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GYNAE SPECTRUM

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Association between sleep, menstrual problems, and menarche in early adolescent girls

Introduction

Menarche is a significant developmental milestone for female adolescents, signifying the start of menstrual cycles. In the United States, the average age for attaining menarche is 12.25 years; Hispanic girls (11.83 years old) and Black girls (12 years old) experience it earlier compared to Asian and white counterparts.[1] Primary dysmenorrhea is the most prevalent gynecological condition in female adolescents, affecting 16–93% of them, with 2%–29% having severe menstrual discomfort.[2] In addition to painful menstruation, menstrual problems are also involved in causing disturbances, either emotional or psychological, and also hormonal imbalances, mood swings, and sleep disturbances. In adult populations, poor sleep quality and/or sleep disturbances have been linked to irregular menstrual cycles, heavy bleeding, dysmenorrhea, and severe premenstrual syndrome.[3] Furthermore, postpubertal females are more likely than boys to experience sleep issues and mental health challenges. So, this study investigated the relationship among sleep, menstruation issues, and menarche in a sample of early teenage females.[4]

Methods

This study used linear mixed effect models to analyze associations between sleep behavior (self- and caregiver-reported) and menstrual problems (self-reported cycle irregularity, premenstrual symptom, and menstrual pain severity and their impact on daily life), as well as menstrual characteristics using the cross-sectional data from the Adolescent Brain Cognitive Development Study (2019-2021), which included 3,037 participants with an age range: 11.58-14.75 years and with menarche at their third-year assessment. Menstrual issues, such as premenstrual symptoms, flow, irregularity, and impact of menstrual pain were assessed by conducting a questionnaire based on the premenstrual symptoms screening tool. Sleep variables such as sleep duration, bedtime, wake-up time, and social jetlag were measured and a sleep distribution scale for children was utilized for analyzing the breathing disorder abnormalities, arousal disorders, transition disorder, and sleep hyperhidrosis. Covariates such as sex, race, ethnicity, parental education (indicator for socioeconomic status), and body mass index were calculated. Wald chi-square test was used for assessing the predictor's significance in Generalized Linear Mixed Models (GLMMs).

Results

In the sample, 26.2% experienced moderate-severe premenstrual symptoms, while 20.8% expressed moderate-severe menstruation discomfort. 23.3% had irregular menstrual cycles,

while 15.9% reported excessive menstrual flow. Shorter sleep duration was linked to increased menstrual pain intensity (β=—0.19), decreased daily activities (β=-0.15), irregular cycles (β=-0.17), and severe premenstrual symptoms (β=-0.04) (Figure 1). Higher sleep disturbance ratings were associated with increased menstrual pain (β=0.18) and premenstrual symptom intensity (β=0.03). Later wake-up times were associated with increased menstrual pain intensity (β=0.14). A shorter period after menarche was linked with decreased menstrual flow (β=0.07), pain intensity (β=0.51), and milder premenstrual symptoms (β=0.07). Being post-menarche was linked to later bedtimes and lower sleep durations (Figure1).

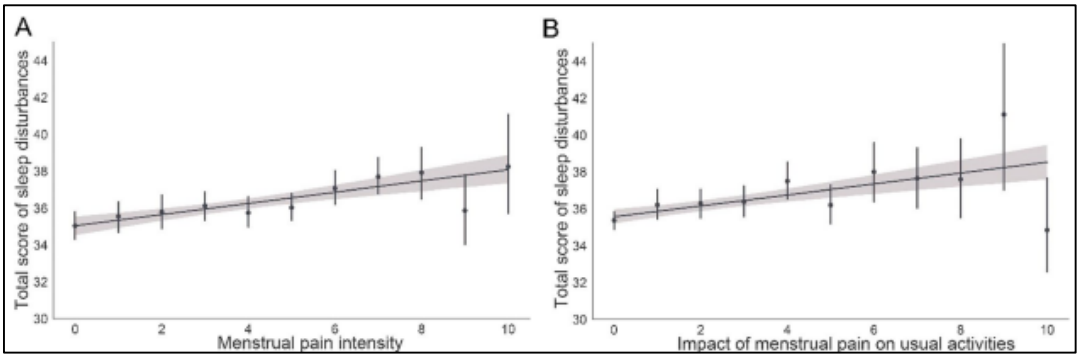

Figure 1: Relationship between overall sleep disruption scores, as judged by the caregiver-reported Sleep Disruption Scale (SDS), and menstrual pain intensity (A) and influence on daily activities (B) in female adolescents.

