Gazi Tıp Dergisi / Gazi Medical Journal

OLGU SUNUMU - CASE REPORT

2008: Cilt 19: Sayı 2: 89-92

OVARIAN CAVERNOUS HEMANGIOMA: A CASE REPORT AND REVIEW OF THE LITERATURE WITH REFERENCE TO CONTROVERSIAL PATHOLOGICAL DIAGNOSES

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ABSTRACT

Vascular tumors of the female genital tract, especially those arising in the ovary, are very rare although the ovary has a rich vascular supply. We report a case of cavernous hemangioma of the right ovary in a 48-year-old woman who underwent total abdominal hysterectomy and right salpingo-oophorectomy for symptomatic uterine leiomyomas. At laparotomy, multiple uterine nodules consistent with leiomyomas were detected but the right ovary was unremarkable. Macroscopically, two intramural leiomyoma nodules, a corpus luteum cyst, a cortical cyst, multiple corpora albicans, and a paratubal cyst were observed. Microscopical examination revealed an incidental cavernous hemangioma, consisting of multiple thin-walled vascular channels, filled with red blood cells in the cortex and medulla of the right ovary, which had not been grossly appreciated. These vascular channels were lined by a single layer of flattened endothelial cells that showed strong immunoreactivity for CD31, CD34, and factor VIII-related antigen.

Key Words: Ovarian Cavernous Hemangioma, Clinicopathological Features, Differential Diagnoses.

OVERYAN KAVERNOZ HEMANJİOM: TARTISMALI PATOLOJİ AYIRICI TANILARIN REFERANS ALINDIĞI LİTERATÜR ESLİĞİNDE OLGU SUNUMU

ÖZ

Overin zengin bir vasküler desteği olmasına karşın kadın genital traktusun vasküler tümörleri özellikle overden köken alanları oldukça nadir görülmektedir. Semptomatik uterus leiomyomlarından dolayı total abdominal histerektomi ve sağ salpingoooforektomi yapılan 48 yaşındaki bir kadın hastanın sağ overindeki kavernoz hemanjiom olgusu bildirilmektedir. Laparotomide leiomyom ile uyumlu multipl uterus nodülü saptanmasına karşın sağ overde anlamlı bir patoloji izlenmemistir. Makroskopik olarak iki intramural leiomyom nodülü, bir korpus luteum kisti, bir kortikal kist, multipl korpora albikans ve bir paratubal kist gözlenmiştir. Mikroskopik inceleme, sağ overin korteks ve medullasında makroskopik olarak görülemeyen, lümenleri eritrosit ile dolu, ince duvarlı multipl vasküler yapıdan oluşan insidental bir kavernoz hemanjiomu ortaya çıkarmıştır. Bu vasküler yapıların CD31, CD34 ve factor VIII-related antigen ile kuvvetli immünreaktivite gösteren tek sıra basıklaşmış endotelyal hücrelerle döseli olduğu izlenmiştir.

Anahtar Kelimeler: Overyan Kavernoz Hemanjiom, Klinikopatolojik Özellikler, Ayırıcı Tanılar.

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INTRODUCTION

Vascular tumors of the female genital tract, especially those arising in the ovary, are very rare. The number of well-documented cases of ovarian hemangiomas does not exceed 60 (1-5). These neoplasms have been reported in both adults and children, with the age ranging from infancy to 81 years (1,6).

The purpose of this paper is to discuss ovarian hemangioma with the emphasis on clinicopathological features and differential diagnoses in light of the most recent literature with reference to controversial pathological diagnoses on this subject.

CASE REPORT

A 48-year-old woman, gravida 1, para 1, underwent total abdominal hysterectomy and right salpingo-oophorectomy for symptomatic uterine leiomyomas. Her medical history was noncontributory except for a left ovarian cyst excision 23 years before. Laboratory data showed no abnormal findings except for hemoglobin concentration being 9.7 g/dL on admission. At laparotomy, multiple nodules consistent with leiomyomas, being 8 cm in greatest diameter, originating from the right and left cornua of the fundus, were detected. The right ovary was unremarkable.

Macroscopically, two well-demarcated intramural nodules, 10 cm and 6 cm in greatest dimension, having a white-tan whorled appearance without hemorrhage and necrosis were observed. The right ovary had a golden-yellow corpus luteum cyst with a hemorrhagic center, 3.5 cm in greatest dimension, a cyst filled with clear fluid that was 1.5 cm in greatest dimension, and multiple corpora albicans. The right tube had a thin-walled paratubal cyst, filled with clear fluid that was 5 cm in greatest dimension.

