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Case Report

A case report on endometrial stromal sarcoma: a diagnostic challenge

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ABSTRACT

Endometrial stromal sarcoma (ESS) is a rare and malignant tumor of the endometrial stroma, predominantly affecting women in their 40s and 50s. Here, we report a unique case of a 60-year-old post-menopausal woman, para 3 live 3 (P3L3), presenting with post-menopausal bleeding, initially thought to be due to a primary vaginal sarcoma. Despite an extensive diagnostic workup, including pelvic exams, Pap smears, and vaginal ultrasound, no abnormalities were detected. However, repeated episodes of post-menopausal bleeding prompted further investigation, including magnetic resonance imaging (MRI) and fractional curettage, which revealed a polypoidal growth in the right fornix extending through the OS. The clinical impression favored a primary vaginal sarcoma metastasizing to the uterus. The patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Surprisingly, histopathological analysis determined the tumor originated from the endometrial stromal tissue with metastasis to the vagina. The tumor was classified as low-grade with significant myometrial invasion (greater than 50%). Post-operatively, lymph node resection was performed, followed by adjuvant radiotherapy to mitigate recurrence risk. This case highlights the diagnostic complexities of ESS, particularly when it mimics primary vaginal tumors, and underscores the importance of histopathological evaluation in determining the correct tumor origin. ESS is rare, constituting about 0.2% of all uterine malignancies, and this case emphasizes the importance of multidisciplinary management and vigilant follow-up to optimize patient outcomes.

Keywords: Endometrial stromal sarcoma, Post-menopausal bleeding, Vaginal metastasis, Uterine sarcoma, Low-grade ESS

INTRODUCTION

Endometrial sarcomas are uncommon gynecological malignancies that originate from the endometrial stromal tissue. Their rarity and diverse clinical presentations can lead to diagnostic complexities. Cancers arising from mesodermal structures like muscles and connective tissue are called sarcomas. Sarcomas of the uterus are uncommon and may arise from connective tissue, smooth muscle, or the endometrial stroma. Uterine sarcoma is a rare form of malignancy, occurring in 2–5% of all patients with uterine malignancy, with an incidence of approximately one to two cases per 100,000 women in the general population. Endometrial stromal sarcomas (ESSs) are very rare malignant tumors that make up approximately 10% of all uterine sarcomas but only around 0.2% of all uterine malignancies.[1]

CASE REPORT

A 60-year-old post-menopausal woman, P3L3, presented with a complaint of post-menopausal bleeding that started in October 2023. She had a history of three pregnancies, all of which resulted in live births. All her deliveries were via normal vaginal delivery, and menopause occurred 20 years ago. During her initial evaluation, physical examination, including a pelvic examination, showed no abnormal findings. Pap smear results were negative for any abnormal cells, and a vaginal ultrasound revealed no visible abnormalities. She underwent fractional curettage

due to persistent post-menopausal bleeding. The endometrial sample obtained during the procedure showed disorderly proliferative changes and the presence of a benign cervical polyp, which was subsequently removed. Despite the initial diagnostic workup, she experienced post-menopausal bleeding again in March 2024. On examination a polypoidal growth measuring 3×2 cm in the right fornix extending through the OS was noted. To further investigate the cause, a magnetic resonance imaging (MRI) was performed, and based on the findings, another fractional curettage was scheduled. Clinical examination and MRI findings showed a tumor which appeared to have originated in the vagina and subsequently spread to the endometrium, mimicking a primary vaginal sarcoma. With the clinical impression of a primary vaginal sarcoma that metastasized to the uterus, the patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Intraoperatively, a tumor measuring 6.5×6×3.5 cm, arising from the right anterior vaginal wall and extending into the right parametrium, was resected. The uterus, tubes, and ovaries appeared normal, and no evidence of deposits or metastasis was found. The specimen was sent for histopathological analysis, and to everyone's surprise, the results revealed that the tumor had originated from the endometrial stromal tissue and had metastasized to the vagina, contrary to the initial clinical impression.

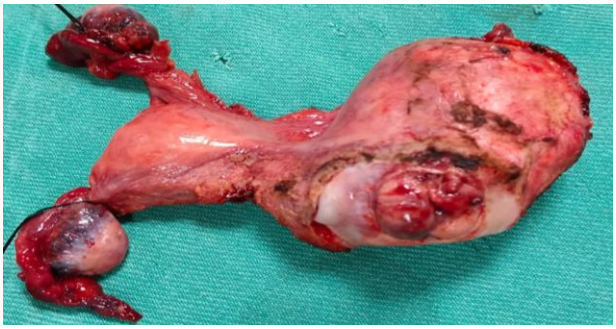

Figure 1: Gross finding of endometrial stromal sarcoma arising from vagina involving the cervix and partly the uterus.

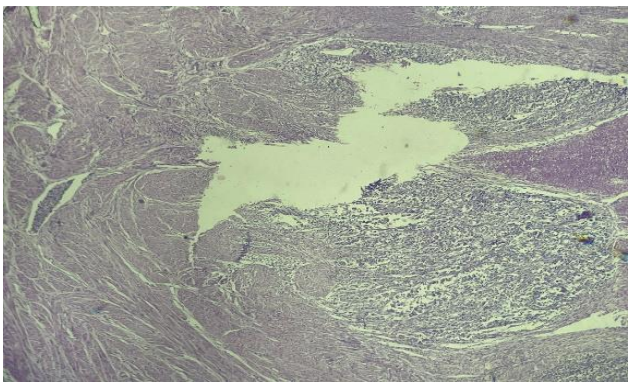

Figure 2: The tumour cells on H&E are densely packed with presence of arterioles and capillaries in an irregular pattern.

