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Case Report

Two-stage resection of a disseminated mixed endometrial stromal sarcoma and smooth muscle tumor with intravascular and intracardiac extension

Ai-Qian Zhang [a], Min Xue [a], Dian-Jun Wang [a], Wan-Pin Nie [a], Da-Bao Xu [a, *], Xiao-Ming Guan [b, **]

[a] Department of Gynecology, Third Xiangya Hospital, Central South University, Changsha City, Hunan Province, China
[b] Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX 77030, USA

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ABSTRACT

Objective: Mixed endometrial stromal and smooth muscle tumor (MESSMT)—a rare mesenchymal uterine tumor of the uterus with atypical clinical symptoms—is susceptible to misdiagnosis and missed diagnosis. We report a case of a disseminated MESSMT with intravenous and intracardiac extensions treated with staging surgery and review previously documented cases of such tumors with intracardiac extension.

Case Report: The case involves a 45-year-old woman with disseminated MESSMT that originated in the uterus and progressed through the iliac vein, inferior vena cava, right atrium, and into the right ventricle, which closely resembled intravenous leiomyomatosis (IVL) grossly and microscopically. She presented with a 1-year history of dyspnea on exertion. IVL was highly suspected preoperatively based on computed tomography and magnetic resonance imaging findings. Two-stage surgeries were performed successfully. The postoperative pathology indicated a disseminated MESSMT.

Conclusion: This case illustrates the important role of pathology and immunohistochemistry in the differential diagnosis of a rare tumor that mimics the characteristics of IVL with intracardiac involvement and demonstrates the therapeutic strategy for this rare entity.

Introduction

Mixed endometrial stromal and smooth muscle tumor (MESSMT) contains both endometrial stromal and smooth muscle tissue with > 30% of each type of tissue. Initially reported as an interstitial myoma [1], it is a rare mesenchymal uterine tumor with atypical clinical symptoms. Owing to the atypical presentation, this tumor is susceptible to misdiagnosis [especially with intravenous leiomyomatosis (IVL)] and missed diagnosis. It has been seldom reported in the literature, and there are only a few previously documented cases of such tumors with intracardiac extension [2–4].

Complete resection of the intravascular and extravascular portions of the tumor, although challenging, is mandatory in order to relieve symptoms and prevent recurrence [4]. In cases with intracardiac extension, the disease condition is particularly complicated, given the venous and cardiac involvement. Surgery for such tumors requires the participation of doctors from various disciplines and is associated with high mortality and postoperative recurrence rates. Single-stage and two-stage operations with cardiopulmonary bypass (CPB) with or without hypothermic circulatory arrest have been used for resection of tumors with caval and cardiac extensions [4–6].

We report a case of a low-grade malignant and disseminated MESSMT that originated in the uterus and progressed through the iliac vein, inferior vena cava (IVC), right atrium, and into the right ventricle that was successfully treated via two-stage operations with CPB.

* Corresponding author. Department of Gynecology, Third Xiangya Hospital, Central South University, 138 Tongzipo Road, Changsha City, Hunan Province 410013, China.
** Corresponding author. Department of Obstetrics and Gynecology, Baylor College of Medicine, 6651 Main Street, Suite F1050, Houston, TX 77030, USA.
E-mail addresses: dabaoxu@yahoo.com (D.-B. Xu), xiaoming@bcm.edu (X.-M. Guan).

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Case Report

A 45-year-old woman presented with a 1-year history of dyspnea on exertion that was alleviated with rest. Four years prior to presentation, the patient underwent myomectomy in a local hospital for a "benign leiomyoma" (no medical notes/pathological specimens were available). One year following the myomectomy, the patient was diagnosed with a recurrence of "uterine leiomyoma" (later found to be MESSMT) during a medical checkup. Regular ultrasound examinations revealed a gradually enlarging "uterine leiomyoma." The patient did not experience any changes in menstruation patterns.

Clinical examination revealed a diastolic murmur at the left sternal border and a slightly distended abdomen. Pelvic examination showed the cervix to be in a very high position; it could not be exposed or palpated. Bimanual examination revealed a pelvic mass consistent in size with a 24-week uterus and of irregular shape. The mass was hard, fixed, and nontender. The uterus could not be palpated, and both adnexal regions were completely occupied by the mass. Computed tomography and magnetic resonance imaging (MRI) confirmed a large mass (measuring 21.3 cm × 10.8 cm × 11.8 cm) in the abdominal cavity (Figures 1A and 1B). Intraluminal filling defects were observed within the right common iliac vein, extending through the IVC, right atrium, and into the right ventricle (Figure 1C). The pulmonary arteries were free of any involvement.

