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Differential Diagnosis of Endometrial Stromal Sarcoma Mimicking Other Types of Fibroids: A Case Study

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Abstract

Methods: A single patient presenting with a pelvic mass was examined. The research included a detailed medical history, physical examination, and imaging studies. The clinical symptoms, imaging characteristics, and histopathological findings were analyzed to distinguish ESS from other fibroid types. **Results:** The patient initially presented with symptoms and imaging suggestive of typical uterine fibroids. However, histopathological evaluation revealed the presence of ESS. This case underscores the critical role of histopathology in differentiating ESS from other benign fibroids, which may appear similar on imaging. The discussion focuses on the diagnostic challenges, the importance of considering ESS in differential diagnoses, and the implications for patient management and prognosis. **Conclusion:** Accurate differential diagnosis between endometrial stromal sarcoma and other fibroids is crucial for effective patient management. This case highlights the necessity of comprehensive diagnostic approaches, including histopathological examination, to avoid misdiagnosis and ensure appropriate treatment strategies.

Keywords: differential diagnosis, endometrial stromal sarcoma, fibroids, histopathology, uterine tumors

Introduction

Uterine sarcomas are rare genuine tumors of mesenchymal cells generated from uterine muscle or endometrial stroma. Malignancies of the endometrial stroma are classified as carcinosarcoma, adenosarcoma, or ESS based on the presence and type of their epithelial components. Endometrial Stromal Sarcoma (ESS) is a malignant tumor that develops from the endometrial stroma, the tissue that supports the endometrial cells.[1] ESS is the second most prevalent kind of uterine sarcoma, following leiomyosarcoma. There are two varieties of ESS: low-grade and high-grade. The distinction between these two varieties of ESS is that low-grade ESS typically increases slowly and has a better prognosis than high-grade ESS. However, these are still malignant illnesses that necessitate prompt and appropriate treatment.[2]

Endometrial Stromal Sarcoma (ESS) is a rare kind of uterine cancer that makes up only 0.2% of all malignant uterine tumors. In the general community, one to two instances of uterine sarcoma are reported per 100,000 people per year. ESS is estimated to account between 7-25% of all uterine mesenchymal tumors and fewer than 1% of all uterine tumors globally. Meanwhile, from 2018 to 2023, the incidence of ESS in Indonesia accounted for just 1.8% of the total incidence of endometrial cancers.[2,3]

Fibroids, sometimes called leiomyomas or myomas, are non-cancerous mass growths that can occur inside or outside the uterus. Fibroids are frequent uterine growths that often form during the years when a woman is able to conceive and give birth. Fibroids range in quantity and size, from as small as a seed to as large as a melon. Although fibroids are benign growths, they can produce a range of unpleasant symptoms, including excessive monthly bleeding, pelvic pain, and fertility issues.[4]

Myomas are classified into numerous forms, including submucosal myomas, which grow in the thinnest layer inside the uterine cavity, and subserosal myomas, which grow outside the uterus. Myomas vary in size from 1 mm to 20 cm. Uterine myoma can affect any race, however it is most prevalent in black women (18%), 10% in Hispanic women, 8% in white women, and seldom in Asian women. The majority of cases are asymptomatic, with about 30% exhibiting symptoms. Approximately 80% of uterine myomas are numerous, with pregnant women accounting for 10.7%.[4,5]

It can be difficult to distinguish between ESS and fibroids because both are uterine growths. However, ESS is a cancerous illness, whereas fibroids are benign growths. As a result, understanding the differences between the two is critical for accurate diagnosis and therapy. One of the primary distinctions between the two is that ESSs frequently exhibit infiltrative growth or lymphovascular invasion, whereas fibroids typically develop as a mass separate from the surrounding tissue.[4,5]

Radiation therapy, Tamoxifen use, and a family history of hereditary leiomyomatosis syndrome and renal cell carcinoma are all risk factors for developing ESS. Fibroids, on the other hand, are benign growths that occur in women of reproductive age and are associated with a number of risk factors such as age, race, obesity, family history, high blood pressure, and vitamin D insufficiency.[4,5]

This case report will look at the diagnostic differences between Endometrial Stromal Sarcoma and other forms of fibroids. Understanding these differences is intended to help medical practitioners make the accurate diagnosis and develop the most effective treatment strategy. Furthermore, the purpose of this report is to provide additional insights on how to discriminate between these two illnesses in clinical practice, so enhancing patient care.

