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Araştırma / *Research Article*

Histopathological Features of Paratesticular Solid Tumors: 5 Years Experience

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Paratestiküler Solid Tümörlerin Histopatolojik Özellikleri: 5 Yıllık Deneyim

ABSTRACT

Objective: *The aim of this study is to determine the types of tumors seen in the paratesticular region, to discuss the most prominent histopathological features and differential diagnoses of rare tumors among our cases as well as to compare the findings with the literatüre.*
Method: *The patients operated in Bezmialem Vakıf University for inguinal hernia and paratesticular tumor between 2014-2019 and diagnosed as paratesticular tumor were added to our study. Diagnosis, clinical findings and demographic data of the cases were recorded.*
Results: *We had a series of 21 paratesticular tumors with a mean age of 58.8 years. The most common; benign tumor was lipoma and malignant tumor was liposarcoma. Hemangioma, ovarian type serous carcinoma and mesothelioma were also rarely seen in the literature.*
Conclusion: *Paratesticular tumors are composed of tumors originating from rete testis, epididymis and tunica vaginalis, soft tissue tumors and metastatic tumors. The most common epithelial tumors are adenomatoid tumors. The most common benign and malignant mesenchymal tumors are lipoma and liposarcoma, respectively. Histomorphological appearance may be difficult especially in malignant epithelial tumors. Although immunohistochemical markers are helpful in differentiation, the transition between the lesion and non-neoplastic epithelium is important. Paratesticular tumors are quite rare. For this reason, at this location both primary tumors -especially malignant- and metastasis can be challenging. They should be kept in mind for differential diagnosis.*

Keywords: *paratesticular, mullerian, adenomatoid*

ÖZ

Amaç: *Bu çalışmada amacımız paratestiküler bölgede görülen tümörlerin tiplerini tayin etmek, en sık karşılaştığımız tümörler yanısıra olgularımız arasında bulunan nadir tümörlerin dikkat çekici histopatolojik özelliklerini ve ayırıcı tanılarını ayrıntılı olarak tartışmak, ve son olarak bulgularımızı literatür verileri ile karşılaştırmaktır.*
Yöntem: *Çalışmaya, 2014-2019 yılları arasında Bezmialem Vakıf Üniversitesi'nde inguinal herni ve paratestiküler kitle nedeniyle opere olmuş vakalar arasından, paratestiküler tümör tanısı alan olgular dahil edildi. Vakaların tanıları, klinik bulguları ve demografik verileri kaydedildi.*
Bulgular: *Yirmi bir olguluk paratestiküler tümörlerimizin yaş ortalaması 58.8'di. En sık görülen benign tümör lipom, malign tümör liposarkomdu. Ayrıca literatürde oldukça nadir görülen, hemangiom, ovaryan tip seröz karsinom ve mezotelyoma da mevcuttu.*
Sonuç: *Paratestiküler tümörler, rete testis, epididim, tunika vaginalis, yumuşak doku tümörleri ve metastatik tümörlerden oluşur. En sık görülen epitelyal tümör adenomatoid tümördür. Mezenkimal benign tümörlerden lipom, malignlerden ise liposarkom görülmektedir. Histomorfolojik görünüm özellikle malign epitelyal tümörlerde güç olabilir. İmmünhistokimyasal belirleyiciler ayrımda değerli olsa da lezyonun neoplastik olmayan epitel ile geçişi önemlidir. Paratestiküler tümörler oldukça oldukça nadirdir, bu lokalizasyonda ve metastazlarda ayırıcı tanıda akılda tutulmalıdır.*

Anahtar kelimeler: *paratestiküler, müllerian, adenomatoid*

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INTRODUCTION

Paratesticular tumors are tumors of rete testis, tubuli efferentes/epididymis, mesothelium, soft tissue and metastatic tumors of this region. Their common findings are nonspecific: pain or swelling due to inguinal hernia, hydrocele sac or inflammation [(1)]. Paratesticular masses account for about 30% of all scrotal masses. Lipoma and adenomatoid tumors are the most common benign tumors [(2)]. Our aim is to draw attention to tumors in the paratesticular region and to compare histopathological features and differential diagnosis with the literature.