With appropriate preoperative preparations, exploratory laparotomy was performed. The large, hard, and fixed mass extended deeply into the pelvis and upward to 5 cm above the umbilicus. The uterus was difficult to identify, although it was eventually located to the left of the mass. The border between the mass and the bladder was indistinct. The bladder walls were studded with multiple 0.5–4-cm tumors that did not penetrate the mucous membranes. The main body of the mass, uterus (Figure 2A), and both fallopian tubes and ovaries were resected. Several disseminated masses were found deep in the pelvis: one on the left side of the vagina, a second adjacent to the right ureter, and a third near the right obturator foramen. The masses on the bladder walls, retroperitoneum, and pelvic floor were removed (Figure 2B). Because of the large size of the tumor and its invasiveness, extensive hemorrhage occurred during the surgery. To avoid further hemorrhage, pelvic lymph node dissection was not performed. The postoperative pathological examination indicated a tumor with endometrial stromal (Figure 3A) and smooth muscle origin (Figure 3B) with low-grade malignancy, which fulfilled the definition of MESSMT. The patient recovered uneventfully.

At 25 days after the first-stage surgery, thoracoabdominal surgery was performed under hypothermic CPB. Through abdominal incisions, the abdominal vessels were completely exposed and explored. The tumor's basal part was found in the right iliac vein. A venotomy was made at the junction of the iliac vein and IVC. Owing to the delicate shape of the tumor in this junction, the tumor was difficult to separate from the iliac vein and was therefore dissected. After incising the right iliac vein, the basal part of the tumor was excised. Simultaneously, right atriotomy under extracorporeal membranous oxygenation with beating heart was performed. A solid tumor mass was found in the right atrium contiguous with the tumor filling the IVC. A portion of the tumor in the right atrium branched into the right ventricle through the tricuspid valve, making a "Y" shape. Although the tumor was space filling, it did not adhere to the venous or cardiac walls. The branching part of the tumor was extracted from the right ventricle through the tricuspid valve; then, the entire tumor was completely pulled out through the IVC. The final specimen measured ~33 cm and was grayish white, cylindrically shaped, smooth, and hard (Figure 2C). The histopathological examination indicated a cellular morphology identical to that of the tumor removed in the first-stage operation.

The patient recovered well from the surgery and was discharged home 12 days postoperatively. We recommended toremifene citrate tablets to prevent tumor recurrence postoperatively. Three months after the surgery, the patient was doing well with no signs of recurrence.

For this report, we obtained the informed consent of the patient and approval from the Independent Ethics Committee of Central South University, Changsha City, China.

Discussion

MESSMT contains both endometrial stromal and smooth muscle tissues, and must contain > 30% of each type of tissue to meet the definition of MESSMT. MESSMT has biological behavior similar to IVL in that it can display vascular invasion—such as in this case, in which the tumor invaded the iliac veins, IVC, right atrium, and right ventricle. MESSMT is easily misdiagnosed as IVL or endometrial stromal tumor (EST). The differential diagnosis is difficult because of the similar clinical presentations; therefore, pathological and

