

PRIMARY LOW-GRADE ENDOMETRIOID STROMAL SARCOMA OF THE OVARY WITH MULTIPLE OMENTAL METASTASES

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ABSTRACT

A 60-year-old diabetic patient, G5P5, presented with postmenopausal bleeding for two months. The clinical assessment was unremarkable. The computed tomography of the chest, abdomen, and pelvis showed a right-sided complex ovarian mass measuring 7 cm with multiple nodular deposits in the omentum, with a dimension of 4 cm for the largest one. Debulking laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, and infracolic omentectomy were performed. A histopathologic examination revealed primary ovarian low-grade endometrioid stromal sarcoma. Postoperatively, the patient received hormonal therapy.

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CASE REPORT

The patient history revealed a 60-year-old female, G5P5, presented with postmenopausal bleeding for two months. The clinical assessment was unremarkable. Computed tomography (CT) (Figure 1) showed a right adnexal (likely ovarian) lesion with marked omental deposits causing right-sided hydronephrosis, mild hydronephrosis with superior mesenteric vein thrombi, and calcified splenic artery aneurysm.

As per external lab reports, readings from tumor marker studies showed the following: CA125: 56.9 U/ml (Normal<35); CA15-3: 14.6 U/ml (N<28); CA19.9: 2 U/ml (N<37); and CEA: 1 ng/ml (N<5).

The complete blood count test revealed the following: hemoglobin: 10.9 gm/dl; white blood cell (WBC) count: $11.7 \times 10^9/L$; and platelet count: $266 \times 10^9/L$.

Other examinations, such as liver and kidney function tests, were normal.

In August 2015, the patient had undergone

total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy, along with mesh insertion. Her postoperative course was complicated by urinoma resulting from an injury to the dome of the urinary bladder, which was repaired successfully. She was discharged seven days postoperatively after a second laparotomy.

The pathology material was referred to the KHCC lab from external medical laboratories. It was received as 20 paraffin blocks and 11 unstained slides. Macroscopically (as per external lab report), the right ovary showed a mass lesion with 7 cm as its largest dimension, having a ruptured capsule and smooth external surface. The maximum dimension of the left ovary was 4 cm. The uterus showed an endometrial polyp. Numerous solid nodules were noted in the omentum, the size of the largest being 5 cm. Upon sectioning, the right ovary showed foci of hemorrhage. In the external pathology report, the tumor was described as a spindle cell lesion; immunohistochemistry was not performed.

Microscopically, the right ovary exhibited a spindle cell lesion comprising cells with scant eosinophilic cytoplasm and vague cell borders showing perivascular whorls around many spiral arterioles (Figures 2 and 3). Foci of necrosis and

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hyalinized blood vessels were noted. However, endometrial glands were not seen. As the uterus was extensively sampled (received as six blocks) and revealed no malignancy, the histopathological findings were consistent with primary low-grade endometrioid stromal sarcoma of the ovary.

Figure 1. Coronal section showing right adnexal lesion, along with multiple omental deposits



Figure 2. High power magnification showing plump spindle cells

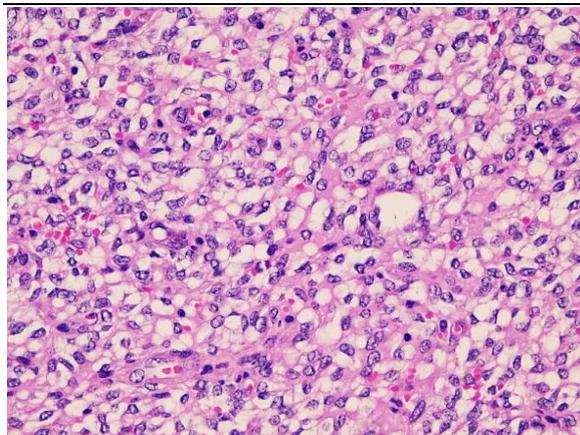
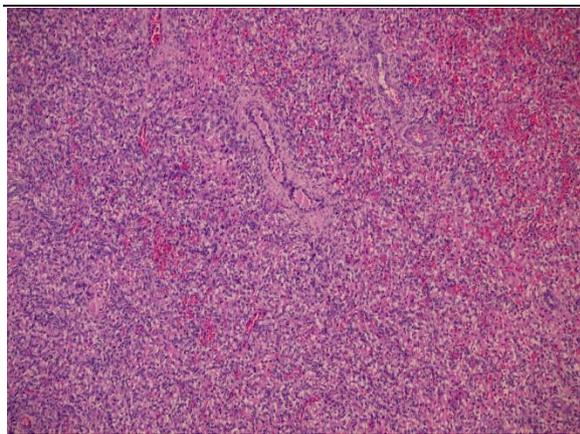
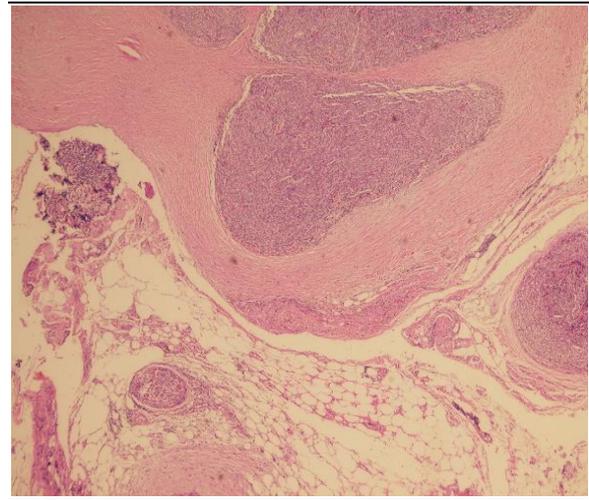


