Large Leiomyosarcoma of The Uterus: A Challenging, Difficult-To-Treat, Case of an Indian Patient

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Citation: Ramya Vandanasetti, Tripura Sundari, Umadevi G. Large Leiomyosarcoma of The Uterus: A Challenging, Difficult-To-Treat, Case of An Indian Patient. ERWEJ. 2022;2(3): 151-156. 10.54136/ERWEJ-0203-10023

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Abstract
Leiomyosarcoma is a rare tumor that accounts for about 2 to 5% of uterine malignancies originating from the smooth muscles of the uterus. Women can be affected at any age group, however, the majority get diagnosed at their perimenopausal age. The early-stage diseases are managed by hysterectomy and complete surgical resection. In the present case report, we discuss a 41-year-old female with a tumor mass of approximately 32-week gestation at the time of examination. The patient had a regular menstrual cycle with no abnormal uterine bleeding except for abdominal pain for three months. A large, lobulated mass (25 x 18 x14 cms) with solid, cystic, and hemorrhagic components was removed surgically (total abdominal hysterectomy) from the uterus's fundus and spalango-oophorectomy. The patient developed severe hypotension and tachycardia post-surgery and required a longer recovery time. We referred the patient to the medical oncologist for further treatment. In our patient, the tumor rapidly increased, and metastasis was noted in the peritoneal fluid. A further follow-up will be needed to understand the course of the disease and its outcome.

Keywords: Leiomyosarcoma; Smooth muscle tumors; Uterine fibroid; Uterine myoma

Introduction
Uterine sarcomas are rare gynecological malignancies classified into three subtypes: leiomyosarcomas (ULMSs), endothelial stromal sarcoma (ESS), and adenosarcoma. ULMS is the most common form of uterine sarcoma identified as highly aggressive tumors with a poor overall prognosis, high recurrence rate, and a tendency to spread hematogenously[1,2]. It accounts for 2% to 5% of all uterine malignancies and differs from the endometrial tumors in management and prognosis[3,4]. Perimenopausal women, usually in their sixth decade of life, are typically affected and may remain asymptomatic till the tumor reaches an advanced stage[5]. Atypical symptoms such as abnormal uterine bleeding, abdominal pressure, and abdominal pain may occur in a few patients[1,3].

For the lack of definitive clinical criteria for diagnosis and imaging features that overlap with uterine leiomyomas, preoperative diagnosis of ULMSs is difficult[6,7]. Most cases are diagnosed accidentally during surgical procedures (myomectomy/hysterectomy) for alleged benign leiomyomas[8].
ULMS is optimally managed through surgery, including total abdominal hysterectomy and bilateral salpingo-oophorectomy[5]. Patients with metastasis to lymph nodes require lymphadenectomy as a cytoreductive effort[9]. Given how uncommon the tumor is, there is a lack of literature on ULMS, and sporadic cases have been reported predominantly in India. We describe a case of large ULMS in an Indian female who underwent successful surgical management.

Case presentation

A thin, pale 41-year-old female (P2L2) hailing from South India presented with complaints of abdominal mass for six months. The mass had increased rapidly over the past three months resulting in lower abdominal pain. Her previous menstrual cycles were regular, with no history of abnormal genital bleeding. Her vital signs were well preserved, and she did not have any relevant past medical history. A mass of approximately 32 weeks gestational size uterus was noted on examination. It appeared to be a solid cystic mass occupying the whole abdomen up to the epigastrium arising from the pelvis. The upper and lateral borders of the mass were distinct and identified, although the lower margin could not be ascertained. The mass was non-tender, firm in consistency, and restricted mobility. The presence of ascites was also noted, with no hepatosplenomegaly. Vaginal examination reaffirmed the per abdominal findings as a large, nodular, irregular mass with restricted mobility occupying the whole pelvis. The perrectal examination did not reveal any abnormalities. The patient underwent routine laboratory tests along with imaging studies for further diagnosis. Findings on the computed tomography (CT) scan were suggestive of a large (18.2 x 26.9 x 27.8 cm), multiloculated, multiseptated growth containing solid and cystic elements arising from the pelvis and extending into the abdomen (Figure 1).

Figure 1. CT scan of abdomen and pelvis showing A. Mass with solid and cystic areas and B. Mass with internal septations and calcification.
Internal necrotic cystic areas of calcifications were noted along with a mass in the posterior wall of the uterus (8.3×7.8 cms). The CA125 levels were elevated at 82 ng/mL (normal range: 0-35 ng/mL), and the chest X-ray showed multiple lung nodules. Positron emission tomography (PET)/CT showed high signal uptake in the mass, low uptake in lung lesion, and no skeletal involvement (Figure 2). Based on these findings, the patient was posted for exploratory laparotomy.

![Figure 2: PET scan showing increased uptake by the mass.](image)

A large hemoperitoneum (1.5 liters) and omental adhesions to the mass were noticed during the surgery. A large, lobulated mass (25 x 18 x 14 cms) with solid, cystic, and hemorrhagic components was seen from the uterus's fundus (Figure 3).

