

## Case Report

# A uterine malignant solitary fibrous tumor accompanied by squamous metaplasia and carcinoma in situ of endometrium

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**Abstract:** Solitary fibrous tumor of the uterus is extremely rare. This paper presents a case who has developed squamous metaplasia and carcinoma in situ of endometrium. The 67-year old female presented with abdominal pain, postmenopausal bleeding, and a 4 cm mass of the uterine serosa. Histological examination with immunohistochemistry of the tumor biopsy revealed diagnosis of malignant SFT. The patient underwent a hysterectomy with right salpingo-oophorectomy and left salpingectomy. No recurrence has been observed for 6 months. Uterine SFT with squamous metaplasia and carcinoma in situ of endometrium has not been reported. Immunohistochemistry was helpful in diagnosis.

**Keywords:** Uterus, solitary fibrous tumor, squamous carcinoma in situ of endometrium, immunohistochemistry

## Introduction

Solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm first described in 1931 by Klemperer and Rabin [1]. Though possible to occur in all parts of the body, most SFTs are found in the pleura, with a low incidence rate of less than 0.1/100000 per year [2]. SFTs can occur at any age, with an equal sex distribution. It is now believed that SFTs originate from dendritic stromal cells expressing CD34 antigens. The tumor rarely occurs in female genital tract. We present a case of a uterine malignant SFT accompanied by diffuse squamous metaplasia and foci carcinoma in situ of endometrium.

## Case presentation

A 67-year-old woman presented with abdomen pain and postmenopausal bleeding for 1 month. Enhanced computed tomography (CT) scan found a heterogeneous mass measured 3.7 cm × 3 cm in the right uterus corner, which was suspected to be leiomyoma of uterus. Cervical secretions were positive for HPV16 and HPV56 detection, but Pap smear of the

cervix was negative for intraepithelial lesions or malignancy. Chest X-ray and essential blood and urine tests were normal. There has been report of this tumor in the myometrium in association with hypoglycemia; in this case, however, the patient had no hypoglycemia. She underwent a hysterectomy with right salpingo-oophorectomy and left salpingectomy.

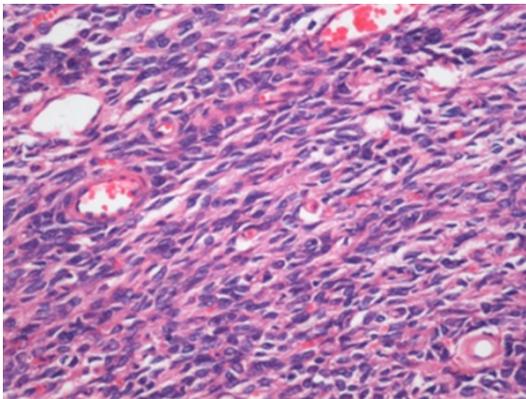
The resected tissues were fixed in 10% buffered formalin. Representative sections were embedded in paraffin, and 4 μm sections were cut for hematoxylin and eosin staining and IHC studies. Immunohistochemical studies were performed using Envision method and the primary antibodies were brought from Dako and Santa Cruz. The Ventana Ultraview detection kit and Benchmark XT staining system were used with diaminobenzidine (DAB) as the chromogen.

On gross examination, the uterus measured 7 × 5.5 × 5.5 cm and its right side was distorted by a 4 × 3 × 3 cm subserous mass which had a pale and solid-cystic sectioned surface, while the content of the cystic area was clear liquid and the solid area was firm (**Figure 1**). The mass

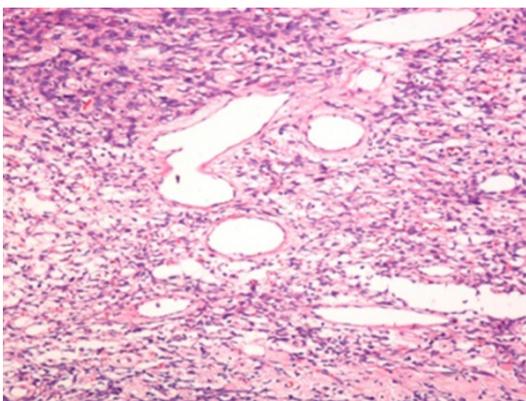
## Uterine malignant solitary fibrous tumor



**Figure 1.** The uterine mass had a pale and solid-cystic sectioned surface.



**Figure 2.** H & E-stained sections showed spindle shape and prominent nuclear atypia in the tumor cells. Original magnification,  $\times 200$ .



**Figure 3.** Thin walled blood vessels showed staghorn-like shape. Original magnification,  $\times 100$ .

was well demarcated. The endometrial cavity was distended and endometrial surface was

dark red and shaggy. The myometrium, right ovary, bilateral fallopian tubes, and cervix were normal.

