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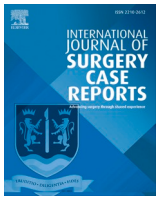

Case report

A case of a recurrent low-grade endometrial stromal sarcoma extending to the inferior vena cava (IVC) after the primary fertility-sparing surgery

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ABSTRACT

Introduction and importance: A case of Low-grade endometrial stromal sarcoma (LG-ESS) invading the great vessels is rare.

Case presentation: A 34-year-old female who had no past history presented to a previous hospital with abdominal distension. Magnetic resonance imaging revealed a 15 cm pelvic mass beside the uterus, and only the pelvic mass was removed at the surgery. The tumor was judged to be a LG-ESS. The patient chose to be observed to preserve her fertility, and no adjuvant treatment was undertaken. Two years later, she was referred to our hospital due to recurrence of the pelvic mass. Enhanced computed tomography revealed a large tumor in the vena cava which extended from the left internal iliac vein and which originated from the pelvic tumor. An operation was performed by a multidisciplinary team. Complete resection of the tumor was achieved with a radical hysterectomy, bilateral salpingo-oophorectomy, removal of recurrent pelvic masses and the intravascular tumor. We diagnosed a recurrence of LG-ESS. She received a postoperative adjuvant therapy of LG-ESS.

Clinical discussion: Patients with fertility-sparing treatment had higher recurrence rates. In cases of tumor intravenous extension, we should make every effort to extract the tumor to avoid sudden death.

Conclusion: This case highlights the importance of a multidisciplinary approach in treating this rare tumor with intravascular extension. In particular, patients with LG-ESS who receive fertility-sparing surgery should undertake postoperative chemotherapy or radiotherapy in order to reduce the risk of recurrence, as was in this case.

1. Introduction

Endometrial stromal sarcoma (ESS) is one of the rare malignant tumors that makes up approximately 0.2 % of all uterine malignancies and approximately 10 % of all uterine mesenchymal neoplasms [1].

Gynecological mesenchymal tumors, such as uterine leiomyomas and low-grade endometrial stromal sarcomas (LG-ESS), on rare occasion may extend and invade the venous system. The incidence of this disease is very uncommon, whether benign or malignant. According to a previous report, there were only 22 cases of advanced LG-ESS that invaded the great vessels with an IVC tumor, compared to the nearly 300 reported cases of intravenous leiomyomatosis (IVL) [2,3]. Moreover, there has been only one reported case where the recurrence of LG-ESS extended into vessels after fertility-sparing treatment [4]. If the tumor extends into large vessels, more than 50 % of LG-ESS cases often show intracardiac extension [5]. Although a potentially life-threatening disease, treatments are not yet clearly defined due to its infrequency. In this manuscript, we present a case of recurrent LG-ESS with intravenous extension two years after the primary surgery for fertility-sparing treatment.

2. Case presentation

A 34-year-old female who had no past or family history presented to a previous hospital with abdominal distension. Magnetic resonance imaging (MRI) revealed a 15 cm pelvic mass beside the uterus, which was considered to be a uterine fibroma, and an operation was performed at the hospital. Since there was no connection between the pelvic mass and the uterus and adnexa at the primary surgery, only the pelvic mass was completely removed. The tumor had little cellular atypia, and the cells were positive for ER, α-SMA and CD 10, but negative for desmine, was judged to be a low-grade endometrial stromal sarcoma after the

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surgery [Fig. 1]. The patient chose to be observed in order to preserve her fertility, and no adjuvant treatment was undertaken.

Two years later, she was referred to our hospital due to recurrence of the pelvic mass which was revealed by pelvic examination. On MRI, the tumor was identified on the left side of the pelvic space with a diameter of 10 cm and without any connection with the endometrium. The tumor was just adjacent to the left ureter. Enhanced computed tomography (CT) revealed a large tumor in the vena cava (IVC) which extended from the left internal iliac vein and which originated from the pelvic tumor [Fig. 2]. The upper margin of the intravenous tumor reached to the third lumber vertebra. Positron emission tomography (PET) showed that part of the pelvic mass was slightly positive. A blood test showed no elevation of LDH, CA 19-9 or CEA. CA-125, however, was slightly elevated at 36 U/ml. There was no malignancy in the endometrial tissue specimen. We carried out a CT-guided biopsy which revealed that the tumor had a similar histology to the specimen of the initial surgery. Therefore, we suspected that the present tumor was a recurrence of the previous LG-ESS.

