A case of multiple metastatic low-grade endometrial stromal sarcoma arising from an ovarian endometriotic lesion

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The development of endometrial stromal sarcomas (ESSs) in foci of endometriosis is extremely rare, and few cases have been reported in the literature to date, particularly with regard to multiple extrauterine ESS. Here we report a case of endometrial stromal sarcoma with multiple metastasis that arose from an ovarian endometriotic lesion. The literature is also briefly reviewed.

Key Words: Endometrial stromal sarcomas, Endometriosis, Ovary

INTRODUCTION

Uterine sarcomas are rare tumors that are characterized by rapid progression and a poor prognosis. Histologically, they are classified as leiomyosarcomas, endometrial stromal sarcomas (ESSs) and mixed mesodermal tumors. ESSs are rare neoplasms that comprise approximately 0.2% of all uterine malignancies and about 10-15% of all uterine sarcomas.1 In particular, the development of ESS in endometriotic lesions is very rarely reported. Such extrauterine ESSs can develop in the ovary, fallopian tube, pelvic cavity, colon and retroperitoneum.2 Since ovarian ESS is so rare, very little is known about its pathogenesis.

However, at least in some cases, it may be a metastatic tumor that originates from a uterine tumor, perhaps years after a hysterectomy was performed to remove the primary tumor.

Here we describe a case of low-grade ESS with multiple metastasis that arose from an ovarian endometriotic lesion after hysterectomy.

CASE REPORT

A 50-year-old gravida 4, para 3, abortion 1 woman presented with lower back pain that had lasted for 1 month. In April 2000, the patient underwent total abdominal hysterectomy due to uterine myoma in our hospital. The uterus was sent for pathohistological analysis. Histologically, the myoma appeared to be an adenomyomtous polyp. In September 2008, the patient returned to our hospital due to back pains. Computed tomography (CT) showed a necrotic solid mass measuring 7 cm in diameter in the left adnexa, a para-aortic solid mass lesion, and left renal vein and inferior vena cava thrombosis, which was suggestive of nodal metastasis, probably pelvic nodal metastasis (Fig. 1). We performed an ultrasound-guided biopsy of the para-aortic solid mass. Histological analysis revealed a spindle cell tumor with malignant features, including high cellularity and abnormal mitotic figures. The data from the tumor marker studies are as follows: cancer antigen (CA)-125, 118.4 IU/ml; CA 19-9, 38.7 IU/ml; carcinoembryonic antigen (CEA), 1.8 ng/ml; alpha-foetoprotein (AFP), 1.6 ng/ml. The complete blood cell count data are as follows: hemoglobin, 12.6 g/dl; white blood cell count, 8,900/mm3; platelet count, 273,000/mm3. Other examinations, including urinalysis, liver function tests and renal function tests, revealed no abnormalities. Esophagoduodenoscopy revealed reflux esophagitis and gastropathy. Colonoscopy detected hemorrhoids and a 0.2 cm diameter polyp 50 cm from the anal verge. Histologically, the tumor appeared to be a tubular adenoma. On the basis of these findings, we performed an exploratory laparotomy followed by a tumor debulking procedure. The surgical procedure consisted of a bilateral salpingoophorectomy, an appendectomy, an omentum biopsy, and a posterior cul-de-sac area biopsy and cytology. In the left adnexa, a 6×5 cm-sized mass was detected. It was composed of a solid and a cystic portion. It adhered to the posterior cul-de-sac and was accidentally ruptured during the operation. In the right adnexa, multiple small nodules approximately 1cm in
diameter were detected. In addition, the right adnexa had adhered to the omentum. A hard nodule about 2-3 cm in diameter was detected at the right infundibulopelvic ligament. The para-aortic lymph node was enlarged to a size of 10×8×5 cm and had invaded the aorta, inferior vena cava and common iliac vessels. Consequently, it was not possible to perform an en bloc excision of the para-aortic mass. The rectum contained numerous nodules up to 0.5 cm in diameter. The appendix, liver surface and diaphragm were normal.

Grossly, the left ovary measured 8.0×6.5×4.0 cm in size and weighed 83 gm. The external surface was pale pink to whitish and smooth. Upon sectioning, the cut surface showed a diffuse dark reddish hemorrhagic lesion containing a focal yellowish solid lesion (Fig. 2). The right ovary had a smooth surface and a unilocular cyst with hemorrhaging. The cul-de-sac mass measured 1.3×0.5 cm in size. The omentum exhibited multiple small nodules.

