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Adenomatoid tumor of the female genital tract: Report of three cases

Kadın genital sisteminde adenomatoid tümör: Üç olgu sunumu

Filiz BOLAT[1], N. Emrah KOÇER[1], Nebil BAL[1], Ümran KÜÇÜKGÖZ[2]

Baskent University Faculty of Medicine, Department of Pathology[1], Department of Gynecology and Obstetrics[2], ANKARA

ÖZET

Adenomatoid tümörler en sık olarak kadın ve erkek genital sistemlerinde görülen iyi huylu üreyişlerdir. Bu az rastlanan tümörün mezotelyal hücrelerden köken aldığına dair pek çok immünhistokimyasal ve elektron mikroskopik çalışma mevcut olmakla birlikte, histogenezisi kesin değildir. Bu çalışmada, kadın genital sisteminde saptanmış üç adenomatiod tümör olgusu sunulmakta ve bu tümörün klinik bulguları, kökeni ve immünhistokimyasal profili tartışılmaktadır. Olgulara ait ait parafin bloklarından hazırlanan kesitlere, immünhistokimyasal olarak kalretinin, HBME-1, vimentin, sitokeratin, EMA ve CD31 uygulandı. Hastaların yaşları 40 ile 46 arasında değişmekteydi (ortanca yaş 43,3). Tümörlerden biri uterusta diğer ikisi fallop tüpünde yerleşmişti. Tümörlerin boyutları 0,6-5 cm arasında değişmekteydi. İmmünhistokimyasal olarak tüm tümörlerde sitokeratin, kalretinin, HBME-1 ve vimentin ile yaygın ve kuvvetli pozitiflik izlenirken, EMA ve CD31 negatifti. İmmünhistokimyasal sonuçlar adenomatoid tümörün benign bir mezotelyoma olduğunu savunan teorileri desteklemektedir. İmmünhistokimyasal fenotipler ayırıcı tanıda önemli bir rol oynamaktadır.

Anahtar sözcükler: Adenomatoid tümör, kadın genital sistemi, histogenez

ABSTRACT

Adenomatoid tumors are benign proliferations that are most often encountered in the female and male genital tracts. The mesothelial phenotype of these unusual tumors has been established by a variety of ultrastructural and immunohistochemical studies, although their histogenesis is by no means certain. In this paper we report three cases that were diagnosed as genital tract adenomatoid tumors and discussed the clinical signs, origin and immunohistochemical characteristics of the this type of tumor. Immunohistochemical expression of calretinin, HBME-1, vimentin, pancytokeratin, EMA, and CD31 were analyzed in three ATs, using formaline -fixed, paraffin-embedded archival tissues. The age of the patients were ranging from 40 to 46 years with a median of 43.3. Tumors were located in uterus (one), and fallopian tube (two). Tumor sizes were ranging between 0.6-5 cm. Immunohistochemically all tumors exhibited strong and diffuse positivity for pancytokeratin, calretinin, HBME-1 and vimentin, but negativity for EMA, and CD31. The immunohistochemical results support histogenetic theories of the adenomatoid tumor that claim it as a type of benign mesothelioma. Immunohistochemical phenotypes can play an important role in the differential diagnosis

Key words: Adenomatoid tumor, female genital tract, histogenesis

INRODUCTION

Adenomatoid tumors (ATs) are specialized benign mesothelial tumors that are preferentially found in the genital systems of both males and females (1-9), and only rarely reported in other sites, such as adrenal glands (10), pleura and peritoneum (11). In the female genital system they are found in the fallopian tubes, uterus and ovarian hilus, whereas they also occur in epididymis, spermatic cord, prostate, and ejaculatory duct in the male (1,6,9). ATs have been observed in women between 30-72 years of the age (median 42 years) (2). It is found in 0.1%-

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Corresponding Author: Dr. Filiz Bolat, Baskent University Faculty of Medicine, Department of Pathology, 06490-Ankara

1% of women, who are hysterectomized for other reasons. Most ATs are localized and usually small incidental tumours, but large lesions have also been reported (3).

Although a variety of ultrastructural and immunohistochemical studies have provided strong support for mesothelial differentiation, their preferential occurence in the genital organs has not yet been well explained. Alternative explanations, including differentiation from muscle, vascular endothelium, and pluripotent mesenchymal cells have also been proposed.

In this study, immunohistochemical phenotypes and the origin of this neoplasm are discussed.

