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Review

Successful pregnancy after laparoscopy-assisted excision of uterine smooth muscle tumor of uncertain malignant potential: A case report and a review of the literature

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Summary

Uterine smooth muscle tumors of uncertain malignant potential (STUMP) are neither benign nor malignant. Herein, we report the case of a successful pregnancy after laparoscopy-assisted excision of uterine cervical STUMP in a 37-year-old woman with secondary infertility. Magnetic resonance imaging showed a tumor, which was suspected to be a uterine cervical leiomyoma. She underwent a laparoscopy-assisted excision, and the final diagnosis was STUMP. The uncertain behavior of STUMP was explained to the couple; since STUMP is an exclusion diagnosis of leiomyoma or leiomyosarcoma, the prognosis was not clear, i.e., the tumor may behave in a benign or malignant fashion. The patient did not undergo further treatment. She conceived naturally 5 months after the operation and delivered a child by cesarean section. Although previous reports have described the recurrence rates of STUMP, they are inconsistent probably due to the challenges encountered to make this diagnosis. At present the diagnosis can only be made postoperatively when histologic features of the tumor, such as necrosis, atypia, or mitotic count, exclude the diagnosis of benign leiomyomas, but do not meet the criteria for leiomyosarcomas. This case highlights that if a patient with infertility is diagnosed with STUMP, she must be counseled about the possibility of recurrence and the need for long-term surveillance.

Key words: STUMP; Leiomyoma; Leiomyosarcoma; Laparoscopic excision; Pregnancy.

Introduction

Uterine leiomyoma is the most common benign gynecologic disorder, occurring in nearly 25% of the general female population [1]. Meanwhile, uterine leiomyosarcoma is a relatively rare malignant disease. However, differentiating between the two conditions is not easy. Furthermore, smooth muscle tumors of uncertain malignant potential (STUMP) can develop, which are neither leiomyomas nor smooth muscle sarcomas of the uterus.

STUMP are defined by the World Health Organization (WHO) as smooth muscle tumors that are neither benign nor malignant, and their clinical management is not well established [2]. STUMP are often benign, but cases of recurrence or metastasis have been reported [3-5].

Herein, we present a case suspected to be a uterine cervical leiomyoma preoperatively but was diagnosed as STUMP after laparoscopy-assisted excision. The patient conceived naturally and no metastasis was observed during the 3-year follow-up.

Presentation of the Case

A 37-year-old Japanese woman (G2P1) was referred to our hospital for surgery. Her chief complaints were secondary infertility and dysmenorrhea for 2 years. Her previous physician diagnosed her with a uterine leiomyoma, approximately 6 cm in size. As the leiomyoma enlarged over 3 months, she was referred to our hospital for surgery and infertility treatment. At the initial visit, a full hemogram revealed a hemoglobin level of 10.7 g/dL, white blood cell count of 3.4 $\times$ $10^3/\mu$L, platelet count of 23.1 $\times$ $10^4/\mu$L, and serum lactate dehydrogenase (LDH) level of 117 IU/L (reference range, 115-245 IU/L at 37 °C).

This tumor demonstrated a high signal intensity on diffusion-weighted magnetic resonance imaging (MRI) and low signal intensity on the apparent diffusion coefficient (ADC) map without contrast enhancement (Figure 1A-D, white arrows), and was diagnosed as a degenerating uterine leiomyoma with high cellularity. This large tumor, measuring 16 $\times$ 13 $\times$ 13 cm, expanded the cervical canal, and the uterine body was pushed from the pelvic cavity to the