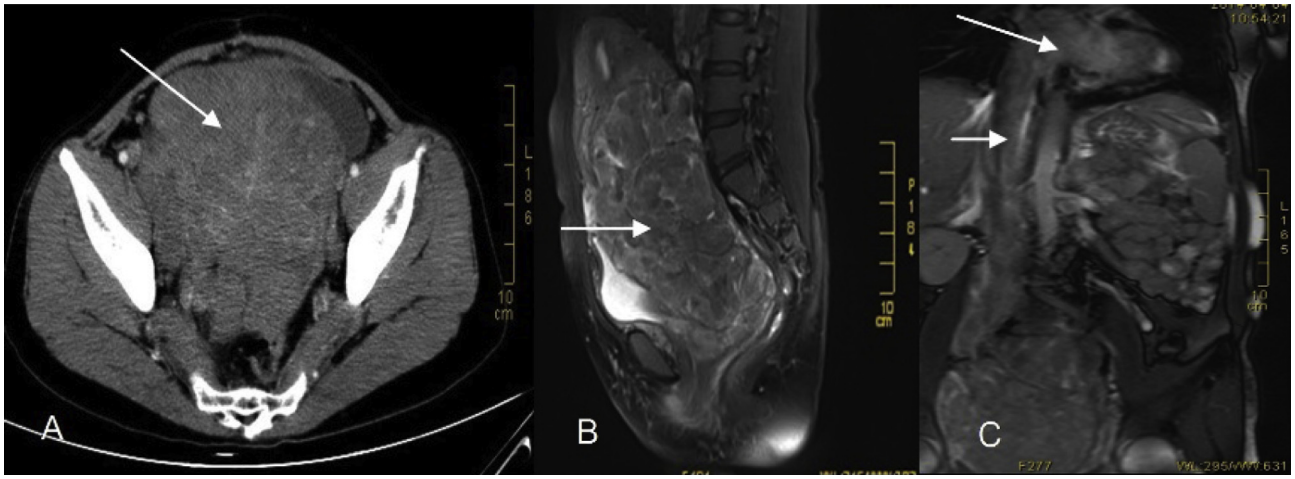

Figure 1. (A) Pelvic computed tomographic image showing a huge pelvic mass. (B) Magnetic resonance image (MRI) showing the uterus and mass. (C) MRI showing the masses in the inferior vena cava and right atrium.

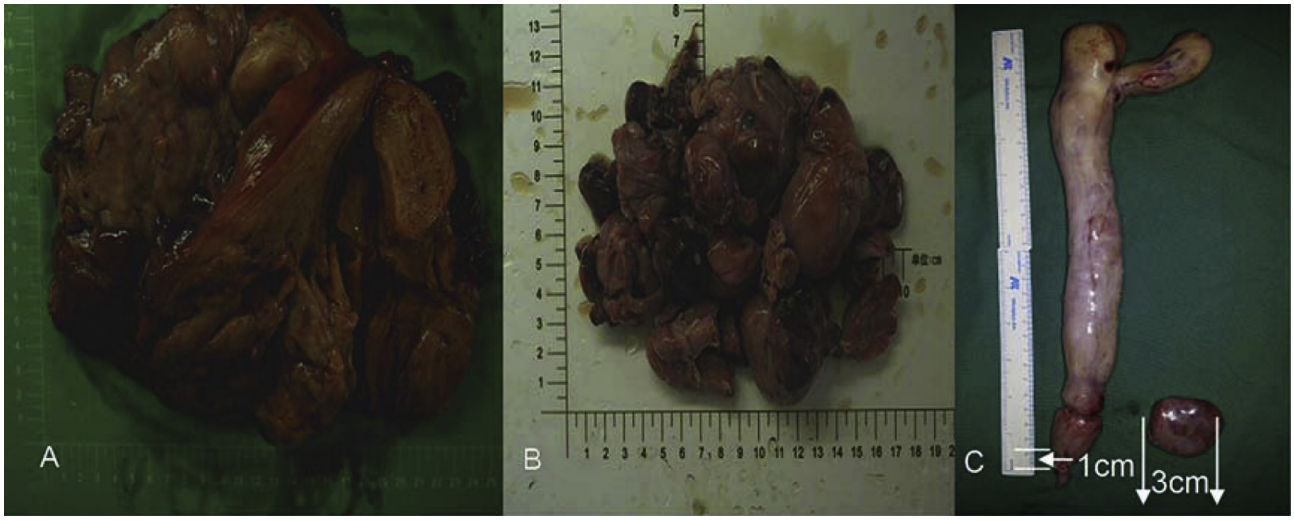

Figure 2. (A) The resected main body of the tumor and uterus. (B) The tumors from the bladder walls, retroperitoneum, and bottom of the pelvis. (C) The tumors in the vein and the heart.

immunohistochemical examinations are essential for differentiation.

IVL is an uncommon benign smooth muscle uterine tumor that grows along the veins. Its biological behaviors are similar to those of malignant tumors with high rates of recurrence and metastasis. It migrates to the endometrial smooth muscle lining the veins, which enables extrauterine extension. So far, the pathogenesis is thought to be one of two possible origins: one theory is that this type of tumor develops from a preexisting benign uterine leiomyoma; the other is that it originates from smooth muscle cells within the walls of a uterine vein [7]. EST is a rare kind of malignant uterine tumor originating from mesenchymal stem cells, which can potentially differentiate into mature endometrial stroma or into endometrial smooth muscle [8]. EST is considered to be an estrogen-dependent sarcoma [9]. This tumor can invade the lymphatic system or vessels, although it rarely involves the large vessels or the heart [3]. ESTs are more aggressive than IVL and have greater propensity for local invasion and systemic metastasis. Low-grade malignant endometrial stromal sarcomas are considered to be biologically similar to pure smooth muscle tumors [2,3].

A literature review revealed three cases of this type of MESSMT with intracardiac extension. These cases differed from the present case: they were diagnosed at a later stage, with the tumors displaying a more aggressive behavior with pelvic, caval, and intracardiac recurrences [2,3]. In the third case, the tumor had extended to the pulmonary vessels, and it had a higher rate of sudden death [4]. Previously documented cases of such tumors with intracardiac extension are reviewed in Table 1.

