Endometrial Stromal Sarcoma of the Uterus with Arterial Tumor Embolus

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Citation

D Feng, D Wolfson. *Endometrial Stromal Sarcoma of the Uterus with Arterial Tumor Embolus*. The Internet Journal of Gynecology and Obstetrics. 2008 Volume 12 Number 1.

Abstract

Endometrial stromal sarcoma (ESS) of the uterus is extremely rare. We report a case of ESS of the uterus with tumor embolus in an artery in a 36 year-old woman.
The patient is a Caucasian woman who presented with vaginal bleeding. Surgical biopsy revealed low grade ESS (LGESS). Subsequently, total abdominal hysterectomy and right salpingo-oophorectomy was performed. A 3.8 cm polypoid mass was identified in the endometrial cavity, invading into the outer half of the anterior uterine wall. About 5-10% of the tumor exhibited undifferentiated sarcoma. Based on the aggressive nature of the tumor, the patient underwent left salpingo-oophorectomy and was subsequently treated with chemotherapy. She was followed up with periodic CT scans and was found to have recurrent ESS in the retroperitoneum 20 months after total hysterectomy and bilateral salpingo-oophorectomy. Rebulking surgery was not performed as the tumor showed diffuse abdominal and retroperitoneal involvement. Although LGESS may behave as an indolent tumor, it can be associated with an aggressive process and a high recurrence rate. A poor prognosis may occur when LGESS is admixed with undifferentiated components especially with evidence of arterial tumor embolus, which is herein reported.

