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Intratesticular adenomatoid tumor: A case report and review of the literature

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Abstract Adenomatoid tumors (ATs) are rare benign neoplasms that typically occur in the male and female genital tract. In men, the most common site of ATs is the epididymis and other paratesticular locations (tunica albuginea, spermatic cord, and ejaculatory ducts). However, intratesticular AT is exceedingly rare and may mimic a malignant neoplasm.

We report a case of an AT occurring in a 27-year-old man with no prior medical, urologic or trauma history, who presented with right-sided scrotal pain of a few days' duration. Physical examination showed no skin change in the scrotum, a normal-sized, nontender left testis and an enlarged, tender right testis. Ultrasound images of the scrotum showed an eccentric, predominantly hypoechoic vascular mass in the posterior aspect of the right testis measuring 2.2 × 2.1 × 2.1 cm. Tumor markers were within normal limits. His workup was negative for metastatic disease. A right radical orchiectomy was performed. Histological examination and immunohistochemical stains confirmed the diagnosis of adenomatoid tumor confined to the right testis.

We report this rare, benign neoplasm of mesothelial origin that more often occurs in a paratesticular location, but rarely has been shown to involve the testicular parenchyma.

1. Introduction

Adenomatoid tumors (ATs) are rare benign neoplasms that typically occur in the male and female genital tract, but have been reported from a variety of extragenital sites such as the adrenal gland, heart, pleura, liver, pancreas, mesentery and omentum, retroperitoneum and lymph node [1]. In men, the most common sites of ATs are the epididymis [2] and other paratesticular locations (spermatic cord, tunica albuginea and ejaculatory ducts) [3]. Despite their rarity, ATs represent the most common paratesticular neoplasms, accounting for about 30% of all such tumors. Some larger primarily paratesticular (epididymal or tunica albuginea) tumors may show infiltration into the testis and intratesticular growth [4], sometimes forming larger intratesticular nodules. However, ATs with complete intratesticular (intraparenchymal) growth are exceedingly rare, with only six well-documented cases previously reported in the world literature [5–10].

We herein report a case of intratesticular adenomatoid tumor occurring in a 27-year-old man, clinically suspected to represent a malignant testicular neoplasm and review the literature on the subject.

2. Case presentation

A 27-year-old male previously healthy nonsmoker with no significant prior medical history, presented to the

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emergency room with right-sided scrotal pain of a few days' duration. The pain was worse with walking and movement. His general physical examination was within normal limits; no skin changes were present on the scrotum. His left testis was normal in size and non-tender, but the right testis was enlarged and tender. There was no lymphadenopathy.

Ultrasound imaging of the scrotum showed an enlarged right testis measuring 4.6 × 2.9 × 3.2 cm. with an eccentric, heterogeneously echoic, but predominantly hypoechoic vascular mass measuring 2.2 × 2.1 × 2.1 cm. The mass was located in the posterior aspect of the right testis, slightly deforming its posterior contour, and showed a rim of hypervascularity. No definite calcifications were noted (Fig. 1). The left testis measured 3.9 × 2.0 × 2.6 cm and appeared normal. Vascularity in the right testicle was relatively increased when compared to the left. The epididymis was normal in appearance.

Abdominal and pelvic CT scan showed a 1.9 cm peripherally enhancing lesion within the enlarged right testis (Fig. 2), corresponding to the abnormality on the ultrasonographic evaluation. No lymphadenopathy or other abnormalities were seen in the abdominal or pelvic organs.

Testicular tumor markers (beta-HCG, AFP and LDH) were within normal limits. His workup was negative for metastatic disease. A malignant testicular tumor was clinically suspected. After discussion of his treatment options, the patient chose to undergo a right radical orchiectomy.

The surgical specimen consisted of the right testis, measuring 4.8 × 3 × 3.2 cm with attached spermatic cord. Upon bivalving the testis, a well-defined, ovoid, tan–white firm tumor with central hemorrhage and necrosis, measuring 2.3 × 2.2 × 2.1 cm was identified. The tumor was confined to the testis and grossly appeared to focally abut the tunica albuginea. The surrounding testicular parenchyma was grossly unremarkable, except for a rim of edematous and erythematous tissue surrounding the tumor (Fig. 3).