MATERIALS and METHODS

The patients were operated in Bezmialem Vakıf University for inguinal hernia and paratesticular mass between January 2014-August 2019. Cases diagnosed with paratesticular tumor were added to our study, and paratesticular cystic lesions and paratesticular spread of intratesticular tumors were excluded. Pathologic diagnoses were reviewed according to the World Health Organization 2016 classification. Diagnosis, clinical findings and demographic data of the cases were recorded. The study was approved by the local ethics committee (permission no:13/264).

RESULTS

21 cases with a mean age of 58.8 (37-78) were included in the study. 61.9% (13 cases) of the tumors were diagnosed as benign, and 38% (8 cases) were diagnosed as malignant. Lipoma was the most common type of benign tumors, constituting the majority (77%). Malignant tumors were very few: 50% (4 cases) were liposarcoma, and 25% (2 cases) were mesothelioma (Figure 1). Lipoma and liposarcomas presented with complaints of inguinal hernia; adenomatoid tumor, hemangioma, mesothelioma, ovarian serous carcinoma and metastasis presented with scrotal swelling. Exceedingly rare cases of ovarian type serous carcinoma and colon adenocarcinoma were also encountered (Figure 2, 3).

DISCUSSION

Paratesticular tumors include primary tumors and metastasis from rete, epididymis, soft tissue and mesothelium [(1)]. Mesothelioma is the most common malignant epithelial tumor in the paratesticular region. It may present as a mass in the hydrocele sac or scrotum. 48% of the cases had asbestos exposure. We mostly encountered epithelial types (75%), followed by biphasic types and rarely sarcomatoid types [(3)]. Among our cases, there were two mesotheliomas that consisted of biphasic and epithelial types. Both had a history of hydrocele sac excision. Skin metastases were seen 6 months after chemotherapy and radiotherapy in the case with epithelioid mesothelioma. This patient had severe pain, admitted to palliative treatment and died 1 month later. The other case had no follow-up.