On microscopic examination, the tumor was composed of spindle-shaped cells and collagenous stroma. These small-to-medium in size cells were in a fascicular and whorled structure, and had poorly defined and pale eosinophilic cytoplasm (**Figure 2**). The nucleus was big, deep-stained, and chromatin granulated, while the prominent nucleoli were not seen. In a few areas, the tumor cells were epithelioid. What's more, thin walled blood vessels were found, which adopted a hemangiopericytoma-like growth pattern (**Figure 3**). Scattered collagen bundles and stromal hyalinization were also noted (**Figure 4**). The high mitotic count (6-8/10 HPFs), focal tumor necrosis and myometrial invasion were noted, so the tumor was defined as malignant. Squamous metaplasia with high-grade squamous intraepithelial lesions of the endometrium was observed. So the endometrium and cervix were thoroughly sampled, but no evidence of intraepithelial lesions and squamous cell carcinoma of cervix was observed. Also no area of invasion was found on the entire endometrium.

Immunohistochemistry was strongly positive for CD34 (**Figure 5**) and Bcl-2, focally weakly positive for CD99. STAT6 was positive in the nuclei of tumor cells (**Figure 6**). H-caldesmon, SMA, desmin, actin ( $\alpha$ -smooth muscle actin), CD10, CD117, ER, PR, Inhibin, CR, CK, EMA and S-100 were all negative in the tumor cells. Ki-67 index was around 30%.

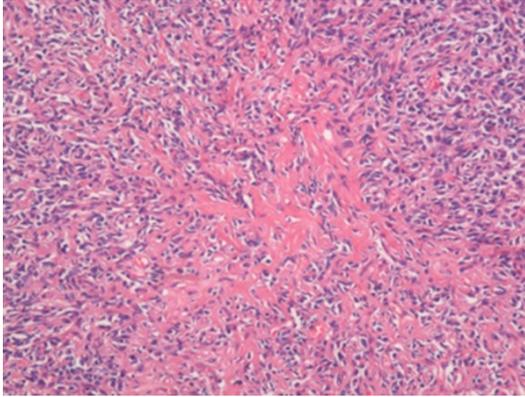
The patient refused further treatment after surgery. At 6-mo telephone follow-up, the patient continued to be alive and asymptomatic.

### Discussion

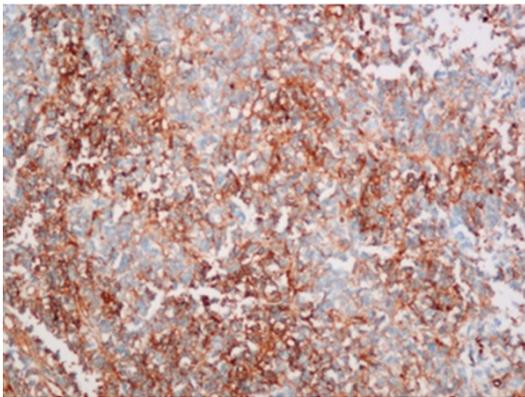
The female genital tract is one of the rarest primary sites for SFT [3]. There have only been 5 cases of SFT of the uterus reported previously in the English literature [4-8] (**Table 1**); undoubtedly, its rarity makes the diagnosis extremely difficult.

At present, SFT and hemangiopericytoma are both classified as SFT and belong to the majority of fibroblast/myofibroblastic tumors. In general, the tumors have a solid and firm cut sur-

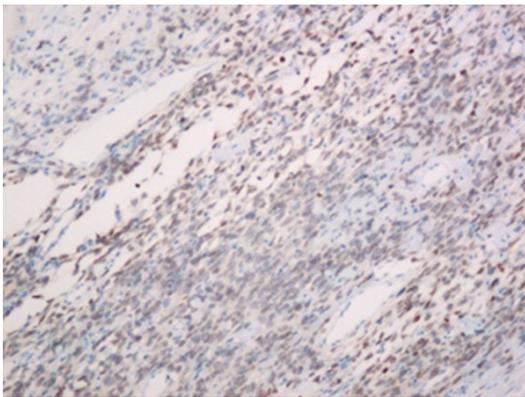
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**Figure 4.** H & E-stained sections showed scattered collagen bundles and stromal hyalinization. Original magnification,  $\times 100$ .



**Figure 5.** Immunohistochemistry for CD34 on the tumor cells was diffusely and strongly positive. Original magnification,  $\times 200$ .



