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## Paratesticular adenomatoid tumor: A report of nine cases

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## A B S T R A C T

**Introduction:** Paratesticular tumors are rare. Most of them are benign, and adenomatoid tumors are most common.

These tumors sometimes infiltrate the testicular parenchyma and require differential diagnosis with malignant tumors. In such cases, intraoperative biopsy allows for performing conservative surgery.

**Materials and methods:** A retrospective study of nine patients with paratesticular adenomatoid tumors seen during a nine-year period (2000-2008) is reported.

**Results and conclusions:** Patient age (mean, 49.6 years) and most common initial signs (tender nodule) are reported. The tumor most commonly occurred as a small, usually oval, nodule in the tail of epididymis.

Our series included a case each of intraparenchymal tumor of the testis and tumor of the tunica vaginalis. Diagnosis was initially made based on a ultrasound scan and subsequently confirmed by histology. Differential diagnosis and surgical treatment, performed in all patients, are reported, and also the pathological features of surgical specimens.

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## Tumor adenomatoide paratesticular: una serie de nueve casos

## R E S U M E N

## Palabras clave:

Teste

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**Introducción:** Los tumores paratesticulares son raros. La mayoría son benignos, siendo el más frecuente el tumor adenomatoide.

En ocasiones estos tumores infiltran el parénquima testicular y es necesario plantear un diagnóstico diferencial con tumores malignos, por lo que la biopsia intraoperatoria, en estos casos, permite realizar una cirugía conservadora.

**Material y métodos:** Presentamos de forma retrospectiva nuestra extraordinaria serie de 9 casos de tumores adenomatoides paratesticulares durante un periodo de 9 años (2000-2008).

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**Resultados y conclusiones:** Describimos la edad de los pacientes (media de 49,6 años) y la clínica de inicio (nódulo palpable doloroso). La localización de la lesión más frecuente fue en el epidídimo, que habitualmente se manifiesta como un nódulo de pequeño tamaño, generalmente oval en la cola del epidídimo.

En nuestra serie tenemos un caso de lesión testicular intraparenquimatosa y otro en túnica vaginal; el resto se localizan en el epidídimo. El diagnóstico de sospecha fue por ecografía, con confirmación histológica posterior. Describimos el diagnóstico diferencial y el tratamiento quirúrgico, que se aplicó en el 100% de los casos, así como sus características anatomopatológicas.

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## Introduction

Paratesticular tumors are generally infrequent, representing less than 5% of all intrascrotal neoplasms. Benign lesions predominate (75% of all cases), and adenomatoid tumor is the most common presentation (30%). The epididymis is the most common location (generally in the lower pole region), though the tunica albuginea can also be affected, as well as the spermatic cord and the ejaculatory duct. In turn, the lesion can extend to the testicle parenchyma, and when such infiltration is extensive, the impression may be that of a primary testicular tumor extending towards the adjacent structures. In any case, however, the clinical course is invariably benign<sup>1</sup>.

From the macroscopic perspective, these tumors are almost always unilateral and single, measuring no more than 5 cm in size and with a predominance of lesions measuring under 2 cm. They typically form a well delimited but non-encapsulated, round or oval mass. Growth in plaque form is rare, and the margins are not always well defined. The tumors are solid and firm, and the white- or pink-colored sectioned surface presents a storiform or fascicular pattern. Necrosis is usually not observed<sup>2,3</sup>.

Microscopically, the cells form cords, nests or channels which in turn show a pseudovascular or pseudoglandular distribution. Depending on the degree of cellular packing, the tumor may appear solid or cystic. The stromal component is fibrous and sometimes hyalinized<sup>4-6</sup>.

Three basic morphological patterns can be seen: angiomatoid, solid and adenoid.

In general, these histological patterns are mixed within a given tumor, though one or other tends to predominate.

The spaces present in the different histological patterns in turn are crossed by bridge-like filiform cords that produce a "spider web" appearance. Ultrastructurally, these fine cords are identified as the flattened cytoplasm of two adjacent mesothelial cells, and are morphologically very specific of these tumors (present in 100% of all cases). In addition, the mentioned spaces are occupied by mucoid material with PAS-negative and alcian blue-positive staining characteristics typical of acid mucopolysaccharides.

A mesothelial origin is predominantly accepted, considering the tumor immunophenotype, with positivity for calretinin, cytokeratin (CK), vimentin and epithelial membrane antigen A (EMA), and negativity for vascular markers.

