎子宮全摘術（広汎子宮頸部切除術）および所属リンパ節摘出を行った、FIGO2008 分類 IB1 期（画像上リンパ節腫大なし）の 210 例を背景とし、カルテ調査に基づく後方視的検討を行った。種々のアウトカムは開腹手術群（O 群）160 例と鏡視下手術群（R 群）50 例で比較を行った。【成績】年齢中央値 43 歳、組織型は扁平上皮癌 133 例（63%）、77 例（37%）であった。リンパ節転移は 12% に認められた。腫瘍径中央値は 19mm であった。年齢、BMI、腫瘍径、組織型、リンパ節転移頻度、既往円錐切除の頻度、追跡期間、高度神経因性膀胱出現頻度、再発率、死亡率は両群間に差を認めなかった。R 群で尿管侵襲陽性例が有意に少なく（46% vs. 20%, $P=0.01$ ）、術後治療の追加率が少なかった（39% vs. 24%, $P=0.046$ ）。手術時間は R 群で有意に長かった（292 分 vs. 459 分, $P<0.0001$ ）が、出血量は有意に少なく（667cc vs. 173cc, $P<0.0001$ ）、入院期間が短かった（26 日 vs. 16 日, $P<0.0001$ ）。【結論】子宮頸癌 IB1 期において、鏡視下広汎子宮全摘術の実施妥当性の余地がある可能性が示唆された。

日本語ポスター
7日(日)

P-66-10 ガットクランパーを用いた腹腔鏡補助下（ハイブリッド）広汎子宮全摘術の検討

神戸大附属病院

長又哲史, 山崎友維, 久保田いろは, 吉本梓希子, 山中啓太郎, 安積麻帆, 鷺尾佳一, 笹川勇樹, 西本昌司, 寺井義人

【目的】子宮頸癌に対する腹腔鏡下子宮悪性腫瘍手術は、LACC trial の結果から開腹手術に比べて再発率が高いことが報告され、その原因としてマニピュレータの使用、腔管切断時の気腹による腫瘍細胞散布などの問題がクローズアップされた。そこで、我々はリスク因子を回避する目的でガットクランパーという腔壁を挟鉗する器具を用いて腫瘍の露出を防ぎ、さらに腔壁切開時に気腹を終了し下腹部小切開を行う腹腔鏡補助下（ハイブリッド）広汎子宮全摘術を開発した。これまでの症例の蓄積や経験を踏まえ、この術式の有用性について報告する。【方法】2020 年 4 月から 2021 年 9 月までに、当院で子宮頸癌に対してハイブリッド広汎子宮全摘術を施行した全 16 症例について後方視的に検討を行った。ハイブリッド術式の手術時間、気腹時間、出血量、術後入院期間、摘出検体における腫瘍最大径および腔壁長、傍腔結合織長、子宮摘出後の洗浄細胞診について検討した。【成績】ハイブリッド手術の手術時間中央値は 485.5 分、気腹時間中央値は 424.5 分、出血量中央値は 190ml であった。術後退院日数の中央値は 10.5 日、摘出検体における腫瘍最大径中央値は 30mm、腔壁長の中央値は 22mm、傍腔結合織長の中央値は 30mm であった。子宮摘出後の洗浄細胞診はすべて陰性であった。【結論】ガットクランパーを用いたハイブリッド広汎子宮全摘術は、従来の腹腔鏡下手術におけるメリットを残したまま、予後不良のリスク因子となる要因を回避した新たな術式である。長期予後については今後の検討が必要であるが、腫瘍細胞を防ぎ腔壁長も十分に確保できており、有用な方法と考えられる。

P-67-1 当院から紹介した子宮頸癌にたいする重粒子線治療後の転帰

高知大

樋口やよい, 氏原悠介, 松浦拓也, 前田長正

進行子宮頸癌には放射線治療が導入されているが、腫瘍径が大きいくほど 5 年生存率は低下する。重粒子線治療は通常の放射線治療と比べて、大きな腫瘍に対する治療効果が高いとされており、当院でも Bulky な子宮頸癌は、重粒子線治療の選択肢を提示している。2013 年から 2019 年に当院から 6 例の子宮頸癌患者を重粒子線治療して頂き、その転帰をまとめた。対象は 6 cm 以上の扁平上皮癌 6 例で、年齢は 28-53 歳（中央値 44 歳）であった。全例骨盤リンパ節転移を認めた。重粒子線治療は全例 total72Gy 照射（全骨盤+子宮+局所）、シスプラチンは 1-5 コース投与された。初回治療後、4 例は腫瘍消失、2 例に局所残存を認めた。局所残存した 2 例のうち 1 例は TC 療法 3 コース追加にて消失、1 例は骨盤除臓術を行った。6 例のうち、5 例で再発を認め、局所再発 2 例、傍大動脈リンパ節再発 2 例、腹膜播種 1 例であった。局所再発の 1 例に前方骨盤除臓術、傍大動脈リンパ節再発の 2 例に摘出術と CCRT、残り 2 例に抗癌剤治療を行った。放射線治療後に手術を行った 3 例に重篤な合併症を認め、2 例は尿管-動脈瘻を、1 例は骨盤内腸管穿孔であった。治療後 5 年を経過した 4 例のうち、現在病変なく生存している症例が 3 例、病変を認め生存している症例が 1 例である。Bulky な子宮頸癌に対する重粒子線治療は従来の CCRT に比較し治療効果が高く、生存率を改善させる可能性があるが、現状では再発のリスクは高く、再発治療後の合併症が重篤となる可能性がある。重粒子線治療後の治療は、他病院・他科と連携をとりながら全身管理をしていく必要があると考える。

P-67-2 子宮頸癌 FIGO2018 治療前進行期分類 IIB および IIIC1r 期の治療方針の検討

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【目的】子宮頸癌において摘出病理所見で子宮傍組織浸潤と骨盤リンパ節転移は再発高リスクに該当し、ガイドラインでは術後同時化学放射線療法 (CCRT) が推奨される。有害事象を考慮すると、FIGO2018 治療前進行期分類 IIB 期、IIIC1r 期では初回治療として CCRT も選択肢となる。当院の治療成績を検討し、今後の治療方針決定の一助とすることを目的とした。【方法】2007 年から 2016 年に当院で初回治療をした FIGO2018 治療前進行期分類 IIB 期、IIIC1r 期症例を後方視的に検討した。なお IIIC1r 期では旧進行期 IIB 以下の症例を対象とした。腺癌と腺扁平上皮癌は全例手術が施行されていたため、扁平上皮癌に限定して解析した。術前化学療法 (NAC) で増悪し CCRT/放射線治療単独 (Rx) が施行された症例は手術群に含めた。生存解析にはログランク検定を用いた。【成績】治療前進行期 IIB 期、IIIC1r 期の扁平上皮癌において手術群 43 例、CCRT/Rx 群 28 例であり、背景として CCRT/Rx 群で年齢が有意に高かった ($p < 0.01$)。5 年生存率は手術群 83%、CCRT/Rx 群 81% と有意差は認めなかった ($p = 0.93$)。手術群 43 例のうち、術後 CCRT/Rx を施行した 16 例、術後化学療法を施行もしくは術後療法なしとした 19 例、NAC 後増悪し CCRT/Rx を施行した 8 例の 3 群で比較すると、NAC 後増悪した群は有意に 5 年生存率が低く、残りの 2 群では有意差は認めなかった。なお術後 CCRT/Rx 群は術後病理結果で傍組織浸潤およびリンパ節転移を認めた頻度が高かった。【結論】治療前進行期 IIB 期、IIIC1r 期の扁平上皮癌では手術と CCRT/Rx で治療成績に有意差は認めなかった。有害事象を考慮すると IIB 期、IIIC1r 期の扁平上皮癌では初回治療で CCRT を行うことも考慮される。

P-67-3 トモセラピーを用いた子宮頸癌根治的同時化学放射線療法後の腫瘍残存リスク因子の検討

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【目的】トモセラピーは強度変調放射線治療法 (IMRT) と画像誘導放射線治療 (IGRT) が一体となった高度放射線治療装置である。正常組織への被曝線量を低減し、有害事象の軽減が期待できる。しかしトモセラピーを用いた根治的同時化学放射線療法 (CCRT) の成績報告は少ない。そこで今回当院における子宮頸癌に対するトモセラピーを用いた根治的 CCRT の治療成績について後方視的検討を行い、治療後の腫瘍残存リスク因子について統計学的解析を行った。【方法】当院倫理審査委員会の承認を得て、2013 年 1 月～2020 年 12 月の期間に当院でトモセラピーを用いて根治的 CCRT を行った子宮頸癌 (IB2 期～IVA 期) 44 例について診療情報を抽出した。【成績】年齢の中央値は 63 歳 (34～77 歳)。組織型は扁平上皮癌 39 例、腺癌 5 例。併用する化学療法 (原則週 1 回投与、5～6 コース) は CDDP 35 例、CDGP 7 例、その他 2 例であった。32 例で高線量率腔内照射 (RALS) を併用。治療効果は CR 33 例 (75.0%)、PR 6 例 (13.6%)、SDI 1 例 (2.3%)、PD 4 例 (9.1%)。Grade3 以上の急性期有害事象は、白血球減少 21 例 (47.7%)、血小板減少 5 例 (11.4%)、下痢 2 例 (4.5%)。Grade3 以上の重篤な晩期消化管障害は認めなかった。治療後の腫瘍残存 (non-CR) リスク因子について多変量解析を行ったところ、腺癌・腫瘍径 5cm 以上・腔内照射併用無しが、独立したリスク因子であった。【結論】トモセラピーを用いた根治的 CCRT は奏効率高く、重篤な晩期有害事象の発生率も低い。有用な治療方法と考えられる。ただし、腺癌・腫瘍径 5cm 以上・腔内照射併用無しは、治療後腫瘍残存の独立したリスク因子であり、治療後更なる追加治療が必要となることが予見される。

P-67-4 PAN 転移の評価を病理診断と画像診断を用いた進行子宮頸癌に対する予後の検討

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【目的】子宮頸癌の重要な予後因子に傍大動脈リンパ節 (PAN) 転移がある。GOG 試験 85・120・165 の後方視的研究では、PAN 転移の評価を病理診断群 (P 群: pathological staging) と画像診断 (R 群: radiological staging) で検討すると、PFS で HR 1.51 ($p = 0.055$) と有意差はないが、OS で HR 1.60 ($p = 0.038$) と P 群の予後が優れていた。当院では、腹腔鏡下 PAN 生検術を施行し病理診断で放射線照射域を決定する先行研究を研究・発表した (JOGR 2021)。今回、それらの症例と画像診断を用いた CCRT 症例の予後について検討した。【方法】2012 年 1 月 1 日～2020 年 12 月 31 日までに治療した子宮頸癌の患者で、局所進行期 IIB～IIIB (FIGO 2008)、扁平上皮癌・腺癌・線扁平上皮癌、骨盤リンパ節転移陽性例に対して、同時化学放射線療法を施行したものを対象とした。傍大動脈リンパ節転移以外の遠隔転移の症例は除外した。統計は Kaplan-Meier 法を用い、log-rank 検定で行った。【成績】R 群が 55 例、P 群が 14 例を対象とした。局所進行期は、R 群で II 期 17 例、III 期 38 例、P 群で II 期 7 例、III 期 7 例で患者背景に有意差は認めなかった。R 群 PAN 転移は、R 群に 14 例、P 群に 3 例含まれた ($p = 0.745$)。2 年 PFS は、R 群で 63.3%、P 群で 59.2% と有意差はなかった ($p = 0.608$)。2 年 OS は、R 群で 76.1%、P 群で 90.7% だが、有意差はなかった ($p = 0.451$)。全体で再発は、R 群で 17 例、P 群で 5 例あったが、PAN の再発は R 群で 10 例に対し、P 群では 0 例と有意差を認めた ($p = 0.030$)。【結論】R 群と P 群で PFS と OS で差はなかった。しかし、P 群では PAN の再発症例がなく、PAN 領域への不要な放射線治療を防ぎ、腸閉塞や放射線性腸炎の合併症を減らす可能性が示唆された。

P-67-5 子宮頸癌における転移骨盤リンパ節への boost 照射と傍大動脈リンパ節再発に関する後方視的検討

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【目的】子宮頸癌の最も重要な予後因子はリンパ節転移である。骨盤リンパ節転移を有する子宮頸癌に放射線治療を行う際、転移リンパ節への boost 照射は多くの施設で行われているがその有効性に関して十分なエビデンスがあるとはいえず、本邦のガイドラインにも boost 照射を推奨する記載はない。boost 照射の有効性を検証するため、当院での治療症例について後方視的検討を行った。【方法】2012年1月から2018年12月に放射線治療による初回治療を開始し、骨盤リンパ節転移に対して boost 照射を行った子宮頸癌 IB 期～IVA 期（日産婦 2011, FIGO 2008）の症例を抽出した。治療開始時に傍大動脈リンパ節転移を認めた例は除外した。診療録を用いて患者背景、治療内容、治療効果、予後について検討した。【成績】全症例数は 31 例で、年齢中央値は 60 歳、組織型は扁平上皮癌が 27 例、腺癌が 1 例、その他が 3 例であった。29 例で同時化学放射線療法が施行され、2 例は放射線単独治療であった。転移骨盤リンパ節に対しては 5.4～10.8Gy の boost 照射が行われた。初回治療により骨盤リンパ節病変は 30 例で消失したが、内 4 例は骨盤内に再発をきたした。残りの 26 例中 9 例に傍大動脈リンパ節再発を認め、内 7 例は遠隔転移を伴った。傍大動脈リンパ節再発が認められなかった 17 例の内、遠隔転移を認めたのは 1 例のみであった。【結論】boost 照射により高い骨盤病変制御率（26/31=83.8%）が得られたが、傍大動脈リンパ節再発率は高く（9/26=34.6%）、遠隔転移も高率にきたすため、新たな治療戦略が必要と考えられる。

P-67-6 局所進行子宮頸部扁平上皮癌について、治療中の血清 SCC 値が持つ臨床的意義の検討

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【目的】子宮頸癌において傍子宮組織浸潤（Para）の存在は、臨床的に重要な因子であるが、正確な推測は困難である。またそれが明らかな場合は再発への懸念が生じる。本研究で我々は、Para 有無の評価と、明らかな場合の再発予測に血清 SCC 値（S 値）の有用性ではないかと考え、検討を行なった。【方法】対象は 2011 年から 2016 年までに当科で手術治療を行なった子宮頸部扁平上皮癌のうち、FIGO2008 において IB2（21 例）、IIB（30 例）を対象とした。治療前 S 値、最大腫瘍径、尿管侵襲（LV）、病理学的リンパ節転移（LN）、病理学的 Para、患者予後を抽出して、S 値と各因子の相関を検証した。当科では IB2、IIB 例には術前化学療法（NAC）を行っており、NAC 後の S 値と腫瘍径も加えて検討した。【成績】IB2 期：NAC 後の S 値は Para（+）とも有意な相関を認めた（ $r=0.669$, $p=0.001$ ）。また NAC 前後 S 値と腫瘍径にもそれぞれ相関を認めた（NAC 前： $r=0.522$, NAC 後： $r=0.583$ ）。Para（+）について、NAC 後腫瘍径、S 値に LN、LV も加えて検討したところ、S 値は独立した有意な相関因子であった（OR：2.2, 95%CI [1.20-12.18]）。IIB：NAC 前後の S 値とともに、再発と有意に相関していた（NAC 前： $p=0.03$, NAC 後： $p=0.0086$ ）。LN、Para、LV も含めた多変量解析にて、特に NAC 後 S 値は再発について有意な独立相関因子であった（ $p=0.0059$ ）。【結論】子宮頸部に留まると予測される場合でも、4cm 以上の大きな腫瘍を形成している場合、S 値が Para（+）の予測のために有用である。また明らかな Para（+）がある場合、S 値は再発の可能性を予測する有用な指標である。S 値は再発スクリーニング以外にも、進行期毎で重要な臨床的意義を持つ。

P-67-7 当院における子宮頸癌 IVB 期（FIGO2008）に関する後方視的検討

大阪医科薬科大

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【目的】遠隔転移や傍大動脈リンパ節転移を伴う子宮頸癌 IVB 期は、5 年生存率が 19.5% と予後が悪く、治療方針は難渋することが多い。治療奏効率や予後を把握することは、患者の症状緩和やそれによる QOL 向上を目的とした治療選択の提示に必要な不可欠と考える。【方法】2013 年以降当院で治療を行った子宮頸癌 IVB 期 31 例を後方視的に検討した。【成績】年齢は 55.9 ± 12.5 歳、組織型は扁平上皮癌 26 例、腺癌 4 例、痛肉腫 1 例だった。また TNM 分類では、T1～2 が 9 例、T3 が 18 例、T4 が 4 例、N1 が 27 例、N0 が 4 例、M1 が 15 例、MA が 16 例であり、M1 は肺が 8 例と最多で、その他骨 4 例、腹膜播種 3 例、Vichow2 例、肝 1 例だった。初回治療は化学療法が 17 例、RT/CCRT が 14 例で、奏効率は化学療法で 7 例（41.2%）、RT/CCRT で 8 例（57.1%）が CR を得られた（ $p=0.376$ ）。全症例中では初回治療後 15 例（48.4%）で CR、7 例（22.6%）で PR、9 例（29.0%）で PD だった。初回治療で CR～PR を得られた症例 22 例中 9 例（40.9%）で再発あるいは腫瘍の再燃を認め、無再発・無増悪生存期間は 10.3 ± 4.6 か月、12 例（38.7%）が死亡し、平均生存期間は 15.4 か月だった。また 2 年生存率は 47.8%（23 例中 11 例）、3 年生存率 35.3%（17 例中 6 例）だった。【結論】今後さらに観察期間を経た上での再検討は必要だが、当院での治療成績は一般的な予後と同等であると予測される。治療内容としては化学療法と放射線療法で奏効率に有意差は認めなかった。予後不良ながらも約 7 割の患者に CR～PR の奏効が得られ、さらにその 6 割に一定期間の病勢低下の維持が期待できる。進行癌において、予後の具体的なデータをふまえた治療計画をたてることは、より QOL の維持もふまえた治療選択に繋がると考える。

P-67-8 骨盤内リンパ節腫大を伴う子宮頸部腺癌 (T1, T2 症例) における治療成績の検討

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【目的】子宮頸部腺癌で広汎子宮全摘出術 (RH) が施行され、骨盤内リンパ節転移陽性例の治療成績を明らかにする。【方法】2004年3月～2018年5月に当院で治療を行った子宮頸部腺癌 (T1, T2) 190例の内、病理学的に骨盤リンパ節転移が証明された19例について、診療録を後方視的に検討しRHの治療成績を検討した。統計学的解析はKaplan-Meier法, log-rank検定, χ^2 検定, Mann-Whitney検定を用いた。【成績】年齢中央値は48 (30-68) 歳, BMI 21.7 (17.4-32.5) kg/m²。腫瘍学的背景は、骨盤MRIの腫瘍径中央値は3 (20-77) mm, 骨盤リンパ節腫大 (画像検査で短径 \geq 10mm) は2例のみだった。UICC分類T1b1は12例 (63.1%), 1b2は4例 (21%), 2bは3例 (15.7%), 骨盤リンパ節転移は複数個が12例, 単発が7例, 遺残例はなかった。18例 (95.7%) で術後補助療法 (化学療法17例, 同時化学放射線療法1例) を施行した。3年生存率は82.5%, 3年無病生存率は42.6% だった。複数個リンパ節転移では, 73.3% ($p=0.053$), 19.4% ($p=0.009$) で予後不良だった。19例中NEDは7例で、術前画像でリンパ節腫大なく、5例は単発リンパ節転移だった。再発例は13例 (56.5%) で、骨盤リンパ節再発が6例, 腔断端再発が3例, 肺再発が2例, 骨, 腹腔内再発が各1例であった。再発後治療は放射線療法が7例に施行され、2例が12, 24か月間無病生存, 担瘤生存2例, 原病死が1例。手術療法は骨盤内リンパ節再発の1例に施行され、26か月の無病生存がえられている。化学療法は3例に施行されたが、9～23か月で原病死された。【結論】複数個のリンパ節転移例は予後不良因子だったが、再発治療として放射線療法や手術療法が選択できれば予後の延長が期待できると思われた。

P-68-1 後腔円蓋部へのトロカー留置による子宮牽引操作を行った早期子宮体癌に対する腹腔鏡下子宮悪性腫瘍手術の手術成績に関する検討

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【目的】後腔円蓋部へのトロカー留置による子宮牽引操作の有効性と安全性を検証するとともに、早期子宮体癌に対する腹腔鏡下子宮悪性腫瘍手術と開腹子宮悪性腫瘍手術の手術成績について後方視的に比較検討する。【方法】2018年11月より2020年12月までに後腔円蓋部へのトロカー留置により子宮牽引操作を行った、早期子宮体癌に対する腹腔鏡下子宮悪性腫瘍手術症例22例の手術成績 (手術時間, 出血量, 摘出リンパ節数), 再発率, 無再発生存期間について、同時期に術前推定進行期1A期の診断で開腹手術を行った54例と比較検討した。また、腹腔鏡手術症例において後腔円蓋部へのトロカー留置による子宮牽引操作の安全性について後方視的に検討した。【成績】骨盤リンパ節郭清施行症例では、手術時間は腹腔鏡手術群で有意に延長し (218.5分 vs 162分, $p=0.003$), 出血量は腹腔鏡手術群で有意に少なかった (50ml vs 150ml, $p=0.01$)。摘出リンパ節個数は、腹腔鏡手術群と開腹手術群で有意差を認めなかった (23.5個 vs 20個, $P=0.38$)。骨盤リンパ節郭清省略症例では、手術時間は腹腔鏡手術群と開腹手術群で有意差を認めなかったが (109分 vs 127分, $p=0.103$), 腹腔鏡手術では出血量が有意に少なかった (12.5ml vs 120ml, $p=0.009$)。腹腔鏡手術群では、子宮牽引操作による出血や臓器損傷等の術中合併症を認めず、開腹手術に移行した症例はみられなかった。腹腔鏡手術群と開腹手術群の無病生存率に有意差は認めなかった ($p=0.896$)。【結論】後腔円蓋部へのトロカー留置により子宮牽引操作を行う腹腔鏡下子宮悪性腫瘍手術は、開腹手術とほぼ同等の腫瘍学的成果をあげ、かつ安全に施行し得る術式である。

P-68-2 早期子宮体がん手術における、骨盤部ドレーン抜去至適時期の検討

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【目的】近年当院でも早期子宮体がんに対し腹腔鏡下手術 (TLH+BSO+PLA) を導入し、経験した12例では①術後退院まで平均10.7日であること②骨盤部ドレーン抜去が平均術後8.9日目であり、ドレーンの抜去時期が退院日の規定要因となっている可能性が示唆された。今回骨盤部ドレーン抜去の至適時期について後方視的に検討を行った。【方法】当院で施行した早期子宮体がん手術 (ATH+BSO+PLA または TLH+BSO+PLA) について、ドレーン抜去日・抜去時ドレーン排液量・術後一年間の間に発生したリンパ嚢胞の有無につき比較検討を行った。【成績】開腹群50例 腹腔鏡群12例の早期子宮体がん手術を検討した。患者の平均年齢・BMIは両群で概ね同等であった。全例に手術終了時骨盤部ドレーンを挿入し、術後主治医判断の上抜去を行った。抜去日 (平均術後日数)・抜去時排液量 (l/日) は開腹群で7.5・162ml, 腹腔鏡群で9.0・196mlであった。大部分の症例で主治医が排出量減少と判断し抜去したが、開腹群10例 腹腔鏡群4例にて他の理由で抜去を要した。後者では抜去時排液量が開腹群362ml 腹腔鏡群238mlと多い傾向であったが、全症例において処置を有するリンパ嚢胞形成を認めなかった。また開腹群6例で絶食を要する消化管症状を呈したが、腹腔鏡群では認めなかった。【結論】排出量減少以外の理由でドレーンを抜去した症例では抜去時排液量が多い傾向であったが、その後処置を有するリンパ嚢胞形成は認めなかった。腹腔鏡群においては消化管障害が軽微であるため、早期のドレーン抜去が早期退院につながる可能性があると考えられた。

P-68-3 腹腔鏡下子宮体癌手術における合併症の検討

琉球大学病院

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【目的】子宮体癌に対する腹腔鏡手術における周術期合併症の検討【方法】2015年1月から2020年12月の期間, 子宮内膜異型増殖症または子宮体癌 IA 期の術前診断にて腹腔鏡手術を施行した症例の診療録を後方視的に調査した。患者背景, 手術時間, 出血量, 入院期間, リンパ節摘出数および周術期合併症について検討した。【成績】109例で腹腔鏡下子宮悪性腫瘍手術が施行された。患者背景は, 年齢中央値53歳(35-84), BMI中央値25.8(18.2-41.8), 腹部手術歴32例(29.3%), 糖尿病合併14例(12.8%), 高血圧合併31例(28.4%)であった。術後診断でstageIB以上へ変更となった症例は9例(8.3%), 組織型が特殊型に変更となった症例は6例(5.5%)であった。手術時間の中央値は216分(100-519), 出血量は100ml(5-950), 輸血施行例は3例(2.8%)であった。周術期合併症は腸管損傷1例(0.9%), 腔断端感染10例(9.2%), 腔断端離開1例であった。膀胱・尿管損傷は1例も認めなかった。リンパ節生検が施行された104例のうち, 生検個数の中央値は右4個(0-13), 左4個(0-13)と左右差は認めなかった。リンパ腫7例(6.7%), リンパ浮腫3例(2.9%)を認め保存的加療にて改善した。これらはリンパ節生検個数とは関連しなかった。腔断端感染は体位やバジパイプ挿入方法の改善により現在は認めていない。4例(3.7%)に再発を認め, 2例は術後に組織型が変更となったもの(癌肉腫, 漿液性腺癌), 2例はIA期G1であったもののいずれも追加治療で寛解に至っている。【結論】当科における子宮体癌に対する腹腔鏡手術の周術期合併症はほとんどが保存的療法で改善できるものであったが, 今後も合併症を起こさないための周術期管理が必要である。

P-68-4 肥満を伴う子宮体癌患者に対して腹腔鏡下手術を施行した2症例の検討

岡山大病院

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【緒言】腹腔鏡下子宮悪性腫瘍手術は2014年4月より保険適応となり, 当院でも2019年より施行している。子宮体癌は肥満が発症リスクとなるが, 腹腔鏡手術において肥満患者は通常の症例より高難易度となる。当院にて子宮体癌を疑い, 腹腔鏡下単純子宮全摘と両側付属器切除術を施行したBMIが40以上の2例につき報告する。【症例】症例1:40歳。0経産。遅延月経を主訴に前医受診し, 異型内膜増殖症の疑いにて, 紹介となった。BMI41であった。造影MRIでは異型内膜増殖症または類内膜癌が疑われ, 手術の方針となった。腹腔鏡下単純子宮全摘と両側付属器切除術を施行した。手術は合併症なく終了し, 術後6日目に退院となった。病理組織は子宮体癌IA期, 類内膜癌 GradeIであった。症例2:60歳。2妊2産。不正出血を主訴に前医受診し, 内膜組織診にて類内膜癌 GradeIの診断のため, 紹介となった。BMI40であった。造影MRIで子宮体癌IA期相当の診断であった。症例1と同手術を施行する方針となった。手術は合併症なく終了し, 術後7日目に退院となった。病理組織は子宮体癌IB期, 類内膜癌 GradeIであった。【考察】肥満患者の腹腔鏡下手術には手術時の過剰な脂肪組織による操作スペースの狭さや腹壁の厚さによる鉗子操作の難しさに加え, 麻酔におけるリスク, 碎石位によるコンパートメント症候群や血栓症など様々なリスクを伴う。当院では合併症の発生リスクを考慮し, 肥満を伴う子宮体癌の患者ではリンパ節郭清を省略としている。【結論】高度肥満を伴う子宮体癌において腹腔鏡手術を施行した2例を経験した。肥満患者における腹腔鏡手術は高リスクでもあるために手術の妥当性を十分に考慮し, 手術に臨むべきである。

P-68-5 早期子宮体癌に対する腹腔鏡・開腹手術において, 肥満が手術に及ぼす影響

JCHO九州病院

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【目的】早期子宮体癌に対する腹腔鏡・開腹手術において, 肥満が手術時間に及ぼす影響を明らかにする。【方法】2014年から2021年に早期子宮体癌に対して根治手術を行った症例を対象とし, 開腹術, 腹腔鏡手術それぞれにおいて肥満と手術時間との相関と, 手術成績, 合併症, 再発の有無を後方視的に検討した。【成績】50例の開腹手術症例(開腹群)と42例の腹腔鏡手術症例(腹腔鏡群)を対象とした。BMI25以上の肥満を開腹群で26例52%, 腹腔鏡群で24例57%に認め, それぞれの手術時間は開腹群で平均184分(95%信頼区間167-202分), 腹腔鏡群で平均309分(95%信頼区間290-328分)で腹腔鏡群で長かった。リンパ節摘出例は開腹群で30例60%, 腹腔鏡群で41例97%で, リンパ節摘出例に限った手術時間も腹腔鏡群で有意に長く, 出血量は腹腔鏡群で有意に少なかった。リンパ節摘出例の手術時間は, 開腹群で肥満例平均234分(95%信頼区間200-267分), 非肥満例平均207分(95%信頼区間180-235分), 腹腔鏡群で肥満例平均315分(95%信頼区間285-344分), 非肥満例で平均299分(95%信頼区間272-327分)であった。手術時間とBMIとの順位相関係数(Spearman)ではリンパ節摘出のない開腹群は $\rho=0.4485$ と有意に正の相関を認めたが腹腔鏡群では有意な相関はなかった。合併症発生率に有意差なく, 開腹例の1例のみに再発を認めた。【結論】当科での早期子宮体癌に対する手術で, 腹腔鏡は開腹に比べ手術時間が延長した。しかし肥満が手術時間に及ぼす影響は少なく, 出血量は腹腔鏡で少なかった。腹腔鏡手術は肥満症例に対して有用と考えた。

P-68-6 当院における術前進行期 IA 期子宮体癌の検討

大阪市立総合医療センター

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【目的】当科では子宮体癌 IA 期に対する手術療法として開腹手術, 腹腔鏡下手術, ロボット支援下手術の 3 つの方法を行なっている。2017 年 1 月から 2021 年 9 月の間に術前進行期子宮体癌 IA 期に対して当科で手術療法を施行した症例について検討したので報告する。【方法】術前に子宮体癌 IA 期と診断した症例は, 開腹手術 34 例, 腹腔鏡下手術 23 例, ロボット支援下手術 32 例であり, それぞれ検討した。また, 2018 年以降リンパ節郭清は省略している。【成績】開腹手術は年齢 29~83 歳 (中央値 57 歳), BMI 15.11~36.64 (23.39), 出血量 10~700ml (225ml), 手術時間 94~305 分 (186.5 分), 子宮重量 60~1020g (170g) であった。腹腔鏡下手術は年齢 37~74 歳 (中央値 56 歳), BMI 17.84~35.3 (21.41), 出血量 5~230ml (60ml), 手術時間 146~408 分 (254 分), 子宮重量 20~380g (110g) であった。ロボット支援下手術は年齢 36~73 歳 (中央値 51 歳), BMI 17.23~36.92 (23.17), 出血量 0~200ml (3ml), 手術時間 116~334 分 (192 分), 子宮重量 50~435g (145g) であった。再発は開腹手術では 1 例認め, 術後診断 Serous carcinoma, IB 期, pT1bN0M0 であったが術後化学療法は拒否された症例で, 術後 11 か月後での再発であった。腹腔鏡下手術では 1 例認めたが, 術後診断 Endometrioid carcinoma G2, IIIA 期, pT3aN0M0 の症例であり術後化学療法施行後で術後 3 年 11 か月後での再発であった。ロボット支援下手術では再発は認めていない。【結論】現在のところ, 術前, 術後進行期が IA 期であった症例では, 開腹手術, 腹腔鏡下手術, ロボット支援下手術で再発症例を認めておらず, 早期子宮体癌には低侵襲手術も有効であると再確認した。

P-68-7 当院でのロボット支援下手術の初期経験—44 例の報告—

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【目的】当院で施行したロボット支援下手術の初期成績と問題点および今後の改善点を検討する。【方法】2019 年 6 月~2021 年 10 月に当院で行ったロボット支援下手術 44 例 (良性 33 例, 初期子宮体癌 11 例) の診療録を後方視的に検討した。【成績】子宮全摘のみの 39 例の手術時間 (中央値) 230 分 (111 分-387 分), コンソール時間 162 分 (68 分-315 分), 手術室使用時間 328 分 (176 分-507 分) であった。いずれも徐々に短縮傾向で, いまだプラトーには達していない。また 44 例全例で, 挿管~手術開始まで 45.4 分 (28 分-65 分), 手術開始からロールインまで 25.5 分 (7 分-63 分), ロールインからコンソール開始まで 14.5 分 (4 分-30 分) であった。ロールインやコンソールまでの時間は, 助手を固定したことやカニューレのオペチュレートをディスプレイに変えたことで短縮した。合併症は, 子宮動脈損傷での大量出血 1 例, 腸間膜血腫 1 例, 小腸損傷 1 例であった。また碎石位で術後の下肢痛・腰痛 (コンパートメント症候群の診断には至らず) を 3 例認めたことから, 開脚位に変更し以後同様の症状は認めていない。開脚位は体位セッティングの短縮にもつながった。手術時間を短縮できたことで, 1 日 2 例執刀することが可能になった。【結論】一般的にロボット支援下手術のラーニングカーブは 20 例程度と言われるが, 専攻医や若手スタッフの多い大学病院では手術時間が一定に落ち着くまでにはそれ以上かかると考えられた。まずは術者を固定し経験を重ねて安全を担保したのちに, 若手医師のトレーニングや手術時間短縮の工夫が必要と考えられた。

P-68-8 子宮体癌に対するロボット支援下手術 130 症例の検討

豊橋市民病院

梅村康太, 河合要介, 岡田真由美, 安藤寿夫, 河井通泰

【目的】子宮体癌 1A 期に対するロボット支援下手術は 2018 年 4 月より保険適応となり全国に拡がりつつある。当院では院内倫理委員会承認の上, 2014 年 8 月から子宮体癌に対するロボット支援下手術を開始し, 2021 年 10 月までに 130 症例を経験した。今回, 手術成績やラーニングカーブなどについて検討した。【方法】ロボット支援下手術機器として, INtuitive 社 da Vinci Si, X, X システムを使用して手術を行った。対象患者は子宮体癌 1A 期, G1, G2 症例, 年齢 75 歳以下, BMI40 を上限とした。頭低位は 25 度, カメラポート膈上 3 cm, 右側に第 1, 3 ポート, 左側に第 2, 助手用ポートを配置, サイドドッキングを施行した。平均年齢, BMI, 総手術時間, コンソール時間, 出血量, 摘出リンパ節個数などを検討した。【成績】平均年齢 57.6 歳 (31-76), BMI25.5kg/m² (18-37.5), 総手術時間 210.4 分 (138-271), コンソール時間 162.7 分 (120-217), 出血量 18.2g (5-250), 摘出リンパ節個数 22.5 個 (13-36), 子宮重量 161.5g (55-330) であった。手術開始からコンソール開始までの時間は, 20 症例を経験して以降明らかに短縮した。ロボット支援下手術から開腹術に移行した症例はなかった。輸血を要した症例はなく, Clavien-Dindo 分類 3 度以上の重篤な周術期合併症は認めなかった。術後病理検査で 1A 期, G1, G2 以外と診断された一部の症例は化学療法を追加した。【結論】子宮体癌に対するロボット支援下手術は術中, 術後の大きな合併症なく安全に施行すること可能であった。手術時間に関しても, 開腹術や腹腔鏡下手術と比較して同等であった。

P-68-9 肥満患者に対するロボット支援子宮体癌手術の検討

鹿児島大病院
福田美香

【目的】低リスク子宮体癌に対するロボット手術が保険適用となり当科では2021年3月までに83症例を施行した。肥満症例におけるリスクを非肥満症例と比較することで検討した。【方法】年1月から2021年3月までに初回治療としてロボット支援子宮体癌手術を施行した術前推定進行期IA期（類内膜癌 grade1, 2）の低リスク体癌83例を対象とした。肥満群（BMI30以上）26例、非肥満群57例における患者背景や手術成績・周術期合併症、予後の比較検討を行った。【成績】背景では年齢中央値は肥満群で57.5歳、非肥満群で56歳、BMIは肥満群で34.5、非肥満群で23であった。高血圧症、糖尿病などの合併症を有する割合に差はなかった。手術成績において手術時間、コンソール時間において肥満群で長く有意差を認めたと、出血量、開腹移行率、合併症については差を認めなかった。出血量中央値は両群ともに20ml程度出会った。開腹移行は非肥満群のみで4例あり、いずれも癌の進行によるものであった。術中合併症は、帝王切開術既往後の膀胱損傷、子宮回収時に会陰切開を加えた際の直腸損傷であり、いずれも術中に修復した。周術期合併症では、BMI56の症例で抜管後、喘息発作が出現しICU管理を要した。【結論】時間に若干の延長を認めるものの、手技の困難さに伴う開腹移行は認めず、合併症においても非肥満群と差を認めなかった。肥満患者に対してもロボット手術は安全に施行可能である。

P-68-10 当科におけるロボット支援下手術の現状

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向井百合香, 工藤美樹

【目的】当院では2020年8月よりロボット支援下手術を導入し、子宮良性腫瘍に対するロボット支援下子宮全摘術（Robot-assisted simple hysterectomy；以下、RASH）から開始した。以後1年間で、子宮体癌に対するロボット支援下子宮悪性腫瘍手術（以下、子宮体癌RASH）、ロボット支援下仙骨腔固定術（Robotic sacrocolpopexy；以下、RSC）、リンパ節郭清と適応を拡大してきた。そこで、ロボット支援下手術の導入、適応拡大における安全性を確認するため本検討を実施した。【方法】2020年8月から2021年10月に実施したロボット支援下手術と腹腔鏡手術を対象に、手術時間、術中出血量、合併症などについて後方視的に比較検討した。腹腔鏡手術は、全腹腔鏡下子宮全摘出術（Total laparoscopic hysterectomy；TLH）、リンパ節郭清を伴う子宮体癌TLH、腹腔鏡下仙骨腔固定術（Laparoscopic sacrocolpopexy；LSC）を対象とした。【成績】RASHが51例、リンパ節郭清を伴う子宮体癌RASHが3例、RSCが6例であった。同時期に実施したTLHは18例、リンパ節郭清を伴う子宮体癌TLHは7例、LSCは13例であった。手術時間中央値と出血量中央値は、RASHが123（77-313）分、25（3-130）g、TLHが147（103-258）分、20（2-245）gと2群間で有意差を認めなかった。リンパ節郭清を伴う子宮体癌症例も同等の成績であった。RSCとLSCでは、205（175-235）分、14（9-20）gと189（159-265）分、20（5-85）gで有意差を認めなかった。また、すべての症例において重篤な周術期合併症を認めなかった。【結論】ロボット支援下手術は導入から1年間で適応も拡大したが、導入時より腹腔鏡手術と同等の質を保ちながら、安全に実施できていると考える。

P-69-1 子宮内膜異型増殖症と子宮体癌に対するMPA療法

防衛医大病院
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【目的】子宮内膜異型増殖症（Atypical endometrial hyperplasia：AEH）や子宮体癌（Endometrial carcinoma：EC）の標準治療は、手術による子宮摘出だが、若年発症で妊孕性温存を希望する場合にMPA療法を行うことがある。当院でMPA療法を施行した症例の後方視的検討を行ったので報告する。【方法】2010年1月～2021年8月の間に、当院でAEHまたはECと診断され、MPA療法を施行した症例を対象とし、患者背景、効果、再発の有無、再発治療、妊娠転帰について後方視的に検討した。【成績】対象は7例で、年齢中央値34.5（27-41）歳、BMI中央値24.4（18.6-63.8、BMI30以上は2例）、全例未経産だった。癌家族歴があった症例は2例で、MPA療法開始前の病理診断はAEHが4例、IA期のEC grade1が3例だった。MPA療法を完遂した例は5例、MPA無効が2例、再発が2例だった。無効例の1例はMPA療法を26週施行したがEC grade1が消退せず、根治手術によりIB期と判明した。もう1例はAEHで投与16週に腔転移が判明、組織型は明細胞癌、IIIB期と診断して根治手術を施行した。再発例の2例は、どちらもEC grade1、初回治療でCRに至ったが、1例は治療後6年目で再発し根治手術を施行してIA期と診断し、もう1例は、治療後11か月で再発し、再度MPA療法を行って再度CRに至った。完遂例のうち1例は、治療後10か月で自然妊娠し、自然分娩で生児を得た。【結論】MPA療法は妊娠に至る例もあるが、無効例が存在し、晩期再発にも注意を要する。再発後も再度MPA療法を行うことで有効な症例もあり、患者の希望と医学的安全性を考慮した慎重な管理が必要である。

P-69-2 進行再発子宮体癌に対する黄体ホルモン療法の経験

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【目的】進行・再発子宮体癌に対する黄体ホルモン療法におけるホルモンレセプター以外の効果予測因子についてのエビデンスは乏しい。今回、進行・再発体癌に対し Medroxyprogesterone acetate (MPA) を使用した症例について報告する。【方法】2005年1月から2020年12月にMPAを処方した176例(乳癌・初期子宮体癌等含む)のうち、再発・進行体癌症例10例を対象とし、投与期間、有効性、有害事象について検討した。【成績】年齢の中央値は62.5(47-81)歳、BMIは20.2(16.9-28.1)、組織型は類内膜癌G1が4例、G2が4例、G3が1例、不明が1例であった。内服期間は3.85(0.5-79.1)か月で、3か月以上内服の継続が可能であった5症例および画像で病変の縮小が確認できた1症例を有効とすると、有効例はG1の4例中2例、G2の4例中3例、G3の1例中0例であった。ER、PgRは各1例のみに検査が行われER陰性1例・PgR陽性1例とともに有効例であった。MPA開始までの化学療法レジメン数は有効6例で1(0-2)、無効4例で3(1-6)、再発部位は有効6例では全例が1臓器、無効4例では1臓器が1例、複数臓器が3例であった。腔断端再発に対し放射線治療が行われた後にMPAが投与された5例中3例が有効であった。1例で視野異常を認め中止により軽快、別の1例では糖尿病が増悪しインスリン導入を要したが、血栓症等の重篤な有害事象は認めなかった。【結論】MPA療法は、類内膜癌G2や、放射線照射後の腔断端再発でも有効な症例があった。前治療の化学療法レジメン数が少ない症例や、再発部位が1臓器のみの症例で3か月以上の投与が可能なが多く、MPA療法により化学療法を行わない期間が延長できる可能性があると考えられた。

P-69-3 子宮腺筋症を合併した子宮体がんについての検討

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【目的】子宮体がんは術前の推定進行期によって術式が異なり、低侵襲手術も考慮されるため、術前に正確に進行期を推定することが重要である。しかし子宮腺筋症を合併した場合、MRIによる筋層浸潤の程度の評価はしばしば困難である。今回、当院で診察した子宮腺筋症を合併した子宮体がんの19例について、術前の画像評価による筋層浸潤の程度と術後の病理組織評価による筋層浸潤の程度の乖離などを検討した。【方法】対象は、2016年1月～2021年10月に当院で手術を施行した子宮腺筋症を合併した子宮体がん19例。診察録より、患者背景、術前推定進行期、術後進行期、筋層浸潤の程度、組織型などを後方視的に調査した。【成績】年齢は46歳～77歳(中央値:56歳, 平均値:60歳)で、手術時に閉経していたのは13例(68%)であった。組織型は、endometrioid carcinomaが17例(89%)、serous carcinomaが1例(5%)、carcinosarcomaが1例(5%)であった。子宮腺筋症と併存していたのは17例(89%)、腺筋症の癌化が疑われたのは2例(11%)であった。術前の画像評価による筋層浸潤の程度に比べて術後の病理組織評価による筋層浸潤が高度であったのは3例(16%)、軽度であったのは2例(11%)、同程度であったのは13例(68%)、評価不能は1例(5%)であった。【結論】子宮腺筋症を合併した子宮体がんでは、画像所見から筋層浸潤の程度を評価することが難しく、過小評価もしくは過大評価のいずれの可能性もあり、術式決定に留意しておく必要がある。

P-69-4 妊孕性温存を希望する子宮体癌および子宮内膜異型増殖症患者に対する子宮内膜全面搔爬に子宮鏡下子宮内膜腫瘍摘出術を併用する試み

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【緒言】子宮内膜に限局する子宮体癌(類内膜癌 GradeI)および子宮内膜異型増殖症患者に対する妊孕性温存療法として子宮内膜全面搔爬による可及的な病巣摘除と黄体ホルモン療法が行われるが、われわれはより徹底的な腫瘍減量を目指し、子宮内膜全面搔爬に子宮鏡下子宮内膜腫瘍摘出術を併施した5症例を経験したので報告する。【症例】子宮体癌2例、子宮内膜異型増殖症3例、年齢は28歳から40歳で、全例に月経不順を認めた。2例が多嚢胞性卵巣、3例がBMI>35の肥満であった。子宮内膜全面搔爬と子宮鏡下子宮内膜腫瘍摘出術を行ったのち、直近の妊娠を希望しない患者には当院臨床研究「子宮体癌(高分化型類内膜癌)および子宮内膜異型増殖症に対する子宮内黄体ホルモン放出システム治療に関する研究」に則り LNG-IUS を装着した。挙児希望のある症例にはMPA療法を行い速やかな妊娠成立のため補助生殖医療を開始した。子宮体癌の1例目は妊孕性温存療法後の再発で、子宮鏡下子宮内膜腫瘍摘出術後MPA療法を施行。寛解後ARTにより妊娠が成立、帝王切開で分娩となった。子宮体癌の2例目は腫瘍量が多く子宮内膜全面搔爬で腫瘍の完全摘除ができず、後日子宮内膜全面搔爬と子宮鏡下子宮内膜腫瘍摘出術・子宮筋層生検を施行。LNG-IUSを装着し41か月間寛解を維持している。子宮内膜異型増殖症の3例はいずれも初回手術で子宮内膜全面搔爬と子宮鏡下子宮内膜腫瘍摘出術を併用、LNG-IUSを装着し20-48か月再発なく経過観察中である。【結語】子宮体癌および子宮内膜異型増殖症に対する妊孕性温存療法のさい、子宮鏡下子宮内膜腫瘍摘出術を行うことにより、子宮内膜全面搔爬単独よりも確実に腫瘍減量ができる可能性が示唆された。

P-69-5 子宮体癌において術前 PET/CT 検査における病巣の SUVmax 値は再発予後因子になり得る

杏林大

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【目的】婦人科腫瘍における PET/CT 検査の有用性は高く、術前の病期診断や治療方針決定、再発診断に重要な画像診断法である。今回、術前に PET/CT 検査を施行した子宮体癌症例について、PET/CT SUVmax 値と再発リスク因子との関連について検討した。【方法】当院にて 2016 年 5 月から 2021 年 8 月までに、術前 PET/CT 検査を行い、開腹または腹腔鏡下手術を行った 105 例を対象とした。PET/CT SUVmax 値を測定し、再発リスク因子とされる組織型、進行期、筋層浸潤・脈管侵襲・頸部間質浸潤・子宮外病変の有無および予後について後方視的に検討した。【成績】術後進行期は IA 期 64 例、IB 期 18 例、II 期 5 例、IIIA 期 3 例、IIIB 期 4 例、IIIC1 期 3 例、IIIC2 期 5 例、IVB 期 3 例、組織型は類内膜癌 G1 72 例、G2 11 例、G3 4 例、特殊型 18 例であった。進行期別、組織型別に比較検討し、SUVmax 値に有意差はなかったが、筋層浸潤、脈管侵襲では有意差を認めた ($P < 0.05$)。腫瘍径 4cm 以上でも有意差を認めた ($P < 0.01$)。頸部間質浸潤・リンパ節転移・子宮外病変の有無や腹水細胞診では有意差は認めなかった。再発低リスク群と中リスク以上群で比較検討したところ、中リスク以上では有意に SUVmax 値が高値であった ($p < 0.001$)。ROC 曲線より SUVmax の Cut off 値を 15.6 と算出し、Kaplan-Meier 法にて予後を検討したが無病生存率に有意差はみられなかった。【結論】術前に PET/CT 検査を施行した子宮体癌症例において、筋層浸潤・脈管侵襲を認め、最大腫瘍径 4cm 以上では SUVmax 値が有意に高値であり、進行期推定の指標として有用である可能性が示唆された。また再発中リスク以上では有意に SUVmax 値が高値であり、SUVmax 値と予後予測との関連性が示唆された。

P-69-6 当科における子宮体がんの治療の変遷と成績について

順天堂大練馬病院

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【目的】子宮体がんへの手術アプローチはこの 10 年間で腹腔鏡下手術、ロボット支援へと低侵襲手術が急速に普及してきた。当院における過去 10 年間の子宮体癌の治療の変遷と成績を報告する。【方法】子宮体がんは増加傾向にあり、早期例に対しては低侵襲手術が急速に普及してきた。当院における過去 10 年間の子宮体癌の治療の変遷と成績を報告する。【成績】総症例数は 407 例 (IA 期 254 例、IB 期 75 例、II 期 12 例、III 期 35 例、IV 期 31 例) で平均年齢は 60.1 歳であった。IA 期 252 例に対して手術 (開腹 202 例、腹腔鏡 52 例、ロボット 16 例) を行った。37 例に対して化学療法を行い、再発は開腹の 11 例 (4.3%) であり (観察期間 57.0 か月)、3 例 (1.2%) が原病死となった。IB 期では 73 例 (開腹 64 例、腹腔鏡 4 例、ロボット 2 例) に手術が行われた。術後化学療法は 52 例 (71.2%) に行われ、再発は開腹の 7 例 (観察期間 52.8 か月) であり、7 例 (9.6%) が原病死となった。II 期の 11 例はすべて開腹手術であった。再発例は 3 例で、2 例が原病死となり、術後化学療法を希望しなかった 1 例が担癌で生存中 (120 か月) である。III 期では 34 例 (開腹 31 例、腹腔鏡 1 例、ロボット 1 例) に手術が行われ、1 例を除きすべてに術後化学療法が行われた。再発例は 11 例であり (観察期間 41.8 か月)、9 例が原病死となった。IV 期 31 例はすべて IVB 期であり、無病生存者が 6 例 (19.4%) であり、外科的切除に加え化学療法が奏効し、残存部位に放射線療法を行った症例である。【結論】今後増加する子宮体がんに対して当院でも安全に低侵襲手術が導入できた。進行例に対しては集学的治療が奏功する例があり、術後化学療法の選択肢が増えることを期待したい。

P-69-7 子宮体癌 IV 期における組織型タイプ別の臨床症状及び予後の検討

宮崎大附属病院

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【目的】当院における子宮体癌 IV 期における組織型タイプ別の臨床症状及び生命予後を明らかにする。【方法】2007 年~2017 年の 11 年間に当院で診療した子宮癌肉腫、子宮肉腫等を除く子宮体癌 230 例のうち IV 期の 22 例 (9.5%) を対象に後方視的に観察研究を行った。進行期分類 (FIGO 2008) は子宮内膜組織診、摘出子宮の病理所見、胸腹部 CT 検査、骨盤部 MRI 検査に基づき行った。類内膜癌 G1, G2 をタイプ 1 群 (1 群, $n=11$) とし、それ以外の G3, 漿液性癌等をタイプ 2 群 (2 群, $n=11$) とし検討を行った。2 群間の検定は χ^2 乗検定、マン・ホイットニー U 検定、ログランク検定を用い $P < 0.05$ を有意差ありとした。【成績】1, 2 群の年齢の中央値は 58 (範囲: 48-86), 62 歳 (範囲: 42-75) で有意差はなかった。病院受診の契機となった臨床症状は不正性器出血が 1 群 91% (10/11), 2 群 33% (3/9) と 1 群に有意に多く、腹部膨満等の腹部症状は 1 群 10% (1/10), 2 群 67% (6/9) と 2 群に多かった。生存期間の中央値は 1 群 41 か月、2 群 12 か月と 2 群で有意に短かった、 $P = 0.005$ 。【結論】子宮体癌 IV 期の症例はタイプ 1 では不正性器出血、タイプ 2 では腹部症状で当院を受診しているのが明らかになった。またタイプ 2 ではタイプ 1 に比較し生命予後は有意に不良であった。

P-70-1 急速に進行し、病理解剖にて診断された SMARCA4 欠損子宮肉腫 (SDUS) の一例

旭川医大

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SMARCA4 欠損子宮肉腫 (SDUS) は、SMARCA4・BRG1 の欠損を特徴とする未分化の子宮間葉系悪性腫瘍である。急速に進行し、病理解剖にて SDUS と診断された症例を経験したため報告する。【症例】46 歳 0 妊の女性で、腹痛と腰痛で初診した。CT で骨盤内に巨大な子宮腫瘍があり、腹膜播種と後腹膜リンパ節腫大を認めた。LDH は 451 と上昇していた。子宮内膜組織診では high grade sarcoma の診断であった。第 11 病日の PET-CT では、リンパ節転移、骨転移、腹膜播種、肝転移を認め、初診時にはなかった両側の水腎症が出現していた。尿管ステント留置を行い、第 14 病日に Doxorubicin 単剤化学療法を開始した。第 28 病日に吐血と Hb 4.6 の貧血で入院し、十二指腸潰瘍からの出血を内視鏡的に止血した。第 33 病日に無尿となりその後も腎機能は改善せず、全身状態が急速に悪化し第 44 病日に死亡した。家族の同意のもと病理解剖を行った。腹腔内は長径 35cm の灰白色の腫瘍で充満し、腹壁への浸潤と癒着を認めた。腫瘍は腎臓・膀胱・直腸周囲を取り巻き骨盤内臓器は一塊となっていた。肉眼的に子宮と両側卵巣は同定困難で、腫大リンパ節との境界も不明瞭であった。組織学的には、類円形に腫大し偏在する核と明瞭な核小体を有する均一な腫瘍細胞が緩い結合性を示して増殖していた。著明な静脈侵襲、リンパ管侵襲を認め、周辺臓器への直接浸潤と肝・肺・肺門リンパ節・腹腔内リンパ節・大網への転移を認めた。免疫染色では BRG1/SMARCA4 陰性で SDUS と診断した。【結論】新たに報告された稀な疾患である SDUS の 1 例を経験した。SDUS の特徴的な病理学的所見を認識することは、正確な診断に必要であり予後予測因子となり得る。

P-70-2 変性子宮筋腫と鑑別が困難であった低異型度子宮内膜間質肉腫の治療経験

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【背景】低異型度子宮内膜間質肉腫はまれな子宮体部悪性腫瘍であり、また術前の画像検査において変性子宮平滑筋腫との鑑別は容易ではない。我々は閉経後に増大する子宮腫瘍に対し、術前には最終的に変性子宮筋腫と画像診断していたが、術後病理検査により低異型度子宮内膜間質肉腫と診断された一例を経験したので報告し文献的考察を加える。【症例】49 歳、3 経産婦。近医で子宮筋腫に対して定期的にフォローされていた。閉経後にも関わらず半年前より腫瘍は増大傾向にあり、精査目的に当院を紹介受診した。骨盤造影 MRI 検査では子宮体部に 39mm 大の腫瘤を認めた。この腫瘤の内部に造影効果を伴う嚢胞構造を認め、さらにその内部に拡散強調像で高信号、ADC map 低値を示す不整な充実部分を伴っていた。以上の所見から子宮肉腫の可能性が考えられたため、全身転移の有無を検索するため全身 FDG-PET/CT 検査を施行したが、子宮腫瘍の嚢胞構造内部の充実部分にのみ軽度の FDG 集積を認め、遠隔転移を疑う所見を認めず、総合的に変性子宮筋腫と画像診断した。腹腔鏡補助下腔式子宮全摘術、両側付属器切除術を施行した。摘出標本は子宮体部に 55mm の腫瘤を認め、病理組織学的には一部に核異型を伴う細胞密度の高い富細胞性局面を認め、免疫染色では α -SMA 陰性、CD10 陽性像を認めた。以上より子宮平滑筋腫および低異型度子宮内膜間質肉腫 stageIB と診断され現在慎重にフォローアップしている。【考察】低異型度子宮内膜間質肉腫は術前の画像診断は困難であり、子宮筋腫などの良性腫瘍として手術加療後に本疾患と診断されることも珍しくない。臨床経過や画像検査などにつき文献的考察を含め検討を行った。

P-70-3 子宮体部術後の難治性リンパ嚢胞に対してリンパ管造影を行い、改善を認めた 2 例

聖マリアンナ医大

石井雅人, 金森 玲, 大原 樹, 八幡将喜, 武永 智, 今井 悠, 竹内 淳, 横道憲幸, 久慈志保, 戸澤晃子, 長谷川潤一, 鈴木 直

【緒言】後腹膜リンパ節郭清では術後合併症で 10~50% にリンパ嚢胞やリンパ漏などを生じ、再発を繰り返す場合もある。難治性リンパ嚢胞に対してリンパ管造影を行った 2 例を経験したので報告する。【症例 1】45 歳、0 妊 0 産。前医で子宮体癌 III 期 (類内膜癌 Grade3) に対して単純子宮全摘+両側付属器切除+後腹膜リンパ節郭清+大網切除術を施行した。術後リンパ液貯留認め持続ドレナージ行い、改善したため退院した。退院 2 日後から呼吸苦出現し当院救急搬送となった。CT 検査で肺動脈血栓、総腸骨・内腸骨静脈血栓、傍大動脈領域に 15cm 大のリンパ嚢胞を認め、穿刺ドレナージ、開胸血栓除去術を施行した。ドレナージ留置後も 1000ml/日程度排液が持続したため、留置後 22 日目にリンパ管造影を施行した。その後排液量は減少し、留置後 44 日目に抜去した。その後再発は認めなかった。【症例 2】72 歳、3 妊 3 産。子宮体癌 IIIC2 期 (明細胞癌) に対して単純子宮全摘+両側付属器切除+後腹膜リンパ節郭清+大網部分切除術を施行した。術後 50 日目の CT 検査で右傍結腸溝に 18cm 大、左骨盤内に 20cm 大のリンパ嚢胞を認めた。穿刺ドレナージを施行した。排液量が 200ml/日程度持続したため、留置後 27 日目にリンパ管造影を施行した。造影翌日より排液量は減少し、留置後 32 日目に両側とも抜去した。抜去 1 か月後も再発は認めなかった。【結語】リンパ漏は、保存的治療で改善しない場合に開腹結紮術などの外科的治療も考慮されるが、2 症例では持続ドレナージで改善なく、リンパ管造影後より効果を認め、再発もなかった。穿刺ドレナージのみで改善しない場合、外科的治療を検討する前に、リンパ管造影が有用となる可能性がある。

P-70-4 内膜病変を伴わず筋層内に嚢胞性病変を示した漿液性癌の1例

大阪医科薬科大

橋田宗祐, 福西智美, 塩見まちこ, 入江惇太, 齊藤駿介, 吉田篤史, 井淵誠吾, 村上 暉, 西江瑠璃, 上田尚子, 田中良道, 大道正英

子宮体部漿液性癌は子宮内膜癌の約10%を占めるが、子宮内膜癌関連死亡の約40%を占める予後不良の疾患である。60代以降の高齢者に多く、社会の高齢化に伴い今後も診療の機会が増加すると予想される。一般に、子宮体部漿液性癌は萎縮性内膜や内膜ポリープを背景に発生する。今回、内膜病変や内膜ポリープを認めず、子宮体部筋層に嚢胞性病変を示した漿液性癌の症例を経験した。症例は72歳、2妊2産。臍部腫瘍を主訴に受診した。造影MRIでは骨盤内に壁肥厚を伴う嚢胞性病変を認め、壁肥厚部位には造影効果を認めた。嚢胞性腫瘍が子宮由来か卵巣由来かは判定困難であった。PET-CTでも嚢胞の壁肥厚部および臍部、腹腔内に異常集積を認め、進行卵巣癌が疑われた。腔鏡診で子宮腔部は大きく腹側に偏位し外子宮口は視認できず、内膜組織の採取は出来なかった。腫瘍マーカーはCA-125:2010U/mlと高値、CA19-9、CEAは正常範囲内であった。試験開腹手術を行ったところ、両側卵巣は肉眼的に正常であり、子宮体下部筋層内に嚢胞状の腫瘍、大網や腸間膜、臍部に転移巣を認めた。腫瘍は直腸筋層に浸潤しており完全摘出には腸切除および人工肛門造設が不可避であったが、予後を考慮して腸切除は行わずに子宮・両側付属器・大網・臍腫瘍を摘出し、腫瘍の一部が直腸漿膜面に残存した状態で手術を終了した。病理診断はmalignant tumor of uterine body, serous carcinomaであった。大網、臍部にも同様の腫瘍を認めた。免疫染色ではp53陽性であった。追加治療としてTC療法を行っている。漿液性癌は内膜病変を伴わず子宮体部筋層に嚢胞性病変を示し得る。骨盤内に嚢胞性病変を認めた場合には、本疾患も考慮するべきである。

P-70-5 傍大動脈リンパ節腫大を伴う子宮体癌症例において腫大したリンパ節は悪性リンパ腫であった1症例

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傍大動脈リンパ節腫大を伴う子宮体癌に対し手術加療を行なった結果、リンパ節腫大は悪性リンパ腫によるものであった症例を経験した。症例は75歳。202X年10月、主訴は不正性器出血で前医受診。子宮内膜肥厚を指摘され子宮体癌疑いとして202X年11月当院紹介受診。術前MRIで子宮体部にDWIで高信号を示す5cm大の腫瘍が確認され、造影CTでの遠隔転移スクリーニングでは傍大動脈リンパ節(326b2領域)の腫大を確認した。cT1aN2M0、IIIC2期として202X年12月腹式筋膜外単純子宮全摘術、両側付属器切除術、骨盤リンパ節郭清、傍大動脈リンパ節郭清を行なった。動脈間リンパ節は著明に腫大しており、破綻のないように完全摘出を行なった。術後病理診断ではEndometrioid Adenocarcinoma G3 pT1aN0M0。リンパ節病変は濾胞性リンパ腫の診断であった。血液内科にて骨髄穿刺を含む精査をし、子宮体癌の治療を優先する方針として術後化学療法6クール施行し現在SDを維持している。

P-70-6 胆のう転移を認めた子宮平滑筋肉腫の長期生存例

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【緒言】子宮平滑筋肉腫は、子宮体部悪性腫瘍の1~2%に発生する。肺や肝臓などへの血行性転移を早期に認めるため、I期の5年生存率でも55.4%と予後が悪い。今回、発症から約11年と長期生存を認め、稀な転移臓器である胆のうへの再発を認めた子宮平滑筋肉腫の1例を経験した。【症例】65歳、3妊2産。54歳時に子宮平滑筋肉腫IB期(pT1bN0M0)に対して、腹式単純子宮全摘術+両側付属器切除術+骨盤・傍大動脈リンパ節郭清術+大網切除術+脾臓摘出術を施行した。後療法としてDocetaxel+Gemcitabine (DG) 6コースを施行し、寛解した。8年後、肺左下葉の平滑筋肉腫再発に対して胸腔鏡補助下左肺底区域切除術を施行した。後療法としてDoxorubicin 6コースを施行し、寛解した。更に2年後、S状結腸と左外腹斜筋への平滑筋肉腫再発と、原発性胆のう癌を疑われ、内視鏡的粘膜炎切除術、腹腔鏡下胆のう摘出術を施行した。術後病理診断はS状結腸、胆のう病変ともに平滑筋肉腫再発だった。後療法としてDG 6コースを施行し、部分奏功だった。現在は、病勢の進行認めず定期的な経過観察を継続している。【結語】胆のう転移を認めた子宮平滑筋肉腫の長期生存例を経験した。転移性胆のう腫瘍の割合は0.46%と非常に稀であり、平滑筋肉腫の胆のう転移はこれまで1例のみの報告である。また、本症例は遠隔転移を繰り返しているが、手術による遠隔制御ができています。予後の悪い子宮平滑筋肉腫においても、定期的な経過観察と手術療法などの積極的な制御を行うことで長期生存が期待できる。

P-70-7 繰り返す子宮内膜ポリープ様病変に対して、免疫染色で子宮腺肉腫の診断に至った一例

関西ろうさい病院

田口友美, 上杉俊太郎, 北島 遼, 国本沙紀, 大久保理恵子, 尾上昌世, 吉岡恵美, 後藤摩耶子, 高田友美, 堀 謙輔, 伊藤公彦

子宮腺肉腫は稀な疾患であり、病理診断で良性疾患と過小評価されることがある。今回、繰り返す子宮内膜ポリープ様病変に対して、免疫染色を用いて子宮腺肉腫と診断し得た症例を経験した。症例は51歳、3経産。不正性器出血、膣からの腫瘍脱出感を主訴に前医を受診。頸管より腔内に脱出する腫瘍を摘除され、病理診断は子宮頸管ポリープであった。その後も2-3か月毎に腫瘍の増大を認め、その都度経腔的に摘出され、病理診断は子宮内膜ポリープであった。精査のために当科に紹介後に実施した経頸管的腫瘍摘出術 (TCR) の病理診断も、子宮内膜ポリープであった。TCR後3か月で再度、頸管より腔内に脱出する腫瘍を認めた。TCR後4か月で、前医で再度腫瘍摘除がなされ、子宮腺肉腫と診断されたため、当科に再紹介となった。TCR時の摘出標本に免疫染色を加えたところ、Desmin (+), SMA (+), ER (一部+), CD10 (-), MIB-1は高い領域で60%であり、腺肉腫と診断修正がなされた。TCR後6か月時に、開腹子宮全摘術+両側付属器摘出術を実施した。最終診断は、Adenosarcoma with sarcomatous overgrowth (FIGO stage IB) となった。子宮腺肉腫の診断は困難な場合があり、子宮内膜ポリープと診断されても病変が繰り返す場合には、免疫染色を含めた標本の再検討による慎重な鑑別が必要である。

P-70-8 活性化リンパ球継続輸注下で、肺転移巣の摘出と左腎摘出を経て完治した子宮平滑筋肉腫の一例

名鉄病院¹, 水谷内科小児科²片平智行^{1,2}, 細井延行¹

A氏女性、75歳、発症時58歳。1994年子宮平滑筋腫が見つかりフォローを開始。1998年子宮頸部高度異形成の治療後、2007年4月にMRI画像で子宮平滑筋肉腫が強く疑われ、同5月子宮全摘および両側卵巣卵管摘出術が施行された。術後の組織学診断において肉腫と診断された。同年7月、1クルールの化療の後、活性化リンパ球輸注療法のみで切り替えた。2008年12月、2か所の右肺転移が検出され、両方の肺転移巣を摘出した。その後、肺における再発は認められなかったが、2010年10月、非常に稀なケースと思われる腎転移を認め摘出した。幸い転移は左腎に限局していたため、摘出で危機を乗りきることができた。2018年10月、完治したと判断し活性化リンパ球輸注療法を中止。その後、新たな転移は認められず、A氏は健康人として生活しており、術前術後を除いて高いQOLを維持し続けた。この研究の中で特記すべきことの一つとして、肺転移巣を成功裏に切除できたことが挙げられる。腎摘出標本の免疫染色結果によれば、腫瘍の周囲及び内部にグランザイムB陽性のCD8陽性細胞障害性Tリンパ球の集簇が証明された。このことから、活性化リンパ球はびまん性の転移を抑える力があつたとも考えている。腎摘出後10年経過、活性化リンパ球輸注療法を中止して3年経過し、患者は通常の社会生活を送っている。子宮平滑筋肉腫と肺・腎転移を含め完治した症例であると思われる。

P-70-9 AP療法が奏功した再発未分化子宮肉腫の1例

千船病院

北口智美, 吉田茂樹, 光岡真優香, 小川史子, 二木ひとみ, 小倉直子, 河谷春那, 北 采加, 三木玲奈, 北井沙和, 大木規義, 村越 誉

【緒言】未分化子宮肉腫はまれな腫瘍であり、いまだ標準治療法は確立されていない。今回、AP療法が奏功した未分化子宮肉腫の1例を経験したので報告する。【症例】症例は51歳女性。腹痛を主訴に当院救急外来を受診し、直腸穿孔・穿孔性腹膜炎の診断でハルトマン手術を施行された。その際に15cm大の子宮腫瘍および両側卵巣腫瘍を認めた。骨盤部造影MRI検査で、子宮悪性腫瘍および付属器転移の可能性が示唆されたため、後日開腹手術を施行した。術中所見でるゝいと腫大して摘出困難な多発リンパ節転移を認め、腹式単純子宮全摘術、両側付属器切除術を施行した。病理組織検査で左卵巣転移を認め、未分化子宮肉腫 pT2aNxM0 の診断だった。術後1か月後で退院し、術後2か月の胸腹部CT検査で骨盤内および複数の後腹膜リンパ節、脾臓に転移・再発を疑う所見があり、他院でパゾパニブによる治療を開始。術後6か月で脳転移を認め、放射線治療が施行された。パゾパニブの治療経過中に直腸断端・腔断端・骨盤内再発巣および腸管に瘻孔形成があり、感染を伴ったため当院でドレナージ術を行った。瘻孔形成・腸管穿孔をきたしたためパゾパニブ治療を中止し、状態安定後、初回治療から1年経過し再発巣に対して当院でAP療法を開始した。骨盤内の再発巣は著明に縮小し、PRと判断した。6コース施行後、画像検査で病巣の指摘が困難となった。約6か月の経過観察後、現在は骨盤内の再々発巣に対して同化学療法を継続している。【結語】未分化子宮肉腫は治療がきわめて困難である。今回、AP療法が奏功した一例を経験し、再発・進行時の化学療法として有用である可能性が示唆された。

P-70-10 TCRを施行または検討した子宮肉腫であった3例佐野病院
井上滋夫

【症例1】39歳。過多月経，貧血。MRI T2強調画像で子宮体部左側後壁に6.9cmの境界明瞭な不均一高信号腫瘍を認め，変性したtype2粘膜下筋腫またはAPAMを疑った。レゴリクス8週服用で4.3cmに縮小しTCRを行った。術中所見では腫瘍切開面に腫瘍性出血や壊死はなく，平滑な小腫瘍が集合する特異な所見が見られた。病理組織診断は低悪性度子宮内膜間質肉腫であった。【症例2】67歳。閉経後増大傾向があり肉腫の可能性が否定できないとして子宮全摘を勧められていたが，TCRを希望し受診した。MRI T2強調画像で子宮体部左側前壁に12.0cmの境界明瞭，T1強調画像で低信号の腫瘍を認め，変性の強いtype2粘膜下筋腫または子宮肉腫を疑った。TCRを強く希望したため生検としてTCRを行った。術中所見では腫瘍切開面に腫瘍性出血や壊死はなく変性子宮筋腫様であった。病理組織診断は平滑筋肉腫であったので腹式子宮全摘が行われた。【症例3】45歳。過多月経，貧血。MRIでは子宮体部右側後壁に9.6cmのT2強調画像で低信号境界明瞭な腫瘍を認め，type2粘膜下筋腫を疑った。TCRを計画し，リュープロレリン3.75を2回投与したところ6.9cmに縮小した。しかし3回投与後に7.9cmと増大傾向に転じたため，子宮肉腫を疑い腹式子宮全摘が行われ，病理組織診断は平滑筋肉腫であった。子宮肉腫の術前診断はMRIにより可能になったが変性子宮筋腫と鑑別困難な例がある。子宮腔内に隆起し筋層との境界が明瞭なら生検としてのTCRが可能で針生検より診断精度が高いが，診断的治療として円錐切除のように確立されたものではない。偽閉経療法で一旦縮小する子宮肉腫があるので，術前治療として行う場合に腫瘍径の正確な測定は重要である。

P-70-11 ドキソルピシンにて手足症候群を来した一例八尾市立病院
永井 景，日野友紀子，松浦美幸，重光愛子，佐々木高綱，山田嘉彦

【緒言】手足症候群（以下HFS）は重症化するとQOLを大きく損なう。ドキソルピシン（以下DOX）でHFSの報告はほとんどない。今回我々はDOX投与によってHFSを来した症例を経験したので報告する。【症例】54歳，未婚，0妊0産。子宮平滑筋肉腫IB期。X年10月に他院で子宮肉腫を疑い腹式子宮全摘術施行。術後に平滑筋肉腫と診断されたX+2年8月に多発肺転移・骨転移が判明し，11月に当科紹介となった。デノスマブとDOX 75mg/m²の投与を開始した。2コース目day20頃より掌蹠に紅斑を認め，徐々に悪化し痛みを伴うようになり，Grade2のHFSと診断した。ステロイド剤塗布で改善したが，治療は4w延期となった。3コース目に保湿剤・アيسグロブ等を使用したところ，HFSは発症しなかったが，病巣の増大と新規病変の出現を認めたため，DOX療法は終了した。【考察】DOXによるHFSの文献報告はなかったが，18例の医薬品副作用報告があり，その内，経過が把握されている6例は全て改善し，投薬の続行は可能であった。動物実験でDOXの微少な漏出が皮膚内の金属イオンと反応し，活性酸素を生じさせ，これが表皮細胞の炎症性サイトカインの産生を即し，表皮細胞のアポトーシスを誘発し皮膚障害を起こすことが報告されている。リポソーム化ドキソルピシンはDOXをリポソーム化することにより骨髄抑制・心毒性・脱毛等の副作用は軽減されたがHFSを認めるようになったとされているが，DOXでも化学療法直後に掌蹠のように皮膚への圧迫が起き易い部位にはDOXの微少な漏出をきたす可能性があり，HFSを起こすリスクがあると考えられた。【結論】DOX単剤投与でのHFSは稀な副作用ではあるが，PLDに準じた指導が必要な可能性が示唆された。

P-71-1 子宮筋腫と子宮肉腫を術前に鑑別するアルゴリズム作成のための研究

Kamogawa Study

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【目的】子宮筋腫と子宮肉腫の治療前に単純MRIと血清LDH値を用いて簡便に子宮肉腫を100%の感度で拾い上げることを目的に作成した診断アルゴリズムを多施設共同研究で検証する。【方法】1986年1月から2005年3月の1,387例（癌肉腫を除く，sample A，子宮肉腫18例，子宮筋腫1,369例）において，MRI画像上①T2WI-high，②T1WI-high，③腫瘍辺縁の不明瞭，④血清LDH値上昇の有無を後方視的に解析し，肉腫診断のためのアルゴリズムを作成した。2011年1月から2013年12月の302例（sample B，肉腫9例，筋腫293例）と，2014年1月から2018年12月の663例（sample C，肉腫11例，筋腫80例）をvalidation setとした。さらに6施設において2006年1月から2020年12月までの124例（多施設sample D，肉腫62例，筋腫62例）で診断アルゴリズムを検証した。【成績】sample Aの解析より，T2WI-lowかT2WI-highの中でも②③④の所見を持たないものは筋腫であり，①に②③④のいずれか1つの所見を併せ持つものは肉腫の可能性があるというアルゴリズムを作成した。sample A+Bの1,689例中，アルゴリズム陽性は75例（約4%）。sample B，Cでは100%の感度で子宮肉腫は診断アルゴリズム陽性であった。多施設sample Dでは放射線診断医が26%（16/62例）で良性の術前診断をしていた中で診断アルゴリズムは95%（59/62例）で子宮肉腫を拾い上げた。DWIは子宮肉腫53例中51例でhigh，子宮筋腫57例中10例でhighであった。【結論】診断アルゴリズムを使用して治療方針を決定することは有意義であり，DWI-highの条件を組み込むことでさらに制度の高い術前診断が期待される。さらなる症例の収集により検討を行う予定である。

P-71-2 当科における子宮癌肉腫, 平滑筋肉腫, 内膜間質肉腫の術前診断についての検討

大阪市大

大上健太, 市村友季, 笠井真理, 今井健至, 山内 真, 福田武史, 安井智代, 角 俊幸

【目的】子宮体部に腫瘤を形成する腫瘍としては平滑筋腫の頻度が最も高いが、癌肉腫 (CS), 平滑筋肉腫 (LMS) および内膜間質肉腫 (ESS) といった子宮肉腫もこれに含まれる。これらは変性した筋腫とMRI所見が類似し、生検による組織診断も困難なため術前診断が容易でないことが多い。当科における子宮肉腫の術前診断に関する検討を行った。【方法】対象は2011年4月から2021年9月に当科で内膜生検あるいは(および)針生検による組織検査を受け、その後子宮摘出術が行われたCS 24例, LMS 8例, ESS 7例で、これらの症例に対し行った術前生検の疑陽性率 (悪性腫瘍を否定できない症例の割合) と正診率に関する後方視的検討を行った。【成績】LMS 1例を除く38例に内膜生検を行い、針生検は内膜生検陰性例および未実施例の16例に行った。CSの内膜生検疑陽性率は87.5%・正診率は29.2%で、針生検は3例のみだが正診率100%であった。CSに対する術前生検の疑陽性率は100%・正診率は41.7%であった。LMSの内膜生検疑陽性率は0%であったため、針生検の疑陽性率87.5%と正診率37.5%がLMSに対する術前生検の疑陽性率・正診率となった。ESSの内膜生検疑陽性率は28.6%・正診率は14.3%、針生検の疑陽性率は80.0%・正診率は40%で、ESSに対する術前生検の疑陽性率は85.7%・正診率は42.9%であった。CSとLMS, CSとESSにおける内膜生検の疑陽性率に有意差 ($p < 0.001$, $p = 0.006$) がみられた。術前生検陰性の症例はLMS 1例とESS 1例のみで、子宮肉腫39例のうち37例 (94.8%) は疑陽性であった。【結論】内膜生検と針生検による術前組織検査は、正診率は高くないものの子宮肉腫の存在を術前に推定するための検査として有用であると考えられた。

P-71-3 腹腔鏡下子宮全摘術または腹腔鏡下/開腹子宮腫瘍核出術に判明した子宮平滑筋肉腫/STUMP 19例の予後に関する検討

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【目的】子宮筋腫などの良性腫瘍を術前診断に、体腔内で核出および細断する手術手技は、術後想定外に悪性腫瘍が判明した場合、腹腔内に腫瘍細胞を散布し、予後を悪化させる可能性がある。今回我々は腹腔鏡下子宮全摘術(LH), または腹腔鏡下/開腹子宮筋腫核出術(LM/AM)を実施した後に、子宮平滑筋肉腫(uLMS: Uterine leiomyosarcoma)またはSTUMP(Smooth-muscle tumors of uncertain malignant potential)の診断となった症例の予後について検討を行ったので報告する。【方法】2019年5月から2021年9月の期間中に当院肉腫総合治療センター受診歴のある症例をもとに上記術式既往のあるuLMS/STUMP症例の予後を検討した。【成績】対象症例は19例, うちuLMSが16例, STUMPは3例であった。初回手術術式はLHが3例で全例体腔内での細断手技あり(バッグ使用1例), LMが6例で電動モルセレーター使用は4例(バッグ使用例0), 他10例はAM(細断手技あり1例)が施行されていた。年齢中央値は41(24-48)歳で、再発が14例(73.7%), 無増悪期間は48(7-99)か月, 全生存期間は92(7-187)か月で死亡例はなかった。初回再発部位は骨盤内播種再発が8例, 肺転移再発が6例(1例は骨転移もあり)だった。10例で再発後に腫瘍減量術が施行されており, 5回以上施行された症例も2例認めた。8例で初回術後または再発に対して化学療法が実施された。【結論】体腔内で核出または細断を伴う手術後にuLMS/STUMPが判明した場合でも、必ずしも予後不良とは言えず、積極的な腫瘍減量術, 化学療法などによって長期生存が得られる可能性がある。

P-71-4 子宮肉腫の腫瘍径は予後予測因子となり得る

杏林大付属病院

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【目的】子宮肉腫は稀な腫瘍であり手術による腫瘍摘出が唯一の有効な治療とされているが、その予後は不良である。今回、当院における子宮肉腫の症例における予後予測因子について後方視的に検討した。【方法】当院において2011年1月~2021年8月の10年間に初回治療を行い、病理診断にて子宮原発の間葉性悪性腫瘍と診断された30例についてその初回治療、再発・増悪の状況、予後等について検討した。【成績】初回治療時の平均年齢は59.5歳(37歳~79歳)で、観察期間は平均38か月(2か月~112か月)、組織型は平滑筋肉腫21例(70%), 低悪性度内膜間質肉腫4例(13.3%), 未分化肉腫5例(16.6%)であった。手術進行期分類はI期15例(50%), II期5例(16.6%), III期3例(10%), IV期7例(23.3%)であった。30例全例で腹式単純子宮全摘出術を施行し、うち14例で術後化学療法を施行し、15例は経過観察とした。化学療法のレジメンはDIP療法7例, GD療法4例, その他3例であった。再発・増悪をきたした症例は17例で再発部位は肺が40%と最も多かった。観察期間中の死亡例は11例(36.6%)であり、うち4例はI期であった。IB期について腫瘍径によりその予後を比較すると、10cm以下の群4例では再発・死亡ともに認めなかったが、10cmを超える群9例中6例で再発・増悪を認め、4例は死亡の転帰であった。【結論】本検討から予後不良な子宮肉腫において初回治療時の腫瘍径は予後予測因子となる可能性が示唆された。

P-71-5 子宮平滑筋肉腫に対する新規治療薬開発を目指した化合物探索

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【目的】悪性間質性腫瘍である子宮平滑筋肉腫 (ULMS) は、現行の化学療法に対する奏効率が非常に限定的な予後不良の疾患である。本研究では、ULMS に選択的に有効な新規治療薬を同定し、その機序を明らかにする。【方法】FDA 承認 1280 既存薬からなるライブラリーを用いて、ULMS 細胞 (SKN 細胞, SKUT-1 細胞) への抗腫瘍効果を評価した。薬剤による阻害率は、生存割合、および Z スコアを用いて評価した。有望な薬剤を皮下移植モデルマウス、および子宮同所移植モデルマウスで効果を検証した。阻害作用機序を明らかにするため、子宮肉腫細胞内での薬剤投与による遺伝子変化を、また、ヒト ULMS 組織内の遺伝子プロファイルを、次世代シーケンサーを用いて検証した。【成績】薬剤濃度 10 μM による一次スクリーニングでは Z スコア 2 以上の 32 剤、二次スクリーニングでは阻害率 80% 以上の 9 剤、3 次スクリーニングではより低濃度 (100 nM) で作用する 4 剤を選択し、最終候補とした。皮下移植マウスによる効果検証では、4 剤のうち、2 剤で抗腫瘍効果を認め、同薬剤は同所移植マウスでの効果も確認した。尚、体重減少などの副作用は認めなかった。2 剤を作用させた ULMS 細胞での RNA シーケンスを用いた機能解析では、抗腫瘍効果に関わる 10 のパスウェイが推定され、同経路を制御する 4 つの標的遺伝子を解析対象とした。同遺伝子変動は定量 PCR でも、その変化が確認できた。また、ヒト ULMS 組織 6 例の RNA シーケンスの結果、同遺伝子は有意に高発現しており、治療標的となる可能性が示唆された。【結論】本研究では ULMS における新しい治療薬および治療標的を同定した。本知見は、ULMS 患者の予後を改善するための治療戦略創生に貢献し得る。

P-71-6 子宮肉腫に対するトラベクテジンの使用経験

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【目的】トラベクテジンは悪性軟部腫瘍に対して使用可能な抗悪性腫瘍薬であるが、子宮肉腫に限った報告は少ない。今回、子宮肉腫に対するトラベクテジンの有効性及び安全性を検証することを目的とし、当科における使用経験について解析した。【方法】2015 年 10 月から 2021 年 9 月に、当科で子宮肉腫に対してトラベクテジンを投与した症例について診療録より後方視的に検討した。有効性については奏効割合、無増悪生存期間 (PFS)、全生存期間 (OS) を、安全性については有害事象を評価した。【成績】対象は 19 例で、年齢の中央値は 45 歳 (34-61 歳)、組織型は子宮平滑筋肉腫が 18 例、線維形成性小円形細胞腫瘍が 1 例であった。治療ラインは二次治療が 4 例 (21%)、三次治療が 7 例 (36%)、四次・五次治療が 8 例 (42%) であった。治療の総合最良効果は部分奏効が 2 例 (10%)、安定が 4 例 (21%)、進行が 13 例 (68%) で、病勢制御割合は 31% であった。PFS ならびに OS の中央値は 2.0 か月と 5.9 か月であった。Grade 3 以上の血液毒性については好中球数減少を 8 例 (42%)、貧血を 3 例 (15%)、肝酵素上昇を 5 例 (29%) に認め、Grade 3 以上の非血液毒性ならびに横紋筋融解症は認めなかった。好中球数減少による投与延期を 3 例 (15%)、減量を 2 例 (12%) に認めたが、有害事象による治療中止例は認めなかった。【結論】子宮肉腫に対するトラベクテジンの使用は三次治療以降が大半を占め、安全に投与が可能で、奏効割合は 10% であった。今後は奏効や病勢制御を示唆するバイオマーカー等を検討することが必要と考えられた。

P-71-7 当院での子宮肉腫に対するエリプリンの使用経験

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【目的】微小管阻害剤であるエリプリンは 2016 年 2 月に悪性軟部腫瘍に対して保険承認されたが、子宮肉腫に限った有効性についての報告は少ない。当院での子宮肉腫に対するエリプリンの使用経験から安全性、有効性について検討した。【方法】2016 年 2 月から 2021 年 9 月に子宮肉腫に対してエリプリンを投与した症例について診療録より後方視的に検討した。【成績】対象は 30 例で、年齢中央値は 52.5 歳 (35-66 歳)、組織型は子宮平滑筋肉腫 24 例、未分化肉腫 2 例、高異型度子宮内膜間質肉腫 1 例、線維形成性小円形細胞腫瘍 2 例、分類不能 1 例であった。治療ラインは二次治療が 13 例 (43%)、三次治療が 11 例 (37%)、四次治療が 6 例 (20%) であった。最良総合効果は完全奏効 (CR) が 0 例、部分奏効 (PR) が 0 例、安定 (SD) が 9 例 (30%)、進行 (PD) が 20 例 (67%)、評価不能が 1 例 (3%) で、奏効割合は 0%、病勢制御割合は 30% であった。無増悪生存期間の中央値は 2.4 か月 (0.73-19.0)、全生存期間の中央値は 7.5 か月 (1.2-51.9)、5 例 (17%) で 6 か月間以上の病勢制御が可能であった。Grade 3 以上の血液毒性は白血球減少 9 例 (30%)、好中球減少 13 例 (43%)、貧血 4 例 (13%)、肝酵素上昇 1 例 (3%) であった。非血液毒性は Grade 2 以上の末梢神経障害を 2 例 (7%) で認めた。有害事象により 7 例 (23%) で減量を要したが、有害事象による治療中止例は認めなかった。【結論】進行再発子宮肉腫に対し、エリプリンは全例で安全に投与可能であった。投与方法が間便なこともあり、約半数が二次治療で選択されていたものの、奏効例は認めなかった。今後は長期間の病勢制御を示唆するバイオマーカー等を検討することが重要と考えられた。

P-71-8 外腸骨動脈周囲の再発腫瘍に対し人工血管置換術を実施した子宮平滑筋肉腫の1例

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【緒言】婦人科悪性腫瘍における再発腫瘍切除術では、人工血管置換術を実施することは稀である。再発子宮平滑筋肉腫に対して外腸骨動脈静脈併切離、外腸骨動脈人工血管置換術を施行した症例を経験したため報告する。【症例】60歳、特記既往、癌家族歴は無い。X年に子宮腫瘍の破裂に対して緊急手術（腹式単純子宮全摘出、両側付属器切除術）を実施。病理組織診断は子宮平滑筋肉腫（pT2ANXM0/stage2A/FIGO2008）の診断であった。術後補助化学療法を実施、以降外来で経過観察した。X+9年に後腹膜から右外腸骨動脈周囲に発育する再発腫瘍を認めた。同年に再発腫瘍切除術を実施、外腸骨動脈から腫瘍を剝離摘出した（病理：平滑筋肉腫）。術後補助化学療法を実施し外来経過観察とした。X+10年に前回と同部位に約7cmの腫瘍増生、FDG-PETで同部位に集積を認めた。右外腸骨動脈、静脈を巻き込んだ腫瘍であり血管と腫瘍を一塊に摘出する方針とした。右外腸骨動脈静脈併切離、右外腸骨動脈人工血管置換術（INTERGARD 8mm 径）、腸腰筋部分切除術、骨盤リンパ節郭清術を実施。摘出標本は平滑筋肉腫の再発であった。現在術後10か月を経過し、再発を疑う所見は無く外来経過観察中である。【考察】子宮平滑筋肉腫は一般的に予後不良かつ化学療法抵抗性である。局所再発に対する積極的な外科介入で長期生存を得られる可能性がある。

P-71-9 腹腔鏡下手術後に子宮肉腫と診断された症例の再発リスクについての検討

手稲溪仁会病院

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【目的】子宮筋腫への腹腔鏡手術は、筋腫の核出操作や検体搬出操作に伴う組織の飛散が起こる可能性がある。術後に肉腫と診断された場合、再発の懸念があるがそのリスクは明らかではない。今回、後方視的に腹腔鏡手術後に子宮肉腫と診断された症例の臨床的経過を明らかにすることを目的とした。【方法】2006年1月～2020年12月、子宮筋腫の術前診断で腹腔鏡手術を施行した6181例のうち、術後に肉腫と診断された11症例について、再発部位、術前MRI所見、回収バッグ使用の有無、電動モルセレーター使用の有無、回収経路について検討した。【成績】年齢は30～51歳、MRIで腫瘍径は3～70mm、9症例で拡散制限を認めた。9例が子宮全摘出術、2例が腹腔鏡下子宮筋腫核出術で、いずれも悪性の可能性についてインフォームドコンセントを得ていた。病理は平滑筋肉腫6例、腺肉腫1例、低悪性度子宮内膜間質肉腫4例、進行期はFIGOIA期6例、IB期5例だった。再発は平滑筋肉腫症例3例で認められた。2例は腹膜播種再発で、うち1例は子宮全摘時、電動モルセレーター使用（回収バッグなし）、1例は筋腫核出だった。回収バッグ使用と経腔回収の症例は腹膜播種再発を認めなかった。残りの1症例は子宮全摘出（分割なし・経腔回収）後、6か月で多発肺転移となり原病死した。【結論】核出術や電動モルセレーター使用は、腹腔内播種再発をきたす可能性があった。対して、経腔回収や回収バッグ使用により、少なくとも腹膜播種再発は回避できる可能性が示唆された。本研究では症例数が少数にとどまるため、今後の多数例の集積の必要と思われる。本研究では症例数が少数にとどまるため、今後、多数例の集積の必要があると考えられる。

P-72-1 多発肝転移をきたした卵巣成人型顆粒膜細胞腫の1例

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卵巣成人型顆粒膜細胞腫は全卵巣腫瘍の1%程度と比較的稀な腫瘍である。初期では一般的に予後良好とされているが、20～30%で再発し、再発までの平均期間は4～6年とされている。20年以上経過してからの晩期再発の報告もある。再発は主に骨盤内に生じ、遠隔転移は稀とされている。今回我々は卵巣成人型顆粒膜細胞腫に対し初回手術を施行した後、半年後に骨盤内再発を認め、さらにその1年後に多発肝転移を認めた症例を経験したので報告する。症例は72歳、3妊3産。不正性器出血と腹部腫瘍感あり、近医より紹介となった。20cm大の左卵巣腫瘍を認め、骨盤MRIでは顆粒膜細胞腫の可能性を指摘された。CA125値、血中E2値の上昇、FSH値の低下を認めた。腹式子宮全摘術、両側付属器切除術、大網部分切除を施行した。病理診断は成人型顆粒膜細胞腫であり、卵巣表面まで浸潤が及ぶところもあり、尿管侵襲も認めた。子宮や卵管への浸潤、大網播種はなく、pT1c2と診断した。術後に血中E2値の低下を確認した。術後半年後のCTで骨盤内右側に35mm大の多房性囊胞性病変を認め、再発病変を疑った。腹式骨盤内腫瘍摘出術を施行したところ、顆粒膜細胞腫の転移との診断であった。さらに1年後のCTで多発肝転移を認めた。腹腔鏡下肝腫瘍部分切除術を施行したところ、顆粒膜細胞腫の転移の診断であった。術後にTC+アバスタチン療法を施行した。初回手術から再発までの期間が早く、肝転移をきたした稀な症例を経験した。初回手術時の病理診断で尿管侵襲や卵巣表面までの浸潤所見あり、早期再発に起因した可能性がある。顆粒膜細胞腫は初期手術後も慎重に経過をみる必要があると考える。

P-72-2 進行癌で発見された顆粒膜細胞腫の1例

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【緒言】成人型顆粒膜細胞腫は性索間質腫瘍のうち悪性腫瘍に分類され、全卵巣悪性腫瘍の2.7%を占める稀な腫瘍である。78%-91%がI期で発見される。進行癌での発見は稀であり、5年生存率は0%-20%と上皮性卵巣癌と同等に予後不良との報告がある。今回我々は進行癌で発見された症例を経験したため報告する。【症例】35歳、3妊1産、X-5年に卵巣腫瘍に対して腹腔鏡下左卵巣腫瘍摘出術を施行し最終病理診断はfollicular cyst。X年9月に偶発的に右卵巣腫瘍を指摘され当院紹介受診。受診時、経口避妊薬を内服しており不正性器出血は認めなかった。経陰超音波断層法では右付属器領域に10cm大の多房性腫瘍を認め一部隔壁に血流を認めた。子宮内膜肥厚なし。CA125, CA19-9の上昇はなくE283.5pg/mLだった。MRI検査では境界明瞭な多房性嚢胞性腫瘍を認め嚢胞内に出血を疑う所見があった。骨盤内に播種を疑う病変を多数認めた。画像上顆粒膜細胞腫が鑑別に挙がり手術の方針となった。開腹で手術を開始し破綻することなく右付属器を摘出し術中迅速病理診断で顆粒膜細胞腫の診断。腹腔内は播種様病変を認めた。単純子宮全摘術、左付属器摘出術、大網部分切除術、播種病変切除術を追加し直腸表面に1mmの播種病変が残存するのみでoptimal surgeryで終了。永久標本の病理組織学的所見から顆粒膜細胞腫IIIB期(pT3bNxM0)と診断し、術後化学療法としてTC療法の方針とした。【結論】進行癌で発見された顆粒膜細胞腫の1例を経験した。当院では過去10年間に7例ありいずれもI期で発見され予後良好だった。本症例では子宮内膜の肥厚や不正性器出血などの典型的なエストロゲン症状がなかったことが早期発見困難となった一因と考えた。

P-72-3 パクリタキセル・カルボプラチン・ペバシズマブ療法が奏功した再発顆粒膜細胞腫の一例

信州大

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卵巣顆粒膜細胞腫(GCT)は10年以上経てからの晩期再発は珍しくない。化学療法の奏効率は約40%と低く、プレオマイシン・エトポシド・シスプラチン療法(BEP)が最も多用されるが、有害事象から施行可能コース数に制限がある。今回、パクリタキセル・カルボプラチン・ペバシズマブ療法(TC-BV)が奏功した初発から26年後の切除不能GCT再発例を経験したので報告する。症例は未経産の女性で、45歳時に左卵巣腫瘍に対し前医で左付属器切除術を施行され、病理診断はGCTで経過観察された。20年後の65歳時に下腹部を占拠し直腸・S状結腸浸潤、横隔膜播種、大網播種、腹膜播種を伴う長径15cmの右卵巣充実性腫瘍を認め、当科で腹式単純子宮全摘術、右付属器摘出術、腹膜播種摘出術、大網全摘術、直腸・S状結腸部分切除術、虫垂切除術が施行された。腫瘍は肉眼的に完全切除され、病理ではGCT再発と診断されたが、術後化学療法には同意されず、経過観察となった。71歳時にCTで骨盤内に多発する充実性腫瘍を認め、2度目のGCT再発と診断した。再発腫瘍の一つは前回の直腸吻合部背側に存在し、径4cmで仙骨に固着して全く可動性がなく、摘出不能と判断した。化学療法の方針としたが、BEPの最大コース数4コースで治療が終了できる見込みはなく、長期間継続可能な治療が望ましいとの判断から再発卵巣癌に準じてTC-BVの方針とした。6コースを施行し、縮小率35%の部分奏功(PR)を認めた。Grade3以上の有害事象はなく、治療継続中である。GCTの切除不能再発例では、再発卵巣癌に準じたTC-BVは長期継続可能で有効性も期待でき、BEP以上に有力な治療選択肢となり得る。今後、更なる症例の集積が必要である。

P-72-4 当院における20歳未満の未熟奇形腫と成熟奇形腫の石灰化に着目した鑑別法

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【目的】20歳未満のAYA世代の卵巣腫瘍は日常診療で遭遇し、妊孕性温存が必要なため術前に画像所見による正確な診断が求められる。当院における20歳未満の卵巣腫瘍の術前画像診断の良悪性を明らかにし、石灰化に着目して鑑別方法について検討した。【方法】2008年から2021年5月までに当院で手術を施行した20歳未満の42例を対象とし、診療録を用いて後方視的に観察した。【成績】平均発症年齢は14.8歳(95%CI:13.7-15.9)、平均腫瘍径は11.8cm(95%CI:9.4-14.2)であった。病理診断は81.0%(34/42例)が良性であった。内訳は、成熟奇形腫27例、粘液性腺腫5例、漿液性腺腫1例、黄体嚢胞1例であった。悪性は19.0%(8/42例)で、内訳は未熟奇形腫4例、漿液性境界悪性腫瘍1例、性腺芽腫1例、卵黄嚢腫瘍1例、小細胞癌1例であった。画像上石灰化を伴う腫瘍は81.1%(30/37)存在した。石灰化を持つ良性腫瘍と悪性腫瘍の頻度は、それぞれ83.3%(25/30)と75.0%(6/8)で統計学的に有意差がなかった。次に、石灰化が粗大で局在しているものと微細で散在しているものに分類した。微細で散在性に存在した石灰化症例における、良性腫瘍と悪性腫瘍の頻度は、それぞれ44.4%(4/9)と55.6%(5/9)であった。次に診断に一番苦慮する成熟奇形腫と未熟奇形腫のみの鑑別では、石灰化が微細で散在しているものが、それぞれ成熟奇形腫では9.1%(2/22)と未熟奇形腫では100%(4/4)で統計学的に有意差を認めた。【結論】石灰化の存在のみで良悪性の鑑別はできないが、石灰化の局在により成熟奇形腫と未熟奇形腫の鑑別ができる可能性が示唆された。現在、両者の鑑別をさらに明確にするため、腫瘍全体に占める石灰化部分の数と面積と体積を数値化することを試みている。

P-72-5 無月経と骨盤内腫瘍を主訴に来院し Swyer 症候群と診断した1例

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【緒言】Swyer 症候群は核型が 46, XY であるにも関わらず内性器・外性器ともに女性型をとる稀な性腺分化異常であり、性腺の悪性腫瘍を高率に合併することが知られている。今回、無月経と両側卵巣腫瘍を契機として Swyer 症候群と診断された症例を経験したので報告する。【症例】16 歳、無月経と骨盤内腫瘍のため紹介受診となった。身長 167cm, 体重 66kg, 腋毛・恥毛を認め、外陰部は女性型で陰核の肥大を認めず。経直腸超音波検査で長径 5cm の子宮の背側に 8cm 径の充実性腫瘍を認めた。血液検査では LH 28.8mIU/mL, FSH 64.8mIU/mL, エストラジオール 21.1pg/mL, テストステロン 0.81ng/mL, CA 125 14.6U/mL, AFP 1.6ng/mL, LDH 414 U/L であった。骨盤部 MRI では右卵巣に 90mm×73mm 大で T1 強調像・T2 強調像いずれも軽度高信号の分葉形腫瘍を認め、左卵巣にも内部に 25mm 径の嚢胞性病変を認めた。胚細胞腫瘍を疑い、開腹による右付属器摘出術および左卵巣生検を行った。腹膜播種病変は認めなかったが、腹水細胞診が陽性であった。術後病理診断は右卵巣は dysgerminoma, 左卵巣も dysgerminoma 疑いであった。術後 BEP 療法と並行して染色体検査を行ったところ 46, XY であり、Swyer 症候群と診断した。BEP 療法 3 サイクル後に腹腔鏡下左付属器摘出術を行ったところ、左卵巣の病理診断は gonadoblastoma であった。現在、外来で経過観察中である。【結語】Swyer 症候群では約 25% に gonadoblastoma や dysgerminoma の発症がみられるため、両側卵巣の予防的摘出が推奨されている。患者本人と家族への説明や予防的摘出の時期については慎重に判断する必要がある。

P-72-6 子宮内膜癌に対する腹腔鏡下手術後に診断された成熟嚢胞奇形腫合併卵巣カルチノイドの一例

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【緒言】卵巣カルチノイドは稀な疾患であり、約半数は成熟嚢胞奇形腫に合併する。今回、子宮内膜癌、成熟嚢胞奇形腫に対し腹腔鏡下手術を施行し、偶発的に卵巣カルチノイドを発見した症例を報告する。【症例】49 歳 2 妊 2 産 不正出血を主訴に受診された。子宮内膜組織診で Endometrioid carcinoma Grade1, MRI 検査で子宮内に 3cm 大の腫瘍性病変を認め、拡散制限および造影効果を伴い子宮内膜癌を疑う所見であった。左卵巣に 4cm 大の嚢胞性腫瘍を認め、T1 脂肪抑制像にて抑制される領域を伴うため成熟嚢胞奇形腫と考えたが、悪性を疑う所見は認めなかった。CT 検査で遠隔転移やリンパ節腫大は認めなかった。腫瘍マーカーは CEA, CA125, CA19-9, SCC 全て正常であった。子宮内膜癌 IA 期, 左成熟嚢胞奇形腫の診断とし腹腔鏡下単純子宮全摘出術, 両側付属器摘出術, 骨盤リンパ節郭清術を施行した。術後病理結果は子宮内膜癌 IA 期 endometrioid carcinoma grade1, 左卵巣は mature teratoma with strumal carcinoid で、カルチノイドにリンパ管侵襲を認めた。【考察】卵巣カルチノイドの約 90% は I 期で診断され、I 期の 5 年生存率は 90% 以上と予後良好だが明確な治療方針は確立されておらず、臨床的には卵巣境界悪性腫瘍に準じた治療方針が考慮される。本症例ではカルチノイドにリンパ管侵襲を認めた。摘出リンパ節ではカルチノイドは検出されなかった。カルチノイド腫瘍の転移好発部位は所属リンパ節、肝臓、骨、肺が挙げられ、晩期の転移症例の報告もあり慎重な経過観察が必要と考えられる。【結語】卵巣カルチノイドは I 期では予後良好だが、晩期再発や死亡例も報告があるため、慎重な経過観察が必要である。

P-72-7 妊娠中急性腹症にて発見された成熟嚢胞奇形腫合併卵巣カルチノイドの一例

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【緒言】神経内分泌細胞由来の腫瘍 (neuroendocrine tumor: NET) であるカルチノイドはほとんどが膵・消化管原発であり、本邦での卵巣原発カルチノイドの頻度は約 1.3% である。我々は妊娠中の急性腹症にて緊急手術となった成熟嚢胞奇形腫合併卵巣カルチノイドの 1 例を経験したので報告する。【症例】28 歳, 1 妊 0 産。妊娠 10 週 6 日当院分娩希望にて紹介。初診時の経膈超音波検査にて右卵巣に 6cm 大の充実成分を伴う腫瘍を認めた。妊娠 14 週で MRI での精査後に手術予定としていたが、検査の 2 日前に下腹部痛が出現。卵巣腫瘍茎捻転が疑われ、緊急腹腔鏡下右卵巣嚢腫核摘出術を施行した。病理検査では皮膚・脂肪織・軟骨組織等を認めたが、極僅かに楕円形の核を有する異型細胞の索状増殖や、類円形の核を有する細胞の胞巣状～索状増殖を示す部分が見られた。chromogranin A, synaptophysin が共に陽性で、Ki-67 陽性細胞は 2% 程度であり、mature cystic teratoma with NET G1 と診断された。NET の範囲が極僅かであったことから追加手術は施行せず、経過観察となった。現時点で再発は認めていない。【考察】卵巣カルチノイドの約 91% は I 期であり、5 年生存率はほぼ 100% であるが、粘液性のもの、成熟嚢胞奇形腫合併を伴わないもの、リンパ管侵襲を伴うものは悪性経過をたどることもある。妊孕性温存症例では病巣の完全切除を目的とした患側付属器切除術が行われるが、成熟嚢胞奇形腫内に極僅かなカルチノイド成分を認めるのみの症例で嚢腫核摘出にとどめ、術後慎重経過観察としている報告もある。【結語】カルチノイド成分が微小な症例に対する保存的治療の選択肢を明確にするためには、さらなる症例の蓄積と検討が必要である。

P-72-8 卵巣成熟嚢胞性奇形腫の腺癌への悪性転化と大腸癌を重複した一例

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【緒言】成熟嚢胞性奇形腫の悪性転化のうち、腺癌は6.3~7%と稀である。腺癌への悪性転化に限定した予後についての報告はなく、術後化学療法についても有効性が確立したレジメンはない。【症例】61歳 G3P2 閉経 57歳。便潜血陽性を契機に横行結腸癌の診断となった。術前 CT で右卵巣に 44*65mm の奇形腫を疑う腫瘍を指摘され当科を受診した。MRI で悪性を疑う所見を認めず、CA125 6 IU/ml, SCC 1.4 ng/ml, CEA 3.1 ng/ml, CA19-9 18 IU/ml と正常範囲内であった。腹腔鏡下結腸拡大右半切除術 D3 郭清/腹腔鏡下両側副属器切除術を施行した。卵巣嚢腫壁の一部に 12mm 大の結節があり、病理学的検査で異型腸型腺上皮を認めた。横行結腸癌の卵巣転移が疑われたが、横行結腸癌は僅かな漿膜下層へ浸潤に留まり、卵巣への転移を生じる可能性は低いとの外科医師の見解により精査を進めた結果、奇形腫の組織内に正常大腸粘膜上皮から癌上皮への移行部位を認め、横行結腸癌 MUC-2 (-) p53 (+), 卵巣内腺癌 MUC-2 (+) p53 (-) であり、右卵巣成熟嚢胞性奇形腫の腸型腺癌への悪性転化の診断となった。横行結腸癌 pT3N0M0/右卵巣癌 pT1aNX の診断となり、XELOX 療法を行なう方針となった。【考察】奇形腫の腸型腺癌への悪性転化と大腸癌を合併した、稀な症例を経験した。正常組織から癌組織へ連続的に移行する部位を確認できたことと、免疫染色による検討が、卵巣嚢腫内の腺癌が大腸癌からの転移なのか悪性転化なのかの診断に有用であった。

P-72-9 悪性卵巣甲状腺腫の一例

市立安佐市民病院

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卵巣甲状腺腫は全卵巣腫瘍の 0.5~1% とされており、そのうち悪性卵巣甲状腺腫 (malignant struma ovarii; MSO) は 5~10% 程度と極めて稀である。高度な腹腔内癒着のため手術に難渋し、術後治療について検討した MSO を経験したので報告する。症例は 46 歳, 3 妊 2 産。発熱, 下腹部痛を主訴に近医を受診し、炎症反応高値, CT 検査で卵巣腫瘍が疑われ当科を紹介受診した。MRI 検査では卵管膿瘍および右卵巣に血液成分を含む 6cm 大の充実性腫瘍を認め、内膜症性嚢胞や卵巣甲状腺腫、粘液嚢胞腺線維腫が鑑別に挙げられた。抗菌薬治療により全身状態が改善した後に卵巣腫瘍に対して開腹手術を施行した。右卵巣腫瘍は下手拳大で内膜症性癒着のため子宮・左付属器と一塊となり、直腸とも強固に癒着していた。癒着剝離時に嚢胞壁の一部が破綻し、チョコレート様の内容液が漏出した。右付属器摘出術を先行し、迅速病理診断で MSO が疑われたため、左付属器摘出術、単純子宮全摘術、大網部分切除術を追加した。高度な腹腔内癒着により出血量 1840 ml となり、RBC 4 単位を輸血した。永久病理組織標本でも MSO (乳頭癌) と診断された。内膜症性嚢胞部分は術中に破綻したが、組織学的に MSO を含む嚢胞壁の破綻は認めず切除縁への癌腫の露出も認めなかった。以上より、右 MSO IA 期 (pT1aNXM0) と診断した。術後 PET/CT 検査で転移や残存腫瘍がないこと、耳鼻科にて甲状腺に異常がないことを確認した。MSO の治療法は確立しておらず、術後治療として①卵巣癌に準じる、②甲状腺癌に準じる、③経過観察が選択肢として考えられた。本症例は再発低リスクと考え、追加治療は行わず慎重な経過観察を選択した。

P-73-1 肺水腫の管理に難渋し、陽圧換気下で化学療法を行った進行期胚細胞性腫瘍の 1 例

大阪国際がんセンター

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【緒言】胚細胞性腫瘍は若年好発の卵巣悪性腫瘍であり、化学療法への感受性が高く、診断時に進行期であることは少ない。進行期胚細胞性腫瘍に対して難治性の肺水腫を合併し、陽圧換気併用下での化学療法を要した 1 例を経験したため報告する。【症例】24 歳女性。腹部膨満感と腹痛を主訴に近医内科を受診し、進行期卵巣癌を疑われ、当科紹介受診となった。画像検査では骨盤内を占拠する右付属器由来の 10cm 大の腫瘍に加え、多数の腹膜播種病変および腹水を認めた。術前に腹水貯留による頻呼吸や腹部膨満感の増悪を認めたが、腹水除去により改善した。初回手術として右付属器摘出術を試みたが、腹腔内に易出血性の腹膜播種を多数認め、骨盤内や腹腔内の観察が不可能であり、腫瘍生検のみを行った。術後 4 時間で肺水腫を認め、再挿管ならびに陽圧換気を開始した。術後、創部より 1 日 3L の腹水の漏出を認め、全身管理に難渋した。加えて、難治性肺水腫と腹腔内腫瘍による胸郭圧迫のため抜管困難となり、術後 1 週間で気管切開術を行った。病理組織検査の結果は卵黄嚢腫瘍であり、術後 12 日目よりプレオマイシン・エトポシド・シスプラチン (BEP) 療法を開始した。BEP 療法 3 コース終了後、腫瘍は著明に縮小し、陽圧換気は不要となった。4 コース終了後、腫瘍減量術を行い、骨盤内に残存していた 8cm 大の腫瘍および播種病変を摘出したが、病理学的には全て腫瘍壊死に至っていた。現在、再発兆候なく外来経過観察中である。【結論】難治性肺水腫のため全身管理に難渋したが、気管切開による陽圧換気を行いながら BEP 療法を実施し、最終的に完全奏功を到達しえた進行期卵黄嚢腫瘍の 1 例を経験した。

P-73-2 卵巣原発の腎芽腫成分を有する成熟嚢胞性奇形腫の一例

函館中央病院

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【緒言】腎芽腫（Wilms 腫瘍）は好発年齢 2 歳～5 歳と主に小児期に発生する腎原発悪性腫瘍とされ小児悪性固形腫瘍では神経芽腫瘍に次いで発生頻度が高く、本邦における年間発生数は約 100 例と推察されている。しかしながら腎外に発生する腎芽腫は報告が少なく、婦人科臓器由来の腎外性腎芽腫は極めて稀である。今回我々は卵巣原発の腎芽腫成分を有する成熟嚢胞性奇形腫の一例を経験したので文献的考察も交え報告する。【症例】患者は 52 歳 3 妊 3 産、48 歳閉経。既往歴：甲状腺機能亢進症。婦人科腫瘍検診で当科受診。その際に 5cm 大に腫大した右卵巣腫瘍を認めた。MRI では成熟嚢胞性奇形腫を第一に考える所見であったが、一部充実性変化を考える部位もあり、外科的切除の方針となった。当科にて腹腔鏡下右付属器切除術施行。腫瘍表面に明らかな浸潤、播種所見なく、術中破綻なく術式終了した。摘出した病変は病理的評価にて重層扁平上皮の被膜や軟骨、脂肪組織等、成熟奇形腫を考える所見を認める一方、不規則な腺管形成や策状配列、スリット様構造を示す由来の特定困難な成分を認めた。当初未熟奇形腫も鑑別には挙がったが明確な神経上皮構造に乏しく、免疫染色の結果も踏まえ、卵巣原発の腎芽腫成分を伴う成熟嚢胞性奇形腫の診断に至った。悪性成分を有する卵巣腫瘍として staging 目的の追加手術も提示したが、本人手術希望されず現在慎重に経過観察中である。【考察】腎外性腎芽腫の発生は稀であり、多くは後腹膜腔に充実性腫瘍として発生する。卵巣を原発とする腎外性腎芽腫は極めて稀で、今回我々が検索した限りでは文献例 12 症例の報告があるのみである。

P-73-3 術後化学療法を省略し妊娠中期に再発をきたした妊娠卵黄嚢腫瘍 IA 期の一例

熊本大

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【緒言】卵巣卵黄嚢腫瘍は若年女性に好発する悪性卵巣胚細胞腫瘍であり、一般に術後化学療法が推奨されるが、NCCN ガイドラインでは経過観察も許容される。今回われわれは、妊娠初期の卵黄嚢腫瘍 IA 期に対して妊孕性温存手術後に化学療法を省略し妊娠管理を行ったところ、妊娠中期に再発をきたした一例を経験したので報告する。【症例】24 歳の初産婦。妊娠初期に充実性右卵巣腫瘍と AFP 高値 (18,068U/ml) を指摘され、妊娠 12 週 2 日に当施設を紹介受診した。病巣は右卵巣に局限しており、妊娠 13 週 1 日に右付属器切除と大網切除術を施行した。病理診断は卵黄嚢腫瘍 IA 期であった。標準治療として術後 BEP 療法 (プレオマイシン+エトポシド+シスプラチン) を説明したが、患者は化学療法の胎児への影響を心配し経過観察を強く希望したため、AFP を 1 週毎に測定し慎重に経過観察を行った。妊娠 22 週 2 日に胎胞形成を認め頸管縫縮術を行った。術後 AFP は 150U/ml 前後と妊娠期の正常範囲内で推移したが、妊娠 27 週 1 日に 708U/ml と再上昇し、画像検査で腹膜播種を認めた。妊娠継続での化学療法は希望されず、切迫早産の治療を終了し妊娠 28 週 0 日に 1,097g の児を Apgar score 4 点/6 点で経陰分娩した。現在、BEP 療法を施行中である。【考察】卵黄嚢腫瘍は他の悪性卵巣胚細胞腫瘍と比較して再発率が高く予後不良である。われわれの知る限り、これまで妊娠初期に卵黄嚢腫瘍 IA 期に対して妊孕性温存手術後に化学療法を省略し、妊娠中期に再発をきたした報告はない。卵黄嚢腫瘍 IA 期での術後化学療法省略は生存率を低下させないとの報告もあるが、妊娠期の卵黄嚢腫瘍 IA 期の取り扱いに一定の見解はなく、今後の症例の蓄積が待たれる。