As the tumor invasion of the ureter and the intestinal loop were suggested in the preoperative evaluation, an operation was performed by a multidisciplinary team including cardiologists, urologists and gastroenterologists. During the operation, an ultrasonography was used to confirm the upper tip of the tumor located in the IVC [Fig. 3]. To remove the intravascular tumor, at first, the left internal iliac vein containing the tumor was isolated, ligated and cut along with the tumor. Thereafter, we clamped the IVC, external iliac vein, and the common iliac vein, each with a margin from the tumor. The wall of left internal iliac vein was then cut, and the intra-internal iliac vein mass was smoothly removed because there was no adhesion to the vessel walls [Fig. 4]. Complete resection of the tumor was achieved with a radical hysterectomy, bilateral salpingo-oophorectomy, removal of recurrent pelvic masses, and the removal of the intravascular tumor with an estimated blood loss of 3769 ml. The patient needed additional treatments for urination disorders after the operation since the hypogastric nerve could not be preserved during removal of the tumor. She was discharged on post-operative day 26 with no other complications.

Pathological findings showed that the tumor invaded the myometrial layer, yet the endometrium was normal. There was no grossly apparent deep endometriosis. The tumor cells showed small, spindle shapes without atypical, but vascular invasions were frequently confirmed [Fig. 5]. The cells were positive for estrogen receptor (ER) and CD10 but negative for STAT6 and h-caldesmon. As for molecular exams, no mutation was detected in JAZF1(Suz12) and PHF1, which mutates relatively frequently in LG-ESS. We therefore diagnosed a recurrence of LG-ESS according to the pathological evaluation and the patient's clinical course.

She received 2.5 mg/day of aromatase inhibitor for 18 months as a postoperative adjuvant therapy of LG-ESS. There were no signs of recurrence at the time of surveillance performed 16 months after surgery.