Discussion

In this study, a strong connection was found between menstrual problems such as pain during menstruation, irregularity, and premenstrual symptoms and caregiver-reported sleep disturbance like short duration of sleep patterns, delayed bedtimes, and noticeable social jetlag.[4] A study carried out on teenagers aged 12 to 18 also showed a linkage between menstrual discomfort, sleeplessness, and daytime sleepiness.[5] These show a crucial linkage between menstrual issues and poor sleep habits even in the early stages of adolescence, since these factors may impair quality of life and have an impact on general and reproductive health in the future.[4]

Conclusion

There are complex relationships between teenage sleep and menarche, as well as between sleep and menstruation disorders, highlighting how common these problems are even in the early stages of adolescence. Menstrual discomfort and disturbances in everyday life are linked to certain sleep patterns, which highlights the need for holistic healthcare treatments that incorporate menstrual and sleep health.

There is a significant association between menstrual problems and sleep disturbances, highlighting the need for integrated approaches in healthcare focusing on improving sleep and menstrual health.

References

1. Biro FM et al. Age of Menarche in a Longitudinal US Cohort. J Pediatr Adolesc Gynecol. 2018 Aug;31(4):339-345.
2. De Sanctis V et al. Primary Dysmenorrhea in Adolescents: Prevalence, Impact and Recent Knowledge. Pediatr Endocrinol Rev. 2015 Dec;13(2):512-20.
3. Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update. 2015 Nov-Dec;21(6):762-78.
4. Kiss O et al. The relationship between sleep and menstrual problems in early adolescent girls. Sleep Sci Pract. 2024;8(1):20.
5. Bahrami A et al. Neuropsychological function in relation to dysmenorrhea in adolescents. Eur J Obstet Gynecol Reprod Biol. 2017 Aug; 215:224-229.

Immunological distinctions between Endometriosis and Uterine fibroids

Introduction

Endometriosis (EN), a prevalent gynecological condition, involves the proliferation of active endometrial tissue. According to estimates, 10% of women of reproductive age had a diagnosis of EN over their lifetime, 50% to 80% of those who experience chronic pelvic discomfort, and up to 50% of those who experience infertility.[1] Many EN cases may go untreated or be misdiagnosed because of their vague symptoms. Genetic, hormonal, immunologic, inflammatory, and environmental factors are thought to play a role in EN, while the precise cause is still unknown.[2] Studies indicate that immune regulation may have a role in reproductive women with EN, but further investigation is needed to completely understand the pattern of peripheral immunological alterations.[3] So, this study aimed to detect immunological indicators in peripheral blood and to provide a complete understanding of the peripheral immune environment in reproductive females with EN.[4]

Methods

This study was a comprehensive and systematic analysis of immune cell subsets within T cells, B cells, NK cells, and γδ T cells conducted in peripheral blood (PB) samples from women with EN, women with uterine fibroids (UF) but no EN (UF-alone), and healthy controls using multi-parameter flow cytometry. Participants in this study were 94 healthy donors between the ages of 25 and 45, 35 UF-alone, and 56 EN patients. For EN and/or UF, all of the patients enrolled in this study had laparoscopic surgery. Before laparoscopic surgery, the patient's peripheral blood (PB) samples were prospectively obtained and never received any pharmacological treatment, and they had no history of autoimmune, chronic inflammatory, or cancerous conditions. A thorough process that includes imaging tests, clinical questionnaires, and interviews was used to choose healthy controls for the study. GraphPad Prism (version 6.0, USA) and IBM SPSS software (version 20.0, USA) were used for statistical analysis.

Results

In the EN group, the proportions of PD-1^{+}γδ1^{+} T cells and CD94^{-}KIR^{+}NK cells were higher compared to the control groups, PD-1^{+}γδ1^{+} T cells showed a notable difference (Figures 1A, B). In addition to the proportions of PD-1^{+}γδ1^{+} T cells and CD94^{-}KIR^{+}NK cells, which were higher in the EN-alone patients, the findings showed that there was a drop in the proportion of CD94^{+}KIR^{-}NK cells and an γδ1^{+} T cells in the same EN-alone cohort (Figure 1C). On the other hand, there was no discernible variations were found in any of the 70 immunological markers between the EN with UF patients and the UF-alone patients (Figure 1A). Upon further comparison, notably, only the percentages of γδ1+ T cells, NKG2D+ γδ2+ T cells, and CD94+ KIR- NK cells showed significant differences between the EN-alone patients and the healthy cohorts.