The differential diagnosis is established with the following types of tumors: hemangioma, metastatic carcinoma, carcinoma of the rete testis, adenocarcinoma, mesothelioma, vitelline sac tumor, leiomyoma and reactive fibroblast proliferations<sup>7,8</sup>.

## Material and method

A retrospective study has been made, evaluating the paratesticular adenomatoid tumors diagnosed and treated in our hospital over a 9-year period (2000-2008). We present a series of 9 cases and describe the age of the patients, the initial clinical manifestations, the preoperative diagnosis, treatment, and posterior histological and immunohistochemical confirmation.

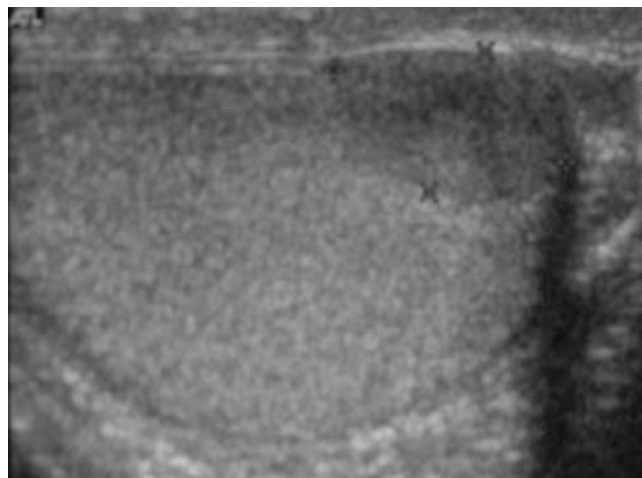
## Results

The mean patient age was 49.6 years (range 33-61). The initial clinical manifestations consisted of a palpable and painful nodule in 8 patients (88.8%), and initial acute orchiepididymitis in one case. The right side was affected in 5 patients and the left side in 4 cases. In all cases the diagnosis was suspected on the basis of the ultrasound findings. The ultrasound appearance is variable in these tumors, though the lesions tend to be isoechoic, of generally small size (< 2 cm), with a characteristic oval shape, and are commonly located in the lower pole or tail region of the epididymis (fig. 1). In our series the epididymis was affected in 7 cases, while one patient presented an intratesticular lesion and another showed involvement of the tunica vaginalis. An intraoperative study was made in three patients, with a diagnosis of adenomatoid tumor in two cases (lesion located in the tunica vaginalis, intratesticular tumor, and lesion in the tail of the epididymis). The intraparenchymal tumor was the smallest of the lesions, and the histopathological diagnosis indicated testicle atrophy.

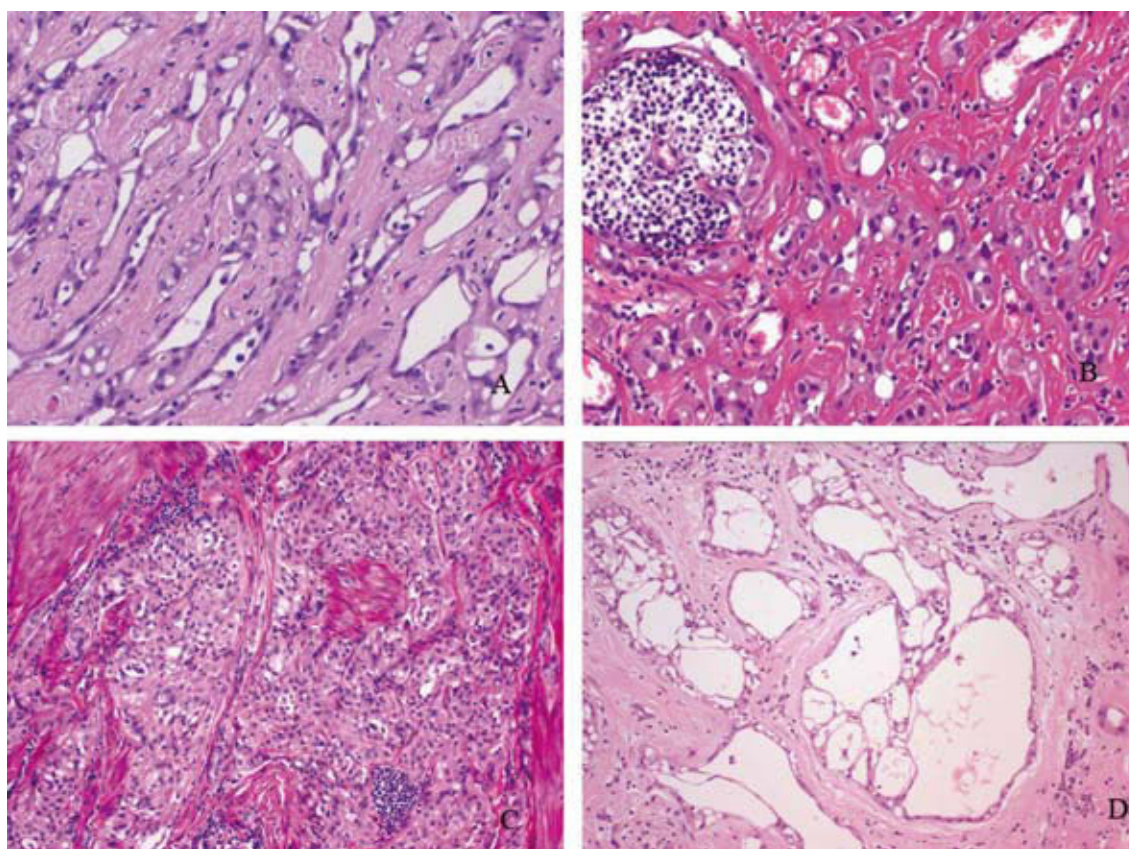
Surgical treatment was provided in all cases. In 8 patients (88.8%) a conservative approach was decided, with excision of the nodule, while an inguinal radical orchiectomy was performed in one patient with ultrasound uncertainties (corresponding to the above mentioned intraparenchymal tumor). The histological study was completed with immune markers for CKpan, calretinin, CD34 and Ki67 in all 9 cases, with a histochemical study comprising PAS diastase and alcian blue in four cases.

