



Case report

Extra-uterine endometrial stromal sarcoma of the left adnexa and distal ureter: A case report

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1. Introduction

Endometrial stromal sarcomas (ESS) are rare, indolent malignancies that account for 15–25% of uterine sarcomas and 0.2% of all genital tract malignancies (Sylvestre and Dunton, 2010; Dahhan et al., 2009; Efareed et al., 2019; Masand et al., 2013; Masand, 2018). Literature on the topic includes case reports, small retrospective case series and literature reviews; no high level evidence exists. The predominant treatment consists of total abdominal hysterectomy and bilateral salpingo-oophorectomy plus or minus adjuvant therapy. Adjuvant treatment typically consists of progesterone therapy, as many ESS tumors are found to be estrogen and progesterone receptor positive.

Primary extra-uterine endometrial stromal sarcomas (EESS) are endometrial stromal sarcomas that occur in the absence of uterine involvement (Efareed et al., 2019; Masand, 2018). These very rare entities are believed to be strongly associated with foci of endometriosis (Efareed et al., 2019; Masand et al., 2013; Masand, 2018; Yadav et al., 2019; Buchholz et al., 2017). Common locations for EESS include the ovaries, abdomen and pelvis (Masand et al., 2013). They usually present a significant diagnostic challenge, partly due to their extra-uterine location, low incidence, non-specific symptoms, and ability to mimic other pathologies (Efareed et al., 2019; Masand, 2018; Buchholz et al., 2017).

We present a case of EESS in a patient with no documented history of endometriosis or previous gynecologic pathology. In addition to invading the left ovary and pelvic side wall, EESS was also found within the lumen of the left distal ureter resulting in hydronephrosis.

2. The case

Our patient was a 53-year-old, G2P2, premenopausal woman who presented with right sided back and flank pain. Past medical history was

significant for multiple sclerosis, two Cesarean sections, a tubal ligation, and a remote re-implantation of the left ureter as a child. Unfortunately, the indication for ureteric reimplantation and potential implications for future malignant transformation are unknown.

On physical examination, there was no cervical or inguinal lymphadenopathy. Abdominal examination was negative. Speculum exam revealed a normal cervix and bimanual exam noted an anteverted, non-bulky uterus with some adjacent fullness to the right parametria. Pelvic-rectal exam was unremarkable.

CT chest, abdomen and pelvis revealed a solid and cystic left adnexal mass measuring 6 × 6.7 cm (Fig. 1). The mass appeared to involve the left ureter, causing hydronephrosis. An enlarged left internal iliac lymph node was measured at 1.6 cm. No extra-pelvic metastatic disease was identified. CA-125 was elevated at 217.

The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, retroperitoneal resection of cancer, infracolic omentectomy, excision of left ureteric mass and left ureteric reimplantation by Gynecologic Oncology at a tertiary center. Intraoperatively, disease was noted in the posterior cul de sac, right pelvic sidewall peritoneum, left pelvic retroperitoneum and left ureter. Retroperitoneal dissection of the ovarian mass off the external iliac artery and vein, as well as the ureter was completed with identification of a 2 cm non-mobile mass in the lumen of the left distal ureter. Urology was consulted intraoperatively. The ureteric lesion was resected and primary reimplantation of the left ureter was performed. There was microscopic residual disease at the end of the procedure. The patient's postoperative course was uncomplicated.

On final pathology, pelvic cytology, omentum, and uterus were negative for malignancy. The left adnexa and retroperitoneal tumor left pelvic lymph node and ureteric mass revealed low grade biphasic proliferation consistent with a low grade endometrial stromal sarcoma with glandular differentiation. FISH for rearrangement of JAZF1 and PHF1

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was negative. ER/PR staining was positive (Fig. 1). Expert gynecologic pathology review confirmed the diagnosis of extrauterine endometrial stromal sarcoma arising in the background of endometriosis.

The patient received adjuvant oral megestrol acetate 160 mg daily. Pelvic MRI eight months postoperatively showed no evidence of recurrent malignancy within the pelvis. Megestrol acetate was discontinued secondary to patient intolerance following 16 months. The patient was transitioned to oral letrozole 2.5 mg daily. She remains free of disease on letrozole after 20 months of follow up. Adjuvant hormonal therapy was started at the lowest therapeutic dose cited in the literature, to minimize the risk of side effects.