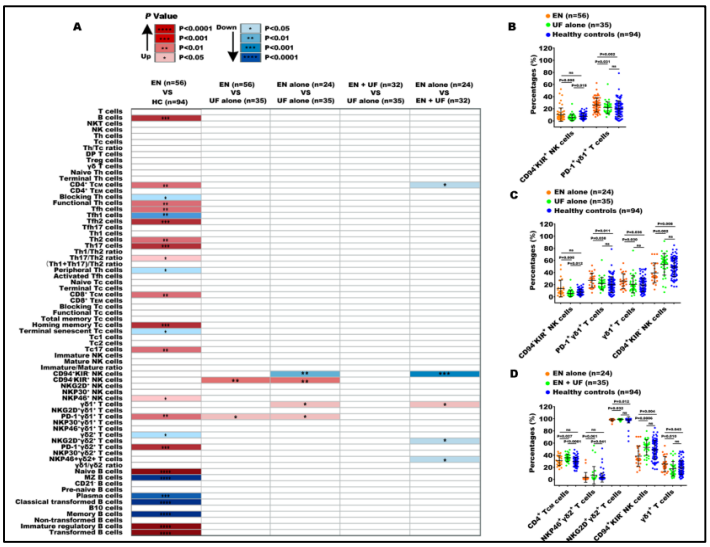

Figure 1: Peripheral immune indexes detected by multipara-meter flow cytometry. (A) overview of changed immune indexes between patients with EN and the HC, and between EN and non-EN patients; (B) immune subsets among EN, UF alone and HC; (C) among EN alone, UF alone and HC; (D) among EN alone, EN with UF and HC

Discussion

The subsets of B cells in EN peripheral blood samples exhibited aberrant patterns of B cell activation and differentiation. A prior analysis examined 22 studies that explored the functions of B cells in EN and noted that there were more B cells and, along with more activated and/or produced autoantibodies.[5] There was a rise in B cells, naive B cells, B cells, and transformed B cells, which is comparable with prior findings. In the setting of the persistent chronic inflammation linked to EN, γδ1^{+} T cells may exhibit a fatigued phenotype after activation. The proportion of γδ1^{+} T cells was also higher in pain-symptomatic patients than in symptomless ones. In contrast, the percentage of γδ2^{+} T cells dropped when pain symptoms were present, and the percentage of NKG2D^{+}γδ2^{+} T cells dropped as the disease severity increased. These results imply that the imbalance in γδ1+ and γδ2^{+} T cell expression might be linked to the development of the disease and the occurrence of pain symptoms, which could result in the development of new EN diagnostic or therapeutic approaches.[4]

Conclusion

The immunological signature in the PB of EN patients was shown in detail for the first time in this study. B cells and their subsets, Th and Tc cell subsets (primarily Th2, Th17, Tc17, and Tfh cells), as well as functional subsets of NK cells and γδ T cells, are linked to the peripheral immunological dysfunction in EN.

The comorbidity between EN and UF is a significant medical concern and needs to be taken into account when treating either EN or UF.

References

1. Zondervan KT et al. Endometriosis. Nat Rev Dis Primers. 2018 Jul 19;4(1):9.
2. Zondervan KT, Becker CM, Missmer SA. Endometriosis. N Engl J Med. 2020 Mar 26;382(13):1244-1256.
3. Abramiuk M et al. The Role of the Immune System in the Development of Endometriosis. Cells. 2022 Jun 25;11(13):2028.
4. Lin KR et al. Peripheral immune characteristics and subset disorder in reproductive females with endometriosis. Front Immunol. 2024 Nov 28; 15:1431175.
5. Riccio LGC et al. The role of the B lymphocytes in endometriosis: A systematic review. J Reprod Immunol. 2017 Sep; 123:29-34.

