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Uterine Myxoid Leiomyosarcoma with Stromal Chondroid Metaplasia: A Rare Case Report

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Abstract

Background: Uterine leiomyosarcoma is a rare gynecological disease. Myxoid leiomyosarcoma (mLMS) is an aggressive and very uncommon type of leiomyosarcoma, with few cases reported in English literature. Stromal metaplasia is rare in leiomyosarcoma. Here we present huge uterine myxoid leiomyosarcoma with stromal chondroid metaplasia. **Case Presentation:** A 48-year-old single woman with lower abdominal pain and increased abdominal circumference. The detected mass on imaging was diagnosed as uterine mLMS with stromal chondroid metaplasia in the histopathological examination after surgery. **Conclusion:** Myxoid leiomyosarcoma should be considered in uterine mass with extensive myxoid change, infiltrative border, low mitotic count, and mild atypia. Stromal chondroid metaplasia can be seen in the myxoid leiomyosarcoma. [GMJ.2021;10:e1817] DOI:[10.31661/gmj.v10i0.1817](https://doi.org/10.31661/gmj.v10i0.1817)

Keywords: Myxoid Leiomyosarcoma; Leiomyosarcoma; Metaplasia; Uterus

Introduction

Leiomyosarcoma (LMS), the most common uterine sarcoma (30%), is generally a rare gynecologic disease, accounting for about 1% of gynecological malignancies and 3–7% of uterine cancers. This malignant tumor of the smooth muscle cells usually manifests itself by vaginal bleeding, pelvic mass, and pain in women >40 years [1]. A rare and aggressive variant of LMS is myxoid leiomyosarcoma of the uterus, first detected and described by King and colleagues in 1982 [1]. Although the pathological features of LMS (hypercellularity and coagulative necrosis, nuclear

atypia, and high mitosis) help differentiate it from leiomyoma, microscopic diagnosis of the epithelial and myxoid LMS is difficult; myxoid leiomyosarcoma (mLMS) is hypocellular with mild nuclear atypia and low mitotic count (less than 3 MF/10 high power field [HPF]). Its diagnosis is a challenge because even its smooth muscle nature cannot be recognized [2]. The 5-year prognosis of mLMS is poor (11%), estimated worse than the survival rate of conventional LMS [3]. Metaplasia in smooth muscle tumor is rare. The most common metaplasia in leiomyoma is adipose metaplasia, while only a few leiomyoma cases with cartilaginous metaplasia are reported [4].

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The presence of metaplasia and heterologous elements such as cartilage and striated muscle are reported in some of the uterine sarcomas, most commonly in carcinosarcoma (malignant mixed mullerian tumor) [5]. To the best of our knowledge, this case is the first chondroid metaplasia in myxoid leiomyosarcoma in English literature.

Case Presentation

A 48-year-old single woman referred to Faghihi Hospital, affiliated to Shiraz University of Medical Sciences, with a chief complaint of sharp lower abdominal pain and rapid increased abdominal circumference over three months. Her medical history was unremarkable. She did not have a positive family history of breast or gynecological cancers.

Abdominopelvic examination by a gynecologist showed that the uterus was palpable as globular and mobile without tenderness. In the initial serum laboratory measurements, increased lactate dehydrogenase (LDH) (665 U/L, normal range 0-480) and anemia (Hb:9.3g/dL, normal range 12-15.6 g/dl) was detected. Other laboratory data, including Ca 125 and HE4 were within normal range.

In ultrasonography of abdominopelvic and retroperitoneal areas, the uterus was significantly enlarged and showed two heterogeneous masses: one at the anterior wall extended to the abdominal cavity (170×130 mm) and the other as an intramural fibroid mass at the fundal area (55×53 mm). Endometrial thickness was 14 mm. Ovaries were unremarkable, without any cystic or solid lesion. The results of ultrasonography also showed a fatty liver grade I and 2.5-mm gravel at the upper pole of the left kidney. Magnetic resonance imaging (MRI) with and without gadolinium was suggested for further details of the mass, which showed a deviation of the uterus to the right side by a huge mass with solid and cystic parts of about 130×200 mm. The solid parts were enhanced after gadolinium administration, and the mass infiltrated the left adnexa and attached to the left posterior side of the uterus, suggestive of a large subserosal malignant uterine mass versus malignant adnexal mass, as well as mild ascites. Endometrium was irregular with a thick junctional zone and mul-