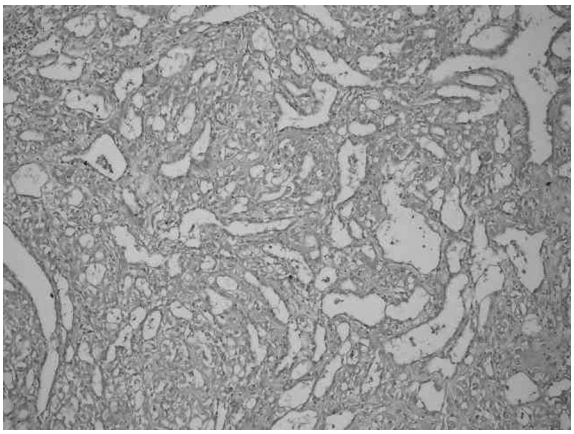
MATERIALS and METHODS

Three AT cases that were diagnosed in the pathology department of Baskent University Hospital, Adana were included in this study. Basic clinical and pathological data as well as paraffin blocks were available. Immunohistochemical stainings were performed on formalin-fixed, paraffin-embedded tissue sections. Sections were cut in a thickness of 5 µm, placed on slides, deparaffinized in xylene, and hydrated in a graded series of alcohol.The sections were immunohistochemically stained with calretinin (clone CRT01, NeoMarkers, Fremont CA, USA), HBME-1 (lot:1494R604A, NeoMarkers, Fremont CA), vimentin Ab-2 (clone V9, NeoMarkers, Fremont CA, USA), EMA (clone E29, code N1504, DakoCytomation, LSAB) pancytokeratin (clone:AE1/AE3, N1590, Lot:00007872, DakoCytomation, LSAB), and CD31 (clone:JC/70A, NeoMarkers, Fremont CA, USA) using avidin-biotine detection system. Each case was scored as positive or negative as for each antibody.

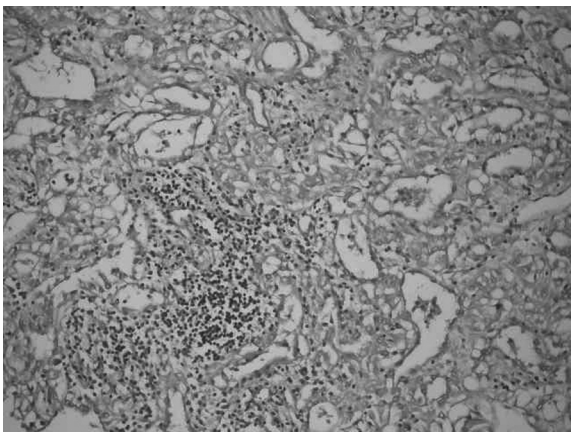
RESULTS

The patients' ages at the time of diagnosis were ranging from 40 to 46 years with a median of 43.3 years. In one case the tumor was located in the uterine corpus, and in the other two in the fallopian tube. All cases were incidental findings in hysterectomy specimens obtained from uterine leiomyomas. Tumor sizes ranged from 0.6-5 cm. The uterine tumor was a white-yellow, nodular mass, with a whorled cut surface, and the tumor borders with the surrounding myometrium were not as sharply defined as a leiomyoma. The cervix, fallopian tubes, and ovaries showed no significant pathologic features.
In the remaining two cases, the tumors were smaller than the uterine one, and the masses were located within the right fallopian tubes nearby the fimbria.

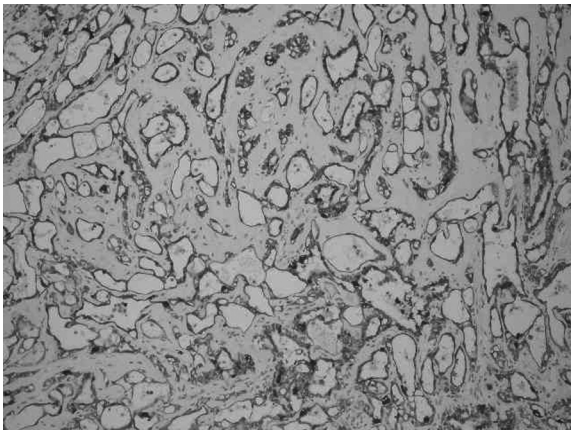
In histologic examination, all adenomatoid



Resim 1. The microscopy shows multiple split-like spaces lined by a single layer of flattened endothelial-like cells (HE x100).



Resim 2. Multiple tubules and adenomatoid spaces and a chronic follicular inflammatory infiltrate (HE x200).



Resim 3. Immunohistochemically, the tumor revealed strong staining for calretinin (Calretinin x100).

tumors were composed of ill-defined, nodular proliferations of variably sized tubules and cysts lined by eosinophilic cuboidal or flattened cells (Figure 1). The cells lining the gland-like structures have small-to-moderate amounts of pale, often vacuolated cytoplasm and small, but conspicuous nucleoli. Nuclear pleomorphism, calcification, and mitotic figures were not seen. All cases contained chronic inflammatory cells either as isolated lymphocytic infiltrates or as true lymphoid follicles (Figure 2).

Immunohistochemically, the neoplastic cells in all tumors were stained strongly positive with pancytokeratin, the mesothelial antigen calretinin and HBME-1 (Figure 3), less intensely with vimentin. EMA and CD31 were consistently negative.

