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**ORIGINAL RESEARCH**

# Endometrial stromal sarcoma: Masquerading as fibroid: A case series

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**ABSTRACT**
Endometrial stromal sarcomas (ESS) constitute around 10% of uterine sarcomas, but only 0.2% of all uterine malignancies. ESS usually present in the peri- menopausal age group. ESS are often clinically misdiagnosed as benign entities like uterine leiomyomas and are usually diagnosed postoperatively, after a histopathological examination of a hysterectomy specimen. We report a case series of three cases of endometrial stromal sarcoma, in age group ranging from 28-47 years. Two out of three cases presented with complaints of heavy menstrual bleeding for 6 months and one case with lower abdominal pain for 8 months. Clinico-sonographically, these cases were diagnosed as fibroid. Out of three cases, two cases underwent MRI (abdomen and pelvis) for evaluation, with Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) and leiomyosarcoma considered as possible differential diagnosis. One patient underwent Myomectomy and later hysterectomy for completion. Two other patients underwent Total Abdominal Hysterectomy with Bilateral Salphingo-oopherectomy. Histopathological examination revealed ESS in all three cases of which two cases were reported as low-grade ESS and one as high-grade ESS. Endometrial stromal neoplasms are rare uterine tumours. They can mimic a variety of benign and malignant neoplasms, making accurate diagnosis challenging. When a singlefibroid exhibits increased vascularity on Ultrasound or MRI, along with signs of hypercellularity and necrosis, the possibility of ESS should be considered. This is crucial for planning the appropriate treatment modality to avoid repeat surgeries.
**Key words:**Endometrial stromal sarcoma (ESS), Uterine malignancies, Misdiagnosed fibroids, Histopathological examination, Differential diagnosis (STUMP, leiomyosarcoma)



## INTRODUCTION

Endometrial stromal sarcoma,is a rare uterine tumour with an incidence of 0.2%. It affects perimenopausal women around 42 to 58 years[1]. Less than 10% of uterine mesenchymal neoplasms are caused by ESS, while 10 to 25% of affected women are premenopausal. ESS are frequently clinically misinterpreted as benign entities suchas uterine leiomyomas. After a histological analysis of a specimen from a hysterectomy or polypectomy, ESS are typically identified postoperatively. Even 20 years after the initial diagnosis, distant metastases and local recurrences are possible in ESS. It is crucial to identify any gross features or radiological features that can raise the possibility of an endometrial stromal tumour while evaluating cases of leiomyoma so that adequate surgery can be done at the time of primary surgery. We are presenting case series of three endometrial stromal sarcoma with detailed clinical, radiological findings, and management which were all clinically misdiagnosed as fibroid at Sri ManakulaVinagayar Medical College and Hospital, Puducherry.

## CASE SERIES

**CASE 1:** A 28-year-old nulliparous woman presented with heavy menstrual bleeding, dysmenorrhea, and an abdominal mass for six months. She had regular and normal menstrual cycles in the past, with no significant family history of malignancies. Abdominal examination-On palpation, a midline mass corresponding to 16 weeks of gestation was noted,

