Endometrial stromal sarcoma: An aggressive uterine malignancy

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ABSTRACT

Endometrial stromal sarcoma (ESS) is an aggressive uterine sarcoma. We report a case of a large endometrial stromal sarcoma in a 42 year nulliparous woman with chronic kidney disease presenting with acute urinary retention and irregular per vaginal bleeding. Ultrasound and Doppler imaging revealed a heterogeneous mass in the endometrial cavity with internal vascularity. Magnetic resonance imaging (MRI) revealed a large lobulated mass in the endometrial cavity extending into the vagina, causing local mass effect. Multiple linear hypointense bands on magnetic resonance T2 weighted (T2wt) images were characteristic of ESS. MRI is a very useful imaging modality in characterizing the lesion and also for the staging. It is necessary to distinguish these tumors from benign as well as other uterine malignancies for better management. We also review relevant literature discussing imaging findings of ESS.

CASE REPORT

CASE REPORT

A 42-year-old nulliparous, premenopausal woman with Chronic kidney disease (CKD) presented with acute urinary retention. She also gave a history of constipation since 1 month and irregular per vaginal bleeding since 3 months. Ultrasound of the abdomen and pelvis done 7 months back revealed thickened endometrium (~20mm). Patient refused further investigation of the uterine thickening at that time. There was no prior history of polycystic ovarian disease or use of hormonal therapy in the past. Clinical examination revealed a mass in the lower abdomen. Transabdominal Sonography showed a large, heterogeneously echogenic lesion (11 x 9 x 10cms) distending the endometrial cavity with extension into the cervix and vagina (Fig 1). Internal vascularity was appreciated on Color Doppler (Fig 2). There was compression of the urinary bladder and distal ureters causing bilateral hydroureteronephrosis (Fig 3). Further imaging with MRI showed a large lobulated mass in the endometrial cavity arising from posterior fundal wall and extending into the vagina (Fig 4 and Fig 5). The mass was hypointense on T1 weighted (T1Wt) images and heterogeneously hyperintense on T2Wt and fat suppressed T2Wt spectral attenuated inversion recovery (SPAIR) images. The uterine endo-myometrial junction was obscured (Fig 6). Posterior and lateral infiltration of the cervix and vaginal vault noted with a small extra-uterine component without pelvic wall or rectal involvement. Multiple linear hypointense bands noted within the mass on T2Wt images. The mass was hyperintense on diffusion weighted images (Fig 7a & 7b and Fig 8). No pelvic lymphadenopathy was seen. Ultrasound of the abdomen did not reveal any liver lesions or abdominal lymphadenopathy. Contrast enhanced MRI was deferred due to CKD status (serum creatinine was 3.5mg/dl). Considering the rapid growth

of the endometrial lesion within a span of 7 months, diagnosis of endometrial malignant neoplasm was made. The patient did not consent for further investigations or surgery and went against medical advice due to personal and financial reasons. Two weeks later she returned for surgery, however, her further investigations were restrained for financial reasons. Radical hysterectomy was performed and histopathology revealed poorly differentiated endometrial stromal sarcoma (Fig 9a, 9b and Fig 10a, 10b). During surgery, pelvic peritoneal nodularity was observed and subsequent non-contrast CT abdomen done for abdominal pain following surgery showed few peritoneal nodules (Fig 11). Pelvic peritoneum was normal on initial MRI suggesting rapid spread and aggressive nature of the neoplasm.

The patient was referred to a tertiary oncology center for further chemoradiotherapy.

DISCUSSION

Etiology & Demographics:

Uterine sarcomas are infrequent mesenchymal tumors with three histological types, malignant mixed Mullerian tumor, leiomyosarcoma and endometrial stromal sarcoma (ESS). ESS is an uncommon neoplasm with the literature showing incidence of about 0.2% of all uterine malignancies and 10-15% of all uterine mesenchymal malignancies [1]. ESS originates from the endometrial stroma and is histologically divided into low-grade and high-grade tumors. Low grade ESS is common in middle aged females with mean age of 39 years at presentation and the high grade ESS are seen in older age group with a mean age of 61 years at presentation and are usually aggressive [2]. Parity appears to reduce the risk of developing uterine sarcomas [3]. High grade sarcomas are currently named as Undifferentiated endometrial sarcoma (UES) [4], and are very aggressive tumors which show no endometrial stromal features.

Specific translocation t(7;17) (p15;q21) with the involvement of zinc finger genes juxtaposed with zinc finger proteins and chromosome deletion on 7p may play a role in the tumor development of ESS [5]. Risk factors include unopposed estrogens, exposure to tamoxifen and conditions like polycystic ovarian disease [5].

Clinical & Imaging Findings:

ESS tumors may be asymptomatic at presentation or could present as postmenopausal or atypical premenopausal bleeding, [5, 6], and rarely present with mass effect causing urinary and bowel obstructive symptoms.