There were no surgical complications apart from a single case of postoperative orchiepididymitis, and in all cases the clinical course proved satisfactory.

Macroscopically, all the lesions were well delimited nodules measuring between 0.3-3.5 cm in size, of a hard or firm elastic consistency, and with a whitish or grayish color. The sectioned surface was of the same color and presented a homogeneous or fascicular appearance. In general, the relation between the tumor and the epididymis or tunica vaginalis was noted, together with good delimitation of the testicle parenchyma.



**Figure 1 – Ultrasound view showing an isoechoic nodule located in the tail of the epididymis, with benign characteristics.**



**Figure 2 – (A) Angiomatoid pattern: channels lined by flattened cells of endothelial appearance. Fibrous stroma. (B) Adenoid pattern: cubic or polygonal cells with abundant eosinophilic cytoplasm and an epithelioid appearance, surrounding luminal spaces that appear to correspond to glands. A lymphoid aggregate: a histological finding present in almost all these tumors. Collagenized stroma. (C) Solid pattern: cords and sheets of epithelioid cells in a stromal component with abundant smooth muscle cells. (D) Detail of the "spider web" structure formed as a result of cell vacuolization and the filiform bridges of the cytoplasm of the tumor cells that cross them.**

**Table 1 – Significant data in our series of 9 patients regarding age, location, intraoperative biopsy, size, histological pattern, testicle infiltration and other parameters**

	Age	Location	Intraoperative	Macro (cm)	Histological pattern	Infiltration ST	Others
1	33	EPID	IDAT	Nodule (1.5)	Solid 50% Angiomatoid 30% Adenoid 20%	Yes	Abundant vessels
2	57	EPID		Nodule (0.8)	Angiomatoid 60% Adenoid 30%		Hyperplasia ML
3	61	EPID		Nodule (2.5)	Solid 70%		Central necrosis. Psammoma bodies
4	42	EPID		Nodule (1.2)	Adenoid 30% Angiomatoid 50% Adenoid 50%		
5	57	EPID		Nodule (1.4)	Solid 50% Adenoid 50%		Hyperplasia ML
6	44	TEST	No IDAT	Nodule (0.3)	Solid 70%	Yes	Atrophy ST
7	59	VAG		Nodule (3.5)	Angiomatoid 90%		Hyperplasia Leydig cells
8	50	EPID		Nodule (2)	Angiomatoid 60% Adenoid 30%		Collagenized stroma
9	44	EPID	IDAT	Nodule (1.5)	Angiomatoid 70% Cystic 30%	Yes	

IDAT: intraoperative diagnosis of adenomatoid tumor; EPID: epididymis; TEST: testicle; ST: seminiferous tubule; VAG: tunica vaginalis.