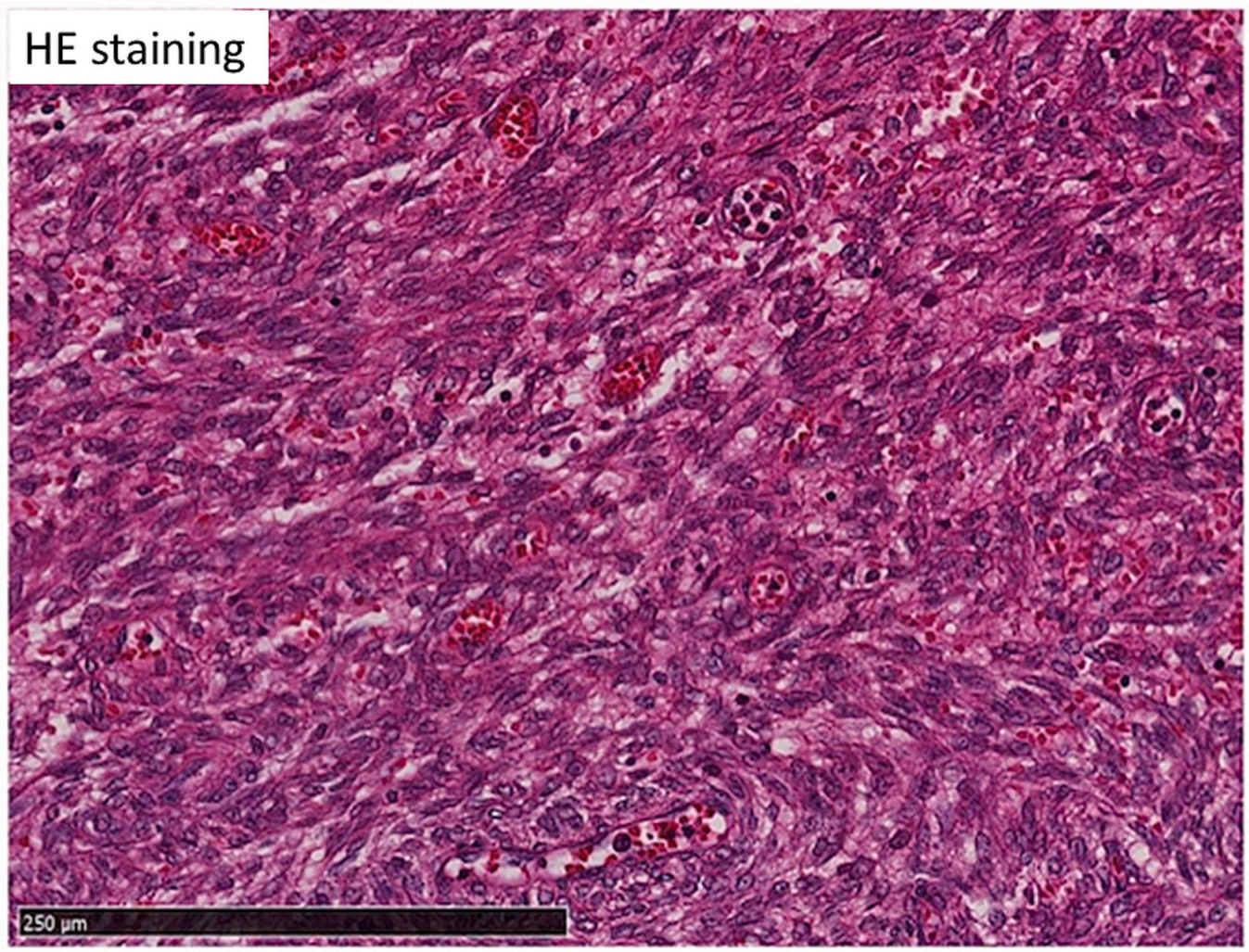

Fig. 1. The tumor had little cellular atypia and was judged to be a low-grade endometrial stromal sarcoma after primary surgery.

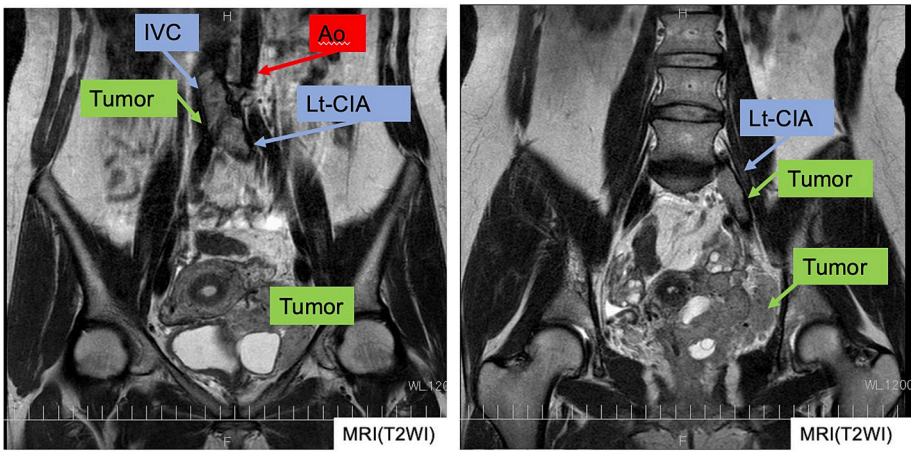

Fig. 2. Contrast-enhanced MRI showed a large tumor in IVC and the left internal iliac vein, which was derived from the tumor in pelvis.