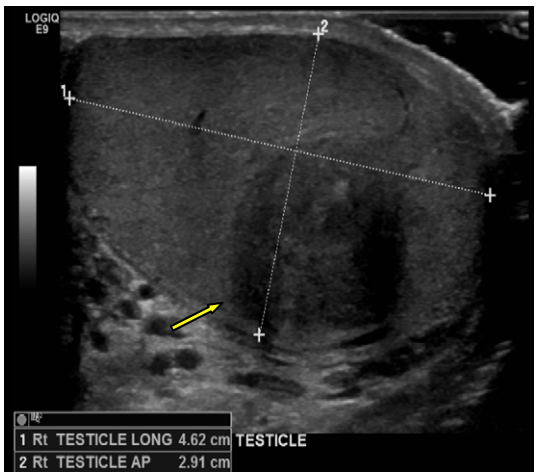

Fig. 1 The ultrasound showed an eccentric, heterogeneously echoic, but predominantly hypoechoic vascular mass in the posterior aspect of the right testicle, measuring 2.2 × 2.1 × 2.1 cm.

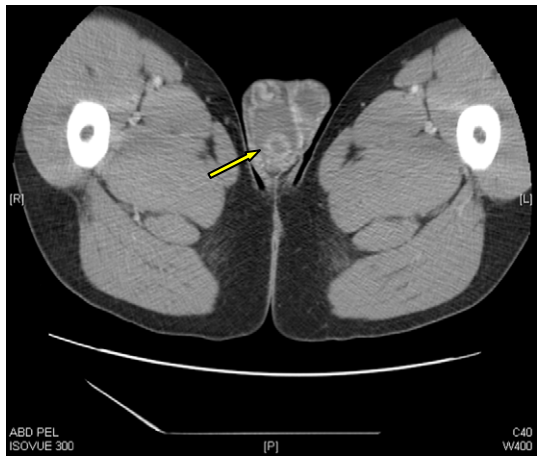

Fig. 2 Abdominal and pelvic CT scan showed a 1.9 cm peripherally enhancing lesion within the enlarged right testicle.

Although the tumor appeared grossly well circumscribed, microscopic examination showed that it was not encapsulated, and infiltrated into the testicular parenchyma, focally entrapping seminiferous tubules (Fig. 4A). Despite the gross impression of the tumor abutting the tunica albuginea, no histologic connection to the tunica could be demonstrated in the planes of the sections examined. Lymphoid aggregates were seen at the periphery of the tumor (Fig. 4B). The tumor was composed of two major elements; polygonal, cuboidal, flattened or vacuolated epithelioid cells arranged in tubular/glandular structures or solid cords, and a hypocellular fibrous stroma interspersed with occasional lymphocytes. The tumor cells were epithelioid, with mild cytologic atypia, and showed ample acidophilic finely granular or vacuolated

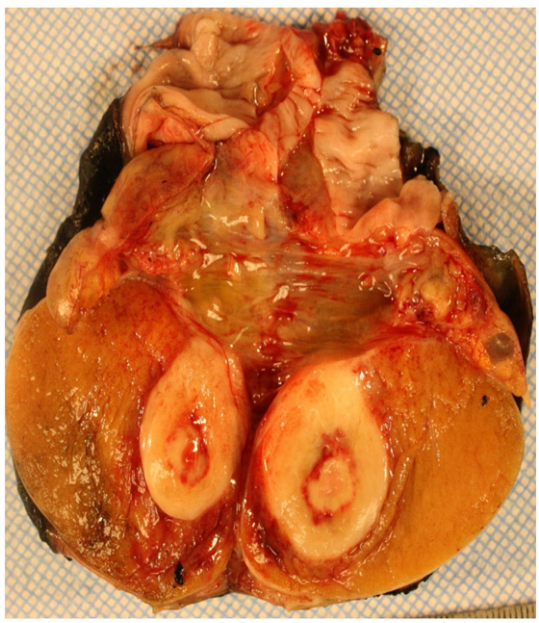

Fig. 3 Orchiectomy specimen: Cut surface of the test showed a well defined, ovoid tan–white tumor with central hemorrhage and necrosis grossly appearing to abut the tunica albuginea.