Case Description

The patient, a 37-year-old woman, first came to the clinic on April 3, 2024 with a chief complaint of heavy and prolonged menstrual bleeding. This bleeding had started since June 2023 with a menstrual cycle that could last for 24 days without stopping. The patient also experienced stabbing pain that sometimes interfered with her activities. The patient had her first menarche at the age of 12 with an initially regular menstrual cycle. The patient had a history of obstetric P2 and both children were born perabdominally and healthy. On physical examination, no pelvic examination was performed. Ultrasound examination showed an antiflexed uterus with an endometrial line of 18 mm. There was a 15 cm firm mass in the uterine posterior that had restricted movement. This mass exhibited hypervascularization.

On April 17, 2024, the patient had an abdominal CT scan. The CT scan results were discussed during the first clinic visit on April 26, 2024. Multiple uterine tumors attached to the vesica urinaria, right distal ureter, attached and restricted sigmoid colon, non-infiltrating. There was no bilateral para-aortic or para-iliac KGB enlargement.

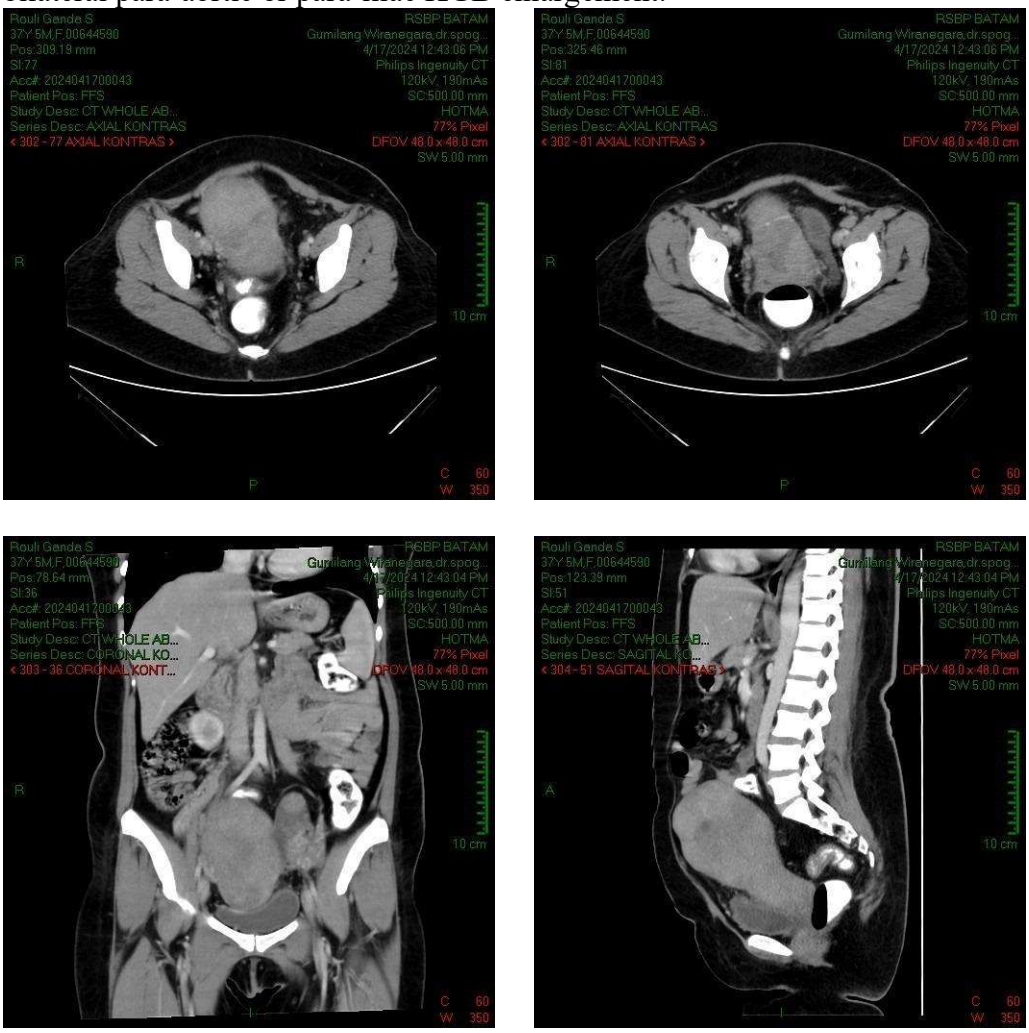

Figure 1. CT Scan Image with Contrast

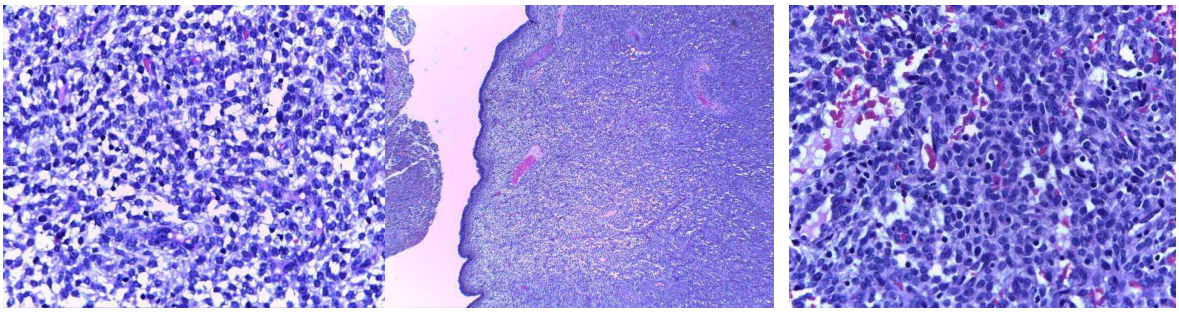

Figure 2. Anatomical pathology of the patient