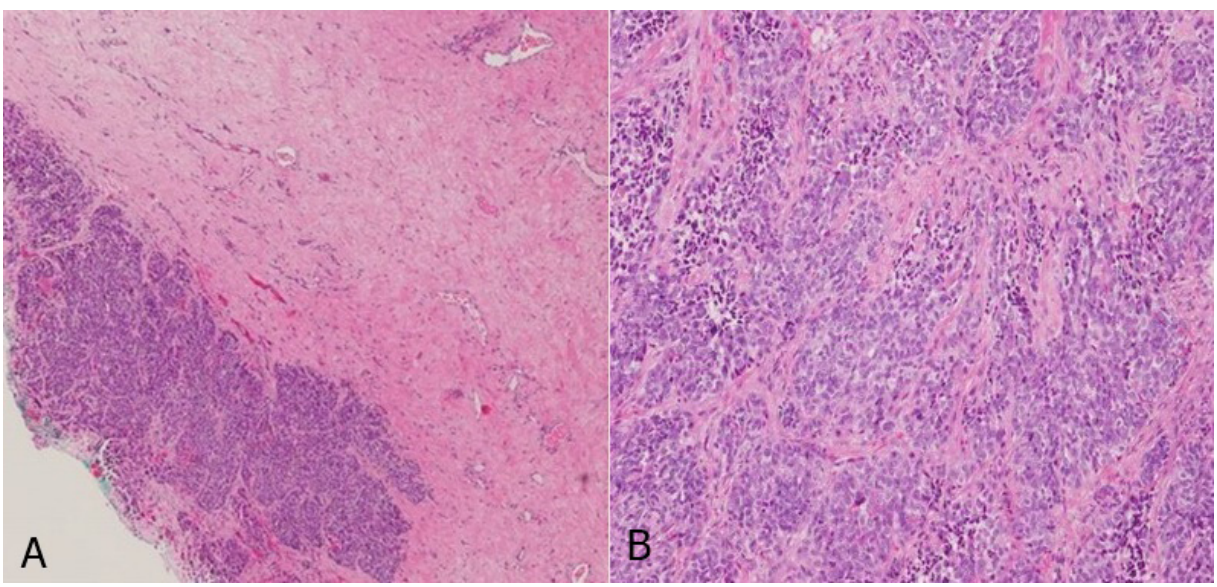

Figure 1. Epithelial tumor forming solid groups (A, HEX100, B, HEX200).

