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Case Report

UTERINE LEIOMYOSARCOMA - A CASE REPORT

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ABSTRACT

Leiomyomas are the most common mesenchymal neoplasms. Smooth muscle cells with variable amounts of fibrous stroma make up these benign tumors. The tumor occurs most frequently in uterus in 20–30% of women of reproductive age. Uterine leiomyosarcoma (uLMS/LMS) is a rare cancer originating from smooth muscle lining the walls of the uterus. We report a case of postmenopausal women of 65 years presented with retention urine, diagnosed as LMS of uterus on histopathology.

Keywords: Uterine leiomyosarcoma, Fibroid, Spindle cells, Atypia, Cancer, Sarcoma.

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INTRODUCTION

A rare cancer arising from the smooth muscle lining the walls of the uterus is termed uterine leiomyosarcoma (uLMS/LMS). It is an aggressive tumor with high mortality and morbidity despite the disease staged at the time of diagnosis [1]. Frequently misdiagnosed as a benign uterine leiomyoma, the pre-operative diagnosis of uterine sarcoma in women following hysterectomy or myomectomy is still a real challenge.

CASE PRESENTATION

We present a 65-year-old P5 L5, referred in view of urinary retention, pelvic pain and pressure for 2.5 months. No h/o abdominal pain, loss of weight, loss of appetite, menstrual and bowel complaints. Menopause attained 15 years ago. Diabetic on oral hypoglycemics.

Clinical examination

Moderately built with 65 kg. Vitals - stable. General examination was normal. CVS and RS were normal. Abdominal examination showed uterus enlarged to 16–18 weeks. Per speculum examination showed cervix with multiparous OS, transformation zone appears normal, no growth or ulcers seen on the cervix, vaginal wall appears healthy. Per vaginal examination showed uterus 18 weeks size, irregularly enlarged and freely mobile mass occupying the POD (Fig. 1). Per rectal examination showed rectal mucosa free. Pap smear done was negative for intraepithelial malignant cells. USG results showed a large heterogeneous calcified mass 11.6*8.5 cm extending from the epigastric region to the pelvic area, indenting the bladder wall.

Magnetic resonance imaging (MRI) abdomen and pelvis were done to look for myometrial invasion and reported a heterogenous enhancing mixed signal intensity lesion arising from the posterior wall of the uterus--*degenerated fibroid* (11.8×9.4×9.64 cm) in the posterolateral wall of the uterus (Fig. 2) noted with endometrial thickening of 4.7 mm in the endometrial cavity and the margin appears smooth and regular in shape. In pre-contrast T1W image – No heterogenicity, no hemorrhage on the cystic lesion was seen. T2W images – the lesion is heterogenous and high intensity areas which can be due to hemorrhage. Post-contrast T1W image – non-homogenous contrast enhancement. No nodal involvement or myometrial invasion/parametrial invasion ovaries normal. After obtaining medical, cardiology, anesthesia fitness, she was taken up for total abdominal hysterectomy with bilateral salpingo oophorectomy (BSO). Intraoperative findings include uterus 18 weeks with calcified, solitary fibroid. Bilateral tubes and ovaries normal. Peritoneum and other organs appeared normal. Bladder-evidence of hypertrophy noted.

Cut section

A circumscribed grey white fleshy lesion with areas of necrosis measuring 3.5×3.5×3.5 cm in right fundal region. The histopathology report was uterine LMS Stage-1b (pT1b NXMX) parametrium free and Serosa free of tumor with a clearance of 2 mm.

In HPE there was coagulative tumor necrosis, severe atypia, No. of mitotic figures - 4-6/10 HPF which confirmed the diagnosis of LMS. Microscopic evaluation of the tissue sections showed infiltrating cellular neoplasm, arranged in fascicles and sheets, spindle cells containing hyperchromatic nuclei and eosinophilic cytoplasm, atypical mitosis (high-power fields [HPF] >10/10), and foci of necrosis.

Conclusion

We found that the surgery is the only treatment for LMS; however, there is a little possibility to diagnose LMS before surgery in the patient with uncertain diagnosis and suspicious of LMS.

DISCUSSION

Malignant change in a leiomyomais termed LMS/u-LMS, seen in 0.5–0.7/100000/women having a poor prognosis which is followed by endometrial stromal sarcoma [2]. Sarcomas are most commonly seen in involuntary muscle, uterus, stomach, intestine, retro peritoneum, and walls of blood vessels and skin. Although the possibility of leiomyoma turning into LMS is only 0.2%, it must always be suspected in postmenopausal women with *submucous fibroid or fibroid showing increased vascularity*. Average age of occurrence is 40–50 years [3-5].