The woman came to the clinic for a second checkup to review the hysterescopy and anatomical pathology findings. The anatomical pathology examination revealed fragments of endometrial tissue that provided the appearance of endometrial stromal sarcoma. Subsequently, the patient's

treatment will include laparoscopic debulking.

Discussion

This case report details the illness of a 37-year-old female patient who had significant and protracted menstrual bleeding. The patient was first diagnosed with a submucosal myoma, but during endometrial resection hysteroscopy surgery, anatomical pathology revealed Endometrial Stromal Sarcoma (ESS).

Submucosal myoma is a form of fibroid that grows inside the uterine cavity and can cause heavy monthly flow and pelvic pain, as this patient has. Although fibroids are benign tumors, they can produce a variety of annoying symptoms and lower the patient's quality of life. Endometrial Stromal Sarcoma (ESS) is a rare malignant tumor that is typically discovered in perimenopausal women with symptoms similar to fibroids, making both ESS and fibroids a differential diagnosis.[6-8]

For fibroid cases, advanced treatments such as biopsy are usually done after the hysteroscopy procedure. The tumor tissue sample taken will then be examined in the laboratory to determine whether the tumor is benign or malignant. On ultrasound, these fibroids are usually seen as broad-based, hypoechoic, solid masses with clear borders with shadows.[9]