3. Discussion

The EESS case presented is unique due its involvement of the urinary tract with disease located within the ureteric lumen in the context of a previous left ureteric surgery and reimplantation. Very few reported cases of EESS have involved the urinary tract. The closest case reported involved a patient presenting with azotemia and found to have disease of the ovaries and periureteral tissue (Masand et al., 2013; Masand, 2018). The only other reported cases of EESS with urinary tract involvement consist of three case reports describing bladder primaries (Yadav et al., 2019). All other cases of urinary tract involvement (bladder or ureter)

found in the literature are residual or recurrent uterine ESS (Sylvestre and Dunton, 2010; Buchholz et al., 2017; Leunen et al., 2004; Tian et al., 2014; Yamaguchi et al., 2015).

EESS is an extremely uncommon subtype of the already rare ESS. Masand et al. published the largest case series to date on EESS, describing 63 cases at a single institution over a 21-year period (Masand et al., 2013). Twenty-five of those cases were primary ovarian EESS. A recent literature review by Efared et al. described 90 published cases of EESS involving the ovaries (Efared et al., 2019). Our case therefore contributes to a body of literature on an entity consisting of approximately 100 cases and is novel due to the separate disease within the left ureter at presentation; it also highlights a question of association with previous ureteric implantation. While the indication for the initial ureteric surgery is not known, theoretically previous ureteric instrumentation may have predisposed to development of this unique pattern of malignancy. Given the paucity of cases reported, this hypothesis is neither supported nor refuted in the literature.

Despite limited cases of EESS and a lack of evidence-directed therapies, most management plans for EESS follow the same guidelines as uterine ESS. Thus, surgical resection plus or minus debulking has been heavily relied upon (Buchholz et al., 2017). As in the case of our patient, a total abdominal hysterectomy and bilateral salpingo-oophorectomy is typically carried out to further rule out the possibility of a uterine