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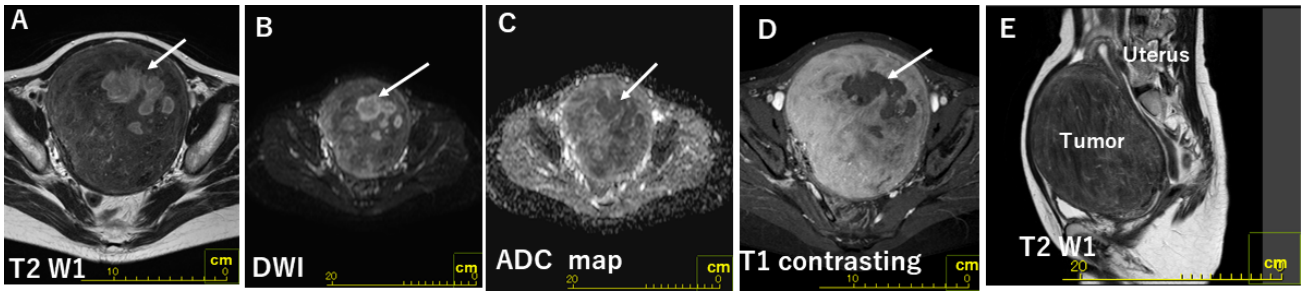

Figure 1. — Preoperative magnetic resonance imaging showing a large tumor on the cervical anterior wall of the uterus. (A) Transaxial T2-weighted image. (B) Transaxial diffusion-weighted image. (C) Transaxial apparent diffusion coefficient (ADC) image. (D) Transaxial T1-weighted contrast-enhanced image. (E) Sagittal T2-weighted image. The tumor volume is 16 × 13 × 13 cm. The inside of the tumor shows a decreased intensity area of the T2 signal, which is a high intensity on diffusion-weighted imaging and low intensity on ADC and contrast-enhanced images (arrow).

abdominal region (Figure 1E); thus, natural pregnancy was deemed difficult.

Consequently, laparoscopic surgery was chosen. A 5-mm trocar was inserted at the umbilicus via direct entry, followed by a 5-mm suprapubic port, and then two 5-mm trocars were positioned in the left and right lateral quadrants. Intra-abdominal visualization revealed an enlarged uterus containing an intramural tumor (Figure 2A). A vertical incision was made on the prominent part of the principal leiomyoma using a monopolar hook (Figure 2B). The cleavage plane between the leiomyoma and its surrounding connective tissues was then dissected (Figure 2C). Thereafter, enucleation was accomplished by traction on the leiomyoma using a tenaculum. The tumor was enucleated. This tumor was too large to attempt in-bag morcellation. After enucleation, the suprapubic incision was extended in a transverse direction to 3 cm, followed by placement of an Alexis wound retractor (small size, Applied Medical, Rancho Santa Margarita, CA) for morcellation and suturing. Extraction of the tumor was performed under direct and careful visualization to prevent any leakage into the abdominal cavity. Then, the myometrial defect and edges were closed with a single suture using a 2-0 PDS in one layer, while a Hegar dilator was inserted to avoid cervical canal closure (Figure 2D). Before abdominal closure, the abdominal cavity was lavaged with 3,000 ml of saline and explored. The uterus was almost normal, the adnexa found on both sides and on other pelvic and abdominal organs were normal, and remnant leiomyoma tissue was not observed (Figure 2E). The total weight of the excised tumor was 954 g (Figure 2F). The total operation time was 176 min, and the total intraoperative blood loss was 1470 mL. Autologous blood transfusion of approximately 400 mL was provided.

She was discharged uneventfully on postoperative day four. She presented at her 4-week postoperative visit without any complaint and no vaginal bleeding. Pathology results showed STUMP of the uterus (Figure 3A, B). The enucleated tumor had the appearance of a leiomyoma, but with high cell density, no atypia, and a low mitotic index. Coagulative necrotic tissues were widely detected. Postoperative positron emission tomography/computed tomography did not detect metastasis.

Management options, diagnostic criteria, and characteristics of the STUMP were explained to the patient. The patient did not proceed with additional treatment.

At 5 months postoperatively, the patient conceived naturally. At 37 weeks' gestation, she delivered a male neonate, weighing 2860 g (Apgar score, 9-10), via a scheduled cesarean section. Intraoperatively, no tumor was found in the abdominal cavity, and the uterus was preserved. No recurrence was reported at 3 years after the first operation.

Discussion

Herein, we presented a case of laparoscopy-assisted excision of STUMP in a woman who conceived postoperatively.

