Case Report

A High-Grade Undifferentiated Endometrial Stromal Sarcoma Presenting as Inversion of the Uterus: A Rare Case

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Abstract

Endometrial stromal sarcoma (ESS) is a rare malignant tumor that constitutes about 0.2% of all uterine malignancies and 10% of uterine sarcomas. ESS is generally misdiagnosed as leiomyoma or endometrial polyp and typically discovered on histopathological examination postoperatively because of its rarity. Endometrial stromal tumors are composed of cells resembling normal endometrial stroma in its proliferative phase. The histologic diagnosis of the high grade is made if there is a high-grade sarcoma with a high mitotic index and nuclear anaplasia. The mean age of presentation of high-grade endometrial sarcoma is about 61 years with the most common presenting complaint is menorrhagia. The median overall survival for high-grade endometrial sarcoma is 53 months with optimal cytoreduction. A 49-year-old woman P2 L2 presented with nonspecific complaint of discharge and spotting per vaginum. In the present case, the provisional diagnosis by clinical findings as well as imaging was in favor of the inversion of submucous fibroid. Preoperative histopathological examination and immunohistochemistry confirmed the diagnosis of high-grade undifferentiated ESS. Haultain's operation followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. The patient was referred to another center for radiotherapy. From there, she was lost to follow-up. Rarity of endometrial stromal tumor limits the clinician view to diagnose it preoperatively. We were fortunate to have preoperative histopathological diagnosis of ESS. Furthermore, as ESS is rare and undifferentiated stromal sarcoma is even rarer, literature is lacking on its optimal management. Hence, it is important for all clinicians to keep the high degree of suspicion for ESS while working up any case of abnormal uterine bleeding.

Keywords: *Low-grade endometrial stromal sarcoma, undifferentiated endometrial stromal sarcoma, uterine inversion, uterine sarcoma*

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Introduction

Sarcoma is a rarely encountered malignancy of the uterus. The site of origin may be connective tissue, smooth muscle, or endometrial stroma.[1]

Endometrial stromal sarcoma (ESS) is a rare malignant tumor that constitutes about 0.2% of all uterine malignancies and 10% of uterine sarcomas.[1] The annual incidence of ESS is 1–2/million women.[2] Past exposure to pelvic radiation, exposure to tamoxifen, unopposed estrogen, and polycystic ovary syndrome are implicated in the pathogenesis of ESS. Chromosomal aberrations are found linked with ESS, deletion on chromosome 7p being the most common finding (55.6%).[2]

On the basis of mitotic activity, vascular invasion and observed differences in prognosis endometrial stromal tumors are divided into the following three types:

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1. Endometrial stromal nodule
2. ESS
3. High grade or undifferentiated stromal sarcoma.[2,3]

Here, we report the rare case of high-grade undifferentiated ESS.