DISCUSSION

ATs are presumed to be of mesothelial origin (benign mesotheliomas). They occur in areas or organs close to mesothelium-lined surfaces (1-6). They are most common in the genital tract of both males (paratesticular and epididymal tissues) and females (tubal, uterine, and ovarian tissues) (1-9).

The histogenesis of adenomatoid tumors is controversial, and mesonephric, mullerian, endothelial, and mesothelial origins have been suggested (5,12-14). Previous studies, based on electron microscopic and immunohistochemical findings support a mesothelial origin (1-6).

Since they are almost merely incidental findings in hysterectomy specimens of adult women, the true incidence of these tumors is unknown. Furthermore, they are frequently mistaken macroscopically for leiomyomas, just as in our cases.

Macroscopically, they most often appear as nodular formations with ill- defined margins with the surrounding myometrium, an observation that helps to differentiate the lesion from leiomyomas, which are much more clearly delineated. Only a small proportion of the cases are not identified macroscopically, because they diffusely involve the myometrial wall and lack nodular arrangement. They may be located intramurally and subserosally (1). The uterine AT in our patient was located intramurally.

There are several histologic types of ATs. Quigley and Hart (15) have described four types: adenoid (also referred as tubular or glandular), angiomatoid, solid, and cystic. Although most tumors feature adenoid or angiomatoid histologic patterns, in our cases all of which represented adenomatoid patterns, and combinations of two or more patterns in each tumor. Tumors are usually solitary, small, and solid, but multiple, multinodular, diffuse, and large cystic lesions have also been described, particularly in the uterus (6). Cytologic atypia and mitoses are typically absent. In the uterus, they often associated with smooth muscle hypertrophy, whereas extrauterine forms frequently contain intermingled fibroblastic tissue. Some believe that, this is a reactive hyperplasia of indigenous myometrial smooth muscle, and this contention is supported by the absence of smooth muscle in ATs that occur in other sites, such as ovary, mesentery, adrenal glands, and omentum (1). Others postulate that, this represents a neoplastic component, and the possibility of a collision tumor composed of leiomyoma and adenomatoid tumor cannot be completely disallowed (16,17).

To date, no recurrence or malignant trans-

formation have been reported in ATs. Therefore, the recommended treatment is simple excision of the tumor, if possible.

The histogenesis of AT is controversial. Some authors have suggested, mesonephric, müllerian, endothelial, and mesothelial origin (5,12-14,18). Their usual subserosal position would suggest an origination from the uterine peritoneum. Alternatively, since most tumors have an intramural location, it has been speculated that the mesothelial component may originate from muscle (1).

It was recently suggested that these tumors originate from mesenchymal stem cells differentiating toward submesothelial or mesothelial cells (18). However, ultrastrucal and immunohistochemical studies indicates that ATs are benign mesotheliomas. Ultrastructurally, tumor cells showed numerous apical microvilli, abundant cytoplasmic filaments, and desmosomes. Immunohistochemically, the tumor cells are strongly positive for cytokeratin, vimentin, HBME-1 (anti-human mesothelioma antibody), and calretinin but negative for EMA, factor VII-I, Ber-EP4, and carcinoembryonic antigen (CEA). These characteristics are all presented in normal mesothelium and in the cells of mesotheliomas.

The reactivity for cytokeratin, calretinin, HBME-1 and vimentin, and consistent negativity for EMA, CD31 in our study suggest a mesothelial origin for adenomatoid tumor, which is compatible with the literature.

A possible explanation of this phenomenon is that ATs arise from inclusions of mesothelium incorporated into subserosal connective tissue or myometrium.

The differential diagnosis is not usually complicated because ATs are easily recognizable. However, macroscopically large cystic tumors may resemble a lymphangioma (19). ATs with a diffuse, infiltrative growth pattern may cause a diagnostic dilemma. In these instances, because of the unusual setting or pseudoinfiltrative pattern, distinguishing ATs from malignant lesions such as metastatic signet-ring cell adenocarcinoma, epitheloid hemangioendothelioma, germ cell tumor, or sex cord-stromal tumor becomes more important (20,21).

Immunohistochemically, the invariably intense cytoplasmic staining with cytokeratin markers in conjunction with the absence of staining for factor VIII and CD31 in adenomatoid tumors is usually sufficient to exclude vascular tumors and other mesenchymal lesions. Similarly, absence of inhibin expression helps to exclude adrenal cortical or sex cord-stromal neoplasm (1). Additionaly, ATs may sometimes contain cells with small intracytoplasmic vacuoles and may be confused with signet-ring cell adenocarcinoma. The bland cytologic features and absence of mitoses, histochemical negativity of mucin stains, immunohistochemical carcinoembryonic antigen (CEA) and EMA negativity support the diagnosis of ATs (1,7).

In summary, our immunohistochemical results confirm that ATs of female genital tract have mesothelial origin. Immunohistochemical phenotypes are important in the differential diagnosis. The biologic behaviour of AT is benign and has a good prognosis.

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