![Figure 3: Extracted tumour and uterus. A. Tumour mass with necrotic, solid and cystic areas B. Uterus with pedunculated tumour](image)
Both ovaries and fallopian tubes were normal. Total abdominal hysterectomy (along with excision of the tumor) and bilateral salpingo-oophorectomy were done. The uterus measuring 8 cm × 5 cm × 3 cm with a subserosal bosselated growth that arose from the fundus was removed. Samples were obtained from omental and external iliac lymph node biopsy and sent for histopathological examination. A neoplastic growth composed of diffuse sheets of tumor cells with abrupt areas of necrosis and hyalinization was observed. The tumor cells showed moderate to marked atypia with frequent bizarre giant cells (Figure 4). Few osteoclasts type of giant cells was also seen. Focal smooth muscle differentiation and tumor extension beyond one-half of the myometrium were observed.

![Figure 4](image)

**Figure 4:** Microscopic examination of surgical specimen showing a cellular tumour arranged in interlacing bundles of spindle cells with elongated hyperchromatic nuclei and nuclear pleomorphism

The post-surgical recovery was delayed leading to a prolonged ICU stay. She developed severe hypotension and tachycardia, managed by IV and oral inotropes. The patient also required several units of blood as well as albumin infusion for hypoproteinaemia. Tigecycline and Meropenem were prescribed as needed. The patient gradually recovered and was discharged in stable condition on the 14th day of admission. She was also referred to a medical oncologist based on a cytological examination of peritoneal fluid, which showed malignant cells.

**Discussion**

Uterine sarcomas, including ULMS, are rare mesenchymal tumors with an increased risk of local recurrence and metastasis\(^{[10]}\). ULMS is also a high-grade tumor typically characterized by a mitotic rate > 15/10 HPF. The patient did not have any menstrual abnormalities in the case described above. However, the tumor was massive and primarily occupied the whole pelvic and abdominal cavity.

In a case study by Ahuja A et al., a 60-year-old woman was operated on for multiple fibroids. The metastasis to the brain with the erosion of overlying skull bone, chest wall, and lungs resulted in further evaluation. The authors used a multidisciplinary approach such as clinical history, critical analysis of FNA slides, archival material review, and histomorphology assay to arrive at a confirmatory diagnosis\(^{[11]}\). In another case by Kaur K et al., a 60-year-old female
presented with postmenopausal bleeding was diagnosed with ULMS. Like our case, the tumor was large, and the uterus was enlarged (20 weeks in size) with distinct necrotic growth. The patient underwent surgery followed by six cycles of chemotherapy and recovered well[12].

Clinical diagnosis of uterine sarcomas is usually tricky and supported by clinical findings like rapidly growing masses and radiological investigations like USG and MRI. The sensitivity of endometrial biopsy to detect ULMS is low. Hence, the diagnosis is only confirmed on histologic examination of the entire uterus postoperatively[13]. Since uterine sarcoma is rare, screening is mostly not suitable; however, given the aggressive nature of the tumor, high-risk cases may be subjected to screening if the clinical picture is suspicious. A retrospective cohort study by Tong A et al. demonstrated that MRI is an effective and potentially economic screening test with 100% sensitivity and 97% specificity[14]. For prospective differentiation between ULMS/ smooth muscle tumor with uncertain malignant potential (STUMP) and benign leiomyoma, contrast-enhanced-MRI can provide accurate information and is preferable to diffusion-weighted MRI[15]. The loss of the normal endometrial stripe (either thickened or not seen) in a postmenopausal patient with a myometrial mass on a non-contrast MRI should raise the alarm for ULMS[16]. Management of ULMS at an early stage involves hysterectomy and complete surgical resection of the gross tumor. Outcomes are poorer in patients who undergo surgery with tumor disruption. Hence surgery with en bloc tumor should be attempted. The power morcellation should be avoided as it is associated with an increased risk of recurrence, shortened time to recurrence, and upstage after re-exploration[17]. Role of adjuvant therapy for early ULMS remains controversial as overall survival benefit has not been demonstrated. In cases of recurrent ULMS, treatment with trabectedin prolonged disease control, with 3-month and 6-month progression-free survival rates exceeding 50 and 30%, respectively[18]. Nevertheless, for advanced and recurrent disease, novel chemotherapeutics, targeted therapies such as olaratumab and pazopanib, and immunotherapies such as nivolumab and pembrolizumab are being considered[19-20]. In our patient, an abdominal hysterectomy with bilateral salpingo-oophorectomy was done, and she was referred to a medical oncologist for further treatment. Post-surgical treatment has not been described here. The tumor also rapidly increased in our patient, and metastasis was noted in the peritoneal fluid. A further follow-up will be needed to understand the course of the disease and its outcome.

Conclusion

Screening for ULMS is not a routine practice, especially in developing countries like India, and most of the patients are still diagnosed post-surgery. In our study, there was successful surgical resection of the tumor, however, the tumor rapidly increased with peritoneal fluid metastasis. Therefore, a post-surgery treatment follow-up would help understand the disease progression and recovery.

Patient consent: N/A
Conflict of Interest: Nil
Financial Disclosure: None
References