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Myxoid leiomyosarcoma of the uterus: a case report and review of the literature

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Summary

A para 1, 52-year-old female was admitted with complaints of irregular vaginal bleeding for the previous six months. Ultrasonography revealed a 4×6-cm tumor extending into the uterine cavity and cervical canal. On vaginal examination, a 2×2-cm tumor protruding from the cervical os was found, and an enlarged uterus was palpated. Vaginal intrauterine tumor resection was performed, and the patient was diagnosed with uterine myxoid leiomyosarcoma. A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed, followed by postoperative chemotherapy. Twenty-one months after surgery, the patient died of tumor recurrence. Uterine myxoid leiomyosarcoma is an extremely rare variant of uterine sarcoma with a poor prognosis and malignant biological behavior.

Key words: Leiomyosarcoma; Myxoid; Uterus.

Introduction

Uterine leiomyosarcoma is an uncommon mesenchymal neoplasm accounting for 1.3% of all uterine malignancies and 30% to 40% of all uterine sarcomas [1]. Very few cases series have been reported. Myxoid leiomyosarcoma of the uterus was first described in 1982 by King *et al.* [2]. These tumors have a striking myxoid appearance and exhibit highly malignant behavior despite their low mitotic index. In this article, the authors report a 50-year-old patient with myxoid leiomyosarcoma.

Case Report

A 50-year-old Chinese woman (gravida 3, para 1) presented with a nearly six-month history of irregular vaginal bleeding. Ultrasonography revealed a 3.5×3.2-cm intrauterine tumor with irregular inner density. On April 2012, ultrasonography revealed a myoma-like tumor measuring 4 ×6 cm extending from the uterine cavity to the cervical canal. On vaginal examination, a 2×2-cm bleeding tumor was protruding from the cervical os and an enlarged uterus was palpated. Vaginal intrauterine tumor excision was performed in a county hospital. Pathologic findings revealed a myxoid leiomyosarcoma with cell necrosis and eight mitotic figures per ten HPF. The patient was transferred to the present hospital seven days after operation. Laboratory data and tumor markers including CA125, CA153, CA199, CEA, and AFP were within the normal range. Magnetic resonance imaging (MRI) demonstrated an enlarged uterus with a 2.5-cm inhomogeneous mass in the cavity (Figure 1A). No enlarged lymph nodes were found. A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed on May 7th, 2012. The uterus was 9×6×5 cm without any obvious mass around it. There were no palpable lymph nodes, thus lymph node dissection was not performed. No evidence of pelvic spread or ascites was found. Peritoneal irrigational cytology was negative. Frozen sections demonstrated myxoid leiomyosarcoma, and no other malignant tumor, such as endometrial cancer, was found; therefore, lymph node dissection was not performed. The uterus was opened, and a 4×4×3-cm mass with an old broken end was found to protrude from the uterine fundus and back wall. The mass had a pale and smooth cut surface with areas of necrosis and hemorrhage. The border with the adjacent myometrium was blurred. Four pale firm nodules measuring 0.5-1.0 cm were found in the muscular layer. On microscopic examination, the largest mass was a myxoid leiomyosarcoma with five to eight mitotic figures/ten high power fields. Myxoid material was present in the extracellular matrix (Figures 2-3). The tumor had invaded halfway through the myometrium. There was no venous or lymphatic invasion. Four small nodules were placenta nodules. In addition, microscopic examination revealed adenomyoma of the uterus. Stage Ib was diagnosed according to FIGO 2014. The patient was treated with five courses of carboplatin 500 mg+epimbicin 80 mg.

At 14 months postoperation, ultrasonography revealed an eight-cm pelvic mass, which suggested tumor recurrence. After three months, an MRI showed a 34×24×13-cm cyst-solid mixed abdomino-pelvic mass. The solid section was obviously enhanced on a contrast-enhanced MRI scan (Figure 1B). In addition, peritoneal dissemination and ascites were found. The patient declined further treatment and died 21 months after surgery.