Sonography usually demonstrates the endometrial mass. However, MRI is a more useful investigation because it helps in defining the local anatomy better, is able to differentiate benign versus malignant subtypes better, for suspecting the histologic subtype of the malignancy and for staging.

Sonographic findings are not characteristic and alone cannot definitively diagnose uterine sarcomas [7]. However, few studies have described four patterns on transvaginal sonography like diffuse myometrial thickening, central cavitary mass, mural mass and polypoidal mass protruding into the endometrial cavity from the myometrium [8]. They may have partially nodular, smooth or ill-defined margins with heterogeneous, hypoechoic and septated cystic echotexture [8]. Color Doppler may show central or peripheral vascularity and low resistivity index (RI) values [6, 9].

MRI of ESS commonly shows polypoidal endometrial mass, heterogeneously isointense on T1Wt and hyperintense on T2Wt images. Low grade ESS shows variable presentation, from a polypoidal mass to an intramyometrial lesion mimicking leiomyoma which can be differentiated by lesser enhancement, extensive necrosis and peripheral hypointense rim on T2Wt images [6, 10]. Lymphatic and vascular invasion may cause worm-like nodular extensions described as a bag of worms appearance in low grade ESS [6]. These appear as hypointense bands on T2Wt images and represent preserved bundles of myometrium [1]. UES may present as heterogeneous signal intensity voluminous polypoidal mass with more frequent myometrial involvement, which can be well demarcated or diffusely infiltrative on T1Wt and T2Wt images [10]. UES frequently have hemorrhage, necrosis and show vascular and lymphatic invasion. Contrast enhancement is heterogeneous and more intense than normal myometrium [1, 7]. Rarely, very extensive myometrial involvement can predominate as myometrial tumor. Large tumors may extend into the adjacent structures along the fallopian tubes, uterine ligaments and ovaries, exhibiting vascular and lymphatic involvement [2]. Increased signal intensity of the lesion on diffusion weighted imaging (DWI) and low apparent diffusion coefficient (ADC) values indicate malignancy [11]. Vascular, lymphatic and peritoneal metastases are known to occur in ESS [12].

Treatment & Prognosis:

On review of available literature, the 10 year overall survival is 65-76% in low grade ESS and overall survival in UES is poor [13].

Surgery and adjuvant hormonal therapy are the important elements in the treatment in ESS [14]. Hysterectomy along with bilateral salpingo-oophorectomy is the standard surgical treatment. Low grade ESS is usually managed by cytoreductive surgery and hormonal treatment which include progestins and aromatase inhibitors as maintenance therapy. However, for High grade ESS; cytotoxic agents like doxorubicin and ifosfamide or gemcitabine with docetaxel and doxorubicin have been used prior to surgery for tumor shrinkage [12].

In our case, the patient underwent radical hysterectomy with removal of uterus, cervix and part of the vagina. She was referred to a tertiary center following surgery for further treatment, after which she was lost to follow up.

Differential Diagnoses:

Endometrial carcinoma

It is commonly seen in the age group of 60-70 years with postmenopausal bleeding as the primary manifestation. A very few may present in a younger age below 35 years of age [15]. Nulliparity, prolonged unopposed estrogen stimulation,

estrogen excess, and long term use of tamoxifen are the associated risk factors [15]. Sonography may demonstrate thickened endometrium and also the depth of myometrium and cervical invasion. It may mimic ESS due to the endo-myometrial involvement. Endometrial carcinoma is isointense with normal endometrium and myometrium on T1Wt images and heterogeneous with variable appearance on T2Wt images [16]. Invasive ones show disruption or irregularity of the junctional zone on T2Wt images [16]. However, Endometrial carcinomas tend to show less contrast enhancement, and are comparatively smaller in size than ESS [6].

Leiomyosarcoma

Second most common uterine sarcoma presenting in the early fifth decade of life and less often below 40 years of age. These sarcomas are generally larger in size and may present as a large solitary tumor with endo-myometrial involving. Doppler shows low RI due to increased tumoral vascularity [6]. Leiomyosarcomas arise from the myometrium and are more heterogeneous due to common necrosis, hemorrhages, calcifications and show early contrast enhancement [4, 10, and 17]. Areas of hyperintensities on T2Wt images suggest necrosis. Marginal irregularity may also be demonstrable [6].

Leiomyoma

Low grade ESS presenting as mural mass mimic leiomyoma on ultrasonography. However, leiomyomas have a well-defined outline, peripheral rim and hyperechoic echotexture with whirling pattern [8]. On MRI, the non-degenerated leiomyomas are low to intermediate signal on T1Wt images and low signal on T2Wt images with variable contrast enhancement. Cystic degeneration in a leiomyoma appears hyperintense on T2Wt images and may simulate sarcoma [1]. DWI shows higher ADC values, suggesting the benign nature of the lesion. Low grade ESS tends to invade into the myometrium and surrounding structures [2].