Effects of lifestyle modification programs on clinical and anthropometric symptoms in adolescents with polycystic ovarian syndrome

Introduction

One of the most prevalent endocrine conditions affecting females of reproductive age globally is polycystic ovarian syndrome, which primarily manifests in adolescence of 8-13%.[1, 2] The primary clinical manifestations of PCOS in adolescents are male-pattern baldness or alopecia, hirsutism, acne, and irregular or absent menstruation. Hyperandrogenism and oligo-anovulation symptoms are common in healthy adolescents with PCOS. Given that the prevalence of obesity among PCOS subjects increased from 51% in the 1990s to 74% in the following decade, lifestyle management is advised as the first-line intervention for women with PCOS in the 2018 International Evidence-based Guideline for the Assessment and Management of PCOS.[3] It has been demonstrated that 75% of lean women and 95% of overweight women with PCOS have insulin resistance, and the difficulties that come with this condition worsen as weight rises. This cluster-randomized experiment sought to determine if lifestyle promotion initiatives centered on behavioral habit modifications may impact teenagers' anthropometric measurements and PCOS symptoms. Also this study involved in evaluating the anthropometric indices experienced by obese adolescents with PCOS like non-PCOS adolescents.[4]

Methods

This was a cluster randomised trial (CRT), conducted among adolescents between the ages of 14 and 18 years. Eligible subjects were free of liver, adrenal, kidney, thyroid, mental, cardiac,

and skeletal disorders, had no history of sexual activity, and had none of these conditions for at least two years after their juvenile menarche. Furthermore, during the previous three months, they had not taken any drugs, smoked, drunk alcohol, worked out professionally, or followed any particular diet. Participants were divided into two subgroups: PCOS and non-PCOS group for the intervention and PCOS and non-PCOS group as control. Anthropometric measures, regular menstruation, hirsutism, acne, and hair loss were the main results. These results were evaluated at baseline, six, and twelve months following enrolment, among other intervals. At baseline and a year following the intervention, the individuals' food habits and level of physical activity were evaluated. Analysis of the data was done with SPSS software (version 25).

Results

For every six months, the average weight of the PCOS intervention group dropped by 3.14(-3.73, -2.55) kg ($p<0.001$), and the average weight of the non-PCOS intervention group dropped by 2.60(-3.23, -1.98) kg ($p<0.001$), while the average waist circumference of adolescents in the non-PCOS intervention group dropped by 4.95(-5.95, -3.93) cm ($p<0.001$) from the non-PCOS control group. Further, there was a 4.68(-5.75, -3.61) cm drop in the waist circumference of the PCOS intervention group ($p<0.001$), compared to the control group for PCOS. In the non-PCOS intervention group, the mean FG score dropped considerably by 3.23 (-4.2, -2.24) scores ($p<0.001$) in contrast to the non-PCOS control group, and by 5(-5.93, -4.00) points ($p<0.001$) when compared to the PCOS control group (Figure 1). After 12 months of intervention, the odds ratio (OR) for monthly regularity in the PCOS intervention group increased to 3.30 (95% CI: 2.06, 5.25), whereas acne scores reduced considerably with an OR of 0.46 (95% CI: 0.31, 0.70). In comparison, the non-PCOS intervention group showed an increase in monthly regularity to 2.45 (95% CI: 1.33, 4.25) and an improvement in acne score to 0.44 (95% CI: 0.28, 0.69). There were no significant variations in nutritional status across all groups after intervention. Both intervention groups showed a significant increase in physical activity levels (MET/min/week) ($p<0.05$).

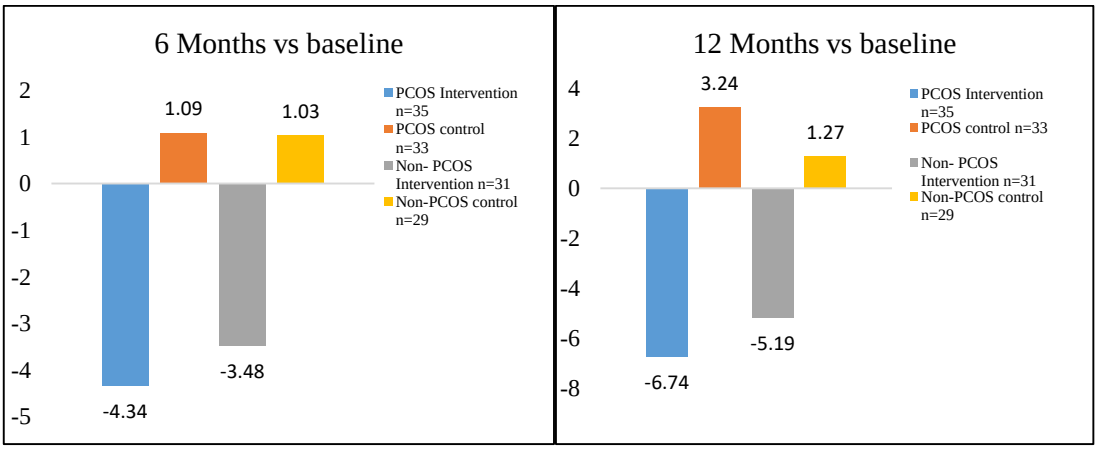

Figure 1: Changes in the FG score according to the PCOS and intervention status during follow ups (6 months vs baseline & 12 months vs baseline)

