Endometrial stromal sarcoma- A study of five cases

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ABSTRACT

Endometrial stromal sarcoma (ESS) is a tumor of endometrial stromal cells that invades the myometrium. Because of its rarity and benign looking appearance, a preoperative diagnosis is difficult. But in few cases if the stromal tumor involves the endometrium, diagnosis can be made by endometrial biopsies and curettings. A definitive diagnosis of stromal sarcoma can be made if myometrial invasion is identified in the tissue fragments or with imaging studies, but hysterectomy is usually required for definitive diagnosis. Prognosis depends on the stage of disease at the time of presentation. Here we are presenting five such cases of endometrial stromal sarcomas.

Keywords : Endometrial stromal sarcoma, plexiform vascular arrangement, undifferentiated stromal sarcoma

INTRODUCTION

ESS is a rare malignant tumor of the uterus. The tumor cells resemble endometrial stromal cells of the proliferative phase of the Endometrium and the annual incidence of ESS is 1-2 per million women. They account for less than 10% of uterine mesenchymal neoplasms.The pathogenesis of ESS is unknown, but exposure to tamoxifen, unopposed estrogen and conditions such as polycystic disease of ovary are implicated[1]. ESS was traditionally divided into two categories low grade ESS and high grade ESS, but in the current WHO classification only low grade stromal sarcomas (LGSS) are called ESS[2], high grade tumors are now designated as Undifferentiated endometrial sarcoma (UES).

Low grade ESS are composed of cells resembling endometrial proliferative stroma with a plexiform vascular arrangement and minimal cytological atypia. High grade endometrial stromal sarcoma (UES) is characterised by tumor cell necrosis, high mitotic activity and absence of uniform proliferation of small blood vessels. High grade sarcomas can be divided into monomorphic and pleomorphic variants. Monomorphic variant is composed of relatively uniform tumor cells, whereas large, pleomorphic tumor cells are seen in pleomorphic variant.

CASE REPORT

We studied five cases of endometrial stromal tumors. All the five cases presented with vaginal bleeding. For all the cases we received hysterectomy specimens. Histological sections were taken from tumor areas and slides were stained with Hematoxylin & Eosin and examined under the microscope. After microscopic examination we diagnosed 4 cases as low grade ESS, and one case as high grade.

In the four cases of low grade sarcomas, two cases presented grossly as a mass in the endometrial cavity (Figure 1) with bulky uterus and two cases presented grossly as focal thickening in the myometrium (Figure 2) and asymmetrical enlargement of uterus as seen in adenomyosis. All these cases presented with vaginal bleeding and age range was 43-55years .

Microscopic examination of these low grade sarcomas revealed tumor cells invading the myometrium as irregular tongues and prongs and tumor cells pushing between bundles of smooth muscle cells (Figure 4). Tumor cells have round to oval nuclei and amphophilic cytoplasm with ill defined cell borders resembling endometrial stromal cells. Nucleus shows finely granular dispersed chromatin and mitotic figures are very low. Uniformly distributed small arterioles are seen among the tumor cells (Figure 5). In many areas whorls of tumor cells surrounding the arterioles were seen resembling endometrial spiral arterioles. Invasion of vascular channels by tumor cells were well appreciated in one case of low grade sarcoma (Figure 6).

In our study we also received one case of High grade endometrial stromal sarcoma . Patient presented at the age of 56 years with vaginal bleeding. Grossly the tumor presented as multiple, soft , fleshy, polypoidal masses in the endometrial cavity (Figure 3). Microscopically tumor is characterised by monomorphic variant of high grade ESS

in which tumor cells are relatively uniform that bear resemblance to endometrial stromal cells (Figure 7). However, the tumor cells are larger and have medium sized atypical nuclei with coarse chromatin. Areas of necrosis were observed (Figure 8) and mitotic activity was about 10 to 12 per 10 HPF. Uniform distribution of blood vessels which is characteristic of low grade sarcoma was not observed in the high grade ESS.

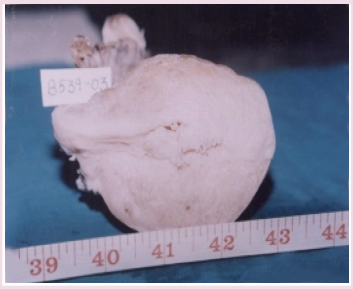

Figure 1: Low grade tumor presenting as polypoid growth

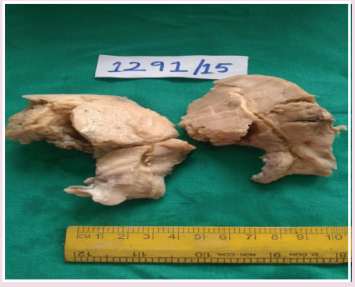

Figure 2 : Low grade tumor presenting as focal thickening in myometrium

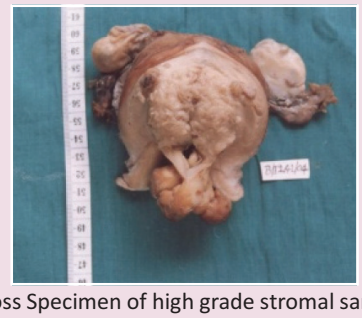

Figure 3: Gross Specimen of high grade stromal sarcoma

DISCUSSION

ESS are rare tumors and the literature shows that about 20% of uterine sarcomas were low grade and 6% were high grade[3]. The mean age for low grade sarcoma is 42 to 53years[4,5] and more than 50% of patients are premenopausal. The main symptoms are abnormal vaginal bleeding and abdominal pain[6]. In our study, all the four cases of low grade sarcomas presented with vaginal bleeding.