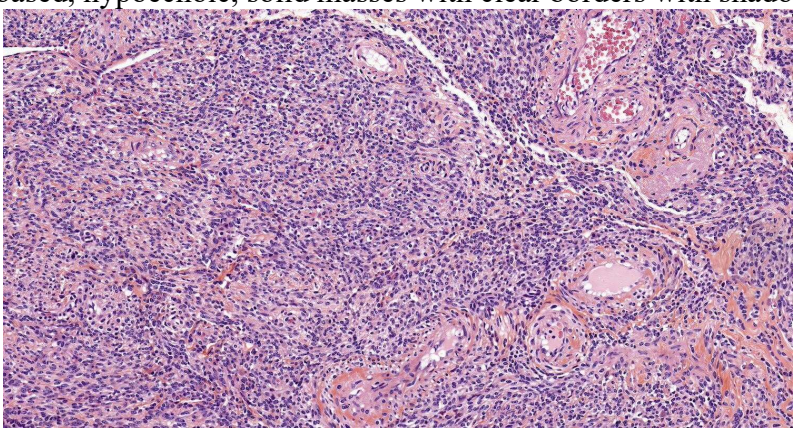

FIgure 3. Myoma Fibroids, showing increased cellularity and little cytoplasm without increased mitotic activity and atypia.
Source: https://www.pathologyoutlines.com/topic/uterusleiomyoma.html

Submucosal myomas are typically well-defined tumors from an anatomical standpoint. They can develop in any area of the uterus, including the cervix. These tumors can grow pedunculated, protruding into the uterine cavity or through the cervix. In terms of microscopic biopsies, each leiomyoma lesion in the uterus may have various isoforms and is thought to develop separately. Cytogenetic anomalies on numerous chromosomes have been found in these smooth muscle tumors, despite normal karyotypes in neighboring non-tumor regions. These cytogenetic mutations have been found in around 40% of uterine leiomyomas. Some mutations affect genes involved in cell growth regulation.[10-12]

Submucosum (spindle) myoma has distinct boundaries and is normocellular. It is made up of interconnecting fascicles of monotonous spindle cells with indistinct boundaries, eosinophilic cytoplasm, cigar-shaped nuclei (tapered ends), and small nucleoli. Atypia is typically absent or moderate. Mitoses are extremely rare, with less than 5 per 10 high field of vision. These

leiomyomas also have thick-walled blood arteries. These leiomyomas may or may not exhibit infarct-type necrosis, hyalinization, calcification, or cystic alterations.[13,14]

Meanwhile, for Endometrial Stromal Sarcoma (ESS), definitive diagnosis and treatment usually require hysterectomy because it must be determined whether stromal cell changes occur as a whole or if cell changes are limited, which will be the basis for grading ESS cases, namely Low Grade Endometrial Stromal Sarcoma or High Grade Endometrial Stromal Sarcoma. As a result, endometrial biopsy or curettage alone are rarely used to diagnose ESS. LG-ESS is defined in pathology reports as stromal cell alterations that spread across the uterine muscle wall and lymph nodes. [15]

LG-ESS histology shows monotonous oval to spindle-shaped cells with low cytologic atypia, vesicular chromatin, and sparse cytoplasm. Mitotic numbers are often low (<5/10 high power fields), and necrosis is frequently absent8. While HG-ESS refers to severe stromal cell alterations that have rapidly split and may have expanded outside the uterus. HG-ESS is distinguished by permeative invasion (tongue-shaped), vaguely nested round-shaped cell development with low to moderate eosinophilic cytoplasm, and homogenous nuclear atypia. Frequently, this image is broad, encompassing not just the endometrium but also the myometrium. Mitosis occurs rapidly (>10/10 high power field), and there is frequently tumor cell necrosis and lymphovascular invasion. Stromal nodule features are also often found as in the results of the anatomical pathology examination in this case[8].

