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CASE REPORT

A case of multiple metastatic low-grade endometrial stromal sarcoma

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Abstract

Endometrial stromal sarcoma (ESS) is a rare low-grade malignancy affecting mainly the uterus. Primary extrauterine occurrence of this tumor, involving most commonly the ovary, is exceedingly uncommon, and is retained after excluding an occult or misdiagnosed EES of the uterus.

A 79 year-old-woman, with a previous history of hysterectomy for prolapse and leiomyoma, presented with a bilateral ovarian mass. Morphological characteristics suggested ESS with extraovarian spread, peritoneal implants and endometriotic foci. The sections of the previous "leiomyoma" revealed ESS with prominent foci of epithelial-like structures. We discuss through this case clinicopathologic features of ESS, with emphasis on its unpredictable outcome.

Key words: uterus, ovary, endometrial stromal sarcoma, sex cord differentiation, metastasis

INTRODUCTION

Endometrial stromal sarcoma (ESS) is an uncommon low grade malignancy, and its occurrence at extrauterine sites is extremely rare in the absence of metastasis or extension of a primary uterine tumor.[1] In a series of ovarian ESS including 23 cases, there was a prior, synchronous or subsequent ESS of the uterus in 9 cases.[2]

The ovary is the most frequent extrauterine primary site of ESS occurring in 76% of cases.[3] The primary ovarian localization is sometimes difficult to definitively establish, particularly if there is a history of a hysterectomy for "leiomyomas".[4]

We report here the case of a 79-year-old woman, with a previous history of hysterectomy, who presented with bilateral ovarian ESS. We discuss through this case clinicopathologic features of this neoplasm, with emphasis on its wide morphologic spectrum and its unpredictable outcome.

CASE REPORT

A 79 year-old, gravida 10, para 6 woman presented with abdominal pain and swelling. Her history was remarkable for a triple operation for prolapse 10 months ago in another institution without preliminary radiologic examinations. On physical examination, a hard-to-define and fixed pelvic mass of 24 cm involving mostly the right side of the pelvis was palpated. Abdominopelvic computed tomography scan revealed a solid, well-circumscribed, lobulated right abdominopelvic mass with liquidian areas and heterogeneous enhancement, measuring 18 cm in diameter. A similar left-sided pelvic mass of 14 cm was also detected (Fig. 1).

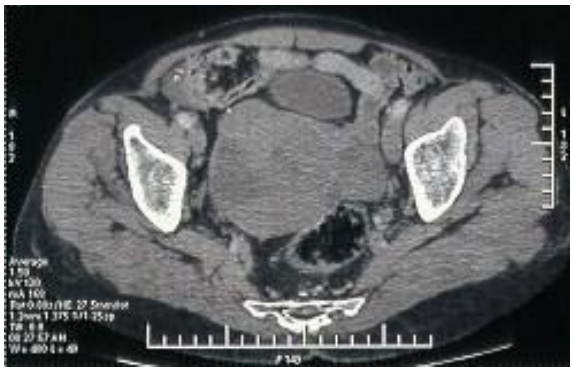

Figure 1 Axial pelvic computed tomography scan showing a bilateral adnexial mass with cystic components

Moreover, a hypodense splenic nodule of 11 mm was seen. No enlarged lymph nodes were identified.

Intraoperatively, both ovaries were transformed into solid tumoral masses. Moreover, a hard and irregular mesenteric nodule of 3 cm was detected suggesting possible metastasis. The left tumor was submitted for frozen section examination, and a diagnosis of

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stromal ovarian tumor was given. The patient underwent bilateral salpingoophorectomy. Grossly, the left and right masses measured 11 and 18 cm in greater size respectively and were soft in consistency. The external surface was lobulated and smooth. There was a tumoral-looking area of infiltration of the capsule extending along 1 cm on the left ovary. The cut surface was white with focal yellowish areas (Fig. 2).