Discussion

This study suggested that weight control and lifestyle promotion can have an impact on teenage hyperandrogenism, and will lower the FG score in PCOS-affected females by five points following intervention. Also it was found that hirsutism can be reduced following an adolescent lifestyle intervention, which was consistent with the findings of previous studies.[4] In line with the findings of this study, lifestyle modifications such as dietary changes at six months and physical activity changes at three months may improve adolescents menstrual cycle regularity.[5]

Conclusion

The lifestyle promotion programs significantly involved in improving the anthropometric and clinical symptoms in adolescents with PCOS, thereby describing its effect as first-line intervention and these sessions also improved hyperandrogenism (i.e., acne and hirsutism), menstrual regulation, and anthropometric parameters.

Lifestyle promotion programs based on changes in behavioral habits such as physical activity can affect the anthropometric parameters and manifestation of PCOS in adolescents.

References

1. Bozdag G et al. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016 Dec;31(12):2841-2855.
2. Naz MSG et al. The prevalence of polycystic ovary syndrome in adolescents: A systematic review and meta-analysis. Int J Reprod Biomed. 2019 Sep 3;17(8):533-542.
3. Teede HJ et al. Longitudinal weight gain in women identified with polycystic ovary syndrome: results of an observational study in young women. Obesity (Silver Spring). 2013 Aug;21(8):1526-32.
4. Nahidi F et al. The impact of a lifestyle promotion program on anthropometric and clinical manifestations in adolescents with polycystic ovarian syndrome: a randomized controlled trial. BMC Womens Health. 2024 Dec 4;24(1):637.
5. Marzouk T, Nabil H, Senna M. Impact of a Lifestyle Modification Program on Menstrual Irregularity among Overweight or Obese Women with Polycystic Ovarian Syndrome. Korean J Women Health Nurs. 2015 Sep;21(3):161-170.

Adenocarcinoma of the cervical region manifested as ovarian torsion

Introduction

The World Health Organization (WHO) ranks cervical cancer as the fourth most frequent cancer affecting women worldwide. There are two main subtypes of cervical neoplasia: adenocarcinoma (AC) and squamous cell carcinoma (SCC). About 25% of all cervical cancers are AC.[1] According to the WHO and the International Endocervical Adenocarcinoma Criteria and Classification (IECC) systems, high-risk human papillomavirus is responsible for the majority of AC (~80%). Based on appearance, the IECC divides cervical AC into two main groups: non-HPV-associated (NHPVA) and human papillomavirus-associated (HPVA). According to reports, 77% of ovarian mucinous adenocarcinomas are metastatic tumors,

despite the fact that only 6–25% of ovarian adenocarcinomas are mucinous. Compared to ovarian original tumors, 94% of bilateral ovarian cancers are metastatic.[2] This was a case of cervical AC that was initially misdiagnosed as mucinous ovarian adenocarcinoma and manifested as bilateral ovarian masses with ovarian torsion.[3]

Case presentation

A 41-year-old woman with a history of ovarian cancer was admitted to the emergency room, due to vomiting and stomach pain. She had three previous caesarean deliveries and had not visited a gynaecologist since her last child's birth over 13 years ago. An abdominal and pelvic CT scan revealed bilateral adnexal masses without ascites, peritoneal or omental illness, and severe hepatic steatosis. The patient had both of her ovarian cysts removed laparoscopically, but intraoperative observations included a 13 cm left ovarian cyst that was clearly venous in congested and had twisted three times on the left infundibulopelvic ligament. The patient's gynecologic oncology consultation found no uterine/parametrial abnormalities, adnexal tumors, or cervical lesions. The proposed treatment included a colonoscopy, an appendectomy, omentectomy, pelvic and para-aortic lymph node biopsy, and a staging procedure using a robotic-assisted TLH BSO. The colonoscopy was normal, and fine peritoneal nodules were discovered throughout the pelvis during surgery. The tumor was classified as AJCC Stage IVB with a PDL1 tumor proportion score (TPS) of 1%. The patient received eight rounds of chemotherapy with carboplatin and paclitaxel, immunotherapy with bevacizumab and pembrolizumab, and maintenance regimen with bevacizumab and pembrolizumab. Radiation therapy was not administered to her. CT scan revealed growing peritoneal and anterior wall implants, indicative of progressing illness. After being moved to Tisotumab, the patient experienced severe ascites and had to be admitted to the hospital. She was switched on carboplatin and taxol while in the hospital. Cardioplatin and taxol were switched on while she was in the hospital. Then she died due to cardio-pulmonary arrest.

