

Case series of uterine smooth muscle tumors of uncertain malignant potential (STUMP)

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Summary

Uterine smooth-muscle tumors of uncertain malignant potential (STUMP) cannot be categorized as benign or malignant. In this paper, the authors describe several cases presenting with STUMP. The authors reported five cases of STUMP treated in Soonchunhyang University Bucheon Hospital from 2013 to 2016. Four patients remain recurrence free (26–60 months) and one patient was lost to follow-up one month after STUMP diagnosis, revisited three years later, and was diagnosed with high-grade (Stage IIa) ovarian serous carcinoma after a staging operation. The authors suggested that regular follow-up after surgery was important in STUMP, and more aggressive surgical management, including salpingo-oophorectomy, should be considered.

Key words: Leiomyoma; Smooth muscle tumor; Uterine neoplasms.

Introduction

Smooth-muscle tumor of uncertain malignant potential (STUMP) is a subcategory of poorly defined uterine smooth-muscle tumors. Pathologists have difficulty definitively diagnosing STUMP, and its clinical behavior is not well known [1]. STUMP features are intermediate between benign and malignant, with a high level of mitotic activity, cellular atypia, and necrosis. No standardized protocol for the management of patients with suspected STUMP has been developed. The management of STUMP is the same as that of classical leiomyoma, but follow-up is recommended. When STUMP is diagnosed from myomectomy specimens, considering the proven possibility of recurrence, hysterectomy is the gold standard for women with these tumors who have completed childbearing. In the case of recurrence with low-grade features, surgery, estrogen-blocking therapy, and/or the use of gonadotropin-releasing hormone agonists and/or aromatase inhibitors can be considered. When recurrence occurs as leiomyosarcoma (LMS), surgery and/or chemotherapy is necessary [2, 3]. The paucity of STUMP cases makes the development of a standardized follow-up plan difficult. Here, the authors report five cases of STUMP with similar courses of diagnosis.

Case Report

Case 1

A 50-year-old Korean woman (gravida 4, para 2) visited the clinic due to vaginal bleeding which started seven days ago and aggravated two days later. She had been diagnosed with uterine

leiomyoma three years prior. The estimated weight of the uterus was more than 1,000 grams, based on bimanual pelvic examination. Blood transfusion was performed, as the patient's hemoglobin level was 4.6 mg/dL. Pelvic ultrasonography (USG) and abdominopelvic CT showed multiple uterine myomas and left ovarian cyst. Total abdominal hysterectomy (TAH) with left ovarian cystectomy was performed, and pathologic analysis revealed a smooth muscle tumor with increased cellularity and mitotic activity, suggestive of STUMP. Mitotic count was 7/10 high power fields (HPFs), whereas nuclear atypia was moderate and necrosis was present (Figure 1). Results of immunohistochemical (IHC) stain showed positive to desmin and increased proliferating activity to Ki-67. After pathologic diagnosis, bilateral salpingo-oophorectomy (BSO) was performed, and pathologic analysis revealed a non-specific finding. Transvaginal USG was performed every three months, abdominopelvic CT and positron emission tomography (PET)-CT every six months, and MRI every year. The patient remains disease and symptom free for 53 months.

Case 2

A 46-year-old premenopausal woman (gravida 2, para 2) visited the clinic due to the presence of a giant palpable pelvic mass. The mass was approximately 37 cm in diameter, and was palpated up to xiphoid process. The patient's cancer antigen 125 level (CA 125) was within the normal range (11.0 U/mL). CT scan showed a giant heterogeneous enhancing mass occupying the abdominal cavity and suggested the possibility of LMS. Mass removal and left salpingo-oophorectomy were performed, and pathological analysis revealed a smooth muscle neoplasm with moderate nuclear atypia, 3 mitotic figures /10 HPFs, and necrosis, consistent with STUMP (Figure 2). After the diagnosis of STUMP, PET-CT and MRI were performed, and revealed no evidence of tumor invasion or metastasis. After pathologic diagnosis, TAH and right salpingo-oophorectomy was performed because of remaining uterus contained leiomyoma. The patient was checked by pelvic USG every three months and CT, PET-CT every six months. The patient has remained disease-free for 26 months.