Adenomyosis

Adenomyosis commonly affects multiparous and premenopausal women. Sonography demonstrates heterogeneity of the myometrium with small myometrial cysts, poorly defined endo-myometrial junction and ill-defined margins between the normal and abnormal myometrium [18]. Typical ones are ill-defined, T2 low signal intensity lesions with tiny cysts appearing as T2 bright spots. Junctional zone is thickened. Contrast enhancement is variable. DWI shows low to intermediate signal intensity [19]. Low grade ESS may occasionally be present within the myometrium mimicking adenomyosis.

TEACHING POINT

Large malignant uterine tumors have varied presentation and have overlapping features due to endo-myometrial involvement. Few characteristic features, on Ultrasound and MRI, especially with T2Wt images, seen as hypointense bands within the tumor with the bag of worms appearance, give clues to consider endometrial stromal sarcoma as one of the differential diagnoses.

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FIGURES

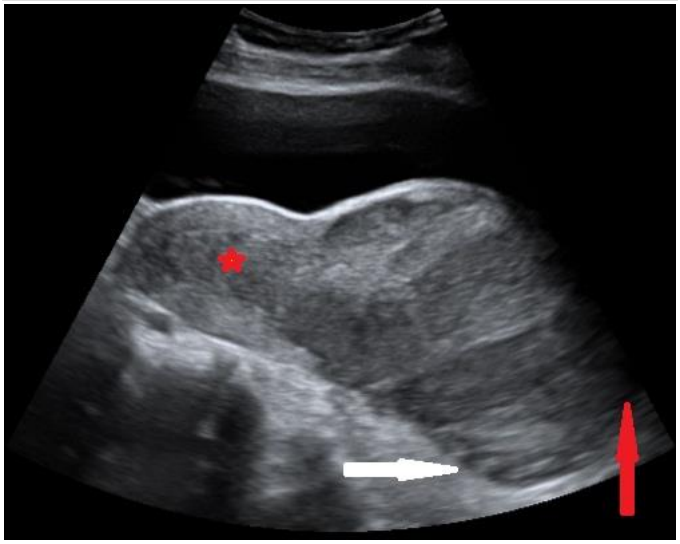

Figure 1: 42 year old female with endometrial stromal sarcoma
Findings: Heterogeneous echogenic mass within the endometrial cavity is shown (red asterisk) which is causing distension and extending into the cervix (white arrow) and vagina (red arrow).
Technique: B-mode Transabdominal sonogram of the pelvis. Longitudinal section of uterus. Ultrasonography was performed using 3-5MHz curvilinear transducer.

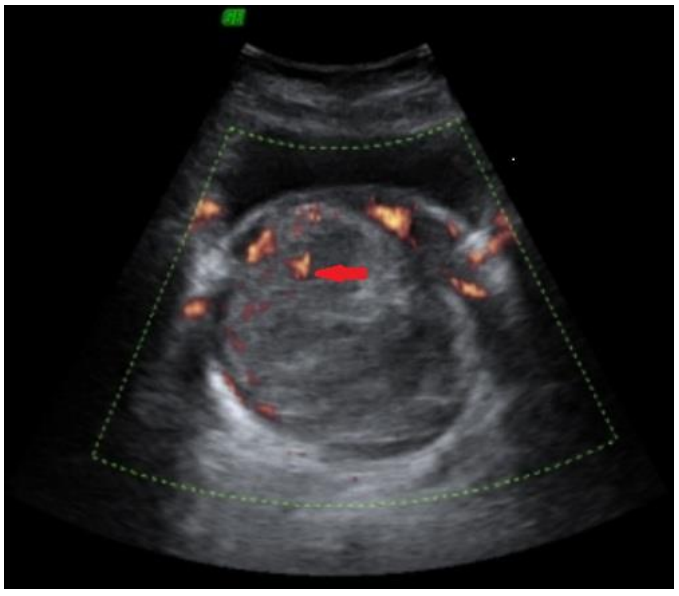

Figure 2: 42 year old female with endometrial stromal sarcoma
Findings: Transabdominal sonogram of transverse section of the uterus showing enlarged uterus with a heterogeneous mass in the endometrial cavity showing internal vascularity (red arrow).
Technique: Power Doppler performed using 3-5MHz curvilinear transducer.

