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Uterine leiomyosarcoma in a premenopausal woman. Clinical case.

Dalia Lucía Gómez Aguilar 1, Claudia Páez 2, Xochitl Margarita Carrillo Nuño 3, Ana Laura Mena Rodríguez 4, Alejandro L. Villalobos Rodríguez 5, Guillermo Padrón Arredondo 6.

1.Resident third grade Gyn-Obs , Clinic app ISSSTE Mérida Susulá Commissary
2.Resident first degree Gyn-Obs , Clinic app ISSSTE Mérida Susulá Commissary
3,4.Gyn-Obs Orcid: 0000-0001-8410-0209
5.pathologist Clinic app ISSSTE Mérida Susulá Commissary
6.General Surgeon. Orcid: 0000-0001-6049-5672

*Correspondence: Alejandro L. Villalobos Rodríguez Gyn- Obs

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ABSTRACT

INTRODUCTION. *Leiomyosarcoma (LMS) of the uterus is a rare soft-tissue tumor of the female pelvis with <1% of uterine tumor. It usually arises from the uterine myometrium de novo or is very rarely transformed from a preexisting benign leiomyoma. These tumors are found mainly in females 40–60 years of age. Leiomyomas seen in the reproductive age group and a strong suspicion of LMS should be in mind in cases of fibroid with postmenopausal bleeding.*

CLINICAL CASE. *A 39-year-old female came to the emergency room complaining of pelvic pain of 8 days duration, treated symptomatically with NSAIDs. It has the following background: hereditary family history, which is unimportant to the case. Gynecobstetric history: menarche 11 years old, regular cycles five to seven days, reports two months with uncontrolled cycle with heavy menstrual bleeding, start active sexual life 24 years old. Papanicolaou: last year reported normal; colposcopy last one and a half ago reported normal.*

DISCUSSION. *Approximately 40-80% of women may develop leiomyomas, the most common benign gynecological disease, during their lifetime. Uterine sarcoma, on the other hand, is a rare disease with an incidence ranging from 1.55 to 1.95 per 100,000 women per year. According to the WHO, in 2011, a LMS is a specific type of rare sarcoma that accounts for over 60% of all cases of uterine sarcoma. It is*

essential to correctly evaluate myometrial tumors before surgery to ensure proper patient management and avoid delayed treatment. However, distinguishing an LMS from fibroids can be difficult due to similar clinical, laboratory, and ultrasound features. Ultrasound is a cost-effective, non-invasive, and widely accepted imaging method for evaluating the myometrium. The reporting of ultrasound characteristics of the myometrium and myometrial lesions was standardized by developing a consensus statement by the Morphological Uterus Sonographic Assessment group.

Keywords: myometrial tumors; uterine leiomyosarcoma; diagnosis; treatment.

INTRODUCTION

Leiomyosarcoma (LMS) of the uterus is a rare soft-tissue tumor of the female pelvis with <1% of uterine tumor. It usually arises from the uterine myometrium de novo or is very rarely transformed from a preexisting benign leiomyoma. These tumors are found mainly in females 40–60 years of age. Leiomyomas in the reproductive age group and a strong suspicion of LMS should be in cases of fibroid with postmenopausal bleeding.

The World Health Organization (WHO) classification of tumors of female genital organs classifies leiomyosarcoma into three types – conventional (spindle cell), epithelioid, and myxoid variant. Conventional LMS is the most common one. Myxoid and epithelioid variants of LMS are rare. WHO classification of female genital tract tumors in the latest 5th edition recommends a diagnosis of epithelioid LMS if there are >50% cells showing epithelioid morphology with tumor cells showing moderate-to-severe atypia along with tumor cell necrosis or ≥1.6 mitoses/mm^2[1].

In the setting of an epithelioid smooth muscle tumor of the uterus, we postulate that the diagnosis of malignancy is in the presence of ≥2 of the following: moderate or severe atypia, ≥4 mitoses/2.4 mm2, and tumor cell necrosis. In their absence, the finding of tumor size ≥5 cm, vascular invasion, infiltrative edges, or atypical mitoses treated with caution, and designation as of at least uncertain malignant potential is warranted [2].

