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# Treatment of low-grade endometrial stromal sarcoma in a nulligravid woman

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ABSTRACT

A 32 year-old nulligravid woman with a uterine mass underwent exploratory laparotomy with myomectomy. Final pathology revealed a low-grade endometrial stromal sarcoma (ESS) with positive margins. She subsequently underwent definitive robotic hysterectomy and bilateral salpingectomy with ovarian preservation. She was diagnosed with a stage IB low-grade ESS. She is currently undergoing observation. Discussion of classification, surgical options, and adjuvant therapy is presented.



## 1. Presentation of case

A 32-year-old nulligravid woman presented to her primary OBGYN for a routine gynecologic exam. The patient reported cyclic pelvic pain and occasional bloating, but otherwise denied vaginal bleeding, discharge, and early satiety. She was found to have an enlarged uterus on bimanual exam. Family history was notable for the patient's mother having been diagnosed with a retroperitoneal liposarcoma. A pelvic ultrasound was performed, which revealed an 11 × 8 × 8 cm uterus with a heterogeneous mass filling the entire uterus. The endometrial stripe was 2 mm and the ovaries were normal appearing with small follicles. An MRI confirmed an enlarged, lobulated uterus with a 10 × 7 × 12 cm intramural mass. The mass enhanced fairly homogenously with internal areas suggestive of degenerative changes. An endometrial biopsy was performed and showed no evidence of malignancy; however, there was scant material in the specimen. The primary working diagnosis was a degenerating uterine fibroid.

After extensive counseling regarding the risks and benefits of fertility preservation, the patient underwent a myomectomy via a Pfannenstiel incision. At the time of surgery, she was found to have a fundal uterine mass measuring approximately 14 × 6 cm. Several other small whorled nodules clinically consistent with leiomyoma were noted, each <1 cm. The rest of her pelvic organs and abdomen appeared normal. After the dominant mass and other palpable uterine masses were removed, the uterus was repaired in multiple layers. She was discharged on postoperative day two without any complications.

Pathology returned as a low-grade endometrial stromal sarcoma (ESS). The size of the tumor measured 12.7 cm in its greatest dimension and there were positive margins present. The patient was counseled on options of close observation, additional tumor resection, and definitive hysterectomy. In order to maximize oncologic outcomes, the patient elected to undergo hysterectomy. Due to concerns related to the side-effects of surgical menopause, the patient desired ovarian preservation. The decision was made to proceed with a robotic-assisted laparoscopic hysterectomy and bilateral salpingectomy with ovarian preservation. She was found to have small and large bowel adhesions to her previous myomectomy scar. Her tubes and ovaries appeared normal and there was no other disease noted in the pelvis and abdomen. The patient was discharged on postoperative day one.

Pathology from the follow-up hysterectomy specimen was notable for a 1.3 cm nodule with residual low-grade ESS; the surgical margins were uninvolved. Final pathology was consistent with stage IB due to tumor limited to the uterus and a combined tumor size of 14 cm. Hormonal therapy with an aromatase inhibitor was considered but the patient opted for observation. At her three-month follow-up, the patient's primary symptoms were vaginal dryness and dyspareunia which improved with vaginal estrogen cream. Follow-up CT scans of the chest, abdomen, and pelvis showed no evidence of disease and the patient is without evidence of disease at 18 months.

## 2. Epidemiology of endometrial stromal sarcoma

ESS tumors are rare and account for <10% of uterine mesenchymal neoplasms and <2% of all uterine neoplasms [1]. The annual incidence is estimated to be 1–2 per million women [2]. The mean age of diagnosis is 50 years old and premenopausal women comprise up to half of affected patients [3]. Due to limitations with preoperative imaging and endometrial sampling to accurately diagnose ESS, the usual presentation is abnormal uterine bleeding or incidental pathologic finding at hysterectomy performed for suspected benign disease, such as fibroids.

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The majority of cases present with early stage disease [3]. Approximately 30–50% of patients will experience recurrence or metastasis after surgical management, including both pelvic and/or extrapelvic locations [4]. Recurrences typically have an indolent course and can occur up to 20 years later [3].

## 3. Pathology of endometrial stromal sarcoma

A single fragment of disrupted soft tissue labeled as "uterine fibroid" was examined (12.7 × 7.7 × 5.2 cm). Sectioning revealed yellow multinodular tissue and low power microscopic examination showed a tumor with irregular tongues and islands of highly cellular tissue infiltrating the myometrium (Fig. 1). Collagen bands and areas of diffuse hyalinization were present (Fig. 2). The tumor extended to the margins of resection. On high power magnification, tumor cells had uniform oval to spindle nuclei with scant cytoplasm resembling proliferative phase endometrial stroma (Fig. 3). Rare mitoses were identified and the stroma had multiple small arterioles and capillaries with collagen bands surrounding the tumor cells. The tumor was positive for CD10, WT-1, estrogen and progesterone receptors. Residual tumor in the hysterectomy specimen showed similar findings.

## 4. Molecular characteristics

The majority of ESS are estrogen and progesterone receptor positive. They are typically reactive for CD10 and smooth muscle actin. Several genetic abnormalities have been reported in low-grade ESS. The most common rearrangement (50%) is a gene translocation involving the short arm of chromosome 7 and the long arm of chromosome 17 t (7;17); this results in the fusion of JAZF1 and SUZ12 genes [5–7]. The JAZF1/SUZ12 protein has not been found in other uterine sarcomas. Although recent advances have expanded our understanding of the molecular characteristics of ESS tumors, further research is needed to better understand the molecular pathways and optimize targeted treatment strategies. These tumors are routinely diagnosed using histologic criteria; however, next generation sequencing assays may assist in the identification of ESS with unusual location or morphology.