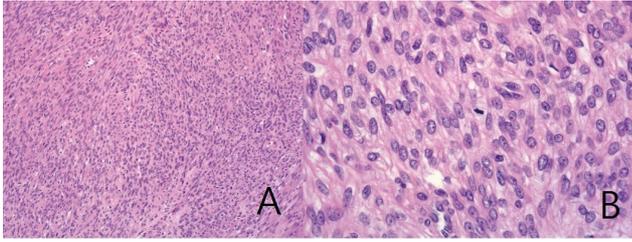


Figure 1. — (A) Section shows bundles of elongated smooth muscle cells exhibiting eosinophilic cytoplasm. The tumor has high cellularity and moderate nuclear atypia. (B) There are frequent 7 mitoses in 10 high power fields (HPFs) (7/10 HPFs).

Case 3

A 45-year-old premenopausal woman (gravidia 3, para 2) visited the clinic due to increased menstrual bleeding for three months and dysmenorrhea. A uterine mass measuring 8 cm was detected by ultrasonography. The patient was transferred to hospital based on the clinician's suspicion of a sarcomatous mass. Uterus was estimated to weigh 400 grams by bimanual pelvic exam. Abdominopelvic CT scan showed well-demarcated low density uterine mass and the impression by it was degenerated myoma, or possibly other uterine tumors including endometrial stromal sarcoma. TAH was performed, and pathological analysis revealed STUMP. Most of the tumor mass was necrotized, mild atypia, and the mitotic count was 9/10 HPFs. However, no atypia of the tumor cells was found, and IHC revealed positivity for progesterone receptor (PR), and for p53 in a few cells. The Ki-67 index was positive, indicating a high level of proliferative activity. PET-CT scan showed no abnormal fluorodeoxyglucose (FDG) uptakes, and disease-free follow-up period was one month. The patient did not follow up in the authors' hospital after surgery and visited the clinic three years later with the primary complaint of abdominal discomfort. Ultrasonography (USG) and abdominopelvic CT revealed a malignant cystic mass measuring 16×13 cm in the right ovary. A staging operation was performed, and the final diagnosis of high-grade (Stage IIa) ovarian serous carcinoma was made. Patients received paclitaxel-carboplatin chemotherapy for six times and have been living without recurrence until now.

Case 4

A 49-year-old postmenopausal woman (gravidia 3, para 2), who had a history of hyperthyroidism, visited the clinic due to sudden increase in the size of uterine leiomyoma after several years of regular follow-up visits since her initial diagnosis. Multiple uterine myoma was detected by ultrasonography with the largest measuring approximately 9 cm. TAH and BSO were performed, and pathological analysis revealed a smooth-muscle neoplasm with moderate nuclear atypia, necrosis and 5 mitotic figures/10 HPFs, consistent with STUMP. IHC staining was positive for estrogen receptor and PR, and the Ki-67 index was <3%. The patient was checked by pelvic USG every three months and CT and PET-CT every six months, and has remained disease free for 44 months.

Case 5

A 42-year-old (gravidia 1, para 0) premenopausal woman presented with the complaints of lower back pain, chronic pelvic pain, and menorrhagia. A myoma measuring approximately 7 cm was detected by USG. The estimated weight of the uterus was 300 grams, based on bimanual pelvic examination. After seven months of follow-up, laparoscopic total hysterectomy was performed, and pathological analysis indicated STUMP with moderate cellular atypia, necrosis, and a geographic hypercellular area with high

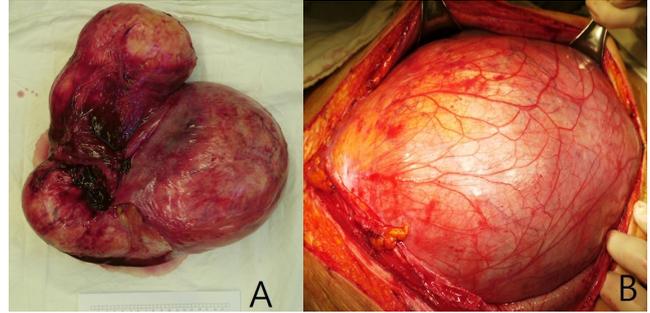


Figure 2. — (A) Photograph showing specimen of mass. (B) Photograph shows abdominal opening.