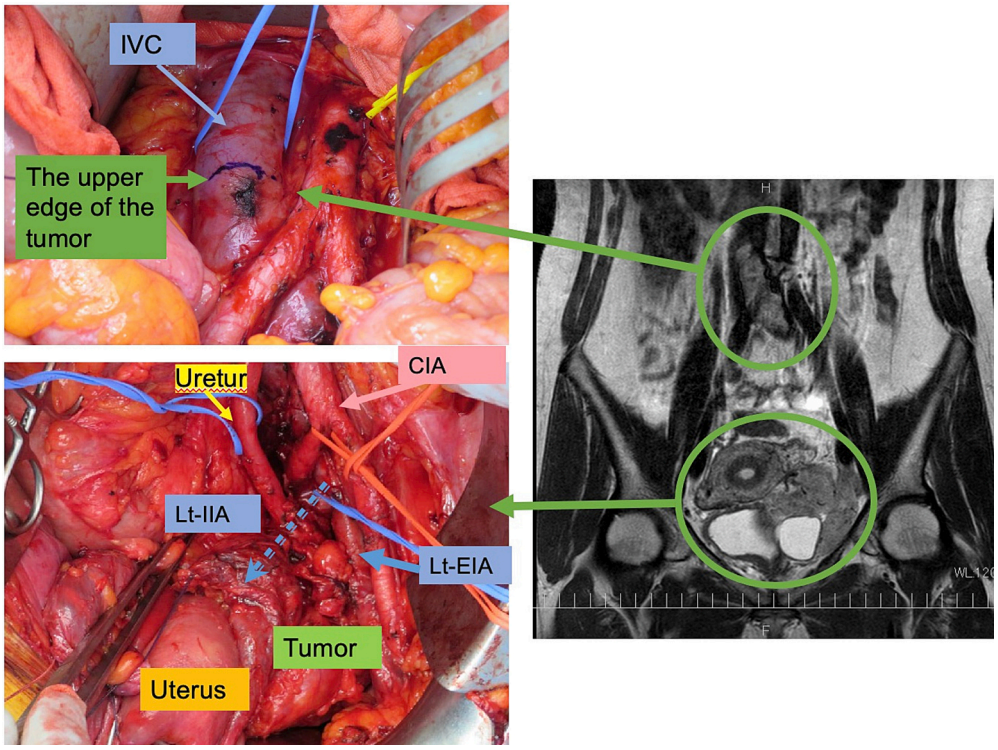

Fig. 3. We checked the upper tip of the tumor located in the IVC during the surgery.

3. Discussion

LG-ESS tends to occur in premenopausal and perimenopausal women with a median age between 45 and 57 years, which is younger than those with other uterine sarcomas. Beck T et al. (2012) reported that patients with fertility-sparing treatment, ovarian preservation, or a treatment modality other than repeated surgeries had significantly higher recurrence rates [6]. The intravenous extension of LG-ESS is very rare, as previously mentioned. More than 50 % of cases are related to endometriosis [7,8]. Our case is the second case report of LG-ESS extending to the greater vessels after fertility-sparing treatment. In the present case, the tumor did not connect to the uterus at the time of the initial surgery, and it was considered that the tumor developed outside of the uterus. According to the pathology of the recurrent tumor, there were some components of LG-ESS in the myometrial layer, which was also found in the pelvic tumor. Moreover, there was no grossly apparent deep endometriosis in the pelvic tumor. Therefore, the recurrent tumor may have developed in the uterus first and then invaded into the pelvis.

Previous report has shown that more than 40 % of LG-ESS extend into the IVC and that more than 50 % extend to the cardiac system in cases of a tumor invading the venous system [5]. In particular, in cases of tumor intravenous extension, like in our case, we should make every effort to extract the tumor in order to completely avoid congestive heart failure or sudden death by, in the worst case, pulmonary embolization [2,8]. Therefore, preoperative evaluation is extremely important in cases of intravascular tumor extension. Imaging examination, like enhanced CT and MRI, are often used for the preoperative assessment to evaluate the size, location, origin and the extent of tumors [2]. However, Nogami et al. (2016) reported that the sensitivity of CT was limited for the detection of free-floating lesions in the bloodstream [9]. In most cases, intracardiac or intravascular tumors grow freely within the endovascular system without invading tissues [9,10]. In our case, we