Smooth muscle tumors of the uterus are categorized usually as leiomyomas and leiomyosarcomas, with the latter having metastatic potential. However, according to the WHO classification, a smooth muscle tumor with features that preclude an unequivocal diagnosis of a leiomyosarcoma, but do not fulfill the criteria for a leiomyoma or its variants, and which raise concerns of malignant behavior, should be called STUMP [6].

Bell *et al.*'s Stanford Criteria (1994) [7] are used for the histopathological differentiation of uterine leiomyomas from smooth muscle sarcomas, which include the mitotic index (MI = number of mitotic figures [mf]/10 high-power fields [hpf]) of $<$ 5 mf/10 hpf (usual leiomyomas), degree of cytologic atypia, and presence or absence of coagulative tumor cell necrosis. Currently, the classification of uterine smooth muscle neoplasms into clinically benign or clinically malignant has shifted to the exclusive reliance on these criteria and not just the MI. Even though all these features are detected in approximately 80% of typical leiomyosarcomas, the presence of two of the three features is sufficient to make the diagnosis of leiomyosarcoma. Moreover, a tumor with coagulative necrosis and significant nuclear atypia, regardless of the mitotic count, should be diagnosed as a leiomyosarcoma [8]. If the histological criteria for ma-

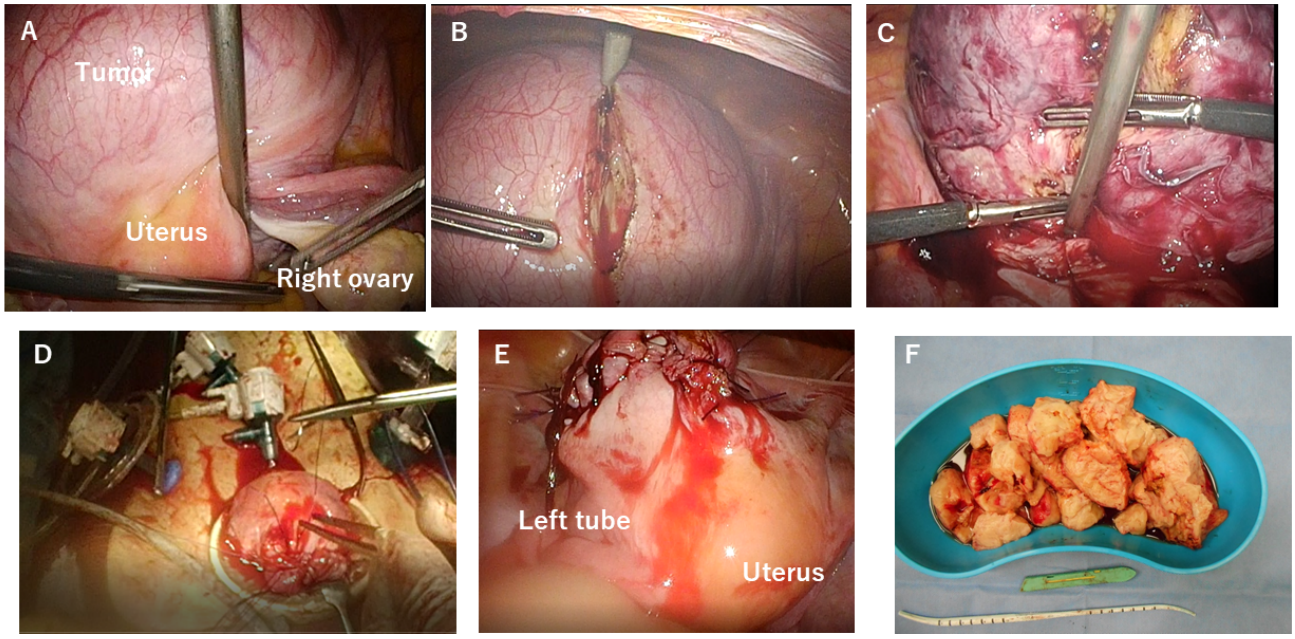

Figure 2. — Laparoscopic surgery. (A) Intra-abdominal visualization of an enlarged uterus containing an intramural tumor. (B) A vertical incision is made on the prominent part of the principal leiomyoma using a monopolar hook. (C) The cleavage plane between the leiomyoma and its surrounding connective tissues is then dissected. (D) The myometrial defect and edges are closed with a single suture using a 2-0 PDS in one layer, while a Hegar dilator is inserted to avoid closure of the cervical canal. (E) Before abdominal closure, the abdominal cavity is explored: the uterus is almost normal, and abdominal organs are normal. (F) The total weight of the excised tumor is 954 g.