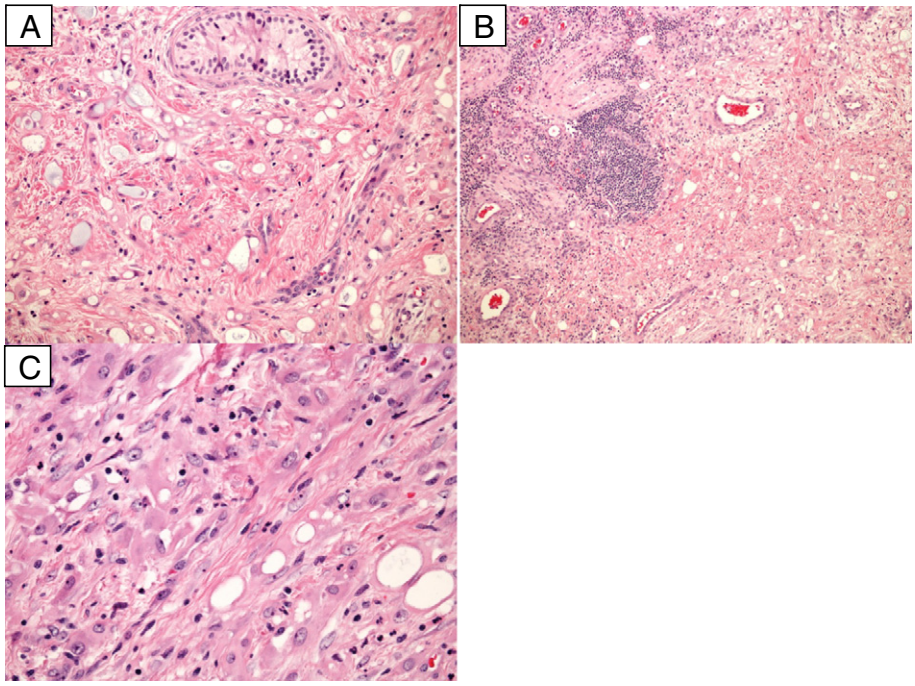

Fig. 4 H&E stain. A–C: Epithelial-like cells and fibrous stroma. The epithelial component has tubular/glandular and solid patterns. B: A lymphoid aggregate is observed at the periphery of the lesion. C: Tumor cells have acidophilic, finely granular and vacuolated cytoplasm. Nuclei are round to ovoid, and have uniform chromatin distribution and a small single central nucleolus.

cytoplasm. The nucleocytoplasmic ratio was low. Mild anisonucleosis was present. The nuclei were located either centrally or eccentrically, and were large, round or ovoid, with evenly distributed chromatin and smooth nuclear membranes and showed single, small, central nucleoli. No mitosis was seen (Fig. 4C).

A large panel of immunostains was performed using the Ventana Benchmark XT IHC platform (Ventana Medical Systems, Inc. Tucson, AZ). The tumor cells were positive for cytokeratin AE1/AE3 (Leica Biosystems), vimentin (clone SRL33, Leica Biosystems), calretinin (clone CAL6, Leica Biosystems), WT-1 (clone WT49, Leica Biosystems) and podoplanin (clone D2-40,Ventana medical system) and were negative for PLAP (clone 8A9, Leica Biosystems), melanoma marker (clone HMB-45, Leica Biosystems), Melan-A (clone A103, Leica Biosystems) and alpha inhibin (clone CR1, Leica Biosystems) (Fig. 5A–D). This staining profile, in conjunction with the histological features, established the diagnosis of adenomatoid tumor.

3. Discussion

We herein report an unusual case of a completely intratesticular adenomatoid tumor. To the best of our knowledge this is only the sixth such tumor reported in the literature. However, in some of the previously reported cases it is difficult to be certain if the tumor was entirely intratesticular or only invaded the testis secondarily, especially since in many of these cases no gross pictures or descriptions were provided.

Previously reported intratesticular AT presented at a similar age (31–65 years) to paratesticular AT (5 to 80 years [11,12]), and occurred mostly in the left testis. Their presentation was more commonly with pain of short duration rather than as an incidental finding or a slow growing scrotal mass [13], which is typical of paratesticular AT. The presentation with pain is most likely due to the stretching of the tunica albuginea or due to infarction. Reported intratesticular ATs were smaller than paratesticular ATs and measured less than 2 cm (range, 0.6–3.2 cm). Grossly, intratesticular ATs were described as rounded or ovoid well-circumscribed unencapsulated tumors, with a gray to white, firm, smooth cut surface, a gross appearance that may mimic that of seminoma [10,14]. Intratesticular ATs were most frequently described as not connected to the tunica or epididymis, but some were in relation to the rete testis.

The case presented herein highlights the difficulty in establishing a preoperative diagnosis of AT, when the tumor is not found in its typical location, which is usually intrascrotal but extratesticular, frequently in the tail of the epididymis. In contrast to paratesticular tumors, which are frequently benign [15], the overwhelming majority (over 90%) of intratesticular tumors are malignant, most commonly germ cell tumors. Therefore, the standard treatment of

