

Vulvar extrauterine endometrial stromal sarcoma: A case report and literature review



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Endometrial stromal sarcoma (ESS) is an extremely rare neoplasm accounting for only 0.2% of all uterine malignancies and for 15–26% of primary uterine sarcomas. The annual incidence of ESS is 1–2 per million women. Herein, to the best of our knowledge, we present the first reported case of ESS of the vulva in a 50-year-old female presenting with per vaginal spotting over a period of three months. Her past surgical history included a subtotal hysterectomy and left salpingo-oophorectomy for uterine fibroids ten years previously. On examination, a 3.5 × 3 × 2 cm cystic mass was found in the right labia majora. The mass was excised and the diagnosis of endometrial stromal sarcoma was made. Subsequent metastatic workup was negative and the patient was started on megestrol acetate. She has remained disease free with no signs or symptoms of recurrent or advanced disease for 28 months.

KEYWORDS: Endometrial stromal sarcoma; Vulva; Uterine sarcoma

INTRODUCTION

Endometrial stromal sarcoma (ESS) is an extremely rare neoplasm accounting for only 0.2% of all uterine malignancies and for 15–26% of primary uterine sarcomas.¹ The annual incidence of ESS is 1–2 per million women. Compared to other uterine malignancies, ESS affects younger women with a mean age of 42–58 years.² ESS resembles stromal cells in the proliferative stage of the normal endometrium and are often low-grade, indolent, but metastatic exhibiting myometrial and/or vascular invasion.³ The incidence of ESS in extrauterine locations is exceedingly rare especially in the absence of metastasis or extension of a primary neoplasm. Principal extrauterine sites of ESS include the ovary, bowel wall, abdomen, peritoneum, pelvis, and vagina.^{4–6}

Herein, to the best of our knowledge, we present the first reported case of ESS of the vulva in a 50-year-old female presenting with per vaginal spotting

of three months' duration. A literature review of ESS is also presented.

CASE REPORT

A 50-year-old female, para 8+0 was referred to our service with per vaginal spotting. Her past medical history was unremarkable; her previous surgical history included a subtotal hysterectomy and left salpingo-oophorectomy for uterine fibroids ten years previously. On clinical examination, a soft yellowish lesion with hemorrhagic foci, measuring 3.5 × 3 × 2 cm, was found and a Bartholin gland cyst was suspected. On February 2012, an excisional biopsy was performed and the rendered histopathological diagnosis was low-grade endometrial stromal sarcoma. Microscopy showed a diffuse cellular infiltrate composed of monotonous bland looking oval to spindle cells (simulating endometrial stromal cells) surrounding arterioles resembling endometrial spiral

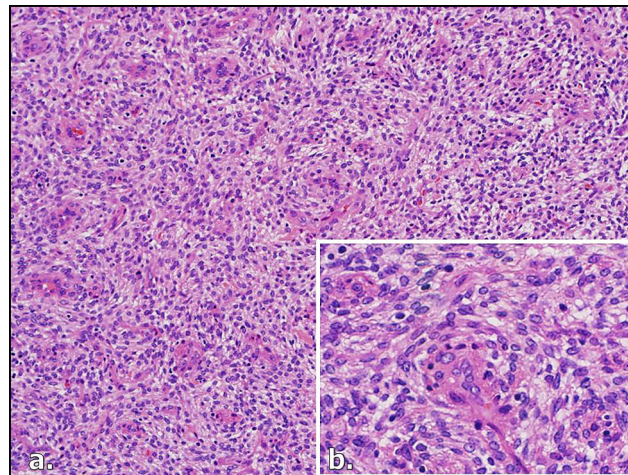


Figure 1. Endometrial stromal sarcoma. (a) A cellular neoplasm composed of bland oval cells surrounding arterioles resembling endometrial spiral arterioles (hematoxylin and eosin stain, $\times 200$ magnification). (b) A higher magnification microphotograph showing the spindle cells surrounding a blood vessel (hematoxylin and eosin stain, $\times 400$ magnification).