Who are at risk?

Patients with uterine mass, age ≥40 years, postmenopausal status and postmenopausal bleeding, AUB, palpable mass and recognition of mass growing rapidly, and ultrasonography detected solitary uterine mass were more likely to be diagnosed as uterine sarcoma [6]. Long-term adjuvant tamoxifen in women with breast cancer also escalates the risk of sarcomas [7,8].

How does LMS present?

Most women with LMS lack symptoms or present with a rapidly enlarging pelvic mass. Pelvic pain/pressure, abdominal distention,

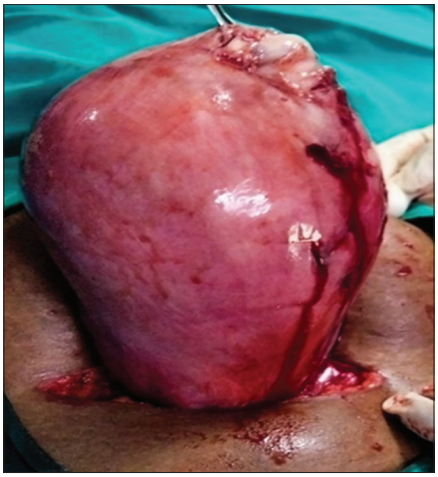

Fig. 1: P/A - Uterus 18 weeks calcified, solitary fibroid present

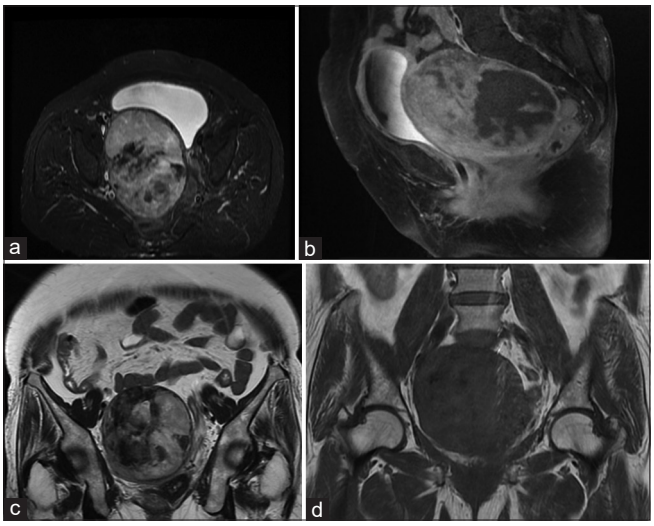

Fig. 2: (a and b) Magnetic resonance imaging (MRI)-LMS frequently manifests as a large, solitary, infiltrating myometrial mass with ill-defined margins and heterogeneous SI. The heterogeneity reflects focal areas of hemorrhage, necrosis. (c and d) MRI abdomen and pelvis were done to look for myometrial invasion and reported as a degenerated Fibroid (11.8×9.4×9.64 cm) in the posterolateral wall of the uterus noted with endometrial thickening of 4.7 mm in the endometrial cavity and the margin appears smooth and regular in shape

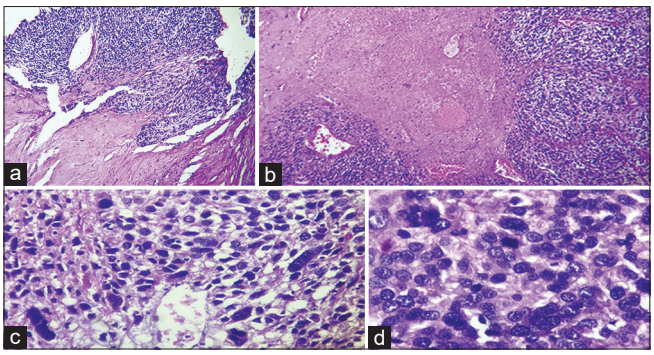

Fig. 3: (a) Leiomyosarcoma with foci of tumor invasion (×40). (b) Foci of necrosis with in the tumor (×10). (c) Malignant spindle cells with severe nuclear atypia (×40). (d) Tumor with atypical mitotic figure (×40)

postmenopausal bleeding, unintentional weight loss, and even AUB could be the presenting features. In most cases, the diagnosis of LMS is made by pathological examination of hysterectomy (0.1–0.3%) or myomectomy specimen [9-11].

