

A Case of Unsuspected Low-grade Endometrial Stromal Sarcoma Successfully Treated with Two Minimally Invasive Surgeries

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Abstract

It is relatively uncommon to treat patients with a preoperative diagnosis of benign leiomyoma that is then unexpectedly rediagnosed as malignant in postoperative histology. We report the case of a 55-year-old woman with low-grade endometrial stromal sarcoma who had been diagnosed as having uterine leiomyoma with myxoid degeneration by preoperative magnetic resonance imaging (MRI). She underwent a laparoscopic hysterectomy. The uterus, after being placed in a retrieval bag, was transvaginally morcellated to prevent spillage of the contents, as the MRI image appeared somewhat atypical. A retrospective survey of MRI findings affirmed that the muscle tissue had the appearance of a low-intensity band-like structure: bag of worms appearance. She underwent a laparoscopic bilateral salpingo-oophorectomy and remains recurrence-free. With somewhat atypical preoperative MRI, it is essential to prevent the spillage of the tumor content as no definitive preoperative exclusion of unsuspected mesenchymal malignancies is feasible.

Keywords: Unsuspected uterine sarcoma, bag of worms, in-bag morcellation

INTRODUCTION

Uterine sarcomas are rare diseases and consist of only 4% of all cancers. There have been reports of patients with unsuspected uterine sarcoma (UUS) who underwent surgery with a diagnosis of uterine leiomyoma.^[1] With the recent rise in a laparoscopic hysterectomy and power morcellation of the uterus, the issue of malignant cell spillage and consequent dissemination had become the main concern.^[2]

Magnetic resonance imaging (MRI) is the preferred diagnostic modality to exclude UUS, but it would be unlikely to do so unless a clinician provides a cytology-/biopsy-based high suspicion of the malignancy, or unless the lesion contains invasive infiltration pattern. We recently experienced a patient with unexpected diagnosis with low-grade endometrial stromal

sarcoma (LG-ESS) who was treated effectively by minimally invasive surgeries.

CASE REPORT

A 51-year-old patient, gravida 0, had a history of rheumatoid arthritis. When she visited a clinic with lower abdominal pain, an enlarged uterus with tenderness at the same site was detected. Blood tests showed inflammation with an elevated white blood cell count of 14,600/ μ L and C-reactive protein levels to 2.5 mg/dl, intravenous antibiotic (ceftriaxone) was administered.

MRI reading suggested uterine leiomyoma with myxoid degeneration. The patient was, thereafter, referred to us. The MRI re-read by our radiologist affirmed a 65-mm

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well-demarcated mass compatible with leiomyoma of O-3 (Palm-COEIN subclassification system)^[3] with degenerative changes, which had compressed the endometrial cavity in the posterior wall [Figure 1a]. A tortuous band-like area of low signal intensity on T1-weighted images and high signal intensity on T2-weighted images was seen inside the mass with contrast enhancement [Figure 1b-d]. Based on these findings, uterine leiomyoma with myxoid degeneration was the primary diagnosis but with a comment on the potential risk of mesenchymal malignancies. Preoperative cervical cytology and endometrial cytology showed benign atrophic changes only. Cancer antigen CA125 levels were 10.6 U/mL (<35 U/ml), and the lactate dehydrogenase levels were 178 U/L (120–245 U/ml) and were both within the normal range. Chest, abdominal, and pelvic contrast-enhanced computed tomography (CT) detected no lesions in any organs other than the uterus.

The patient requested a minimally invasive surgical removal of the uterus with the preservation of the ovaries for concerns of menopausal symptoms. A single dose of gonadotropin-releasing hormone agonist (leuporelin acetate) was administered to reduce the size of the uterus *in toto*. Consequently, the mass volume was reduced by 67% in 1 month. At the laparoscopic surgery, an enlarged uterus and grossly normal but atrophic ovaries and fallopian tubes were observed [Figure 2a]. Neither adhesion nor peritoneal dissemination was seen. A total laparoscopic hysterectomy was carried in a usual manner. The isolated uterus was placed in a LiNA EasyBag (LiNA, EB125) [Figure 2b]. During the vaginal retrieval, the opening of the bag was

fixed extracorporeally through the vagina. A double ring self-retaining soft wound retractor of 2–4 cm (Applied Medical, C8312) was placed in the vagina to dilate it, as the vagina was atrophic and small [Figure 2c]. The uterus was power morcellated exclusively in the bag, and the tissue was thoroughly retrieved without any visible spillage of the contents. The morcellated tissue weighed 155 g. A nodular intramural lesion measuring approximately 45 mm was macroscopically observed and there was no infiltration to the endometrium. The postoperative clinical diagnosis of degenerated myoma was entertained.