Uterine LMS is a rare and heterogeneous entity with unknown etiology, accounting for approximately 60–70% of uterine sarcomas. It occurs most frequently in perimenopausal women and shows indistinct manifestations, such as vaginal bleeding and increasing abdominal girth. Approximately 60% of cases are diagnosed at the International Federation of Gynecology and Obstetrics (FIGO) stage I, and the stage is the most important prognostic factor. However, patients with uterine-confined disease unexceptionally exhibited unfavorable prognoses. The reported 5-year overall survival rate was as low as 50–61% for stage I while decreasing to 22–48 %, 16-38%, and 10-17% for stage II, III, and IV disease, respectively [3].

CLINICAL CASE

A 39-year-old female came to the emergency room complaining of pelvic pain of 8 days duration, treated symptomatically with NSAIDs (ibuprofen). It has the following background: hereditary family history, which is unimportant to the case. Gynecobstetric history: menarche 11 years old, regular cycles 5 to 7 days, reports two months with uncontrolled cycle with heavy menstrual bleeding, start active sexual life 24 years old. Papanicolaou: last year reported normal; colposcopy last one and a half ago reported normal.

The current condition began two months ago with changes in the menstrual cycle (polyproiomenorrhea) and dysmenorrhea, which increased in the last eight days, accompanied by dysuria, tenesmus, polakiuria, and constipation. Speculoscopy revealed: complex visualization of the cervix; it is lateralized to the right due to the presence of a mass, with slight residual bleeding, a mass with regular and smooth edges on vaginal examination, with pain on cervical mobilization. A pelvic scan revealed a mass dependent on the uterus measuring approximately 8x9 cm and another measuring approximately 3 cm.

Ultrasound: the uterus in the ante version, with heterogeneous echogenicity, is identified as entirely occupied by a hypoechogenic, heterogeneous image, with central vascularity of 148 x 123 x 95 mm, which causes deformity of the anterior wall of the uterine body, as well as the uterine fundus—non-assessable endometrial cavity. The right ovary, with a volume of 13 cc, is of regular shape, size, and echogenicity, measuring 42 x 25 x 23 mm, with few follicles of less than 4 mm, without evidence of focal or diffuse lesions. The left ovary has a volume of 30 cc, has a standard shape and echogenicity, measures 47 x 37 x 32 mm, and has a 12 x 6mm follicle inside. Diagnostic impression: uterine myomatosis of the sub-serous type.

Laboratories typically and the patient is admitted and scheduled for a hysterectomy. During the trans-surgical procedure, a myoma was seen in the posterior wall of the segment, measuring approximately 18 x 15 x 10 cm. A subtotal hysterectomy was performed due to the loss of the anatomy of the parameters. To the anterior and posterior cul de sac, a 12 x 8 cm tumor with fibroid characteristics on the surface was dissected; however, fetid caseous discharge is observed, gray in color, with granulomatous tissue, significantly bleeding and fragile; intraoperative biopsy reports atypical myoma, cytological characteristics of malignant mesenchymal neoplasms (necrosis, marked atypia and mitosis), two red blood cell packets and two fresh plasmas are transfused due to hemorrhage with WHO grade IV anemia, requiring monitoring in the intensive care unit. Subsequently, laboratories requested control with the following results: Hb 10.9 with leucocytes 31.47/uL, rest routine and continuous floor surveillance of gynecology, contrast-enhanced abdominopelvic tomography was requested, and a third-level referral to oncology service (Figs. 1-5).

Figure 1. macroscopic image of an irregular mass of 12x10x10cm of fleshy appearance, with partially necrotic and hemorrhagic areas.

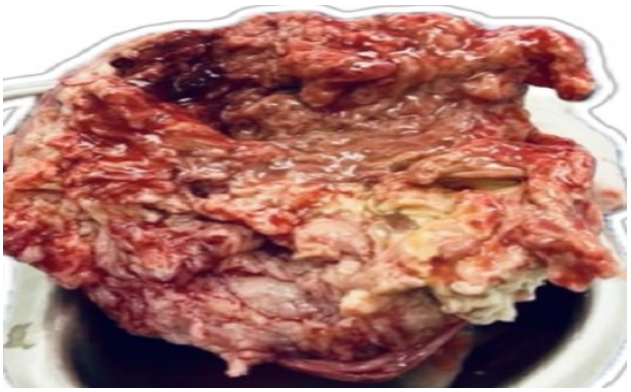


Figure 2. Uterine body without adnexa and without neck measuring 5x5x3 cm, closed smooth serous to the cut endometrial cavity of 1.5 cm from horn to horn and 3 cm in length has a thickness of 1.5 cm, no invasion of the myometrium.