iple cystic changes in favor of adenomyosis. Based on the imaging results, the patient was scheduled for surgery. A huge uterine mass was observed, which arising from the uterus and extended to the pelvic cavity and ruptured in one area (Figure-1). The uterine mass was resected and sent for frozen sectioning. Gross examination of the uterine mass revealed a large bosselated creamy-pink ruptured mass of 20×20×15 cm. Cut sections showed creamy lobulated surface, with predominant myxoid changes and large hemorrhagic areas. Microscopic examination revealed a hypocellular spindle cell tumor with mild nuclear atypia without mitosis in few representative frozen sections. The frozen section diagnosis was a spindle cell tumor with myxoid change and hemorrhagic area. The ruptured huge mass with myxoid areas underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with lymph node dissection with impression of malignant myxoid tumor. One section for each centimeter of the maximum diameter of the mass was prepared for histological evaluation. Myxoid leiomyosarcoma was diagnosed for the subserosal mass. Microscopic examination showed stellate cells with moderate nuclear atypia and focal necrosis (Figure-2 A, B, C). The cells were surrounded by abundant myxoid stroma. Alcian blue staining showed mucoid material deposition at the stroma (Figure-2D). Chondroid differentiation was seen focally in the tumor stroma (Figure-3). Fifty high-power fields (x400) were evaluated, and an average of 2-3 mitotic figures per 10 HPF was noted. Examination of the pedicle of the uterine mass showed infiltration of the tumor into the adjacent myometrium. A benign intramural leiomyoma measuring 6×5.5 cm was also present. Five dissected lymph nodes were free of tumor. Due to the large size of the tumor (stage II), the patient received radiotherapy, followed by ultrasonography and serum LDH level. After 12 months, the patient has no evidence of recurrence.

Discussion

Leiomyosarcoma is the most common type of uterine sarcoma, easily differentiated from leiomyoma by the malignant pathological fea-

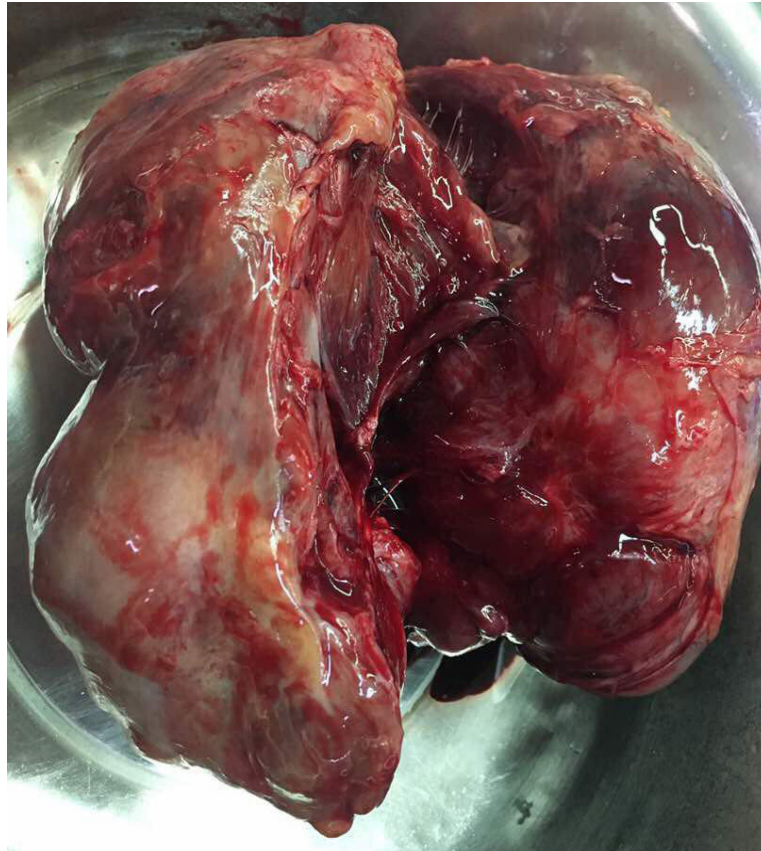


Figure 1. Huge ruptured uterine mass.