Hematoxylin and eosin (H and E) staining, however, presented the proliferation of atypical cells with oval- to spindle-shaped nuclei and a high nuclear/cytoplasmic ratio that formed an irregular-shaped alveolar structure. Although it was partly necrotic, the cells were relatively small and homogeneous. Mitotic figures were not prominent. Immunostaining revealed that the specimen was positive for CD10 and negative for smooth muscle actin and desmin. Ki-67-positive cells accounted for 5% or less. The histological diagnosis was LG-ESS. Based on the histological results and the clinicopathological diagnosis of LG-ESS, the patient was counseled that preservation of the ovaries would carry a higher risk of recurrence of the disease. Six weeks after the initial surgery, the laparoscopic bilateral salpingo-oophorectomy was

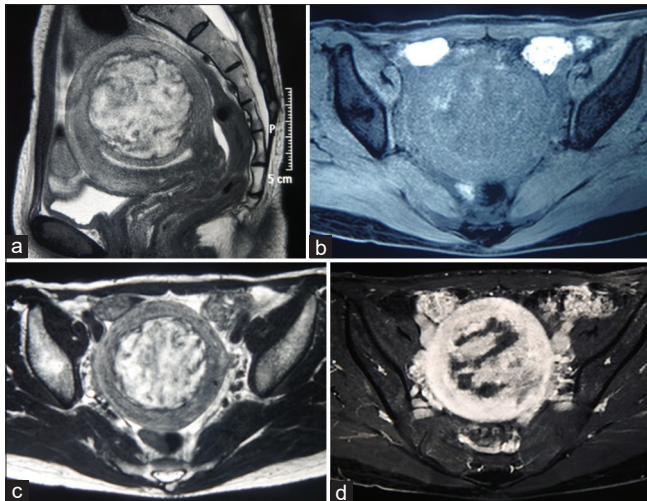


Figure 1: Magnetic resonance imaging. (a) T2-weighted magnetic resonance image shows a well-demarcated mass compressing the endometrial cavity. (b) T1-weighted magnetic resonance image shows low signal intensity. (c) T2-weighted magnetic resonance image shows high signal intensity with low signal bands. (d) T1 fat suppression contrast magnetic resonance imaging shows enhancement in the band area

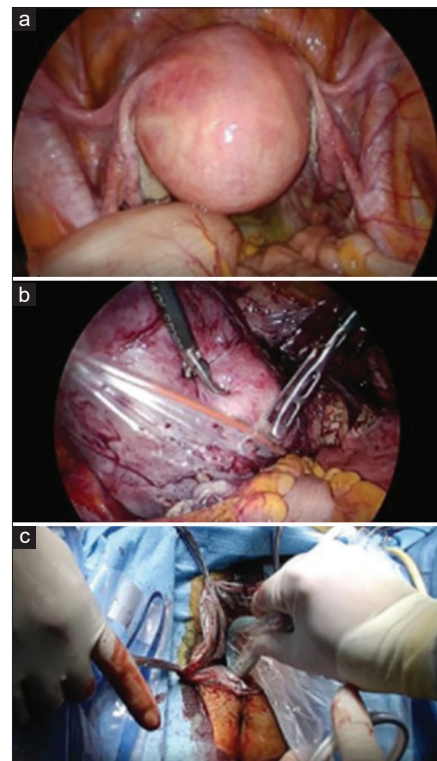


Figure 2: Transvaginal retrieval. (a) An enlarged uterus and grossly normal ovaries and fallopian tubes were observed. (b) The uterus was placed in a specimen bag. (c) A wound retractor was placed in the specimen bag, and the vagina was dilated

performed. There was no enlargement in any of the ovaries and was no intraperitoneal dissemination (FIGO Stage IB). No additional treatment was given to the patient. Postoperative examinations by cytology, ultrasonography, and CT images have been performed every 3 months. To date, ≥ 2 years after the initial surgery, the patient remains recurrence free.

DISCUSSION

UUS occurs around the frequency of 0.28% in patients undergoing hysterectomy and 0.20% in those undergoing myomectomy.^[1] The Food and Drug Administration of the United States issued an alarm in April 2014 that the use of power morcellator in laparoscopic hysterectomy was not recommended because of the potential risk of unrecognized uterine malignancies and the consequential intraperitoneal dissemination of malignant cells.^[1] The Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy consequently conducted a national questionnaire-based survey and reported that UUS was detected in 12 in 10,679 patients (0.11%) undergoing laparoscopic hysterectomy and four in 13,545 patients (0.03%) undergoing laparoscopic myomectomy.^[4] It is clear that preoperative MRI failed to detect UUS at the estimated rate of 16/24,224 (0.07%), and UUS is an unavoidable *de facto* event presently.