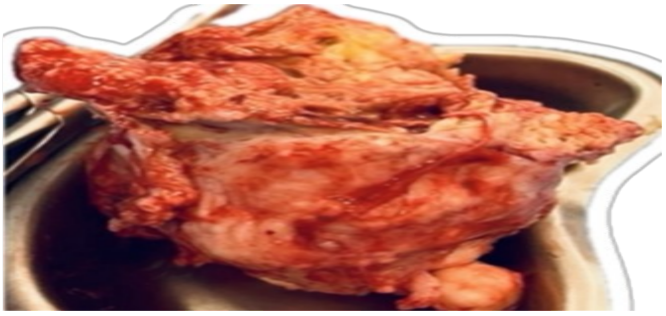


Figure 3. Transoperative study, cytology with atypia, marked pleomorphism and mitosis in a hemorrhagic background.

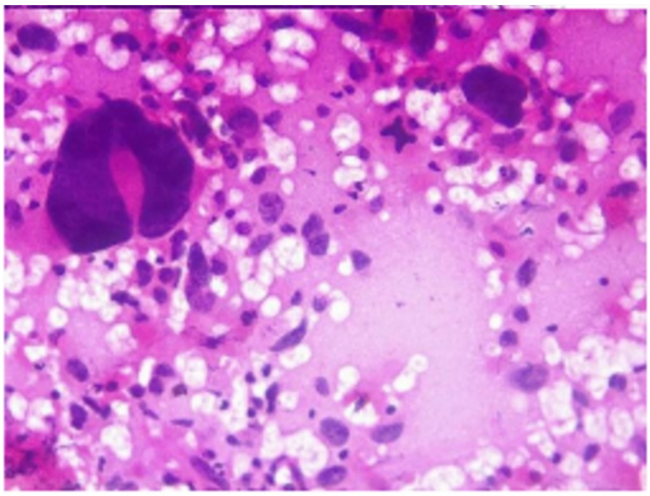


Figure 4. Hematoxylin and eosin stain: Fusocellular neoplasia with marked cellular pleomorphism and abundant mitoses (50 in 10 fields at 40x).

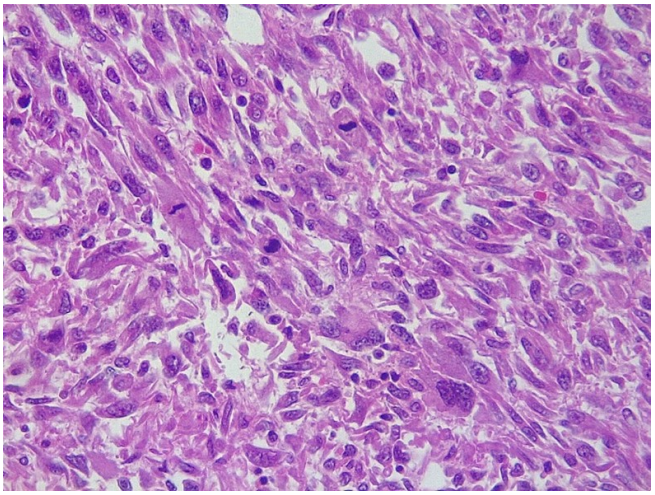
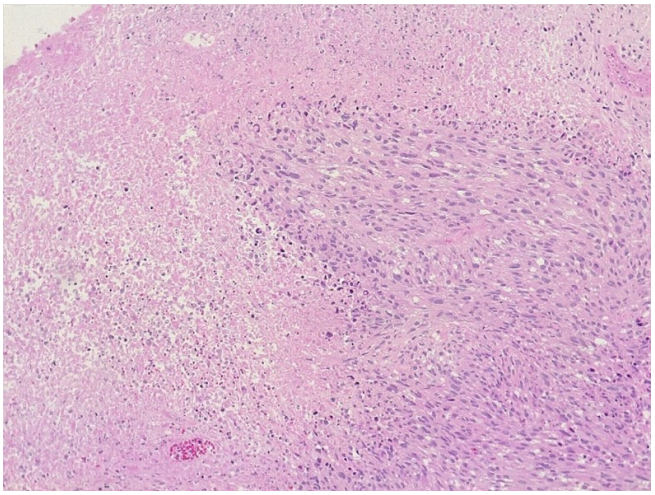


Figure 5. Areas of lesion with abrupt transition from viable tumor cells to necrotic cells.