P-73-4 TC 療法が著効した粘液性腫瘍を合併した異所性成分を伴う巨大なセルトリ・ライディッヒ細胞腫の 1 例

市立奈良病院

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【緒言】卵巣悪性腫瘍の 0.1% に発生するセルトリ・ライディッヒ細胞腫 (SLCT) の術後化学療法に関しては、胚細胞腫瘍あるいは上皮性卵巣癌のレジメンが混在し、未だ統一した見解が得られていない。今回、TC 療法にて完全寛解 (CR) が得られた IV 期の SLCT を経験したので報告する。【症例】65 歳、下腹部の膨満感を主訴に来院。コロナ禍で受診を控えていたため、来院時には心窩部までの可動性のある超成人頭大の腫瘍を下腹部に認めた。陰毛が濃く、陰核の腫大も認め、CA125 296.3U/mL, E2 31.5pg/mL, testosterone 3.42ng/mL であった。胸部 XP で右胸水、横隔膜の挙上、骨盤 MRI で 40cm ほどの多房性嚢胞性腫瘍を認めた。胸腹部 CT では多発肺転移も描出され、卵巣の粘液性癌や悪性の性索間質性腫瘍を疑い手術を行った。上腹部にまで達する腫瘍は右卵巣由来であり、当初、骨盤部の腫瘍は左卵巣由来と考えた。骨盤部の腫瘍はダグラス窩で後腹膜と強固に癒着していたため挙上せず、左右腫瘍の境界面と思われる部分を剝離しつつ摘出を試みた。しかし操作を進める過程で、萎縮した左の付属器を認め、右の巨大な卵巣腫瘍 (4,365g) を分割していることが判明。左付属器と子宮、大網も切除した。術後 13 日目に、腫瘍が広範囲に壊死を伴う異型の強い腫瘍細胞で構成されていたことから、TC 療法を開始した。術後 26 日目に永久標本で、腹膜や大網にも転移を伴う異所性成分として粘液性腫瘍部分を含む SLCT (中分化+低分化、脈管侵襲あり) と診断された (IV 期, pT3bNxM1)。合計 6 コースを行い、術後 1 年が経過した現在、CT を繰り返し行うも胸部病変にも変化なく、CR を維持している。【結語】TC 療法は進行 SLCT にも有用で、著効する可能性がある。

P-73-5 硬化性腹膜炎を伴う黄体化莢膜細胞腫の一例

市立秋田総合病院

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Luteinized thecoma with sclerosing peritonitis (LTSP) は、黄体化莢膜細胞腫 luteinized thecoma (LT) に硬化性腹膜炎 sclerosing peritonitis (SP) を合併する非常に稀な疾患である。1994年の初報告以降、全世界で50例程度の報告に留まり、標準療法は確立していない。今回我々は消化器症状の改善を得たLTSPの1例を経験したので報告する。症例は66歳、2妊2産。59歳時に罹患した悪性リンパ腫はR-CHOP, fludarabineで完全奏効を得られているが、化学療法に伴う薬剤性間質性肺炎に加え、細菌性肺炎の反復により呼吸機能は低下し、在宅酸素療法を導入されている。64歳時に胸腹水の貯留と骨盤内腫瘍を指摘され、当科に紹介となった。MRIで両側卵巣の充実性腫瘍を認め、病理学的診断目的に両側付属器摘出の方針とした。術中、腹膜の硬化および大網との癒着が強く、手術が長時間に及ぶことが予想されたため、呼吸機能を鑑み二期的な手術とした。初回手術標本(左卵巣)よりLTSPと診断した。術後よりSPによるイレウスをきたし、経鼻胃管(NGT)による減圧と中心静脈栄養による管理を行った。SPの消化器症状に対して症例報告を参考にホルモン療法(Tamoxifen×61日間)/ステロイドパルス療法(Methylprednisolone1000mg/日×3日間)を行ったが、著明な効果はなく消化管拡張不良による通過障害は続いた。状態の改善をみては段階的に食上げを試みるも、誤嚥性肺炎を繰り返し、経口摂取はスープ食までが限界でありNGTによる減圧も必須だった。しかし、要因は不明ながら発症から1年8か月後にNGTは不要となり、常食の摂取まで可能となった。その後は肺性心にもなう胸水と呼吸機能低下による呼吸苦を来すことがあるが、SPによる消化管通過障害は再発なく経過している。

P-73-6 卵巣ステロイド細胞腫瘍 not otherwise specified (NOS) の1例

高松赤十字病院

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【緒言】卵巣ステロイド細胞腫瘍 NOS は全卵巣腫瘍の0.1%以下の稀な腫瘍である。男性化徴候を示した卵巣ステロイド細胞腫瘍 NOS を経験したので報告する。【症例】37歳未婚妊。糖尿病、高血圧、脂質異常症、睡眠時無呼吸症候群、肥満(BMI 39)を併存していた。22歳ごろから稀発月経で、多嚢胞性卵巣症候群と診断されていた。半年ほど前から頭髪の脱毛や体毛増加などの男性化徴候があり、受診した。血中テストステロン値は476.5 ng/dLと異常高値であった。腹部CTで7cm大の右卵巣腫瘍を認めた。ホルモン産生卵巣腫瘍と診断し、腹腔鏡下右付属器切除術を施行した。摘出組織の病理検査で卵巣ステロイド腫瘍 NOS と診断した。術後血中テストステロン値は37.1 ng/dLに低下し、男性化徴候は改善した。卵巣ステロイド腫瘍 NOS の悪性転帰を予測する因子として①腫瘍径7cm以上、②核分裂像の増加、③壊死、④出血、⑤Grade2-3の核異型が報告されている。本症例は①と②が該当し、悪性腫瘍の可能性は否定できなかった。しかし、効果のある化学療法レジメンが確立していないこと、術後PET-CTで残存病巣が検出されなかったこと、患者の妊孕性温存希望があったことから、追加治療は行わず、厳重経過観察の方針とした。【結語】卵巣ステロイド細胞腫瘍 NOS の1症例を経験した。稀な腫瘍のため管理方針は確立しておらず、更なる症例の集積が必要である。

P-73-7 術前に悪性転化を考慮した上皮内癌を伴う成熟嚢胞性奇形腫の1例

八尾市立病院

松浦美幸, 日野友紀子, 重光愛子, 佐々木高綱, 永井 景, 山田嘉彦

【緒言】成熟嚢胞性奇形腫は全卵巣腫瘍の約20%を占める良性疾患であり、日常診療でよく遭遇する疾患である。若年女性に好発するが閉経後女性にも認められ、約1-2%に悪性転化を来すが術前診断は困難であることが多い。今回我々は術前MRIでは良性を疑ったが、年齢、腫瘍マーカー、腫瘍径から悪性転化の可能性を念頭に置き開腹付属器切除術を行い、術後病理検査にて上皮内癌を伴う成熟嚢胞性奇形腫と診断した1例を経験したので文献的考察を加え報告する。【症例】55歳閉経後女性。5経妊3経産。既往歴、家族歴に特記なし。健康診断にて血清CA19-9値の上昇を指摘され精査的に当科紹介となった。MRIでは左卵巣にT1強調像で高信号、T2強調像で低信号、脂肪抑制T1強調像で低信号を示す長径105mmの腫瘍を認めた。充実性部分は造影効果を示さず、成熟嚢胞性奇形腫を疑った。しかし、年齢が55歳、血清SCC値が4.5ng/ml、腫瘍径が10cm超であることから悪性転化の可能性を念頭に開腹左付属器切除術を行い腫瘍を破綻なく摘出した。術後病理診断は上皮内癌を伴う成熟嚢胞性奇形腫であり、後日腹式単純子宮全摘術、右付属器切除術、大網切除術を行った。病変は左卵巣に局限しており術後は経過観察の方針とし、現在に至るまで再発を認めていない。【結語】術前MRIでは良性を疑ったが、その他の因子から悪性転化を考慮し加療を行った上皮内癌を伴う成熟嚢胞性奇形腫の症例を経験した。成熟嚢胞性奇形腫はそのほとんどが良性であることから腹腔鏡手術が選択されることが多いが、悪性転化のリスクが上昇するとされる因子を有する症例においては術式選択に慎重を期すべきである。

P-73-8 閉経後に発症した Dysgerminoma に対して Secondary debulking surgery を施行した1例

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【緒言】Dysgerminoma は主に小児から若年者で発症する悪性腫瘍である。今回、閉経後に発症した Dysgerminoma に対する治療を経験したので報告する。【症例】51歳、2妊2産、閉経50歳。腹部膨満感で前医初診。MRIで卵巣悪性腫瘍もしくは子宮癌肉腫の疑いで当院紹介され、診断目的で手術となった。開腹すると弾性硬の腫瘍が下腹部に充満し、左卵巣由来と判断。腫瘍とS状結腸が強固に癒着しており、S状結腸の損傷を避けるべく、腫瘍に切り込むように左付属器を摘出した。迅速病理では悪性腫瘍の診断、組織型は診断困難であった。子宮全摘、右付属器摘出、大網部分切除、骨盤リンパ節生検を実施。S状結腸に強固に癒着した5cm大の腫瘍は摘出困難と判断し閉腹した。最終病理診断で卵巣 Dysgerminoma FIGO stage IIICの診断。術後後療法としてBEP療法を3コース施行した。PET-CTでS状結腸間膜に3cm大の腫瘍あり、Secondary debulking surgery (SDS)により完全摘出。最終病理では悪性の遺残は無く、さらなる後療法は施行しない方針。最終治療から6か月間無再発で経過している。【考察】卵巣 Dysgerminoma は若年での発症が主であり、51歳での発症は極めて稀である。治療としてはシスプラチンを含む化学療法の奏効率が高いとされている。一方で Dysgerminoma 初回治療後の残存腫瘍に対する治療は一定の見解が無い。本症例はSDSにより完全摘出が可能であり、結果的には病理学的に術後BEP療法の完全奏功が証明された。【結論】51歳で発症した卵巣 Dysgerminoma の治療を経験した。閉経後に発症した Dysgerminoma の残存腫瘍に対してSDSを施行された症例は稀であり、今後さらなる症例の蓄積が望まれる。

P-74-1 進行・再発卵巣癌に対するニラバリブ11例の使用成績

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【目的】ニラバリブの有効性、安全性を検討する。【方法】当科でニラバリブを使用した卵巣癌症例の臨床データを診療録より抽出し、「人を対象とする生命科学・医学系研究に関する倫理指針」に従い、後方視的に検討した。【成績】2021年1月以降、当科で11例の使用経験があった。内服開始用量は200mg/日が10例、100mg/日が1例であった。1)卵巣癌における初回化学療法後の維持療法として2例に使用した。1例にグレード3の血小板減少を認めたが100mg/日に減量して内服継続中である。残る1例は患者希望で早期に中止となった。2)白金系抗悪性腫瘍剤感受性の再発卵巣がんにおける維持療法として5例に投与した。ニラバリブによる維持療法を行っている。1例に8か月後に再燃を認め中止したが、残る4例は内服継続中である。3)前治療として3ライン以上の抗がん剤治療が行われた、白金系抗悪性腫瘍剤感受性の相同組み換え修復欠損(HRD)を有する再発卵巣癌4例に対し使用したが、4例とも内服2か月以内に病勢進行(PD)に至った。【結論】エビデンスに基づきニラバリブを使用したのが、実臨床における効果、安全性はさらなる検討が必要である。

P-74-2 卵巣癌に対する維持療法における PAOLA レジメンの当科使用経験

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【緒言】相同組み換え修復欠損(HRD)を有する卵巣癌における初回化学療法後のオラバリブとベバシズマブの併用維持療法であるいわゆるPAOLAレジメンが、本邦で2020年12月に承認された。当科でも卵巣癌維持療法として2021年3月よりPAOLAレジメンを使用しており、これまでに3例の投与経験がある。【症例】症例1は、51歳、卵巣癌IIIC期、High-grade serous carcinoma。術前化学療法としてdose-dense TCおよびTC療法を行った後に卵巣癌根治手術を行い、残存腫瘍なし。HRD陽性を確認して、術後補助化学療法としてTC+ベバシズマブ併用療法を3サイクル行った後にPAOLAレジメンに移行した。症例2は、49歳、卵巣癌IVB期、High-grade serous carcinoma。術前化学療法としてTCおよびdose-dense TC療法を行った後に卵巣癌根治手術を行い、残存腫瘍なし。HRD陽性を確認して、術後補助化学療法としてTC+ベバシズマブ併用療法を4サイクル行った後にPAOLAレジメンに移行した。グレード3の貧血と血小板減少を認めたため現在休業している。症例3は、48歳、卵巣癌IVB期、High-grade serous carcinoma。術前化学療法としてdose-dense TC療法を行った後に卵巣癌根治手術を行い、残存腫瘍なし。HRD陽性を確認して、術後補助化学療法としてTCおよびTC+ベバシズマブ併用療法2サイクルを行った後にPAOLAレジメンに移行した。【考察】1例で副作用のため休業しているが、その他2例にはグレード3以上の副作用は認めていない。最長投与症例は7か月で、全例で現在まで再発を認めていない。PAOLAレジメン導入後の使用経験と安全性を検討し、文献的考察を含めて報告する。

P-74-3 ニラバリブにより出血傾向を伴う血小板減少を認めた卵巣がん IVB 期の一例

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【症例】70歳代3妊3産【主訴】便秘【現病歴】内科で施行した下部消化管内視鏡検査で直腸粘膜下腫瘍を認め、生検で漿液性癌のため、婦人科臓器由来と考えられ当科紹介。【検査所見】画像で右卵巣が腫大し、子宮と直腸へ浸潤を認め、播種巣により結腸狭窄を認めた。また、胸腹水、骨盤・鼠径リンパ節の有意な腫大、臍・肝臓・肺に腫瘍を認め、臍の穿刺吸引細胞診で腺癌を認めた。CA125 6449U/ml (基準値 35 U/ml>)。【診断】卵巣がん IVB 期、漿液性癌、T3cN1M1【経過】化学療法 (ddTC 療法) 8 コース施行し、原発巣の著明な縮小・転移巣の消失、CA125 陰性化を認めたため、腫瘍減量術を施行し、完全切除であった。術後1か月、CTで明らかな残存病変を認めず、ニラバリブによる維持療法を開始した。ニラバリブ投与開始前の血小板は28万/μlであったが、day14に7万/μlと低下し、投与中止した。しかしながら、day16に2.2万/μl、day21に1000/μlとさらに低下し、出血傾向を認めたため緊急入院し、同日および第6病日に血小板輸血を施行、その後徐々に血小板上昇傾向となった。またG4の好中球減少も併発したため、G-CSFと抗生剤を投与した。その後骨髄抑制改善したため、第15病日に退院。現在、維持療法は行わずに経過観察中であり、原疾患の再発は認めていない。【まとめ】ニラバリブ投与開始間もなく急激な骨髄抑制を認め、自然回復に約2週間を要した症例を経験した。ニラバリブによる骨髄抑制、特に血小板減少に留意した管理は重要であると考ええる。

P-74-4 当院での Niraparib の使用経験について

大阪はびきの医療センター

西川恭平, 中野和俊, 藤田由布, 小川憲二, 安川久吉, 赤田 忍

【目的】Niraparibは進行卵巣癌の初回化学療法後の維持療法ならびに白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法などの適応で2020年11月より本邦で販売開始となった。卵巣癌に幅広く使えるPARP阻害剤であるが、同じPARP阻害剤であるOlaparibに比べて本邦での使用経験がまだ少ない。そのため、今回我々が当院でNiraparibを使用した13例をまとめ、これを報告する。【方法】当院でNiraparibを使用した症例を後方視的に検討した。【成績】年齢は45-77歳であり、中央値は63歳であった。投与期間は2-10か月であり、中央値は6か月であった。進行卵巣癌の初回化学療法後の維持療法が6例、再発卵巣癌における維持療法が7例であった。組織型は高異型度漿液性癌10例、類内膜癌2例、低異型度漿液性癌1例であった。BRCA遺伝子変異を認めた症例はなく、HRDを認めた症例もなかった。有害事象として最も多かったものが血小板低下であり5例で減量となった。嘔気/食思不振で休薬が必要となった症例がそれぞれ1例ずつ認められたが休薬によって症状が改善し、200mgのまま再開可能であった。その他重篤な副作用として間質性肺炎を認めた症例が2例あった。内服中止となった症例は上記2例と再発を認めた3例であった。【結論】PARP阻害剤であるNiraparibは適応が広く、今後使用が増えると考えられる。当院での経験では嘔気による中止や減量などはなく症状のコントロール可能であるが、血小板低下など開始から4週間以内に有害事象が起こることも多く、間質性肺炎のような副作用報告も存在する。内服での維持療法であり患者のQOLも高い反面、Bevacizumabでの維持療法では起こらない副作用も多い為注意が必要である。

P-74-5 当院におけるオラパリブの使用経験

杏林大付属病院

春名佑美, 百村麻衣, 西尾南紗, 對馬可葉, 富岡紀子, 渡邊百恵, 澁谷裕美, 西ヶ谷順子, 松本浩範, 森定 徹, 小林陽一

【目的】プラチナ感受性再発卵巣癌の維持療法としてオラパリブが登場して3年が経過し、最近ではMychoice診断システムやBRCAanalysis診断システムなどのコンパニオン検査により初回化学療法後の維持療法としても用いられるようになった。当院のオラパリブ投与例を対象に、安全性や治療効果について検討した。【方法】2018年4月から2021年7月に当院でオラパリブを投与された、卵巣癌、卵管癌、腹膜癌患者36症例を対象とし、後方視的に検討した。【成績】原発部位は、卵巣癌26例、卵管癌3例、腹膜癌6例、卵巣・卵管・腹膜(分類不能)が1例であった。年齢の中央値は62歳(39-80)であった。組織型は、高異型度漿液性癌が28例、類内膜癌が1例、明細胞癌が2例、その他5例であった。進行期は、I期1例、II期1例、III期26例、IV期8例であった。36例中6例が初回治療の維持、30例が再発に使用した。G3以上の副作用が発現したものが9例あり、その半数は貧血であった。いずれも投与開始から4か月以内に発症していた。オラパリブ投与期間は、1か月~24か月で、初回投与量600mgでの継続率は55%であった。減量の原因は貧血と腎機能障害が多かった。再発30例中7例でTFIの延長を認めた。延長した7例のオラパリブ開始前の化学療法効果判定は、CRが3例、PRが3例、SD1例であった。前レジメン数は2レジメン5例、3レジメン1例、5レジメン1例であった。【結論】プラチナ感受性卵巣癌の維持療法としてのオラパリブは投与早期に副作用が発現することが多いが、休薬・減量基準を順守することで安全に使用することができた。またプラチナ感受性再発卵巣癌では直前の化学療法での奏功がPRであっても有用であることが示唆された。

P-74-6 多施設共同研究におけるプラチナ感受性再発卵巣癌に対するオラパリブの奏効期間についての後方視的検討

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【目的】再発卵巣癌に対しオラパリブ投与症例の中で約15%の患者は5年以上の長期無増悪期間が得られることが報告されているが、長期奏効例の効果予測因子は明らかになっていない。今回我々は、多施設共同研究において再発卵巣癌に対するオラパリブの奏効期間について検討した。【方法】対象はプラチナ感受性再発卵巣癌46例、卵管癌6例、腹膜癌7例の59例であり、①オラパリブ投与直前に施行した化学療法の治療成績とオラパリブ奏効期間について②オラパリブの2年以上の長期奏効例について検討を行った。【成績】①患者のオラパリブ開始時の年齢中央値は63歳(34-78歳)、オラパリブ維持療法前のプラチナ併用化学療法の直接効果はcomplete response (CR):21例(36%)、partial response (PR):27例(46%)、stable disease (SD):9例(15%)、progressive disease (PD):2例(3%)であった。②オラパリブ投与直前化学療法での無増悪生存期間とオラパリブ投与開始後の無増悪生存期間を比較した結果、CR例でのみオラパリブ投与後の無増悪生存期間の方が長い傾向にあった。③オラパリブ投与後無増悪生存期間は、BRCA変異陰性よりBRCA変異陽性で長い傾向にあった。④2年以上長期奏効例は16症例あり、BRCA変異は4例で陽性、1例で陰性、11例は未検で今後パネル検査を行う予定である。【結論】前治療CR例やBRCA変異例はオラパリブが奏効しやすい可能性がある。今後2年以上の長期奏効例について、遺伝子パネル検査を行う予定である。

P-74-7 減量を行なったが投与継続ができなかった niraparib の一例

横浜労災病院

相原隆充, 松永竜也, 佐藤理穂, 宇都宮真理子, 道佛美帆子, 瀬川恵子, 大井由佳, 笠井絢子, 茶木 修

【緒言】卵巣癌治療においてPARP阻害薬はプラチナ製剤による化学療法後の維持療法として大幅なPFSの延長を認め、2018年にolaparibが、2020年よりniraparibが使用可能となった。PARP阻害薬は投与開始後早期から消化器症状や血球減少を生じるが、中止/減量基準に従うことで投与継続が可能とされる。しかし、実臨床ではその程度や頻度が臨床試験と異なることもある。血小板減少による有害事象によりniraparibの投与継続が困難となった症例を経験したため、経過から血小板減少について考察する。【症例】57歳、1妊1産。40歳閉経。下腹部腫瘍を契機に卵巣悪性腫瘍の疑いで手術を行い、卵巣癌IIIC期、pT3cNXM0、高異型度漿液性癌と診断した。術後化学療法としてdd-TC療法を6サイクル行い、効果判定PRで経過観察とした。7か月後に再発し、プラチナ感受性再発としてTC療法6サイクルを行い、再びPRの判定の後、niraparib200mg/日による維持療法を開始した。内服開始18日後に頻回な鼻出血が出現し、血小板がG4まで低下し、血小板20単位輸血を行った。26日間休業し、血小板14.9万まで回復を確認した後に100mgで再開したが、3か月後に再び血小板がG4まで低下し、血小板20単位輸血を行った。【結語】今回適正使用基準に従い100mgまで減量したが、再びG4の血小板減少にてniraparibの投与継続が困難となった症例を経験した。臨床試験では血小板減少による投与中止は3%程度と報告されているが、有害事象のリスク因子については不明な点も多い。また、nadirがわからないため輸血のタイミングにも苦慮した。niraparibの血小板減少に関し、体重や血小板数以外のリスク因子、出現のタイミングについて文献を交えて考察する。

P-74-8 当院でプラチナ感受性再発卵巣癌におけるPARP阻害薬維持療法中に増悪を認めた症例の検討

市立広島市民病院

田中奈緒子, 植田麻衣子, 保崎憲人, 久保倫子, 森川恵司, 片山陽介, 玉田祥子, 関野 和, 依光正枝, 上野高子, 石田 理, 児玉順一

【目的】近年、PARP阻害薬に対する耐性獲得について、腫瘍細胞における相同組換え修復機構の回復が示唆されている。プラチナ感受性卵巣癌では、相同組み換え修復機構が破綻している場合が多く、PARP阻害薬に耐性を獲得した腫瘍ではプラチナ製剤の効果が低い可能性が考えられる。今回、当院におけるオラパリブ維持療法後の化学療法の治療効果を検討することを目的とした。【方法】2018年4月~2021年4月にプラチナ感受性再発卵巣癌に対しオラパリブによる維持療法中に増悪を認めた症例を対象とし、オラパリブ維持療法後の化学療法の治療内容、治療効果および治療効果に影響する因子(PFI、プラチナ製剤の有無)を検討した。【成績】期間中にオラパリブによる維持療法を行ったのは52例であり、増悪のため治療終了した症例は27例(52%)であった。年齢中央値は69歳、組織型は漿液性癌17例、粘液性癌2例、明細胞癌1例、類内膜癌1例、混合癌1例、癌肉腫1例、不明4例であった。オラパリブ治療期間中央値は3か月(1-14か月)、PFI6か月未満16例、6か月以上11例であった。1例を除いた26例に対しオラパリブ維持療法後に化学療法を行い、プラチナ製剤17例、非プラチナ製剤9例であった。画像診断で治療効果を判定した21例の治療効果はCR2例、PR3例、SD2例、PD14例であり、病勢コントロール率(DCR)は33%であった。プラチナ製剤と非プラチナ製剤のDCRはそれぞれ43%と0%であった。PFI6か月未満と6か月以上のDCRは27%と40%であった。【結論】オラパリブ維持療法中に増悪を認めた症例にもプラチナ製剤の効果は認められた。オラパリブ維持療法後の化学療法はPFI6か月以上の症例において治療効果が高い傾向がみられた。

P-74-9 再発卵巣癌に対するPARP阻害薬による維持療法の検討

大阪国際がんセンター

久 毅, 小泉 舞, 坂口仁美, 前田通秀, 角田紗保里, 渡辺正洋, 松崎慎哉, 馬淵誠士, 上浦祥司

【目的】当院で再発卵巣癌にたいしPARP阻害薬による維持療法を行った症例について、PFI (Platinum Free Interval) の延長効果やその後のプラチナ製剤を含めた多剤併用療法の治療成績を中心に検討を行った。【方法】2006年5月から2021年9月の期間で、卵巣癌の診断で治療を開始した症例のうち、再発に対しPARP阻害剤による治療を行った46例を対象とし、その治療成績を後方視的に検討した。PFI延長効果については組織型、進行期、PARP阻害剤投与前の治療効果を中心にその要因について検討した。再発に対し外科治療および放射線治療を行った症例は除外した。【成績】年齢中央値は58歳(41-80)、進行期はI期からIV期までそれぞれ3/3/26/14例であった。術前化学療法を行った症例は24例、組織型別では高異型度漿液性癌37例、類内膜癌3例、明細胞癌2例、粘液性癌1例、その他3例であった。一次再発で投与した症例が59% (27/46例)であり、PARP阻害剤投与前の奏効はCR/PR/SDがそれぞれ12/29/5例であった。PFIについては前回のPFIより延長した症例を11例(24%)に認め、延長期間の中央値は12か月で漿液性癌症例で延長する傾向にあった(42.3% : 11/26)。PARP阻害剤投与後のプラチナ製剤の奏効率はPFI6-12か月の群で25% (1/4)、12か月以上の群で56% (5/9)であった。【結論】再発卵巣癌治療においてPARP阻害剤によるPFIの延長する症例を認めた。今回の検討ではPARP阻害剤投与後のプラチナ製剤の奏効はある程度得られているが症例が少なく、プラチナ感受性再発か否かの判断基準はPFIの期間を含めて今後検討されるべき課題である。

P-75-1 PARP阻害剤導入によるプラチナ感受性再発卵巣癌に対する化学療法選択の変化

群馬大附属病院

周藤 周, 東 杏莉, 小林 梓, 尾池 妙, 中尾光資郎, 池田禎智, 平川隆史, 岩瀬 明

【目的】PARP阻害剤導入前後のPSRに対する化学療法の実施状況を後方視的に評価し、それに関連する要因を考察することを目的とした。【方法】2015~2020年に当院で施行した、PSRに対する化学療法について、PARP導入前後の2群に分け、投薬内容、コース数を比較した。前期、後期における最良効果判定、奏効率、病勢制御率および、レジメン毎のHSRの発生状況を比較した。【成績】症例数は前期22名、後期39名、レジメン数は前期25、後期45であった。年齢の中央値は前期62歳、後期59歳、進行期、組織型の患者背景に大きな差は認めなかった。レジメンは前期ではTC/DCベースが15例、PLD-Cが4例、単剤が4例であったのに対して、後期ではTC/DCベースが25例、PLD-Cが15例、単剤が5例であった。コース数の中央値は前期が6、後期は4であった。最良効果判定は前期CR17、PR1、SD4、PD3、後期はCR12、PR18、SD6、PD9であり、奏効率は前期が72%、後期が67%であった。後期ではPARP阻害剤投与の基準を満たした30レジメンのうち19レジメンでPARP阻害剤が投与された。HSRの発生頻度はTC/DCが18%、PLD-Cが5%であった。【結論】PARP阻害剤の導入後、化学療法の施行回数は少なくなり、早期に維持療法に移行していることが示された。今後はPFSなどのパラメーターについて評価し、PARP阻害剤の長期的な効果を明らかにするとともに薬剤選択の適正化を図っていきたい。

P-75-2 当施設における卵巣癌初回化学療法後のニラバリブ維持療法の治療経験

藤田医大

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【目的】PARP阻害薬であるニラバリブは、進行卵巣癌に対する初回プラチナベース化学療法に奏効後の維持療法としての有効性が示されている。しかしながら、現時点で本邦における使用経験は多くなく、安全性等に関する報告は十分ではない。本研究では、当施設におけるニラバリブの実地臨床での使用経験につき報告する。【方法】当施設において進行卵巣癌、卵管癌、原発性腹膜癌の初回化学療法後の維持療法としてニラバリブを投与した患者を対象とした。対象患者の臨床的背景、ニラバリブ投与状況、有害事象、治療効果等について診療録を用いて後方視的に検討した。【成績】初回化学療法後の維持療法として10例の患者にニラバリブを投与した。年齢中央値は62.5 (50-78)歳、進行期はIII期が9例、IV期が1例であり、組織型はいずれの患者も高異型度漿液性癌であった。BRCA1/2変異は9例が陰性、1例が不明であった。初回化学療法のサイクル数は3-7回、ニラバリブ開始用量は200mg/日であった。ニラバリブ投与開始からの観察期間(中央値158日、幅27-252日)内で、6例にGrade3以上の有害事象を認めた。内訳は、好中球減少1例、血小板減少1例、貧血1例、高血圧2例、肝機能異常1例であった。1例は投与中止し、5例は休薬・減量を要したが投与継続可能であった。ニラバリブ維持療法中に2例で再発を認め、それぞれ投与開始後4.6か月、5.0か月の時点で中止となった。【結論】ニラバリブを投与した患者の60%でGrade3以上の有害事象がみられ、休薬や減量の対応を要した。維持療法開始後早期に治療中止となった症例もあり、有害事象管理や奏効予測につきさらなる蓄積が必要である。

P-75-3 プラチナ感受性再発卵巣癌に対する PARP 阻害剤オラパリブの使用経験～長期投与可能症例の検討～

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【目的】プラチナ感受性再発卵巣癌治療後の維持療法として、2018年1月にPARP阻害剤オラパリブが承認され約4年が経過した。使用する症例が増加し長期継続投与できている症例も経験した。再発卵巣癌に対しオラパリブを使用した症例の有効性及び安全性を検討し、長期投与可能となる因子を見出すことを目的とした。【方法】2018年1月～2020年10月にオラパリブを処方したプラチナ感受性再発卵巣癌において、年齢、組織型、前治療内容、BRCA遺伝子変異、投与直前の腫瘍マーカー値、投与前画像による効果判定について検討した。その中で2年以上継続投与できている症例に共通する項目を調査した。【成績】対象症例は20例で、投与開始時の年齢中央値(範囲)は64歳(39-74)であった。卵巣癌17例、卵管癌1例、腹膜癌2例で、組織型は漿液性癌17例、明細胞癌1例、分類不能の腺癌2例であった。前化学療法レジメン数の中央値(範囲)は3(1-4)であり、18例にペバシズマブ投与歴があった。投与期間の中央値(範囲)は10.5か月(1-40)であり、2年以上投与している症例は5例であった。現在治療中の症例は11例で、9例は中止となった(病状進行6例、有害事象3例)。BRCA遺伝子変異は不明17例、陽性1例、陰性2例であった。有害事象によって休薬や減量を要した症例は10例であった。長期投与できている症例に共通する所見として、効果判定がCRである、腫瘍マーカーが正常化している、漿液性癌であることが挙げられた。【結論】適切な休薬や減量にて安全に長期維持投与が可能であった。維持療法としてPARP阻害剤か血管新生阻害剤のどちらを選択するべきか判別可能になる因子を選択できるように、今後さらに症例数を重ねて検討が必要である。

P-75-4 進行卵巣癌における初回化学療法後の維持療法選択に関する後方視的検討

東北大病院

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【目的】分子標的治療薬の開発により、進行卵巣癌に対する初回がん薬物療法後の治療戦略は新たな局面を迎えた。2013年にペバシズマブ、2019年にオラパリブ、2020年にはニラパリブ、ペバシズマブ/オラパリブ併用(PAOLAレジメン)による初回化学療法後の維持療法が臨床実装された。当院での進行卵巣癌における初回化学療法後の維持療法について文献的考察を加えて報告する。【方法】当院で治療した進行卵巣癌患者(III/IV期)のうち、初回化学療法後の維持療法について、①経過観察群②ペバシズマブ維持療法群、③オラパリブ維持療法群、④ニラパリブ維持療法群、およびPAOLAレジメン維持療法群に関する後方視的検討を行った。【成績】2019年6月より経口薬(PARP阻害薬)による初回維持療法の治療選択が拡充された。ペバシズマブ、ニラパリブ、オラパリブ、PAOLAレジメンの順に多かった。オラパリブ導入時、BRCAバリエントを認めない症例、未検査の症例においてペバシズマブ維持療法が選択されていた可能性が考えられた。【結論】初回維持療法後の維持療法の選択に関しては、有効性に加えて、合併症、投与経路、コンパニオン診断の費用などが影響している可能性が示された。治療成績も含めて、引き続き診療情報を集積して検証を行う必要がある。

P-75-5 再発卵巣癌に対する PARP 阻害剤維持療法の施行状況と安全性の検討

岡山大病院

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【目的】再発卵巣癌に対するPARP阻害剤維持療法の有害事象発生について検討を行った。【方法】2018年1月から2021年8月までに当院でPARP阻害剤を維持療法として投与開始した再発卵巣癌28症例に対する維持療法の施行状況と有害事象の発生状況、減量または中止の有無について検索した。【成績】患者背景は初回再発23例、再々発5例、使用薬剤の内訳はオラパリブ23例、ニラパリブ5例であった。投与期間の中央値は6か月(2週-41か月)、14例(50%)が病勢増悪しており化学療法終了後のtreatment free intervalの中央値は11か月(1-41か月)であった。初回投与量を有害事象のために減量したのは13例(46%)であった一方で、最大投与量を初回から継続している症例は15例(33%)であった。減量を要した13例のうち9例は1か月以内の早期に減量していた。オラパリブ投与例では4例で有害事象による投与中止があり、腎機能異常によるものが2例と嘔気・食不振によるものが2例であった。G2以上の骨髄抑制は貧血が28%、好中球減少が17%、血小板減少が10%、腎機能低下は32%、嘔気・食不振は21%であった。再々発では5例中3例でG3以上の貧血を認め、4例で減量を要した。【結論】PARP阻害剤投与では投与開始後早期に嘔気や食不振のために治療継続困難になる症例があり、早期から対応する必要がある。また再々発群では貧血が重症化しやすいためより慎重な経過観察が必要である。

P-75-6 再発卵巣癌に対するオラパリブ維持療法後に再燃した14例の検討

関西ろうさい病院

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【目的】卵巣癌治療はPARP阻害薬の登場によって大きな変化を迎えた。今後はPARP阻害薬維持療法後の再燃例の後治療が問題となるため、今回これらの症例を検討した。【方法】2018年4月から2020年1月の間に、当科でプラチナ(Pt)感受性再発(PSR)に対するオラパリブ維持療法を開始し、その治療中に再燃した症例の臨床データを「人を対象とする生命科学・医学系研究に関する倫理指針」に基づき後方視的に診療録より抽出し検討した。【成績】対象症例は14例(卵巣癌10例, 腹膜癌3例, 卵管癌1例)で、組織型は高異型度漿液腺癌11例, 類内膜癌2例, 明細胞癌1例であった。前治療レジメン数の中央値(範囲)は2(1-3), platinum-free intervalの中央値(範囲)は16(6-27)か月であった。再燃までのオラパリブ投与期間の中央値(範囲)は7(2-17)か月であった。再燃時にPt最終投与から6か月以上のPSRは10例, 6か月未満のPt抵抗性再発(PRR)は4例であった。PSRには再度Pt併用化学療法±ベバシズマブが, PRRには非Pt単剤±ベバシズマブが後治療として実施された。後治療の効果はPSRで20%(PR2, SD3, PD4, NE1/10), PRRで25%(PR1, SD1, PD2/4)であった。フォローアップ期間の中央値(範囲)が23.5(17-35)か月の現在, PRの3例は担癌生存(AWD)中だが, SD以下の11例は5例がAWD, 6例が原癌死に至っている。【結論】オラパリブ維持療法後の再燃例では, PSRでもPt併用化学療法の効果が高く, 今後はPARP阻害薬耐性克服を目指したさらなる臨床試験の結果が待たれる。

P-75-7 進行卵巣癌に対するPARP阻害薬(ニラパリブ)の臨床像および有害事象に関する検討

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【目的】海外での臨床試験であるPRIMA試験, NOVA試験, QUADRA試験の結果に基づき, 本邦では2020年9月にニラパリブが進行卵巣癌に対する治療薬として承認された。先述した3つの臨床試験では300mg/日の投与量によりそれぞれ, 12.2%, 21.2%, 16.3%が血小板減少を主とした有害事象により投与中止に至っており, 本邦では200mg/日の投与量が適応されたがその安全性については明らかになっていない。今回, 当科でニラパリブを使用した症例を後方視的に検討し, その安全性について検討を行った。【方法】2020年9月から2021年5月までに当科でニラパリブを使用した卵巣癌症例15例を対象とし, その有害事象を後方視的に解析した。【成績】年齢の中央値は68歳[49-82]で, 初回治療後の11例(IIIA期:1例, IIIB期:2例, IIIC期:4例, IVB期:4例)と再発後の4例(IIIC期:3例, IVB期:1例)にニラパリブが投与された。投与期間の中央値は10週間[1-20]で, 有害事象は嘔気が7例(46.7%), 高血圧が4例(26.7%), 貧血が3例(20.0%), 血小板減少が3例(20.0%), 全身倦怠感が3例(20.0%)であった。15例中8例(53.3%)に投与量の減量もしくは一時休業を要したが, 病勢の悪化により投与中止となった1例を除いて, 全例で有害事象の再燃なく治療継続が可能であった。【結論】今後, 症例の蓄積によるさらなる検討を要するが, 本邦において進行卵巣癌に対するニラパリブ200mg/日による管理は安全に行える可能性が示唆された。

P-75-8 再発卵巣癌におけるPARP阻害剤使用の検討 オラパリブ使用後のニラパリブ使用例を通じて

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【はじめに】ボリアデノシン5'ニリン酸リボースポリメラーゼ(PARP)阻害剤は, 卵巣癌における初回化学療法後の維持療法や白金系抗悪性腫瘍剤感受性の再発卵巣癌における維持療法で使用可能となっているが, 血液毒性などの有害事象に留意した使用が求められる。白金系抗悪性腫瘍剤感受性の再発卵巣癌においてオラパリブの使用歴あるも血液毒性強く中断した後に, ニラパリブでの維持療法を試みた症例を経験したため, 若干の文献的考察を加え報告する。【症例】66歳女性, 妊娠分娩歴は3妊3産, 既往に高血圧症と糖尿病あり。卵巣癌IIIb期の診断で術後にTC療法6コース施行。PET-CTでの腹腔内播種疑いで再発の診断となり, 再度TC療法6コース施行。維持療法としてオラパリブ内服行っても骨髄抑制強く休業の上経過観察中に, CA125の上昇及びPET-CTで上行結腸腹側, 縦隔リンパ節への転移を認め再再発の診断。TC療法行ってもカルボプラチンによる過敏性反応が疑われ, 脱感作TC+Bev療法を施行した。維持療法としてニラパリブを使用の上経過観察中である。【考察】PARP阻害剤は, 本邦ではオラパリブとニラパリブが使用可能となっている。再発卵巣癌における維持療法はもちろんのこと, 初発卵巣癌治療への適応拡大, またPARP阻害剤と血管新生阻害薬などの併用も再発卵巣癌治療に有効な可能性がある。【結語】PARP阻害剤による維持療法を試みた症例を通じて, 再発卵巣癌におけるPARP阻害剤使用について検討した。血液毒性をはじめとする重篤な有害事象に留意して使用することで, 再発卵巣癌治療の選択肢が広がるものと考えられた。

P-75-9 再発卵巣癌に対する Schlafen11 発現と PARP 阻害剤の効果に関する検討

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【目的】プラチナ感受性再発卵巣癌では PARP 阻害剤 (PARPi) 維持療法が治療選択肢の一つとなる。PARPi のバイオマーカーには BRCA variant を含めた相同組換え修復異常 (HRD) とプラチナ感受性がある。近年、DNA 複製停止作用を持つ *Schlafen (SLFN) 11* の発現がプラチナ製剤や PARPi の感受性と相関することが報告されている。再発卵巣癌で *SLFN11* が PARPi の新たなバイオマーカーとなり得るかを検討した。【方法】2018 年~2021 年まで再発卵巣癌に対し PARPi 投与を行った 30 例を対象とした。手術による摘出検体を *SLFN11* 抗体で免疫染色し、陽性群と陰性群で臨床病理学的因子と予後を後方視的に解析した。【成績】*SLFN11* 陽性群は 9 例 (30%)、陰性群は 21 例 (70%) であった。組織型は高異型度漿液性癌が陽性群で 6 例 (67%)、陰性群で 15 例 (71%) であり、陽性群に明細胞癌は認めなかった。PARPi 投与前のプラチナ製剤を含む化学療法の効果は陽性群が全例 PR であったのに対して陰性群では PR が 13 例 (62%) であった。PARPi 投与開始後の PD は陽性群で 6 例 (67%)、陰性群では 16 例 (76%) であった。PARPi 投与開始日からの無増悪生存期間中央値は陽性群で 235 (43-672) 日、陰性群で 182 (42-1029) 日であり、全生存期間中央値は陽性群で未到達 (死亡数 0 例)、陰性群では 579 (143-1029) 日 (死亡数 10 例) であった (有意差なし)。【結論】再発卵巣癌における *SLFN11* の発現は、PARPi 投与後の無増悪生存期間に影響を及ぼさないが、プラチナ感受性と関連し、全生存期間と相関する可能性がある。

P-76-1 悪性転化が疑われた卵巣粘液性境界悪性腫瘍の一例

宮崎大附属病院

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【緒言】卵巣境界悪性腫瘍の頻度は全卵巣腫瘍の約 9% 程度であり、5 年生存率は 98% と予後良好とされているが、悪性転化として再発する報告もある。今回、初回手術時に粘液性境界悪性腫瘍と診断され、9 年後に浸潤癌として再発した一例を経験した。【症例】32 歳女性、未経妊。X 年 2 月頃より腹部膨満を自覚し、7 月に急速に増大傾向を認めたため前医受診となった。腹部 CT 検査で腹腔内を占拠する巨大卵巣腫瘍、多量の腹水貯留を認めた。8 月に右付属器切除術を施行し、病理組織診断で粘液性境界悪性腫瘍 IC 期と診断された。妊孕性温存を希望され、術後化学療法として TC 療法 4 コースを施行した。初回手術から 5 年後の胸腹部 CT 検査では再発所見を認めなかった。初回手術から 8 年後、CA125 が 39.5U/mL と上昇しており、腹部 CT 検査で左横隔膜下に約 8cm 大の腫瘍性病変を認めた。初回手術+9 年 1 月に PET-CT 検査を施行し、左横隔膜下、腹腔動脈根部リンパ節、右鎖骨上窩リンパ節、縦隔リンパ節、右乳房に異常集積を認めた。左横隔膜下腫瘍に対して超音波ガイド下経胃的腫瘍生検を施行し adenocarcinoma と診断された。消化管に腫瘍性病変を認めず、原発不明癌として当院血液内科紹介受診となった。右鎖骨上リンパ節の細胞診では、腺癌の転移の所見であり、既往歴から卵巣腫瘍の悪性転化として当科紹介となった。TC+Bev 療法 6 コース施行したところ、腫瘍の縮小傾向を認めたため、同年 10 月に左横隔膜下腫瘍・脾臓・横隔膜合併切除術を施行した。病理組織診断は adenocarcinoma であり、卵巣腫瘍の悪性転化が疑われた。今後、化学療法施行予定である。本症例について文献的考察を加えて報告する。

P-76-2 若年境界悪性卵巣腫瘍患者に対する腫瘍核出術の妊孕性温存治療としての可能性

名古屋大附属病院

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【目的】片側付属器摘出術既往がある若年卵巣腫瘍患者が妊孕性温存を希望された際、術前診断として良性とはい切れずかつ悪性を強く疑う所見がない場合には、治療方針を検討するにあたり参考となるデータは限られている。本研究では、境界悪性卵巣腫瘍に対する腫瘍核出術が再発に与える影響を付属器摘出術と比較して検討した。【方法】1986 年から 2017 年までの東海卵巣腫瘍研究会の悪性卵巣腫瘍登録 4708 例から 45 歳以下の 1 期境界悪性卵巣腫瘍患者 285 例を抽出した。内訳は腫瘍核出術 27 例、患側付属器摘出術 184 例、妊孕性非温存手術 74 例であった。統計解析には Cox 比例ハザードモデルおよび Kaplan-Meier 法等を用いた。また、傾向スコアを用いた逆数重み付け法により調整を行った。【成績】観察期間の中央値は 62.0 (1.2-270.4) か月であった。腫瘍核出術で 1 例 (3.7%)、患側付属器摘出術で 7 例 (3.8%)、妊孕性非温存手術で 2 例 (2.7%) の計 10 例 (全体の 3.5%) に再発を認めた。多変量解析では、腫瘍核出術は無再発生存に対する有意な予後因子ではなかった (ハザード比 1.276, 95% 信頼区間 0.150-10.864, $P=0.823$)。逆数重み付け法で調整した 5 年無再発生存率は腫瘍核出術 95.8%、患側付属器摘出術 96.0% で有意差はなかった ($P=0.378$)。【結論】早期の境界悪性卵巣腫瘍若年患者において腫瘍核出術は再発を増加させなかった。今後さらなる検証は必要ではあるが、片側付属器摘出術既往がある若年卵巣腫瘍患者が妊孕性温存を希望された場合、境界悪性腫瘍に対しては腫瘍核出術が治療選択肢の一つとなり得る可能性が示された。

P-76-3 卵巣境界悪性腫瘍の再発診断について—当科で経験した再発例6例の検討—

田附興風会医学北野病院

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【目的】卵巣境界悪性腫瘍は5年生存率が95%, 10年生存率が90%と予後良好であるが, 晩期再発の報告もされている。2017年4月より当院で再発した卵巣境界悪性腫瘍の再発様式・診断に至った経緯を中心に文献的な考察を踏まえて報告する。【方法】2017年4月から2021年9月までの間に当科で経験した卵巣境界悪性腫瘍の再発6例を検討した。【成績】患者年齢は32歳から76歳であった。初発時の組織型は顆粒膜細胞腫が1例, 漿液性境界悪性腫瘍が4例, 粘液性境界悪性腫瘍が1例であった。初回手術術式は基本術式(腹式単純子宮全摘術+両側付属器切除術+大網切除術)が2例であり, 妊孕性温存手術は4例であった。再発までの期間の中央値は3年2か月(1年1か月から6年4か月)であり, 再発部位は, 2例は前回核出術を行い残存していた卵巣, 1例は対側卵巣, 残りの3例はリンパ節や腹腔播種での再発であった。また2例は単発で, 4例は多発再発であった。初回手術後の経過観察中の画像診断は症例によりCT検査やMRI検査が定期的に行われていたが, 再発の診断時にCT検査では確定診断に至らず, MRI検査で診断に至った症例を認めた。再発を疑った際にPET-CT検査は4例で行われたが, 3例ではFDG集積を認めなかった。腫瘍マーカーは全例測定していたが, 上昇を認めない症例が4例あった。【結論】卵巣境界悪性腫瘍の経過観察中には定期的なCT検査, 腫瘍マーカーに加え, 子宮や付属器の残存症例では特に適宜MRI検査を行うことが再発診断に有用と考えられた。

P-76-4 Peutz-Jeghers 症候群に合併した Atypical Lobular Endocervical Glandular Hyperplasia (LEGH) 様卵巣粘液性境界悪性腫瘍の一例

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Peutz-Jeghers syndrome (PJS) では, 若年からの様々な悪性腫瘍や Lobular Endocervical Glandular Hyperplasia (LEGH) の合併が知られている。PJS に Atypical LEGH 様卵巣粘液性境界悪性腫瘍を合併した一例を経験したので報告する。症例は60歳, 3妊2産。既往歴として10歳時, 16歳時に腸閉塞があり, 23歳時に消化管に多発ポリープを指摘され, PJS と診断。腹部膨満感を主訴に当院を紹介受診し, CT, MRI で多房性嚢胞性腫瘍を認め, 境界悪性または悪性腫瘍を疑う卵巣腫瘍と診断された。腹式単純子宮全摘出術, 両側付属器摘出術, 骨盤リンパ節生検を施行され, 卵巣粘液性境界悪性腫瘍 pT1cIN0M0, FIGOIC1期と診断。術後, 複数回の腸閉塞をきたし, 試験開腹が施行された。開腹時, 小腸から小腸間膜にかけての播種が認められ, 生検による病理組織学的検査で胃または卵巣原発の胃型腺癌と診断。術後の上部消化管内視鏡検査では, 胃のポリポーシスが認められたが, 悪性所見はなかった。このため, 初回手術時の検体を再検討したところ, 卵巣腫瘍には, 大型の導管様腺管の周囲に小型腺房様の腺管が分葉状に分布しており, 免疫組織化学染色で MUC5AC (+), MUC6 (+), p53 (wild type pattern), ER (-) を呈していた。細胞異型を示す上皮が領域性をもち多巣性にみられ, Ki-67 陽性細胞の増数も認められ, 子宮頸部における Atypical LEGH の基準をみたすものと考えられた。PJS 症例における Atypical LEGH の基準を満たす卵巣腫瘍の報告は稀であり, 文献的考察を加えて報告する。

P-76-5 稀な両側傍卵巣境界悪性腫瘍に対する治療経験

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【目的】傍卵巣境界悪性腫瘍の発生はまれである。傍卵巣嚢腫全体でも発生頻度は付属器腫瘍の発生頻度の10%程度とされている。今回, 腹腔鏡補助下核出術後の病理学的検索にて両側傍卵巣境界悪性腫瘍の診断に至った一例を経験したので報告, 文献的考察を加える。【方法】症例は20歳, 下腹部痛で近医へ受診した際に施行した超音波検査で骨盤内の巨大卵巣嚢胞を指摘され, 精査目的に当科へ紹介となった。撮影した骨盤部単純MRIで24cm大, 二房性の巨大卵巣嚢腫を指摘され, 腹腔鏡補助下腫瘍摘出術を施行した。【成績】術中, 左右付属器に1つずつ嚢腫を確認した。サンドバルーンで漿液性の内容物を合計4600ml吸引し観察したところ, 両側傍卵巣嚢腫であることが判明した。体外法にて両側傍卵巣嚢腫腫瘍壁を核出, 核出部を連続縫合で修復し手術を終了した。経過良好につき, 術後6日目に退院の運びとなった。病理学的検索では大半は良性漿液性腺腫の所見であったが, 一部上皮の旺盛な増殖形態や砂粒体像を認め, 両側傍卵巣境界悪性漿液腫瘍の診断に至った。【結論】本症例では両側傍卵巣管境界悪性腫瘍であり, 妊孕性温存の観点から核出術のみで経過観察を行っている。腹腔鏡下手術を行った傍卵巣境界悪性腫瘍の症例報告は国内外散見され, 検討を行った。

P-76-6 卵巣境界悪性腫瘍の臨床背景・検査所見の多様性の検討

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【目的】卵巣境界悪性腫瘍 (BT) の中には粘液性 (MBT), 漿液性 (SBT), 漿液粘液性 (SMBT) の頻度が多い。これらは病理学的な分類だが, 臨床所見や患者背景は画一でない。本研究ではこの3種のBTそれぞれについて, 発症年齢, 腫瘍マーカー, 腫瘍径のばらつき程度に着目し, 病態や発生メカニズムの違いを考察することを目的とした。【方法】対象: 2005~2016年に当院で手術を行ったMBT34例, SBT18例, SMBT24例。発症年齢(歳), CA19-9値(IU), CA125値(IU), 画像上最大腫瘍径(cm)を比較すると共に, ばらつきは変動係数(CV:%)を用いて評価した。【成績】発症年齢の中央値/CVはMBT: 42.0/36.3, SBT: 43.5/35.9, SMBT: 43.5/27.3で, 発症年齢に有意差は無かった。腫瘍径の中央値/CVはMBT: 20.2/35.3, SBT: 6.1/40.2, SMBT: 7.5/63.8で, MBTが有意に他よりも大きく($p<0.0001$), CVはSMBTで最も大きかった。CA125の中央値と対数変換後のCVは, MBT: 29.2/20.7, SBT: 24.7/53.6, SMBT: 24.7/40.2で, SBT, SMBTでCVが大きかった。CA19-9についてはMBT: 18.7/41.9, SBT: 22.5/27.9, SMBT: 26.0/57.6で, SMBTのCVが特に大きかった。SMBTのCA19-9は発症年齢と正の相関を認めた($r=0.334$)。【結論】MBTは大きな腫瘍を形成し, SBTは小さめの腫瘍でCA19-9のばらつきは少ないという特徴がある。それに比してSMBTは, 症例間での腫瘍容積, CA19-9, CA125の値が症例間で異なるという多様性が見られる。特にCA19-9の多様性には, 発症年齢との関与が示唆され, SMBT特有の病態や発生メカニズムに時間的要因が部分的に関与している可能性が考えられる。

P-76-7 悪性を疑うも茎捻転であった奇形腫を伴う巨大な粘液性境界悪性腫瘍

大津赤十字病院

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腹腔内を占拠する巨大な卵巣腫瘍は捻転することは珍しいと考えられている。今回, 30cmを超える卵巣腫瘍が茎捻転を起こし, 術前検査では悪性腫瘍が疑われた1例を経験した。68歳経産婦。初診の2-3年前から腹部膨満感あるも放置。初診2週間前に右下腹部痛が出現し前医を受診, 腹部CT検査で巨大卵巣腫瘍を認め当科に紹介となった。当科初診時には腹痛は軽減していたが, 腹腔内を占拠する巨大腫瘍を認めた。腫瘍マーカーはCA19-9: 4495.0U/mL, CA125: 247.9U/mL, SCC: 2.8ng/mLといずれも高値であった。造影MRI検査では石灰化や脂肪を含む部分と粘液部分とでなる多房性の巨大腫瘍で, 一部に拡散制限を伴う充実部を認めた。PET-CT検査では壁に結節にFDGの集積を認めるも, 遠隔転移・リンパ節転移は認めなかった。検査結果から, 成熟奇形腫と粘液性癌の混在もしくは奇形腫の悪性転化と考え, 初診から1か月後に開腹手術を施行した。腹水細胞診は陰性。腫瘍は周囲組織と癒着があり, 特に大網と強固に癒着していた。癒着剝離を進めると腫瘍背側で右骨盤漏斗靭帯が360度捻転していることが確認された。術中迅速組織診では良悪性の判定困難であり, 子宮全摘+両側付属器切除+大網部分切除を施行した。術後の病理検査は奇形腫を伴う粘液性境界悪性腫瘍(pT1aNXMX)の診断であった。術前画像を後方視的に確認すると, 捻転を示唆する所見を認めた。捻転により循環障害があると良悪性の評価は困難である。巨大な卵巣腫瘍でも捻転の可能性を考慮する必要があると考えられた。

P-77-1 当院で経験した巨大卵巣腫瘍の3症例

兵庫県立尼崎総合医療センター

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【緒言】巨大卵巣腫瘍は血栓症の合併や腫瘍摘出時の循環動態の変動, 術後の再膨張性肺水腫による呼吸不全など周術期管理に留意が必要である。今回, 呼吸や循環動態へ影響を及ぼす可能性のある巨大卵巣腫瘍を3例経験したので報告する。【症例】手術は全症例で局所麻酔下の小開腹し, 腫瘍内容液を緩徐に吸引し循環動態の安定などを確認後, 全身麻酔に切り替えた。症例1: 52歳腹部膨満, 全身脱力で前医に搬送。CTで40cm大の卵巣腫瘍を指摘された。呼吸状態悪化し気管挿管され, 当院に転院搬送。十二指腸潰瘍による高度貧血を合併。腫瘍内容液を約20L吸引し右付属器切除を施行。術後抜管するも喀痰排出できず気管切開した。また, 術後に腓骨神経麻痺や廃用症候群を発症し, リハビリ目的に転院した。症例2: 44歳自覚症状なく, 異常な腹部突出を周囲に指摘され受診。MRIで46cm大の右卵巣境界悪性腫瘍の疑い。合併症は認めず。腫瘍内容液を約20L吸引し右付属器切除を施行。術中迅速検査で粘液性境界悪性腫瘍のため根治術を行い, 術後経過は良好であった。症例3: 86歳腹部膨満, 食思不振で前医に搬送され, 肺炎の診断で入院。CTで巨大卵巣腫瘍を指摘され当院に転院搬送。MRIで30cm大の右卵巣良性腫瘍の疑い。深部静脈血栓症を合併。手術時は循環器科でIVCフィルターを挿入し, 卵巣腫瘍内容液を約10L吸引し, IVCフィルターを腎静脈下に留置後, 両側付属器切除を施行。術後経過は良好でリハビリ目的に転院した。【結論】巨大卵巣腫瘍の周術期管理を安全に行うためには, 術前の深部静脈血栓症の評価やIVCフィルター留置の必要性, 手術時の循環動態変動, 術後の再膨張性肺水腫や廃用症候群の対応を検討する必要がある。

P-77-2 進行卵巣がん手術における横隔膜切除の安全性

千葉大附属病院

錦見恭子, 楯 真一, 松岡 歩, 大塚聡代, 生水真紀夫

【目的】進行卵巣がん手術において、肉眼的残存腫瘍ゼロを目指すために横隔膜切除は高頻度に必要な術式である。横隔膜切除は難しい手技ではないが、ときに合併症がおこることがある。短期予後としては胸水・気胸等が報告されているが、長期合併症の報告は少ない。今回われわれは、横隔膜切除における術中合併症・短期合併症に加えて長期合併症を調査し、安全性について検討した。【方法】2008年から2020年までのあいだに当科で初回治療を行ったFIGOIII/IV期卵巣がんのうち、右横隔膜切除は264例、左横隔膜切除は118例(両側切除115例を含む)を対象とした。横隔膜切除方法・閉鎖方法、術中合併症・術後早期合併症(術後30日以内)・術後晩期合併症(術後30日以降)について検討した。【成績】右横隔膜切除264例のうち、235例に分層全層切除、29例に分層切除を行った。左横隔膜切除118例のうち23例に分層全層切除、95例に分層切除をおこなった。術中合併症は5例に発症し、右肝静脈から大量出血が1例、横隔膜に癒着した肝を切除中に出血が多くなったのが1例、肺損傷が3例であった。術後30日以内の合併症は、左横隔膜切除後のドレーンをいれていなかった2例に、ドレナージを必要とした胸水貯留が発症した。また、ドレーン抜去後の気胸が右横隔膜切除症例の2例に発症した。術後30日以降の合併症は、右横隔膜切除後の右横隔膜ヘルニア1例と、左横隔膜切除後の左横隔膜ヘルニア2例、膿性胸水1例であった。【結論】横隔膜切除後の早期・晩期合併症の頻度は大変低く、安全な手術であることが確認された。

P-77-3 当院の卵巣癌に対する Staging laparotomy での傍大動脈リンパ節・骨盤内リンパ節摘出の病期診断に対する有用性の評価

千葉県がんセンター

後藤裕磨, 田中尚武, 糸井瑞恵, 草西多香子, 井尻美輪, 海老沢桂子, 鈴鹿清美

【目的】進行卵巣癌に対しては、近年新規の分子標的薬が適応となっており、治療の選択肢が増えている。このため、卵巣癌のステージングの重要性が高まっている。当院で行った卵巣癌手術においてリンパ節郭清・生検を行った症例について検討した。【方法】2010年1月～2021年3月に当院で初回治療を開始、または他院で手術施行し卵巣癌の診断となり当院で手術治療を行った卵巣癌・卵管癌・腹膜癌症例222例のうち、傍大動脈リンパ節や骨盤内リンパ節の郭清または生検を行われた症例が157例あった。このうち術前化学療法を行わなかった131例について検討した。【成績】131例のうち20例(15%)で組織学的にリンパ節転移陽性であったが、5例は術前評価でリンパ節転移を疑われていなかった。特に5例中3例はpT1またはpT2であった。リンパ節転移のあった症例の組織型の内訳は、高異型度漿液性癌13例、明細胞癌2例、類内膜癌Grade3 2例、粘液性癌、低異型度漿液性癌、癌肉腫が1例ずつであった。20例中1例でsuboptimal surgeryとなったが、他の19例はcomplete surgeryまたはoptimal surgeryを達成できた。リンパ節の転移部位は骨盤内のみが3例、傍大動脈のみが7例、双方に転移があったものが10例であった。組織学的にリンパ節転移のなかった111例についても7例は術前評価でリンパ節転移を疑われていたが、系統的リンパ節郭清を行った結果、転移を否定された。術前の画像診断でリンパ節転移を疑われていなかった109例中5例(4.6%)でリンパ節転移を認めた。【結論】術前評価でリンパ節転移が指摘されていない場合でも系統的リンパ節郭清を行うことで正確な診断を行い卵巣癌患者に対する術後の適切な治療選択に寄与し得る。

P-77-4 長径6cm未満の子宮付属器悪性・境界悪性腫瘍についての検討

高知医療センター

山本寄人, 難波孝臣, 塩田さあや, 山本真緒, 高橋成彦, 森田聡美, 脇川晃子, 上野晃子, 松島幸生, 川瀬史愛, 南 晋, 林 和俊

【目的】長径6cm以上の卵巣嚢胞では、莖捻転のリスクが高いため、手術を勧めるが、長径6cm未満では、莖捻転のリスクが低いため、経過観察を勧める報告が多い。しかし、長径6cm未満でも悪性腫瘍の場合がある。今回、長径6cm未満の子宮付属器悪性・境界悪性腫瘍について検討した。【方法】2011年9月から2021年5月の間に当科で手術を施行した長径6cm未満の子宮付属器悪性・境界悪性腫瘍症例を対象とし、超音波所見、血清CA125値などの臨床的特徴と、同時期に手術を施行した長径6cm以上の症例と組織型、進行期を比較し後方的に検討した。【成績】対象は悪性腫瘍41例(7例は転移性腫瘍)、境界悪性腫瘍13例の54例で、年齢中央値は63歳であった。転移性腫瘍の原発巣は、乳癌2例、結腸癌2例、虫垂癌2例、直腸癌1例であった。超音波検査では充実性所見を59.3%、腹水貯留を57.4%、多房性所見を25.9%の症例に認めた。血清CA125値の中央値は、255.5IU/l(悪性腫瘍485.9IU/l、境界悪性腫瘍13.8IU/l)で、75.4%の症例(悪性腫瘍87.8%、境界悪性腫瘍33.3%)で上昇を認めた。長径6cm以上の197例(悪性腫瘍146例、境界悪性腫瘍51例)と比較すると、長径6cm未満の悪性腫瘍例は、組織型では漿液性癌、転移性腫瘍、進行期ではIII期・IV期症例が有意に多く認められた。境界悪性腫瘍例は、粘液性腫瘍が有意に少なく認められた。I期の占める割合には差を認めなかった。【結論】長径6cm未満の症例でも超音波検査で充実性所見や腹水を認め、血清CA125値が上昇している場合は、転移性腫瘍も含め悪性腫瘍を念頭に置き精査することが必要で有る。

P-77-5 当院における進行卵巣癌の審査腹腔鏡手術の現状

水戸赤十字病院

高田佳苗, 李 佳陽, 藤岡淳朗, 横野佑太郎, 角藤結莉, 豊澤秀康, 満川元一, 杉山将樹

【目的】進行卵巣癌における審査腹腔鏡手術は、腹腔内観察や組織診断の目的で近年多くの施設で導入されている。今回当院における審査腹腔鏡の現状について報告する。【方法】2020年より1年間で審査腹腔鏡手術した進行卵巣癌または腹膜癌9症例を対象に後方視的に検討した。【成績】年齢の中央値は66歳(54-79)であった。手術時間は39分(27-104)で、出血量は全例少量であった。化学療法導入までの術後日数は10日(7-24)であった。癌腫は卵巣癌5例、腹膜癌4例で、組織型は高度漿液性腺癌5例、類内膜腺癌3例、癌肉腫1例、その中でIDS施行症例は6例あり、手術完遂度はOptimal2例、Complete4例であった。IDS施行症例での術中有害事象は認めなかった。HRD検査施行症例は5例で、HRD陽性例は3例であった。【結論】PDSが困難と予想される症例に対しての審査腹腔鏡手術は、腹腔内観察、腫瘍検体採取ができるため正確な診断をすることができ、治療戦略の一助となり有用である。

P-77-6 初回化学療法前に審査腹腔鏡・試験開腹術を行った症例の検討

関西医大附属病院

武田恵美, 久松洋司, 鈴木健太郎, 牧野琴音, 牧野博朗, 横江巧也, 佛原悠介, 村田紘未, 北 正人, 岡田英孝

本邦では2021年1月からMy Choice[®]診断システムが保険適用となったが、化学療法後の組織採取では偽陰性となる可能性があるため、化学療法導入前の組織採取が重要である。そのため当院では進行卵巣癌・卵管癌・腹膜癌を疑う症例に対して積極的に審査腹腔鏡・試験開腹術を行っている。これらの手術では速やかな化学療法開始が求められるため合併症を引き起こすことは回避したい、可能な限り腹腔鏡下で付属器摘出術や可及的な腹膜播種病変の摘出を心掛けているが、ダグラス窩閉鎖症例などでは臓器損傷のリスクがあるため、壁側腹膜切除術も選択肢としている。2021年1月から9月までに5症例を経験した。術式は付属器摘出術3例・腹膜播種病変切除術2例、組織型はHigh-grade serous carcinoma4例・消化器系由来の腺癌1例、My Choiceは4例に実施しHRDは2例だった。その中で合併症を引き起こした1症例を提示する。症例は76歳女性、大腸癌術後の卵巣癌または腹膜癌に対して試験開腹術を施行し、高度な癒着のため組織採取に難渋した。採取した組織よりHigh-grade serous carcinomaを検出し、卵巣癌IIIC期の診断となった。術後化学療法としてPaclitaxel+Carboplatin, 2コース目よりBevacizumabを併用し、3コース終了後に小腸穿孔を起こしたため化学療法を中断した。My Choice[®]診断システムではHRD陽性であるため、全身状態が安定すれば化学療法を再開する方針である。今後、審査腹腔鏡または試験開腹術の対象となる症例が増加し、本症例のような高難度の症例も経験することが予想される。組織を十分かつ安全に採取するために症例に応じて工夫が必要である。当院で経験した他の症例も含めて、今後の課題について検討する。

P-78-1 本県における卵巣明細胞癌の予後調査

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【目的】卵巣明細胞癌は化学療法抵抗性の疾患で、進行例では非常に予後不良である。今回、本県における卵巣明細胞癌の予後調査を行った。【方法】2012年1月~2019年12月の期間に、県下関連施設で卵巣明細胞癌と診断された91例において、臨床情報を後方視的に検討した。【成績】年齢は56歳(32-87歳)、進行期は1A:27例, 1C:40例, 2A:4例, 2B:5例, 3A:1例, 3B:3例, 3C:7例, 4A:1例, 4B:3例であった。観察期間は中央値50か月であった。初回手術例87例、うちリンパ節郭清施行は29例、残存腫瘍なし:80例、残存腫瘍1-2cm:2例、残存腫瘍2cm以上:5例、術前化学療法例は4例であった。全体の再発は18例(19.7%)、死亡例は9例(9.8%)であった。進行期別のprogression free survivalは1期:53か月, 2期:61か月, 3期:12か月, 4期:7.5か月であった。5年overall survival rateは1期:98%, 2期:100%, 3/4期:32%であった。【結論】卵巣明細胞癌は予後不良とされるが、本検討では1期, 2期で診断された症例の治療成績は良好であった。しかし、卵巣明細胞癌の進行・再発例は予後不良であり、早期診断の確立が重要と考えられた。

P-78-2 プラチナ抵抗性再発卵巣癌に対して非プラチナ製剤を投与した後、プラチナ製剤を再投与した症例の検討

岡山大病院

依田尚之, 入江恭平, 岡本和浩, 松岡敬典, 小川千加子, 中村圭一郎, 長尾昌二, 増山 寿

【目的】プラチナ抵抗性再発卵巣癌に対して非プラチナ製剤を投与した後、プラチナ製剤の再投与が奏功した報告は散見される。標準治療の終了したプラチナ抵抗性再発卵巣癌に対しプラチナ製剤を再投与した症例につき現況報告する。【方法】2010年1月から2020年12月に当院でプラチナ抵抗性再発卵巣癌に対し非プラチナ製剤投与後にプラチナ製剤を再投与した12症例につき後方視的に検討した。【成績】非プラチナ製剤投与期間を含むPlatinum-free intervalは6か月未満0例、6-12か月は4例(33.3%)、12か月以上は8例(66.7%)。非プラチナ製剤の使用数は2以下2例(16.7%)、3以上10例(83.3%)。PARP阻害剤の使用歴はあり3例(25.0%)、なし9例(75.0%)。以前使用したプラチナ製剤数は1が6例(50.0%)、2以上が6例(50.0%)。プラチナ製剤再投与後のORR (overall response rate)は25.0%、DCR (disease control rate)は75.0%であった。プラチナ製剤再投与後のTime to Progressionの中央値は3(0-50)か月であった。病勢制御できた8例については全例が高異型度漿液性癌であった。7例(87.5%)は非プラチナ製剤投与期間を含むPlatinum-free intervalが6か月以上で、6か月未満の1例(12.5%)はBRCA1病的変異陽性であった。5例(62.5%)は初回治療にのみプラチナ製剤を使用した。【結論】現行の標準治療が終了したプラチナ抵抗性再発卵巣癌の中にはプラチナ製剤再投与により病勢制御のできる症例が含まれている可能性が示唆された。

P-78-3 再発卵巣癌患者における、寛解後無病生存期間に関する多施設後方視的検討

KAMOGAWA Study Group

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【目的】再発上皮性卵巣癌(卵管癌, 腹膜癌を含む, 以下同)は非常に予後不良であり, その大部分が原病死するとされている。ごく一部の症例のみ再発後に長期寛解生存するが, どのような症例が長期寛解生存するのか, そもそもどの程度寛解していれば完治と考えられるのかといったことは明らかになっていない。本研究では多施設より再発後卵巣癌症例を集積し, 再発後長期寛解生存症例の寛解期間及びそれら症例の臨床病理学的特徴を解析した。【方法】多施設共同研究にて後方視的に解析した。各施設の倫理委員会で承認を得た後, 卵巣癌患者の治療経過を集積した。まずA大学病院の症例から, 再発後原病死症例及び再発後寛解生存症例を抽出し, 再発後完治と考えられる基準を設定した。次に多施設の症例に前述の基準を適応し, 抽出された症例の臨床病理学的特徴を調べた。【成績】7施設合計で1469例の上皮性卵巣癌症例の治療経過を集積した。A大学病院症例のうち, 再発後に寛解に至りその後無病生存している症例, またはその後原病死に至った症例は42例であった。この42例中, 初回再発までの無病生存期間が12か月未満の予後不良症例を除外した後, 再発後の無病生存期間が初回再発までの無病生存期間を越えた症例は, 全例長期間寛解生存していた。この基準を多施設の症例に適応したところ, 全症例のうち28例(全症例の1.9%)が該当した。【結論】初回治療後無治療生存期間が12か月以上を経て再発し, 再発後の治療で寛解に至り, その後の無治療生存期間が再発前の無治療再発期間を越えた症例は, 再発後完治したものと考えられた。この基準を用いると, 全卵巣癌症例の1.9%が再発後に長期寛解生存していることが明らかとなった。

P-78-4 卵巣明細胞癌のMRI画像によるパターン分類と推定診断

獨協医大病院

鈴木紫穂, 長谷川清志, 香坂信明, 三橋 暁

【目的】卵巣明細胞癌(CCC)は組織発生として子宮内膜症由来や腺線維腫由来などがあり, MRIでの腫瘍形態にもバリエーションが認められる。今回, CCC FIGO I期症例のMRI画像のパターン分類を行い, どの程度CCCの術前推定診断が可能か後方視的に検討した。【方法】MRI読影レポートに推定組織型が記載されていた28例を対象とした。MRI画像の特徴により, A群:単房性囊胞性+壁在結節, B群:単房性囊胞性+充実部分, C群:多房性囊胞性+壁在結節, D群:多房性囊胞性+充実部分, E群:充実性にパターン分類し, 推定組織型との関連を検討した。なお, 充実性は充実部分が腫瘍全体の80%以上を占める場合とした。【成績】パターン分類は, A群8例, B群8例, C群3例, D群4例, E群5例であった。病理学的に子宮内膜症が認められたのは, 壁在結節を有するA+C群11例では全例であったが, 充実部分を有するB+D+E群17例では9例と約半数であった。B群の1例は粘液性癌, C群の1例は漿液性癌と推定されていた。E群の5例中1例は卵管癌, 2例はCCCが推定されるもプレナー腫瘍あるいは顆粒膜細胞腫との鑑別が必要とされた。【結論】内膜症性囊胞を背景に単房性・多房性腫瘍内の壁在結節や充実部分に造影効果が認められ, 拡散強調像で高信号かつADC低値を示す囊胞性CCCの推定診断は十分可能である(23例中21例)。一方, 充実部分が優位の充実性CCCは頻度が少なく(28例中5例), 種々の組織型との鑑別診断が必要である。脂肪抑制T1WIで腫瘍内に囊胞状あるいは帯状の高信号域(出血成分)が認められ, T1WIで低信号を示す充実部分がGd造影T1WIで強い増強効果を示した場合には充実性CCCも鑑別診断に挙げる必要がある。

P-78-5 卵巣癌診断における新規腫瘍マーカー TFPI2 の有用性

奈良県立医大附属病院

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【目的】Tissue Factor Pathway Inhibitor 2 (TFPI2) は、卵巣明細胞癌と非明細胞癌を高い特異度で鑑別できる腫瘍マーカーとして、2021年4月に保険収載となった。実臨床でのデータはまだ蓄積されておらず、既存の卵巣癌腫瘍マーカー(CA125, HE4, CA19-9, CEA)との比較検討は行われていない。今回の研究の目的は、卵巣癌の診断におけるTFPI2の有用性を検討することである。【方法】2008年1月から2020年8月の間に、卵巣腫瘍に対して初回治療をおこなった患者を対象とし、術前に血清サンプルを採取した。良性腫瘍+境界悪性腫瘍と卵巣癌の鑑別におけるTFPI2の診断性能を、既存の卵巣癌腫瘍マーカー(CA125, HE4, CA19-9, CEA)と比較した。【成績】症例は良性卵巣腫瘍317例、境界悪性腫瘍52例、卵巣癌118例であった。卵巣癌症例におけるTFPI2値は、253.6pg/mL(範囲:106.2-5824.2)であり、良性腫瘍+境界悪性腫瘍症例のTFPI2値123.5pg/mL(範囲:0-490.6)と比較して有意に高値であった($p < 0.05$)。CA125, HE4, CA19-9に関しても、卵巣癌症例で高値となったが、CEAでは差を認めなかった。卵巣癌の診断性能を比較するためにROC曲線の曲線下面積(AUC)を比較すると、TFPI2のAUCは0.887であり、CA125(AUC=0.828), HE4(AUC=0.845), CA19-9(AUC=0.585), CEA(AUC=0.544)と比較して良好な診断性能を有していた。Youden Indexより算出したTFPI2値171pg/mLをカットオフ値とすると、感度78.8%、特異度85.8%で卵巣癌を診断することが可能であった。【結論】新規卵巣癌マーカーTFPI2は、明細胞癌の診断だけではなく、卵巣腫瘍の良悪性の診断においても高い診断性能を有していることがわかった。

P-78-6 当院における初回卵巣癌治療に対するベパシズマブ、オラパリブ併用療法の使用経験

大阪医科薬科大病院

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【目的】2021年1月PAOLA-1試験の結果から、相同組み換え修復欠損(HRD)を有する初回進行卵巣癌に対し、ベパシズマブとオラパリブの併用療法が本邦で保険承認となった。当科でのベパシズマブ、オラパリブ併用療法の使用経験を報告する。【方法】2021年1月から7月までの間、当院でベパシズマブ・オラパリブ併用療法を行った6例を対象に安全性と有効性について後方視的検討を行った。【成績】6例の観察期間中央値は19.2週(10-28週)である。組織型は全例が高異型度漿液性癌であり、BRCA variant例は4例(67%)であった。6例中3例に腫瘍減量術で完全切除、1例にoptimal surgery、2例にsuboptimal surgeryを施行した。全例で術後ベパシズマブ併用の化学療法を行った。残存腫瘍を有した3例も化学療法が奏功し、全例で評価病変が無い状態でベパシズマブ・オラパリブ併用療法へ移行した。現在全例で再燃なく維持療法継続中である。有害事象は、非血液毒性は嘔気を3例(50%)に認めたがGrade1であり約2か月経過時で消失した。高血圧の発症はなく、蛋白尿は3例(50%)に認めたがベパシズマブの休薬はなく継続投与可能であった。血液毒性として、Grade3の貧血3例(50%)、好中球減少2例(33%)を認めた。2例で貧血による減量を要したが、オラパリブについても全例で投与を継続している。【結論】併用療法の有害事象は各単剤による維持療法と比較し重篤な発症はなく、全例で継続投与中である。しかし観察期間は短期であり、今後症例数の重ね長期の経過観察を行う必要がある。

P-78-7 卵巣癌治療の初期に発症したヘパリン起因性血小板減少症の3例

筑波大附属病院

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【緒言】ヘパリン起因性血小板減少症(heparin-induced thrombocytopenia: HIT)を発症し、異なる臨床経過を辿った卵巣癌の3例を経験したので報告する。(症例1)35歳, 0妊0産。卵巣癌IIIC期, 右大腿静脈に亜急性期血栓, 肺動脈末梢に多発血栓を認めた。ヘパリン投与開始後13日目に腫瘍生検を施行, 15日目に血小板7.0万に低下, HITを疑いDOAC内服に変更した。肺動脈主幹部に新規血栓を認めた。DOAC開始後の血栓増悪がないことを確認し, wTC療法施行。化学療法5日後にTrousseau症候群を発症しアルガトロバンを開始したが, 状態悪化し原病死した。明細胞癌であった。(症例2)47歳, 2妊1産。卵巣癌IIIC期, 右肺動脈主幹部に粗大血栓を認めた。ヘパリン投与開始後13日目に血小板3.0万に低下, DOAC内服に変更した。右肺動脈起始部から下葉枝にかけて血栓の進展を認めた。血栓増悪がないことを確認し, wTC療法を施行。化学療法4コース後にIDSを施行した。高異型度漿液性癌であった。(症例3)50歳, 2妊2産。卵巣癌IVA期, 右ひらめ筋静脈に亜急性期血栓を認めた。ヘパリン投与開始後8日目に腫瘍生検, 12日目にTC療法を施行, 13日目に血小板5.4万に低下, DOAC内服に変更した。血栓の増悪は認めなかった。化学療法4コース後IDSを予定している。高異型度漿液性癌であった。いずれの症例もHIT発症予測の4Tsスコアは中間群であったが, HIT抗体陽性だった。【まとめ】HIT発症後は, 血栓の増悪により原病の治療が困難なことがある。特に明細胞癌は注意を要すると考えられた。

P-79-1 腔原発悪性末梢神経鞘腫の一例

田附興風会医学北野病院

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【緒言】悪性末梢神経鞘腫はその半数が神経鞘腫1型から、残りは特発的に発症し、末梢神経に関連して生じることから神経堤由来とされている肉腫である。本腫瘍の多くは四肢近位部や体幹、頭頸部より発生し婦人科臓器からの発生は稀である。今回、腔原発の悪性末梢神経鞘腫と診断した一例を経験したので報告する。【症例】55歳、2妊1産、特記すべき既往歴なし。外陰部腫瘍を主訴に近医を受診し、子宮下部より腔入口部に下垂する腫瘤を認め、当院に紹介となった。MRIでは長径7cmの腫瘤が腔を占拠しており、拡散制限を伴い腔左側壁に茎様構造を認めた。PET-CTでは腫瘤に強いFDGの集積を認めたが、リンパ節を含めた遠隔病変は認めなかった。静脈麻酔下の腔鏡診により、腫瘤は腔入口部上方1cmの腔壁より有茎性に発育しており、生検にて高悪性度子宮内膜間質肉腫或いは平滑筋肉腫が疑われた。腔内腫と診断にて腫瘍起始部の周囲腔壁を含めた経腔的腫瘍摘出術を施行、腔原発の悪性末梢神経鞘腫(S-100+, HMB45-, MelanA-, alpha SMA-, Desmin-, Caldesmon-, CD34-), 切除断端陰性の診断に至った。腫瘍径5cm以上で多数の核分裂像を認めた点から高悪性度病変として、術後放射線治療を行った。【結論】本腫瘍に対しては手術による完全切除が標準的な治療法であり、特に高悪性度のものは切除断端の状態が生存率と強く相関することが知られている。今回下位腔壁より有茎性に発育する病変であったため、十分なマージン確保の上で腫瘤を含めた腔部分切除を施行した。腔原発悪性末梢神経鞘腫の報告は極めて稀であり、今後症例の集積により適切な術式・後治療を含めた治療戦略を検討する必要があると考えられた。

P-79-2 抜去困難なIUD長期留置に対して施行した腹腔鏡下子宮全摘術の半年後、直腸腔瘻にて発見された腔癌の1例

JA 江南厚生病院

近藤恵美, 樋口和宏, 橋本 陽, 内村優太, 柴田茉里, 小崎章子, 水野輝子, 松川 泰, 木村直美, 池内政弘

【緒言】腔癌は婦人科悪性腫瘍のうちの約1%と稀な疾患である。今回、腹腔鏡子宮全摘術の約半年後に、直腸腔瘻を発症したことを契機に発見された腔癌の症例を経験した。【症例】67歳、2経妊2経産。不正性器出血があり当院受診。腔鏡診にて避妊具の糸を認め、一部は子宮腔部周囲の肉芽組織に埋没していた。避妊具は数十年間放置されており抜去不可能であった。子宮腔部細胞診はNILM、子宮内膜細胞診は陰性で、不正性器出血は子宮内避妊具が原因として腹腔鏡下子宮全摘術を施行した。摘出した子宮の内膜は膿瘍形成を伴う肉芽組織に広く置換されていたが、悪性所見を認めなかった。術後6か月で多量の膿性帯下を主訴に受診されたところ、直腸腔瘻を形成し、腔壁には全周性に不整な易出血性の隆起病変を認め、腔壁より生検した病理組織学検査にてSCCが検出された。腔癌IVA期の診断で放射線療法と化学療法を施行したが、腔癌の診断から1年後に原病により死亡された。【結論】進行期の腔癌は非常に予後が悪く、直腸腔瘻や膀胱腔瘻などにより著しいQOLの低下を引き起こすため、早期の発見と治療が重要である。腔癌は稀な疾患であり、IUDの長期留置との関連は不明であるが、不正性器出血を訴える場合には腔癌も念頭に置いた十分な診察と検査が必要と考えられる。

P-79-3 婦人科領域悪性黒色腫に対し免疫チェックポイント阻害剤で治療した3症例

兵庫医大病院

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婦人科領域の悪性黒色腫に対し免疫チェックポイント阻害剤で治療を行った3症例を報告する。【症例1】60代、腔原発悪性黒色腫、鼠径リンパ節転移、脳転移。抗PD-L1抗体は陰性で、BRAFは陽性であった。脳転移巣に対してガンマナイフ治療後、ニボルマブを開始した。7サイクル施行し、原発巣腫瘍増大傾向のため腫瘍減量術を行い8サイクル目を施行した。肝酵素上昇および原因不明の下肢脱力のため、中止し、緩和治療を行った。【症例2】40代、子宮頸部原発悪性黒色腫に対し広汎子宮全摘出術を施行、3か月後多発肺転移、多発リンパ節転移が出現した。抗PD-L1抗体が陽性で、BRAFは陰性であった。ニボルマブ単剤で治療を開始、その後ニボルマブとイビリムマブの併用療法を開始した。下垂体炎を発症したためステロイド治療を行った。画像上、転移病巣は縮小していた。3か月後にニボルマブ単剤で治療を再開し、現在も継続中である。【症例3】80代、外陰原発悪性黒色腫、脳転移、肺転移、鼠径リンパ節転移と診断した。ニボルマブを開始し、副作用なく継続し10か月経過。原発巣および転移巣は縮小傾向である。3症例中2症例で腫瘍縮小効果をもとめ、ニボルマブ投与継続中である。重篤な副作用を認めた症例もあり、さまざまな起こりうる副作用の理解と早期発見・早期治療が重要である。

P-79-4 当院における子宮全摘出術後 VAIN 症例の臨床的検討

富山大附属病院

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【緒言】 膣上皮内腫瘍 (VAIN) は子宮頸部上皮内腫瘍 (CIN) や浸潤癌の子宮全摘出後に発症しやすいといわれている。一方、VAIN は稀な疾患であるためフォローアップ期間や治療方法について定まった見解はない。今回、自験例から膣断端細胞診で VAIN が疑われた場合の対応を検討した。【症例 1】子宮筋腫で 46 歳時に腹式単純子宮全摘出術を施行した。62 歳時の膣断端細胞診で VAIN1 が疑われたが、9 か月で細胞診所見は正常化した。【症例 2】CIS で 61 歳時に腹式単純子宮全摘出術を施行した。術後膣断端細胞診 class IIIa, 生検で VAIN1 であった。71 歳時の細胞診で VAIN3 が疑われ、生検でも VAIN3 と診断されたため膣断端切除術を施行した。【症例 3】CIN3 で 50 歳時に腔式子宮全摘出術を施行した。73 歳時の膣断端細胞診で VAIN3 が疑われ、生検でも VAIN3 と診断されたため膣断端切除術を施行した。【症例 4】CIN3 で 50 歳時に腹腔鏡下子宮全摘出術を施行した。53 歳時の膣断端細胞診で VAIN3 疑い、生検で VAIN2 であり経過観察とした。54 歳時の細胞診で VAIN3 が疑われ、生検でも VAIN3 と診断されたため膣断端切除術を施行した。摘出標本は膣上皮内癌の診断であった。【結論】自験例のうち 3 例は CIN/CIS での子宮全摘出術後 10 年以上を経て VAIN3 が出現していた。米国コルボスコピー子宮頸部病理学会でも推奨されるように CIN3 以上の病変が存在する子宮全摘出後には、長期的な膣断端細胞診のフォローアップが必要と考えられる。VAIN3 が疑われる時点でコルボスコープ下に生検、膣断端切除術の適応を判断することで浸潤癌への移行を回避できる可能性が示唆された。

P-79-5 Molecular Mapping 法による VaIN 誘発 HPV タイプの検索

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【目的】 膣癌の前癌病変は膣上皮内腫瘍 (VaIN or Vag-SIL) と呼ばれ、多くは HPV 感染が関与するとされている。また CIN と合併する症例は予想以上に多い。VaIN, および CIN における HPV 感染との寒冷性と、それぞれの原因となる HPV タイプについて比較検討した。【方法】 VaIN99 症例のうち評価可能な 65 例 (VaIN+CIN: 26 例, VAIN 単独: 32 例, 膣扁平上皮癌 (VaSCC): 7 例) を検討した。FFPE 組織ブロックから 4 μ m, 10 μ m の厚さで標本を作成した。4 μ m の標本には HE 染色, p16 染色, ki67 染色を行い病変評価を行い 10 μ m の標本は用手的 microdissection 法で病変部のみから DNA 抽出し, E6/E7 PCR 法で HPV タイピングを行った (Molecular Mapping)。本法では High-risk (HR), possibly high-risk (pHR), Low-risk (LR) 39 タイプを検出できる。【成績】 VaIN および VaSCC 組織において、HPV 陽性率は VaIN で 91.2%, VaSCC で 85.7% であった。ほとんどすべて 1 つの病変に 1 つの HPV タイプが同定された。VaIN+CIN 症例の 92.3% で VaIN と CIN の HPV タイプは異なっていた。VaIN1 病変では HR, pHR, LR を含む 17 タイプが同定された。VaIN2/3 では、6 つの HR (16/18/51/52/56/58), 1 つの pHR, および 1 つの LR が同定された。VaSCC では 3 つの HR (45/58/68), および 3 つの pHR (66) が同定された。VAIN は CIN に比べ多くの HPV 型が検出され、数は少ないが VaSCC で HPV18 型は認められず、HPV16 型は 1 例のみであった。【結論】 VaIN および CIN の合併症例は多く認めるが、それぞれが感染している HPV タイプは異なり、それぞれの発生は独立したものである可能性がある。CIN に比べ VaIN では pHR 型や LR 型 HPV が多く検出されたことより、膣は HPV 感染しやすい場所と思われる、子宮頸癌と膣癌では発生の自然史が異なる可能性も示唆された。

P-79-6 膣 adenosis を背景とした膣原発明細胞癌の一例

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【緒言】 膣癌は女性生殖器悪性腫瘍の 1-2% に発生し、組織型として腺癌は 15% を占める。流産予防目的の Diethylstilbestrol の母体内暴露や先天性の泌尿生殖器異常に関連した膣 adenosis からの発症が報告されているが、今回、それらの既往がない膣 adenosis から発生したと考えられる膣原発明細胞癌の一例を経験したので報告する。【症例】 57 歳, 0 妊 0 産。帯下増加を主訴に受診した。月経困難症の既往歴はなかった。膣鏡診で子宮腔部は異常なかったが、後膣円蓋から後膣壁上 1/2 までの範囲に易出血性の腫瘍を認め、同部位を生検したところ、腺癌の結果であった。内診で傍子宮結合織の抵抗はなく、直腸診で直腸粘膜面への露出を認めなかった。MRI 検査で後膣円蓋から後膣壁にかけて T2 強調画像で高信号, DWI 高信号, ADC 低値の 33 \times 25mm 大の腫瘍を認めた。CT 検査でリンパ節腫大や遠隔転移を認めなかった。膣癌 I 期相当として、広汎子宮全摘出術、両側付属器切除術を施行した。術中迅速組織診で膣側断端陽性であったため、膣を全周性に追加切除し、膣断端陰性となったことを確認し手術を終了した。病理組織診の結果は明細胞癌、膣癌 I 期 (pT1N0M0) で、リンパ管侵襲陽性、脈管侵襲陰性、切除断端陰性であった。子宮頸部や子宮内膜および両側付属器には悪性所見はなく、膣粘膜から膣壁浅層に adenosis の所見を認め、これを背景とした膣原発癌と診断した。残存病変はないもののリンパ管侵襲陽性であったことをふまえた術後補助治療の選択肢についての IC のうえで、慎重に経過観察していく方針となった。【結語】 膣原発明細胞癌は稀な疾患であり、術後補助療法等の十分なエビデンスが乏しいため、さらなる症例の蓄積が必要である。

P-79-7 腹腔鏡下に切除した腔壁 Angiomyfibroblastoma の一例

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【症例】52歳, 女性, 未経妊。ASC-USの精査のため紹介された。当院受診時の子宮頸部細胞診はASC-US, 子宮頸部からのHPVは陰性であった。経腔エコーで筋層内子宮筋腫を指摘された。また腔鏡診の際に腔壁3時方向に小径のポリープを発見した。半年後の子宮頸部細胞診でもASC-USが持続し, 子宮筋腫による過多月経が継続するため腹腔鏡下子宮全摘術および両側付属器切除と同時に腔壁ポリープの切除を計画した。【手術所見】手術時間は2時間11分, 出血量は少量であった。子宮筋腫は底部筋層内に5cm大であり, 腔管切開した際に腔壁にポリープが切除可能範囲内に位置していたため腹腔鏡下に切除した。術後経過は良好で術後5日目に退院した。【病理検査結果】腔壁ポリープは短紡錘形細胞が一様に増殖し, アクチン陰性, デスミン陽性, ER陽性, PR陽性であり, Angiomyfibroblastomaと診断した。子宮頸部には異型な扁平上皮は認めなかった。子宮体部に腺筋症と平滑筋腫を認めた。子宮内膜, 両側卵巣には悪性像はなかった。【考察】Angiomyfibroblastomaは女性外陰部を主な発症部位とする間質系良性腫瘍である。急速に浸潤性に増大するAggressive angiomyomaとの鑑別が重要となる。Angiomyfibroblastomaは通常切除後の再発はないが, Aggressive angiomyomaは高頻度に切除後局所再発をきたし, 性機能障害, 排尿障害などを生ずる可能性があるため慎重な経過観察が必要となる。病理学的に両者の鑑別が難しいことがあるため, Angiomyfibroblastomaと診断された症例においても定期的な経過観察が必要と考えられたため, 本症例も術後経過観察を行なっている。

P-79-8 子宮摘出後に発生した腔異形成 (VAIN) の検討

徳島大

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【目的】子宮摘出後に腔異形成 (VAIN) を発症し治療を要することがある。CINや子宮頸癌ではVAINのハイリスクであると報告されているが, その詳細や管理についての検討は少ない。今回, 当院で子宮摘出後にVAINの診断で治療をした症例を検討し現状, 特徴を明らかにすることを目的に後方視的検討を行った。【方法】2016年1月~2021年8月までにVAIN3と診断され治療を行った9例を対象とした。年齢, 基礎疾患, コルポスコピー所見, 治療内容と予後を後方視的に検討した。【成績】年齢は50~84歳, 平均66歳であった。基礎疾患を有する者は1例で, DMとサルコイドーシスで投薬治療中であった。子宮摘出時の診断は, CIN3が4例, 子宮頸癌が4例, 子宮体癌が1例であった。子宮摘出からVAIN発生までの期間は, 3か月~30年であった。全例無症状で, すべて細胞診陽性でコルポスコピー下生検により診断された。子宮摘出後の断端陽性は1例で, 術後3か月で細胞診異常を認めた。コルポスコピー所見は, 白色上皮が6例, 明らかな病変を認めないものが2例であった。2例がレーザー蒸散を行い, 6例はRALSにて治療を行った。治療後現在までに再発は認めていない。【結論】VAINはHPV感染が関与していると報告されており, CINや子宮頸癌症例はVAINのハイリスクである。子宮頸癌では30年経過後にVAINと診断される症例もあり, 子宮摘出後も細胞診での長期的なフォローアップが必要であると思われる。

P-80-1 当医院での外陰部疣贅における外陰部上皮内腫瘍 (VIN) の割合

ちはるクリニック

金森千春

【目的】当医院では外陰部の疣贅, 尖圭コンジローマを主訴に多数の患者が来院する。自覚によりインターネットで検索し来院した患者, 他院で難治だとして転院希望のもの, 紹介患者などが存在する。自覚により来院されたものは発病よりの期間が短い, 難治性だとして来院したのものには数年間の治療期間があるものも少なくはない。その中で病理検査により尖圭コンジローマでなくVINと診断し得るものも存在する。VINはHPV16, 18の感染によるものであり尖圭コンジローマとはHPV型が異なり, がんの原因となるHPV感染であるため, 癌化を念頭に入れた注意深い治療と観察が必要である。にもかかわらず, 漫然と治療観察のみが繰り返され, 子宮頸部細胞診すら実施されておらず, 当医院診療後直ちに癌根治手術を余儀なくされる症例も存在する。【方法】当医院において, 外診上外陰部疣贅と診断し手術治療を実施した患者の病理検査結果を検討し, VINと診断し得た患者の割合を後方視的に解析した。【成績】2019年5月より2021年9月までに当医院で手術した外陰部疣贅 (主に尖圭コンジローマを強く疑ったもの) 362人中, VINとして病理診断されたものは23例 (6.35%)。そのうちVIN3と診断されたものは14例 (3.87%)であった。【結論】HPV感染はその性質上, 外陰部のみならず, 尿管内, 膣内, 子宮頸部, 肛門管内にもおよび, いずれの場所においても癌化の可能性がある。外陰の皮膚疣贅を診断した場合, その性状をよく見極めること, 病理診断が必要であれば躊躇なく実施すること, 骨盤部すべての診察を細かく行い, 経過を観察することが必要であると警鐘する。

P-80-2 当院における外陰癌鼠径リンパ節転移の術前画像評価の精度について

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【目的】外陰癌鼠径リンパ節転移における術前画像評価の精度につき検討する。【方法】術前に施行されたCT, PET-CTもしくはPET-MRIの放射線診断科医による読影結果と、摘出したリンパ節の病理結果を比較した。リンパ節転移の診断はCTでは短径1cm以上, PETでは異常集積がある場合を有意な所見とした。【成績】2015年10月から2021年7月までの期間に当院で初回手術を行った外陰扁平上皮癌17例を対象とした。症例の年齢中央値は70歳(34-90), FIGO進行期(2008年)IA期1例, IB期4例, II期1例, IIIA期3例, IIIB期3例, IIIC期4例, IV期1例であった。画像評価方法として10例にCTのみ, 4例にPET-CT, 3例にPET-MRIを用いた。術前画像診断でリンパ節転移が疑われた12症例のうち, 実際には転移を認めなかった症例は2例(16.7%)だった。反対に, 術前画像診断でリンパ節転移なしとしたが, 実際には転移を認めた症例は1例だった(20%)。本検討における画像評価の感度90.9%, 特異度66.7%, 陽性的中率83.3%, 陰性的中率80%であった。また, CTとPET個々の精度を比較した場合, CTの感度100%, 特異度80%, PETの感度83.3%, 特異度0%であった。【結論】外陰癌鼠径リンパ節転移の術前画像診断として, 本検討は少数例の検討でもありPETの優位性は示されなかった。

P-80-3 妊娠中に合併したと思われる乳がんと外陰 mammary gland-like adenocarcinoma の同時性重複癌の一例

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【緒言】悪性腫瘍合併妊娠は約0.1%とされるが, 妊娠年齢の高齢化に伴い増加傾向にある。妊娠中に診断される悪性腫瘍で頻度の多いものは乳癌の他, 子宮・付属器悪性腫瘍や造血管悪性腫瘍があるが, 外陰癌は非常に稀である。また外陰部の異所性乳腺組織から発生するとされる mammary gland-like adenocarcinoma は外陰部腺癌としても極めてまれである。今回, 産褥期にこれらの同時性重複癌と診断された一例について報告する。【症例】患者は44歳, 1経妊1経産。妊娠36週に帝王切開術を施行。妊娠中から左外陰部に次第に増大する腫瘤を自覚し, 産後健診ではバルトリン腺のう胞とされていた。産褥3か月目に血性乳汁分泌を伴う左乳房のしこりを指摘され産褥6か月目に乳癌(Invasive ductal carcinoma)と診断され手術をうけた。産褥8か月目に左外陰部腫瘤が増大したため生検したところ adenocarcinoma と診断され当科に紹介となった。画像検査では外陰部腫瘤のほかに, 左鼠径リンパ節に3cm大の腫大が認められた。広汎外陰切除及び両側鼠径リンパ節郭清術を施行し病理学的には mammary gland-like adenocarcinoma of vulva, StageIIIA (i) であった。乳癌・外陰癌の病理組織学的所見, 及び腫瘍としての臨床所見から, これらは同時性重複癌と診断された。【結語】乳癌と外陰 mammary gland-like adenocarcinoma の同時性重複癌はまれであり, 後方視的に考えると妊娠中に合併していたと思われる。妊娠中のこれらの同時性重複癌の報告は現在我々が検索し得た限りではこれが初の症例である。

P-80-4 外陰癌術後創部離解に対し閉鎖陰圧療法にて良好な創治癒が得られた2例

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【緒言】外陰癌は稀な疾患であり, 術後閉鎖鎖に関し有用な治療報告は殆ど無い。患者背景より高齢, 合併症を有する割合は高く治癒遷延し易い。今回, 外陰癌 SCC 術後の創部離解を来した2症例について閉鎖陰圧療法(以下 NPWT: negative pressure wound therapy)にて良好な創治癒を得られたので報告する。【症例提示】症例1: 80歳台, stageIVB, T2病変に対し単純外陰切除を施行。創部は単純縫縮とした。術後6日目に離解あり徐々に拡大, 10日目に開放創とし洗浄, デブリードマンを施行したが肉芽形成緩徐でありNPWT開始。処置に伴い外尿道口を覆うため尿カテーテルを挿入し, 創部をポリウレタンフォームで充填, その上に創全体を覆うフィルムを貼付し吸引を施行した。吸引圧は-125mmHg, 装具は3-4日毎交換とした。開始後7日目で肉芽形成, 創縮小を認め, 18日目で創閉鎖, 上皮化が得られ治療終了とした。症例2: 80歳台, stageIIIA, T1b病変に対し広範外陰切除後, 再発にて局所切除を施行。術後4日目に離解あり再縫合としたが皮膚緊張強く開放し自然治癒を期待した。13日目よりNPWT開始し各条件は症例1と同様とした。開始後3日目で肉芽認め, その後創縮小し上皮化, 13日目で治療終了とした。両症例とも, 既往に糖尿病は無く手術翌日より離床可能であった。NPWT開始後に創感染やその他の合併症は認めず, 治療後も外尿道口は保たれており排尿も自立していた。【考察】NPWTにより再縫合など侵襲性の高い処置は不要で保存的治療が可能であった。また自然閉鎖より早期の治癒が期待できると考えられQOL向上が期待出来る。【結論】外陰癌術後創部離解に対しNPWTは治癒促進に有用であり, 今後の活用が期待される。

P-80-5 外陰部に発生した Eccrine porocarcinoma の一例

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【緒言】Eccrine porocarcinoma (EPC) とはエクリン汗腺由来の非常に稀な皮膚腫瘍であり, 良性病変からの悪性化による発生も知られている。全ての皮膚腫瘍の 0.005 から 0.01% と頻度は低く, 下肢に最も多く発生する。60 から 70 歳代に多く, 男女差はない。外陰部に発生した EPC は Pubmed で検索する限り, 2017 年までの報告で 9 例のみである。【症例】60 代女性。7 年前より自覚していた外陰部の腫瘍に痛みを伴うようになり, 切除目的に受診した。左外陰部に 10×5mm 大の腫瘍を認めた。増大速度が緩徐で擦過細胞診は陰性であり, 良性外陰部腫瘍の診断で腫瘍切除術を施行した。組織標本では病変は表皮より連続して索状や粗大網状に不規則に増生し, 好塩基性の細胞質を有するやや小型で N/C 比の高い細胞と, それより大型で好酸性胞体を有する細胞がみられ, それぞれに異型細胞や核分裂像を多数認めた。一部に良性の汗孔腫もみられ, 間質浸潤は明らかではなかった。これら病理所見より EPC と診断した。そのため全身 CT にて検索したが転移は認めなかった。しかし切除断端にも腫瘍細胞を認めたため, 前回切除部位から周囲 2cm 程度の幅を取り追加切除した所, 一部にわずかな残存病変を認めたが, 追加切除断端には腫瘍病変は認めなかった。【考察】EPC は 20% に局所リンパ節転移, 10% に遠隔転移し, 20% に再発する。治療は外科的切除であり, 非転移症例では 80% が治癒するが, リンパ節転移例の死亡率は 70% とされている。転移例に対しては化学療法も行われるが, 有効なレジメンはなく, 放射線療法も効果が乏しいとされている。本症例は転移なく, 根治的外陰部切除術を行った症例である。今後も外来にて経過観察を予定している。

P-81-1 骨盤リンパ節郭清後に併発した骨盤内リンパ腫瘍の 5 症例に対する治療とその予後

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婦人科悪性腫瘍の骨盤リンパ節郭清後 (PLA) に骨盤内にリンパ嚢胞 (LC) を発症する症例がある。症状がなく治療が不要なものから, 嚢胞が増大し水腎を来すものや, 感染を伴い処置が必要な症例もある。今回我々はリンパ腫瘍に対してドレナージを要した 5 症例の経過と予後について報告する。症例 1 は子宮頸癌 (IVB 期), 術後 1 週間で LC が出現し術後 3 か月で 20 cm に増大, 腹痛と水腎を来した。持続ドレナージ (CD) で 500ml/日以上以上の排液が持続した。ミノサイクリンを用いた硬化療法では改善せず, OK-432 を用いた硬化療法を施行し消失した。現在までの 10 年間で LC の再発はないが右下肢の慢性的なリンパ浮腫 (LE) と頻りにリンパ管炎を発症している。症例 2 は子宮頸部腺癌 (IB2 期), 術後 4 週に LC を形成し, 術後 6 か月で 9cm に増大し水腎を発症, MRCNS 感染を伴い, 開腹下で膿瘍摘出し, 術後 CD を施行した。以後術後 10 年間 LC 再発や LE はなく経過良好である。症例 3 は子宮体癌 (IB 期), 術後 5 週で最大 18cm のリンパ腫瘍と水腎を認め, CD 施行により消失し以後再発は認めていない。症例 4 は卵巣癌 IC 期, 術後 3 か月で 9cm の LC を認めた。術後 6 年で同部位に感染を伴い CD 施行により消失し以後再発は認めていない。症例 5 は卵巣癌 IIIC 期, 術後 3 か月で 5cm の LC を形成し感染を伴ったため CD を施行し消失し以後再発を認めてない。なお, 5 症例ともに抗がん剤投与を併用した。以上より, PLA 後の LC は, 感染を伴う大きな嚢胞であっても CD により改善したものは LC の再燃や LE 発症を来した症例はなかった。一方, LC に対する硬化療法では LC の改善は期待できるが, LE が増悪する可能性があり, 施行する場合には慎重な対応が必要と考えられた。

P-81-2 介入を必要としたリンパ節郭清術後リンパ嚢胞の 4 例とリンパ管シンチグラフィの治療的意義について

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【緒言】リンパ節郭清を伴う婦人科悪性腫瘍手術後にリンパ液が腹腔内へ漏出し, リンパ嚢胞が形成されることはしばしば経験される。多くは無症候性であり自然軽快を認めるが, 一部は難治性となる。多量の腹水貯留を認めるリンパ漏や巨大な嚢胞形成を呈した場合には, 患者の QOL 低下の原因となる。今回我々は難治性術後リンパ嚢胞に対しリンパ管シンチグラフィ (lymphoscintigraphy : LS) が有用であったので報告する。【方法】2012 年 1 月から 2021 年 2 月までに当院で施行されたリンパ節郭清を含む婦人科悪性腫瘍手術 115 例のうち, 術後リンパ嚢胞をきたし治療的介入を要した症例 4 例について検討した。【結果】手術後にリンパ嚢胞を認めた症例は 115 例中 20 例。自然治癒を認めなかったのは 20 例中 4 例。2 例は感染を合併し抗菌薬投与または外科的ドレナージを行い改善を得た。もう 2 例は腹部膨満が主訴であり, 複数回リンパ液を穿刺吸引するも症状の改善が得られなかった例である。経過として, 第 1 例は卵巣癌術後 38 日目にリンパ嚢胞を認め, LS 施行後リンパ液が減少し施行後 55 日目には腹腔内のリンパ液が消失し現在まで再発を認めていない。もう 1 例は子宮体癌術後 14 日目にリンパ嚢胞を認め, 術後 35 日目に LS を施行後, 徐々に腹水の減量を認めた。少量の腹水は認めるが, リンパ液の再貯留は認めていない。【結論】LS 施行後にリンパ嚢胞が改善する機序についてはいまだ解明に至っていないが, リンパ管内への薬液流入で生じる微小な炎症が漏出部位の修復に関与する可能性がある。保存的治療で改善を認めない難治性リンパ嚢胞に対して行う LS は検査的意義だけではなく治療的意義を持つ可能性があり, 更なる検討を行っていく。

P-81-3 腹腔鏡下に摘出を行った後腹膜原発漿液性癌の一例

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【緒言】後腹膜原発漿液性癌はまれな疾患であり、報告は散見されるのみであるが、そのほとんどが女性で、発生部位は傍大動脈リンパ節領域や腎周囲が多い。今回我々は、直腸横の後腹膜内に発生し、腹腔鏡下に摘出し得た漿液性癌の一例を経験したので報告する。【症例】44歳女性、2妊2産。過多月経のため近医受診。Hb6.4g/dlの貧血と子宮筋腫を認めため、精査加療目的に当科を紹介受診。経膈超音波で最大5cmの多発子宮筋腫と右付属器領域に充実部分を伴う3cm大の嚢胞性腫瘍を認めた。MRI検査で子宮右側背側、直腸に近接して3cm大の嚢胞性腫瘍を認め、内部には造影される充実部分を認めた。両側卵巣は正常であった。また子宮には最大5cmまでの多発子宮筋腫を認めた。腫瘍マーカーは正常範囲内であった。下部消化管内視鏡検査では粘膜面は正常で壁外腫瘍による圧排を認めた。手術の方針とし、腹腔鏡下腔式子宮全摘、右付属器切除、左卵管切除、後腹膜腫瘍摘出術を施行した。嚢胞性腫瘍は右仙骨子宮韧带根部あたりに表面が一部露出していたが、ほとんどが後腹膜腔内に発生していた。腫瘍は直腸からも剝離でき、破綻なく摘出できた。病理結果は漿液性癌であり、免疫染色ではエストロゲンおよびプロゲステロンレセプター陽性であった。子宮および右卵巣、両側卵管にSTICなど悪性所見を認めず、後腹膜原発と考えられた。【考察】後腹膜原発漿液性癌は非常にまれな疾患であり、女性に多く、卵管病変との関連も示唆されているが、本症例は卵管に病変を認めなかった。また本症例の嚢胞性腫瘍は骨盤深部の病変であり、腹腔鏡下手術は視野確保に優れ、腫瘍摘出するのに有用であった。

P-81-4 悪性腫瘍との鑑別を要した、直腸穿孔をとまなう多発膿瘍を形成したIUDによる骨盤放線菌感染症の1例

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【緒言】放線菌は、咽頭、消化管、女性器の常在菌で、炎症、手術、外傷により放線菌が組織内へ侵入すると慢性化膿性肉芽腫を形成する。今回我々は、直腸穿孔、肝膿瘍を伴うまれな骨盤放線菌感染症を経験したので報告する。【症例】症例は55歳女性。20年前に子宮内にIUDを留置した。特記すべき既往歴、併存症なし。2週間前からの便秘と体重減少、腹痛を訴え近医より当科紹介。来院時体温38.1度、CRP20mg/dl、WBC15600/μLと炎症反応上昇あり、腔内には膿性分泌物を認めた。CTで右付属器腫瘍、直腸左側腫瘍、肝膿瘍が認められた。下部内視鏡検査では直腸左側腫瘍と直腸との瘻孔所見を認めたのみで直腸瘻は否定された。IUD留置もしくは婦人科悪性腫瘍にともなう骨盤腹膜炎と考え、ABPC/SBTの投与を開始し入院後3日目で試験開腹術を施行した。子宮、両側付属器摘出に加えて、小腸部分切除、S状結腸人工肛門造設術、直腸左側膿瘍の解放を施行した。術後病理検査では切除標本に放線菌菌塊を含む膿瘍形成が認められ、直腸周囲膿瘍、肝膿瘍を合併した骨盤放線菌感染症と診断した。術後発熱が持続し、肝膿瘍の増大をみとめ経皮的ドレナージを試行したが穿刺吸引は不可能だった。術後4週間保存的治療を継続し抗菌剤を内服へ変更し退院となった。現在外来通院中である。【考察及び結語】腸管穿孔、肝膿瘍まできたた骨盤放線菌症の報告は少ない。放線菌はその性質により肉芽腫性の多発膿瘍形成をきたしうるため臨床像は悪性腫瘍に類似する。放線菌の培養同定は困難であるが、周囲の組織への浸潤傾向をとまなう膿瘍形成で、子宮内にIUD挿入がある場合には、骨盤放線菌感染も念頭に鑑別を行う必要がある。

P-81-5 悪性腹膜中皮腫の一例

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【緒言】悪性中皮腫は、非常に稀な疾患であり、その中でも悪性腹膜中皮腫はさらに発生頻度が低い。術前の診断に苦慮することも多く、予後不良であるが確立した治療法もない。今回、術前に悪性腹膜中皮腫を疑い、手術により腫瘍を完全切除した症例を経験したので報告する。【症例】67歳、X年5月頃より腹部膨満感を自覚し近医を受診。腹腔内腫瘍を指摘され、精査加療目的に当科紹介となった。アスベスト暴露歴なし。血液検査はCA125 628.8 U/ml、HE4 46.0 pmol/L、IL-2R 204 U/ml、ヒアルロン酸 79.1 ng/ml、CA15-3 10.1 U/mLであった。CT、MRIで上腹部に121mm、59mmの分葉状の腫瘍があり、内部は変性・壊死を疑った。横行結腸と接してはいるものの、腸管壁との境界は保たれていると考えた。腹水は認めなかった。鑑別疾患として悪性腹膜中皮腫、腹膜癌、GIST、悪性リンパ腫等を考えたが、上記検査所見から悪性腹膜中皮腫、腹膜癌を疑った。手術による腫瘍摘出、病理学的診断が必要と考え、同7月に腫瘍切除術を行った。腹腔内には播種はなく、腫瘍と腸管は剝離可能であった。術中迅速検査は上皮型中皮腫、もしくは腺癌の結果であった。検査所見、開腹所見から中皮腫の可能性が高いと考え、腫瘍切除のみで手術を終了した。最終病理診断は悪性腹膜中皮腫であった。腫瘍の肉眼的完全切除がなされており、有効な術後治療も確立していないことから追加治療は行わずに経過観察中である。【結語】術前から悪性腹膜中皮腫を強く疑い、手術により腫瘍を肉眼的に完全切除した症例を経験した。非常に稀な疾患であり、診断、治療に苦慮する場合が多い。適切な診断・治療方法の確立のために今後も症例の蓄積が望まれる。

P-81-6 後腹膜膿瘍との鑑別に苦慮した後腹膜悪性リンパ腫の一例

静岡赤十字病院
荒木 甫

【緒言】後腹膜腫瘍は比較的稀な疾患で、様々な部位で発生するため携わる診療科は多岐にわたる。後腹膜膿瘍の中では悪性リンパ腫の頻度が高く、見逃すことなく早期に診断することが重要である。今回、後腹膜膿瘍との鑑別に苦慮した後腹膜悪性リンパ腫の一例を経験したので、報告する。【症例】50歳、4経産。発熱、左鼠径部痛を主訴に近医を受診し、経腹エコーで左鼠径部・腸腰筋に腫瘤を認め、腸腰筋膿瘍疑いで救急外来を紹介受診した。採血でCRP/WBC上昇を認め、造影CTで左外腸骨領域に、辺縁に造影効果を伴う5cm大の腫瘤と両側多発リンパ節腫大を認めた。後腹膜膿瘍や悪性腫瘍のリンパ節転移を考え、入院加療方針となった。原因菌判明のための経皮的腫瘍穿刺を施行するも、内容液を吸引できなかった。腫瘍マーカーは陰性で、抗生剤治療により臨床症状が速やかに改善したため、1週間で退院となった。退院後、臨床症状の再燃は認めなかったが、経腹エコーで後腹膜腫瘤と多発リンパ節腫大が残存していた。診断確定目的に腹腔鏡下後腹膜腫瘍摘出も考慮したが、侵襲が高いと考え、鼠径リンパ節生検を施行した。病理検査の結果、びまん性大細胞型B細胞性リンパ腫と診断し、血液内科で紹介となった。PET-CTで後腹膜腫瘍や骨髄内リンパ節に多数集積を認め、R-CHOP療法導入となった。【結語】保存的加療後も縮小しない後腹膜腫瘤を認めた場合、悪性腫瘍の可能性を考え診断目的に組織生検すべきである。後腹膜膿瘍の中では悪性リンパ腫の頻度が高いため、表にリンパ節腫大を認めた場合は、低侵襲のリンパ節生検が考慮される。