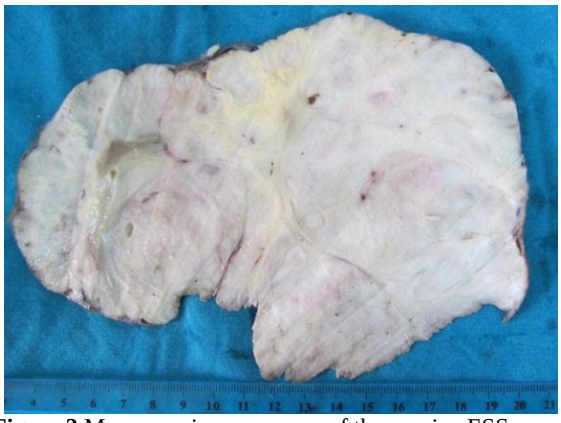

Figure 2 Macroscopic appearance of the ovarian ESS

Representative sections from the tumors were taken. Histologic examination of the two masses (Fig. 3)

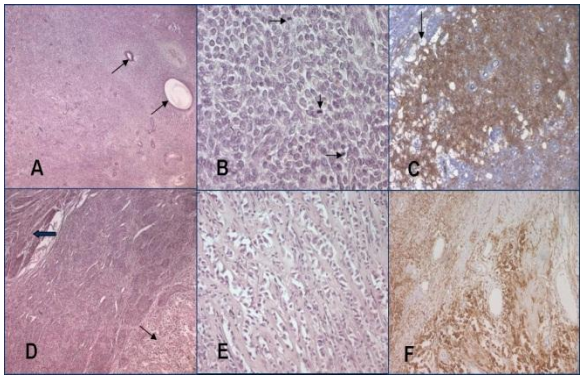

Figure 3 Histologic appearance:
A: Ovarian ESS composed of monotonous stromal cells with abundant small vessels and sparse endometrium-like glands (arrows) (hematoxylin-eosin stain, original magnification ×40)
B: Detail of stromal cells. Note the numerous mitoses (arrows) (hematoxylin-eosin stain, original magnification ×400)
C: Strong immunostaining for CD10 in the ovarian tumor. Note the foam cells (arrows) (immunohistochemistry x 100)
D: Uterine ESS infiltrating the myometrium (thick arrow) with epithelial-like areas (thin arrow) (hematoxylin-eosin stain, original magnification ×40)
E: Detail of epithelial-like structures in the uterine tumor (hematoxylin-eosin stain, original magnification ×200)
F: CD10 staining in the uterine tumor (immunohistochemistry x 100)

revealed a multinodular growth pattern and ovoid uniform cells resembling endometrial stromal cells. Cytological atypia were minimal to mild, and mitotic figures were frequent, namely up to 18 mitotic figures per 10 high power fields. Large areas of foamy cells were seen. Sparse benign endometrial glands were observed at the periphery of the left tumor as well as foci of ovarian endometriosis in the residual ovarian parenchyma. Call-Exner bodies were not identified. There were not necrotic areas. Extensive sampling failed to disclose lymphovascular invasion. Tumor cells infiltrated the ovarian capsules. Additionally, a reticulin-staining was performed. Reticulin fibers surrounded single tumor cells and demonstrated a network of interstitial thin walled blood vessels. Fallopian tubes were not involved by the tumor. The mesenteric nodule had the same histological features as the ovarian tumors. The neoplastic cells were immunoreactive to antibodies specific for CD10 and beta-catenin. All tumor cells expressed estrogen and progesterone receptors strongly. The immunostaining for desmin was sparse. No reactivities were found for epithelial markers (AE1/AE3, EMA), sml and melan A. On the basis of these features, a diagnosis of bilateral ovarian ESS with mesenteric metastasis was made. Since the patient had a history of leiomyoma, we reviewed the corresponding slides in order to rule out a primary uterine ESS. The leiomyoma was described macroscopically as a fairly well-circumscribed submucosal and intramural mass, 25 mm in diameter, protruding into the uterine cavity. Review of the slides showed that most parts of the tumor were composed of epithelial-like structures arranged in cords and small nests in hyaline background with foci of ischemic necrosis. Features of conventional ESS sarcoma were seen at the periphery. Nuclear atypia was mild and mitotic activity was low (one to two mitoses per 10 high-power fields). The tumor was focally infiltrative. There were discrete foci of adenomyosis. Based on these findings, the tumor was interpreted as ESS and epithelial-like areas were thought to be sex cord-like differentiation but immunohistochemical analysis failed to show reactivity for sex cord markers (inhibin, calretinin, CD99), the epithelial-like structures were only positive for CD10 and desmin and were negative for sml, caldesmon, AE1/AE3, estrogen and progesterone receptors. The typical ESS component was also strongly positive for CD10 but not for desmin. Final pathologic diagnosis was uterine ESS with epithelial structures reminiscent of sex cord-like differentiation.