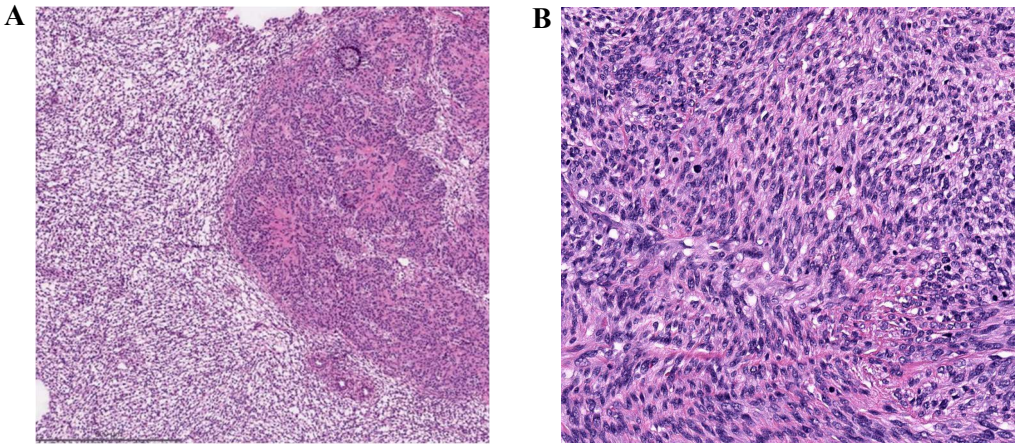

Figure 4. (A) LG-ESS with coiled splinded cells around blood vessels and foci of differentiation around areas of smooth muscle (B) HG-ESS with uniform atypical spindled cells and rapid mitosis. Source: https://www.pathologyoutlines.com/topic/uterusESShighgrade.html

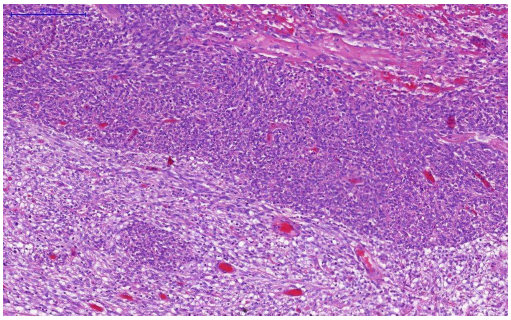

Figure 5. HG-ESS Small round cells (top) and spindled cells (bottom).
Source: https://www.pathologyoutlines.com/topic/uterusESShighgrade.html

In the context of this case report, it is important to note that, while the patient's initial symptoms may indicate the presence of fibroids, the final diagnosis of Endometrial Stromal Sarcoma (ESS) can only be determined after anatomical pathology examination, as there are no specific radiological findings, serum markers, or symptoms. This highlights the significance of anatomical pathology examinations in distinguishing between ESS and fibroids[16].

In theory, ultrasonography imaging shows ESS as an intramural mass extending into the endometrial cavity or as a purely intramural mass. The characteristics of ESS vary greatly: some cases have a mainly solid mass with cystic degeneration, while others have unclear infiltrative solid masses.[16]

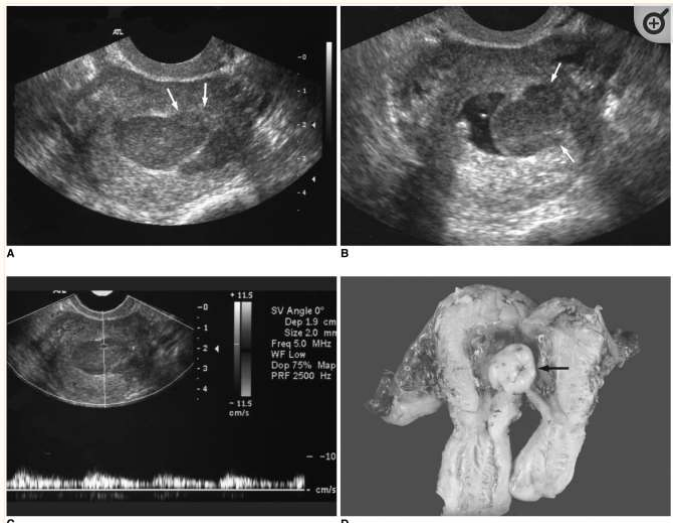

Figure 6. An ultrasound image of ESS (A) and a sonohysterographic image (B) indicate a hypoechoic mass in the myometrium with partially unclear borders against the endometrium and apparent nodular invasion of the myometrium. Figure C depicts vascularization with low resistance pulsatile flow in the mass via pulsed Doppler imaging. Figure D depicts a gross hysterectomy specimen with a polypoid mass (arrow) projecting into the endometrial cavity from the myometrium.

Source: Kim JA, Lee MS, Choi JS. Sonographic findings for uterine endometrial stromal sarcoma. Korean J Radiol. 2006 Oct-Dec;7(4):281-6. DOI: 10.3348/kjr.2006.7.4.281. PMID: 17143032, PMCID: PMC2667615.