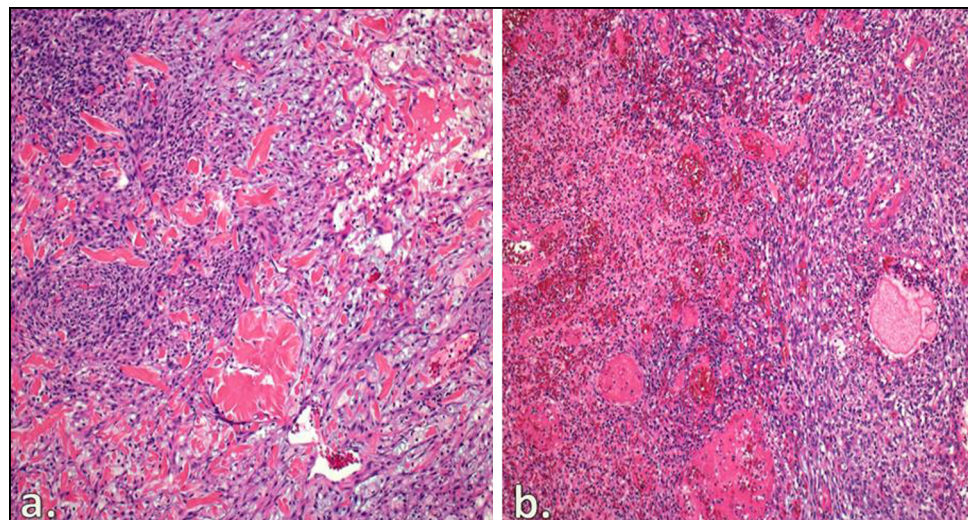


Figure 2. Endometrial stromal sarcoma. (a) Plaques of hyalinized fibrosis (hematoxylin and eosin stain, $\times 200$ magnification). (b) Areas of tumor necrosis on the left of the image in contrast to the viable tumor on the right (hematoxylin and eosin stain, $\times 100$ magnification).

arterioles (Figure 1). Few mitoses and large foci of tumor necrosis and hemorrhage were seen, as well as plaques of hyaline fibrosis (Figure 2). The lesion was infiltrative with poorly defined margins. The surgical resection margins were negative for tumor and there was no evidence of associated endometriosis. Moreover, immunohistochemical staining was strongly positive for CD10, vimentin, estrogen receptor and progesterone receptor (ER and PR) (Figures 3 and 4). Cytokeratin cocktail (CKAE1/AE3) was moderately positive, whereas h-caldesmon, desmin, CD34, SMA and S-100 were all negative (Figure 5). The patient was started on megestrol acetate. In May 2012, surveillance computed tomography of the

chest, abdomen, and pelvis displayed an unremarkable cervix and no signs of metastasis or recurrence. In January 2013, the patient had a positron emission tomography (PET) scan which was unremarkable; the patient was therefore kept on megestrol. In July 2013, magnetic resonance imaging (MRI) revealed an ill-defined lesion in the right side of her perineum and lower vagina, encasing the urethra, with no lymph node involvement (Figure 6). The patient was referred to urology, and a cystoscopy was performed with unremarkable results. An excisional biopsy was performed showing a benign polypoid piece of endocervical mucosa with chronic inflammation. Subsequent cervical smears throughout the patient's

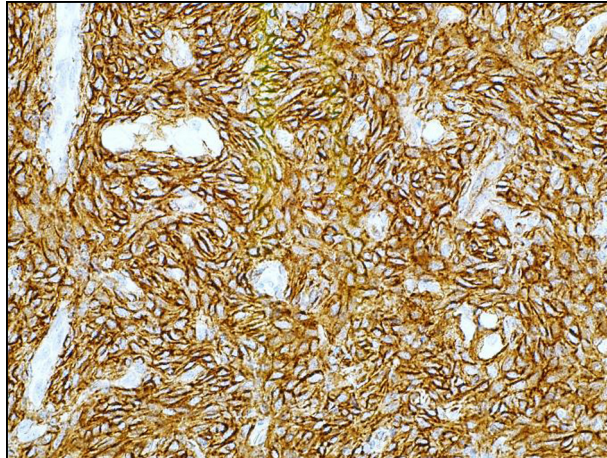


Figure 3. CD10 immunostain showing a strong and diffuse membranous staining of the tumor cells (CD10, Dako, ×400 magnification).

