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Case Report

Obstetrics and Gynaecology Section

# Endometrial Stromal Sarcoma in a Young, Nulliparous Woman: A Case Report

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## ABSTRACT

Endometrial stromal tumours are tumours of endometrial stromal origin and are classified into Endometrial Stromal Nodule (ESN), Low-Grade Endometrial Stromal Sarcoma (LG-ESS), and High-Grade Endometrial Stromal Sarcoma (HG-ESS). LG-ESS and HG-ESS are rare tumours, accounting for 1% of uterine malignancies and 10% of uterine sarcomas. These tumours commonly occur in perimenopausal women between the ages of 45 and 50 years. Their incidence is rare in younger women. Endometrial stromal tumours are usually confused with leiomyoma, uterine Leiomyosarcoma (LMS), or other sarcomas. The authors here present a case report of a 28-year-old nulligravid patient who presented with a history of heavy menstrual bleeding and dysmenorrhea for a duration of six months. Ultrasonography of the abdomen and pelvis suggested fibroid with degenerative changes, and Magnetic Resonance Imaging (MRI) indicated leiomyoma variants such as: i) Stromal Tumours of Uncertain Malignant Potential (STUMP)/atypical/cellular leiomyoma; ii) myxoid degeneration of leiomyoma. To arrive at a definitive diagnosis, myomectomy was performed considering the woman's young age and nulliparity. Histopathology allowed for a differential diagnosis of LG-ESS, LMS, and cellular leiomyoma. Consequently, the patient underwent total abdominal hysterectomy with left salphingo opherectomy, right salpingectomy, and preservation of the right ovary. The definitive diagnosis is made by histopathological examination coupled with immunohistochemistry of the hysterectomy specimen. Hysterectomy is the definitive treatment of LG-ESS considering their ability to infiltrate and become malignant.

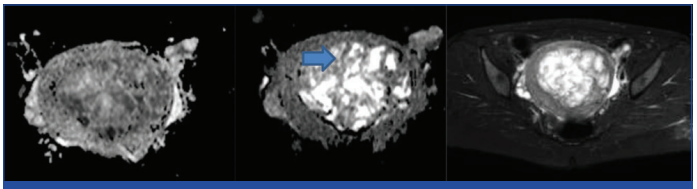

**Keywords:** Leiomyosarcoma, Low grade, Uterine malignancy

## CASE REPORT

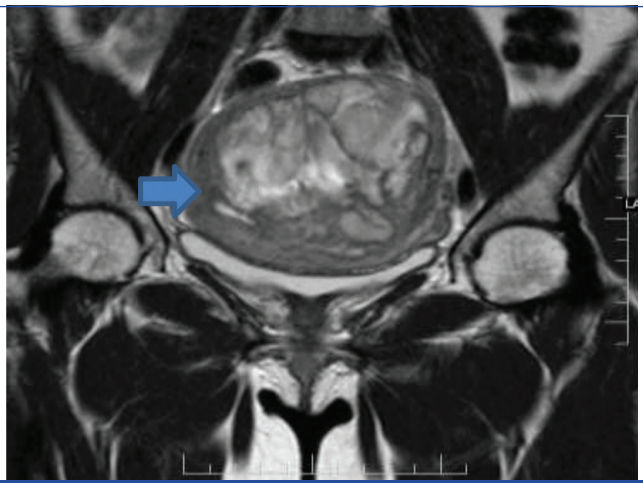
A 28-year-old nulligravida presented with a history of heavy menstrual bleeding and dysmenorrhea for a duration of six months. She attained menarche at the age of 14, with regular and normal menstrual cycles. She has no history of contraceptive use or any significant medical or family history. Upon presentation at the hospital, she did not appear pale, and no palpable abdominal mass was found. As she was not sexually active, a bimanual examination was deferred.

Ultrasonography of the abdomen and pelvis showed a heterogeneous mixed solid to cystic lesion in the uterus, suggestive of fibroid with degenerative changes. Magnetic Resonance Imaging (MRI) of the abdomen and pelvis revealed a bulky uterus measuring 10.4×8.7×9.9 cm, with a well-encapsulated heterogeneous lesion predominantly hyperintense on both T1 and T2, with a peripheral T2 hypointense rim arising from the posterior and left lateral wall of the uterus. There was no suppression on fat saturation images, no blooming on gradient images, no pelvic/para-aortic lymphadenopathy, and no ascites. The differential diagnosis included: i) leiomyoma variants like STUMP/atypical/cellular leiomyoma; ii) myxoid degeneration of leiomyoma [Table/Fig-1-3]. Given these findings, she underwent examination under anaesthesia and hysteroscopic-guided endometrial biopsy.