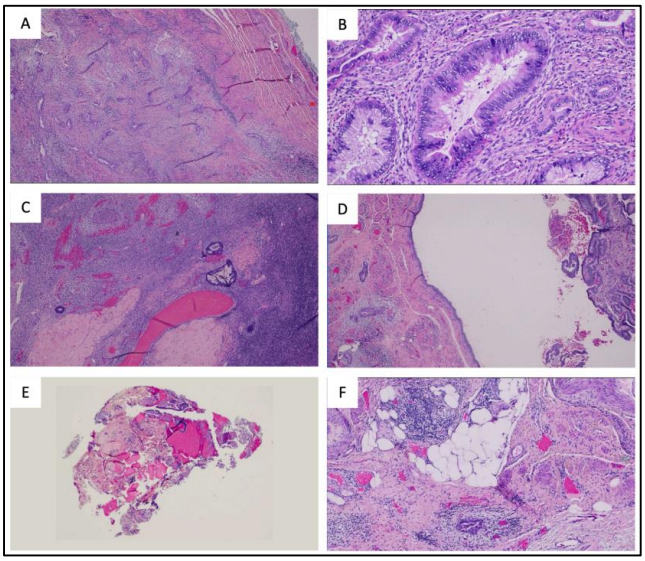

Figure 1: A) Cervical stromal involvement by invasive adenocarcinoma (40x); B) Cervical stromal involvement by invasive adenocarcinoma (200 x); C) Metastatic adenocarcinoma involving ovary (40x); D) Metastatic adenocarcinoma involving fallopian tube (40x); E) Metastatic adenocarcinoma involving diaphragm (40x). F) Metastatic carcinoma involving parametrium (40x)

Discussion

In this case, the patient was treated with pembrolizumab after developing pathology with PD-L1 and TPS 1%. Pembrolizumab was added to cervical cancer patients in a phase 3 trial, which decreased disease progression by 35% and death by 36% in patients with a PD-L1 positive score greater than 1. Most patients in that study had squamous cell carcinoma; adenocarcinoma affected 18% of individuals in the pembrolizumab group and 27% of patients in the placebo group. Squamous cell carcinoma has a greater PD-L1 positive than adenocarcinoma. PD-L1 testing is required since TPS is a marker for the effectiveness of monoclonal antibodies like pembrolizumab, even though PD-L1 is less prevalent in adenocarcinoma.[3] It has been noted that surgically removing adnexal tumors can improve treatment results for advanced cervical cancer.[4]

Conclusion

Although the case is uncommon, it illustrates how clinical skills have improved to enable us to make a precise pre-operative diagnosis. Because of cytologic screening and the HPV vaccine, the incidence of cervical AC is rising while that of SCC is declining. However, mucinous ovarian AC is typically a metastasis, and in order to try to find the original tumor, a thorough and detailed work-up is necessary.

Cervical Adenocarcinoma is increasing in incidence while squamous cell carcinoma is decreasing due to cytologic screening and the HPV vaccine.

References

1. Hodgson A, Park KJ. Cervical Adenocarcinomas: A Heterogeneous Group of Tumors with Variable Etiologies and Clinical Outcomes. Arch Pathol Lab Med. 2019 Jan;143(1):34-46.
2. Seidman JD, Kurman RJ, Ronnett BM. Primary and metastatic mucinous adenocarcinomas in the ovaries: incidence in routine practice with a new approach to improve intraoperative diagnosis. Am J Surg Pathol. 2003 Jul;27(7):985-93.
3. Mvula M et al. Cervical adenocarcinoma presenting as an ovarian torsion. Gynecol Oncol Rep. 2024 Nov 19; 56:101546.
4. Nagel CI et al. Adnexal masses requiring surgical intervention in women with advanced cervical cancer. Gynecol Oncol. 2014 Sep;134(3):552-5.