Because of its rarity and preoperative benign looking appearance, resembling other tumors like uterine myomas, a preoperative diagnosis is difficult. Gross presentation of this tumor varies widely, with extensive involvement of endometrium it sometimes presents as polyp in the endometrial cavity and in some cases it may present as nodular growth in myometrium mimicking leiomyoma. In some cases tumor appears as ill defined tumor causing thickening of myometrium and in the fourth and most frequent pattern of growth the myometrium is permeated by poorly demarcated pink, tan, or yellow cords and nodules of tumor. For accurate diagnosis microscopic examination is must. In our study also two cases of ESS presented as polyp in the endometrial cavity, two cases presented as focal thickening of myometrium. Only after microscopic examination of tumor, we made the diagnosis of ESS. Differential diagnosis include several soft tissue neoplasms demonstrating arborizing vasculature, highly cellular leiomyoma, cellular endometrial polyp, low grade mullarian adenosarcoma and adenomyosis[7].

Low grade ESS grows slowly and the tumor stage is the most significant prognostic factor. Hysterectomy and bilateral salpingo-oophorectomy is the standard treatment for stage 1 stromal sarcoma, with debulking of extrauterine tumor performed in more advanced cases. Adjuvant hormone therapy in the form of progesterone, gonadotropin

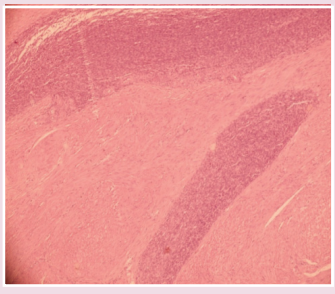

Figure 4: Tongue shaped invasion of tumor cells in myometrium(10X,H&E).

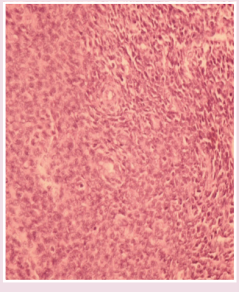

Figure 5: Uniformly arranged small vessels resembling spiral arterioles in low grade stromal sarcoma(40X,H&E).

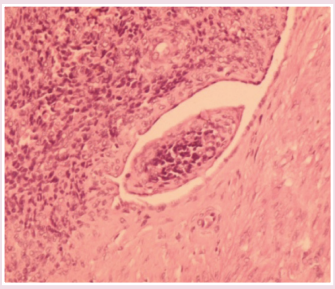

Figure 6: Vascular invasion of tumor cells in ESS(40X,H&E)

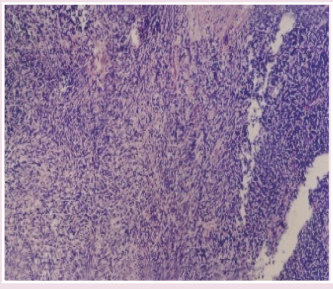

Figure 7: High grade stromal sarcoma,mono morphic variant(10X,H&E).

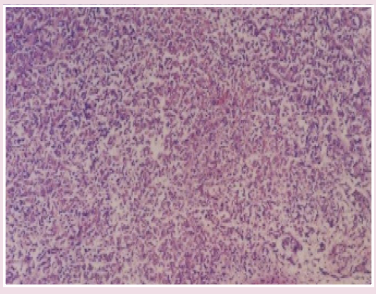

Figure 8: Necrosis in high grade stromal sarcoma.(10X,H&E).

releasing hormone analogues, and aromatase inhibitors are found to be effective in preventing recurrences. Recurrences are often not seen many years after the intial treatment. Most recurrences are in the pelvis and involve the pelvic soft tissues, ureter, bladder, vagina or bowel[8]. Recurrent ESS occasionally transforms into high grade sarcoma, with increased nuclear atypia and mitotic activity and loss of response to hormone therapy[9].

The average age of women with high grade stromal sarcoma is 55 – 60 years[10], in our case patient age was 56 years of age and tumor was confined to uterus,no pelvic lymphadenopathy noted. Grossly this tumor presents as soft flesy, polypoid tumors that bulge into and often fills the endometrial cavity, in our study also tumor presented as multiple polypoid growth filling the endometrial cavity (figure 3). A significant proportion of patients have extra uterine tumor spread at diagnosis, either to the pelvic lymphnode, upper abdomen, or to distant sites such as the lungs[5].Treatment includes hysterectomy and, in most cases,radiation therapy and/or chemotherapy depending on the stage of the tumor. For women with high grade ESS overall survival is significantly lower than for those with Low grade ESS [5,8].

In the immunohistochemical study of Low grade ESS , CD10 is the most useful positive marker. The tumor cell cytoplasm often shows strong positive staining for CD10. Smooth muscle tumors tend to be CD10 negative or show focal weak staining. WT-1 is positive in the tumor cell nuclei in most Low grade ESS. Nuclear staining for beta-catenin is present in 40% cases of Low gade ESS, but not in cellular lieomyoma. Estrogen and progesterone receptors are positive in most cases. Immunohistochemistry is not helpful in the evaluation of high grade ESS. This is because reactivity for many antigens , including hormone receptors, is lost in some of these poorly differentiated tumors.

CONCLUSION

ESS are rare mesenchymal tumors of the uterus. Preoperative clinical diagnosis is difficult but histological diagnosis of these tumors is easy because of their typical microscopic appearance. Tumor staging being the most important prognostic factor, early diagnosis can prolong the life of the patients.

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