P-82-1 エトボシド脱感作プロトコールで治療した絨毛癌の2症例

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エトボシド (ETP) は絨毛癌治療のキードラッグであり、ETP 過敏症を発症した場合、どのように絨毛癌治療を行うか悩ましい。脱感作プロトコールにより MEA 療法を行った絨毛癌患者 2 例を報告する。【症例 1】51 歳、8 妊 3 産、49 歳で全胎奇胎。hCG 陰性化確認後、通院中断。不正出血で A 病院を受診した。hCG 901, 000 mIU/mL、子宮に局限した腫瘍を認めた。止血目的で単純子宮全摘が行われ絨毛癌と診断された。化学療法目的に当院へ紹介された。MEA 療法を開始した。初回 ETP 点滴開始 15 分後に全身の熱感・発赤、咽頭違和感の訴えがあり、ETP を中止した。デキサメタゾンのフルメディケーション、ETP を少量から漸増する脱感作プロトコール (1 ボトル 6 ステップ) で、その後は問題なく MEA 療法が継続できた。12 コース行い、再発なく経過している。【症例 2】30 歳、2 妊 1 産、胎状奇胎寛解後の臨床的絨毛癌として、B 病院で EMACO 療法が開始された。初回 ETP 開始直後に呼吸苦が出現した。ETP を用いない FA 療法などで寛解し、その後第 2 子を分娩した。分娩終了後 (34 歳) に絨毛癌再発が判明した。C 病院で TIP 療法と肝切除で寛解したが、6 か月で hCG 再上昇したため当院で紹介された。ETP 脱感作プロトコール (3 ボトル 8 ステップ→2 ボトル 6 ステップ) で MEA 療法を施行し、過敏症をおこさず治療が継続できた。3 コース目からは、B 病院で MEA 療法を継続している。【結語】脱感作プロトコールでは、薬剤濃度、薬剤投与速度、点滴ラインのプライミング量、点滴管理の複雑さ等を考慮する必要がある。脱感作プロトコールにより、ETP を含むレジメンでの治療を行うことができた。

P-82-2 MTX-Folic acid 療法を施行した臨床的侵入奇胎の 3 例

三重大
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【緒言】侵入奇胎の標準療法は化学療法で、子宮体がん治療ガイドライン 2018 年版ではメトトレキサート (MTX) またはアクチノマイシン D (ACT-D) 単剤が推奨されるが、いずれの薬剤も複数の投与方法が存在する。NCCN ガイドライン Ver 1.2022 でも同様に MTX もしくは ACT-D の単剤が推奨されている。しかし weekly MTX 療法は推奨されておらず、FIGO スコア 2~4 点での奏効率は 40% との報告がある。今回 MTX-Folic acid 療法 (MTX1mg/kg 1, 3, 5, 7 日目, ロイコポリン 0.1 mg/kg 2, 4, 6, 8 日目を 14 日間隔で投与) を施行した 3 例の臨床的侵入奇胎を経験したので文献的考察を加え報告する。【症例】①23 歳 1 妊 0 妊。妊娠 8 週で子宮内容除去術を施行し全胎奇胎と診断された。その後血中 hCG が経過非順調型となり紹介となった。画像上肺転移が疑われた。FIGO スコア 2 点の臨床的侵入奇胎と診断した。MTX-Folic acid 療法 3 サイクルで hCG 陰性化した。②28 歳 3 妊 1 妊。妊娠 7 週で部分胎奇胎が疑われ紹介となった。子宮内容除去術を施行し流産と診断された。術後子宮内に血流を伴う腫瘤を認め、術後 5 週の hCG が判定線を超えたため、FIGO スコア 4 点の臨床的侵入奇胎と診断した。MTX-Folic acid 療法 5 サイクルで hCG 陰性化した。③34 歳 1 妊 0 妊。稽留流産で妊娠 8 週に子宮内容除去術を施行。組織診は絨毛性疾患を認めなかった。術後子宮体部に血流豊富な腫瘍を認め当院紹介となった。FIGO スコア 4 点の臨床的侵入奇胎と診断した。MTX-Folic acid 療法を 1 サイクル後、大量出血し子宮動脈塞栓術を施行した。その後 3 サイクルで hCG 陰性化した。【結語】FIGO スコア 2~4 点の臨床的侵入奇胎 3 症例に MTX-Folic acid 療法は有効であった。

P-82-3 絨毛癌 MTX 耐性株の作成と解析

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【目的】絨毛癌は化学療法への感受性がよく、メソトレキセート（以下 MTX）、アクチノマイシン D、エトポシドを用いた化学療法で奏効率は 80% に達するが、残りは治療抵抗性となり治療に難渋する。化学療法の耐性機序の解明が絨毛癌の予後改善に重要だと考えられる。今回、絨毛癌治療の key drug として MTX に注目し、MTX 耐性絨毛癌細胞株を作成し、解析した。【方法】絨毛癌細胞株 JAR に対し MTX を添加した培地で継代・培養を繰り返し、耐性株を作成した。MTX の濃度を 1×10^9 M より開始し、徐々に濃度を上昇させ、 1×10^6 M でも生存する細胞の集団を MTX 耐性株とした。MTS assay を行い、親株と MTX 耐性株の増殖能を評価した。次に、親株と MTX 耐性株の IC50 を測定した。親株と MTX 耐性株から、蛋白を抽出し、Western blot にて耐性に関与する既知の蛋白発現を検討した。さらに、未知の耐性に関与する因子を明らかにするため、RNA を抽出し、網羅的 RNA sequence 解析を用いて親株と MTX 耐性株について比較した。【成績】親株と MTX 耐性株では増殖能に有意差はなかった。MTX に対する IC50 はそれぞれ 2.6×10^6 M、 2.9×10^6 M とおよそ 1000 倍程度の差を認めた。Western blot では MTX 耐性の主要な因子である DHFR の蛋白発現が、親株に比べて MTX 耐性株で 10.9 倍増加していた。RNA sequence では親株に対し、MTX 耐性株で DHFR、TYMS など、MTX 耐性に関与する既知の RNA の発現増加が確認されたほか、有意に発現増加または低下する RNA が複数検出された。【結論】絨毛癌細胞株 JAR の MTX 耐性株を作成した。RNA sequence で MTX 耐性に関与する因子が検出され、今後それらの MTX 耐性のメカニズムを検討することが、絨毛癌の予後改善の糸口となる可能性がある。

P-82-4 子宮内容除去術時、大量出血のため子宮摘出を行い侵入奇胎の診断に至った 1 例

豊中病院

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【緒言】侵入奇胎は胎状奇胎絨毛が子宮筋層内に浸潤したもので、抗がん剤治療によりほぼ 100% の寛解率が得られる疾患である。今回、稽留流産または絨毛性疾患を疑い子宮内容除去術後、子宮摘出を行った結果、侵入奇胎の診断に至った症例を経験した。追加治療について文献的考察をふまえ報告する。【症例】34 歳、2 妊 1 産（帝王切開既往あり）。不正性器出血および下腹部痛を認め、最終月経起算 7 週 6 日に前医を受診した。尿中 hCG 陽性。経陰超音波で子宮腔内に辺縁不整な 5 cm 大のエコーリースペースを認めた。胎嚢と考え経過観察をしたが、1 週間後の診察で一部に血流豊富な病変を認め、胎盤ポリープが疑われ、精査加療目的に当院に紹介となった。最終月経起算 8 週 6 日に当院を初回受診した。血清 hCG は、123,025 mIU/ml であった。経陰超音波で子宮腔内に 45 mm 大の胎嚢を認めた。明らかな胎児成分は認めなかった。稽留流産または絨毛性疾患を疑い、翌日、手動真空吸引法にて子宮内容除去術を施行した。処置中、制御不能な大量出血を認め、緊急で腹式単純子宮全摘出術を施行した。内容除去術にて得られた検体は、部分胎状奇胎、また摘出子宮は、侵入奇胎と病理診断された。術後 14 日目、頭部単純 CT および胸腹部造影 CT にて転移病変は認めなかった。術後 21 日目、血清 hCG は 59.5 mIU/ml であった。術後 38 日目よりメソトレキセート（MTX）による抗がん剤治療を 2 週間毎に 3 コース行った。現在、血清 hCG は陰性のまま経過観察中である。【結語】今回我々は、子宮内容除去術時、大量出血のため子宮摘出を行い、侵入奇胎の診断に至った症例を経験した。

P-82-5 先行妊娠の部分胎状奇胎が責任妊娠であることが判明した絨毛癌の一例

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【はじめに】妊娠性絨毛癌は、胎盤絨毛を形成する栄養膜細胞が癌化したものであり、正常分娩、流産、中絶、胎状奇胎など、あらゆる妊娠が絨毛癌の原因（責任妊娠）となり得る。胎状奇胎が責任妊娠の場合は、ほとんどが全胎状奇胎に由来するものであり、部分胎状奇胎に由来する症例はまれで、世界的に数例のみしか報告されていない。今回、患者、パートナー、胎状奇胎組織、及び、絨毛癌組織から抽出した DNA を用いた STR 解析により、部分胎状奇胎を責任妊娠とする絨毛癌と診断した極めて稀な症例を経験したので報告する。【症例】症例は 36 歳。2020 年 X 月、A 病院で胎状奇胎除去術を施行され、部分胎状奇胎と病理診断されたが、一次管理を受けずに放置していた。その後、月経様の不正性器出血が持続したため、2020 年 X +7 月、B 病院へ紹介となったが、採血や CT などの画像診断により絨毛癌の疑いと診断されたため、当院へ紹介となった。当院来院時、多量性器出血を認めたため、緊急子宮摘出術を施行し、病理診断により絨毛癌と診断された。術後に MEA 療法を 5 コース追加し、寛解に至った。本症例は、部分胎状奇胎に罹患する以前に複数回の妊娠、正常分娩、流産、中絶を経験しており、絨毛癌の責任妊娠の同定のため、患者、パートナー、部分胎状奇胎組織、及び、絨毛癌組織から DNA を抽出し、STR 解析を行ったところ、奇胎組織と絨毛癌の遺伝型判定が一致し、かつ、それらが 3 倍体と判明したため、部分胎状奇胎を責任妊娠とする絨毛癌と判断した。【結語】本症例を通して、侵入奇胎や絨毛癌への続発率が低いとされている部分胎状奇胎においても、一次管理が極めて重要であることが再認識された。

P-82-6 経過非順調型を呈した絨毛性疾患の当病院での臨床経過の検討

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【目的】 存続絨毛症は主に胞状奇胎娩出後に続発する。胞状奇胎娩出後のhCG推移により経過順調型(順調型)、経過非順調型(非順調型)に分けられ、非順調型が存続絨毛症と診断される。存続絨毛症は奇胎後hCG存続症、臨床的侵入奇胎、臨床的絨毛癌に分類される。本研究では胞状奇胎娩出後に存続絨毛症となるリスク因子を抽出することを目的とした。【方法】2010年1月から2021年9月までに当科で診断・管理を行った胞状奇胎娩出後の症例につき、後方視的検討を行った。順調型・非順調型を呈した2群において病理診断、年齢、血中hCG、治療や予後について検討した。【成績】胞状奇胎娩出後管理を行った46症例のうち全胞状奇胎36例、部分胞状奇胎8例、その他2例であった。順調型は36例、非順調型は10例であった。奇胎後hCG存続症が1例、臨床的侵入奇胎が8例、臨床的絨毛癌が1例であった。臨床的侵入奇胎・絨毛癌の病巣は子宮筋層5例、肺5例、骨盤内1例であった。非順調型全例に化学療法を行い8例は1stラインで、絨毛癌を含む2例は3rdラインで寛解に至った。非順調型の年齢は中央値33.5歳(範囲22~50歳)で、順調型は中央値32.0歳(範囲18~43歳)であり有意差を認めなかった。奇胎娩出前のhCGは非順調型で中央値109426mIU/ml(範囲73011~374999 mIU/ml)、順調型で中央値88820mIU/ml(範囲22274~553300 mIU/ml)であり有意差を認めなかった。非順調型を呈するかについて病理診断間で有意差は無かった。非順調型は全例で奇胎娩出後4週時点の血中hCG値が100mIU/ml以上であった。【結論】存続絨毛症を予測することは困難であるが、奇胎娩出後4週時点の血中hCG値が100mIU/ml以上の場合は慎重なフォローが必要となる。

P-83-1 子宮内膜ポリープの形態を呈し絨毛癌への分化をみとめた子宮体部未分化癌の一例

湘南鎌倉総合病院

渋谷茉莉, 井上裕美, 松本愛世, 青柳 遼, 柴崎 聡, 渡邊零美, 鶴澤芳枝, 大沼一也, 福田貴則, 木幡 豊

【背景】 絨毛癌は妊娠性と非妊娠性に分類され、非妊娠性絨毛癌の中には、卵巣胚細胞腫瘍から発生する腫瘍、胚形成期に性腺組織へ移動できずに残存した胚細胞が悪性転化し発生する腫瘍、他の腫瘍が脱分化や逆分化を起こし発生する腫瘍が含まれる。今回我々は、子宮内膜ポリープの形態を呈した子宮体部腫瘍に対し手術を施行したところ、絨毛癌への分化を認めた子宮体部未分化癌の一例を経験したため報告する。【症例】53歳女性、2妊2産。2か月続く不正出血を主訴に前医受診し、子宮内腔に6×3cmのポリープ様腫瘍を認め紹介となった。内膜細胞診は陰性であり、子宮内膜ポリープ病変に対してTCRを施行したところ、組織診で子宮癌肉腫の診断となった。PET-CT検査ではリンパ節・他臓器転移は認めず、子宮全摘、両側付属器切除、骨盤リンパ節郭清、傍大動脈リンパ節生検を施行した。病理組織所見は、腫瘍細胞の多くはAE1/AE3弱陽性、p53陽性、p16陽性を示す未分化癌であり、一方一部に栄養膜細胞に類似した腫瘍細胞を認め、hCG強陽性を示した。腫瘍は浅い筋層浸潤は認めなが脈管侵襲はなく摘出したリンパ節にも転移は認めず、子宮体部未分化癌StageIAの診断となった。術後に検査したhCGβは2.4mIU/mとやや正常を超える値であった。術後TC療法を6コース行い、現在術後8か月経過しているが再発なくフォロー中である。【結語】非妊娠性絨毛癌を認めた場合、発生機序により選択する化学療法の種類も異なるが、今症例では子宮体部の分化異常により発生した絨毛癌と考えTC療法を行った。また、今症例では一般的なCA125を含めた腫瘍マーカーは陰性であったが、今後の再発に関してはhCGβ値の推移が参考になる可能性がある。

P-83-2 臨床的侵入奇胎治療後動静脈瘻をみとめIVRを施行した症例

近畿大病院

山本貴子, 村上幸祐, 佐藤華子, 藤島理沙, 宮川知保, 貫戸明子, 小谷泰史, 中井英勝, 松村謙臣

症例は34歳G2P1(39週経産分娩)。挙児希望にて他院で、クロミフェンクエン酸塩、タイミング法で妊娠成立した。その後流産となり、妊娠6週で子宮内容除去術を行った。病理結果が部分胞状奇胎であったため以後HCGβサブユニットで経過観察していたが、半年経過しても低下不良、少量の性器出血が持続しており、経過非順調型にて流産処置後から半年後に当院紹介となった。CTで多発肺転移、MRIで右基鞘帯に約40mmの腫瘍を認めた。絨毛がんスコアにて、合計4点の臨床的侵入奇胎の診断でMTXにて治療開始した。(20mg/day×5日間、2週間毎)治療開始前の血中HCGは1370730mIU/mlと著明に上昇していた。⑤コース終了後、血中HCG26mIU/mlにまで順調に低下したが、その後血中HCGが軽度上昇傾向になることがあったが、⑩コースまで継続し血中HCGが4.1mIU/mlまで低下した。しかし、⑫コース開始時に血中HCGが8.3mIU/mlまで上昇認めたためMTX抵抗性と判断しACT-D(0.5mg/day×5日間、2週間毎)に変更した。④コース施行後血中HCGは陰性化したため、追加で③コース行い経過観察となった。初診時から認めていた、基鞘帯の腫瘍は消失したが、同部位に血流豊富な動静脈瘻をみとめ、尿管圧迫による水腎症も認めたため、今後挙児希望があり、妊娠時の破裂などのリスクも考え、IVRにて動静脈瘻の治療を行い消失を確認した。月経も正常に再開し現在1年以上の血中HCGの陰性化を確認しているため不妊治療を再開している。治療開始時多発肺転移、HCG高値であり、治療方法の選択に難渋したが、単剤療法のみで加療した臨床的侵入奇胎を経験した。文献的考察も含め提示する。

P-83-3 帝王切開術後の子宮筋層離開に対し、子宮全摘出術を施行後に判明した類上皮性トロホプラスト腫瘍の一例

新潟市民病院

廣川哲太郎, 常木郁之輔, 小川裕太郎, 上村直美, 森川香子, 田村正毅, 柳瀬 徹, 倉林 工

類上皮性トロホプラスト腫瘍 (epithelioid trophoblastic tumor (ETT)) は、中間型トロホプラスト腫瘍の一つであり、絨毛膜無毛部の中間型栄養膜細胞に類似する腫瘍細胞から構成される。発症当初は無症状のことが多いが、性器出血もしくは無月経を起すこともあり、増悪すると肺などへ遠隔転移を来とし悪性腫瘍の性格を持っているとされる。先行妊娠としては満期産が最も多いとされる。今回我々は、帝王切開施行後に筋層離開を来し子宮全摘術を行った際に、ETT を認めた症例を経験したので報告する。症例は44歳女性、G3P2(SA, C/S, C/S)。既往帝王切開後妊娠に対し、X年3月選択的帝王切開術施行された。この際子宮筋層非薄化が認められたが、異常血管等は認められなかった。1か月健診にて子宮筋層の離開・同部分に血腫を認めた。腹痛・性器出血等の症状は認められなかった。病状説明を行ったうえ、術後半年後に単純子宮全摘術を施行した。摘出子宮より、免疫染色にてCAM52, PLAP, inhibin, P63 陽性を示す中間型栄養膜細胞の増殖・一部筋層への浸潤を認め ETT と判明した。術後 CT では、肺・縦隔・肝臓等への遠隔転移等は認められなかった。原因となる先行妊娠としては、本疾患が比較的緩やかに増殖する腫瘍であるため、過去にあった自然流産・帝王切開の両方が推測された。今回の症例は子宮内に局限した病変であった為、追加治療を施行せず外来で嚴重に経過観察を行う方針とした。本疾患は明確な治療指針が無く、数年後に局所再発・肺転移等で再発した例もあり今後も慎重に経過観察する必要がある。

P-83-4 当院で治療した絨毛性腫瘍の検討

沖縄県立中部病院

高橋慶行, 三浦耕子, 中澤 毅, 大畑尚子

【目的】絨毛性腫瘍は近年減少傾向と言われ、日本産科婦人科学会の婦人科腫瘍登録でも2019年は175例の登録で(同時期の子宮体癌は12631例)遭遇する機会が少なくなっている。本邦では2011年に絨毛生疾患取扱い規約第3版が上梓され、これに基づき適切に治療すれば大半で予後良好と思われるが、一部の難治性絨毛癌や PSTT などに対する化学療法は確立していない。当院で治療した絨毛性腫瘍について検討し今後の診療に役立てる。【方法】1990~2020年に当院で治療した絨毛性腫瘍は26例を診療録をもとに後方視的に検討。【成績】内訳は奇胎後 hCG 存続症4例、臨床的侵入奇胎13例、侵入胞状奇胎5例、臨床的絨毛癌1例、絨毛癌3例で、PSTT と ETT 0例であった。年齢は17歳から53歳で2015年以降に45歳以上が4例あった。50歳以上の症例で奇胎娩出術前に絨毛性疾患を予想していない例があった。治療は全例化学療法が行われ、初回レジメンは MTX 22例、EMA/CO 2例、MAC 2例であった。7例で子宮摘出が併用されていた。当院の症例では、FIGO2000 staging IV の症例はなく、FIGO scoring で7点以上の high risk GTN は3例のみということもあって全例寛解しており、追跡可能症例で死亡や再発はなかった。文献では難治性症例の報告もあり、分子標的薬剤による治療など検討されている。【結論】絨毛性腫瘍、特に絨毛癌はかなり希少で、一般施設では治療に精通するのは困難で、ハイリスク症例は治療経験豊富な重点施設で治療することが望まれる。

P-83-5 PSTT を疑う過大着床部症例を対象とした子宮温存療法の適応と限界

秋田大附属病院

富樫嘉津恵, 熊澤由紀代, 藤島綾香, 尾野夏紀, 白澤弘光, 佐藤 亘, 寺田幸弘

【緒言】当院で子宮温存した過大着床部 (exaggerated placental site ; EPS) 3例と、その後絨毛性疾患 (placental site trophoblastic tumor ; PSTT) が判明した1例を報告し、子宮温存治療について考察する。【EPS 症例1】33歳 G1P0 妊娠6週で自然流産した。21日後に持続する性器出血あり、子宮内腔に21mm大の腫瘤像あり。血中 β hCG=105.0mIU/mL、開腹下子宮腫瘍除去術を実施し、EPS と診断された。【EPS 症例2】31歳 G2P1 妊娠8週で稽留流産と診断された。子宮内容除去30日後に出血し、子宮内腔に17mm大の腫瘤像あり。血中 β hCG=196.0mIU/mL、子宮鏡下腫瘍摘出術を実施し、EPS と診断された。【EPS 症例3】26歳 G1P0 妊娠17週の人工妊娠中絶術後に出血し、血中 β hCG=160.0mIU/mL、子宮内容除去組織の病理検査で EPS と診断された。91日後に多量出血し、両側子宮動脈塞栓後に子宮鏡下腫瘍摘出術を施行した。【PSTT 症例】32歳 G2P1 化学流産後ネフローゼ症候群の全身検索 CT 検査で微小な子宮内病変を認めた。血中 β hCG=116.0mIU/mL、子宮鏡下腫瘍掻爬術を施行して病理組織はわずかであったが EPS と診断された。以降血中 hCG は低下したが、7か月後子宮異常血流像が出現し、子宮動脈塞栓の術前診断で子宮全摘した標本から PSTT と最終診断された。術後5年まで再発徴候なし。【考察】EPS と PSTT の術前診断は困難であり、鑑別には子宮全摘を含めた病理検査が有効とされる一方、子宮の温存治療を希望する症例は少ない。子宮温存症例では厳重な管理を要するとされるが、子宮温存療法後の長期予後をまとめた報告は少ない。PSTT を疑う症例を対象とした子宮温存療法の適応と限界について、文献的考察を加え報告する。

P-83-6 卵管間質部妊娠破裂に伴う出血性ショックの後に存続絨毛症をきたした53歳の一例

石巻赤十字病院¹, 大崎市民病院²

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【緒言】卵管間質部妊娠は全異所性妊娠の2~4%と稀な病態だが、致死率が高いため早期の診断治療が必要である。また、存続絨毛症を起こしやすい病態としても知られている。53歳という超高齢で卵管間質部妊娠破裂後に存続絨毛症を呈した症例を経験したため、報告する。【症例】53歳、女性、G1P0。受診日3週間前より持続的な不正性器出血を認めていた。激しい腹痛を主訴に前医を受診した。造影CTで腹腔内出血を認め、卵巣出血疑いとして当院に転院搬送となった。当院到着時バイタルサインはショック状態であった。血中βhCG値18410.9 mIU/mLであり、肝周囲、脾周囲に及ぶ多量の腹腔内出血と子宮体部左側にextravasationを認めることから異所性妊娠破裂に伴う出血性ショックと診断し緊急手術の方針となった。開腹手術にて左卵管角部に膨隆する病変を認め、同部位より持続的な出血をきたしていた。左卵管角部を楔状に切除し、止血を得た。術後、血中βhCG値は低下傾向であったが、術後24日目に血中βhCG値の再上昇を認めた。術後38日目には血中βhCG値44596 mIU/mLまで上昇していた。画像検査上、明らかな器質的病変を伴わないことから、存続絨毛症と診断した。同日よりメソトレキセート(MTX)50mg/m²×2の単回投与を1週間ごと3回行った。血中βhCG値順調に低下し、術後122日目に陰転化を確認した。【考察】卵管間質部妊娠破裂は存続絨毛症をきたしやすい疾患であるため、術後早期のMTX投与の検討や長期間の血中βhCG値フォローを行うべきである。また、年齢から妊娠の可能性を除外すると致死的な疾患を見逃したり、治療開始が遅れたりすることから50歳代に対しても積極的に妊娠反応検査を行うことが肝要である。

P-84-1 早期診断と集学的治療により救命しえた原発不明癌の腫瘍塞栓性肺微小血管障害の1例

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【緒言】腫瘍塞栓性肺微小血管障害(PTTM)は腫瘍塞栓を契機に肺細動脈が繊維細胞性内膜肥厚から狭窄を来し、急速に肺高血圧症が進行する極めて予後不良な病態である。我々は原発不明癌のPTTMの対応に成功した一例を経験したので報告する。【症例】症例は58歳の女性で、腹膜播種、両側水腎症、小腸壁肥厚、瀰漫性子宮壁肥厚のため、泌尿器科、消化器内科と当科で精査中であった。内膜吸引組織診で腺癌組織が少量認められたが、原発性か転移性かの判別ができず、播種組織生検を予定した。入院時(第1病日)、SpO₂88%と低下を認め、造影CTで肺血栓なく、心エコーで著明な肺高血圧を認めたため循環器内科管理となった。病状悪化により第2病日に人工呼吸、経皮的心肺補助法(PCPS)が導入され、肺動脈血中に腺癌細胞を認めたためPTTMと診断された。抗PDGF作用による肺細動脈狭窄改善を期待し、第4病日よりimatinib投与を開始したところ、呼吸循環の改善傾向が認められ、第13病日でPCPSを離脱した。原疾患に対しては、腺癌細胞は婦人科系、消化器系などの特異的マーカーは全て陰性で原発巣特定は困難であったが、院内がんサーボードで婦人科病として治療することとなった。第17病日よりゲムシタビン-カルボプラチン療法を2コース行い、肺高血圧からも離脱し、第87病日に退院した。その後原疾患の進行を認めたがPTTM再発はなく、第229病日に永眠された。【結論】急速に進行するPTTMに対し、早期診断と集学的治療で救命しえた。本例より、担痛状態での急性呼吸循環不全では、肺血栓塞栓症とともにPTTMも念頭に置く必要があり、血中酸素化不良の際には造影CTだけでなく、心エコーを施行する重要性が示唆された。

P-84-2 子宮筋腫など骨盤内良性腫瘍を基礎疾患として血栓症を発症し、子宮全摘術を行った症例

津山中央病院

片山沙希, 河原義文, 佐藤麻夕子, 岡真由子, 石川陽子, 片山菜月

【緒言】子宮筋腫や子宮腺筋症は時に子宮を腫大させ、血流をうっ滞させることで血栓症のリスクとなりうる。今回、血栓症を契機に子宮に腫瘤を指摘され、婦人科にて子宮全摘術を行った症例を経験したので報告する。【症例1】52歳、3妊2産、肥満やホルモン剤の内服はなし。閉経後に持続する不正出血を認めていた。めまいを主訴に救急外来を受診し、小脳梗塞と貧血を認めた。骨盤MRIにて悪性腫瘍を疑う子宮体部腫瘤を認めたため当科紹介となり、手術の方針となった。術前に経腔的に腫瘍の一部排出を認め、分娩筋腫の可能性も考慮されたが子宮鏡下にて腫瘍の完全切除ができず、腹式単純子宮全摘術+両側付属器切除を施行。病理診断は子宮筋腫、腺筋症であった。術後経過は良好である。【症例2】37歳、2妊2産、BMI26と肥満あり。筋腫核出術の既往があった。下肢の腫脹・疼痛と労作時呼吸苦を主訴に受診。画像検査にて10cm大の子宮筋腫と、圧迫部位に深部静脈血栓症、また肺血栓塞栓症を認めたため当科紹介となった。血液検査にて抗リン脂質抗体症候群と診断された。IVCフィルター挿入下にて腹式単純子宮全摘術+両側卵管切除を施行。術後経過は良好でありDOAC内服にて退院した。【考察】骨盤内腫瘍は血管を圧迫することで血液のうっ滞が起こり、血栓が生じうる。筋腫も腺筋症も良性疾患であるが、本症例のように血栓症の原因となり致命的にもなりかねない。抗リン脂質抗体症候群のように、潜在的に危険因子を有している可能性もあることも考慮し、慎重なfollowをすべきであると考えた。【結語】巨大な骨盤内腫瘍は良悪性に関わらず、血栓症を発症する危険性があることをふまえて外来followしていく必要がある。

P-84-3 婦人科悪性腫瘍における直接経口抗凝固薬の使用下での静脈血栓塞栓症再発または抗凝固薬変更の予測モデル

東北大病院

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【目的】直接経口抗凝固薬 (DOAC) 使用中の婦人科悪性腫瘍症例において、静脈血栓塞栓症 (VTE) 増悪/再発または抗凝固薬変更の予測モデルを作成する。【方法】2016年1月から2019年10月に当院を受診した婦人科悪性腫瘍症例のうち、VTEのためDOACを開始した症例を対象として、後ろ向きコホート研究を実施した。アウトカムを静脈血栓塞栓症増悪/再発または抗凝固薬変更とし、DOAC開始後から1年6か月間追跡した。アウトカムと関連する説明変数をLASSOロジスティック回帰分析で選択し、リスクスコアによる予測モデルを作成した。リスクスコアによるアウトカムの判別能を評価し、ブートストラップ法で内的検証を行った。Youden indexをもとにリスクスコアのカットオフ値を算出した。【成績】解析対象者63人のうち、アウトカムは10人(15.9%)に認められた。選択された説明変数は、VTE初発が肺血栓塞栓症または肺血栓塞栓症を伴わない近位深部静脈血栓症(スコア=3)、VTE初発時のD-dimer ≥ 7.6 $\mu\text{g}/\text{dl}$ (スコア=1)、卵巣癌(スコア=1)であった。リスクスコアによるアウトカムの判別能は、C統計量で0.873(95%信頼区間[CI]:0.720-0.930)であった。内的検証によるC統計量は0.884(95%CI:0.55-1.00)であった。Youden indexをもとに算出されたリスクスコアのカットオフ値は4であり、感度:0.90(95%CI:0.55-1.00)、特異度:0.70(95%CI:0.56-0.82)、陽性的中率:0.36(95%CI:0.18-0.57)、陰性的中率:0.97(95%CI:0.86-1.00)であった。【結論】リスクスコアによるアウトカムの判別能は優れていた。以上から婦人科悪性腫瘍でVTE増悪/再発リスクが高い症例やDOAC不応症例の予測に有用な可能性がある。

P-84-4 婦人科腫瘍領域におけるトルソー症候群の臨床的検討

東北婦人科腫瘍研究会 (Tohoku Gynecologic Cancer Unit : TGCU)

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【目的】トルソー症候群の原因となる悪性腫瘍では婦人科癌の頻度が高いとされるが、診断基準は明確ではなく、まとまった報告は少ない。トルソー症候群と診断した症例について臨床的病理学的因子や治療や予後を多施設共同試験で検討した。【方法】過去15年間で各施設においてトルソー症候群と診断した症例について後方視的に検討を行った。【成績】症例は88例で、年齢中央値は60歳、卵巣・腹膜癌53例(60%)、子宮体癌22例(25%)、子宮頸癌11例(12.5%)であった。病期は65%がIII期以上で、I期の多くは卵巣明細胞癌であった。発症時期は悪性腫瘍の診断時が34例(39%)で最も多く、次いで初回治療中25例(28%)、再発治療中23例(26%)であった。トルソー症候群の診断は、画像検査、血液検査で総合的に診断されており、心エコー検査は38例(43%)で施行され、非細菌性血栓性心内膜炎を認めた症例は6例であった。血栓への治療としてはヘパリン持続静注が52例(59%)で施行されていた。またその後ワーファリンやDOAC内服へ切り替えた症例がある一方で、ワーファリンやDOAC内服中に脳梗塞を発症した症例も認めた。トルソー発症後の予後因子では、発症時期が初発時の群、原疾患に対して手術を施行できた群でそれぞれ、有意に予後良好であった($p=0.04$, $p=0.001$)。一方で、発症時の血小板が低値、D-dimerが高値、組織型が明細胞癌では予後不良な傾向を認めた。5年生存率はI期:43%、II期:50%、III期:20%、IV期:6%であった。【結論】婦人科悪性腫瘍に限定したトルソー症候群について、多施設かつ知りうる限りでは最多の症例数について検討した。今後は診断方法や遺伝子解析を含めた病因についての検討を進めたい。

P-84-5 婦人科悪性腫瘍患者における化学療法または放射線療法中のがん関連血栓症 (CAT) の発症と理学的予防法 (弾性ストッキング着用) を中心とする積極的予防対策

九州大病院

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【目的】婦人科悪性腫瘍患者における化学療法や放射線療法中のがん関連血栓症 (Cancer Associated Thrombosis : CAT) の発症状況を把握し、理学的予防法 (弾性ストッキング着用) を中心とする積極的予防対策の効果を検証する。【方法】当科で入院治療を行った婦人科悪性腫瘍患者を診療データベースより抽出し、患者背景とCATの発症状況について電子カルテを用いて後方視的に調査した。続いて、全ての婦人科悪性腫瘍患者に対して入院時の静脈血栓塞栓症リスク評価を導入し、化学療法または放射線療法中の患者に対して弾性ストッキングによる理学的予防法と看護師による日常生活指導を導入した。最後に、この積極的予防対策の効果を前方視的に検証した。【成績】2012年4月からの5年間に入院治療を行った婦人科悪性腫瘍患者は1008例であった。そのうちCATを発症したのは95例(9.4%)で、発症時期は50.5%が化学療法または放射線療法中であった。また、2019年1月より導入した入院時の静脈血栓症リスク評価では、化学療法および放射線療法中の全ての患者が中リスク以上であった。そこで、2019年4月からの2年間に化学療法および放射線療法目的で入院した439例の患者に対して積極的予防対策を実施し、CAT発症は21例(4.8%)であった。積極的予防対策の導入前4年間における対照群(676例)のCAT発症は49例(7.3%)で統計学的有意差はなかったが、減少傾向であった。また化学療法症例に限れば4.6%と8.1%で、統計学的有意に減少した。【結論】婦人科悪性腫瘍患者におけるCATの発症は、化学療法や放射線療法中が過半数を占めていた。これらの症例に対する理学的予防法を中心とする積極的予防対策は有効である可能性が示唆された。

P-84-6 静脈血栓塞栓症の診断における TFPI2 の有用性

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【目的】外因系抗凝固因子 Tissue Factor Pathway Inhibitor 2 (TFPI2) は、新しい卵巣癌の腫瘍マーカーとして保険収載された。静脈血栓塞栓症(venous thromboembolism; VTE)が多い卵巣明細胞癌で、TFPI2 の高発現が認められている。現在 VTE のスクリーニングには D タイマーが広く用いられているが、TFPI2 と VTE に関する研究はこれまで行われていない。今回、VTE の診断に TFPI2 が有用かどうかを検証した。【方法】2008 年 1 月から 2015 年 12 月に、当科で上皮性卵巣癌と診断され初回治療を受けた患者を対象とした。術前の採血で D タイマー陽性 (>1.0 μ g/mL) となった 81 人を対象に下肢静脈超音波検査を実施し、VTE の有無を調べた。また ROC 曲線を用いて VTE の診断における TFPI2 の有用性を比較した。【成績】患者年齢の中央値は 60 歳 (範囲: 37-83) であった。対象患者の 22.2% が卵巣明細胞癌であり、66.7% が stage III/IV 期の進行癌であった。下肢超音波検査の結果は VTE 有りが 25 名、VTE 無しが 56 名であった。VTE 患者の TFPI2 値は非 VTE 患者と比較して有意に高値であった (中央値 472.2 pg/mL vs. 279.1 pg/mL, $p < 0.001$)。VTE の診断における TFPI2 の ROC 曲線の曲線下面積 (AUC) は 0.729 (95% CI: 0.614-0.844) であり、Youden index より 398.9pg/mL をカットオフ値と設定すると、感度 64.0%、特異度 80.4%、陽性適中率 59.3%、陰性適中率 83.3% で VTE を診断することができた。また TFPI2 が 199.0pg/mL 以下の場合、VTE 発症は無かった。また D タイマーと TFPI2 値に相関関係は認めなかった ($p = 0.574$) 【結論】D タイマー陽性の卵巣癌患者において、TFPI2 は VTE の有無を診断する有用なマーカーとなる可能性が示唆された。

P-84-7 右室内浮遊性血栓症を伴った Trousseau 症候群合併卵巣癌に対し抗凝固療法後に試験開腹術を施行した 1 例

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【緒言】悪性腫瘍では血液凝固能が亢進し Trousseau 症候群に代表される血栓塞栓症を来す事がある。今回我々は卵巣癌の診断時に右室内浮遊性血栓症を伴った Trousseau 症候群に対し抗凝固療法後に試験開腹術を施行した一例を経験したので報告する。【症例】38 歳, 0 妊 0 産, 未婚, 橋本病で当院通院中, 不正性器出血を主訴に当科受診し, 造影 CT にて左卵巣癌が疑われた。同 CT にて肺動脈塞栓症及び脾梗塞, 腎梗塞を指摘され, 入院しエンドキサパン 60 mg を開始したが, 第 11 病日に意識消失発作あり, 頭部 MRI にて脳梗塞を認め Trousseau 症候群の診断となった。同日行った心臓超音波検査で右室内に浮遊性血栓を認めたため循環器内科転科しヘパリンへ変更した。血栓は残存していたが第 22 病日に試験開腹術を施行した。術中, 骨盤内に多数の播種を認め完全切除は困難であり, 左付属器切除のみを行い, 左卵巣明細胞癌 IIB 期と診断した。術後はワーファリンで抗凝固療法を行い, 術後 15 日目にパクリタキセル+カルボプラチン療法を施行したが, パクリタキセルによるアナフィラキシーショックを認め, 術後 29 日目にゲムシタピン+カルボプラチン (GC) 療法 1 コース目を施行し退院となった。今後は右心室内血栓消失後に二期的根治術を予定している。【結論】右室内浮遊性血栓症を伴った卵巣癌に対して抗凝固療法後に試験開腹術を施行した一例を経験した。血栓症のため脳梗塞などの重篤な合併症を併発することが十分考えられるが, 手術をせざるを得ない症例もあり, 血栓症合併卵巣癌では他科との連携を強化し診療にあたる事が重要である。

P-84-8 Trousseau 症候群を呈した卵巣癌 3 症例の検討

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 前田大伸

【目的】Trousseau 症候群 (TS) は悪性腫瘍に伴う血液凝固亢進により脳卒中を生じる病態と捉え婦人科腫瘍との関係も深い。【方法】今回我々は 2011 年 4 月~2021 年 10 月までに、3 例の脳梗塞を発症した TS を経験したので報告する。〈症例 1〉46 歳女性, 脳梗塞発症にて前医入院中に、線溶系亢進を認めた。腹部 CT 検査を施し 130×110mm 大の腫瘍を認め、精査・加療目的に当科受診となった。〈症例 2〉69 歳女性, 構語障害および左上下肢の不全麻痺が出現したため当院救急外来受診。頭部 MRI を施行し、大脳皮質・小脳に散在性梗塞を認めた。凝固線溶系の異常と腹部 CT 検査にて 110×95mm 大の腫瘍を認めた。〈症例 3〉65 歳女性, 血便にて消化器外科より精査紹介。CT, MRI 検査で 80×70mm 大の腹部腫瘍を認めた。【成績】症例 1 と 2 は、卵巣癌と脳梗塞および深部静脈血栓症を合併し線溶系も亢進していた。循環器内科, 神経内科に併診し、ヘパリン療法および IVC フィルターを挿入し手術を行った。術後病理検査で、卵巣明細胞癌と診断され追加化学療法を施行した。症例 3 は脳梗塞にヘパリン療法を開始し手術施行。術後病理検査は卵巣類内膜癌と診断され、化学療法を追加した。【結論】脳卒中と悪性腫瘍との関連性については、原発巣として肺, 卵巣, 大腸, 胃, 睪由来の腺癌が圧倒的に多く、CA125, CA19-9 などの腫瘍マーカーの臨床的意義が高い。これらのマーカーは高分子ムチンで、近年血栓形成に直接関与していることが明らかにされている。TS の治療としては、早期に抗凝固療法を開始し、手術による腫瘍摘出と抗癌剤治療により原疾患のコントロールができた場合に、凝固線溶異常が正常化し予後改善が期待できると考えられる。

P-85-1 当院における過去10年の腹腔鏡下・腹腔鏡補助下子宮筋腫核出術の検討

市立広島市民病院

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【目的】近年、腹腔鏡手術の普及に伴い、子宮筋腫核出術においても腹腔鏡下子宮筋腫核出術 (Total Laparoscopic Myomectomy: TLM) と腹腔鏡補助下子宮筋腫核出術 (Laparoscopic Assisted Myomectomy: LAM) が増加傾向である。当院においても、TLM と LAM は主要な術式となっており、近年の傾向について検討することを目的とした。【方法】2011年1月から2020年12月までの10年間に当院で施行した514例のTLMと43例のLAMについて、摘出検体量、出血量、手術時間、手術前投薬、術後経過、合併症について、診療録をもとに後方視的に検討を行った。【成績】当院での子宮筋腫核出術 (TLM, LAM, 開腹手術) の件数は年間76~119件で推移し、増加・減少傾向は示さなかった。一方、子宮筋腫核出術全体におけるTLMとLAMの割合は2011年に24.3%であったものが2020年には75.0%と増加傾向であった。摘出検体量の中央値はTLMが120g (2~726g), LAMは中央値247g (15~816g)。出血量の中央値はTLMが60g (0~900g), LAMが150g (10~2050g)であった。手術時間の中央値はTLMが113分 (33~265分), LAMが112分 (58~192分)であった。術前はほとんどの症例でGnRHアナログ製剤を使用した。退院延期や治療を要した合併症として、術後血腫を生じ輸血を要する貧血を生じた症例は2例であり、術前に貯血していた自己血を返血した。他は皮下血腫2例、仮性動脈瘤1例、尿管狭窄を1例で認めた。【結論】当院における子宮筋腫核出術におけるTLM, LAMの割合は増加傾向であった。10年間における重大な合併症の頻度は低く、安全性を確保した手術が可能であった。腹腔鏡下手術の普及と技術向上に伴い、今後も腹腔鏡での筋腫核出術の増加が予想される。

P-85-2 閉経後子宮筋腫の臨床病理学的所見に関する後方視的研究

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【目的】子宮平滑筋腫は性成熟期女性に高率に認められる良性腫瘍であり、発生率は217-3745/100,000¹と報告されている。また、子宮平滑筋腫はestrogen依存性であるため、一般的に閉経と共に自然縮小が認められる。しかし、しばしば閉経後であっても増大傾向を示す子宮筋腫が経験され、子宮平滑筋肉腫あるいは卵巣腫瘍との鑑別のため手術が適用されているが、閉経後の子宮筋腫の臨床病理学的特徴の詳細は未だ不明である。閉経後子宮筋腫 (子宮平滑筋腫) の臨床病理学的特徴について、当院において手術を行った20症例から後方視的に検討する。【方法】2017年4月1日~2021年9月1日の期間のうち子宮筋腫の手術をした閉経女性20症例を診療録を用いた後方視的調査、病理組織学的検討、免疫組織学的検討を行った。【成績】臨床所見として閉経前後の患者の主訴を比較した。閉経前の症例の主訴は過多月経が最も多く、次に不正性器出血が多かった。一方で閉経後の症例の主訴で最も多かったのは疼痛であった。血液検査所見に関しては閉経前後で有意差を認める項目は見られなかった。病理組織学的検討については閉経後の症例で20例中12例に変性を伴う筋腫が認められた。閉経後の症例では硝子化が9例、脂肪化が4例、そのほか石灰化、水腫状化、粘液変性がそれぞれ1例あった。【結論】閉経後子宮筋腫は縮小傾向にあると言われているが、変性している筋腫も多く子宮肉腫との鑑別が必要になるような症例もみられた。閉経後においても増大したり悪性化する例もあり、長期的な経過観察が必要と思われる。

P-85-3 腹腔内自然脱落后に増大傾向を示したと考えられる parasitic myoma の1例

国立神戸医療センター

嘉納 萌, 浅見里紗, 白國あかり, 吉田 愛, 杉本 誠, 武内享介

Parasitic myoma とは子宮筋腫が異所性に生着した病態である。腹腔鏡下子宮筋腫核出術におけるモルセレーター使用に関連した医原性と、自然発生で生じる非医原性がある。今回、子宮筋腫を経過観察中に増大傾向を示し、腹腔鏡下に parasitic myoma と診断・摘出した症例を経験したため報告する。症例は38歳、未妊、既往歴なし。6年前に下腹部痛で受診した。最大6cmの子宮筋腫を複数指摘された。変性痛を疑い手術加療をすすめたが、本人の希望で経過観察をしていた。筋腫の増大を認め、腹腔鏡下子宮筋腫核出術の方針となった。術中所見では最大9cmの筋腫4個と、ダグラス窩に5cmの子宮とは連続性のない腫瘍を認めた。腹腔鏡下子宮筋腫核出術およびダグラス窩腫瘍摘出術を行った。ダグラス窩の腫瘍は広間膜後葉および直腸間膜に癒着していた。腹腔鏡の拡大視を利用して栄養血管を検索しながら全周性に剝離した。明らかな血管は認めなかったが、主に直腸間膜に生着していた。剝離面からの出血はわずかであった。病理検査にてダグラス窩腫瘍も子宮筋腫であった。6年前と術前のMRI検査を見返して比較すると、漿膜下筋腫に付着していた2cm大の筋腫が、ダグラス窩左側に脱落し増大していると考えられた。また、経過観察中に左背部痛の訴えも度々あり、筋腫の生着・増大に伴う疼痛であった可能性が示唆された。本症例のように自然脱落后にも増大する parasitic myoma があり、術中後腹膜腫瘍との鑑別が困難であった。多発子宮筋腫に併存する後腹膜腫瘍は parasitic myoma も念頭に置いて慎重な手術操作が必要と考える。

P-85-4 レルゴリクス療法を多数例に施行した中で見えてくる光と影

メディカルトピア草加病院

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【目的】子宮筋腫に対する治療薬であるレルゴリクスはまだ発売されて間もないため、知見が少なく使用中のトラブルに触れることもある。術前治療目的にレルゴリクスを多数例に使用し、使用中の貧血やエストロゲンの抑制障害症例について検討したので報告する。【方法】2020年10月より2021年2月の間にレルゴリクスの処方を行い、その後手術を施行した症例を対象とした。検討項目として、手術の概ね1か月前に施行した術前検査におけるヘモグロビン値（以下Hb値）ならびにエストロゲン値（以下E2値）について調査した。【成績】観察期間中に当科でレルゴリクスの投与を行った症例は244例であり、このうち60日以上服用をした212例について検討した。患者の平均年齢は43.7±5.8歳であった。術前検査時に貧血（Hb11.0g/dl未満）を認めた症例は24例（11.3%）であり、そのうち投与前よりもHb値が低下していた症例は7例（3.3%）であった。また、術前評価時のE2値が50pg/ml以上であった症例は7例（3.3%）であった。E2値の抑制障害を示した症例と全体集団の患者背景（BMIや年齢）については大きな差異は認めなかった。【結論】術前にレルゴリクスを投与することにより得られる無月経によって、Hb値の改善や子宮筋腫の縮小効果が期待される。一方で、一部症例において今回検討したような貧血の進行やE2値の低下障害も散見されることから、レルゴリクスの使用を躊躇する医師もみられる。今回の検討結果における課題症例の割合はそれぞれ3%程度であり、実臨床での許容範囲であると思われる。

P-85-5 当院における子宮筋腫手術前の薬物治療の治療効果に関する比較検討

岐阜大附属病院

合田知弘, 菊野享子, 村瀬紗姫, 森美奈子, 竹中基記, 早崎 容, 古井辰郎, 森重健一郎

【目的】子宮筋腫は一般診療において非常に多く遭遇する疾患の一つである。2019年3月より、GnRHアンタゴニストのレルゴリクス（商品名レルミナ）が発売された。発売後の子宮筋腫手術の術前管理について後方視的検討を行い、GnRHアナログの使い分けについて検討した。【方法】後方視的研究。対象は術前にリュープロレリンもしくはレルゴリクスを使用した閉経前の子宮筋腫患者で全身麻酔下に手術を行った症例。実施期間はリュープロレリン：2014年1月1日～2018年12月31日、レルミナ：2019年3月1日～2021年2月28日。主要評価項目は筋腫縮小率、副次評価項目は副作用や縮小率に関する因子。統計学的検討を行った。【成績】レルゴリクス群（37例）とリュープロレリン群（120例）で比較検討した。平均投与期間とレルゴリクス群で18.2週間、リュープロレリン群で4.7回（4週間に1回投与）であった。平均縮小率はそれぞれ20%と19%であった。ホットフラッシュはレルゴリクス群の方がリュープロレリン群と比べて多く（それぞれ51%、37%）、その他の項目に関しては同程度であった。【結論】レルゴリクスとリュープロレリンは、筋腫の縮小効果や副作用に関してそれほど違いは認めず、同じように使用できるものと思われる。レルゴリクスは経口投与であるため、副作用による治療中断が行いやすく、患者側も内服開始しやすい印象がある。服薬コンプライアンスを考慮し、患者本人と相談して決定するのが良いと考える。

P-85-6 多血症を呈しエリスロポエチン産生が疑われた閉経後子宮筋腫の一例

新潟大病院

佐藤仁美, 島 英里, 谷地田希, 齋藤宏美, 工藤梨沙, 磯部真倫, 西野幸治, 西川伸道, 関根正幸, 榎本隆之

【緒言】エリスロポエチン（Erythropoietin：EPO）産生腫瘍の代表的なものに腎細胞癌や肝細胞癌などがあるが、子宮筋腫においてもEPO産生を来すことが報告されており、関連赤血球増多症（myomatous erythrocytosis syndrome：MES）と言われている。今回我々はMESが疑われた子宮筋腫の1例を経験したので報告する。【症例】75歳3妊3産。3cm程の筋腫を指摘されていたが、50歳で閉経後は受診せず。1年前に他疾患精査目的のCTで子宮腫瘍を疑われ初診。超音波検査にて8cm大の子宮筋腫を認めたが、無症状のため経過観察となった。その後RBC $591 \times 10^4/\mu\text{l}$ 、Hb 18.3g/dl、Ht 54.3%と多血症が出現してきたため、血液内科で精査が行われた。血清EPO 19.5IU/mlと正常範囲内であったが、他の血液学的所見から二次性多血症が疑われた。再検したCTで子宮筋腫の増大を認め、原因として筋腫以外に想定されるものがなく、一旦終診となっていた婦人科に再度紹介された。経過から悪性またEPO産生腫瘍の可能性も考慮し、腹式単純子宮全摘術および両側付属器切除術を施行した。術後1週間で血清EPO 2.80IU/mlに低下、RBC $470 \times 10^4/\mu\text{l}$ 、14.0g/dl、Ht 41.6%と多血の所見は消失、その後の経過観察でも多血症の再燃は認めず経過している。病理組織診断は平滑筋腫で悪性所見は認めなかった。【考察】術前の血清EPO値は正常範囲内であったが、子宮摘出後にEPO値の低下と多血症の改善を得たことから、EPO産生子宮平滑筋腫であると考えられた。EPO産生子宮筋腫は閉経後に増大傾向を示すといった報告が散見されるが、巨大な筋腫例が多くを占める。本症例では閉経前には有意なサイズではなかったものの、MESを発症していたと考えられた。

P-85-7 腹腔鏡下子宮粘膜下筋腫核出時の内膜穿破予防の工夫

東海大八王子病院

間邊貴俊, 牧野田佳, 牧野田知奈美, 重盛波留子, 泉 顕治, 大岩一平, 橋山知紗, 橋山知明, 西島義博, 杉山太郎, 前田大伸, 村松俊成

【緒言】子宮筋腫核出術において、子宮内膜に近い筋腫を核出した場合に内膜穿破を来すことがしばしばある。内膜を穿破した場合の合併症として子宮腔内癒着が知られているがその発生頻度や予防対策はまだまだ確立していない。今回術中に子宮腔内へインジゴカルミンを注入し子宮内膜を確認しつつ粘膜下筋腫を内膜穿破することなく核出できた症例を経験したので報告する。【症例】42歳0妊0産 粘膜下筋腫、過多月経のため手術的に当院へ紹介となった。MRI検査にて子宮底部に4cm大の粘膜下筋腫を認めた。腹腔鏡下子宮筋腫核出術を施行した(トロッカー配置はdiamond style, 手術時間1時間57分, 出血量5ml, 自己血2単位使用)。手術開始時にインジゴカルミン希釈液(インジゴカルミン1A/生食100ml)を子宮マニピュレーターから子宮腔内に注入し卵管疎通性を確認した。その後超音波凝固切開装置にて筋層切開を開始し、内膜近くに達したところでハサミ鉗子で慎重に筋腫を剝離した。インジゴカルミンを注入したことで染色された内膜が膨隆し筋腫と内膜との境界が明瞭になり内膜穿破することなく核出することが可能となった。また筋層縫合の際にも子宮内膜を視認しながらのより丁寧な縫合が可能であった。【結語】腹腔鏡下筋腫核出術時の内膜穿破予防としてインジゴカルミン希釈液の子宮腔内への注入は、簡便であり内膜穿破の予防として有用な方法であると考えられた。

日本語ポスター
7日(日)

P-85-8 腹腔鏡下筋腫核出術の術前療法薬としてのGnRHアゴニストとGnRHアンタゴニスト比較検討

メディカルトピア草加病院

加藤紀子, 小堀宏之, 野路千智, 山本憲子, 熊切優子, 萩原聖子

【目的】筋腫の手術において術前療法薬は長い間GnRHアゴニスト(リュープリン塩酸塩)が使用されてきたが近年GnRHアンタゴニスト(レルゴリクス)も使用可能となった。腹腔鏡下子宮筋腫核出術(LM)前の使用で両者の効果に相違があるのか検討した。【方法】2019年4月から2020年12月まで当院で施行されたLMで選択バイアスを考慮し、最大筋腫径が5cm~10cm大の筋腫症例を対象として、術前療法がリュープロレリン酢酸塩であった84症例(L群)と、術前療法がレルゴリクスであった39症例(R群)について後方視的に比較検討した。年齢、BMI、投与期間(月)、術直前のE2値、骨盤MRIで計測した投与前と比較した投与後の最大子宮筋腫の縮小率(%), 術中出血量(g), 手術時間(分), 摘出した子宮筋腫の個数をそれぞれL群とR群とで比較し、2群間をMann-Whitney's U testを用いて有意差検定をおこなった。【成績】L群とR群で年齢: 36.6±5.4歳, 36.2±5.1歳, BMI: 21.8±3.0, 21.6±2.8, 筋腫個数: 5.0±4.0個, 5.5±5.5個, 縮小率: 72.1±22.8%, 77.8±32.4%, 術前E2値: 15.0±12.1, 16.5±15.3, 手術時間: 81.1±31.0分, 86.1±33.7分, 出血量: 63.3±86.2g, 63.3±97.4gで有意差を認めなかったが投与期間のみL群4.2±0.9か月, R群3.3±0.8か月と有意差を認めた。【結論】投与期間はR群で有意に短くなっていたが縮小率, 術前E2値, 手術時間, 出血量にL群とR群の有意差は認められなかった。このことより術前療法としてレルゴリクスはリュープリン塩酸塩と比較して投与期間を短くしても遜色なく使用できると考えられた。

P-85-9 乳癌術後タモキシフェン療法後に腹膜子宮内膜症の悪性転化を認めた一例

JA 旭川厚生病院

三坂琴美, 小田切哲二, 今田冴紀, 杉山沙織, 中嶋えりか, 野崎綾子, 光部兼六郎, 吉田俊明, 山田和佳

【目的】タモキシフェン(TAM)療法が子宮体癌のリスクとなることは知られている。今回、子宮全摘、両側付属器切除術10年後に、タモキシフェン療法の影響が考えられる腹膜子宮内膜症病変の悪性転化を認めた一例を報告する。【症例】症例は62歳女性。1妊1産。20XX年5月、子宮内膜症のため腹腔鏡補助下子宮全摘術、両側付属器切除術を施され、同年甲状腺癌のため甲状腺全摘術施行された。20XX+1年4月、乳癌手術施行し、TAM療法を開始された。20XX+9年12月、乳癌術後再発評価目的のCTで直腸両脇に腫瘤を指摘された。20XX+10年5月、骨盤内腫瘍精査目的に当科へ紹介された。骨盤内腫瘍にはエコーで充実成分を認めず、経腔超音波検査での定期検診としていたが、20XX+12年7月嚢胞内に充実成分が出現し、MRIでも悪性を疑う所見を認めたため、手術の方針となった。腹腔鏡下直腸低位前方切除術、骨盤内腫瘍摘出術、回腸ストマ造設術を行った。病理では、類内膜癌G2であった。ER, PgR共に陽性を示し、内膜間質細胞と推測され、内膜症に連続して生じた類内膜癌を考える結果だった。腹膜癌に準じて、IIB期と診断し、画像上リンパ節転移は認めないためリンパ節郭清は行わず、化学療法を追加する方針となった。【考察】今回、両側付属器切除後の子宮内膜症腹膜病変が悪性転化した症例を経験した。腹膜子宮内膜症の悪性転化は非常に稀であり、さらに本症例では乳癌術後TAM療法が悪性転化に寄与した可能性が考えられ、こちらに関して若干の文献的考察を加えて報告する。

P-86-1 術中に肺血栓塞栓症をきたした閉経後子宮捻転の一例

JCHO 九州病院

松本裕佳, 西村和泉, 進本かれん, 池之上李都子, 安東明子, 魚住友信, 大塚慶太郎, 愛甲悠希代, 東條伸平, 川上剛史, 河野善明

子宮捻転は子宮が長軸に沿って45度以上回転した状態と定義される。今回我々は子宮筋腫を伴う閉経後子宮捻転に対する手術中に肺塞栓を発症し、迅速な集学的治療を開始して救命し得た一例を経験したので報告する。症例は81歳、2妊1産。下腹部痛と食欲不振を数日間認めた後、意識消失し倒れているところを家族に発見され前医に救急搬送された。CT検査で骨盤内に巨大な充実性腫瘍を認め、婦人科疾患を疑われ当科に搬送された。MRI検査で長径20cm以上の子宮筋腫を認め、子宮筋腫の捻転を疑われた。下肢静脈超音波検査で右ヒラメ静脈のみに血栓を認め、CT検査で下大静脈は腫瘍により圧排されていたが明らかな血栓は同定できなかった。入院翌日より下腹部痛が増強し、入院3日目(発症5日目)に開腹手術を施行する方針とした。循環器内科に相談し、中枢型の静脈血栓を認めないため、下大静脈フィルターは留置しなかった。開腹時所見で、20cm大に腫大した子宮体部は暗赤色に変色し、内子宮口の高さで頭側から見て時計回りに540度、両側付属器を巻き込んで捻転していた。捻転を解除後に心肺停止状態となり、蘇生を開始して自己心拍は再開した。心臓超音波断層法で肺塞栓が疑われ、術中よりヘパリン投与を開始した。蘇生と並行して腹式単純子宮全摘術、両側付属器摘出術を施行した。術直後のCT検査で肺血栓塞栓症を認め、その後DICも発症した。集中治療室で抗凝固療法を含めた全身管理を行い、術後33日目に後遺症なく独歩退院した。子宮体部腫瘍は組織学的には平滑筋腫であった。

P-86-2 消化管間質腫瘍(GIST)との鑑別を要した寄生筋腫の1例信州大附属病院¹, JA 南長野医療センター篠ノ井総合病院²山本さやか¹, 小原久典¹, 井田耕一¹, 遠藤瑞穂¹, 品川真奈花¹, 竹内穂高¹, 山田 靖¹, 鹿島大靖², 宮本 強¹, 塩沢丹里¹

寄生筋腫は子宮筋腫が子宮との連続を持たない臓器から栄養血管を獲得し増生する腫瘍で、腹腔鏡下子宮筋腫核出術(LM)での小片遺残が医原性発生要因として問題となっている。今回、LM後に消化管間質腫瘍(GIST)との鑑別を要した寄生筋腫の1例を経験した。症例は38歳女性で34歳時にLMを施行され、摘出筋腫核の腹腔外搬出はin-bagで行われ、病理結果は富細胞性平滑筋腫であった。この4年後に子宮背側に上直腸動脈からの血流支配を受け、子宮との連続性のない長径10cmの骨盤内腫瘍を指摘された。MRIでは腫瘍は直腸に連続し、T2強調像で高信号、T1強調像で低信号の造影効果を伴う充実性腫瘍で内部に嚢胞部分を伴い、充実性部分は拡散制限を示し、4年前に摘出した筋腫の信号と類似していた。以上から寄生筋腫を第一に考えたが、GISTは否定できず、術中迅速診断での両者の鑑別は不可能であり、短期間で増大していたこともありGISTを念頭に置いた手術療法の方針とした。妊孕性温存希望はなく、子宮筋腫再発も認めていたため、腹式単純子宮全摘術、両側卵管切除術、直腸低位前方切除術を施行した。術中所見は腸管と連続した腫瘍がダグラス窩に存在し、腫瘍と子宮や付属器との連続性はなかった。摘出腫瘍の病理検査では直腸筋層と腫瘍の連続性は明らかではなく、紡錘形細胞が錯綜配列し、エストロゲン受容体陽性で子宮由来の平滑筋腫と判断し、寄生筋腫と診断した。LM後の寄生筋腫ではGISTとの鑑別を要する場合があるが、摘出した筋腫のMRI所見と比較することが診断の一助になると思われる。またLMではin-bagでの子宮外搬出でも寄生筋腫を生じる可能性があり、術前に十分説明しておく必要があると考えられた。

P-86-3 子宮悪性腫瘍と鑑別が困難であった閉経後子宮筋腫の一例

兵庫県立西宮病院

高木江利華, 山部エリ, 向田直人, 元山貴仁, 西森早苗, 尹 純奈, 石田享相, 小寺花織, 増原完治, 信永敏克

子宮筋腫および子宮腺筋症は婦人科領域で高頻度に認められる良性疾患であるが、閉経後に増大する事は珍しく、増大した場合は悪性腫瘍を考慮に入れるべきである。今回、子宮筋腫および子宮腺筋症にて経過観察中の患者が、閉経後に子宮の増大をきたし、子宮腺筋症の悪性転化または子宮肉腫を疑った症例を経験したので、文献的考察を加えて報告する。症例は59歳女性、1経妊1経産、51歳閉経。併存症に神経線維腫症I型があるも皮膚病変のみで病状は安定していた。46歳から5cm大の子宮筋腫および子宮腺筋症に対し当院で経過観察されていた。閉経後は1年毎の婦人科検診目的に当院へ通院を継続していた。59歳時、1年前には認めなかった、骨盤内に子宮と連続する充実部分を伴う12cm大の腫瘍が認められた。子宮内膜組織診は悪性所見を認めず。CEA, CA19-9, CA125の腫瘍マーカーの上昇は認められなかった。骨盤MRIを施行したところ、子宮筋層内に拡散制限および造影効果のある充実成分と、その周囲に出血を伴う15cm大の腫瘍が認められた。子宮腺筋症の悪性転化または子宮内膜間質肉腫などの子宮肉腫が疑われたため、手術の方針とした。術中迅速病理診断の結果が子宮筋腫であったため、腹式単純子宮全摘・両側付属器摘出術を実施し、手術を終了とした。永久病理結果は、奇怪核を伴う平滑筋腫に分類される良性腫瘍の異型平滑筋腫であった。閉経後の子宮筋腫増大は子宮肉腫などの悪性疾患との鑑別が必要であるが、本症例のように良性腫瘍の事もあり、慎重な検討が必要である。

P-86-4 当院で経験した稀少部位子宮内膜症の3例

大阪市立大附属病院

中島安紗海, 安井智代, 市村友季, 福田武史, 笠井真理, 山内 真, 今井健至, 角 俊幸

【緒言】稀少部位子宮内膜症は common site 以外の部位に発症した子宮内膜症と定義されている。当院で経験した3例を報告する。【症例】症例1: 44歳, 未経妊。既往歴に31歳時卵巣チョコレート嚢胞摘出術がある。月経開始4日目に右気胸を発症。翌々月に2度目を発症し偽閉経療法を開始した。治療開始3日目に3度目を発症し胸腔鏡下手術を実施。摘出標本に子宮内膜症を認めた。偽閉経療法後ジェノゲスト投与中で術後3年間再発を認めていない。症例2: 41歳, 1経産。既往歴に40歳時卵巣嚢腫摘出術がある。数年前より月経開始とともに排尿時に陰に違和感出現。月経終了とともに消失するということを繰り返していた。排尿時腰痛が出現するようになり来院。後陰門蓋部に出血部位と硬結を認め、生検にて子宮内膜症と診断。LEPでは症状軽快せず、偽閉経療法に引き続き現在ジェノゲスト投与中で症状消失している。症例3: 45歳, 未経妊。既往歴に42歳時に子宮筋腫に対し腹式子宮全摘出術がある。術後3年頃より月に1回程度の性器出血を認めるため来院。陰道断部に blueberry spot を伴う腫瘤を認め、生検で子宮内膜症疑いと診断された。BBT 上の性器出血の時期から子宮内膜症と診断し偽閉経療法を実施した。その後症状は再燃したが51歳時に症状は消失した。【結語】稀少部位子宮内膜症に対しては手術療法や薬物療法の有効性が報告されている。今回胸腔に発症したものは手術療法を行ったが、3例ともホルモン療法により長期管理が可能となった。大変まれな疾患ではあるが、症例に応じて治療方法を選択することにより長期管理が可能と考えられる。

P-86-5 後腹膜に発生した粘液性平滑筋腫の1例

ハートライフ病院

武田 理, 宮崎優樹, 比嘉博香, 堀本直幹, 大西 勉

粘液性平滑筋腫は子宮平滑筋腫の特殊型の1つで時に肉腫との鑑別が重要である。今回我々は悪性の可能性も疑いながら手術後に粘液性平滑筋腫と診断された1例を経験したので報告する。症例は60歳。G4P2。既往歴に子宮頸部円錐切除術(CIN 3)。子宮頸部細胞診異常を指摘され当科紹介。経膈超音波検査で骨盤内腫瘤を疑われた。初診時検査では末梢血生化学検査、出血傾向で異常を認めず腫瘍マーカーの上昇なし。超音波検査で子宮左側に充実性腫瘤を認め、子宮筋層との境界は明瞭。造影MRIでは子宮右側に74x42mmの腫瘤で内部ではT2強調で低信号の点状構造や不整な網状影、T1強調像で高信号域も一部認め脂肪含有の可能性もあり。明らかな拡散制限はなし。変性筋腫を念頭に成熟奇形腫や充実性腫瘤が鑑別に上げられた。開腹手術を施行した。子宮、右付属器は異常なし。左卵巣は軽度腫大。腫瘤は右円靭帯下部の後腹膜に存在。円靭帯を結紮切断し広間膜前葉を開き目的の腫瘤を周囲から鈍的に剝離、骨盤底から遊離すると子宮頸部側壁から有茎発生していた。これを摘出。迅速病理検査結果は平滑筋腫瘍で異型度は低い。型通りに子宮、両付属器を摘出した。永久標本による病理組織検査では白色充実性病変と粘液腫様病変が混在、紡錘形細胞が粘液を背景に増殖、成熟した脂肪細胞を混している。核異型は軽度で核分裂像も明らかではなく腫瘍壊死も認めず。免疫染色でh-caldesmon陽性、Desmin陽性、PAS陰性、アルシアンブルー陽性、Ki-67 index<1%で最終的に粘液性平滑筋腫と診断した。粘液性平滑筋腫は特に粘液性平滑筋肉腫との鑑別が常に問題となるが、臨床上肉腫の報告がほとんどであり、粘液性平滑筋腫自体の報告は稀有である。文献の考察も含め報告する。

P-86-6 大量出血をきたし子宮鏡手術を要した若年性子宮内膜ポリープの1例

国立神戸医療センター

白國あかり, 武内享介, 浅見里紗, 嘉納 萌, 吉田 愛, 杉本 誠

【緒言】子宮内膜ポリープは、子宮内膜が過剰に増殖し、子宮内腔に腫瘍ができる疾患で、内膜腺と線維性間質の限局性増生で構成される境界明瞭な隆起性病変である。主な症状は不正性器出血であるが、無症状で偶発的に見つけられることもある。若年の不正性器出血の場合、ホルモンバランスが安定していないことで機能的出血をきたすことが多い。今回若年で不正性器出血を認め、ホルモン剤を投与するも止血が得られず、診察にて子宮内膜ポリープが疑われたため手術加療を行った症例を経験したので、報告する。【症例】15歳女性。0妊0産。性行為歴なし。既往歴なし。身長150cm, 体重49kg。不正出血にて近医を受診し、機能的出血の診断にてLEPを処方された。しかし、出血が持続し、貧血の進行が認められたため当科紹介となった。診察にて子宮口奥に腫瘤下端を確認した。経膈超音波検査にて頸管内に1-2cm大の腫瘤を認めた。出血が持続しており、血液検査にてHb 9.0mg/dLと貧血の進行を認めたため、緊急入院の上、子宮鏡下手術を行った。術中所見では、頸管内に明らかなポリープは認めなかったが、子宮内膜の肥厚を認めた。子宮鏡下に肥厚した内膜を切除した後、愛護的に内膜搔爬を行い、手術を終了した。術後病理検査では子宮内膜ポリープの結果であり、異型は認めなかった。術後性器出血の増加はなく、超音波検査でも異常は認めなかった。【考察】若年女性では月経周期が不規則であり、ホルモンバランスの乱れによる不正性器出血を認めることがある。ホルモン剤投与でも止血が得られない場合には、若年であっても器質的疾患の有無を確認する必要がある。

P-86-7 子宮平滑筋より発生し、右内腸骨静脈に進展した静脈内平滑筋腫症を切除した一例

誠光会草津総合病院

十河進仁, 卜部 諭, 小暮 藍, 中川渥裕, 藤城直宣, 鳥井裕子, 卜部優子

【緒言】静脈内平滑筋腫症 (intravenous leiomyomatosis) は、組織学的に良性の平滑筋腫が子宮平滑筋または静脈壁平滑筋もしくはその両者から発生し下大静脈内に進展する疾患である。今回、子宮平滑筋より発生し、右内腸骨静脈に進展する静脈内平滑筋腫症を早期に摘出することができたため報告する。【症例】57歳, G1P1, 閉経52歳。近医より閉経後に増大する子宮腫瘍の精査加療目的で当院紹介受診した。造影MRI検査で子宮体部右側より発育する不整形で長径9cmの腫瘍を認め、一部右内腸骨静脈内に腫瘍栓を認めた。閉経後に増大する子宮腫瘍であり、悪性も考慮し手術による摘出を行った。術中所見として子宮体部右側より数珠状に連なる子宮腫瘍を認めた。腹腔鏡下に子宮、両側付属器、右内腸骨リンパ節を切除した。子宮腫瘍と右内腸骨周囲組織との剝離時に右内腸骨静脈より出血あり。圧迫、バイポーラによる凝固止血、止血剤により止血した。手術時間は4時間45分、術中出血量は1600ml、摘出組織重量は350gであった。病理結果は子宮平滑筋腫であり、一部血管内腔にも筋腫組織を認め静脈内平滑筋腫症と考えられる所見を認めた。【考察】静脈内平滑筋腫症は子宮に好発するまれな平滑筋腫であり、静脈血管腔内での平滑筋細胞の増殖を特徴とし、組織学的には良性腫瘍に分類される。しかしながら、まれに骨盤内から下大静脈に進展した場合、三尖弁陥頓や肺塞栓症となり血管置換などの心臓血管領域の手術が必要となることがある。本症例では比較的早期に発見摘出した為、血管を温存しながら腫瘍を摘出することが出来た。文献的考察を含めて報告する。

P-86-8 後腹膜血管平滑筋腫に対して腹腔鏡下手術を行った1例

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【緒言】血管平滑筋腫 (angioleiomyoma; 以下 ALM) は、軟部組織に由来する比較的まれな良性腫瘍で、豊富な血流を受けることが多い。後腹膜 ALM は非常に稀で、これまで英文で7例の症例報告を認めるのみである。今回、後腹膜 ALM に対して腹腔鏡下手術を行った1例を経験したので報告する。【症例】45歳, 2妊2産。40歳時に腹腔鏡下筋腫核出術の既往がある。他院で骨盤部腫瘍を指摘され紹介となった。診察では、右付属器領域に5.8cmの充実性腫瘍を認めた。腫瘍マーカーは、CA125は57U/mlと微増、他は上昇を認めなかった。MRIでは、T2強調画像で右卵巣および骨盤壁と接する、子宮平滑筋に比し高低信号が混在する充実性腫瘍を認めた。ダイナミック造影MRIでは早期より不均一に強い造影効果を認めた。拡散強調画像では高信号だが、ADC値は低下を認めなかった。以上より、卵巣ないし骨盤壁由来の多血性良性腫瘍と診断し、腹腔鏡下右付属器切除術の方針とした。手術所見では、右付属器と連続性のない後腹膜から発生する淡紅色で鶯卵大の腫瘍を認めた。腫瘍には周囲から多数の栄養血管が流入し、これらの血管をシールしながら右付属器および腫瘍切除術を施行した。病理診断では、紡錘形細胞の不規則束状の増殖および大小多数の血管形成を認めた。免疫染色では、 α -SMAとdesminはびまん性に陽性、CD34は陰性であった。以上より、後腹膜由来のALMと診断した。【結語】画像で、骨盤内に非常に強く造影される腫瘍を認めた場合は、稀ではあるがALMの可能性も考慮する。手術に際しては、多方向から栄養血管が流入している可能性を念頭に置いた慎重な手技が望ましい。

P-86-9 GnRH アンタゴニスト投与後に多量出血を併発した4症例

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【緒言】GnRH アンタゴニストはGnRH アゴニストと比較し投与初期のフラアアップが無く、大量性器出血が少ない。しかし我々はGnRH アンタゴニスト投与中に大量出血を生じた4例を経験した。【症例1】51歳, 2妊2産。子宮筋腫・過多月経に対しGnRH アンタゴニスト使用歴あり。月経再開後多量の性器出血・Hb 6.0g/dLの貧血を認め紹介。超音波で50mmの子宮筋腫を認めた。GnRH アンタゴニストを再開したが止血せず、腹腔鏡下単純子宮全摘術を施行。【症例2】53歳, 1妊0産。過多月経、貧血で紹介。初診時Hb 6.3g/dL。MRIで70mmの筋層内筋腫と判断し、GnRH アンタゴニストを開始したが止血せず貧血が進行し、腹式単純子宮全摘術を施行。病理組織検査は平滑筋肉腫であった。【症例3】43歳, 0妊0産。既往症は狭心症(抗血小板薬)・腎不全(透析)。過多月経、貧血に対し前医でGnRH アンタゴニストが投与されたが、不正性器出血が持続し、Hb 5.3g/dLとなり紹介。初診時のE2 212.0pg/mL。MRIで器質的疾患なく、子宮内膜生検も異常なし。保存的治療では止血せず、腹腔鏡下単純子宮全摘術を施行。【症例4】31歳, 1妊0産。子宮筋腫核出術後。過多月経を認め、MRIで50mmの筋層内・粘膜下筋腫の再発を認めた。GnRH アンタゴニスト投与後に手術方針とした。内服開始後一旦止血したが56日目に出血増量あり、腹式筋腫核出術+子宮鏡下筋腫核出術を施行。【考察】GnRH アンタゴニストでも大量性器出血を来すことがあり、特に粘膜下筋腫の症例はGnRH アゴニスト同様注意を要す。また、長期に不正出血が持続する場合は悪性腫瘍を疑って早期の精密検査や外科的介入が必要である。さらに、透析患者では内服時間の工夫が必要であった可能性がある。

P-87-1 腹腔鏡手術後に診断された卵管内膜炎の2症例

富山県立中央病院

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【緒言】卵管内膜炎 (endosalpingiosis) は、卵管型上皮に類似した上皮で裏打ちされた腺組織が異所性に存在する病変だが、子宮内膜症とは異なり症状が乏しいため腹腔内腫瘍として発見され偶発的に診断されることが多い。今回、腹腔鏡手術中に腹腔内に散発する微小な病変を認め、卵管内膜炎と診断された2症例を報告する。【症例】症例1: 73歳, 2妊2産, 閉経54歳。症例2: 69歳, 3妊2産, 閉経50歳。2例とも腹腔鏡下仙骨腔固定術中に、骨盤内の直腸子宮窩腹膜に中央に1mm大の透明な嚢胞形成を伴う全長3mm径の白色の病変を複数箇所に認め、一部を切除し病理検査へ提出した。病理組織像では、一部線毛を有する円柱上皮で被覆された嚢胞があり内膜間質様の組織はなく、卵管内膜炎と診断された。【考察】良性疾患で摘出した付属器で卵管内膜炎の有病率は22%にまで達するとする報告や、観察される腹膜病変のうち16.1%が卵管内膜炎と診断されると報告する文献もある。高悪性度漿液性卵巣癌の発生源は卵管上皮である可能性が最も高いと言われるが、低悪性度漿液性卵巣癌の発生機序は依然として不明である。卵管内膜炎の臨床的な意義は不明であるが、低悪性度漿液性卵巣癌によく併発することが報告され、境界悪性腫瘍と卵管内膜炎との関連も示唆されている。卵管内膜炎の肉眼的所見は明らかでなく報告は少ないが、我々は今回、閉経後の直腸子宮窩腹膜に存在する中央に1mm大の透明な嚢胞形成を伴う3mm大の白色病変が、卵管子宮内膜症であることを示した。【結語】卵管内膜炎の微小な腹膜病変の形態について報告した。卵管内膜炎の肉眼的所見を明らかにし、正しい診断を行っていくことが今後の研究に不可欠である。

P-87-2 当院での子宮頸部筋腫に対する腹腔鏡下単純子宮全摘出術の検討

松山赤十字病院

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【目的】過去21年間に当院で施行した子宮頸部筋腫に対する子宮摘出術で腹腔鏡手術と開腹手術の差異を検討することを目的とした。【方法】2000年1月1日から2021年9月30日までの期間に当院で子宮頸部筋腫に対して子宮摘出術を施行した腹腔鏡手術11例(以下A群)及び開腹手術5例(以下B群)を対象として診療録より後方視的に検討した。検討項目は年齢、経妊経産回数、GnRHα投与後最大筋腫径、出血量、手術時間、子宮重量、術中合併症の有無、腹腔鏡手術における尿管ステント留置の有無、開腹移行の有無とした。統計解析はMann-Whitney U検定を使用し、p値0.05以下で有意差ありとした。【成績】A群とB群で上記の各検討項目の中央値(最小値-最大値)p値を下記に示した。年齢、経妊経産回数に有意差はなかった。GnRHα投与後最大筋腫径はA群98mm(73-130)vs B群136mm(90-184)p=0.02でA群が有意に小さかった。出血量はA群219mL(少量-850)vs B群572mL(389-3845)p=0.02でA群が有意に少なかった。手術時間はA群278分(100-364)vs B群220分(157-303)p=0.26で有意差はなかった。子宮重量はA群450g(247-623)vs B群1350g(462-1816)p=0.02でA群が有意に小さかった。術中合併症及び開腹移行症例はなく、A群の子宮重量が中央値で450gであったことから、子宮重量を450g前後まで縮小できれば腹腔鏡手術が可能であることが示唆された。【結論】GnRHαにより子宮重量が450g前後まで縮小できれば、尿管ステント留置、子宮動脈幹処理、子宮頸部筋腫核出手技を組み合わせることで、子宮頸部筋腫に対しても腹腔鏡下子宮全摘出術を施行できると考えられた。

P-87-3 蛍光尿管カテーテルと子宮トランスイルミネーターの両者を用いて施行した腹腔鏡下子宮全摘術3症例の検討

浜松医大附属病院

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【緒言】巨大筋腫や頸部筋腫、子宮内膜症に対する腹腔鏡下子宮全摘術では、視野不良や癒着によって尿管の走行や陰門蓋部の位置の把握が困難な場合があり、誤認から多量出血や尿路損傷を来すリスクが上昇する。このような高難度症例においても安全で確実な子宮全摘を行うため、蛍光尿管カテーテルと子宮トランスイルミネーターを使用した腹腔鏡下子宮全摘術の3症例でその有用性を検討した。【症例】症例1は巨大筋腫(検体重量2,450g)、症例2は頸部筋腫(検体重量1,470g)、症例3は高度な癒着が予想された子宮内膜症症例で、症例1, 2に対し腹腔鏡下子宮全摘術を、症例3に対しロボット支援腹腔鏡下子宮全摘術を行った。3例とも全身麻酔導入後に泌尿器科医師が蛍光尿管カテーテルを挿入した後、子宮トランスイルミネーターを陰門蓋部に挿入した。術中にICG検出モードに切り替えることで、蛍光尿管カテーテルと子宮トランスイルミネーターの両者が緑の蛍光色で視認できた。いずれの症例でも、尿管の走行と陰門蓋部を視認することで、切除部位と尿管との距離を確認することが可能となり、過不足のない子宮傍組織処理と安全な陰管切開が可能だった。それぞれの手術時間、出血量は症例1: 4時間2分, 305g, 症例2: 3時間16分, 12g, 症例3: 4時間17分, 30gで、3例ともに手術合併症はなく、術後経過は良好だった。【結語】蛍光尿管カテーテルと子宮トランスイルミネーターの両者を用いることにより、尿管の走行と陰門蓋部を確実に視認することが可能となり、高難度症例に対し腹腔鏡下子宮全摘術は安全に施行することが可能だ。また、両者を用いることは、手術教育の観点からも有用と考えられる。

P-87-4 当院の婦人科腹腔鏡手術の術中に遭遇した腸管子宮内膜症の5症例

四谷メディカルキューブ

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【はじめに】腸管子宮内膜症は稀少部位子宮内膜症の中では最も発症頻度が高く、子宮内膜症全体の12-37%を占め、もっとも高頻度に認められる部位は直腸・S状結腸で小腸（回腸）、虫垂の順に頻度は低下する。1989年の松隈らの報告した本邦78例の報告では84%が直腸・S状結腸、回腸7%、回盲部5%、虫垂3%の頻度である。腸管子宮内膜症では約70%に両側付属器やダグラス窩に子宮内膜症病巣が認められ、下血やイレウスなどの症状がなければ術前に診断できるケースは少ない。【当院の症例】当院で2015年から2021年9月までに子宮・卵巣の腹腔鏡手術において、5例の腸管内膜症を遭遇し診断した。いずれも子宮や卵巣・ダグラス窩に著明な内膜症所見を認めた。発生部位はS状結腸子宮内膜症1例、小腸内膜症3例、虫垂内膜症1例であった。術中に外科医介入により1例の回腸部分切除と1例の虫垂切除症例は病理検査で確定診断した。S状結腸子宮内膜症例は術後の大腸内視鏡検査下の病理検査で診断し、GnRHaとジェノゲストによるホルモン治療で排便痛の症状緩解となった。2例の小腸内膜症は術後LEPのホルモン治療で腹痛症状の改善により臨床的診断となった。【結論】稀少性子宮内膜症は病理診断による確定診断に至らない場合もあり、診断に苦慮するが、腸管内膜症が進行すると腸管狭窄による急激なイレウスや緊急手術等が必要となるため、早い段階での診断と治療の介入が有用である。腹腔鏡手術は腹腔内の観察に優れているため、目的病巣以外の観察も注視して検索することが望ましい。当院の腸管内膜症の腹腔鏡所見と術後診断・治療の経緯について報告する。

P-87-5 腎移植後に腹腔鏡下子宮全摘出術を行った1例

愛媛県立中央病院

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【緒言】近年、末期腎不全患者に対する腎移植件数は増加傾向にあり、2019年には年間2057件の腎移植が行われた。そのレシピエントの女性比率は約36.5%で、年齢分布では40歳代が約21.7%と最も多く、腎移植既往の婦人科疾患による手術症例は今後増えると考えられる。今回、腎移植後6年経過した後、子宮筋腫のため腹腔鏡下子宮全摘出術を行った症例を経験したので報告する。【症例】46歳、G2P2。腎硬化症による慢性腎不全のため39歳より血液透析を行い、40歳時に生体腎移植を施行された。過多月経を主訴に当科紹介受診し、長径3cmの粘膜炎筋腫を認めたため腹腔鏡下子宮全摘出術の方針となった。手術は、臍上から5mmトロッカーをダイレクト法にて穿刺し、気腹開始した。左下腹部5mmトロッカーを穿刺した後、腹腔内を観察すると移植腎は右腸骨窩に位置しており、右下腹部のトロッカー穿刺が移植腎を損傷しないように右下腹部、および下腹部正中に5mmトロッカーを穿刺した。移植腎からの尿管は視認できなかったが、腹壁に沿って走行しており手術に影響しないことを移植外科医の立ち会いにより確認した。また移植腎は内腸骨動脈に吻合されていたため右子宮動脈の結紮は行わなかった。その他は特に問題なく、定型的に手術可能であった。術後はモルヒネを含まないIV-PCAとアセトアミノフェン内服で疼痛コントロールを行い、尿量減少や感染などの合併症なく経過し、術後3日目に退院した。【結語】腎移植後患者の手術時には、移植による解剖学的差異を意識した手術手技、および腎機能障害、免疫抑制に伴う感染等に留意した周術期管理が必要となると考えられる。

P-87-6 ジェノゲスト投与によって縮小し子宮鏡下切除したポリープ状異型腺筋腫の1例

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【緒言】ポリープ状異型腺筋腫（APAM: atypical polypoid adenomyoma）は、未閉経女性の子宮体部に発生する稀な腫瘍である。ポリープ状に子宮内に突出し過多月経や不正性器出血、不妊症をもたらす。腫瘍では、平滑筋腫様の紡錘形細胞が増生した間質内に、子宮内膜様の異型腺組織が不規則に増殖している。時に子宮体癌を合併することもあり、正確な診断と治療のための摘出が必要となる。今回我々は、ジェノゲスト投与によって著明に縮小し子宮鏡下切除したAPAMの1例を経験したので報告する。【症例】症例は、26歳女性。BMI 21.5、月経は35-40日周期、性行経験なし。過多過長月経の精査で子宮内腫瘍を指摘され紹介受診した。MRIでは、体部後壁から発生する拡散能低下を示す49x44x32mmのポリープ状腫瘍を認めた。全身麻酔下に細胞診、組織診を行いAPAMの診断に至った。摘出術前に月経困難症に対しジェノゲスト療法を施行すると、腫瘍は著明に縮小し、再手術では子宮鏡下に完全切除が可能となった。最終診断は、APAMだった。【考察】APAMは若年女性に発生することが多く、再発や子宮体癌発生のリスクがある。稀な疾患であるため定まった管理方針はない。プロゲステロン療法には腫瘍縮小の可能性があり、妊孕性温存希望の症例では、腫瘍摘出術前後の管理としての使用が考慮される。今後の症例集積による検討が必要である。

P-87-7 Parasitic leiomyoma に対しレルゴリクスによる保存的加療を行った1例

大阪赤十字病院

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今回我々は医原性と考えられる腹壁に発生した parasitic leiomyoma (以下 PL) に対して経口 GnRH アゴニスト製剤であるレルゴリクスによる保存的加療を行った症例を経験したため報告する。症例は48歳2妊2産, 30歳時に他院で腹腔鏡下筋腫核出術, 32歳, 35歳時に帝王切開術の既往があった。47歳頃から過多月経と右下腹部の膨隆を自覚するようになり, 近医で子宮筋腫と腹直筋内に7cm大の腫瘤を指摘され当院消化器外科に紹介となった。MRI検査所見では腹壁腫瘍は帝王切開の瘢痕部に位置し, 子宮には筋腫と腺筋症を認め, 腹直筋腫瘍生検にて平滑筋腫と診断され PL を疑われ当科紹介となった。腹壁腫瘍摘出時には腹直筋と筋膜の欠損部が大きくなり腹壁メッシュ留置が必須と考えられた。患者に手術摘出を勧めたが強く拒否されたため保存的加療としてレルゴリクス投与を開始した。腹壁腫瘍は縮小し, 投薬6か月後も手術は希望されず, 骨塩定量を測定しながらレルゴリクスを継続した。投薬後260日目の骨塩定量の Young Adult Mean (YAM) 値では腰椎88%, 大腿骨近位部81%と正常域であった。腹壁腫瘍はさらに縮小したが投薬後518日目の骨塩定量では腰椎YAM83%, 大腿骨近位YAM73%と減少し, レルゴリクス中止をした。エルデカルシトールを開始し現在骨塩定量をフォロー中である。PLは遊離した子宮筋腫が異所性に他臓器からの栄養血管を得て生着する疾患で, 手術時の筋腫断片より発生する医原性 PL が近年報告されている。PLは手術摘出例の報告が多いが, 長期投与による骨粗鬆症リスクに十分留意した上でのレルゴリクスを用いた保存的治療は有用である可能性があると考えられた。

P-87-8 TLH を施行した感染性子宮頸部嚢胞性腺筋症の1例

岡山済生会総合病院

杉原花子, 秋定 幸, 假谷奈生子, 太田友香, 関 典子, 平野由紀夫, 春間朋子

【緒言】嚢胞性腺筋症は子宮内膜組織が限局的に出血を繰り返すことで嚢胞を形成する稀な病態である。今回我々は感染を伴った子宮頸部嚢胞性腺筋症に対して腹腔鏡下子宮全摘術 (TLH: Total laparoscopic hysterectomy) を施行した症例を経験したので報告する。【症例】54歳女性, 1妊1産。腹痛を主訴に近医を受診し, 炎症反応の上昇とCTで子宮腫瘤を認め精査のため当院受診。MRIで子宮頸部に7.5cm大の嚢胞性病変を認め, 子宮頸管と交通しており腫瘍内容液が移動している所見を認めた。入院後抗生剤を開始し炎症反応は改善した。退院時よりジェノゲストを開始したが, その後も腹痛持続し, 膿瘍形成の可能性も疑われ外科的治療の方針となり, TLHを施行した。画像所見同様, 腫瘍と膀胱は高度に癒着しており, 術中に膀胱損傷を認め泌尿器科と修復術を行った。術前診断は困難であったが, 術後病理は嚢胞性腺筋症の診断であった。【考察】子宮に発生する嚢胞性病変の頻度は全子宮腫瘤の0.35%にすぎないとされており, 中でも頸部に発生した嚢胞性腺筋症は報告が極めて少ない。薬物治療と外科的治療があるが, 薬物治療ではコントロールが困難であり, 外科的治療が選択されることが多く, 感染を伴っている場合, 外科的治療以外の選択肢が制限される。さらに, 本症例では抗生剤使用による保存的治療では疼痛改善なく, 外科的治療を選択せざるを得なかった。しかし, 予想以上に膀胱の脆弱化が著しく, 術中に多発膀胱損傷が生じた。そのため, 術中の膀胱損傷の際に, 色素注入法やステント挿入等の合併症予防を行った。【結語】今回, 感染を伴った子宮頸部嚢胞性腺筋症に対して, 根治的な治療を行い得た症例を経験した。

P-88-1 卵巣腫瘍茎捻転を契機に診断された Mayer-Rokitansky-Kuester-Hauser 症候群の1例

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症例は51歳, 未経妊, 生涯無月経であった。下腹部痛を主訴に内科を受診し, CT検査により骨盤内腫瘍と子宮欠損を疑われ, 当科を紹介受診した。外性器は正常女性型で, 膣は閉鎖しているようで, わずかな陥凹のみみられるだけであった。MRI検査では右付属器には長径8cmの多房性腫瘍を認め, 様々な輝度の内容液を含み, 壁の一部には充実性部分を認めた。左付属器は腫大を認めず, 子宮は痕跡様であった。術前診断: 右付属器腫瘍に対して開腹手術を実施したところ, 右卵巣は手拳大に腫大し, 1080度捻転していた。子宮は索状物のようにみえ, 左卵巣は萎縮していた。画像診断上, 悪性腫瘍の可能性を考えていたため, 両側付属器摘出術を実施した。組織学的に, 右卵巣腫瘍は良性的な嚢腫と診断したが, 茎捻転により上皮成分は壊死しており, 嚢腫の上皮成分に関する詳細な診断は困難であった。Mayer-Rokitansky-Kuester-Hauser 症候群は胎生期の Muller 管の形成異常により子宮の形成不全, 膣の形成不全を生じる先天性異常である。女兒の5,000例に1例の頻度でみられ, 原発性無月経の精査で発見されることが多い疾患である。今回の症例は, 生涯無月経であるも, 婦人科を受診することではなく, 51歳で卵巣腫瘍茎捻転を契機に Mayer-Rokitansky-Kuester-Hauser 症候群と診断された。Mayer-Rokitansky-Kuester-Hauser 症候群における卵巣腫瘍茎捻転の報告はまれであるが, 解剖学的には卵巣の支持組織が短いことから, 小児期同様に捻転しやすいことを示唆する報告もある。文献的考察を加え, 本症例を報告する。

P-88-2 卵巣滑脱に茎捻転を伴った鼠径ヘルニアの一例

鳥取県立中央病院

圓井孝志, 高橋弘幸, 竹中泰子, 荒田和也, 野中道子, 上垣 崇

【緒言】鼠径ヘルニアは鼠径部筋膜の脆弱性により腹膜の一部が脱出することにより発症する。ヘルニア門が拡大すると、主に小腸などの内臓臓器が脱出することが一般的である。今回、卵巣滑脱に捻転を伴い緊急手術に至った鼠径ヘルニアの一例を経験したので報告する。【症例】68歳、G3P3。幼少期より左鼠径部の膨隆を自覚していたが、自身で手動的に還納していた。3年前より還納が困難となった。突然の下腹部痛を主訴に近医を受診し、当院へ救急搬送となった。左鼠径部に手拳大の膨隆を認め、CTにて卵巣嵌頓を伴う左鼠径ヘルニアと診断した。手動的還納は困難であり、緊急手術とした。鏡視下に腹腔内を観察すると、左卵巣が捻転を伴い内鼠径輪より腹腔外に嵌頓していた。腹腔内への還納は困難であった。鏡視下に左卵巣支持靭帯を切断した。左付属器を摘出した後、ヘルニア修復術を施行した。摘出卵巣は充実性腫瘍により手拳大に腫大していた。病理組織診断は卵巣繊維腫であった。【考察】小児においては鼠径ヘルニアに卵巣滑脱を認める症例が散見されるが、成人例はまれである。本症例は拡大したヘルニア門より滑脱した卵巣が経時的に腫大したと考える。ヘルニア門に対して卵巣が著しく大きく、還納に難渋した。【結語】卵巣滑脱に捻転を伴った鼠径ヘルニアの一例を経験した。ヘルニア門が拡大した症例では卵巣が嵌頓する可能性があることに留意する。

P-88-3 卵巣茎捻転を契機に発見し治療方針に苦慮した広汎性卵巣浮腫の2例

武蔵野赤十字病院

大坪 翔, 小林織恵, 飯田理央子, 黒木李穂, 松本友里, 菊池友美, 梅澤 聡

広汎性卵巣浮腫 (Massive Ovarian Edema: 以下 MOE) は卵巣間質に液体成分が貯留し、卵巣に浮腫状腫大を来す稀な疾患であり、若年者に多い。一様な組織であることから手術療法としては捻転解除が挙げられ、一般的な卵巣嚢腫茎捻転に比し治療効果と手術の侵襲のバランスを考慮する必要がある。今回我々は治療方針に苦慮した MOE の2例を経験したため報告する。【症例1】18歳、0妊0産。2日前から持続する強い右下腹部痛、嘔吐で受診。MRIで両側卵巣の浮腫状腫大、右卵巣捻転茎を認め、両側 MOE、右卵巣茎捻転と診断。症状が強く軽減しないため腹腔鏡下手術の方針とした。術中所見では右付属器が720度捻転し暗紫色の色調変化も認めたが捻転解除を行ったところ速やかに血行不良は改善した。術後1か月で両側卵巣は縮小しており終診とした。【症例2】8歳、女児。7日前から持続する強い下腹部痛を主訴に来院。MRIで左卵巣が6cm大に腫大し、同部位の造影効果が乏しく、左 MOE、左卵巣茎捻転の疑いと診断。しかしその時点では腹痛改善傾向であり手術加療せず、症状増悪時の手術対応が可能な小児外科へ転院となった。転院後の造影 CT で卵巣への血流は保たれており、症状消失傾向であったため保存的加療のみで退院となった。MOE は若年者に好発し、茎捻転に対する治療として捻転解除が挙げられるが、卵巣嚢腫茎捻転と異なり部分的な切除ができないため解除後も腫大卵巣の再捻転の可能性が残るため、手術の侵襲に見合う治療となりえるのか考慮しなければならない。年齢や症状の経過、画像診断など個々の症例を十分に検討し治療方針を決定することが必要である。

P-88-4 両側水腎症を契機に発見された小児の良性卵巣腫瘍の一例

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症例は11歳。身長141cm、体重32.9kg。月経発来なし。既往歴は特記事項なし。当科受診1か月前から嘔気と下痢が出現したため近医小児科を受診し、整腸剤処方にて経過観察となった。症状は軽快したが受診2週間前より症状が再燃し、同院を受診した。血液検査で Cre 1.7 mg/dl、BUN 24.7 mg/dl と上昇を認め、原因精査のため施行した腹部単純 CT 検査で両側水腎症と卵巣腫瘍を認めたため当科に紹介受診となり、同日入院となった。骨盤部単純 MRI 検査では径10cm大の嚢胞性腫瘍を認めた。内部の大部分は漿液性成分を疑う所見で、一部脂肪抑制効果を伴う箇所を認めた。尿管は下部より拡張していた。良性卵巣腫瘍による尿管圧迫を疑い、入院3日目に腹腔鏡下卵巣嚢腫摘出術を施行した。腹腔内を観察すると、右付属器由来の骨盤内を占拠する卵巣腫瘍を認めた。尿管は拡張傾向であったが、腫瘍が原因かどうかは術中には断定できなかった。卵巣表面に切開を加えて内容液を吸引し、卵巣腫瘍を摘出した。内容液は淡黄色透明な漿液性で、一部毛髪と脂肪成分を認めた。術後より尿量の増加を認め、1日4Lほどの排尿を認めた。それに伴い Cre と BUN も正常域まで低下し、経腹超音波検査でも水腎症が消失した。脱水に注意し、適宜補液を追加していった。術後4日目には尿量も落ち着いたので補液を終了し、術後6日目に退院となった。経過より、水腎症の原因は卵巣腫瘍であったと判断した。術後病理組織診断は Mature Cystic Teratoma で悪性所見は認めなかった。体格の小さい小児の場合、卵巣腫瘍が増大した場合には水腎症を発症することもあり、卵巣腫瘍を認めた場合には水腎症の評価は重要である。

P-88-5 黄体嚢胞莖捻転に対して腹腔鏡手術を施行した1例

自衛隊札幌病院

海士洋平, 高崎和樹, 三宅太郎, 濱口大志

【緒言】非妊娠女性における卵巣腫瘍莖捻転において、黄体嚢胞が原因であることは稀である。黄体嚢胞莖捻転に対して、緊急手術を行った1例を経験したため報告する。【症例】症例は19歳、0妊0産。腹痛を主訴に当院を受診した。既往歴、家族歴に特記事項なし。初経は13歳で性交歴はなく、月経周期は30日～90日と不順であった。体温37.1℃、血圧112/47mmHg、HR72回/分、SpO2 98% (room air)。経腹超音波検査で右卵巣に圧痛を伴う6cm大の単房性嚢胞を認めた。骨盤MRI検査では、右卵巣にT1低信号、T2高信号を示す6cm大の嚢胞を認めた。血液検査で腫瘍マーカーは、CA125 15.8 U/ml、CA19-9 4.2 U/ml、CEA 0.6 ng/dlと正常範囲内であった。右卵巣腫瘍莖捻転と診断し、腹腔鏡手術を実施した。術中右卵巣は6cmに腫大しており、捻転・壊死の所見はなく、右卵巣嚢腫を核出した。左付属器および子宮は正常であった。組織所見では、血液を貯留した顆粒膜黄体嚢胞を認め、最大径20mmであった。壊死の所見を認めなかったが、強いうっ血を認めたことから、捻転の可能性が示唆された。腹水細胞診はClass Iであった。術後経過良好であり、術後4日目に退院となった。【考察】卵巣腫瘍莖捻転を疑い、卵巣嚢腫を核出した結果、組織所見から黄体嚢胞莖捻転と診断された症例を経験した。黄体嚢胞莖捻転は妊娠女性、女児では頻度が高いが、非妊娠女性では稀である。術前の予測は容易ではないが、若年者において鑑別が必要と考えられる。

P-88-6 多様な付属器捻転における経陰超音波断層法を用いた Whirlpool Sign の描出

医科歯科大

東出 凌, 齊藤和毅, 石川智則, 宮坂尚幸

【目的】Whirlpool Sign (WS) は超音波検査で同定される卵巣嚢腫莖捻転の軸の断面図である。診断におけるWSの陽性的率は高いものの、その描出は容易ではなく、一般的な診断法としては認知されていない。また傍卵巣嚢腫や子宮摘出後などの付属器捻転におけるWSの診断的有用性は明らかでない。本報告では我々が行っている系統的なWS描出法を紹介し、同手法で診断した様々な付属器捻転の症例を提示する。【方法】卵巣嚢腫莖捻転では、骨盤漏斗韧带と卵巣固有韧带が捻転軸を作り、その際に子宮と骨盤壁は捻転に牽引される。捻転側の卵管角と骨盤壁との間に捻転の起始部は位置し、起始部と卵巣嚢腫を結ぶ線に捻転軸は存在する。子宮の横断面から捻転の起始部に超音波プローブを移動し、捻転軸に垂直にプローブを動かすことによりWSが描出される。【成績】症例1. 56歳。持続する下腹部痛を主訴に当院を受診した。経陰超音波断層法で長径7cmの右卵巣嚢腫を認め、右卵管角と骨盤壁の間にWSを同定した。症例2. 28歳。急性発症の左下腹部痛を主訴に当院を受診した。超音波検査で正常大の両側卵巣と、ダグラス窩に長径5cmの単房性嚢腫を認め、左卵管角と嚢腫の間にWSを確認した。症例3. 80歳。陰式子宮全摘術後。間欠的腹痛を主訴に当院を受診した。超音波検査で8cmの卵巣嚢腫を認め、嚢腫と骨盤壁との間にWSを描出した。上記3症例に対して腹腔鏡下に卵巣嚢腫(症例1, 3)および傍卵巣嚢腫(症例2)の捻転を確認し、それぞれ摘出した。【結論】WSは多様な付属器捻転の診断において有用である。我々の系統的な検査手技が多くの婦人科医に活用され、付属器捻転の診断に寄与することを期待する。

P-88-7 卵巣腫瘍莖捻転に対する術前CT値と病理学的壊死・出血に関する後ろ向き研究

千船病院

胡 脩平, 安田立子, 村越 誉, 大木規義, 稲垣美恵子, 岡田十三, 吉田茂樹, 本山 覚

【目的】卵巣腫瘍莖捻転では壊死が予測される場合、卵巣摘出を選択する。術前捻転卵巣腫瘍のCT値から病理学的壊死が術前に推測可能であれば卵巣機能温存がより可能になると考えられ、その関連を検討した。【方法】2008年1月から2020年11月までの良性卵巣腫瘍莖捻転手術のうち術前に単純CTを撮像した症例は131件、症例数が少ない組織型は省き、奇形腫74件、漿液性腺腫17件、粘液性腺腫15件を対象症例とした。病理学的壊死の有無によってCT値を比較検討し、莖捻転によってCT値に影響すると考えられる病理学的出血と鬱血の有無に関しても比較検討を行った。さらに同時期の予定良性卵巣腫瘍手術で術前に単純CT撮像を行った症例を正常群として各々組織型ごとに腫瘍卵巣のCT値の比較検討を行った。また、術中肉眼的壊死所見と病理学的壊死の有無も比較検討した。【成績】どの組織型も病理学的壊死の有無ではCT値平均に有意差はなく、病理学的壊死群は正常群との比較でも有意差はなかった。病理学的出血のみ、CT値平均に奇形腫、漿液性腺腫、粘液性腺腫と正常群間に有意差があった(p=0.034)。術中肉眼的壊死所見があった症例は50件、そのうち、病理学的壊死があった症例は16件(32%)、なかった症例が34件(68%)、術中肉眼的壊死所見がなく、病理学的壊死があった症例はなかった【結論】術前CT値による病理学的壊死は予測困難と考えられた。現時点では、術中肉眼的壊死所見が病理学的壊死を推測する有効な手段ではあるが、肉眼的壊死を疑う症例のうち、病理学的壊死を認める割合は低く、妊娠性温存が必要な症例では捻転解除あるいは腫瘍核出が卵巣温存に寄与する可能性が示唆された。

P-88-8 当院における良性卵巣腫瘍の再発手術率と再発リスク因子に関する検討—卵巣嚢腫摘出後に定期検診は必要か—

福岡赤十字病院

和田智子, 藤玄一郎, 野田龍之介, 中島 京, 田中大智, 嶋田幸世, 友延 寛, 貴島雅子, 濱崎洋一郎, 松本 恵, 遠城幸子, 西田 眞

【目的】良性卵巣腫瘍に対して嚢腫摘出術を施行した場合、その後再発することがあるが、これについて詳細に検討した報告は少ない。当院における過去の良性卵巣腫瘍の再発手術症例を検索し、再発手術率と再発リスク因子について検討する。【方法】2011年4月から2019年12月までに良性卵巣嚢腫摘出術を施行した783例の中から、再発卵巣腫瘍に対して当院で再手術を行った症例を抽出して、年齢、手術方法（開腹か腹腔鏡下手術）、組織型、腫瘍径、術中被膜破綻の有無等について検討した。【成績】783例中10例（1.3%）で再発に対して手術を行い、組織型別では粘液性嚢胞腺腫（45例中4例：8.8%）、成熟奇形腫（368例中4例：1.1%）、子宮内膜症性嚢胞（298例中2例：0.7%）の順に再発手術率が高かった。粘液性嚢胞腺腫は全て同側卵巣に再発しており、再発群（4例）では無再発群（41例）に比べ、有意に若年で（mean±SD：19.3±3.6 vs. 32.0±10.2歳）、腫瘍径が大きかった（15.0±6.5 vs. 8.3±3.7cm）。手術方法、術中被膜破綻の有無と再発手術率には明らかな関連はなかった。【結論】良性卵巣腫瘍の再発手術率は1.3%であったが、他院で再発手術を行った症例や再発し経過観察中の症例も含めると、再発率はさらに高いと考えられる。粘液性嚢胞腺腫は全て同側に再発しており、再発の原因として初回手術時の腫瘍の遺残が推測される。卵巣嚢腫摘出術の際に腫瘍遺残を正確に確認する方法はなく、今回の検討で明らかとなった再発リスク因子を有する症例では、術後に定期的な検診を行った方がよいと考えた。

P-88-9 上腹部に偏位し大網奇形腫が疑われた卵巣成熟奇形腫の1例

岡山済生会総合病院

秋定 幸, 春間朋子, 杉原花子, 假谷奈生子, 平野由紀夫

卵巣成熟奇形腫は全卵巣腫瘍の15～25%を占める良性胚細胞腫瘍であり、遭遇する頻度の高い疾患である。一方性腺外奇形腫は全奇形腫の0.4%程度と稀である。発生部位は頭蓋内、縦隔、後腹膜、尾仙骨部などがあり、大網成熟奇形腫が最も多く報告されている。われわれは上腹部に偏位し、大網から血流を受ける卵巣成熟奇形腫を経験した。症例は47歳、GIP1で下腹部痛と嘔吐下痢のため前医を受診した。腹部CT検査で上腹部正中に10cm大の腫瘍を認めた。卵巣成熟奇形腫が疑われ当科に紹介された。経膈超音波検査で骨盤内に左卵巣は描出できなかった。大網奇形腫の可能性もあったが、いずれにしろ腫瘍切除は必要と考えられたため、消化器外科と合同で腹腔鏡下手術を施行した。上腹部正中に大網と癒着し血流を受ける腫瘍を認めた。骨盤内には左卵巣は認めず、左卵管が上腹部まで延長し腫瘍と接続していた。右付属器は正常であった。左の卵巣堤索や卵巣固有索は存在しなかった。左卵巣腫瘍と診断し、大網部分切除と左付属器切除を施行した。病理組織検査では腫瘍に卵巣成分を認めており、卵巣成熟奇形腫と診断した。大網成熟奇形腫の発生機序として大網原発説と卵巣原発説が存在する。本症例は大網成熟奇形腫が卵巣原発であることを示唆すると思われた。

P-89-1 脱落膜化子宮内膜間質細胞におけるLGALS9の転写制御機構の解明

関西医大

村田絃未, 服部 葵, 安原由貴, 中尾朋子, 小野淑子, 岡田英孝

【目的】子宮内膜の主要な免疫細胞である子宮NK細胞は、子宮内膜間質細胞（Endometrial Stromal Cells：ESC）が分泌するIL15ならびにLGALS9によって分化し、ヒト子宮内膜の免疫寛容を促す。本研究では、脱落膜化ESCにおけるLGALS9の発現動態および転写制御機構を明らかにしたので報告する。【方法】本研究は倫理委員会により承認され、すべて文書による同意を得た後、婦人科良性腫瘍のため子宮摘出された正常月経周期のある年齢31—50歳の女性41人から子宮内膜を採取した。ヒト子宮内膜におけるLGALS9発現と脱落膜化転写制御因子HAND2ならびにFOXO1のLGALS9転写制御への関与を検討した。【成績】子宮内膜のLGALS9は分泌期早期—中期で低下し、分泌期中期—後期に増殖期と同等にまで回復した。分離培養したESCのLGALS9はプロゲステロン（MPA）刺激1日で低下、刺激12日で増加した。LGALS9の転写制御領域活性はHAND2によって増加しFOXO1によって減少した。ESCのHAND2はMPA刺激後12日間増加し続ける一方で、FOXO1は刺激後1日に増加し以降変化なく、刺激後6日に再び増加した。FOXO1のリン酸化を検討し、MPA刺激0h、3日後には認めなかったが、刺激後12日で有意な増加を認めた。FOXO1リン酸化によって、FOXO1のDNA結合量の減少とそれに伴うLGALS9発現抑制の開放が起こる可能性が示された。【結論】脱落膜化過程のESCにおいてLGALS9発現は、HAND2およびFOXO1リン酸化によって制御されている。

P-89-2 妊娠前から妊娠初期にかけての母体末梢血 NK 細胞における網羅的遺伝子発現解析

自治医大

石田洋一, 大口昭英, 高橋宏典, 藤原寛行

【目的】脱着膜 NK 細胞が妊娠維持機構に関わっていることは知られているが、絨毛と接する母体血中に存在する末梢血 NK 細胞が妊娠維持機構に関わっているかどうかは分かっていない。母体末梢血 NK 細胞が着床や妊娠維持機構に関わっている、という仮説を立て、これまでに検討した結果では、卵胞期、黄体期、妊娠初期、妊娠後期にかけて母体末梢血 NK 細胞数の有意な変動を認めた。また妊娠初期と後期における母体末梢血 NK 細胞の遺伝子発現マイクロアレイの実験では多数の遺伝子発現に有意な変動を認めた。今回、妊娠前(卵胞期及び黄体期)と妊娠初期の母体末梢血 NK 細胞における網羅的遺伝子発現解析を行った。【方法】当院に通院している患者から同意を得て、妊娠前(卵胞期・黄体期)、妊娠初期に末梢血を採取した。その血液から磁気ビーズを用いて CD56 陽性細胞の母体末梢血 NK 細胞をネガティブ分離した。そして、卵胞期、黄体期、妊娠初期における母体末梢血 NK 細胞の遺伝子発現マイクロアレイを、卵胞期-黄体期 6 例、黄体期-妊娠初期 5 例、卵胞期-妊娠初期 6 例に施行した。比較は同一人物において比較した。【成績】卵胞期-黄体期、黄体期-妊娠初期、卵胞期-妊娠初期に有意な発現変動を認めた。とくに卵胞期-黄体期では IL-6, CDK9, 黄体期-妊娠初期では IL-10, MMP9, DUSP13, 卵胞期-妊娠初期では IL-18, MMP9, DUSP13 の遺伝子発現の顕著な変動を認めた。【結論】妊娠前から妊娠初期にかけても多数の遺伝子発現が変動していたため、母体末梢血 NK 細胞が着床や妊娠維持機構に関わっている可能性が示唆された。

P-89-3 子宮移植手術の安全性向上のためのカニクイザルを用いた基礎動物研究

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【目的】2014 年にスウェーデンで世界初の子宮移植後の妊娠出産が報告され、その後各国で子宮移植による出産の臨床報告が相次いでいる。我々は 2017 年 5 月より子宮移植プロジェクトチームを立ち上げ、献体遺体やブタを用いた子宮移植研究を実施してきた。今回、手術の安全性と低侵襲性の向上を目指し、カニクイザルを用いて自家子宮移植手術研究を実施したので報告する。【方法】年齢 9 歳 6 か月、体重 5.0kg のカニクイザル 1 頭を用い、全身麻酔下に開腹し子宮を摘出し、再び同一個体へ子宮を移植し、血流の再開を確認した。本研究は研究施設より動物実験計画の承認を得て、所定の動物実験の適正実施講習を受講し、動物実験の倫理規定を順守して行われた。【成績】カニクイザルの内腸骨動脈(両側内径 2.0mm)と卵巣静脈(内径右 2.5mm, 左 2mm)を吻合血管として選択した。血管走行を確認できるまで婦人科医が露出操作を行い、腔管切除後に移植外科医が血管を剝離切断し子宮摘出した。移植外科医による臓器灌流後、形成外科医が右内腸骨動脈を右外腸骨動脈へ、右卵巣静脈を右総腸骨静脈へと吻合を行い、右側からの血流の再開を血管拍動の再開と子宮色調にて確認した。手術時間 6 時間 0 分、総阻血時間は 1 時間 47 分であった。【結論】サルを用いた子宮移植研究においては血管縫合にヒトにおいて要求される以上の細密な手術手技が必要であり、ヒトにおける臨床手技との乖離があることに研究の限界がある。今回の手術や阻血時間は過去の動物実験報告と比較しても遜色のない結果であった。献体や動物を用いた手術研究の積み重ねと適切な執刀医交代時期を含めたチーム医療の習熟が、子宮移植手術成功の鍵であると思われた。

P-89-4 miR-424&503 は FOXO1-SCARA5 を介して子宮内膜の脱着膜化を制御する

埼玉医大病院

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【目的】昨年、本学会において、miR-424 と miR-503 は FOXO1 の発現を制御することにより、脱着膜化過程を制御することを報告した。本研究においては miR-424 と miR-503 が関連するさらなる脱着膜化制御機構を明らかにすることを目的とした。【方法】良性疾患により子宮摘出を行った患者から同意を得て、常法にて子宮内膜間質細胞を分離・培養した。脱着膜化刺激は 8-bro-cAMP と MPA で行った。脱着膜化刺激を施行した群(脱着膜化群)と施行しない群(control 群)から miRNA を含む total RNA を抽出し定量的 PCR 法を行った。また、Scara5 の発現量に伴う遊走能の変化を評価するため、sRNAi 法にて SCARA5 をノックダウンし脱着膜化刺激を施行した群(si 群)と非ノックダウン群(control 群)を蛍光免疫染色及び imageJ を用いて評価を行った。【成績】脱着膜化群では control 群と比較して FOXO1 とその標的遺伝子である SCARA5 の発現は共に有意に上昇していた。またヒト子宮間質細胞に miR-424 と miR-503 を同時に強制発現させると、FOXO1 とともに SCARA5 の発現は有意に抑制された。脱着膜化細胞において FOXO1 の発現を sRNAi 法にてノックダウンすると SCARA5 の発現も抑制されたが、SCARA5 の発現を sRNAi 法にてノックダウンしても FOXO1 の発現量は変化しなかった。脱着膜化における形態変化は SCARA5 の発現をノックダウンすることにより抑制され、遊走能は亢進した。【結論】miR-424 と miR-503 は FOXO1-SCARA5 の発現を制御することにより、脱着膜化過程において重要な役割を担っている事が示唆された。