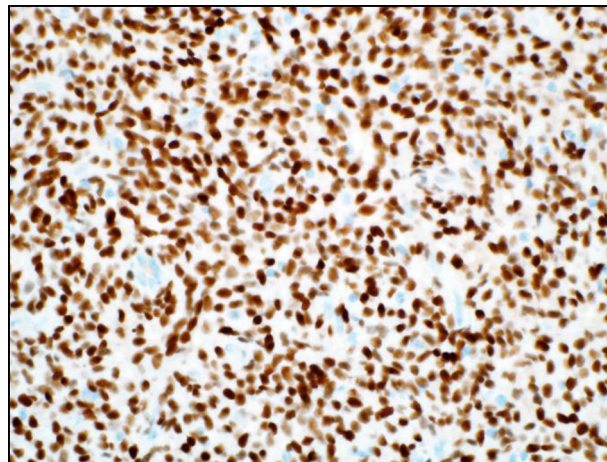


Figure 4. Estrogen receptor immunostain showing a diffuse nuclear reactivity in the tumor cells (ER, Dako, ×400 magnification).

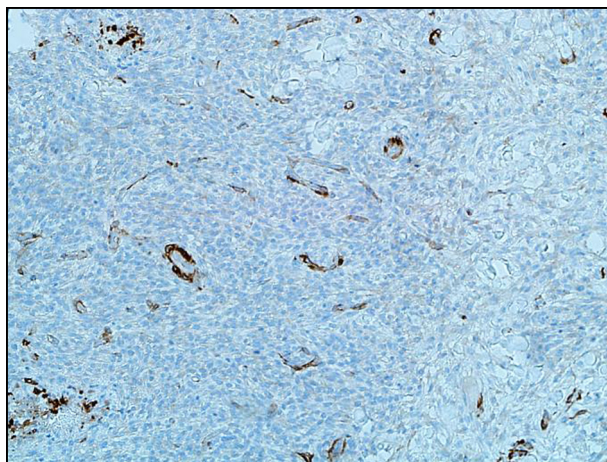


Figure 5. H-caldesmon immunostain showing negative tumor cells in contrast to the internal control smooth muscle cells in the walls of the blood vessels. (H-caldesmon, Dako, ×200 magnification).



Figure 6. T1-weighted axial magnetic resonance imaging (MRI) scan showing slight high signal intensity around an ill-defined lesion encasing the urethra from the right side.

follow-up were all negative. The patient was maintained on megestrol 80 mg once daily and has remained disease free with no signs or symptoms of recurrent or advanced disease for the subsequent 28 months of follow-up.

DISCUSSION

ESS is an extremely rare neoplasm accounting for only 0.2% of all uterine malignancies and for 15–26% of primary uterine sarcomas.¹ The annual incidence of ESS is 1–2 per million women. Compared to other uterine malignancies, ESS affects younger women with a mean age of 42–58 years.² The pathogenesis of ESS is still vague, but hormonal exposure through tamoxifen, estrogens, and conditions such as polycystic disease of the ovary have been implicated.⁷ Clinically, symptoms of ESS are non-specific and usually include irregular vaginal bleeding pelvic pain/pressure and an abdominal mass or discomfort. Diagnosis should therefore be based on pathological examination.