Case Report

A 49-year-old woman, P2 L2, presented to the gynae outpatient department with complaints of discharge and spotting per vaginum for the past 3 months. Her previous menstrual cycles were regular. Her personal and family history was not significant. There was no history of radiation, tamoxifen, or estrogen use. She was a known case of hypertension. On general examination, pallor was present, and blood pressure was 150/90 mmHg. There was no tachycardia, clubbing, cyanosis, or lymphadenopathy. On systemic examination, cardiorespiratory and neurological systems were normal. On per abdominal examination, there was no organomegaly or lump. On per speculum examination, a cauliflower-like growth of about 6 cm × 8 cm was present completely filling the vagina [Figure 1]. Growth was friable and bled on touch. On pervaginal examination, same growth was felt, and the whole mass was of 10 weeks size and fornices were free. Due to friability, few fragments from the mass were separated and the same sent for histopathological examination. The clinical impression was of advanced-stage cancer cervix. Except for her Hb which was 7.9% g, other blood investigations were within the normal limits. Her ultrasonography reported a large 5.9 cm × 3.4 cm × 6.3 cm heterogeneous mass in the vaginal canal with inferiorly displaced uterine fundus and body with the impression of large prolapsed submucosal fibroid with resultant inversion of uterus or a large cervical growth. Her contrast-enhanced computed tomography of the abdomen reported the inversion of the uterus and occupying the vaginal canal [Figure 2]. The hypodense lesion was noted surrounding the inverted uterus with a thickness measuring 3.5 cm. The final impression was submucosal fibroid with uterine inversion. Histopathological examination reported the possibility of ESS with a heterologous element or leiomyosarcoma with a heterologous element. On immunohistochemistry, it was CD10-positive weakly [Figure 3], and tumor cells were negative for desmin, and thus the diagnosis of high-grade ESS with smooth muscle differentiation and heterologous element was made [Figure 4]. The case was discussed in the institute's multidisciplinary therapy board and was planned for surgery. Preoperatively, two units of packed red cell were transfused. On opening the abdomen, uterine fundus was not visualized. A vas-like appearance was seen [Figure 5] with both the ovaries, tubes, and round ligaments entering into the crater. Debulking was done vaginally, and Haultain's operation was performed. The uterus was then reposited followed by hysterectomy and bilateral salpingo-oophorectomy. Postoperative period was uneventful. Her final histopathological report was high-grade endometrial stromal sarcoma with more than 10 mitosis/10 high-power field and extensive hemorrhage and necrosis with more than 50% of myometrial invasion with estrogen and progesterone receptor positivity. In view of high-grade undifferentiated sarcoma, the patient was referred for radiotherapy postoperatively.

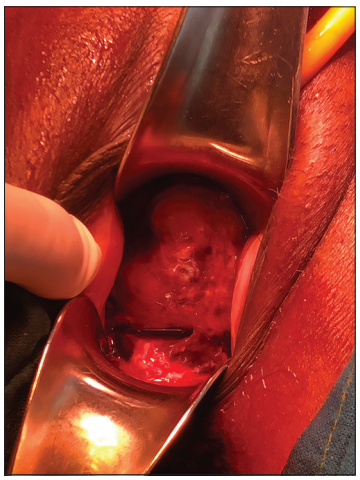

Figure 1: On per speculum examination, cauliflower-like growth was seen

Discussion

ESS is generally misdiagnosed with leiomyoma or endometrial polyp and typically discovered on

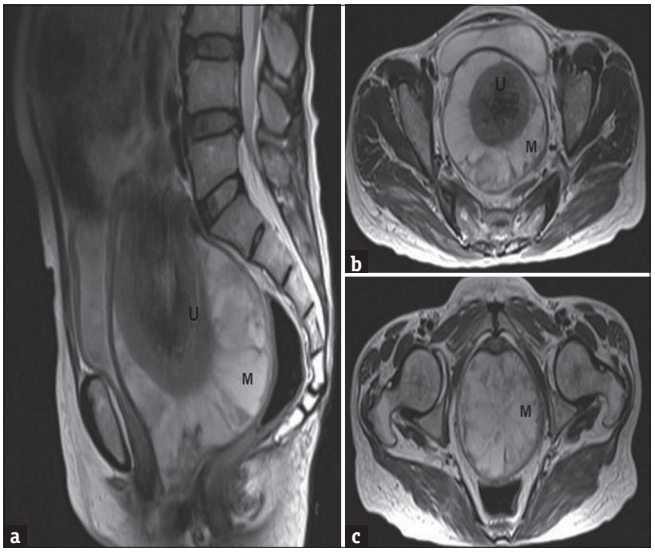

Figure 2: (a) Sagittal T2-weighted magnetic resonance imaging shows T2 hyperintense mass (M) in the pelvis causing inversion of the uterus (U) seen as "V-shape" fundus; (b) axial T2-weighted magnetic resonance imaging shows inverted uterus (U) with "Bull's eye" configuration; (c) axial T2-weighted magnetic resonance imaging at a lower level shows the mass (M)

