Journal of Experimental Research

June 2014, Vol 2 No 1
www.er-journal.com
Email: editor_in_chief@er-journal.com

Received: June, 2013
Accepted for publication: February, 2014

Endometrial Stromal Sarcoma: Case Report And Review Of Literature

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Abstract

Endometrial stromal sarcoma is a very rare tumour. It usually presents with abnormal vaginal bleeding. Preoperative diagnosis based on clinical and radiological evaluation is usually impossible. Though endometrial sampling may help, diagnosis is mostly based on histological analysis of hysterectomy specimen. In some cases, immunohistochemistry may be required. Total hysterectomy with bilateral salpingo-oopherectomy is the accepted s tandard of treatment. The ovaries may be conserved in young women with early stage disease. The role of lymphadenectomy as well as adjuvant therapy is controversial.

Keywords: endometrial stromal sarcoma, diagnosis, histology, hysterectomy

INTRODUCTION

Endometrial stromal sarcoma (ESS) is rare accounting for only 0.2% of uterine malignancies and approximately 10% of all uterine sarcomas. The mean age range of occurrence is 42 – 58 years and 10 – 25% of those affected are premenopausal (Jassal et al, 2012; Chang et al, 1990).

ESS was previously classified as low grade (LGESS) and high grade (HGESS) based on cellular uniformity, mitotic activity rate (<10 per ten high-power fields vs. >10 per ten high-power fields) and presence of haemorrhage and necrosis. Currently, HGESS is called undifferentiated or poorly differentiated endometrial sarcoma (UES) while ESS is the term for the previous LGESS (Jassal et al, 2012).

ESS is slow growing and recurs locally but distant metastasis may take up to 20 years after initial diagnosis to develop. Commonest presenting complaints in ESS are abnormal uterine bleeding (about 90% of cases) and uterine enlargement (about 70% of cases). Some may present with pelvic pain and dysmenorrhoea though ESS may be asymptomatic in 25% individuals (Puliyath and Nair, 2012).

Clinical features and radiology are usually inadequate for definitive diagnosis making histopathological evaluation the mainstay of diagnosis (Ashraf-Ganjooei et al, 2006; Halbwed et al, 2005).

We present here a case of endometrial sarcoma which confounded clinical and radiological diagnostic attempts and whose prognosis was compounded by patient's refusal of surgery.

Case Presentation

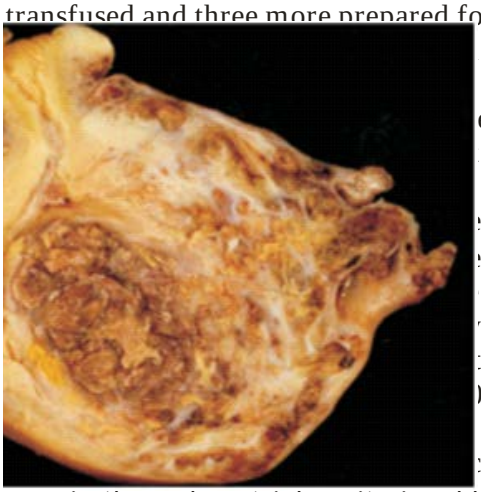
Mrs. NF, a 45-year old, G4P4[0] mid-level civil servant presented to the Gynaecology Emergency Unit with 3-day history of heavy bleeding through the vagina. She first presented to our hospital 8 months previously with a 3-year history of abnormal vaginal bleeding which she had thought was a premenopausal symptom. A clinical and sonographic diagnosis of uterine leiomyoma was made as in three other hospitals she visited afterwards. Also she was advised but refused to get surgery in all cases. Efforts were then focused on controlling vaginal bleeding which did not yield good result.

The patient attained menarche at 13 years and had regular menstrual cycle until onset of symptoms. As time passed, she began to notice discomfort in the lower abdomen, an abdominal mass and associated weight loss with bouts of heavy vaginal bleeding till the last episode which led to her collapsing some hours before presentation.

On examination, she was weak, markedly pale and bleeding from the vagina. Her pulse was 94/min and BP, 92/58mmHg. The uterus was

bulky measuring 16 weeks size. Her haemoglobin was 6.2g/dl. Abdominal ultrasound showed an 11cm submucosal, well-circumscribed mass consisting of cystic and solid parts. The ovaries and the tubes were normal.