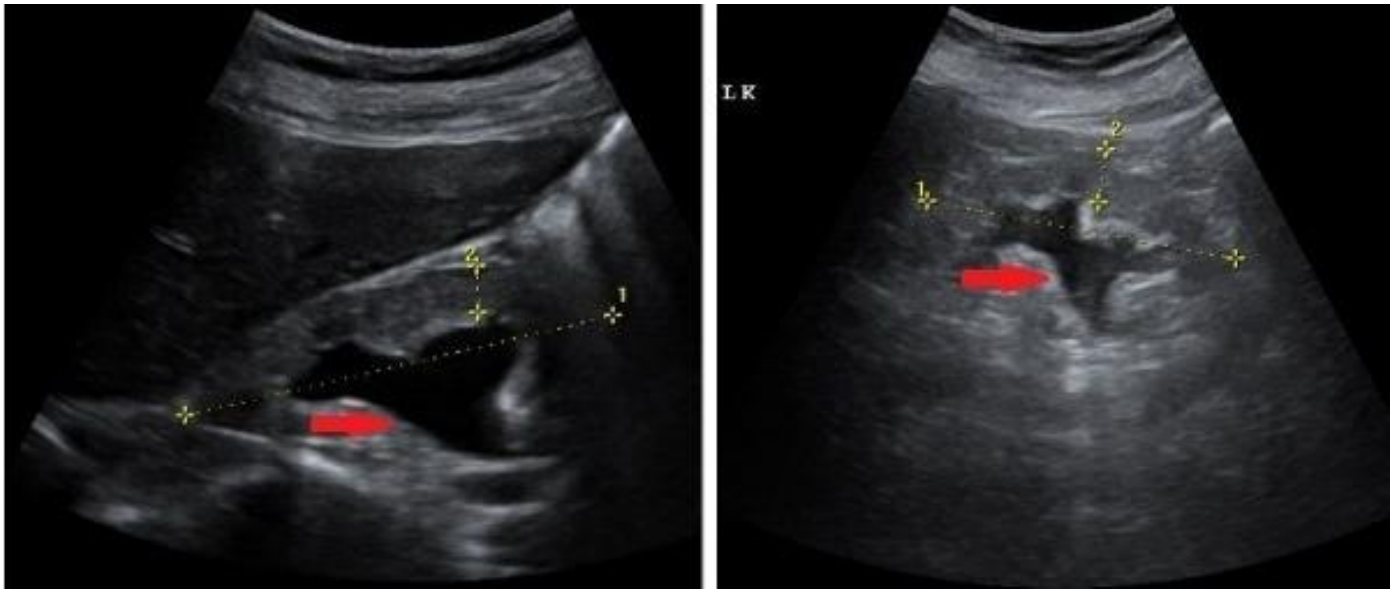

Figure 3: 42 year old female with endometrial stromal sarcoma
Findings: Transabdominal sonogram of longitudinal section of both kidneys shows dilatation of pelvicalyceal system and ureters indicating hydroureteronephrosis (red arrows).
Technique: Transabdominal sonogram of the abdomen at lumbar regions performed using 3-5MHz curvilinear transducer.

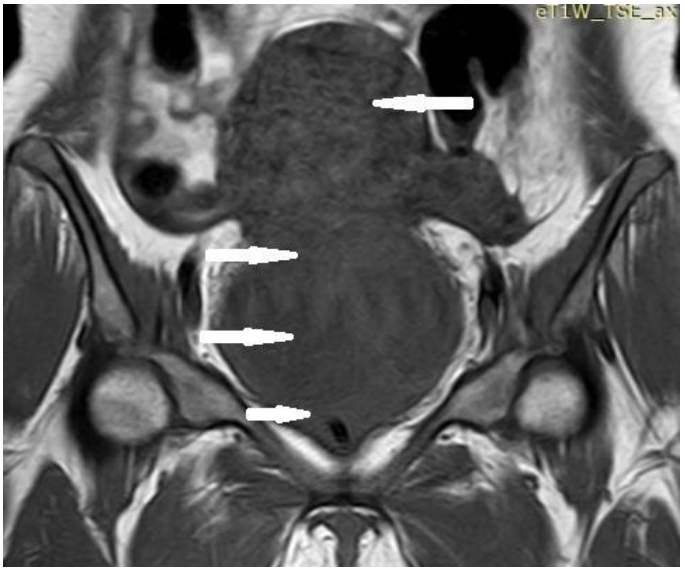

Figure 4: 42 year old female with endometrial stromal sarcoma
Findings: Coronal T1Wt image showing enlarged uterus with hypointense mass extending up to vagina distending the cervical canal (white arrows).
Technique: Philips 1.5 Tesla MRI, Coronal T1Wt image of pelvis, TR/TE - 612ms/10ms, 4.0mm slice thickness, noncontrast. FOV - 240. Matrix - 320 x 320.