Microscopically, an incidental hemangioma of cavernous type was noted, which had not been grossly appreciated in the right ovary. Numerous thin-walled vascular channels having different sizes and configurations, some of which were dilated and filled with red blood cells, were observed to replace the cortex and medulla in a haphazard fashion. Although the lesion was not well-demarcated from the surrounding parenchyma, its approximate diameter was measured as 28 mm microscopically. These vascular channels were lined by a single layer of flattened endothelial cells without atypical features. A variable amount of connective tissue stroma separated the vessels, in which no inflammatory reaction, hemorrhage, or calcification were observed (Fig. 1).

The endothelial cells showed strong immunoreactivity for CD31 (Fig. 2), CD34, and factor VIII-related antigen. At first glance, the main differential diagnosis that had to be taken into consideration in the current case was vascular proliferations, which have a tendency to be diffuse and smaller in dimension when compared with hemangioma, which is considered a more circumscribed lesion. Although the lesion was located haphazardly in the cortex and medulla, the presence of numerous thin-walled

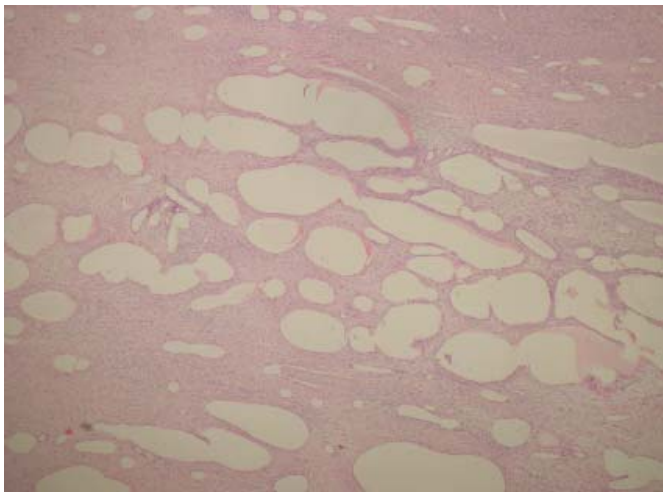

Figure 1: Numerous thin-walled vascular channels with different sizes and configurations, lined by a single layer of flattened endothelial cells (Hematoxylin and eosin, x40).

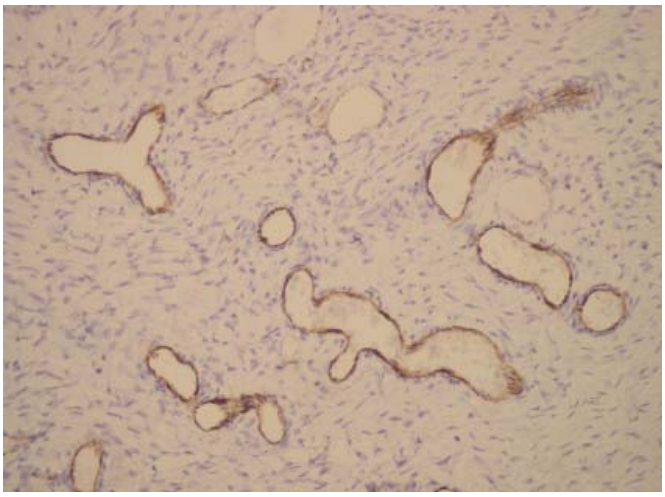

Figure 2: The endothelial cells showing immunoreactivity for CD31 (Diaminobenzidine, x200).

vascular channels, some of which were filled with red blood cells, ranging from small to large sizes with variable configurations, separated by a variable amount of connective tissue, was the most important morphological feature that led to this lesion being interpreted as hemangioma rather than vascular proliferations in the current case. Lymphangioma, which was considered in the differential diagnosis of this case because of a similar morphological appearance, was excluded due to the absence of pale eosinophilic homogeneous material within the vascular channels.

DISCUSSION

Vascular tumors of the female genital tract, especially those of the ovary, are very rare. This is not expected since the ovary has a rich vascular supply. Cyclic changes in the female genital organs during the reproductive period and the asymptomatic nature and small size of the neoplasm have been attributed to explain its rarity of occurrence (7).