She was admitted and worked up for surgery. Efforts were made to secure haemostasis while three units of blood were transfused and three more prepared for intra-op



day, total bilateral e. The ted for care unit teriorated day. ed for erus with gm. The were no lots were seen in the endometrial cavity in additi 11.6cm x 6.5cm x 3.0cm bosselated attached to the anterior uterine wall. Th was limited to the uterine corpus and invaded up to half of the myometrium. O sections, the mass showed yellowish,

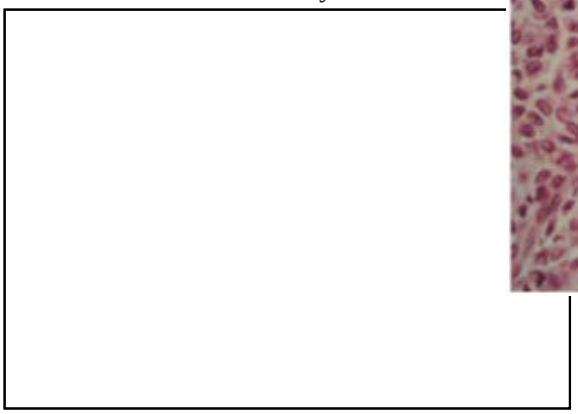


Fig. 1: Gross: uterus with a bosselated mass within endometrial cavity

hemorrhagic surfaces with alternating and solid areas. The uterine adnexae normal. Histological analysis showed cel plump round to oval spindle- shaped nucl mild nuclear atypia, few mitoses myometrial and vascular invasion. (Figu 3)

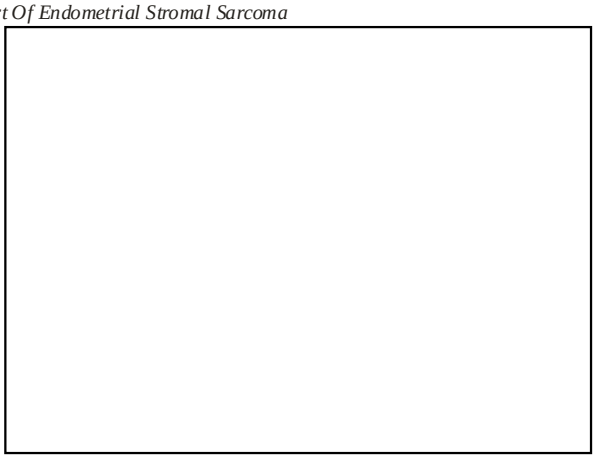
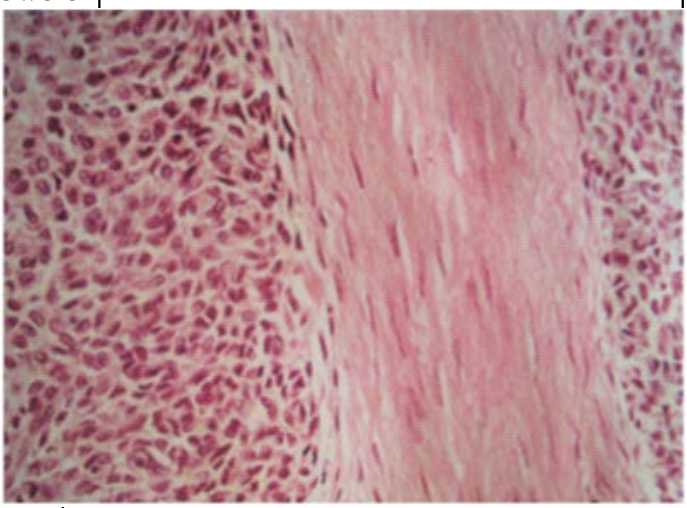
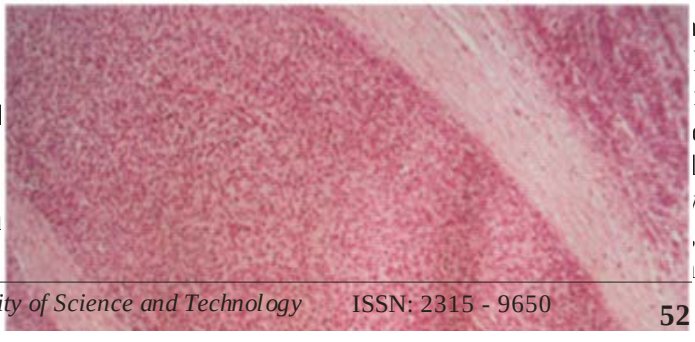