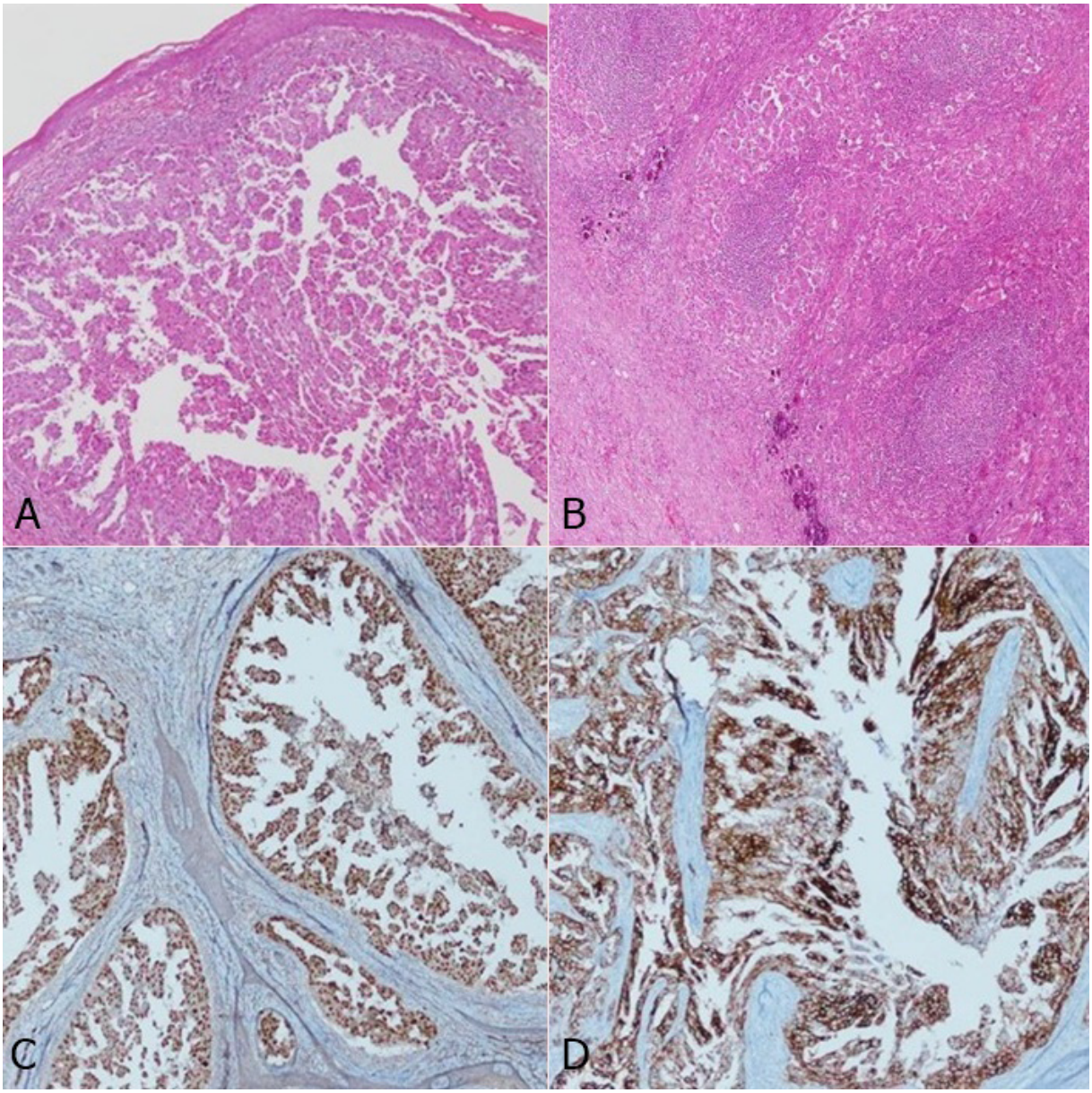

Figure 2. Tumoral tissue forming micropapillary structures in the dermis (A, HEX100), tumor deposit and psammoma bodies in the lymph node (B, HEX100), nuclear-positive staining with PAX-8 in tumor (C, 200), membranous-positive staining with CA125 in tumor (D, X200).

Adenomatoid tumor (AT) is another paratesticular tumor with mesothelial origin. Adenomatoid tumors are rare but account for about 30% of paratesticular tumors. It is most frequently located in the epididymis, less frequently in the spermatic cord, ejaculatory duct, testis parenchyma, prostate and adrenal gland [4]. It is common in 3rd-4th decades. Microscopic cords, nests and tubules constitute the epithelioid appearance. Cells have moderate to significant cuboidal-shaped eosinophilic or vacuolar cytoplasm. Liposarcoma and signet ring cell carcinoma should be considered for differential diagnosis because of this vacuolated appearance. Eosinophilic cytoplasm and cords are important in the differential diagnosis of Sertoli cell and Leydig cell tumors. These tumors show immunoreactivity with mesothelial markers such as Calretinin and D2-40 [4,5]. One of our cases was adenomatoid tumor consisting of cuboidal cells, forming solid groups and cords. Vascular lesions were taken into differential diagnosis. As mentioned above, immunohistochemical positivity for calretinin and negativity for D2-40 and CD34 supported the adenomatoid tumor diagnosis versus hemangioma.

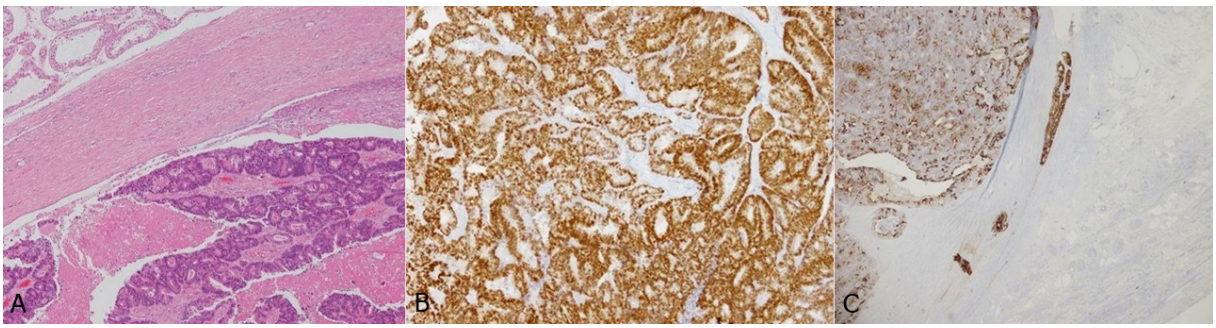

Figure 3. Adenocarcinoma infiltration, cribriform pattern with central necrosis (A, HEX40), Diffuse strong nuclear staining with CDX2 in tumor (B, X100), CK20 positivity in the tumor (C, X40).