Course of LMS

A rapid clinical course with a doubling time of 4 weeks is common in LMS. About 60% of the women with LMS present with the disease limited to the uterus on first diagnosis. On the basis of the FIGO 2009 classification, 68% of LMSs are diagnosed as stage1 and only 22% are diagnosed as Stage IV [12].

Imaging modalities

CT and MRI are not reliable diagnostic tools as the diagnosis of LMS is made microscopically [13]. Ludovisi *et al*. opined that LMSs are suspected if the mass is large (largest diameter 106 mm) and solitary even if they may coexist in same uterus with benign myomas [14]. In 50% of cases, LMSs are solid mass with inhomogeneous echogenicity with irregular border and irregular cystic areas with minimal or absent blood flow in one third of them. Solid tissue necrosis, defined as *"cooked appearance,"* a homogeneous avascular area with blurred borders was termed by Ludovisi *et al.*

LMS frequently manifests as a large, solitary, infiltrating myometrial mass with ill-defined margins and heterogeneous SI reflecting focal areas of hemorrhage, necrosis, or both on T1- weighted images, with irregular and ill-defined margins. On T2-weighted images, intermediate to high signal intensity, with central hyperintensity indicative of extensive necrosis are seen [15]. Early heterogenous enhancement due to the areas of necrosis and hemorrhage are classically seen post contrast [16-18].

Prognosis

Early tumor stage, age <50 years, and absence of vascular space involvement were independently associated with good prognosis. Histological type and lymph node metastasis have prognostic implications [19]. Tumor more than 5 cm and LMS extending beyond uterus and cervix have poor prognosis [20-22]. Mitotic count was detected to be a strong prognostic parameter in early tumor stage, but failed to act as an independent prognostic parameter in patients with tumor Stage II–IV disease [23,24].

Metastasis

Mainly to lung, liver, brain, kidney, and bones. Secondary's to ovary from uterine LMSs are, however, very rare (3.5%).

Criteria for the diagnosis

LMS is an aggressive tumor associated with a high risk of recurrence and death, regardless of stage at presentation and differ from other types of endometrial cancer. LMS is diagnosed based on the Stanford criteria, requiring the presence of at least two of the following characteristics: (a) High mitotic rate >10 figures per 10 high-power fields, (b) moderate to severe cellular atypia, and (c) areas of coagulative tumor cell necrosis [25].

Gross appearance

These tumors usually grow as solitary, irregular, bulky masses that invade the uterine wall with a grey-white, fleshy lobulated cut surface with foci of hemorrhage.

Microscopy

LMS are tumors of smooth muscle differentiation. Well-differentiated tumors show typical architecture of smooth muscle with broad fascicles of plump spindle cells intersecting at right angles with varying degrees of hyalinization which contain abundant brightly eosinophilic fibrillary cytoplasm, with distinct cell borders, and cigar-shaped nuclei. Microscopic examination reveals the coagulation tumor cell necrosis with hyper cellularity and abundant mitosis (>10 MF/10 HPF). Presence of aneuploidy, high MIB-1 activity and negative p53, and focal "bizarre" changes is also reported with cellular atypia (Fig. 3a-d) [26].

Immunohistochemistry

LMSs typically expresses smooth muscle markers, including smooth muscle actin and h-caldesmon [27]. Ki 67 proliferation index - 8–10%. Desmin, SMA – Positive. Vimentin – positive.

Management

Surgical staging should include a hysterectomy and a BSO with the resection of any visible metastatic disease. About 60% of the women with LMS present with the disease limited to the uterus upon first diagnosis. Advanced cases need neoadjuvant chemotherapy. The impressive efficiency of the doxorubicin plus trabectedin combination is given in first-line therapy for patients with locally advanced/metastatic LMS in terms of survival [28]. No proven benefit of using further chemotherapy or radiotherapy after complete surgical removal is the evidence.

CONCLUSION

U LMS is a rare malignant smooth muscle tumor with significant cellularity, nuclear atypia, necrosis, high mitotic rate, invasion, and metastases.

Consent

Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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AUTHORS' CONTRIBUTIONS

All authors had participated in the management of this case and the realization of this work. All authors read and agreed to the final version of this manuscript.

CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

Not required.

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