Previous research, reported by Sqalli et al. in 2023, revealed that on CT scan imaging, ESS typically presents as a mass in the myometrium and can demonstrate widespread and multinodular distribution inside the myometrium. These masses may contain both solid and cystic portions, with heterogeneous contrast enhancement of the solid component and visible septae. This is consistent with the findings from this patient's abdominal CT scan, which show a mass with contrast enhancement linked to both the vesica urinaria and the right distal ureter.[16]

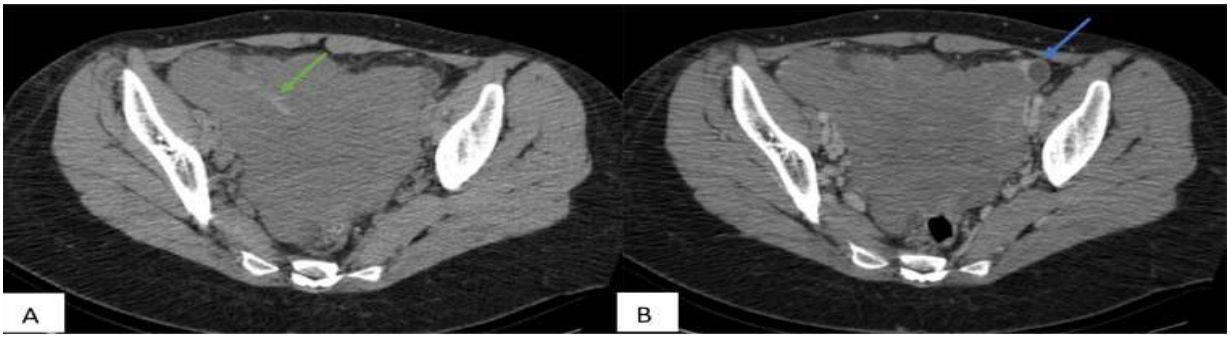

Figure 7. Axial computed tomography scans of the abdomen and pelvis before (A) and after contrast (B) show bilateral ovarian tumors with heterogeneous contrast enhancement, including hemorrhagic (green arrows) and cystic (blue arrows) areas.

Source: Sqalli Houssaini M, Haloua M, Mourabiti AY, Tahiri L, Fdili Alaoui FZ, Akammar A, El Bouardi N, Alami B, Alaoui Lamrani MY, Maaroufi M, Boubbou M. A case of ovarian endometrial stromal sarcoma: Radiological and histopathological findings. Radiol Case Rep. 2023 Jul 28;18(10):3529-3534. doi: 10.1016/j.radcr.2023.07.027. PMID: 37547797; PMCID: PMC10400806.

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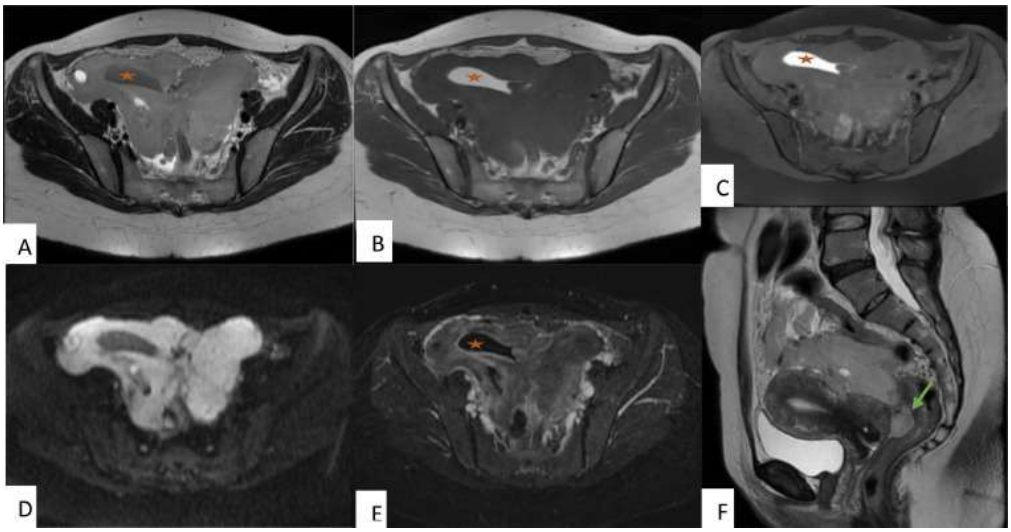