Figure 3. Low power magnification showing spiral arterioles



The tumor showed metastasis to the omentum and displayed multifocal lymphovascular invasion (Figure 4). As the tumor involves one ovary with implants in pelvic tissues, the tumor stage was FIGO stage II.

Figure 4. Low power magnification showing characteristic nodular pattern of ESS in omental deposits



Immunostains for CD10 were positive in the tumor cells (Figure 5). In addition, estrogen receptors (Figure 6) and progesterone receptors (Figure 7) were strongly positive in 95% of the tumor cells. The tumor cells, however, were only focally and weakly positive for cyclin D1. The following immunostains were negative: SF1, CK-MNF, EMA, inhibin, calretinin, TTF1, synaptophysin, CD99, DOG1, and HMB45.

Figure 5. CD10 immunostain

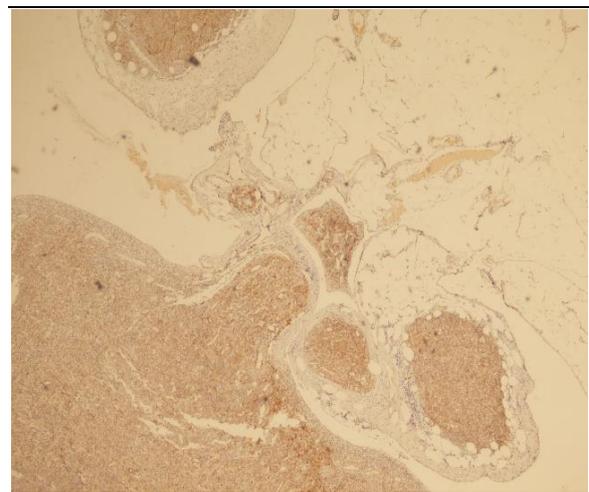


Figure 6. ER immunostain showing nuclear positivity

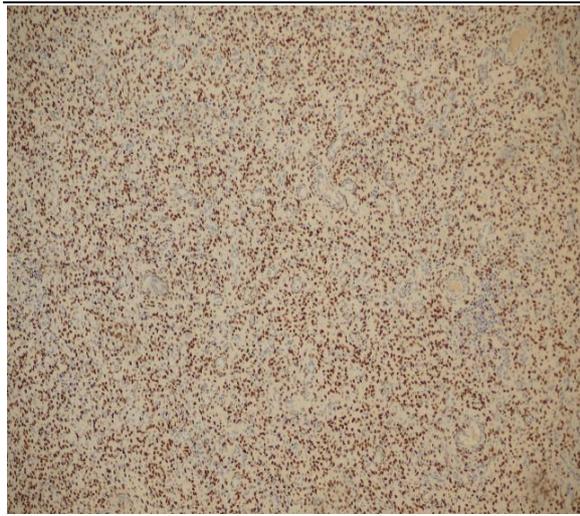
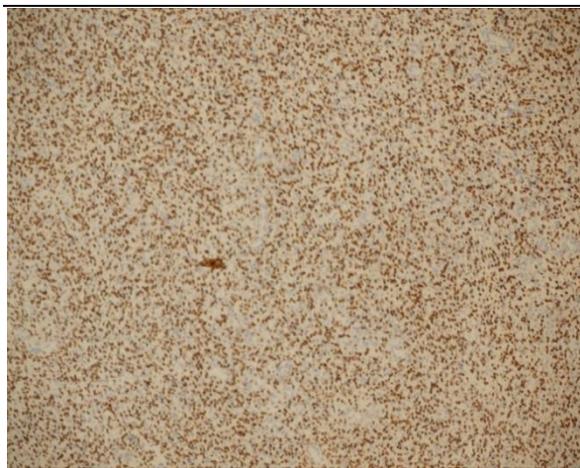


Figure 7. PR immunostain showing nuclear positivity



Postoperatively, the patient was maintained on megestrol acetate 250 mg/day.

Follow-up information over 10 months revealed no signs of recurrence or distant metastasis.