Microscopically, the left ovary exhibited perivascular whoring proliferation of plump spindle cells with scanty cytoplasm and indistinct cell borders. There were many irregular small
from submesothelial pluripotent mullerian cells. Ovarian tumors such as gastrointestinal stromal tumors (GISTs) are extremely rare and differentiating such tumors from other tumors. The development of ESS in foci of endometriosis is extremely rare and differentiating such tumors from other tumors. The microscopic differential diagnosis of ovarian ESS includes three major categories of neoplasms: namely, other pure sarcomas; malignant mesodermal mixed tumors, particularly mesodermal adenosarcoma; and sex cord-stromal tumors. The major diagnostic features that are helpful in identifying the endometrioid stromal nature of an ovarian tumor are listed in Table 2. The possible origins of ESS of the ovary are endometriosis of the usual type and pure sarcoma endometriosis (foci of gland-free endometrial stroma in the ovary). Similar neoplasms have arisen in association with endometriosis in various other locations. It is also possible that some ESSs of the ovary arise directly from ovarian stromal cells that have undergone neometaplasia into endometrial stromal-type cells. In this case, the left ovary showed gradual progression of usual endometrioid foci to low grade ESS (Fig. 3A) with multiple metastatic nodules in the right ovary, cul-de-sac and omentum. ESS has traditionally been divided into two categories, namely, low-grade and high-grade stromal sarcoma. In most studies, ESS comprises less than 10% of uterine sarcomas. The mitotic activity of LGSSs is low, namely, less than 10/10 HPF. High-grade stromal sarcomas (HGSSs), on the other hand, are tumors with mitotic activities that generally exceed 10/10 HPF. Histological analyses of extrauterine extraovarian ESS reveal infiltrative or tongue-like multinodular growth patterns. Cytological atypia is minimal to mild, and mitotic figures are infrequently seen, namely, up to 5 mitotic figures per 10 HPF. Vascular and lymphatic invasion by the tumor is occasionally present. Characteristic immunohistochemical features of ESS include reactivity to antibodies specific for Vimentin, ER and CD10, and nonreactivity to antibodies against CD117, smooth muscle actin (SMA) and cytokeratin (CK). A recent study has shown that among the cases of ESS that were examined, all cases were immunoreactive to anti-CD10 (5/5 cases) and anti-progesterone receptor (10/10 cases) antibody, most reacted with anti-estrogen receptor antibody (9/11 cases), 5/9 and 3/7 were focally positive for smooth muscle actin and desmin, respectively, and all were negative for CD34 (0/7 cases).

<table>
<thead>
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<th>Ab</th>
<th>Endometrial stromal sarcoma</th>
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<tr>
<td>CD10</td>
<td>+</td>
</tr>
<tr>
<td>Vimentin</td>
<td>+</td>
</tr>
<tr>
<td>Ki-67</td>
<td>+</td>
</tr>
<tr>
<td>ER</td>
<td>3+</td>
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<tr>
<td>PR</td>
<td>3+</td>
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<tr>
<td>SMA</td>
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CD10: cluster of differentiation 10, ER: estrogen receptor, PR: progesterone receptor, SMA: smooth muscle actin

Table 1. Result of immunohistochemical examination

Table 2. Microscopic features of ovarian endometrioid stromal sarcoma

<table>
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<th>Diffuse growth pattern</th>
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<tr>
<td>Extraovarian intravascular growth</td>
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<tr>
<td>Small round or oval cells with scanty cytoplasm</td>
</tr>
<tr>
<td>Pericellular reticulum</td>
</tr>
<tr>
<td>Fibromatous component</td>
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<td>Associated endometriosis</td>
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Of the extrauterine ESSs, the ovary is the primary site in 76% of cases, while extragonadal sites accounts for the remaining 24%. The microscopic differential diagnosis of ovarian ESS includes three major categories of neoplasms: namely, other pure sarcomas; malignant mesodermal mixed tumors, particularly mesodermal adenosarcoma; and sex cord-stromal tumors. The major diagnostic features that are helpful in identifying the endometrioid stromal nature of an ovarian tumor are listed in Table 2. The possible origins of ESS of the ovary are endometriosis of the usual type and pure sarcoma endometriosis (foci of gland-free endometrial stroma in the ovary). Similar neoplasms have arisen in association with endometriosis in various other locations. It is also possible that some ESSs of the ovary arise directly from ovarian stromal cells that have undergone neometaplasia into endometrial stromal-type cells. In this case, the left ovary showed gradual progression of usual endometrioid foci to low grade ESS (Fig. 3A) with multiple metastatic nodules in the right ovary, cul-de-sac and omentum. ESS has traditionally been divided into two categories, namely, low-grade and high-grade stromal sarcoma. In most studies, ESS comprises less than 10% of uterine sarcomas and most are low-grade stromal sarcomas (LGSSs). The mitotic activity of LGSSs is low, namely, less than 10/10 HPF. High-grade stromal sarcomas (HGSSs), on the other hand, are tumors with mitotic activities that generally exceed 10/10 HPF, although some HGSSs can also have mitotic activities below 10/10 HPF. Histological analyses of extrauterine extraovarian ESS reveal infiltrative or tongue-like multinodular growth patterns. Cytological atypia is minimal to mild, and mitotic figures are infrequently seen, namely, up to 5 mitotic figures per 10 HPF. Vascular and lymphatic invasion by the tumor is occasionally present. Characteristic immunohistochemical features of ESS include reactivity to antibodies specific for Vimentin, ER and CD10, and nonreactivity to antibodies against CD117, smooth muscle actin (SMA) and cytokeratin (CK). A recent study has shown that among the cases of ESS that were examined, all cases were immunoreactive to anti-CD10 (5/5 cases) and anti-progesterone receptor (10/10 cases) antibody, most reacted with anti-estrogen receptor antibody (9/11 cases), 5/9 and 3/7 were focally positive for smooth muscle actin and desmin, respectively, and all were negative for CD34 (0/7 cases).
activity being of major prognostic significance. The prognosis of patients with low-grade tumors is considerably better than that of patients with other pure ovarian sarcomas. This case illustrates the findings of low-grade ESS with multiple metastasis arising from an ovarian endometriotic lesion.

REFERENCES