Uterine Tumor Resembling Ovarian Sex Cord Tumor; A Rare Case Report with Histopathology, Immunohistochemical Findings and P53 Expression

Overin Seks Kord Tümörüne Benzeyen Uterin Tümör; Histopatoloji, İmmunohistokimyasal Bulgular ve P53 İfadesi İçeren Nadir Bir Olgu Sunumu

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Abstract
Uterine tumors resembling ovarian sex cord tumors, is a rare mesenchymal tumor of the uterus that displays similar histological features of sex cord tumors. The pathogenesis for this tumor, which was first described by Morehead and Bowman in 1945 and about 100 cases of which have been published so far, is still unknown . It is frequently seen in perimenopausal or menopausal women around the age of 45. It can manifest itself with gynecological symptoms such as menorrhagia, postmenopausal bleeding, abdominal pain, or it can be detected incidentally with no symptoms. Although it behaves like benign tumors, its attitude is unpredictable due to publications reporting that it recurs and metastases and it can be considered as a low malignancy potential tumor. Therefore, bilateral salpingooferectomy and hysterectomy is the most reliable method in the treatment, except for the reproductive age where only tumor resection is performed. Here, I present a case of this rare tumor accompanied by histomorphological findings and immunohistochemical studies including P53. P53 marker study in uterine tumor resembling ovarian sex cord tumor has been reported in only four cases in the literature; three of them showed P53 marker positivity and one mentioned that it could be associated with recurrence or tumor progression. More studies need to be done in terms of prognostic or diagnostic value between uterine tumors resembling ovarian sex cord tumors and P53 marker. Our case showed overt expression with p53.

Keywords: Sex cord tumor, uterine tumor, P53 marker

Özet
Overin seks kord-stromal tümörüne benzeyen uterin tümör, seks kord tümörlerine benzer histolojik özellikler gösteren, uterusun nadir görülen mezenkimal tümörleridir. İlk kez 1945 yılında Morehead ve Bowman tarafından tanımlanan ve bugüne kadar 100'e yakın vakası yayınlanmış olan bu tümörün patogenezi halen bilinmemektedir. Sıklıkla 45 yaş civarında perimenopozal veya menopozal kadınlarda görülür. Menoraji, postmenopozal kanama, karın ağrısı gibi jinekolojik semptomlarla kendini gösterebileceği gibi herhangi bir semptom olmadan tesadüfi tesbit edilebilir. İyi huylu tümörler gibi davranmasına rağmen, rekürrens ve metastaz yaptığını bildiren yayınlar nedeniyle tutumu öngörülemez ve düşük malignite potansiyelli bir tümör olarak kabul edilebilir. Bu nedenle üreme yaşı dışında sadece tümör rezeksiyonu yapılan olgularda, tedavide iki taraflı salpingooferektomi ve histerektomi en güvenilir yöntemdir. Burada nadir görülen bu tümörün bir olgusunu histomorfolojik bulgular ve P53 dahil immünohistokimyasal çalışmalar eşliğinde sunuyorum. Overin seks kord-stromal tümörüne benzeyen uterin tümöre ait P53 marker çalışması literatürde sadece dört olguda rapor edilmiş olup; üçü P53 marker pozitifliği göstermiş ve biri bunun nüks veya tümör ilerlemesi ile ilişkili olabileceğinden bahsetmiştir. Overin seks kord-stromal tümörüne benzeyen uterin tümöri ile P53 belirteci arasında prognostik veya tanısal değer açısından daha fazla çalışma yapılması gerekmektedir. Bizim olgumuzda p53 ile belirgin ekspresyon görüldü.