Currently, the patient is under hormonal therapy with tamoxifen and is alive 5 months after diagnosis of

ovarian metastases. The follow-up scan showed enlarged pelvic lymph nodes.

DISCUSSION

ESS is a very rare sarcoma accounting for 0.25% of uterine malignancies.[5] It was initially divided into low grade ESS and high grade ESS. Current World Health Organization classification recognizes ESS and undifferentiated endometrial sarcoma.[6]

ESS tends to occur in premenopausal women. Histologically, it is a low-grade tumor but its relatively good prognosis is worsened by a high potential for local recurrence and possible metastasis.[1] In one series, the incidence of extrauterine spread was 25% and that of lymph node metastasis was 7%.[7]

In this case, the patient was first diagnosed with bilateral ovarian ESS which was thought to be primitive especially as there were foci of ovarian endometriosis. It was suggested in fact that ovarian ESS may arise with endometriosis.[3] However, bilaterality, multinodular ovarian growth pattern and surface implants plead for corpus primary with ovarian metastasis. Moreover, extrauterine sites of ESS are very uncommon and since the patient had a history of leiomyoma, we had to exclude ESS metastatic from the uterus, which is much more frequent, before giving a diagnosis of primary ovarian ESS.[8] We reviewed the slides to eliminate the uterine origin and we discovered an ESS with prominent foci of epithelial-like structures.

Pathological features of the tumors described in our case were similar to those of previous reports including an infiltrative and diffuse proliferation of uniform round or oval stromal cells and abundant small vessels resembling endometrial spiral arterioles. Presence of foam cells has also been described. Other forms of differentiation may be seen in ESS, namely smooth muscle differentiation and epithelial patterns including endometrioid-type glands as seen in the ovarian tumor of our case and sex cord differentiation.[4,8,10] In the latter form, the tumor contains epithelial-like or sex cord-like elements often with epithelioid appearance, arranged in nests, cords, trabeculae, solid, or tubular structures.[5]

CD10 is currently regarded as a specific marker for endometrial stromal tumors and is also expressed in normal endometrial stromal cells. Other characteristic immunohistochemical features of ESS include reactivity to antibodies specific for vimentin, estrogen receptors and progesterone receptors. Most endometrial stromal sarcomas express also beta-catenin.[6,11] Alpha smooth muscle actin and keratin may be positive.[12] Desmin and h-caldesmon are generally negative. Areas of smooth muscle differentiation are reactive for smooth muscle markers (h-caldesmon, desmin, smooth muscle actin) as well as for CD10.[13] Calretinin, inhibin, CD99 and MelanA seem to be the most characteristic sex cord markers and ESS with sex cord-like elements usually express only 1 sex cord marker, mostly calretinin.[14]

The histologic features of the metastases may not be similar to those of the primary[15] In this case, the uterine tumor, unlike the ovarian ones, showed large areas of epithelial-like structures thought to be sex cord differentiation, but immunohistochemistry was inconsistent with this diagnosis as sex cord markers were negative. The differential diagnosis included epithelioid leiomyoma and epithelial neoplasm. These tumours were ruled out on immunohistochemistry as CD10 was positive. Expression of desmin, found in these epithelial-like areas, is reported in sex cords elements[6] and morphology, negativity of smooth muscle actin were not consistent with smooth muscle differentiation, so we retained the diagnosis of ESS with sex cord-like differentiation.

Light microscopic analysis suffices in the majority of cases to establish the diagnosis of ESS[4] but this neoplasm may be confused, especially when present at an extrauterine site, with several neoplasms such as solitary fibrous tumor, adenosarcoma, epithelioid smooth muscle tumors, synovial sarcomas sex cord-stromal tumors.[3,12] Immunohistochemistry play a role in evaluating these tumors.

Since ESS frequently express estrogen and progesterone receptors, treatment with hormonal therapies may be efficacious for patients with advanced, residual or recurrent disease.[3]

CONCLUSION

We present here a rare case of a multiple metastatic malignancy, which consisted of bilateral ESS, revealing a misdiagnosed ESS of the uterine corpus. In this case, there was a significant delay in diagnosis because of lack of adequate radiologic explorations before hysterectomy for prolapse. ESS is a low grade tumor with high rate of local recurrences; it may also disseminate beyond its site of origin and cause multiple metastases. In some cases, identification of the site of origin has prognostic implications and is necessary for appropriate staging and treatment.

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