**Figure 6.** Immunohistochemistry for STAT6 was positive in nuclei of the tumor cells. Original magnification,  $\times 200$ .

face, but cystic changes may occur in the section of the tumors. The typical SFTs often show

a patternless architecture characterized by spindle cells and bands of hyalinised collagen. In most cases, the tumor cells alternately distribute in high and low cellularity. In some cases, the tumor cells are round or short fusiform with vague boundary, and they contain lightly eosinophilic cytoplasm and vacuolated nucleus. The stroma may appear myxoid degeneration and adipocyte differentiation [9]. In addition to this classical SFT morphology, a few of SFTs with papillary structure and without staghorn vessels typical of SFT/HPC and some SFTs with epithelial components have also been reported in the literature [10]. Currently, the diagnostic criteria of malignant SFT depend mainly on morphological changes: high cellularity, nuclear pleomorphism, mitotic activity ( $> 4/10\text{HPF}$ ), diffuse hemorrhage and necrosis, the positive percentage of Ki-67 index  $> 20\%$  [11]. Yokoi [12] et al proposed two possible mechanisms for the origin of malignant SFT: one believed that the original benign SFT had undergone malignant transformation; the other believed that the tumor was malignant and grew rapidly at first. The first mechanism is supported by the benign histological features of MSFT seen in SFT; the second mechanism is of the opposite: there is no benign region in the tumor. In this case, there is no benign region, and it seems to support the second mechanism.

SFTs generally have positive staining for vimentin, CD34, and CK negative. In addition, CD99 and bcl-2 are positive in  $\approx 50\%$  of SFTs [13]. The positive rate of NAB2-STAT6 fusion gene is 100% in SFT [14]. Strong nuclear STAT6 is largely specific for SFT. The expression rate of STAT6 displayed 97% for SFTs and that in other soft tissue tumors was 3.3%. So strong nuclear staining for STAT6 is a useful diagnostic marker for solitary fibrous tumors [15].

The uterine SFT should mainly be differentiated from benign and malignant spindle cell lesions, such as leiomyoma or leiomyosarcoma, monophasic synovial sarcoma and low-grade endometrial stromal sarcoma.

(1) Leiomyoma: tumor cells are long spindle shaped and arranged in bundles. The nuclei are rod-shaped and both ends are rounded, and the cytoplasm is eosinophilic. Immunohistochemical staining is positive for SMA, H-caldesmon and Desmin, but negative for CD34.

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**Table 1.** Five cases so far reported in the medical literature

Reference	Author	Age	Maximal diameter of tumour (cm)	Symptoms	Treatment	Follow-up	Outcome
4	Wakami K	78	24	Hypoglycemic unconsciousness	Local resection of tumor	24	Alive, NR
5	Thaung C	47	10.5	Menorrhagia and urinary compression	Hysterectomy with bilateral salpingo-oophorectomy	NA	NA
6	Chu PW	78	-	Low abdominal pain	Hysterectomy with bilateral salpingo-oophorectomy	12	Alive, NR
7	Casanova J	30	-	Diffuse abdominal pain and menorrhagia	Transabdominal myomectomy	50	Alive, NR
8	Strickland KC	81	10	Shortness of breath	Hysterectomy	6	Alive, NR

NA - data not available, NR - no recurrence.

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(2) Low-grade endometrial stromal sarcoma: The tumor cells are oval or spindle-shaped with little cytoplasm. The cells spiral around the arteriole, with a infiltrative growth in the myometrium (“tongue like” growth). The atypia of the cell is not obvious, and the mitotic figures are rare. Over 80% of low-grade endometrial stromal sarcomas express CD10, WT1, ER and PR, and endometrial stromal sarcoma almost never expresses CD34.

(3) Monophasic fibrous synovial sarcoma: the tumor is composed of spindle shaped cells resembling fibroblasts, and its cells are consistent and arranged in bundles or sheets, without obvious collagen formation. The irregular intercellular clefts often can be noted. Immunohistochemistry shows that, in this case, CK, EMA, CD99 and Bcl-2 should be positive, while negative for CD34.

The treatment of solitary fibrous tumor is mainly based on surgical treatment, followed by radiotherapy and chemotherapy. Targeted therapy with the tyrosine kinase inhibitor (Sunitinib) may be useful prospectively [16].

All SFTs are considered to have malignant potential regardless of histological appearance, and may locally recur, but rarely metastasize. The common sites of distant spread are lung, liver, and bone. Malignant SFTs are characterized by tumor cell polymorphism, increased mitotic figures, marked tumor necrosis and tumor edge invasive growth. Therefore, they are more aggressive and have a higher recurrence rate. The diversity of tissue structure and cell composition, the variability of stroma and the different mitotic activity constitute a broad spectrum of SFT clinical pathology. So it is difficult to accurately judge the benign SFTs from the malignant ones. To do so, it is necessary to combine the clinical manifestations and imaging data. The prognosis is mainly determined by the complete resection of the tumor. It is also suggested that the extra pleural SFT is more invasive than the pleura, but it needs to be confirmed by studies with larger samples.

In conclusion, the uterine malignant SFT and presence of squamous metaplasia of endometrium are both extremely rare, and we have presented the first clinical case in this paper.

### Disclosure of conflict of interest

None.

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