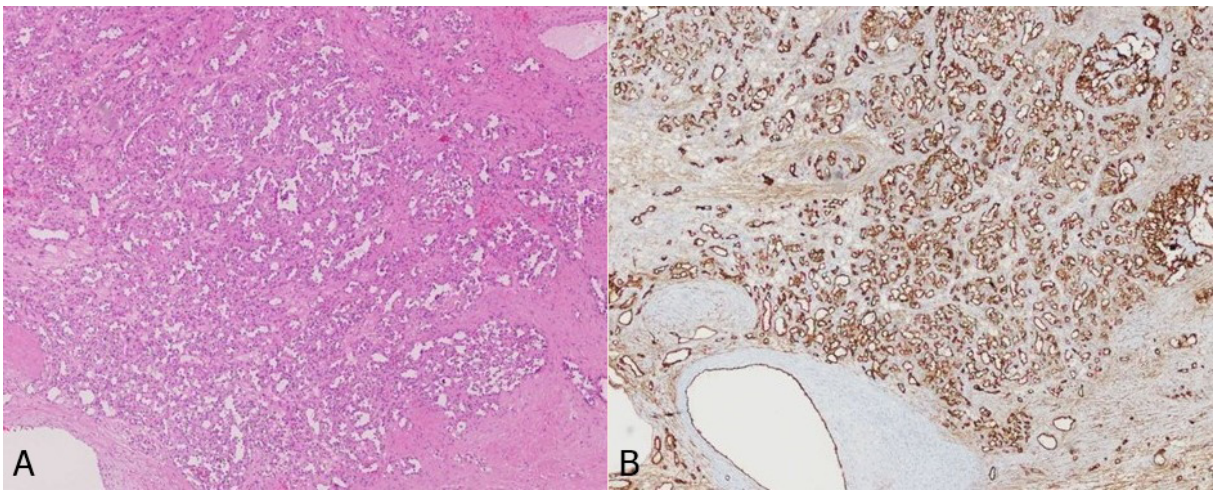

Figure 4. Vascular structures lined by a single row of epithelium in the fibrous tissue (A, HEX100), Diffuse strong staining with CD34 (B, X200).

Other epithelial tumors are cystadenoma and cystadenocarcinoma of rete and epididymis. The diagnosis of rete testis adenocarcinoma is difficult, as both morphological and immunohistochemical features are challenging. Although there was no rete adenocarcinoma among our cases, it should be taken into the differential diagnosis of malignant tumors in this region. The diagnosis of primary rete adenocarcinoma can be valid only under the following circumstances: there should be no tumor in the intratesticular or paratesticular areas, there should be primary tumor focus on the extrascrotal region, the tumor should be located at the hilus, and most importantly, transition from normal epithelium to neoplastic epithelium should be detected [(6)]. These hilar located tumors are aggressive tumors that can be seen in a wide range of age. Most rete located testicular tumors can be tubular or tubulopapillary, and lesser solid, tubular, retiform and kaposiform patterns can be detected. The cells have cuboidal, columnar and eosinophilic cytoplasm. This appearance may also be the pagetoid spread of intratesticular germ cell neoplasia through the rete testis. It should be kept in mind that even if there is no mass in the testis parenchyma, it could spread from a regressed tumor through rete testis [(7)].

Cystadenoma and cystadenocarcinomas of the epididymis can be seen in a wide age range. Histopathologically, tubular and tubulopapillary structures are lined by cuboidal and low columnar cells with low-grade nuclear features. Immunohistochemical tumor cells are stained with CK7, CAIX, PAX8 [(8)]. Unfortunately, we had neither cystadenoma nor cystadenocarcinomas of the epididymis in our series.

Mullerian type epithelial tumors can be seen as cystadenomas, borderline tumors and carcinomas, likewise in ovary. The most common serous type tumors

are the endometrioid, clear cell, mucinous and Brenner tumors. It is known that these tumors develop from appendix testis, appendix epididymis and other Müllerian residues. Müllerian markers CK7, PAX 8 and CA125 can be positive in these tumors [9]. One of our cases was high-grade serous carcinoma and was positively stained with Müllerian markers. This case was 66 years old and presented with scrotal swelling. Scrotal ultrasonography revealed a hydrocele sac, and the case was operated. Microscopic examination revealed papillary and solid tumor tumoral infiltration in the stroma and focally on the surface of the tissue.