During bimanual examination, a uterus of 14 weeks in size and a posterior wall fibroid measuring 5×5 cm felt through the pouch of Douglas were noted. Hysteroscopic-guided endometrial biopsy revealed a thickened polypoidal endometrium, and the histopathological report indicated endometrial hyperplasia without atypia. Considering the woman's young age and nulliparity, myomectomy was performed to arrive at a definitive diagnosis. Intraoperative findings revealed a posterior uterine wall tumour measuring 7×6 cm with variable consistency, which was enucleated

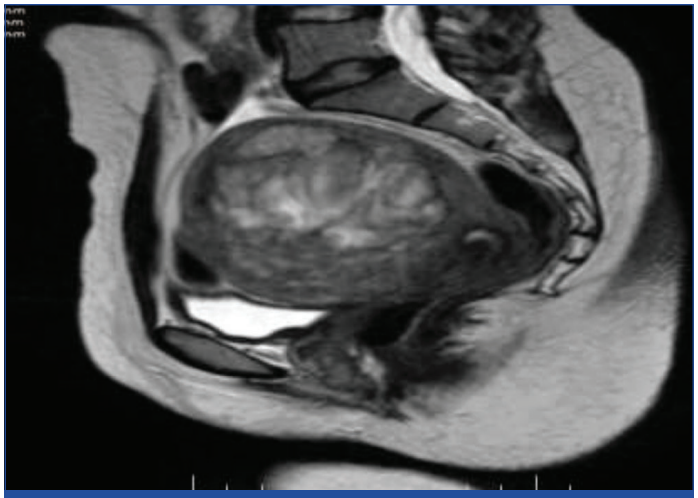


**[Table/Fig-1]:** MRI imaging showing postcontrast axial enhancement suggestive of heterogenous areas of diffusion restriction.

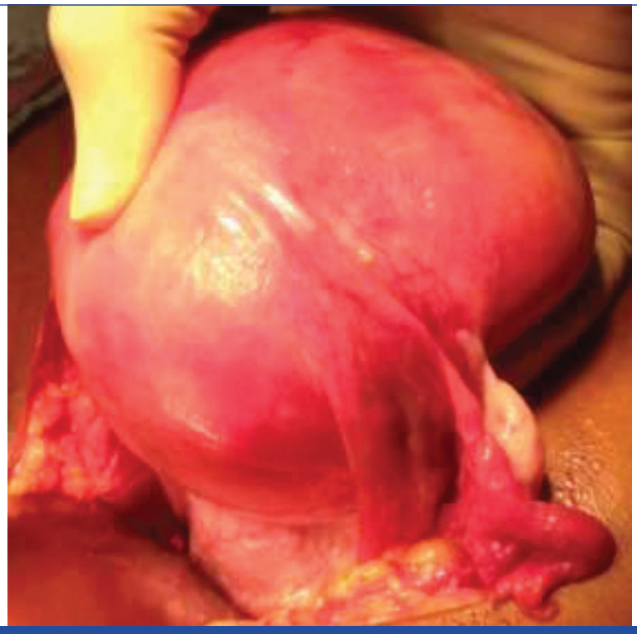


**[Table/Fig-2]:** Axial view of Magnetic Resonance Imaging (MRI) showing T1 heterogenous hyperintense lesion in uterus.

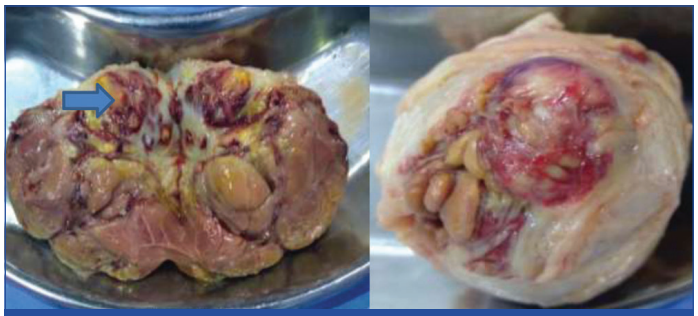
in toto [Table/Fig-4]. Grossly, the specimen had a yellowish tan color [Table/Fig-5]. Microscopic examination revealed necrotic tissue with tumour cells arranged as nodules with interlacing fascicles of smooth muscle cells. The individual tumour cells were round to spindle-shaped with bland nuclear features and occasional mild atypia. One focus showed vascular and muscular invasion of tumour cells. The



**[Table/Fig-3]:** Sagittal view of Magnetic Resonance Imaging (MRI) showing T2 heterogenous hyperintense lesion with hypointense rim.