P-89-5 SR-16234のNF κ B経路を介した子宮内膜症間質細胞の増殖および炎症抑制効果

鳥取大

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【目的】SR-16234 (SR) はエストロゲン受容体 (ER) α に対しては antagonist として働き, ER β に対しては partial agonist として働く選択的 ER 調節薬 (Selective Estrogen Receptor Modulator: SERM) である。これまでに, 子宮内膜症に伴う月経困難症を有する女性において, 骨盤痛の改善効果, 卵巣チョコレート嚢胞の縮小効果があることを報告した。本研究では培養子宮内膜症間質細胞への SR 添加が細胞増殖や炎症関連因子発現に及ぼす効果ならびに, その分子メカニズムを明らかにすることを目的とした。【方法】手術で摘出した卵巣チョコレート嚢胞壁より, 間質細胞を分離培養した。SR (10^6 - 10^8 M) と炎症を惹起する目的で TNF α (1ng/ml) を併用添加したのちに, WST-8 アッセイを用いて細胞増殖能を評価した。ELISA で培養上清中の IL-6 と IL-8 タンパク量, RT-PCR により COX-2 と TRPV1 mRNA 発現について評価した。また, I κ B α , ERK 1/2 および AKT リン酸化タンパクの発現についてウエスタンブロットで評価した。【成績】すべての濃度において SR 添加による約 10% の細胞増殖抑制効果がみられた。IL-6 と IL-8 タンパク量はそれぞれ 20% 減少し, COX-2 mRNA と TRPV1 mRNA の発現低下もみられた。また, SR 添加によりリン酸化 I κ B α タンパクの発現が増加したが, 他のシグナル分子のリン酸化タンパクの発現には変化はみられなかった。【結論】SR は NF κ B 経路を介して, 子宮内膜間質細胞に対する増殖や炎症を抑制することが示唆された。

P-89-6 当院における POI 症例の現状と課題

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【目的】早発卵巣不全 (Premature ovarian insufficiency 以下 POI) の臨床的問題点として不妊症や骨密度低下が挙げられる。当院における POI 患者の ART 成績および骨密度結果について検討する。【方法】2014 年 4 月から 2021 年 5 月に POI と診断された 34 例を対象とした。①挙児希望があり低卵巣刺激や調節卵巣刺激で採卵を試みた 15 例において, 採卵可能例 (n=5) と採卵不可例 (n=10) の患者背景, 採卵可能であった 5 例 (14 周期) の ART 成績の検討, ②HRT 前に DEXA 法にて骨密度測定を行った 12 人の骨密度評価, および骨密度低下群 (大腿骨/腰椎 YAM 値 <80%) と非低下群 ($\geq 80\%$) におけるリスク因子の検討を行った。【成績】①採卵可能例は採卵不可例と比較し, FSH 値が 55.2 IU/L vs. 82.4 IU/L と有意に低く, 月経異常から診断までの期間が 6.8 か月 vs. 25.8 か月と有意に短かった。採卵可能であった 5 例 ART14 周期のうち, 卵子獲得率は 50% (7/14 周期), 凍結卵子・胚獲得率は 28.6% (4/14 周期) であったが, 挙児希望のある症例あたり妊娠率は 6.6% (1/15) と低値であった。卵子獲得周期 (n=7) と非獲得周期 (n=7) では採卵前の E2 値が卵子獲得周期で有意に高かった (p=0.03)。②HRT 前に骨密度測定を施行したのは 35% (12/34 例) と少なかった。月経異常から診断までの期間の平均は 30.5 か月 vs. 9.1 か月 (p=0.03) と骨密度低下群で有意に長く, 平均 FSH 値は 105.6 IU/L vs. 81.2 IU/L (p=0.09) と骨密度低下群で高い傾向があった。【結論】POI 患者では採卵を試みても採卵に至る症例は少なく, ART を用いても妊娠率は低かった。また, POI 診断の遅れは, 更なる骨密度低下を引き起こす可能性があり, 積極的な骨密度測定と早期の HRT 導入が望まれる。

P-89-7 IL17B/IL17RB pathway による子宮内膜老化メカニズムの解明

九州大

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【目的】生殖補助医療では, 子宮内膜の老化が着床不全の原因として疑われる症例を認める。先行研究で我々は子宮内膜老化マーカー遺伝子として IL17RB を同定した。IL17RB は上皮細胞や免疫細胞に発現する受容体で, 様々なシグナル経路を介してサイトカイン分泌や炎症に関与する。今回, 我々は IL17RB 発現により子宮内膜に生じる変化および老化との関連を明らかにすることを目的とした。【方法】(1) ヒト子宮内膜不死化細胞株 (hEM) の IL17RB 強制発現株を作成し, リガンドを添加した際の phenotype を解析した。(2) ヒト子宮内膜オルガノイドを作成し, IL17RB 発現の有無による違いを観察した。(3) IL17RB シグナル経路の下流で発現するサイトカインが子宮内膜に及ぼす影響についてヒト子宮内膜オルガノイドを用いて解析した。(4) 血液から分離した単球由来のマクロファージを LPS で刺激し, マクロファージが分泌するサイトカインについて分析した。【成績】(1) IL17RB 強制発現株では SAPK/JNK や NF- κ B のシグナル経路を介して IL-6, IL-8, IL1 β の mRNA 発現が上昇していた。(2) IL17RB 発現細胞は非発現細胞と比し細胞増殖能が低下していた。(3) IL1 β 存在下では子宮内膜オルガノイドの増殖能は低下し, p21 および senescence-associated β -galactosidase (SA- β -gal) の発現が上昇した。(4) マクロファージへの LPS 刺激で IL17RB のリガンドである IL17B の mRNA 発現が上昇していた。【結論】子宮内膜は IL17B/IL17RB pathway を介したシグナルにより炎症を惹起し, 下流に発現する IL1 β により自己の老化を誘導する可能性が示唆された。

P-89-8 早発卵巣不全患者における染色体異常に関する後方視的検討

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【目的】早発卵巣不全 (primary ovarian insufficiency : POI) 患者のうち染色体異常が関連する症例は 10-13% とされており、今回我々は、染色体異常を呈した POI 症例に対して、染色体異常の頻度や内訳及び臨床所見を検討した。【方法】1994 年 1 月～2021 年 7 月に当院の生殖内分泌外来を受診し、染色体検査 (G-一分染法) を実施した POI 症例 1804 例の中から染色体異常を認めた症例を診療録から後方視的に抽出し、染色体検査 (G-分染法) 結果、診療記録に記載の確認できた症例における無月経の診断 (原発性無月経あるいは続発性無月経)、身長、体重について検討した。【成績】1804 例のうち、7 例は骨髄移植後であり除外した。POI 患者のうち、染色体異常は 166 例であり、全体の 9.2% を呈していた。この 167 例の染色体異常の詳細は、数的異常 80 例 (48%)、構造異常 53 例 (32%)、数的異常と構造異常を併せ持つものが 23 例 (14%)、常染色体異常 6 例 (4%)、46, XY が 4 例 (2%) であった。数的異常は Turner 症候群、Triple X 症候群に関連するものが 80 例 (48%) を占めた。診療録に記載があった症例における臨床所見の検討では、平均身長は 154.5cm、平均体重は 52.08kg であった。原発性無月経が 9% (15/158 例)、続発性無月経が 91% (145/158 例) であった。【結論】POI では染色体異常例が 1 割程度認められるが、今回の検討では 9.2% であった。数的異常を認める 48% (80 例/166 例) のうち、全例が Turner 症候群もしくは Triple X 症候群に関連していた。構造異常では、POI 関連遺伝子の存在する領域として POI1 (Xq26-28)、POI2 (Xq13.3-q21.1) が報告されている。本検討においては X 染色体 q22 及び q26 に POI 関連遺伝子が存在する可能性が示唆された。

P-89-9 早発卵巣不全関連遺伝子発現下での、顆粒膜細胞における網羅的遺伝子発現解析

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【目的】早発卵巣不全 (POI ; Primary Ovarian Insufficiency) と自己免疫疾患の関連は以前から指摘されている。当教室では、甲状腺自己抗体陽性の POI 患者血清中の抗卵巣抗体の抗原分子として POTEF タンパクを同定、同タンパクの卵巣における機能解析を行った。顆粒膜細胞における POTEF 発現が細胞増殖能を変化させ卵胞発育を制御していることを見出し報告した (Cell Death Discovery 2021 7 : 186)。本研究では顆粒膜細胞において POTEF 発現に伴い発現変動を呈する遺伝子を探索するため、RNA-Sequence (RNA-Seq) による網羅的な解析を行った。【方法】ヒト非黄体化顆粒膜細胞株 (HGRC1) を用い、薬剤誘導により POTEF を強制発現した細胞株を 2 株作成、発現誘導後 48 時間で 2 株から回収した RNA と、POTEF を発現誘導していない同細胞株 2 株から回収した RNA の RNA-Seq 解析を行い、各々の株につき POTEF 発現により発現変動した遺伝子の検出を行った。【成績】|Fold Change|>2、P 値<0.05 の条件で解析を行った結果、POTEF 発現により 2 株に共通して 28 遺伝子の発現量が増加、51 遺伝子の発現量が低下した。KEGGnetwork 解析 (Q 値≤0.05) より、発現量が増加した 5 遺伝子、低下した 5 遺伝子は Autophagy に関連、発現量が増加した 5 遺伝子、低下した 4 遺伝子は mitophagy に関連していた。また、今回の 2 株に共通して発現量が低下した遺伝子には、すでに POI 関連候補として報告のある AMHR2 を認めた。【結論】RNA-seq 解析では、当教室の先行研究でも POTEF 発現と関連が見出されている autophagy と関連する遺伝子や、卵胞発育において重要な役割を担う AMHR2 の発現変動を認めた。今後は、これらの遺伝子と POTEF 発現との関連について追加検討を行いたい。

P-90-1 自然周期凍結胚盤胞移植後の妊娠初期胎状卵胞数の検討

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【目的】妊娠初期の胎状卵胞数 (AFC) を計測し、卵巣年齢のマーカーとして使用することにより、胎児染色体異常性の背景リスクを評価する試みの報告があるが、妊娠初期の AFC の動態は明らかでない。今回我々は、自然周期凍結胚盤胞移植 (N-FET) 後における妊娠初期 (5 週 1 日、6 週 4 日、8 週 0 日) の AFC の推移を検討した。【方法】2020 年 7 月から 2021 年 6 月まで当院で N-FET 後に妊娠 10 週まで妊娠継続し、妊娠 5 週 1 日、6 週 4 日、8 週 0 日に経陰超音波にて平均直径 2~10mm の AFC を計測した 214 例を対象とし、平均 AFC を反復測定分散分析にて検討した。【成績】平均年齢 37.4±3.23 歳、採卵周期平均 AMH3.17±2.62ng/ml、平均 AFC 妊娠 5 週 1 日 8.32±7.05 個、6 週 4 日 9.13±8.54 個、8 週 0 日 9.96±9.31 個であった。妊娠 5 週から 8 週で平均 AFC は増加した (p<0.0007)。【結論】今回の結果は、妊娠 10 週まで妊娠継続した場合、妊娠 5 週から 8 週で AFC が増加すること示唆され、妊娠初期の卵巣年齢マーカーとしての AFC 測定は妊娠週数も考慮する必要があると考えられた。N-FET 後の妊娠初期 AFC の推移は、ホルモン補充周期凍結胚移植と比較して、自然妊娠と同様の動態が予想される。妊娠初期の高 E₂、高 P_r 環境による低 FSH 下でも胎状卵胞は新たに成長する可能性がある。また妊娠初期の高 βHCG 環境により胎状卵胞の退縮が抑制される可能性もある。

P-90-2 インドシアニングリーンを用いた捻転卵巣の予後予測

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【目的】インドシアニンググリーン・アンギオグラフィー (ICGA) を用いた捻転卵巣血流の定量的評価が、捻転解除後の機能温存の指標になるかを調査する。【方法】18匹のWistar種ラットを用い、片側の卵巣を阻血した。24時間後に、阻血解除する前後でICGAをし、そのグラフから以下の8つのパラメータを抽出した。F_{max} (阻血解除前の最大輝度)、T_{max} (輝度上昇時からF_{max}に達するまでの時間)、T_{1/2max} (輝度上昇時からF_{max}の半分に達するまでの時間)、slope (F_{max}/T_{max})、time ratio (T_{1/2max}/T_{max})、F_{max}' (阻血解除後の最大輝度)、reperfusion rate (F_{max}'/F_{max})、reperfusion gap (F_{max}'-F_{max})。4週間後に卵巣を摘出し、primordial follicleとprimary follicleを計測し、functional群/non-functional群に分けた。【成績】13匹のラットがfunctional群、5匹がnon-functional群となった。各パラメータのAUCは以下の通り。F_{max}: 0.908, T_{max}: 0.569, T_{1/2max}: 0.546, time ratio: 0.746, slope: 0.877, F_{max}': 0.723, reperfusion rate: 0.938, reperfusion gap: 0.862。【結論】ICGAは捻転卵巣の血流を定量的に評価することができた。捻転解除直前の血流、さらに再灌流の大きさが、重要な予測因子であった。

P-90-3 妊娠中の食餌介入が次世代の脂質代謝に与える影響：高脂肪食誘発性肥満モデルを用いた研究

愛媛大附属病院

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【目的】子宮内低栄養環境のみならず、過栄養環境も次世代の健康に悪影響を及ぼすことが知られているが、妊娠中の食事介入が次世代に及ぼす影響は不明瞭な点が多い。そこで我々は高脂肪食誘発性肥満モデルマウスを用いて妊娠中の食餌介入効果に関する検討を行った。【方法】5週齢から6週間高脂肪食 (45% 脂肪: HFD) を摂餌させ高脂肪食誘発性肥満モデルマウスを作成し、妊娠10日目より食餌介入 (14% 脂肪: Diet) を行った後、新生仔、3週齢での解析を行った。更に授乳期の食餌内容 (コントロール食, HFD食あるいはDiet食) により群別し、12週齢まで仔の追跡を行った。【成績】新生仔、3週齢においてDNAマイクロアレイ解析を施行し変動遺伝子を抽出 (対照群 vs 高脂肪食群 vs 食餌介入群)、新生仔、3週齢で共通して変動がみられた11遺伝子を特定した。12週齢における仔の解析では、妊娠中Diet食、出生後HFD群が、妊娠中から出生後にかけてHFD食を継続した群と比較し、体重増加量は有意に減少し、血中総コレステロール・血中トリグリセリド値の有意な低下を認めた。睥島の免疫染色では、妊娠中Diet群の仔において有意にβ細胞面積の減少を認めた。ただし、コントロール群に比し、β細胞面積の増加を認めた。更に、妊娠中のDiet群は、妊娠中HFD群と比較して、糖負荷試験、インスリン負荷試験においても、有意な血糖値の低下を認めた。授乳期の食餌内容に関わらず、妊娠期母体のHFD群はDiet群と比較して血中トリグリセリド値の上昇、睥β細胞の肥大化を認めていた。【結論】今回の研究から、妊娠中の母体への食事介入は胎内環境の改善を介し、仔の成人期における糖・脂質代謝に好影響を及ぼす可能性が示唆された。

P-90-4 フィブリンを介した初期ヒト栄養膜の成長制限は、線溶活性化により成長促進に切り替えられる

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【目的】ヒト胎盤の正常所見であるフィブリノイド層は、妊娠維持に必須の物質だが、初期の胚着床に対するフィブリンの効果は殆ど知られていない。本研究ではフィブリンがヒトとマウスの着床期胚に与える影響を、栄養膜の成長に着目して調査した。【方法】研究同意が得られたヒト凍結胚と、ICR系マウス凍結胚を使用した。解凍した胚盤胞をフィブリン上で培養し、栄養膜の成長とフィブリン分解を評価した。サイモグラフィで培養上清中の線溶因子を、リアルタイムqPCRで線溶遺伝子の発現を調べた。線溶因子のウロキナーゼ型プラスミノゲンアクチベーター (uPA) に着目し、uPA阻害剤、uPA添加剤、uPAインヒビター (PAI-1) 阻害剤、およびフィブリン分解産物 (FDP) を用いて栄養膜成長との関連を調べた。本研究は学内および院内倫理委員会、日本産科婦人科学会の承認後に実施された。【成績】マウス栄養膜の成長はフィブリンの影響を受けず、急速にフィブリンを分解した。一方、ヒトはフィブリンにより栄養膜成長が顕著に抑制され、緩慢なフィブリン分解と共に栄養膜が成長した。培養上清に認められたuPA活性はヒトはマウスより弱く、そしてuPAの阻害により栄養膜の成長は抑制された。uPAのインヒビター *Serp1b2* (PAI-2) のmRNAは、ヒトでは発現し、マウスでは検出されなかった。さらに、ヒトではフィブリン存在下のuPA活性の上昇及びFDPが栄養膜の成長を促進した。【結論】ヒトではフィブリンは栄養膜の成長を抑制したが、uPA活性上昇による線溶亢進が栄養膜の成長を促進させた。フィブリンとの接触はヒト栄養膜の表現型変換を誘導すると考えられ、マウスでは示されないこの性質はヒトに制限されると示唆された。

P-90-5 2波長性電解質インジケータを用いた胚盤胞期マウス胚におけるNa⁺濃度の経時的変化の解析

秋田大

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【目的】胚発育における電解質の役割は、いままでそれらの構造および機能に対する阻害剤等を使用した間接知見より類推されていた。近年、当施設では胚発育の観察に電解質インジケータを使用し、Na⁺濃度とK⁺濃度を直接可視化することに成功した(PLoS ONE, 2021)。しかし、前研究で用いた1波長性の電解質インジケータでの解析では、その細胞内分布を明らかにできず客観性に関して改善の余地が考えられた。今回、試料の濃度や退色による輝度変化成分の影響を受けない2波長性電解質インジケータを用いて、マウス胚におけるNa⁺濃度の挙動を観察した。【方法】胚盤胞期のマウス胚に10 μ MのSBFI-AMを添加した後、Fura2 レシオイメージング装置で観察を行った。340nmおよび380nmの励起光を照射したときのSBFIの蛍光強度比(340nm/380nm)を5分毎に8時間測定した。また、Na⁺-K⁺ ATPase 阻害薬であるouabain 1mMを付加した条件でも観察を行った。【成績】統計解析を行った15個のマウス胚盤胞のNa⁺濃度と胚盤胞面積において、8個の胚が有意な正の相関、7個の胚が有意な負の相関を示した。相関の正負については、胚盤胞に対する胞胚腔の割合すなわち胚盤胞の発育段階に依存する可能性が示唆された。ouabainを付加した5個では4個の胚で有意に正の相関を示し、1個は有意な相関を認めなかった。【結論】今回、我々は胚発育の観察に初めて2波長性電解質インジケータを用いて、その経時的変化を可視化することに成功し、胚盤胞におけるNa⁺濃度と胚盤胞面積について正あるいは負の相関があることを明らかにした。このことからNa⁺イオンは胚の発育動態に密接かつ複雑に関与していることが示唆される。

P-90-6 未受精卵子凍結におけるミトコンドリア動態の検討

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【目的】未受精卵子凍結保存の技術および治療成績の向上を目指し、MII 卵子の凍結融解過程に起こる障害を検討した。【方法】6-12 週齢 ICR マウスより獲得した MII 卵子を新鮮卵子群、凍結融解卵子群の2群に分け、走査型電子顕微鏡を用いてミトコンドリアを観察した。また、それぞれのミトコンドリアの分布および膜電位の評価として MitoTracker[®] Green (MTG), TMRE における蛍光試薬による染色施行後、共焦点レーザー顕微鏡にてミトコンドリアのクラスター分布、膜電位およびその面積を解析した。またデジタル PCR にてミトコンドリア DNA コピー数の評価を行った。【成績】走査型電子顕微鏡による評価では、凍結融解卵子群においてミトコンドリアの密度の低下と膨化を確認した。ミトコンドリアのクラスター分布およびその面積の解析では、クラスター数は新鮮卵子群が有意に多く、クラスターあたりの面積は凍結融解卵子群が有意に増大した。また、ミトコンドリア DNA コピー数の評価では、両群間に有意な差は認めなかった。【結論】凍結融解過程によりミトコンドリアに障害が引き起こされるが、アポトーシスに至るほどの大きなダメージは受けにくいことが考えられた。ミトコンドリアの変化が、何らかの障害を引き起こし未受精卵子凍結における妊娠率の低下の原因となる可能性が示唆された。

P-90-7 ホルモン補充周期凍結融解胚移植は遅発型妊娠高血圧症候群の危険因子

三重大附属病院

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【目的】日本において生殖補助医療(ART)での妊娠は増加しており、ARTと周産期予後の関係について様々な報告がなされている。その一つとして、ホルモン補充周期凍結融解胚移植では排卵周期凍結融解胚移植と比較して有意に周産期合併症が増加することが指摘されている。本研究ではホルモン補充周期凍結融解胚移植と周産期予後、特に妊娠高血圧症候群(HDP)に着目し、その関係について明らかにすることを目的とした。【方法】体外受精により妊娠成立し、2018年から2020年に当院で分娩した症例の内、診療録に移植時の情報(新鮮胚移植・排卵周期凍結融解胚移植・ホルモン補充周期凍結融解胚移植)が記載されていた症例を抽出した。それらの症例の母体情報・周産期合併症を後方視的に収集した。新鮮胚移植症例と排卵周期凍結融解胚移植症例を自然周期群(n=58)とし、ホルモン補充周期群(n=145)と周産期予後に関して比較検討した。【成績】ホルモン補充周期群vs自然周期群で、年齢、経産、人工妊娠中絶歴、帝王切開歴はいずれも有意差を認めなかった。産科合併症として臨床的癒着胎盤が21例(14%)vs2例(3%)(p=0.025)、慢性高血圧症を除くHDPが19例(13%)vs2例(3%)(p=0.041)と有意差を認めた。HDPの発症時期に関して、遅発型がホルモン補充周期群と自然周期群それぞれで18/19例(95%)、1/2例(50%)と大半を占めていた。【結論】ホルモン補充周期凍結融解胚移植では、黄体ホルモンやリラキシンなどの濃度が影響し、着床から胎盤形成不全が起き早発型HDPが増加するのではないかと考えられていた。本研究で早発型ではなく遅発型HDPが増加することが明らかとなり、今後その成因について再構築しなければならない。

P-90-8 低用量エストロゲン・プロゲステン配合薬の静脈血栓症リスクに関する検討—多変量解析による検討—

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【目的】子宮内膜症治療に使用する低用量エストロゲン・プロゲステン配合薬 (LEP) には、投与3か月以内に、静脈血栓症 (VTE) リスクをわずかながら増加させる有害作用が知られている。OC・LEP ガイドライン 2020 年度版にも、リスクファクターとして 50 歳以上・肥満・高血圧のリスクファクターが記載されている。今回、LEP 投与時の VTE のマーカーである D タイマー上昇が、どのようなパラメーターによって影響を受けているかを後方視的に検討した。【方法】同意を得た内膜症女性 37 人 (22~48 歳) を対象とした。LEP を 3 か月間投与し、D タイマーの上昇をアウトカムとして、年齢、BMI、収縮期・拡張期血圧、血管炎症の指標である高感度 CRP 前値を説明変数とし、ロジステック回帰分析を用いて検討した。本研究は倫理委員会の承認を受けている。【成績】D タイマーは投与前: 0.48 ± 0.20 から投与後: 0.66 ± 0.33 ($\mu\text{g/ml}$) と有意に上昇した。治療による D タイマー上昇と有意に関係したのは BMI ($\chi^2=7.425$, $P<0.006$) と、収縮期血圧 ($\chi^2=4.044$, $P<0.04$)、高感度 CRP 前値 ($\chi^2=14.233$, $P<0.002$) であった。年齢、拡張期血圧には有意な関連はなかった。【結論】内膜症女性への LEP 投与の VTE リスクは、BMI、血圧、血管炎症に影響される可能性が判明した。

P-90-9 世代別 OC・LEP がプロテイン S 活性に与える影響

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【目的】OC・LEP は女性の QOL 向上に限らず、女性アスリートのパフォーマンス向上にも有用であるが、現在 OC・LEP 服用時に血栓症を予測できる有用なコンパニオン診断はない。プロテイン S (PS) は OC 内服中に低下し、活性化プロテイン C 抵抗性をきたす。海外では OC・LEP の含有する黄体ホルモンにより PS 低下の程度が異なるとの報告がある。世代別 OC・LEP が PS に与える影響を調べる。【方法】13 歳以上の女性で OC・LEP 治療予定患者及び治療中の患者の血液検体を用いて PS 活性を測定した。【成績】ノルエチステロン (NET)/エチニルエストラジオール (EE) 7 例, レボノルゲストレル (LNG)/EE 10 例, デゾゲストレル (DSG)/EE 6 例, ドロスビレノン (DRSP)/EE 11 例であった。治療中の PS 活性平均値は NET/EE 群 $81.7 \pm 10.6\%$, LNG/EE 群 $90.7 \pm 16.7\%$, DSG/EE 群 $77.8 \pm 18.0\%$, DRSP/EE $63.3 \pm 15.8\%$ で、DRSP/EE 群の PS 活性は NET/EE 群及び LNG/EE 群の PS 活性と比較して有意に低値であった。治療前と治療中を観察できたのは LNG/EE 7 例及び DRSP/EE 5 例であった。PS 活性平均値は LNG/EE 群で治療前 99%, 治療中 90%, DRSP/EE 群で治療前 88.2%, 治療中 65% であり、DRSP/EE 群は治療により PS 活性が有意に低下した。【結論】PS 活性は OC・LEP 服用で低下するが、DRSP/EE 服用で著明に低下し、他世代 OC・LEP 治療中の値より低値であった。LNG/EE は PS に与える影響が最少なかった。含有黄体ホルモンの違いが血栓症の起こしやすさに影響する可能性があり、さらなる検討が必要である。

P-91-1 子宮内膜症性嚢胞が顆粒膜細胞に及ぼす影響

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【目的】卵巣子宮内膜症性嚢胞 (OE) は卵巣機能障害の一因とされているが、その機序は明らかにされていない。当研究室で確立した OE モデルマウスとヒト非黄体化顆粒膜細胞株 (HGrC1) を使用し、OE が顆粒膜細胞および卵胞発育に与える影響を検討した。【方法】OE モデルマウスにおいて OE 群, control 群 (C) および sham 群 (S) で、原始・一次・二次・前胞状・胞状卵胞でのオートファジー関連蛋白 (LC3, Atg7, VEGF) の発現を免疫染色で評価した。また $1.0\text{-}20\mu\text{M}$ の H_2O_2 で HGrC1 を刺激し western blot 法にて LC3 抗体を用いてオートファジーの誘導を確認し CYP19A1 発現を RT-PCR 法にて評価した。【成績】合計 268 個の卵胞を評価した。OE 群において、LC3 は全卵胞発育段階で C および S 群に対して有意に発現が亢進していた ($p=0.0004$, $p=0.0208$, $p=0.0012$, $p=0.0405$, $p=0.0093$)。OE 群で Atg7 は胞状卵胞で有意に亢進 ($p=0.0407$)、VEGF は前胞状・胞状卵胞で有意に亢進していた ($p=0.0492$, $p=0.0077$)。HGrC1 は $10\mu\text{M}$ H_2O_2 にてオートファジーが誘導され、RT-PCR にて CYP19A1 の発現は有意に低下していた ($1.0\mu\text{M}$: $p=0.0412$, $10\mu\text{M}$: $p=1.24 \times 10^7$, $20\mu\text{M}$: $p=1.75 \times 10^9$)。【結論】OE モデルマウスでは、卵胞顆粒膜細胞でオートファジーが起きている可能性が示唆された。過剰なオートファジーは顆粒膜細胞の機能低下を来し、OE における卵巣機能障害に関与している可能性が示唆された。

P-91-2 HPG axis 中枢における AMH の作用について

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【目的】抗ミュラー管ホルモン (AMH) が視床下部・下垂体性腺軸 (HPG axis) 中枢においてどのような作用を持つのか検討することを目的とした。【方法】キスペプチン及び GnRH 発現細胞であるラット視床下部前腹側室周囲核 (AVPV) 領域由来の mHypoA-50 細胞と視床下部弓状核 (ARC) 由来の KNDy ニューロンである mHypoA-55 細胞, また下垂体ゴナドトロピン産生 LbT2 細胞における AMH 受容体の有無と AMH の作用について検討した。【成績】視床下部 mHypoA-50 細胞 (AVPV), mHypoA-55 細胞 (ARC) 及びゴナドトロピン産生 LbT2 細胞には AMH 及び AMH2 受容体が発現していた。視床下部 mHypoA-50 細胞及び mHypoA-55 細胞において AMH はキスペプチン遺伝子である Kiss-1 発現を変化させなかったが, GnRH 発現が有意に増加した。mHypoA-55 細胞においてキスペプチン (KP10) 刺激は Kiss-1 発現を有意に増加させるが, AMH 存在下では KP10 による Kiss-1 の上昇は抑制された。mHypoA-55 細胞におけるキスペプチン受容体, Neurokinin B, Dynorphin A 発現は AMH 刺激で変化しなかった。ゴナドトロピン LbT2 細胞において, AMH はゴナドトロピン FSHb サブユニットのみを増加させた。KP10 は LbT2 細胞において全てのゴナドトロピンサブユニット発現を増加させるが, AMH の存在下で KP10 によるゴナドトロピンサブユニット発現はすべて抑制された。AMH は GnRH によるゴナドトロピンサブユニット発現に対しては影響を与えなかった。【結論】AMH は HPG axis の中枢である視床下部においてキスペプチン及び GnRH の発現に影響を与える他, 下垂体ゴナドトロピン産生に対しても直接作用を持つことが示された。

P-91-3 エストロゲンによるラットの摂食・体重の変化と視床下部オキシトシンの動態について

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【目的】エストロゲンは子宮に作用するだけでなく, 中枢神経や脂肪細胞を含む全身に作用する。オキシトシン (OXT) は視床下部の視索上核 (SON) と空傍核 (PVN) で産生され, 下垂体後葉 (PP) から血中に分泌される。OXT の作用には, 分娩に関わる末梢作用と, 直接脳内に作用する中枢神経作用があるが, エストロゲンの OXT への影響は不明である。OXT 産生を定量評価することが可能な OXT-monomeric red fluorescent protein 1 (mRFPI) トランスジェニック (TG) ラットを用いて, エストロゲンと視床下部 OXT との関連を調べた。【方法】成熟雌性の OXT-mRFPI TG ラットを用い, 動物実験倫理委員会の承認を得た。雄群と雌群 (発情前期, 発情期, 発情後期, 休止期, 両側卵巣摘出術 (OVX)) 群, エストロゲン補充群 (低用量エストロジオール (E2) 35pg/日, 高用量 E2 514pg/H) 群に分けた。各群の摂食量, Micro-CT 装置で脂肪量を測定した。蛍光顕微鏡を用いて視床下部 (SON・PVN) と PP の OXT-mRFPI 蛍光輝度を測定し, *in situ* hybridization 法を用いて SON と PVN の OXT-mRNA を測定した。【成績】OVX 群では, 摂食量と皮下・内臓脂肪は増加したが, エストロゲン補充では, 摂食量と皮下脂肪が低下した。OXT-mRFPI TG ラットの SON, PVN および PP の mRFPI 蛍光輝度は, 雌の発情期で高く, OVX 群では低下, エストロゲン補充では蛍光輝度が高くなった。*in situ* hybridization 法では, エストロゲン補充で OXT-mRNA は増加した。【結論】エストロゲンにより, 摂食や脂肪量は変化し, SON・PVN の OXT 蛍光輝度と mRNA も変化した。エストロゲン投与は OXT 産生を増加させることが示唆された。臨床, エストロゲン補充療法の更なる効果が期待できる。

P-91-4 卵巣摘出及びステロイド補充ラットにおける下垂体前葉の変化について

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【目的】卵巣摘出による下垂体前葉ホルモン産生細胞の変化及び性ステロイドホルモン補充の影響について検討した。【方法】6 週齢の雌ラットの卵巣を摘出し, 摘出 7 日後の下垂体前葉におけるゴナドトロピンサブユニット及びプロラクチン発現の変化, 関連する視床下部因子の受容体発現及び下垂体インヒビンサブユニット発現について定量 PCR で検討した。【成績】卵巣摘出により下垂体前葉の LHb サブユニットは約 6 倍, α 及び FSHb サブユニットは約 2 倍に増加した。卵巣摘出後に E2 を補充したラットではゴナドトロピンサブユニットの上昇は完全に抑制された。アンドロゲンであるジヒドロテストステロン (DHT) の補充は卵巣除去による α 及び LHb サブユニットの増加を抑制しなかったが, FSHb サブユニットの増加は DHT 補充で抑制された。卵巣摘出により下垂体前葉のプロラクチン発現は有意に減少し, E2 及び DHT 補充ラットではプロラクチンは減少しなかった。卵巣摘出により下垂体前葉に発現する GnRH 受容体遺伝子は有意に増加し, E2 補充でこの増加は完全に抑制された。TRH 受容体, PACAP 受容体, キスペプチン受容体遺伝子発現は変化しなかった。下垂体前葉に存在するインヒビン α bA, bB サブユニット発現に卵巣摘出による影響は見られなかったが, 下垂体前葉のフォリスタチン発現は約 3.3 倍に増加し, この増加は E2 補充で完全に抑制された。【結論】卵巣除去による E2 の欠乏はネガティブフィードバックによるゴナドトロピン発現の上昇の他, 下垂体前葉内でプロラクチン発現を減少させ, GnRH 受容体遺伝子及びフォリスタチン発現を増加させることが分かった。E2 の欠乏により下垂体局所でも様々な変化が生じていることが示唆された。

P-91-5 排卵時の顆粒膜細胞のエネルギー代謝は卵母細胞の能力と相関しており、肥満と老化により負の影響を受ける

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【目的】加齢と肥満は、生殖医療においても重要な懸案事項である。根本的な原因としてミトコンドリア機能障害が示唆されているが、卵胞のエネルギー代謝の全貌はこれまで明らかにされていない。本研究ではマウスにおける排卵時の顆粒膜細胞 (GC) と卵丘卵母細胞複合体 (COC) のエネルギー代謝動態を明確にし、肥満と加齢の影響を明らかにすることと、ヒトにおける GC の代謝を検討し、加齢と肥満による影響を解明することを目的とした。【方法】リアルタイム代謝アナライザー (SeahorseXFe96) を使用し、マウスにおける排卵時の GC および COC の動的なエネルギー代謝 (ミトコンドリア機能、解糖系機能、および脂肪酸代謝) を検討した。またヒトでは IVF/ICSI 患者 85 人の採卵時に GC を回収し、その細胞代謝を検討した。【成績】マウス GC における ATP 産生は、ミトコンドリア、解糖系、および脂肪酸代謝の増加により hCG 投与後 8 時間で増加し、12 時間で最大となった。COC の ATP 産生は hCG 後 4 時間で最大となり、その後減少した。肥満マウスでは主にミトコンドリア機能が低下し、加齢マウスではミトコンドリア機能と解糖系機能の両方が低下した。加齢肥満マウスでは、より著しい代謝の低下を観察した。一方、ヒトでは胚培養結果との相関があり、年齢と BMI はエネルギー代謝に有意な影響を与えていた。【結論】今回の結果から、排卵時の顆粒膜細胞は LH に応答し、複数のエネルギー代謝経路が動的に増加することを示している。マウス、ヒトともエネルギー代謝経路は肥満と加齢による負の影響を受け、卵母細胞の質の低下に関連していた。今後は加齢および肥満が影響する代謝経路を特定し、不妊症の発症機序の解明に繋げていきたい。

P-91-6 月経困難症に対するホルモン治療が女性の気分障害や性機能障害に及ぼす影響についてのアンケート調査

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【目的】海外では低用量エストロゲン・プロゲステン配合剤 (LEP) やプロゲステン製剤で女性性機能障害を起こすことが知られているが、日本人女性における報告は少なく実態は明らかではない。そこで、これらの薬剤による副作用の頻度について調査し、特に性機能については国際的指標である FSFI を用いて評価する。【方法】2021 年 6 月から約 1 か月間に 3 施設に受診した、月経困難症をホルモン治療中の患者にアンケート用紙を配布し、回収できた回答結果を集計・解析した。本研究は当院の倫理委員会の承認を得、プライバシーに配慮して実施した。【成績】回収できたアンケート 108 を調査した。回答者の年齢は 14 歳~51 歳 (平均 35.4 歳) で、使用中の薬剤は LEP69, 経口プロゲステン 28, IUS-LNG5, 無回答 6 例だった。うつ病や不安障害などのスクリーニングに用いられる K6 のスコアの平均値は 4.4, 最頻値 0, 最高値 24 で、治療により気分障害が改善した 26, 変化なし 62, 悪化した 4, 無回答 16 であった。女性性機能の指標である FSFI は完全回答数 73, 部分回答 7, 無回答 28 で、いずれかの項目で改善か悪化があったのは 18 例だった。詳細の例数 (改善, 悪化) は、性欲 (1, 12), 性的高まり (1, 7), 潤滑 (1, 5), オルガズム (2, 2), 満足度 (2, 4), 性交痛 (2, 10) であった。【結論】月経困難症の治療で原疾患の症状は改善しているが、気分障害の悪化や性機能障害、特に性欲、性的高まり、性交痛で悪化を感じている症例が少なくなかった。性機能障害については、自覚があっても外来で主治医に相談しにくいことも考えられ、ホルモン治療の副作用としての医師・患者相互の認識と、症例に応じた細やかな対応が必要である。

P-91-7 ノビレチンが閉経後骨粗鬆症モデルラットの骨密度に及ぼす影響

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【目的】ノビレチン (Nobiletin: Nob) はシークワーサー等の柑橘類果皮に含まれるポリメトキシフラボノイド (PMF) の一種で、抗酸化作用により、腫瘍、神経、代謝性疾患などの疾患モデルで治療効果が報告されている。閉経後骨粗鬆症の原因の一つとしてエストロゲン低下による酸化ストレスの増加が考えられており、また PMF は骨芽細胞における PGE2 の産生抑制、破骨細胞分化抑制作用を有することから、閉経後骨量減少に対する予防効果が期待される。今回、我々は卵巣摘出ラットを用い、Nob が骨代謝に及ぼす影響を検討した。【方法】10 週齢の雌 Wistar ラットを Sham, Ovx, Nob の 3 群 (n=11) に分割し、麻酔下に Ovx 及び Nob 群には両側卵巣摘出術 (Ovx) を、Sham 群には偽手術を施行した。術後、Ovx, Sham 群は通常食、Nob 群は特餌 (Nob0.5% 含有) を自由摂取とし、14 週後に屠殺した。右大腿骨を摘出し、DXA 法にて骨密度 (BMD) を測定した。【成績】1) 子宮重量: Ovx, Nob 群は Sham 群に比較し、有意に低値であった (p<0.001)。2) 体重: Sham 群と比較し Ovx 群では有意に大きかったが (p<0.05), Nob 群では有意差は認めなかった。3) DXA: Sham, Ovx, Nob 群の全骨密度はそれぞれ、 0.223 ± 0.008 , 0.204 ± 0.005 , $0.201 \pm 0.008 \text{g/cm}^2$ であり Ovx により有意に低下したが、Nob 投与による BMD の改善は認められなかった。遠位端、中央部、近位端で 3 等分した検討でも Nob 群と Ovx 群で BMD の有意差はみられなかった。【結論】今回の条件下においては Nob 投与により Ovx による BMD 低下を抑制できないことが示された。

P-91-8 コーヒーポリフェノールが閉経後骨粗鬆症モデルラットの骨密度に及ぼす影響

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【目的】加齢や閉経により増大する酸化ストレスが閉経後骨粗鬆症の原因の一つとして考えられている。コーヒーに含まれるポリフェノール (coffee polyphenol : CPP) は強い抗酸化作用を持ち、2型糖尿病や肝疾患の発症リスクを低下させるなどの効果が報告されており、閉経後骨量減少の抑制効果も期待される。今回卵巣摘出ラットを用い、CPP が骨代謝に及ぼす影響を検討した。【方法】10 週齢の雌 Wistar ラットを Sham, Ovx, CPP の 3 群 (n=11) に分割し、麻酔下に Ovx 及び CPP 群には両側卵巣摘出術 (Ovx) を、Sham 群には偽手術を施行した。術後 Ovx 群, Sham 群は通常食を、CPP 群は特餌 (飼料中 CPP 1.5% 含有) を自由摂取とし、14 週後に屠殺し、右大腿骨を摘出、DXA 法にて骨密度 (BMD) を測定した。【成績】1) 子宮重量 : Ovx, CPP 群は Sham 群と比較し有意に低値であった ($p < 0.001$)。2) 体重 : Sham 群と比較し Ovx 群は有意に大きく ($p < 0.05$)、さらに Ovx 群と比較し CPP 群は有意に大きかった ($p < 0.05$)。3) DXA : 全骨密度は Sham, Ovx, CPP 群の BMD は、それぞれ 0.223 ± 0.008 , 0.204 ± 0.005 , $0.208 \pm 0.006 \text{g/cm}^2$ であり、Ovx により有意に低下したが、CPP 投与による BMD 改善は認められなかった。遠位端・中央部・近位部で 3 等分した検討でも、CPP 群と Ovx 群で BMD の有意差はみられなかった。【結論】今回の条件下においては、CPP の閉経後骨粗鬆症モデルラットにおける BMD 低下を抑制する効果はないことが示唆された。

P-91-9 ジェノゲスト (0.5mg) はピルの不適症例の代わりとなりうるか

佐々木レディスクリニック

山田俊夫, 佐々木義和, 佐々木真一

【目的】月経困難症や月経前症候群 (PMS) を訴える方にはピルが用いられている。しかしピル不適例には、ジェノゲスト (0.5mg, JG と略す) が適応と考えられる。今回 JG が月経困難症や PMS に対して、継続可能な治療法であるか、また副作用、投与時のホルモン状態についても検討した。【方法】2020 年 6 月より 2021 年 6 月迄に、過多月経、月経困難症、PMS の為に治療を希望する 114 人に対して、十分な IC の上 JG の投与を行った。投与 6 か月経過した 31 例について血中 E2, FSH を測定した。【成績】投与した 114 例は、10 代は 11 例、20 代は 10 例、30 代は 13 例、40 代は 74 例、50 代は 6 例で、平均 39.5 \pm 10.4 歳。投与 114 例中、4 か月以上継続出来たのは 62 例で、4~16 か月 (8.2 ± 3.2 か月)。3 か月以内に中止となった 52 例では、27 例が出血で中止、来院せずに中止となった 20 例のうち 15 例が 1 か月で中止となった。継続出来た 62 例は、前治療がピルの 19 例中 11 例、ジドロゲステロンの 11 例中 9 例、LNG-IUS 脱落の 7 例中 5 例、JG (1.0mg) の 2 例、前投与なしが 75 例中 35 例でした。50 代の 6 人は継続中である。JG 投与 31 人の FSH 値 $7.1 \pm 10.5 \text{mIU/ml}$, E2 値 $66.4 \pm 54.1 \text{pg/ml}$ でホルモン状態は保たれていた。投与中全く出血がなかったのは 114 例中 8 例で、他は必ず不正出血を認めた。出血の治療には芍薬湯を併用した。出血以外で継続中止となった副作用は、鬱状態が 2 例、脱毛が 1 例、頭痛が 1 例、体重増加が 2 例でした。【結論】JG (0.5mg) は不正出血が起こりやすく最初の 3 か月間に脱落する症例が多い為、出血に対して十分に説明する必要がある。4 か月以上継続出来ればピルの代用となりうるが、ピル代用にはこの不正出血をコントロールする必要があると考えられた。

P-92-1 不育症患者における anti-phosphatidylserine/prothrombin antibodies (抗 PS/PT 抗体) の新しい病原性の検討

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【目的】我々は既に、不育症患者には、第 XII 因子やプロテイン S に対する自己抗体が存在し、それぞれの epidermal growth factor (EGF) 様領域を認識する事を報告した。さらに、抗第 XII 因子抗体や抗プロテイン S 抗体は、EGF や Heparin-binding (HB)-EGF など EGF family protein にも結合する事がわかってきた。そこで、不育症患者の EGF に対する自己抗体を測定したところ、抗 EGF 抗体は抗プロテイン S 抗体、抗第 XII 因子抗体だけでなく、抗 PS/PT 抗体と強い相関関係にあった。プロトロンビンには EGF 様領域が無いため、不可解なデータであり、その解析を行なった。【方法】【成績】先ず、Western blot 上で、不育症患者の抗 PS/PT 抗体は、プロトロンビン F1+2 と α -thrombin の両方を認識した。さらに、抗 human EGF ポリクローナル抗体 (PoAb) は、プロトロンビンを認識し、F1+2 領域ではなく、 α -thrombin 領域を認識した。次に、抗プロトロンビン PoAb と抗 α -thrombin PoAb は、human EGF を認識した。従って、 α -thrombin と human EGF の抗原性は cross reactive である事が判明した。【結論】抗 EGF 抗体は抗 PS/PT 抗体と有意な相関関係にあり、プロトロンビンの protease domain は EGF 系と cross reactive である。不育症患者の持つ EGF に対する自己抗体は、第 XII 因子、プロテイン S や EGF family protein を認識し、EGF 系を破壊させ、子宮内膜や胎盤の血管新生を阻害し、着床障害、流産を引き起こしている可能性があるが、今回、抗 PS/PT 抗体にも同様の病原性がある事が示唆された。

P-92-2 均衡型染色体構造異常をもつ不育症カップルの診療におけるピットフォール札幌医大¹, エナ麻生 ART クリニック²馬場 剛¹, 遠藤俊明^{1,2}, 春日美貴子¹, 小川万梨絵¹, 森下美幸¹, 久野芳佳¹, 木谷 保², 齋藤 豪¹

【目的】不育症カップルにおいて染色体均衡型構造異常を認めた場合、流産回避と生児獲得のため着床前診断 (PGT-SR) を選択するが、正倍数性胚の移植が必ずしも生児獲得とならない。そこで PGT-SR がどの程度妊娠・出産に寄与するかを検討したので報告する。【方法】当院でこれまでに PGT-SR を試みた不育症カップル 15 例について、胚移植と妊娠転帰について後方視的に検討した。【成績】15 例中 1 例は移植可能胚が得られず治療を断念した。初回胚移植で 14 例中 10 例 (71.4%) が着床した。そのうち生化学的妊娠を含む初期流産が 3 例 (30.0%)、妊娠 12 週以降の妊娠継続中が 1 例 (10.0%)、生児獲得が 6 例 (60.0%) であった。初回胚移植で生児獲得に至らず 2 回目以降の胚移植に進んだ 6 例 (流産: 3 例, 着床不成立: 3 例) のうち、3 例で 3 回目までに妊娠継続に至り (2 回目で 2 例, 3 回目で 1 例)、最終的に 14 例中 10 例 (71.4%) で妊娠継続が可能であった。初回胚移植で初期流産となった 3 例のうち 2 例は 3 回の正倍数性胚移植で生児獲得に至らなかった。【結論】PGT-SR によりほとんどの症例で生児獲得が期待されるが、一部の症例では 3 回の胚移植によっても生児獲得に至らず、染色体構造異常以外の不育症リスク因子の存在が疑われた。リスク因子の精査や PGT の適用には慎重な対応が求められる。

P-92-3 不育症に対する OPTIMUM (Optimization of Thyroid function, Thrombophilia, Immunity and Uterine Milieu) treatment strategy の治療効果の検討杉山産婦人科新宿¹, 順天堂大²黒田恵司¹, 池本裕子², 堀川 隆¹, 森山 梓¹, 中尾佳月¹, 壽圓裕康¹, 月花瑤子¹, 小代裕子¹, 高見澤聡¹, 中川浩次¹, 杉山力一¹

【目的】不育症はリスク因子が複雑に影響するため、多因子性疾患と考えられている。我々は以前に、複数回胚移植をしても妊娠しない着床不全に対し、OPTIMUM treatment strategy (OPTimization of Thyroid function, Thrombophilia, IMMunity and Uterine Milieu) の治療効果を報告した。今回、不育症に対する OPTIMUM の治療効果を解析した。【方法】2018 年から 2019 年に、2 回以上の臨床的流産の既往のある不育症女性に、以下の検査を行った: 子宮鏡検査, 子宮内膜組織の CD138 免疫染色および子宮内細菌培養検査, 血清 Th1 (IFN- γ 産生細胞) および Th2 細胞値 (IL-4 産生細胞), 血清ビタミン D 値, TSH と TPO 抗体。慢性子宮内膜炎を含む子宮内病変を子宮鏡手術・抗菌薬, Th1/Th2 細胞比高値をビタミン D (+タクロリムス), 顕性・潜在性甲状腺機能低下症をレボチロキシシン, 血栓性素因を低用量アスピリンで治療した。43 歳以下の 168 名のうち 115 名が不育症検査を受けた。OPTIMUM を行った 90 名 (100 妊娠) と行わなかった 41 名 (46 妊娠) を比較した。【成績】不育症検査で、子宮内病変 66 例 (57.4%), Th1/Th2 細胞比高値 50 例 (43.5%), 甲状腺機能異常 33 例 (28.7%), 血栓性素因 33 例 (28.7%) を認めた。OPTIMUM 群とコントロール群のそれぞれの初回妊娠後の生産率は、40 歳未満で 78.1%, 42.3% ($p=0.002$), 40 歳以上で 55.6%, 30.0% ($p=0.09$) で、40 歳未満で OPTIMUM 群が有意に高かった。【結論】OPTIMUM は、世界で初めて着床不全と不育症を同時に治療が可能な方法である。40 歳以上では年齢に伴う流産率が高く、有意差を認めなかったが、着床前スクリーニングなどを併用することで妊娠成績の向上が期待できる。

P-92-4 流産時脱着膜 NK 細胞に発現する NKp46 から不育症のリスク因子を知る

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【目的】不育症の約 60% はリスク因子不明とされ、未知のリスク因子の解明は重要な課題である。今回、脱着膜 NK (dNK) 細胞における CD16 と CD56 発現から見た NK 細胞サブセット, NKp46 発現, サイトカイン産生を測定し、不育症のリスク因子としての NK 細胞の意義につき検討した。【方法】本学倫理審査委員会の承認および患者への説明と同意のもと、流産手術あるいは人工妊娠中絶術 (AA) 後の脱着膜組織を回収し、物理的分散のうえ、脱着膜細胞浮遊液を作成した。CD56⁺dNK 細胞における CD16, NKp46 発現およびサイトカイン (IFN- γ , TNF- α , IL-4, IL-10, TGF- β) 産生をフローサイトメトリーで測定し、絨毛染色体検査が正常であった不育症患者群 (染色体正常流産群 $n=11$)、医学的適応による AA 群 (AA 群 $n=12$) における差異を検討した。【成績】CD16⁺/CD56^{dim} 細胞, CD16⁺/CD56^{bright} 細胞には両群間に差を認めなかった。一方, NKp46⁺dNK 細胞 ($p<0.01$), NKp46^{bright}dNK 細胞 ($p<0.05$) は、染色体正常流産群で AA 群に比して有意に低値であった。NKp46⁺dNK 細胞, NKp46^{bright}dNK 細胞の不育症のカットオフ値を 86.52% および 70.85% とすると、感度は 83.3% および 67.7%, 特異度は 100% および 90.9% であった。カットオフ値に基づき NKp46 高値群と低値群の 2 群に分け、dNK 細胞産生サイトカイン産生を解析すると、NKp46 低値群では NKp46 高値群に比して IFN- γ /IL-4 比 ($p<0.05$) および TNF- α /IL-10 比 ($p<0.05$) が有意に高値であった。【結論】不育症患者の脱着膜では、NKp46 の低下およびタイプ 1 サイトカイン産生の上昇がみられ、リスク因子不明不育症の中には dNK 細胞における NKp46 発現異常を有するものが存在することが示唆された。

P-92-5 不妊症における慢性子宮内膜炎と子宮内膜 microbiota の関連および妊娠予後

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【目的】慢性子宮内膜炎(chronic endometritis; CE)は不妊症に合併することが報告されているが、子宮内膜 microbiota (uterine endometrial microbiota; UEM)との関連についての報告は少ない。前向きコホート研究として CE と UEM に関連があるか調べた。また CE と妊娠予後について検討した。【方法】倫理委員会承認と同意の下、2回以上の流産産歴がある不妊症患者を対象に黄体期中期の子宮内膜組織を吸引法で採取した。CD138 免疫染色を行い McQueen score 1 以上ないし Liu 法 (>0.515/mm²) 陽性を CE と診断した。UEM は 16S ribosomal RNA sequence 法で解析した。【成績】23 人中、McQueen score 1 が 10 人、score 2 が 1 人、score 3 が 1 人、また Liu 法陽性は 3 人で、12 人 (52%) が CE と診断された。CE 群 vs non-CE 群の比較で、*Lactobacillus* 相対占有率 (中央値 93.1% vs 96.6%, p=0.5) や Shannon diversity index (0.15 vs 0.19, p=0.6) に有意差を認めなかった。妊娠率は 42% (5/12 人) vs 64% (7/11 人), p=0.4, 妊娠 12 週未満の流産率は 20% (1/5 人) vs 43% (3/7 人), p=0.6 で有意差を認めなかった。【結論】不妊症において CE は *Lactobacillus* depletion に影響を与えなかった。流産率は本研究では有意差を認めなかった。

P-92-6 慢性子宮脱落膜炎 (Chronic deciduitis) の不妊症への関与

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【目的】子宮内膜の免疫組織染色法による CD138 陽性形質細胞の有無で慢性子宮内膜炎を診断する方法が近年用いられているが、同様に子宮脱落膜での CD138 陽性形質細胞の存在を慢性子宮脱落膜炎 (CD) とする概念が提唱されてきている。CD と不妊症病態との関連は報告が少なく、今回不妊症患者の流産脱落膜における CD の影響を後方視的に検討した。【方法】2011 年から 2019 年にかけて稽留流産の診断で子宮内容除去術を行った、40 歳未満の不妊症患者を対象とし、抗リン脂質抗体症候群、子宮奇形、夫婦の染色体異常をみとめるものは除外した。絨毛染色体検査を行い、染色体正常流産群 (n=13)、染色体異数性流産群 (n=13) と、不妊症でない妊娠初期中絶検体で絨毛染色体正常を確認したもの (n=19) を対照群として、CD138 陽性形質細胞の有無を比較検討した。今回、CD138 陽性形質細胞を 1 つ以上みとめたものを弱陽性、HPF で 2 個以上集簇しているものを陽性とした。本研究は IRB 承認のもとインフォームドコンセントを得て行った。【成績】染色体正常流産で陽性は 30.7%、弱陽性を含むと 53.8%、染色体異数性流産で陽性は 38.5%、弱陽性を含むと 92.3%、中絶で陽性は 10.5%、弱陽性を含むと 36.8% の CD を認めた。それぞれにおいて Fisher の正確比検定を用い比較検討をしたところ、染色体異数性流産では中絶と比較して有意に弱陽性を含む CD 陽性率が高かった (P=0.003)。染色体正常流産は中絶と比較して、CD は多い傾向があるが、有意な差はみとめなかった (p=0.19)。【結論】不妊症において CD の頻度が高いことが明らかになったが、染色体正常ではなく異数性群に多いことから CD が不妊症の原因とは判断できないと考えられた。その機序も含めて今後の検討が必要である。

P-93-1 挙児希望を主訴とする帝王切開癒痕症候群に対する子宮鏡手術の安全性と有効性

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【目的】帝王切開癒痕症候群 (Cesarean Scar Syndrome; CSS) は帝王切開術後に異常子宮出血、月経痛、不妊症をきたす症候群として知られている。しかし、挙児希望を主訴とする CSS 症例に対する治療法は未だ確立されていない。そこで当院では低侵襲とされる子宮鏡手術を行った。そこで今回、子宮鏡手術の安全性と有効性について検討を行った。【方法】2014 年 7 月から 2020 年 4 月まで当院で挙児希望を主訴とする CSS に対して腹腔鏡補助下子宮鏡手術を行った 49 症例を対象とした。当院の子宮鏡手術の術式は、子宮頸部側をループ電極にて切除し、陥凹部を露出させた後に癒痕部およびその周囲をポール電極で焼灼させる術式である。安全性は術中、術後の合併症の有無、およびその後の妊娠における産科合併症の有無で評価した。有効性は術後の妊娠率で評価した。【成績】すべての症例で術中合併症は認めなかった。追跡できた症例は 45 例であった。術後妊娠例は 34 例 (76%) であった。妊娠例の平均年齢は 36.6 歳、非妊娠例は 34.9 歳であり両群間に有意な差は認めなかった。周産期予後については、流産が 4 例、現在継続中が 1 例であるが、その他は 35 週が 1 例、36 週が 4 例、37 週が 10 例、38 週が 14 例ですべて帝王切開分娩であった。出生児の生下時平均体重は 2962g であった。妊娠経過中に子宮破裂等子宮鏡手術に起因すると思われる産科合併症は認めなかった。【結論】挙児希望を主訴とする CSS に対して腹腔鏡補助下子宮鏡下帝王切開癒痕部焼灼術は安全でありかつ有効であることが示唆された。

P-93-2 帝王切開癒痕症候群 63 例における子宮峡部創陥凹の病理組織学的検討

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【目的】帝王切開後に子宮峡部創陥凹 (Cesarean scar defect ; CSD) が形成され、月経終了後の不正子宮出血、月経痛や不妊症等をきたす疾患を帝王切開癒痕症候群 (Cesarean scar syndrome ; CSS) という。しかし CSS の CSD の病理組織学的検討は未だなされていない。そこで病理組織学的検討を行い CSS の病態に迫ることを本研究の目的とした。【方法】本研究は当院倫理委員会の許可を得て後方指的に検討した。対象は CSS のため CSD を切除した症例 63 症例 (CSS 群) と帝王切開既往があり良性疾患のため子宮全摘術を行った 21 症例 (control 群) を比較対象として検討した。方法は、HE 染色、免疫染色 (CD 3, CD20, CD56, CD68, CD138, myeloperoxidase, tryptase) を行い検討した。【成績】CSS 群は control 群に比べ CSD 部の子宮内膜が覆っている症例は有意に少なく (22% vs 62%, $p=0.0023$)、異所性子宮内膜を CSD 部に認める症例は有意に多かった (43% vs 14%, $p=0.0195$)。CD3, CD20, CD68, tryptase 陽性細胞は CSS 群で有意に少なく ($p<0.0001$, $p=0.0015$, $p=0.0006$, $p<0.0001$)、CD138 陽性細胞は CSS 群で有意に多かった ($p=0.0042$)。【結論】CSS では子宮内膜が覆っておらず、子宮筋腫および慢性炎症のマーカーを特徴的に認めることが明らかとなった。これらの所見が CSS の妊孕能低下の一因となっていることが示唆された。

P-93-3 帝王切開癒痕症候群に対する Gambee 縫合を用いた腹腔鏡下癒痕部切除術の試み

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【目的】帝王切開により月経終了後不正子宮出血、月経痛および不妊症をきたす疾患を帝王切開癒痕症候群という。当院では本症候群に対し子宮鏡下手術を中心に行ってきた。しかし子宮鏡での治療が困難な症例に遭遇することもあり、これらに対し腹腔鏡下に癒痕部を切除する手術を行っている。そこで本術式の短期予後を評価した。【方法】当院での腹腔鏡下癒痕部切除術は以下の手順で行っている。まず 4 孔ダイヤモンド式にポートを配置し、膀胱を子宮から剝離し、子宮鏡の光源を透過させながら菲薄部のマーキングを行う。バソプレシンを局所注射した後にマーキングに沿って癒痕部を切除し、子宮筋層を 2 層縫合 (1 層目 Gambee 縫合, 2 層目単結節縫合) にて縫合する。その後円靭帯を縫縮する。術前と術後 3 か月に MRI 検査を行い残存子宮筋層厚 (residual myometrium thickness ; RMT) を測定し比較した。【成績】これまで本手術を 10 例行った。患者平均年齢は 37.6 歳であり、既往帝王切開数は 1 回が 5 例、2 回が 4 例であった。手術時間は平均値 240 分 (171-292 分)、出血量は中央値 38ml (0-150ml) であり全例術中合併症は認めなかった。術後 3 か月の経過観察期間を経た症例は抄録作成時点で 7 例あった。7 例の術前 RMT は平均 2.5mm であったが、術後 9.0mm まで有意に増加していた ($p=0.0001$)。また全例で RMT の増加を認めた。【結論】当院で施行している腹腔鏡下癒痕部切除術は RMT の増加に寄与すると考えられた。妊孕能の回復効果については今後検討していく必要がある。

P-93-4 帝王切開癒痕部症候群に対する鏡視下手術

琉球大学病院
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【目的】帝王切開癒痕部症候群に対して鏡視下手術を施行した症例について検討し、その効果や課題を明らかにする。【方法】2019 年 1 月～2020 年 2 月の期間、帝王切開癒痕部症候群として治療的に腹腔鏡もしくは子宮鏡手術を受けた 5 症例を対象とし、その臨床的背景、手術成績、妊娠を含む治療効果について診療録を後方視的に検討。当科では症状を有する帝王切開癒痕部症候群を手術適応とし、癒痕部の筋層 2.5mm 未満であれば腹腔鏡手術を、癒痕部の筋層 2.5mm 以上あれば子宮鏡手術を選択している。腹腔鏡下手術では、1. 癒痕部同定のために子宮体下部に Foley カテーテルを挿入、2. 術中経陰超音波検査を併用、3. 縫合部の治癒を補助するため子宮後屈を修正する、などの工夫を行っている。子宮鏡下手術では腹腔鏡を併用し、膀胱子宮窩腹膜の癒着を剝離した後に子宮鏡下癒痕部切除を行った。妊娠許可は 6 か月後とした。【成績】5 症例の平均年齢は 33 歳、前回帝王切開からの経年数は平均 3.6 年、平均の帝王切開回数は 1.6 回であった。5 例とも不正性器出血を認め、不妊症を 3 例認めた。5 例中 4 例に挙児希望を認め、腹腔鏡手術 4 例、子宮鏡下手術 1 例を施行。平均手術時間は 208 分で、術中出血量の平均は 12.6ml と少量であった。全症例で症状の改善を認め、手術合併症は認めなかった。挙児希望のある 4 例のうち、不妊治療を行った 3 例で妊娠成立し、うち 1 例は ART、2 例は一般不妊治療であった。妊娠した 3 例中 2 例で生児獲得し、1 例は妊娠継続中で、早産や子宮破裂はなかった。【結論】鏡視下手術によって全例で症状改善し、4 例中 3 例で妊娠した。症状を有する帝王切開癒痕部症候群に対し、腹腔鏡手術や子宮鏡手術は選択肢の一つとなる。

P-93-5 子宮峡部にチョコレート様のう胞を認めた帝王切開癒痕症候群の4症例

滋賀医大

渡邊大祐, 辻俊一郎, 信田侑里, 花田哲郎, 北澤 純, 森宗愛菜, 天野 創, 村上 節

【背景】帝王切開により子宮峡部創陥凹が形成され、術後に異常子宮出血、月経痛や不妊症をきたす疾患を帝王切開癒痕症候群 (Cesarean Scar Syndrome ; CSS) と称す。我々は CSS の症例に対して積極的に内視鏡手術を行ってきたが、子宮峡部にチョコレート様のう胞を認めた4症例を経験したので報告する。【症例】症例1: 39歳1妊1産。タイミング療法にて妊娠せず、月経後に続く異常子宮出血を認めるため当院紹介となった。子宮鏡手術時に子宮峡部側壁に青変した領域を認め、ループ電極により割を入れるとチョコレート様内容液の流出を認めた。症例2: 42歳2妊1産。ART施行するも妊娠に至らず当院紹介となった。子宮鏡手術中に子宮峡部側壁からチョコレート様液体の流出を認めた。症例3: 39歳3妊1産。月経後から断続的に粘性茶色の帯下を認めるようになった。ARTを行うも妊娠に至らず当院に紹介となった。子宮鏡手術中に子宮峡部側壁からチョコレート様の液体の流出を認めた。症例4: 43歳1妊1産。過長月経を主訴当院紹介。癒痕部が大きく漿膜側に膨隆するほどであった。子宮鏡補助下に腹腔鏡で癒痕部の切除と再建を行った。術中の子宮鏡所見で癒痕部に black lesion およびチョコレート様の分泌物の流出を認めた。切除した術後病理標本で、異所性子宮内膜組織を認めた。【考察】CSSの病態は未だその全容が明らかとなっていない。今回の4症例はいずれも卵巣に存在するチョコレート様のう胞と同様の所見であった。これらは CSS が子宮内膜症関連疾患であることを想起させる4症例であったと考えられた。

P-94-1 当院における医学的適応による未受精卵子凍結の現状

歳本ウイメンズクリニック

小川尚子, 吉岡尚美, 藤田智之, 古川雄一, 大塚未砂子, 歳本武志

当院では2010年より院内倫理委員会の承認を得て、医学的適応による卵子凍結を開始した。当院の現状について報告する。2021年3月までに23症例31周期の卵子凍結を実施した。乳癌15例、血液がん6例、その他、悪性黒色腫、骨軟部腫瘍が各1例であった。乳癌症例の年齢の中央値は38(27-47)歳、血液がん他の症例は23(15-32)歳であり、乳癌症例で高齢者が多かった。周期毎の採卵数は中央値で9(1-41)個、うち採卵時の成熟卵数(MII)は3(0-37)個で、未熟卵は未熟卵体外成熟(in vitro maturation ; IVM)を行い、症例毎の凍結卵子数の中央値は10(2-40)個であった。乳癌症例で9個、血液がん他の症例で14.5個であった。これまでに凍結卵子を用いてICSI-ETを行ったのは2例であった。1例は乳癌の術前化学療法前に37歳で卵子凍結し、担当医の妊娠許可後、40歳で妊娠し正期産に至った。もう1例は骨髄異形成症候群の骨髄移植前に26歳で卵子凍結し、34歳で妊娠したが、高血圧のコントロール不良のため中期中絶となった。37歳で再度妊娠したが、妊娠26週6日に切迫早産および早発型加重型妊娠高血圧腎症の診断で緊急帝王切開分娩となった。一方で、すでに凍結卵子の破棄を希望した症例が5例あり、さらに、本人が死亡し卵子が破棄となった乳癌症例が2例あった。乳癌症例では卵子凍結時の年齢が高いことによる妊娠率の低下が危惧される。血液がん症例では原疾患の治療による臓器障害が妊娠により顕在化することもあり、妊娠前の母体評価および周産期管理目的に高次医療機関へコンサルトすることが重要である。さらに、卵子破棄症例も多く、死亡症例もみられることから、卵子凍結について原疾患の担当科との情報共有が今後重要となってくると考えられた。

P-94-2 妊娠後期に急性リンパ性白血病を発症し、分娩後の化学療法中に受精卵凍結を行った一例

信州大附属病院

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急性リンパ性白血病 (Acute Lymphoblastic Leukemia : ALL) は進行が非常に早く、診断後は迅速に化学療法を開始する必要がある。治療後に妊孕性を喪失するリスクが高いが原疾患治療を優先するため、化学療法前の受精卵凍結は時間的余裕がなく困難である。今回、妊娠後期に ALL を発症し、分娩後に速やかに化学療法を開始しつつ化学療法中に合併症なく受精卵を凍結し、妊孕性を温存した一例を経験したため報告する。症例は33歳の女性で第一子妊娠中の妊娠33週6日白血球増多、血小板低下から ALL が疑われ、当科に紹介となった。妊娠34週1日、原疾患の増悪および胎児機能不全のため帝王切開術を施行した。産褥2日目に ALL と診断し、産褥4日目からダサチニブ、シタラビン、メトトレキサートによる化学療法を開始した。AMH 0.31ng/ml と低く、化学療法および造血幹細胞移植前の全身放射線照射による妊孕性喪失が危惧され、ご夫婦が化学療法中の受精卵凍結を希望された。排卵誘発に伴い腹水が多量に貯留した場合はメトトレキサートの血中濃度が上昇し、毒性が増すことが報告されているため、卵巣過剰刺激症候群のリスクが低いクロミフェン+ゴナドトロピン法により排卵誘発した。12個の卵子を得て、3個の受精卵を凍結した。採卵後はカベルゴリンの内服により、腹水貯留は少量であり化学療法を遅延なく再開できた。迅速に化学療法を開始する必要がある ALL において、化学療法中の排卵誘発および採卵は妊孕性温存に有効であることが示唆された。化学療法中の採卵では骨髄抑制や腹水貯留による薬物濃度への影響に注意しつつ、適切な排卵誘発法を選択し、卵巣過剰刺激症候群の予防に努めることが必要であると考えられた。

P-94-3 小児・AYA 世代の女性がん患者に対する妊孕性温存療法と治療後の月経状況

三重大附属病院

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【目的】妊孕性低下リスクの高い治療を受ける小児・AYA 世代の女性がん患者に対する、妊孕性温存療法の提示と実施、また治療後のヘルスケアは重要な課題である。当院での小児・AYA 世代女性がん患者に対する妊孕性温存療法と治療後の月経状況について報告する。【方法】2017年4月から2021年8月までに当院高度生殖医療センターを受診し、妊孕性温存を行った女性患者50例を対象に背景、原疾患、妊孕性温存療法の方法、治療後の月経状況等を診療録から後方視的に検討した。【成績】初診時年齢は8-43(平均28.2)歳、原疾患は乳癌31例(62%)、白血病6例(12%)、悪性リンパ腫4例(8%)、横紋筋肉腫2例(4%)、骨肉腫2例(4%)、その他5例であった。妊孕性温存療法の方法は未受精卵子凍結19例、胚凍結12例、卵巣凍結19例であった。月経は初診時に順調32例、不順9例、初経前4例、ホルモン療法中3例、不明2例であった。ASCO2013ガイドラインで治療後閉経リスク中等度以上の化学療法終了後から6か月以上経過し、偽閉経療法を行っていない患者は28例であった。治療後6か月時の月経状況は、月経再開3例、無月経遷延10例、不明12例、初経未発来1例、HRT中2例であった。治療後1年時の月経状況は、月経再開9例、無月経遷延3例、不明12例、HRT中4例であった。治療後月経状況不明を除く16例中、7例(44%)が無月経遷延もしくは無月経に対しHRT施行していた。【結論】ASCO2013ガイドライン治療後閉経リスク中等度以上の化学療法終了後1年時の月経状況は、ガイドラインと同等の無月経率であった。妊孕性温存療法だけでなく、がんサバイバーの月経状況を確認し、必要時にホルモン補充療法を行うなど、継続的なフォローが必要と考える。

日本語ポスター
7日(日)

P-94-4 AYA 世代造血器腫瘍患者における妊孕性温存療法 84 例の検討

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【目的】より効率的で安全ながん・生殖医療の実現のために、疾患治療別に妊孕性温存治療を評価することが求められている。今回我々は、AYA 世代造血器腫瘍患者における妊孕性温存治療の現況について検討した。【方法】2010年から2021年6月までに妊孕性温存目的で受診した造血器腫瘍の成人女性患者84例を対象とし、受診時の状況、妊孕性温存の有無とその後の妊娠成績を後方視的に検討した。なお、本研究は筆頭演者施設の臨床試験部会で承認され実施した(承認番号3464)。【成績】原疾患は悪性リンパ腫40例、AML19例、ALL11例、MDS6例、CML4例、再生不良性貧血3例、CLL1例であった。受診時の年齢中央値は26歳(18-46)、化学療法開始後であった症例は63.1%(53/84)であった。妊孕性温存療法施行率は39.3%(33/84)であったが、造血幹細胞移植が予定されていた33例においては63.6%(21/33)であった。卵巣組織凍結は14例に行われ、希望されていたが体調不良で施行を断念した症例が2例あった。採卵は19例に行われたが、化学療法による遺伝毒性のリスクを説明した上で化学療法中に採卵した3例の採卵数は0~1個と少数であった。なお、治療後に5例が自然妊娠し出産に至り、造血幹細胞移植後に閉経した2例は温存凍結胚の融解移植を行い2例とも妊娠出産に至った。凍結保存した33例(観察期間中央値:1501日)のうち4例が原疾患死した。【結論】造血器腫瘍患者に対する標準的の化学療法は性腺毒性の低リスク群に含まれるが、造血幹細胞移植が行われた場合には閉経に至ることが多い。診断時には温存の時間的猶予がないことも多く、その後の治療経過と内容から妊孕性温存の必要性和時期を適切に判断することが肝要である。

P-94-5 BRCA1/2 に病的バリエントを認める乳癌患者に対する妊孕性温存治療の転帰

聖路加国際病院

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【目的】BRCA1/2 に病的バリエントを認める乳癌患者の妊孕性温存治療施行後の乳癌・卵巣癌発症に関する報告は、欧米からはあり、短期間の排卵誘発剤の使用や治療の遅延は影響がないとされているが、本邦からの報告は少ない。このため、当院で行った場合の転帰を把握することを目的とした。【方法】当院で2006年から2020年までに乳癌を発症後にBRCA1/2生殖細胞系列の検査を行い、病的バリエントを保持している患者で妊孕性温存治療を行った後の転帰を、診療録を後方視的に検討した。【成績】乳癌かつBRCA1/2に病的バリエントを保持し妊孕性温存治療を行った患者は12人(BRCA1病的バリエント保持6人、BRCA2病的バリエント保持6人)だった。BRCA1/2の検査は妊孕性温存前に行った:5人、温存後に行った:5人、再発した卵巣癌発症後に行った:2人だった。行った妊孕性温存治療は胚凍結保存6人、卵子凍結保存4人、卵巣組織凍結保存2人だった。妊孕性温存後に乳癌再発3人、卵巣癌発症1人に認めた。【結論】当院で乳癌かつBRCA1/2に病的バリエントを認め妊孕性温存治療を行った12人のうち、乳癌再発・卵巣癌発症者は4人と比較的高く、今後も把握していく必要があると考えられた。

P-94-6 当院における医学的適応による未受精卵子と受精卵凍結・保存～近年の動向～

東京医大病院

上野啓子, 小野政徳, 山田悦子, 中崎千晶, 忽那ともみ, 長谷川朋也, 久慈直昭, 西 洋孝

【目的】当院では2015年より倫理委員会の承認を得て、医学的適応による未受精卵子および卵巣組織の凍結・保存に関する臨床研究を始め、2017年からは受精卵凍結・保存も追加し行ってきた。今回、当院における妊孕性温存療法の動向を調査することとした。【方法】2015年11月から2021年9月までに当院で医学的適応による妊孕性温存療法を施行した22例を対象とし、患者背景、治療経過、さらに年次別受診者数の動向を後方視的に調査した。【成績】未受精卵子凍結の施行例は11例で、9例は乳癌であった。全例が未婚で、平均年齢は33.2±5.4歳(23-39歳)であった。9例はantagonist法、1例はlong法、1例は同一周期内に2回卵巣刺激を行うDouble Stimulation (DuoStim)法で行った。乳癌症例には全例letrozoleを併用した。平均卵子凍結数は11.3±7.7個(5-32個)であった。受精卵凍結の施行例は11例で、7例は乳癌以外のがんであった。全例が既婚で、経産が2例、平均年齢は34±5.7歳(26-43歳)であった。2015年に受精卵凍結した1例が2020年に40週に2,790gの女児の出産に至った。また、2021年の施行例が7例と全症例の約32%を占めていた。【結論】当院での施行数増加の背景には、第1に不妊治療専門のセンター開設による他科との連携の強化、第2に院内スタッフへがん・生殖医療が周知されたこと、第3に妊孕性温存療法に対する公的助成制度の開始がある。今後、妊孕性温存療法のニーズの増加に応えるべく、個々の症例に合わせた適切な卵巣刺激法の施行が重要であると認識した。

P-95-1 思春期に悪性腫瘍を罹患し卵巣組織凍結保存を施行した2症例

愛媛大附属病院

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【緒言】近年、若年がん患者に対する卵巣組織凍結保存が、わが国でも普及してきている。今回、思春期の患者に対し卵巣組織凍結保存を施行した2症例を経験したので報告する。【症例】症例1:13歳、未妊、未性交、初経11歳。急性骨髄性白血病と診断され、FLT-ITD変異陽性であった。寛解導入療法を施行中に妊孕性温存について当科に相談された。イダマイシン、シタラビン、メソトレキサート、エトポシドがすでに投与され、今後はさらに造血幹細胞移植が計画されていた。血液検査はE₂:<10pg/ml, LH:117.5mIU/ml, FSH:139.0mIU/ml, AMH:0.22ng/mlであった。症例2:15歳、未妊、未性交、初経12歳。右大腿骨限局ユーイング肉腫の術前化学療法に、卵巣毒性高リスクのイホスファミド、シクロホスファミドと、中等度リスクのドキシソルピシン、エトポシドが含まれるVDC-IE療法を施行されている間、妊孕性温存について当科に相談された。術前化学療法が終了し大腿骨の手術を施行する前に卵巣組織凍結保存を希望された。血液検査はE₂:<10pg/ml, LH:66.8mIU/ml, FSH:76.3mIU/ml, AMH:0.40ng/mlであった。【考察】今回卵巣組織凍結保存を施行した症例は、相談した時点においてすでに卵巣機能不全を来していた。また、凍結した卵巣組織に微小残存癌病巣(MRD: Minimal Residual Disease)が混入するリスクは、白血病は高リスク群であり、ユーイング肉腫は中リスク群に分類されており、凍結保存した卵巣を移植することもリスクがある。MRDの検出方法や卵胞の完全体外培養に関する研究の進行も期待されており、今後も症例の蓄積が望まれる。

P-95-2 卵巣移植における微小残存病変再移植のリスク低減を目指した人工卵巣の開発について

聖マリアンナ医大

岩端秀之, 高江正道, 杉下陽堂, 戸澤晃子, 長谷川潤一, 鈴木 直

【目的】卵巣組織内に微小残存病変(MRD)が存在する場合、卵巣移植にはがん細胞が体内に再移入されることによるがん再発への懸念がある。その懸念を払拭する目的で人工卵巣を用いて卵巣から単離した未熟卵胞を生体内へ移植する新たな方法が検討されている。MRDリスクの高い造血器腫瘍や卵巣がんの患者にとって本法の臨床実用化は急務を要する。今回我々はマウス卵胞を用いて適切な人工卵巣デバイスの評価を行った。【方法】天然高分子であるアガロース(A)とコラーゲン(C)を素材とし、作製した人工卵巣デバイスを用いて15-16日齢ICRマウス卵胞を8日間体外培養した。それぞれの素材を用いた培養の経過を卵胞径、タイムラプス(TL)による観察、培養液中エストラジオール(E2)値、採取した卵子を評価し比較検討を行った。【成績】A群と比較しC群で卵胞径の増大が認められた。またE2はC群で8日目まで上昇が認められたが、A群では認められなかった。C群のTL観察では顆粒膜細胞の増加と卵胞径の増大が確認された。観察4日以降で形態が崩壊する卵胞が認められたが、形態崩壊後も顆粒膜細胞の増殖は確認できた。さらにC群から成熟卵子を観察できた。【結論】Cは比較的硬度が低く生体接着性が乏しく硬度の高いAに比べて良好な発育経過を確認することができた。しかし、形態が崩壊した卵胞では長期の生存は困難であり、卵胞に対し最適な圧をかけられるデバイスの作成を検討する必要があると考えられた。本研究の成果は人工卵巣開発に限らず、今まで明かされていない原始卵胞の発育に関する生理学的解明や*in vitro*での卵胞への薬剤毒性の新たな評価方法の開発につながる可能性があると考えている。

P-95-3 白血病モデルマウスを用いた卵巣組織凍結における微小残存病変 (MRD) の評価

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【目的】卵巣組織の凍結保存と移植は、性腺毒性治療後の若いがん患者の妊孕性を温存するための現実的な選択肢である。しかし、凍結保存した卵巣組織に悪性細胞が存在するリスクと移植後の原発性疾患の再発リスクを考慮する必要がある。そこで本研究は、卵巣組織凍結の対象となる疾患の中でもとくに若年層で罹患率が高い白血病を研究対象として、卵巣内の微小残存病変 (MRD) をマウスモデルで評価することを目的とした。【方法】白血病モデルマウスは白血病細胞株を腹腔内あるいは尾静脈への移植により作製した。MRD モデルマウスの卵巣を摘出し、卵巣内の悪性細胞を組織学的解析と qPCR により検出した。さらに凍結保存した MRD モデル卵巣の同所移植により、残存悪性細胞数と再発性との関係を検討した。【成績】組織学的解析の結果、白血病モデルマウスの卵巣には白血病細胞が存在しており、この MRD 卵巣を同種マウスへ移植することで白血病が伝播されることを確認した。また Venus タンパク質標識した白血病細胞株を用いて MRD 卵巣内の悪性細胞数を qPCR により決定した。さらに凍結保存した MRD 卵巣組織の同所移植により再発に必要な最小悪性細胞数を決定した。【結論】白血病患者における凍結保存卵巣組織の自家移植を検討する際の重要な懸念は、がんの再播種のリスクである。今日まで、凍結保存された卵巣組織における白血病細胞の存在を評価する研究はほとんどなく、本研究による卵巣組織の微小残存病変を正確に評価し原発性疾患の最小伝播細胞数を特定することは、白血病患者の受胎能回復に対する大きな進歩となり臨床的にも意義深いと考える。

P-95-4 卵巣組織移植術前における融解卵巣組織の至適培養時間の検討

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【目的】卵巣組織移植術では緩慢凍結が主流であるが、近年より簡便に実施可能な Vitrification 法による凍結が評価されている。Vitrification 法による凍結の安全性や組織生存率の向上を目指すため、融解凍結卵巣組織片の組織生存率を最大化する至適培養時間を検討する。【方法】ウシ卵巣組織片 (10×10×1mm を新鮮組織群と凍結融解群に分けた。凍結融解群ではそれぞれ 15 分、30 分、1 時間、2 時間、5 時間、24 時間と培養液中で融解卵巣を培養した。培養前後の組織片重量と培養液の浸透圧変化を測定し、遺残凍結保護剤を確認した。次に 2 群の培養時間ごとの培養液中 LDH 融解卵巣組織中の ROS Reactive Oxygen Species 測定、そしてアポトーシス、DNA ダメージ、卵胞増殖マーカー、卵巣予備能マーカーを PCR および免疫組織化学染色にて評価を行なった。また、卵巣組織片内にある卵胞の活性を確認するため両群をそれぞれ 0 時間、1 時間、2 時間、24 時間培養し、ニュートラルレッド染色にて卵胞生存率、TMRE 染色にてミトコンドリア膜活性を検討した。【成績】卵巣内遺残 CPA 濃度の検討では、培養 1 時間で低値を示した。また LDH ROS 測定では、新鮮組織群と比較し 0-2 時間培養の間に有意差は認めなかった。一方、ミトコンドリア膜活性の評価では培養 1 時間で膜活性の低下を認めた他、両群間に有意差は認めなかった。【結論】ガラス化凍結を実施した卵巣組織では、卵巣組織移植術の術前 1-2 時間前に卵巣組織融解を行うことが移植片の組織生存率を最大化させる可能性が示唆された。

P-95-5 妊娠成績と原疾患予後調査による卵巣組織移植の有効性と安全性の検証

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【目的】がん患者に対する妊孕性温存療法として卵巣組織凍結 (OTC)・卵巣組織移植 (OTT) が実施されている。本法による生産例は既に 200 を超えたと推測されているが、いまだ臨床研究段階であり、わが国での生産例の報告はない。今回、我々は当院で経験した症例を解析し、本法の有効性と安全性について検証した。【方法】当院で実施された OTT 症例 11 例の背景、移植部位、移植後の月経周期回復や採卵数の変化、妊娠の有無、手術合併症や疾患再発の有無について後方視的検討を行った。【成績】OTT 11 例の原疾患は全例が乳がんで、がん治療前にガラス化法による OTC が施行された。OTC 施行時の年齢は 35.7 ± 3.5 歳であり、がん治療後に OTT が施行され、その年齢は 40.7 ± 3.7 歳で、OTC より平均 5.0 ± 1.3 年後に実施された。OTT 施行時の AMH 値は 0.32 ± 0.40 ng/ml で、2 例が無月経、2 例が月経不順、7 例が月経周期整であった。6 例に異所性+同所性移植、5 例に同所性移植が施行された。移植後平均 36.9 ± 19 か月の観察期間で全例に卵胞発育を認め、月経周期の改善や採卵数の増加を認めた。さらに 4 例が妊娠 (3 回自然、1 回 IUI、2 回 ART) し、2 例で計 3 回の健康児の出産が得られ、2 例で計 3 回の初期流産を認めた。手術合併症はなく、1 例のみが術後 8 年で腋窩リンパ節再発を認めたが、OTT との明らかな関連性は無いと考えられた。【結論】本検討により、OTT による妊娠・出産例が得られたこと、術直後の再発例がないことなどから、OTT の有効性や安全性が示唆された。ただし、疾患や年齢に偏りがあり、さらなる検証が必要と考えられる。

P-95-6 当院で卵巣組織凍結を選択した乳癌症例の検討

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【目的】乳癌は生殖可能年齢の女性に最も多いがんである。出産の高年齢化により、乳癌診断時に出産を経験していない女性が増加している。そのため、乳癌の妊孕性温存療法は重要であり、近年助成金事業も拡充されたこともあり社会的注目度は高くそのデータ集積は急務である。がん治療の開始を遅らせることが困難な場合や思春期前の女兒への妊孕性温存療法として卵巣組織凍結は選択されるが、乳癌の場合には進行例で発見されることが少ないため卵巣組織凍結を選択する機会は少ない。当院では2008年からがん生殖外来を設置しており、卵巣組織凍結を選択した乳癌症例を検討する。【方法】2008年9月～2021年9月までの14年間で卵巣組織凍結のために腹腔鏡下卵巣摘出術を施行した23例のうち、乳癌症例の5例を後方視的に検討した。なお、本法を施行するにあたっては当院倫理委員会の承認を得ている。【成績】年齢中央値は33歳(17-40歳)。初診日から手術までの日数中央値は8日(5-26日)、手術時間中央値52分(40-58分)、出血量中央値10ml(5-57ml)、入院期間中央値5日(4-8日)、転帰は全員生存であり、その後腹腔鏡下卵巣組織移植を施行した症例は1例であった。また5例のうち1例がBRCA2陽性、1例がCowden syndromeであった。【結論】卵巣組織凍結は初診から手術施行までの準備期間が短い、術中術後を通して特にトラブルは認めなかった。ただし、妊孕性温存療法で本手法を選択せざるを得ない進行乳癌症例は好発年齢よりも若年発症であるため、背景に家族性腫瘍がある可能性を考慮して卵巣組織移植をする際に問題となることを情報提供する必要がある。

P-96-1 子宮頸癌に対する妊孕性温存手術(Trachelectomy)後の生殖補助医療の治療成績

歳本ウイメンズクリニック

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【目的】広汎、準広汎子宮頸部摘出術(Trachelectomy)は、子宮頸癌に対する妊孕性温存手術である。同手術を受けた症例で妊娠が成立するためには生殖補助医療(Assisted Reproductive Technology, ART)を含む不妊治療が必要なケースが多いと言われている。しかし、Trachelectomyを受けた後にARTを実施した症例に関する報告は多くない。今回、我々は当院で経験したTrachelectomy後のART症例について検討する。【方法】対象を当院で2012年1月から2021年4月の期間に他院でTrachelectomyを受けた後にARTを実施した12例(広汎6例, 準広汎5例, 単純1例:以下T群)と同等の条件で抽出した手術を受けていない48例をcontrol群(以下C群)に設定し治療成績を検討した。【成績】患者背景、卵巣刺激のゴナドトロピン総投与量などに有意差は認めなかった。採卵数の中央値はT群で9個(1-29)、C群で12個(1-34)と有意差はなかったが、凍結胚数の中央値ではT群で1.5個(0-7)、C群3個(0-8)と有意差が認められた。生児獲得までに要した移植胚の個数の中央値はT群で4個(1-8)、C群で1個(1-8)とT群で多い結果となった。症例あたりの累積妊娠率はT群で67%、C群で75%となった。【結論】子宮頸癌に対して妊孕性温存手術を受けた症例のART成績では、コントロール群に比べて生児獲得までにはより多くの胚を移植する必要があったが、累積妊娠率はコントロール群と比較して遜色のない結果となった。

P-96-2 妊孕性温存検体の長期保管管理体制の必要性について—安全性の担保を志向して

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【目的】がん治療成績の向上に伴い、妊孕性温存療法のニーズは高まっている。体外受精の技術を利用して妊孕性温存療法は実施されているが、検体の保存期間は通常の不妊治療よりも長期になるため、厳格な管理体制が必要である。これまで本邦では凍結保存検体の長期保管に対する大規模な調査は実施されていない。今回、我々は厚労科研究班により全国の妊孕性温存療法実施施設に対して凍結保管体制について調査を行った。【方法】2020年12月～2021年3月に、本学会より医学的適応による妊孕性温存施設認可を受けている130施設にアンケートを送付し回答を得た。施設における保管責任者、検体の保管継続が困難になった場合の対処法、災害時の対策、液体窒素保存容器の管理体制、保存費用、保存期間の更新について調査を施行した。なお、本研究は筆頭演者施設の臨床試験部会で承認され実施した(承認番号:H2020-183)。【成績】回答率は63.8%であった。閉院時の対応は、移送先を決定済みの施設は20.5%、何も決めていない施設が59.0%であった。液体窒素の管理体制は、定期的な日時、時間での補充が83.1%、定期的な残量確認は65.1%、アラーム等の警告システム設置施設は16.9%であった。災害等の非常時の対策の実施施設は70.9%であった。保存期間の更新時の意思確認は、医師が61.4%と最も多く診察時に確認していた。なお、更新時に原疾患治療医とは54.2%が連携していた。【結論】今回の調査で、検体長期保管体制に関する施設間格差等の課題があることが明らかになった。妊孕性温存療法を実施する施設は一定の管理基準が設けられる必要性があり、今後は管理指針等を作成し、日本中に広げていく必要がある。

P-96-3 乳癌術後に投与されたGnRHアゴニスト徐放性製剤の影響下で治療抵抗性OHSSに対しGnRHアンタゴニスト製剤による治療を行った一例

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【背景】ホルモン感受性乳癌患者への術後ホルモン療法は、再発予防のために重要である。ホルモン療法のみであれば妊孕性温存療法は不要だが、今回、術後治療計画がホルモン療法から化学療法に途中で変更された乳癌患者に妊孕性温存療法を行った症例を経験したので報告する。【症例】症例は24歳、0妊0産。術前に初期の左乳痛と診断され、手術2週間後から24週間作用型GnRHアゴニスト徐放性製剤を投与された。その後の病理診断で追加化学療法が必要と判断され、GnRHアゴニスト投与7日後に妊孕性温存療法施行目的に当科紹介となった。ゴナドトロピンが抑制されていることを確認し、GnRHアゴニスト投与13日目から10日間HMGで調節卵巣刺激を行い、12個採卵した。採卵後はレトロゾールとカベルゴリンを投与していたが、腹痛、呼吸困難、多量の腹水と乏尿を伴う重症卵巣過剰刺激症候群(OHSS)を発症し、補液、低用量ドパミン投与、腹水穿刺を行ったが症状は持続した。しかしGnRHアンタゴニスト製剤の経口投与を行ったところ症状は速やかに改善し、術後治療計画への影響は無かった。【考察】GnRHアゴニストは、卵巣に対し下垂体を介した間接的な作用だけでなく、卵巣黄体化顆粒膜細胞に発現したGnRH受容体への直接的な作用を有する。GnRHアゴニスト徐放性製剤は卵巣黄体化顆粒膜細胞への持続的な刺激によりOHSSの原因となったが、GnRHアンタゴニストが症状を抑制したと考えられる。【結論】がん生殖医療への関心が高まる中、妊孕性温存療法が原疾患の治療計画に与える影響は最小とすべきである。GnRHアゴニスト徐放性製剤影響下のOHSSに対するGnRHアンタゴニストの投与は、考慮すべき治療選択肢の一つである。

P-96-4 悪性腫瘍の罹患歴が卵子の発育能力や臨床成績に与える影響

虎の門病院

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【目的】悪性腫瘍の罹患歴が卵子の発育能力に与える影響を検討した。【方法】悪性腫瘍の既往がある女性(症例群)に実施したART52周期と、年齢とBMIを調整した悪性腫瘍の既往がない女性(対照群)のART52周期を比較した。卵子の発育能力、妊娠率および生産率を比較した。【成績】受精卵、分割期胚、良好分割期胚の数は、対照群に比べて症例群では有意に少なかった。また、受精率、および卵母細胞・受精卵それぞれから良好分割期胚への発育率、分割期胚における良好分割期胚の割合も、症例群では対照群に比べて低かった(63, 25, 39, and 43% vs. 83, 36, 50, and 55%)。症例群の胚移植1回あたりの臨床妊娠率および生産率は、対照群に比べて有意に低かった(7.6 and 1.5% vs. 20.4 and 14.0%)。【結論】女性の悪性腫瘍の既往歴は卵子の発育能力の低下と有意に関連していた。妊娠率や生産率の低下について、がん・生殖を行うにあたり患者へ情報提供していく必要があると考える。

P-96-5 妊孕性温存治療の医療連携体制の構築

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【目的】がん治療の進歩にがん治療はがんの治療のみではなく、その後のQOLについても重要視されるようになった。その1つに妊孕性温存治療がある。若いがん患者等が希望をもって病氣と闘い、将来子どもをもつことの希望を繋ぐ取り組みの全国展開を図ることを1つの目的とした小児・AYA世代のがん患者等の妊孕性温存療法研究促進事業が2021年4月より開始し、今後さらに妊孕性温存療法を希望する症例が増加すると考えられる。このため、今回その医療連携体制をどのように構築すべきかその取り組みを含め検討する。【方法】がん治療施設から当院への情報提供書の定型化、連携施設との定期的な会議、2021年度よりAYA世代がん相談情報センターおよび妊娠とがんホットラインの開設を行うことにより、がん治療施設と妊孕性温存施設との円滑な連携がはかっているか検討する。【成績】2021年1月から9月までで精子凍結保存目的での受診数は45例であり、その中で43例(96%)が院外からの症例であった。受診希望から1週間以内に精子凍結での受診となった症例は44例(98%)であった。同時期に妊孕性温存治療を希望または詳細の説明を求めて受診した女性症例は52例であり、その中の33例(63%)で卵子・胚凍結保存を施行した。院外からの症例は17例(33%)であった。受診希望から1週間以内に受診した症例は10例(59%)であった。【結論】がん治療施設から当院への情報提供書の定型化、連携施設との定期的な会議などの医療連携体制の構築により、がん治療施設と当院間での妊孕性温存体制は比較的円滑に行われていると考えられる。今後、他の妊孕性温存施設との連携も含め、さらなる医療連携体制を整える必要がある。

P-96-6 当院における男性患者への妊孕性温存治療の取り組み

東京医大病院

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【目的】精子凍結保存技術の歴史は、1953年に Bunge と Sherman がこの技術を用いて人工授精を行なったのが始まりとされている。医学的適応による精子凍結保存は、性腺毒性を持つ化学療法を要するがん患者で一般的に施行されてきたが、昨今男性の妊孕性温存の適応が自己免疫疾患等の非がん疾患を含めて拡大してきている。当院では2003年から化学療法や性腺摘出による造精機能障害を来す可能性のある思春期年齢以降の男性患者を対象として、精子凍結保存を行っている。今回、当院における男性患者への妊孕性温存治療の取り組みについて現況を報告したい。【方法】2003年5月から2021年9月までに当院に妊孕性温存希望で受診した男性62人を対象とし、患者背景と治療経過を後方視的に調査した。【成績】精子凍結施行例は58症例で、平均年齢は31.8±9.0歳(15-62歳)であった。悪性腫瘍は血液疾患が22例、精巣腫瘍が14例、頭頸部腫瘍は6例、消化器系悪性腫瘍が4例、前立腺癌が3例、脳腫瘍が3例、肺腫瘍が2例、停留精巣が2例、自己免疫性疾患を2例認めた。うち22例が精子凍結保存継続中で、3例が凍結精子を用いて妊娠し、2例が出産まで至った。【結論】精原細胞は思春期以降分裂を繰り返しており、思春期以降にシクロホスファミドの治療を受けた男性の妊孕性喪失のリスクは女性よりも高い。近年、男性患者への妊孕性温存治療の重要性が認識されており、当院においても本治療後に出産に至った症例が2例あった。原疾患の治療が第一優先であるが、今後も個々の症例への迅速かつ適切な治療法の選択を行っていくことが重要であると再認識した。

P-96-7 妊孕性温存目的に精子凍結保存を実施した悪性腫瘍患者271名の転帰

東北生殖医療研究会

高橋俊文, 福原理恵, 横山良仁, 馬場 長, 寺田幸弘, 永瀬 智, 八重樫伸生, 藤森敬也

【目的】悪性腫瘍患者に対して妊孕性温存目的に実施した精子凍結保存の長期予後について明らかにすることを目的とした。【方法】本研究は後ろ向きコホート研究である。対象は、1997年1月から2017年12月に妊孕性温存目的に精子凍結保存を実施した悪性腫瘍患者271名である。精子凍結保存時の患者背景について分析を行い、長期予後として、患者の生命予後、凍結保存精子の使用について、カプラン・マイヤー法を用い累積生存率、累積精子利用率を算出した。【成績】精子凍結保存時の年齢はメジアン値28歳(15~58歳)であった。疾患(n=251)の内訳は、精巣腫瘍84人(33%)、白血病54人(22%)、悪性リンパ腫44人(18%)、骨軟部腫瘍26人(10%)、その他43人(17%)であった。凍結保存前に化学療法が施行されていたのは230人中74人(32%)であった。凍結保存回数はメジアン値2回(0~6回)であった。精液所見は、化学療法実施群と未実施群と比較すると、精液量は両群で有意差(P=0.38)を認めないが、精液濃度(P=0.01)と運動率(P<0.01)が有意に化学療法実施群で低下していた。長期予後：観察期間はメジアン値5.2年(0~20.5年)で、死亡数は252人中48人(19%)であった。累積生存率は、1年(96%)、3年(90%)、5年(84%)、10年(81%)であった。凍結保存精子は271人中28人(10%)に使用され、14人が妊娠(体外受精1人、顕微授精13人)した。累積精子利用率は、1年(1.8%)、3年(2.8%)、5年(5.3%)、8年(10.6%)であった。【結論】この結果は、妊孕性温存希望のある男性悪性腫瘍患者に対して有益な情報提供となり得る。

P-97-1 高度凝固異常を伴う胎児機能不全を発症し、胎盤病理組織検査にて massive perivillous fibrin deposition を認めた COVID-19 合併妊婦の一例

市立広島市民病院

坂井裕樹, 上野尚子, 岩間かれん, 久保倫子, 森川恵司, 植田麻衣子, 片山陽介, 玉田祥子, 関野 和, 依光正枝, 石田 理, 児玉順一

【緒言】COVID-19 合併妊婦の凝固異常や、胎盤の組織学的所見についての検討は十分ではない。今回、高度凝固異常を併発した COVID-19 合併妊婦が、NRFS のため緊急帝王切開術を要し、胎盤病理検査にて massive perivillous fibrin deposition (MPFD) を認めた一例を経験したので報告する。【症例】42歳7妊4産。妊娠32週4日に発熱、咽頭痛が出現、COVID-19 PCR 陽性と判明。呼吸不全なく COVID-19 軽症であったが、発症5日目より行政の方針にて当院隔離病棟に入院。発症10日目より頻回の子宮収縮を認め tocolysis を開始。発症11日目に血小板減少(6.0×10⁹/μL)、発症13日目に高度凝固異常(Fib161 mg/dL, FDP100.4μg/mL, Dダイマー 32.0μg/mL)を認めた。発症14日目に、胎動減少と CTG にて variability 減少を伴う反復性の高度遅発性一過性徐脈を認め、NRFS の適応で緊急帝王切開の方針とした。児は2023g、男児、AS 4/7点、UApH7.277で出生、術中出血量は950ml(羊水込み)、胎盤の肉眼的に赤黒色調を呈しており早期剝離の所見はなかった。術後1日目の全身造影 CT で血栓を認めず、凝固異常は急速に改善していた(血小板 29.2×10⁴/μL, Fib 311 mg/dL, FDP 4.3μg/mL, Dダイマー 2.3μg/mL)。出血・血栓傾向を認めず術後5日目に退院。胎盤病理検査にて、絨毛管腔の著明なフィブリン沈着および栄養膜細胞の壊死を認め、MPFD と診断した。【考察】MPFD は、COVID 合併妊娠の予後不良例で報告されている胎盤病理所見である。本症例は、COVID-19 感染を契機に母体凝固異常を来し、胎盤の絨毛間腔にフィブリンが沈着した結果、NRFS を来したと考えられた。【結語】COVID-19 合併妊娠において、母体凝固異常や NRFS の発症のリスクを念頭に置く必要がある。

P-97-2 遠隔胎児心拍数モニタリングとオンライン診療で管理した COVID-19 陽性妊婦の1例

亀田総合病院

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【緒言】2021年はCOVID-19の感染拡大に伴い、感染妊婦の管理が課題となった。36週以降の感染妊婦は原則入院管理が推奨されているが、病床確保や設備やスタッフの感染管理が問題となる。今回病床確保が困難で、無症状であったことから遠隔胎児心拍数モニタリング（以下遠隔CTG）及びオンライン診療を導入し、在宅での管理を行った。本発表については患者の同意を得た。【症例】40歳、2回の帝王切開術の既往があった。自然妊娠成立後近医にて管理されていた。夫がCOVID-19陽性となり、濃厚接触者のためPCR検査を行なった所陽性となり、当科に対応依頼があった。病床が逼迫し、無症状かつ分娩切迫も認めなかったため36週6日から在宅管理の方針とした。1度当科受診とし遠隔CTG装着指導、全身状態、急変時の対応方法等の確認を行い、以降は自己でのCTG装着及び連日のオンライン診療にて母児状態の管理を行った。10日間の隔離後、既往帝王切開術を適応に38週3日で選択帝王切開術を施行した。手術時間は65分、出血量930ml。児は3524g、アプガールスコア8/9。PH7.365。母児ともに問題なく血栓や呼吸器症状は認めず術後8日目で退院となった。【結論】今回は無症状妊婦を母児状態を評価しながら在宅で管理し得た。感染拡大の状態では病床確保が重要であり、かつ医療従事者の暴露を減らすためにも遠隔CTG及びオンライン診療は有効であると考えられた。

P-97-3 COVID-19 妊婦に対して抗体カクテル療法を施行した2症例

市立伊丹病院

金 美娘, 城戸絵里奈, 福井 薫, 神谷章子, 角張玲沙, 田中江里子, 三好ゆかり, 雨宮京夏

新型コロナウイルス感染症(COVID-19)は妊娠後期に生じた場合は重症化しやすいとされる。今回、当院にて2人のCOVID-19妊婦に対して抗体カクテル療法を施行した経験を得たため経過を含め報告する。症例1は42歳の初産婦で基礎疾患に高血圧症を認めた。妊娠34週時に咳嗽と発熱が出現しコロナPCR陽性と判明した。十分なインフォームドコンセント後、抗体カクテル療法カシリマブ(ロナプリーブ[®])を入院のもと投与した。Infusion reactionを認めず翌日退院となった。退院後症状は軽減したが、隔離期間終了後の妊娠36週に血圧が重症域となり緊急入院後血圧コントロール不良にて緊急帝王切開となった。症例2は30歳の経産婦で、妊娠37週時に鼻汁と味覚異常が出現しコロナPCR陽性と判明した。抗体カクテル療法を希望し症例1と同様に入院下で投与した。副作用なく翌日退院となった。症状は味覚異常のみ継続したがその他の症状悪化はなく経過した。しかし、隔離期間中に陣痛発来し当院はCOVID-19妊婦の分娩は取り扱っていないため感染症指定医療機関病院で経陰分娩となった。当院ではICT医師の先導のもと、これまで妊婦以外の患者に対して抗体カクテル療法を数十例施行し、効果を認め副作用も少ないことを経験していた。妊婦への抗体カクテル療法は禁忌ではなく有益性投与となっているが、当県の感染症指定医療機関病院で妊婦に1例使用していたこと、他の抗体薬ではあるものの欧米では妊婦への投与報告があり、有害事象が生じていないことも踏まえインフォームドコンセントの上使用した。2例と少ないながらも抗体カクテル療法の効果と安全性を感じた症例であった。

P-97-4 COVID-19 罹患妊娠に対する抗凝固療法中に腹直筋下縁巨大筋膜下血腫を生じ緊急手術を要した妊婦の1例

聖路加国際病院

館恵美里, 杉山美智子, 栗山恵里沙, 川野さりあ, 浅見夕菜, 岡田有香, 松岡咲子, 小山田瑞紀, 菅沼牧知子, 斎藤理恵, 山中美智子, 百枝幹雄

【症例】40歳、5妊0産3自然流産1人工流産。体外受精、凍結胚盤胞移植により妊娠に到り、高血圧症・腺筋症合併妊娠として初期より当科で管理していた。また、不育症に対してアスピリン100mgを内服していた。妊娠26週6日COVID-19中等症のため第6病日に入院となった。入院後、緊急帝王切開の可能性を考慮し血栓予防目的にヘパリンカルシウム持続静注を開始し、アスピリンを中止した。同日より子宮収縮増強を認めリトドリン持続点滴を開始した。肝酵素上昇・尿蛋白を認め加重量型妊娠高血圧腎症と診断した。妊娠27週5日(第12病日)酸素需要が増加し、High-flow nasal cannula 40L, FiO2 0.5となったが、第16病日に酸素需要は漸減した。妊娠28週5日より左下腹部痛が出現し、妊娠29週0日夜間、同部位に長径10cm大の腫瘍を認めた。貧血を認めず腫瘍の増大なく、疼痛も軽度であったため経過を診ていたが、妊娠29週2日には疼痛コントロール不良となり、貧血進行を認めた為、緊急手術を行った。術中、腹直筋下縁に筋膜下血腫を認め、血腫除去術・緊急帝王切開術を施行した。児は1533g, Apgar8(1')/9(5'), UapH7.30で経過は良好であった。母体術後経過は良好で、COVID-19の再増悪も認めなかった。血腫を生じた契機は不明であった。【考察と結論】COVID-19中等症以上の患者では抗凝固療法を要するが、予期せぬ出血を来しうる。また、今回は加重量型妊娠高血圧腎症と診断したが、COVID-19合併妊婦では子癇前症候群を呈するという報告があり鑑別を要する。

P-97-5 当院における SARS-CoV-2 陽性妊婦の臨床的検討

泉大津市立病院

田中和東, 野田拓也, 植村 遼, 和田卓磨, 岡嶋晋加, 林 雅美, 長嶋愛子, 中川佳代子, 西尾順子, 石河 修

【目的】SARS-CoV-2 はパンデミックとなり、その感染経路は飛沫感染であると考えられている。現時点で、SARS-CoV-2 が母体から胎児へどのように感染するかは不明である。当院で管理した SARS-CoV-2 陽性妊婦の臨床的特徴について検討した。【方法】2020 年 4 月から 2021 年 10 月までに当院へ受診した、鼻咽頭 SARS-CoV-2 PCR 検査陽性妊婦 14 例を対象とした。発症年齢は、中央値：29 歳 (26~42 歳) で、発症もしくは鼻咽頭 PCR 陽性となった妊娠日数は、中央値 160 日 (62~268 日) であった。発症もしくは鼻咽頭 PCR 陽性となってから分娩までの期間と、臍帯血 SARS-CoV-2 抗体 (ECLIA 法) の抗体価について回帰分析を行った。【成績】14 例のうち、軽症は 10 例、中等症 I は 4 例であった。中等症 I で、受診日に他院へ転院搬送となった 1 例を除いた 3 例に対し、2 例にレムデシビル、1 例にカシリビマブ/イムデビマブ治療を行った。1 例は流産となった。当院で分娩となった 5 例はすべて、経陰分娩となった。分娩時妊娠日数は、中央値 275 日 (271~276 日) で、発症もしくは鼻咽頭 PCR 陽性となってからの分娩までの期間は、中央値 87 日 (8~205 日) であった。出生児の鼻咽頭 SARS-CoV-2 PCR もしくは抗原定量検査は全例陰性であった。臍帯血 SARS-CoV-2 抗体 (ECLIA 法) は、80% (4/5) で陽性であった。SARS-CoV-2 IgG (CLIA 法) 及び SARS-CoV-2 IgM (CLIA 法) は測定した症例すべて陰性であった。発症もしくは鼻咽頭 PCR 陽性となってから分娩までの期間と、臍帯血 SARS-CoV-2 抗体 (ECLIA 法) の抗体価に正の相関関係 ($r=0.95$, $p=0.013$) を認めた。【結論】SARS-CoV-2 陽性妊婦では、待機的に管理することで、母体が産生した抗体が胎児に移行し、出生児に対して有益であると考えられた。

P-97-6 胎児機能不全を呈し緊急帝王切開を施行した COVID-19 の一例

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山内 綾¹, 徳田温子¹, 菅野知佳¹, 山田直史², 児玉由紀², 大塚晃生¹, 寺尾公成¹

【緒言】新型コロナウイルス感染症 (COVID-19) は周産期医療にも様々な影響を及ぼし、母子感染率は 2-3% と推測されている。COVID-19 第 5 波では若年層の感染が多く報告され、妊婦の感染者も急増した。今回、COVID-19 軽症で入院中の妊婦が、切迫早産のため当院に搬送となり、胎児機能不全のため緊急帝王切開術を施行したところ、胎盤に SARS-CoV-2 感染所見を認めたので報告する。【症例】23 歳、2 妊 1 産、妊娠 30 週から発熱があり、SARS-CoV-2 PCR 検査陽性のため入院となった。妊娠 32 週、下腹痛増強のため当院に搬送。胎児心拍数モニタリングで基線細変動の消失、遅発一過性徐脈を認め、胎児機能不全の診断で緊急帝王切開術を施行。児は 1495g の女児、Apgar score 1 点/5 点/8 点 (1 分値/5 分値/10 分値)、臍帯動脈血 pH は 6.915 であった。NICU で集中治療を行った。4 度の脳室内出血を認めたが、痙攣等の神経学的異常所見なく、日齢 49 に退院となった。なお、出生直後、出生 48 時間後、日齢 15 の新生児咽頭ぬぐい液 SARS-CoV-2 PCR 検査は陰性であった。胎盤剖面には白色調の部分が見られ、組織所見では、絨毛間質に好中球や組織球の集簇像が散見された。また、合体栄養膜細胞には核の変性所見を認め、免疫染色で合体栄養膜細胞に SARS-CoV-2 が証明された。【考察】本症例は母体が軽症であったにもかかわらず、胎盤への感染所見を認め、胎児機能不全を呈した。COVID-19 妊婦の管理に関して一石を投じる症例と考え報告する。

P-97-7 COVID-19 妊婦に対するワクチン・抗体薬使用例と非使用例の経験

東京女子医大

松田望帆, 藏本吾郎, 小野澤真弓, 柏崎咲絵, 鈴木正人, 鈴木 崇, 永田怜子, 鈴木優人, 中林 章, 水主川純, 正岡直樹, 田畑 務

【緒言】新型コロナウイルス感染症 (COVID-19) の対策として、ワクチン接種と抗体薬が提示されてまだ日は浅い。我々は、ワクチン未接種で COVID-19 を発症し抗体薬を使用しなかった妊婦と、ワクチン接種後に COVID-19 を発症し抗体薬を投与した妊婦を経験したので報告する。【症例】症例 1: 37 歳 1 妊 0 産、妊娠糖尿病合併妊娠。妊娠 26 週 5 日に発熱、咳嗽、咽頭痛、関節痛を認め当院にて新型コロナ PCR 検査陽性のため入院となった。感染時、ワクチンは未接種であった。投薬はせず症状改善を認め入院 7 日目に退院となった。36 週 1 日の PCR 検査で陽性が持続していたが 4 日後の PCR 検査では陰性が確認され帝王切開ではなく通常管理下に経陰分娩となった。症例 2: 33 歳 3 妊 2 産、SLE 合併妊娠。33 週 3 日に発熱、咽頭痛、嗅覚障害、頭痛を認め前医にて新型コロナ抗原検査陽性のため当院に入院となった。発症時、ワクチンは 2 回接種済みであった。入院 3 日目、カシリビマブ/イムデビマブ投与した。症状改善を認め入院 7 日目に退院となった。36 週 3 日、前期破水で入院したが、PCR 検査は陰性であり通常管理下に経陰分娩となった。【考察】COVID-19 は無症状でも検査の結果により分娩方法が決定されることが多い。感染既往のある妊婦も同様であり、当院では入院前の PCR 検査で陽性であれば帝王切開、陰性であれば通常管理としている。今回経験した症例では、症例 1 は陰性まで 10 週間程度かかり、症例 2 は 3 週間程度で陰性化した。感染後の症状改善は同時期だったが PCR 検査の陰性化の時期は異なった。ワクチンや抗体薬は新型コロナ検査陽性を理由とする帝王切開を回避できると考えられる。

P-97-8 当院産科領域における新型コロナウイルス感染症に対する対応について

愛媛県立中央病院

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【目的】新型コロナウイルスの感染拡大は産科領域においても、妊婦健診、分娩方法、母児管理に影響を与え、多大な負担を強いる状況が続いている。当院は感染症指定医療機関かつ総合周産期医療センターとして新型コロナウイルス感染妊婦、濃厚接触妊婦の対応にあたってきた。地方における新型コロナ対応につき、これまでの状況と今後の課題について検討を行った。【方法】2021年10月までで当院で入院対応した新型コロナPCR陽性妊婦と濃厚接触者となった妊婦について検討した。【成績】当院に入院となった新型コロナPCR陽性妊婦は2名であったが、2名とも重症化することなく、また分娩に至ることなく退院した。濃厚接触者として自宅待機中に分娩に至ったのは3名であった。当院は濃厚接触者の妊婦は経陰分娩の方針だが、2名は経陰分娩し、1名は産科的適応で帝王切開術を施行した。帝王切開術はPCR陽性妊婦に準じて陰圧手術室で行ったが、感染対策のための手順が多く、超緊急帝王切開術などへのスムーズな対応は困難と考えられた。児は母体の状況に応じてPCR検査を施行してから母児同床とした児と、分娩後より母児同床とした児にわかれた。【結論】新型コロナPCR陽性妊婦や濃厚接触者の妊婦は多くはなかったが、分娩には多大な負担がかかり、今後、患者数が増加すると、医療資源に制限がある地方では対応が困難となることが懸念される。妊婦への感染予防への啓蒙と分娩・帝王切開術の更なる手順の見直しが必要と考えられる。加えて今後の流行波に備えて医療体制を整えていく必要がある。