In the microscopic study, practically all the lesions showed a combination of at least two of the characteristic histological patterns of this type of tumor. The angiomatoid and adenoid patterns are the two most common presentations, being composed of anastomosed tubes and channels of flattened cells of an endothelial appearance, or cubic cells with an eosinophilic cytoplasm, respectively. These cells presenting an eosinophilic cytoplasm and epitheloid appearance are distributed in the form of more packed cords and nests, forming the solid pattern (fig. 2).

Both types of cells show vacuolization in all cases, often giving rise to signet ring-like cells.

The angiomatoid pattern was practically the only pattern in the largest of the lesions, while the solid pattern predominated in the smallest tumor (that located within the testicle parenchyma).

Tumor infiltration of the seminiferous tubules was seen in two cases in addition to the intratesticular tumor, associated with extensive atrophy of the tubules.

The stromal component in turn consisted of fibrous tissue mixed with the tumor, and was highly collagenized in two of the lesions, with smooth muscle cells sometimes forming hyperplastic nodules and in some cases also presenting numerous blood vessels – particularly at the periphery of the tumor.

The lymphoid aggregates at the tumor periphery and the so-called filiform bridges crossing the pseudovascular spaces were present in all but one of the lesions (that located at intratesticular level) (Table 1).

The immunohistochemical study in turn proved positive in all cases for CKpan and calretinin, and negative for CD34, which marked the vascular endothelium – thus supporting the mesothelial nature of the tumor. Calretinin is a calcium binding protein belonging to the protein S100 family that is located both in the cytoplasm and in the cell

nucleus. It is very sensitive in identifying mesotheliomas and mesothelial cells, and its expression in malignant tumors is very rare. In all cases the proliferation index was under 2% (fig. 3).

PAS and PAS diastase staining proved negative in all cases, showing the absence of glycogen and neutral mucopolysaccharides. In turn, alcian blue staining proved positive in all cases either focally or diffusely, particularly in the large pseudovascular spaces - thus revealing the presence of acid mucopolysaccharides (Table 2).

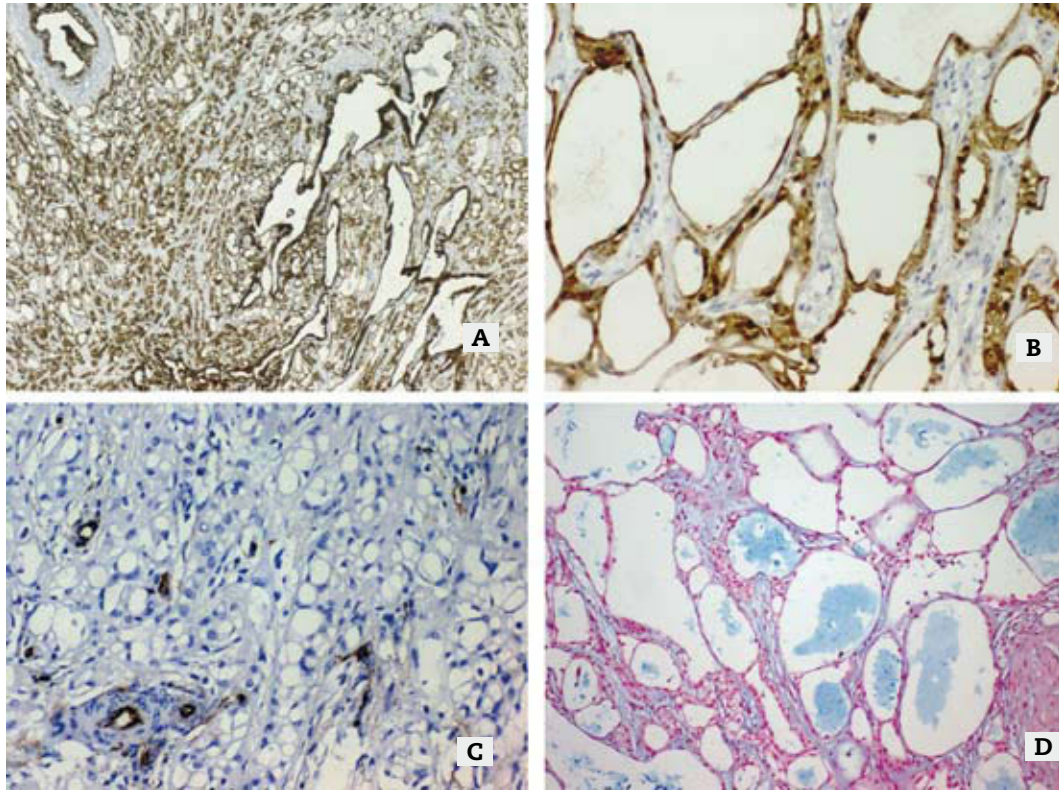
## Discussion

Paratesticular tumors are generally infrequent, and are mostly benign. Adenoid tumor is the most common presentation. The epididymis is the most common location (generally in the lower pole region), though the tunica albuginea can also be affected, as well as the spermatic cord and the ejaculatory duct. In turn, the lesion can also extend to the testicle parenchyma.