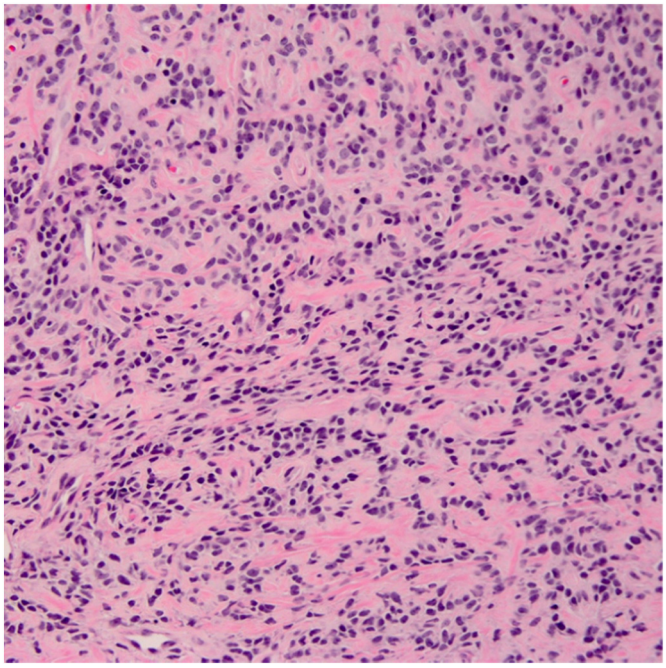

**Fig. 2.** Collagen bands surrounding tumor cells were present (H&E stain, 200× magnification).

## 5. Classification system

Endometrial stromal tumors are a subset of uterine mesenchymal neoplasms that account for <10% of uterine sarcomas and approximately 1% of all uterine malignant neoplasms. The terminology and classification system of endometrial stromal neoplasms has changed numerous times. The 2014 World Health Organization (WHO) classifies these tumors into four categories: (a) endometrial stromal nodule, (b) low-grade endometrial stromal sarcoma, (c) high-grade endometrial

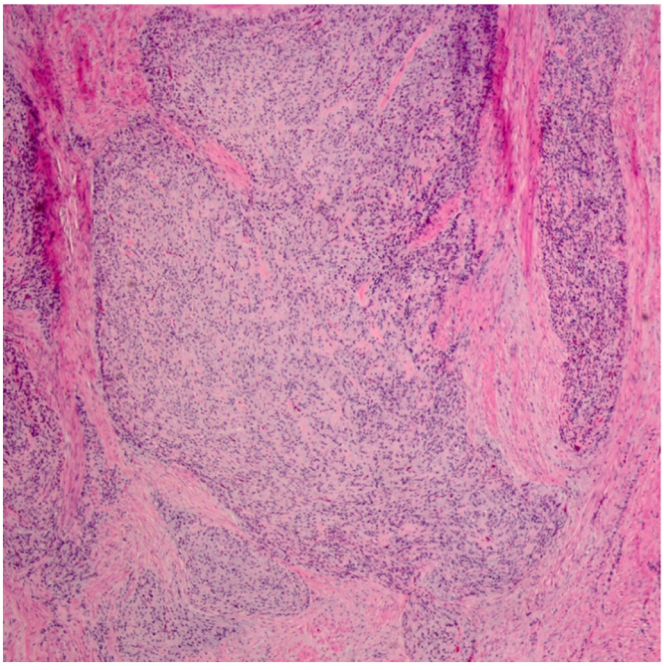

**Fig. 1.** Low-grade endometrial stromal sarcoma with irregular tongues of highly cellular tissue infiltrating myometrium (H&E stain, 40× magnification).

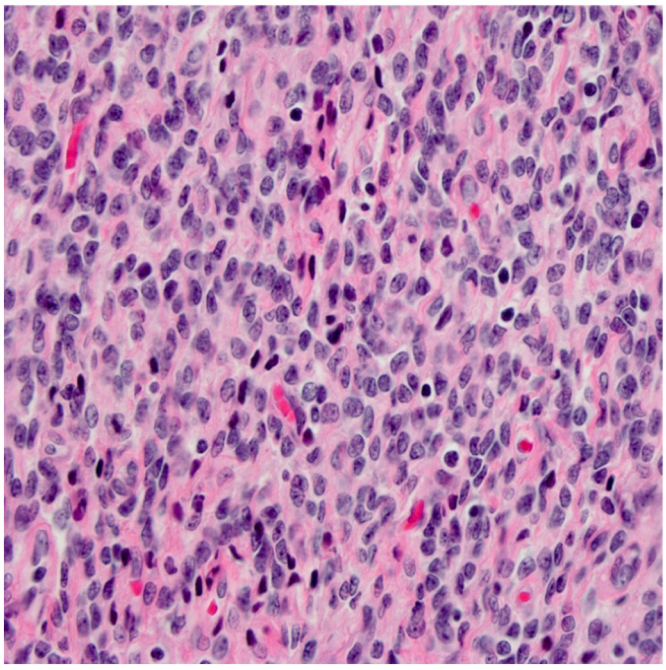

**Fig. 3.** High power examination shows tumor with uniform oval to spindle shape nuclei with scant cytoplasm resembling proliferative phase endometrial stroma (H&E stain, 400× magnification).

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