DISCUSSIÓN

Sarcomas of the genital tract is 3% of all gynecological malignancies, with uterine sarcomas being the most common subtype in 80% of the cases. Cervical LMS constitute <1% of all cervical malignancies, and they mainly occur in perimenopausal women with an average age at diagnosis of 46 years. Of all cervical sarcomas, Carcinosarcoma (malignant mixed Müllerian tumors) is the most common subtype, with cervical LMS being the most common, followed by adenosarcoma, rhabdomyosarcoma and endometrial stromal sarcoma. Clinical symptoms typically include abnormal vaginal blood loss, abdominal distension, a cervical mass, and pelvic pain. Preoperative imaging characteristics with an ultrasound scan and magnetic resonance imaging (MRI) have been investigated and can raise suspicion of a sarcoma. With ultrasound scans, uterine LMS are often larger, solitary, and with increased central/peripheral vascularity compared to benign uterine masses. The final diagnosis is based on pathology and immunohistochemical analysis [4]

Approximately 40-80% of women may develop leiomyomas, the most common benign gynecological disease during their lifetime. Uterine sarcoma, on the other hand, is a rare disease with an incidence ranging from 1.55 to 1.95 per 100,000 women per year. According to the WHO, in 2011, a LMS is a specific type of rare sarcoma that accounts for over 60% of all cases of uterine sarcoma. It is essential to correctly evaluate myometrium tumors before surgery to ensure proper patient management and avoid delayed treatment. However, distinguishing an LMS from fibroids can be difficult due to similar clinical, laboratory, and ultrasound features. Ultrasound is a cost-effective, non-invasive, and widely accepted imaging method

for evaluating the myometrium. The reporting of ultrasound characteristics of the myometrium and myometrium lesions has been standardized by developing a consensus statement by the Morphological Uterus Sonographic Assessment group [5].

The diagnostic evaluation of uterine sarcomas includes, in addition to a physical examination, a transvaginal ultrasound and Magnetic Resonance Imaging (MRI), eventually combined with a Positron Emission Tomography (PET) scan. Nevertheless, definite diagnosis always requires hysteroscopic endometrial biopsy and tissue sampling in order to define the tumor grade and the hormone receptor status. The markers Cancer Antigen 125 (CA-125), Lactate Dehydrogenase (LDH), C-reactive protein (CRP), and D-dimers could theoretically indicate uterine sarcoma but are influenced by various other factors and, consequently, lack specificity. Despite being a cheap and convenient screening method, ultrasound may not conclusively determine the benignity or malignancy of uterine masses. On the contrary, MRI exhibits excellent soft tissue resolution, and certain degenerative types of uterine fibroids show comparable signal intensities that account for a specific rate of misdiagnosis. PET-CT is costly and complicated to promote but assures the highest accuracy [6].

LMS often demonstrates aggressive tumor biology, with a higher risk of developing distant metastatic disease than most sarcoma histologic types. The prognosis is poor, particularly in patients with uterine disease, and there is a need for the development of more effective therapies. Genetically, LMS is karyotypically complex and characterized by a low tumor mutational burden, with frequent alterations in TP53, RB1, PTEN, and DNA damage response pathways that may contribute to resistance against immune checkpoint blockade monotherapy. The LMS immune microenvironment is infiltrated with tumor-associated macrophages and tumor-infiltrating lymphocytes, which may represent promising biomarkers [7].

A Nomogram is a chart-based algorithm that integrates clinical variables to achieve accurate prediction without complex mathematical formulas. Nomograms for various malignant tumors have demonstrated practical value. Furthermore, web-based graphical nomograms can assess prognoses conveniently and intuitively. Nomograms have been developed to predict STS prognosis, as well as 12-year sarcoma-specific deaths. Histology-specific and site-specific nomograms have been developed to predict overall survival for patients with uterine LMS or limb LMS. We recently established an internal validation web-based Nomogram for LMS with lung metastasis to predict overall and cancer-specific survival. DM is an independent risk factor for poor prognosis in patients with LMS. Therefore, early identification of patients with a high risk of DM can improve patient outcomes [8].

A LMS can arise in almost all organs other than neurogenic organs. Many LMS have been reported in the digestive tract, mesentery, uterus, vessels, retroperitoneum, and soft tissues. A solitary, lobular, soft, fleshy solid mass with hemorrhage and cystic degeneration characterizes its macroscopic appearance. Microscopically, it presents 2/3 moderate/severe cytologic atypia, 10 + MF/10 HPF, and tumor cell necrosis as our case [9].