P-97-9 COVID-19により胎児機能不全を認め子宮内胎児死亡に至った一例

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【緒言】COVID-19は血管内皮障害やサイトカインストームによる母体の血栓症や胎盤循環不全が問題となる。今回、軽症COVID-19妊婦が急激な凝固障害を生じた後に、子宮内胎児死亡に至った症例を経験したので報告する。【症例】22歳、2妊1産。妊娠21週にSARS-CoV-2の感染を認め、管理入院となった。入院時、母体は無症状で、血液検査では異常なく明らかな肺炎像も認めなかった。妊娠21週6日に38度台の発熱を認め、妊娠22週1日には、血小板8.6万/μLと低下、D-Dimer 13.3μg/ml, FDP50.0μg/mlと上昇を認めたため、未分画ヘパリン1万単位/日の皮下注射を開始した。妊娠22週3日、胎動減少を自覚するも胎児心拍数モニタリングでは基線160-170bpm、基線細変動中等度、一過性頻脈を認めた。妊娠22週4日、基線細変動が消失し、繰り返す軽度遅発一過性徐脈を認めた。経腹超音波検査では、呼吸様運動、胎動、筋緊張は確認できなかった。同日よりヘパリンCa10000~15000単位/日の持続静脈注射に変更したが、妊娠22週5日、子宮内胎児死亡を確認した。翌日、流産処置を行い、骨盤位にて児娩出となった。児は男児で384g、明らかな外表奇形は認めなかった。児の咽頭スワブのPCRは陽性、臍帯血中・胎盤組織からSARS-CoV-2 RNAが検出された。また、胎盤には高度の変性がみられた。【考察】SARS-CoV-2の垂直感染あるいは母体の凝固障害による胎盤機能不全が子宮内胎児死亡の原因と考えられた。【結語】COVID-19妊娠ではたとえ軽症例であっても慎重な母体管理の上、胎児心拍数モニタリングを含めた胎児機能評価が重要である。

P-98-1 COVID-19感染寛解後早期にワクチンを接種しIUFDに至った妊娠21週妊婦の一例

帝京大ちば総合医療センター

根本一成, 馬場 聡, 前田加奈子, 永井紗恵子, 尾本恵里菜, 山口広平, 足立克之, 五十嵐敏雄, 梁 善光

【緒言】COVID-19感染により流産や死産が増えるという報告はないが、少数ながら母子感染や死産の報告はある。また妊婦に対するCOVID-19ワクチン接種も安全とされているが症例の集積は十分とはいえない。我々はCOVID-19感染寛解後早期にワクチン接種した2日後にIUFDに至った妊娠21週の一例を経験したので報告する。【症例】32歳、2経産、自然妊娠による前置胎盤症例。妊娠19週0日に発熱があり、COVID-19陽性と診断され自宅療養し、妊娠20週5日に解熱した。翌日に少量の性器出血を認め、前医で入院管理して軽快した。妊娠21週2日に本人の希望でCOVID-19ワクチン接種したところ、2日後にIUFDが確認された。同日、当院へ紹介され、妊娠21週6日にPGE2錠による処置により児を娩出した。出血量は225g。児は290g女児で、外表奇形はなく、剖検の希望はなかった。胎児付属物の病理所見では、臍帯は異常なかったが、胎盤は血管低形成による胎盤機能不全の存在が示唆された。なお、その後の血液凝固能検査では異常は認めなかった。【考察】COVID-19罹患患者の胎盤には血管還流障害や血栓形成などの異常がみられるという報告がある。また一般的にCOVID-19罹患既往者に対するワクチン接種は未感染者より副反応が出やすいとされ、英国公衆衛生庁や米国CDCも延期を推奨、容認している。本症例は、胎盤の病理所見からCOVID-19感染やワクチン接種がIUFDの契機になった可能性は否定できない。【結論】COVID-19感染寛解後早期にワクチン接種しIUFDに至った一例を経験した。COVID-19の感染やワクチン接種が原因となった可能性は否定できず、COVID-19感染既往の妊婦のワクチン接種時期については再考する必要性が示唆された。

P-98-2 当院における COVID-19 妊産婦 14 例の診療経験

岡山赤十字病院

江口武志, 道満佳衣, 角南華子, 柏原麻子, 大村由紀子, 高取明正

【緒言】2021年5月の時点では、岡山県では人口10万人あたりの新規感染者数は580人(2021年5月7-13日)、全国4位であり、新規感染者数は高い水準であった。2021年10月の時点では、妊産婦へのワクチン接種が普及して妊産婦の新規感染者数は減少している。新規治療薬の妊産婦への使用も含めてCOVID-19妊産婦・分娩取り扱い病院である当院で経験したCOVID-19妊産婦14例の臨床経過を報告する。【症例】入院時の妊娠週数は24-36週で14例の内訳は、中等症II1例、中等症I7例、軽症6例で、感染経路は家庭内感染が8例であった。中等症II1例は酸素療法、ステロイド療法、抗ウイルス薬(レムデシビル)を投与し、発症から13日目で症状軽快した。中等症Iのうち1例は抗ウイルス薬(レムデシビル)を投与し、発症から6日目で症状軽快した。また中等症Iのうち4例は中和抗体薬(カシリビマブ/イムデビマブ)を入院2日目に投与していずれも3日以内に症状軽快したが、24時間以内に38度以上の発熱、倦怠感が出現して48時間以内の解熱、呼吸器症状の軽減が得られた。中等症Iのうち2例は対症療法で発症から8日目、13日目に症状軽快した。軽症6例は対症療法で発症から平均7.2日目(6-8日目)に症状軽快した。妊娠合併症は、母体発熱に伴い胎児頻脈を認めたが、胎児機能不全を疑う所見は全例で認めなかった。また、妊娠26週に発症した軽症1例で-3.0SD程度の小頭症が新規で出現した。全例で血栓予防を行い血栓症は全例で認めなかった。【結語】岡山県の第5波の特徴として若年者に多く、それにより妊産婦の感染も増加していた。中和抗体薬の出現により発症から早期入院、早期治療を行うことで早期改善と重症化を防ぐ可能性がある。

P-98-3 当院で経験した COVID-19 関連妊婦 30 例の検討

石川県立中央病院

山田野々花, 桑原陽祐, 東 恭子, 田中良明, 黒岩征洋, 平吹信弥, 佐々木博正, 干場 勉

【目的】石川県では2021年9月下旬までに、約8000人の新型コロナウイルス(COVID-19)感染が確認された。当院は県内の周産期医療の中核を担っており、COVID-19感染が疑われる妊婦の多くが当院へ紹介となった。当院でCOVID-19感染が疑われた妊婦30例の臨床背景、妊娠分娩管理について検討した。【方法】2020年8月上旬から2021年9月下旬までに当院で経験した、COVID-19のため特別な管理を要した妊婦30例を後方視的に検討した。【結果】対応開始日時点での平均年齢は29歳であり、妊娠初期が3例、妊娠中期が10例、妊娠後期が17例であった。妊娠後期の患者17例のうち入院したのは14例であり、そのうち当院で帝王切開を行ったのは5例、経膈分娩が2例であった。帝王切開が選択された5例のうち帝王切開の既往がある患者は2例であった。第5波(2021年6月下旬以降)で経験した妊婦は16例で、そのうち抗体カクテル療法を行ったのは10例であった。【考察】抗体カクテル療法が導入されたことで入院後の重症化を防ぐことができ、無症状または軽症例ではホテル療養も可能となった。また、第4波以前では陰性が確認できたとしても経過観察期間が過ぎるまでは全例帝王切開を選択せざるを得ない状況であったが、第5波以降ではゾーニングを工夫しスタッフの精神面も配慮することで経膈分娩を選択することが可能となった。このような症例は未だ数が少ないのが現状であり今後もさらに体制を整えていく必要があると考える。

P-98-4 広島県および当院で入院管理を行った COVID-19 陽性妊婦の検討

県立広島病院¹, 国立呉医療センター・中国がんセンター²中島祐美子¹, 松島彩子¹, 伊勢田侖鼓¹, 山根高史², 加藤俊平¹, 浦山彩子¹, 白山裕子¹, 三好博史¹

【目的】広島県での新型コロナウイルス(SARS-CoV-2)感染症(以下COVID-19)陽性妊婦は、広島県健康福祉局の指導の下、県立広島病院(以下当院)を中心に対応を準備してきた。2021年9月末までの期間における、広島県でのCOVID-19陽性妊婦の感染状況や当院での対応を振り返り検討した。【方法】県内初めてのCOVID-19陽性妊婦を認めた2020年5月から2021年9月の期間における県内症例、また当院に入院した症例を対象として、妊娠分娩経過、当院での対応について診療録を用いて後方視的に検討した。【成績】2021年9月30日までの広島県におけるCOVID-19陽性妊婦は累計134人であり、入院患者は73人(54.5%)であった。このうちの39.7%にあたる29症例が当院に入院し、軽症25例、中等症12例、中等症II2例であった。感染時期は妊娠前期7例、中期10例、後期12例であり、感染経路としては家庭内感染が最も多く13例(44.8%)であった。中等症II2例にはステロイド投与を行い、その他の症例は対症療法と、Dタイマーが3μg/ml以上の場合はヘパリン療法を施行した。入院中に分娩となった8例は、全例帝王切開術を施行した。7例が妊娠36週以降であり、帝王切開の適応はCOVID-19適応5例、胎児機能不全1例、既往帝切1例であった。また35週で感染診断され切迫早産であった1例も帝王切開を行った。出生した児はNICUに入院し母児隔離としたが、児の生後2回のPCR検査結果は全例陰性であった。【結論】妊婦は罹患しても治療に使用できる薬剤が限られており、感染予防が重要である。ワクチン接種妊婦が増加傾向となっているが、これまでの当院入院患者、そして今後の症例の治療、妊娠経過について文献的考察も含めて報告する。

P-98-5 当院にて管理した COVID-19 感染妊婦の臨床像

沖縄県立中部病院

大畑尚子, 小松泰生, 田所宏樹, 林 伯宣, 青木大芽, 金城国仁, 橋口幹夫

【目的】沖縄県は人口あたりの COVID-19 罹患者が多い地域であり, 学会医会対策チームと県対策本部周産期リエゾンが協働し妊婦陽性者対応スキームを作り対応を続けている。当院はトリアージ及び療養調整を担当し, 周産期センター内の陰圧室を使用して多くの陽性妊婦に対応しており, その臨床像を検討した。【方法】2021年9月末までに当院にて対応した COVID-19 罹患妊婦に関して, その臨床像や療養経過を診療録より後方視的に検討した。【成績】対象期間の県全体の妊婦陽性者は409名であり, 当院は189名に対応した。療養形態は自宅療養及び宿泊療養109名, 入院管理68名, 分娩管理12名, 流行時期別では第1~4波で80名, 第5波で109名であった。第1~4波では軽症79%, 中等症21%であったが, 第5波では軽症68%, 中等症32%となった。第1~4波では軽症者の67%, 第5波では88%が自宅療養となり, 連日電話体調確認を行った。分娩管理は12例あり, 9例は正常, 3例は早産期であった。分娩様式は経陰分娩7, 緊急帝王切開4(NRFS 3, 母体重症 HDP 1), 選択的帝王切開1であった。妊娠37週以降の陽性者17名のうち8名は待機的管理にて分娩前に隔離解除となった。【結論】沖縄県においては第3波より症例を選んで妊婦の自宅療養サポートを行ってきた。第5波においては, 県内の他協力医療機関との役割分担にてより重症例を当院で対応することとなった。経陰分娩や妊娠37週以降の待機的管理は院内各部署の緊急分娩対応への全面的な協力が不可欠である。

P-98-6 妊娠36週以降に診断された新型コロナウイルス感染妊婦の周産期臨床像に関する検討

国立埼玉病院

福武麻里絵, 松田亜季, 白根照見, 世良亜紗子, 河村 佑, 岩佐尚美, 境 委美, 藤岡陽子, 和田美智子, 樋野牧子, 倉橋 崇, 服部純尚

【目的】妊娠後期は新型コロナウイルス感染症 (COVID-19) が重症化するリスク因子であることから, 慎重な周産期管理が求められる。しかし, 現状では感染妊婦の分娩様式に一定の指針はない。今回我々は, 妊娠36週以降に COVID-19 と診断された妊婦の周産期臨床像について分娩様式を中心に検討した。【方法】2020年1月から2021年9月までに当院で入院管理した感染妊婦61例のうち, 妊娠36週以降に診断された21例を対象とした。当院では産科的適応に準じて分娩様式を決定しているが, 医療従事者の業務軽減を目的とした帝王切開 (COVID-19 適応) も許容している。【成績】初産婦3例, 経産婦18例であり, 重症度は軽症が20例, 中等症IIが1例であった。診断週数中央値は38 [36-40] 週, 分娩週数中央値は39 [37-40] 週であった。分娩様式は経陰12例/帝王切開9例 (産科的適応5例, COVID-19 適応4例), 感染重症化による帝王切開はなく, 重篤な周産期合併症は認められなかった。出生時体重中央値は3155 [2672-3668] g, Small for Gestational Age 児はなかった。臍帯動脈血 pH 7.15 未満は1例, 新生児感染・死産・新生児死亡はなかった。隔離期間中の分娩は17例 (81%) であり, 分娩様式は経陰9例/帝王切開8例, 経陰分娩の分娩所要時間の中央値は252 [121-742] 分であった。【結論】妊娠36週以降に感染診断された全症例で, 母児の周産期予後は良好であった。当院では, COVID-19 妊婦の病床数拡充や新生児科との連携により急増する患者数に対応が可能であった。また, 隔離期間中であっても医療体制や患者状態に応じて分娩様式を選択可能であると考えられた。今後, 集積されたデータをもとにした分娩様式の議論が期待される。

P-98-7 当院における新型コロナウイルス感染妊婦の検討

大阪医科薬科大病院

井淵誠吾, 澤田雅美, 塩見まちこ, 入江惇太, 夏山幸一郎, 増田ゆうき, 森田奈津子, 上田尚子, 寺田信一, 藤田太輔, 大道正英

【目的】新型コロナウイルス感染症は, 妊婦に感染した場合, 重症化リスクが高いことが報告されている。しかし本邦における, 感染妊婦の詳細な経過については, 受け入れ施設からの報告が待たれている。今回, 当院で管理を行った, 新型コロナウイルス感染妊婦の詳細な経過を明らかにし, 管理方法について言及する事を目的とし, 検討を行った。【方法】2021年8月25日から10月21日までに当院の妊婦コロナ ICU にて管理を行った, 新型コロナウイルス感染妊婦27例について, 入院後経過, 分娩経過, 新生児予後を後方視的に検討した。【成績】平均年齢は30.1歳であり, 胸部 CT 検査で肺炎像を認めた例は, 18例だった。入院時の重症度は, 軽症19例, 中等症 (I) 2例, 中等症 (II) 6例だった。軽症例の内, 発症から7日以内だった11例には, 抗体カクテル療法を行い, その内1例が経過中に中等症 (I) へ悪化した。入院時, 中等症以上だった8例中, 発症から7日以内だった7例には, レムデシベルを投与し, 重症化例はなかった。Nasal High Flow が必要だった例は2例であり, 人工呼吸器を要した例はなかった。10例が, 隔離期間中に分娩となり, 7例が経陰分娩, 3例が帝王切開だった。帝王切開3例の適応は, 2例が既往帝王切開の陣痛発来で, 1例は陣痛発来後の胎児機能不全だった。早産例はなかった。新生児への垂直感染は認めなかった。【結論】新型コロナウイルス感染妊婦の管理について, 抗体カクテル療法やレムデシベル投与の方法など, さらなる議論の余地がある。今回, 産婦人科, 呼吸器内科, 感染症内科などの多職種が連携して, 治療方針を決定し, 積極的に治療を行ない, 良好な結果を得ることができた。

P-98-8 当院における軽症および中等症の新型コロナウイルス感染妊産婦 151 例の検討

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【目的】2020年1月に国内で初めて新型コロナウイルスによって引き起こされる新型コロナウイルス感染症 (COVID-19) の患者が報告されて以降, 当院では軽症および中等症の COVID-19 妊産婦の受け入れを行っている。これまで当院に入院した COVID-19 妊産婦について検討したため報告する。【方法】2020年4月~2021年9月までに COVID-19 と診断され入院した 151 例の妊産婦を対象とした。統計学的手法は Fisher の正確確率検定を用い, $p < 0.05$ を有意差ありと判断した。【成績】150 例は妊婦, 1 例が褥婦であった。年齢中央値 (四分位範囲) は 31 歳 (26-34 歳), 陽性判明時の妊娠週数は 23.6 週 (14.2-30.0 週) で妊娠 1・2 三半期が 90 例, 妊娠 3 三半期・産褥期が 61 例, 入院日数は 8 日 (6-9 日) であった。軽症は 123 例, 中等症は 28 例であった。症状は咳嗽が 91 例, 発熱が 86 例, 倦怠感が 40 例であった。胸部レントゲン写真で肺炎像を認めたのは 21 例であった。また 17 例が無症候であった。13 例で緊急帝王切開術を行い, そのうち妊娠 37 週未満の早産は 3 例で, 1 例は産科適応, 2 例が感染理由であった。出生児の感染はなかった。治療は酸素投与が 23 例, レムデシビル投与が 15 例, プレドニゾロン内服が 18 例, 抗凝固薬投与が 31 例, 中和抗体薬の投与は 3 例に行われた。酸素投与例とレムデシビル投与例 (重複あり) は, 妊娠 3 三半期・産褥期が妊娠 1・2 三半期と比較し有意に多かった ($p < 0.05$)。3 例が重症化し転院となった。【結論】当院に入院した COVID-19 妊産婦の検討では, 妊娠後期の妊産婦が妊娠前半と比較し重症化するリスクが高い可能性が示唆された。妊娠後期では感染予防対策を徹底し早期入院加療の体制を十分に整える必要があると考えられる。

P-99-1 当院で経験した妊娠中の COVID-19 陽性症例 16 例の報告

ベルランド総合病院

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【目的】当院での COVID-19 スクリーニング検査体制と, 当院で経験した妊娠中の COVID-19 陽性症例 16 例の周産期の転帰を報告する。【背景】当院の COVID-19 スクリーニング検査は, 予定入院患者は入院前日に唾液による PCR 検査 (LAMP 法) を実施し, 緊急入院もしくは有症状者は鼻咽頭ぬぐい液の抗原定量検査を実施している。【方法】2020年12月から2021年10月までに当院で経験した妊娠中の COVID-19 陽性症例を対象として, 電子カルテにて後方視的に患者情報を抽出した。【結果】対象となった COVID-19 陽性症例 16 例のうち, 入院時のスクリーニング検査で判明したのは 3 例, 健診時に症状があり判明したのが 1 例, 他院で判明したのが 12 例であった。発症時期は妊娠初期が 2 例, 妊娠中期が 4 例, 妊娠後期が 10 例であった。有症状が 14 例, 無症状が 2 例であった。感染経路は家庭内感染が 6 例, 感染経路不明が 10 例であった。重症度は軽症が 6 例, 中等症 I が 2 例, 中等症 II が 1 例, その他 7 例は追跡はできていなかった。COVID-19 陽性妊婦を介した二次感染例は認めなかった。分娩時に COVID-19 陽性であった症例は 4 例であり, 分娩様式は経陰分娩が 3 例, 帝王切開分娩が 1 例であった。分娩直後から母子分離を行っており, 搾乳による母乳栄養を行っていた。新生児は NICU 入室時および日齢 3 に鼻咽頭ぬぐい液の抗原定量検査を実施しており, COVID-19 陽性例は認めなかった。【結論】当院で行っているスクリーニング検査で COVID-19 陽性妊婦を早期に発見することができ, 2 次感染を予防することができた。2021年10月現在, 16 例のうち 9 例が分娩に至った。9 例すべてにおいて, 周産期の転帰が悪化したものはなく, 新生児への感染も認めなかった。

P-99-2 当院における新型コロナウイルス感染妊婦 67 例の周産期管理について

琉球大学病院

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【目的】沖縄県では, 新型コロナウイルス感染症が若年者へ拡大したことから, 妊婦の感染者が急増し, NUCU を含めた病床確保に対して周産期医療連携で対応した。当科において管理した新型コロナウイルス感染妊婦の特徴と妊娠転帰を評価することを目的とした。【方法】2020年7月から2021年9月までの期間, 当科で管理した新型コロナウイルス感染妊婦 67 例を対象とした。妊婦は原則入院, 37 週以降は帝王切開の方針とし, 出生した児は濃厚接触者として NICU で隔離, 人工栄養とした。【成績】年齢と感染時週数の中央値はそれぞれ 30 歳 (18-44) と 31 週 (5-40) であった。新型コロナ感染症の重症度は, 軽症 40%, 中等症 I 48%, 中等症 II 11%, 重症 1.5%, 自宅療養中に悪化して入院となったのが 12% であった。軽症と中等症 I (A 群), 中等症 II と重症 (B 群) の 2 群間比較では, BMI (24.6 vs 27.7) と初診時 CRP (1.66 vs 3.78) は有意に B 群で高値であった。16 人に分娩管理を行い, 帝王切開が 81%, 早産を 37.5% に認め, その原因は陣痛発来 3 例 (36, 28, 24 週), 胎児機能不全 2 例 (32, 36 週), 肺炎重症化 (34 週) 1 例であった。濃厚接触者として自宅療養中に陣発し, 自宅分娩になりかねなかった 24 週の症例, 陰圧室で破水し, 医療者に濃厚接触者が発生した 28 週の症例など, 想定外の事象に新たな方針決定を迫られることが次々に発生した。【結論】中等症 II 以上では BMI, 初診時 CRP が高い。新興感染症パンデミックにおける母子管理は, 周産期医療連携のもと, 次々に発生する想定外の事象に対する速やかな決断と対応が重要である。

P-99-3 当院における SARS-CoV-2 陽性妊婦の周産期管理の経験

トヨタ記念病院

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【目的】妊娠中の severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) 感染は早産のリスクとされ、妊娠後期は coronavirus disease 2019 (COVID-19) 重症化のリスク要因と考えられ、COVID-19 と診断された妊婦は感染症に対応できる病院での周産期管理が推奨されている。感染症指定医療機関ではない当院において周産期管理を行った SARS-CoV-2 陽性妊婦について後方視的に検討した。【方法】2020年7月から2021年9月までに当院で周産期管理を行った SARS-CoV-2 が陽性であった妊産婦17例を対象とした。年齢、陽性が判明した週数、COVID-19の重症度、周産期経過、新生児の SARS-CoV-2 検査の結果について検討した。【成績】17例の平均年齢は30.0歳で SARS-CoV-2 陽性が確認された時期は、第1三半期が4例、第2三半期が6例、第3三半期が7例であった。軽症14例、無症状3例であった。周産期合併症として、妊娠糖尿病が3例、切迫早産が1例、preterm PROMが1例、PROMが1例あった。これまでに17例中13例が分娩に至った。13例中11例は隔離解除後に陣痛が来し、10例が経陰分娩となり、1例は産科的適応により帝王切開となった。残りの2例は分娩直前に SARS-CoV-2 陽性が確認され、帝王切開後に隔離管理となった。第3三半期に SARS-CoV-2 陽性となった母体から出生した新生児7例の SARS-CoV-2 検査はいずれも陰性であった。【結論】感染症指定医療機関でなくても感染対策に留意し SARS-CoV-2 陽性妊婦の周産期管理を行うことは可能であった。

P-99-4 COVID-19 陽性妊婦の感染隔離入院中の経陰分娩の試み

豊中病院

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【緒言】当院は大阪府北摂地域における基幹病院および第二種感染症指定医療機関であり、当科は地域周産期母子医療センターの役割を担っている。COVID-19 流行初期より大阪府入院フォローアップセンターからの要請を受けて軽症から中等症の COVID-19 陽性妊産婦の入院管理を行ってきた。妊産婦の受入に際し、COVID-19 感染患者専用病棟内に産科病床最大3床と分娩室1室を設け、感染対応可能な陰圧手術室を1室準備した。また、他科や多職種と連携しシミュレーションを行い、体制を整えた。【症例】当院では2020年3月から2021年9月までに計50症例の COVID-19 陽性妊産婦の入院を受け入れ、入院中の分娩としては、帝王切開7例、経陰分娩11例を経験した。感染病棟内で急速な分娩進行を認め経陰分娩に至った症例を経験し、経陰分娩対応の体制作りの一助となった。当院では妊娠週数、全身状態、分娩所要時間の予測、隔離解除までの予想日数などから、分娩様式の見直しや妊娠継続のまま待機的管理可能かについて症例毎に検討した。経陰分娩と帝王切開術の比較では、経陰分娩の方が分娩所要時間は長くなるものの、術後管理は不要で入院日数を短くすることが可能となった。【考察】COVID-19 のワクチンや治療薬の普及に伴い、COVID-19 陽性妊産婦の入院・分娩管理方針が今後変わっていくことが予想される。当院では COVID-19 陽性妊婦の経陰分娩にも対応できるような体制を整えることで、分娩時期や分娩様式について産科的適応に準じた管理を行うことが可能となった。当院での COVID-19 陽性妊婦の感染隔離入院中の経陰分娩の試みについて、文献的考察を加え報告する。

P-99-5 当院における COVID-19 陽性妊婦の分娩管理について

国立三重中央医療センター

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【目的】三重県では、COVID-19 陽性妊婦の分娩は感染症対策のしっかりした周産期センターが担う方針とし、三重中央医療センターがそのほとんどを管理してきた。今後の感染拡大に備える目的で、第5波までの分娩症例について検討した。【方法】2020年3月から2021年9月末までに当院で管理した COVID-19 陽性妊婦53例のうち、分娩に至った11例を対象とした。母児の診療録を参照し、後方視的に検討した。【結果】感染の第1波・第2波では感染管理中に分娩に至った症例はなく、第3波・第4波で4例、第5波で7例の分娩管理を行った。第3・4波では、1例は母体の肺炎増悪のため35wでC-S、2例は COVID-19 感染管理のために選択的C-Sを行い、1例のみ経陰分娩となった。妊娠中に胎児心拍モニタリングの異常がみられた症例はなかった。第5波では、COVID-19 感染によると思われる22wでのIUFD症例が1例あり、この症例のみ経陰分娩となったが、他の6例はC-Sを行った。母体は無症状だが、胎児頰脈の持続のために緊急C-Sを行った症例と、遅発一過性徐脈の反復がみられた症例があり、第5波では、7例中1例がIUFDとなり、2例にNRFSの所見がみられた。また、1例はC-S後に母体が重症化し、人工呼吸器管理となった。【結論】デルタ株では、母体の重症化リスクだけでなく、胎盤機能・胎児にも COVID-19 が影響している可能性が示唆された。胎児 NRFS の可能性を考慮して、妊婦は全例入院管理、分娩は原則C-Sとしたが、今後、新たな変異株が出現した場合も、胎児の well-being についても評価し、慎重な管理が必要であると考える。

P-99-6 当院での COVID-19 陽性妊婦の検討

大阪市立十三市民病院
沖 絵梨

行政の指導により 2020 年 5 月 1 日より当院が国内で初めての新型コロナウイルス感染症 (COVID-19) 専門病院となって以来、我々は産科診療休止を余儀なくされ、呼吸器内科医として COVID-19 陽性患者を診療する傍ら、COVID-19 陽性妊婦の対応にもあたってきた。当院では 2020 年 8 月から 2021 年 10 月 15 日までの間に計 80 例の COVID-19 陽性妊婦の治療を行った。これは COVID-19 での全入院患者 1491 名の約 5.4% にあたる。感染時期としては妊娠中期 (14 週-27 週) の感染が 42.5% と最も多く、感染経路は 47.5% が家庭内感染であった。しかし 2020 年 4 月以降の第 4 波・第 5 波となるにつれ、感染経路不明の症例の割合が増加する傾向を示した。また、第 4 波・第 5 波では入院時 37.5 度以上の発熱を認める症例や、血液検査にて CRP が高値である場合には胸部 CT を撮像し、肺炎像を認めた中等症 I の 12 例にはレムデシベルの投与を行い、軽症の 1 例に重症化予防のためカシリビマブ/イムデビマブの投与を行った。また COVID-19 陽性妊婦受け入れ開始後、5 例が呼吸状態悪化にて、4 例が切迫早産にて高次医療機関への転院を要しており、産直体制の無い当院での妊娠管理に苦慮することも多かった。COVID-19 陽性妊婦の疫学・治療・重症化因子 (CRP, LDH, リンパ球数, フェリチン, TARC (COVID-19) など) につき当院での症例・治療経験をもとに若干の文献的考察を含め検討・報告する。

P-99-7 当院における COVID-19 妊婦の傾向と県内における対応の変遷

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【目的】COVID-19 感染者の増加に伴い、県内でも COVID-19 妊婦が急激に増加した。今回、当院で入院管理を行った COVID-19 陽性妊婦の傾向、さらに第 5 波における県内の COVID-19 妊婦の入院受け入れ態勢について報告する。【方法】2020 年 3 月 1 日から 2021 年 9 月 30 日までに県内で発生した COVID-19 陽性妊婦 89 例のうち、当院で入院管理を行った 53 例を対象とし、診療録を参照して後方視的に検討した。【成績】COVID-19 妊婦の国籍は、日本人 36 例 (67.9%)、外国籍 17 例 (32.1%) であった。年齢内訳は、10 代 1 例 (1.9%)、20 代 29 例 (54.7%)、30 代 22 例 (41.5%)、40 代 1 例 (1.9%) であった。第 1 波～第 4 波までの COVID-19 妊婦は 23 例、軽症例が多く、中等症 I が 4 例 (17.4%)、中等症 II が 1 例 (4.3%) であったのに対し、第 5 波のみで 30 例の COVID-19 妊婦が入院管理となり、中等症 I が 14 例 (46.7%)、中等症 II が 1 例 (3.3%)、重症が 1 例 (3.3%) であった。県内では、当初 2 施設で COVID-19 妊婦を管理していたが、第 5 波で感染症病床が逼迫したため、急遽受け入れ病院を 5 施設に増やした。また、専任の産婦人科医師が県の調整本部から直接連絡を受けてコーディネートし、関連病院が参加するテレビ会議で、毎日各施設の状況を情報共有した。COVID-19 妊婦は自宅療養者も含めて、全例産婦人科医師が把握し、直接管理した。【結論】COVID-19 妊婦は、危機意識が低いと思われる外国人・若年者の感染者が多くなり、家族も含めた患者教育が重要と考えられた。第 5 波では患者数の急増に加え、中等症以上の症例が多かったが、県内の産婦人科医師の連携と、柔軟な対応で危機を乗り切ることができた。今後同様の事態が発生した際にも活用可能と考える。

P-99-8 コロナ禍における妊産婦の生活の変化による周産期予後の検討

大阪医科薬科大病院
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【目的】本邦では Covid-19 の感染拡大に伴い 2019 年 3 月から始まった緊急事態宣言から、不要不急の外出を避けた自粛を呈されてきた。今回、我々はコロナ禍における妊産婦の生活の変化による周産期予後の検討を行ったので報告する。【方法】コントロール群 (2019 年 1 月～12 月) とコロナ禍群 (2020 年 8 月～2021 年 7 月) に当院で妊娠 22 週以降に分娩となった単胎妊娠を診療録より抽出し、周産期予後 (エジンバラ産後うつ評価を含む) について後方視的に検討した。【成績】コントロール群とコロナ禍群はそれぞれ 405 例と 397 例であった。分娩時年齢の中央値 (範囲) は 33.0 (12-47) 歳と 33.0 (18-43) 歳であった。母体搬送はコロナ禍群 (12.0%) がコントロール群 (17.0%) より有意に少なかった ($p < 0.05$)。また、胎児発育不全 (7.1% vs 5.0%, $p < 0.05$)、分娩時出血量 (中央値, 範囲) (590 (70-3900) g, 700 (10-7000) g, $p < 0.01$) で有意に差を認めた。また、羊水過多においてコロナ禍群 (1.5%) でコントロール群 (0.5%) より多い傾向にあった ($p < 0.1$)。1 か月検診時のエジンバラ産後うつ評価は両群に有意な差を認めなかった。【結論】当院のコロナ禍と以前の検討結果は、コロナ禍での母体搬送の減少が関与している可能性があるが、胎児発育不全の減少および羊水過多が多い傾向にあることは、妊婦の外出自粛による影響がある可能性があると考えられた。コロナ禍における妊婦の行動変容が、どのような原因で周産期アウトカムに影響を与えたのかについては引き続き検討していきたい。

P-99-9 当院で入院管理した COVID-19 罹患妊婦の医療圏を越えた受入状況の後方視的検討

都立多摩総合医療センター

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【目的】当院では2020年3月よりCOVID-19罹患妊婦の対応についてマニュアルを作成し、産科医が主治医となって受け入れを行ってきた。妊婦の搬送調整困難例があるなか、二次医療圏および都県境界を越えて受け入れた症例があった。妊婦と妊婦以外の全症例で医療圏を越えた受け入れ状況に差があるか検討することを目的とした。【方法】2021年4月～2021年9月までに当院に搬送依頼があった妊婦と妊婦以外のCOVID-19罹患症例について、後方視的に検討した。入院した妊婦症例は産科で全例把握しており、リストをもとに検討した。妊婦以外の症例は当院COVID-19患者受け入れ決定リスト、キャンセルリスト、入院症例リストをもとに、COVID-19診断時期、居住地域を収集した。妊婦と非妊婦の医療圏内外受入人数の割合の比較は χ^2 乗検定をもちいた。【成績】同期間当院で入院対応した妊婦は59例であった。二次医療圏内からの症例は39例(66%)、二次医療圏外からの症例は20例(34%)であった。妊婦以外の受け入れは同期間855例で二次医療圏内から666例(78%)、二次医療圏外から189例(22%)であった。妊婦のほうが二次医療圏外からの受け入れ割合が多かった($p=0.02$)。同期間のCOVID-19罹患妊婦の受け入れ数の増加は社会全体の流行と概ね一致した。【結論】当院では妊婦は妊婦以外の全症例と比較して二次医療圏外からの受け入れが多く、医療圏内での受け入れ調整困難例が多かった可能性がある。感染爆発の状況下においては、産科主体での受け入れ調整が必要と考えられた。

P-100-1 新型コロナウイルス感染症蔓延の母乳栄養への影響についての検討

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【目的】新型コロナウイルス感染症の世界的蔓延により、人と人との関わりが制限され、里帰り分娩や立ち会い分娩、母親学級や両親学級などが多くの施設で中止された。当院では母乳育児を積極的に支援しているが、パンデミックによる環境変化が母乳育児にもたらしている影響について検討した。【方法】2020年に当院で出産した単胎、正期産の妊産婦における退院時、産後1か月健診時での栄養法について、診療録に基づき後方視的に検討した。新型コロナウイルス感染症の流行との関連性を分析するため、退院時と産後1か月時点における母乳栄養をそれぞれ目的変数として2つの多変量ロジスティック回帰分析を行った。共変量として年齢層、初産・経産、分娩様式、入院有無を調整し、分娩月ごとのオッズ比と95%信頼区間を算出した。産後1か月における母乳栄養に関する回帰分析には退院時母乳栄養も共変量に加えた。【成績】地区陽性者が最少であった1月と比べ、6, 8, 10, 12月は退院時母乳栄養に対するオッズ比が有意に低く、3, 5, 7, 10, 11月では1か月健診時母乳栄養に対するオッズ比が有意に低かった。なお、1か月健診時母乳栄養に対する退院時母乳栄養のオッズ比は10.3(95%信頼区間7.7-13.9)だった。【結論】地区陽性者数の推移と母乳栄養には関連があると考えられた。1か月健診時の母乳栄養は退院時母乳栄養の影響を強く受けており、入院中からの母乳育児支援が重要と考えられる。感染対策により対面でのカウンセリングや支援の機会が減少しており、退院後はオンラインでのサポートを積極的に行うなどの継続支援が求められる。

P-100-2 COVID-19 妊婦の転帰予測因子の検討

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【目的】新型コロナウイルス感染症(COVID-19)の流行に伴う医療の逼迫は喫緊の課題である。限られた医療資源を効果的に利用するためにはCOVID-19症例の転帰を予測する必要があるものの、妊娠中の重症化予測因子は明らかではない。そこで本研究では妊娠中のCOVID-19における医療介入の必要性を予測する因子を明らかにすることを目的とした。【方法】2020年4月から2021年6月16日までに当院で入院加療したCOVID-19妊婦を後方視的に検討した。補液、酸素投与、ステロイド投与、帝王切開術のいずれかを行った症例を介入群、いずれも行わなかった症例を非介入群とした。症状出現日を発症0日とし、0～3日、4～6日、7日以降に分けて、両群間の臨床所見を比較した。【成績】当院に入院した妊婦は42例で、介入群と非介入群はそれぞれ21例ずつだった。年齢・妊娠週数・既往歴の有無について両群間に有意差を認めなかった。発症初期の発熱を介入群21例、非介入群10例で認めた($p=0.007$)。血液検査値では、発症4～6日目のCRP値の予測確率が最も高く(AUC=0.913)、カットオフ値を1.28 mg/dLとした時の医療介入の有無に対する感度は81.25%、特異度は100%だった。【結論】発症初期の発熱および発症4～6日目のCRP値はCOVID-19妊婦の医療介入の必要性を予測する因子になる可能性が示唆された。

P-100-3 新型コロナウイルス感染症に対する当院の産科病棟での対応

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【目的】2019年12月に発生した新型コロナウイルス感染症(以下, COVID-19)は, 中国湖北省武漢市を発端とし世界的な大流行に発展し, 本邦でも本年10月時点で総感染者数は170万人を超え, 死亡者は18000人を超えている。第5波ではCOVID-19の爆発的な感染拡大によって, 連日, 多くの都道府県で若い世代を中心に新規感染者数が増加した。新規感染者数の推移と並行して, COVID-19陽性妊婦も急増し, 一般産科病棟でも対応せざるを得ない状況であったと考える。当院では昨年8月より迅速抗原定量検査を導入し, 本年2月より入院時に全例検査が開始となった。産科病棟でクラスター発生子防を目的に当院で行っている, COVID-19陽性例や抗原定量検査結果未判明症例の分娩対応方法を検討したので報告する。【方法】【成績】当院においてもCOVID-19陽性妊婦, 検査結果未判明妊婦の分娩に対応する体制を整えた。抗原定量検査開始後現在までの分娩件数は254件あり, その内51件の抗原定量検査が行われ, 分娩前に1件の陽性が判明した。検査結果未判明の段階ではゾーニングされた分娩室, 陣痛室への徹底した隔離と感染防御を行っており, 院内感染は認めず陽性妊婦は搬送となった。また, 2件が分娩時に結果未判明であったためゾーニングされた分娩室での分娩となった。現時点では前述の1件を除き陽性者は確認されており, 感染の拡大なく治療・看護の継続が図れている。【結論】施設ごとに院内の構造や人員の関係で, 一律の方策は立てがたいと思われるが, COVID-19陽性妊婦の非受け入れ施設においても, 診療体制を工夫することでより安全な分娩管理につながる可能性がある。

P-100-4 COVID-19流行がもたらした影響～当院における変化と, COVID-19感染妊婦診療の実際～

日赤医療センター

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【目的】COVID-19流行に伴い, 長期間の外出自粛や心理的ストレスなど妊婦を取り巻く環境が大きく変化した。当院における変化と, 感染妊婦診療の実際を報告する。【方法】緊急事態宣言が発令された2020/4/7を妊娠成立日とした分娩予定日は2020/12/31であることから, COVID-19流行が影響した2021/1/1～2021/10/20の妊娠22週以降の分娩(死産, 母体搬送症例を除く)1401例に関して, 患者層, 分娩週数, 産科疾病への罹患, 出生児の特徴, 分娩方法について2015/1/1～2019/12/31の分娩13941例と比較検討を行う。またCOVID-19感染妊婦の診療指針と分娩様式, 感染対策について紹介し, 新規感染症流行時の対策について考察する。【成績】2021年の分娩数は37%減少し, 過去5年と比較して初産婦が減少(48.3 vs 57.2%)した。初産婦において, 早産は上昇傾向(8.7 vs 6.8%)にあり, 妊娠糖尿病は減少(3.4 vs 5.8%)した。経産婦においては, 帝王切開率が上昇(28.8 vs 23.1%)した以外に変化がなかった。当院では36名のCOVID-19感染妊婦の診療を行った。肺炎, 酸素需要の有無によって治療方針をアルゴリズム化した。治療期間中の分娩に関しては, 重症例は帝王切開としたが, それ以外は産科的適応がなければ経陰分娩とした。夫の立ち合いは継続したが, 感染管理により院内感染したスタッフはいなかった。【結論】COVID-19感染流行により分娩数は大幅に減少し, 外出自粛によって安静がもたらされ早産率は減少することが想定されたが, 初産婦において早産率は増加傾向にあった。感染妊婦の診療に際しては, 感染症科医師との連携, アルゴリズムの作成により, 内科管理への不安が解消され要請に対してスムーズな受け入れを行うことができた。

P-100-5 妊婦における新型コロナウイルス抗体陽性率の調査研究

近畿大病院

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【目的】現在, 新型コロナウイルス感染症の拡大は未だ収束に至っておらず, 妊婦においても感染の報告が続いている。分娩入院は時期の推定が困難であり, 休日夜間の緊急入院も多いが, 施設によっては緊急でのPCR検査は実施できず, また無症候性の患者も多く存在するため, 分娩時の感染対策やスクリーニングの難しさが, 感染拡大当初より問題となっていた。今回, 妊婦における新型コロナウイルスのIgG抗体の陽性率を調べ, 妊婦における感染動向を検討することとした。【方法】2021年8月から2022年3月までに当院および近隣の医療施設で妊婦健診を施行している妊婦において, 血液検査を施行し, 新型コロナウイルス感染症のIgG抗体の陽性率を検討した。血液検査は原則後期検査で実施したが, 周産期合併症に伴い早期の分娩終了が想定される症例では分娩前に検査を施行した。【成績】2022年9月末時点で22例の妊婦に対して検査を施行し, 1例でIgG抗体が陽性となった。陽性例は, 新型コロナウイルス感染者の濃厚接触者として, PCR検査を実施され, 結果陰性のため経過観察となっていた症例であり, 本人の自覚症状はなかった。【結論】妊婦においては, 新型コロナウイルス感染症の感染率は低いものの感染時の重症化率は高いとの報告もあるが, 若年のため無症候性患者も多く存在するため, その実情把握は困難である。本検討では, 今後800例相当のデータを集積予定で, 症状によらず既感染者を抽出することが可能であり, 妊婦における新型コロナウイルス感染症の感染動向を把握する一助になると考えられる。

P-100-6 待機的管理を軸とした COVID-19 感染妊婦の新たな集学的妊娠分娩管理と経膈分娩における臨床的知見

りんくう総合医療センター

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【目的】COVID-19 感染妊婦の分娩管理は依然明らかでない。感染妊婦の分娩の特徴を研究した報告も我々の知る限り無い。欧米では感染妊婦に対する帝王切開は産科的適応で行われているが、我が国ではウイルス曝露時間短縮や垂直感染リスクなどを理由に多くの施設で帝王切開分娩が行われてきた。しかし、現在の状況が継続した場合、既往帝王切開後妊娠・癒着胎盤の増加など女性のヘルスケアに重大な影響を与える懸念がある。我々の目的は、1) COVID-19 治療と共に可能な限り待機的に母体を経膈分娩可能な状態へ回復させ、2) 隔離中の分娩進行時は経膈分娩を軸とした産科的適応に則した分娩管理を集学的管理下で行うことである。【方法】我々は感染症内科・NICU・救命科・助産師と共に、COVID-19 感染妊婦に対し集学的感染治療・待機的な母体管理を行いつつ正常産での経膈分娩を目指す体制を構築し、感染妊婦の経膈分娩に関する特徴について検討した。【成績】COVID-19 感染妊婦 70 名が当院に搬送され、40 名が隔離解除後前医へ帰院、30 名が隔離中・隔離解除後に正常産で分娩した。緊急帝王切開は 5 名(産科的適応 3 名、母体挿管適応 2 名)で、残り 25 名が正常産で経膈分娩した。COVID-19 感染妊婦の経膈分娩で以下の新たな臨床的知見を得た：①非感染妊婦と比して分娩進行が速く、急速な分娩(陣発～3h 以内の分娩)が多い ②分娩検体の網羅的 COVID-19 検査上、全例で垂直感染を否定 ③母体・新生児合併症発生なし ④早産・妊娠分娩合併症なし【結論】集学的管理下で COVID-19 感染妊婦の経膈分娩が母体・新生児・医療者の面から安全に遂行可能なことが示唆され、特徴的な COVID-19 感染/感染治療妊婦の分娩の臨床的特徴が明らかになった。我々の取り組みが今後多くの施設で実施・洗練されることで、感染妊婦の経膈分娩管理に寄与すると確信する。

P-100-7 埼玉県におけるコロナ陽性妊婦の分娩予後調査結果について

埼玉県産婦人科医会

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【目的】2021 年 6 月現在、埼玉県における新型コロナ陽性妊婦の実数や分娩転帰などの実態把握は出来ていない。保健所を介した実態把握も個人情報保護法のためほぼ不可能である。そこで埼玉県産婦人科医会では 2021 年 6 月末まで陽性が判明し入院管理を行った陽性妊婦患者の全数と分娩予後の把握のため、埼玉県でコロナ陽性妊婦の入院管理を行った高次医療機関にアンケート調査した。なお同期間は陽性妊婦の管理は原則入院である。【方法】12 の医療機関に陽性判明時期・分娩管理の有無・分娩週数・分娩時陽性の有無・分娩様式・帝王切開適応・児体重・新生児仮死の有無についてエクセルシートを用いてアンケート調査した。【成績】アンケートを依頼した全医療機関から回答が得られた。6 月末までの陽性妊婦数は 96 例あり、陽性診断は初期 15 例中期 25 例後期 56 例に行われた。同施設で分娩管理まで行った症例は 53 例あり、分娩時陽性例は初期陽性例 0/6、中期陽性例 2/10、後期陽性例 24/37 であった。分娩時陽性症例 26 例のうち 4 例の経膈分娩と 1 例の産科適応での帝王切開を除く 21 例がコロナ陽性を理由とした帝王切開分娩であった。53 例のうち早産は 11 例(20.8%)に見られた。分娩時陽性症例の中で新生児仮死を認めた症例はなかった。【結論】今回の調査は第 4 波までの陽性例の分娩予後をまとめたものとなっており陽性例は帝王切開での分娩が主であること、早産が約 2 割と多いことが分かった。第 5 波以降は変異株の違いを反映し異なる特徴がある可能性があり、迅速に実態把握が出来るシステム確立が急務と考えられた。

P-100-8 COVID-19 対応産科リエゾンシステムの構築：埼玉県産婦人科医会のコロナ対策

埼玉県産婦人科医会

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【目的】新型コロナウイルス感染症が蔓延し、第 5 波では多くの感染者が出た。妊婦も例外ではなく感染し、各地の周産期センターでは患者対応に追われた。感染症法上、感染妊婦の入院決定権限は保健所にあるが、妊娠週数や合併症から産科的受入可能施設の選定をする必要があった。埼玉県産婦人科医会では、県内の感染妊婦が安心して妊娠・分娩期を過ごせるように、COVID-19 対応産科リエゾンシステムを構築し、運用した。【方法】日々の担当リエゾンの役割として、以下の 3 点を整備した。①保健所や県に適切な受入先を助言し、急な入院調整の場合には、かかりつけ医と県との橋渡しを行った、②かかりつけ医から濃厚接触妊婦を含めた報告を受け、システム登録し、特に予定日近い妊婦情報を管轄地域周産期センターで把握できるようにした、③iCTG 等を活用したオンライン診療を整備し、自宅療養中の妊婦の健康管理が行えるようにした【成績】9 月 3 日のシステム登録開始以降、60 名の陽性妊婦と 26 名の濃厚接触妊婦が登録された。ECMO 導入となった重症妊婦は 2 名であった。陽性妊婦の年齢中央値は 30 歳、診断週数中央値は妊娠 26 週であった。県調整本部からの相談電話は、第 5 波ピークで 1 日 2～3 件あった。【結論】埼玉県内での感染妊婦に対し、妊娠中の入院先調整や分娩受入調整、自宅での健康管理に対する産科リエゾンシステムを構築し、運用した。第 5 波終盤からの運用であったが、県などから好評を得た。今後はシステムを見直し、第 6 波以降への対応、陽性妊婦への抗体カクテル投与を行いながら、重症者を出さない対策と、コロナ以外の災害時にも運用できるシステムにしていきたい。

P-101-1 腎機能障害が遷延した産褥期発症遷延性 HELLP 症候群の一例

三次中央病院

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【緒言】近年 HELLP 症候群や非典型的溶血性尿毒症症候群 (aHUS) などを統括した妊娠関連血栓性微小血管症 (妊娠関連 TMA) という概念があり, 微小血管症性溶血性貧血, 消費性血小板減少, 微小血管内血小板血栓による臓器症状を 3 主徴とする病態である. 今回, 腎機能障害が遷延したために妊娠関連 TMA として, 血漿交換療法と透析療法を行い改善を得られた一例を経験したため報告する. 【症例】36 歳 3 妊 2 産, 特記すべき異常なし. 甲状腺機能低下症合併妊娠でありチラージン内服あり. 妊娠 38 週 6 日の健診時に高血圧 (144/95mmHg) と尿蛋白 1+, 下腿浮腫を認めた. 翌日 (妊娠 39 週 0 日) 陣痛発来で入院し, 入院時血圧は 170/96mmHg であった. 分娩は急速に進行し入院後 30 分で分娩となった. 分娩後も高血圧が持続しニカルジピンと硫酸マグネシウムの持続点滴を行った. 分娩後 3 時間で悪心・嘔吐, 褐色尿出現, 血液検査にて肝逸脱酵素および LDH の著明な上昇, 血小板減少を認めたため HELLP 症候群と診断した. この時点での腎機能は正常であった. ニカルジピンにて血圧管理を行うもコントロールは不良で, 第 2 病日より進行性の腎機能悪化を認め, 第 6 病日には血清クレアチニン値 4.76 mg/dL となり, 肺水腫が出現した. aHUS を疑い第 7~8 病日に血漿交換を施行したが腎機能の改善が乏しかったため第 10 病日に腎代替療法として人工透析を施行した. その後は腎機能や血圧は緩徐に改善傾向となり, 第 18 病日に退院となった. 【結語】腎機能障害が遷延した産褥期発症遷延性 HELLP 症候群の一例を経験した. HELLP 症候群症例において重篤な腎機能障害が遷延した場合は aHUS をはじめとした妊娠関連 TMA としての対応を考慮する必要がある.

P-101-2 日本の Posterior reversible encephalopathy syndrome 妊婦症例の特徴—review

自治医大

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【目的】妊婦の Posterior reversible encephalopathy syndrome (PRES) の報告は症例報告や症例シリーズが多く, 日本の症例をまとめた報告はない. 今回, 日本の報告例をレビューしその特徴を調べた. 【方法】PubMed, 医中誌のデータベースにおいて英語または日本語で書かれた妊婦の PRES の症例報告または症例シリーズの抄録や論文を収集した. PRES 発症前の旧妊娠高血圧症候群 (PIH) 分類, 発症時の症状, 画像所見の局在部位を検討した. 【成績】重複や関連しない論文を除き, 122 例 (75 文献) が収集された. 平均年齢は 31.4±5.3 歳, 初産/経産が 63.9%/24.6% (不明 11.5%), 発症時期は妊娠時/分娩時/産褥時が 39.3%/18.9%/41.8%, 発症時血圧値は重症域/非重症域/正常域が 65.6%/12.3%/9.8% (不明 12.3%), 合併症 (重複あり) は子癇発作/HELLP 症候群/脳出血/クモ膜下出血/脳梗塞が 69.7%/29.6%/2.4%/2.4%/0.8% であった. 発症前の高血圧・蛋白尿は旧 PIH 分類で, 妊娠高血圧腎症/妊娠高血圧/加重型妊娠高血圧腎症/慢性高血圧/PIH 病型不明/非 PIH が 42.6%/28.7%/0.8%/0.0%/13.9%/14.0% であった. 発症時の症状 (重複あり) は, 痙攣, 頭痛, 視野障害が 72.1%/36.9%/34.4% にみられた. また PRES 画像所見の局在 (重複あり) は, 後頭葉/大脳基底核/頭頂葉/前頭葉/脳幹/小脳/側頭葉が 79.3%/52.1%/41.3%/25.6%/15.7%/11.6%/6.6% であった. 【結論】高血圧合併妊娠では PRES 発症率が低いかもしれない. PRES 所見局在は, 後頭葉のみならず, 大脳基底核, 前頭葉, 脳幹でもしばしば観察されていた. 脳出血も 5% に発生していた. 今後, 多機関横断研究を行い, 妊娠関連の PRES の特徴を検討する必要があると思われる.

P-101-3 妊娠高血圧症候群を発症した母から生まれた早産児における呼吸器合併症の検討

名古屋大

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【目的】妊娠高血圧症候群 (HDP) を発症した母から出生した早産児における呼吸器合併症については, これまで報告はあるものの一定の見解を得ていない. 今回我々は在胎 32 週未満の早産児を対象として, HDP による児の呼吸器合併症への影響について検討した. 【方法】Neonatal Research Network Japan に参加する約 200 施設において, 2003 年~2017 年に在胎 22~31 週, 1500g 以下で出生した新生児 50599 例のうち, 多胎, 胎児奇形, 院外出生, 新生児死亡, データ不備例を除外した 24373 例 (HDP 群 5258 例, 非 HDP 群 19115 例) を対象とした. HDP 群と非 HDP 群を層別化マッチング (母体年齢, 在胎週数, 初産・経産, 分娩年度) を行い, 各群 5137 例を抽出した. その後, 単変量および多変量解析を施行した. 【成績】単変量解析では HDP による呼吸窮迫症候群, 新生児遷延性肺高血圧症, 慢性肺疾患, 在宅酸素 (NICU 退院時) の crude odds ratio は 1.79 (1.65-1.95), 0.37 (0.29-0.47), 1.36 (1.23-1.50), 1.06 (0.90-1.26) であった. 多変量解析では, HDP による adjusted odds ratio はそれぞれ 1.79 (1.61-2.00), 0.29 (0.22-0.39), 0.97 (0.85-1.10), 0.73 (0.59-0.91) であった. 【結論】HDP による児の呼吸器合併症への影響は疾患ごとに異なっており, 呼吸窮迫症候群や慢性肺疾患は有意に増加するが, 新生児遷延性肺高血圧症と在宅酸素は有意に減少することが明らかになった.

P-101-4 妊娠高血圧症候群における心筋細胞間質の変化

三重大附属病院

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【目的】妊娠高血圧症候群（HDP）は周産期心筋症（PPCM）の最大危険因子であり、周産期心筋症はHDP関連疾患のひとつに挙げられている。炎症、浮腫、線維化など心筋組織間質の変化を示す心筋 native T1 は、正常妊娠では変化せず、PPCMの急性期では上昇することが知られている。今回、心機能と心筋組織間質変化の関係について検討することを目的とした。【方法】2018年10月から2021年10月に、心不全症状があり、ヒト脳性Na利尿ペプチド（BNP） $\geq 100\text{pg/ml}$ を示した14例を対象とした。14例をEF $\leq 45\%$ の6例（A群）、EF $> 45\%$ の8例（B群）に分け、各群の急性期に、Cine MRI, T1 mapping (modified look-locker inversion recovery) を3T心臓MRI検査で施行し、BNP, EF, 心筋 native T1 について、比較検討を行った。統計解析は、t検定で行い、 $p < 0.05$ を有意差ありとした。研究倫理審査委員会の承認を得て行った。【成績】A群6例は、PPCMの診断基準を満たし、リスク因子として、HDP3例、多胎2例、2週間以上の塩酸リトドリン投与2例（重複あり）があった。B群は、全例HDPであった。A, B両群において、平均値は、BNP: $387 \pm 222\text{pg/ml}$, $173 \pm 60\text{pg/ml}$, $p = 0.07$, EF: $36 \pm 9\%$, $58 \pm 6\%$, $p < 0.01$, 心筋 native T1: $1384 \pm 92\text{ms}$, $1356 \pm 74\text{ms}$, $p = 0.526$ であった。また、心筋 native T1 は、いずれの群でも施設基準値 $1294 \pm 39\text{ms}$ を上回っていた。【結論】EF低下のないHDPでも、心筋組織間質に、炎症、浮腫や線維化などの変化が生じていることが示唆された。

P-101-5 妊娠高血圧腎症と胎児発育不全における母体血中 furin に関する検討

藤田医大

大脇晶子

【目的】ナトリウム利尿ペプチドの代謝酵素である furin は、プロレニン受容体を切断してレニン-アンジオテンシン系に作用するとともに、胎盤形成に重要な役割を有することが報告されている。そこで本研究では、妊娠高血圧腎症および胎児発育不全の母体血中 furin について検討した。【方法】施設内倫理委員会の承認を得た後に、研究内容に同意の得られた重症妊娠高血圧腎症妊婦（以下PE群）43例、高血圧を伴わない胎児発育不全妊婦（以下FGR群）20例、コントロール妊婦（以下NC群）40例を対象とした。ELISA法により母体血中 furin, プロレニン受容体について各群間の比較を行い、臨床パラメータである血圧や胎児・胎盤発育との相関についても検討した。【成績】母体血中 furin (pg/ml) は、PE群: 343.0 ± 99.3 , FGR群: 255.8 ± 42.4 , NC群 503.4 ± 234.0 と、PE群およびFGR群で有意に低下し（各 $p < 0.01$ ）、血中プロレニン受容体 (pg/ml) は、PE群: 3.9 ± 2.2 , FGR群: 3.2 ± 1.4 , NC群 2.0 ± 0.9 と、PE群およびFGR群で有意に高値であった（各 $p < 0.01$ ）。また、血中 furin は出生児体重かつ胎盤重量と有意な正の相関を認め（各 $r = 0.61$, $p < 0.01$, $r = 0.65$, $p < 0.01$ ）、血中プロレニン受容体は収縮期かつ拡張期血圧と有意な正の相関を認めるとともに（各 $r = 0.36$, $p < 0.01$, $r = 0.39$, $p < 0.01$ ）、出生児体重かつ胎盤重量と有意な負の相関を認めた（各 $r = -0.39$, $p < 0.01$, $r = -0.45$, $p < 0.01$ ）。【結論】妊娠高血圧腎症と胎児発育不全において、妊娠母体における furin の低下とプロレニン受容体の増加が胎盤形成不全やレニン-アンジオテンシン系の活性化に基づく血圧上昇に関連することが示された。

P-101-6 重症妊娠高血圧腎症による当院搬送例の産後経過の検討

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【目的】妊娠高血圧症候群の患者に於いては、産褥1か月の健診時に血圧・尿蛋白が正常化していても、その後本態性高血圧症に移行する場合があることが知られており長期的なフォローが必要である。また妊娠を契機に腎疾患が明らかとなる場合もある。当院で加療した重症妊娠高血圧腎症例の産褥の経過を調査し、その実態を確認する。【方法】2012年から2015年に当院に重症妊娠高血圧腎症にて母体搬送となった妊婦を対象とした。このうち、産褥搬送及び退院後他院にて分娩した症例を除外した全125名を後方視的に検討した。【成績】産褥1か月以内に尿蛋白の陰性化及び血圧の正常化が認められたのは全125名中91名（72%）。腎臓内科併診となったのは全125名中100名（80%）で、フォローを続けた結果、膜性増殖性糸球体腎炎1名、原発性アルドステロン症1名、本態性高血圧症3名の診断に至っている。腎臓内科通院の自己中断例は全100名中18名（18%）にも及んでいる。次回妊娠が確認されたのは20名であり、うち4名がLDA内服し再度妊娠高血圧症候群を発症したのは1名、LDA内服しなかった14名のうち再度妊娠高血圧症候群を発症したのは3名、1名は経過不明、1名は産後受診ないまま3度飛び込み出産し毎回血圧高値だった。【結論】妊娠高血圧症候群を発症した女性は将来、高血圧、脳血管障害、虚血性心疾患、糖尿病、脂質異常症、慢性腎臓病などを発症しやすいことが多くの疫学研究で指摘されている。妊娠高血圧症候群既往女性には次回妊娠時のリスク説明とともに長期的予後についても十分に説明を行い、長期的フォローアップを行えるよう導く必要性を改めて確認した。

P-101-7 ENDOU が胎盤における小胞体ストレス関連因子 CHOP の発現を制御する

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【目的】妊娠高血圧腎症の胎盤由来 Cytotrophoblast のプロテオーム解析により妊娠高血圧症候群発症に関わる因子の一つとして ENDOU に着目した。これまでに ENDOU が妊娠高血圧腎症を発症した妊婦の胎盤において亢進していることを報告したが、その機能は不明である。ゼブラフィッシュにおいては小胞体ストレスを亢進させアポトーシスを誘導することが報告されていることから、ストレス下にある妊娠高血圧腎症の胎盤において ENDOU 発現により小胞体ストレスを亢進させているのではないかと考えた。【方法】EVT 細胞株の HTR8/SVneo 細胞および絨毛癌由来 Bewo 細胞に過酸化水素処理を行い ENDOU や小胞体ストレス関連因子の発現をリアルタイム PCR とウエスタンブロットで解析した。HTR8/SVneo 細胞および Bewo 細胞にレトロウイルスを用いて ENDOU 遺伝子の強制過剰発現を行い、アポトーシスや小胞体ストレス関連因子の発現をリアルタイム PCR とウエスタンブロットで解析した。【成績】HTR8/SVneo 細胞、Bewo 細胞において過酸化水素処理を行ったところ ENDOU の発現が亢進した。さらに低酸素状態で培養を行った場合でも ENDOU の発現が亢進していた。過酸化水素処理及び低酸素状態での培養で ENDOU だけでなく小胞体ストレス関連因子 CHOP の発現も亢進していた。ENDOU 強制発現細胞において、HTR8/SVneo 細胞及び Bewo 細胞において CHOP の発現が亢進した。【結論】胎盤においても酸化ストレスや低酸素などにより小胞体ストレスが生じた場合、ENDOU が亢進することで CHOP の発現が亢進し Cytotrophoblast にアポトーシスが誘因されることが示唆された。

P-101-8 絨毛外栄養膜細胞の機能発現に、HMGA1 は WNT 系を介して関与する

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【目的】妊娠高血圧腎症 (PE) では、絨毛外栄養膜細胞 (EVT) の浸潤不全が胎盤形成を障害している。これまで我々は、PE における EVT の増殖・浸潤に HMGA1 関与することを報告してきた。本研究では、これらの蛋白発現に HMGA1 がどのように関与しているのかについて検討を行った。【方法】EVT 細胞株を用い、1) HMGA1 の transfection・knock down を行い、MMPs の発現を real time-PCR・western blotting によって評価した。2) HMGA1 を添加して Matrigel invasion assay を行い、EVT の浸潤能について検討を行った。3) 細胞上清中にサイトカインを添加し、EVT からの HMGA1 の分泌の変化について検討を行った。4) HMGA1 を knock down することで Wnt 5a・catenin b1・c-myc の変化について RT-PCR を用いて検討を行った。【成績】1) HMGA1 transfection によって EVT における MMP2・MMP9 の発現がそれぞれ 1.4 倍・1.6 倍に増加した。TIMP1・TIMP2 の発現に影響は無かった。WB でも MMP2・MMP9 の発現は HMGA1 の transfection で増加した。2) HMGA1 の添加により EVT の浸潤能は約 2 倍に促進された。3) 逆に培養上清中に cytokine を添加・低酸素 (2% O₂) とした際、HMGA1 濃度は IL-1β・LPS・IFN-γ 添加によって著明に増加した。一方、TNF-α・IL-4・低酸素下では変化を認めなかった。4) HMGA1 の knock down により Wnt 5a・Catenin・c-myc の発現が著明に減少した。【結論】HMGA1 は EVT の浸潤に影響することを報告してきたが、HMGA1 は向炎症サイトカインによって細胞外に放出され、EVT における MMP2・MMP9 産生を autocrine・paracrine 的に促進することで浸潤能亢進に作用していると考えられた。さらに、これらは Wnt-Catenin 系を介していることが明らかとなった。

P-101-9 妊娠高血圧症候群における帝王切開術後の血腫形成に関する後方視的解析

順天堂大順天堂医院

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【目的】深部静脈血栓症のリスク因子を有する帝王切開症例では術後の抗凝固療法が推奨されている。当院では血栓症の危険性を重要視し、帝王切開全症例にエノキサパリンを投与する方針としているが、抗凝固薬投与後に血腫形成をきたす症例を認める。妊娠高血圧症候群 (HDP) は血栓症のリスク因子であるが、術後の血腫形成の危険性も有しており、HDP 症例における術後抗凝固療法の血腫形成に関与するリスク因子を明らかにすることを目的として後方視的に検討を行った。【方法】2018 年から 2020 年に当院で帝王切開術を実施した妊婦を対象とした。対象の症例において、妊娠関連項目、手術関連項目、HDP の有無、術前後の血液データについて後方視的検討を行った。主要評価項目は血腫形成におけるリスク因子の同定とした。【成績】対象例 937 例のうち血腫群は 39 例 (4.2%) であった。血腫形成率は、HDP 症例 (38.5%, $p < 0.001$) において有意に高かった。HDP 症例 (80 例) における比較において、非血腫群に比べ、血腫群は術後のヘモグロビン値 (9.9 ± 1.7 vs 10.9 ± 1.6 , $p = 0.029$)、ヘマトクリット値 (29.2 ± 5.0 vs 32.3 ± 4.2 , $p = 0.022$)、推定糸球体濾過率 (eGFR) (82.2 ± 22.3 vs 98.0 ± 26.7 , $p = 0.036$) が有意に低く、クレアチニン値 (0.69 ± 0.16 vs 0.59 ± 0.14 , $p = 0.014$) が有意に高かった。【結論】HDP 症例における帝王切開術後の血清クレアチニン値は抗凝固療法による血腫形成のリスク予測因子となる可能性が示唆された。

P-102-1 妊娠高血圧腎症における胎児発育不全の取り扱いの検討

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【目的】本邦では2015年より妊娠高血圧腎症 (Preeclampsia; PE) の診断基準に胎児発育不全 (Fetal growth restriction; FGR) を含めたが, FGRの発症時期に関する検討は十分にされていない。妊娠高血圧症 (Gestational hypertension; GH) にFGRを伴うPEの周産期転帰とFGRの発症時期の関連性を検討した。【方法】当院で2010年1月から2021年6月に分娩したFGRを伴うPE症例 (n=108) を, GHが先行またはFGRと同時に発症した群 (GH群; n=60) とFGRが先行した群 (FGR群; n=48) で母体背景と母体転帰, 新生児予後を比較検討した。胎児染色体異常や出生時体重が400g未満の症例は除外した。【成績】PE診断週数はGH群30.2 (22.6-39.4) 週, FGR群34.7 (26.0-40.1) 週でありGH群で有意に早かった (P=0.0027) だった。妊娠延長期間が2日以上だった割合はGH群85.0%, FGR群72.3%で中央値はGH群11 (2-43) 日, FGR群8 (2-30) 日で有意差は認めなかった (P=0.27) だった。常位胎盤早期剝離や子癩など重篤な母体有害転帰の発症率はGH群26.7%, FGR群10.4%であり有意にGH群で多かった (P=0.049, 95%CI 1.05-9.29)。子宮内胎児死亡はFGR群で1例あったが, 新生児死亡は両群ともなかった。NICU入室率はGH群73.3%, FGR群74.5%で, 慢性肺疾患や敗血症など新生児複合合併症の発症率はGH群25.0%, FGR群17.0%であり, いずれも有意差は認めなかった。【結論】GHとFGRを同時またはGHを先行するPEは, FGRが先行するPEよりも早期にPEと診断され, 母体有害転帰の発症率が有意に高かった。

P-102-2 妊娠高血圧腎症妊婦における尿中蛋白排泄量と母体重症度との関連性

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【目的】妊娠高血圧症候群の重症度分類は, 尿中蛋白排泄量が2g以上/日の場合に重症と分類していたが, 2018年の改訂によって尿中蛋白排泄量による分類は廃止となった。しかし, 尿中蛋白排泄量が増加する場合に母体の病状が悪化することがしばしば認められる。今回, 妊娠高血圧腎症妊婦の尿中蛋白排泄量と母体重症度との関連性を検討した。【方法】2008年4月1日から2021年9月30日までに当院で分娩となった妊娠高血圧腎症の妊婦を対象とし, 以下の検討を行った。尿中蛋白排泄量2g未満/日 (44例), 2g以上/日 (94例) の2群に分別し, それぞれ母体の重症度を評価し, 比較検討した。母体の重症度評価は, 米国家産婦人科学会が示す母体重症度分類を用いた。I, 血圧160/110mmHg以上 II, 血小板数10万/ μ L未満 III, 肝機能障害 IV, 腎機能障害 V, 肺水腫 VI, 新規発症した頭痛 VII, 視覚障害。また, ROC曲線を用いて母体が重症と考えられる尿中蛋白排泄量を検討した。【成績】尿中蛋白排泄量2g未満/日に比較し, 2g以上/日で血圧160/110mmHg以上となる妊婦が有意に増加し (P<0.001), 新規発症した頭痛の頻度も2g以上/日で有意に高値であった (P<0.05)。また, 重症度分類の重症に該当する妊婦数は2g未満/日で13人 (29.5%) に比較して2g以上/日で74人 (78.7%) と有意な高値を認めた (P<0.001)。感度・特異度が最も高値となるROC曲線では, 尿中蛋白排泄量のカットオフ値は2.20g/日であり, 感度83.9%, 特異度66.7%であった (AUC=0.78, 95%CI=0.70-0.86)。【結論】旧重症度分類で重症とされていた尿中蛋白排泄量2g以上/日の妊婦では, 重症度は高く, 2.20g以上/日が母体の重症度を判定する最適な蛋白排泄量と考えられた。

P-102-3 妊娠高血圧腎症の新分類における追加項目と周産期予後の検討

トヨタ記念病院

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【目的】2018年に日本妊娠高血圧学会により妊娠高血圧症候群 (HDP) の定義, 分類が改定された。新定義では蛋白尿, 子宮胎盤機能不全, 血液凝固障害, 神経障害, 肝機能障害, 腎障害のいずれかを認めた場合に妊娠高血圧腎症 (PE) と診断する。新定義による周産期予後への影響についての報告は限られている。今回我々は, 当院におけるHDP患者を旧定義, および新定義に基づき分類し, その周産期予後について検討したので報告する。【方法】2018年1月から2019年12月に当院で分娩した, 新定義でHDPと診断された妊婦のうち高血圧合併妊娠を除いた71例を対象とした。新定義で追加された蛋白尿以外の項目を認める群と対照群において, 児のNICU入院率, 緊急帝王切開率, 分娩週数, HDP発症週数について後方視的に検討した。【成績】HDP71例のうち, 新定義でのPE診断基準の蛋白尿以外の項目を認めた症例は39例 (54.9%) であった。39例のうち蛋白尿は28例, 子宮胎盤機能不全を21例, 血液凝固障害を17例, 神経障害を11例, 肝機能障害を6例, 腎障害を1例で認めた。蛋白尿以外の追加項目のいずれかを認めた39例と, 対照群32例を比較した。追加項目を認めた群では, 出生児のNICU入院率 (61.5% vs 28.1%; P=0.008), 緊急帝王切開率 (59.0% vs 15.6%; P<0.001) が高く, 平均分娩週数は早く (36.3週 vs 38.8週; P<0.001), HDP発症週数は早かった (34.6週 vs 36.5週; P=0.020)。【結論】新定義でHDPと診断される症例のうち, 妊娠高血圧腎症の診断基準に新たに追加された項目のいずれかを認める症例では, いずれも認めない症例と比較し, HDPの発症時期が早く, NICU入院率や緊急帝王切開率が増加し, 分娩週数は早かった。

P-102-4 頭蓋内出血を発症した妊娠高血圧症候群妊婦3症例の血圧管理の問題点

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杉浦一優

【概要】母体の3大死亡原因の1つとして頭蓋内出血が知られている。妊娠高血圧症候群（HDP）に伴う高血圧は子癇および頭蓋内出血を発症することから、適切な降圧管理がその予防として重要である。今回、頭蓋内出血を発症したHDP妊婦3症例について、血圧管理の問題点を検討した。【症例】〈症例1〉37歳、1妊0産、高血圧合併妊娠（CH）。妊娠初期より血圧160/110 mmHg以上を認めCHと診断されたが、降圧治療せずに外来管理されていた。妊娠36週4日に自宅で意識障害、左不全麻痺を呈し当院に搬送された。CTでも膜下出血と診断し、緊急帝王切開術後、開頭血腫除去術を施行した。〈症例2〉32歳、1妊0産、妊娠高血圧腎症（PE）。妊娠35週より尿蛋白が持続し、妊娠37週より血圧140/90 mmHg以上となるも、PEと診断されず外来管理されていた。妊娠39週3日に血圧150/100 mmHg台で頭痛、嘔吐を認め当院に搬送された。CTで大脳皮質下出血、くも膜下出血を認め、緊急帝王切開術後、開頭血腫除去術を施行した。〈症例3〉41歳、3妊2産、PE。妊娠34週に妊娠糖尿病の診断で当院に紹介された。外来管理中は血圧異常、蛋白尿は認めていなかった。妊娠37週3日、既往帝王切開術後妊娠に対する予定帝王切開術のため入院となった。入院後に血圧140/90 mmHgを認め、脊椎麻酔時には血圧190/130 mmHg以上が持続していた。術中、母体の全身性痙攣が出現し、術後CTでも膜下出血を認めた。出血量少量のため、保存的に経過観察した。術後蛋白尿を認め、PEと診断した。【考察】今回の3症例は、いずれも血圧管理が不十分であった。HDP妊婦の頭蓋内出血を予防するためには、適切な血圧管理が重要であると考えられた。

P-102-5 妊婦健診時の一過性高血圧と妊娠高血圧症候群発症との関連

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【目的】妊娠20週以降に一過性の血圧上昇（transient gestational hypertension, TGH）を認め、家庭血圧測定を開始し経過を観察していると、最終的に妊娠高血圧症候群（hypertensive disorders of pregnancy, HDP）を発症する症例をしばしば経験する。妊婦健診時のTGHとその後のHDP発症との関連を後方視的に検討した。【方法】2016年9月から2021年6月までに当院で妊婦健診と分娩を行った症例を対象として、産科部門システムより患者基本情報、基礎疾患・合併症、健診時および分娩経過中の血圧測定値、分娩・産褥情報を含むデータを一括して取得した。妊婦健診での来院時に収縮期血圧 ≥ 140 mmHgまたは拡張期血圧 ≥ 90 mmHgを示した妊婦が、外来診察室での再検では正常血圧であった場合をTGHと定義した。白衣性高血圧または高血圧合併妊娠と考えられる症例は除外した。【成績】2108症例を対象とした。症例の年齢中央値は33歳（18-45歳）、妊娠経過中にHDPと診断された症例は85症例（4.0%）であった。妊婦健診時の血圧データは22473レコードで、このうちTGHの基準を満たすレコードは204症例（9.7%）にみられた。後にHDPを発症した症例の割合はTGH群では15.2%、非TGH群では2.8%で、TGH群の方が高率にHDPを発症していた（リスク比5.4, 95%信頼区間3.5-8.1）。またTGH群のうち血圧再検値が $140 >$ 収縮期血圧 ≥ 130 mmHgまたは $90 >$ 拡張期血圧 ≥ 80 mmHgであった77症例に限ると、HDP発症のリスク比は7.6（95%信頼区間4.8-12.0）に上昇した。【結論】産科外来における血圧上昇をみた場合は、たとえ一過性であっても後にHDPを発症する可能性を考慮した慎重な経過観察が必要である。

P-102-6 妊娠高血圧腎症妊婦で発症する低Alb血症に対する尿中蛋白排泄とCRPの関連性

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【目的】妊娠高血圧症候群（HDP）妊婦での血管内皮機能障害は、母体や胎盤で発生する活性酸素（FR）が関連する。我々はこれまで妊娠高血圧腎症（PE）妊婦での血中アルブミン（Alb）は抗酸化作用を担っていること、PE妊婦は尿中蛋白排泄することから低Alb血症となり、FRの増加の一因であることを報告してきた。近年Albは炎症により肝臓での合成が抑制され、C反応性蛋白（CRP）の合成に傾くため、AlbとCRPは負の相関を示すことが報告されている。また、PE妊婦では血管内皮機能障害の原因として、酸化ストレスとともに慢性炎症も主な要因であることが知られている。今回、PE妊婦で発症する低Alb血症に対する尿中蛋白排泄とCRPとの関連性につき検討した。【方法】2020年1月から2021年9月までの同意を得た正常妊婦（Control群）15例、PE妊婦（PE群）27例について、母体血中総蛋白濃度（TP）、Alb、CRP、1日尿中Alb量の指標として尿Alb/Crea比を測定し関連性を検討した。【成績】母体血中TP、AlbはControl群に比較しPE群で有意な低値を認めた。CRPは、Control群と比較しPE群で有意な高値を認めた。尿Alb/Crea比はControl群に比較してPE群で有意な高値を示した。PE群ではAlbとCRPでは負の相関（ $r = -0.48$, $p < 0.05$ ）を認めたが、Control群では関連性を認めなかった。また、PE群では血中Albと尿Alb/Crea比とは有意な負の相関（ $r = -0.53$, $p < 0.05$ ）を認めた。【結論】PE妊婦のAlb低下は、尿中Alb排泄に加え、慢性炎症による肝でのAlb産生障害が寄与している可能性が考えられた。

P-102-7 Soluble fms-like tyrosine kinase-1 と Placental growth factor を用いた妊娠高血圧症候群における妊娠継続期間についての検討

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【目的】Hypertensive disorder of pregnancy (以下 HDP) は、発症すると進行性に悪化し、妊娠を終了する以外に根治的な治療がない。そのため、血管新生・阻害因子を用いた発症予測など様々な取り組みが行われている。本研究は、HDP 発症後に Soluble fms-like tyrosine kinase-1 (以下 sFlt-1) と Placental growth factor (以下 PlGF) を測定し、妊娠継続期間との関係を明らかにすることを目的とした。【方法】2020年4月から2021年3月において、sFlt-1 と PlGF を測定した 367 例のうち、測定前に HDP の診断を受けた患者 29 例を対象とした。測定された sFlt-1・PlGF と測定した時点から 1 週間以内に妊娠が終了するまでの期間について検討した。【成績】HDP 患者 29 例のうち、Preeclampsia が 19 例、Gestational Hypertension が 6 例、Superimposed preeclampsia が 2 例、Chronic hypertension が 2 例であった。Preeclampsia の 19 例のうち Late onset が 17 例、Early onset が 2 例であった。年齢、分娩週数、出生体重の中央値はそれぞれ 34 (28-43) 歳、36 (23-39) 週、1744 (403-2776) g であった。初産婦、帝王切開、胎児発育不全を合併した割合はそれぞれ 63%、73%、31% であった。1 週間以内に分娩した群と 1 週間以上妊娠を継続できた群と比較して sFlt-1 は 11155 vs 5810 pg/ml ($p=0.01$)、PlGF は 26 vs 79 pg/ml ($p=0.20$)、sFlt-1/PlGF 比は 554 vs 106 ($p=0.02$)、であった。1 週間以内に妊娠を終了するかを判定する sFlt-1 のカットオフ値を ROC 曲線による解析に基づいて設定すると 8800pg/ml であった (特異度: 100%、感度: 78%)。【結論】HDP 発症後の 1 週間以内の妊娠終了を予測する上で、sFlt-1 単独の特異度が最も有用であった。

P-102-8 当院での妊娠 34 週未満の妊娠高血圧症候群の分娩時期の決定条件の検討

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【目的】妊娠高血圧症候群は、周産期領域における重要な疾患である。しかし、有効な治療方法は確立されておらず、その管理方法の基本は妊娠の終結であり、特に妊娠 34 週未満は児の未熟性を考慮しなければならず、分娩時期の決定は重要な検討課題である。34 週未満で分娩した妊娠高血圧症候群の周産期管理と母体の転帰を調査し、今後の当院での管理に活用することを目的とした。【方法】2018年4月～2021年3月までに当院で妊娠・分娩管理し、34 週未満で分娩した妊娠高血圧症候群の症例を対象とする。診療録を用いて後方視的に調査し、当院における母体の予後に影響する要因について検討した。【成績】全分娩総数は 3604 例であり、該当症例は 53 例であった。加重型妊娠高血圧腎症が 28.3%、妊娠高血圧腎症が 71.7% であった。分娩時期は妊娠 22-28 週が 13 例、妊娠 29-33 週が 40 例であった。妊娠終結の決定は (重複あり) 母体臓器障害が 45.3%、胎児機能不全が 22.6%、母体の血圧コントロール不良が 22.6% であった。入院中の産褥経過は 28.3% で退院延期 (術後 6-12 日) となり、胎児適応での妊娠終結の場合は、退院延期が 1/13 例 (7.7%) に対して母体適応の場合は 15/35 (42.8%) と差を認めた。母体に重篤な合併症が起きた症例はなかった。退院後の経過は、72.2% は産褥 12 週までに血圧等が正常化した。27.8% は内科で外来通院が継続となった。【結論】当院での妊娠 34 週未満の妊娠高血圧症候群の分娩時期の決定条件の検討したところ、早産の時期によって決定条件に大きな差はなかった。また、母体の転帰は重篤な合併症はなく母体にとっては予後良好と考えられた。今後は児の転帰を調査し、母児にとって最良の分娩時期となっているか検討したい。

P-103-1 減量手術後の妊娠・分娩では妊娠高血圧腎症のリスクが高い

関西医大附属病院

森川 守

【目的】減量手術 (BS) 後に妊娠・分娩した妊婦の転帰を明らかにする。【方法】2018年にわが国で総合・地域周産期母子医療センターすべて (408 施設) にアンケートを配布した。減量手術 (BS) 後に妊娠し 2018 年に分娩した妊婦について調査した。回答した 229 施設 (56.1%) のうち、4 施設に BS 後に妊娠・分娩した単胎妊婦計 5 名 (BS 群) の転帰を調査した。【成績】229 施設の 2018 年の全分娩数は合計 127,355 であったため、全分娩に占める減量手術 (BS) 後に妊娠・分娩した妊婦の割合は 0.0039% (5/127,355) だった。5 名の受けた BS の術式は、4 名が腹腔鏡下スリーブ状胃切除、1 名が腹腔鏡下調節性胃パンディンク術であった。BS 群 5 名のうち、3 名 (60.0%) が妊娠高血圧腎症 (高血圧と蛋白尿) を発症した。2 名では妊娠時に慢性高血圧があり、その後に妊娠高血圧腎症へ進展した。残りの 1 名では妊娠時に慢性高血圧がなかったが、妊娠 20 週以後に妊娠高血圧腎症を発症した。【結論】減量手術後の妊婦 (特に糖尿病合併妊娠) において妊娠高血圧腎症の発症率が高かった。

P-103-2 双胎妊娠における妊娠高血圧症候群発症予防に低用量アスピリンは有効か

筑波大附属病院

築比地彩香, 西田恵子, 鮎澤 萌, 角 央彦, 渡辺麻紀子, 筑田陽子, 阿部春奈, 眞弓みゆき, 大原玲奈, 小島真奈, 濱田洋実, 佐藤豊実

【目的】低用量アスピリン (LDA) の服用による双胎妊娠の妊娠高血圧症候群 (HDP) 発症予防効果について明らかにすること。【方法】2019年12月から2021年9月までに当院で妊娠・分娩管理を行った双胎妊娠を対象とした。HDP発症を予防するためのLDA服用について文書および口頭で説明し、希望して服用したLDA群と服用しなかったnon-LDA群に分け、後方視的に妊婦背景や周産期転帰について比較した。【成績】双胎妊娠94例 (二絨毛膜二羊膜双胎58例, 一絨毛膜二羊膜双胎35例, 一絨毛膜一羊膜双胎1例)が対象となり、LDA群は22例, non-LDA群は72例であった。母体年齢, 経産回数, 妊娠方法, 膜性, GDM合併の有無について両群で比較したところ有意差はなかったが, 妊娠前BMIについてはLDA群が 25.1 ± 3.9 (平均 \pm 標準偏差)であり, non-LDA群の 22.3 ± 4.5 と比較して有意に高かった ($p=0.007$)。周産期転帰のうち分娩様式, 分娩週数, 児出生体重, 出血量については両群に有意差はなかった。LDA群の8例 (36.4%), non-LDA群の15例 (20.8%)がHDPを発症したが, その頻度に有意差は認めなかった ($p=0.162$)。病型は妊娠高血圧腎症がそれぞれ3例, 4例, 妊娠高血圧がそれぞれ5例, 11例と有意差はなく, 発症時期についても早発型がそれぞれ1例, 2例, 遅発型がそれぞれ7例, 13例と有意差はなかった。HDP発症に関して多変量ロジスティック回帰分析を行ったところ, LDA服用との関連は認めず, 妊娠前BMI 30以上で調整オッズ比5.79 (95%信頼区間1.19-28.2)と有意な関連を認めた。【結論】双胎妊娠におけるHDP発症のLDAによる予防効果は明らかではなかった。今後さらに症例を蓄積し, 検討していく必要がある。

P-103-3 初診時血圧と妊娠高血圧腎症の発症の関連について

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【目的】妊娠初期の血圧が高血圧の定義に満たない場合でも, 血圧が高いほど妊娠高血圧腎症 (PE) の発症リスクが高くなる事が知られているが, 本邦からの報告は乏しい。初診時血圧とPE発症の関連について, 本邦のデータを用いて検証する事を目的とした。【方法】2006年1月1日から2018年4月30日までに当院で分娩した妊婦のうち, 初診が22週未満の者を対象とした。ACA (The American College of Cardiology) の診断基準に従って, 正常群 (収縮期血圧120mmHg未満かつ拡張期血圧80mmHg未満), 上昇群 (収縮期血圧120-129mmHgかつ拡張期血圧80mmHg未満), 1度高血圧 (収縮期血圧130-139mmHg又は拡張期血圧80-89mmHg), 2度高血圧 (収縮期血圧140mmHg以上または拡張期血圧90mmHg以上) の4群に分類し, PEの発症頻度及びその他の妊娠分娩転帰を比較した。ロジスティック回帰分析により, 母体背景を調整したオッズ比 (aOR) と95%信頼区間 (95% CI) を算出した。【成績】対象は10,482例で, 正常群: 8,637例, 上昇群: 948例, 1度高血圧群: 627例, 2度高血圧群: 270例に分類された。PEの発症率はそれぞれ1.4%, 3.3%, 6.5%, 16.7%と血圧の高い群ほど高かった。さらに正常群を参照とした各群のaOR (95% CI) は, 2.11 (1.40-3.17), 3.85 (2.62-5.65), 9.84 (6.47-14.97) と, 上昇群, 1度高血圧, 2度高血圧群すべてで有意に高かった。【結論】初診時の血圧が正常であっても, 上昇群 (収縮期血圧120-129mmHgかつ拡張期血圧80mmHg未満) 以上の場合, 血圧が高いほどPE発症の発症リスクが高くなるため, より注意した管理が必要である。

P-103-4 低用量アスピリンによる妊娠高血圧腎症発症予防効果

弘前大附属病院

大石舞香, 横山美奈子, 飯野香理, 伊東麻美, 田中幹二, 横山良仁

【目的】近年, 妊娠初期からの低用量アスピリン (LDA) 投与が妊娠高血圧症候群発症予防に有用であることが報告されている。特に妊娠高血圧腎症を発症した女性に対しては, 再発予防目的に次回妊娠時のLDA投与が考慮されている。しかしながら, 日本ではLDAの使用は, 出産予定日12週以内 (妊娠28週以降) は添付文書上禁忌とされており, 妊娠高血圧症候群予防として保険適応はないのが現状である。今回, LDA予防内服によって実際に妊娠高血圧症候群予防が可能か否かを検討した。【方法】カルテベースの後方視的検討を行った。2017年~2019年当院で周産期管理を行った症例より, 米国産婦人科学会 (ACOG) のLDA内服推奨基準を満たすハイリスク症例を抽出し, その中でLDA内服群, 非内服群の2群に分類し, 妊娠高血圧腎症発症の有無について検討した。また, 2群間での周産期予後の比較を行った。【成績】854分娩の内, ACOGのLDA内服推奨基準を満たす妊娠高血圧症候群ハイリスク症例は673分娩であった (分娩時平均年齢 33.7 ± 5.5 歳, 平均分娩週数 38.5 ± 2.0 週)。673分娩の内, 患者の同意が得られ初期よりLDAを内服して周産期管理を行った症例は40例であった。妊娠高血圧腎症は673例中35例 (5.2%) に発症し, 35例全てがLDA内服が行われていない症例であった。【結論】統計学的有意差は認められなかったが, 妊娠高血圧症候群ハイリスク症例にもかかわらず, LDA投与を行った40例において妊娠高血圧腎症の発症はなかったことから, LDA投与は妊娠高血圧腎症発症予防に有用であると考えられた。

P-103-5 当センターでの妊娠高血圧症候群のハイリスク症例に対する低用量アスピリンの効果

大阪急性期・総合医療センター

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【目的】妊娠高血圧症候群 (HDP) の予防には低用量アスピリン (LDA, low dose aspirin) の有効性が多数報告されている。本研究では HDP のハイリスク妊婦での LDA 内服が妊娠高血圧腎症 (PE) 発症を予防するかを検討した。【方法】本研究は単施設における後方視的コホート研究である。研究対象は 2017 年 1 月から 2021 年 6 月に当センターで分娩した HDP ハイリスク群の単胎妊婦である。診療録から情報を収集した。不育症などでアスピリンを使用している症例や、胎児構造異常を有する症例は除外とした。当センターでの LDA の適応には妊娠高血圧症候群の既往 (早発型もしくは重症型)、多胎妊娠、慢性高血圧、1 型/2 型糖尿病、慢性腎疾患、自己免疫性疾患 (全身性エリテマトーデス、抗リン脂質抗体症候群) である。アスピリン 100mg を 1 日 1 回、妊娠 12 週から 16 週の間に開始し、31 週 6 日まで投与した。LDA 内服群と対照群で PE、早産、胎児発育不全、分娩時出血量の項目を比較検討した。P 値は 0.05 未満を有意差ありとした。【成績】対象は 138 例、LDA 内服群は 70 例 (50.7%)、対照群は 68 例 (49.3%) であった。PE (20% vs. 16.2%, $P=0.56$)、37 週未満の早産 (14.3% vs 16.2%, $P=0.76$)、胎児発育不全 (15.7% vs 5.9%, $P=0.06$)、分娩時出血量 (中央値 438mL vs 459mL, $P=0.95$) であり、いずれも有意差を認めなかった。【結論】LDA 内服による HDP 予防効果は本研究では示されなかった。有効性について先行研究と異なる結果となった要因には LDA の内服期間や HDP ハイリスク妊婦の抽出方法 (子宮動脈拍動指数や母体バイオマーカーの活用) が挙げられる。

P-103-6 妊娠高血圧症のハイリスク要因をもつ妊婦におけるバイアスピリン内服による発症予防効果についての検討

島根大附属病院

原 友美, 皆本敏子, 野々村由紀, 金崎春彦, 京 哲

【目的】世界妊娠高血圧学会では妊娠高血圧症候群 (HDP) 予防目的に、臨床的危険因子を有する患者に妊娠 16 週までに低用量アスピリンの内服を開始することを推奨している。当院の症例でこの予防効果について検証した。【方法】当院では 2018 年より①HDP 既往 ②BMI30 以上の肥満 ③抗リン脂質抗体症候群 ④生殖補助医療による妊娠 ⑤妊娠前からの高血圧 ⑥妊娠前からの糖尿病のいずれかの因子がある妊婦に HDP 予防目的に低用量アスピリン内服 100mg/日 (保険適用外) を説明し、希望者には妊娠 16 週までに内服を開始している。2015 年から 2016 年 3 月に出産した 350 例と 2021 年から 2021 年に出産した 350 例の全 700 例を対象に後方視的に検討した。有意差検定にはカイ 2 乗検定を用い、 $P<0.05$ を有意差ありとした。【成績】少なくとも一つの臨床的危険因子をもつ妊婦は 145 人、そのうちアスピリンを非内服群は 89 人、内服群 56 人だった。リスク毎の内訳は①28 人 (内服群 14 人) ②37 人 (8 人) ③5 人 (4 人) ④75 人 (30 人) ⑤14 人 (6 人) ⑥3 人 (1 人) だった。HDP 発症は非内服群 24 人、内服群で 21 人であり、HDP 発症率はアスピリン内服群と非内服群で差は認めなかった ($p=0.609$)。リスク要因毎に分類してもアスピリン内服による HDP 発症予防効果は認めなかった。【結論】当院の症例では臨床的危険因子を有する妊婦においてアスピリン内服による HDP 発症予防効果は認めなかった。症例が少なかったことも一因と思われるがハイリスク群におけるアスピリン内服には子宮動脈波形測定などの組み合わせも今後検討したい。

P-103-7 妊娠高血圧腎症既往妊婦に対するアスピリン投与効果の検討

鹿児島市立病院

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【目的】妊娠高血圧腎症発症予防を目的とした母体へのアスピリン投与の有効性が多くの研究により示されている。今回我々は、妊娠高血圧腎症の既往のある妊婦に対する、アスピリン投与の妊娠高血圧腎症再発予防効果を検討することを目的とした。【方法】2015 年 1 月から 2021 年 3 月までに、当院で周産期管理を行った 4422 分娩中、妊娠高血圧腎症の既往のある妊婦 59 例を対象とした。アスピリン投与群 18 例 (1 日に 81mg 投与 : 12 例, 1 日に 100mg 投与 : 6 例) と非投与群 41 例に分けて妊娠週数、出生体重、胎児発育不全の有無、早発型妊娠高血圧腎症再発の有無について検討した。統計には EZR を使用し χ^2 乗検定または t 検定を用い、 $P<0.05$ をもって有意とした。【成績】分娩週数は、アスピリン内服群は平均値 37.2 ± 13.1 週であり、非投与群の 35.3 週 ± 24.3 と比較して有意に延長できていた ($P=0.006$)。その他、出生体重、胎児発育不全の有無、早発型妊娠高血圧腎症再発の有無に関しては有意な差は認められなかった。【結論】今回の検討では、妊娠高血圧腎症の既往がある妊婦に対するバイアスピリン内服により出生体重、早発型妊娠高血圧腎症発症、胎児発育不全の発生に差は認められなかったが、妊娠週数の延長が期待できることが示唆された。

P-104-1 当院における臨床型羊水塞栓症に関する検討

東海大

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【目的】羊水塞栓症（心肺虚脱型，子宮型）は現在母体死亡の主要な原因の一つであり，発症早期からの集学的治療が必要である．当院における臨床型羊水塞栓症について検討した．【方法】2011年4月から2021年10月までに臨床的羊水塞栓症と診断された18例に関して診療録を用いて後方視的に検討を行った．【成績】18例の中央値は年齢38（22-45）歳，出血量が5515（1500-14055）gで，全例で出血性ショックをきたしていた．初産が9例，経産が9例，分娩方法は経陰5例，吸引6例，帝王切開7例（うち緊急3例）で，分娩誘発が行われていたものが12例，麻酔分娩が6例であった．治療としては全例で輸血が行われ，5例でクリオプレシペートの投与が行われた．8例でBakriバルーンが使用され，12例で動脈塞栓術が行なわれた．4例では動脈塞栓術においても出血のコントロールが困難であり，子宮摘出を要した．来院時心停止の心肺虚脱型の1例では母体死亡に至った．また，意識障害のために呼吸器症状ははっきりしなかったもののCTで肺血栓塞栓症を認めた症例が2例あった．17例でフィブリノゲン値の低下を認め（そのうち35mg/dl未満の著明な低下が8例，35-150mg/dlが11例），15例で血清補体値が測定されており，うち14例で補体低値を認めた．【結論】羊水塞栓症においては発症早期から著明な凝固障害と補体低下を呈する症例が多く，輸血療法を含めた集学的治療を行いつつ，この特徴を捉えていくことが補助診断となる．今回の検討では動脈塞栓術を含めた保存的治療で止血が完遂できた症例が多かったが，出血コントロールが困難である場合には子宮摘出が必要となり，その判断を躊躇してはならないと思われる．

P-104-2 トロンボモジュリンが子宮型羊水塞栓症によるDICに有効だったと思われた1例

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【緒言】子宮型羊水塞栓症に伴うDICに対して，トロンボモジュリンアルファが有効であるとした報告は少ない．今回，トロンボモジュリンアルファが有効であったと思われた1例を経験したため報告する．【症例】44歳4妊2産．胎児発育不全，羊水過多のため当院紹介となり，妊娠27週6日羊水染色体検査で18トリソミーの診断となった．妊娠32週4日子宮内胎児死亡となり，分娩誘発で分娩となった．児娩出直後に母体はショックバイタルとなり，子宮弛緩と非凝固性の性器出血，血尿を認めた．分娩後2時間で676gの出血を認め，フィブリノゲンは55mg/dLと著明に低下していた．産科DIC scoreは15点であり，フィブリノゲン3g，アンチトロンビンガンマ1800単位を投与した．投与後フィブリノゲンは120mg/dLと上昇し，性器出血は止血傾向となったが，FDP，D-dimer高値は持続し，産科DIC scoreは9点とDICが残存した．そのためDICに対しトロンボモジュリンアルファ19000単位を追加投与することでDICから脱却できた．STN（Sialyl Tn）72.0U/mL，Zn-CP（Zinc-coproporphyrin）<1.6pmol/mLとSTNの高値を認め，子宮型羊水塞栓症と診断した．【考察】今回，子宮型羊水塞栓症によるDICに対してフィブリノゲン補充，アンチトロンビンガンマに加えトロンボモジュリンアルファを投与することでDICから離脱できた症例を経験した．子宮型羊水塞栓症は羊水中の組織因子などの凝固促進因子が母体血と反応し，凝固因子の消費が亢進することでDICが起る．トロンボモジュリンアルファはプロテインCの活性化を促進し凝固反応を阻害するため，凝固因子の消費が亢進している子宮型羊水塞栓症に対し有用であったかもしれない．

P-104-3 臨床的羊水塞栓症4例と産科危機的出血に対する当院の取り組み

自衛隊中央病院

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産科危機的出血は約300分娩に1の頻度で起こるとされ，子宮型羊水塞栓症はそのうちの約半数程度を占めるとされる．「産科危機的出血への対応ガイドライン」では，早期の非常事態宣言，コマンドーの決定と指揮命令系統の確立，救命を最優先した薬剤・輸血の投与等が基本的事項として示されている．当院の特性として年間分娩400件程度の地域の2次医療機関であり，輸血ストックが僅少である点が挙げられる．過去5年の当院での取り組みを紹介する．第1に指揮命令系統の確立（コマンドーの決定，産科危機的出血宣言）とそれに伴う人員・資器材の補充，第2に情報共有を円滑化するための院内緊急連絡網図と専用ホットラインの設置，第3にフィブリノゲン製剤を含む危機的出血時使用薬剤類のセット化及び紙伝票を用いた追加輸血オーダーの簡略化及び迅速化，第4に定期的なシミュレーション実施による練度維持である．最近の危機的出血3例では上記の取り組みにより3例とも子宮を温存し母体救命が可能であった．その後もシミュレーション訓練や実際の症例のデブリーフィングを通じてさらなる取り組みの改善，スタッフの教育及び基本動作・手順の徹底を図っている．産科危機的出血は事前に予測できないため，いつどのような状況でも誰もが迅速に対応できるようなマニュアルの整備・システム構築が不可欠である．今後もさらにこの取り組みを改善させ，妊産婦死亡ゼロを目指したい．

P-104-4 羊水塞栓症と常位胎盤早期剝離に合併したDICの病態比較：線溶亢進の観点から

浜松医大

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【目的】消費性凝固障害をきたす産科疾患として羊水塞栓症 (AFE) と常位胎盤早期剝離 (早剝) が知られている。AFE では凝固亢進の程度に見合わない著明な線溶亢進が認められたが、その機序は解明されていない。本研究は、AFE における線溶亢進の病態を早剝との比較により解析することを目的とした。【方法】当教室では2003年よりAFE診断事業を委託され展開している。本事業登録症例と当院症例の中から、Erezの基準でDICと診断された、日本の臨床的AFEエントリー基準に該当する症例および病理学的に診断された早剝症例を対象とした。2009年8月から2020年3月までの該当症例の血漿を用いてTissue factor (TF), Annexin A2, Plasminogen activator inhibitor type 1 (PAI-1), Thrombin activatable fibrinolysis inhibitor (TAFI) を測定した。連続変数を中央値 [最小値-最大値] で示す。【成績】研究対象者はAFE群25例および早剝群9例であった。TF, PAI-1は両群間で有意差を認めなかった。Annexin A2は早剝群で有意に高値(12.0[4.7-2392] vs 72.4[20.9-266.4] ng/mL, $p < 0.01$)、TAFIはAFE群で有意に低値であった(2.6[0.9-6] vs 4.1[2.7-9.2] $\mu\text{g/mL}$, $p < 0.01$)。【結論】TAFIは線溶系酵素のフィブリンへの結合を阻害し、線溶反応を抑制する。血中TAFIの低下がAFEにおける凝固亢進の程度に見合わない線溶亢進に関与している可能性がある。

P-104-5 羊水塞栓症発症リスク因子としての遺伝子バリエーションの解析

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【目的】羊水塞栓症 (Amniotic fluid embolism, AFE) は胎児羊水成分の母体循環への流入が契機となって生じる肥満細胞と補体系の活性化 (アナフィラクトイド反応) が主病態と考えられる。特に心肺虚脱型 AFE は、急激に全身状態が悪化し妊産婦死亡に至ることも多いが、発症を予測することは困難である。将来的に発症の予防・予知・治療に応用するため、何らかの遺伝子バリエーションがAFEのリスク因子になるという仮説を立て、そのバリエーションを同定することを目的とした。【方法】本学AFE事業に登録された心肺虚脱型AFEの子宮組織21検体のパラフィン包埋ホルマリン固定切片からゲノムDNAを抽出し、次世代シーケンサーで全ゲノムシーケンス (Whole genome sequence, WGS) を行った。対照群 (末梢血) と比較しAFE群で頻度が高く、特定のGene Ontologyでアノテーションされた遺伝子バリエーションからPathway解析, Enrichment解析などをもとに絞込みを行った。【成績】21例から最終的に16例の全ゲノムシーケンス結果を得た。16例中8例はバリエーション数が対照群と比べ約2倍 (B:ゲノム品質不良群) であったが、その他8例は対照群と同程度のバリエーション数であった (A:ゲノム品質良好群)。バリエーション総数18831個から、対照群で認められず、A群のうち6例以上かつ全16例中8例以上でみられるバリエーションを抽出し、さらに解析を行い、免疫系や受容体等に関連する18遺伝子に絞込んだ。【結論】AFE発症に関連する可能性のある18個の遺伝子バリエーションを同定した。今後、肥満細胞株や実験動物におけるゲノム編集技術等を用いた実験により、それぞれの遺伝子バリエーションの機能解析やAFEとの関連について検討を行う予定である。

P-104-6 タイプ別に見た羊水塞栓症の発症時期に関する研究

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【目的】羊水塞栓症の病態は母体流入した胎児成分、組織の物理的塞栓だけでなく、組織や液性成分に対するアナフィラクトイド反応であると考えられているが、心肺虚脱型および子宮型の羊水塞栓症の臨床症状の差異の病因については明らかになっていない。それぞれの発症に子宮収縮の有無や発症時期との関連性を明らかにすることを目的とした。【方法】2010年以降、妊産婦症例評価検討委員会に報告された妊産婦死亡症例のうち、死亡原因が心肺虚脱型および子宮型の羊水塞栓症であった症例の発症時期の違いについて検討した。発症時期は、分娩開始前、予定帝王切時、分娩第1期、分娩第2期、分娩第3期、および分娩後2時間以降に分類した。また、児の娩出前後で両者の頻度の違いについて検討した。【成績】2010~2020年の検討期間における妊産婦死亡症例は487例であった。そのうち、子宮 (混合) 型の羊水塞栓症が8% (39例)、心肺虚脱型羊水塞栓症は11% (52例) であった。子宮 (混合) 方および心肺虚脱型の羊水塞栓症の頻度はそれぞれ、分娩開始前、5% (2) と12% (6)、予定帝王切時、0% と10% (5)、分娩第1期、5% (2) と25% (13) *, 分娩第2期、3% (1) と17% (9) *, 分娩第3期、26% (10) と14% (7)、分娩後2時間以降62% (24) と23% (12) *であった (*: $p < 0.05$)。【結論】分娩第1-2期で心肺虚脱型羊水塞栓症が、分娩第3期および胎盤娩出後には子宮型羊水塞栓症が有意に多かった。心肺虚脱型羊水塞栓症は子宮型羊水塞栓症に対して肺などの遠隔部位にも羊水流入の影響が出現している状況であり、それには子宮収縮による子宮内圧上昇が関与している可能性が示唆された。

P-104-7 当院における常位胎盤早期剝離症例の予後因子に関する検討

大津赤十字病院

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【目的】常位胎盤早期剝離（以下早剝）は周産期予後に関わる産科的救急疾患である。今回、当院における早剝症例の臨床経過を振り返り、母児の予後不良に関わる因子について検討した。【方法】2015年1月～2021年7月に早剝と診断し分娩に至った24例を対象とし、入院時の臨床、検査所見や発症から娩出までの時間と母児の予後不良に関わる因子を検討した。母体の予後不良を子宮摘出、UAE、輸血、ICU入室例、児の予後不良をIUFDおよびAp5分値7点未満と定義した。【成績】母体の予後良好群は17例、不良群は7例であった。両群で母体年齢や分娩週数には差を認めず、妊産婦死亡例は認めなかった。予後良好群は全例帝王切開術による分娩であり、予後不良群のうち2例（28.6%）は経陰分娩であった。また予後不良群は予後良好群と比較して分娩前DICスコア（点）が高く（9 vs 4）が高く、発症から娩出までの時間（分）が長く（479 vs 257）、出血量（ml）は多く（1328 vs 958）、分娩前Hb値（g/dL）（8.6 vs 10.7）、血小板数（万/ μ L）（13.1 vs 18.6）、フィブリノゲン値（mg/dl）（137 vs 349）は低値であった。一方、児の予後良好群は8例で、予後不良群16例のうち4例がIUFDであった。予後不良群では予後良好群と比較して、分娩週数が早く、発症から娩出までの時間が長く、母体の分娩前Hb値や血小板数、フィブリノゲン値が低い傾向にあったが有意差は認めなかった。【結論】早剝症例では母体の予後不良に関して、分娩前DICスコア高値や発症から娩出までの時間、出血量、分娩前フィブリノゲン低値がリスク因子であることを再認識して管理を行うべきである。

P-104-8 当センターにおける子宮内胎児死亡を伴う常位胎盤早期剝離19例の分娩様式の解析

日赤医療センター

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【目的】子宮内胎児死亡を伴う常位胎盤早期剝離（以下早剝 IUFD）に対し、わが国では帝王切開術による急速遂娩が行われてきたが、近年は経陰分娩を選択する施設が増加傾向にある。また早剝 IUFDは播種性血管内凝固（DIC）を伴うことが多いことが知られている。当センターでは以前より抗DIC療法を併用しながら積極的に経陰分娩を選択してきた。今回当センターで経験した早剝 IUFD症例の分娩管理について報告する。【方法】対象は、2010年以降に当センターで分娩に至った妊娠22週以降の早剝 IUFD症例とし、診療録を用いて後方視的に解析した。①経陰分娩完遂群（以下VD群）、②経陰分娩を選択したが帝王切開術へ移行した群（以下CS移行群）、③はじめから帝王切開術を選択した群（以下CS選択群）に分け、それぞれ総出血量、分娩所要時間、退院までの入院日数、転帰などについて解析した。【成績】対象は19例で、VD群は13例（初産8例）、CS移行群は3例（初産2例）、CS選択群は3例（初産3例）で、VD完遂率は81.3%であった。CSに移行した3例の理由は、経過中に妊娠高血圧（前回CS）、意識低下（前回CS）、頸管熟化不良を認めたからであった。VD群の平均総出血量は3199mlで非VD群は2305mlであった。VD後の平均入院期間は3.8日で、非VD群は7.3日であった。19例のうちDICスコアが13点以上となったものは8例で、うちVD群は5例であった。子宮摘出を要した症例や母体死亡例はいずれの群にもなかった。【結論】早剝 IUFD症例は、初産婦や頸管熟化が不良な症例であっても抗DIC療法を併用することで経陰分娩を完遂することが可能である。母体の状態により緊急帝王切開術が必要な症例も存在するが、可能な限り経陰分娩を選択することが望まれる。

P-105-1 産科危機的出血動物モデルの確立と人工赤血球の蘇生効果についての検証

防衛医大病院

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【目的】産科危機的出血は母体死亡原因の第一位であり、輸血不足は喫緊の課題となっている。輸血代替治療として人工赤血球 Hemoglobin vesicles (HbV) が注目されている。HbVは血液型に依存せず、感染源がなく長期保存可能で、高い酸素運搬能を持つことが大きな特徴である。既に出血性ショックに対するHbVの有効性は示されているが、産科危機的出血に対する有効性の検討はされていない。そこで我々は新たに産科危機的出血動物モデルを確立し、HbVの有効性の検証を行った。【方法】まず妊娠ウサギの帝王切開を行い胎仔娩出後、創部閉創後に子宮動脈を切離し出血を惹起させた。まず初期治療として輸液（代用血漿剤）投与を全例行った。出血量が100mL又は出血後30分を超えた時点で産科危機的出血状態と定義し、以後の治療は輸液群（代用血漿剤, n=7）、HbV群（HbV+25%アルブミン, n=10）、輸血群（赤血球+血漿, n=8）の3群に分類し、救命治療を開始した。出血後60分又は出血量が200mLに達した時点で止血し、各群の生存時間や血行動態等を比較検討した。【成績】出血開始後30分で、全例がHb6g/dL以下となり産科危機的出血の状態に達していた。HES群が止血後6時間で全例死亡したが、輸血群は全例生存していた。救命治療後、HbV群は平均動脈圧が45mmHg以上、Hb6g/dL以上となっており、6時間後の時点では8例（80%）が生存することができた。全生存期間はHbV群が輸血群より予後不良だったが（ $p < 0.01$ ）、HES群と比較し有意に予後良好であった（ $p=0.01$ ）。【結論】新たな産科危機的出血モデルを確立することができた。致死出血性ショックに至る産科危機的出血の輸血の代替治療として、HbVは有効な手段となり得る。

P-105-2 当院で対応した心停止に至った産後過多出血症例の検討

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【目的】本邦では妊産婦死亡報告事業として母体死亡の症例が集積されているが、心停止後蘇生した症例に関してはまとまった報告がない。当院では2016年より産後過多出血の症例に対して速やかに集学的治療が行える院内コールシステム（以下産褥コール）を運用し多くの症例を受け入れている。本検討では産後過多出血で当院に搬送となり、心停止に至った症例の背景・転帰の解析および産褥コールの有用性を検討することを目的とした。【方法】2010年から2021年に産後過多出血で当院に搬送となった症例のうち、母体の心停止となった症例を後方視的に集積し、各症例の背景・転帰の解析および産褥コール導入前後の予後の比較を行った。【成績】対象症例は8例認めた。搬送元の医療機関は6例が産科単科の一次施設、1例が助産院、1例が総合病院であり、分娩方法は総合病院の1例が帝王切開術で、残りの7例は経陰分娩であり、そのうち2例は無痛分娩を実施していた。産褥コール導入後の症例は5例あり、1例は低酸素脳症に伴う高度神経学的後遺症を残し、1例は多臓器不全により一時的な人工透析を要したが退院時には後遺症は認めず、死亡例は見られなかった。一方産褥コール導入前の3例は、全例死亡に至った。心停止は5例が当院に搬送後にみられ、来院時にすでに心停止に至っていた3症例のうち、産褥コール導入後の2例は蘇生し得た。蘇生し得た5症例の心停止から心肺蘇生までの平均時間は14.2分（5-30分）だった。【結論】早期より集学的治療が行えるコールシステムの運用は産後過多出血症例の母体生命予後の向上につながる可能性がある。

P-105-3 院外発症の産科危機的出血搬送例の時間軸との関連性：ケースシリーズ

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【目的】今般の産科危機的出血（PPH）による周産期死亡例は減少を認める一方で、産後の超緊急搬送例の最多理由である。PPHの搬送例に特化した文献は散見されるのみで、患者の状態は軽症から最重症まで多岐にわたる。分娩後から当院到着までの時間との関連性とその特徴を単一施設のケースシリーズとして後方視的に検討した。【方法】倫理委員会承認（研1703-061）。2015年5月から2021年3月に当院に緊急搬送されたPPH例94例を検討した。なお、「分娩から当院まで180分以内の急要例」かつ「重症化項目：出血量4L以上、フィブリノゲン（Fib）<100 mg/dL値、ICU入院3日以上」を各々従属変数とした「超重症化関連因子」を、多重ロジスティック回帰分析で抽出した【成績】母体死亡4例、産後10時間以上経過12例、データ欠損3例、出血量1000ml未満15例を除外し計60例を対象とした。解析の結果、「急要例かつ出血量4L以上・Fib<100 mg/dL・ICU3日以上入院」の症例では、重症化関連項目は、特定の分娩取扱施設が全項目に該当した（p-Value<0.05）。出産年齢1歳増加ごとに出血量とFib値が該当した（p-Value<0.05）。【結論】急激に増悪し、重篤な搬送レベルに至る超ハイリスクPPHは、高齢出産への注意喚起の必要性が示唆された。また、特定の分娩取扱施設からの搬送が血液因子欠乏と集中治療の長期化の両方で独立して該当した。高次救急センターを有する施設として、地域医療体制・個別指導も含めた教育体制の再構築など、患者負担軽減の解決策を見出す必要がある。

P-105-4 分娩後異常出血に対するフィブリノゲン製剤の使用経験

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【目的】分娩後異常出血（Postpartum hemorrhage：PPH）はわが国の妊産婦死亡の2割を占める。PPHには、凝固因子の補充を目的に新鮮凍結血漿製剤（FFP）やフィブリノゲン（Fibrinogen：Fib）製剤が投与されるが、PPHに対するFib製剤の有効性は確立されていない。そこで当院でのFib製剤使用例について有用性を検討した。【方法】2012年1月から2021年3月の間、当院で治療したPPH症例のうち、輸血製剤を用いた症例を対象に、FFPのみを使用した群（A群）と、FFPとFib製剤を使用した群（B群）に分類し、患者背景、臨床経過について後方視的に検討した。【成績】PPH症例は956例あり、A群が22例（2.3%）、B群が30例（3.1%）だった。両群間の患者背景、出血量に差はなかった。B群では治療前の血小板数、Fib値が有意に低く、PT、APTTは有意に高かった。輸血使用量は、濃厚赤血球液 [6単位（4-10）vs 18単位（11.5-26）；中央値（25%IQR-75%IQR）；p<0.01]、FFP [5単位（4-8.5）vs 16単位（9.5-22）；p<0.01]、濃厚血小板液 [0単位（0-2.5）vs 25単位（0-45）；p<0.01]の全てでB群の使用量が有意に多かった。治療後は、B群のHb、血小板数、Fib値、APTT、PTが有意に改善したが、FFP/RCCは有意差がなかった。母体死亡例はなかった。【結論】本検討では、重症度の高いB群にFib製剤が投与され、輸血量も多かったが、Fib製剤の早期投与により、凝固異常の速やかな改善が得られた可能性がある。同量のFibを投与する場合では、Fib製剤はFFPより低コストかつ短時間で投与できるという利点がある。本検討では、PPHに対するFib製剤の有用性は明らかではなかったが、Fib製剤の投与基準や、特に有用となる症例についての検討が必要である。

