



Case report

Primary low-grade endometrial stromal sarcoma of the omentum

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1. Background

Endometrial stromal sarcoma (ESS) is a rare mesenchymal tumor, comprising approximately 0.2% of uterine malignancies and up to 15% of uterine sarcomas (Back et al., 2016). Patients typically present with an enlarged uterus, pelvic pain, and vaginal bleeding. Management of these tumors includes surgical resection with or without adjuvant therapy (Masand et al., 2013). Extra-uterine endometrial stromal sarcoma (EESS) has been documented in the literature and is a rare occurrence that is the result of malignant transformation of endometriotic implants. Our literature review of PubMed indexed articles (1970 to 2016) identified 75 total cases of EESS, none of which described an isolated implant involving the omentum. Importantly, the majority of EESS cases reported are confined to the ovaries, although other common sites include the pelvic peritoneum, rectovaginal septum, vagina, and colorectal serosa (Heaps et al., 1990; Masand et al., 2013). We report a case of a woman with low-grade endometrial stromal sarcoma arising from malignant transformation of omental endometriosis managed with surgical resection followed by adjuvant hormonal therapy.

2. Case

A 42-year-old Caucasian gravida 5 para 3 with a history of stage IV endometriosis presented for consultation for persistent pelvic pain and left adnexal mass. The patient previously underwent colonoscopy with biopsy confirming rectal involvement by endometriosis. Despite leuprolide depot injections, the patient continued to have refractory cyclic pelvic pain. Her past medical history was remarkable for Hepatitis C. The patient strongly desired surgical management of her endometriosis after failing multiple lines of conservative therapy. Pre-operative pelvic magnetic resonance imaging (MRI) demonstrated several solid and cystic lesions consistent with endometriosis adjacent to the rectum, sigmoid colon and cervix including a 5.4 cm left adnexal mass and thickening of the posterior vaginal wall. On bimanual palpation, the uterus was fixed and immobile, with firmness and induration noted along the distal apical portion of the recto-vaginal septum.

Following informed consent, the patient underwent an exploratory laparotomy, class 2 radical hysterectomy, bilateral salpingo-

oophorectomy with en bloc resection of the rectum and sigmoid colon followed by primary end-to-end anastomosis. At the time of surgery, the patient was found to have extensive pelvic endometriosis with obliteration of normal tissue planes. Importantly, exploration and palpation of the upper abdomen was notable for several nodular, hemorrhagic omental lesions, measuring 4.0 cm in greatest dimension. Given these findings, a total infragastric omentectomy was performed. Intra-operative pathologic evaluation of the resected specimen was consistent with endometriosis. Additional anterior abdominal wall and pelvic peritoneal endometriotic implants were identified and resected. The patient's post-operative course was uncomplicated, and she was discharged home on post-operative day 4.

Gross pathologic examination of the surgical specimens consisted of a uterus and cervix, parametria, bilateral ovaries and fallopian tubes, a sigmoidal mesenteric nodule, omentum, and abdominal peritoneal wall nodules. Multiple hemorrhagic nodules, histologically consistent with endometriosis involved the left para-uterine and adnexal soft tissues, colonic wall, peri-colonic fibroadipose tissue, abdominal peritoneal



Fig. 1. Gross specimen. (A) Exophytic and polypoid mass involved the colonic mucosa and (B) diffusely nodular and fibrotic omentum.

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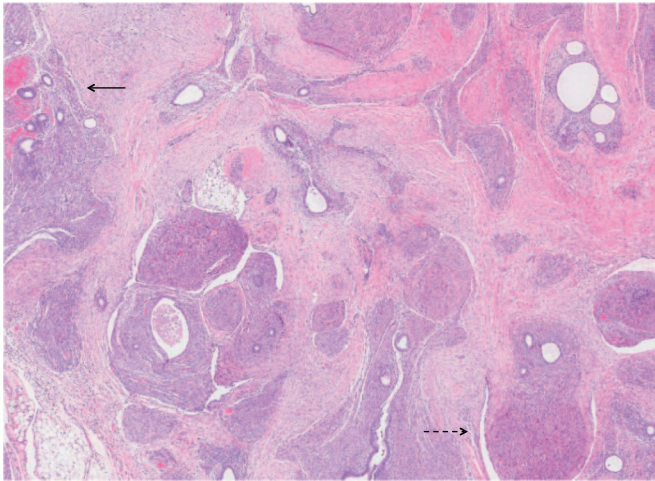


Fig. 2. Image of a focus of endometriosis top left (solid arrow) with classic features of endometrial stromal sarcoma protruding into vascular space in bottom right (dashed arrow).

wall and sigmoid mesentery. Additionally, the left ovary contained an endometriotic cyst. An exophytic, polypoid mass involving the omentum was diffusely nodular and fibrotic. The colon and omentum were extensively sampled given the atypical gross findings (Fig. 1). The omental mass had multiple foci of stromal proliferation without glands, diagnostic for low-grade endometrial stromal sarcoma, arising in a background of extensive endometriosis (Fig. 2). Immunohistochemical studies demonstrated that tumor cells of the omentum were diffusely positive for estrogen receptor (99%), progesterone receptor (99%), CD10, and negative for cyclin-D1 (Fig. 3). This diagnosis was confirmed on outside consultation at the University of Texas M.D. Anderson Cancer Center. All other surgical specimens were negative for malignancy, although found to have extensive endometriosis.

After discussion and counseling, the patient was started on adjuvant hormonal therapy with Letrozole given strong tumor expression of estrogen and progesterone receptors. She remains without evidence of disease recurrence nine months following surgery based on examination and diagnostic imaging.

