Case Report

Endometrial stromal sarcoma in an adolescent girl: A case study and review

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ABSTRACT

Endometrial stromal sarcoma (ESS) is a rare mesenchymal tumor which usually occurs in the age group 40-60 years. Our patient is an adolescent girl of 17. A case of ESS in a 30 year old female has been reported once before. A high level of suspicion is required for pre-operative diagnosis in younger age group. Type 1 hysterectomy with removal of tubes and ovaries is the treatment. The patient requires regular follow up

Key words: Endometrial stromal sarcoma, Mesenchymal tumors, Adolescent girl, Type 1 hysterectomy

INTRODUCTION

Endometrial stromal tumor accounts for 0.2% of all malignant uterine tumors[1] and 10% of mesenchymal stromal tumors of the uterus.[2] The incidence peaks in the perimenopausal age group.[2] Patient may present with mass abdomen, pain abdomen and heavy menstrual bleeding.[3] The differential diagnosis include benign leiomyoma of uterus. Leiomyoma is also rare in younger age group as the peak incidence is over 40 years (40-60%).[4] During diagnosis and management of endometrial stromal sarcoma (ESS) a high index of suspicion is required.

CASE REPORT

The present case report is about a 17-year-old unmarried girl presented to our out-patient department with the complaints of severe abdominal pain for 2 days. She had regular 28-30 days cycle with normal flow for 4-5 days. She gave a history of progressive dysmenorrhea since 1 year. She had no other relevant past medical, surgical or family history.

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On examination, she was an average built person with body mass index of 19.

Her general examination and systemic examinations were within normal limits.

Per abdomen

A mass arising from the pelvis of 14 weeks size was palpable in the hypogastrium, firm in consistency, non-tender with restricted mobility. No evidence of ascites.

Bimanual pelvic examination was not performed.

An ultrasound (USG) revealed well-defined solid lesion 10 cm × 8.5 cm in the pelvis posterior to the bladder impression? Uterine mass.

Magnetic resonance imaging (MRI) was advised due to the uncertainty of the USG findings. Her parents were not willing for the same. We proceeded with exploratory laparotomy under general anesthesia [Table 1].

Per-operative findings

There was no ascites, peritoneal washings were taken. Uterus enlarged to 14 weeks with a well-defined 5 cm × 5 cm firm mass anteriorly near the fundus. On incising over the mass copious amount of friable necrotic material protruded. There was no evidence of capsule. The necrotic material was removed as much as possible and cavity obliterated. B/L ovaries and tubes were normal.

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Post-operative period was uneventful. Patient was discharged on day 6.

HISTOPATHOLOGICAL REPORT

Gross

Multiple brownish tissue fragments aggregating measuring 9 cm × 7 cm × 2 cm cut section brownish areas which appears friable and necrotic.

Microscopy

Section shows fragments of myometrial tissue with an infiltrating neoplasm composed of irregular nodules and lobules separated by dense fibrous stroma. In areas, the cells are seen in linear or serpentine fashion infiltrating myometrial tissue. In areas, neoplastic cells are seen into vascular spaces. The neoplastic cells are oval with scanty cytoplasm and vesicular nuclei. Some shows grooving. 5-10 mitotic figures are seen per 10-15 high power field. Areas of collagenization are seen. The neoplasm was richly vascular. In areas, the cells showed hemangio cryptic pattern. Large areas of necrosis and foci of dense inflammatory reaction seen. Reticulin stain-shows reticulin fibers around individual cells impression-ESS.

Patient was further advised type 1 hysterectomy with removal of ovaries. Since, she was not willing for surgery at that time she was treated with injection hydroxylprogesterone caproate. After extensive counseling and follow-up for 2 years, she finally agreed for the definitive surgery. MRI was carried out prior to the surgery.

Findings of the MRI

Ill-defined hypo-intense lesion on the right lateral and anterior uterine wall of 3 cm × 2 cm × 1.5 cm. No definitive enhancement in myometrium. Bilateral ovaries were normal. No lymph node enlargement.