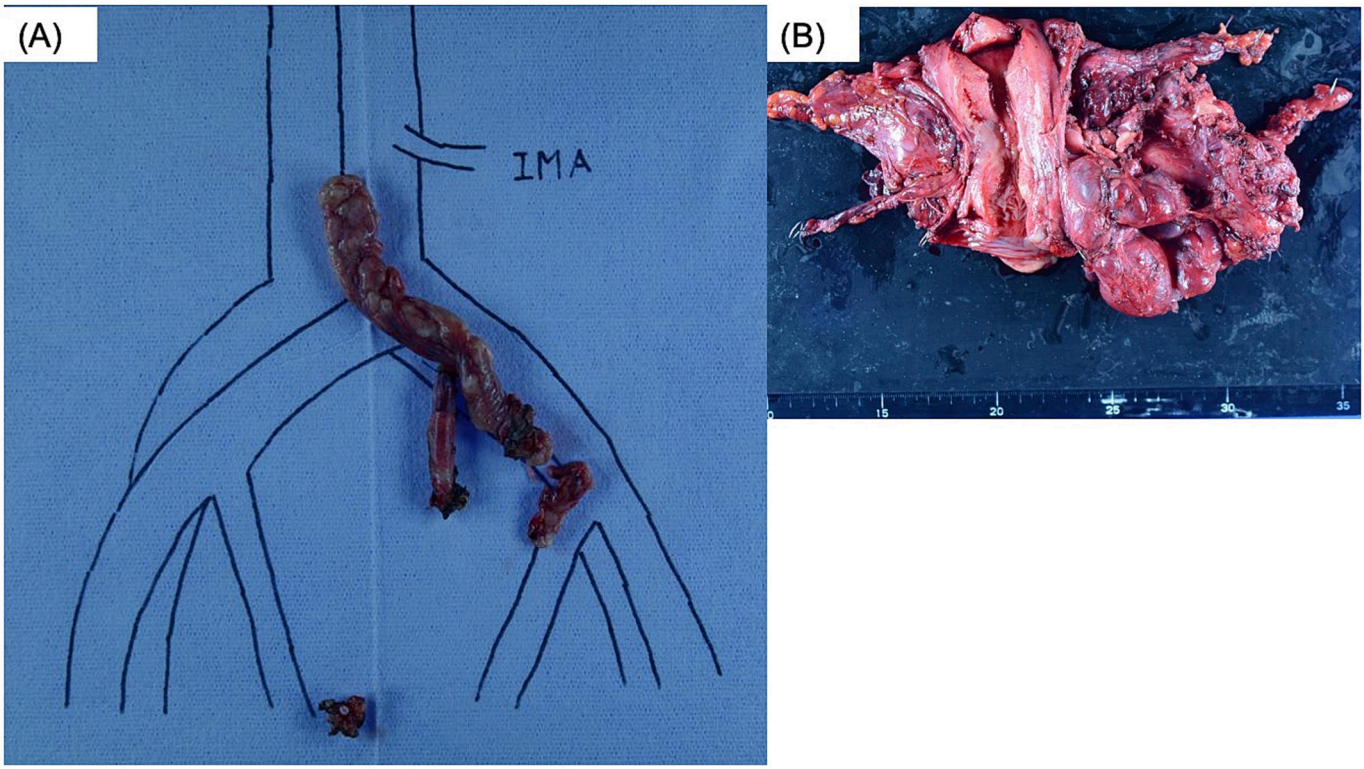

Fig. 4. (A) The intra-internal iliac vein mass was removed smoothly because there was no adhesion to the vessel walls. (B) Weight of tumor: 403 g.