3. Discussion

Endometriosis is the presence of estrogen dependent endometrial tissue outside the uterus and is a common benign gynecologic condition that affects up to 10% of reproductive aged women (Giudice, 2010). Ovarian carcinoma arising in the background of endometriosis was first documented in 1925 by Irvin et al. (Irvin et al., 1998). Since that time, multiple case reports have described malignant transformation of endometriotic implants, most commonly arising within the ovary. In those with endometriosis, malignant transformation takes place in approximately 0.7–1.0% of patients (Irvin et al., 1998). Malignant transformation of extra-ovarian endometrial implants is uncommon and generally found to have clear cell or endometrioid histology, and very rarely, endometrial stromal sarcoma (Irvin et al., 1998).

In the largest series published of extra-uterine endometrial stromal sarcoma (EESS) cases, Masand et al. reported on 63 cases from MD Anderson Cancer Center. They report that EESS is commonly associated with endometriosis and given its indolent nature, long-term follow-up is recommended for late recurrences. The most frequent presenting symptoms included an abdominal or pelvic mass, pain, vaginal bleeding, and gastrointestinal symptoms. The most common sites involved included the ovaries, rectal wall, pelvic peritoneum and vagina. Endometriosis was noted in 30 of the 63 cases, and close to 25% of the cases had an initial pathologic diagnosis other than EESS including sex cord stromal tumor, gastrointestinal stromal tumor, and leiomyosarcoma. Of the 53 patients that were followed, 33 patients had recurrent disease, 9 patients died of the disease, 7 of which had bowel involvement, and 3 patients had tumors with areas of dedifferentiation (Masand et al., 2013). A critical review of patients who died of disease

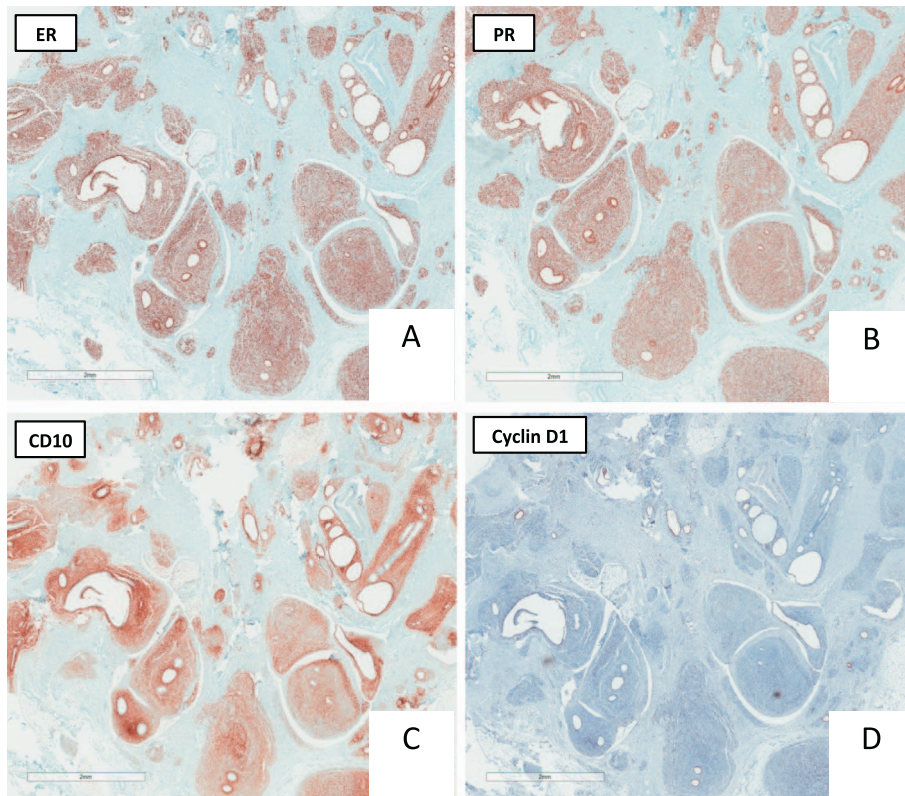


Fig. 3. Immunohistochemical studies (panel of four IHCs) demonstrate that the tumor cells of the omentum are diffusely positive for (A) estrogen receptor (99%), (B) progesterone receptor (99%), (C) CD10, and (D) negative for cyclin-D1.

failed to identify clinical-pathologic characteristic predictive of poor oncologic outcome.

The treatment of EESS has been adapted from paradigms used in management of the more common endometrial stromal sarcomas. Surgical resection remains the primary treatment for these tumors (Chang et al., 1993). The role of radiation, chemotherapy, and hormonal therapy remains relatively unknown (Chang et al., 1993) (Rauh-Hain and del Carmen, 2013). Given the near ubiquitous expression of estrogen and progesterone receptors, hormonal therapy is commonly employed in an effort to suppress stromal proliferation (Reich and Regauer, 2007) (Masand et al., 2013). In our case, given bilateral oophorectomy at the time of surgery, the patient was started on an oral aromatase inhibitor.

Despite complete surgical resection, delayed recurrence is possible and close follow-up, inclusive of regular pelvic examinations and imaging based on symptoms and physical findings is warranted (Reich and Regauer, 2007). While rare, EESS may arise in the background of endometriosis, and a careful intraoperative assessment of the abdominal cavity during operative exploration for severe endometriosis should be performed to assess for extra pelvic disease. Adequate and appropriate tissue sampling can then be conducted to exclude malignant transformation where appropriate. EESS arising from extra-uterine endometriosis can be multifocal, and it is critical to sample the endometriotic implants adequately, especially those forming mass-like lesions, so as to not overlook a malignancy that may require therapy and appropriate long term follow up.

Conflict of interest statement

The authors declare no conflicts of interest as they relate to the published material. RNE has received honoraria from AZ Oncology, Genentech and Clovis Oncology.

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