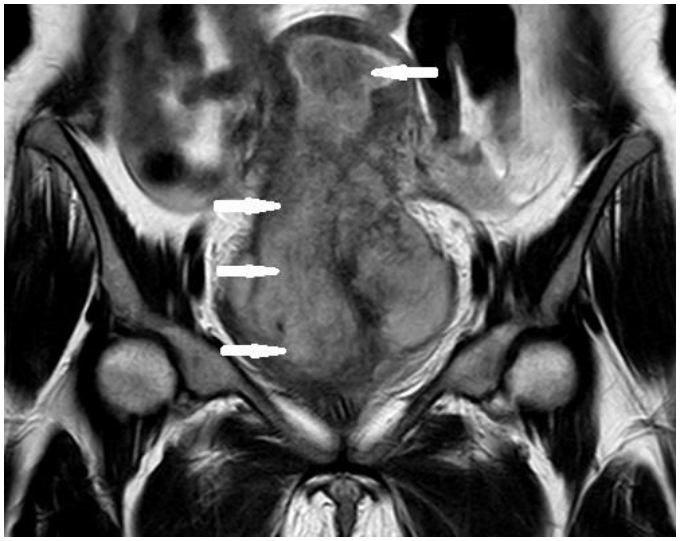

Figure 5: 42 year old female with endometrial stromal sarcoma
Findings: Coronal T2Wt image showing a large heterogeneous hyperintense mass in the endometrial cavity extending from the fundal region up to the vagina, causing distension of the cervical canal (white arrows). Uterus appears superiorly displaced by the mass.
Technique: Philips 1.5 Tesla MRI, Coronal T2Wt image of pelvis, TR/TE - 2800ms/90ms, 4.7mm slice thickness, noncontrast. FOV - 240. Matrix - 320 x 320.

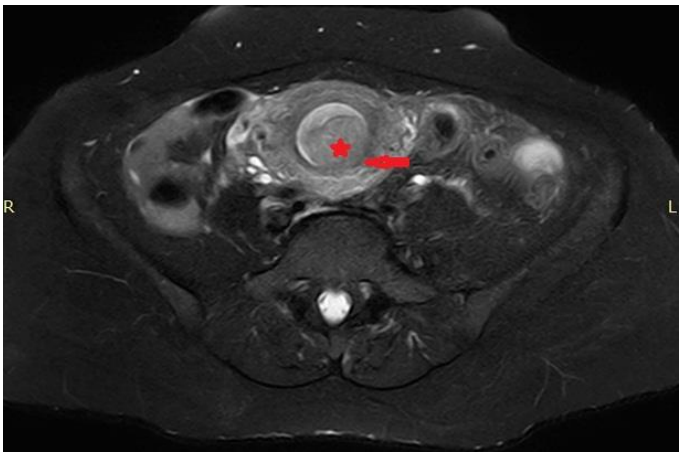

Figure 6: 42 year old female with endometrial stromal sarcoma.
Findings: Axial Fat suppressed T2Wt image of the pelvis at the level of the uterine fundus showing enlarged uterine endometrial cavity with a hyperintense lesion arising from the posterior aspect of the endometrium (red asterisk). The endo-myometrial junction is not clearly delineated in the posterior aspect (red arrow).
Technique: Philips 1.5 Tesla MRI, Axial Fat suppressed T2Wt image of the pelvis, TR/TE - 3700ms/70ms, 5mm slice thickness, noncontrast. Fat suppression technique - SPAIR. FOV - 240. Matrix - 320 x 320.

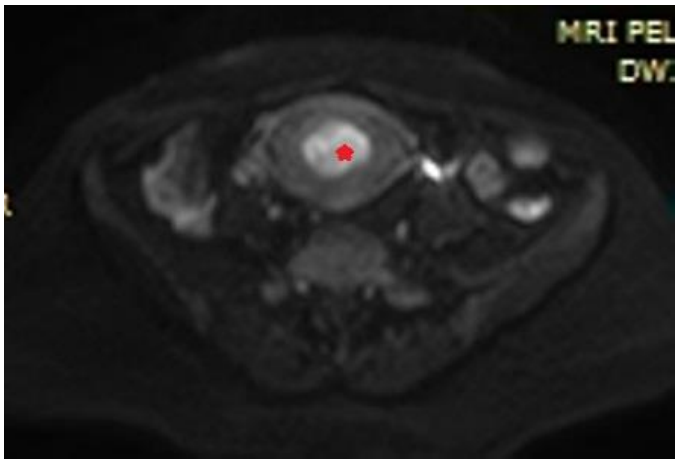

Figure 8: 42 year old female with endometrial stromal sarcoma
Findings: Axial Diffusion weighted image showing high signal intensity mass within the endometrial cavity (red asterisk).
Technique: Philips 1.5 Tesla MRI, Axial DWI of pelvis, b-factor =800s/mm2, TR - 2000ms, TE - 60ms, 5.0mm slice thickness. FOV - 240. Matrix- 192 x 192