DISCUSSION

Endometrial stromal sarcoma is a rare neoplasm that constitutes 0.2% of uterine malignancies and is characterized by indolent behavior¹. The mean age of presentation is 54 years and most cases present with postmenopausal bleeding¹. In the newest WHO classification (WHO 2014), endometrial stromal tumors are classified into four categories: endometrial stromal nodule, low-grade endometrial stromal sarcoma (LG-ESS), high-grade endometrial stromal sarcoma (HG-ESS), and undifferentiated uterine sarcoma². The high-grade category was reintroduced in this classification; although it is not well defined currently, three subtypes of

HG-ESS were described: HG-ESS with YWHAE-NUTM2 rearrangement (which is the most important to recognize), dedifferentiated HG-ESS, and HG-ESS, not otherwise specified³. ESN and LG-ESS are characterized by JAZF1-JJAZ1 translocation, whereas the YWHAE-NUTM2 genetic fusion can be identified in HG-ESSs². Extruterine sites for endometrial stromal sarcomas are uncommon, so the pathogenesis is not well understood¹. However, their frequent association with endometriosis implies that it can be an origin for these extruterine ESSs⁴. The ovary can be a primary site for the malignant transformation of endometriosis in 76% of cases. This transformation can also occur in extragonadal sites in the remaining 24% of cases⁵. To date, fewer than 40 cases of primary ovarian ESSs have been reported in literature. The ESS would be considered as primary ovarian when the uterus is not encompassed by the tumor and the largest mass is identified in the ovary, along with the clinical presentation of ovarian tumor⁶.

In literature, the largest series was published by Oliva *et al.*, in which 27 cases of primary ovarian ESSs were collected over 32 years. The tumor was bilateral in 26% of the cases, and the frequency of this bilaterality was attributed to an origin from endometriosis, which commonly involves both ovaries⁶. Therefore, bilaterality is not considered as evidence of metastasis. Notably, 55% of the cases were associated with endometriosis. The stage varied, but most patients presented at stage III. The tumor size was 1–20 cm⁶.

According to the aforementioned study, patients with endometrioid stromal sarcoma have a much better overall prognosis than those with other sarcomas presented in the ovaries; 16 of 21 lived for 1–21 years postoperatively, of which 10 were disease-free for 10 years⁶.

CD10 is a known immunomarker for low-grade endometrial stromal sarcoma, but can also be positive in granulosa cell tumors, which can be part of the differential diagnosis⁷. However, calretinin and inhibin can be helpful as they are known to be negative in endometrial

stromal tumors and positive in granulosa cell tumors⁷. Immunohistochemical markers such as h-caldesmon, desmin, and oxytocin receptors will help differentiate ESS from another entity that appears in the differential diagnosis, i.e., cellular leiomyoma. The latter will be positive for these markers and negative for CD10⁸. The differential diagnosis of ovarian ESS includes thecomas, especially when hyaline plaques are present⁶. It also includes fibromas, which are negative or only focally positive for CD10⁶.

Metastatic GISTs are also considered part of the differential diagnosis of ESS. CD34, c-kit and DOG1 are positive in most GISTs, and negative in endometrial stromal tumors⁹. The exceptions to this are endometrial stromal tumors with the genetic fusion of YWHAE-NUTM2, which will show positivity for c-kit immunostain without c-kit mutation, but they will still be negative for DOG1¹⁰.

The differential diagnosis of extrauterine LG-ESS depends on location. In ovaries, primary uterine endometrial stromal sarcoma and ovarian sex cord stromal tumors should be excluded. When ESS arises from the abdominal cavity, GIST appears in the differential diagnosis¹¹.

Molecular testing may be helpful, especially in unusual locations or morphology. The most common rearrangement in LG-ESS is t (7,17) with genetic fusion JAZF1-SUZ12 (also named JAZF1-JJAZ1); other genetic fusions that are much less common are JAZF1-PHF1, EPC1-PHF1, and MEAF6-PHF1¹¹. However, molecular testing is not routinely conducted; therefore, in this case, as morphology and immunohistochemical studies were consistent with the diagnosis of primary ovarian LG-ESS, molecular studies were not performed in the KHCC lab or the referral lab.

Low-grade endometrial stromal sarcoma has indolent clinical behavior, with a relapse rate of up to 56%. A relapse may occur as late as 20 years after the hysterectomy and may be local, distant, or both¹¹; however, owing to the uncommon presentation of this tumor as primary ovarian, the prognosis is not well

known. Nevertheless, according to the largest series of cases studied recently, the prognosis is variable and better than other ovarian sarcomas⁶.

CONCLUSION

The tumor was described as a spindle cell lesion and diagnosed outside the institution as an ovarian stromal tumor, which is a differential diagnosis of ESS. Awareness of this entity and the possibility of an extrauterine primary location are important to arrive at the right diagnosis and appropriate management.

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