Although the exact number of ovarian hemangiomas is disputed, the number of well documented cases seems to be 50 or more but does not exceed 60 (1-5). Eight of these cases have been reported in children (1). Since the diagnoses of two of the cases have been regarded as controversial (8,9), the number of ovarian hemangiomas in childhood could remain restricted to six.

Ovarian hemangiomas are usually asymptomatic and present as incidental findings during operation, autopsy (4), or histological evaluation as in our case. Large lesions tend to present clinically with symptoms of a painful adnexal mass such as acute abdomen due to torsion or abdominal enlargement or distention because of the mass itself. However, the mode of clinical presentation seems to be different in the pediatric age group since they present with symptoms more frequently than adults. They present either with an abdominal or pelvic mass and/or with lower abdominal pain with nausea and vomiting, and torsion is noted as a frequent sign (1).

Ovarian hemangiomas have been reported to be associated with massive ascites clinically mimicking an ovarian carcinoma (2,10), pseudo-Meigs' syndrome (2), elevated serum CA-125 levels (2,3,10), stromal luteinization, stromal hyperplasia (3,10,11-16), and thrombocytopenia as a complication in which decreased platelet count is regarded as one of the manifestations of Kasabach and Merritt syndrome, particularly in bilateral cases associated with diffuse abdominopelvic hemangiomatosis (4,17). Ovarian hemangiomas coexistent with non-ovarian neoplasms such as endometrial carcinoma (3), cervical carcinoma (5), rectosigmoid carcinoma (14), and tubal carcinoma (15) have also been reported.

The etiology of ovarian hemangiomas remains unknown. These lesions have been considered either hamartomatous malformations or true neoplasms in which pregnancy, other hormonal effects, or infection (18) have been implicated as factors enhancing the growth of hemangiomas. There have been some speculations concerning the relationship between hemangiomas of the ovary and hormonal status/disorders in the literature. It has been suggested that pre-existing stromal luteinization of the ovaries may stimulate the development of an ovarian hemangioma in which the inciting event seems to be hyperestrogenism due to the growth stimulatory effects of estrogens on vessels and expression of estrogen receptors by hemangiomas (12,14). According to another hypothesis, the presence of an expansile ovarian hemangioma induces stromal luteinization by mass effect. This is based on the fact that, although hemangiomas are non-functional neoplasms, luteinization of stromal cells restricted to the stroma of the neoplasm or the stroma adjacent to the neoplasm commonly occurs as a reactive process to the presence of any expansile ovarian lesion (3,4). These luteinized stromal cells produce steroid hormones, mainly androgens, which are subsequently converted to estrogens in adipose tissue, potentially causing unopposed estrogenic stimulation to the endometrium. The end result of this cascade manifests itself as estrogenic, androgenic, or a combination of both such as postmenopausal or dysfunctional uterine bleeding (3,12,13,15), aching breasts (13), advanced male type hair loss (3), and elevated androgen and estradiol levels (3) on clinical and biochemical grounds. Ovarian hemangioma induced endometrial stimulation has been reported in a few patients with endometrial hyperplasia (11-13,15,19).

Macroscopically, ovarian hemangiomas are usually small and the size of the lesions has been reported to range from 5 mm to 24 cm in greatest diameter (4). However, regarding the size in relation to age, cases concerning children demonstrate comparatively large tumors (1). Grossly, enlarged ovaries with a smooth glistening outer surface showing a red or purplish cut surface of a spongy texture and honeycomb appearance due to multioculated cystic spaces filled with frank blood or serous fluid are observed. They are usually unilateral and occasional bilateral cases have been reported (4,17). Although they may be encountered in any part of the ovary, the medulla and hilum appear to be the most common sites. Histologically, they demonstrate either a cavernous, capillary, or mixed type with the cavernous type predominating (4), as in this case, in contrast to hemangiomas in other parts of the body. This has been considered to be due to the specificity of female organs and their sensitivity to hormonal effects. Microscopically, they are composed of dilated, blood-filled, generally thin-walled vessels ranging from small to large sizes, lined by a single layer of flattened endothelial cells. The vessels may be haphazardly located or display a roughly lobular arrangement in a variable amount of connective tissue stroma in which inflammation, hemorrhage, hemosiderin deposits, and calcification can be detected.