mitotic counts (average, 5–6/10 HPFs). IHC revealed positivity for desmin and smooth-muscle actin, and negativity for CD10. The Ki-67 index was approximately 10%–20%. After pathologic diagnosis, laparoscopic bilateral salpingo-oophorectomy was performed, and pathologic analysis revealed a non-specific finding. After the operation, PET-CT was performed and showed no uptake. The patient was checked by pelvic USG every three months and had CT and PET-CT every six months. The patient was followed for 60 months with no evidence of disease recurrence.

Discussion

Smooth-muscle tumors range from benign leiomyoma to low- and high-grade LMS. Uterine LMS is a rare malignancy that can be divided into three histological subtypes based on cellular characteristics and constituents of the intercellular stroma [4]. The most common type is spindle cell (usual differentiation), whereas LMS with epithelioid or myxoid differentiation is relatively rare and the diagnostic criteria differ. The diagnosis of spindle cell-type LMS can be made when any two of the following features are present: diffuse, moderate to severe atypia, ≥ 10 mitotic figures/10 HPFs, and tumor cell necrosis [4]. Kempson [5] first used the term “STUMP” in 1973 to refer to tumors that acted malignant clinically, but could not be diagnosed as sarcoma based on the diagnostic criteria available at the time [6]. Bell *et al.* [7] suggested that few uterine smooth-muscle tumors with tumor cell necrosis, but otherwise benign appearances, are clinically malignant, and thus that such tumors should be considered to be STUMPs. At the present institute, tumors exhibiting unusual combinations of histopathological features that do not satisfy the Stanford criteria for LMS are diagnosed as uterine STUMPs, in accordance with the current World Health Organization classification [4].

STUMP has recurrence potential. However, this disease is considered to be of intermediate seriousness in Korea, as it is practically a borderline disease. Guntupalli *et al.* [1] reported that 3 of 41 (7.3%) patients developed recurrent disease. As the mean disease-free period was 42 months, longer follow-up periods are necessary. In addition, further studies are needed to reach consensus regarding the appropriate length of follow-up. Pelvic examination and USG are

basic procedures that should be performed at follow-up visits. For the cases reported here, the authors' clinic recommended six-month follow-up visits. Pelvic transvaginal USG was performed at each visit. At the time of publication, four cases have shown no sign of recurrence. The fifth patient developed ovarian cancer, underwent a staging operation, and was treated with chemotherapy.

Perioperative study has not been standardized for several reasons, including the national insurance policy. As STUMP can be diagnosed only by postoperative pathological examination, therapeutic planning prior to surgery is difficult.

Radiological findings suggestive of STUMP are not clearly distinct from those indicating benign leiomyoma or LMS. Intraoperative frozen biopsy is not dependable for the confirmation of a STUMP diagnosis. If possible, MRI should be performed in such patients before surgery to aid diagnosis. Therefore, the best option is to perform total hysterectomy and bilateral salpingo-oophorectomy after diagnosis in patients beyond childbearing age. Continual follow-up with appropriate imaging studies should be performed after diagnosis, as for other tumors with malignant potential. Although recurrence is not common in cases of STUMP, it may occur; follow-up studies are thus critical. Indeed, ovarian cancer was detected during follow-up in one case reported here.

Pelvic transvaginal USG and abdominopelvic CT were performed as follow-up examinations, and MRI was performed preoperatively. PET-CT was performed immediately after pathological diagnosis. Follow-up imaging by abdominopelvic CT and MRI in addition to pelvic USG every 3–6 months is performed at the present institute.

One patient seemed to have double primary cancers developing at different times, as STUMP and ovarian epithelial carcinoma are not thought to be related. Thus, aggressive salpingo-oophorectomy should be considered in cases of STUMP, taking each patient's age and menopausal status into account. Even when the tumor does not recur, more invasive surgical treatment should be performed in such cases.

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Conflicts of interest

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

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