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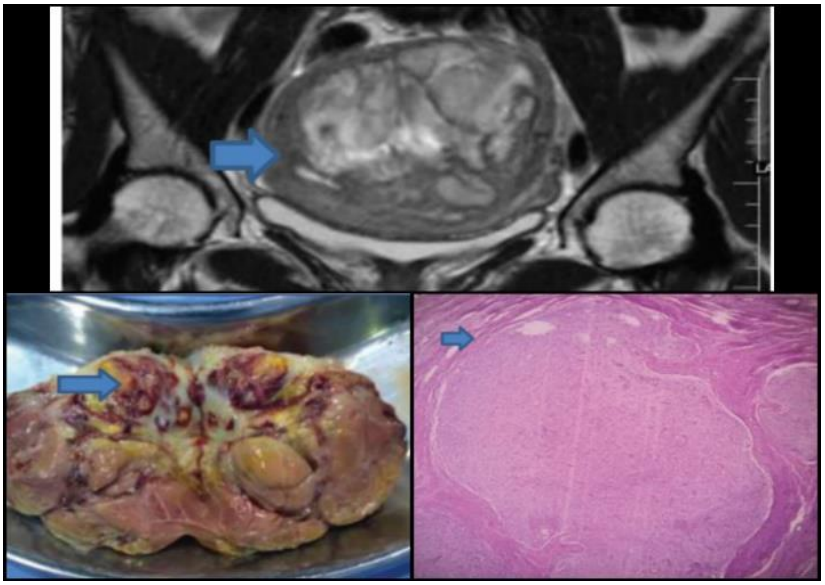
which was firm in consistency, had a regular surface, and its lower border could not be reached. During the speculum examination, the vagina and cervix appeared healthy. Per vaginal examination confirmed abdominal findings. It was provisionally diagnosed as fibroid uterus. Ultrasound findings-a heterogeneous mixed solid-to-cystic lesion in the uterus, measuring 10 × 7 × 10 cm in the posterior wall, suggestive of fibroid with degenerative features. MRI findings-a well-encapsulated heterogeneous lesion of 10.4 × 8.7 × 9.9 cm, arising from the posterior and left lateral wall of the uterus. The differential diagnosis included STUMP (smooth muscle tumors of uncertain malignant potential), atypical leiomyoma, cellular leiomyoma, and myxoid degeneration of leiomyoma. Given that the patient was 28 years old and nulliparous, we proceeded with myomectomy. The gross specimen showed a posterior uterine wall tumor measuring 7 × 6 cm with variable consistency; cut section-yellowish-tan in color. Histopathology of myomectomy specimen presented a differential diagnosis of low-grade endometrial stromal sarcoma (ESS), leiomyosarcoma, and cellular leiomyoma. Total abdominal hysterectomy with left salpingooophorectomy, right salpingectomy, and preservation of the right ovary were performed. The final histopathological examination confirmed endometrial stromal sarcoma, FIGO stage IB, low grade (>50% myometrial invasion), with all margins free of tumor. Both tubes and the left ovary appeared normal, and LVSI was negative. Additional immunohistochemistry studies revealed positive staining for CD10, confirming the diagnosis of low-grade ESS. At the third and sixth months postoperatively, follow-up visits included pelvic ultrasound, MRI of the pelvis, and chest X-ray, all of which were normal. The patient will be followed up annually with the same investigations.



**CASE2:** A 40-year-old woman, P3L3, presented with heavy menstrual bleeding, dysmenorrhea, and an abdominal mass for eight months. No significant family history of malignancies. Abdominal examination revealed a midline mass corresponding to 16 weeks of gestation. The mass was firm in consistency, had a regular surface, was mobile, and its lower border could not be reached. During the speculum examination, the vagina and cervix appeared healthy. Per vaginal examination confirmed abdominal findings. The case was provisionally diagnosed as fibroid uterus. Ultrasound showed a well-defined hypoechoic lesion measuring 6.6 × 5.9 × 5.4 cm in the anterior wall of the uterus, with multiple internal septations and internal vascularity, displacing the endometrium posteriorly. The impression was an intramural fibroid. Clinical and ultrasound findings suggested fibroid uterus; hence, the patient underwent total laparoscopic hysterectomy with bilateral salpingectomy. The histopathological examination later revealed endometrial stromal sarcoma (ESS), FIGO stage IB, high grade (>50% myometrial invasion), with all margins free of tumor. Both tubes and the left ovary were normal, and LVSI was negative. In this case, ESS was diagnosed postoperatively, and the patient is being followed up.

**CASE 3:** A 47-year-old woman, P3L3, presented with heavy menstrual bleeding, dysmenorrhea, abdominal mass, weight loss, and loss of appetite for six months. No significant family history of malignancies. Abdominal examination-On palpation, a midline mass corresponding to 24 weeks of gestation was noted. The mass was firm in consistency, had a regular surface, was mobile, and its lower border could not be reached. During the speculum examination, the vagina and cervix appeared healthy. Per vaginal examination confirmed abdominal findings. The patient was provisionally diagnosed as fibroid uterus. Ultrasound showed a heteroechoic mass measuring approximately