While the clinical differential diagnoses of ovarian hemangiomas include tubo-ovarian mass, twisted ovarian cyst, and chocolate cyst (5), the main pathological differential diagnoses are those of vascular proliferations, lymphangioma, and monodermal teratoma composed of a prominent vascular component. However, angiosarcoma and steroid (lipid) cell tumor of the ovary can be added to the list. The most problematic entity that enters into the differential diagnosis is proliferations of dilated hilar blood vessels since the number of true ovarian hemangiomas has been questioned because of the difficulty in distinguishing a small hemangioma from such vascular proliferations. However, the hemangioma usually forms a reasonably circumscribed nodule or a small mass composed of vascular channels, ranging from small to large sizes with a variable amount of stroma when compared with vascular proliferations, which tend to be smaller and diffuse. Although haphazardly located, the presence of numerous thin-walled vascular channels having different sizes and configurations, separated by a variable amount of connective tissue, was the key morphological feature that led to this lesion being interpreted as hemangioma rather than vascular proliferations in the current case. It should also be kept in mind that the medullary blood vessels may appear particularly numerous and closely packed in postmenopausal women and should not be mistaken for a hemangioma. One of the main characteristics of these vessels is that they may be calcified or have thickened walls and narrowed lumina due to medial deposition of a hyaline, amyloid-like material (20). The presence of numerous blood cells within the vascular channels and the absence of pale eosinophilic homogeneous material usually distinguish hemangioma from lymphangioma. One of the controversial issues regarding the differential diagnosis involves distinguishing a monodermal teratoma having an angiomatous component from a pure hemangioma. Although vascular elements are not generally a component of ovarian teratomas, bilateral ovarian teratomas with a large hemangiomatous component have been reported in which the lesions were distinguished from a pure hemangioma by the presence of a focus of respiratory epithelium (21). While one of the reported cases of hemangioma in a 4-year-old child (8) was criticized as it contained dermoid elements (21), the other one suggested that the lesion, reported as an ovarian hemangioma, may have actually been a teratoma since a small cyst lined by squamous epithelium adjacent to the main lesion was detected (19). In the case reported as the first Turner's syndrome associated with ovarian hemangioma, there was a combination of mixed germ cell tumor and a cavernous hemangiomatous lesion in the right gonad in which the hemangiomatous lesion was, indeed, accepted histogenetically as being most likely of germ cell origin by the authors later (9). In fact, it has been debated that hemangiomas may actually represent monodermal teratomas. However, this was rejected by Prus et al. (22), who examined simple sequence repeat (SSR) polymorphic markers in the tumor tissue, as well as in the patient's and her parents' blood in order to further confirm whether the tumor in their case represented a germ cell neoplasm or not. They observed that the SSR markers were found to be identical in the tumor and in the patient's somatic cells. Therefore, it was suggested that the tumor described was a congenital infantile hemangioendothelioma most probably arising from ovarian parenchymal cells rather than a monodermal teratoma of germ cell derivation. Thus, in the case of a teratoma with a prominent vascular component, extensive and careful sampling will detect other teratomatous elements, the presence of which will help in distinguishing the lesion from a hemangioma.

Angiosarcomas have vascular spaces lined by endothelial cells showing papillary tufting, marked cytologic atypia, pleomorphism, and increased mitotic activity. The presence of degenerative changes may mimic vascular spaces in a stromal luteoma or intraoperative microscopical appearance could be suggestive of a stromal luteoma (3). Although stromal luteinization can be detected in ovarian hemangiomas, more classical features of a lipid cell tumor such as hyperthecosis, steroid (lipid) cell, or Leydig's cells are not evident in a hemangioma. Furthermore, the presence of immunoreactivity with some vascular endothelial markers also confirms the diagnosis of a vascular neoplasm. Inhibin, while staining characteristically a steroid cell tumor, points against a vascular neoplasm.

In conclusion, hemangiomas of the ovary are very rare neoplasms with a broad age range that are usually discovered incidentally during operation or autopsy. These neoplasms should be considered in the differential diagnosis of a hemorrhagic ovarian lesion grossly. Surgical extirpation of the involved areas is the treatment of choice and risk of Kasabach and Merritt coagulopathy has to be considered in larger tumors, thus necessitating correct diagnosis and definitive surgical treatment.

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