Primary extrauterine endometrial stromal sarcoma: response to hormone therapy

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Introduction

Endometrial stromal sarcomas (ESS) of the uterus are hormone-sensitive tumors. There have been reports in the literature confirming the regression of ESS with progestins, gonadotropin analogues, and aromatase inhibitors. We report a case of primary extrauterine ESS of the rectovaginal septum (RVS), which was poorly responsive and, in fact, progressed on progestin therapy. The question arises: is the evident lack of response to oral progestin in our case an exception or a trend more commonly seen in primary extrauterine, extraovarian ESS? To the best of our knowledge, there has been no report in the literature to address this question. Therefore, we conducted a review of the literature to evaluate the response of these tumors to hormone therapy in relation to their estrogen and progesterone receptor status.

Case Report

A 45-year-old G3P0030 African American woman underwent a supracervical hysterectomy and bilateral salpingo-oophorectomy for chronic pelvic pain. The pathology report of the surgical specimen confirmed the presence of endometriosis. Subsequently, six years later, the patient presented with vaginal bleeding, lower abdominal pain, dyspareunia, and difficult defecation. Vaginal examination showed active bleeding from an exophytic polypoid mass in the posterior vaginal fornix. Rectovaginal examination revealed a 4x3 cm mass in the rectovaginal septum (RVS) and a smooth rectal mucosa. Narrowing was noted on proctoscopy at 8 cm distance owing to extrinsic compression from the mass. The vaginal polyp was removed and biopsies were obtained from the adjacent normal-appearing vaginal mucosa at the base of the mass. On pathological examination, the lesion showed an overgrowth of endometrial-like stromal cells with scattered benign-appearing endometrial-type glands. Stromal cells showed mild to moderate cytological atypia. The tumor was positive for both estrogen and progesterone receptors. The differential diagnosis included polypoid endometriosis; however, stromal overgrowth with atypia and mitosis favored a low-grade Mullerian adenosarcoma. Gastrointestinal stromal tumor (GIST), though a strong possibility when masses are encountered in this location, was ruled out effectively by morphology. Additionally, immunohistochemical staining with CD117 (not performed in our case) is considered valuable in the diagnosis of GIST.

Given that the tumor was hormone receptor positive, megestrol acetate was prescribed initially for the patient in an attempt to shrink the mass in the RVS. Despite hormone therapy progression of the tumor with increased vaginal bleeding was noted. Therefore, the patient underwent a posterior exenteration with end-sigmoid colostomy four months after her initial presentation. Pathological examination revealed a low-grade endometrial stromal sarcoma (ESS). Subsequently, the patient also received adjuvant radiation because of copious mucoid material being present on debulking, and she has remained disease free at 18 months follow-up.

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Key words: extrauterine, endometrial stromal sarcoma, rectovaginal septum, hormone therapy

Contributions: ET conception and design; GG, AA and ET manuscript writing; ET final approval of the manuscript.

Conflict of interest: the authors report no conflicts of interest.

Received for publication: 12 July 2009.
Revision received: 16 September 2009.
Accepted for publication: 16 September 2009.

Rare Tumors 2009; 1:e39
doi:10.4081/rt.2009.e39

Discussion

Endometrial stromal sarcoma is a rare mesenchymal neoplasm that usually occurs as a primary tumor of the uterus. However, it rarely

Table 1. Response to hormone therapy in primary extrauterine endometrial stromal sarcoma.

Author	Site of tumor	Treatment	Treatment response	ER/PR status
*Kusaka *et al.*	Cul-de-sac	GnRH analogue, danazol	Disease progression	Strongly positive
Lacroix-Trilki *et al.*	Sciatic nerve	GnRH analogue	Disease progression	Strongly positive
Present case	Rectovaginal septum	Megestrol acetate	Disease progression	Strongly positive

Only case reports of patients with extrauterine extraovarian ESS with follow-up data were included in the review. ER, estrogen receptor; PR, progesterone receptor; GnRH, gonadotropin releasing hormone *High-grade tumor arising from endometriosis (all other cases had low-grade tumors).

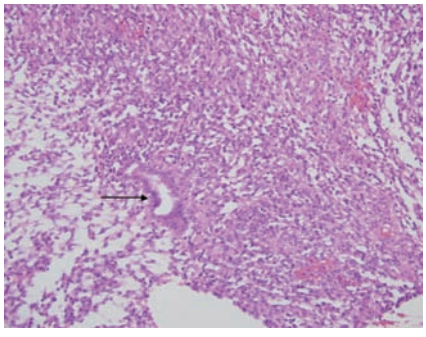

Figure 1. High power view (magnification: 400X) of endometrial stromal sarcoma with an entrapped benign gland (indicated by the arrow) (Stain: hematoxylin and eosin.)

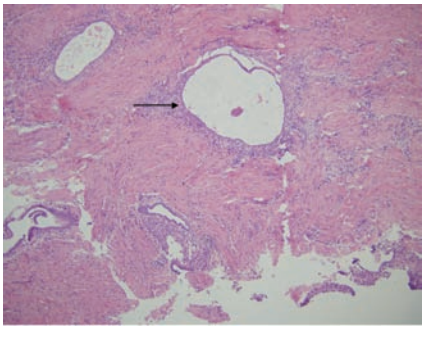

Figure 2. Arrow indicating the area of extensive endometriosis. (Stain: hematoxylin and eosin; magnification: 200X.)

originates in sites other than the uterus and ovaries. The role of hormone therapy is well documented in primary low-grade ESS of the uterus, in patients with no evidence of residual disease after surgical treatment as well as in patients with advanced and recurrent disease. It has been shown to be effective, particularly in tumors that express both estrogen and progesterone receptors and which have demonstrable evidence of concomitant endometriosis. Our case is unique, however, because it was a low-grade tumor positive for both estrogen and progesterone receptors; yet the tumor progressed on progestin therapy. In our review of the literature, we found two other reports (Kusaka *et al.*,[1] Lacroix-Triki *et al*.[2]) describing patients with primary extrauterine, extraovarian ESS in whom hormone therapy alone was administered. The treatment used and the clinical response relative to estrogen and progesterone receptor status is summarized in Table 1.

Interestingly, all three patients (including our case) shown in Table 1 did not respond to hormone therapy. All reported associated endometriosis. Two other patients[3,4] received hormone therapy in conjunction with chemotherapy; however, it is not feasible to assess independently the role of hormone therapy in these cases. One explanation for the observed lack of response may be that, in spite of the hormonal receptorship, not all low-grade ESS respond to hormone therapy. Various factors have been shown to influence hormone responsiveness: concentration of the sex steroid receptor, and relative expression of the progesterone receptor (PR) isoforms (PR-A and PR-B). It is conceivable that receptor concentration and the predominant isoform may vary in ESS originating in the uterus versus extrauterine sites, such as to make the latter less hormone responsive.

In summary, we report a trend favoring poor responsiveness of extrauterine, extraovarian ESS to hormone therapy. This is significant given the predilection to extrapolate from the treatment responses observed in uterine ESS. Although our conclusion is based on a limited number of cases, our report raises an important question that needs to be investigated further.

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