Discussion

Myxoid leiomyosarcoma is an extremely rare variant of the uterine leiomyosarcoma. Only a few cases of myxoid leiomyosarcoma of the uterus have been reported in the English literature. Because of its rarity, there is limited knowledge about this type of tumor. The patient age ranges from 20

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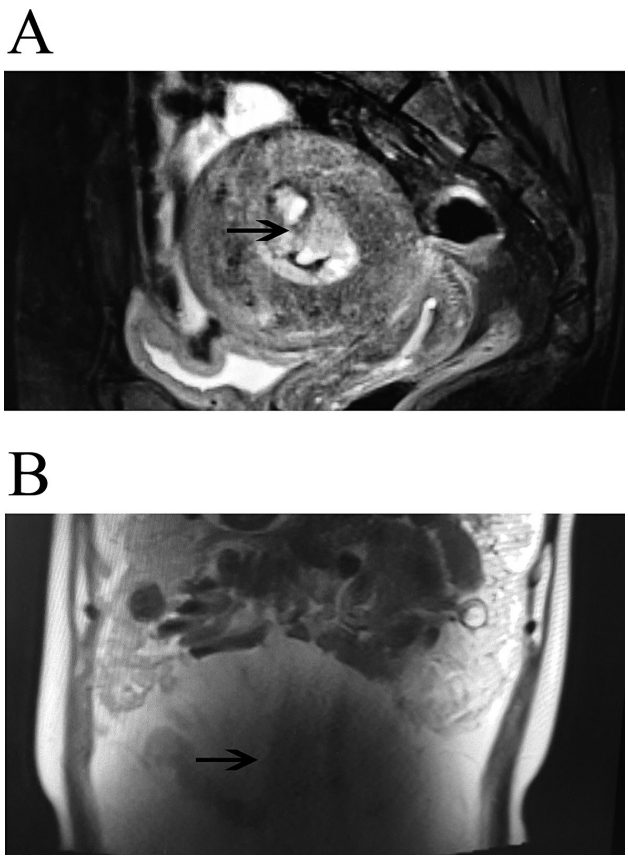

Figure 1. — A. MRI showing a non-homogeneous mass in the uterine cavity before operation (arrow: tumor). B. MRI demonstrated a large cyst-solid mixed abdomino-pelvic mass, which suggests tumor recurrence at 17 months postoperation (arrow: recurrent tumor).

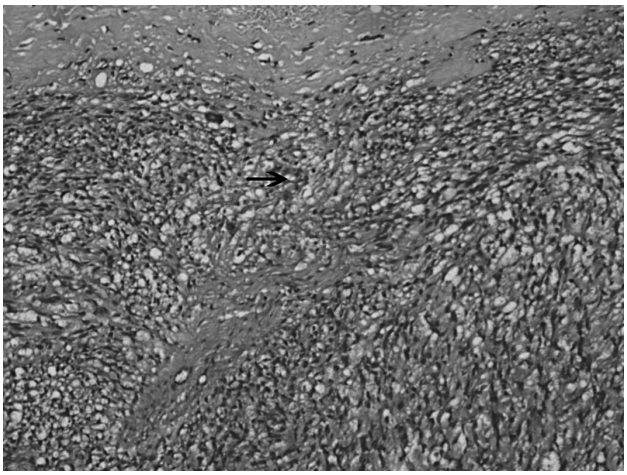

Figure 2. — Histological section of the uterine sarcoma showing a myxomatous stroma and leiomyosarcoma cells with infiltrative margins (arrow: infiltrative margin; Hematoxylin and Eosin,×100).

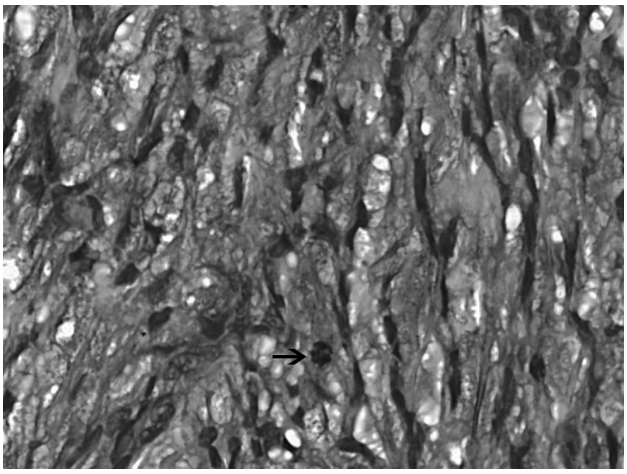

Figure 3. — Stellate and bipolar spindle tumor cells in a background of myxoid stroma with mitosis (arrow: mitotic figure; Hematoxylin and Eosin,×400).

to 74 years, with a mean age of 55 years [3]. Myxoid leiomyosarcoma has not been shown to be related to the known risk factors for endometrial carcinoma (nulliparity, obesity, diabetes mellitus, hypertension, etc.) [4] or carcinosarcomas (prior radiation therapy) [5]. This case had no risk factors for endometrial carcinoma or carcinosarcoma. Some authors have reported that uterine myxoid leiomyosarcoma arise from leiomyoma [6-8]. Typical uterine myomas may or may not coexist in the uterus. In this article, the patient was 50-years-old and in the peri-menopausal period. No myomas were found in the uterus.