tures, including tumor cell necrosis, hypercellularity, nuclear atypia, and high mitosis. One of the rare variants of uterine leiomyosarcoma is mLMS that has an aggressive nature [2, 6]. As the presenting symptoms, including abdominal pain and mass sensation, are non-specific, the final diagnosis is usually made by histopathological examination [6]. The presented case also had abdominal pain as the only chief complaint. Similar to previous reports [7], the results of ultrasonography and MRI showed a non-specific mass, and final diagnosis was only possible by histopathological examination. Gelatinous or mucoid gross appearance and low mitotic rate have been described as the main histopathological features of mLMS [1]. Nevertheless, as these microscopic features (low mitosis and mild nuclear atypia) resemble those of benign lesions, special attention should be paid during histopathological examinations. In our case, gross examination revealed creamy bosselated surface, and microscopic examination documented moderate nuclear atypia, 2–3 mitotic figures per 10 HPF, and focal tumor

cell necrosis. [3]. Tumor cell necrosis is reported in some cases, but the assessment of tumor necrosis can be difficult and challenging. Other microscopic features suggested for the diagnosis of mLMS include focal nuclear enlargement and infiltrative tumor border. The latter is associated with aggressive behavior but requires careful examination and extensive sampling [3]. Cartilaginous metaplasia has also been reported in the leiomyoma of the uterus, while the exact nature of these cartilaginous foci is not well-known. According to our recent search in English articles, the major heterologous elements have been reported in carcinosarcomas. No cartilaginous or chondroid metaplasia has been reported in leiomyosarcoma, and the metaplastic foci in the endometrium or myometrium have been observed in relation to the previous miscarriage and interpreted as a reactive process [4, 8]. Some laboratory measurements suggested helping the diagnosis of mLMS include immunohistochemistry and serum levels of LDH [9]. Cell-cycle regulatory markers such as