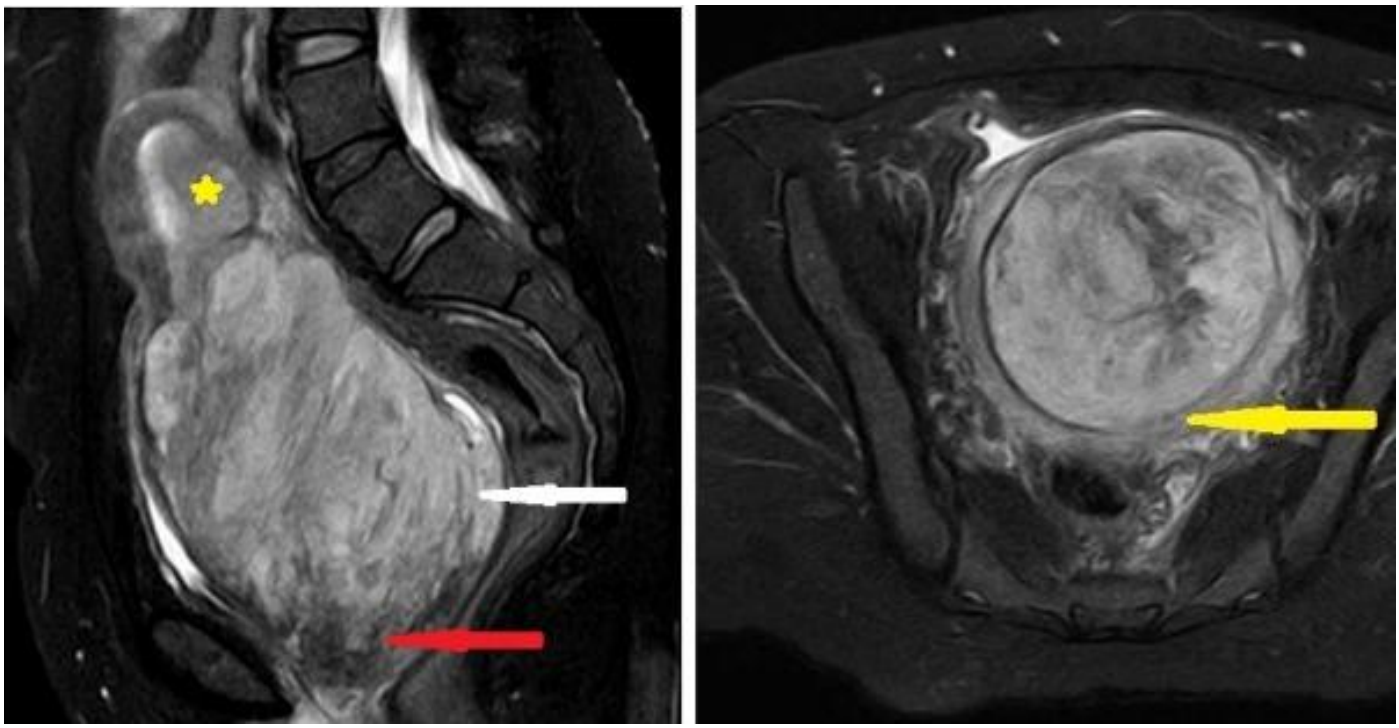

Figure 7: 42 year old female with endometrial stromal sarcoma.
Findings: Sagittal Fat suppressed T2Wt image of the pelvis showing a large, heterogeneously hyperintense large mass arising from the fundal endometrial cavity (yellow asterisk) extending into the cervix (white arrow) and vagina (red arrow). Few hypointense linear bands are noted which are characteristic for ESS. Note the posterior wall infiltration beyond the cervix (yellow arrow).
Technique: Philips 1.5 Tesla MRI, sagittal Fat suppressed T2Wt image of the pelvis, TR/TE-3700ms/70ms, 5mm slice thickness, noncontrast. Fat suppression technique - SPAIR. FOV - 240 .Matrix - 320 x 320.