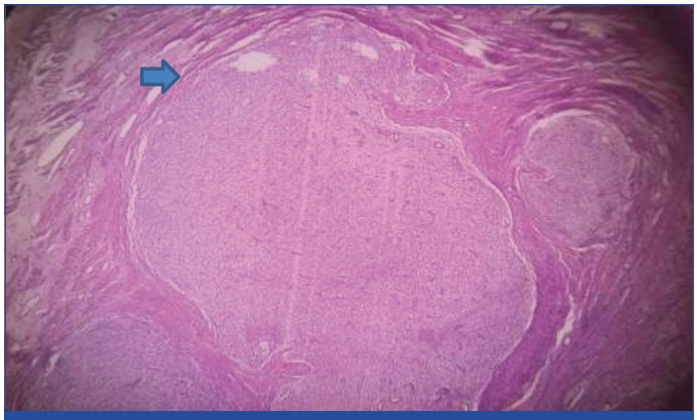
**[Table/Fig-4]:** Gross appearance of uterus.



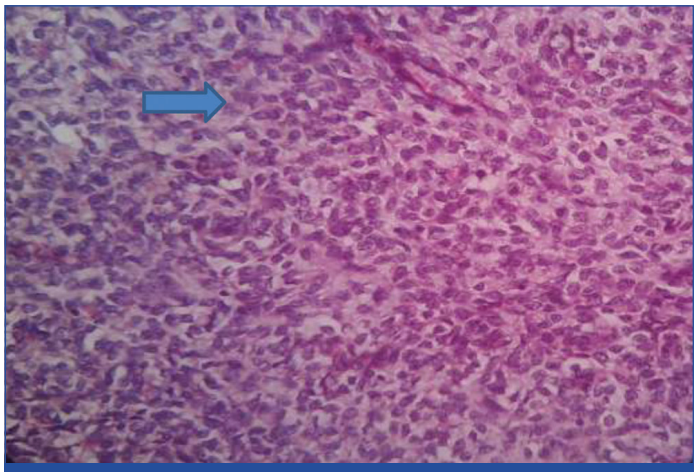
**[Table/Fig-5]:** Cut section of myomectomy specimen showed yellowish tan colour.

histopathological diagnosis included a differential diagnosis of LG-ESS, LMS, and cellular leiomyoma, and the patient was posted for definitive surgery.

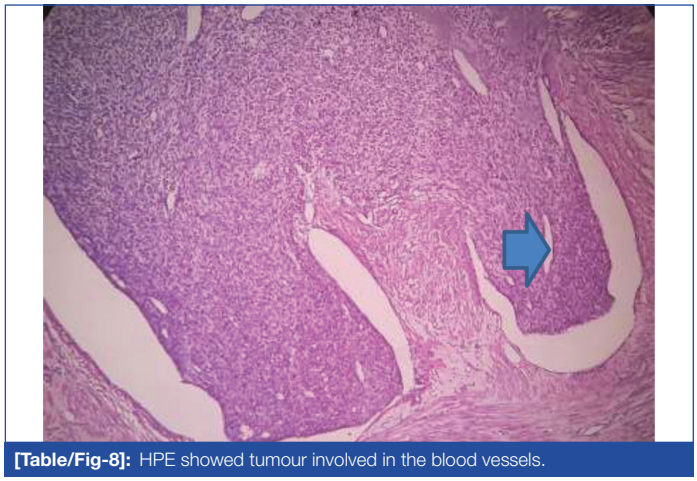
Total abdominal hysterectomy with left salphingo opherectomy, right salpingectomy, and right ovarian preservation were performed. Microscopy showed tumour cells arranged in nodules and sheets infiltrating the myometrial wall for more than 50% of the myometrium. The tumour cells had round to oval hyperchromatic nuclei, with 8 to 12 mitoses per 10 high-power fields [Table/Fig-6,7]. The tumour was involved in the blood vessels [Table/Fig-8]. Additional immunohistochemistry studies revealed positive staining for CD10 [Table/Fig-9]. HPE and immunohistochemistry with CD10 confirmed the diagnosis of LG-ESS. According to International Federation of Gynecology and Obstetrics (FIGO) staging, it was classified as



**[Table/Fig-6]:** Microscopy showed tumour cells arranged in nodules and sheets infiltrating the myometrial wall for more than 50% of myometrium.



**[Table/Fig-7]:** Microscopy showed tumour cells with round to oval hyperchromatic nuclei, with 8 to 12 mitosis per 10HPF.



**[Table/Fig-8]:** HPE showed tumour involved in the blood vessels.

**[Table/Fig-9]:** Endometrial stromal cells positive for CD10 stain

Stage-Ib disease. The postoperative clinical course was uneventful. At the three-month follow-up visit, pelvic ultrasound, MRI pelvis, and chest X-ray were performed, and all were normal. The plan is to continue follow-up with clinical examination and the same investigations after six months, followed by annual check-ups.