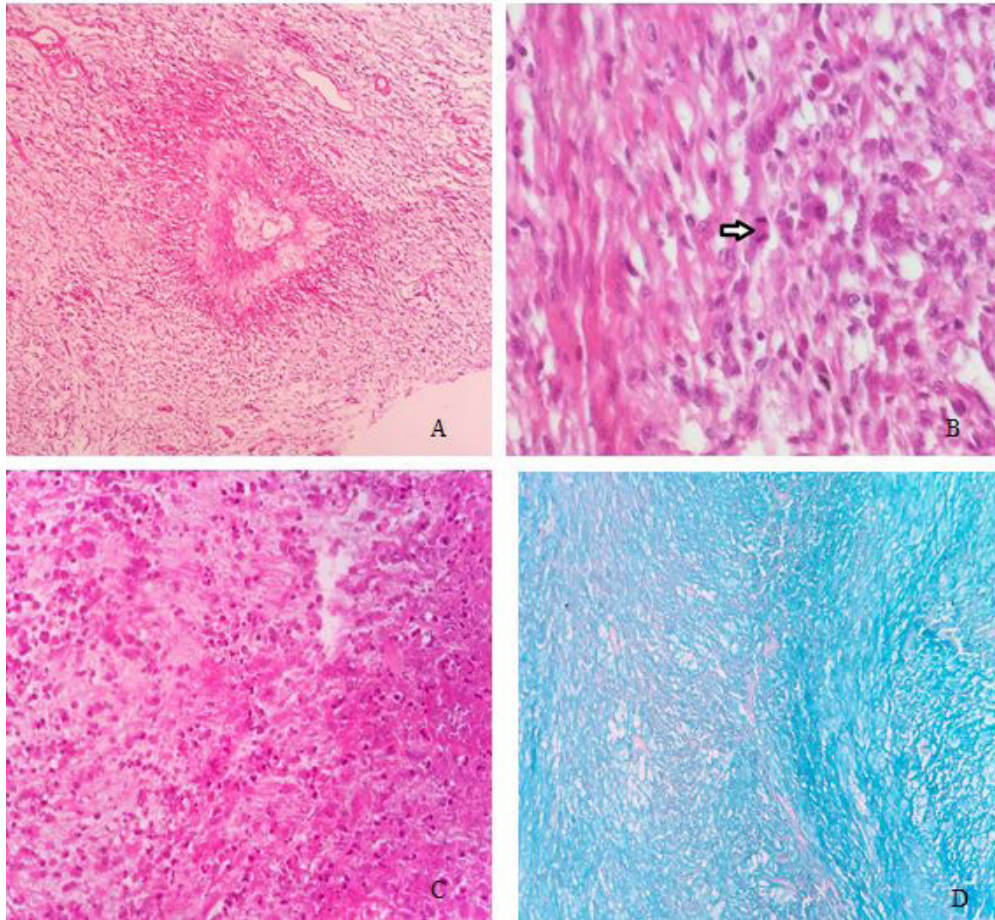


Figure 2. A&B- Spindle cells with mild nuclear atypia and rare mitosis in the myxoid background and (C) necrotic area, H&E staining X 100 (A) and x 400 (B,C). D- Mucoid material deposition at stroma, Alcian blue staining x100.

p16, p53, Ki-67; nevertheless, the latter markers cannot distinguish between benign and malignant cases, and mLMS may show less immunoreaction than conventional LMS [10]. The serum parameters evaluated in our patient showed an increased LDH level, which is critically important in presurgical diagnosis [9]. Uterine mLMS can have a wide range of differential diagnoses, including different benign and malignant lesions. It is also important to distinguish myxoid changes from hydropic degenerative changes in the uterine leiomyomas, which is characterized by watery edema [11]. Myxoid material is rich in glycosaminoglycans and proteoglycans and shows a positive response to the Alcian blue staining. Conversely, hydropic change, and edema have negative results by Alcian blue [12]. Myxoid leiomyosarcoma could be differentiated from myxoid leiomyoma by the infiltrative tumor border and at least one of the following: two

or more mitoses per 10HPF, moderate to severe (2+/3+) nuclear atypia, or unequivocal coagulative tumor necrosis [3]. The inflammatory myofibroblastic tumor is another uncommon neoplasm in the female genital tract, characterized by a spindle cell population in a myxoid to collagenous stroma admixed with a lymphoplasmacytic infiltrate. It has morphological overlap with smooth muscle tumors, which is considered as an important differential diagnosis for mLMS. The distinction between these two can be achieved by immunohistochemistry assay, resulting in anaplastic lymphoma kinase (ALK) overexpression in uterine inflammatory myofibroblastic tumor [13]. The myofibroblastic tumor had a benign clinical course in the past, while aggressive behavior has been recently reported for this entity, resulting in its classification as an entity with intermediate malignant potential [3]. The distinction between inflammatory