Anahtar Kelimeler: Seks kord tümör, uterin tümör, P53 marker

Introduction

Uterine tumors resembling ovarian sex cord tumors, is a rare mesenchymal tumor of the uterus that displays similar histological features of sex cord tumors. The pathogenesis for this tumor, which was first described by Morehead and Bowman in 1945 and about 100 cases of which have been published so far, is still unknown (1). It is frequently seen in perimenopausal or menopausal women around the age of 45 (2). It can manifest itself with gynecological symptoms such as menorrhagia, postmenopausal bleeding, abdominal pain, or it can be detected incidentally with no symptoms (3). Although it behaves like benign tumors, its attitude is unpredictable due to publications reporting that it recurs and metastases and it can be considered as a low malignancy potential tumor (4-6). Therefore, bilateral salpingooferectomy and hysterectomy is the most reliable method in the treatment, except for the reproductive age where only tumor resection is performed (7).

Histopathologically, they show varying features such as glandular, macrofollicular, microfollicular, trabecular, tubular, cords, retiform, solid clusters, diffuse or mixed. Immunohistochemically, it displays a pattern of unknown origin due to its staining with epithelial, smooth muscle and sex cord markers. For this reason, it is among the miscellaneous mesenchymal tumors of the corpus uteri in the World Health Organization classification (8).

Here, it is presented a case of this rare tumor accompanied by histomorphological findings and immunohistochemical studies including P53. P53 marker study in uterine tumor resembling ovarian sex cord tumor has been reported in only four cases in the literature; three of them showed P53 marker positivity and one mentioned that it could be associated with recurrence or tumor progression (3,7,9). More studies need to be done in terms of prognostic or diagnostic value between uterine tumors resembling ovarian sex cord tumors and P53 marker. Our case showed overt expression with p53.

Case Report

In a 47-year-old patient who did not have any complaints and came for intrauterine contraseptive device control, a 16 mm diameter polyps in the uterine cavity was detected in ultrasound. Sampling is done by curettage from the patient.

Microscopic examination of 1.5 cc endometrial sampling revealed two endocervical polyps showing squamous metaplasia between endometrial tissues in the early secretory phase. Besides, very dense cellular and vascularized polypoid tumor fragments were observed. These fragments were mostly solid layers with a focal trabecular and retiform pattern of neoplastic cells with focal pleomorphism, usually with monotonous oval-round nuclei with faint nucleoli and scant to abundant eosinophilic cytoplasm. There was no mitosis and necrosis (Figure 1).

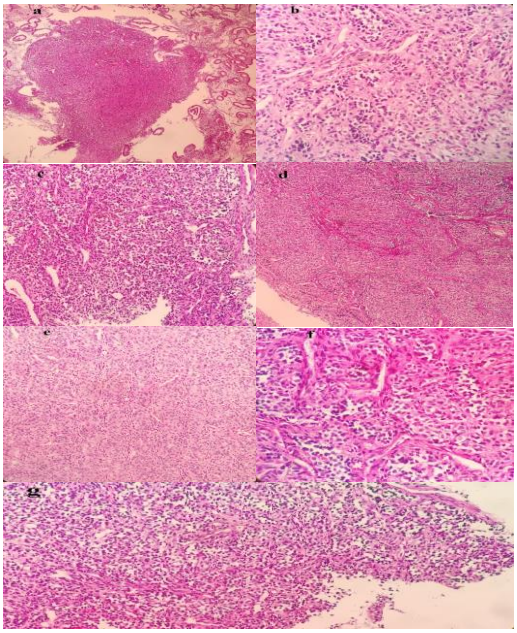

Figure 1. Histology of the uterine tumor resembling ovarian sex-cord tumor (a) Polypoid tumor, (b) trabecular pattern, (c,g) retiform pattern, (d,e) solid areas, (f) densely cellular and vascular (Hematoxylin-eosin staining, a: × 40, d, e**:** × 100, the others ×200)

In immunohistochemical studies, neoplastic cells showed patch staining with the epithelial marker pancytokeratin, diffuse staining with desmin and calphonin, the myoid markers, diffuse staining with the ovarian sex-cord marker CD56, focal staining with calretinin and cell clusters with melan A. In addition, diffuse staining with vimentin and patchy staining with BCL2 was observed (Figure 2).