Myxoid LMS (MLMS) is a tumor variant of the uterine LMS variant, extremely rare with an annual incidence of 0.64. It is exceedingly challenging

to identify because of the aggressive disease course, clinical and histological heterogeneity, and ostensibly benign and bland cellularity. MLMS are tumors that include myxoid stroma in at least 60% of the tumor area, have undergone microscopic examination, and exhibit light microscopy and immunohistochemical evidence of smooth muscle differentiation. Correct diagnosis of MLMS is essential since, unlike other cancers, mitotic figures and abundant cellularity are not usual. Despite having a low mitotic index, these tumors have a startling myxoid look and behave very malignantly [10].

Ijaz I et al. [11] Conducted a meta-analysis of 51 reports, including 1664 patients. Among patients who received adjuvant chemotherapy (916 patients; 55%), gemcitabine and docetaxel were the most frequently used drugs. First-line monotherapy with alkylating agents and second-line with protein kinase inhibitors resulted in favorable prognoses. The combinations of anthracycline plus alkylating therapy and gemcitabine plus docetaxel showed the most significant benefits when used as first-line and second-line chemotherapies, respectively. Subgroup meta-analysis results revealed that dual-regimen therapies comprising anthracycline plus alkylating therapy and gemcitabine plus docetaxel are practical therapeutic choices for International Federation of Gynecology and Obstetrics stages III –IVb with distant metastases when assessed by computed tomography. Furthermore, neoadjuvant chemotherapy and local radiotherapy resulted in favorable outcomes for patients with earlier stages of distant relapsed uLMS. Our findings provide a basis for designing new therapeutic strategies and can potentially guide clinical practice toward better prognoses for uLMS patients with advanced, metastatic, and relapsing disease.

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REFERENCES

1. Aden D, Zaheer S, Singh S, Ranga S. Epithelioid leiomyosarcoma of the uterus and the diagnostic challenge in diagnosing it on small biopsy. J Mid-life Health. 2022; 13:241-3.
2. Chapel DB, Nucci MR, Quade BJ, Parra-Herran C. Epithelioid leiomyosarcoma of the uterus: Modern outcome-based appraisal of diagnostic criteria in a large institutional series. Am J Surg Pathol. 2022; 46:464-75.
3. Chen S, Deng Y, Zhai Y, et al. Clinical Analysis and Prognostic Prediction Model for Patients with Uterine Leiomyosarcoma at FIGO Stage I. Int J Women's Health. 2023; 15: 545-57.
4. Lebbe I, DeCuypere E, Claes N, et al. Primary leiomyosarcoma of the uterine cervix: an unusual case and critical appraisal. J Surg Case Rep. 2023; 8: 1-3.
5. Arezzo F, Cormio G, Putino C, et al. Overlap of Suspicious and Non-Suspicious Features in the Ultrasound Evaluations of Leiomyosarcoma: a Single-Center Experience. Diagnostics 2023; 13:543.
6. Psilopatis I, Vrettou K, Kokkali S, Theocharis S. The Role of MicroRNAs in Uterine Leiomyosarcoma Diagnosis and Treatment. Cancers 2023; 15: 2420.
7. Cope BM, Traweek RS, Lazcano R, et al. Targeting the Molecular and Immunologic Fea-

tures of Leiomyosarcoma. Cancers. 2023; 15:2099.

8. Wei J, Liu L, Li Z, et al. Web-based nomogram to predict post-resection risk of distant metastasis in patients with leiomyosarcoma: retrospective analysis of the SEER database and a Chinese cohort. J Int Med Res. 2023; 51(7): 1-14.

9. Mandato VD, Torricelli F, Mastrofilippo V, et al. Primary Ovarian Leiomyosarcoma Is a Very Rare Entity: A Narrative Review of the Literature. Cancers. 2023; 15:2953.

10. Wankhade R, Sajjanar A, Dawande P, et al. A Rare Case of Uterine Myxoid Leiomyosarcoma. Cureus. Aug 29, 2023; 15(8):e44303.

11. Ijaz I, Shahzad MN, Hosseinifard H, et al. Evaluation of the efficacy of systemic therapy for advanced uterine leiomyosarcoma: A systematic review, meta-analysis, and meta-regression analysis. Cancer Med. 2023; 12:13894-911.