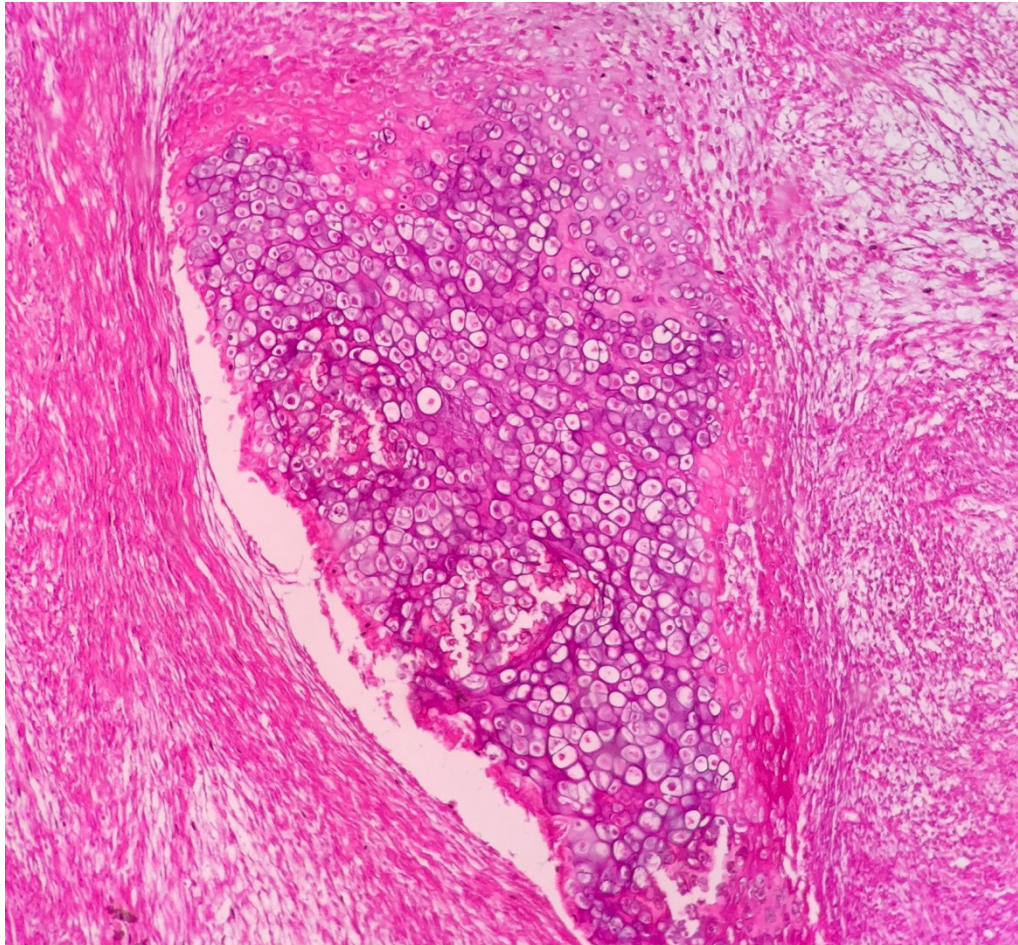


Figure 3. Chondroid differentiation of stroma. H&E staining X 200

myofibroblastic tumor and mLMS is critical because targeted therapy with tyrosine-kinase inhibitors can be used to treat recurrent or unresectable inflammatory myofibroblastic tumor [3]. Also, endometrial stromal sarcomas may occasionally have a predominant fibromyxoid pattern [14], and purely myxoid endometrial stromal sarcomas are among differential diagnoses of mLMS. Other entities, such as myxoma or low-grade fibromyxoid sarcoma, should be considered in the differential diagnoses of mLMS, too [3]. The distinction can be made by classic architectural and cytologic features of endometrial stromal neoplasms, particularly the absence of severe nuclear pleomorphism and the presence of a uniform vascular network composed of thin-walled vessels, while negativity of smooth muscle markers will favor an endometrial stromal neoplasm [3]. The study by Parra-Herran and co-workers showed poor prog-

nosis of mLMS, and almost half the patients died. Local or distant tumor recurrences were found in one-third of the patients. The reported five-year survival rate of 11.1% is significantly lower than the survival rates reported for conventional LMS [3]. The prognosis was also related to high mitotic rates, infiltrative tumor border, and intravascular extension [3]. Large size (>80 mm) and p53 positivity have been reported as important features associated with recurrence, while expression of estrogen and progesterone receptors in mLMS and its effect on the patient's survival is still controversial. Further evaluation of the influence of p53 positivity on long-term recurrence in future studies would be worthwhile [15]. Despite the few mLMS cases reported in the literature, evidence suggests that surgery remains the most appropriate treatment. Radiotherapy has been recommended to treat deep sarcomas before and after surgery since 2002. mLMS

has shown favorable responses to radiotherapy; specifically, preoperative radiotherapy has been found to reduce the size of mLMS [16]. The patient had no recurrence and responded well to surgical removal and radiotherapy until the report of this case.

Conclusion

The case presented here, similar to the few cases reported before, had abdominal pain and mass. On microscopic examination, extensive

myxoid matrix and infiltrative border helped final diagnosis by the pathologist despite low mitotic rates and mild cellular atypia. Metaplasia is rare in leiomyoma and very rare in leiomyosarcoma. To the best of our knowledge, this case is the first with chondroid metaplasia in mLMS.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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