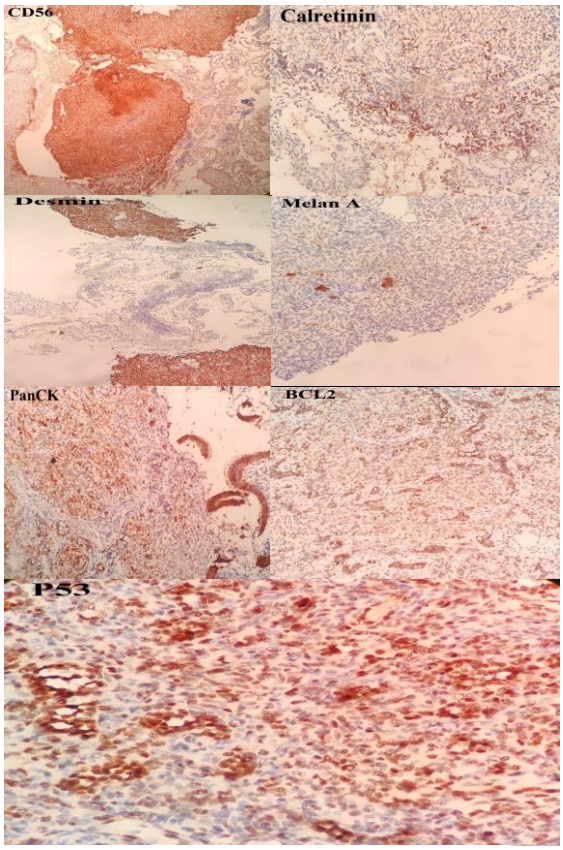

Figure 2. Immunohistochemistry of the uterine tumor resembling ovarian sex-cord tumor (× 40)

Diffuse nuclear staining with estrogen, progesterone and P53, and point nuclear staining with cyclin D1 was remarkable. No staining was seen with EMA, CD99, inhibin, SMA, P16, CD34, CD117, S100, HMB45, β catenin. Ki 67 proliferation index was evaluated as 5-10%. This staining pattern supports the diagnosis of a uterine tumors resembling ovarian sex cord tumors.

Discussion

First described by Morehead and Bowman in 1945 (1), it was divided into two groups according to the proportion of ovarian sex cord tumors-like components in 1976 by Clement and Scully, and this tumor, which was named as ovarian sex cord tumor (UTROSCT), was 50% -100%. sex cord-like histomorphology is in question. The other group was named as endometrial stromal tumors with sex cord-like elements (ESTSCLE), with less than 50% sex cord tumor-like components (10).

UTROSCT; it often presents clinical symptoms such as menorrhagia, postmenopausal bleeding, abdominal distention, abdominal or pelvic pain (11). It may also appear asymptomatically. Usually manifests as an intramural, submucosal or subserosal mass in the uterine corpus (12). It is often interpreted as intracavitary polyps or intramural myomatous lesions. The diagnosis is made by histopathological and immunohistochemical examinations.

It may show histomorphological variants as solid layers or small clusters, or as retiform or plexiform pattern, or as intersecting cords of two cell widths, or in a trabecular or tubular form, or with macrofollicular or microfollicular characteristics, or diffuse or mixed pattern within the hyalinized or fibroblastic stroma (11). Rarely, formations similar to Call-Exner bodies observed in granulosa cell tumors and cells with eosinophilic or foamy cytoplasm resembling luteinized stromal cells can be seen (13-16). Mild cellular atypia may be observed, but it is generally composed of cells with round or oval nuclei in uniform appearance, indeterminate nucleolus and eosinophilic cytoplasm. Nuclei can be hyperchromasic or a nuclear groove can be observed in between (11,17-19). Rare lymphocytic infiltration, foamy histiocytes, focal

hemosiderin may appear as other uncommon microscopic findings (20). Necrosis, vascular invasion, 2-3 (10 hpf) mitosis are extremely rare; their presence indicates aggressive progression (21)