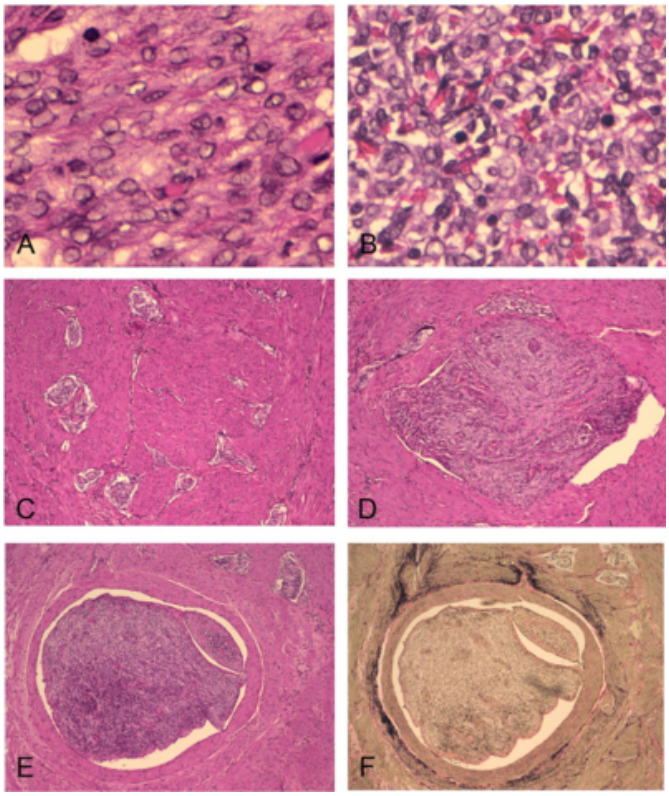
CASE REPORT

A 36-year-old Caucasian woman, G2, P1-0-1-1 with a history of vaginal bleeding presented to our institution. A large polypoid mass was identified in the uterus by radiographic studies. Surgical biopsy of the lesion was performed. Morphologically, the lesion displayed a polypoid neoplasm composed of monotonous ovoid to spindly cells whirling around spiral arterioles. Immunohistochemically, the tumor cells were positive for vimentin, CD10, estrogen receptor, progesterone receptor, weakly positive for p53, MIB-1, and negative for desmin, CD31, S100, and AE1/3. Histochemical special staining was negative for mucicarmine. Given the patient's clinical history, morphological findings along with immunostaining pattern, a pathological diagnosis of LGESS) was rendered. Subsequently, a diagnostic laparoscopic exploratory laparotomy with total abdominal hysterectomy and a left salphingo-oophorectomy was undertaken. Gross examination revealed that the enlarged uterus weighed 145 gram, and measured 12 x 8 x 6 cm in size. A 3.8 cm polypoid mass was identified in the endometrial cavity involving the anterior endometrium and myometrum. On cut surfaces, the tumor appeared solid, fleshy growth with areas of hemorrhage, invading more than one half of the myometrial thickness. Microscopic examination found that the tumor extended into the myometrum up to 0.3 cm from the serosal surface. Tumor cells appeared with typical LGESS morphology with tongue-like infiltration between muscle bundles of the myometrium and extensive worm-like lymphvascular invasion (Fig.1A, C and D). Focal transformation into undifferentiated endometrial sarcoma (UES) was identified in 5-10% of the tumor burden, characterized by increased cellular atypia, uniform pleomorphism, markedly increased mitotic index, > 20/10 high power field, prominent hemorrhage, and absence of spiral arterioles (Fig.1B). Focal arterial tumor embolus was identified (Fig. 1E) and special staining for elastic fibers confirmed the tumor embolus within the lumen of a small artery (Fig. 1F). Necrosis was absent. Subsequently, the patient underwent right salpingo-oophorectomy. She was placed on norethindrone acetate 5 mg daily, ibuprofen and serotinal. A repeat CT demonstrated an approximately 2.5 cm cystic mass in the left pelvis 17 months after the total hysterectomy. A follow up CT scan demonstrated a large mass in the retroperitonium, suspicious for metastasis. Therefore, a CT guided core needle biopsy was performed

on this mass, which revealed metastatic ESS (Fig. 2A to 2D). Three months after the core needle biopsy, the patient underwent an extensive exploratory laparotomy, which, unfortunately, demonstrated unresectable recurrent tumor secondary to involvement of the aorta, vena cava, pancreas and duodenum. Currently, the patient is still alive.

Figure 1

Fig 1



A. High power view of LGESS showing monotonously ovoid to spindly cells with occasional mitosis on the left upper portion. . (H&E, original magnification ×400).

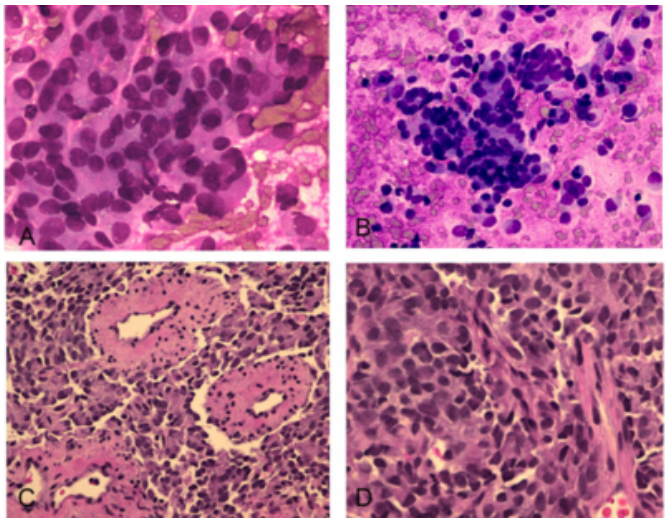
B. High power view of UES-U showing increased atypia, hypercellularity, nuclear pleomorphism and hemorrhage with increased mitosis. (H&E, original magnification ×400).

C and D. LGESS showing monotonously ovoid to spindly neoplastic cells with extensive worm-like lymphvascular invasion and intimately associated with prominent arterioles (H&E, original magnification ×100).

E and F. LGESS tumor embolus in the lumen of a small artery. (E. H&E, F. Elastic special stain. Both original magnification ×100).

Figure 2

Fig 2.



A & B. Imprinting smears of the core needle biopsy demonstrating monotonous oval neoplastic cells with scant cytoplasm, with high nuclear to cytoplasmic ratio in clusters or isolated single cells . (Diff Quik, original magnification A x 400, B x 200).

C and D. Sections of the core needle biopsy exhibiting classic morphological features of LGESS with a sheet of uniformly sized neoplastic cells whirling around prominent arterioles. (H&E, original magnification C x 200, D x 400).