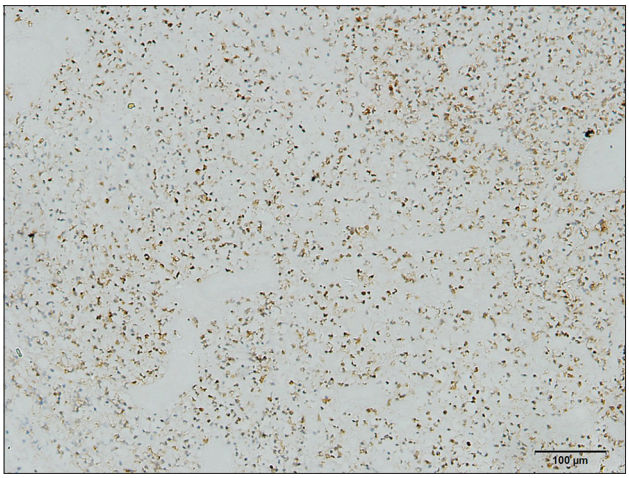

Figure 3: ×10 is showing sprinkling positivity of CD10, consistent with high-grade stromal sarcoma

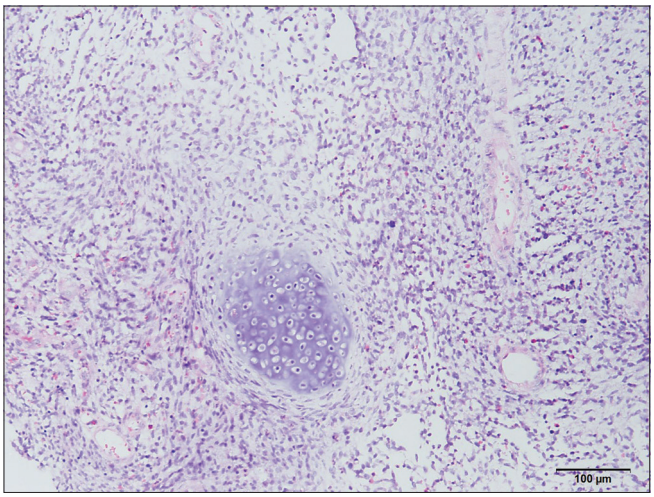

Figure 4: It showing frank areas of endometrial stromal tumor with foci of heterologous cartilaginous formation

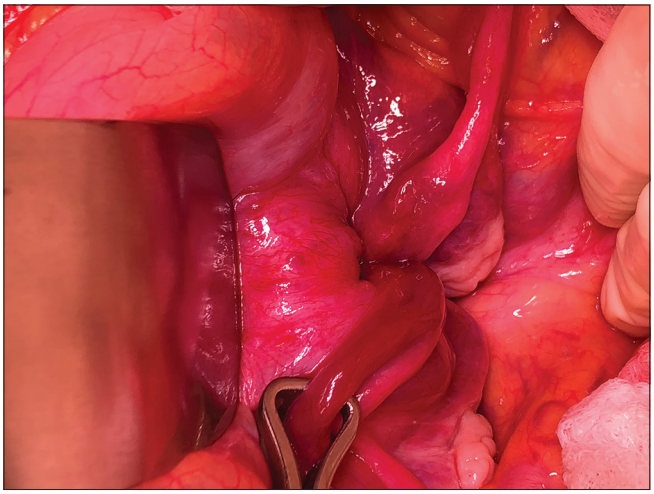

Figure 5: Intraoperatively, vas-like appearance was seen

histopathological examination postoperatively because of its rarity.[4,5] It affects a younger age group, and the mean age is 42–58 years.[2] Nearly 10%–25% affected women are premenopausal.[2] High-grade ESS are seen in the older age group, with a median age of 61 years at presentation and are usually aggressive.[6]

Endometrial stromal tumors are composed of cells resembling normal endometrial stroma in its proliferative phase.

Although menorrhagia is present in 90% of cases, 70% of patients present with uterine enlargement, pelvic pain, and dysmenorrhea. However, many patients can be asymptomatic.[1,2,7] In spite of presenting with typical symptoms and signs, it is rarely suspected as the first diagnosis and more common causes of abnormal uterine bleeding (AUB) such as leiomyoma, endometrial polyps, or submucous fibroid are considered as the etiology.