Fig. 2: Photomicrograph showing sheets of neoplastic endometrial stromal cell with nuclear atypia, few mitoses and interspersing fibrous tissue bands. (H&E: x 60)



of ur us g for less than 1% of malignancies of the female genital tract and occur mostly in the uterus (Stefan et al, 2007). Sarcomas comprise 2% to 5% of all uterine cancers (Ashraf-Ganjoei et al, 2006). There are various subtypes of uterine sarcoma the commonest of which is



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cystic lesions (Ashraf-Ganjoei et al, 2006). Our case was of the solid-cystic pattern. It may arise in the endometrium, adenomyosis and rarely, in endometriosis (Eun et al, 2008) in previous sites of endometriosis or following metaplasia of the pelvic peritoneal wall (Ashraf-Ganjoei et al, 2006). ESS constitutes 10%-15% of all uterine sarcomas and 0.2% of total uterine neoplasias (Ramia et al, 2012).

The pathogenesis of ESS is unknown, but exposure to tamoxifen, unopposed estrogens, and conditions such as polycystic disease of ovary are implicated (Cohen, 2004). Other hypothetical risk factors include pelvic irradiation and long-term tamoxifen therapy (Yildrim et al, 2005).

The commonest symptoms are menorrhagia and an abdominal mass (Puliyath and Nair, 2012). Our patient had both symptoms with vaginal bleeding being particularly excessive and uncontrollable at presentation.

Differential diagnoses include several soft-tissue neoplasms with arborizing vasculature, highly cellular leiomyoma, uterine leiomyosarcoma (LMS), cellular endometrial polyp, low-grade mullerian adenosarcoma, and adenomyosis (Ashraf-Ganjooei et al, 2006; Halbwed et al, 2005).

The close resemblance of ESS to normal endometrium or some uterine pathologies namely endometrial cancer, uterine myoma, or adenomyosis makes diagnosing ESS with certainty on curettage specimens or imaging studies such as magnetic resonance imaging or sonography very difficult definitive diagnosis can only be made by histological analysis of a hysterectomy specimen (Ashraf- Ganjooei et al, 2006; Halbwed et al, 2005; Bohr and Thomsen, 1991; Ueda et al, 2001). However, some authors argue that for ESS involving the endometrium, as is mostly the case, uterine curettage may be helpful in preoperative diagnosis (Berkowitz and Goldstein, 2005; Jin, 2010).When the lesion is completely within the myometrium, endometrial scrapings may not be helpful (Puliyath and Nair 2012). In one study of 28 cases of ESS, only 5 were diagnosed following D&C while 16 patients (57.1%) had been referred from local clinics after hysterectomy, myomectomy, D&C, or hysteroscopy for presumed benign gynecologic conditions (Eun et al 2008). Our case typified this diagnostic dilemma. Though D&C was not done in the c ase we report because of our patient's refusal, four different pelvic sonographies at four different centers including ours had returned a diagnosis of leiomyoma.

In cases in which histological diagnosis is difficult, e.g. when ESS is associated with myxoid, epithelioid, and fibrous changes, immunohistochemistry may then be relied upon. Yet ESS share certain immunohistochemical profile with leiomyoma and LMS including expression of muscle-specific actin (MSA), SMA, and desmin (Jassal et al, 2012). However, endometrial stromal tumours show strong and/or diffuse CD10 immunoreactivity. In a series of 34 cases, (Chu et al, 2001) found 100 % positive result for CD10 and like some other workers (Eun et al, 2008; Chu and Arber, 2000) accept CD10 as a specific marker of ESTs. However, the antibody is now known to be negative in fibrous tissue variants of ESS and to be expressed in smooth muscle tumours of the uterus, most commonly in leiomyosarcomas and highly cellular leiomyomas (HCLs) (McCluggage, 2007). Other antibodies useful in this differential diagnosis include h caldesmon (Loddenkemper et al, 2003; Rush et al, 2001), histone deacetylase 8 and smooth muscle myosin (De Leval, 2006). Because ESTs may have smooth muscle differentiation that expresses these markers, there is the need to correlate immunohistochemical results with the morphological findings (Loddenkemper et al, 2003; De Leval, 2006). Also, because leiomyosarcomas may be h caldesmon negative, a panel of antibodies rather than a single antibody should be used in the differentiating between ESTs and smooth muscle tumours (Rush et al, 2001). Oxytocin receptor which is expressed in all leimyomas, HCLs and leiomyosarcomas but not in ESTs (Loddenkemper et al, 2003) is useful for differential diagnosis.