Figure 8. Axial T2WI (A), T1WI (B), T1 fat-weighted suppression image (C), diffusion (D), dynamic contrast-enhanced image (E) and sagittal T2WI (F) of the tumor showing heterogeneous intensity on T2WI and diffusion-limited T1WI, including areas "that are hyperintense on T1WI, not erased on T1 fat-weighted suppression image, hypointense on T2WI, and not enhanced after contrast (orange stars)." This mass extends into Douglas and invades the uterus and serous rectum (green arrow).

Source: Sqalli Houssaini M, Haloua M, Mourabiti AY, Tahiri L, Fdili Alaoui FZ, Akammar A, El Bouardi N, Alami B, Alaoui Lamrani MY, Maaroufi M, Boubbou M. A case of ovarian endometrial stromal sarcoma: Radiological and histopathological findings. Radiol Case Rep. 2023 Jul 28;18(10):3529-3534. doi: 10.1016/j.radcr.2023.07.027. PMID: 37547797; PMCID: PMC10400806.

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In the case of ESS, hysteroscopy can serve both diagnostic and therapeutic reasons. As a diagnostic tool, hysteroscopy can assist doctors in determining the cause of abnormal bleeding, such as excessive bleeding during menstruation or bleeding after menopause. Hysteroscopy and curettage methods can be used to collect endometrial tissue samples, which can then be examined under a microscope for typical signs of ESS cells. However, ESS is rarely detected with endometrial biopsy or curettage. Thus, while this approach can provide a definite diagnosis, its sensitivity may be limited. The sensitivity is approximately 46% and the specificity is 96%. [14-16]

Low sensitivity during endometrial biopsy using the Endometrial Sampling System (ESS) can be caused by a variety of causes. One of these is the variability in sampling. For example, the sample collected may not encompass the afflicted area, and the pathologist's interpretation of the data may vary. High specificity, on the other hand, means that if the endometrial biopsy results are positive, the individual is very likely to have the suspected illness. In other words, endometrial biopsies rarely produce false-positive results. [10]

However, it is crucial to highlight that sensitivity and specificity are not the sole considerations when evaluating diagnostic tests. Other aspects to consider include the condition's prevalence, the dangers and repercussions of false positive or false negative results, as well as the test's cost and availability. Hysterescopy is a therapeutic tool for tiny lesions (<1cm) that allow for full excision.

Conclusion:

This case report focuses on the diagnostic problems in distinguishing endometrial stromal sarcoma (ESS) from other uterine fibroids. Patients with ESS may appear with general symptoms such as pelvic pain, irregular uterine bleeding, or a pelvic mass resembling a uterine fibroid, hence the initial diagnosis is frequently fibroid-related. Imaging assessment methods typically reveal a

homogeneous mass with distinct boundaries, which is also prevalent in fibroids. However, ESS can occasionally exhibit specific traits such as enhanced vascularization or an infiltrative growth pattern, distinguishing it from normal fibroids. A biopsy and histological analysis can confirm the diagnosis of ESS, which is characterized by tiny, monomorphic endometrial stromal cells with an infiltrative growth pattern. Treatment for ESS differs from that for fibroids, with a more aggressive approach that may include hysterectomy and adjuvant therapy such as radiation or chemotherapy. However, as a beginning point in treating patients, undergoing hysteroscopy to check intra-uterine cavity abnormalities is critical, especially in young instances with vaginal bleeding disorders, since it eliminates different possibilities that could lead to a misdiagnosis. As a result, doctors must consider ESS when making a differential diagnosis of uterine masses, particularly in cases when clinical and radiological characteristics are not entirely consistent with fibroids.

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