ESS often forms distinctive finger-like projections that invade the myometrium, veins, and lymphatics. Histologically, ESS is characterized by densely uniform stromal cells with minimal cellular pleomorphism, mild nuclear atypia, and variable mitoses. The differential diagnosis of our lesion included: smooth muscle tumors (leiomyosarcoma, cellular leiomyoma), adenosarcoma, hemangiopericytoma/solitary fibrous tumor (HPC/SFT), and cellular angiofibroma.

Smooth muscle tumors tend to have larger cells with typical cigar-shaped nuclei. Large thick-walled

blood vessels are commonly present, and the small arterioles that are characteristic of ESS are usually absent. Immunostains are also helpful in making the distinction, as smooth muscle tumors are strongly positive for SMA, desmin and h-caldesmon, and extensive staining for CD10 is unusual. HPC/SFT form well-circumscribed masses with neoplastic cells intimately arranged around a myriad of thin-walled vessels and partially collapsed branching capillaries. The absence of large vessels, which often exhibit a staghorn-like appearance, and the immunostains did not support this diagnosis. HPC/SFT are strongly positive for CD34 and SMA. In comparison with HPC/SFT, ESS shows strong expression of CD10 and PR. ESS is also ER positive and CD34 negative. We also excluded adenosarcoma with stromal overgrowth because of the lack of any epithelial elements, and, subsequently, any periglandular stromal condensations. Furthermore, the possibility of cellular angiofibroma was considered. However, cellular angiofibromas tend to be well-circumscribed with uniformly distributed small blood vessels, thick collagen bundles and variable amounts of fat. Cellular angiofibromas can show variable mitotic activity, though atypical forms, including tumor necrosis, are absent. There are notable differences in the reported immunoprofile of this tumor. SMA and desmin expression are positive in <20% and <10% respectively; however, strong diffuse reactivity for CD34 is reported in about half of such cases.⁸

The origin of the ESS in our case is unclear. Despite an unknown route of metastasis and negative

metastatic workup, a primary metastasizing ESS should be considered because remote recurrences occurring after decades from the primary diagnosis have been previously documented in the literature.⁹ In a series of 78 patients, Gloor et al. reported higher local and metastatic recurrence rates in cases where one or both ovaries were preserved;¹⁰ such is the case in our patient. ESS has also been shown to arise from ovarian and extraovarian endometriosis.¹¹ Yet our patient did not have any pathological or radiological evidence of endometriosis.

According to the hypothesis postulated by Lauchlan et al., mesenchymal cells present in tissues derived from the coelomic epithelium have the potential to differentiate into Müllerian-type epithelium and stroma. This could explain the occurrence of ESS in extrauterine sites lined by a coelomic-type of epithelium such as the ovaries, fallopian tube, and pelvic peritoneum, but not the vulva or vagina.^{12,13} However, four cases of primary ESS occurring in the vagina without evidence of endometriosis or metastasis have been reported in the literature.¹⁴

Treatment of ESS has been challenging due to the rarity of the disease. Performing prospective randomized clinical trials to adjust treatment is difficult; management has therefore been mainly guided by retrospective case series and case reports. Treatment involves various approaches including radiation,

surgical excision, chemotherapy, or a combination of surgery and chemotherapy. Hormonal therapy remains the most studied in the management of ESS. We therefore report the successful control of this neoplasm on megestrol acetate after local excision with negative margins.

ESS has a highly recurrent nature with around 50% of patients presenting with recurrence mostly after long latency periods.¹⁵ They most commonly recur in the abdomen/pelvis (40–50%) followed by the lung (25%). However, spine and hematologic recurrences have also been described in the literature.^{16–19}

ESS has shown overall survival rates of 65% at five years but of 32% in those with extrauterine disease.²⁰ In conclusion, although extremely rare, the diagnosis of ESS presenting as a Bartholin gland cyst should be kept in mind especially in patients between the ages of 40–50 presenting with symptoms of menorrhagia, dysmenorrhea, and pelvic pain or pressure.

DISCLOSURE OF CONFLICT OF INTEREST

None.

CONSENT

Informed consent was obtained from the patient.

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