Although LG-ESS, as presented in the current patient, accounts for <1% of uterine malignancies, it is considered the second-most common malignant mesenchymal tumors of the uterus after leiomyosarcoma.^[5] LG-ESS occurs in a wide range of ages but is more likely to occur in women in their 40s and 50s.^[5] It tends to occur in younger women than other types of uterine sarcomas.^[5] The common symptoms are genital bleeding and abdominal pain.^[5] Our patient also presented with abdominal pain but no genital bleeding. Tumor cells in LG-ESS resemble endometrial stromal cells of the proliferative phase, forming irregular-shaped alveolar structures. They may infiltrate myometrium in tongue-like or worm-like patterns.^[5] Based on the results of immuno-histochemical examinations, the positive rates for CD10, smooth muscle actin, estrogen receptor, and progesterone receptor are 88.2%, 66.7%, 75.0%, and 88.9%, respectively. Those for desmin and S-100 are 16.7% and 0%, respectively.^[6] A combination of these markers has contributed to improve diagnostic accuracy.^[6] In the present case, LG-ESS was also diagnosed based on the combination of H and E and immunohistochemical staining.

Typical MRIs of leiomyoma is hypointense mass in myometrium on T1-weighted and more hypointense than the myometrium on T2-weighted images. Once the myxoid degeneration develops in leiomyomas, the differential

diagnosis from uterine sarcoma became challenging because the degeneration exhibits atypical appearance. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient may be useful for the differentiation although they have low specificity with high sensitivity.^[7] Uterine sarcoma is difficult to diagnose with positron emission tomography (PET)/CT alone.^[7] A combination of PET/CT and MRI/DWI is considered to be preferable.^[7] Chino *et al.* reported that the extent of the lesion of intravenous leiomyomatosis was accurately determined by PET/MRI.^[8] The clinical application of the combination may become applicable in future. In our case, when MRI/DWI was performed at a high b value, the DWI signals decreased. Therefore, uterine leiomyoma with myxoid degeneration was diagnosed, instead of typical uterine sarcoma. Meanwhile, the mass of high signal intensity contained a bundle of muscle fibers appearing as a band-like structure of low signal intensity on T2-weighted images and was contrast enhanced. This suggests that the mass exhibited the typical bag of worms appearance. This MRI finding is characteristic to LG-ESS because it grows, as the preexisting myometrium is engulfed and kept intact.^[9,10]

Unlike laparotomy, laparoscopic surgery requires morcellation of the uterus before the retrieval, and the spillage of the tissues is unavoidable. Park compared patients with early LG-ESS undergoing hysterectomy with and without morcellation and reported that the 5-year disease-free survival was significantly lower with morcellation than without (55% vs. 84%).^[11] We performed the total laparoscopic hysterectomy with power morcellation using an endo bag because of the atypical findings on the preoperative MRI. The patient was postmenopausal nulliparous, and her vagina was small. A good visual field was secured by dilating the vagina with a double ring self-retaining soft wound retractor. The wound retractor was useful because it did not damage a specimen bag-like metallic hooks.

Early-stage LG-ESS has a low recurrence rate. The 10-year recurrence rate is 10% or less, and hysterectomy and bilateral oophorectomy are the treatment of choice in stage I and II diseases.^[12] For LG-ESS of stage I, hysterectomy plus oophorectomy is considered adequate, and postoperative endocrine (progestin) adjuvant therapy may be applied if necessary.^[13] We used preoperative gonadotropin-releasing hormone agonists, and consequently, the mass volume was markedly reduced from 65 to 45 mm in a period of 1 month. Since the present LG-ESS tissue had 77.0% estrogen receptor-positive cell population, the use of the agonist may have possibly reduced the size of the LG-ESS through the hypoestrogenic mechanism. It is, therefore, conceivable that the secondary oophorectomy should have reduced the risk of recurrence in future.

LG-ESS with the bag of worms appearance, such as in this case, could be diagnosed preoperatively, but no definitive preoperative exclusion of unsuspected malignancies is feasible. With somewhat atypical preoperative MRI, it is essential to prevent the spillage of the tumor content during minimally invasive surgery.

Ethical approval

This study was approved by the Tokyo Women's Medical University. Institutional Review Board approval for Project#5540 was obtained on March 24, 2020.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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