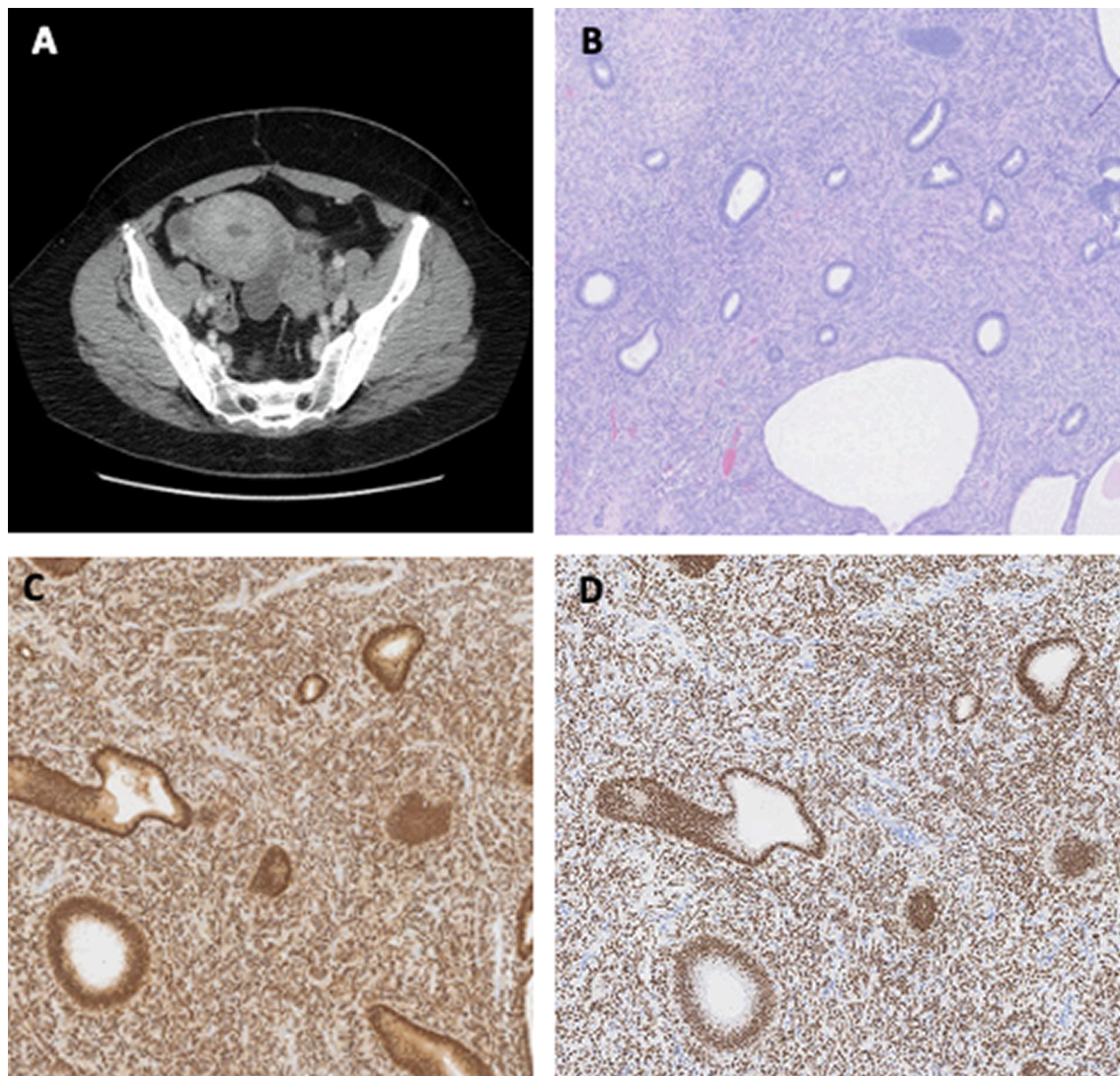


Fig. 1. Radiologic and histologic images. A – Preoperative axial CT of adnexal mass. B – Representative H&E stain from surgical specimen. C – Representative image of ER positivity. D – Representative image of PR positivity.

primary.

A significant portion of the EESS literature discuss the utility of adjuvant therapy. There appears to be very limited benefit to adjuvant chemotherapy or radiation in treatment of EESS. The majority of the literature focuses on hormonal adjuvant therapies given the known PR and ER positivity of these tumors (Sylvestre and Dunton, 2010; Dahhan et al., 2009; Buchholz et al., 2017; Leunen et al., 2004; Yamaguchi et al., 2015). The benefit of hormonal therapy in ESS and EESS appears to be limited to advanced or metastatic disease (Dahhan et al., 2009; Leunen et al., 2004; Yamaguchi et al., 2015). Studied hormonal therapy options include aromatase inhibitors (e.g., letrozole) and synthetic anti-estrogenic progestins (e.g., megestrol acetate).

Given that many of these cases are initially misdiagnosed, our case further emphasizes the importance of keeping EESS on the differential for ovarian, pelvic and urinary tract tumors (Masand, 2018; Yadav et al., 2019). Symptoms are non-specific and often not typical for gynecological cancers. Roughly two-thirds have been linked to previous endometriosis and possible malignant transformation of its stromal components (Efared et al., 2019; Masand et al., 2013; Masand, 2018; Yadav et al., 2019; Buchholz et al., 2017). Genetic studies looking for rearrangements in JAZF1/SUZ12 and JAZF1/PHF1 may help with diagnosis (Efared et al., 2019; Yadav et al., 2019). These rearrangements have been isolated in ESS. Unfortunately, the sensitivity of these rearrangements is quite low (Efared et al., 2019). For now, high clinical suspicion and thorough pathological review of samples remains the de facto method for diagnosis. Hopefully, as the evidence continues to accumulate, our knowledge and ability to identify and treat these rare tumors will only improve.

4. Conclusion

This case involves the incidental finding of an extremely rare multifocal EESS, involving the left ovary and ureter. With two-thirds of patients having corresponding endometriosis, malignant transformation of diseased foci is a theoretical etiology of this presentation. However, many women will have no prior clinical history of endometriosis (Buchholz et al., 2017). Given their rarity, these cases present diagnostic challenges and often require expert pathologic review. While rare, these tumors should remain on the differential in pre- and postmenopausal women who present with abdominal and/or pelvic masses. A combination of surgical debulking and adjuvant hormonal therapy is standard of care, although no prospective studies currently exist.

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contribution

All authors contributed to the development of this manuscript. Drs. Roberts and Altman were clinically involved in the case as well as contributing to writing and editing of the manuscript. Dr. Nora-Beth Mercier conducted the literature review and was the primary author of the manuscript. Dr. Azordegan reviewed the pathology, did the additional staining, took photos and reviewed the final manuscript.

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