Definitive surgery was carried out with removal of the uterus, both tubes and ovaries.

Table 1: Pre-operative investigations

Investigations	Value	Normal
Hb	12.4 g%	12-15
TC	11,400 cells/mm^3	4000-10,000
ESR	10 mm/h	0-10
DC	N:74, L:24, E:02	N:50-60, L:20-40, E:1-4
HIV	Negative	
HbsAg	Negative	
HCV	Negative	
Creatinine	0.6	0.2-1.2
RBS	101	<140
Urea	16	20-40

Hb: Hemoglobin, TC: Total count, ESR: Erythrocyte sedimentation rate, DC: Differential count, HIV: Human immunodeficiency virus, HCV: Hepatitis C virus, HbsAg: Hepatitis B surface antigen, RBS: Random blood sugar

THE HISTOPATHOLOGICAL REPORT

Gross

Uterus measures 10 cm × 5.5 cm × 3.5 cm.

Cut section of uterus shows ill-defined grey white areas involving more than half of the myometrium. The abnormal areas are seen over 3.2 cm × 3 cm. Endo cervix and ecto cervix on cut section unremarkable. Cut section of both ovaries and fallopian tubes were unremarkable.

Microscopy

Section shows a neoplasm infiltrating full thickness of the myometrium and serosa. The neoplastic cells are arranged in nests within the myometrium [Figure 1]. The cells are oval or spindle shaped with scanty to moderate cytoplasm and oval nuclei [Figure 2]. Capillary sized vessels are seen. Mitotic figures noted. Lymphovascular tumor emboli seen.

