

Endometrial Stromal Sarcoma: Report of Two Cases

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A rare entity in gynecologic oncology, endometrial stromal sarcoma diagnosed in two women aged 45 and 46 years. was presented with discussion on similar mesenchymal lesions.

Key words : Gynecologic oncology, endometrial cancer, endometrial stromal sarcoma

Endometrial Stromal Sarkom (İki Olgu)

Jinekolojik onkolojide seyrek görülen endometrial stromal sarkom tanısı almış olan biri 45 , diğeri 46 yaşlarında iki kadın hasta sunuldu ve benzer mezenşimal lezyonlardan ayırıcı tanılar tartışıldı.

Anahtar kelimeler : Jinekolojik onkoloji, endometrium kanseri, endometrial stromal sarkom

Endometrial stromal tumors are rare tumors, which have an incidence of 12.5-23% among uterine sarcomas. Features of these tumors are outlined by the studies of Norris and Taylor, as classical knowledge (1-3, 6-8).

The identification of the tumor cells, which closely resemble the proliferative or hyperplastic endometrial stromal cells, is essential for histopathological diagnosis(1-7). Also arterial vascular architecture which is highly characteristic for endometrial stromal differentiation is often encountered property of endometrial stromal tumors.

This group of tumors are classified as stromal nodule which does not have a myoinvasive and/or intravascular growing pattern, and infiltratively growing stromal sarcomas. Endometrial stromal sarcomas(ESS) are also classified, by Norris and Taylor, as 'low grade' and 'high grade' according to its mitotic rate (1,2,6,7,8).

Endometrial stromal nodule: The rarest stromal tumors which are clinically benign, well circumscribed. They neither have myoinvasive nor intravascular growth pattern. They are almost always diagnosed incidentally. Histologically, the tumor cells resemble proliferative endometrium cells. Mitotic counts are not important in these tumors and are always under 10 mitotic figures per 10 high power fields (HPF).

Simple hysterectomy is an adequate therapy for these tumors.

Low grade ESS: This is the most common endometrial stromal tumor. Although cytological and architectural properties resemble endometrial stromal nodules, these tumors show myoinvasive and/or intravascular infiltrative pattern (1,2, 6-8). Pleomorphism is minimal and they have no anaplastic changes. Mitotic figures are less than 10/ 10 HPF.

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High grade ESS: Tumor cells, in these tumors show at least a moderate nuclear pleomorphism and hyperchromasia and have higher counts of mitotic figures than 10 / 10 HPF.

According to a controversial classification suggested by Evans(3,8), which is also widely accepted, tumors having endometrial stromal differentiation are defined as 'ESS', whereas the tumors not having endometrial stromal differentiation are defined as 'poorly differentiated endometrial sarcomas', regardless their mitotic figure counts

CASE REPORTS:

Case 1: A 45 year old woman was admitted to Obstetrics and Gynecology Department of İnönü University Faculty of Medicine, with complaints of inguinale and flank pain. Findings of her physical examination were within normal limits. Her bimanual pelvic examination revealed the uterus to be two weeks size and there was a 2x1cm myoma uteri at the right corneal region. Her pelvic ultrasound revealed a septated, hyperechoic mass in fundus, which was well circumscribed from peripheral tissues with irregular internal borders,. The probable diagnosis of this mass was degenerated myoma uteri. The uterine cavity was

measured to be 10 cm, during the endometrial biopsy, which was later diagnosed as 'proliferative endometrium'. The patient underwent TAH+BSO, with the diagnosis of myoma uteri.

The surgical specimen contained a 3x2 cm yellowish mass with necrotic areas. The lesion was confined with corpus. On the histological examination, small, relatively uniform cells with oval or round nuclei, which closely resemble endometrial stromal cells (Figure 1). Tumor cells have infiltrated the myometrium and some vessels and were seen as irregular solid groups. There was not serosal infiltration. The tumor contained necrotic areas and foamy histiocytes. Mitotic figures were 2-3/10 HPF (Figure 2).

The patient was diagnosed as stage I low grade ESS, and planned to be followed with 3 month intervals postoperatively.

Postoperative progestational therapy (200 mg/day medroxyprogesterone acetate) was started to prevent long term recurrence

Case 2: A 46 year old woman was admitted to Obstetrics and Gynecology Department of İnönü University Faculty of Medicine, with complaints of vaginal bleeding for the last two months. Findings of her physical examination were within normal limits. Uterus was found to be slightly bigger in



Figure 1: Regularly distributed small blood vessels and uniform tumor cells (Case 1).
(H&E x 50)



Figure 2: Dilated and slit-like vessels and myometrial infiltration of the tumor cells. (Case 1)
(H&E x 20)

size than the normal on bimanual examination of the pelvis. Since the bleeding continued, despite the three months of therapy, the patient underwent TAH+BSO.

The surgical specimen contained a polypoid lesion which irregularly filled the endometrial cavity and its dimensions were 3x2 cm. Histopathologically the tumor was found to be irregularly distributed to cervix and reached to inferior surgical border. There was wide necrotic and haemorrhagic areas. Mitotic figures were more than 10/10 HPF. The patient was diagnosed as Stage II, high grade ESS and transferred to Oncology department of Hacettepe University. She has received seven sessions of chemotherapy (Cisplatin 100 mg + Isophosphamide 3 gm + Mesna 3 gm). No evidence of recurrences or metastasis was found in her follow-up examinations.