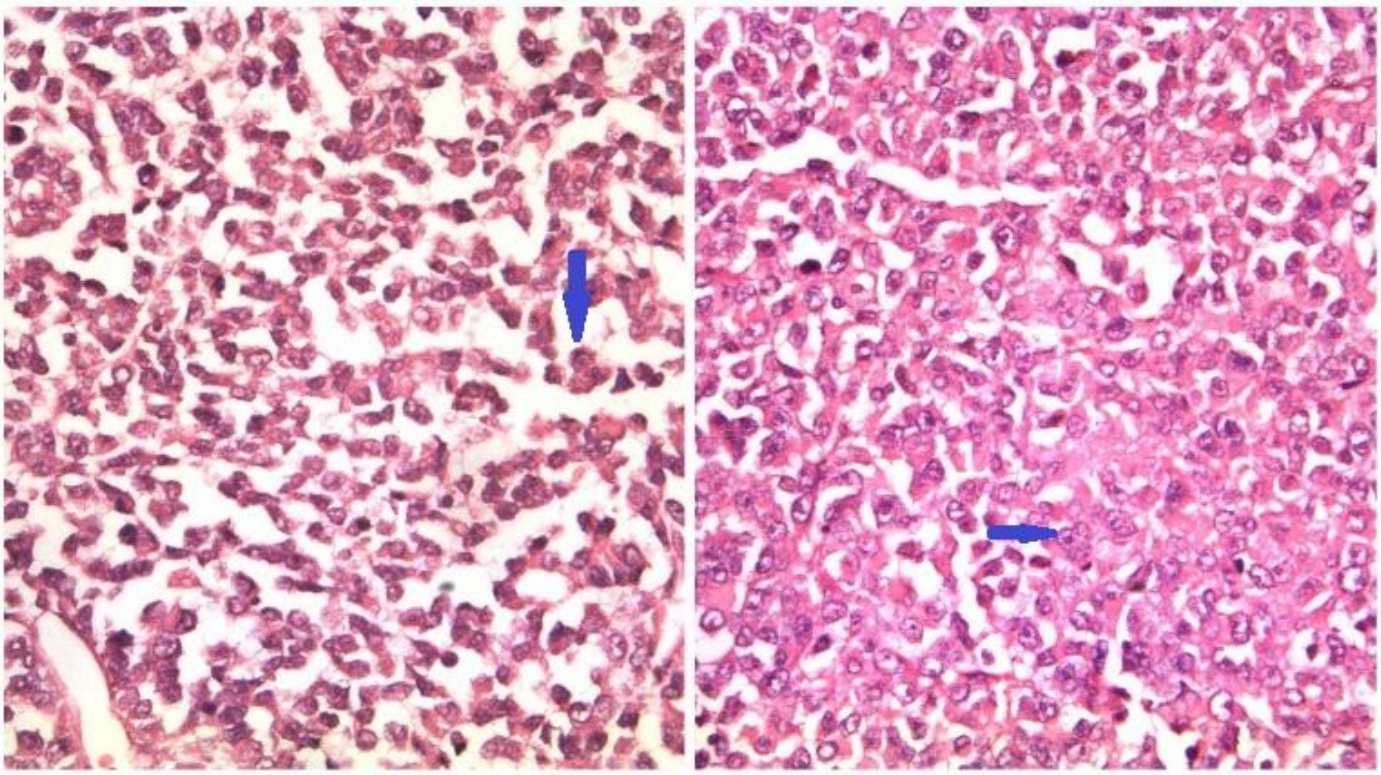

Figure 9: 42 year old female with endometrial stromal sarcoma.
H & E 40x showing diffuse sheets of cells showing fine chromatin with occasional prominent nucleoli with mitotic figures (blue arrows).

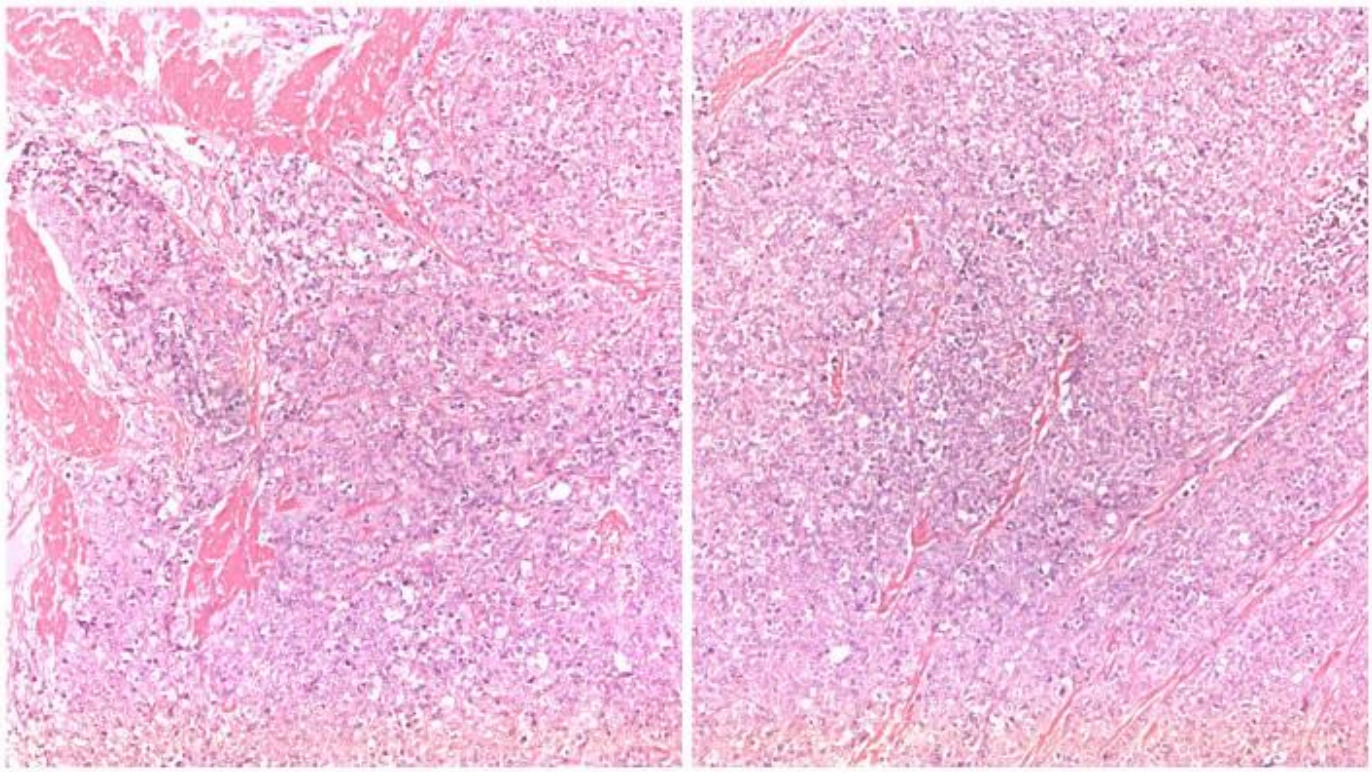

Figure 10: 42 year old female with endometrial stromal sarcoma.
H & E 10x showing uniform oval to spindle shaped cells with scant to moderate cytoplasm.