Although endometrial curettage is the frequently used diagnostic modality for AUB, it is not sensitive for ESS, particularly when the lesion is entirely rooted in the myometrium. Furthermore, because of similarity between ESS and normal endometrial tissue curettage fragments, the diagnosis of ESS can be missed.[2] Ultrasound, especially, transvaginal can be helpful in diagnosing uterine leiomyoma, adenomyosis, or endometrial polyps but unpredictable in diagnosing ESS. Transvaginal Doppler can play a role in diagnosing ESS in which ESS has a low-impedance flow and hence delineates it from the rest of uterine tissue. Magnetic resonance imaging scan can also diagnose it by the presence of low-intensity bands within the area of myometrial invasion due to worm-like permeations of tumor.[2] This can help in the preoperative diagnosis of ESS. Undifferentiated endometrial sarcoma (UES) may present as heterogeneous signal intensity voluminous polypoidal mass with more frequent myometrial involvement which can be demarcated or diffusely infiltrative on T1- and T2-weighted images.[8] UES frequently has hemorrhage and necrosis and shows vascular and lymphatic invasion. While often indolent in behavior, ESS is malignant and can spread to the vagina, Fallopian tubes, ovaries, bladder, and ureters. Distant metastasis to the lung, heart, and other sites has also been reported.[9,10] High-grade undifferentiated tumor tends to be larger, more polypoidal as presented in the index case (Stage IB). Due to the large growth, the uterus got inverted. High-grade undifferentiated tumor displaces the myometrium more destructively, leading to prominent hemorrhage and necrosis.[11]

At times, it is very difficult to differentiate ESS from cellular leiomyoma. In these cases, immunohistochemistry is particularly helpful to get the final diagnosis. The immunohistochemical markers such

as h-caldesmon and CD 10 may solve the diagnostic problem as CD 10 staining is positive in ESS but not in leiomyosarcoma. We performed CD-10 staining to establish the diagnosis. Survival in patients with undifferentiated ESS appears to be related to the extent of residual disease after initial surgery and would suggest the necessity for aggressive cytoreduction as a main modality of the treatment.[2] Limited clinical data suggest that patients presenting at higher stage have a worse prognosis as compared to published outcomes in low-grade ESS. Moreover, in the same study, the mean age of presentation was 54 years, and they were predominantly based in endomyometrium and demonstrated tongue-like projections.[12]

The treatment includes debulking surgery followed by total hysterectomy with bilateral salpingo-oophorectomy).[13]

Postoperative radiotherapy or progesterone is an effective adjuvant treatment providing high local control rates in uterine sarcomas. Hormone therapy with medroxyprogesterone, tamoxifen, gonadotropin-releasing hormone analogs, and aromatase inhibitors are suggested for low-grade ESS Stage 3-4 and for recurrent disease.[14,15] In contrast, high-grade undifferentiated tumors are not responsive to progestin therapy, and the poor therapeutic result suggests that radiation therapy, chemotherapy, or both should be used in combination to the surgery.[16] Our patient was referred for radiotherapy postoperatively. One of the retrospective studies reported that adjuvant radiotherapy and chemotherapy appear to improve overall survival.[17]

For high-grade ESS cytotoxic agents such as doxorubicin and ifosfamide or gemcitabine with docetaxel and doxorubicin have been used before surgery for tumor shrinkage.[18]

In another retrospective study, vaginal vault brachytherapy as part of a multimodal adjuvant treatment was associated with a high locoregional control rate and with acceptable side effects in localized high-grade ESS.[19]

Long-term follow-up is necessary in these tumors as local recurrence and distant metastasis can occur even after 20 years of initial diagnosis. It shall be once in 3 months for the 1st year and half yearly for the next 4 years, and thereafter, annual follow-up is recommended.[2] We referred our patient to another center for radiotherapy, and from there, she was lost to follow-up. She did not report to our center thereafter.

Conclusion

Rarity of endometrial stromal tumor limits the clinician view to diagnose it preoperatively. In the present case, even though provisional diagnosis by clinical findings as well as imaging was in favor of submucous fibroid, we were fortunate to have the preoperative histopathological diagnosis of ESS. Furthermore, as ESS is rare and undifferentiated stromal sarcoma is even rarer literature is lacking on its optimal management. Hence, it is important for all clinicians to keep a high degree of suspicion for ESS while working up any case of AUB.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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