Histopathological analysis

Tumor was classified as low grade, with myometrial invasion above 50%. The ovaries, tubes, and vaginal cuff were uninvolved, and no lymphovascular invasion or peritoneal ascites fluid deposits were detected. Staging of the tumor was categorized as pTIIb.

This case highlights the complexities involved in diagnosing endometrial stromal sarcoma, particularly when they mimic primary vaginal tumors. It emphasizes the importance of accurate histopathological analysis to determine the true origin of the tumor and guide appropriate management.

Treatment and follow-up

Given the potential risk of lymph node involvement, lymph nodes were removed, and adjuvant radiotherapy was initiated to address potential residual disease and minimize recurrence risk.

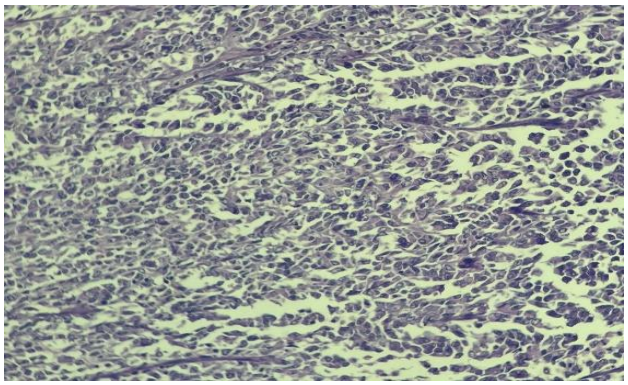

Figure 3: The tumour cells are dense and relatively uniform population of small, spindle-shaped cells with irregular borders.

DISCUSSION

ESS is an exceptionally rare malignancy, accounting for a mere 0.2% of all uterine malignancies. Its annual incidence is estimated to be 1-2 cases per million women, underscoring its infrequent occurrence in the spectrum of gynecological tumors.[1] While most ESS cases arise within the uterus, extra uterine occurrences are also documented, albeit rarely, involving sites such as the pelvic cavity, ovary, abdominal cavity, fallopian tube, retroperitoneum, vagina, and vulva. Among these sites, vaginal origin and spread is exceedingly uncommon, with only a handful of reported cases in the existing literature.[2]

Origin of tumor cells

Interestingly, the origin of extra uterine ESS tumor cells remains an enigma. The presence of endometriosis in proximity to neoplasms in many cases suggests a plausible association, with the hypothesis of the secondary

Müllerian system proposing that mesenchymal cells within celomic epithelium-derived tissues could differentiate into Müllerian-type epithelium and stroma, contributing to tumor formation.[2] Nonetheless, in sites lacking endometriosis, an alternative origin from primitive cells of the pelvis and retroperitoneum is suggested.[2]

Classification

The current World Health Organization (WHO) classification categorizes endometrial stromal tumors into four distinct groups: endometrial stromal nodule (ESN), low-grade endometrial stromal sarcoma (LG-ESS), high-grade endometrial stromal sarcoma (HG-ESS), and undifferentiated uterine sarcoma (UUS).[3] Low-grade ESS is often characterized by the presence of chromosomal rearrangements leading to JAZF1-SUZ12 fusion or equivalent genetic fusions, reflecting its close resemblance to proliferative-phase endometrial stromal cells.[4] Conversely, high-grade ESS, now termed undifferentiated endometrial sarcoma (UES), is defined by the YWHAE-NUTM2A/B (YWHAE-FAM22A/B) genetic fusion and is marked by distinct histological features, including myometrial invasion, hemorrhage, necrosis, nuclear pleomorphism, and high mitotic activity.[4]

Differential diagnosis

Distinguishing low-grade ESS from histological mimics such as endometrial stromal nodules, cellular leiomyomas, and cellular intravenous leiomyomatosis is imperative for accurate diagnosis.[5] Notably, cellular leiomyomas exhibit characteristic spindle-shaped nuclei with fascicular growth patterns and thick muscular-walled vessels, aiding differentiation from ESS. Microscopic analysis revealing infiltrative margins and worm-like cord growth patterns further aids in the distinction between low-grade ESS and other entities.[5]

Immunohistochemical markers, such as CD10, have proven valuable in distinguishing ESS from its mimics. Strong and diffuse positivity for CD10 aids in differentiating ESS from cellular leiomyoma and other histological mimics, complementing the diagnostic arsenal.[6]

Prognostic factors

In terms of prognosis, early tumor stage, low myometrial invasion, and low mitotic count emerged as favorable prognostic factors for overall survival in ESS patients, highlighting the importance of these parameters in clinical management decisions.[7] Hormone receptor expression, particularly the predominance of PRA over PRB, was found in primary LGESS, mirroring the profile of normal endometrial stroma.[8] A shift in receptor expression between primary and recurrent disease was observed in some cases, underlining the dynamic nature of these tumors.[8]

Treatment

Hysterectomy and bilateral salpingo-oophorectomy is the cornerstone of treatment for early-stage (I or II) disease. Surgical resection when feasible may also be appropriate for patients presenting with advanced-stage tumors. The value of adjuvant therapy for early-stage disease remains unproven. Hormone therapy continues to be the most efficacious treatment modality for patients with advanced-stage or recurrent disease.[9]

CONCLUSION

In conclusion, the presented case sheds light on the diagnostic intricacies of ESS, particularly their mimicry of primary vaginal tumors. Accurate histopathological analysis remains paramount in determining the true tumor origin, enabling informed management decisions. The rarity of ESS, further emphasizes the need for heightened clinical awareness. This case of endometrial stromal sarcoma metastasis to vagina underscores the need for multidisciplinary collaboration and vigilant follow-up in managing such rare malignancies. Awareness of these challenging presentations is crucial for improving diagnostic accuracy and optimizing patient outcomes. Further research and reporting of similar cases are essential to expand our understanding of these rare gynecological tumors.

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