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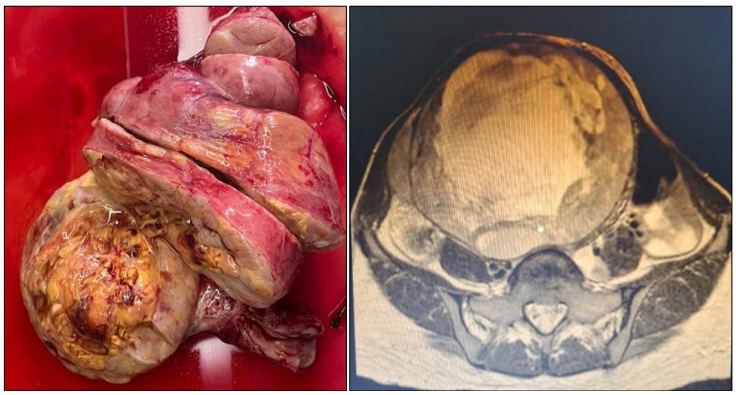
12.8 × 12 cm in the fundus, with cystic degeneration and increased vascularity and diagnosed as fibroid with cystic degeneration. MRI showed a heterogeneous solid lesion measuring 14.8 × 12.5 × 14.7 cm, extending from L3 to S5, with a central necrotic component and blooming present. The differential diagnosis included subserosal/pedunculated leiomyosarcoma, subserosal/pedunculated STUMP, atypical leiomyoma, and cellular leiomyoma. The initial differential diagnoses were suggestive of leiomyosarcoma, leading to the decision to proceed with a total abdominal hysterectomy with bilateral salpingectomy and frozen section.The gross specimen showed a mass of 15 × 12 cm in the fundus of the uterus with variable consistency; the cut section revealed necrosis and degenerative changes. The frozen section reported cellular leiomyoma with atypical cells, indicating that malignancy could not be ruled out. Later, the histopathological examination showed endometrial stromal sarcoma (ESS), FIGO stage IB, low grade (>50% myometrial invasion), with all margins free of tumor. Both tubes were normal, and LVSI was negative. The patient was advised for immunohistochemistry, but patient denied. The patient is kept in follow-up.



| | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| **Age (years)** | **28** | **40** | **47** |
| Signs and symptoms | Heavy menstrual bleeding, dysmenorrhea, mass abdomen | Heavy menstrual bleeding, dysmenorrhea, mass abdomen | Heavy menstrual bleeding, dysmenorrhea, mass abdomen, loss of appetite and loss of weight |
| Clinical diagnosis | Fibroid uterus | Fibroid uterus | Fibroid uterus |
| Ultrasound diagnosis | Fibroid with degenerative changes | Intramural fibroid | Fibroid with cystic degeneration |
| MRI differentialdiagnosis | STUMP<br>Atypical leiomyoma<br>Cellular leiomyoma<br>Myxoid degeneration of leiomyoma | Not done | Subserosal/pedunculated leiomyosarcoma<br>Subserosal/pedunculated STUMP, atypical leiomyoma, cellular leiomyoma |
| Management | Myomectomy followed by abdominal hysterectomy with right ovarian preservation | Laparoscopic hysterectomy | Abdominal hysterectomy |
| Histological diagnosis | LGESS | HGESS | LGESS |
| IHC | Positive for CD10 | | |

## DISCUSSION

Endometrial stromal sarcoma (ESS) is a rare malignant tumor of the uterus that primarily affects perimenopausal women aged 42 to 58 years[1]. It accounts for approximately 0.2% of uterine malignancies. In the present series, two women presented at the age between 40-50 years and one was younger. According to the 2014 WHO classification, ESS is divided into four categories: Endometrial Stromal Nodule, Low-Grade Endometrial Stromal Sarcoma, High-Grade Endometrial Stromal Sarcoma, and Undifferentiated Uterine Sarcoma (UUS). Presenting symptoms are similar to those of uterine leiomyomas, including abnormal uterine bleeding, lower abdominal pain, pelvic mass, and approximately 5% of patients may be asymptomatic. In the current series, all three patients presented with abnormal uterine bleeding.

Risk factors associated with ESS include ovarian polycystic disease, unopposed estrogens, and tamoxifen exposure. The most common location for these tumors is intramyometrial[2]; however, they can also develop in extrauterine locations such as the ovaries, pelvis, and abdominal cavity, with the ovary

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being the most common extrauterine site. The endometrium is involved in the majority of ESS cases, and uterine curettage may assist in the preoperative diagnosis, although scrapings may not be useful if the lesion is entirely within the myometrium. The final diagnosis can only be confirmed with a hysterectomy specimen.

Ultrasonographic findings may be confused with those of uterine leiomyomas and adenomyosis. Transvaginal color Doppler may show low impedance flow compared to other benign tumors. In this study, all the three cases were clinically and sonographically labeled as leiomyomas.