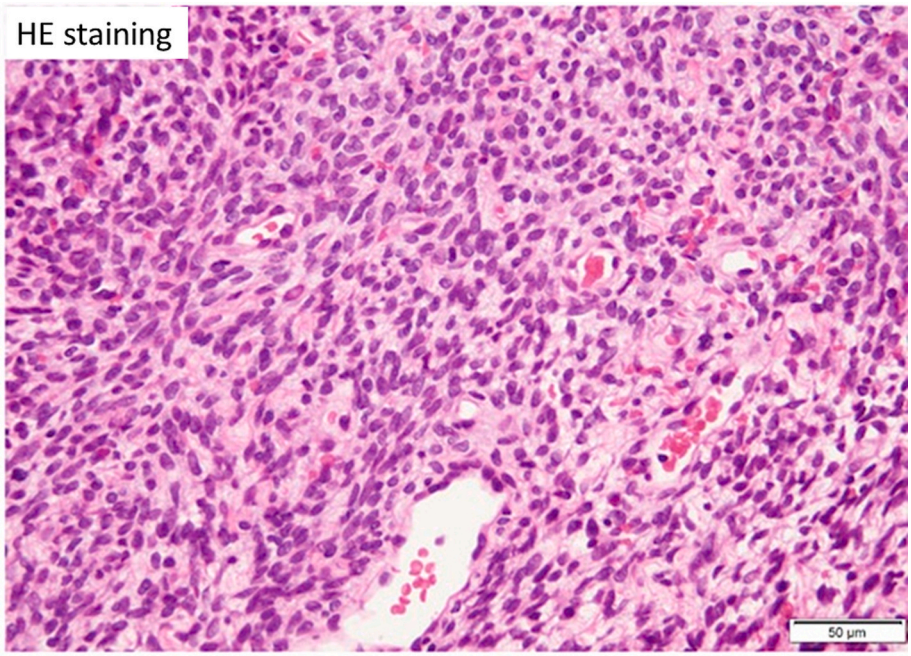

Fig. 5. The tumor cells showed small, spindle shapes without atypia; however, numerous vascular invasions were confirmed.

planned strategies preoperatively and involving a multidisciplinary team, including cardiovascular surgeons. Because of their mobility inside vessels or the heart ultrasonography, including transthoracic or transesophageal echocardiography and transabdominal sonography, during surgery play an important role in predicting and guiding the surgical approach to extract intravascular tumors completely [9].

In general, NCCN guidelines do not recommended adjuvant treatment for patients with stage I LG-ESS [11]. According to Zang Y et al. (2019), hormonal therapy, for example progestin, aromatase inhibitors and gonadotropin-releasing hormone analogue (GnRH-a), showed a high therapeutic effect in recurrent, metastatic or unresectable LG-ESS [12]. Leath C et al. (2007) also reported no difference in the outcomes in patients treated with either observation or with hormonal therapy, but hormonal therapy was associated with improved survival, as the risk of death was higher in the observation group [13]. Some reports show that adjuvant treatment for LG-ESS may be effective for patients who

want to preserve their fertility [14,15]. Therefore, there is some possibility that the patient in this case wouldn't have recurred if she had received adjuvant therapy.

In conclusion, patients with LG-ESS who receive fertility-sparing surgery should undertake postoperative chemotherapy or radiotherapy in order to reduce the risk of recurrence, as was in this case. Intravascular extension of LG-ESS, although rare, should be further investigated in future studies.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Methods

The work has been reported in line with the SCARE criteria.

Agha RA, Franchi T, Sohrab C, Mathew G, Kirwan A, Thomas A, et al. The SCARE 2020 guideline: updating consensus Surgical Case Report (SCARE) guidelines. International Journal of Surgery. 2020; 84 (1):226–30.

Ethical approval

The Ethics Committee of our institution confirms that ethics approval for case report or case series are waived.

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Guarantor

Prof. Yoshito Terai.

CRediT authorship contribution statement

Yoko Yano: Writing – original draft, Investigation, Visualization. **Yui Yamasaki:** Resources, Writing – review & editing, Supervision. **Keitaro Yamanaka:** Resources. **Masashi Nishimoto:** Resources. **Satoshi Nagamata:** Resources. **Yoshito Terai:** Resources, Visualization, Supervision, Project administration.

Declaration of competing interest

The authors declare no conflicts of interest.

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