Diagnosis

Uterus with low grade ESS. Neoplasm infiltrating full

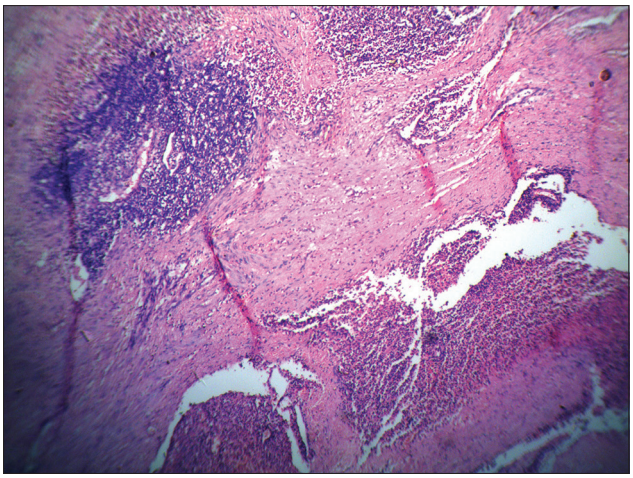

Figure 1: Endometrial stromal sarcoma with irregular infiltrating margins

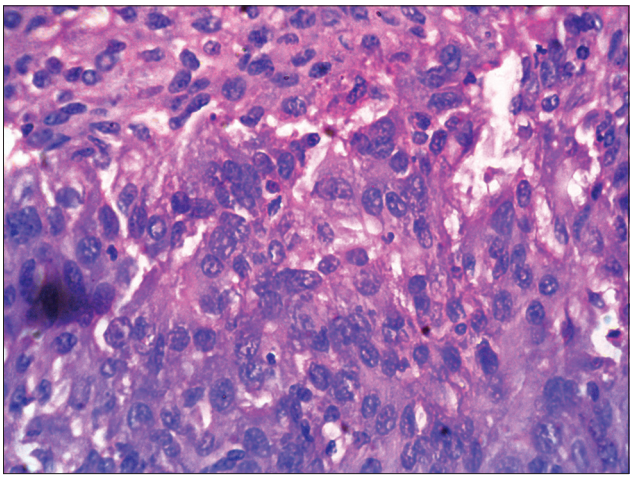

Figure 2: Malignant transitional cells-high power view

Table 2: Classification WHO-2003

Classification	Type	Histopathology
A	Endometrial stromal nodule	Well circumscribed, soft non-encapsulated neoplasm tan to yellow cut surface M/E-non-infiltrating border Lobulated or finger like projections into the myometrium that are <3 mm and <3 in number No vascular invasion
B	Low grade ESS or ESS	Irregular nodular growth involving the endometrium with varying degrees of permeation to myometrium including worm like plugs of tumor that fill the myometrial veins Proliferation of uniformly small cells closely resembling those of endometrial stroma in the proliferative stage. The cells have scanty cytoplasm, oval to round nuclei and inconspicuous nucleoli. Significant atypia and pleomorphism are absent. Mitotic activity is usually <5/10 high-power fields
C	Undifferentiated endometrial/ uterine sarcoma	Polypoid, fleshy grey to yellow endometrial masses and often show prominent hemorrhage and necrosis Marked cellular atypia and abundant mitotic activity, often including atypical forms They lack the typical growth pattern and vascularity of low grade ESS and displace the myometrium in contrast to infiltrative pattern of low grade ESS They resemble the sarcomatous component of carcinoma sarcoma

ESS: Endometrial stromal sarcoma, WHO: World Health Organization

thickness of the myometrium and serosa. Sections from cervix ovaries tubes and parametrium do not show any significant pathology.

Patient is on regular follow-up for the past 3 years with clinical examination and USG. There is no evidence of recurrence.

DISCUSSION

World Health Organization in 2003 has classified endometrial stromal tumors based on mitotic activity, vascular invasion and prognosis. Endometrial stromal tumors account for < 10% of the mesenchymal tumors of the uterus. These are divided into [Table 2]

- Endometrial stromal nodule
- ESS (low grade)
- High grade or undifferentiated stromal sarcoma.

Endometrial stromal tumors are very rare accounting for approximately 0.2% of all malignant uterine tumors.[2] Usually the peri-menopausal age group is affected.[3] A study including 14 patients in USA by Gezginç *et al*. had a median age distribution of 55.69 ± 11 years.[5] A study by Jin *et al*. the median age was 43.5 years.[4] A case of ESS in a 30 year old female has been reported once.[6] Some low grade endometrial stromal nodules has also been reported in women with polycystic ovarian disease, tamoxifen therapy or estrogen use.[7]

Nearly 70% of patients present with abnormal uterine bleeding, 25% with uterine mass. In 40% of patients, it is an incidental finding as they are asymptomatic.

Endometrial stromal nodule is an expansive non-infiltrating solitary lesion confined to uterus. These tumors should be considered benign as there is no recurrence or deaths reported after surgery. The differential diagnosis includes cellular leiomyoma.[5] Diagnosis may be aided by immunohistochemistry. Endometrial stromal nodules are positive for CD10; leiomyoma are positive for caldesmon and desmin and sometimes CD10.[8]

ESS-low grade has a more protracted clinical course. Recurrences occur late and local recurrence is more common than distant metastasis.[9] The tumor lacks aneuploid deoxyribonucleic acid content. The cells express estrogen/ progesterone-receptors.

The Federation of Gynecology and Obstetrics staging for endometrial stromal tumor is the same as that for carcinoma of corpus uteri.

ESS extends beyond uterus in 40% of cases. However, the spread is limited to pelvis in 2/3 of the cases. Lymph node metastasis is rare and 5 year recurrence rate is 50%. Prolonged survival and cure is a rule even after recurrence.[5]

The treatment is type 1 hysterectomy. The adnexa should always be removed due to the possibility of the tumor metastasis to the parametria, broad ligament and adnexal structures. Furthermore, there is a possibility of estrogen stimulating effect on tumor cells if the ovaries are retained. Pelvic radiation is advised in inadequately excised tumors to prevent local recurrence.[10]

The evidence also suggests that endometrial stromal tumors are highly hormone sensitive. The objective response to progestin was reported in 48% of patients in a series studied.[11]

Treatment with medroxy progesterone acetate, aromatase inhibitors, tamoxifen, hydroxyprogesterone caproate, gonadotropin-releasing hormone analogs has been suggested for low grade ESS and for recurrent diseases.[12]

Recurrences are also managed surgically. Long-term survival and apparent cures are excellent.