Immunohistochemically, UTROSCT has a highly variable staining pattern just like its histology. For diagnosis, it should be stained with one or more of the markers of both ovarian sex cord, smooth muscle and epithelial. The sex cord markers it is dyed frequently include CD56, inhibin, calretinin, WT1, CD99, melan A. It is also expected to be stained with SMA, caldesmon, calponin, desmin as myoid and pancytokeratin, EMA, CK AE1 / 3 as epithelial markers. Additionally, it stains with hormone markers such as estrogen, progesterone, androgen and various markers such as vimentin, CD10, BCL2, CD117, S100. Staining with P53 has been reported in the literature in a total of three cases, one of which was associated with recurrence (3,7,22). Immunohistochemical markers and staining diffusions for UTROSCT are different from each other (16,23). Not staining with CD34, chromogranin and HMB45 is important in differential diagnosis (4-6,24).

UTROSCT can be similar to many uterine tumors. Our case was predominantly solid component histologically. Therefore, endometrial polyp, ESTSCLE, endometrial stromal tumors, PEComa, cellular leimyoma, epithelioid hemangioendothelioma were considered in the differential diagnosis.

ESTSCLE is more similar to endometrial stromal tumors. Its molecular structure, clinical course and treatment protocol are different from UTROSCT (17). However, it is microscopically quite similar to UTROSCT. JAZF1 and JJAZ1 fusion monitored in ESTSCLE. It is not seen in UTROSCT and its molecular structure is still unresolved. In UTROSCT, it is expected to be painted with at least two sex cord markers, especially the calretinin. In ESTSCLE, staining is observed with only one sex cord marker (inhibin, CD99, Melan-A and Wilms tumor 1), mostly calretinin (17).

In 2020, the World Health Organization; Endometrial Stromal Tumors classified in 4 groups as endometrial stromal nodüle, low grade endometrial stromal sarcoma, high grade endometrial stromal sarcoma and undifferentiated stromal sarcoma (25). Endometrial stromal nodules usually show diffuse staining with CD10, SMA, vimentin, CD56, estrogen receptors, and focal staining with pancytokeratin, desmin, and progesterone receptors. No staining expected with WT1, S100, CD117, EMA, CD34, Cyclin D1 (26). Diffuse or focal staining with CD10, SMA, desmin, estrogen receptor, progesterone receptor, cyclin D1, pancytokeratin, WT1, CD34, BCL2, vimentin may occur in low grade endometrial stromal sarcoma; however, they do not stain with S100, CD117, EMA, HMB45, CD99, melan A, synaptophysin, chromogranin, inhibin and P53 (27-29). High grade endometrial stromal sarcomas are stained with CD56, CD117, CD99, cyclin D1, staining with CD1O is variable. Usually staining is not expected with pancytokeratin, DOG1, EMA, SMA, desmin, calretinin, inhibin, estrogen receptor and progesterone receptor (30,31). While stromal cells were stained with P16, CD10, P63 in endometrial polyps; no staining with pancytokeratin, EMA (32). PEComa is almost always positive with SMA, cathepsin K, HMB45, desmin, and melan A markers (33). They are not stained with the markers pancytokeratin, PAX8, S100, CD10 (34). Epithelioid hemangioendothelioma is expected to be CD34 positive, but not staining with desmin (35).

There are a number of studies done with P53 marker in UTROSCT (9). The differential diagnosis and prognostic value of p53 marker positivity are not yet known. New studies may clarify this issue in the future.

As a last word, mastering the pathology of this rare tumor, which is considered to be tumors with uncertain attitude or low malignant potential, enables accurate clinical follow-up and treatment.

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