Most patients complain of genital bleeding and/or a pelvic mass [2]. The mass was large (20 cm at the greatest diameter), which falls within the five to 45 cm range [9]. In the present case, the patient presented with symptoms of abnormal vaginal bleeding but with no obvious abdomino-pelvic mass. In contrast to previous reports, the mass was in the uterine cavity and protruded from the cervical os. Perhaps an intrauterine mass was the primary cause of vaginal bleeding. Some authors have reported that the serum CA125 level is elevated [6, 10], but the significance of this marker has not been established. In the present case, the serum CA125 and other tumor markers levels were within normal limits. Unfortunately, tumor markers levels were not evaluated prior to tumor excision.

Uterine myxoid leiomyosarcomas have a characteristically gelatinous appearance and many have well-circumscribed borders macroscopically. However, in this case, the mass had a smooth appearance. Myxoid leiomyosarcoma, although rare, should be included in the differential diagnosis of any uterine tumor with a predominantly myxomatous composition, such as myxoid endometrial stromal sarcoma, myxoid leiomyoma, and low-grade myxofibrosarcoma. To differentiate myxoid leiomyosarcoma from

a benign leiomyoma, one cannot rely solely on intraoperative frozen sections because these tumors are characterized by a low mitotic count without atypia in most instances [11]. Kaleli *et al.* [12] reported that frozen section diagnosis has failed to recognize the myxoid variant of uterine leiomyosarcoma. However the presence of myxomatous stroma on frozen section should warn the surgeon about the possibility of myxoid leiomyosarcoma. In the present case, the pathologists made the right diagnosis based on the highly atypical nuclei and infiltrative margin by frozen section examination. The presence of tumor cell necrosis, atypia, and mitotic figures are major features in the differentiation between myxoid leiomyosarcomas and myxoid leiomyomas [7]. Conventional pathologic diagnosis of sarcoma depends primarily on the number of mitotic figures per ten HPF [13]. Myxoid leiomyosarcomas are characterized by low cellularity and a low mitotic index [14]. King *et al.* [2] reported a low mitotic index (range zero to two per ten HPF). However, some cases occur with high mitotic rates. Mitrache *et al.* [15] reported a mitotic index with 20 mitotic figures per ten HPF. The present case had five to eight mitotic figures per ten HPF. Traditionally, the mitotic count has separated leiomyosarcomas from cellular leiomyomas. However the diagnosis of myxoid leiomyosarcoma is primarily based on gross and microscopic features rather than the mitotic index. Moreover, the mitotic count cannot determine the malignant potential of this type of tumor.

Although the numbers are small, adjuvant radiation therapy does not appear to be effective. Likewise, chemotherapy does not seem to improve long-term survival as the effects of chemotherapy have been unclear [7, 9]. Five courses of carboplatin + epimbicin were performed in this case.

This variant of leiomyosarcoma tends to recur and metastasize whether mitotic figures are scanty or numerous. A better prognosis is associated with premenopausal status, circumscribed margins, and low mitotic counts [11]. Many patients experience disease recurrence with a time to recurrence ranging from two months to ten years [10, 12]. Although regular chemotherapy was performed, this case experienced recurrence 14 months after surgery and died 21 months after. Burch *et al.* [7] reported 12 uterine smooth muscle tumors with myxoid leiomyosarcoma change. Of these, nine had an infiltrative growth pattern, and all five recurrent tumors were from this group. Their results suggested an infiltrative margin which was a major factor in myxoid leiomyosarcoma aggression. Patients with a leiomyoma component have a favorable prognosis [8]. A five-year survival rate of 15- 35% with a more favorable prognosis has been reported for patients with Stage I tumors and for premenopausal females [14]. In this article, this patient had no leiomyoma and the tumor had infiltrative margins with high mitotic activity. These factors likely contributed to the poor prognosis.

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