High grade ESS is a highly malignant neoplasm. The tumor is aggressive with poor prognosis. This is usually reported in perimenopausal and post-menopausal age group. 5 year survival is only 25%. Treatment is surgery followed by chemoradiation. These tumors are not responsive to progestins.

CYTOGENETICS OF ESS

There is uncertainty regarding the origin of ESS A recurrent translocation of chromosome, t (7;17)(p15;q21), occurs in ESS. This translocation leads to the fusion of two polycomb group genes, JAZF1 and JJAZ1, with production of a fusion transcript with anti-apoptotic properties. Interestingly, even normal endometrial stroma cells express the fusion gene, derived not by translocation, but by the "stitching" together of messenger ribonucleic acids. Thus, it appears that a pro-survival gene in the normal endometrium is somehow subverted to become pro-neoplastic.[13]

CONCLUSION

The ESS is a rare mesenchymal sarcoma of the uterus occurring in perimenopausal and post-menopausal age group. The mean age is between 42 and 58 years.[3] Review of literature has revealed only very few cases of ESS in the younger age group. Hence a high index of suspicion is required in young patients especially in the adolescent age group. The tumor may be mistaken for leiomyoma uterus and a conservative approach may be hazardous. In our patient, the availability of frozen section would have helped us to proceed with the definitive surgery during the initial laparotomy itself.

REFERENCES

1. Ashraf-Ganjoei T, Behtash N, Shariat M, Mosavi A. Low grade endometrial stromal sarcoma of uterine corpus, a clinico-pathological and survey study in 14 cases. World J Surg Oncol 2006;4:50.
2. Tavassoli FA, Devilee P. WHO Classification of Pathology and Genetics of Tumors of Breast and Female Genital Organs. IARC Press Lyon; 2003. p. 233-6.
3. Jin Y, Pan L, Wang X, Dai Z, Huang H, Guo L, *et al*. Clinical characteristics of endometrial stromal sarcoma from an academic medical hospital in China. Int J Gynecol Cancer 2010;20:1535-9.
4. Oliva E, Clement PB, Young RH. Endometrial stromal tumors: An update on a group of tumors with a protean phenotype. Adv Anat Pathol 2000;7:257-81.
5. Gezginç K, Karatayli R, Yazici F, Acar A, Çelik Ç, Çapar M, *et al*. Malignant Brenner tumor of the ovary: Analysis of 13 cases. Int J Clin Oncol 2012;17:324-9.
6. Puliyath G, Nair VR, Singh S. Endometrial stromal sarcoma. Indian J Med Paediatr Oncol 2010;31:21-3.
7. Cohen I. Endometrial pathologies associated with postmenopausal tamoxifen treatment. Gynecological Oncology 2004;2:256-66.
8. Baker P, Oliva E. Endometrial stromal tumours of the uterus: A practical approach using conventional morphology and ancillary techniques. J Clin Pathol 2007;60:235-43.
9. Berek JS. Bereks and Novaks Text Book of Gynecology. 15th ed. New Delhi: Lippinco Williams and Wilkins; 2012.
10. Norris HJ, Taylor HB. Mesenchymal tumors of the uterus 3. A clinical and pathologic study of 31 carcinosarcomas. Cancer 1966;19:1459-65.
11. Kreigner PD, Gusberg SB. Endolymphatic stromal myosis a grade 1 endometrial sarcoma. Gynecol Oncol 1973;1:299-313.
12. Linder T, Pink D, Kretzschmar A, Mrozek A, Patience PC, Reichardt P. Hormone treatment of endometrial stromal sarcomas: A possible indication for aromatase inhibitors. J Clin Oncol 2005;23:16S-9057.
13. Li H, Wang J, Ma X, Sklar J. Gene fusions and RNA trans-splicing in normal and neoplastic human cells. Cell Cycle 2009;8:218-22.

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