P-105-5 一高次施設における血液製剤と自己血の使用状況

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【目的】高次施設においては、妊娠高血圧症候群や前置胎盤、多胎妊娠など、分娩時出血が増加する症例を扱う機会が多い。今回我々は自施設における同種血輸血や自己血の使用状況を後方視的に検討し報告する。【方法】2016年4月から2021年3月までに当院で分娩となった症例において、分娩時に同種血の投与を要した症例及び自己血貯血・輸血を行った症例を抽出し、その特徴を明らかにするとともに、同種血・自己血の有効利用の可能性について統計学的手法を併用して検討を行った。【成績】同期間内の分娩件数は1599件であり、自己血は93例(5.8%)で延べ132件貯血されていた。同種血投与を要した症例は52例(3.3%)、自己血投与を行った症例は72例(4.5%)であり、そのうち自己血投与に加えて同種血を併用した症例が15例(1.0%)あった。自己血のみの症例における分娩時出血量の平均は1167g、同種血輸血のみの症例では1800gであったが、両者を併用した症例では3643gと有意に多かった。自己血全体としては77%が返血されていた。自己血貯血の主要な理由は低置・前置胎盤であり、事前に診断された低置・前置胎盤91例においては58例(64%)で自己血貯血が行われ、返血は50例(86%)とその他の適応(63%)と比較して有意に高率であった。観察期間内で同種血輸血による重度の副反応として輸血関連肺障害(TRALI)が1例認められたが、輸血関連感染症の発症は確認されなかった。【結論】高次施設においては約3~4%の分娩において同種血輸血が必要となり、自己血投与を行った症例においても約20%で同種血の追加が必要となる。自己血貯血の適応症例としては、特に低置・前置胎盤症例においては有効利用が期待できる。

P-105-6 産科危機的出血に対する地域特性に即した当院での対応

京都府立医大附属北部医療センター

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【緒言】京都府北部に位置する当院では血液製剤到着や高次施設への搬送は時間を要し、産科異常出血への対応は早期の子宮全摘術を余儀なくされたが、血管内治療が可能な放射線科医師の赴任によりIVR(Interventional Radiology)による出血源に適したアプローチが可能になった。今回、当院での産科異常出血に対するIVR症例を報告する。【症例1】28歳, G2P1, 経陰分娩後21日目に大量出血のため他院より当院搬送となった。MRI検査で造影効果のある胎盤ポリープを認め、子宮動脈塞栓術後に用手的胎盤剝離を施行した。再出血はなく、術後3日目に退院した。【症例2】31歳, G1P0, IVF-ETにて妊娠成立。妊娠経過に特記異常はなく経陰分娩にて児娩出に至ったが、癒着胎盤による大量出血を認めた。緊急IVRによる動脈塞栓術にて止血を得た。術後5日目に胎盤用手剝離を行い出血増加は認めず産後15日目に退院し、術後10か月で自然妊娠にて妊娠成立し現在妊娠継続中である。【症例3】28歳, G2P1, 全前置胎盤にて当院に紹介受診となった。MRI検査で全前置胎盤の診断で、さらに癒着胎盤の可能性も指摘されたため、分娩時大量出血に備え大動脈バルーン留置下に帝王切開術を施行した。術後大動脈バルーンは使用することなく経過良好で術後8日目に退院した。【結語】事前に大量出血が予想される症例に対して、放射線科医と情報共有することや緊急時にIVRを早期に考慮することで常時対応可能であり、術後妊孕性温存という点においても良好な結果を得た。より安全に管理ができるよう今後症例集積を重ね、更なる検討を行う予定である。

P-105-7 当院における産後出血に対するフィブリノゲン製剤の使用経験

市立広島市民病院

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【目的】当院では2018年9月よりフィブリノゲン製剤が導入され、産後出血症例等に対して保険適応外使用を行ってきた。今回、輸血を要した産後出血の症例(自院分娩例, 搬送例)において、フィブリノゲン製剤導入前後での臨床成績を後方視的に検討した。またフィブリノゲン製剤を使用した症例と使用しなかった症例について比較検討した。【方法】2015年1月1日から2018年8月31日まで(フィブリノゲン製剤導入以前)をI期, 2018年9月1日から2021年9月31日まで(フィブリノゲン製剤導入以後)をII期とし、輸血を要した産後出血症例において総出血量, 総輸血量, フィブリノゲン製剤を使用した割合, 輸血関連合併症についてI期とII期で検討した。また、フィブリノゲン製剤を使用した症例と使用しなかった症例についても検討した。【成績】I期25例, II期40例の輸血を要した産後出血の症例を認めた。診断時の出血量, ショックインデックス, Hb値, Plt値, フィブリノゲン値に差を認めなかった。II期では40例中10例(25%)にフィブリノゲン製剤が使用されていた。I期とII期で総出血量, 総輸血量, 産後入院日数, 多量輸血後の肺水腫発症に差を認めなかった。次にDICスコア8点以上, DICスコア13点以上, 常位胎盤早期剝離・羊水塞栓と診断した症例において、フィブリノゲン製剤を使用した症例と使用しなかった症例の比較検討を行ったが、総出血量, 総輸血量, 子宮動脈塞栓を要した症例, 子宮全摘を要した症例, 産後入院日数, 多量輸血後の肺水腫発症に差を認めなかった。【結論】フィブリノゲン製剤使用による明らかな臨床成績の変化は認めなかったが、症例数がまだ十分でないこともふまえ今後さらなる検討が必要である。

P-105-8 Alcian Blue 染色を利用した産褥大量出血に寄与する因子についての検討

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【目的】羊水塞栓(AFE)は急速進行性の重篤な産科合併症である。当院では原因不明の産後大量出血で子宮摘出し従来のAFE診断基準に合致しない症例に対し、Alcian Blue (AB) 染色を用い、AFE診断基準に当てはまらない子宮型AFE様の病態が存在することを明らかにしてきた。今回、AFE臨床基準に合致しないAB陽性症例において、手術回数・内膜症・羊水暴露時間・フィブリノーゲン値など大量出血関連性因子について後方視的に検討を行った。【方法】2008年～2020年に当院にて産科大量出血で腹式単純子宮全摘を行った31症例のうち、出血量が統計解析上外れ値であった1例を除く30例を対象とした。全例でAB染色を実施。30例のうち、AFEの診断基準を満たさぬ24例のうち、AB染色陰性(AB-群)は13例、AB染色陽性(AB+群)は11例だった。分娩第3期～子宮摘出までの出血量をアウトカムとし、両群における出血量の差、及びその原因となる背景因子を検討した。【成績】出血量はAB-群 4058.92±2068.55 (ml) vs. AB+群 6321.54±3320.81 (ml) (p=0.0538)と統計学的に有意ではないものの、AB+群で出血量が多くなる傾向を認めた。出血量増加寄与因子として年齢、妊娠高血圧症候群、妊娠糖尿病、子宮内膜症、手術回数、喫煙、羊水暴露時間、フィブリノーゲンについてそれぞれ単変量解析を行ったが、いずれの項目においても出血量との有意な相関は認められなかった。【結論】従来のAFE診断基準に合致しないAFE様症例において、胎児・羊水成分の混入により出血量増加の可能性が示唆された。産褥大量出血関連性因子の検討については症例数が少なく、特定には至らなかったが、子宮筋への羊水混入の関与が示唆された。

P-105-9 分娩後腔壁血腫のリスク因子の後方視的検討

信州大

浅香亮一、横川裕亮、品川真奈花、田中泰裕、小野元紀、布施谷千穂、菊地範彦、塩沢丹里

【目的】経陰分娩後に腔壁や外陰に血腫ができる症例を稀に経験するが、その危険因子は不明で、治療方法も確立していない。今回我々が経験した22例の経陰分娩後の腔壁・外陰血腫を後方視的に検討し、その危険因子と適切な治療法の選択法を検討した。【方法】2006年から2020年までに当科で分娩、または分娩後に母体搬送された22例につき、母体年齢、経産数、分娩時週数、児の出生体重、分娩時の血圧、血腫認知までの時間、陣痛増強剤の使用、会陰切開の有無、吸引分娩の有無、総出血量、バイタルサイン、造影CTの所見、治療法、輸血につき検討した。【成績】母体年齢、児の体重、分娩時週数に有意な差は認められなかった。リスク因子と考えられたのは初産(68%:15/22)、分娩時の血圧上昇(85.7%:12/14)、陣痛増強剤の使用(45%:9/20)、吸引分娩(31%:6/19)、会陰切開の施行(76%:13/17)であった。分娩終了から血腫を認知するまでの平均時間は3.3±3.5時間であった。出血量の平均は1515.9±1491.7gであったが、血腫認知時のShock Indexは86%(18/21)で1未満と状態は安定していた。造影CTは22例中19例で施行され、12例で動脈性の出血を認め、血管造影を行っている。12例中1例のみ出血点が特定できなかったが、11例で動脈塞栓術を施行し、10例は1回の塞栓術で止血を得た。22例中9例で輸血を必要とした。【結論】初産、陣痛促進、機械分娩、会陰切開に加え、分娩時に血圧上昇がみられる場合には、分娩後数時間経過してからの腔壁、外陰血腫の形成に注意が必要である。患者状態は安定していても結果的に輸血を必要とすることが多い。治療方針決定には造影CTを施行し、動脈性出血を認める場合には動脈塞栓術の有効性が高い。

P-105-10 分娩時大量出血と常位胎盤早期剥離における凝固線溶系分子マーカー活性からみた新しいフィブリノーゲン境界値の妥当性の検証

NHO 小児・周産期ネットワーク研究

多田克彦、宮木康成、安日一郎、野見山亮、兒玉尚志、前田和寿、江本郁子、大蔵尚文、水之江知哉、前川有香

【目的】分娩時大量出血(PPH)と常位胎盤早期剥離(早剥)において、fibrinogen (Fbg) 値と凝固線溶系分子マーカーの活性化の関係を解析し、我々が提唱した凝固の亢進を反映する新しいFbg境界値の妥当性を検証すること。【方法】2020年9月から開始した多施設共同前向き研究で、分娩時出血量2000g以上のPPH47例と臨床的に早剥と診断された17例を対象として、新しいFbg (mg/dL) 境界値を用い凝固障害を以下の3群に分類した:Fbg≥237、凝固障害なし(N)群;170≤Fbg<237、軽度凝固障害(M)群:Fbg<170、高度凝固障害(S)群。分子マーカー活性からみた凝固線溶系の異常亢進は、内科領域の基準を用い以下の如く定義し、各群における発生率を比較した:凝固系、thrombin-antithrombin complex≥20 ng/mL;線溶系、plasmin-α₂plasmin inhibitor complex≥10 μg/mL。M群では、凝固障害の発生に注意すべきFbg値とされてきた200を境界値として、さらに2群に分けて検討した。【成績】PPHにおけるN群(n=23)、M群(n=16)、S群(n=8)の凝固/線溶系の異常亢進の発生率(%)は、それぞれ39.1/0.0、50.0/31.3、87.5/62.5だった。早剥のN群(n=8)、M群(n=4)、S群(n=5)では、75.0/0.0、100/50.0、60.0/60.0だった。M群を2群に分けた検討の200≤Fbg<237における凝固/線溶系の異常亢進の発生率は、PPH(n=8)で62.5/25.0、早剥(n=3)で100/66.7だった。【結論】200≤Fbg<237における凝固線溶系の異常亢進の発生率は、PPH、早剥共にN群に比べて高率であり、凝固障害の存在を考慮すべきFbg値として237 mg/dLは妥当であると考えられた。

P-106-1 弛緩出血に対して集学的治療で母体救命できた一例

宮崎大¹, 下村産婦人科医院²小畑 静¹, 松澤聡史¹, 榎原康平¹, 長島陽子¹, 大澤綾子¹, 魏 馨予¹, 吉本 望¹, 下村直也², 桂木真司¹, 鮫島 浩¹

【緒言】産科危機的出血による妊産婦死亡は近年減少傾向にあるが、死亡原因第一位で全体の19%を占める。我々は総出血量5000mlに及ぶ弛緩出血例を救命したが重症妊産婦の救命における課題を見つけたので共有する。【症例】24歳、初産婦。一次施設で骨盤位のため妊娠38週で選択的帝王切開術を施行した。術中より子宮収縮不良に伴う弛緩出血にて当院に搬送となった。分娩室にて来院時体温35.5度、末梢冷感を認め持続的な出血を認めた。凝固因子を含む血液製剤の投与、子宮収縮剤持続静注、Bakriバルーンタンポナーデ法の加療を行ったが子宮収縮は不良で出血が持続した。この間血圧120-130/70-80mmHg、心拍数80-90bpmで推移した。治療開始1時間後の電解質はNa138, K4.3, Ca1.0 mmol/L。総出血量4660ml、輸血総量はRBC18U, FFP66U, 血小板10U, フィブリノゲン製剤1gであった。Interventional Radiologyによる両側子宮動脈上行枝塞栓後に確実な止血が得られ以後経過良好であった。【考察】以下の改善点が検討会で指摘された。1) バイタル異常、DICに陥らずに管理しえたが救急部での初期対応が望ましかった。2) 大量輸血に伴う低体温、高カリウム血症、アシドーシスに対する評価、適宜のカルシウム製剤補充に対する意識不足。【結論】危機的状況では総括指揮者による適確なリーダーシップが重要である。救急医との連携という体制整備、チーム医療実現の重要性を認識しコマンダーシステムや多職種連携を日常診療から行う事とした。

P-106-2 妊娠中に発症し、子宮内膜症関連のSHiPと鑑別を要した脾動脈破裂の1例

千船病院

光岡真優香, 城 道久, 北 采加, 安田立子, 吉田茂樹

【緒言】妊娠中の特発性腹腔内出血 (Spontaneous hemoperitoneum in pregnancy, SHiP) は子宮内膜症に関連し子宮・付属器からの出血が多いと報告されている。しかしSHiPの中には脾動脈瘤破裂に伴う出血が稀ながら存在し、その母体救命率は25%と低い。今回妊娠21週にSHiPを認め、試験開腹術にて脾動脈瘤破裂と診断し、脾摘出術により母体救命ができた1例を経験した。【症例】35歳、1妊0産。妊娠21週に突然の上腹部痛を発症し救急搬送となった。超音波検査で子宮周囲に血性腹水を認め、腹部単純CTで肝周囲まで広がる腹腔内出血を認めた。子宮内膜症に関連したSHiPを疑い、造影CTを検討したがその後出血性ショックとなったため、集中的な輸液・輸血を行った上で試験開腹術を実施した。子宮・付属器領域に明らかな出血は認めず、上腹部の皮膚切開を追加し観察すると胃の大彎左側の大網より湧出性出血を認めた。消化器領域の出血を疑い、外科医へ応援の上で手術を進めると、脾門部からの動脈性出血を認めた。脾動脈瘤破裂による出血を疑い、脾摘出術を実施した。胎児は術中に超音波検査で子宮内胎児死亡を確認し、術後3日目に自然陣痛発来し死産となった。母体は全身状態改善し、術後8日目に退院した。【結語】大量のエストロゲンにより血管壁が脆弱化し、妊娠中に脾動脈瘤が形成され、循環血液量の増大により破裂する例が稀であるが報告されている。SHiPの多くは子宮内膜症関連の出血であるが、脾動脈瘤破裂の可能性も考え、外科医との協同した救命処置が重要である。また今回の経験からSHiPを超音波で認めた時点で可能な限り造影CTを撮影することは、治療方針を決定するうえで極めて重要であると考えられた。

P-106-3 経陰分娩後の腹腔内出血に対し審査腹腔鏡で出血源の特定をできた1例

八戸赤十字病院

深川大輔, 深川安寿子, 会田剛史

【はじめに】分娩後に腹腔内出血が生じることは極めて稀であり、出血源特定と大量出血を考慮し緊急手術を要する。今回我々は経陰分娩後に子宮静脈叢の破綻による腹腔内出血を来した症例を経験したので報告する。【症例】33歳、3妊2産。自然妊娠成立後、妊娠17週1日妊娠糖尿病、切迫早産既往のため当院紹介初診となった。妊娠28週4日より子宮頸管長18mmと短縮を認め入院加療を行った。妊娠37週0日に経陰分娩し、子宮収縮は良好であったが、分娩4時間後より持続する腹部膨満感、呼吸苦、血圧低下を認めた。経腹超音波検査ではモリソン窩に腹水貯留を認めた。血液検査ではHb7.3g/dLと貧血の進行を認めた。造影CTでは大量の腹腔内出血を認めたが、出血源を特定することはできなかった。貧血の進行・出血源が不明であることより直ちに輸血を行い、審査腹腔鏡を施行した。腹腔内は大量の腹腔内出血を認め、出血源を探ったところ、右側子宮傍結合織の子宮静脈叢から持続的な出血を認めた。手術開始から20分で出血源の特定をしたが、すでに腹腔内出血量は1500mlを越えたため、直ちに開腹術に移行した。開腹後、出血源の右側子宮傍結合織を挟鉗するも容易に破綻するため、止血を得られず、出血量が2500mlを越えたため、止血目的に子宮腔上部切開術を行ったのち、改めて右尿管の走行を確認しながら止血操作を行った。術後経過は良好で術後8日目に退院となった。【結語】分娩後腹腔内出血という極めて稀な症例を経験した。今回は腹腔鏡下に止血は得られなかったものの、出血源の特定のため、審査腹腔鏡も選択肢の一つと考える。

P-106-4 妊娠関連の大量出血で救急搬送され輸血を要した症例の特徴

手稲溪仁会病院

太田 創, 足立岳貴, 小池和生, 小林雄大, 浅井美香, 浅井聡子, 小嶋一司, 島袋朋乃, 小野洋輔, 滝本可奈子, 福土義将, 和田真一郎

【目的】妊娠関連大量出血で救急搬送され輸血を要した症例の特徴を検証する。【方法】2016年1月から2021年7月に妊娠関連の大量出血で当院が応需した救急搬送症例86例を後方視的に解析した。産科DICスコアが8点以上を産科DICと定義した。当院では初療から関連する部署と連携して治療にあっている。【成績】原因疾患の内訳は地緩出血が33例、子宮仮性動脈瘤・子宮動静脈奇形が16例、胎盤遺残が11例、産道裂傷・産道血腫が10例、後期分娩後異常出血が6例、その他は子宮破裂、後腹膜血腫、RPOC、子宮内反、低置胎盤、流産、筋腫分娩であった。輸血を要した76例のうち産科DICと診断された症例は44例で、搬送前出血量と総出血量の中央値はそれぞれ2000gと2800gであった。搬送前出血量が1000g、1500g、2000gを超えたのはそれぞれ63例、53例、36例で、産科DIC併発率は68%、74%、88%であった。輸血例76例と産科DIC症例44例のうち平日日勤帯以外で応需したのはそれぞれ62例と37例であった。産科DICの主な原因は地緩出血が22例、胎盤遺残が8例、産道裂傷が4例だった。輸血療法に併用した治療は子宮内バルン留置31例、子宮動脈塞栓術17例、胎盤用手剥離術11例、子宮全摘出術7例、子宮圧迫縫合術4例、鏡視下止血術2例であり、全例を救命し得た。【結論】搬送前出血量が多いほど産科DICと診断される傾向にあり、輸血症例や産科DIC併発例の8割強は土日祝日や夜勤帯に應需した。妊娠関連大量出血の搬送症例では初療から関連診療科や多職種と協働し、迅速に診断して治療する必要がある。

P-106-5 産科危機的出血の集中治療後に、神経障害およびSheehan症候群を発症し治療に難渋した一例

大津赤十字病院

林真麻子, 高折 彩, 星本泰文, 上田 匡, 藤田浩平

産科危機的出血への対応として、大量輸血、子宮全摘出術、動脈塞栓術や大動脈閉塞バルーン (IABO) 留置術がある。これらの処置により急性期を離脱しても、続発症により長期的な影響が残る場合がある。報告する症例は35歳初産婦、妊娠38週前期破水後に胎児機能不全で脊髄/硬膜外麻酔下に緊急帝王切開術を受けていた。術中大量出血(約3L)を認めB-Lynch縫合され当院へ母体搬送された。まず子宮動脈塞栓を試みたが処置中に心停止となり、直ちに蘇生を行った。IABO併用下に子宮腔上部切断術を行い、同日(分娩後1日目)さらに右内腸骨動脈塞栓に加えて大動脈ステントグラフト留置術で止血を得た。また、両側下肢麻痺を認め、硬膜外血腫による神経障害やカテーテル治療による脊髄梗塞が疑われたが全身状態が安定しておらず、精査や積極的治療はせず経過観察となった。分娩から止血までの総出血量は5.5L、総輸血はRBC68、FFP52、PC60単位であった。分娩後6日目に副腎皮質ホルモンの低値を認め、相対的副腎不全としてホルモン補充を開始した。分娩後11日目の頭部MRI検査で、下垂体卒中所見を認めたことからSheehan症候群を考え甲狀腺ホルモンの補充も開始した。分娩後58日目に退院となり、分娩後3か月からエストロゲン製剤の補充も開始し、1年以上経過した現在もホルモン補充療法目的に通院継続中である。産科危機的出血後の続発症として稀ではあるが神経障害やSheehan症候群があり、救命後も長期にわたる経過観察が必要であることを認識しておかなければならない。

P-106-6 産褥期にatypical HUSを発症し、治療後に自然妊娠した1例

奈良県総合医療センター

上林潤也, 樋口 渚, 渡辺しおか, 石橋理子, 吉元千陽, 佐道俊幸, 喜多恒和

【緒言】溶血性尿毒症症候群 (Hemolytic Uremic Syndrome : HUS) は血栓性微血管症 (Thrombotic Microangiopathy : TMA) の1つである。腸管出血性大腸菌を検出しない症例は非典型 (atypical) HUSとされ、妊娠を契機に発症することもある。【症例】28歳の特に既往歴のない女性。来院7日前に前医にて硬膜外麻酔による無痛分娩で出産、3日前に退院となった。退院後より発熱あり、抗菌薬投与を受けていたが改善しないため当院に母体搬送となった。搬送時、意識清明、血圧100/58mmHg、心拍数130/分であった。身体所見では明らかな外出血や特記すべき異常は見られなかったが、血液検査でFDP: 788mg/dL、Dダイマー: 369.5μg/mLと著明な線溶系亢進、PT: 37%、APTT: 61.7秒と凝固系延長が見られた。SOFAScore6点であり、敗血症に伴うDICが疑われてICU入室となった。呼吸状態徐々に悪化し、尿量低下傾向となったため第3病日に人工呼吸管理、血漿交換、血液透析導入された。溶血性貧血、血小板減少、腎機能障害があることからTMAによるDICを考慮し、ADAMTS13活性を測定すると23%と低下を認めなかったことからaHUSとして第4病日より5日間ラブリズマブを投与した。第6病日には人工呼吸器より離脱し、第8病日にはICU退室となり、血液内科にて治療継続し、第29病日に退院となった。退院後は血液内科に通院しており、経過中に自然妊娠成立し経過良好である。【結語】DICの原因として感染症やTMAなど鑑別となったが、血液検査所見やADAMTS13活性低下がないことからaHUSの診断に至った。治療後の経過観察中に自然妊娠成立したが、妊娠契機のaHUSは再発例も報告されており今後、十分に注意しながら経過観察する必要がある。

P-106-7 分娩時大量出血症例における頭部MRI検査での下垂体評価についての検討

大阪市立総合医療センター

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【目的】Sheehan 症候群は分娩時の大量出血後に下垂体の梗塞・壊死を生じ、下垂体前葉機能低下症を呈する病態である。症状は下垂体ホルモンの減少または欠乏に起因し、副腎不全などの重篤な合併症を引き起こす場合もある。そのため、早期発見、早期治療介入が重要であるが、発症時期は分娩直後～数十年後と幅広く、全ての大量出血症例で長期予後を観察するのは困難である。そこで、Sheehan 症候群発症リスクの高い症例において分娩直後に頭部MRIを撮像することで、下垂体ホルモン欠乏による症状が出現する前に比較的鋭敏に下垂体機能低下を評価できると考える。【方法】2010年4月1日から2021年9月15日に当院及び他院で分娩時大量出血及びショックバイタルを来した症例15例を対象とした。診療録より患者背景、出血量、出血原因、精査の有無、Sheehan 症候群発症の有無などを後方視的に検討した。【成績】頭部MRI検査を行った症例は15例中9例であり、その内Sheehan 症候群と診断された症例は4例であった。診断された4例の内訳は、分娩直後の発症が2例、分娩20年後の発症が1例、1例は無症状であったが頭部MRIにて偶発的に発見された。5例は頭部MRIにて異常所見を認めず、6例は分娩時大量出血及びショックバイタルを来したが画像精査は行われていなかった。【結論】Sheehan 症候群と診断された症例は時間当たりの出血量が多い傾向があり、急激な血液喪失がSheehan 症候群の発症に深く関与している可能性があった。今回の検討から、分娩時大量出血症例において、一定の基準をもって分娩直後に頭部MRIを撮像することはSheehan 症候群早期発見において有用であると考えられる。

P-106-8 子宮内反症9例の検討

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【目的】急性産褥子宮内反症は産科危機的出血の原因となり得る疾患である。当院で経験した9例の急性産褥子宮内反症の臨床経過や原因について検討する。【方法】2012年9月から2021年8月の期間で当院で治療した急性産褥子宮内反症9例について診療録より後方視的に検討した。【成績】10年間で子宮内反症は9例であり、院内発症4例、院外発症(発症後に当院へ搬送)5例であった。発症率は0.015%(院内発症4例/総分娩数26662例)であった。発症年齢は30-42歳、9例のうち8例が初産婦、完全子宮内反6例、不完全子宮内反3例であり、ショックインデックス>1は、8例で昇圧剤投与などの全身管理を要した症例は4例であった。平均出血量は3283ml(1695-7250ml)で、院内発症は2654ml、院外発症は3787mlであり、輸血は全例に実施した。不穏・疼痛・腔内腫瘍、子宮底を触れないなどの臨床症状から子宮内反症を疑い、経腹超音波検査で診断されていた。全例が用手的に整復成功し、静脈麻酔下8例、全身麻酔下1例だった。院内発症症例は、発症から整復までに要した時間は平均で13分間であった。徒手整復時の緊急子宮弛緩薬投与は4例(全例ニトログリセリン)、整復後の子宮内バルーン留置は5例に施行した。子宮内反の原因は、臍帯牽引7例、癒着胎盤2例であった。全例で術後の子宮内反症の再発を認めず、母児退院した。【結論】分娩第3期に大量出血、疼痛を認めた際は、急性産褥子宮内反症を念頭に置き、速やかな診断と介入が必要となる。輸血を含めた全身管理を要することもあり、高次施設との連携が重要である。

P-106-9 妊娠初期に大量性器出血に伴う出血性ショックを発症したが、妊娠を継続し得た子宮動脈奇形合併妊娠の1例

手稲溪仁会病院

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【緒言】子宮動脈奇形(Uterine arteriovenous malformation: AVM)は、分娩や流産後の不正性器出血を契機に診断される症例報告は散見されるが、妊娠初期に大量性器出血をきたしたにも関わらず妊娠を継続した症例の報告はまれである。今回、妊娠4週で大量性器出血により出血性ショックをきたし、その後妊娠が継続できたAVMの1例を経験したので報告する。【症例】症例は29歳、3妊0産(人工妊娠中絶2回)、挙児希望のある初産婦で、突然の大量性器出血を主訴に近医へ救急搬送された。その後、妊娠4週の進行流産に伴う出血性ショックの診断で当科へ転院搬送された。血清hCG値は113mIU/mlで、経腹超音波検査では子宮内に胎嚢を同定できず血塊の貯留があり、子宮体部後壁筋層内にカラードプラー法で豊富な血流を伴う12×12mmの肥厚した領域を認め、AVMと診断した。性器出血が持続していたため、子宮卵管造影検査用バルンカテーテルを子宮内に挿入し、蒸留水2mlで固定して止血を得た。1,500ml以上の出血と、Hbが14.0から8.1g/dlまで低下する急激な貧血の進行を認めたため、濃厚赤血球液6単位を輸血した。子宮内バルンカテーテルは2日後に抜去したが再出血は無く、さらに7日後の経腹超音波検査でAVMに隣接する直径8mmの胎嚢を子宮内に認めた。本人が妊娠継続を希望したため妊婦健診を継続した。【結論】妊娠初期の大量性器出血を子宮内バルンカテーテルで圧迫止血し妊娠を継続したAVM症例を経験した。本症例は現在妊娠24週であるが、妊娠分娩経過も併せて報告する予定である。

P-106-10 トラネキサム酸を投与した産後出血で腎皮質壊死を呈した一例

大阪赤十字病院

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【緒言】産後出血へのトラネキサム酸 (TXA) の効果をみた国際的多施設共同の WOMAN trial によると、出血後3時間以内に TXA 投与を行うことにより、母体死亡率が有意に減少することが報告されており、TXA 投与に伴う血栓イベントのリスクは増加しないと結論づけられている。今回我々は、産後出血で搬送された褥婦に TXA を投与し腎皮質壊死 (RCN) を呈した一例を経験したので報告する。【症例】32歳, G1P0。前医で妊娠高血圧腎症のため帝王切開が行われ、術後大量出血のため当院へ母体搬送となった。来院時 JCSII-10, 収縮期血圧 110 mmHg, 脈拍 110 bpm, 尿流出はほぼない状態。陸鏡診にて、子宮内より噴出するような出血を認めた。すでに Hb 5.2 g/dL と貧血進行し、Fib 108 mg/dL と低値であったため、大量輸血とともに、TXA 1g を投与した。dynamic CT にて子宮内に造影剤の血管外漏出を認め、同時に腎皮質に限局した造影不良域を認めていた。パルーションポンナーデによる止血が困難であり、バイタルサインが保たれていたため、IVR による止血を施行した。来院時 sCr1.74mg/dL と腎障害を認めていたが、その後も利尿が得られず、腎障害の進行を認め透析導入。精査にて血栓性血小板減少性紫斑病 (TTP) および非典型型溶血性尿毒症症候群 (aHUS) は否定され、特徴的な画像所見より RCN と診断、透析離脱できず腹膜透析導入し退院となった。【考察】産後大量出血においては、早期に TXA を投与することが推奨されている。一方で、TXA の投与は、その血栓形成作用により RCN を引き起こす可能性のあることが報告されている。産後出血への TXA の使用は、投与のタイミングや投与時の母体の病態を考慮する必要があることが考えられた。

P-107-1 切迫早産に対する塩酸リトドリンの short term tocolysis trial の効果に関する前方視的コホート研究

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【目的】切迫早産に対する塩酸リトドリンの短期投与への移行のために計画した当院の short term tocolysis trial (STTT) protocol の有用性を明らかにすること。【方法】2018年12月-2021年4月に、当院に入院した切迫早産例に以下の protocol で前方視的検討を行った。妊娠22-34週間に、子宮収縮を主訴に予約外で来院もしくは、搬送された妊婦を対象とし、所見の変化がある場合に塩酸リトドリンの持続点滴静注を開始し、48時間後に終了とした。終了できた群と出来なかった群を比較し検討した。【成績】対象期間の分娩1513例のうち、切迫早産は151例(10%)あり、双胎妊娠、前置胎盤、前期破水を除いた対象は、妊娠28週未満18例、以降26例を検討した。妊娠28週未満の症例の44%は短期投与後の再開はなく、分娩週数(中央値, 範囲), 妊娠延長期間は34(26-39), 8(0-12)週であったが、短期投与できなかった群では30(22-39), 5(0-8)週であった (ns)。妊娠28週以降の症例の50%は短期投与後の再開はなく、分娩週数, 妊娠延長期間は36(30-40), 3(0-11)週であったが、短期投与できなかった群では35(29-40), 3(0-8)週であった (ns)。短期投与できた群, できなかった群でそれぞれ、軽快退院率は妊娠28週未満で50%, 0% (p<0.01), 妊娠28週以降で69%, 2% (p<0.01), リトドリン総投与量は妊娠28週未満で0mg (0-144), 144mg (144-1166) (p<0.01), 0mg (0-216), 2196mg (216-3024) (p<0.01) であった。絨毛膜炎 stage II 以上は妊娠28週未満で0%, 70% (p<0.01) であった。【結論】塩酸リトドリンを短期投与をしても妊娠延長期間が短縮することはなかった。副作用軽減のためにも短期で塩酸リトドリン使用の終了を試みる意義があると考えられた。

P-107-2 当院における子宮頸管不全症に対する治療的頸管縫縮術とプロゲステロン療法の治療成績の検討

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【目的】当院では、産科既往および子宮頸管の所見から子宮頸管不全症を診断している。その中で頸管長 (CL) が 25mm 未満の場合、産科既往も考慮して治療的頸管縫縮術 (C) またはプロゲステロン療法 (P) の適応を検討し、両者を併用する場合もある。それらの治療成績について検討した。【方法】当院で 2012~2019 年に上記治療を行った症例を対象として後方視的に診療録をもとに、C 単独, P 単独, CP 併用それぞれの治療適応・診断時期・早産の割合などについて検討した。症例は、診断時の頸管所見から、 $10 \leq CL < 25$ mm の低リスク群と、 $CL < 10$ mm または胎胞形成 (可視や脱出など、 $CL = 0$ mm として計算) の高リスク群に分類した。【成績】治療法の内訳は、低リスク群では C 単独 42 例, P 単独 45 例, CP 併用 13 例, 高リスク群では、C 単独 42 例, P 単独 6 例, CP 併用 7 例だった。診断時期は C 単独, P 単独が妊娠 23 週 (平均値) に対し、CP 併用は妊娠 20~21 週と早い傾向を認めた。治療時の CL 平均値は、低リスク群で C 単独 15.3mm, P 単独 18.7mm, CP 併用 16.2mm, 高リスク群で C 単独 2.7mm, P 単独 5.4mm, CP 併用 2.0mm だった。37 週未満の早産率は、低リスク群で C 単独 10%, P 単独 24%, CP 併用 8%, 高リスク群で C 単独 38%, P 単独 50%, CP 併用 43% だった。【結論】早産率は、P 単独に比較して C 単独, CP 併用群の方が少ない傾向を認め、縫縮術の有用性が示唆された。C 単独と CP 併用では早産率はほぼ同等だったが、CP 併用の方が診断時期が約 2 週間ほど早く、より早産リスクの高い症例を対象としていると考えられ、CP 併用療法の有用性を示唆するものと考えられた。

P-107-3 当院における早産ハイリスク症例に対する子宮頸管アラビンペッサリーの使用経験

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【目的】早産予防目的の子宮頸管アラビンペッサリーの研究は海外でも行われ、対象の設定により有効な報告も見られる。現在、日本でも臨床試験が行われている。当院では子宮頸管長短縮例の早産ハイリスク症例に対して頸管ペッサリーを補助ツールとして使用しており安全性や有効性に関して検討した。【方法】2019年7月から2021年7月に当院でペッサリーを使用して分娩に至った83例のうち人工早産8例と12週流産1例を除いた74例を対象として有害事象、症例の臨床的背景、双胎の経過、単胎のリスク因子別経過について検討した。倫理委員会の承認を受け、文書での同意を得て施行している。【成績】背景は双胎5例(6.8%)、円錐切除後11例(14.9%)、自然流早産既往14例(18.9%)(9例は34週未満)とハイリスク症例を含む。結果は挿入時頸管長(中央値)15mm、週数は妊娠25週3日、分娩週数は妊娠37週3日で妊娠延長期間83日あった。単胎ではそれぞれ15mm、妊娠25週4日、妊娠37週6日、83日で48例(69.6%)が正期産だった。リスク因子別では円錐切除後で21.5mm、妊娠15週3.5日、妊娠35週6日、125日。37週未満早産既往で11.5mm、妊娠24週4.5日、妊娠36週3日、76.5日。34週未満早産既往で11mm、妊娠23週6日、妊娠31週1日、67日であった。主な有害事象(因果関係は問わない)はペッサリーのずれによる疼痛1例、自然脱着2例、絨毛膜羊膜炎10例であった。【結論】約70%が正期産に至っており、また重篤な有害事象はみられずペッサリーを用いた追加治療は早産予防に安全かつ有効であることが示唆された。既存の治療でも管理がむづかしい早産ハイリスク因子を持つ妊娠においても頸管ペッサリーによる追加治療の一助になる可能性がある。

P-107-4 当院における早産の治療方法についての検討

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【目的】切迫早産の治療薬として、本邦では子宮収縮抑制剤が多用されているが、その使用方法や投与期間は諸外国と大きく異なる。当院では2015年に母体への副作用を考慮した切迫早産治療プロトコルを作成し、治療薬の第一選択を塩酸リトドリンから硫酸マグネシウムに変更した。変更前後の治療効果について比較検討を行った。【方法】切迫早産の診断で入院管理を行った単胎妊婦を対象とした。プロトコル作成前の2009~2011年をA群(400症例)、作成後の2018~2020年をB群(269症例)とし、治療を塩酸リトドリン単体、硫酸マグネシウム単体、両剤併用、点滴無しにわけ、治療効果を後方視的に検討した。A群では外来経過中に子宮頸管長短縮または頻回な子宮収縮を認めた症例を切迫早産と診断し、塩酸リトドリン点滴を第一選択とした。B群ではA群での診断方法に加え妊娠18~24週間に2回子宮頸管長測定を必須とし、子宮収縮抑制剤の第一選択を硫酸マグネシウム点滴とした。【成績】治療方法を塩酸リトドリン単体、硫酸マグネシウム単体、両剤併用、点滴なしとした場合、A群ではそれぞれ39%、10.3%、26.5%、24.2%だったが、B群では5.2%、39.4%、25.2%、30.1%と有意差を認めた。28週未満、34週未満、37週未満の早産率はA群では4.0%、22.0%、27.3%、B群では5.0%、14.0%、26.3%であり治療効果に有意差は認めなかった。【結論】切迫早産治療の第一選択薬変更による早産率に変化は認めなかった。副作用や長期安静入院など母体へのデメリットも勘案し、子宮収縮抑制剤の適応および使用期間に関して再度検討する必要があると考える。

P-107-5 当院における切迫早産治療 long term tocolysis から short term tocolysis へ変更による比較検討

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林 立弘, 北本愛依, 江藤千佳, 福地千恵, 田中 晶, 村上裕介

【目的】日本では切迫早産の治療として長期安静と塩酸リトドリン低用量持続投与(long term tocolysis)が行われていたが、欧米では塩酸リトドリン48時間投与(short term tocolysis)による切迫早産管理が一般的であり、日本でも増加している。当院の切迫早産管理をlong term tocolysisからshort term tocolysisへ変更したので、臨床転帰について報告する。【方法】当院の切迫早産管理指針を2018年10月よりshort term tocolysisへ変更した。切迫早産入院となった時期が2013年5月1日から2018年9月30日までを前期(long term tocolysis)、2018年10月1日から2021年8月31日までを後期(short term tocolysis)とした。両群を入院期間、37週未満の早産率、NICU入院率などについて比較検討した。多胎、前置胎盤、既往帝王切開後妊娠症例は除外した。【成績】前期分娩総数は3102件、対象症例は185例。後期分娩総数は1373件、対象症例は70例であった。入院期間は前期、後期でそれぞれ33.9±24.5日、18.6±18.9日であり有意に減少した(p<0.00001)。一方、分娩週数は前期、後期で37.3±2.07週、37.5±2.25週と差を認めなかった(p=0.37)。それぞれの分娩転帰は37週未満の早産が11% vs 20%(p=0.097)と有意差を認めなかった。出生児のNICU入院率は35.6% vs 28.5%(p=0.284)と有意差を認めなかった。【結論】切迫早産管理方法をlong term tocolysisからshort term tocolysisへ変更した結果、入院期間は減少したが、在胎週数、37週未満の早産率、NICU入院率に差は認めなかった。

P-107-6 絨毛膜下血腫に対する予防的抗菌薬（腔錠）投与の有用性に対する検討

静岡県立こども病院

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【目的】絨毛膜下血腫（SCH）は流早産のハイリスク因子であるがコンセンサスの得られた治療法はまだない。当院における妊娠24週以下の流早産症例（37例：2010～2012年）の胎盤病理でSCHは60%を占め、そのうち70%が絨毛膜用膜炎（CAM）を合併していた。このため、SCH症例に対する予防的抗菌薬（腔錠）投与の有用性について検討した。【方法】2010年1月から2020年12月に当院で管理したSCH症例148例を対象とした。SCHが妊娠16週以降にも存続し、性器出血を認める症例とした。1週間に1回、メトロニダゾール腔錠（250mg）を投与した。無投与群（～2012年）と投与群（2013年～）にわけ、妊娠32週未満の流早産、CAMに加えて周産期合併症の発生率について後方視的に比較検討した。【成績】SCH症例148例のうち投与群65例、無投与群83例であった。投与群は無投与群と比較して、妊娠32週未満の流早産率は有意に低かった（50.8% vs 71.1%, $p=0.018$ ）。CAM、早期前期破水、子宮内胎児発育不全の発生率については2群間に有意差を認めなかったが、投与群で低い傾向が示された。【結論】存続するSCHに対する予防的メトロニダゾール腔錠の投与は32週未満の流早産率を減少させる可能性がある。今後さらに症例を重ね検討していく予定である。

P-107-7 リトドリン塩酸塩と硫酸マグネシウムとの併用で発生リスクが高まる新生児高カリウム血症：多施設共同後方視的研究

子宮収縮抑制剤の新生児への影響調査・検討ワーキンググループ

大口昭英, 大槻克文, 齋藤 滋

【目的】2017年に産科医療補償制度原因委員会から日本周産期・新生児医学会に対して、硫酸マグネシウムあるいはリトドリン塩酸塩で切迫早産の治療を受けた母体から出生した新生児を対象に、高カリウム血症および低血糖症についての発生状況の調査が依頼された。【方法】ワーキンググループが立ち上がり、2014年に32～36週で出生した新生児を対象に後方視的調査が企画された。本研究は、日本周産期・新生児医学会の協力を得て調査した。78施設、新生児6136例について、Web上のデータベースを利用してデータが収集された。主要評価項目は、新生児高カリウム血症及び新生児低血糖であった。副次評価項目は3歳時の脳性麻痺、何らかの神経学的異常であった。産科・小児科に関連した14リスク因子について多重ロジスティック回帰分析を行った。【成績】高カリウム血症は7.6%、低血糖は32.4%にみられた。リトドリン塩酸塩と硫酸マグネシウムの併用療法は、子宮収縮抑制剤未使用例と比較して、新生児高カリウム血症の調整オッズ比は1.53（95%信頼区間：1.09-2.15）であった。また、リトドリン塩酸塩単独の新生児低血糖発症の調整オッズ比は2.58（2.21-3.01）、併用療法の新生児低血糖発症の調整オッズ比は2.59（2.13-3.15）であった。新生児低血糖は3歳時の何らかの神経学的異常と有意な関連を認めた。【結論】リトドリン塩酸塩と硫酸マグネシウムを併用すると、新生児高カリウム血症発症リスクが高まった。2021年4月に添付文書に本事象が追記された。母体が子宮収縮抑制剤の投与を受けていた場合には、高カリウム血症および低血糖の発生頻度が上昇することを念頭において新生児管理を行う事が重要である。

P-107-8 流早産予防目的にプロゲステロン製剤を投与した症例の周産期予後についての検討

愛染橋病院

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【目的】流早産既往のある妊婦で早産予防目的にプロゲステロン製剤を投与した症例の周産期予後を後方視的に検討した。【方法】2013年10月から2021年7月に当院で分娩となった症例のうち、妊娠20週以降の流早産既往のある妊婦で早産予防目的にプロゲステロン製剤の投与を希望した症例を対象とした。プロゲステロン製剤は妊娠16週から20週までに開始され、妊娠36週まで毎週投与した。他院で分娩となり詳細不明な症例、途中でプロゲステロン製剤の投与を断念した症例、今回の妊娠経過において未破水での子宮内胎児死亡症例、頸管縫縮術実施例は除き、妊娠20週以降に分娩となった単胎妊娠について検討した。【成績】106症例においてプロゲステロン製剤が投与されていたが、20症例において頸管縫縮術が実施されていた。頸管縫縮術を行っていない86症例において早産となったのは24症例（27.9%）であった。また前回の子宮切開法によるリスクを考慮した人工早産、前置胎盤や妊娠高血圧症候群による人工早産は合計5症例あり、それらを除いた早産は19症例（23.5%）であった。早産した19症例のうち、34週未満は9例あり、全例胎盤病理検査が実施され7例に絨毛膜羊膜炎を認めた。34週以降37週未満は10例あり、7例において胎盤病理検査が実施され、いずれも絨毛膜羊膜炎を認めなかった。残り3例は36週であったため検査へ提出されていなかった。流早産症例と正常産症例の既往早産回数を比較したところ有意差は認めなかった。（ $p=0.08$ ）【結論】プロゲステロン製剤投与後における流早産率は過去の報告と比較してほぼ同様の結果であった。34週未満の流早産のうち77.8%において絨毛膜羊膜炎を認め、感染が流早産の原因と考えられた。

P-107-9 プロゲステロン消退型早産マウスの頸管熟化過程における CCL11 を介した好酸球性炎症の検討

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【目的】子宮頸管熟化は頸部間質への免疫細胞の浸潤を特徴とする炎症反応と類似した無菌のプロセスであり、プロゲステロン (P4) 作用の機能的消退を起点として誘導されると推測される。本研究では P4 消退型早産モデルマウスを用い、子宮頸管組織学的変化と同期した炎症性変化について解析した。【方法】妊娠 15 日目のマウスに、プロゲステロン受容体拮抗薬 (mifepristone) or 溶媒を皮下注射し (n=5 vs n=5), 12 時間後に子宮頸部を摘出した。組織から RNA を抽出し、PCR array (Inflammatory Cytokines and Receptors) を行った。mifepristone 投与でアップレギュレーションされる分子をターゲットに、リアルタイム PCR, 抽出蛋白のウェスタンブロッティング (WB), 組織切片の免疫組織化学染色 (IH), および子宮頸管粘液の ELISA 法による比較解析を行なった。さらに、mifepristone 投与により子宮頸部に特異的に誘導される免疫細胞をフローサイトメトリーで解析した。【成績】mifepristone 投与マウスでは、頸管間質の膨化を特徴とする頸管熟化変化が認められた。PCR array およびリアルタイム PCR 法で、mifepristone 投与により著明に発現誘導される分子として、好酸球の主要な走化因子であるケモカイン CCL11 (eotaxin-1) が同定された。WB では mifepristone 投与による CCL11 の増加を認め、IH では子宮頸管上皮および間質全域における発現増強が認められた。CCL11 の特異的受容体である好酸球の細胞表面マーカー CCR3 が広範囲に検出された。【結論】P4 消退を起点とした子宮頸管熟化のメカニズムへの CCL11 のアップレギュレーションによる好酸球性炎症の関与が示唆された。

P-108-1 早産妊婦における腔内細菌叢の経時的変化

藤田医大
坂部慶子

【目的】早産は子宮内感染がその危険因子とされる。早産に特異的な腔内細菌を次世代シーケンサーにて評価し、経時的な変化を解析して早産を予測するためのバイオマーカーについて検討した。【方法】早産 5 例, 切迫早産 12 例, 正常産 23 例を比較した。メタゲノム解析は細菌ゲノム DNA の 16S rRNA 遺伝子 V3-4 領域を PCR で増幅後、次世代シーケンサーにて解析した。細菌同定は GreenGene 等のデータベースを用い、解析ソフトウェアである QIIME にて主成分分析、ボルカノプロットを作成し、統計学的有意性検定はロジスティック回帰分析、Mann-Whitney U 検定、一元配置分散分析した。【成績】主成分分析で早産群はクラスター化し、切迫早産群は非早産群に比べて Firmicutes 門の有意な増加、Actinobacteria 門の有意な低下を認めた (各 $P < 0.01$)。ボルカノプロットで Firmicutes 門の *Fingoldia* 属と *Lactobacillus* 属の増加あり (各 20-fold; $P = 0.17$, 2-fold; $P = 0.10$)。 *Lactobacillus* 属は早産群 90.5%, 非早産群 48.5% と早産群で有意に増加した ($P < 0.05$)。 *Lactobacillus* 属のうち *L. iners* は早産群 20.7%, 非早産群 12.6%, *L. crispatus* は早産群 61.5%, 非早産群 19.4% と早産群で高値だが (各 $P = 0.73$, $P = 0.14$)。 *L. gasseri* は早産群 0.1%, 非早産群 9.1% ($P = 0.01$) と早産群で有意に低下した。同一症例の入院時と治療後の比較で *L. iners* の増減率は切迫早産群で -48.2% と減少し早産群では 3.0% であった。【結論】 *Lactobacillus* 属は腔内における主要な細菌叢として pH の調節を通じて防御機能に寄与すると考えられているが、異なる *Lactobacillus* 種の変化が早産に影響すると考えられた。 *L. iners* が治療に伴い減少しないことは、早産予測のバイオマーカーとなり得ることが期待された。

P-108-2 当院の切迫早産例における、ウレアプラズマ感染と早産の関連性について

日赤医療センター
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【目的】腔内ウレアプラズマ感染が早産の原因となる可能性が指摘されている。当院での分娩統計を用いて、腔内ウレアプラズマ感染の有無と早産の関連性についての検討を行った。【方法】2019 年 4 月から 2021 年 7 月の間に、切迫早産の臨床症状を認め当院で腔内ウレアプラズマの培養検査を行った単胎妊娠例のうち、妊娠 22 週以降に分娩に至った症例を抽出した。培養陽性群と培養陰性群 (対照群) に分類し、分娩日数に関してログランク検定と Cox 比例ハザードモデルによる多変量解析を行った。【成績】陽性群 73 例, 対照群 275 例が抽出された。年齢の中央値はそれぞれ 32 歳, 35 歳であり、母体搬送例は 24.5%, 29.8% であった。また、分娩日数の中央値はそれぞれ 255 日, 262 日であり、陽性群は対照群と比較して有意に分娩日数が早かった (ハザード比 1.33, 95% 信頼区間 1.01-1.74)。年齢、ウレアプラズマ以外の細菌感染の有無、妊娠高血圧症候群の合併、子宮頸部円錐切除歴、早産歴、子宮筋腫の合併、前置胎盤の有無を説明変数として多変量解析を行うと、陽性群で分娩日数が早い傾向がみられた (ハザード比 1.31, 95% 信頼区間 0.98-1.74)。切迫早産の臨床症状を認めた日数や早産期前期破水を発症した日数には有意差はなかった。【結論】腔内ウレアプラズマ感染は早産の原因因子のひとつと考えられる。

P-108-3 胎盤病理から見る早期産の病態と妊娠中期流産既往妊娠管理の試み

浜松医大

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【目的】妊娠中期流産既往の妊婦は、次回妊娠時に流産を反復するリスクがある。今回早期産胎盤を組織学的に検討し、更に妊娠中期流産既往妊婦に対し流産時の胎盤病理における炎症所見の特徴から次回妊娠管理方法を決定し妊娠転帰につき検討を行った。【方法】早期産の胎盤は2016年1月から2020年12月までの妊娠22週から33週までの多胎を除く症例について子宮収縮(+)群と子宮収縮(-)群の2群に分類し、胎盤組織にHE染色を行いmaternal vascular malperfusion(MVM), Maternal inflammatory response(MIR), Deciduitisの有無につき検討した。更に子宮収縮を伴う妊娠16週から28週までの中期流産既往の妊娠例について流産時の胎盤病理所見から①感染を伴わない非炎症型(N群)②絨毛膜羊膜炎に炎症反応を示す絨毛膜羊膜炎型(C群)③炎症反応が脱落膜にも認められる脱落膜炎共存型(D群)の3群に分類し、2014年1月から2020年12月までの期間に妊娠した例につきを各々、N群は予防的頸管縫縮術、C群は予防的頸管縫縮術および陰洗浄・ウリナスタチン(UTI)陰錠挿入、D群は陰洗浄・UTI陰洗浄の管理方針とした。【成績】総分娩数3921件中、33週以下の早期産は140例(3.6%)であった。対象の114例につき検討を行ったところ子宮収縮(+)群はMIRとDeciduitisが、子宮収縮(-)群はMVMが有意に認められた。中期流産既往妊娠では対象症例N群4例、C群7例、D群13例であり管理により正産となったものは各々3例(75%)、5例(71%)、11例(85%)であった。【結論】胎盤病理検査は早産原因の病態把握に有用であり、妊娠中期流産症例について胎盤病理所見により管理方針を決定すると次回妊娠時に早産を回避できる可能性が示唆される。

P-108-4 妊娠中の性交渉の有無は早産に関係するか

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葉 宜慧

【目的】日本人での妊娠中の性交渉の有無と早産との関係を究明することを目的に、コホート研究を行った。主評価項目として、妊娠中の性交渉の有無と早産率の関係。副次評価項目は、妊娠中の性交渉の有無と細菌性陰症の関係と性交渉のあった症例の細菌性陰症が早産率を増加させたか。【方法】2018年5月~2019年9月までに当院で妊婦健診、分娩した205人のうち、アンケートに回答した164人とした。1.①妊娠14週以降28週まで②28週以降分娩までの性交渉の有無と早産率を検討した。2.妊娠初期と中期の妊婦健診時に、腔内細菌検査を行い、Nugent score7点以上を細菌性陰症として早産率を検討した。【成績】妊娠14週から28週までの性交渉の有無と早産率は、性交渉有り群23% VS.無し群12%(P=0.047)。妊娠28週以降分娩時までの性交渉の有無と早産率は、性交渉有り群17% VS.無し群12%(P=0.466)。性交渉なしで細菌性陰症なし VS.性交渉有り細菌性陰症なしは、2% VS.25%(P=0.0001)性交渉有り細菌性陰症 VS.性交渉なし細菌性陰症は、33% VS.25%(P=1)【結論】妊娠14週から28週での妊娠中の性交渉は有意に早産率を上昇させるが、28週以降の妊娠中の性交渉は早産率を上昇させなかった。妊娠中の性交渉による早産のリスクは、細菌性陰症以外の因子が関与している可能性が示唆された。

P-108-5 妊娠中期流産既往症例における子宮内細菌叢に関する pilot study

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【目的】早産の原因として絨毛膜羊膜炎が最多であり、腔内細菌叢と関連するとされている。一方、子宮内細菌叢が不良の場合着床率が低下するという報告が散見されるが、周産期予後との関連に関する報告は乏しい。そこで妊娠中期流産と子宮内細菌叢の関連性について検討した。【方法】12週から28週の流産既往のある14例を対象とし、非月経期に子宮内膜を採取し、細菌の16S rRNA 遺伝子を対象に次世代シーケンサーを用いて細菌叢を解析した。流産時の胎盤病理検査で絨毛膜羊膜炎(CAM: chorioamnionitis)を認めた症例をCAM群、認めなかった症例を非CAM群、他院分娩例のため胎盤病理検査未実施症例を不明群とした。細菌叢中のLactobacillus属(以下Lac)の占有率90%以上をLDM(Lactobacillus-dominated microbiota), 90%未満をNLDM(Non-LDM)と定義し関連性を検討した。また、妊娠中や子宮内膜組織採取時の腔分泌物培養検査所見との関連性についても検討した。【成績】NLDMはCAM群で7/9例(77.8%)、非CAM群で2/3例(66.7%)、不明群で2/2例(100.0%)を占めた。妊娠中の腔分泌物でLac優勢と判断された症例3例のうちNLDMは1例のみだった。子宮内膜と同時期に採取された腔分泌物でLac優勢とされても子宮内細菌叢ではNLDMと判定された症例を認めた。【結論】一般女性より妊娠しにくい不妊症女性を対象とした日本からの報告(Kyono et al, 2018)ではNLDMが45/92例(48.9%)を占め、妊娠中期流産既往症例におけるNLDM(11/14例, 78.6%)の方が有意に多かった(P<0.05)。また、腔分泌物培養検査でLac優勢であっても子宮内細菌叢でLDMとは限らず、採取部位と解析法の違いに起因すると思われる。

P-108-6 胎盤形成期の前期破水症例における胎児肺成熟の評価と結果

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【緒言】妊娠 16 週未満の胎盤形成期における破水は、自然治癒した症例を除くと流産として取り扱われることも多く、予後や治療方法に関するエビデンスが乏しい。今回、妊娠 14 週で完全破水後、治療なく妊娠 25 週で死産分娩に至った症例に関して、肺成熟の観点から考察する。【症例】37 歳 4 妊 0 産、凍結融解胚移植で妊娠成立、妊娠 10 週で紹介受診後は、当院で妊娠管理していた。既往に腹腔鏡下子宮筋腫核出術、子宮内膜ポリープ切除術あり。妊娠 14 週 5 日に完全破水、入院管理で抗生剤治療（アンピシリン 8g/day, アジスロマイシン 500mg/day）を開始した。感染兆候なく経過し、妊娠 16 週で子宮収縮のためリトドリン塩酸塩で子宮収縮抑制を開始するも、羊水流出は持続していた。本人と家族の強い希望から妊娠継続方針となり、妊娠 24 週に胎児肺成熟目的でベタメタゾン 12g を 2 回投与、硫酸マグネシウムを併用するも子宮収縮抑制困難のため、妊娠 25 週 5 日に骨盤位の適応で帝王切開術での娩出とした。出生児は 880g の男児、Apgar score 1/1/1 点 (1/5/10 分值)、蘇生実施するも反応せず、新生児死亡を確認した。【考察】本症例は妊娠 14 週、肺の発生段階としては腺様期 (pseudoglandular period) の破水だが、分娩は妊娠 25 週と管状期 (canalicular period) 末期であり、終末囊の発生も期待された。死産児の剖検では、肺組織は acinar/canalicular phase と週数相当であったが、肺総重量は 8.9g と児体重比 0.010 で肺低形成を示した。MRI 検査は妊娠 22 週・25 週で実施しており、胎児胸郭は狭小で、妊娠 25 週での肺肝臓信号強度比は 1.65 と低値であった。破水後の子宮内圧上昇による胸郭形成不全も、肺形成の妨げとなった可能性が考えられる。

P-108-7 分娩中の臨床的絨毛膜羊膜炎が新生児に与える影響

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【目的】正期産期妊婦における分娩中の臨床的絨毛膜羊膜炎 (cCAM) と新生児有害事象との関連を明らかにする。【方法】2018 年 1 月からの 3 年間に、妊娠 37 週 0 日以降に分娩となった単胎児を対象とした後方視的コホート研究である。胎児死亡、胎児構造異常、経陰分娩未試行例、分娩開始前の cCAM、生後一か月時点の新生児の評価が無い症例は除外した。評価項目は新生児複合有害事象 (死亡、低酸素性虚血性脳症、敗血症、髄膜炎、痙攣、挿管、胎便吸引症候群) の頻度とした。母体高齢、初産、体外受精、分娩時 BMI \geq 25、妊娠高血圧症候群、妊娠糖尿病、母体 B 群溶血性レンサ球菌陽性、硬膜外麻酔、オキシトシン、破水～分娩 \geq 24 時間、帝王切開、small for gestational age のうち単変量解析で $P < 0.2$ であった因子を調整因子として、多変量ロジスティック回帰分析を用いて cCAM の有害事象に対する調整オッズ比 (95% 信頼区間) を算出した。分娩中に 38.0°C 以上の発熱を認めた場合に身体診察及び血液検査を行い、Lencki の基準に合致しその他の感染源を認めない場合に cCAM と診断した。診断後、速やかに抗菌薬投与を行い、医師の判断で陣痛促進や器械分娩による分娩時間の短縮を図った。【成績】対象 2930 例のうち cCAM は 113 例 (3.9%) であった。有害事象は 27 例 (0.92%) であり、挿管が 9 例、胎便吸引症候群が 20 例 (重複あり) であった。cCAM 例と非 cCAM 例における新生児複合有害事象の頻度はそれぞれ 0.88%、0.92% であった。オキシトシンの調整オッズ比は 4.62 (1.55-17.2) で有害事象に対する関連を認めたが、cCAM は関連が無かった。【結論】正期産期妊婦における分娩中の cCAM は新生児有害事象と関連しなかった。

P-108-8 絨毛膜羊膜炎起因菌同定にむけた 16S rRNA 解析におけるシーケンス領域の差異による影響

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【目的】絨毛膜羊膜炎 (CAM) の起因菌診断へ 16S rRNA のシーケンスによる菌叢解析が試みられ、ターゲットとして V1-V2 または V3-V4 領域が用いられている。今回我々は、これら 2 領域での属レベルの解析と腔分泌物培養の結果を比較し、方法論を考察した。【方法】対象は、帝王切開 (帝切) で分娩し、胎盤病理組織学的検査で CAM と診断された 8 例 (III 度 3 例, II 度 3 例, I 度 2 例のうち 1 例は DD 双胎) 及び非 CAM 3 例。帝切時採取の羊水と腔分泌物を 16S rRNA の V1-V2 (V1-2 解析) 及び V3-V4 領域 (V3-4 解析) で菌叢解析を行った。帝切前採取の腔分泌物は当院検査室で培養、菌を同定した (院内培養)。【成績】腔分泌物の結果は、非 CAM で V1-2 及び V3-4 解析とも検出リードの大半が *Lactobacillus* であり、院内培養と同様であった。CAM では、4 例で院内培養の検査項目に含まれない *Ureaplasma* が V1-2 及び V3-4 解析とも検出され、分娩は全例妊娠 34 週以前であった。腔分泌物の α 多様性は、I 度及び II 度で増加し、III 度で低下していた。III 度羊水は、V1-2 及び V3-4 解析とも腔分泌物で検出した CAM 関連菌種を認めた。また II 度以下及び非 CAM 羊水の菌叢と α 多様性は、ほぼ同様であったが、III 度羊水の α 多様性は著明に低下していた。V1-2 と V3-4 解析で最優勢の属は、ほぼ同じだったが、次位以降は羊水の半数、腔分泌物の 4 例で異なり、その菌種は陰性コントロールでも検出された。【結論】現在 CAM を惹起し治療対象と考えられている *Ureaplasma* 等の検出や α 多様性の評価は、シーケンス領域によらず 16S rRNA 解析が有用であり、重症 CAM 診断への羊水解析の重要性も示唆された。今後、治療対象の拡大や新たな病態解明時には、解析手法を精査することが求められる。

P-109-1 経産婦の早産リスクについての検討

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【目的】経産婦の早産リスクには早産や分娩停止, 第2期遷延, 中期中絶, 頸管裂傷, 在胎不当過少, 妊娠高血圧症候群, 常位胎盤早期剝離, 子宮内胎児死亡等の既往が影響すると報告があるが, 自然早産に特化したリスク因子については詳細が不明である。妊娠初期に自然早産のリスクが高いか否かを評価することができれば, より慎重な妊娠管理を行うことが可能となる。今回, 経産婦の自然早産を予測するリスク因子を抽出することを目的とした。【方法】2017年8月~2021年7月に妊娠37週未満で単胎を分娩した経産婦のうち人工早産を除外した69人を対象とした。経産回数を入れた正常産168人をコントロール群とした。評価項目は, 切迫早産既往, 早産既往, 分娩停止後の帝王切開, 妊娠中期分娩, 頸管裂傷, 生殖補助医療, 初期流産もしくは中絶, 3回以上の経産分娩, 第1子の分娩所要時間6時間以下, 器械分娩, 円錐切除既往とした。【成績】早産既往ではオッズ比8.84 (95%信頼区間4.22-18.5, $P<0.01$), 妊娠中期分娩ではオッズ比5.79 (1.53-21.9, $P<0.01$), 円錐切除既往ではオッズ比5.080 (1.310-19.7 $P=0.019$), 3回以上の経産分娩ではオッズ比3.930 (1.42-10.80 $P<0.01$) であり, これらの4項目と経産婦の早産との関連性が示唆された。【結論】前回妊娠, 出産時の情報を詳細に確認する事で, 早産のハイリスク群を把握し安全な妊娠分娩管理を行える可能性がある。

P-109-2 妊娠初期の妊産婦における細菌性陰症と早産率の検討

青森県立中央病院

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【目的】妊娠初期の細菌性陰症(以下BV)のスコアリングおよび治療を行い, 早産率を評価した。【方法】2017年1月~2021年9月まで, 妊娠初期より当科でフォローし, 当院で分娩となった妊産婦516例において, 妊娠初期に細菌性陰症スコア(以下BVスコア)を用いてBVスクリーニングを施行した。A群0~3点, B群4~6点, C群7~10点に群分けし, それぞれの群内で早産率を算出し, BVスコアにより差があるかを比較した。また, 途中から外来紹介・母体搬送を含めた2018年-2019年の総分娩数(1242例)の早産率と, 同年の妊娠初期から分娩まで当院で経過を見ていた妊産婦の早産率のデータを比較した。【成績】A群391例中35例(8.9%), B群68例中15例(22.0%), C群57例中6例(10.5%)で, 各群間で早産率を比較した。早産率では, A群とB群およびC群の早産率には有意差はなかったが(P 値=0.085, 0.700), B群とC群の早産率には有意差があった(P 値=0.001)。各群間での早産率ではB群が最も高いため, 錠剤使用の有無での早産率を比較したが, 有意差は認めなかった(P 値=0.380)。また, 2018年~2019年の当院での総早産率は28週未満46例(3.7%), 28-36週168例(13.5%), 22-36週214例(17.2%), 妊娠初期より分娩まで当科管理の妊婦早産率は28週未満8例(0.6%), 28-36週45例(3.6%), 22-36週53例(4.2%)だった。【結論】当院で妊娠初期より経過を見ていた妊産婦の場合, BVスコアによる早産率に有意な差は見られなかった。また, 妊娠初期より分娩まで当院で経過を見ていた症例では, 早産率は他院からの搬送や紹介例を合わせた場合より低値であった。

P-109-3 子宮頸部円錐切除術後の妊娠についての検討

国立弘前病院

追切裕江, 横山万智, 當麻絢子, 横田 恵, 丹藤伴江

【目的】子宮頸部円錐切除術(以下, 円錐切除術)後の妊娠は早産ハイリスクといわれているが, どのような症例がよりハイリスクであるのか, リスク因子を抽出することを目的とした。【方法】2016年1月から2020年12月に分娩となった円錐切除術後の妊娠66例において, 早産群と正常産群にわけて, 母体年齢, 妊娠分娩歴, 喫煙歴, 子宮収縮抑制剤使用の有無, 頸管縫縮術の有無, 細菌性陰症の有無, 術後から妊娠までの期間, 頸管長, 妊娠37週前の子宮口開大の有無, 切迫早産の入院の有無について, 診療記録をもとに後方視的に検討した。また, 切迫早産として入院管理した15例を早産群と正常産群にわけて同様に後方視的に検討した。【成績】早産11例(17%), 正常産55例(83%)であった。早産群と正常産群で有意差のあったものは, 喫煙歴, 子宮収縮抑制剤使用の有無, 妊娠12週の頸管長, 妊娠16週の頸管長, 妊娠24週の頸管長, 妊娠37週前の子宮口開大の有無, 入院の有無であった。切迫早産入院管理症例の早産群と正常産群で有意差のあったものは, 分娩歴と妊娠16週の頸管長であった。母体年齢, 縫縮術の有無, 術後から妊娠までの期間, 細菌性陰症の有無, 早産既往や切迫早産既往は早産と関連を認めなかった。切迫早産入院管理症例において子宮収縮剤使用開始時期や入院時期は早産群と正常産群で有意差を認めなかった。【結論】妊娠初期から頸管長が短縮している症例や早期に子宮口開大がみられる症例は早産ハイリスクであり慎重な管理が必要である。ただし, 子宮収縮抑制剤の使用や縫縮術により早産を有意に低下させるとはいえない。また, 円錐切除術後特有のリスク因子の抽出には至らず, 分娩時期の予測は困難である。

P-109-4 子宮頸部円錐切除術後の妊娠予後に関する臨床的検討

友愛医療センター

池端舞子, 延壽桃子, 高島望海, 西村拓也, 吉川和泉, 山田真司, 大城大介, 比嘉 健, 野坂舞子, 前濱俊之

【目的】子宮頸部円錐切除術(円切)は若年者に発症する子宮頸部上皮内腫瘍(CIN)に対し、最もよく施行されている手術である。しかし、円切後妊娠例における早産発症が課題として多数報告されている。我々は円切後妊娠例の頸管切除長を中心に臨床的予後を解析した。【方法】2006年から2019年において円切を施行した症例は479例あり、その適応はCIN1:3例、CIN2:25例、CIN3:425例、頸癌Ia1期:26例であった。円切後妊娠した66例を対象とし、その妊娠予後を解析した。腺系病変と電気外科的ループ切除法は除外した。解析方法は妊娠予後を早産例、切迫早産治療を要した正常産例、無治療正常産例の3群に分類し、その頻度を分析した。さらに、3群間における平均頸管切除長の比較検討を行った。【成績】円切後妊娠例66例中、早産が16例(24.2%)、切迫早産治療を要した正常産例が18例(27.3%)、無治療正常産例が32例(48.5%)であった。早産例における平均切除頸管長は13.6mm、切迫早産治療を要した正常産例では13.3mm、正常産例では12.2mmであり、3群間に関連性は認めなかった。正常産となった全症例は50例あるが、そのなかで、切迫早産治療を要した例が18例(36.0%)存在した。【結論】円切後妊娠例において切除頸管長と妊娠予後との関連性は認めなかった。円切後妊娠例の早産率は24.2%であり、さらに正常産例のなかで切迫早産治療を要した例が36.0%も認めることが明確となった。したがって、円切後妊娠の予後改善策と円切以外の治療法が求められている。

P-109-5 妊娠34週から36週の分娩転帰

獨協医大病院

多田和美, 鈴木紫穂, 茂木絵美, 久野達也, 宮下 進, 三橋 暁

【目的】妊娠34週以降37週未満の早産を後期早産(Late Preterm)と定義されているが、その期間に分娩に至った母体の管理に一定の見解はなく、各医療機関での対応となっている。新生児においては、37週以降で出生した児と比較し低血糖や呼吸障害が起りやすく注意深い管理が必要とされている。今回当院で経験した後期早産症例の管理について後方指摘に検討した。【方法】2013年から2020年に当院で出産した後期早産症例548例(11.6%)を対象とし、母体と新生児の転帰について後方指摘に調査を行った。この期間を前半(2013年-2016年)と後半(2017年-2020年)に分け比較検討も行った。【成績】この期間の早産は1218例(25.9%)だった。母体搬送による入院は146例(26.6%)、母体の入院理由として切迫早産・双胎・胎盤位置異常・胎児異常などで、陣発・胎児機能不全等の理由で入院当日分娩に至っている症例は113例(20.6%)だった。母体情報として、期間中の多胎妊娠は133例(24.2%)、35歳以上の高齢妊娠は214例(39.0%)、初産は276例(50.3%)だった。前半と後半で比較検討を行なったが、差は認めなかった。当院では、35週以降で2200g以上の児に関しては、産科病棟での管理を行うが、管理困難な場合はNICUに転棟し管理することになっている。このため34週での出生児は全例NICU入室になっている。この期間の出生児は681例だった。NICU入室は347例(50.9%)で、前半よりも後半が多かった。在胎35週から36週は211例(30.9%)で、入室理由は低出生体重児がほとんどで246例(70.8%)だった。【結論】後期早産の理由は様々だったが、NICU入室は半数以上だったため、慎重な管理が必要である。

P-109-6 当院で出産を行った外国人妊婦と日本人妊婦のCOVID-19パンデミック前後での早産率の検討

大阪赤十字病院

米山華蓮, 清川 晶, 田村年規, 石田憲太郎, 定本怜子, 徳重 悠, 小林弘尚, 前田万里紗, 芦原隆仁, 中川江里子, 野々垣多加史

【目的】COVID-19パンデミック下に、諸外国からは早産率が減少したという報告や変わらないという報告がある中で、日本での知見はまだ少ない。また、近年増加している日本在住の外国人妊婦のパンデミック前後の妊娠転帰について比較した知見はこれまでに見当たらない。COVID-19感染拡大前後の外国人妊婦と日本人妊婦の早産率について、当院での実態を調査し考察する。【方法】2018年1月より2021年9月までの期間に当院で出産した2582人のうち、22週未満、母体合併症や胎児適応による人工早産、双胎、FGR、他院からの搬送症例は除外し、Pre-COVID19群(n=1413人)とPost-COVID19群(n=920人)の2群に分けて、早産率について比較を行った。【成績】Pre-COVID19群は、日本人33.1±5.1歳、外国人29.2±4.3歳、Post-COVID19群は、日本人33.3±5.1歳、外国人29.7±4.6歳と母体年齢はパンデミック前後でいずれも差がなく、初産経産も差がなかった。Pre-COVID19では、日本人早産率1.6%に対し、外国人では早産したものはなかった。一方、Post-COVID19では、日本人早産率1.7%とパンデミック前後で差がないのに対し、外国人早産率は6.3%と上昇を認め、有意に日本人より早産が増加した。【結論】当院では、パンデミック後に婦人出産できなくなったと考えられる外国人の出産が増加しており、日本人ではパンデミック前後に早産率に差がないのに対し、外国人ではパンデミック後に早産率の有意な増加を認めた。早産の要因には様々なものが考えられるため、原因を明らかにすることは困難であるが、COVID-19パンデミックが影響している可能性が示唆された。

P-110-1 オンライン症例検討会—コロナ禍での新しい施設間交流のかたち—

長野県立木曽病院¹, 信州大附属病院², 長野赤十字病院³, 飯田市立病院⁴
上條恭佑¹, 菊地範彦², 堀澤 信³, 池田枝里⁴, 窪田文香¹, 吉岡郁郎¹

【目的】COVID-19 感染拡大を受け、多くの学術集会はオンライン開催へと移行した。これに伴い学会発表は一方性となり、若手医師の症例発表や施設間交流の機会は減少した。この問題を解消すべく、オンライン症例検討会を開催した。【方法】Zoomを用いてオンライン検討会を開催した。参加者にアンケート調査を行い、その内容や課題について検討した。また、Web会議システムの使用経験について長野県内の産婦人科医にアンケート調査を行った。【成績】2020年10月から2021年9月までに6回の検討会を開催した。参加人数は平均30名で、計17施設から参加があった。参加者の内訳は初期研修医、専攻医、10年未満、10年以上、その他がそれぞれ5%、21%、26%、44%、4%であった。検討会では母体搬送症例の搬送元と搬送先の双方からの症例提示、切迫早産等の施設毎の管理方針の違いについて、リアルタイムの投票機能を用いたディスカッションが行われた。検討会終了後のアンケート(n=109)では、97%の参加者が満足と回答し、産休・育休中でも参加しやすいという意見があった。一方で若手医師が発言しにくい、議論が延長する等の指摘もあった。また、Web会議システムの使用経験についてのアンケート(n=63)では、86%がWeb会議システムを使い慣れる必要があると感じていた一方、その使用に自信がある回答者はわずか21%だった。【結論】オンライン症例検討会は、若手医師にとってオンライン開催の学会発表では経験しにくいリアルタイムで双方向性の議論ができ、施設間交流も行える貴重な機会となる。また、Web会議システムに習熟した医師は少なく、その使用経験を積めることもオンライン検討会の利点と考えられた。

P-110-2 福岡県内の産科医療施設に対する母性健康管理指導事項連絡カードの使用状況調査

産業医大

金城泰幸, 内村貴之, 村上 緑, 櫻木俊秀, 福田頌子, 森 博士, 荒牧 聡, 近藤恵美, 柴田英治, 吉野 潔

【目的】妊娠や出産を機に退職する女性は未だ4割に達するとされている。キャリアアップを目指し就労継続を希望する女性が妊娠した場合、就労による妊娠中の体調変化を職場へ適切に情報提供できる体制が整えば、退職することなく就労を継続することが期待できる。その情報提供ツールとして、母性健康管理指導事項連絡カード(以下、母健連絡カード)が知られている。このように退職者が多い現状を踏まえ、母健連絡カードがどのように使用されているかの状況調査を行う目的に、福岡県内の産科医療施設に対してアンケート調査を実施した。【方法】2019年10月から12月にWebのアンケート調査を実施した。送付した医療施設の内訳は、単科15施設、複数科6施設、大学病院4施設であった。質問事項は、回答者の属性(職種・経験年数・施設規模)、母健連絡カードを見たことがあるか、記載したことがあるか、母健連絡カードと診断書の作成はどちらが多いか、改善が必要と思われる事項は何か、とした。【成績】151名から回答が得られ、内訳は医師67名、助産師47名、看護師37名であった。母健連絡カードを見たことがないのは、医師13名(19.4%)、助産師15名(31.9%)、看護師16名(43.2%)であった。記載したことがない医師は25名(37.3%)であり、その内21名が診断書を作成すると回答した。医師から得られた改善すべき事項は、周知や啓蒙が15名、内容の充実が11名、料金の設定が1名であった。【結論】就労妊婦の母性健康管理を行う上で母健連絡カードは有効なツールと考えられるが、事業所に対する周知や啓蒙、さらには内容の充実が課題であると考えられる。

P-110-3 新型コロナウイルス感染症罹患妊婦及び疑い妊産婦に対しての妊娠・分娩管理と母乳育児支援

日赤医療センター

石川久美子, 笠井靖代, 有馬香織, 鈴木研資, 井出早苗, 山田 学, 木戸道子, 宮内彰人

【目的】新型コロナウイルス感染症罹患(以下COVID19)妊婦の分娩は、立ち会い出産が行えずまた母子分離などの問題が生じる。本研究は、当センターで隔離中に分娩となった妊産婦の精神的支援を含めた分娩管理と母乳育児支援のアウトカムを明らかにする。【方法】対象は、2020年4月から2021年8月に、当センターでCOVID19罹患による隔離期間中に分娩となった7症例とCOVID19疑いによる隔離下に分娩となった7症例とする。診療録から、妊娠・分娩管理、本人が記載したバースレビュー、母乳育児支援の内容と1か月後の母乳率を後方視的に解析した。【結論】陽性例7例のうち3例は経陰分娩、4例は帝王切開分娩。その適応は産科的適応が2例、COVID19肺炎の悪化が2例であった。疑い症例7例は全例経陰分娩であった。1か月の栄養法は、陽性例7例のうち2例が母乳栄養、2例が人工栄養、1例が混合栄養、1例は不明であった。疑い7例のうち5例が母乳栄養、1例が人工栄養、1例が不明だった。COVID19対応初期に記載されたバースレビューでは、孤独感や不安感を訴えるものがあり、授乳が中止になる症例があった。その後担当医師・助産師による継続的なサポート体制と精神的支援に力を入れ、マンツーマンの搾乳支援を施行したところ、ある程度の満足度が伺えるバースレビューとともに、母乳栄養が継続できる症例が増えてきた。全14例の1か月の母乳率は70%であった。【考察】COVID19罹患妊産婦では急性期の治療だけでなく、長期的な視点で継続的な育児支援を行うことが重要である。隔離下にあった母親の1か月の母乳率は、2019年の当センターの1か月の母乳率66%と同等であり、母子分離となっても、適切な支援を行うことで母乳育児が可能であると考えられる。

P-110-4 日本とカナダにおける早産の周産期アプローチの比較～それぞれの強みから見てきた、早産のケアの向上と研究の優先課題～

富山大学
米田徳子, 齋藤 滋

【目的】早産は、世界中の児の死亡率および罹患率の主な原因となっている。日本とカナダはそれぞれ、早産ならびに早産児の後遺症の予防に関する臨床的意思決定、研究、ヘルスケアに役立つ強みを持っている。日本とカナダにおける早産の発生率、リスク因子、管理および転帰を比較し、将来の共同研究の機会を促進しつつ、研究の優先順位を設定することを目的とした。【方法】日本とカナダにおける、早産率、早産リスク因子、早産の予防・管理法、転帰について文献レビューをおこなった。また、日本とカナダの周産期センターにおいて両親、新生児科医、母体・胎児専門医、研究者と情報交換をした。【成績】日本はカナダに比べて早産率、新生児死亡率、いくつかの早産リスク因子の発生率が低かった。しかし、カナダの早産データベースは population-based であるのに対し、日本の早産率は population-based だが、転帰については population-based ではなかった。日本では、児の重篤な神経学的障害と壊死性腸炎の発生率が低く、カナダでは慢性肺疾患や未熟児網膜症の発生率が低かった。早産の予防法にも違いがあり、日本ではプロゲステロンの使用が少なく、長期の tocolysis が多かった。日本では、新生児搬送や当直医のいない施設での出生が少なかったが、出生前ステロイド投与や臍帯遅延結紮が少なかった。情報交換会では、早期の skin-to-skin contact、早産児の両親や同胞のメンタルヘルスサポート、NICU 退院後の児のケアなどが研究の優先課題にあげられた。【結論】早産の管理と早産児の転帰に影響を与える要因について、日本とカナダには重要な違いがあることがわかり、今後の研究課題が明らかになった。

P-110-5 周産期専門医不在の地方病院において高次医療機関と連携した遠隔妊婦診療の取り組み

砂川市立病院¹, 北海道大病院²
宇田智浩¹, 佐藤元哉¹, 佐野友字子¹, 櫻井愛美¹, 山下陽一郎¹, 津田加都哉¹, 馬詰 武²

【目的】当院は中空知医療圏唯一の周産期施設であるものの周産期専門医が不在であり、日々の妊婦診療において胎児超音波診断に悩むケースがある。しかし胎児診断精査ができる高次医療機関までは遠距離であり、地方に住む妊婦が精査のために遠くの施設を受診することは大きな負担となる。さらに新型コロナウイルス感染拡大のため地域を跨ぐ移動が簡単ではない現状がある。そのような妊婦の負担および医療の地域格差を解消するため当院で行っている高次医療機関と連携した遠隔妊婦診療の取り組みを報告する。【方法】2021年1月から10月までに外来通院または入院した妊婦に対し胎児診断精査が必要と判断した6例に遠隔診療を行った。遠隔診療にはオンライン診療システム会社 (Cisco Webex Meetings[®]) を利用した。胎児超音波画像をライブ映像で転送し、医師同士はビデオ通話にてカンファレンスを行った。なお患者には事前で文書での同意を取得した。【成績】遠隔診療を行った6例の内訳は腸管拡張疑い2例、胆のう拡張疑い2例、骨盤腫瘍1例、食道閉鎖疑い1例であった。これらのうち2例は高次医療機関への転院がその場で決定し、そのうち1例は分娩後外科治療を要した。残り4例は当院で管理しつつ適宜情報共有する方針となった。【結論】遠隔妊婦診療により胎児超音波診断に悩む症例であっても適正な周産期管理を行うことができた。また高次医療機関との情報共有も行うことができた。精査目的に遠距離を移動する妊婦の負担も軽減でき、専門医の意見をその場で聞くことができるため妊婦の不安解消にも役立った。日々の妊婦健診の補助ツールの1つとして遠隔妊婦診療は今後有益ではないかと思われた。

P-110-6 当院における事後スーパー母体症例の後方視的検討

杏林大付属病院
平野稚子, 小林千絵, 浅野史男, 石川美佳, 佐藤泰紀, 北村亜也, 松島実穂, 田嶋 敦, 谷垣伸治, 小林陽一

【目的】東京都では、母体救命処置を要する搬送例をスーパー母体搬送とし、6ヶ所の病院が必ず受け入れるシステムとしている。過去に通常搬送として受け入れた例の中には、搬送受け入れ後にスーパー母体例と判断した(事後スーパー母体)例がある。事後スーパー母体例を振り返り、今後の課題を検討した。【方法】2015年4月から2021年8月の当院スーパー母体91例のうち、事後スーパー母体と判断された4例について、後方視的に検討した。【成績】4例とも初産の産褥症例であった。症例1は痙攣発作、症例2は意識障害であった。症例3は救急車内で出血量が増加した弛緩出血であり、画像検査実施までに134分、動脈塞栓術までに188分要していた。類似スーパー母体例16例の中央値は各々41分、71分であった。症例4は癒着胎盤であり、救急車内での血圧70/30mmHg、Shock Index1.6と悪化していたが、輸血開始までに来院後103分を要した。【結論】スーパー母体搬送例は、搬送前から他科との連携準備をし、救急初療室において救急科とともに対応している。当院救急初療室は画像検査室、血管造影室が隣接しており速やかな対応が可能である。通常の搬送では人手を当科で全て担う必要もあり、時間を要する。当システムでは、搬送元医療機関もしくは救急隊によりスーパー母体症例かどうか判断され、受け入れ側はそれが適切かどうか議論は行わない。搬送元で全身状態が安定していても急変する可能性はあり、時には受け入れ側からのスーパー母体宣言の提案も必要と考える。また、今後地域との連携を深め、症例振り返り機会を設け、適切な宣言がなされるようにしたい。

P-110-7 当院における妊娠期からの育児支援（マタニティーサポート）活動について

松山赤十字病院

井上奈美, 横山幹文, 駒水達哉, 吉里美慧, 矢野晶子, 高杉篤志, 信田絢美, 青石優子, 梶原涼子, 栗原秀一, 本田直利

【目的】当院では児童虐待や妊産婦自殺の妊娠期からの予防を目的とし、2005年6月より妊娠期からの育児支援として育児支援活動（マタニティーサポート）を行っている。その活動状況を報告する。【方法】妊娠中から出産後を通して母親やその家族を対象に傾聴を行い、必要な情報共有や院内外の連携を行った。対象とする妊婦は以下の基準に従った。虐待の4因子すなわち①虐待しやすい親②家庭環境（生活のストレス）③虐待されやすい子供④社会的孤立を有する妊婦、あるいは母体合併症（精神疾患、知的障害等）でサポートを要する妊婦を対象とした。周産期カウンセラーあるいは療養支援看護師が妊婦の傾聴を行なった。連携が必要な事例は院内産科小児科スタッフ、精神科医、愛媛県児童相談所、松山市子ども総合支援センター、周産期カウンセラー、医療ソーシャルワーカーなど必要に応じて多職種でケースカンファレンスを行い、県内外の地域、行政の協力を得ながら様々な院内院外のサポートを行った。【成績】2005年6月より2021年3月までの産婦合計8725人のうち1770人（20.3%）が何らかの連携を必要とする症例であった。連携理由は育児不安が40.8%と最も多く、母の疾患（16.8%）、シングルマザー（7.5%）、高齢出産（7.0%）、若年出産（5.8%）、子供の疾患（4.3%）、虐待（2.9%）等であった。また2017年以降5年間でケースカンファレンスを行った症例は174件であり、そのうち児童虐待のリスクが高く母児分離が必要と判断され特別養子縁組への移行や乳児院施設入所となった事例が11例（6.3%）であった。なお、このサポート対象者に自殺例はなかった。【結論】これらの活動は虐待予防や妊産婦自殺予防に貢献できると考えられた。

P-110-8 日本居住妊産婦における新型コロナウイルスワクチン接種の実態

たて産婦人科¹, 千葉大附属病院²楯 浩行¹, 齊藤佳子^{1,2}, 楯 真一^{1,2}, 楯 健司¹, 楯 高子¹, 楯 二郎¹

【目的】日本居住妊産婦における新型コロナウイルスワクチン接種の実態を明らかにすること。【方法】当院で妊産婦に接種を開始した2021年6月から2021年10月までにカルテにて接種・妊娠転帰の判明した504人の妊産婦を対象としワクチン接種率・副反応・転帰を調査した。【成績】対象者中に接種予定者28名（6%）ワクチン忌避15名（3%）接種できず分娩に至った95名（19%）妊娠前に接種した39名（8%）2回とも妊娠中に接種した288名（57%）（2週0日から11週6日までの63名を含む）授乳中に接種した39名（8%）（妊娠中のワクチン忌避1名を含む）を認めた。接種したワクチンの種類：ファイザー360名（98%）モデルナ6名（2%）であった。妊娠中に接種した週数は1回目中央値20週（3-36）2回目中央値23週（6-39）であった。感染時期は妊娠前1例、妊娠後1回目接種前5例、1回目接種後2回目接種前1例、2回目接種後8日目1例、未感染279例であった。当院で感染が確認された10名中すべてが2回目接種後10日以前であり、2回目接種後10日以降の感染者は認められていない。妊娠中の副反応は1回目（発熱11%（21/251）発熱（38.0度以上）0.8%（2/251）頭痛16%（39/243）全身倦怠感24%（58/241）接種部位の痛み86%（208/242）解熱剤の内服4.8%（12/249）、2回目（発熱51%（101/200）発熱（38.0度以上）17%（33/200）頭痛37%（73/193）全身倦怠感54%（103/191）接種部位の痛み84%（160/191）解熱剤の内服31%（63/196））であった。抄録作成時までの妊娠転帰は、経産分娩90%（63/70）帝王切開7%（5/70）早産1%（1/70）流産1%（1/70）異所性妊娠1%（1/70）である。新生児転帰、体重、先天奇形に異常は認められない。【結論】日本居住妊産婦に対する新型コロナワクチン接種の実態を報告した。

P-110-9 当院における院内助産と医師立ち会い分娩との分娩成績の比較検討

済生会富田林病院¹, 生駒市立病院²島岡昌生¹, 山本嘉一郎²

【目的】院内助産とは助産師主導で分娩を取り扱うシステムで、産科医不足解消の手段として提唱された。当院は2012年11月から常勤医2名の院内助産単独施設として分娩を取り扱ってきた。2019年8月から院内助産を廃止し、2019年11月から常勤医1名となった。当院での院内助産と医師立ち会い分娩の分娩成績を比較検討する。【方法】院内助産群（以下I群）は2012年11月から2019年7月まで当院で分娩した588名で、平均年齢は30歳、初産婦208名、経産婦380名。医師立ち会い群（以下II群）は2019年8月から2021年6月まで当院で分娩した276名で、平均年齢は30歳、初産婦129名、経産婦147名。データの公表について全症例に文書による説明を行い、同意を取得した。I群とII群での母児の分娩成績について後方視的に比較検討した。【成績】I群の分娩時間の平均は8時間36分で、II群の分娩時間の平均は8時間48分であった。I群の分娩時出血量の平均は474mlで、500ml以上が205名（33.5%）であった。II群の分娩時出血量の平均は386mlで、500ml以上が55名（19.9%）であった。500ml以上の割合はI群で有意に高かった（ $p=0.0001$ ）。分娩時に医師がコールされたのは220名（37.4%）であった。I群の臍帯血ガスpH値の平均は7.29で、7.2未満の症例は65例（11%）であった。II群の臍帯血ガスpH値の平均は7.30で、7.2未満の症例は16例（5.8%）であった。臍帯血ガスpH7.2未満の症例の割合はI群で有意に高かった（ $p=0.0148$ ）。【結論】分娩時に医師が立ち会うことにより、分娩時出血量が減少し、臍帯血ガスpH値が7.2未満の児が減少することが確認された。院内助産における母児の安全性の向上が今後の課題である。

P-110-10 産科医療集約化をめざした取り組み

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春田祥治¹、細川奈月¹、喜多恒和²、佐道俊幸²

【目的】地域基幹病院において医師数が減少し、従来夜間休日の産科診療を支えてきた当直医オンコール体制を維持することが困難となり、医師および助産師の負担が増大した。この問題を解決するために、母児の安全・安心を高め、産科医療の質を維持し、そして医師散在を解消することによる働き方改革への対応を図ることを目的とした、産科診療集約化への取り組みとその成果について述べる。【方法】同一法人内の中核病院との医療連携を実現するために、両院間で電子カルテをリアルタイムで参照できるシステムを導入した。このシステムを通して診療情報を共有化することで、地域基幹病院で妊婦健康診査を実施して、分娩および夜間休日の緊急診療は中核病院が対応し、そして産後健康診査および乳幼児健康診査を地域基幹病院で実施する産科診療連携を確立した。患者および家族に対し、電話および面談で集約化に伴う分娩休止について丁寧に説明し、理解を得た。また、医師を一体的に管理して適切な人員の配置を行い、働き方改革の推進を行った。【成績】産科診療集約化が決定した時点で分娩施設の変更を要した67例のうち、52例が中核病院での分娩を選択し、15例が他施設での分娩を選択した。移行期において、診療面および事務面での問題は生じなかった。中核病院で出産し産科的合併がなかった50症例のうち、47例が地域基幹病院で産後健康診査および乳幼児健康診査を受診した。【結論】産科診療の集約化を安全に実現することができた。働き方改革を実現するためには、病院間における連携ないしは統合が必要であり、人的資源の有効活用とQOLの向上が達成できる。

P-110-11 一次産科医療施設で発症した母体急変のバイタルサインと産褥搬送のタイミングに関する検討

聖マリアンナ医科大学病院

山本紗希、西村陽子、古谷菜摘、美馬康幸、本間千夏、岩端秀之、倉崎昭子、近藤春裕、仲村将光、戸澤晃子、長谷川潤一、鈴木直

【目的】一次産科医療施設で発生した母体急変におけるバイタルサインの感知から周産期センターへの産褥母体搬送のタイミングが適切に行われているかどうかを明らかにすること。【方法】2017-2021年、当総合周産期母子医療センターに産褥母体搬送された症例を対象に後方視的検討を行った。日本母体救命普及協議会のコース(J-MELS)の提唱する母体急変(搬送決定)とするバイタルサイン出現のタイミングで搬送が決定されているかどうかを調査した。本研究は、倫理委員会の承認を得て行った。【成績】対象は53例あった。搬送理由は、分娩後早期の出血性ショックは36例、産褥晩期出血が5例、妊娠高血圧症候群6例、産褥熱、感染が2例などであった。搬送を、出血持続とShock Index(SI)>1で決定したものが12例、SI>1.5で決定したものが8例あったが、意識レベル低下で決定したものが2例、SaO₂<95%で決定したものが1例、呼吸数22回/分以上で決定した例はなかった。分娩後異常出血(PPH)41例の中で、上記基準を満たさなくともSI<1で早めの搬送判断をした症例は20例あり、それらの総出血量と輸血量の中央値(範囲)はそれぞれ、1030g(20-6141)、280ml(0-6180)に対し、SI>1(n=14)では3000g(892-8902)、3320g(280-28385)であった(p<0.01)。【結論】一次施設においてはいかに早く高次機関へ搬送するかが母体の予後を左右する。J-MELSの搬送基準は、当センターの地域においても、簡便で役に立っていると考えられたが、患者の全身状態を観察して先読みし、基準を満たさなくともそれ以前の早期搬送をすることによって予後が改善することが明らかになった。

P-110-12 大規模災害時の周産期医療体制に関するアンケート調査

都立多摩総合医療センター

馬場慎司、本多泉、有山悠乃、松田美奈子、大城早紀子、齋藤麻祐子、曾我江里、高原めぐみ、中村浩敬、光山聡、谷口義実

【目的】当院は東京都多摩地域の災害拠点病院(以後拠点)で、総合周産期母子医療センターでもある。多摩地域の出生数は約3万件と宮城県約2倍であり、災害時に甚大な被害が予想される。診療機能が低下する一般分娩施設(以後一般)も想定した体制整備が重要で、医療資源の精査、各施設の災害時の対応等を確認するため、アンケート調査を行った。【方法】多摩地域の助産院以外の分娩施設56施設(拠点は16)を対象とした。質問紙による記名式調査とし、平成31年4月にアンケートには医療圏を超えた搬送の受け入れの可否、《一般》には分娩対応が困難な際に、他院からの褥婦および新生児の受け入れ可否について調査を追加した。【成績】回答率は拠点10(63%)、一般18(39%)であった。分娩数が月50を超える施設は、拠点6、一般7であった。拠点では全施設で、災害マニュアルを有し、防災訓練も行ってた。一般でも約半数の施設で災害マニュアルを有し、防災訓練も行ってた。一般では分娩対応が困難となる施設が半数あり、拠点でも2施設あった。医療圏を超えた搬送も9施設で可能で、他院からの褥婦などの受け入れ困難な施設は5であった。【結論】一般で対応困難となった分娩などを、拠点で補完する必要がある。一方で、産後早期の一般褥婦、新生児の受け入れを一般に依頼できれば、拠点の負担が軽減できる可能性がある。拠点でも被災した際には分娩対応が困難となる場合があり、医療圏を超えて対応を協議する事が重要である。

P-111-1 当院での初期研修医の帝王切開に対する指導とその意義についての検討

成田赤十字病院

塙 真輔, 伊藤孝輔, 竹原直希, 佐藤史朗, 西方紀子, 山ノ内美紀, 真田道夫, 清水久美子, 小幡新太郎

【目的】当院では産婦人科医になることを志望している初期臨床研修医の研修態度, 臨床能力, 産婦人科研修期間を考慮し, 一定レベル以上に達していると判断した初期研修医は上級医の指導のもと帝王切開を執刀している。今回, 初期臨床研修医の執刀した帝王切開の検討とその意義について検討した。【方法】2014年-2021年の初期臨床研修医8名の執刀した帝王切開の執刀数, 手術時間, 出血量, 術後合併症を検討した。また①産婦人科医になるのに影響を与えたか, ②与えたとしたらどのような影響だったか, ③初期に行う帝王切開のデメリットなどはあったか, について自由記載で回答をもらった。【成績】8名の総執刀数は61例であった。一人あたりの執刀数, 手術時間, 出血量の中央値 (range) はそれぞれ8 (range1-12) 例, 手術時間86 (49-137) 分, 出血量890 (423-2530) g 術後合併症としての周囲の臓器損傷は無かった。インタビューの回答では①について全員産婦人科医になるのに影響があると回答し, ②については産婦人科医になる自覚や志が一層強くなったという意見は共通していた。またこれまで実際に手術を行うことで, 手術を違う視点で見られるようになった, 後期研修の効率がよくなったなど, 前向きな意見がみられた。③症例を選べばデメリットはないが手術に手間取ると患者に申し訳ない気持ちになるという意見がみられた。【結論】初期臨床研修医が上級医の指導下で帝王切開を執刀した場合手術時間はやや長くなる傾向であったが大きな合併症は見られず産婦人科医になる決定に寄与するほか, 医師としての資質を高めることに一定の効果がある。

P-111-2 産婦人科専攻医が術者である帝王切開術の手術成績に関する検討

日赤医療センター

愛葉美奈, 木戸道子, 有馬香織, 細川さつき, 渡邊理子, 山田 学, 笠井靖代, 宮内彰人

【目的】専攻医が専門医の指導下で帝王切開術の術者を務める際の安全性など手術成績について検討する。【方法】2018年4月から2021年3月までに当院で行われた帝王切開術のうち, 術者経験数30例以下の専攻医による手術症例 (A群) 260例と産婦人科専門医が術者を務めた症例 (B群) 54例について比較解析した。A群の第一助手は全例専門医である。【成績】対象例の平均妊娠週数はA群で38.4±1.6週, B群で35.0±4.7週で, うち34週未満は2例 (0.77%) vs 16例 (29.6%) とB群に早産例が多かった。母体年齢は35.1±5.0歳 vs 35.3±5.1歳で差はない。出血量 (430±272 ml vs 519±390 ml), Apgar score (1分値: 8.01±0.93 vs 7.29±1.89, 5分値: 9.00±0.63 vs 8.78±1.48), 臍帯動脈血 pH (7.28±0.05 vs 7.28±0.12) は両群に有意差はなかった。児の入院率は12.7% vs 50.0% (p<0.05) とB群で高いが, 37週以降に限定すると8.7% vs 10.0% (p=0.48) で差はなかった。術後に再手術を要した例はA群1例, B群2例で, いずれも腹壁創部出血で予後は良好であった。児の損傷等の合併症は両群とも皆無であった。平均手術時間はA群で70.0±1.6分であり, B群の55.0±6.2分よりも長かったが術後の血栓症などの合併症は両群ともなかった。【結論】専攻医が専門医の指導下で帝王切開術を執刀する場合は, 手術時間は長い傾向があるが, 母児の安全性に影響はみとめない。

P-111-3 死戦期帝王切開シミュレーション～新たな周産期シミュレータ “Konoha” の有用性～

岡山大病院

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【目的】死戦期帝王切開 (perimortem cesarean delivery: PMCD) とは, 心肺停止となった妊婦に対して行う母体蘇生処置の1つである。PMCD 施行には多職種連携が必須である。これまで他部署と院内連携を高めるため様々な場面を想定しシミュレーションを行ってきたが, 今回, 新たに周産期全身シミュレータを用いた多職種連携 PMCD シミュレーションを施行したので報告する。【方法】参加部署は産婦人科, 新生児科, 救急科, 麻酔科, 心臓血管外科, 臨床工学センター, 手術部, 助産師, NICU 看護師である。「絶え間ない高質な CPR から10分以内に PMCD を施行し児を娩出する」ことを目標とし, 平日日勤帯, 分娩室で分娩誘発中の CPA 妊婦に対し手術室で PMCD 施行後 ECMO まで導入するシナリオを作成。患者役は新たに当科で共同開発中の会話可能でモニタにバイタル表示でき, 胸骨圧迫や開腹, 挿管可能な周産期全身シミュレータ “Konoha” を使用し, PMCD 用のプログラミングを構築した。【成績】シミュレーション当日は全部署に動画撮影者を準備, またタブレットを用いて達成項目を評価した。当日は心肺停止後7分で児娩出に至った。今回新たなシミュレータを導入したことにより, より臨場感のあるシミュレーションと時系列毎かつ客観的なフィードバックが可能となり, 全体の流れの把握, 問題点が抽出できた。その後 PMCD 運用マニュアルの運用を開始した。【結論】参加部署が多い PMCD の円滑な運用のためにはシミュレーショントレーニングは必要不可欠である。多職種連携シミュレーション教育を行う上で, 本シミュレータは非常に有用であると考えられた。

P-111-4 神奈川県における4次元超音波技術を用いた胎児心臓超音波勉強会

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【目的】4次元超音波技術である spatio-temporal image correlation (STIC) を用いた遠隔胎児心臓勉強会による教育効果について検討する。【方法】神奈川県産科婦人科医会が主催し、希望した施設を対象に毎月胎児心臓病超音波勉強会を開催した。STIC データ (疾患の超音波データ) の入ったパソコンを参加施設へ配送した。受講者は講義を WEB 会議室上で視聴しながら、パソコンで STIC データをハンズオンのように動かし、患者を実際に検査するのと同じような感覚で学習した。またリアルタイム参加できない方のために録画 URL を送り受講者が好きな時間に参加できるようにした。講義の前後でクイズ、アンケートを行い、Kirkpatrick の4段階教育評価モデルで評価した。【成績】2021年5月から9月までに勉強会を4回行った。21施設、延べ275人が参加した。アンケートに返答したのは73人であり、返答率は27%であった。Kirkpatrickのレベル1: 満足度は非常に満足、満足を合わせ88%であった。レベル2: 学習到達度については講義前後のテストの平均点で比べ、有意な平均点上昇を認めた。レベル3: 行動変容は、86%が胎児心エコーを今後積極的にやりたいという結果であった。レベル4: 結果 (心疾患の診断) については今後アンケート施行予定である。【結論】STICを用いた胎児心臓病超音波勉強会は、遠隔教育を拡大させ、より効果的な学習に応用できる。

P-111-5 SDGsの実現を目標としたリカレント教育プログラム“学びなおし講座”のコロナ禍におけるweb展開の試み

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【目的】持続可能な開発目標 (SDGs) 実現の一環として、リカレント教育プログラム“学びなおし講座”を実施している。新型コロナウイルス感染症 (COVID-19) の感染拡大の影響下でリモート開催を試みたのでその効果を報告する。【方法】A大学の市民公開講座の一環として2009年より「周産期多職種連携とシミュレーション教育“学びなおし講座”」を開催した。2017年度より出張コースを敢行した。2020年度からは、COVID-19感染対策として受講生及び講師の移動を伴わないリモートハンズオンを含むweb開催に変更した。アンケートと筆記テストを行い満足度と習熟度を確認した。本発表内容は全受講生及び講師の同意を得ている。【成績】2021年度までに20コースを開催し、のべ506人が受講した。90%が女性で30から50歳代が70%であった。助産師が60%で看護師、薬剤師、心理士、医師、保健師、管理栄養士や救急救命士が参加した。県内は80%で県外17都道府県からの受講があった。本年度のアンケート回答率は62.5%であった。講義内容に対しては100%が良い以上で、難易度は92%が適切以上だった。web開催とした2020年度からは海外からの参加者を含む受講者数が倍増し、参加地域、受講率、理解度、満足度及び収益が増大した。一方で、対面方式でないことにより手技習得やコミュニケーションを取ることの難しさや、通信環境の問題が指摘された。【結論】リカレント教育プログラムを継続的かつwebを用いて進化的に提供することが、COVID-19禍においても「安全なお産を守る」ことに貢献できる可能性が示唆された。またSDGs (目標3, 4, 8及び17) 実現のための一つのツールとして非常に効果的であることが考えられた。

P-111-6 Plus One Seminar 2021②～多視点映像と実況中継による参加型オンライン分娩シミュレーションへの挑戦～

岡山大病院

三苫智裕, 横畑理美, 三島桜子, 大平安希子, 桐野智江, 谷 和祐, 牧 尉太, 衛藤英理子, 早田 桂, 増山 寿

【目的】産科部門のシミュレーション教育は、これまで分娩シミュレーターを使用して正常分娩や異常分娩などを指導者とマンツーマンによる指導で教育を行ってきた。しかし、今回 plus one seminar を開催するに際し、参加者が越県し集合してのセミナー開催が困難となった。そのため、同期型オンライン会議システム及び事前収録の多視点映像により、シミュレーションの利点を生かしながら、現場に即した学習の場の提供するための工夫を行なった。【方法】開催1か月前より制作チームを編成し、シナリオ制作、レクチャー制作、シミュレーション動画などに役割を分割した。映像は分娩の各フェーズごとに事前収録を行い、編集を加え動画を制作した。セミナー当日は動画を繋ぎ合わせ、ナレーションによる進行により分娩シナリオを進行させた。【成績】1. 多視点映像により、オンラインでありながら、体験・実践しているような視点を再現し具体的経験を再現した。2. レクチャーの事前収録を行い動画編集をすることで学習効果を高める工夫ができ、さらにセミナー進行への時間的配慮を行うことが可能となった。3. オンライン会議システムを使用し、課題、考察とフィードバックをリアルタイムで行うことで、学習効果を高めることができた。4. 事前収録動画とシナリオナレーションを組み合わせることで、入院から分娩までを実臨床に沿った内容で学習者へ提供することができた。5. セミナー自体を収録し、再編集することで、医学生・看護学生向けのレクチャー動画に繋げ、セミナー資料の二次活用に繋げた。【結論】動画編集による多視点映像とオンラインによる講義とシナリオ作成は、新たな産科教育の手段となり得る。

P-111-7 コロナ禍の「技術革新と自由学習の効率性を重視」した体感型 CCS 実施の試みと学生から得た評価の検討

岡山大病院

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【目的】コロナ禍は、大いにクリニカルクラクシップ(CCS)の弊害となった。2017年度より多機能女性全身シミュレーターモデル(Sim)開発を行い、2019年完成、2020年2月よりCCSの学生教育に導入。コロナ時代にSimとICTを融合したOFF-JT(ジョブトレーニング)を取り入れつつON-JTを行う新教育展開とした。コロナ禍のCCSへの新教育展開に学生が、どう認識し評価したかを探索的に調査、分析した。【方法】対象は2020年2月から2021年10月に当科でCCSを行った5・6年の学生履修者。On-JTでは「女性の救急疾患(腹痛)、妊婦と薬、国家試験対策」等、Sim+OFF-JTで「陣痛発来後の対応」等の学習とした。CCSの開始前(プレ)と最終日(ポスト)の2度アンケート調査を行い、分析した。【成績】プレ288例、ポスト222例が回答。プレでは、当科CCSまでにSim機器を用いた実習は、正常分娩・心肺蘇生・超音波検査を除き、他12項目の全てで10%以下であった。学生が求める教育レベルは学生程度68.4%、研修医程度24.3%、知識の到達レベルは国家試験合格が64.6%、研修医程度が20.5%。ポストでは、研修到達目標の達成度で「すべて・かなり達成できた」が76%であった。Simでは「手技・チーム医療の6つの設問」全てで90%を超えた。また、指導医評価・Sim・ICT教育・スキルアップ・フィードバック・行動目標の達成度、斬新さ、全て90%以上で好意的な回答を得た。【結論】学生はコロナ禍でもSim教育が欠乏していた。「技術革新と自由学習の効率性を重視」できるSimやON-JT、OFF-JTを組み合わせて体感型CCSを導入することで、コロナ禍で従来型CCSが困難でも、学生が求める教育欲求に合致する新展開は従来型CSSに勝る可能性が示唆された。

P-111-8 Plus One Seminar 2021①~ICTを駆使した産婦人科領域ハイフレックス型教育システムの構築~

岡山大病院

衛藤英理子, 長谷川徹, 牧 尉太, 久保光太郎, 松岡敬典, 早田 桂, 増山 寿

【目的】コロナ禍においてICT(information communication technology:情報通信技術)を活用した教育システムの重要性が高まっている。ハイフレックス型教育は、対面・同期オンライン・非同期オンラインが提供され学修者が選択することができる新しい教育スタイルである。Web開催でも効率的かつ効果的なセミナーの主催が求められている中で、最新のICTを駆使した多施設合同の産婦人科教育を実践し、産婦人科領域でのハイフレックス型教育システムを構築することを目的とした。【方法】初期研修医および医学生38名を対象に、Plus One Seminar 2021を開催した。周産期と腹腔鏡に関する2つの対面・同期オンライン教育を実施した。周産期プログラムでは、回旋や内診などの現実味を最大限追及した当科開発の新型シミュレーターを用い、VOD(Video On Demand)とリアルタイム配信を組み合わせた仮想経陰分娩の実況中継という形式を考案した。腹腔鏡プログラムでは、中四国10大学に同型のドライボックスと操作機器を設置し、全施設でディスカッションを行う遠隔シミュレーションを実施した。非同期オンライン教育素材の全行程動画を作成した。【成績】Web会議システムZoomを用いて双方向のコミュニケーションが可能な状況で、それぞれ80分間のプログラムが提供された。経陰分娩、腹腔鏡トレーニングを通じた産婦人科業務の追体験により、オンザジョブトレーニングにつながる学修が行われた。作成動画を用いて非同期オンライン教育も実施された。【結論】ICTを駆使することにより、産婦人科領域でのハイフレックス型教育システムの構築が可能であった。

P-111-9 産婦人科医学教育における反転授業の中止とその影響

山梨大

深澤宏子, 平田修司

【目的】われわれは学習効率の向上をめざし2017年から産婦人科の系統講義にアクティブラーニングの手法の一つである反転授業を導入してきた。しかし、教育効率の向上は期待できるが、解決すべき諸問題があることが明らかとなった。さらに2020年春から、Covid-19(新型コロナウイルス感染症)の拡大により、臨床医学の講義教育が遠隔講義となったため、遠隔講義ではこれまで継続してきた反転授業を行うことができなかった。今回、われわれは反転授業の中止が学習に与えた影響に関して検討した。【方法】昨年の産科の講義は22時限あった。そのほとんどは遠隔講義で行ったが、講義内容の特性から、全員を対象とした対面講義を2時限のみ行った。この2時限の対面講義では、遠隔講義の教育効果を検討する目的で、この講義に先立って一昨年までと同一の反転授業課題を同一の指示方式で課し、対面講義の冒頭で、一昨年と同一の小テストを計2回行った。【成績】2020年の小テストの結果を2019年と比較すると、2019年は 76.0 ± 22.4 (平均 \pm 標準偏差)ならびに 91.8 ± 12.6 であったのに対し、2020年は 42.6 ± 16.1 ならびに 75.8 ± 22.4 と2回とも2020年の方が有意に低かった。【結論】以上より、日常的に反転授業を用いた講義を経験しておらず、かつ、遠隔講義を受けている学生の知識習得意欲が制約され、結果的に学習到達度が低くなったことを意味するのではないかと考えた。対面講義が再開できても、今後も遠隔講義を余儀なくされる可能性はあるため、対面講義で反転授業を再開すると同時に、遠隔講義においても通用する反転授業の手法を考案する必要がある。

P-111-10 周産期センターのチーム医療における Non Technical Skills の課題をチェックリストを用いて「見える化」する試み—より安全な周産期医療をめざして—

昭和大江東豊洲病院

山下有加, 田淵明彦, 竹村有理, 対馬杏奈, 高林綾乃, 中林裕貴, 河野春香, 小松玲奈, 西 健, 土肥 聡, 近藤哲郎, 大槻克文

【目的】Non Technical Skills (NTS) とは、安全で効率的なチームパフォーマンスに寄与する認知的、社会的機能であり、Technical Skills をサポートする役割として重要である。NTS は、医療業界においては、『教育する技術』としては認識がされていないことが多い。そこで我々の施設スタッフに NTS の向上に必要な要素 (状況認識/意思決定/ワークロード/チームワーク/コミュニケーション) についてチェックリストを用いて、意識的に行動をしているか否かをアンケート調査し、教育における課題を抽出した。【方法】2021 年 1-7 月の期間に当院周産期センターに勤務している医師 21 名、助産師 18 名にアンケート調査を行ない、その結果を分析した。【成績】アンケートの回収率は 100% であった。状況認識の要素では認識をリセットすることを意識しているスタッフは半数程度、状況の変化の予測について経験が浅いスタッフで苦手の傾向がみられた。意思決定の要素では根拠を伝えているという医師が 92.9% に対し、それを確認していると回答した助産師が 60% と認識に解離が見られた。ワークロードの要素ではチーム全体のタスクの把握と不要な業務負荷の排除、効率的な計画の立案に課題があるスタッフが多かった。コミュニケーションの要素では切迫した現場で意見や疑問を素直に言えるスタッフが 60% と低かった。【結論】NTS のチェックリストを用いることは、問題点が要素別に分類されているので個人、職種別の教育課題の明確化に有用と考えられた。当院においてはチームの意思決定における伝達とその確認、チームメンバーのタスクの把握と適度な分配、誰もが意見、疑問を言いやすく、それを傾聴できる風土作りが課題と考えられた。

P-112-1 低リスクの初産婦における自然分娩と誘発分娩の比較検討

北里大病院産母子成育医療センター

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【目的】新型コロナウイルス感染症の流行に伴いユニバーサルスクリーニングを行うため、2020 年 3 月以降の分娩は自然分娩希望の場合でも全例未陣発で入院する計画分娩としている。一般的に分娩誘発では器械分娩や帝王切開率の上昇、分娩所要時間延長が懸念される。そこで当院における自然分娩と計画分娩を比較し、分娩誘発が周産期予後に与える影響について検討した。【方法】対象は当院で分娩した正期産の単胎、頭位、母児に合併症を認めない初産婦。2019 年 4 月～2020 年 2 月に陣発入院し自然分娩管理を行った 53 例 (N 群) と、2020 年 3 月～2021 年 9 月に分娩誘発を行った 45 例 (I 群) を比較し、診療録を用いて後方視的検討を行った。統計学的解析は Mann-Whitney's U test, χ^2 検定, t 検定を用いて $p < 0.01$ を有意とした。【成績】母体背景、児の出生体重に差は認めなかった。入院時 Bishop score は I 群で有意に低く (N/I 群: 7/3 点)、34 例にメトロイリンテルを使用した。I 群の 1 例は分娩停止で帝王切開を施行したが、器械分娩頻度 (13/16 例)、回旋異常 (0/2 例)、分娩所要時間 (第 1 期 8/7.6h・第 2 期 0.5/0.7h)、出血量 (670/663g)、会陰裂傷 (III・IV 度) の頻度 (2/4 例) に有意差を認めなかった。アプガースコア 7 点未満 (1 分値 2/4 例・5 分値 1/1 例)、臍動脈血 pH (7.3/7.3) も有意差を認めなかった。NICU 入室は N 群が 2 例 (一過性多呼吸 1 例、新生児仮死 1 例)、I 群は一過性多呼吸の 1 例であった。入院日数は誘発前日入院のため、I 群で有意に長かった (5/6 日)。【結論】分娩誘発では入院日数が 1 日程度延長する欠点はあるが、適切な器械的頸管熟化と子宮収縮薬投与により自然分娩と同様の周産期予後を得ることが可能であった。