Mesothelioma should be taken into consideration for the differential diagnosis of this tumor. In our case, the detection of Müllerian residues in the vicinity of the tumor, the presence of psammoma bodies and positive immunoreactivity with Müllerian markers supported the diagnosis of ovarian type serous carcinoma. The tumor was located in rete testis, epididymis and soft tissue; scrotal resection, omentectomy and lymph node dissection were performed. Recurrence and lymph node metastasis were detected 6 months later.

Paratesticular mesenchymal tumors are especially located in the spermatic cord. Similar to the study of Lioe and Biggart, the most common tumor in our study was lipoma [10]. In sarcomas, liposarcoma, rhabdomyosarcoma and leiomyosarcoma are the most common, and 19% of our cases were diagnosed as liposarcoma. Two of the cases were followed up with no problem detected after radiotherapy treatment.

As in our series, they are most frequently located in the spermatic cord. As in other regions, all types of liposarcoma can be detected [11,12].

Another group of tumors among mesenchymal tumors is vascular lesions. There was one hemangioma among our cases. Priemer et al. had one hemangioma in their series, and they are very rare in this region [13]. In the differential diagnosis, adenomatoid tumor was initially included, and D2-40 and Calretinin negativity and immunoreactivity with CD34 supported the hemangioma (Figure 4).

Secondary tumor involvement can also be seen in the paratesticular region. Dissemination of intratesticular tumors, hematolymphoid tumors and metastatic tumors can be seen. 8.1% of paratesticular malignant tumors are metastatic [1]. It is rarely detected as the first settlement of metastasis. Prostate, colon, and gastric metastases are the most common metastases, whereas lung, malignant melanoma, appendix, kidney, pancreas, and carcinoid tumors have lower proportion in these groups [14,15]. In addition, lymphomas and sarcomas also have metastases. The criteria defined by Amin et al. may be a clue for the metastasis. The findings included the presence of a primary tumor history, being older than 50, bilateral or multifocal tumors, no evidence to support primary testis or paratesticular tumors, extensive vascular/lymphatic invasion and interstitial growth pattern [6]. One of our cases was colon adenocarcinoma metastasis of a 60 years old man with primarily paratesticular location. The presence of widespread vascular invasion and interstitial growth pattern and absence of rete testis, epididymis and tunica vaginalis invasion supported the diagnosis of metastasis. The tumor was morphologically and immunohistochemically (CK20, CDX2 and SATB2 positivity, CK7 negativity) compatible with colon adenocarcinoma metastasis. A computed tomography scan of the abdomen revealed a 5 cm mass in the sigmoid colon wall, and the largest in the liver was 4.6 cm in diameter. The case was diagnosed as adenocarcinoma on colonoscopy, but unfortunately had no follow-up.

Due to the similar morphological appearance in malignant epithelial tumors in the paratesticular region, mesothelioma-associated markers (calretinin, WT-1, CK 5/6), adenocarcinoma-associated antibodies (CEA, Leu-M1, Ber EP4 and B72.3) and Müllerian origin (CA125, PAX8, ER, PR, WT1) markers should be applied. Rete testis and epididymis located tumors have similar morphologic and immunohistochemical patterns. Müllerian tumors and mesothelioma can be distinguished from these tumors by immunohistochemistry.

As a result, paratesticular tumors are rare and may have similar clinical findings. Although benign tumors are morphologically similar, immunohistochemistry helps differential diagnosis. Malignant tumors constitute a small part in paratesticular tumors. Although morphological and immunohistochemical findings are valuable, it is important to show the transition from non-neoplastic to neoplastic epithelium, espe-

cially in primary tumors, also to deepen the history of the patient to evaluate metastasis.

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