Complete surgical tumor resection is the best treatment for this tumor. The surgical approach should be guided by preoperative determination of the site of origin of the tumor and the degree of extension into the veins, heart, and pulmonary arteries. In these patients, venous cannulation for CPB may be challenging. Coganow et al [4] successfully performed single-stage resection of this tumor with CPB. Staged surgical approaches have also been used for tumor resection involving cardiac extension [6]. We chose a staged surgical approach for the following reasons. (1) Preoperatively, the pathological diagnosis and true extent of the tumor was unclear. The large size of the pelvic mass with its extensive abdominal invasion and infiltration was expected to render the removal of the intravascular tumor extremely difficult in a one-stage procedure. (2) Single-stage surgery requires longer procedural duration, results in a large surgical pedicle, and carries a greater risk of massive hemorrhage from the surgical field because of heparinization

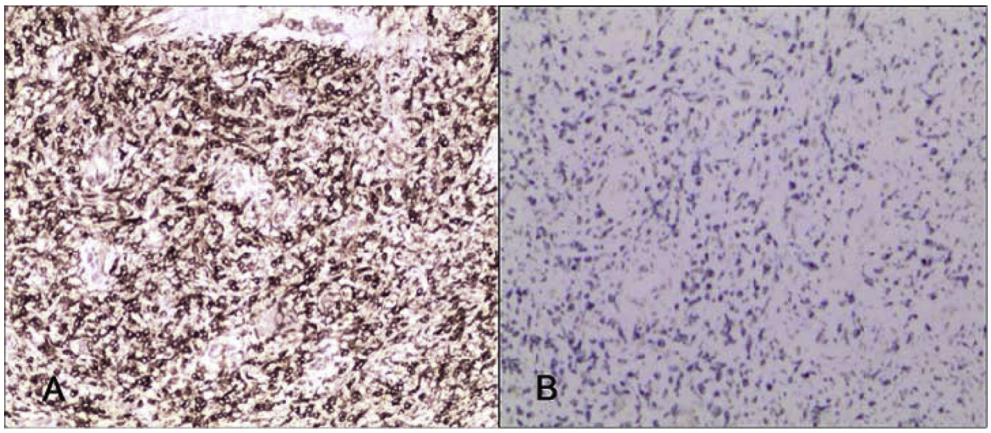

Figure 3. The final diagnosis is mixed endometrial stromal and smooth muscle tumor. Histological examination of the resected specimen with immunohistochemical staining for (A) CD10 (endometrial stromal cells) and (B) desmin (smooth muscle differentiation).

Table 1
Clinical summary of documented cases of MESSMT with intracardiac extension.

Ref.	Year	Age (y)	Original diagnosis	Final diagnosis	Metastasis	Surgery	Follow-up
[2]	1987	50	IVL	MESSMT	IVC, right atrium	Staging surgery	Patient died after 8 y
[3]	1999	24	IVL	MESSMT	IVC, right atrium right lung	Staging surgery	Asymptomatic at 12 y
[4]	2006	47	No record	MESSMT	IVC, right atrial pulmonary	Multiple-stage operation	No recurrence at 9 mo
Our case	2014	45	IVL	MESSMT	IVC, right atrial right ventricle	Staging surgery	No recurrence at 3 mo

IVL = intravenous leiomyomatosis; IVC = inferior vena cava; MESSMT = mixed endometrial stromal and smooth muscle tumor.

during CPB. Therefore, a two-stage surgical approach was selected. In the first stage, the pelvic and abdominal tumors were removed. In the second stage, the right cardiac and venous tumors were removed under CPB.

Because MESSMT is an estrogen-dependent tumor, postoperative antiestrogen medication, such as toremifene citrate tablets or tamoxifen, may have therapeutic effects on preventing tumor relapse, particularly for patients with incompletely removed tumors [3].

Preoperative diagnosis with computed tomography and MRI is important for pelvic tumors with intravenous extension, particularly when complicated by venous and/or cardiac involvement. MRI can provide clarity regarding the relationship of the tumor with the vessel wall, i.e., whether the tumor is densely adhesive to the vessel wall. Such information is critical to the successful removal of the tumor because sloughing of the tumor thrombus can cause pulmonary artery embolism and sudden death. Owing to the similar biological behaviors of MESSMT and IVL, postoperative pathological and immunohistochemical examinations are vital to distinguish the two diseases. In patients with MESSMT, long-term surveillance is necessary because of the high mortality and postoperative recurrence rates associated with this tumor.

Conflicts of interest

The authors have no conflicts of interests relevant to this article.

Acknowledgments

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