P-112-2 IoT 胎児モニター iCTG を COVID-19 感染妊婦の入院・自宅・救急搬送時モニタリングに活用した当院での試み

小樽病院¹, 札幌医大附属病院²

黒田敬史¹, 今 沙織¹, 谷垣 学¹, 齋藤 豪²

【目的】当院は 2019 年に IoT 胎児モニター iCTG を導入し、助産師外来における遠隔妊婦健診へと活用してきた。COVID-19 感染妊婦診療においては発熱妊婦の外来応需や軽症感染妊婦の入院対応を行う中、感染・疑似症・濃厚接触妊婦における入院中・在宅・救急搬送時のモニタリングツールとして iCTG を活用したので、その有用性を検討すべく報告する。【方法】COVID-19 の国内感染拡大後 18 か月間に当院で診療した感染妊婦の重症度および臨床経過、また同時期に COVID-19 感染に関連して iCTG を使用した症例の分析から、iCTG の有用性を検討した。【成績】当該期間に当院で診療した COVID-19 感染妊婦患者は 11 例であり、重症度は軽症 8 例、中等症 I が 1 例、中等症 II が 1 例、重症 1 例であった。診療経過については 7 例が当院で入院後軽快退院したが、2 例が増悪のため高次医療施設へ転院搬送、1 例は満期のため感染発覚後高次医療施設へ入院、1 例は自宅観察となった。iCTG は COVID-19 感染妊婦 4 例と濃厚接触妊婦 1 例において使用した。当院入院中に用いた 3 例では自主計測を指示したが 2 例 (妊娠 19 週に用いた例と、妊娠 31 週で BMI が高値であった例) において測定困難で、のち救急搬送にも用いた 1 例において入院中、搬送中ともに CTG 波形表出が可能であった。自宅観察中に自主計測を指示した妊娠 38 週および 40 週の 2 症例では良好に波形データが表出された。増悪のため救急搬送した妊娠 33 週症例では CTG 波形をリアルタイム送信するため搬送先へ URL を伝え、データを共有することができた。【結論】少数症例からの検討であるが、COVID-19 感染妊婦への iCTG 利用は、医療従事者の接触時間に配慮を要する局面で有用である可能性が示唆された。

P-112-3 子宮頸管熟化不全に対する処置の有用性に関する検討～ジノプロストン腔用剤と器械的熟化法の比較～

新潟大病院

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【目的】当科では2020年12月より新規子宮頸管熟化剤であるジノプロストン腔用剤を妊娠37週以降の頸管熟化不全症例の第一選択薬として使用している。本検討はジノプロストン腔用剤と器械的熟化法の臨床成績の違いを比較検討することを目的とした。【方法】妊娠37週以降子宮頸管熟化不全の適応で2020年12月から2021年9月までにジノプロストン腔用剤を使用した28例(以下、腔剤群)と、2019年1月から2020年11月までに器械的熟化法を行った61例(以下、器械群)の患者背景や治療成績を、診療録を元に後方視的に比較検討した。子宮頸管熟化不全はBishop score 7点未満と定義した。【成績】患者背景は両群で有意差を認めず、初産婦は腔剤群17例(61%) vs 器械群41例(67%)であった。Bishop scoreは両群ともに治療前後で有意な上昇を認め(p<0.01)、経陰分娩は腔剤群23例(82%) vs 器械群45例(74%)で成功し、両群で経陰分娩成功率に有意差を認めなかった(p=0.43)。処置開始から分娩までの時間は腔剤群22.5±15.2時間 vs 器械群55.4±46.2時間、処置開始から退院までの日数は腔剤群6.6±1.3日 vs 器械群8.8±2.7日であり、ともに腔剤群で有意に短縮していた(p<0.01, p<0.01)。処置に伴う母体合併症は両群ともに発症はなく、出生体重、Apgar score(1分値/5分値)、臍帯動脈血pH値には両群で有意差を認めなかった。【結論】ジノプロストン腔用剤は熟化成功率や経陰分娩成功率は器械的熟化法と同等であり、かつ分娩時間を短縮しうる有用な薬剤である。

P-112-4 当施設におけるジノプロストン腔内留置用製剤の使用症例の検討

大垣市民病院

中尾優里, 勅使河原利哉, 小林祐太, 孫 麻子, 市田啓佑, 大塚直紀, 石井美佳, 古井俊光

【目的】分娩誘発の成功率は頸管熟化の状態に依存する。本邦では2020年1月にジノプロストン腔内留置用製剤が承認され、分娩誘発における効果が期待されている。当施設におけるジノプロストンの使用症例を検討する。【方法】2020年8月から2021年9月までの期間に当院でジノプロストンを使用した妊婦12例を対象とした。分娩転機、Bishop scoreの変化、副作用について後方視的に検討した。【成績】初産婦8例、経産婦4例であり、分娩誘発の適応は、前期破水4例、予定日超過3例、巨大児2例、妊娠高血圧症候群2例、FGR1例であった。平均母体年齢は29.3歳(25-40歳)、挿入時の平均妊娠週数は39.1週(37-41.1週)であった。開始時のBishop scoreの平均値は2.58点(1-4点)、抜去時は4.58点(1-10点)であった。平均挿入時間は457.9分(300-620分)であった。12例のうちジノプロストン使用により陣痛発来した症例は5例であった。それらの抜去時のBishop scoreの平均値は7点(5-10点)であり、陣痛開始までの平均所要時間は284分(30-495分)、平均分娩所要時間は431.6分(112-884分)であった。陣痛発来しなかった7例の抜去時のBishop scoreの平均値は2.85点(1-5点)であった。そのうち5例は誘発の継続または自然陣痛発来により経陰分娩に至り、2例は緊急帝王切開にて分娩に至った。適応は臨床的絨毛膜羊膜炎と分娩停止であった。副作用としては3例に胎児徐脈を認めた。そのうちの2例では新規破水直後に認めた。【結論】当施設では、ジノプロストンにより子宮頸管熟化が得られた割合は既報より少なかったが、その後の誘発継続により経陰分娩に至る症例が多く認められた。新規破水後の胎児徐脈出現に注意が必要であると考えられる。

P-112-5 当院でのジノプロストン腔用留置剤の使用成績および留置時間についての考察

倉敷中央病院

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【目的】当院でのジノプロストン腔用留置剤の使用成績と留置時間について検討する。【方法】2020年3月～8月に当院での従来法による分娩誘発された妊婦(初日に機械的拡張; 以下従来群, 61例)、2020年9月～2021年7月に初日にジノプロストン腔用留置剤使用による分娩誘発された妊婦(以下ジノプロストン群, 58例)(両群とも単胎, 妊娠37週以降, 誘発前のBishop Score(以下BS)≤4点)を対象に、分娩成績を後方視的に比較検討する。【成績】両群間で経陰分娩率は大きな差は認めなかった。(初産婦; 53% vs. 50%, 経産婦; 100% vs. 93%)初産婦では、分娩前BS0-2点の症例が多く(80% vs. 47%)、経陰分娩までの平均期間はプロウペス群でやや長かった。(2.4日 vs. 1.7日)誘発前BS0-2点の初産婦では、ジノプロストン群の分娩成績が良好な傾向であった。(経陰分娩率; 50% vs. 38%, 24時間以内の経陰分娩率; 17% vs. 6%)ジノプロストン群を留置時間で分けて比較すると抜去基準にかかり9時間以内に抜去した群で有意に経陰分娩率, 24時間以内の経陰分娩率が高かった。(経陰分娩率; 74% vs. 54%, p=0.164, 24時間以内の経陰分娩率; 45% vs. 4%, p=0.0005)【結論】誘発前頸管熟化不良例では、特に初産婦でジノプロストン腔用留置剤の成績が良好な傾向にあり、有用である可能性が示唆される。抜去基準にかかり9時間以内にジノプロストン腔用留置剤を抜去した例では分娩成績が良好である。

P-112-6 当センターでの前期破水症例に対するジノプロストン腔用剤の使用経験

大阪急性期・総合医療センター

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【目的】ジノプロストン腔用剤は妊娠37週以降の頸管熟化不全の症例に対して使用される子宮頸管熟化剤であり、本邦では2020年4月より販売開始され使用可能となった。ジノプロストン腔用剤は急激なpH上昇への曝露により薬剤の放出速度が高まることが知られており、投与開始後に新たな破水が生じた場合は速やかに除去する必要がある。その一方、投与時点で前期破水のある妊婦にも投与可能となっている。今回、前期破水の妊婦に対してジノプロストン腔用剤を用いた症例での分娩への影響について検討した。【方法】当センターで2020年9月から2021年8月までにジノプロストン腔用剤による分娩誘発を実施した正期産の単胎妊婦34症例を対象とした。投与時点での前期破水群は12例、非前期破水群は22例であった。薬剤除去を要したかどうかおよび分娩結果について後方視的に検討した。【成績】前期破水群と非前期破水群の母体年齢は 31.5 ± 6.8 歳 vs. 33.7 ± 6.6 歳、分娩誘発時の妊娠週数は 39.5 ± 0.9 週 vs. 39.3 ± 1.8 週、薬剤投与時点でのBishop scoreは 2.4 ± 1.8 点 vs. 1.2 ± 1.3 点であった。薬剤除去を要する割合は前期破水群では41.7% (5/12例)、非前期破水群では72.7% (16/22例)であった。前期破水群と非前期破水群の帝王切開率は25.0% vs. 31.8%、臍動脈血液ガスのpHは 7.31 ± 0.06 vs. 7.27 ± 0.07 、NICU入室率は8.3% vs. 18.2%であった。【結論】今回の検討では前期破水症例に対してジノプロストン腔用剤を使用した場合、薬剤除去を要する割合は増加がみられず、帝王切開率や出生児の状態に大きな差は認めなかった。前期破水の症例でのジノプロストン腔用剤の使用は分娩への影響を増悪させないことが示唆された。

P-112-7 分娩誘発にPGE2腔座剤（プロウベス）を使用した15症例の検討

西神戸医療センター

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【目的】従来我が国では、分娩誘発の際に頸管熟化不良な症例にはあらかじめ機械的頸管熟化を用いてきた。2020年4月にPGE2腔座剤（商品名：プロウベス）が販売されるようになってから、機械的頸管熟化の代わりに使用できるようになった。当院でPGE2腔座剤を用いて分娩誘発を行った15症例を検討することとした。【方法】当院で2020年12月から2021年8月までの間でPGE2腔座剤を用いて頸管熟化および分娩誘発を行った18症例を対象とした。同一入院で分娩に至らなかった3症例は除外した。それぞれの症例の分娩週数、妊娠分娩歴、Bishop Score、誘発の適応、合併症、最終的な分娩方法、出生体重、Apgar Scoreを比較検討した。必要に応じてオキシトシンやプロスタグランジンF2 α の点滴で分娩誘発を行った。【成績】15例すべて満期で、経陰分娩成功は7例（46.7%）、帝王切開症例は8例（53.3%）であった。14例は初産婦であった。適応はHDPとFGRが5例、予定日超過が4例であった。予定日超過4症例の分娩様式はすべて帝王切開となっていた。HDP症例は4症例が経陰分娩成功となった。【結論】PGE2腔座剤は機械的頸管熟化に代わる頸管熟化方法であり、当院で経験した症例では予定日前のHDP症例で誘発成功となる傾向があった。一方予定日超過症例は帝王切開となる傾向があった。今回は15症例での検討となったが、今後症例数を増やしてさらにPGE2腔座剤有効症例を検討する必要があると考える。

P-112-8 当院におけるoxytocin challenge test (OCT) の成績

JA尾道総合病院

張本 姿, 藤田真理子, 上田明子, 坂下知久

【目的】oxytocin challenge test (OCT) は1960年代に考案され、以後、胎盤機能不全を疑う胎児予備能検査として活用されていたが、胎児超音波検査の進歩に伴いその利用頻度は低下している。しかし、超音波検査で子宮収縮に伴う胎児の低酸素による変化を予測することは難しく、経陰分娩の可能性についての評価には向いていない可能性がある。当院では約4年前から帝王切開率低減の取り組みを進めており、その一環として胎児の健全性を疑う症例に対するOCTを積極的に行っている。当院におけるOCT施行症例の成績を報告する。【方法】当院で2018年から2020年に羊水減少、胎児発育不全 (FGR)、NST異常、FGRを伴う妊娠高血圧症候群などの胎児の健全性を疑う症例に対してOCTを施行した47例を対象とし、診療録を用いて後方視的に検討した。【成績】対象症例のうち、帝王切開に至ったのは8例（17%）であった。OCT陽性は4例（8.5%）あり、全例帝王切開（非緊急）を行った。OCT陰性は42例（89.4%）であり全例分娩誘発を行い、経陰分娩成功39例、緊急帝王切開3例であった。OCT判定不能は1例あり、別の適応で帝王切開となっていた。【結論】OCT陽性は全て非緊急での帝王切開を行うことで、潜在的な緊急帝王切開を回避できた可能性がある。OCT陰性では93%が経陰分娩可能あり、OCTは帝王切開率の低減に寄与している可能性がある。OCTは防御的な適応での帝王切開を減少させる方法であり、今後その有用性に関して見直されるべきである。

P-112-9 吸湿性頸管拡張剤を用いた分娩誘発における、帝王切開のリスク因子の検討

秋田大

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【目的】分娩誘発において物理的開大を行わない海外において、Bishop's Score (BS) の中で、特に子宮口開大・展退度・児頭下降度の3項目(以下、修正BS)が、帝王切開と関連するという報告が散見される。当院で実施している、分娩誘発例に対し吸湿性頸管拡張剤にて頸管開大後に子宮収縮剤を投与する方法においても、修正BSが有用であるか後方視的に検討した。【方法】2011-2019年の9年間に、当院において妊娠37週以降に分娩誘発を受けた単胎初産婦204例を抽出した。分娩停止が主な手術適応となるよう、母体ないしは胎児適応で帝王切開した24例を除外し、180例を解析対象とした(経陰分娩155例、帝王切開25例)。頸管開大後(分娩当日朝)の、BSと修正BSのどちらが帝王切開と関連するか検討した。また、患者背景として、母体の分娩時BMI、年齢、妊娠週数、頸管開大前BS、および新生児出生体重について帝王切開との関連を調べた。【成績】頸管開大後の、BS($p=0.007$)と修正BS($p=0.003$)はどちらも帝王切開と関連するが、ROC曲線のAUCに差はなかった(0.667 vs. 0.682)。頸管開大後BSを項目別にみると、子宮口開大度と展退度は帝王切開と関連が無く、児頭下降度($p=0.006$)、頸管硬度($p=0.028$)、子宮口の向き($p=0.020$)は関連があった。患者背景では、新生児出生体重($p=0.017$)のみが帝王切開と関連があった。【結論】修正BS自体は帝王切開のリスク評価に有用であるものの、BSの項目別にみると、むしろ修正BSに含まれない項目が関連する結果であった。明確な原因は不明であるが、吸湿性頸管拡張剤は子宮頸管に物理的な影響を与えるため既報と違いが見られたのかもしれない。

P-112-10 プロウベス使用中の過強陣痛に対するニトログリセリンの有用性

三重大

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【緒言】ジノプロストン腔内留置用製剤(プロウベス)は、日本において2020年に薬事承認された新たな子宮頸管熟化剤である。特に注意すべき副作用は、過強陣痛である。プロウベスによる過強陣痛に対して有効であった対処法について報告する。【症例1】32歳4妊2産、妊娠39週から分娩誘発を計画し、子宮頸管熟化のため、プロウベスを使用した。挿入から30分後、過強陣痛に伴う軽度～高度の遷延一過性徐脈を繰り返し認めた。体位変換、酸素投与を行い、プロウベスを速やかに抜去したが、改善せず、ニトログリセリン100 μ gを静注した。過強陣痛は減弱し、胎児心拍の波形レベルは1まで回復した。その後、自然陣痛発来し、挿入から4時間15分、経陰分娩で2832gの児(Apgar score 8/9, UA pH 7.328)を得た。【症例2】27歳1妊0産、妊娠41週から分娩誘発を計画し、子宮頸管熟化のため、プロウベスを使用した。挿入から34分後、過強陣痛に伴う高度遷延一過性徐脈が出現した。体位変換、酸素投与を行い、7分後にプロウベスを抜去したが、胎児心拍の波形レベル4から改善せず、超緊急帝王切開術を決定した。ニトログリセリン100 μ gを静注し、手術室へ向かう際、過強陣痛は減弱し、胎児心拍の回復を確認した。3072gの児(Apgar score 7/9, UA pH 7.195)を得た。【結論】プロウベスによる過強陣痛は、プロウベス抜去だけでは過強陣痛は抑制されることがしばしば認められる。ニトログリセリンは、効果発現が極めて速く、副作用の低血圧も起こりにくいため、有効な対応法と考えられる。

P-113-1 当院における胎児外回転術における成功因子の抽出

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【目的】胎児外回転術(External Cephalic Version: ECV)は手動的に骨盤位の胎児を頭位に整復する処置である。しかし破水、常位胎盤早期剝離などの合併症を引き起こす可能性があるため、ECVの成功を予測する因子の抽出は重要である。今回当院で行われたECV症例について後方視的に検討し、ECVにおける成功予測因子の抽出を試みた。【方法】対象は2016年2月から2021年7月の間、当院において単胎骨盤位でECVを行った症例とした。ECV成功の有無、ECV前の超音波所見、非妊娠時から分娩までの母児の情報を診療録より抽出し解析した。単変量解析で $p<0.2$ となる因子についてはROC曲線を用いてカットオフを決定し、多変量解析を行った。【成績】対象症例は50症例(対象期間の全分娩2148例中2.3%)であった。対象症例の年齢は 33.5 ± 4.7 歳、外回転週数は 37.1 ± 0.6 週であった。ECV成功例は34例(68%)で過去の報告でのECVの成功率と同等であった。 $p<0.2$ となる因子は非妊娠時BMI($p=0.06$)、経産の有無($p=0.13$)、AFI($p=0.10$)であった。ROC曲線にて最も有用なカットオフ値をそれぞれ非妊娠時BMI <22 (AUC=0.66)、AFI >11 (AUC=0.65)と定め単変量解析を行ったところ、それぞれにおいて有意差を認めた($p=0.04$, $p=0.03$)。非妊娠時BMI、経産の有無、AFIについて多変量解析をおこなったところ、非妊時BMI <22 ($p=0.02$, OR 5.46: 95%CI 1.24-24.0)、AFI >11 ($p=0.03$, OR 5.47: 95%CI 1.15-26.0)ともに有意差を認め、両者は独立した成功予測因子であることが示された。【結論】非妊娠時BMIとAFIがECVの成功を予測する因子と考えられた。単一施設で症例数も少ないため更なる症例数の取積と検討が望まれる。

P-113-2 当院で施行した骨盤位外回転術 132 例の検討

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【目的】近年、わが国では胎児骨盤位の約 95% が帝王切開 (C/S) となる。しかし経陰分娩には、母体侵襲の回避に加え、出生児の呼吸・循環・代謝のスムーズな安定や健康な腸内細菌叢形成など成長・発達におけるメリットが多い。骨盤位外回転術 (ECV) の臨床成績を検討し、その有効性と成否に関わる因子について考察した。【方法】適応となる妊婦の約半数が ECV を希望し、実際に施行した症例 (2010 年~2021 年 8 月) の診療録をもとに検討した。妊娠 35-36 週にリトドリン点滴による Tocolysis、骨盤高位、経腹超音波を併用して実施し、脊髄くも膜下麻酔や硬膜外麻酔は行っていない。【成績】他院からの ECV 目的の紹介を加え 132 例に ECV を行い、76 例 (57.6%) が成功した。成功/不成功例の平均値に有意差 ($p < 0.05$) を認められたのは、経産回数 (0.85/0.32)、外回転回数 (35.8/35.4)、外回転時の胎児推定体重 (g) (2,316/2,124) だった。年齢、身長、妊娠前 BMI、外回転時 BMI、臍帯巻絡、骨盤位の定まった週数、羊水ポケットの平均値には差がなかった。合併症は、性器出血が 2 例、36 週早産が 3 例だった。成功 76 例中、最終的に 73 例で経陰分娩となり、3 例は C/S となった。その適応は、2 例が NRFS、1 例は再度の骨盤位だった。期間中の骨盤位 C/S は 144 例であり、ECV を行わなければ骨盤位 C/S は約 1.5 倍増加していたことになる。【結論】当院での ECV 成功率は 57.6% で、常位胎盤早期剝離などの重篤な合併症はなかった。特に腹壁の柔軟な経産婦は胎児を扱いやすく、また、児が小さいと先進部が深く嵌入して臀部を拳上しにくい傾向があった。ECV は帝王切開の減少に有用であり、特に経産婦はその良い適応と考える。骨盤位妊婦には ECV の施行を考慮すべきである。

P-113-3 前回分娩からの期間は分娩所要時間に影響するのか

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【目的】前回の分娩から長期間経過している経産婦の妊娠例をしばしば経験する。経産婦の分娩所要時間は初産時のおおよそ半分とされているが、分娩間隔と分娩所要時間に関する検討は少ない。今回我々は、当院における経産婦の分娩所要時間を分娩間隔ごとに検討した。【方法】2017 年 1 月から 2021 年 8 月に当院にて経陰分娩をした経産婦 921 例を対象とし、分娩間隔と分娩時年齢、経産回数、分娩週数、出生児の体重、陣痛誘発および促進の有無、初産時の分娩所要時間を後方視的に検討した。妊娠 22 週未満の分娩は除外し、分娩間隔は年単位で振り分けた。統計には Mann-Whitney 検定、カイ二乗検定を用いた。【成績】分娩間隔の中央値は 3 年で、最長 19 年であった。1~4 年が 680 例と全体の 75.0% を占め、5~9 年が 208 例 (21.3%)、10 年以上が 33 例 (3.6%) であった。分娩所要時間の中央値は、分娩間隔 1~4 年では 238 分、5~9 年では 254 分、10 年以上では 330 分であり、分娩間隔を 10 年で区切った場合に、10 年以上の群は 10 年未満の群 (以下対照群) と比較して分娩所要時間が有意に長くなった ($p=0.03$)。分娩週数や出生児の体重に有意差は認めなかった。陣痛誘発および促進率は、10 年以上の群において有意に高くなった (10 年以上の群 36.3%, 対照群 24.5% $p=0.04$)。また、10 年以上の群における初産時の分娩所要時間の中央値は 510 分であり、今回の分娩所要時間のほうが有意に短かった ($p=0.04$)。【結論】分娩間隔が 10 年以上経過していても、初産時と比較すれば分娩所要時間は短縮されるが、経産婦の分娩所要時間としては長く、陣痛誘発および促進率も高かった。10 年以上の分娩間隔は、分娩ハイリスク因子の一つとして考慮する必要性が考えられた。

P-113-4 帝王切開既往のある妊婦は次回経陰分娩時の分娩所要時間が延長する：傾向スコアを用いた生存時間解析

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【目的】帝王切開の既往のある妊婦の経陰分娩 (帝王切開既往群) と帝王切開の既往のない妊婦の経陰分娩 (非帝王切開既往群) の分娩所要時間を比較した報告は過去に見当たらない。今回我々は帝王切開既往の有無により、分娩所要時間に差があるかを検討した。【方法】2012 年 1 月 1 日から 2020 年 12 月 31 日までに当院で経陰分娩を試みた妊婦を対象とした。日本産婦人科学会周産期登録データベースのデータを用いて傾向スコアによる最近傍マッチングを行い、生存時間解析を行った。傾向スコアに組み込む因子として 23 の因子を選択した。37 週未満の早産例、子宮内胎児死亡例、双胎例は除外した。解析ソフトは R を使用した。【成績】2984 名の経産婦が解析に組み込まれ、傾向スコアによるマッチングで各群 68 名の妊婦が抽出された。非帝王切開既往群のうち初産婦は 31 名、経産婦は 37 名であった。陣痛発来から分娩までの時間の中央値は帝王切開既往群で 552 分 (95% 信頼区間: 436-710 分)、非帝王切開既往初産婦群で 317 分 (95% 信頼区間: 229-357 分)、非帝王切開既往初産婦群で 733 分 (95% 信頼区間: 445-1006 分) であった ($p < 0.05$)。経陰分娩の回数、初産婦/経産婦の別を共変量とする Cox 比例ハザード回帰分析では、帝王切開既往群の非帝王切開既往群に対するハザード比は 0.42 (95% 信頼区間: 0.31-0.56, $p < 0.05$) であった。これらの傾向は感度分析を行っても同様であった。【結論】帝王切開既往のある妊婦は、帝王切開既往の無い妊婦と比較して分娩所要時間が長くなることが示唆された。帝王切開既往のある妊婦の経陰分娩管理を行う際は、通常の妊婦よりも分娩所要時間が長くなることを考慮して管理を行うことが必要と考えられた。

P-113-5 分娩中に人工羊水注入療法を実施した85例の検討

トヨタ記念病院

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【目的】分娩中の人工羊水注入療法は、羊水量増加に伴う臍帯圧迫の解除、軽減により、胎児心拍数波形の異常を改善させるとする報告が多いが、その適応や有効性に関しては一定の見解が得られておらず、症例の蓄積が必要である。今回我々は人工羊水注入療法の有効性を後方視的に検討した。【方法】2019年1月1日から2021年9月31日までに、当院で緊急帝王切開が必要となる可能性が高いと判断し、人工羊水注入療法を行った85例を対象とした。人工羊水注入療法の適応は羊水過少症、non-reassuring fetal status (NRFS)、羊水混濁とした。胎児心拍数波形の判定は日本産科婦人科学会の提唱する胎児心拍数波形のレベル分類に基づいて行い、レベル3以上をNRFSとした。【成績】人工羊水注入療法の適応は、羊水過少症が58例(68%)、NRFSが50例(59%)、羊水混濁が16例(19%)であった(重複あり)。NRFSの内訳は、レベル3が27例(54%)、レベル4が21例(42%)、レベル5が2例(4%)であった。羊水注入前にNRFSであった症例では、31例(62%)で注入後に一過性徐脈が改善した。分娩転帰は経陰分娩が65例(77%)、緊急帝王切開が20例(24%)であった。緊急帝王切開の適応はNRFSが12例(60%)、分娩停止が7例(35%)、絨毛膜羊膜炎が1例(5%)であった。羊水注入によるamniotic fluid index増加量が3cm未満の症例での緊急帝王切開の割合は40%である一方、3cm以上の症例では18%と低い傾向を認めしたが、有意差はなかった($p=0.07$)。人工羊水注入療法に伴う重篤な合併症は認めなかった。【結論】人工羊水注入療法を実施した症例では、62%でNRFSが改善し、77%で経陰分娩となり、その有効性が示唆された。

P-113-6 当院におけるTOLACの検討

香川大附属病院

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【目的】当院では、施設の規定条件を満たす既往帝王切開後妊婦に対し、積極的にTOLAC(Trial of labor after caesarean delivery)の情報提供を行っている。1回の帝王切開既往妊娠におけるVBAC(Vaginal birth after caesarean section)群と選択的帝王切開(elective caesarean section: eCS)群の間で母児の予後について後方視的に検討した。【対象と方法】2010年1月から2020年12月の11年間に当院で分娩した帝王切開1回既往妊娠について、TOLAC希望率と年次推移、TOLAC成功率を算出した。また、在胎週数、児の出生体重、Apgar score、分娩時出血量についてVBAC群とeCS群を比較検討した。【成績】期間中の帝王切開1回既往妊娠は586例で、TOLAC希望は315例(53.8%)、TOLAC成功(VBAC)は282例(89.5%)だった。不成功例での帝王切開適応の内訳は、胎児機能不全10例、分娩停止8例、陣痛誘発・促進拒否8例、母体異常高血圧2例、切迫子宮破裂4例、子宮破裂1例であった。TOLAC希望率は、近年では減少傾向だった。VBAC群とeCS群の年齢(歳)は32.9 vs 34.1 ($p<0.05$)、非妊時BMI (kg/m^2)は21.3 vs 23.6 ($p<0.001$)だった。在胎週数(週)は39.1 vs 37.8 ($p<0.001$)、児の出生体重(g)は3,052 vs 2,985 ($p<0.05$)、Apgar score 1分値は8 (1-9) vs 8 (4-9) ($p<0.05$)、5分値は9 (7-10) vs 9 (7-10) ($p<0.05$)、分娩時出血量(ml)は487 vs 1,321 ($p<0.001$)だった。【結論】当院でのTOLACを希望する妊婦は減少傾向である一方、これまでの諸家の報告と比較して高い成功率であった。VBAC群はeCS群と比較してfull termでの分娩が多く、出生体重も大きく、分娩時出血量が少ないことから、TOLACは母児にとって有益性が高いと考えられた。

P-113-7 本県における帝王切開後試験分娩の実施状況について

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【目的】本県における帝王切開後試験分娩(TOLAC)の現状と周産期合併症について検討すること。【方法】県内の周産期母子医療センター5施設のうちTOLACを行なっている2施設において、2016年1月から2020年12月までの5年間の帝王切開既往一回の妊婦を対象とした。子宮内胎児死亡を除外した妊娠32週から41週に単胎を分娩した妊婦を抽出し、TOLAC希望の有無、最終的分娩方法、帝王切開後経陰分娩(VBAC)母体の有害事象の有無、児の出生時体重、Apgar score、臍帯動脈血pH、血糖値(BS)、Base Excess (BE)を評価した。【成績】抽出された患者は363人で、前置胎盤7人(1.2%)は除外した。TOLAC希望者は102人(28.1%)で、最終的にTOLAC適応となった患者は79人(21.8%)で、2人(0.5%)が回旋異常で緊急帝王切開となり、VBAC施行患者は77人(抽出された患者の21.2%、TOLAC成功率は97.5%)であった。TOLAC患者に、妊産婦死亡や子宮破裂等の有害事象、周産期死亡はなかった。VBAC患者の平均分娩時出血量は392ml、分娩時出血量が1,000ml以上は4人(5.1%)でいずれも弛緩出血が原因であった。分娩週数、児の出生時体重、Apgar score 1分値及び5分値、臍帯動脈血pH、BS、BEについて、帝王切開群とVBAC群の2群間に分けて比較したところ、分娩週数、児の出生時体重、BS、BEで有意差($p<0.01$)を認めた。このうち、分娩週数、出生時体重、BSはVBAC群の数値が高く、VBAC群の非劣性が確認された。【結論】帝王切開術による合併症は、前置癒着胎盤など次回以降の妊娠にも発症し得るものである。2施設ではVBAC率は非常に高く、合併症予防への取り組みは有効である。海外でもTOLAC実施国は増加傾向にあり、この取り組みを継続する方針である。

P-113-8 臀部触知は骨盤位外回転術の成功因子に成り得るか

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【目的】骨盤位外回転術において、子宮収縮のコントロールが可能な症例、経産婦、AFI>7.5cm、児が開脚していない胎位の4因子が、成功因子であることを2018年に当科より報告した。骨盤位外回転術の第一段階は臀部を触知し、拳上することと明記する報告があるが、骨盤位外回転術において臀部触知自体が成功因子とする報告はない。我々が、2018年までの症例を検討した際に骨盤位外回転術が不成功であった症例に臀部触知が困難であった症例を複数確認した。今回、この臀部触知という因子が、骨盤位外回転術の新たな成功因子に成り得るかということを中心に改めて骨盤位外回転術の成功因子を検討する。臀部触知の定義は、子宮収縮のために臀部が不明瞭な症例と臀部が先進し骨盤に嵌入している症例以外とした。【方法】外来で骨盤位外回転術を施行した症例は、薬剤投与なし、またはリトドリン塩酸塩錠の内服とした。入院症例は、リトドリン塩酸塩の点滴投与と下で施行した。臀部触知は骨盤位外回転術の成功因子かということを中心に主要評価項目としてその他の項目を副次評価項目として統計学的手法を用いて検討した。【成績】胎児の臀部触知可能群は202例で、その中の189例(93.5%)が成功した。臀部触知不可能群は40例で、その中の21例(52.5%)が成功した(p値<.001)。【結論】臀部触知が可能な場合の骨盤位外回転術の成功率は、93.5%であり、臀部触知は、骨盤位外回転術の成功因子であった。また、AFI \geq 10cm以上という条件が、骨盤位外回転術の独立した成功因子であった。

P-113-9 骨盤位外回転術における成功・不成功に関わる因子の検討

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【目的】今回、骨盤位外回転術における成功・不成功に関わる因子を明らかにするため、当科で過去10年間に施行した骨盤位外回転術の臨床所見を後方視的に検討した。【方法】2011年6月から2020年11月までの約10年間に骨盤位外回転術を行った40例を対象とした。臨床所見として、年齢、経妊経産、妊娠週数、子宮収縮の有無、リトドリンの使用の有無、骨盤内嵌入の有無、臍帯巻絡の有無、胎盤位置について調査し、成功・不成功に関わる因子について後方視的に検討した。統計学的解析はロジスティック回帰分析を用いて行った。【成績】40例のうち成功は27例(67.5%)、不成功は13例(32.5%)であった。外回転術を施行した妊娠週数は妊娠36週1日~37週1日で、児の推定体重の平均値は2473.6g \pm 265.6g(平均 \pm 標準偏差)、母体の平均年齢は31.5歳(18歳~43歳)であった。不成功例において有害事象を生じたものは2例で、1例は外回転術後に子宮収縮が増強し2日間のリトドリンによる子宮収縮抑制を要し、もう1例は外回転術の翌日(37週0日)に破水し、緊急帝王切開術を施行した。外回転術は、経産婦【OR 0.12(95%CI: 0.01-0.70), p=0.0158】、リトドリン使用あり【OR 5.83(95%CI: 1.14-29.86), p=0.0343】、臍帯巻絡なしの群【OR 0.16(95%CI: 0.02-0.93), p=0.0411】において有意に成功していた。母体年齢、施行時推定体重には有意差を認めなかったが、胎盤位置(前壁以外)は成功しやすい傾向が認められた。【結論】外回転術には、経産婦、臍帯巻絡無し、リトドリンの使用が成功因子として関連していた。よって、外回転術施行前の妊娠・分娩歴の確認と胎児・胎盤の観察、そして施行に際して十分な子宮弛緩の必要性が示唆された。

P-113-10 経会陰超音波検査による鉗子分娩難易度評価の研究

昭和大病院

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【目的】鉗子分娩には試行はなく、施行にあたっては確実に娩出できる児頭下降度の評価が必要となる。経会陰超音波検査は主観的な内診所見を客観的に評価可能な検査であり、鉗子分娩の難易度の評価に有用かどうかを検討した。【方法】2019年3月~2021年6月で、鉗子分娩を施行した72症例を、Case:不成功または2回以上に分けて牽引、Control:1回の牽引で娩出の2群に分け、後方視的に母体背景(経産回数、年齢、身長、分娩時BMI、分娩時妊娠週数)、鉗子施行前の経会陰超音波所見(陣痛間欠時と発作時のB-station、 Δ B-station(発作時と間欠時の差)、分娩結果(分娩第1期所要時間、分娩第2期所要時間、出血量、出生体重、Apgar score、臍帯動脈血液ガスpH)を検討した。なお、B-stationは経会陰超音波画像上に仮想のstation \pm 0を規定した内診下降度を表す評価法である。【成績】CaseとControlで、母体背景に有意差を認めなかった。陣痛間欠時のB-station(1.7 \pm 1.0 vs 2.7 \pm 1.1cm)、陣痛発作時のB-station(2.8 \pm 1.1 vs 4.5 \pm 1.2cm)、 Δ B-station(1.2 \pm 0.6 vs 1.8 \pm 0.9cm)に有意差を認めた。また、分娩結果では出血量(1383.0 \pm 806.3 vs 786.0 \pm 419.1g)に有意差を認めた。【結論】内診のみだけでなく、経会陰超音波による児頭下降度の評価は鉗子分娩の難易度を評価する方法として有用と思われた。

P-113-11 前3回以上の帝王切開既往を有する妊娠症例の検討

青梅市立総合病院

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【目的】帝王切開回数が増加するに従い、胎盤異常や周術期合併症が増加することが知られている。そのため、一般に3回程度を帝王切開回数の上限と説明される場合もあるが、明確なエビデンスはない。今回、前3回以上の帝王切開既往を有する妊娠症例について、患者背景、妊娠予後を検討した。【方法】2010年1月から2021年9月までに当院で妊婦健診を行った、前3回以上の帝王切開既往を有する妊婦について、診療録を用いて後方視的に検討した。【成績】症例は6例。年齢は37-41歳。既往帝王切開回数は全例3回であった。2例は妊婦健診を未受診で、陣痛発来により当院を救急受診していた。その他の4例は妊娠初期より健診を受診し、妊娠経過に有意な異常を認めなかった。全例が帝王切開により分娩となり、手術時間は54-98分、出血量は480-1800mlで、周術期合併症は認めなかった。全例が帝王切開時に希望による不妊手術を受けていた。全例とも児の経過は順調であった。4例は前回帝王切開時に不妊手術の説明を聞いていたが、以後の妊娠も通常通り可能と理解していた。【結論】前3回以上の帝王切開既往を有する妊娠においても、母児の予後は良好であり、必ずしも3回を帝王切開の上限とする必要性は認めなかった。一方で、前回分娩時の説明により以後の妊娠リスクを理解していた患者は少なく、反復帝王切開のリスクに関する情報提供は不足していると考えられた。反復帝王切開症例では、以後の妊娠に関する適切な情報提供を行い、妊娠や避妊に関する自己決定の機会を提供する必要があると考えられた。

P-114-1 器械分娩翌日の母体白血球数とその後の母体合併症との関連：DPCデータベースを用いた後方視的コホート研究

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【目的】器械分娩患者において産道裂傷の縫合不全や続発性感染症は注意すべき合併症であり、分娩翌日に血液検査が実施されることが多い。一方で、分娩翌日の母体白血球数と母体合併症発生との関連について分析した先行研究は乏しい。本研究では、分娩翌日の母体白血球数とその後の母体合併症発生と関連しているかを検討した。【方法】本研究はDPC(Diagnosis Procedure Combination)データベースを用いた後方視的コホート研究で、2008年4月から2020年11月までに器械分娩で出産し、かつ検査データを含む患者を対象とした。分娩翌日の母体白血球数の記述統計を示すとともに、多変数制限付き3次スプライン(Restricted cubic spline)を用いた回帰分析により白血球数の連続的な変化と主要アウトカム(入院中の産道裂傷への追加縫合・デブリドマンまたは集中治療室への入室)の関連を評価した。共変量として年齢、body mass index、入院年、医療機関規模、分娩時の妊娠週数、分娩方法(吸引分娩、鉗子分娩)、母体合併症(糖尿病、妊娠糖尿病、子宮内感染、遷延分娩、微弱陣痛、分娩時重度会陰裂傷)、分娩当日の抗生剤点滴投与を調整した。【成績】対象患者は485名で、うち94%は吸引分娩だった。分娩翌日の母体白血球数の中央値は15170(四分位範囲12610-18300)/mLで、主要アウトカムの発生割合は10.5%だった。回帰分析の結果、母体白血球数は7000-25000/mLの範囲で主要アウトカムの発生との間に統計学的に有意な関連は認められなかった。【結論】器械分娩翌日の母体白血球数は多くの患者で平常時より高値だったが、その後の母体合併症発生との間に有意な関連は認められなかった。

P-114-2 妊婦における周期性四肢運動についてFMAM recorderによる解析

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【目的】周期性四肢運動(periodic limb movements: PLM)は、睡眠中に主に下肢が規則的な周期で出現する不随意運動のことをいい、周期性四肢運動障害や、むずむず脚症候群と関連が指摘されている。妊婦はPLMが多いと推測されているが、実態は明らかではない。胎動計(Fetal movement acceleration measurement recorder: FMAM recorder)は母体動を検出するために大腿部にもセンサーを付けている為、母体のPLMも検出することができる。今回は妊婦のPLMについて報告する。【方法】当院で妊婦健診、分娩を行った妊婦324人を対象に行った。妊娠28~39週までに週1回程度、妊婦自身が自宅でFMAM recorderを装着してもらった。4時間以上計測できたデータを使用し、解析を行なった。これを元に①PLMの出現率②PLMが出現した人としなかった人の2群に分けて、母体年齢、BMI、初産経産、貧血の有無、睡眠時間、中途覚醒回数、胎動占有割合、分娩時期、出生時体重を比較した。③5回以上の記録が可能であった人を対象として、毎回PLMが出現した人と、しなかった人の2群に分けて、②と同じ項目を比較検討した。【成績】解析可能データ数は1,736回、合計約11,400時間であった。①PLMの出現を認めた人は236人(72.8%)であった。②全ての項目で2群間に有意差を認めなかった。③PLM出現群はBMIが高く(P<0.05)、分娩時期が早い(P=0.002)が、その他は有意差を認めなかった。【結論】PLMの出現頻度は一般的に10%程度といわれ、妊婦では明らかに多かった。また、機序は不明だが、PLMが多く出現する妊婦はBMIが高く、分娩時期が早い傾向を示した。しかし、一般妊婦において、病的な意味は少なく、多くは生理的な現象と思われた。

P-114-3 経陰分娩後、産褥10日目に診断した遅発性の外陰血腫の1例

千船病院

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【緒言】経陰分娩後に外陰部や陰壁に血腫を形成することがあるが、分娩後数時間で発生することが多い。今回は経陰分娩で経過が問題無く退院後、産褥10日目に打撲などの誘因無く外陰部に血腫を生じた、遅発性の産褥外陰血腫の症例を経験したので報告する。【症例】34歳、2妊1産の女性で、妊娠40週2日に硬膜外麻酔併用下に経陰分娩した。分娩第1期は8時間32分、第2期は2時間5分で、出生児は女兒、体重は3870gであった。吸収分娩や会陰切開は実施しなかった。6時方向の陰壁裂傷、6時方向の2度会陰裂傷があり、合成吸収糸で縫合した。産褥経過は良好で、退院前の内診でも明らかな異常は認めず、産褥4日目に退院した。産褥9日目より外陰部の腫脹と鎮痛薬でも改善しない疼痛を認め、産褥10日目に受診した。視診・触診で左大陰唇・左側壁の陰壁に腫脹を認め、外陰部からの超音波検査で5cm大の外陰血腫と診断した。造影CTでも左大陰唇に血腫を認め、血腫の周囲に仮性動脈瘤を疑う結節状の濃染像を認めた。緊急手術が必要と判断し、同日外陰血腫除去術を実施した。術後経過は良好で、術後2日目に退院した。その後血腫の再発は無かった。【結論】分娩時に生じた外陰部の仮性動脈瘤の破裂に伴うものと推定される遅発性の外陰血腫を経験した。退院後に外陰部の強い疼痛を自覚した場合、会陰縫合部の疼痛以外に、遅発性に生じる外陰血腫も念頭に置く必要がある。

P-114-4 血漿交換を要する急性腎障害を呈した産褥HELLP症候群の一例—非典型溶血性尿毒症症候群(aHUS)との鑑別を中心に—

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【緒言】HELLP症候群の7-15%に急性腎障害(AKI)が合併するが、産褥期発症では非定型溶血性尿毒症症候群(aHUS)との鑑別が問題となる。【症例】33歳G1P0。前医で妊娠41週1日妊娠高血圧腎症の診断で緊急帝王切開術を施行後、弛緩出血・出血性ショックのため出産後5時間で当院へ母体搬送となった。入院時の血液検査でHELLP症候群と診断、輸血および子宮動脈塞栓術を行い全身状態は安定した。分娩後約15時間で乏尿、24時間で無尿となった。血性LD 3083 U/L, Cr 2.11 mg/dLへ上昇し、持続的血液濾過透析(CHDF)を開始したが、Crは2.5mg/dLとさらに増悪した。ASTは212 U/L, ASTは49 U/Lを上限とし推移した。ADAMTS13活性は50%でTTPは否定的であり、腎炎血清マーカーは陰性であった。aHUSの可能性を念頭に、産後2日目から血漿交換(PF)を開始した。その後Cr値は3.46 g/dLまで悪化した。計4回PFの後、分娩後6日目より自尿を認め、8日目CHDFを離脱した。産後2週間で施行した腎生検では、局所的な急性尿管管障害を認めたが、毛細血管内の強い微小血栓や免疫グロブリン・補体の沈着を認めなかった。分娩後2か月でCr 0.99 mg/dLと腎機能は軽快傾向である。【考察】aHUSとHELLP症候群は、ともに妊娠関連性微小血管症(TMA)に含有される病態である。本症例は、HELLP症候群による二次性TMAに合併したAKIとして説明できる。一方、肝機能の推移と乖離した急激な腎機能障害は一次性TMAであるaHUSとも矛盾せず、早期のPF導入により、慢性腎臓病への移行が回避された可能性も考えられる。妊娠関連TMAの鑑別は難しいが、AKIに際しては急性期の適切な治療介入が予後に直結することから、症例の集積による詳細な検討が必要である。

P-114-5 当地域における12年間の墜落分娩についての検討

名寄市立総合病院

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【目的】当地域は過疎化のため高度に分娩集約化が進んでおり、秋田県全域とほぼ同等の面積の医療圏に分娩可能施設は2箇所のみである。今後の妊娠分娩管理について改善点を模索するために検討を実施した。【方法】2010年1月から2021年9月までに当院で経験した墜落分娩について、保存されている診療録から後方視的に検討した。【成績】総分娩数は4558例、墜落分娩数は14例で発生率は0.31%であった。母体年齢の中央値は30.5±4.1歳であった。13例が経産婦で、1例は初産婦だった。分娩週数の中央値は39週3日±2.5日、早産は1例であった。母体の居住地域については、市内が5例(35.7%)、当院から50km以内の近郊地域3例(21.4%)、50km以上の遠方地域6例(42.9%)であった。分娩場所は自家用車内5例(35.7%)、自宅5例(35.7%)が最多であった。診療録の保存されていた母体9例のうち、妊娠合併症で入院加療を伴う切迫早産は1例であった。分娩産褥期合併症では1-2度会陰裂傷5例(55.6%)、頸管裂傷2例(22.2%)、1000g以上の産後過多出血1例(11.1%)を認めた。また新生児14例に関しては、多血症6例(42.9%)、呼吸障害6例(42.9%)、低体温症4例(28.5%)の発症頻度が高かった。【結論】遠方在住の経産婦の自家用車内の墜落分娩症例が多かった。分娩集約化が進む海外の既報と比較して矛盾せず、集約化による医療圏の拡大が墜落分娩の発症原因の1つと考えた。墜落分娩に初期対応できるよう、救急救命士や患者本人・家族に対して適切な情報提供と教育を行うことが母児の予後を改善するため重要である。

P-114-6 第3度、第4度会陰裂傷の褥婦に対して、3-Dimension 経会陰超音波を用いた創部修復までの評価

帝京大病院

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【目的】分娩時に肛門括約筋の断裂を伴う第3~4度会陰裂傷は全経産分娩のおよそ0.7~8%で発生すると言われている。会陰裂傷は産後便秘発生原因の1つとされており、分娩直後の適切な裂傷縫合を行うことで便秘の発生を少なくできる可能性がある。しかし、その修復の成否は自覚症状によって判定されることが殆どである。近年、3-Dimension (以下3D) 経会陰超音波を使用した報告が散見されるようになったが、まだ症例数が少なく一般的な検査になっていない。今回、2020年11月~2021年4月の期間において当院で経産分娩を行い、分娩直後に産科医が第3~4度会陰裂傷と診断した8例について、3D 経会陰超音波で内外肛門括約筋の観察を産後3か月まで行い、創部の修復の評価を行った。【結果】8例の内訳は自然分娩6例(いずれも第3度会陰裂傷)、鉗子分娩2例(いずれも第4度会陰裂傷)であった。第4度会陰裂傷例はいずれも Albert-Lembert 縫合で修復を行った。1か月健診では第3度会陰裂傷6例中5例(83.3%)、第4度会陰裂傷2例中2例(100%)の修復を確認した。残る1例に関しても産後3か月で修復されていることを確認できた。【結論】第3~4度会陰裂傷の修復は産後1か月の時点では不十分である症例が存在した。修復が不十分な症例に関しても、産後1か月健診以降に創部修復を確認できる可能性がある。しかし創部修復を確認出来た症例の中には括約筋が非薄している症例も認められた。産後1か月健診の間診では便秘などの症状を認めた症例は認めなかったが、創部の修復が不十分であると判断した症例に関しては、産後1か月健診以降も長期的な経過を観察することが望ましい。

P-114-7 母体救急搬送時におけるIoT 胎児モニターの有用性に関する検討

岩手県立大船渡病院

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【目的】母体救急搬送時におけるIoT (Internet of things) 胎児モニターの有用性を検討すること。【方法】2018年8月から2021年8月までに、連携病院から地域周産期母子医療センターである当院に救急搬送された妊娠33週から41週の妊婦47例を対象に、IoT 胎児モニターの超音波ドップラーセンサーを装着後、タブレットデバイスでの波形受信状況、胎児心拍数陣痛波形の判読、および搬送後の臨床転帰について評価した。【成績】救急車内で助産師による超音波ドップラーセンサーの装着により、全例で胎児心拍数および子宮収縮圧を計測シグナラ化することができ、機器等のトラブルなく移動している救急車内から胎児心拍数および子宮収縮圧波形データをリアルタイムに送信できた。受信した胎児心拍数陣痛波形は47例中41例において胎児心拍数波形レベル分類による判定が可能であった。判定困難な症例はすべて陣痛発来症例であった。搬送された全47例すべてにおいて、母児ともに予後は良好であったが、搬送中の胎児心拍数波形レベル分類が良好例と判定困難例それぞれ1例で搬送先において胎児因子による緊急帝王切開となった。また分娩停止症例の搬送中に偶然胎児機能不全のモニターリング所見を示した例が1例あった。【結論】今回の検討において、移動中の救急車内から機器トラブルもなく全例で胎児心拍数陣痛波形を送受信することができた。IoT 胎児モニターを装着することで、母体救急搬送中も連続した胎児心拍数陣痛波形の監視が可能となり、搬送先医療機関での治療方針決定に有用であるが、特に胎児機能不全例において胎児の状態が搬送中または搬送後に予期せぬ変化が生じうることには留意すべきである。

P-115-1 前回帝王切開創部非薄化症例に対する帝王切開時トリミング手術の試み

滋賀医大

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【目的】帝王切開時に児が透見するほど高度な非薄化を呈している症例を時に経験する。非薄化した部位を切除しても非薄化部位同士を縫合することは困難である。そこで、非薄化した部位を切除し、再建するトリミング術を考案し実践したのでその有効性を検討した。【方法】術式は膀胱子宮窩腹膜を開放し、子宮筋層にメスを入れる前に膀胱を可及的に子宮から剝離して子宮頸部側へ展開し、非薄化部分をビオクタンでトリミング予定線をマーキングする。次に、非薄化中央部をメスにて切開する。児娩出後に膜状筋層を切除し、子宮筋層を Gambee 縫合と単結紮の2層に縫合した。症例は、妊娠前に撮像した骨盤MRIで子宮筋層の高度非薄化が指摘されていた2症例。帝王切開時にトリミング術を施行した6か月経過した後に再びMRIを撮像し、術前のMRIと比較した。評価は残存子宮筋層厚(residual myometrial thickness; RMT)の変化とした。【成績】症例1は31歳2胎1産。RMTは術前1.5mmであったが術後8.9mmとなった。妊娠前には月経終了後に茶色帯下を断続的に認め帝王切開癒着症候群と診断されていたが、産後に症状は消失した。症例2は37歳2胎1産。術前に癒着部に嚢胞性病変を認める帝王切開癒着症候群の症例であった。帝王切開時には非薄化した筋層の上に膀胱が吊り上がり癒着している所見を呈していた。RMTは術前1.5mmであったが術後5.5mmとなった。【結論】症例数は少ないが、帝王切開時に我々が考案したトリミング手術を行うことで帝王切開癒着症候群からの離脱が可能となると考えられた。

P-115-2 帝王切開術後創部の肥厚性瘢痕化に対する、ハイドロコロイドドレッシング材の予防的効果についての研究—前向きコホート試験—

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【目的】ハイドロコロイドドレッシング材の貼付による、帝王切開術後創部の肥厚性瘢痕化に対する予防的効果を明らかにする【方法】当院で帝王切開術を施行された患者に対してインフォームドコンセントをとり、ランダムに介入群及び非介入群に割り付けを行った。介入群は術後7～8日目に創部にハイドロコロイドドレッシング材の貼付を開始、半年間継続する。非介入群は何も貼付せずに経過観察した。各群において、術後6か月と12か月の時点で創部の状態を評価した。評価方法は、The Patient and Observer Scar Assessment Scale v.2.0(POSAS)、Japan Scar Workshop Scar Scale 2015(JSS)、modified Vancouver Scar Scale (mVSS)、Patient Reported Outcomes questionnaire (PRO)を用いた。【成績】2019年5月～2020年2月において、当院で帝王切開した患者は135人であり、その内、強いアレルギーや通院困難などの除外症例は33人、研究に同意されなかった患者は40人で、残りの同意が得られた62人をランダムに割り付けた。1年後までフォローを完遂できた症例は、介入群では31人中23人であり、非介入群では31人中24人であった。1年後まで完遂できたこの47人に対して統計学的に検討を行った。その結果、術後6か月の時点において、いずれの評価方法においても介入群の方が有意に瘢痕スコア低値であった。術後12か月の時点でも、同様に介入群が優位に低値を示した。術後12か月において、肥厚性瘢痕の性質とされるJSS:6点～15点となるリスク比は、0.177 (95%CI: 0.041-0.76)であった。【結論】帝王切開術後、ハイドロコロイドドレッシング材を創部に貼付することにより、肥厚性瘢痕のリスクを低減することができる。

P-115-3 多発子宮筋腫による妊娠後屈子宮嵌頓症に対し術中超音波検査を行い安全に帝王切開術を実施できた1例

千船病院

中村達矢、城 道久、小川史子、大木規義、安田立子、岡田十三、吉田茂樹

【緒言】妊娠後屈子宮嵌頓症では、子宮筋腫合併などにより妊娠子宮が後屈したまま発育し、骨盤内に嵌頓した状態となる。本疾患の症例では経陰分娩は困難で、陣痛発来により子宮破裂の可能性がある。また、子宮体部の後屈により子宮頸部が頭側に伸展しているため、術前に診断されず帝王切開術を行うと子宮頸管損傷や陰切開などの様々な合併症が生じる。今回我々は、多発子宮筋腫による妊娠後屈子宮嵌頓症に対し、術中超音波検査を行い安全に帝王切開術を実施できた1例を経験した。【症例】39歳、1妊0産。妊娠初期より経陰超音波検査で多発子宮筋腫を認め、子宮体部後屈を認めていた。妊娠31週にMRI検査を実施し、体部が前傾後屈した妊娠子宮に75mm大までの筋腫を複数認め、頸管の伸展が認められた。子宮体部は骨盤底側に偏位し、それに伴って内子宮口は頭側へ恥骨上縁から10cm偏位していた。腔鏡診では子宮頸部の偏位により子宮陰部を確認できなかった。妊娠後屈子宮嵌頓症と診断し、妊娠37週に選択的帝王切開術を行った。下腹部正中切開し、術中超音波検査で確実に子宮体部を切開できる位置を確認した上で横切開を加え、児を娩出した。児は女児、3400g、Apgar Score5/9であった。術後経過は順調であった。【結論】妊娠初期から超音波検査で強い子宮後屈を認める多発子宮筋腫合併妊娠の場合、妊娠後屈子宮嵌頓症を念頭におくことが重要であると考えられた。術中超音波検査を行うことで、安全に帝王切開術を行うことができた。

P-115-4 頭痛を伴わず明識困難状態に陥った脊椎麻酔後脳脊髄液漏出症—症例報告

自治医大附属病院

藤本揚子

【緒言】脊椎麻酔下の帝王切開術後に脳脊髄液漏出症を生じた場合、起立性の頭痛（硬膜穿刺後頭痛）を示すことが多いが、意識障害に至ることは非常に稀である。今回、術後の起立直後に頭痛を伴わず明識困難状態に陥った脳脊髄液漏出症症例を提示する。【症例】34歳、2妊1産。自然妊娠。妊娠32週3日、辺縁前置胎盤、既往帝王切開術後妊娠の管理目的に当科へ入院した。子宮側壁に付着する胎盤の一部が既往帝王切開術創部付近に付着しており、癒着胎盤の可能性が否定できなかったため、妊娠36週2日、脊椎麻酔下(25G穿刺針)に選択的帝王切開術を行った。児は2535gの男児でApgar-9であった。癒着胎盤は認めず出血量は500gであった。術後1日目、初回歩行直後、頭痛は訴えなかったが、めまいを訴え意識混濁状態に陥った。自発性が低下し軽度構語障害も認めしたが、認知機能は保たれ明識困難状態と判断した(JCSI-I)。血圧98/52mmHg、脈拍56/分、SpO₂98%とバイタルに変化はなかった。神経学的所見を認めず、CT検査やMRI検査でも脳血管疾患や頭蓋内占拠病変を認めず、MR angiography検査でも動脈奇形や血栓も認めなかった。臥位安静と補液で経過を診ていたところ、7時間後、明識困難状態から意識清明に回復した。脊椎麻酔後、初回歩行直後の発症で、安静と補液とで7時間後に意識が回復していることから、脊椎麻酔後の脳脊髄液漏出症と診断した。術後7日目、神経学的後遺症もなく退院した。【結語】術後の起立後に頭痛を伴わないが意識障害を認める場合、本症例のように脳脊髄液漏出症が原因である可能性がある。脊椎麻酔後の起立後に意識障害を認めた場合、脳脊髄液漏出症を鑑別診断に含めた精査が必要である。

P-115-5 選択的帝王切開の施行時期について分娩時状況だけでなく新生児発育を考慮した上で38週以降を推奨するための検討

厚生中央病院

中村 華, 川村 良, 坂本絵璃子, 中島怜美, 里井映利, 大垣洋子, 松田美保, 神田理恵子, 池田俊一

【目的】当院の選択的帝王切開の施行時期は37週以降であるが、本邦では38週以降が増加している。施設の体制や水準により総合的に判断しやむを得ないと判断し決定した37週群と、38週群の分娩時状況と其後の新生児発育について比較し施行時期を検討した。【方法】2012年9月から2020年12月に当院で施行した選択的帝王切開術397例を対象とした。37週群141例(35.5%)と38週群235例(59.2%)について出生時体重、新生児搬送例、アプガールスコア(APS)、臍帯血pH、出生後体重(3, 5日目)、体重増加(3日目から5日目)を比較した。当院の医師構成は5名の指導医(研究開始時平均約54歳)と2から4名の専攻医および更新前の専攻医である。【成績】37週群と38週群の出生時体重は $2886 \pm 291\text{g}$ と $2934 \pm 290\text{g}$ ($P=0.120$)、新生児搬送例は9例(6.4%)と12例(5.1%)($P=0.590$)、APS1分は 8.7 ± 0.6 と 8.4 ± 0.6 ($P<0.001$)、APS5分は 9.4 ± 0.5 と 9.3 ± 0.5 ($P=0.039$)、臍帯血pHは 7.302 ± 0.046 と 7.291 ± 0.048 ($P=0.024$)で、必ずしも38週群が37週群より優位ではなく、逆に37週群に有意な差が複数に認められた。37週群と38週群の新生児体重の3日目は $2776 \pm 272\text{g}$ と $2837 \pm 285\text{g}$ ($P=0.046$)、5日目は $2802 \pm 268\text{g}$ と $2880 \pm 284\text{g}$ ($P=0.011$)、3日目から5日目の体重増加は $27 \pm 45\text{g}$ と $43 \pm 48\text{g}$ ($P=0.002$)で、37週群よりも38週群で明らかに有意な増加が認められた。【結論】経験豊かな医師の判断で決定された37週群は、分娩時に38週群より劣る状況は全くなかった。しかしながら、其後の新生児発育には38週群と比較して明らかな差が認められた。この結果から新生児の分娩時状況に問題ないと予想できても、37週での選択的帝王切開術は極力避けるべきであることが示唆され、38週以降の時期が推奨された。

P-115-6 帝王切開後の後腹膜血腫により、尿路閉塞をきたした1例

新潟県立新発田病院

八幡夏美, 山田大輔, 横尾朋和, 浅野堅策

帝王切開後の子宮動脈損傷により後腹膜血腫を形成し、尿路閉塞をきたした症例を経験したので報告する。症例は、35歳、3妊2産。前医にて、妊娠38週4日に既往帝王切開術を適応として選択的帝王切開術を施行され、3270gの男児を出産した。術中出血は314g(羊水込み)であった。術後3時間経過してから下腹部痛が増悪し、冷や汗、血圧低下、頰脈が出現した。経腹超音波検査にて左下腹部に血腫を認め、当院へ救急搬送された。搬送時にはバイタルサインは安定していたが、激しい疼痛が持続し、造影CTにて両側水腎症と13cm大の後腹膜血腫および血腫内部に左子宮動脈からの造影剤の血管外漏出像を認めた。緊急経カテーテル的動脈塞栓術(transcatheter arterial embolization: TAE)により止血後、再開腹術を行い、後腹膜血腫を除去したところ、スムーズな排尿が得られた。左子宮動脈からの出血は帝王切開創部左端付近であったことから、手術時の損傷により後腹膜血腫をきたし、それにより外因性に尿路閉塞をきたしたと考えられた。帝王切開後に後腹膜血腫を合併することは稀であるが、さらに、それにより尿路閉塞をきたした症例を経験したので、若干の文献的な考察を踏まえて報告する。

P-115-7 帝王切開時のShock Index と分娩時出血量についての検討

名古屋大附属病院

水谷栄介, 牛田貴文, 中村紀友喜, 飯谷友佳子, 今井健史, 小林知子, 小谷友美, 梶山広明

【目的】Shock Index (1分間の心拍数÷収縮期血圧mmHg:以下SI)は、分娩時異常出血(PPH)における出血量の推測や「産科危機的出血」への対応時に用いられ、産科救急では重要な指標の一つである。これまで、経陰分娩時のShock Indexの検討は比較的報告があるものの、帝王切開時のSI値の推移、またSI値と実際の出血量との関連についてはあまり検討されていない。【方法】2018~2020年に当院で帝王切開術を行った正期産症例を対象とし、緊急帝王切開、全身麻酔、子宮摘出、双胎、羊水過多、胎児奇形、妊娠高血圧症候群などの症例を除外した。このうち羊水を含む術中出血が500mL未満(A群:n=34)、500~999mL(B群:n=71)、1000~1499mL(C群:n=24)、1500mL以上(D群:n=19)に分類し、麻酔記録から入室時、執刀直前、胎児娩出直後、胎児娩出後(5分、10分、15分、20分、以降10分毎)、手術終了時のSIを評価した。【成績】A・B群ではSIは児娩出から15分で最大となり、その後徐々に減少し手術終了時には入室時とほぼ同等まで戻った。C・D群では児娩出から10分で最大となるものの、A・B群とはほぼ同等の推移をたどった。SIの最大値は、A群 0.85 ± 0.16 、B群 0.91 ± 0.11 、C群 0.91 ± 0.16 、D群 0.87 ± 0.15 であり、SIの最大値と出血量との相関は低かった($R^2=0.062$)。SIの最大値が1以上となった症例はA~D群でそれぞれ9、29、13、6例で、SI ≥ 1 における出血量1500mL以上の感度、特異度はそれぞれ0.11、0.86であった。【結論】本研究により帝王切開時のSIの推移が初めて明らかになった。また、予想外にも帝王切開時のSIは出血量との相関は低く、出血量1500mL以上でもSI ≥ 1 になるとは限らないため、帝王切開時のSIの解釈には注意を要する。

P-115-8 当院における子宮筋腫核出術と帝王切開時術中出血量の検討

松山赤十字病院

矢野晶子, 井上奈美, 駒水達哉, 吉里美慧, 高杉篤志, 信田絢美, 青石優子, 梶原涼子, 栗原秀一, 本田直利, 横山幹文

【目的】当院で施行された子宮筋腫核出 (LM) 後妊娠の帝王切開時の術中出血量に及ぼす因子について後方視的に検討することを目的とした。【方法】2016年4月1日から2021年3月31日までのLM後妊娠に対する初回帝王切開症例56例(以下LM群)と同期間に施行した2回目の帝王切開症例232例(以下CS群)を検討対象とした。除外症例は多胎妊娠, 前置胎盤, 低置胎盤, LM以外の子宮手術後とした。検討項目はLM群とCS群における年齢, 妊娠回数, 分娩回数, 術中出血量(羊水量を含む)とした。またLM群内の出血量比較としてLM時の①筋腫総重量②筋腫数③筋腫の最大径④筋腫径の合計⑤LM施行から帝王切開施行までの年数⑥核出筋腫と胎盤位置の相関関係の検討も行った。統計的解析はMann-Whitney-U検定を用い, p値が0.05以下を有意とした。【成績】LM群とCS群における検討項目の中央値(最小値-最大値)は年齢が37歳(28-46), 33歳(19-46), 妊娠回数が1回(1-5), 2回(2-7), 分娩回数が0回(0-2), 1回(1-4), 術中出血量がLM群で963mL(220-3139), CS群で775.5mL(194-3066)であった。年齢, 妊娠回数, 分娩回数, 術中出血量のp値は0.01未満となり統計学的有意差を認めた。LM群内比較では出血量1000ml以上の症例(n=25)の内, ①筋腫総重量150g以上の群の術中出血量は1509ml(1085-2801)と150g以下の群は1300ml(1004-1557)となり有意差は認めなかった(p値0.0556)が, 筋腫総重量が150g以上の群で術中出血量が多い傾向があった。上記検討項目②-⑥に有意差を認めなかった。【結論】LM群では術中出血量に有意に多くなることが示され, 影響する因子は核出筋腫総重量150g以上である可能性が示唆された。

P-115-9 帝王切開後のX線検査で異常陰影を認めた3症例の検討

順天堂大練馬病院

前田智佳子, 丸山洋二郎, 寺尾純奈, 田中元基, 九鬼紗葵, 瀬尾瑛美, 長澤さや, 伊藤陽介, 笠原華子, 濱村憲佑, 松岡正造, 萩島大貴

【目的】帝王切開後の異物検索目的のX線検査は広く行われているが, 異常陰影が術中遺残かどうかの鑑別を要する場合もある。今回, 術後X線検査で異常陰影を認めた3症例を比較, 検討した。【症例】症例1: 29歳, 39週5日, 分娩停止で緊急帝王切開を実施した。皮下縫合時, 針先端の欠損に気づき, 術後X線検査で恥骨結合より5cm頭側に約2cmの異常陰影を認めた。単純CT検査では針先端と形状の一致する高吸収域を認めた。同部位を抜糸し, 腹直筋正中に針の先端を認めたため除去して手術終了とした。症例2: 41歳, 41週5日, 分娩停止で緊急帝王切開を実施した。術中出血性DICとなり止血に難渋した。術後X線検査で腹腔内に異常陰影を認め, 形状からタオルガーゼが疑われたため再開腹を実施し, ガーゼを除去して手術終了とした。症例3: 32歳, 35週0日, 切迫子宮破裂で緊急帝王切開を実施した。術後X線検査で右付属器領域に約1cmの異常陰影を認めたが, 術中器具と形状は異なっていた。単純CT検査では同領域に約1cmの高吸収域を認めた。吸収値が骨皮質の約5倍で生体組織ではないと考え, 術中器具を単純CTで撮影し比較したが, 吸収値は異なっていた。再度の問診で卵管造影既往が判明し, 当時の画像で同部位に造影剤の貯留を認めた。造影剤であれば高い吸収値にも矛盾しないため, 再開腹は実施しなかった。【結論】近年, 遺残防止のリスクマネジメントの観点から, 手術室退室前にX線検査を行うことが多い。異常陰影を認めた場合, 術中遺残を疑うと共に器械カウントや破損, 形状, CTでの吸収値, 造影剤使用の既往などを確認し, 再開腹の必要性を検討する必要がある。

P-115-10 一次施設における選択的帝王切開でのERAS(Enhanced Recovery After Surgery)に関する後方視的検討

立花レディースクリニック

立花康成, 立花 崇

【目的】近年, 帝王切開の管理方法は術後早期回復を目的に, 医的根拠に基づく周術期管理方法であるERAS(Enhanced Recovery After Surgery)に沿った術後管理が多くの施設で導入されている。しかし, 一次施設での帝王切開の管理方法は, 術前後の長期絶食, 術後数日間の安静など慣習に基づいた周術期管理方法を行なっている施設も少なくない。今回, ERASに準じた周術期管理が一次施設においても安全に行えるかどうかを目的に後方視的検討を行った。【方法】当クリニックで予定帝王切開術を行なった2019年6月~2020年4月(ERAS導入前)と2020年6月~2021年5月(ERAS導入後)の各々29例と42例を後方視的に比較検討した。評価項目として, 両群間での術後初回排ガス時期, 術後初回排便時期, 術後麻痺性腸閉塞発症の有無とした。【成績】術後初回排ガス時期はERAS導入前群(pre-ERAS群): 1.86 ± 0.74 日, ERAS導入後群(ERAS群): 1.19 ± 0.45 日($p=0.835$), 術後初回排便時期はpre-ERAS群: 3.21 ± 0.86 日, ERAS群: 2.81 ± 1.15 日($p=0.110$)で共に有意差を認めなかった。術後麻痺性イレウス発症はpre-ERAS群: 0/29例, ERAS群: 0/42例で共に認めず, またその他の有害事象も認めなかった。【結論】ERASに準じた周術期管理は一次施設における帝王切開の周術期管理に対しても安全に行える。

P-116-1 切迫流・早産例に対する単繊維合成吸収糸二重縫縮による治療的頸管縫縮術の検討

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【目的】妊娠21週-23週間に頸管短縮を認めた切迫流・早産例に対する単繊維合成吸収糸二重縫縮による治療的頸管縫縮術の治療成績を検討する。【方法】2016年5月～2020年6月に当院で管理した単胎妊娠のうち妊娠21週0日-23週6日に頸管短縮(頸管長 \leq 25mm)を認めた118例を対象とし後方視的に検討した。院外出生, 入院時に絨毛膜羊膜, CAOS, 前期破水, 陣痛発来しているもの, 胎胞が腔管内に充満しているもの, 頸管縫縮術が前医で施行されているもの, 胎児死亡, 死産, 常位胎盤早期剥離となった症例は除外した。縫縮術はマクドナルド式で単繊維合成吸収糸の二重縫縮で行った。縫縮術を行なった群をA群, 行わなかった群をB群に分け, 妊娠継続期間と出生時体重を主要評価項目とし, 妊娠転機を比較した。【成績】A群は9例, B群は42例。両群で母体背景に差はなかった。A群の縫縮術施行週数は, 23週4日(21週4日-24週0日)。入院日から分娩までの妊娠継続期間は, それぞれ中央値が14.3週(9-18)/4.3週(0-15.4)であり($P<0.01$), 出生時体重はそれぞれ中央値2,416g(1,764-3,880)/935g(481-2,934)であった($P<0.01$)。妊娠継続期間, 出生体重ともにA群で有意に高かった。全例で縫縮術に伴う合併症はなかった。【結論】切迫流・早産例を適応とした頸管縫縮術は妊娠継続期間, 出生体重について有用である可能性が示唆された。

P-116-2 当科における治療的子宮頸管縫縮術の治療成績

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【目的】妊娠経過中に子宮頸管短縮を認めた場合, 治療的子宮頸管縫縮術の施行が有用であると報告されているが, 適応となる妊娠週数に関しては一致した見解は得られていない。当科では妊娠25週前後までの頸管短縮例に手術治療を行っている。当科において過去10年間に施行した治療的頸管縫縮術に対してその治療成績を検討した。【方法】当科にて, 2011年1月から2021年2月までに治療的子宮頸管縫縮術を施行した全61例を対象とした。妊娠16週から27週未満に, 頸管長短縮や頸管開大を認め頸管無力症と診断され, 治療的頸管短縮術を施行した症例の周産期予後を検討した。【成績】全61例の平均手術施行週数は21週3日(16週1日から26週5日)であり, 術後他院へ搬送・転院となった症例が7例, 死産が2例, 当院にて生児を得た症例は52例であるが1例では早期新生児死亡となった。当院で分娩に至った症例のうち他院からの緊急母体搬送例が23例, 胎胞脱出例は16例であった。手術方法はシロッカー法が40例, マクドナルド法が14例であった。生児を得た52例において, 分娩週数は36週以降が33例(63.4%), 30から35週が9例(17.3%), 30週未満が10例(33.3%)であった。術後の妊娠継続期間は30から35週までの分娩に至った症例では平均14週2日間, 30週未満での分娩に至った症例では平均3週7日間であった。胎胞脱出例では平均9週3日間の妊娠期間延長を得た。【結論】治療的子宮頸管縫縮術の施行により妊娠期間の延長が期待され, 限られた医療環境下ではその施行が考慮される。

P-116-3 品胎妊娠に対する予防的頸管縫縮術後に大量出血を認め, 仮性動脈瘤が疑われた1例

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頸管縫縮術の稀な合併症の一つに仮性動脈瘤がある。今回我々は, 品胎妊娠に対する予防的頸管縫縮術後に大量出血を認め, 仮性動脈瘤形成が疑われた1例を経験したので報告する。症例は31歳3妊1産。流産2回。ICSI後の妊娠, 一絨毛膜三羊膜品胎として初期より当院で妊婦健診を行った。妊娠13週3日に予防的頸管縫縮術(Shirodkar法)を施行し, 経過良好で術後6日に退院, 外来で定期健診を行った。妊娠26週3日より管理入院を開始するため来院した際に, 突然の性器出血を認めた。診察時は止血しており経過観察としたが, 同日に再度大量出血があり, 再度診察を行うと, 縫縮糸の近傍に31mm大の動脈性の血流を有する瘤を認めた。仮性動脈瘤形成からの出血を疑った。腔部圧迫にて止血が得られたが, その際の出血量は約2000mlでRBC12単位の輸血を要した。その後も間欠的に出血を認めたが少量であったため児の未熟性を考慮し妊娠継続とした。仮性動脈瘤は増大なく経過していたが, 妊娠30週4日に再度大量の出血があり, 圧迫止血困難のため, 同日緊急帝王切開を行った。児は第1子, 男児, 1623g, ApgarScore1分値/5分値:1/9, UmApH=7.358, 第2子, 男児, 1546g, 8/9, 7.369, 第3子, 男児, 1506g, 5/3, 7.370であった。胎内では羊水量差を認めなかったが, 分娩後に第2子が受血児, 第3子が供血児としてTTTSの診断加療が行われた。母体術後経過は良好で, 退院時・1か月健診時には仮性動脈瘤は消失していた。頸管縫縮術の稀な合併症である仮性動脈瘤を疑う症例を経験した。同部位からの大量出血・止血困難のため, 妊娠終了を余儀なくされた。頸管縫縮術後の大量出血時には仮性動脈瘤の形成の可能性を考慮する必要がある。

P-116-4 経腹的子宮頸管縫縮術 (transabdominal cervical cerclage : TAC) を行い、出産後に再度妊娠し2回目のTACを要した1例

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【緒言】子宮頸管縫縮術は頸管無力症や子宮頸管短縮症例に対し、流・早産の予防目的で施行される。経腹的子宮頸管縫縮術 (transabdominal cervical cerclage : TAC) は経陰的子宮頸管縫縮 (transvaginal cervical cerclage : TVC) が困難な症例に考慮される術式であり、これまで我々もTACを4例経験し、その有用性を報告してきた。このうち今回は円錐切除術後の子宮腔部短縮症例に対し計画的TACを施行し、正期産で分娩後に再度妊娠し、2回目のTACを要した1例を経験したので報告する。【症例】症例は、26歳、3妊2産。19歳の時に帝王切開で第1子を分娩後、21歳の時にCIN3に対し円錐切除術を施行された。24歳で第2子を妊娠して当院を受診したが、子宮腔部は高度に短縮していた。妊娠13週で子宮頸管長は20mmであり、TVCが困難なため直ちにTACを施行した。術後妊娠経過は良好で、妊娠37週0日で選択的帝王切開術により2368gの男児を出産し、再度の妊娠希望はなくTAC糸を抜糸した。その後離婚し、新たな配偶者との第3子を妊娠し当院を再受診した。前回と同様に妊娠13週でTACを施行後、慎重に妊娠経過観察中である。【考察】TACはTVCより明らかに手技が煩雑で、TAC施行時と帝王切開の際に2度の手術が必要となる点で母体への侵襲は大きい。また症例により次回の妊娠について考慮する必要もあり、今回のように再度TACを行う場合は非常に患者負担も大きい。一般に再度の妊娠を強く希望する場合は、縫合糸を残存させた状態で次回の妊娠を考慮する。今後も慎重にその適応を判断した上でTACを施行し、少しでも良好な周産期予後を得られるよう努力していきたい。

P-116-5 子宮圧迫縫合術 (Uterine compression suture : UCS) 後のAsherman症候群に対して外来子宮鏡手術が有効であった一例

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【緒言】Asherman症候群の主たる原因は子宮腔内操作である。報告は少ないが、弛緩出血に対して行うUCS後にも発症しうる。今回我々は、UCSを施行後、Asherman症候群と診断した症例に対し、外来で細径硬性子宮鏡下子宮腔内癒着剥離術が有効であった症例を経験したので報告する。【症例】31歳、2妊1産。自然流産1回。3歳時に膣ヘルニア手術の既往がある。また青色強膜、骨密度低下、関節可動域が広く反跳膝と反復関節脱臼の既往があり、家族歴として妹に先天性股関節脱臼の既往もあり、マルファン症候群等の遺伝性疾患も疑われていた。里帰り分娩目的に妊娠19週で当院紹介となった。経陰分娩のリスクを考慮して分娩方式は帝王切開とし、妊娠38週4日に選択的帝王切開術を施行した。児娩出後に弛緩出血を認め、子宮体部前後壁を貫いて縦方向に3針のUCSを加え、子宮を温存し得た。分娩後10か月で月経再来し、分娩前と比べて経血量は若干減少していた。分娩後11か月でUCSの影響を評価するため子宮鏡検査を施行したところ、子宮底部中央に中隔様の索状構造を認めAsherman症候群と診断した。索状部は局所的であり、外来での細径硬性子宮鏡下手術により索状構造をハサミ鉗子で切除することで良好な子宮内腔の拡張を得た。2か月後に子宮鏡検査で子宮内腔に異常のないことを確認し次子妊娠許可とした。【結語】UCSはAsherman症候群の原因となり得るため、術後の慎重な経過観察が必要である。局所的な子宮腔癒着に対する治療法として、外来細径硬性子宮鏡下手術は低侵襲で有効な手段である。

P-116-6 手動吸引法による人工中絶術後に子宮動脈奇形を発症し子宮動脈塞栓術を行った1症例

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2012年WHOは妊娠初期の人工妊娠中絶術には薬剤もしくは吸引法にて行うことを推奨した。本邦では薬剤による方法は認可されていないが、プラスチック製の手動式吸引法 (Manual vacuum Aspiration : MVA) キットが2015年10月に認可され、以降吸引法による人工妊娠中絶術がD&Cに代わって施行されるようになっていく。一方子宮動脈奇形 (Arteriovenous Malformation : AVM) は内膜搔爬や分娩後など後天的な原因により発症する、多量の出血により生命をも脅かす可能性のある疾患である。今回われわれはMVAによる人工妊娠中絶後に子宮AVMを発症し子宮動脈塞栓術を行った症例を経験したので報告する。症例は24歳、4妊2産。自然妊娠成立後、妊娠5週時に当科初診、妊娠8週時にMVAによる人工妊娠中絶術を施行した。手術時間5分、出血量少量でとくに問題なく終了した。その後はっきりとした月経はなく、少量の不正出血が続いていた。中絶術後71日目に多量の性器出血を訴え当院受診、経陰超音波によるカラードプラー法にて子宮粘膜下に強い異常血流像を認めた。本人の希望あり外来経過観察としていたが、79日目に再度同様の症状で救急外来受診、ダイナミックCTにて子宮内腔に動脈相での出血をみとめたため、子宮AVMと診断し同日両側子宮動脈塞栓術を施行、術後経過良好で施行3日後に退院した。D&C施行後のAVM発症は諸家からの報告を散見する。しかしMVA施行後にAVMを発症したとする報告は我々が調べた範囲では見られない。MVAによる人工妊娠中絶術がD&Cにくらべ安全であることは異論がないと考えるが、MVAであってもAVMの原因となる事を念頭におくべきである。

P-116-7 妊娠初期稽留流産の治療成績～待機的管理と外科的治療～

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【目的】現在、わが国での妊娠12週未満の稽留流産や不全流産の治療は、薬物療法が未認可であるため待機的管理と外科的治療のいずれかが選択されているが、どちらが優れた治療法かは不明である。今回、当科における妊娠初期稽留流産の治療成績を検討した。【方法】2017年1月から2020年12月に当科で妊娠12週未満の稽留流産と診断した単胎妊娠173例を対象とした。待機的管理か外科的治療を行うかは患者の希望により決定し、治療成績を検討した。【成績】待機的管理(待機群)は66例、外科的治療(手術群)は107例であった。診断時の待機群の平均妊娠週数は 6.2 ± 1.1 週で手術群の 6.8 ± 1.5 週と比較し有意に低値であった($p < 0.01$)。待機群では、52例(78.8%)が完全流産となり、1例は不全流産の状態が持続したため予定手術を施行し、13例(19.7%)は患者の希望で予定手術に変更した。待機群で診断から完全流産に至るまでの期間は中央値10(1~68)日で、34例(65.4%)が14日以内に、49例(94.2%)が21日以内に完全流産となった。手術群では、手術予定日までに30例(28.0%)が完全流産となったが、緊急手術が必要な症例は認めなかった。合併症は、待機群で入院管理を要した大量出血2例と緊急手術を要した不全流産1例を認め、手術群で存続絨毛症2例と子宮穿孔1例を認めた。【結論】待機的管理も外科的治療もそれぞれ合併症を認めており、治療前の十分なインフォームド・コンセントが必要である。待機的管理では3週間以内に9割以上が完全流産に至っており、待機期間の参考になると思われた。

P-117-1 MRIを使用した前置癒着胎盤の予測

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【目的】前置癒着胎盤は産科危機的出血をきたす代表的な病態であり、既往帝王切開妊娠の増加に伴い増加している。このため、前置癒着胎盤の術前予測は母体死亡回避のためにも重大な意義を持つ。今回、MRIが前置癒着胎盤の術前予測に有用であるかを検討した。【方法】2008年から2020年の13年間に当院でMRIを施行した前置胎盤94例(うち癒着胎盤22例)を対象とし、学習群(71例, うち癒着胎盤16例)と検証群(23例, うち癒着胎盤6例)に分けた。全症例でMRI所見9項目(筋層非薄化, 子宮壁膨隆, 胎盤不均一性, T2低信号帯, 内子宮口への胎盤突出, 異常血管像, 胎盤筋層低信号境界面消失, 胎盤付着部筋層内血管怒張, 漿膜血管像(Flow void))の有無を評価した。学習群を用いて解析ソフトJMP Proのpartitionにて決定木モデルを作成し、検証群を用いて癒着胎盤予測に有用かを検討した。【成績】MRI撮影時の年齢, 妊娠週数, 帝王切開時出血量の中央値は31歳(IQR: 19-39歳), 31週(IQR: 24週-36週), 1235ml(IQR: 250-1000ml)であった。癒着胎盤は22例で、うち21例が既往帝王切開妊娠であった。検討したMRI所見のうち7項目は癒着胎盤と有意に相関していた($p < 0.05$)。決定木モデルからは、癒着胎盤の予測に対し筋層非薄化, 子宮壁膨隆, flow voidの寄与が大きかったことが明らかとなった。この決定木モデルに検証群を適用したところ、癒着胎盤の有無を有意に分類できた(感度50%, 特異度100%, 陽性的中率100%, 陰性的中率85%, $p < 0.05$)。【結論】MRIは前置癒着胎盤の予測に有用であり、特に筋層非薄化, 子宮壁膨隆, flow voidが重要な因子である可能性が示された。

P-117-2 当院における過去10年間の癒着胎盤症例の検討

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【緒言】癒着胎盤は大量出血をきたすことがあり迅速な対応が必要である。一方で、活動性の出血がなく全身状態が安定している場合には保存的に管理されることもある。【方法】2011年6月~2021年6月の当院における癒着胎盤49例を対象とし、診療録を基に後方視的に検討した。【結果】年齢の中央値は34歳(20~44歳), 28例が経産婦, 16例に子宮手術既往があり, 21例がART妊娠, 1例は全前置胎盤であった。34例は分娩時に胎盤用手剥離が可能であった。用手剥離困難だった15例中, 9例は当日中に子宮摘出術を行った。6例は保存的管理を行ったが、そのうち1例は胎盤が吸収され, 2例は自然または用手剥離, 3例は子宮全摘となった。転機が異なった3例について経過を示す。【症例①】30歳, 帝王切開1回既往, 妊娠36週2日, 切迫子宮破裂が疑われ緊急帝王切開術を施行。癒着胎盤のため胎盤を残し閉創し, 術後2日目に自然剥離した。【症例②】40歳, 初産婦, ICSI妊娠, 妊娠38週0日に妊娠高血圧症候群のため緊急帝王切開術を施行。部分癒着胎盤のため胎盤を残し閉創した。出血が持続するため同日IVRを施行。その後は出血や感染徴候なく経過し, 術後11か月目に遺残胎盤は吸収された。【症例③】33歳, 帝王切開2回既往, 帝切瘢痕部にかかる全前置胎盤であった。妊娠35週0日に予定帝王切開術を施行し, 胎盤を残して閉創した。術後46日目に性器出血と凝固異常を認めたため術後47日目に子宮全摘術を施行した。【結語】癒着胎盤を保存的に管理することで子宮温存が可能であった例が報告されているが, 経過観察中に突然の大量出血や凝固異常を認める例もあり, 十分なインフォームド・コンセントの下, 慎重な管理が求められる。

P-117-3 当院における低置・前置胎盤の出血量の検討および自己血貯血の適応について

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【目的】当院は地域周産期母子医療センターとして年間7~17件の低置・前置胎盤症例を受け入れ、主治医の判断で自己血貯血を行っている。自己血輸血は同種血輸血に伴う感染性および免疫性副作用を回避しうる利点がある一方、同種血輸血の安全性や手術技術の向上により自己血貯血が施行されることは世界的に減少傾向にある。今回、当院での低置・前置胎盤症例における出血量および自己血貯血の適応について検討したので報告する。【方法】2013年1月から2020年12月までの当院で管理した低置・前置胎盤症例101例を、後方視的に検討した。【成績】101例の平均術中出血量(羊水込み)は1,469mL(510~4,870mL)であった。出血量が1,500mL以上の症例は、1,500mL未満の群に比較して有意に全前置胎盤が多く($p=0.012$)、有意差は認めなかったが警告出血を認めた症例も多かった。同種血輸血を要したのは5.0%(5例)、自己血輸血を行ったのは14.0%(14例)であった。自己血貯血を行ったのは31例であり、自己血貯血を行った際の合併症は母体血圧低下35.5%(11例)、母体気分不良3.2%(1例)、胎児心音低下0例であった。自己血廃棄率は54.8%(17例)、一部廃棄した例を含めると67.7%(21例)であった。自己血を使用した群は廃棄した群に比べ、有意差は認めなかったが全前置胎盤およびIVF-ETによる妊娠例が多かった。【結論】今回、一般の帝王切開術に比べ低置・前置胎盤では出血が多いことが再確認され、有意に全前置胎盤が多いことがわかった。妊婦での自己血貯血は、母体失血による胎児への明らかな影響は報告されていないものの、懸念する意見も存在し、よりリスクの高い症例に限ってもいいのではないかと考えられた。

P-117-4 出血を伴う前置胎盤における分娩前出血量と新生児脳室周囲白質軟化症に関する検討

宮崎大

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【目的】我々は以前、前置胎盤で分娩前8時間の出血量500mL以上は新生児の脳室周囲白質軟化症(periventricular leukomalacia: PVL)のリスク因子である事を報告した。今回、この基準に準拠し管理を行った際のPVLの発症率について検討した。【方法】2011年1月から2020年12月に、単施設で分娩管理を行った妊娠36週未満の前置胎盤症例60例を対象とし、分娩8時間前の出血量と出生児のPVL発症の有無について後方視的に検討を行った。【成績】新生児の頭部MRI検査、頭部超音波検査でPVLと診断されたのは60例中1例(1.7%)であった。妊娠32週未満では8例中1例(12.5%)、32週以降36週未満は20例中0例(0%)であった。また分娩前に出血があった症例は60例中14例(23.3%)で、14例中1例(7.1%)にPVLを認めた。分娩前8時間の出血量の中央値は197.5mL(範囲:10-1589mL)であり、分娩前8時間で1589mL出血した症例で出生児にPVLを認めた。【結論】出血を伴う前置胎盤を管理する上で、分娩前8時間での出血量が500mLを越える前に娩出できれば、出生児のPVLのリスクを軽減することができる可能性がある。

P-117-5 当院での前置胎盤の管理について

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【目的】前置胎盤はしばしば出血等により早期娩出が必要となり、産科ガイドラインでは平均分娩週数は34-35週で、5-10%に癒着胎盤を合併し、3.5%に子宮摘出が必要であったと報告されている。今回我々は、当科で経験した前置胎盤症例について検討を行ったので報告する。【方法】2018年1月から2020年12月に当科で経験した前置胎盤症例について後方視的に検討を行った。【成績】平均分娩週数は34.7週であり、前置胎盤は35例で、全前置胎盤20例、辺縁もしくは部分前置胎盤15例であった。平均出血量は1950gで自己血輸血のみは16例、同種血輸血を行ったのは3例、16例が輸血不要であった。胎盤付着部位の主体が後壁であったのが30例で、5例が前壁主体であり、すべて全前置胎盤であった。前壁が主体であった5例中4例は今後の挙児希望がなく、底部横切開にて分娩とし、そのうち術前に癒着胎盤が強く疑われた2例は両側尿管ステントを留置し、子宮全摘術を行った。術後病理組織にて癒着胎盤との結果であり、5.7%に癒着胎盤が合併し、子宮全摘術が必要であったとの結果であった。また底部横切開を行ったうち同種血輸血を必要としたのは1例のみであった。【結論】当院での前置胎盤における平均分娩週数、癒着胎盤の合併率はガイドラインに示されている通りである。挙児希望のない前壁主体の全前置胎盤には底部横切開での分娩は有効であると考えられる。

P-117-6 既往帝王切開後前置胎盤症例におけるMRI検査での子宮下部表面Flow Voidの癒着胎盤および分娩時出血量の予測に対する有用性の検討

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【目的】既往帝王切開後妊娠の前置胎盤症例で、子宮下部表面に通常では認めない怒張した血管（以下、異常血管）が目立つ症例があり、このような症例では胎盤剝離困難や分娩出血量の増加を伴う場合がある。この異常血管をMRI検査の血管像（Flow Void）として評価し、実際の開腹所見や癒着胎盤の有無、および分娩時出血量との相関について検討した。【方法】2008年1月～2020年12月までの13年間に当施設で管理した既往帝王切開後妊娠の前置胎盤症例で、妊娠中に癒着胎盤の診断目的にMRI検査を行なった40症例を対象に、Flow Voidの所見と子宮下部表面の異常血管、癒着胎盤、および分娩時出血量との相関を後方視的に検討した。【成績】MRI撮影時の妊娠週数の中央値は妊娠31週（IQR：24週-35週）であり、Flow Voidを認めた症例は12症例（30.0%）あった。Flow Voidを認め異常血管を認めた症例は10症例（83.3%）あり、Flow Voidを認めずに異常血管を認めた症例は5症例（17.9%）で、Flow Voidは異常血管と有意に相関した（ $p < 0.05$ ）。また、Flow Voidを認めた12症例は全て癒着胎盤であり、Flow Voidを認めずに癒着胎盤であった症例は11症例（39.3%）で、Flow Voidは癒着胎盤とも有意に相関した（ $p < 0.05$ ）。さらに、Flow Voidを認めた症例では分娩時出血量が有意に増加した（3187.5 g vs. 1395.7 g, $p < 0.05$ ）。【結論】既往帝王切開後妊娠の前置胎盤症例においてMRI検査での子宮下部表面のFlow Voidの存在は、子宮下部表面の異常血管、癒着胎盤、分娩時出血量との相関が高く、術前の評価項目として有用である可能性が示唆された。

P-117-7 異常浸潤性胎盤における胎盤絨毛の血管構造の病理組織学的解析

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柏木葉月

【目的】異常浸潤性胎盤（PAS：Placenta accreta spectrum）は、多量出血や隣接臓器損傷をおこし、母体死亡の原因になりうる産科的に重要な疾患である。近年、母体の高齢化や生殖補助医療の増加などに関連し、増加傾向であると報告されている。分娩後に胎盤の遺残がある、または用手剝離でも剝離できない時に臨床的に癒着胎盤を疑う。組織学的には、子宮摘出標本の病理検査により、脱落膜の有無や、筋層に直接接着・浸潤する胎盤絨毛の有無により診断されているが、胎盤絨毛の血管構造に関して言及されている文献は少ない。今回我々は、異常浸潤性胎盤と正常胎盤の絨毛の血管構造の差異について免疫染色を行って評価した。【方法】当院で分娩となった侵入胎盤2例、穿通胎盤3例、正常胎盤群は既往帝王切開の症例3例の合計8症例を対象とした。CD34抗体を用いて免疫染色を行い、胎盤絨毛の血管構造及び絨毛に占める血管面積比について検討を行った。【成績】正常胎盤群と比較して、異常浸潤性胎盤群では胎盤絨毛の血管面積が小さいことを確認した。また絨毛間質に占める血管面積の割合も小さかった。しかし1絨毛あたりの血管数に差はなかった。【結論】今回我々は正常胎盤と異常浸潤性胎盤の胎盤絨毛の血管構造の差異について病理組織学的解析を行い、1絨毛あたりの血管数に差はなかったが、血管面積は小さく、また絨毛に占める血管面積比も小さいことを確認した。今後は、これらの特徴的な血管構造に起因する分子病態機序の解明をすすめる。

P-117-8 前置胎盤・癒着胎盤への血流コントロール下帝王切開（Hybrid帝切）は低侵襲治療になり得るか？

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【目的】産科出血は時に致死的であり、大量輸血や子宮摘出が回避困難な事もある。大量出血発症リスクが高い病態の一つが前置胎盤や癒着胎盤だが、我々は同症例に対し血流コントロール下帝王切開術（Hybrid帝切）を導入し精度を高めてきた。既存帝切に比しHybrid帝切は低侵襲治療となり得るかを検証した。【方法】直近6年間に胎盤位置異常で帝王切開分娩を行った中で、前壁付着・癒着胎盤等で大量出血ハイリスクと判断した32例を対象。従来法帝切群（C群）とHybrid帝切群（H群）の二群に分け、患者背景、出血量、輸血有無、手術手法（皮膚切開や子宮内バルーン等）、追加処置有無（子宮摘出や血管塞栓術）等を後方視観察研究として比較検討した。Hybrid帝切群は、ハイブリッド手術室で行い、遮断ゾーン変更可能な大動脈遮断バルーン（IABO）カテーテルで、児娩出直後以降に術野の止血操作状況にあわせて血流・血圧コントロールし、必要に応じ血管撮影・塞栓術を行った。【成績】C群（ $n=18$ ）vs H群（ $n=14$ ）で、患者背景ではH群で前壁付着が多い傾向（22% vs 43%, $p=0.23$ ）はあったが、すべて有意差なし。術中出血量（2641ml vs 1315ml）、同種血輸血率（33% vs 0%）、皮膚縦切開率（100% vs 29%）、尿管ステント留置率（89% vs 7%）、パクリバルーン使用率（67% vs 0%）、腔内ガーゼパッキング率（56% vs 7%）はH群で有意に低く、子宮摘出率（6% vs 0%）、動脈塞栓施行率（6% vs 7%）に有意差なし。【結論】大量出血ハイリスクの胎盤位置異常症例へのHybrid帝王切開は、出血量や術中・後の処置等が低減でき、従来法に比し低侵襲治療となり得る可能性がある。

P-118-1 分娩第2期に発症した重症急性膵炎合併妊娠の1例

昭和と横浜市北部病院

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【緒言】妊娠に急性膵炎を合併する頻度は約0.02%程度と非常に稀である。今回我々は、重症急性膵炎を合併しながらも適切に分娩管理を行い、母児共に救命し得た1例を経験したため文献的考察を加え報告する。【症例】33歳2妊1産。既往に特記事項はなく、母体合併症は妊娠糖尿病(GDM)のみであり、食事療法と血糖測定を実施していた。妊娠40週0日に陣痛発来し入院した。分娩第2期に37.7度の発熱、腹膜刺激徴候、嘔吐を認めたため血液検査を施行したところ、高アミラーゼ血症(AMY 751 U/L)、高トリグリセリド血症(TG 3000 mg/dL)等を認めた。CTG所見はレベル1で経過しており、分娩は急速に進行していたため、慎重に経過観察し、その後速やかに経陰分娩に至った。児は男児、3496g, Apgar score 9点(1分値)、9点(5分値)、臍帯動脈pH 7.35であった。分娩直後に造影CTを施行し、CT grade 2の重症急性膵炎と診断した。直ちに集中治療室に入室し、絶飲食、大量輸液、蛋白分解酵素阻害薬、抗生剤等による治療を開始した。治療により炎症反応は改善したが、発熱と上腹部痛が遷延し、産褥7日目に造影CTを再施行したところ、膵周囲に膿瘍形成を認めた。内視鏡洗浄や外科的ドレナージの適応も考慮されたため、産褥13日目に高度専門施設へ転院した。転院後は保存的治療で状態は改善し、現在は当院外来で経過観察中である。【考察】血中TG濃度の異常高値は膵炎のリスク因子である。妊娠中は生理的に血中TG濃度が上昇するため注意が必要である。適切な脂質管理で膵炎の発症予防に努め、妊娠中に非典型的な臨床症状を認めた際は、急性膵炎も鑑別に挙げて早期診断・治療を行うことが母児の良好な転帰に重要であると思われた。

P-118-2 膵体尾部切除術後に生児を獲得した1例

大津赤十字病院

家村洋子, 大谷遼子, 恩地孝尚, 林真麻子, 松坂直, 中村彩加, 星本泰文, 多賀敦子, 北村幸子, 金共子, 藤田浩平

膵臓部分切除術後にはインスリン分泌の低下から糖尿病を発症する可能性が高くなるが、妊娠報告例は少ない。今回、膵体尾部切除術後に生児を獲得した1例を経験したため報告する。患者は33歳初産婦。家族歴は祖父に膵臓癌がある。既往歴は30歳時に当院外科で膵内分分泌腫瘍G1, G2に対して腹腔鏡下膵体尾部切除術を行われている。術後は血液検査やCT、超音波検査などで経過観察が行われ、再発はなく耐糖能異常も認めていなかった。多発性内分泌腫瘍(MEN)の可能性も考慮されたが、下垂体腫瘍と甲状腺腫瘍は認めず、妊娠前に遺伝子検査は行われなかった。今回自然妊娠し、妊娠11週時の75g経口糖負荷試験の結果、空腹時、1時間値、2時間値がそれぞれ94, 91, 171mg/dLであり妊娠糖尿病と診断した。糖尿病内分分泌内科併診の元で自己血糖測定が開始され、食後血糖値が125mg/dLを頻回に上回るため、妊娠15週時よりインスリン強化療法が開始された。導入時は速効型インスリン14単位を使用していたが、分娩前には持続型インスリン4単位、速効型インスリン25単位にまで増量となった。妊娠中に低血糖発作はなく、その他の周産期合併症も生じずに経過した。妊娠40週時に自然経陰分娩となり、児は女児、体重:3335g(+0.9SD)、身長:50cm(+0.2SD)であった。分娩後よりスライディングスケール法へ変更するも、食前血糖値85-110mg/dL程度で推移したためインスリン投与は行わず、退院時にもインスリンの投与は不要と判断した。膵臓部分切除術後の場合、妊娠前に糖尿病の発症がなくても、妊娠を契機に耐糖能異常を呈する場合がある。厳格な血糖コントロール管理を行うことで安全に妊娠分娩を行うことが可能である。

P-118-3 妊娠中期に家族性大腸腺腫症の診断に至った若年妊婦の1例

橋本市民病院¹, 和歌山県立医科大学²藤野めぐみ¹, 堀内優子¹, 池島美和¹, 太田菜美², 南佐和子², 井篁一彦², 古川健一¹

家族性大腸腺腫症(Familial adenomatous polyposis:FAP)は大腸の多発性腺腫を主徴とし、将来、高率に大腸癌を発病する常染色体優性遺伝疾患である。これまで国内外のFAP合併妊娠の症例報告は極めて少なく、管理指針は明確ではない。今回、妊娠中期に貧血の精査中にFAPの診断に至り、分娩まで保存的に管理した症例を経験したので報告する。症例は17歳の若年初産婦。他院で妊娠管理中、妊娠21週3日に発熱、腹痛、下痢、腰痛症状を認め当院に紹介受診となった。腎盂腎炎、感染性胃腸炎の診断で入院管理、抗菌薬加療を行った。入院中より鉄剤投与では有意な改善がみられない小球性低色素性貧血があった(Hb:6.6~7.8mg/dL)。妊娠22週5日に軽快退院後も貧血が持続し、下血症状を訴え、妊娠26週0日に初回の下部消化管内視鏡検査(CF)にて大腸全体に多数のポリープを認めた。詳細な家族歴を聞き取り、妊娠27週0日に2回目のCFを施行し、FAPと診断確定し、その時点で痛化したポリープ病変はないと判断した。消化器内科、外科と協議を重ね、分娩まで保存的に管理し、分娩後に予防的大腸全摘術を実施する方針となった。妊娠後期では下血症状持続したものの鉄剤静注を適宜行い、Hb:8.2~9.9mg/dLを推移した。また和歌山県立医科大学遺伝外来に紹介し、本人、家族へカウンセリングを実施した。妊娠41週3日より誘発分娩を開始し、妊娠41週5日に3488gの男児を経陰分娩した。妊娠性の貧血や外痔核の出血だけでは説明できない場合は妊娠中のCFも検討が必要である。FAP合併妊娠は個々の症例のライフステージや家族背景を配慮し、他科と連携をとり、疾患の進行度に合わせた慎重な妊娠分娩管理を行う必要がある。

P-118-4 腸リンパ管拡張症および蛋白漏出性胃腸症合併妊娠の一例

姫路赤十字病院

真田知佳, 西田友美, 西田康平, 大前彩乃, 相本法慧, 平田智子, 西條昌之, 河合清日, 中山朋子, 関典子, 小高晃嗣, 水谷靖司

【緒言】腸リンパ管拡張症とは、腸管壁内のリンパ管内圧が亢進し、リンパ管の拡張や破綻をきたした結果、リンパ液と共に蛋白成分が漏出し低蛋白血症をきたす稀な疾患である。非対称性の全身性浮腫や胸腹水の貯留を認め、低 γ グロブリン血症やリンパ球減少により免疫不全状態を伴う。原則、妊娠継続は不可能とされ国内での蛋白漏出性胃腸症合併妊娠の報告は1例のみである。今回蛋白漏出性胃腸症合併妊娠を経験したため報告する。【症例】34歳、1妊0産、初産婦。4歳時に顔面浮腫にて腸リンパ管拡張症および蛋白漏出性胃腸症と診断され、エンターール、中鎖脂肪酸の補充、食事療法で経過観察されていた。血清蛋白は3.5~4.5g/dLで推移し、成長発達に明らかな異常を認めず。本人の育児希望の思いが強く、リスクを説明した上で妊娠を許可した。前医での6回目の人工授精にて妊娠成立、管理目的に当院紹介となった。9週時に妊娠悪阻にて2週間程度の入院加療を要した。20週時に切迫流産に対して入院にてリトドリン点滴を行った。明らかな胎児発育遅延は認めず、40週6日で陣痛発来。経陰分娩にて3455gの男児を娩出。Apgar score 8/9。妊娠期間中は血清蛋白5.2~6.5g/dL、アルブミン2.7~3.7g/dLで推移、明らかな腎機能障害や浮腫の増悪は認めず。産褥5日目で母児ともに退院となった。【考察】蛋白漏出性症候群合併妊娠は非常に稀であり、妊娠に伴う浮腫や胸腹水、腎機能障害の出現が懸念されるため妊娠は回避されているが、本症例では妊娠期間中、母児共に明らかな異常を認めなかった。慎重な周産期管理の下では、蛋白漏出性胃腸症合併妊娠は可能であると思われた。

P-118-5 フィブリノゲン製剤を使用し母児の救命できた急性妊娠性脂肪肝の一例

新潟市民病院

小川裕太郎, 倉林工, 柳瀬徹, 田村正毅, 常木郁之輔, 森川香子, 上村直美, 廣川哲太郎

【目的】急性妊娠性脂肪肝は10,000妊娠に1例と稀な疾患である。今回、総ビリルビン(T-bil)10mg/dlを超え臨床的に急性妊娠性脂肪肝と診断された症例に対して緊急帝王切開を施行し、術後2回の子宮動脈塞栓術、大量輸血およびフィブリノゲン製剤の使用により、母児を救命できた1例を経験したので報告する。【症例】38歳、未経産、自然妊娠成立後に前医で妊娠管理を行っていた。妊娠32週2日に黄疸が出現し、当科母体搬送となった。入院時の血液検査ではT-bil 10.7mg/dl、AST 216 U/L、ALT 124 U/L、Cre 1.83mg/dl、PT 秒 15.4秒、白血球数 17,800/ml、尿酸 8.2mg/dl、血糖 74mg/dl、アンモニア 30 μ g/dlであり、SwanseaCriteriaを6項目以上満たし、急性妊娠性脂肪肝の診断に至った。同日全身麻酔下に緊急帝王切開を施行し、術中出血量は1424gであった。出生児は1402g、ApgarScore1 分値 2点、5分値 7点で、気管内挿管後にNICU入院となった。術後2日目に大量の子宮出血を認め、子宮動脈塞栓術を施行した。その後、再度子宮からの出血をきたし、再度子宮動脈塞栓術を施行した。術直後から赤血球輸血 22単位、新鮮凍結血浆 36単位を輸血していたが、止血困難のため同時にフィブリノゲン製剤投与、濃厚血小板輸血 20単位を行った。術後3日目からは輸血をせず保存的療法を行った。術後14日目の血液検査ではT-bil 2.0mg/dlとなり、術後16日目に退院となった。【結論】急性妊娠性脂肪肝は、適切な診断や治療がなせられない場合には母児ともに死亡率が高い疾患であるが、早期の胎児娩出および術後の適切な管理を行い母児を救命することができた。止血困難の産褥出血に対してフィブリノゲン製剤の使用も考慮することが必要である。

P-118-6 妊産婦における胆石症の検討

島根県立中央病院

西木正明, 奈良井曜子, 障子章大, 江川恵子, 田中綾子, 山上育子, 坪倉かおり, 森山政司, 岩成治, 栗岡裕子

【目的】妊娠中の胆嚢炎は妊娠1,600~10,000に1例とされており、原因の90%以上は胆嚢結石である。妊産婦の急性腹痛となる急性胆嚢炎・胆嚢胆管結石について、当院で周産期管理を行った症例の背景などを検討し解析する。【方法】2010年1月から2021年6月の11年半の間に当院で周産期管理を行った妊産婦で、胆道系疾患を発症した妊産婦の背景・周産期経過および胆道系疾患の転機について検討を行った。【成績】同期間に周産期管理を行った9966例のうち、胆道系疾患を発症したのは13例で0.13%であった。診断時年齢は25~36歳で、平均値は30.3歳であった。妊娠中に診断された症例は7例で、うち1例は非妊娠時に胆石を指摘された既往があった。妊娠9週から33週で診断されており、2nd trimesterでの発症が4例で多かった。胆道系疾患が原因で早産となった症例は認めなかった。7例中2例で産後に腹腔鏡下胆嚢摘出術を施行され、5例は経過観察となっていた。産後に胆道系疾患を発症したのは6例であった。発症時期は産褥1日から産褥3か月であった。全例に腹腔鏡下胆嚢摘出術が施行されていた。【結論】近年の妊産婦の高齢化とは反し、胆道系疾患を発症する妊産婦の平均年齢は30歳で、比較的若年者が多かった。妊娠中はエストロゲンによるコレステロールの過飽和と、プロゲステロンによる胆嚢平滑筋の弛緩に伴う胆汁鬱滞で胆泥が増加し、胆石の形成に関連している。妊産婦の急性腹痛においては、胆道系疾患の可能性を考慮した診療が必要である。

P-118-7 産褥期に巨大肝嚢胞の自然破裂を産症した一例

静岡県立総合病院

佐伯綾香, 堀川直城, 金井亜未, 吉田旭輝, 牧尾 悟, 伊田昂平, 梅宮植樹, 辻 満, 敖 礼, 谷 洋彦, 小阪謙三

【緒言】肝嚢胞は内科的には日常臨床でよく遭遇する良性疾患であるが、巨大肝嚢胞や肝嚢胞破裂は稀である。さらに、妊娠中に巨大肝嚢胞を合併した報告はこれまで認められない。今回、産褥期の卵巣嚢腫の破裂が疑われ近医より搬送されたが、実際には肝嚢胞破裂であった一例について報告する。【症例】34歳1妊1産。自然妊娠が成立し妊娠16週0日以後近医で妊婦健診を受けていた。妊娠35週2日の診察時に初めて経腹超音波で上腹部に180mm大の多房性嚢胞を認め、卵巣嚢腫と判断され経過観察していた。妊娠40週0日に自然経陰分娩に至り、産後2日目にも嚢胞が確認され後日当院へ紹介予定であった。産後5日目に突然の上腹部痛を認め、嚢胞が消失していたため卵巣嚢腫の破裂を疑い当院へ救急搬送された。経腹超音波では壁が破綻し緊張性を失った嚢胞と多量の腹水を認めた。来院時は血圧125/83mmHg、脈拍97回/分とバイタルサインは安定していた。胸部腹部造影CTでは肝左葉から発育する嚢胞を認め、嚢胞壁が破綻し腹腔内に出血が貯留していたため、出血性肝嚢胞の破裂が疑われた。徐々に疼痛が増悪し、ショックバイタル(血圧78/44mmHg、脈拍98回/分)、Hb4.8g/dlとなり、赤血球輸血8単位を実施しながら腹腔鏡下肝嚢胞閉塞術が行われた。肝左葉外側区から発育する嚢胞の破綻部位から出血を認めた。腹腔内には1.2Lの血液が貯留し、出血部位を含むように嚢胞壁を部分的に切除し手術終了となった。術後経過は良好で術後6日目に退院となった。【考察】妊娠中に腹腔内嚢胞性病変を認めた際には肝嚢胞を鑑別診断に挙げ、破裂のリスクを認識しておく必要がある。

P-119-1 産婦人科診療ガイドライン産科編2020における妊婦の耐糖能異常検査変更について妥当性の検討—当院における妊娠初期75gOGTT陽性者の検討—

近江八幡市立総合医療センター

小野哲男, 前田倫子, 岡田奈津実, 草場紗智子, 竹川哲史, 松島 洋, 初田和勝

【目的】産婦人科診療ガイドライン産科編2020において、妊婦の耐糖能異常検査について変更がなされた。これまで妊娠初期随時血糖で陽性となった症例には75gOGTTを行い診断検査としていたのが、HbA1cの測定のみで診断して良いと変更された。しかし、その根拠についてのエビデンスは示されておらず、その妥当性は不明である。当院での妊娠初期75gOGTT陽性症例を検討することにより、産婦人科診療ガイドライン産科編2020における変更が妥当であるかの検討を行った。【方法】当院で2016年1月より2020年12月までの間に分娩となった症例の中で、妊娠初期に75gOGTTで陽性となった単胎妊娠症例を対象とし、HbA1cが6.5%以上の症例と、6.5未満の症例で周産期予後に差があるかどうかを検討する。【成績】妊娠初期75gOGTT陽性73症例のうち、HbA1c6.5%以上は3症例(4.1%)であった。HbA1c6.5%未満と6.5%以上で母体・胎児の予後(帝王切開率、HDP発症率、インスリン導入率、在胎週数、出生体重、Apgarスコア、NICU入室率、人工呼吸管理率、新生児低血糖率)には差を認めなかった。HbA1c6.5%未満の70症例のうち、インスリン導入を要した症例は32症例(45.7%)存在し、新生児低血糖を呈した症例も8症例(11.4%)認めた。【結論】GDM症例の減少はGDMと診断されることで紹介される高次医療施設の産婦人科・内分泌内科の負担軽減につながる可能性がある。一方、HbA1cが6.5%未満でも内科的な血糖管理が必要と思われる症例が存在し、75gOGTTを行わず、HbA1c6.5%以上だけで判断した場合、そのような症例が見逃される恐れがある。妊娠初期耐糖能異常精密検査の変更にあたっては慎重な検討が必要と考えられる。

P-119-2 当院での妊娠初期妊娠糖尿病のスクリーニングの有用性についての検討

JCHO 大阪病院

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【目的】妊娠初期の随時血糖測定後の耐糖能スクリーニングに関しては、産婦人科診療ガイドラインでは、75gOGTTかHbA1cを行うとされている。妊娠初期の妊娠糖尿病(GDM)診断や管理では、75gOGTTのGDM診断の基準値が妊娠中期以降のものを流用していることや食事療法においてつわりの時期での実施には困難があることなどが問題点となる。そこで、当施設では、2021年4月より産婦人科診療ガイドラインに基づき、随時血糖値がカットオフ以上の症例に対して、HbA1c測定か75gOGTTの実施を使い分けるアルゴリズムに基づくGDMスクリーニング方法としている。過去に当院で妊娠初期に75gOGTTでGDMと診断された症例の転帰を確認し、アルゴリズムの妥当性を検証した。【方法】2016年1月から2021年1月までの期間に当院で分娩された、GDMの症例を対象とした。妊娠初期血糖値や75gOGTT結果、分娩転帰、妊娠糖尿病のリスクファクターの有無を抽出し、妊娠初期にGDMと診断された症例の転帰に関して、後方視的に検討した【成績】上記の対象期間に当院で分娩したGDMは、134例であった。妊娠初期にGDMと診断された症例は、41例(30.6%)であった。妊娠初期からのGDM症例のうち、妊娠中の明らかな糖尿病が2例(4.9%)、インスリン使用例は、16例(39%)で、インスリン使用例のうちアルゴリズムで75gOGTTに該当しない症例は、1例(6.3%)であった。アルゴリズムでスクリーニングした場合に75gOGTTの実施をしない症例は、10例(24.3%)であるが、9例が食事療法のみでコントロールされていた。【結論】当院の妊娠初期GDMスクリーニング法では、インスリンを使用するハイリスクのGDMは見逃す可能性は低く、今後も継続可能と判断された。

P-119-3 妊娠初期のHbA1cは、early onset GDMの診断に有用か？

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田野島美城¹、青木 茂¹、宮城悦子²

【目的】妊娠初期のHbA1c値が妊娠初期に診断される妊娠糖尿病（early onset GDM）の診断や予知に有用かは不明である。本研究では、妊娠初期のHbA1c値と妊娠初期75g糖負荷試験（75gOGTT）の結果が相関するか検討することを目的とした。【方法】2018年4月から2020年12月までに当院で単胎分娩した妊婦で、GDMリスク因子をもつために妊娠20週までに75gOGTTを施行した1113例を対象とした。【成績】妊娠20週までに診断されたGDMは265例（24%）だった。GDM群、非GDM群ともに、母体年齢中央値は36歳で差を認めなかったが、非妊時BMI中央値はGDM群22.7kg/m²、非GDM群20.8kg/m²（ $p<0.001$ ）、HbA1c中央値はGDM群5.4%、非GDM群5.3%（ <0.001 ）と有意にGDM群が高かった。75gOGTTの異常値の有無とHbA1c値との関係においては、空腹時血糖異常（ $\geq 92\text{mg/dl}$ ）、1時間値異常（ $\geq 180\text{mg/dl}$ ）、2時間値異常（ $\geq 153\text{mg/dl}$ ）を認めた妊婦は、それぞれ異常値を認めなかった妊婦に比べて有意にHbA1c値が高値であった。HbA1cによる妊娠初期GDM診断のROC曲線のAUCは0.635、カットオフ値はHbA1c5.5%であり、カットオフ値での感度は40%、特異度は80%だった。【結論】妊娠初期のHbA1cはearly onset GDMと相関関係を認めた。しかしながら、ROC曲線から導かれるカットオフ値での感度は低く、妊娠初期HbA1c値は、early onset GDMの診断、予知に有用とは言えなかった。