DISCUSSION

ESS are very rare malignant tumors that constitute approximately 10% of all uterine sarcomas but only around 0.2% of all uterine malignancies. [1] The annual incidence of ESS is 1–2 per million women accounting for 400 to 700 new cases each year in the USA or Europe. ESS occur primarily in the perimenopausal age group, between 45 and 50 years with about one-third being in the post menopausal age group. [2] historically ESS were classified into three types: endometrial stromal nodule, LGESS, and high-grade ESS (HGESS). The endometrial stromal nodule is a lesion confined to the uterus with pushing margins, less than three mitosis per ten high power field and no lymphatic or vascular spread. The prognosis of this disease is usually good and there are no reported recurrences or deaths following surgical removal of the tumor. LGESS has an infiltrating margin and typically shows extensive worm-like vessel invasion. [3, 4] . At present, mitotic counts are no longer used to differentiate high-grade from low-grade lesions. Mitotic rates of 10 or more per 10 high power fields can be encountered in LGESS and a high mitotic index does not in

itself alter the diagnosis. LGESS is almost always positive for both estrogen and progesterone receptors. [5] LGESS is characterized by indolent growth and late recurrences, up to one-half of patients develop one or more pelvic or abdominal recurrences. The 5-year survival rate for LGESS ranges from 67% to nearly 100%. Patients with LGESS are associated with late metastases and a relatively long term survival despite tumor dissemination. The surgical stage is the best predictor of recurrence and survival for LGESS. The division of endometrial stromal sarcomas into low-grade and high-grade categories has fallen out of favor. According to the WHO classification, the term endometrial stromal sarcoma is now considered best restricted to neoplasms that were formally referred to as LGESS. High-grade tumors without recognizable evidence of a definite endometrial stromal phenotype are now termed undifferentiated endometrial sarcomas instead of HGESS [4, 6.]

UES represents a high grade endometrial sarcoma that lacks specific differentiation and bears no histological resemblance to endometrial stroma. UES often show prominent hemorrhage and necrosis with marked cellular atypia and abundant mitotic activity, often including atypical forms. They lack the typical growth pattern and vascularity of LGESS and they resemble the sarcomatous component of a carcinosarcoma. They are negative for estrogen and progesterone receptors. These tumors are aggressive and death occurs from tumor dissemination within three years after hysterectomy in most cases. Studies have found no significant association between mitotic count, myometrial invasion and risk of recurrence. However, pleomorphisim and necrosis are related to poor prognosis. [4, 5, 6, 7] Another study has described a case of UES in an adolescent girl, arising in a rudimentary uterine horn, who presented with an acute abdomen. The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy due to a stage IVA UES. She died of the disease 1 month after her first admission to the hospital secondary to diffused metastases into the lungs and the abdomen. [8]

The pathogenesis of ESS is unknown, but exposure to tamoxifen and unopposed estrogens has been implicated in some cases. [9] Tamoxifen has been widely used in breast cancer treatment. In recent years, the occurrence of uterine malignancies in patients receiving long-term tamoxifen therapy has attracted attention. Most of these malignancies are endometrial adenocarcinomas, but LGESS and UES have occasionally been reported. [9]

Recently, Kurihara et al found that LGESS and undifferentiated endometrial sarcoma with nuclear uniformity (UES-U) frequently showed positive immunoreaction for estrogen receptor (LGESS: 94%, UES-U: 57%) and progesterone receptor (LGESS: 94%, UES-U: 57%), whereas all the undifferentiated endometrial sarcoma with nuclear pleomorphism (UES-P) were negative for these receptors. Moreover, nuclear accumulation of p53 and TP53 gene missense mutations were limited to UES-P cases. JAZF1-JJAZ1 fusion transcript was detected in 55% of LGESS and in 33% of UES-U, whereas it was not detected in any of the cases of UES-P. [10]

In our case, the patient is a premenopausal young woman with predominantly LGESS admixed with a small component of UES-U. The aggressiveness and survival theoretically would expect to may be between the LGESS and UES-P. However, the histopathology in this patient demonstrated an arterial tumor embolus along with extensive lymphangiovascular invasion, which indicated the extremely high risk of rapid recurrence and distant metastasis.

Treatment of ESS is typically surgical. Preservation of ovarian tissue is not recommended because of the likelihood of ovarian metastasis. In addition, bilateral oopherectomy is recommended in cases of ESS with UES-U due to the possibility that ovarian estrogen production may stimulate residual disease. [10] Current treatment for recurrent or metastatic disease has not been particularly effective. Our case demonstrates the complexity of the WHO classification for ESS as it applies to patient care, prognosis, and treatment. Perhaps, further research into the molecular pathogenesis of ESS will improve patient treatment and outcomes.

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