Without sophisticated radiologic studies and immunohistochemistry, our reliance on haematoxylin and eosin (light microscopic) analysis for diagnosis was aided by a well differentiated tumour morphology.

Extrauterine ESS exists in 45% of patients (Thomas et al 2009). It may be secondary or primary. Primary extrauterine ESS is more

common in premenopausal women (Kim et al, 2008; Pink et al, 2006). The commonest extrauterine site is the pelvis. It may be associated with endometriosis or metaplasia of the pelvic peritoneum (Moura et al, 2001; Kovac et al, 2005; Cho et al, 2002).

Surgeons vary with respect to the optimal therapeutic guidelines. Surgery is accepted as the most effective treatment for uterine sarcomas (Lin et al, 1995; Bodner et al, 2001)but the extent of surgery, especially the role of lymphadenectomy, is controversial (Amant et al, 2009; Eun et al, 2008; Gadducci et al, 2008). Some workers recommend total hysterectomy with bilateral salpingo-ophorectomy for all but stage I of ESS (Puliyath and Nair, 2012; Berchuk et al, 1990; Gadducci et al, 1996). Others advocate radiation therapy as primary treatment for patients diagnosed post-hysterectomy and surgical staging, including total hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy for those diagnosed following D&C or myomectomy (Eun et al, 2008). The rate of lymph node involvement in low-grade ESSs may be higher than expected (Riopel et al, 2005; Goff et al, 1993; Reich et al, 2005). Though the therapeutic benefit of radical lymphadenectomy is still uncertain, lymph node dissection is believed to provide prognostic information and treatment guidance (Puliyath and Nair, 2012). Patients with positive nodal metastasis at the time of lymphadenectomy had significantly poorer survival (35.3%) compared with those with negative nodes (80.1%) (Puliyath and Nair, 2012).

Recurrence of ESS despite radical surgery is common and occurs in 36% to 56% of patients with early tumours (Ashraf-Ganjoei et al, 2006; Halbwed et al, 2005).

The role of adjuvant therapy for patients with ESSs is still controversial (Riopel et al, 2005). One study reported no difference in the recurrence rate in patients who had surgery with adjuvant therapy versus surgery alone (Amant et al, 2007) while another reported that the postoperative adjuvant therapy regardless of the treatment modality was associated with relatively increased overall survival when compared to no adjuvant therapy (Eun et al, 2008). The fact that ESS patients experience late recurrence or metastasis could be the rationale for adjuvant therapy. However, the optimal choice of adjuvant therapy for ESSs is unknown, with options including radiation therapy, chemotherapy, and hormonal therapy either alone or in varying combinations.

ESS has a better life expectancy than other sarcomas though there is also controversy over its prognostic factors. Several authors believe that the grade of tumour is the most significant prognostic factor noting that patients with low-grade ESSs had better survival compared to those patients with high-grade ESSs (Eun et al, 2008; Haberal et al, 2003; Leath et al, 2007) while some believe that a combination of grade and extent of tumour if the best indicator. Some others believe that certain independent factors like older age (age more than 50 years), black race, advanced stage, lack of primary surgery, nodal metastasis, high mitotic count more than 5 per 10 high-power fields, CD10 negativity or low expression and lack of oestrogen and progesterone receptors result lead to poor survival (Chan et al, 2008; Lai et al, 2005). Yet some argue that whereas early tumour stage, low myometrial invasion, and low mitotic count are associated with lengthened survival, other factors like age, histologic grade, and adjuvant therapy showed no influence on the overall survival of patients with ESS (Bodner eet al, 2001). These tumours usually run an indolent clinical course with 80–100% 5-year survival, but about 37–60% of patients eventually have recurrence after a very long time and 15–25% die of the disease (Li et al, 2005; Inayama et al, 2000). 5-year survival falls to 32% with extrauterine spread of the disease (Ramia et al, 2012).

Prolonged survival and even cure is possible after surgical resection of recurrent or metastatic lesions (Livi et al, 2003) though death commonly occurs from tumour dissemination within 3 years after diagnosis (Yildrim et al, 2005). In our case, death occurred within 3 years of onset of symptoms and was likely facilitated by the patient's refusal of all forms of surgical intervention.

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