## DISCUSSION

Endometrial stromal sarcoma is a rare malignant tumour. It was first reported by Norris HJ and Taylor HB in 1966, who classified ESS into low-grade and high-grade types based on the mitotic index [1]. According to the 2014 WHO classification, ESS is divided into four categories: ESN, LG-ESS, HG-ESS, and Undifferentiated Uterine Sarcoma (UUS) [2]. LG-ESS and HG-ESS are rare malignancies, accounting for 1% of uterine malignancies and 10% of uterine sarcomas [3].

ESS most often affects perimenopausal women around 45 to 55 years. The presenting complaints are similar to leiomyoma of the uterus: abnormal uterine bleeding, abdominal pain, or pelvic mass. An enlarging pelvic mass can cause pressure, and some patients may be asymptomatic [4]. Martinez M and Jacinto E reported a different presentation in the form of a polypoidal fleshy mass projecting through the cervix [5]. This tumour has a high tendency for local recurrence and metastasis; and hence, an early diagnosis is important as patient survival is determined by the stage of the tumour [6].

The pathogenesis of ESS remains largely unknown, although specific somatic mutations have been discovered through cytogenetic, Fluorescence In Situ Hybridisation (FISH), and Polymerase Chain Reaction (PCR) analysis [7]. Most ESS cases are characterised by an overexpression of estrogen and progesterone receptors [6]. Diagnosing ESS is usually difficult preoperatively as it may be mistaken for leiomyoma, uterine LMS, or other sarcomas. The definitive diagnosis is made through histopathological examination coupled with immunohistochemistry of the hysterectomy specimen [8].

Ultrasonographic findings may be confused with uterine leiomyoma and adenomyosis. However, MRI can be used for a preoperative diagnosis with some accuracy. The lesion of endometrial stromal sarcoma is isointense relative to the myometrium on T1-weighted MRI and hyperintense on T2-weighted MRI. It also shows heterogeneous but prominent enhancement in contrast-enhanced images due to its rich vascularity [9]. The characteristic findings of ESS on MRI are worm-like permeation of cancerous cells in the myometrium [9]. The main tumour mass is almost always intramyometrial, but most ESS cases involve the endometrium. Uterine curettage may be helpful in preoperative diagnosis, but when the lesion is within the myometrium, the scrapings may not be useful [10].

The immunohistochemical markers, such as CD10, H-caldesmon, and hormone receptors, are helpful in the diagnosis. CD10 staining is positive in LG-ESS but not in HG-ESS and leiomyoma [11]. These tumours are estrogen and progesterone receptor positive. CD10 has a sensitivity of 100% and specificity of 90%, while ER/PR shows a sensitivity and specificity of 80% and 100%, respectively, in diagnosing LG-ESS [12]. In our patient, there was cytoplasmic positivity of CD10 staining, indicating a provisional diagnosis of LG-ESS.

The International Federation of Gynecology and Obstetrics staging of uterine sarcoma is used to determine the stage of ESS [13]. Stage I is the most significant prognostic factor, and the 5-year Overall Survival (OS) rate for Stage I LG-ESS patients is more than 90%, but it decreases to 50% for Stage III and IV [14].

The treatment for LG-ESS involves total abdominal hysterectomy; however, ovary removal and pelvic and para-aortic lymphadenectomy remain debatable. Bilateral salphingo opherectomy has been recommended, even in premenopausal women with Stage I ESS disease, as it is a hormone-sensitive tumour, and the recurrence rate is high in women in whom ovaries were retained [15].

Recent reports suggest that preserving the ovaries may be possible in premenopausal women with Stage I ESS if the tumour is completely removed [16]. Fertility-sparing treatment, along with adjuvant treatment, has been reported in cases of LG-ESS using local excision, hormone therapy, and photodynamic therapy [17]. Studies have indicated that lymphadenectomy does not have a significant role in recurrence-free survival or OS in LG-ESS [16]. Postoperative hormone therapy is an effective adjuvant treatment providing high local control and preventing recurrences. Hormone therapy with medroxyprogesterone, tamoxifen, Gonadotropin Releasing Hormone (GnRH) analogues, and aromatase inhibitors is suggested for LG-ESS stage 3-4 and recurrent disease [18].

The mechanism of action of progestins is to bind progesterone receptors and cause downregulation of gene transcription, leading to decreased endometrial gland and stromal proliferation [19]. In our patient, the decision for hysterectomy was based on the currently available diagnostic tools and the lack of knowledge regarding the long-term consequences of conservative treatment.

## CONCLUSION(S)

Endometrial stromal sarcoma is a rarely encountered malignancy, especially in young individuals. Despite its rarity, ESS holds significant clinical importance due to the diagnostic and therapeutic challenges it presents. The authors reported this case to emphasise the need for a high level of suspicion and thorough evaluation of fibroid masses causing prolonged bleeding in young women, in order to promptly rule out malignancy at an early stage. The timely diagnosis and intervention are crucial for improving patient survival.

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