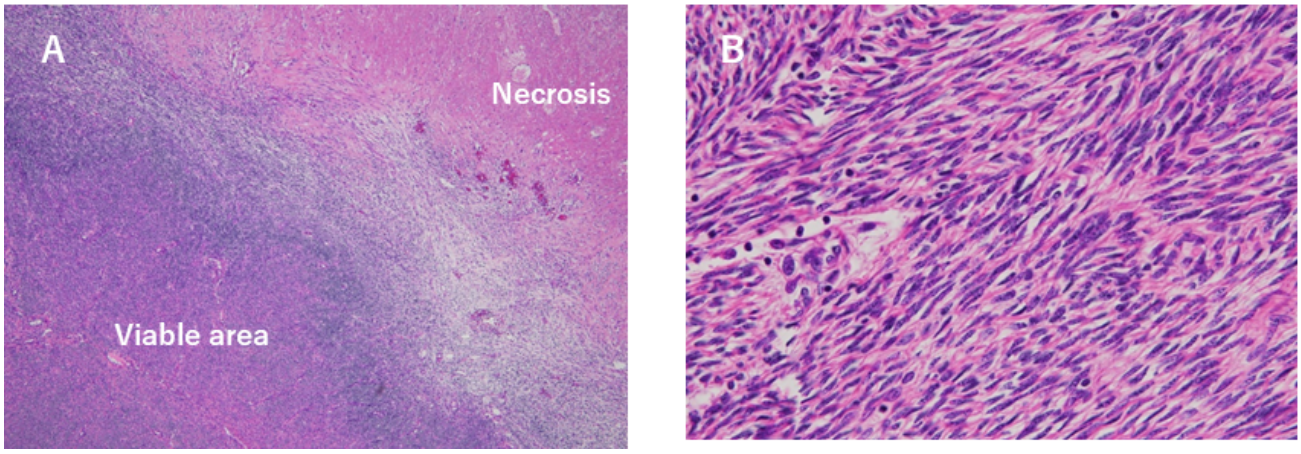

Figure 3. — Histopathological image of the tumor. Hematoxylin and eosin staining of the tumor. (A) Coagulative necrosis next to an area of viable smoot muscal tumor (×4 magnification). (B) Magnified view of (A) (×40). These areas have high cellularity, but not atypia, and a very low mitotic index.

lignancy are not fulfilled, e.g., the type of necrosis is unclear, the interpretation of mitotic activity is ambiguous, and the tumor cannot reliably be classified as a leiomyoma, the tumor is classified as STUMP; however, there was no consensus on the diagnostic criteria for STUMP in Bell *et al.*'s study (1994) [7]. Our patient was diagnosed with STUMP because of the presence of many areas of coagulative necrosis; however, the degree of cytologic atypia was not severe.

Preoperatively, MRI can provide details about the fibroid size, location, signal intensity, and enhancement characteristics. However, it is difficult to diagnose STUMP, because this requires exclusion of leiomyoma and leiomyosarcoma of the uterus by pathological examination. Moreover, there are no diagnostic criteria for leiomyosarcomas based on MRI. An intratumoral hyperintense signal on T2-weighted magnetic resonance image suggests high cellularity or high vascularity, and a hyperintense signal on T1-weighted im-

ages is thought to indicate intratumoral hemorrhage and coagulative necrosis [9]. In contrast, a typical leiomyoma of the uterine body has a signal lower than the muscular layer on T2-weighted MRI and the same signal level as the muscular layer on T1-weighted MRI; moreover, the border between a leiomyoma and the normal uterine muscular layer is clear. Bonneau *et al.* (2014) [10] compared sonography and MRI findings of leiomyomas, malignant mesenchymal tumors (MMTs), and STUMP, and found that the presence of a single tumor, absence of acoustic shadowing, and presence of free fluid are associated with MMTs and STUMP. Tanos and Berry (2018) [11] reported that leiomyosarcoma risk is higher in older women with fibroids larger than 8 cm. However, these findings can also be seen with uterine leiomyomas, which have varying features.