Three basic morphological patterns can be seen from the microscopic perspective:

1. Angiomatoid: composed of more or less dilated channels of vascular appearance, and lined by flattened cells of endothelial morphology.
2. Solid: the cords, channels and cell nests are more closely packed, leaving fewer spaces and forming sheets of cells. The principal cell type is epitheloid, with an abundant eosinophilic cytoplasm, a small nucleus and a non-prominent nucleolus.
3. Adenoid: characterized by anastomosed tubes of cubic cells producing a pseudoglandular histological appearance.





**Figure 3 – (A) Pan cytokeratin positivity in the tumor cells and in other tubular structures corresponding to trapped epididymis. (B) Calretinin positivity in both the cytoplasm and nucleus of the flattened tumor cells lining pseudovascular spaces. The stromal cells are negative for this marker. (C) CD34 positivity in the endothelial cells of the vessels, and negativity in the tumor cells, which show vacuolization and a signet ring cell morphology. (D) Alcian blue staining of the amorphous material occupying the spaces delimited by the tumor cells, expressing the secretory capacity of the latter and the acid mucin nature of the secretion.**

**Table 2 – Immunohistochemical findings in our series of 9 patients**

	Copan	Calretinin	CD34	Ki67	PAS	PAS-D	Alcian blue
1	+	+	–	<2	–	–	+
2	+	+	–	<1			
3	+	+	–	<1			
4	+	+	–	<1			
5	+	+	–	<1			
6	+	+	–	<1			
7	+	+	–	<1	–	–	+
8	+	+	–	<2	–	–	+
9	+	+	–	<2	–	–	+

In addition to the described cell types, other cells with a vacuolated cytoplasm that can adopt a signet ring cell-like appearance are often seen.

No mitotic figures, nuclear pleomorphism or prominent nucleoli are observed. Likewise, no papillary structures characteristic of mesothelial proliferations in the pleura and peritoneum are seen<sup>9,10</sup>.

From the macroscopic perspective, these tumors are almost always unilateral and single, and most measure under 2 cm in size. They typically form a well delimited but non-

encapsulated, round or oval mass. Growth in plaque form is rare, and the margins are not always well defined.

The present review presents an important number of these tumors documented over a 9-year period, since they are quite infrequent. Our series effectively confirms the rarity of these tumors, and the fact that the most common location is the epididymis. In addition, the data obtained support the mesothelial origin of these neoplasms.

The benign nature of these lesions and their paratesticular location makes it possible to preserve the testicle. In this

context, we recommend an intraoperative study of those cases involving a mass in this location, even when parenchymal infiltration is suspected. The intraoperative diagnosis is relatively simple, considering the characteristic histological features in most cases. In the case in our series where a radical orchiectomy was performed due to diagnostic doubts (corresponding to the single recorded intraparenchymal lesion), small solid cords were observed between the atrophic and hyalinized seminiferous tubules.

Two patients showed parenchymal infiltration as demonstrated by the immunohistochemical study, despite the nodular and well delimited macroscopic appearance, and the fact that the tumor did not extend to the resection margin. It is therefore advisable to leave a small margin beyond the macroscopically detected nodule.

We consider the employed markers to be important not only for diagnosing the mesothelial nature of the tumor, but also for identifying the epididymis (positive for CKpan), and for distinguishing it from the parenchyma (negative for CKpan) – such differentiation sometimes being difficult due to atrophy. CD34 or some other vascular marker is needed to determine that the pseudovascular structures are not true blood vessels<sup>11</sup>.

Alcian blue is not necessary for the diagnosis, but it is of help in differentiating neutral mucopolysaccharides inherent to adenocarcinoma (negative in our patients) from the acid mucin secreted by mesothelial cells, which are positive for this stain (as in our patients).

We wish to underscore the great morphological plasticity of the mesothelium at both cytological and structural level, and the absence of papillary structures in this type of tumor – such structures being frequent in reactive and neoplastic proliferations of the mesothelial tissue in the pleura and peritoneum<sup>12,13</sup>.

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