P-119-4 False positive early GDMの妊娠分娩転帰は正常耐糖能妊婦と同じか？

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青木 茂¹、宮城悦子²

【目的】妊娠初期から妊娠糖尿病（GDM）を診断し治療することは是非は国際的にも結論が出ていない。我々は過去に妊娠初期にGDMと診断された妊婦を無治療経過観察としても、約半数は妊娠中期には正常パターンとなることを報告した。本研究では妊娠初期には75g糖負荷試験でGDMパターンを呈したが、無治療経過観察とし、妊娠中期に再度75g糖負荷試験を行うと正常パターンを呈したfalse-positive early GDMは正常耐糖能として扱ってよいのかを検証することを目的とした。【方法】当センターで分娩した、false-positive early GDM妊婦（falseGDM群）117人と正常耐糖能妊婦（NGT群）1774人を後方視的に妊娠分娩転帰について検討した。【成績】母体年齢およびfalseGDM群で36歳とNGT群33歳と比して有意に高値だった。（ $p<0.001$ ）非妊時BMIもfalseGDM群で21.9と、NGT群20.5と比して有意に高値だった。（ $p<0.001$ ）分娩週数、出生体重、帝王切開率、Large for gestational age率は両群間に単変量解析および多変量解析ともに有意差はなかったが、妊娠中の体重増加はfalseGDM群で8.7kgとNGT群の10.3kgより有意に少なかった。（ $p<0.001$ aRC(95%CI)-0.51(-0.919- -0.116)）出生後に全例血糖測定を行われたfalseGDM群で、出生後に血糖測定を一部にしか行われなかったNGT群より新生児低血糖が有意に多かった（ $p=0.002$ 、aOR(95%CI)7.453(2.233-24.875)）が、そのほかの新生児転帰に両群間で差は認めなかった。【結論】False-positive early GDMは正常耐糖能妊婦と同等に取り扱ってよいと考えられ、妊娠初期のみGDMパターンを呈するGDMに臨床的意義は乏しい。

P-119-5 妊娠中期に診断された妊娠糖尿病のインスリン治療開始時期の検討：いつまで血糖自己測定を行う必要があるか？

国立長崎医療センター

網師本健佑、倉田奈史、福岡 操、山下 洋、安日一郎

【目的】妊娠糖尿病（GDM）のインスリン導入は、栄養指導下での血糖自己測定（SMBG）による目標血糖値達成の有無によって判断するが、いつまでSMBGを続ける必要があるかについては一定の見解がない。今回、妊娠中期診断GDMのインスリン導入のタイミングを検討し、SMBGの中止が可能な妊娠時期の推定を行なった。【方法】単施設の後方視的研究として、妊娠24~32週にGDMと診断された単胎妊娠を対象とした。GDM診断後に栄養指導下のSMBG評価によって導入したインスリン開始週数を検討した。インスリン非導入例のSMBGの継続・中止は主治医の判断によった。【成績】対象GDM症例は311例で、食事療法のみ症例（D群）は179例（58%）、インスリン療法群（I群）は132例（42%）であった。両群で年齢、GDM診断およびSMBG開始週数に差はなく、非妊時肥満度はI群で有意に高値であった。I群のインスリン導入週数は 29 ± 2 （範囲24~36）週。SMBG開始からインスリン導入までの期間は 1.8 ± 1.6 （0~10）週で、最大インスリン投与量は 32 ± 23 （4~148）単位/日であった。妊娠33週以降のインスリン導入は13例（I群の10%）に認めたが、34週以降は1例（I群の0.8%）のみであった。D群の30%は分娩までSMBGが継続され、D群のSMBG中止症例の中止週数は 31 ± 3 （25~39）週であった。【結論】妊娠中期診断の単胎GDM症例のインスリン療法導入は、そのほとんどが妊娠33週までに開始されていた。インスリン導入判断のためのSMBGは妊娠34週以降に中止できる可能性が示唆された。

P-119-6 妊娠糖尿病妊婦における1日食塩推定摂取量と周産期予後の検討

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【目的】妊娠糖尿病患者は食事療法が重要である。1日食塩推定摂取量と妊娠高血圧症候群等の合併、周産期予後を検討することを目的とした。【方法】妊娠糖尿病患者は診断されたのち、1泊2日の教育入院を実施している。入院時の随時尿で1日食塩推定摂取量を測定している。2020.5.1より2021.4.30までの1年間で教育入院した239人のうち1日食塩推定摂取量7g未満(A群)43人と7g以上(B群)196人について妊娠高血圧症候群の合併と、周産期予後を検討した。【成績】患者背景は年齢A群35.4±4.7歳、B群35.1±4.3歳、非妊時BMI A群21.1±3.5、B群21.0±3.0、分娩週数A群264±4日、B群264±4日であった。1日食塩推定摂取量はA群5.8±1.0g(2.55~6.98)、B群9.9±1.7g(7.07~14.23)(有意差ありP<0.01)であった。分娩時出血量A群495±428ml、B群381±296ml。新生児出生時体重A群2783±318g、B群2799±326g。Apgar5分値A群9±0.5点、B群9±0.5点。臍動脈血pH A群7.28±0.05、B群7.28±0.06で有意差はなかった。妊娠高血圧症候群(HDP)合併は55人でありA群10人(23%) B群45人(23%)。遅発型はA群3人(0.7%) B群13人(0.7%)、早発型はA群7人(16%) B群32人(16%)。緊急帝王切開A群3人(7%)、B群19人(10%)であった。【結論】教育入院時の1日食塩摂取量には大きく差があるものの、予想していた妊娠高血圧症候群発症については有意差がなかった。周産期予後も差がなかった。教育入院により食事内容が改善された可能性がある。今回は教育入院時1回の検査であり、教育入院後の減塩について改善したかどうかの検証は行っていない。今後は教育入院後の食事についても検討する必要があると考えた。

P-119-7 妊娠糖尿病を発症した妊婦の産褥期における耐糖能異常の検討

トヨタ記念病院
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【目的】妊娠糖尿病は妊娠中に初めて発症した糖代謝異常である。妊娠中期以降に母体のインスリン抵抗性が上昇することが原因であり、分娩後には改善することが多い。しかし、妊娠糖尿病妊婦の2型糖尿病を発症する相対危険度は、正常妊婦の7.43倍と高率であるという報告があり、分娩後に経過観察することが重要である。今回我々は当院で周産期管理を行った妊娠糖尿病妊婦の分娩後の耐糖能異常を検討した。【方法】2020年1月から12月に当院で周産期管理中に妊娠糖尿病と診断された妊産婦50例を対象とした。Overt diabetes in pregnancyと糖尿病の既往のある妊婦は除外した。分娩12週後に75g OGTTを実施した。対象患者の妊娠時の血糖管理方法、12週後の受診率、耐糖能異常の有無を評価した。【成績】食事療法で管理を行ったのが28例(56%)、インスリン療法で管理を行ったのが22例(44%)であった。分娩12週後の受診率は44例(88%)であった。44例のうち75g OGTTで耐糖能が正常型は30例(68%)、境界型は14例(32%)であった。糖尿病型はなかった。境界型の14例のうち、Impaired Glucose Toleranceは13例(93%)、Impaired Glucose ToleranceとImpaired Fasting Glucoseの合併は1例(7%)であった。【結論】分娩後に境界型であったのは32%であり、妊娠糖尿病患者に対して分娩後に耐糖能異常を評価することが重要であることが示唆された。

P-119-8 当院における妊娠糖尿病症例の分娩後フォロー状況に関する検討

榎原記念病院
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【目的】当院では以前より妊娠糖尿病(GDM)症例の分娩後フォローからのドロップアウト例が多いことに苦慮しており、COVID-19流行によりさらに増加することが危惧されている。今回、分娩後のよりよいフォロー体制の構築を目指すことを目標とし、現在までの当院での分娩後フォローの状況を調査した。【方法】2016年4月から2020年12月までの間に当院で分娩した症例のうち妊娠中にGDMと診断された132例につき、分娩後フォロー状況を診療録記載に基づき後方視的に検討した。なお、妊娠前に診断されていた糖尿病の症例は検討対象から除外している。【成績】132例中、産後血糖正常化確認のためのOGTTを実施していなかった例が24例(18.2%)あった。OGTT実施例中101例は分娩後12週以内に実施されていたが、7例(6.5%)では12週以降に実施されていた。調査時点で最終受診より1年以上経過していた例が76例(57.6%)あり、うち26例(34.2%)は当院受診を指示していたが未受診であった。一方1年以上経過例のうち10例(13.2%)は最終受診の時点で次回受診の指示に関する記載がなかった。【結論】当院でGDMと診断された例のうち過半数が分娩後フォローからドロップアウトしていた。その理由として、COVID-19流行により患者の受診行動に制限が生じた可能性もあるが、COVID-19流行以前から未受診となっている例もあり患者自身の何らかの判断による可能性も考えられた。また最終受診時点で次回の受診に関する指示がなされていない例もあり、医療者側の理解が不十分である可能性も示唆された。今後、未受診者に対するアンケートにより未受診例の詳細な状況を調査する予定である。

P-119-9 妊娠糖尿病単胎妊婦におけるインスリン療法の導入のリスク因子

旭川医大

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【目的】妊娠糖尿病 (GDM) 単胎妊婦におけるインスリン療法の導入のリスク因子について調査する。【方法】2016年1月から2020年12月に当院で分娩したGDM単胎妊婦を対象とした後方視的コホート研究である。非妊時体重が不明、血糖管理を他院で行った症例、染色体異常児妊娠は除外した。血糖管理は当院糖尿病内科で行われた。妊娠中に食事療法のみ行われた群とインスリン療法が行われた群の2群に分けてインスリン療法の導入のリスク因子を調査した。説明変数は、母体年齢 ≥ 35 歳、経産婦、GDM既往、糖尿病の家族歴、非妊時体格指数 (BMI) < 18.5 および $\geq 25.0 \text{ kg/m}^2$ 、2点または3点陽性のGDMとした。インスリン療法と独立して関連する調整オッズ比を多変量ロジスティック回帰分析を用いて算出し、 $P < 0.05$ を統計学的有意とした。【成績】対象症例は262例であった。食事療法群が147例 (56.1%)、インスリン療法群が115例 (43.9%)であった。インスリン療法と統計学的有意に関連したリスク因子 (調整オッズ比 [95%信頼区間]) は、GDM既往 (2.8 [1.1-7.1])、非妊時BMI $\geq 25.0 \text{ kg/m}^2$ (1.9 [1.1-3.4])、2点または3点陽性のGDM (3.1 [1.8-5.3])であった。【結論】GDM単胎妊婦においてGDM既往、非妊時肥満、2点または3点陽性のGDMがインスリン療法の導入に独立して関連した。

P-119-10 妊娠糖尿病における簡素化インスリン療法の有効性

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【目的】妊娠糖尿病 (GDM) 妊婦の30-40%がインスリン療法を必要とし、一般的にその多くは糖尿病合併妊娠に準じて食前の頻回インスリン投与を行う強化インスリン療法 (MDI) で管理されている。当院では2008年以降、母体の負担軽減のため、インスリン導入時には、中間型インスリン (NPH) を早朝に1回投与 (必要に応じ就寝前に1回追加投与) する簡素化インスリン療法 (SII法) で開始し、SII法でコントロール不良例はMDI法に移行している。今回SII法のみで管理できた症例の血糖コントロールと周産期予後を評価するとともに、中間型インスリンで危惧される過剰な体重増加について検討した。【方法】24週以降に診断した単胎GDM症例のうち、2015年1月から4年間的前方視的コホートを対象に検討した。【成績】対象症例は403例のうち、59%が食事療法のみ、41%がインスリン療法で管理された。インスリン群の48%はSII法のみで管理し、残る52%はMDI法を必要とした。診断時の血糖値、HbA1c値は、MDI群 $>$ SII群 $>$ 食事療法群の順に高値であった。各群の分娩前の血糖コントロール、分娩週数、児出生体重およびzスコア、および新生児合併症に差を認めず、SII法による母体の過剰な体重増加も認めなかった。【結論】インスリン療法を必要とするGDM症例の約半数は簡素化インスリン療法によって過剰な体重増加を来すことなく十分な血糖コントロールが得られ、その周産期予後も良好であった。本法による母体の負担軽減が期待される。

P-119-11 COVID-19パンデミック期における妊娠中の糖代謝異常合併に関連した周産期アウトカム

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【目的】COVID-19パンデミックに伴い、病院滞在時間を短縮する目的で、糖代謝異常スクリーニングを簡略化する指針が出された。この条件下で当院における妊娠中の糖代謝異常合併率と周産期アウトカムを検討した。【方法】当院で管理した単胎妊娠のうち、パンデミック前 (2019年1月-12月) とパンデミック期 (2020年9月-2021年8月) それぞれにおいて、糖代謝異常合併率 (糖尿病合併妊娠は除く) および糖代謝異常妊婦の周産期アウトカムを比較検討した。2020年5月から、日本糖尿病・妊娠学会発行の「妊娠中の糖代謝異常スクリーニング~COVID-19パンデミック対応~」を導入した。【成績】パンデミック前 (802例) とパンデミック期 (782例) において、糖代謝異常合併率はパンデミック期で低かった (前18% [144/802] vs. 期9.3% [73/782]; $p < 0.0001$)。この中で、Overt DMの割合はパンデミック期で高い傾向がみられた (前3% [5/144] vs. 期6.8% [5/73]; $p = 0.31$)。パンデミック期でインスリン必要例が高率 (前30% [43/144] vs. 期56% [41/73]; $p = 0.0001$) であった。有意差は認めなかったが、糖代謝異常合併妊婦のBMIは高く (前 24.3 ± 5.5 vs. 期 25.4 ± 5.2 ; $p = 0.16$)、体重増加量は少なかった (前 $7.27 \pm 4.7 \text{ kg}$ vs. 期 $6.4 \pm 5.7 \text{ kg}$; $p = 0.23$)。早産率 (前13.9% [20/144] vs. 期12.3% [9/73]; $p = 0.83$)、帝王切開率 (前49.3% [71/144] vs. 期49.3% [36/73]; $p = 1.00$)、児NICU入院率 (前22.9% [33/144] vs. 期30.1% [22/73]; $p = 0.25$) に有意差はなかった。【結論】診断基準の変更に伴い、パンデミック期で妊娠糖尿病の発症率が減少したが、糖代謝異常に関連した周産期アウトカムは大きく変化しないことが示唆された。

P-120-1 COVID-19 流行期に発熱・全身倦怠感の初発症状を呈した劇症1型糖尿病合併妊娠の1例

兵庫県立尼崎総合医療センター

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【緒言】劇症1型糖尿病は1型糖尿病の亜型の1つであり急激な発症経過を辿り、妊娠中に発症すると母児にとって致命的になりうる疾患である。今回、妊娠32週台の妊婦でCOVID-19流行期に劇症1型糖尿病を発症し胎児死亡を来した症例を経験したので報告する。【症例】40歳の初産婦で、糖尿病の既往歴と家族歴はなく、妊娠中の耐糖能検査は正常であった。妊娠32週1日の夜から頻尿の症状が出現し、食思不振、倦怠感も伴った。妊娠32週2日から頻回の嘔吐、38度の熱発および流出感があり前医に連絡した。前医で発熱患者受け入れ困難のため当院に搬送された。当院到着後、COVID-19疑い患者としてPCR検査で陰性を確認するまで隔離対応した。来院時の産科的診察で異常所見なく、胎児心拍数陣痛図(CTG)では胎児心拍120bpmであった。隔離状況下で脱水・不穏に加え、採血困難であった。血糖値489mg/dL、静脈血液ガスでpH7.01、pCO₂10.4、Anion gap16であり糖尿病性ケトアシドーシス(DKA)と診断した。当院到着4時間後にCTGを再開し子宮内胎児死亡が判明した。母体救命のため、大量補液、インスリン治療を行いアシドーシス・高血糖を是正し、翌日には不穏症状が消失した。全身状態が改善した状態で誘発分娩を開始し、3日後に経膈分娩した。その後、精査により劇症1型糖尿病と診断し、インスリン量の調整を行い16日目に退院した。【結論】妊娠中は正常血糖値でもDKAを引き起こすことがあるため、発熱、不穏などの非特異的な症状でもDKAを速やかに鑑別すべきである。またCOVID-19流行期では隔離対応をしつつ、重篤な疾患の診断・治療に遅れが生じないように留意する必要がある。

P-120-2 妊娠初期の高血糖から先端巨大症の診断に至った一例～血糖異常高値から二次性糖尿病を疑う～

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先端巨大症(以下AMと略記)は、成長ホルモン(以下GHと略記)の自律的過分泌とその結果過剰産生されるインスリン様成長因子-I(以下IGF-Iと略記)によって生じる、下垂体腺腫を原因とした全身性代謝性疾患である。AM合併妊娠は腫瘍圧排による下垂体機能不全に伴う不妊症で診断に至り、ホルモンコントロール後に妊娠し良好な周産期経過を辿ることが多いとされている。また未診断例に関しても、妊娠中の高エストロゲンによるGH分泌抑制の影響で、高GHが顕在化せず妊娠終了後に診断となる症例が多く、妊娠中にAMの診断に至ることは少ない。34歳1妊0産、2年前にHbA_{1c}7%前後の2型糖尿病の診断となり内服治療開始となったが治療自己中断された既往があり、今回妊娠初期検査でHbA_{1c}15%と血糖異常高値を指摘された。胎児に明らかな形態異常は認めず、週数相当の発育を認めていた。急激な血糖値の増悪のため二次性糖尿病の存在を疑い、以前の写真と比較して特徴的顔貌(眉弓部の膨隆、前額・下顎の突出および鼻・口唇の肥大)への変化および高血糖下でのIGF-1高値、磁気共鳴画像検査で下垂体腺腫を認め、AMの診断に至った。妊娠と並行した下垂体腺腫の治療も検討されたが、妊娠11週での中絶手術を選択され、その後外科的療法を行う方針となった。妊娠初期の段階で血中エストロゲン値が少量であったために、抑制される前のIGF-1高値を検出した症例である。妊娠初期血糖検査で異常高値を示した症例では、二次性糖尿病の精査が必要となる教訓を得た。

P-120-3 1型糖尿病合併妊娠における妊娠中の血糖コントロールが周産期子後に与える影響

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【目的】1型糖尿病合併妊婦の周産期・新生児子後と、妊娠中の血糖コントロールが周産期子後に与える影響について検討する。【方法】2016年1月から2020年12月までに当科で管理した1型糖尿病合併妊娠34例を対象とし、周産期合併症の頻度について診療録を用いて後方視的に調査した。また、妊娠期間を通じて血糖コントロール良好であった群(n=14)、血糖コントロール不良であった群(n=10)を比較検討した。【成績】妊娠初期で血糖管理目標であるHbA_{1c}:6.2%以上の症例が24例(70.6%)、妊娠許容基準であるHbA_{1c}:7.0%以上の症例が13例(38.2%)とコントロール不良例が多かった。早産12例(35.3%)、帝王切開16例(47.1%)、妊娠高血圧症10例(29.4%)、Heavy-For-Date児9例(26.5%)、胎児形態異常5例(14.7%)であった。妊娠期間を通じて血糖コントロール良好であった群と、血糖コントロール不良であった群において、糖尿病罹患年数、合併症(網膜症・腎症・神経症)、血糖コントロール方法(インスリン頻回注射、持続皮下注射)に関して有意差はなかったが、肥満例(BMI:25kg/m²以上)が有意に血糖コントロール不良群で多かった(P=0.004)。早産率、分娩方法および周産期合併症(妊娠高血圧症、胎児発育不全、胎児機能不全)に関して有意差は認めなかった。児に関しては、形態異常が有意に多く(P=0.015)、うち1例は心血管奇形を含む多発奇形であった。【結論】1型糖尿病合併妊娠は周産期および新生児合併症の発症率が高い。さらに、妊娠期間を通じて血糖コントロール不良な症例は有意に肥満症例が多く、児の形態異常が有意に高率になることが示された。

P-120-4 1型糖尿病合併妊娠と2型糖尿病合併妊娠の周産期予後の検討

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【目的】糖尿病 (DM) 合併妊娠では母児の周産期合併症のリスクが高くなるが, 1型 DM と 2型 DM で周産期予後に差異が生じるかは明らかでない。本研究では1型および2型 DM 合併妊娠の周産期予後を比較検討することを目的とした。【方法】当院で管理し2015年から2021年に分娩に至ったDM合併妊婦28人, 34分娩症例について, 分娩週数, 妊娠合併症, 妊娠前および分娩時のHbA1c, 児出生体重, 新生児血糖値, 持続インスリン皮下注療法および持続血糖測定の有無を解析した。【成績】1型DM合併妊娠は14人, 19分娩, 2型DM合併妊娠は14人, 15分娩であった。分娩週数は38週5日と37週4日で有意差はなかった。妊娠合併症として妊娠高血圧症候群が最多であり, 1型では19分娩中2例, 2型では15分娩中7例と2型で多く認めた。出生体重は1型で有意に高かった ($p=0.0122$, 3406g vs 2811g)。妊娠前HbA1cに有意差はない一方, 分娩時HbA1cは1型で高い傾向を認め ($p=0.0540$, 7.1 vs 6.4), 妊娠中の血糖管理は2型で良好であった。さらに出生体重と分娩時HbA1cで強い相関を認めた ($R=0.5726$, $p=0.0005$)。持続血糖管理および持続インスリン皮下注の有無で血糖管理の改善は認めなかった。新生児血糖2時間値は1型で有意に低かった ($p=0.0329$, 53.17 vs 70.07)。【結論】1型DM合併妊娠は血糖管理が困難で児体重増加や新生児低血糖を起しやす一方, 2型DM合併妊娠は妊娠高血圧症候群を起しやす傾向にあることが分かった。

P-120-5 高トリグリセリド血症を伴った急性膵炎を発症し, 母児ともに不良な転帰をたどった2型糖尿病合併妊娠の一例

熊本大

平尾佳奈, 小寺千聡, 大場 隆, 近藤英治

重症の急性膵炎 (AP) は致死率の高い重篤な病態であり, 妊娠女性やその胎児においても例外ではない。今回われわれはコントロール不良の2型糖尿病合併妊婦が急性膵炎を発症し母児ともに死亡の転帰を辿った症例を経験したので報告する。症例は33歳の1妊0産女性で, 併存症に2型糖尿病と脂質異常症があった。自然周期で妊娠成立したのを機に近医A内科でインスリン自己注射が開始されたが通院を自己中断していた。妊婦健診はB産婦人科クリニックで行われていたが, 妊娠27週1日に腹痛のためC総合病院へ搬送され, 糖尿病性ケトアシドーシスと診断され同日産科を有する当施設へ転院となった。血中トリグリセリド (TG) 14,030 mg/dL と著明な高TG血症およびアミラーゼの上昇が認められ, 高TG血症を伴う急性膵炎 (HTG-AP) が疑われた。急性膵炎に対する加療が開始されたが, 転院の4時間後に循環不全の急速な進行がみられ, 突然の意識障害とともに胎児死亡に至り, 翌日1,050gの死児を経産分娩した。集中治療室での集学的管理によりいったんは会話が可能な状態まで回復がみられたが, 膵炎後に形成された仮性膵嚢胞への感染や繰り返す消化管出血に伴うDICの制御が困難となり, 発症から7か月後に死亡した。妊娠中は, エストロゲンの増加やインスリン抵抗性の増大に伴い高TG血症が助長されることでHTG-APの危険が増大する。本症例はコントロール不良の2型糖尿病の存在が予後不良な転帰に寄与したと考えられる。他診療科との連携を要する耐糖能異常合併妊娠の管理においては, 的確なリスク評価と診療科間の密な連携が求められる。

P-120-6 胎生期低栄養による肝脂肪変性増悪マウスモデルにおける網羅的DNAメチル化解析

浜松医大附属病院

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【目的】疫学研究から胎生期に低栄養環境に曝されることは, 非アルコール性脂肪性肝疾患 (NAFLD) 発症のリスク因子となる。我々は既に, 胎生期低栄養マウスモデルの産生仔において肝脂肪変性が増悪し, 二次胆汁酸である Tauroursodeoxycholic acid (TUDCA) を経口投与することで改善することを報告した。今回, 肝臓におけるDNAメチル化の変化によるエピゲノムの変容が関与する可能性を想定し網羅的解析を行った。【方法】妊娠マウスを自由摂餌群 (NN群) と摂餌制限群 (UN群) に分け, 産生仔に高脂肪餌を与え, Vehicle (Veh) または二次胆汁酸 (Tauroursodeoxycholic acid : TU) を投与し, 23週齢で肝臓をサンプリングした。採取した肝臓組織を用いMBD法並びに次世代シーケンサーを用いてDNAメチル化の網羅的な解析を行った。【成績】UN群で肝脂肪変性の著しい増悪を認めたが, TU投与により著明な改善を認めた。胎生期低栄養により74遺伝子に有意なメチル化を認め (NN-Veh vs UN-Veh), 胎生期低栄養かつTU投与により19遺伝子に有意なメチル化を認め (UN-Veh vs UN-TU), 胎生期の正常栄養かつTU投与により122遺伝子に有意なメチル化を認めた (UN-Veh vs UN-TU)。DNAメチル化の変容を認めた遺伝子群で有意な pathway あるいは遺伝子 ontology を同定することは出来なかった。【結論】胎生期における低栄養環境による肝脂肪変性増悪モデルにおいて, DNAメチル化単独ではプログラム機序を解明できなかった。

P-120-7 非妊娠時 BMI 別の妊娠中体重増加と産科合併症の発症についての検討

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【目的】2021年3月に新たに公表された妊娠中の増加体重目安が、従来と比べ2~3kg引き上げられた背景にはDOHaD学説をはじめとした低出生体重児の様々な疾患リスクが明らかになってきていることが挙げられる。一方で、非妊娠時に肥満である妊婦は帝王切開率や妊娠高血圧症候群(HDP)、妊娠糖尿病(GDM)等の発症頻度が高くなることが知られている。今回当院での非妊娠時BMI別の妊娠中体重増加と産科合併症発症について後方視的に検討した。【方法】2017年~2019年の3年間に37週0日から40週6日に当院で分娩した、単胎、初産婦を対象とした。筋腫核出などの子宮手術歴、骨盤位、前置胎盤、常位胎盤早期剝離、妊娠前からの糖尿病、母体搬送、未受診の妊婦は除外した。非妊娠時BMIは、やせ群(BMI18.5未満)、標準群(BMI18.5以上25未満)、肥満群(BMI25以上)の3つに分類し、妊娠中の体重増加は、A群(9kg未満)、B群(9kg以上12kg未満)、C群(12kg以上)の3つに分類し、分娩方式、HDP、GDM、微弱陣痛、胎児機能不全の発症率、出血量について調べた。【成績】総数2058人中、やせ群は443人(21.4%)、標準群は1521人(74.0%)、肥満群は94人(4.6%)であった。肥満群全体では従来の報告と同様に、帝王切開率、HDP、GDMの発症が有意に高く、出血量が有意に多かった。一方、やせ群・標準群においてA群でGDMの発症が有意に高かった。その他の項目で有意差はなかった。【結論】当院ではやせ群の割合が21.5%と、全国の20代女性の20.7%、30代女性の16.4%と比べて高い。肥満でない妊婦に対する厳格な体重増加制限によりGDMの発症を高める可能性がある。

P-120-8 過去5年間の肥満妊婦の転帰についてのコホート調査

岩手医大

阿部真璃奈

【目的】胎児期の環境は遺伝子発現調節のエピゲノム変化をもたらし、将来の生活習慣病発症に関与すると報告されている。今回我々は、当院で分娩した妊婦の背景を後方視的に分析し転帰について検討した。【方法】対象は、過去5年間に当周産科センターで管理を行なった妊婦1733例のうち初診時のBMIが25以上を対象とした。調査項目は年齢・初診時体重およびBMI、糖代謝異常・精神疾患合併・分娩週数・出生児の出生体重等のデータを収集した。統計はノンパラメトリック検定、回帰分析、因子分析を行なった。統計ソフトはSPSS19.0を用い $p < 0.05$ を有意とした。【成績】対象は318例(18.4%)。年齢、BMI、初診時体重、分娩時体重、産後体重の中央値は、34歳(20~46)、 $28\text{kg}/\text{m}^2$ (25.1~51.4)、70kg(55~140)、75kg(61~124)、69kg(41.2~108)。回帰分析では、母体体重と分娩週数・出生時体重との間に相関を見ない。因子分析は、初診時体重が分娩週数と出生時体重の影響因子になり得る可能性を示した(妥当性:0.49)。NICU入院は82例(23.4%)、精神疾患合併は37例(10.5%)であり、精神疾患合併において低出生体重($p=0.012$)と分娩週数($p=0.05$)が相関を示した。【結論】初診時体重は周産期の転帰に寄与すると考えた。母体栄養状態は、精神疾患合併や胎児発達に影響を及ぼし、結果的にDOHaD説につながると推察する。今後は、肥満妊婦について多施設と共同しデータ収集および解析によって母体栄養と胎児発達・予後の関連について多角的検証が必要と考えた。

P-120-9 胎生期低栄養環境に引き続く生後の急速な Catch-up growth が脂肪組織に及ぼす遺伝子発現の解析:新たな責任遺伝子の同定を目指して

浜松医大附属病院

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【目的】胎生期低栄養環境を経験し、生後に Catch-up growth を来すと肥満や生活習慣病を発症するハイリスク群となる。今回、マウスモデルを用い脂肪組織の網羅的遺伝子発現解析を行った。【方法】妊娠マウスを自由摂餌群(NN群)と摂餌制限群(UN群)に分け、授乳匹数を調整し catch-up growth を促した。産生仔に高脂肪餌を与え、Vehicle(Veh)または二次胆汁酸(Tauroursodeoxycholic acid:TU)を投与した。16週齢の精巣周囲脂肪組織のマイクロアレイ・遺伝子エンリッチメント解析を行い、定量PCRを行った。【成績】16週齢産生仔の体重・脂肪重量は、NN群と比べUN群で有意に増加し、TU投与で改善した($p < 0.05$)。胎生期低栄養ならびにTU投与で共通して変化した44遺伝子をターゲットとして遺伝子エンリッチメント解析を行ったが、有意な Gene Ontology は特定できなかった。そこで、遺伝子改変動物の既報を調査し遺伝子Xに着目した。遺伝子Xは orphan receptor で、ノックアウトマウスの既報で高脂肪餌に対し抗肥満性を示す。マウス全身臓器の遺伝子Xの発現を解析したところ、通常餌投与では脂肪組織における発現量は少ないが、高脂肪餌により脂肪組織特異的に遺伝子発現が増加し全身の臓器の中で最も遺伝子発現が多くなることが明らかとなった。現在、3T3-L1細胞を用いて遺伝子Xの脂肪細胞における機能解析を行っている。【結論】胎生期低栄養環境ならびに生後 Catch-up growth を来すマウスモデルの遺伝子発現解析から遺伝子Xを gene of interest (GOI) として特定し、解析中である。

P-121-1 子宮筋層内妊娠の2症例

松江市立病院

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子宮筋層内妊娠は異所性妊娠の一つであるが、その頻度は非常にまれであり、早期診断が難しい。今回、2例を経験したので報告する。症例1は38歳、2妊0産でART妊娠の流産後、自然妊娠が成立した。妊娠6週時、経陰超音波検査で子宮内に胎嚢を認めず、左付属器付近に胎嚢様像を認め、血中hCG値1373mIU/mlと高値であったため、異所性妊娠を疑われた。妊娠7週時も所見が変わらず、診断と治療目的に腹腔鏡下手術を行った。術中は卵管に腫大なく、妊娠部位は特定できず、術後にMRI検査を行って、子宮筋層内の胎嚢像を確認して子宮筋層内妊娠と診断した。治療は薬物療法を希望されたため、MTX(50mg/m²)を投与し、血中hCG値は速やかに陰性化した。症例2は36歳、0妊で人工授精にて妊娠成立した。妊娠6週時、子宮内に胎嚢を認めず、血中hCG値4740mIU/mlと高値であった。3日後の当院初診時も子宮内に胎嚢はみられず、血中hCG値10470mIU/mlと上昇していた。経陰超音波検査では胎嚢様の囊胞像が子宮後壁筋層内の右卵管角近傍に確認できたため、子宮筋層内妊娠を強く疑った。腹腔鏡下手術を行い、術中に超音波検査を併用して妊娠部位を特定し、子宮後壁筋層を切開して絨毛組織を摘出した。術後は、血中hCG値は速やかに低下し、治療終了となった。【結語】非常にまれな異所性妊娠である子宮筋層内妊娠の症例を経験した。血中hCG値が高値であるにもかかわらず、妊娠部位が特定できない場合は、筋層内妊娠も念頭に超音波検査並びに術中所見を慎重に観察する必要があると考えられた。

P-121-2 穿孔部位から子宮筋層内妊娠破裂の可能性が考えられた一例

神戸大附属病院

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異所性妊娠の部位の約95%は卵管妊娠であり、筋層内妊娠は非常にまれである。原因としては子宮筋層の損傷が原因の一つとされており、帝王切開術や筋腫核出術だけではなく生殖補助医療の関与も指摘されている。今回は妊娠初期に子宮破裂から出血性ショックとなり、術中所見から子宮筋層内妊娠破裂の可能性も考えられた症例を経験したので報告する。症例は41歳、2経妊1経産、自然妊娠成立後、前医診察にて子宮腔内に胎嚢を認めていたものの、間質部妊娠の可能性も指摘されていた。予定日決定後、妊娠8週6日に突然の腹痛、嘔吐を認め、当院救急へ救急車搬送となった。救急医による経腹超音波にて腹腔内出血を疑う所見を認め、当科診察にて子宮外タグラス窩に胎嚢を確認した。出血性ショックに至っており、輸血を施行しながら同日緊急で腹腔鏡下手術を施行した。術中所見では子宮後壁左寄りに穿孔部位を認めたが、卵管間質部からはやや離れた位置であり、筋層内妊娠であった可能性が示唆された。同部位に100倍希釈ピトレシン局注後、子宮筋層を楔状に切除を行い、さらに左卵管切除を施行した。内膜、筋層を縫合し止血確認後、手術終了となった。術後はhCGも低下し経過は良好であり、術後7日目に退院となった。本症例は破裂部位から筋層内妊娠の可能性が示唆されたが、過去に子宮内容除去術の既往があり、筋層内に損傷があった可能性も考えられる。筋層内妊娠は非常に稀で診断も困難な場合があるが、破裂によるリスクも高く、若干の文献的考察を含めて報告する。

P-121-3 当院における帝王切開瘢痕部妊娠4例についての検討

関西医大附属病院

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【緒言】帝王切開瘢痕部妊娠(cesarean scar pregnancy:CSP)は帝王切開率の上昇に伴い報告数が増加しているが、定まった治療方針がない。当院で経験した4例のCSPの経過を示し治療方針について検討した。【症例1】32歳、3妊2産(帝王切開2回)。治療前の血中hCGは51506.0IU/Lで胎児心拍あり。D&E施行し、術後74日目にhCG陰性化。【症例2】32歳、4妊3産(帝王切開3回)。治療前の血中hCGは58201.7IU/Lで胎児心拍なし。D&E施行し、術後44日目にhCG陰性化。【症例3】34歳、7妊2産(帝王切開2回)。治療前の血中hCGは16328.0IU/Lで胎児心拍あり。前回帝切から1年以内でありMTX療法を選択。MTX50mg/m²を胎嚢内投与したが効果不良にてday7に再度MTX50mg/m²を胎嚢内投与した。day54にhCG陰性化。【症例4】32歳、6妊5産(帝王切開5回)。治療前の血中hCGは50640.6IU/Lで胎児心拍あり。子宮温存希望が強くMTX治療後に子宮形成術を試みる方針とした。MTX50mg/m²とエタノールを胎嚢内投与したが効果不良にてday7にMTX50mg/m²を全身投与。day81にhCGは陰性化した。瘢痕部血腫の増大を認め子宮温存は不可能と判断しday108に腹腔鏡下単純子宮全摘術を施行した。症例1,2は妊娠9週未満、筋層が保たれており、D&E単独で治療を完遂することができた。症例3,4は推奨される適応基準より治療前hCG値が高く追加投与を要し、症例4は結果的に子宮全摘術を施行した。【結語】CSPには標準治療を示すガイドラインはなく、治療方針は各施設の判断に委ねられる。患者の希望を尊重しながら、適応と時期を見極め、症例ごとに治療法を選択することが重要と考える。

P-121-4 高度な子宮腺筋症に発症した異所性妊娠の一例

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【緒言】異所性妊娠は全妊娠の約1-2%で、近年、生殖補助医療（ART）による妊娠数の増加に伴い増加傾向にあると言われている。今回、子宮奇形および高度な子宮腺筋症の患者でART後に異所性妊娠をきたした症例を経験した。【症例】37歳2妊0産（人工妊娠中絶1回）、双頸双角子宮であり、12歳で腔留血腫に対して手術の既往がある。36歳から不妊治療を開始し、今回顕微授精-胚移植で妊娠が成立した。妊娠7週で胎嚢が確認できず前医へ紹介となり、MRIで右側子宮の角部から卵管間質部周囲に胎嚢が確認されたものの胎芽は確認できなかった。胎嚢周囲の子宮筋層は非薄化しており、筋層への浸潤が疑われた。血中hCGは上昇を続け、11.8万mIU/mLまで上昇した。妊娠10週で当院紹介となり、少量の出血もみられたことから入院での経過観察とした。経過観察のみでhCGは低下がみられ、約6週間で退院し、外来加療とした。その後妊娠組織の縮小がみられ、hCGは陰性化を認めた。【考察】本症例ではメトトレキサートによる薬物療法や外科的治療を検討していたところ、自然にhCGの低下が得られ、そのまま入念な経過観察を継続したところ軽快を得られた。MRIから着床部位は子宮角部から卵管間質部にかけてと診断し、子宮筋層への妊娠組織の浸潤が疑われた。この着床機序には子宮腺筋症が関与したのではないかと考えられたため、文献的考察を交えて発表する。

P-121-5 当院で経験したダグラス窩腹膜妊娠の2症例

八尾市立病院

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【緒言】腹膜妊娠は稀な疾患であり、全異所性妊娠の約1%程度に発生すると報告されている。当初卵管妊娠を疑い試験腹腔鏡手術を施行したが、ダグラス窩腹膜妊娠であった2症例を経験したので報告する。【症例1】38歳、0妊0産。最終月経より6週5日の時点で子宮内に胎嚢を認めず、血清hCGは1,998mIU/mlであった。その後も子宮内に胎嚢を認められず異所性妊娠を疑われ、7週5日に当科紹介受診した。経腔超音波検査でダグラス窩に左卵巣に接した29mm大の腫瘤を認め胎児心拍を確認した。左卵管妊娠の疑いで同日腹腔鏡下手術を行った。両側付属器に異常を認めず、ダグラス窩に持続的に出血する部位を認めた。術中に経腔超音波検査を行い、同部位と術前に腫瘤を認めた部位が一致した。出血部を焼灼し手術を終了した。腹腔内吸引液には組織が含まれており、病理検査にて絨毛組織であることが判明した。【症例2】44歳、2妊1産。最終月経より6週6日の時点で子宮内に胎嚢を認めず、血清hCGは3,385mIU/mlであった。異所性妊娠を疑われ、3日後に当科紹介受診した。5日後でも子宮内に胎嚢を認めず右付属器領域に低輝度領域を認めた。血清hCGは8,420mIU/mlであった。右卵管妊娠の疑いで同日腹腔鏡下手術を行った。両側付属器に異常を認めず、ダグラス窩に埋没するように絨毛組織を認めた。【結語】今回の2症例の経験を踏まえ、腹膜妊娠の可能性を視野に入れながら手術を行うことが重要である。

P-121-6 当院で腹腔鏡下手術により診断および治療し得た腹膜妊娠の3症例

坂総合病院

増井紗帆, 佐藤孝洋, 藤本久美子, 片平敦子, 船山由有子

【緒言】異所性妊娠のうち腹膜妊娠の頻度は約1%程度とされる。2002年～2021年に当院で異所性妊娠に対して手術を行った144症例（腹腔鏡下132件、開腹12件）のうち、腹膜妊娠は腹腔鏡下手術3症例で、頻度は2.08%であった。【症例】症例①：28歳、1妊0産。主訴は腹痛、不正性器出血で前医受診し、異所性妊娠疑いで当科紹介。最終月経より妊娠6週2日。経腔超音波でダグラス窩右側に4cm大の血腫を、入院後のMRIにて左卵管～ダグラス窩に胎のう様構造と血腫を認め、腹腔鏡下手術を施行した。ダグラス窩の血腫除去時に共に腹膜が挙上し着床部位と判断した。症例②：22歳、1妊0産。徐々に増悪する腹痛のため受診。最終月経より妊娠8週相当。経腹超音波にてダグラス窩、モリソン窩に血腫を認めた。腹腔鏡下で両側卵管は正常で、ダグラス窩の血腫に絨毛組織を、ダグラス窩右側の直腸側より出血点を確認し着床部位と判断し、腹膜妊娠の診断。症例③：37歳、1妊0産。最終月経より妊娠5週相当。主訴は不正性器出血と腹痛にて受診。経腔超音波にてダグラス窩右側に4cm大の血腫と2cm大の胎のう様構造を認め、MRIで同部位に辺縁増強効果を伴う胎のう構造と血腫を確認。腹腔鏡下にてダグラス窩右側骨盤壁に被包化された血腫が付着し、剝離面より出血を認め着床部位と判断した。3症例とも腹腔鏡下に着床部位の診断、止血可能で治療を完遂できた。【考察】腹膜妊娠は異所性妊娠の中でも稀な疾患で、経腔超音波では診断が困難な場合も少なくない。異所性妊娠を疑う症例には診断と治療を兼ねた腹腔鏡下手術が有用で、臨床的に時間の余裕がある際にはMRIも有効な診断方法と考える。

P-121-7 術前に着床部位同定が困難であった腹膜妊娠の1例

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【緒言】腹膜妊娠は異所性妊娠のうち1%程度と稀な疾患であり、術前診断に苦慮することが多い。【症例】34歳、2経妊1経産。第1子は分娩停止の適応での緊急帝王切開術にて分娩となった。今回自然妊娠にて妊娠成立した。最終月経より5週6日、前医受診時は子宮内腔に胎嚢を認めなかった。6週1日、急激な下腹部痛を自覚し前医受診し、左卵管妊娠疑いの診断で当院に搬送となった。来院時の血清hCG値は2985mIU/ml、症状は左下腹部痛のみであり、性器出血は認めなかった。経腔超音波断層法にて左卵管の峡部～卵管角部に胎芽を認め、緊急腹腔鏡手術を行う方針とした。腹腔内を観察すると、膀胱子宮窩に凝血塊および血液貯溜を認め、左卵管間膜は一部穿破しており、子宮体部左前面の漿膜上に妊娠組織を疑う出血交じりの腫瘍の存在を認めた。帝王切開術既往であり、帝王切開痕跡部妊娠も疑ったが明らかな筋層への浸潤所見は認めなかった。一部子宮体部表層からの剝離もし得る状況であり、腹膜表面への着床が疑われる所見であった。腫瘍を慎重に剝離し、欠損させることなく摘出を行い、絨毛組織が含まれていることを確認し手術を終了した。術後6時間後の血清hCG値は1700mIU/ml、術後3日目は553mIU/mlと低下を示した。術後経過良好であり、術後3日目に退院となった。以降は当科外来管理となり、月経の再開も確認し、術後21日目には血清hCG値は検出感度以下となったことを確認した。【結語】術前に着床部位の同定が困難であった腹膜妊娠に対して腹腔鏡下手術で治療を完遂した1例を経験した。

P-121-8 卵管切除術後に同側異所妊娠を繰り返した1症例

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卵管切除術後に同側異所性妊娠を繰り返した症例を経験したので報告する。症例は31歳、3妊0産。18歳時に異所性妊娠にて開腹手術歴あるが詳細不明。中絶1回、初期流産1回。妊娠反応陽性のため当院受診、経腔エコーにて左付属器あたりに胎児心拍を認めたため異所性妊娠の診断下に腹腔鏡手術を施行したところ、左卵管は中央の大部分が欠損し、左卵管角の突起と卵管采のみ認め、過去の手術によるものと考えた。切断されている卵管采から妊娠物が露出していたためこれを卵管采ごと摘出し、また卵管角側の突起を電気凝固装置にてシーリングした。術後経過良好で毎月の排卵を確認し、4か月後妊娠反応陽性となった。しかし今回も子宮内にGSを認めず、腹腔鏡を施行したところ左卵管間質部の膨大を認め左卵管間質部妊娠の診断下に左間質部切除と縫合術を施行した。

P-122-1 妊娠反応陰性の急性腹症が子宮外妊娠であった一症例

成田赤十字病院

佐藤史朗, 小幡新太郎, 伊藤孝輔, 竹原直希, 西方紀子, 真田道夫, 山ノ内美紀, 清水久美子, 埜 真輔

症例は27歳女性、2妊1産(帝王切開1回)、特記すべき既往歴なし。最終月経はX-29日から8日間、整。X-1日から特に誘因なく腹痛が出現して同日17時ごろ前医受診。妊娠反応陰性、腹腔内出血あり、Hb 12.0g/dl。卵巣出血疑いで前医入院して経過観察となっていたが、X日0時の採血でHb 9.5g/dlと貧血の進行を認めたため当院救急搬送となった。当院での診察では意識清明、経腔エコーで肝周囲にまでおよぶ腹腔内出血を認めた。採血・採尿所見はWBC 12000/ μ l, Hb 8.9g/dl, Plt 239000/ μ l, CRP 0.26mg/dl, 血中HCG 3.8mIU/ml, 血糖 218mg/dl, APTT 30.8秒, PT-INR 1.13, Dダイマー 2.6 μ g/ml, 妊娠反応(-)であった。持続出血を伴う卵巣出血疑いで同日全身麻酔下に腹腔鏡での緊急手術施行。腹腔内には上腹部にまでおよぶ多量の腹腔内出血貯留あり。吸引を進めていくと卵巣には腫大や出血なし。腹腔内には明らかな癒着なし。子宮表面に子宮内膜症病変あり。左卵管の腫大と持続出血を認めたため左卵管妊娠の診断で左卵管切除を施行した。手術時間は52分、腹腔内出血650mlであった。術後経過は良好であり、術後4日目に退院となった。病理は拡張した卵管内の血腫に変性絨毛を認めており、左卵管妊娠の診断であった。術後に聴取した月経歴、性交渉歴では1周期前の月経はX-62日から8日間、性交渉はX-47日に避妊なし、X-16日に2日後に緊急避妊薬内服、X-3日の3回であった。経過からは妊娠反応陰性は卵管流産であり、X-62日が最終月経、X-29日の出血が妊娠初期の不正出血であった可能性が考えられた。当院での過去の症例や文献的考察も交えて報告することとする。

P-122-2 出血性ショックを伴い鑑別が困難であった子宮頸管妊娠の一症例

誠光会草津総合病院
中川渥裕

【緒言】子宮頸管妊娠は、2400 妊娠に 1 例とまれな疾患であり、止血困難な大量出血をきたしうる疾患で臨床的に重篤な結果をたどる可能性がある。今回、近医より性器出血・妊娠反応陽性で来院し絨毛性疾患との鑑別が困難であった子宮頸管妊娠の症例を経験したので報告する。【症例】2 妊 2 産 20XX 年 6 月ごろより不正性器出血を自覚しており、同年 9 月に性器出血が多量になったため、近医を受診した。近医にて妊娠反応陽性・多量性器出血を認めため、当院に救急搬送となった。最終月経は不明で、当科で施行した HCG34949 と高値を認め、内診では多量の性器出血、子宮頸部より脱出する腫瘍を認めた。内診後血圧 85/40mmHg、脈拍 120 回/分とショック状態を認め ICU 入院となった。入院翌日に多量性器出血 Hb7.8mg/dl を認め、骨盤部 MRI 検査では絨毛性疾患も否定できなかったため、緊急で腹腔鏡下子宮全摘術を施行。手術時間：3 時感 6 分、出血量 10mL、摘出標本は妊娠に伴う脱落膜化であり絨毛性疾患も否定的であった。術後経過は良好で術後 6 日目に退院となった。【結語】多量の性器出血・妊娠反応陽性にて子宮頸管妊娠と診断した症例を経験したので報告した。子宮外妊娠の頻度や経過について文献的考察を含めて発表する。

P-122-3 卵管膨大部妊娠で卵管切除後に同側残存卵管峡部双胎妊娠を来した 1 例

砂川市立病院
櫻井愛美, 宇田智浩, 佐藤元哉, 佐野友宇子, 山下陽一郎, 津田加都哉

【緒言】卵管異所性妊娠のうち、峡部や間質部妊娠は稀であり、卵管切除後の同側卵管への異所性妊娠の発生はさらに稀であるが、国内でも数十例報告を認める。今回、卵管膨大部妊娠で卵管切除後、残存した同側卵管峡部へ双胎妊娠を来した 1 例を経験したので報告する。【症例】38 歳、G4P0SA2。36 歳時に右卵管膨大部妊娠のため当院で腹腔鏡下右卵管切除術を施行したが、その際わずかに卵管峡部が残存していた。その後他院で生殖補助医療を受け、今回凍結胚移植が行われた。妊娠 5 週 6 日、子宮内に胎嚢を確認できず、右付属器領域に 10mm 大の 1 つの胎嚢および 2 つの卵黄嚢様構造物を認めたことから異所性妊娠が疑われ当院紹介となった。紹介時の画像所見では妊娠部位が確定できず精査目的に管理入院とした。妊娠 6 週 1 日、同部位は 16mm 大へ増大し画像検査にて右卵管峡部への妊娠が疑われた。さらに一絨毛膜双胎妊娠の状態であり胎児心拍も確認されたため同日腹腔鏡下手術の方針とした。術中所見は前回手術で残存した右卵管峡部への妊娠で相違なく、子宮筋層と卵管妊娠部との境界が認識できたため、同部位に希釈パソプレシンを局注し、異所性妊娠部を切除した。一部筋層に切り込んだ状態となり同部位の縫合を行い手術は終了した。術後血清 hCG 値の低下はやや緩徐であったが、術後 38 日目に陰性化が確認できた。【考察】卵管切除後の残存卵管峡部への妊娠を予防するには、卵管切除時にできるだけ子宮に近い卵管角での切除が大切であり、今回反省すべき点と考える。一方、間質部妊娠に関しては確実な予防法の報告はない。卵管切除後も同側卵管妊娠となる可能性を考慮した上で診療にあたるのが大切と考えられる。

P-122-4 卵管間質部管腔外妊娠に対して腹腔鏡下卵管角部切開術を行い、卵管疎通性を温存しえた一例

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黒澤大樹¹, 渡辺 正¹, 佐藤直人¹, 村岡由真², 松澤由記子², 中西 透², 酒井啓治², 渡部 洋²

36 歳 2 妊 0 産 (35 歳 稽留流産で流産手術)【既往歴】28 歳 腹腔鏡下子宮筋腫核出術 (他院), 31 歳 下垂体腺腫手術, 35 歳 子宮鏡下筋腫摘出術 (当院)【現病歴】最終月経より 5 週 4 日、妊娠成立し当科受診。経陰超音波断層法で子宮内に胎嚢を認めず、血中 hCG は 2213mIU/ml であった。6 週 1 日、血中 hCG は 5661mIU/ml と上昇し、経腹超音波断層法で右卵管角部に 10 mm の胎嚢様の嚢胞を認めた。経過より正常妊娠は否定的と判断し、造影 CT 検査を行い、同部位に 12mm の嚢胞を認め、右卵管間質部妊娠が疑われた。同日、腹腔鏡手術を行い、右卵管間質部妊娠と診断し、右卵管角部切開術を行った。腫大部に 200 倍希釈パソプレシンを局注後、超音波凝固切開装置で切開し、絨毛組織を剝離摘出し、E・Z パースを用いて搬出した。絨毛組織摘出直後に卵管通色素検査を行ったところ、角部切開創からはインジゴカルミンの流出は認めず、右卵管采より流出を認めた。MTX50mg を着床部に局注し、切開部を 2-0PDS を用いて単結紮縫合した。手術時間 72 分、出血少量であった。手術翌日、血中 hCG2314mIU/ml と低下し、術後 58 日目に血中 hCG は陰性化した。術後 3 か月で子宮卵管造影検査を行い、両側卵管疎通を確認した。術後 7 か月で自然妊娠成立し、継続中である。卵管間質部妊娠に対し、角部楔状切除の報告が多くみられる。しかし、楔状切除では患側卵管は摘出となり、その後の妊娠における子宮破裂の報告も散見される。今回の症例は管腔外妊娠と考えられ、右卵管角部切開術によって患側卵管を温存することができ、子宮切開も最小限に抑えることができた。本術式は子宮、卵管に対する損傷が少ない優れた術式である。

P-122-5 当院の異所性妊娠手術における開腹手術と腹腔鏡下手術の比較

防衛医大病院

角倉 仁, 宮本守員, 岸本直久, 伊藤 翼, 大塚由花, 岩橋秀樹, 垣本壮一郎, 鈴木理絵, 笹 秀典, 高野政志

【目的】当院での異所性妊娠手術の術式の違い（開腹手術、腹腔鏡下手術）によって、周術期患者予後に影響があるか比較、検討すること。【方法】2015年5月から2021年5月まで当院で施行された異所性妊娠手術を施行された症例を対象とし後方視的に検討した。基本的に2015年5月～2018年11月は開腹手術、2018年12月～2021年5月は腹腔鏡下手術を主体に実施施行した。【成績】異所性妊娠手術は49例、開腹手術が28例、腹腔鏡下手術が21例だった。妊娠部位は右卵管妊娠26例、左卵管妊娠が19例、右子宮間質部妊娠が1例、左卵管間質部妊娠が3例だった。術式（開腹手術/腹腔鏡下手術）によって、術後入院日数は7日間/3日間（中央値、 $p < 0.01$ ）で有意に腹腔鏡下手術が少なかった。出血量は239ml/100ml（中央値、 $p = 0.04$ ）で有意に開腹手術の出血が多かった。患者背景（年齢、身長、体重、BMI、経妊経産歴、妊娠週数、手術時間）で両群に差はなかった。【結論】異所性妊娠手術において腹腔鏡下手術は開腹手術と比較して有意に入院日数を短縮できる。また腹腔鏡下手術の方が出血量が少ない結果となった。手術時間は術式によって差はなかった。今後さらなる症例の蓄積が求められる。

P-122-6 当院における異所性妊娠症例に関する検討

市立砺波総合病院

稲田真三子, 寺西穂波, 古村恭子, 佐々木泰

【目的】当院の異所性妊娠症例について現状と治療の妥当性について検討する。【方法】2017年1月～2021年9月に、当院で異所性妊娠と診断した症例を対象に、診断・治療・転帰に関する諸項目に関して後方視的に検討した。【成績】異所性妊娠は22例で、年齢31(24-42)歳、経妊2(1-4)回、経産0(0-2)回であった（中央値（最小-最大））。妊娠成立方法は、14例(63.6%)が自然妊娠、3例(13.6%)がAIH妊娠、5例(22.7%)がIVF/ICSI妊娠であった。治療方法は手術（全例腹腔鏡手術、卵管妊娠では卵管切除術）が17例(77.3%)、MTX全身投与が2例(9.1%)、待機療法が3例(13.6%)であった。手術症例における妊娠部位別症例数は、卵管膨大部11例、卵管狭部3例、卵管間質部1例、腹膜1例、子宮内1例で、術前の異所性妊娠の正診率は94.1%であった。手術タイミングでは、緊急手術6例、準緊急手術（診断日に手術）4例、待機手術（診断翌日以降の手術）が7例で、予定通り待機手術を行えたのは70%であった。腹腔内貯留血液を含む手術時出血量は、緊急手術で487.5(0-1300)g、準緊急手術/待機手術で0(0-600)gであり、緊急手術の方が出血量は有意に多かった（ $p = 0.04$ ）（中央値（最小-最大）、出血少量は0gで計算）。初回治療後に追加治療をした症例はなく、persistent ectopic pregnancy (PEP) の発症はなかった。自然妊娠/AIH妊娠で成立した異所性妊娠の治療後の自然妊娠率は46.2%であった。【結論】異所性妊娠の症例背景や妊娠部位については、これまでの報告と同程度であった。PEPの発症はなく適切な治療ができていた。今後は術前の診断精度をさらに向上させ、手術時期を適切に判断する必要があると思われる。

P-122-7 異所性妊娠における腹水中 HCG- β 値の有用性の検討

セント・ルカ産婦人科

伊東裕子, 津野晃寿, 甲斐由布子, 宇津宮隆史

【目的】異所性妊娠は早期診断および早期の外科的治療が卵管破裂等の発症予防に繋がる。当院では妊娠判明時血中 HCG- β 値を測定、超音波検査での診断を行う。異所性妊娠を疑う場合、腹腔内に腹水を認めた場合少量であっても IVF の採卵の手技によりダグラス窩穿刺を施行し腹水中 HCG- β 値を測定することで、早期診断・手術への移行を目指している。今回、腹水中 HCG- β 値と血中 HCG- β 値との関連性と有用性を検討した。【方法】当院にて1992年6月～2021年8月までに異所性妊娠で腹腔鏡下手術を施行した219例のうち、術後病理検査によって異所性妊娠と確定診断され、かつ血中 HCG- β 値測定とダグラス窩穿刺による腹水中 HCG- β 値を同日に測定し得た77症例を対象とした。症例の年齢、妊娠週数、血中および腹水中 HCG- β 値、異所性妊娠部位、術式および術後妊娠の有無を検討した。【成績】症例の平均年齢33.8歳、妊娠週数 5.8 ± 0.77 週、妊娠部位は卵管妊娠71例、卵巣妊娠3例、腹膜妊娠3例。血中 HCG- β 値 $41.0 \sim 57,300.0$ IU/L（平均 $2,807.0$ IU/L）、腹水中 HCG- β 値 $211.0 \sim 60,830.3$ IU/L（平均 $12,747.3$ IU/L）。術式は腹腔鏡下卵管切開術46例、腹腔鏡下卵管切除術21例、腹腔鏡下腹腔内洗浄（卵巣・腹膜妊娠も含む）10例。術後妊娠に至ったのは術式別にそれぞれ26例(56.5%)、16例(76.2%)、5例(50.0%)と77例中47例(61.03%)であった。【結論】腹水中 HCG- β 値は血中 HCG- β 値より数倍から十倍以上高かったことから、異所性妊娠の診断を早期に行えることが示めされた。腹水が少量であっても採卵の手技を用いることで安全に検査を行え、早期診断し腹腔鏡下手術へ移行できることが卵管破裂など重症化の予防に繋がると示唆された。

P-123-1 子宮鏡下筋腫核出術後に生じる Asherman 症候群の発生に関する検討

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【目的】子宮鏡下筋腫核出術では、術後に子宮腔癒着が生じると、再手術、子宮内膜菲薄化や癒着胎盤などの問題がある。当院で子宮鏡下筋腫核出術を施行した症例を対象に、子宮腔癒着の発生に関する検討を行なった。【方法】2008年3月から2021年8月までに子宮鏡下筋腫核出術を施行した症例を対象とした。一部症例では、癒着防止として術後にFD-1やシリコンプレート挿入し、ホルモン補充療法を併用した。術後1か月後を目安にセカンドルック子宮鏡を行い、癒着の有無を評価した。手術時に子宮筋腫の位置や突出率、直径、重量を評価し、また複数の筋腫を認める場合は、筋腫が対面に存在する (apposing submucous myoma : ASM) 群と、それ以外 (non-apposing submucous myoma : NASM) の群に分けて、1個のみ (Single : SL) の群と比較して癒着率を検討した。【成績】217人の患者を対象とし、SL175人、NASM31人であった。そのうち、術後子宮腔癒着を認めたのは18人 (10.3%)、4人 (36.4%)、1人 (3.2%) と、ASM群で多かった。SL群では、癒着発生に関して、筋腫の位置 (底部とそれ以外)、突出率、癒着防止の有無で有意差を認めなかった。癒着防止はASM8人 (72.7%)、NASM9人 (29.0%) で、ASMの方が有意に多かった ($p=0.03$) が、両群ともに癒着防止の有無で、癒着発生に関して有意差は認めなかった (いずれも $p=0.49$)。【結論】子宮鏡下筋腫核出術において、子宮筋腫が対面に存在する場合は、術後子宮腔癒着のリスクが高いと予測できる。

P-123-2 細径シェーバー型子宮鏡 TruClear[®]による子宮内膜ポリープ切除の安全性、有用性の検討

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【目的】子宮内膜ポリープは頻度の高い疾患で、超音波検査で簡単に見つかり、再発も多い。そのため、子宮鏡下ポリープ切除術は、不妊治療中の患者において、着床環境の改善のために選択されることが多い。近年、新しく細径シェーバー型子宮鏡システム (以下S法) が発売になり、当院でも導入したため、その経験をまとめ、従来法のループ電極型子宮鏡システム (以下L法) との比較検討を行った。【方法】S法を導入した2020年5月から2021年9月中旬までの子宮鏡下ポリープ切除術62件中、S法28件とL法3件の実施状況を比較検討した。【成績】術前の頸管拡張に関して、S法は導入当初の4例のみ施行で、その後は必要なく、L法では全例頸管拡張を要している。術中の頸管把持・牽引・頸管拡張についてもS法では不要で、L法では全例施行していた。L法が止血に優れていると考えられるが、S法で追加のパワースーツを必要とした症例はなかった。手術時間はS法平均11分、L法16分と有意にS法の方が短時間だった ($p=0.013$; t 検定)。術後に痛み止めを要する症例はS法5例、L法13例で有意差はない ($p=0.0974$; Fisher検定) が、S法で痛みが少ない印象を得た。【結論】S法は頸管拡張を要しないため、術前処置の省略、術中及び術後の痛みの軽減や無麻酔での外来子宮鏡手術を可能とするばかりではなく、頸管無力症のリスクを軽減する。また、パワースーツを使わないことは子宮内膜の損傷を極力抑えられ、内膜の菲薄化を回避できる。システムは非常に簡単で、子宮鏡初心者にも導入しやすい手術と考える。

P-123-3 子宮鏡下子宮筋腫切除術一周術期・周産期管理の実態調査—

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池本裕子¹, 竹田 純², 長井咲樹¹, 手島 薫¹, 齊藤寿一郎¹

【目的】子宮鏡下子宮筋腫切除術 (TCR-M) は一般的に低侵襲とされるが、術者の力量による差が大きく、実際の手術対象は不明である。また、TCR-M術後の避妊期間や分娩方法、患者・家族へのインフォームド・コンセント (IC) の状況など周術期管理や周産期管理についての実態も不明である。今回、その実態を把握すべく、アンケート調査を行った。【方法】2020年8月から10月に子宮鏡手術執刀医 (A)、周産期担当医 (B) それぞれを対象とした匿名アンケート調査を実施した。本研究は当院倫理委員会、MFICU連絡協議会共同研究として承認されている。【成績】回答率はA、Bそれぞれ57.8% (85/147)、74.9% (182/243) であった。子宮鏡手術執刀医の28.2%が子宮筋腫4個以上、30.8%が突出度50%未満、41.0%が30mm以上の病変も手術対象としていた。術後妊娠許可までの期間は、74.3%が術後3か月以下であった。子宮鏡手術執刀医からの診療情報提供書による積極的な診療情報提供は20.5%に留まり、78.2%は間接的、受動的な対応であった。分娩方針は、周産期担当医の72.3%が手術内容を確認して決定していたが、2.9%は手術内容の確認なく、選択的帝王切開術を予定すると回答した。また、周産期合併症の患者・家族に対するICは子宮鏡手術執刀医の39.0%、周産期担当医の17.6%が行っていない。【結論】本検討より多発粘膜下筋腫や突出率が低い子宮筋腫などの困難症例も一定数行われていることが分かった。術後妊娠時に十分な診療情報提供やICが行われず、適切な分娩方法が選択されていない可能性が少なからずあることが示唆された。TCR-M術後妊娠の管理方針について標準化するためのエビデンスを構築することが望まれる。

P-123-4 凍結融解胚移植を契機に診断された帝王切開・流産手術後の子宮内腔癒着症2例

東邦大医療センター大森病院

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自覚症状なく、融解胚移植を契機に診断された子宮内腔癒着症2例について報告する。【症例1】40歳, G2P1SA1。融解胚移植により妊娠成立、胎児機能不全のため緊急帝王切開術を実施。術後持続する性器出血を認め子宮仮性動脈瘤の診断となり左子宮動脈塞栓術を実施した。塞栓術から1年6か月時に自然妊娠したが流産しMVAを実施。術後3か月時に、第2子妊娠に向けた融解胚移植前スクリーニングの子宮鏡で内腔癒着を認めた。軟性子宮鏡で癒着は解除可能で、その後再癒着を認めず融解胚移植実施。妊娠成立した。【症例2】43歳, G4P1SA2mole1。融解胚移植により妊娠成立、妊娠高血圧のため緊急帝王切開術を実施。分娩後1年3か月時に第2子希望し解胚移植周期を計画したが内膜菲薄のため子宮鏡を実施したところ内腔に強固な癒着を認めた。経血の減少などの自覚症状を認めていなかった。子宮鏡下手術にて癒着を解除し、IUDを留置しカウフマン療法を2周期実施。今後、IUDを抜去し子宮鏡予定である。子宮内腔癒着症では続発性無月経などの自覚症状を契機として診断されるが、本症例はいずれも月経は規則的であり胚移植前の子宮鏡で診断された。流産手術や帝王切開など子宮内処置後に、一定の割合で子宮内腔癒着が生じている可能性が示唆された。

P-123-5 直角針型電極を用いて子宮鏡下癒着剝離術を行った Asherman 症候群の3例

日本生命病院

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Asherman 症候群に対する治療として、直角針型電極を用いて子宮鏡下に癒着剝離術を行った3例を経験したので報告する。【症例1】41歳, G0, 38歳時に粘膜炎筋腫に対し子宮鏡下切除術(以下TCR)を受けていた。月経量の著明な減少と挙児希望にて他院受診、Asherman 症候群を疑われ当科受診した。子宮鏡にて子宮内腔右側の閉塞を認めたため子宮鏡下癒着剝離術を実施した。直角針型電極を用いて線維性癒着の中央部を切離し、鈍的剝離にて子宮底部まで内腔を開放した。子宮内器具(以下IUD)を挿入しKaufmann療法を開始。術後約4週間の子宮鏡で新たな癒着形成のないことを確認した。【症例2】43歳, G0, 40歳時に粘膜炎筋腫に対しTCRを受けていた。他院での不妊治療の際に子宮内腔狭小化を指摘され当科受診した。子宮鏡で子宮底部左側の癒着を認めたため、直角針型電極を用いて子宮鏡下癒着剝離術を実施した。【症例3】41歳, G5P1, 34歳時と39歳時に子宮内膜ポリープに対しTCRを受けていた。体外受精を複数回試みるも妊娠せず、子宮内膜ポリープの再発を指摘されTCRを実施した。IUDを挿入の上術後7週間で子宮鏡を実施したところ、子宮内腔の癒着を認めた。直角針型電極を用いて子宮鏡下に子宮底部に認めた癒着の中央を切離し、鈍的に剝離し両側卵管口を確認した。IUDを挿入しKaufmann療法開始の上術後4週間で子宮鏡を実施し、子宮内の新たな癒着形成がないことを確認した。直角針型電極は癒着部位に対し垂直に接触しピンポイントで切離することが可能であることから、最小限の操作で治療できるため子宮鏡下癒着剝離術の際に有用であることが示唆された。

P-123-6 子宮鏡下手術に幅広く応用可能なボール電極による剝離操作～いわゆる「押し切り」との相違点について

大阪警察病院

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【目的】子宮鏡下手術は現在子宮粘膜炎筋腫に代表される子宮内隆起性病変摘出、中隔子宮や子宮内腔癒着などの修復を主な対象としている。演者はこれまでにFIGO Type 2粘膜炎筋腫に対するボール電極による剝離法について報告してきたが、この方法は異所性妊娠(帝王切開癒着部妊娠および子宮頸管妊娠)組織摘出や、子宮中隔の切開についても有用であったので報告する。【方法】ボール電極による剝離には低出力通電による切開と通電を行わない鈍的剝離がある。1)粘膜炎筋腫摘出:2003年にLittaらにより提唱されたニードル電極によるEnucleation in totoを原法とし、より腰が強く剝離に有利なボール電極を用いた。筋腫の剝離層に入る際には内膜組織切開で開始し、剝離層に達した後は原則鈍的剝離を用いる。2)異所性妊娠:原則鈍的剝離のみで操作が可能である。拡大視野下での凝固止血を剝離と同時に進めることが利点である。3)子宮中隔切開:低出力切開を細かく繰り返し残余の中隔を確認しながら進める。ループ電極に比べ、一度に深く切り込む危険が少ない。【成績】粘膜炎筋腫については2018年9月から2021年5月までの2年9か月に実施した71例について、筋腫サイズ、FIGO分類、手術時間、1期的完遂率、合併症等について検討した。Type 2筋腫の22症例中19例で1期的に摘出でき、2例は2期的手術で摘出を完遂した。Type 2症例1例に子宮穿孔が発生し開腹移行した。子宮内腔癒着の発生はみられなかった。異所性妊娠、中隔切開については各々症例提示を行う。【結論】ボール電極による子宮鏡下剝離操作は筋腫摘出以外の目的にも有効かつ安全な手術手技と考えられた。いわゆる「押し切り」の概念との相違点についても述べる。

P-123-7 子宮腔内病変に対する妊孕性回復のための子宮鏡手術についての検討

大分大

岡本真実子, 山田知徳, 栗山 周, 衛藤 聡, 井上尚実, 河野康志

【目的】生殖年齢の女性において、子宮腔内病変は胚の着床の妨げとなり不妊症の原因となりうる。子宮腔内病変として子宮内膜ポリープ、子宮粘膜下筋腫や子宮形態異常が挙げられ、それに対して子宮鏡手術が治療法として選択されることが多い。今回、インフォームドコンセントが得られ、当科で子宮鏡手術を行った症例の妊娠後について検討を行った。【方法】2015年1月から2020年12月にかけて、当院で子宮鏡手術を行った213症例について、患者背景と挙児希望の有無、その後の不妊治療ならびに妊娠後について検討した。【成績】子宮鏡手術を行った213例中、挙児希望があったものは88例であった。子宮粘膜下筋腫が15例、子宮内膜ポリープが57例、子宮形態異常が5例であった。挙児希望があり子宮鏡手術後に不妊治療を行ったものは他院への紹介も含めて66例、当科での不妊治療症例は53例であった。治療内容としては人工授精が26.4%、高度生殖補助医療が35.8%であった。その後に妊娠が確認できたものが22例(41.5%)であり、うち自然妊娠は6例認め、粘膜下筋腫の術後の妊娠は13%、子宮内膜ポリープ術後の妊娠は37%と粘膜下筋腫術後の方が妊娠率は低かった。【結論】子宮腔内病変は不妊診療でしばしば遭遇する疾患であり、当科で行った子宮鏡手術と妊娠について検討した。子宮腔内に病変をもつ症例には妊孕性の回復のための子宮鏡手術は有用であり、積極的な子宮鏡手術の検討が求められる。子宮内膜ポリープと比較すると粘膜下筋腫術後の妊娠率は低い傾向を示したが、年齢や他の不妊原因の可能性もある。また、粘膜下筋腫に対しては大きさ、数、突出度、位置等により手術法を工夫する必要性が示唆された。

P-124-1 子宮・上部腔留血症を伴う下部腔欠損症に対して腹腔鏡下膀胱直腸剝離・進展上部腔陰陰側牽引及び腔式造腔術を施行した一例

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【緒言】腔欠損症はミューラー管の発生異常によって腔を欠く疾患であり原発性無月経や下腹部痛で発症する。我々は原発性無月経、子宮・腔留血症を来した下部腔欠損症の一例を腹腔鏡併用で造腔術を行った。【方法】15歳、性交渉歴なし。来院2週間前からの下腹部痛・腰痛、原発性無月経を主訴に近医を受診した。経直腸超音波にて70mm大の血腫様嚢胞を認め、視診で腔に開口部を認めず、子宮留血腫症、処女膜閉鎖又は腔欠損が疑われ当院紹介された。外診上は腔に陥凹のみを認めるのみで、MRIでは子宮内部から腔上部にかけて血液の信号を示す貯留があり、尿道・直腸間に正常な腔は確認できなかった。その他合併奇形は認めなかった。手術では直腸尿道間の剝離と同時進行で、腹腔鏡下に膀胱子宮窩腹膜を剝離し、腔側ガイド下に膀胱腔間隙を造腔腔に開窓し、開窓部より腔管通過部をヘガールで拡張した。ネラトンカテーテルを会陰から腹腔へ通し、腔最下端となる部分の左右に固定した。ネラトンカテーテルを会陰方向に牽引し、腔下端を触診で確認し、正中縦切開すると、チョコレート様経血が大量に流出した。上部腔を造腔した腔腔の陰陰側に縫合し、腔内にFoley catheterを留置し手術終了した。術後経過は良好で、現在も腔狭窄なく経過している。【結論】造腔術は、剝離層の無い空間を拡張するため難易度が高い。本症例は、上部腔があり、その拡張があったため、腹腔側と同時に手術をすることで、難易度の高い剝離の距離を短縮できた。また上皮のある拡張上部腔は腔側に牽引・外陰に固定ができ閉塞しにくい。性器奇形は症例毎に形態が異なるためベストな術式も異なる。事前に手術計画をよく立てることが重要である。

P-124-2 再閉鎖予防のために術式の工夫をしたOHVIRA症候群の1例

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【緒言】obstructed hemivagina and ipsilateral renal anomaly syndrome (OHVIRA症候群)は、重複子宮、片側腔閉鎖、同側腎欠損を合併する稀な疾患である。経血貯留による症状がある場合は、開窓術とドレナージが治療の基本となるが、一般的な開窓術のみでは腔再閉鎖のリスクがあり、腔プロテラーゼ等挿入による予防が必要となる。今回腔再閉鎖予防のため、器具挿入が不要となるよう術式を工夫した。【症例】11歳、0妊、既往歴：特記事項なし、家族歴：特記事項なし。下腹痛を主訴に前医を受診し、MRI検査で子宮・腔留血腫、重複子宮、右腎無形性を指摘され、OHVIRA症候群を疑われ当院に紹介となった。経直腸超音波断層法検査で、充滿した経血を膀胱の背側に認め、OHVIRA症候群と診断し、全身麻酔下で手術施行した。【術中所見】膨隆した腔壁を右腔門蓋部付近に認めた。膨隆部の上端と下端に縫合糸をかけ、牽引用とした。中央に16ゲージ針を穿刺し、暗赤色の経血80gを吸引した。中央から十字に電気メスで切開を入れ、開窓術を施行した。切開した腔壁を外反させ、腔壁を縫合することで、腔再閉鎖の予防とした。経直腸超音波断層法検査で、子宮留血腫が解除されたことを確認し、手術終了した。手術時間は30分で、出血量は80gであった。合併症なく経過し、術後2日目に退院となった。術後3か月後で、腔再閉鎖を認めていない。【結語】OHVIRA症候群に対して、腔再閉鎖予防のため、術式を工夫した。OHVIRA症候群は初経周辺時期の若年発症が多く、腔再閉鎖予防用の腔プロテラーゼの使用は、精神的苦痛を伴う。今回施行した術式を用いることで、術後に器具を使用することなく、腔再閉鎖の予防が可能である。

P-124-3 双角単頸子宮症例に対して腹腔鏡下の Strassmann 手術により妊娠に至った一例

高の原中央病院

谷口文章, 曾山浩明, 山口昌美, 吉田剛祥

【背景】双角単頸子宮は、不妊や不育症の原因となることがあり、そのような場合に、開腹手術にて Strassmann 手術を行うことにより、妊娠、分娩に至った報告もある。今回、反復胚移植を行うも妊娠に至らなかった双角単頸子宮症例に対し、腹腔鏡下に Strassmann 手術後に妊娠に至った症例を報告することである。【症例】年齢は 35 歳、0 経妊、身長は 152cm、体重は 51 kg。難聴を合併。前医で不妊治療を受け、体外受精で胚移植を 8 回行ったが妊娠に至らなかった。HSG で双角単頸子宮、右卵管水腫疑いを認め、手術目的で当院に紹介された。MRI でも双角単頸子宮を認めたため腹腔鏡下手術を行った。腹腔内を観察すると、子宮はハート型であり、両側卵巣には異常なかった。インジゴカルミンによる通色素検査では、左卵管は良好なる通過を認め、右卵管は、やや水腫状で采部で狭窄を認めたが、少量采部より流れていた。腹腔鏡下に Strassmann 手術を行うとともに左卵管を切除した。手術時間は、161 分、出血量は、80ml であり、術後 4 日目に退院した。3 か月間の避妊期間の後、1 回目の胚移植で患者は妊娠し、現在妊娠 10 週で流産兆候なく、経過良好である。【結論】双角単頸子宮に対して腹腔鏡下に Strassmann 手術を行って妊娠に至った症例を提示したが、腹腔鏡下に Strassmann 手術を行った報告は、非常に少なく、この方法で手術後に妊娠に至った報告は、調べる限り 1 報告のみである。双角単頸子宮が必ずしも不妊になるわけではないが、反復して胚移植を行っても妊娠に至らない場合は、Strassmann 手術は有効な方法かもしれない。そのような場合、開腹手術よりも腹腔鏡下手術の方が手技は難しいが低侵襲である。

P-124-4 卵管切除により妊娠に至った先天性卵管部分欠損の 1 例

高の原中央病院

曾山浩明, 山口昌美, 吉田剛祥, 谷口文章

【目的】先天性卵管部分欠損は稀な病態である。多くは無症状であり、不妊治療による子宮卵管造影 (HSG) により卵管閉塞を認め、その手術時に偶発的に発見されることがある。今回 HSG で卵管水腫様の病態を呈した症例に対する手術の際に卵管部分欠損を認め、その卵管を切除することにより妊娠・分娩に至った 1 例を経験したので文献的考察を加え報告する。【症例】年齢は 35 歳、0 経妊、身長は 163cm、体重は 68kg。前医で不妊治療を受けていたが妊娠に至らなかった。HSG で左卵管水腫を指摘され、手術目的で当院に紹介された。経腔超音波検査では左付属器に水腫様の所見を認めた。血液検査では異常を認めなかった。不妊の精査、左卵管水腫の切除目的に腹腔鏡下手術を行った。左卵管は、膨大部で細くなっており部分欠損が疑われた。術中の卵管疎通性検査ではその狭小箇所手前でインジゴカルミンの貯留を認めた。今後、体外受精を前医で行う方針であったので欠損部を含む左卵管を切除した。病理検査では膨大部の狭小箇所には正常卵管構造が無く、先天性卵管膨大部欠損の診断となった。術後 1 回目の胚移植で患者は妊娠し、妊娠 41 週微弱陣痛で帝王切開分娩を行い生児を得た。【結論】先天性卵管部分欠損は、卵管の近位、中間、および遠位の部分で発生するとされており、遠位部分で発生した場合、卵管水腫の状態を認めることがある。卵管水腫の場合、その卵管内の液体が妊娠へ悪影響を及ぼすと言われている。そのため卵管部分欠損の場合でも卵管水腫様の所見がある場合は、切除は重要と思われた。

P-124-5 双角子宮と鑑別が困難であったエリスロポイエチン産生巨大子宮筋腫を伴う子宮頸部憩室の一例

市立秋田総合病院

佐藤 綾, 福田 淳, 小野有紀, 下田勇輝, 軽部裕子, 高橋 道

【緒言】子宮頸部憩室は極めて稀な子宮奇形であり、ミューラー管の部分的な重複や癒合不全によって起こると考えられている。今回、エリスロポイエチン産生巨大筋腫を伴う子宮頸部憩室の一例を経験したので文献的考察も含めて報告する。【症例】患者は 37 歳女性、0 妊 0 産、未婚。32 歳時に子宮筋腫を指摘され、近医にてフォローされていた。36 歳時、多血症 (Hb : 17.0 g/dl) と巨大子宮筋腫を指摘され当院紹介となった。術前のエリスロポイエチンが 20.9mIU/ml と高値であり、エリスロポイエチン産生巨大子宮筋腫の疑いとなった。MRI では内腔が子宮頸部から 2 方向性に伸展しており、左側は正常子宮体部に、右側は 23×13cm の巨大筋腫に連続していた。術前診断では双角・副角子宮の片側に発生した筋腫の可能性も考慮されたが確定診断には至らなかった。多血症の治療も含め手術の方針となった。挙児希望あり、開腹所見で術式を決定する方針とした。巨大筋腫は右韌帯内筋腫で子宮頸部に茎を持つ漿膜下筋腫の所見であった。正常な子宮体部は左側に存在し、両側付属器とも左側体部に附着していたことから、双角・副角子宮は否定的であった。茎の部分で切離して筋腫 (2450g) を摘出した。切離部は管腔を形成しており、その部を切除後、縫合閉鎖し手術を終了した。組織学的には巨大腫瘍は平滑筋種であった。子宮筋腫の茎の内腔は頸管腺組織に被覆されており、最終的に子宮頸部憩室と診断された。術後血液検査では Hb・エリスロポイエチンとも正常化していた。【結語】子宮頸部から 2 方向性の内腔を確認できるが、一方が正常筋層を確認できない場合は子宮頸部憩室の可能性があることを念頭に入れ、治療方針を考慮すべきである。

P-124-6 機能性子宮を有する膣欠損症に対する腹腔鏡補助下造陰術 (Luge 変法) 及び子宮腔吻合術の1例: 手術手技の詳細と文献的考察

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【背景】膣欠損症に対する造陰術には遊離皮膚や骨盤腹膜・腸管の移植による形成や、人工真皮を利用した形成など様々な方法が行われている。また、機能性子宮を有し妊孕性温存を希望する場合、造陰術に加え経血ドレナージのため子宮腔吻合が必要であり、手術の難易度は高い。今回我々は腹腔鏡補助下に有茎S状結腸を利用した造陰術 (Luge 変法) と子宮腔吻合術を行った1例を経験したため報告する。【症例】症例は初診時13歳、子宮留血腫と腔閉鎖を他院で診断され、当院紹介となった。外陰部は正常女性型であったが、腔口は処女膜の高さで閉鎖していた。骨盤部MRI検査で子宮留血腫をみとめ体部・頸部は共に著明に拡張し、腔は同定できなかった。腹痛が持続しており症状改善のため超音波ガイド下に子宮内容物の経皮的ドレナージを行った。性交希望が出現し腔の術後管理可能な年齢となるまで保存的に管理する方針を本人・両親と相談し決定した。頻回な子宮穿刺を回避するため、骨端線や卵巣機能を評価しつつジェノゲスト内服を継続し、再貯留に伴う腹痛の増強のため5年間に計3回の子宮穿刺を要した。将来的な性交渉の希望から18歳時に造陰術を希望された。術式は、術後の腔狭窄が起こりにくく自己拡張の必要性が少ない腸管利用の造陰術を選択した。腹腔鏡補助下に有茎S状結腸を新生腔として移植し、新生腔に新生子宮頸部を埋め込み縫合した。新生腔の長さは8cm以上確保でき、月経血の流出も確認できた。【考察】機能性子宮を有する膣欠損症の管理には、手術時期の決定や、術前の月経管理、術後の腔狭窄予防法など様々な問題点がある。同様の症例が検索しえた文献上70例あったので、これらを合わせて提示したい。

P-124-7 Wunderlich 症候群に腸管子宮内膜症を合併した一例

岡山大病院

谷岡桃子, 榎野千明, 岡本遼太, 楠元理恵, 久保光太郎, 長谷川徹, 光井 崇, 鎌田泰彦, 増山 寿

Wunderlich 症候群は、Wolff 管の発育障害と Müller 管の癒合不全により発生し、重複子宮、患側子宮頸部の留血腫、患側腎低形成を伴う稀な疾患で、月経血貯留による周期的な下腹部痛や子宮内膜症を合併することがある。一方、小腸子宮内膜症は腸管子宮内膜症の約10%と比較的稀な疾患であり、下腹部痛や嘔吐など腸閉塞症状を呈することがある。今回、Wunderlich 症候群に腸管子宮内膜症を合併し、腸閉塞に対し小腸部分切除を行った1例を経験したので報告する。症例は31歳、0妊。5年前に子宮内膜症を指摘され、低用量エストロゲン・プロゲステン配合薬を1年前まで内服していた。X年10月上旬に嘔吐、下痢、腹痛があり、経口摂取困難となり前医に入院。MRI検査で重複子宮、卵巣子宮内膜症性嚢胞を認めたため当科紹介となった。11月上旬の月経中にも嘔吐、腹痛のため前医救急外来を受診。CT検査で小腸の拡張、超音波断層法で左子宮頸管内に月経血貯留を認め、月経モリミナと月経血逆流による腹膜刺激症状と考えられた。完全中隔子宮、左腎欠損、左子宮頸部の留血腫から Wunderlich 症候群および両側卵巣子宮内膜症性嚢胞と診断し、手術の方針となった。全身麻酔下に腹腔鏡下右卵巣子宮内膜症性嚢胞焼灼、左卵巣子宮内膜症性嚢胞核出および子宮鏡下子宮中隔切除術を施行した。術後2日目に排便はあるも嘔気が継続し腹部単純X線検査より腸閉塞と診断した。イレウス管挿入後の造影検査にて小腸狭窄を認め、月経時の症状は腸管子宮内膜症が顕在化したものと考えられた。術後13日目に腹腔鏡下小腸部分切除術を施行し、病理組織学的に腸管子宮内膜症を確認した。術後経過は問題なく、術後27日目に退院となった。

P-124-8 当科で経験した OHVIRA 症候群の3例

旭川医大

市川英俊, 早坂美紗, 板橋 彩, 寶田健平, 高橋知昭, 片山英人, 加藤育民

Obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) 症候群は重複子宮、重複腔、片側腔閉鎖による腔留血腫および同側腎欠損を合併する稀な疾患である。近年は Herlyn-Werner 症候群、Wunderlich 症候群、OHVIRA 症候群を広義の OHVIRA 症候群として総称する傾向がみられる。今回我々は、広義の OHVIRA 症候群の3例を経験したので報告する。【症例1】16歳、未妊。下腹部痛、不正出血を主訴に当科初診。経腹エコーで子宮形態異常に気づかずカウフマン療法で経過観察していたが、再度腹痛で受診しMRI撮影。重複子宮、子宮留血腫、腔閉鎖を認めた。腎欠損で泌尿器科で follow されていたことも判明し OHVIRA 症候群疑いで腔壁開窓術を施行した。術後7か月経過する現在、再発兆候なく外来経過観察中である。【症例2】13歳、未妊。腎欠損にて小児科・泌尿器科で follow されていたが、エコーで5cmの骨盤内腫瘍を認め、OHVIRA 症候群疑いで当科紹介初診となった。当科でのCT・MRIでも OHVIRA 症候群を疑い、腔壁開窓術を施行した。術後1年経過する現在、再発兆候なく外来経過観察中である。【症例3】17歳、未妊。下腹部痛にて近医受診、骨盤内腫瘍認め、卵巣腫瘍捻転疑いで当科紹介初診となった。CTで重複子宮、腔閉鎖、左腎欠損、MRIで重複子宮の一侧腔閉鎖、子宮留血腫を認め、OHVIRA 症候群を疑い腔壁開窓術を施行した。術後経過良好で、5年後、妊娠37週2日で自然経産分娩に至った。子宮腔形成異常を高頻度に伴う腎欠損の確認は臨床的に有用である。稀ではあるが本疾患も念頭に置き診療にあたることが重要と考える。

P-125-1 徳島県全体の不妊治療による多胎妊娠の発生状況と多胎妊娠を減らす取り組みについて

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【目的】生殖補助医療（ART）による多胎妊娠の発生状況は日本産婦人科学会への症例登録制度により把握可能であるが、一般不妊治療を含めた多胎妊娠の発生状況は明らかではない。徳島県内の複産率は全国的に見ても高い時期があり、この原因として特に一般不妊治療による影響が懸念されていた。このような背景から、不妊治療により発生した多胎に関する調査を実施し、結果をフィードバックすることで、多胎を減らす取り組みを継続してきたので報告する。【方法】徳島県下で不妊治療を行なっている全施設を対象に、2012年から2020年にかけて調査前年度に発生した多胎に関するアンケート調査を行った。卵巣刺激(排卵障害のない症例に対する刺激)、排卵誘発、ARTの3つの治療毎の多胎発生状況および妊娠・分娩転帰等を調査項目とした。【成績】2011年の各治療における多胎率は卵巣刺激7.7%、排卵誘発4.8%、ART8.4%と高率であった。その後、単一胚移植(SET)の普及によりARTでの多胎発生は減少し、2013年以降多胎率は4%未満で推移していた。本調査開始後は、一般不妊治療による多胎発生、複産率も減少傾向となったが、排卵誘発では依然として多胎率が高く、4~10%で推移し品胎以上の超多胎妊娠の発生も認めている。また不妊治療により発生した多胎の約半数は早産となり、10%程度は32週未満での分娩となっていた。【結論】本調査開始以降、不妊治療による多胎発生率は減少しており、一連の取り組みが多胎発生の予防に寄与していると思われる。今後さらに多胎を減少させるにはSETのさらなる徹底、一般不妊治療における発育卵胞数のコントロール、厳密なhCG投与基準の設定が必要になるとと思われる。

P-125-2 ART妊娠症例における出生前遺伝学的検査および患者背景に関する検討

加藤レディスクリニック

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【目的】生殖補助医療（ART）による妊婦は様々な背景から出生前検査を受ける傾向が高いと報告され、特に近年では母体血を用いた出生前遺伝学的検査(NIPT)を選択する妊婦が見受けられる。今回、当院ARTで妊娠した症例における出生前遺伝学的検査の実施状況や、患者背景、ART治療内容との相関について検討する。【方法】2017年~2019年の3年間で、当院ARTで妊娠し胎児心拍を認めた症例を対象とした。血清マーカー、NIPT、羊水検査、絨毛検査の実施について検査群と非検査群に分け、それぞれの実施状況、両群の患者背景(本人・夫年齢、採卵・移植・流産回数)、ART治療内容(移植法、媒精法、アシストハッチングの有無等)に対し単・多変量解析を行った。【成績】対象例13,706例のうち3,873例(28.9%)が出生前検査を実施し、非確定的遺伝学的検査におけるNIPTの割合は73.4%であった。検査群は非検査群と比較して、本人・夫の年齢が高く(38.3 vs 36.8, $P < 0.001$; 38.6 vs 37.0, $P = 0.04$)、採卵・移植・流産回数が有意に多かった(3.8 vs 3.3, $P = 0.02$; 3.2 vs 2.2, $P = 0.02$; 0.71 vs 0.66, $P = 0.005$)。ART治療内容では明らかな差は認めなかった。【結論】夫婦の年齢上昇に伴う児の染色体疾患に対する懸念や、不妊治療の不成功、流産の経験等により不安が増強され、採血のみの容易さと流産リスクがなく、検査精度の高いNIPTが多く選択されていると考えられた。しかし、無認定施設でのNIPT実施が問題視されており、検査前後に適切な遺伝カウンセリングや産科的な対応が可能な認定施設で受けられるような体制づくりとこれらの施設にアクセスできるよう適切な情報提供が重要であると考えられた。

P-125-3 ウェブ検索から把握可能な本邦の医学的・社会的卵子凍結実施施設および凍結コストの実態について

秋田大附属病院

白澤弘光, 熊澤由紀代, 佐藤 亘, 富樫嘉津恵, 尾野夏紀, 藤島綾香, 寺田幸弘

【目的】国内外において医学的・社会的理由による卵子凍結が広まっている。しかし本邦では社会的未受精卵子凍結は非登録制であり、実際に施行している施設の把握は困難となっている。一方で、利用者視点からは諸費用を含め、情報への簡便なアクセスが望まれる他、諸外国と本邦の比較のためにも現状の把握は急務の課題である。【方法】各施設のホームページ(HP)から、医学的・社会的卵子凍結実施の有無および凍結・更新費用の記載有無を調査した。体外受精・胚移植に関する登録621施設(2021年7月時点)のHPを2021年10月中に生殖医療専門医が閲覧し、記載有無を確認した。また卵子凍結については医学的適応のみ施行しているM群と、その他のNon-M群に分け、費用は卵子凍結1個、5個の場合を試算した。刺激・採卵費用は除外した。【成績】621施設中、医学的・社会的卵子凍結実施の明記は146施設(23.5%)、M群88施設、Non-M群58施設であった。M群の凍結費用明記は24施設(27.3%)で1個凍結平均45,527円、5個凍結平均65,179円、更新費明記は28施設(31.8%)で更新費は1個平均22,327円/年、5個平均22,530円/年であった。Non-M群の凍結費用明記は43施設(71.4%)で1個凍結平均56,822円、5個凍結平均88,429円、更新費明記は44施設(75.9%)で1個更新平均40,178円/年、5個更新平均56,502円/年であった。各費用は全てにおいてNon-M群で有意に高額であった。【結論】本調査は卵子凍結費用を各施設のHPから調査した初めての報告である。費用記載割合は医学的適応施設で少なく、今後の改善が望まれる。また施設間により費用は10-20倍程度と大きく異なり、患者のニーズに沿った施設選択が可能となるような情報公開が今後望まれる。

P-125-4 生殖補助医療における医療従事者へのアンケート調査

協協医大埼玉医療センター
正木希世

【目的】生殖医療に携わる医療従事者の特別養子縁組制度・里親制度の情報提供に対する意識を明らかにする。【方法】上体外受精説明会に参加した医療者に対して、特別養子縁組制度・里親制度の情報提供に対するアンケート調査を実施した。【成績】体外受精説明会に参加した医師7人、コメディカルスタッフ17人から回答を得た。「特別養子縁組・里親制度を知っているか」の質問に対して「身近にありよく知っている」16.7%、「両制度の違いを説明できるくらい知っている」45.8%、「あまりよく分からない」33.3%であった。「両制度の情報提供を行なってきたか」の質問に対して最も多かったのは「全く行っていない」66.7%であり、行っていない理由に対して、医師の回答は「専門知識がないから」80%、「患者が不快に思うことが予想されるから」20%であった。コメディカルの回答は「患者と特別養子縁組・里親制度の話をする機会がないから」66.7%、「専門知識がないから」53.3%、「患者が不快に思うことが予想されるから」13.3%であった。情報提供のあり方として「医療施設での情報提供、体外受精説明会での情報提供が必要」、「今後情報提供を積極的に行なっていきたい」という回答がいずれも過半数を占めた。【結論】今回の検討より、生殖医療従事者は患者に対して特別養子縁組・里親制度の情報提供を行うことに対して肯定的であるが、患者の不快感に対する懸念も抱えていることが明らかになった。両制度についての研修、パンフレットなど資料の活用や福祉専門家との連携により適切な情報提供体制を整える必要があると考えられた。

P-125-5 地方自治体の支援による社会的卵子凍結の重要性と転帰

順天堂大浦安病院
大野基晴, 伊地知航司, 水上奈津子, 牧野祐也, 市山卓彦, 牧野真太郎, 吉田幸洋

【目的】少子化の背景には、女性の社会進出に伴う晩婚化や高齢出産があげられる。子育て費用や社会福祉のサポートは進まず、妊娠出産を延期せざるを得ない状況があるが、高齢女性の不妊治療成績は芳しくない。解決策として社会的卵子凍結保存による妊孕性温存があげられるが賛否両論あり、コスト負担も問題である。【方法】市から提供された研究資金を使用し前向き研究を実施した。2016年4月から2018年3月まで参加者を募集し、参加者は市に住む35歳未満の女性とした。毎月講習会を開催し出産に対する意識の向上・採卵の実際と将来の妊娠率・研究のコンセプトとリスクを説明した。採卵・保管管理費は3年間無料とし、その後は実費負担とした。【成績】講習会には市外在住を含む105名が参加、その後他地域から転居した者を含め市内在住対象者は62名で、講習会での説明後、早めの妊娠を考え自然妊娠したものが2名いた。最終的に34名が採卵に至った。採卵希望理由は「社会性」のみならず、子宮内膜症やターナー症候群など様々であった。現在までに2名が自然妊娠、2名が卵子を使用した。うち1名は出産に至った。出産した例は、凍結保存時に7個の卵が得られた。結婚を機に改めて4年後に採卵を行うも3個のみで、採卵卵子より凍結卵子の方がGrade良好な胚となった。ホルモン補充周期で胚盤胞1個を移植し妊娠成立。経過に異常なく骨盤位のため予定帝王切開で出産した。【結論】この研究と卵子凍結保存について市民に啓発する効果は高く、少なくとも初期費用を支えているように見えた。地方自治体など、公的な支援により初期費用を削減することも有用な手段のひとつであると考えられる。

P-125-6 一般集団における高度生殖補助医療治療歴の有無による出生前検査に対する意識についての検討

成育疾患克服等次世代育成基盤研究事業白土班疾患克服白土班
坂本美和, 白土なほ子, 宮上景子, 池本 舞, 和泉美希子, 廣瀬達子, 水谷あかね, 池袋 真, 佐村 修, 山田崇弘, 清野仁美, 吉橋博史, 鈴森伸宏, 山田重人, 奥山虎之, 澤井英明, 左合治彦, 関沢明彦

【目的】高度生殖補助医療(ART)治療歴のある患者の出生前検査についての知識や意識の客観的なデータがないため、それらを明確にする事を目的とした。【方法】20~59歳の全国の有配偶女性を対象に、基本属性(年齢, 経妊有無等)ART治療歴, 出生前検査の知識, 経験等に関して109問のWEB調査を実施した。妊娠経験が有り, ART治療歴のある群; A群とART治療歴のない群; NA群の回答を比較した。検定は χ^2 検定, **t検定を用い $p < 0.05$ を有意差ありとした。【成績】対象はA群393人, NA群1032人で、両群の平均年齢に差はなかった**。A群は精密超音波検査, 母体血清マーカー検査, NIPTの受検率が高い一方, 羊水検査の受検率は低かった*。出生前検査の知識はA群の方が精密超音波検査(A群26.2%*, NA群16.2%), 羊水検査(6.6%*, 3.5%)を全く知らない割合が高く*, 母体血清マーカー検査, NIPT, 遺伝カウンセリングの知識に差はなかった。「医療者が出生前検査の説明をすべての妊婦に伝える方が良い」と両群の半数以上(A群50.1%, NA群58.4%*)が回答した。「条件をつけて伝える」または「伝えない方が良い」はA群が多かった*。「出生前検査はすべての妊娠に対して行う方が良いか」という問いに「条件に合う人だけ行う」はA群に多く、「だれでも希望する人に行う」はNA群が多かった*。【結論】妊娠既往のあるART群では全く知らない出生前検査項目があり, 半数は「医療者からすべての妊婦に説明」と考える一方, 「条件付きで伝える」また, 出生前検査受検対象も「条件に合う人だけ」という慎重に考える傾向が見られた。出生前検査に対し知識や意識の違いがあることも踏まえた遺伝カウンセリングの必要性が示唆された。

P-125-7 日本人女性における骨盤臓器脱の有病率と形態的傾向について

JA 中濃厚生病院

加藤順子, 増田美和, 太田俊治, 伊藤直樹

【目的】骨盤臓器脱 (pelvic organ prolapse : POP) は日常診療で多くみられるものの, その疫学データは国内にほとんどない。POP は進行するまで症状が乏しく, また正確に診断するには婦人科診察が必須である。我々は倫理委員会承認のもと, 検診受診者を対象に観察的横断研究を行ったので報告する。【方法】2018年7月から2019年5月の期間に当院健診センターへ子宮がん検診目的で来院した20歳以上の日本人女性を対象とした。妊婦, 産後6か月以内の褥婦は対象から除外した。研究参加の同意が得られた受診者には婦人科診察と同時に単一検者によってPOP-Quantification (POP-Q) system の計測を行い, stage 分類した。【成績】研究参加者は21から84歳までの1032名 (参加率83.5%), 平均年齢52.3歳, 経産回数2回 (中央値) であった。全体のPOP-Q stage 内訳は, stage 0, 38.0%, I, 45.0%, II, 16.5%, III, 0.6%, stage IV はいなかった。年代別にみたstage II以上の割合 (95%信頼区間 confidence interval : CI) は, 20代と30代で6.6% (2.4-10.8), 40代で17.6% (13.3-21.9), 50代で17.1% (12.9-21.3), 60代で18.0% (12.6-23.4), 70歳以上で28.7% (19.6-37.9) であった。部位別にみた下垂臓器は膀胱瘤45.7%, 子宮脱または陰道端脱21.5%, 直腸瘤32%であった。【結論】今回, 幅広い年齢層の日本人女性1000人余りの骨盤臓器支持について評価することができ, その17.1% (95% CI 14.7-19.5) にstage II以上のPOPを認めた。加齢によって有病率は上昇し, 70歳以上においては約3人に1人に臨床的なPOPを認める結果であった。POPの発生については以前から人種間の違いが指摘されており, 今回の調査によって日本人女性の傾向を明らかにした。

日本語ポスター
7日(日)

P-125-8 骨盤臓器脱患者の受診経路と転帰に関する検討

国立岩国医療センター

杉井裕和, 谷岡桃子, 兼森美帆, 伊藤裕徳

【目的】骨盤臓器脱 (以下POP) は高齢化とともに増加し, 80歳までに11%が医学的介入を要する。患者のQOL低下もあり適切な治療選択が望ましいが, 患者側もPOP症状の相談は恥ずかしく, どの診療科を受診していいかわからないという訴えも多くある。そこで当院におけるPOP患者の受診経路を明らかにし, その転帰について検討することにした。【方法】対象は2020年1月から12月までの1年間に, 当院外来をPOP症状で初回受診した全41症例を対象とし, 診療録より後方視的に検討した。【成績】41例中婦人科を初診したのは32例 (以下ギネ群), 泌尿器科を初診したのは7例 (以下ウロ群), 外科を初診したのは2例であった。ギネ群の紹介元は他院婦人科からが7例, 他院内科からが12例であった。ウロ群の紹介元は他院泌尿器科からが6例, 他院内科からが1例であった。他院婦人科から当院泌尿器科に紹介になった例, 他院泌尿器科から当院婦人科に紹介になった例はなかった。外科を初診した2例は直腸脱であり, 当院外科は肛門疾患の手術を行っていないため専門施設に再紹介になっていた。ギネ群は22例がNative Tissue Repair, 9例が保存療法, 1例が当院泌尿器科へ院内紹介になりロボット支援下仙骨陰固定術 (以下RASC) を施行されていた。ウロ群は全例がRASCを施行されていた。【結論】紹介元の治療科によって紹介先の診療科が固定されている現状, 術式選択が固定されつつある現状が明らかになった。POPは複数の診療科にまたがる疾患であり, 正確な診断が必要となる。婦人科医, 泌尿器科医, 肛門外科医がそれぞれの手術療法, 保存療法のメリットデメリットを理解し, 患者にとって適切な治療法を検討, 提案する必要がある。

P-126-1 医学部新入生女子のHPVワクチン接種状況の11年間の経年的変化

横浜市大

助川明子, 鈴木幸雄, 水島大一, 宮城悦子

【目的】現在の大学新入生はHPVワクチン接種を受ける機会があった世代である。2013年からの積極的勧奨中止前後でワクチンの接種状況, 学校の性教育で子宮頸がん予防の扱いなどを明らかにすることを目的とした。【方法】医学部新入生女子を対象とし2011年からの11年間, 経年的に調査した。HPVワクチンの接種の有無や性教育の内容などを無記名自己記入式質問紙法で調査した。2020年以降はCOVID-19のため同内容のWeb調査とした。書面と口頭 (Webの際はメール) で本研究の説明と協力の依頼を行い, 質問紙の提出をもって研究への参加同意とみなした。【成績】医学部新入生女子は毎年120人前後で年齢中央値は18歳であった。HPVワクチン接種率はワクチンが発売された当初に自費接種のみだった2011年4.1%, 2012年20.0%だったが, 緊急促進事業で公費助成が使用できるようになった2013年以降は上昇した。2014年69.8%と最も高いが, その後やや減少していた。定期接種になったものの3か月後には積極的勧奨中止となった世代の2019年は14.3%, 2020年5.1%, 2021年5.4%と急激に低下した。大学入学前までに受けた性教育の中で性感染が含まれていた割合は毎年90%前後と高いが, 子宮頸がん予防が含まれていた割合は2013~2018年は50%前後であったが, 2019年以降は30%に届いていない。【結論】HPVワクチン接種率は積極的勧奨中止を受けて低下していた。学習指導要領で必須ではなかった時代に性教育の中で子宮頸がん予防を取り上げてくれた教育者がいたが, 近年減少傾向となっていた。今後, 子宮頸がん予防の啓発のために定期接種対象者のいる小学校, 中学校, 高校などの教育の場と産婦人科医が連携していく必要があると考えた。

P-126-2 女性ヘルスケアを対象とした初期臨床研修医漢方卒業教育カリキュラム作成

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【目的】女性は一生のなかの劇的な内分泌環境変化のため、男性より心身不調を来しやすい。更年期障害・月経関連疾患がその代表であるが、ホルモン製剤の特殊性から一般家庭医での対応は不十分である。漢方は古来よりこれら疾患に汎用されており、臨床各科で容易に処方可能であることから、現状打開に有効な手段となりえる。そこで、必修化された産婦人科臨床研修制度を利用し、女性ヘルスケアを対象とした漢方卒業教育実施を最終目標とし、初期研修医が習得すべき必須処方選定を目的とした。【方法】対象は臨床研修指定病院16病棟の産婦人科医123名。最初に診療ガイドライン等に記載された漢方処方を参考に重要処方18処方を選定した。この中で、①「産婦人科全般の漢方治療をテーマとした講義で、教えるべき薬剤」と②「特に女性ヘルスケア分野で教えるべき薬剤」を選択するアンケート調査を実施した。【成績】有効回答42例を解析した(平均卒業後年数14年、産婦人科専門医37名、女性ヘルスケアサブスペシャリティ6名、初期研修教育従事者26名)。初期研修医対象であることを考慮し、8処方を選定した。②の汎用上位7処方から当帰芍薬散、加味逍遙散、桂枝茯苓丸、抑肝散、葛根湯、芍薬甘草湯、加味帰脾湯を選定した。これに①の汎用第4位処方である大建中湯を加えた8処方を選定した。背景因子とこれら薬剤選択の関連性を検討したところ、抑肝散選択者は卒業後年数が長く($p=0.048$)、女性ヘルスケアサブスペシャリティが多かった($p=0.032$)。【結論】女性ヘルスケアを対象とした漢方卒業教育として、研修医が習得すべき8処方を選定した。教育スライドを作成し、現在これを用いた教育実施と効果検証中である。

P-126-3 HPV ワクチン普及に向けた、高校生に対する出張授業の取り組み

日本医科大学

豊島将文, 川瀬里衣子, 山本晃人, 池田真利子, 明樂重夫, 鈴木俊治

【目的】子宮頸がんやHPV ワクチンに関する知識が、高校生への授業によってどの程度変化するかを調べることが本研究の目的である。【方法】事前に希望のあった3か所の高校で延べ7回の授業を行い、聴講した生徒は延べ人数で約2200人であった。聴講する学年、男女は学校側に一任した。「月経への対処法」「子宮頸がん予防とHPV ワクチン」「避妊法」について約50分授業を行った。2017-2020年は対面式で、2021年はオンラインセミナー形式で授業を行い、授業の事前・事後に生徒に無記名でのアンケート調査を行った。【成績】子宮頸がんに関する授業前の知識は、女子生徒の方が男子生徒より高い傾向を認めた。頸がんの原因がHPV感染である事を授業前に知っていた高校生は10-20%程度であったが、講話後のアンケートでは50-65%の学生が子宮頸がんの原因がHPVと正しく答えることができた。授業後にHPV ワクチン接種の公費対象を正しく答えることができた学生は約半数であった。2021年度の授業後には17%の女子生徒がすでにHPV ワクチンを接種済みと回答し、42%は今後接種したいと回答した。また授業後には40%の男子生徒が今後HPV ワクチン接種を考えると回答した。【結論】産婦人科医が高校生に授業を行うことは、子宮頸がんやHPV ワクチンについて正しい知識を植え付けるためには非常に有用である。男子生徒の中にも、HPV ワクチンの接種を希望するものが相当数いることが確認できた。公費接種の年齢を鑑みて、今後は中学生や保護者を対象とした授業も予定している。

P-126-4 臨床実習とアクティブラーニング

近畿大病院

貫戸明子, 森内 芳, 葉 宜慧, 川崎 薫, 小谷泰史, 中井英勝, 松村謙臣

【目的】COVID-19を契機に当科で取り入れたアクティブラーニングを主とした実習方法が、従来の実習方法と比較して医学生や指導医に与えた影響と効果について検討し、今後力を入れるべき内容の洗い出しを行う。【方法】当院で臨床実習のため産婦人科をローテーションした学生の2020年度以前(従来)と2021年度以降(アクティブラーニング)での実習内容の比較と、学生アンケートおよび成績評価、指導医の意識の変化を点数化して比較した。【成績】従来の実習方法では、医学生の知識を深めることに重点を置いており、問に対する答えの正誤を評価する形式が多かった。アクティブラーニングでは、個人の工夫や配慮なども評価の対象としたため、医学生の取り組むべき内容が従来の方法に比べて実践に近いものとなった。学生アンケートおよび成績評価では、アクティブラーニングを開始してからの結果が少ないため、有意な違いは見いだせなかった。指導医の意識の変化は、従来の方法とアクティブラーニングで関わった医師の指導年数などが大きく異なっているが、指導にファシリテートやフィードバックが必要となることから、指導医にとっても従来の方法では指導しにくかったより実臨床に近い形で状況設定をしたり、医学生のレベルに応じて高次の知識や技能を指導する傾向が見られた。当科で設定した内容の中では従来から継続していたシミュレーションセンターでの分娩介助や腹腔鏡の実習が医学生、指導医とも満足度が高かった。【結論】臨床実習にアクティブラーニングを取り入れることで、医学生と指導医双方にとって質の高い医学教育が行うことができた。成績に応じた内容変更で一定の成果が出る可能性がある。

P-126-5 医学生および産婦人科医による HPV ワクチン学生アンケート調査

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【目的】この調査は、学生の HPV ワクチンに対する認識等を解析し、今後の HPV ワクチンの啓発・普及活動に活用することを目的とした。【方法】医学生と産婦人科医の共同研究として、高校生・大学生を対象にしたインターネットアンケートを実施した(2021年10月13日開始)。学生団体 Vcan の公式 Twitter, Instagram などにて公報し、Google フォームまたは PDF への直接記入によって回答を収集した。【成績】2021年10月25日現在、162件の有効回答を得た(大学生の女子114名・男子48名、生まれ年度は1984~93年度・1994~99年度・2000年度以降・記入なしが、各6名・57名・98名・1名)。女子は114名中56名が接種していたが、男子では接種者はいなかった。接種した56名中14名は厚労省の積極的勧奨一時中止後に接種を開始していた。本人が接種を決めたのが34名、親が決めたのが20名であった。本人が決定した34名中21名が親の勧めによるものであった。接種していない107名のうち将来接種したいと答えたのは29名で、まだ接種していない理由として金銭的負担が11名であった。普段利用している SNS については LINE, 日常生活の主な情報源についてはネットニュースが、各162名・139名で最多であった。【結論】HPV ワクチンの再普及には親へのアプローチが必要と考えられた。一方で、学生本人が主体的に HPV ワクチン接種を考えることも重要であり、LINE などの SNS やネットニュースなどの媒体を活用することが有効と考えられる。また、接種の機会を逃した学生のキャッチアップ接種に対する費用補助も求められる。今後、回答数をさらに増やして検討する。

P-126-6 医療従事者をめざす大学に通う女子大学生の女性医学知識の普及程度とその課題

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【目的】インターネットやスマートホンの普及など能動的に女性医学の知識を得られる機会が増えている。今回、医療系女子大学生を対象にインターネットやスマートホンを利用した女性医学情報や知識取得についてアンケート調査し、今後の女性医学の知識普及に有効な方法を検討した。【方法】医療職を目指す女子大学生61名を対象とした。平均年齢20.5+1.4歳。母性看護学などを学ぶ機会のある看護学科の女子学生35名、それらを学習しない臨床工学技士、理学療法士を志望する女子学生26名である。アンケートは Google フォームを用いた。そのほか、PMS, 月経困難症, LEP-OC, インターネット遠隔診療、かかりつけ産婦人科医療機関などに関する質問も加えた。【成績】自分自身が女性医学に関する知識を十分持っていると考ええる者67%であった。婦人科疾患を調べた経験のある者は77%であり、内容は月経痛、月経不順について調べた者が多数であった。調べた方法はインターネット98%、教科書57%、スマートホンのアプリ20%であった。自らの月経管理には、87%がスマートホンのアプリを用いていた。オンライン診療の実際の利用経験者は4%であったが、利用希望者は54%であった。かかりつけ産婦人科を持つ者は57%であり、受診のきっかけは家族の勧め、近所である、などの理由が多数であった。受診機会は、異常を感じて3月後が38%であった。女性医師の診察を希望する者は28%であり、既報より少なかった。将来の職種志望と婦人科受診行動の間の有意差はなかった。【結論】医療職を志望する女子学生の婦人科学の知識取得にインターネットが大きな役割を果たしており、これらを利用する知識普及が重要である。

P-126-7 エージェントベースモデルを用いた HPV 感染シミュレーションとワクチン接種のシナリオ分析

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【目的】日本では子宮頸がんによる罹患・死亡者数は年々増加している。本研究では、HPV 感染プロセスモデルを構築し、シミュレーションにより感染者数の推移を可視化する。さらに、ワクチン接種政策とその強度をモデル上で再現することで、政策効果と HPV 根絶に至るシナリオを分析する。【方法】インターネット上で取得可能な調査より HPV 感染に至るまでの行動モデルをエージェントベースモデル(ABM)のアプローチを用いて設計した。ABM を使うことで、人の年齢や性別、出会いや性交渉の意思決定を考慮できるため、現実に近い再現が可能である。人の意思決定は調査等で得た数値を用いて表現している。また、ワクチン接種率をパラメータとして変化させることで罹患者の削減を実現した。【成績】行動モデルを設計した結果、男女の出会い・交際・結婚の再現と感染・ワクチン接種・定期検診を行う行動モデルの構築を行い、男女間の年齢差や性交渉を行う年齢等の情報も加えた。シミュレーションの結果、ワクチンの接種率を変動させると HPV 感染者数の推移の可視化が可能となり、現状の接種率は全体の感染者数削減には繋がらないことを示した。また、現状のモデルでは、若年層の接種率の増加やキャッチアップ接種に、感染者数の削減の効果があることが示された。【結論】HPV 感染に至るまでの人間の行動モデルを構築することで、人間が子宮頸がんを罹患するまでの再現が可能となり、ワクチン接種の有用性を、HPV 感染シミュレーションにより示した。本研究で構築したモデルを基に、HPV 根絶までのシナリオ分析を策定し、積極的勧奨やキャッチアップ等の政策検証の支援へと繋げる。

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