Figure 11: 42 year old female with endometrial stromal sarcoma, postoperative.
Findings: CT abdomen showing soft tissue density nodules along the inner aspect of parietal peritoneal layer suggesting peritoneal spread.
Technique: Multidetector 128 slice Computed tomography of the abdomen and pelvis, 120kVp, Auto mAs, 1mm slice thickness, noncontrast.

Etiology	Origin is poorly understood. However, specific translocation t(7;17) (p15;q21) and chromosomal deletion on 7p may play a role in tumor development
Incidence	0.2% of all uterine malignancies and 10-15% of all uterine mesenchymal malignancies
Gender ratio	Only females
Age predilection	A low grade subtype of endometrial stromal sarcoma (ESS) presents at the mean age of 39 years High grade ESS presents at the mean age of 61 years
Risk factors	Exposure to tamoxifen, unopposed estrogens, and conditions such as polycystic disease of ovary
Presentation	Asymptomatic/post-menopausal bleeding/ atypical premenopausal bleeding / bladder – bowel symptoms due to extrinsic compression
Findings on imaging	Ultrasonography – Diffuse myometrial thickening, central cavity mass, mural mass and polypoidal mass protruding into the endometrial cavity from the myometrium are the four patterns described. MRI – Heterogeneously isointense on T1 weighted and hyperintense on T2 weighted images. Low grade ESS may show myometrial involvement, giving rise to an appearance of bag of worms on T2 weighted images. High grade ESS shows peripheral hypointense rim and extensive necrosis.
Treatment	Surgery and adjuvant hormonal therapy.
Prognosis	Low grade ESS has a better prognosis than High grade ESS. 10yr overall survival is 65 – 76% in Low grade ESS and overall survival is poor regardless of stage.

Table 1: Summary table for Endometrial stromal sarcoma.

Differentials	Ultrasound	MRI T1	MRI T2	DWI	Contrast MRI
Low grade endometrial stromal sarcoma	Four patterns: Diffuse myometrial thickening, central cavitary mass, mural mass, polypoidal mass	Heterogeneously isointense polypoidal/ intramyometrial mass	Heterogeneously hyperintense polypoidal endometrial/ intramyometrial mass. Diffusely infiltrative into the myometrium with low signal bands with worm like nodular extensions of the margins described as a bag of worms appearance representing preserved myometrial fibers	High signal and lower apparent diffusion co-efficient (ADC) values	Moderate and heterogeneous
Undifferentiated endometrial sarcoma	Ill defined, heterogeneous with necrosis	Heterogeneously hypointense mass, hemorrhage may be seen	Hyperintense mass with myometrial involvement, hemorrhage and necrosis	High signal and lower ADC values	Heterogeneous enhancement and more intense than normal myometrium
Endometrial carcinoma	Thickened endometrium, Myometrial and cervical extension	Hypo to isointense to normal endometrium	Heterogeneously hyperintense relative to normal endometrium	High signal and lower ADC values	Less contrast enhancement compared to normal myometrium
Leiomyosarcoma	Large solitary heterogeneous myometrial neoplasm with increased vascularity and low resistive index on Doppler study	Heterogeneously hypointense, hemorrhage and calcification	Heterogeneously hyperintense, necrosis and hemorrhage	Lower ADC values	Early contrast enhancement
Leiomyoma	Well defined, hyperechoic echotexture, peripheral rim, whirling pattern	Low to intermediate signal intensity. Hemorrhagic degeneration appears as hyperintense signal changes	Non-degenerated fibroids are hypointense. Cystic degeneration appears as a high signal intensity lesion	Higher ADC values	Variable contrast enhancement
Adenomyosis	Heterogeneous myometrium with small myometrial cysts and ill-defined endo-myometrial junction	Foci of high signal due to hemorrhages	Ill-defined, heterogeneous low signal with small bright foci	Low to intermediate signal	Variable enhancement

Table 2: Differential table for Endometrial stromal sarcoma.

ABBREVIATIONS

ADC - Apparent diffusion coefficient
CKD - Chronic kidney disease
DWI - Diffusion weighted imaging
ESS - Endometrial stromal sarcoma
MRI - Magnetic resonance imaging
RI - Resistivity index
SPAIR - Spectral attenuated inversion recovery
T1Wt - T1 weighted
T2Wt - T2 weighted
UES - Undifferentiated endometrial sarcoma

KEYWORDS

MRI; Uterus; Endometrial stromal sarcomas; undifferentiated endometrial sarcomas; high grade sarcomas; uterine mesenchymal neoplasms; myometrial bands

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