With regard to blood markers, Seki *et al.* (1992) [12] reported that a degenerative change within the uterine mass and the presence of an elevated LDH level should suggest leiomyosarcoma. In addition, Nishigaya *et al.* (2019) [13] reported that a combination of LDH, D-dimer, and C-reactive protein could be useful for distinguishing leiomyosarcoma from degenerated or atypical leiomyoma. However, they did not mention STUMP.

In the present case, the tumor was approximately 16 cm in size and had high intensity on diffusion-weighted MRI and low intensity on the ADC map, which may have had high cellularity and malignant potential, but the LDH level was normal. Clinical preoperative differentiation between leiomyomas, leiomyosarcomas, and STUMP is difficult.

Regarding fertility in women with STUMP, Şahin *et al.* (2019) [13] reported that 10 of 27 patients who underwent abdominal excision of STUMP desired fertility. Seven pregnancies were recorded. Thus, even if women are diagnosed with STUMP, it may not be necessary for them to give up the possibility of future pregnancy. However, Şahin *et al.* (2019) [13] reported that for 57 patients with STUMP, eight patients (14%) had recurrence during the follow-up. Recurrent STUMPs were seen in seven patients and leiomyosarcoma after 14 months in one patient. Seven patients with recurrent STUMP survived, while the remaining patient died.

Moreover, regarding the prognosis of STUMP, Ng *et al.* (2010) [14] reported no recurrences in 18 cases of STUMP, with all cases being registered as disease-free after 5 years. However, Guntupalli *et al.* (2009) [3] reported that uterine STUMP have a recurrence rate of 7%. Ip *et al.* (2009) [4] reported that two of 16 STUMP cases recurred, but these two cases had areas that were indistinguishable from benign leiomyomas. Although several studies have revealed various recurrence rates, it may be difficult to interpret the recurrence rate from a large group of patients in a single study, as the definition of STUMP varies. Certainly, many STUMP cases may follow a benign process. On the contrary, Oda *et al.* (2018) [5] reported a case that became malignant. In their report, a patient was diagnosed with STUMP after an abdominal total hysterectomy and bilateral salpingo-oophorectomy. The patient had recurrence 8 months following surgery and died 3 years later. This diagnosis was revised to a leiomyosarcoma from STUMP. A pathologist's interpretation can also be particularly difficult and subjective, especially for patients who have ischemic or epithelioid features in leiomyomas. Therefore, true STUMP are rare; in fact, leiomyomas and leiomyosarcomas can be misdiagnosed as STUMP when considering varying factors such as sampling, experience, and diagnosis skillset of the pathologist, even if it is thought that STUMP may present as "transition" tumors between leiomyomas and leiomyosarcomas, or possibly undiagnosed low-grade leiomyosarcomas [2].

Conclusions

When a woman who desires to bear children is diagnosed with STUMP after (laparoscopic) myomectomy, she must be aware of the uncertainties associated with the biologic behavior of STUMP and the possibility of recurrence inside or outside of the abdominal cavity. The current case highlights that, although previous reports have described the recurrence rate of STUMP, these are inconsistent. This is because the diagnosis of a tumor as STUMP should be reserved for lesions with postoperative histologic features, such as necrosis, atypia, or borderline mitotic count, that exclude the diagnosis of benign leiomyoma, but do not meet the criteria for leiomyosarcoma (Bell *et al.*, 1994) [7]. Even when strict criteria are used to diagnose STUMP there is interobserver variability. Since the clinical behavior of these tumors is unpredicfi, these patients require long-term monitoring for possible recurrences.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. Ethics approval was acquired from Fukuchiyama City Hospital (approval number: 2-23).

Authors' contributions

Tomohiro Okuda, Masahiro Otani and, Yoshio Ogino participated in the treatment of the patient, Yuki Imura, Suguru Yamashita, and Tomoharu Okubo helped write the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare no competing interests.

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