Magnetic resonance imaging (MRI) can be useful preoperatively in some cases. Characteristic findings of ESS on MRI include worm-like permeation of cancerous cells within the myometrium[3]. In the present study, MRI of two cases gave a differential diagnosis of Leiomyosarcoma, STUMP (smooth muscle tumors of uncertain malignant potential), atypical leiomyoma and cellular leiomyoma.

To differentiate between cellular leiomyoma and other tumors, immunomarkers such as desmin, h-caldesmon, oxytocin receptors, CD10, and inhibin are helpful[4]. On immunohistochemistry, low-grade ESS is 100% positive for CD10 and 83% positive for estrogen and progesterone receptors[5]. IHC of one case in this series, reported positive for CD10 and histopathology was confirmed as LGESS. High-grade ESS is positive for Cyclin D1, while leiomyomas express h-caldesmon, desmin, and oxytocin receptors[4,5].

Several soft-tissue neoplasms with arborizing vasculature, highly cellular leiomyomas, cellular endometrial polyps, low-grade müllerian adenosarcomas, and adenomyosis are included in the differential diagnosis. Independent risk factors for poor survival have been identified, including age greater than 50, advanced stage, high mitotic count (greater than 5 per 10 high-power fields), lack of primary surgery, nodal metastasis, negative expression of CD10, and absence of estrogen and progesterone receptors[6,7]. In contrast, ESS generally has a longer survival rate than other sarcomas.

For ESS, surgery is the most effective treatment, similar to other sarcomas. A total hysterectomy with bilateral salpingo-oophorectomy is the standard surgical procedure. These tumors are responsive to progesterone and estrogen receptors; therefore, hormone replacement therapy is contraindicated postoperatively[8,9]. Studies suggest that in stage I ESS, bilateral salpingo-oophorectomy does not appear to impact overall survival or recurrence[10-13]. In premenopausal women with stage I ESS, considering the side effects of early menopausal symptoms, retention of ovarian function may be an option[14]. In the present series, all three cases underwent hysterectomy with ovarian preservation. For other stages of ESS, total hysterectomy with bilateral salpingo-oophorectomy is recommended. A significant rate of lymph node involvement has been reported in ESS, thus lymph node dissection important for providing prognostic information and management options.

For stage I ESS, only postoperative observation is required. For stages II, III, and IVA, hormonal therapy and/or tumor-directed radiotherapy may be indicated, while for stage IVB, hormonal therapy and/or palliative treatment are recommended[15]. Hormones used include megestrol/medroxyprogesterone, gonadotropin-releasing hormone (GnRH) analogues, and aromatase inhibitors[15]. Adjuvant treatment may involve radiation therapy in advanced or recurrent cases, either in the form of brachytherapy or with pelvic radiation[15,16].

Recurrences occur in one-third to one-half of ESS patients and are often confined to the lower genital tract and pelvis. Distant metastases to the lungs can occur after a few years[17,18]. Recurrence may be exacerbated by estrogen stimulation of residual tumor cells. Following oophorectomy, hormone replacement therapy or the production of estrogens from peripheral tissues or exogenous administration could contribute to recurrences. Currently, there is no standard management for patients with recurrent disease. Treatment options for recurrent ESS may include hormone therapy, radiotherapy, surgical re-excision, or a combination of these.

The 5-year survival rate for ESS ranges from 54% to almost 100% at FIGO stage I and approximately 30% at stage II. Only 11% of patients with advanced disease (stages III and IV) survive[3]. Due to the tendency for late recurrence of these cancers, long-term surveillance is crucial. For the first year, follow-up should be every three months, followed by every six months for the next four years, and then annual follow-up is advised. Factors influencing the chance of relapse-free survival include tumor stage, myometrial invasion, adjuvant therapy, and bilateral salpingo-oophorectomy[19,20].

## CONCLUSIONS

Endometrial stromal sarcoma is a rarely encountered uterine malignancy. Because of its rarity, the diagnosis of endometrial stromal sarcoma is misdiagnosed as benign entities and are usually diagnosed postoperatively, after a histopathological examination of a hysterectomy specimen. To our experience, when a single large fibroid exhibits increased vascularity on Ultrasound or MRI, along with signs of hypercellularity and necrosis, the possibility of ESS should be considered. This is crucial for planning the appropriate pre operative evaluation and treatment modality as it is difficult to diagnose endometrial stromal sarcoma by frozen section also to avoid repeat interventions. The importance of early diagnosis, often through a combination of clinical history and examination, imaging, histopathological examination and molecular profiling is important in further treatment options.

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