DISCUSSION:

There are two different aspects in the classification of endometrial stromal tumors. In the classification proposed by Norris and Taylor, according to the mitotic rate, ESS has been divided into two groups as low grade ESS and high grade ESS (1,6,7). According to the next classification proposed by Evans, tumors which show endometrial stromal differentiation (i.e. cells resemble the endometrial stromal cells and vascular elements like spiral arterioles) are regarded as ESS, whereas the tumors which are thought to originate from endometrium but not showing any evidence of endometrial stromal differentiation are described as 'poorly differentiated endometrial sarcomas' (2,3,8).

ESS, especially low grade ESS, are seen under 50 years of age, whereas high grade ESS is mostly diagnosed in patients over 50 years of age (3). There are also ESS cases diagnosed in the adolescence (4). Both of our cases are diagnosed in the fourth decade.

The most common symptom of ESS is dysfunctional vaginal bleeding. Less frequent symptoms are asymptomatic uterine enlargement, pelvic pain and pelvic mass. One of our cases has admitted to hospital with the complaints of

bleeding and the other one with uterine enlargement.

ESS are sometimes lethal tumors, with the ability of recurrences and metastasis. Chang et al. have reported 73 patients with grade I ESS, with a recurrence rate of %45 and a single mortality due to tumor (2). In another study, four recurrences in eleven patients has been reported, whereas 7 patients were followed without recurrence after operation and radiotherapy (3). Among the series reported in literature, the follow-up time varies between 36-370 months. Evans has reported 7 poorly differentiated endometrial sarcoma cases, of which 6 of them were lost due to distant metastases, despite the postoperative chemotherapy and radiotherapy. Only one patient survived for 228 months without tumor (3).

According to Norris and Taylor's classification, one of our cases is regarded as low grade ESS and the other one as high grade ESS. According to Evans classification, our first case is ESS, but the second one can probably be regarded as poorly differentiated endometrial carcinoma. Since there is not a prognostic and therapeutic difference between poorly differentiated endometrial sarcoma and high grade ESS, this difference among classifications do not seem to be important.

The general conclusion of the reports about ESS, clinical stage and mitotic index are univariant parameter. Although mitotic index, does not provide further prognostic information in patients whose clinical stage is known; in late stage cases it turns to be an independent parameter in estimating the prognosis (2). In our first case, when stage and mitotic index is taken into account, the prognosis can be estimated to be good. We also believe in a prolonged remission period with the progesterone therapy, as stated in literature (2,3). In our second case, we do not have a good prognostic expectation, since she has a stage II tumor with high mitotic index. We have been following both patients for more than two years without any evidence of recurrence or metastasis.

In addition to the cells resemble the endometrial stromal cells and vascular elements like spiral arterioles, histopathologic features of ESS also include the existence of large collagen

fibers, hyalinized or necrotic areas, foamy macrophages, calcium deposition and the existence of smooth muscle and epithelioid differentiation (2,7).

The features such as necrosis, hemorrhage or foamy histiocytes are the diagnostic parameters concerning only the endometrial stromal differentiation, but not the prognosis (2,3). The frequent existence of epithelioid cells in ESS is described as 'uterine tumors resemble ovarian sex-cord stromal tumors,' by Clement and Scully (9). There is an attribution about tumors containing epithelioid or glandular foci to be more aggressive (2). Both of our cases do not have this pattern.

Differential diagnosis of ESS should initially be made from stromal nodule and low grade ESS. Stromal nodules do not have myoinvasive and/or intravascular growing pattern. The differential diagnosis of ESS from poorly differentiated endometrial sarcoma can be made by the existence of endometrial stromal differentiation. Due to the prominent vascular pattern, ESS can be mis-diagnosed as hemangioperistoma of the uterus, which may sometimes need the pericytic differentiation to be shown ultrastructurally.

Smooth muscle tumors are also another group to be kept in mind in differential diagnosis. Uterine leiomyomatosis and intravascular leiomyomatosis are the infiltrative and/or intravascular growing benign smooth muscle tumors in which mitosis is rarely observed (2,6). Differentiation of the tumor cells towards smooth muscle or endometrial cells, is helpful in the differential diagnosis of ESS from benign smooth muscle tumors and leiomyosarcomas.

Another clinical entity to be kept in mind in the differential diagnosis is the malignant müllerian tumor, which contain both the carcinoma and sarcoma areas (7).

ESS should be differential diagnosed from metastatic carcinomas, lymphomas and leuchemias.

A focus of adenomyosis, in which the endometrial glands are sparse or not observed, can be diagnosed as low grade ESS (4). The most useful features in the differential diagnosis of adenomyosis with sparse glands are the absence

of grossly evident tumor, the absence of mitosis or nuclear atypia, presence of other adenomyosis foci in uterus and the absence of the diagnostic criteria for low grade ESS.

The standard therapy for the sarcomas which are within the uterus is hysterectomy. Recurrence is observed in more than one third of the patients. Pre- and postoperative radiotherapy and chemotherapy (hormonal or non-hormonal) are recommended in patients with late stage and high grade ESS (10,11). In patients with stage I tumors, a significant difference was not found between the therapeutic modalities of surgery and surgery + radiotherapy. Progesterone increases the time for tumor recurrence. In late stage tumors, rate of response to chemotherapy is found to be 20% and to surgery+radiotherapy as 33 %.

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