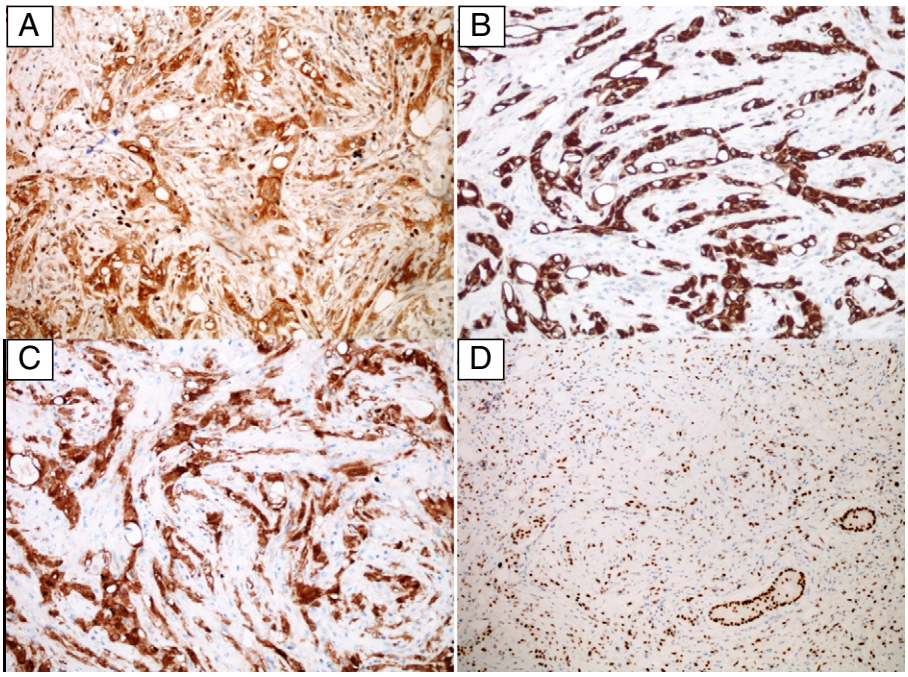

Fig. 5 The tumor cells have strong and diffuse cytoplasmic positivity for D2-40 (A), AE1/AE3 (B), and calretinin (C) and nuclear positivity for WT-1 (D).

intratesticular tumors is radical orchiectomy. However, ATs can be treated by testis-sparing surgery [16], provided that a specific preoperative or intraoperative diagnosis is made. The use of less aggressive surgery is based on the favorable prognosis of ATs in which there are currently no reported cases of recurrence or metastasis, despite the possible presence of nuclear atypia and local infiltrating pattern [8,12]. Based on clinical and imaging features, it is therefore very difficult, if not impossible to differentiate intratesticular ATs from malignant intratesticular solid tumors [17], leading to unnecessary orchiectomies in most of the reported cases. Attempts to obtain a preoperative diagnosis by FNA may also be unsuccessful, as demonstrated by a case in which an AT was misinterpreted as seminoma on FNA due to the presence of a tigroid background, usually seen in seminomas [18]. In addition to the intratesticular location of the tumor, challenges encountered in the pathologic diagnosis of these tumors, especially during frozen section diagnosis, can be created by the infiltrative growth pattern [3], and the histologic pattern mimicking metastatic adenocarcinomas and other malignancies. Therefore, even when testis-sparing surgery is attempted, an intraoperative frozen section diagnosis may not provide an accurate diagnosis or may only provide an equivocal diagnosis, due to the frequent misidentification of ATs with a variety of malignant neoplasms [19,20].

The definitive histopathologic diagnosis of ATs is therefore most often made only after histologic examination and the performance of appropriate immunohistochemical stains. Microscopically, the tumor is composed of two major elements; epithelial like cells and fibrous stroma. The epithelial-like component forms a variety of histological patterns, such as microcystic, adenoid or tubular/glandular, angiomatoid, solid, cystic or transitional, which can occur in the same tumor and are frequently admixed. Intrascrotal ATs usually have a mixed microcystic/trabecular or retiform pattern and show prominent lymphoid infiltrates [21], often localized at the periphery of the tumor, which may help in the diagnosis of ATs [8]. The spindle cell stroma, which is usually sparse and fibroblastic may be more cellular and show myoid features, mimicking leiomyoma or adenomyoma.

Due to the wide spectrum of possible histologic appearances and patterns mimicking the appearance of other neoplasms, ATs pose a range of diagnostic problems in their differential diagnosis from other primary or secondary testicular tumors. The differential diagnoses include primary and metastatic adenocarcinoma of testis, epithelioid hemangioendothelioma, malignant mesothelioma, yolk sac tumor, and other testicular tumors like leiomyoma, Leydig cell tumor and Sertoli cell tumor [8].

The characteristic mesothelial immunostaining pattern with consistent expression of cytokeratin AE1/AE3 and EMA, HBME-1, WT1, podoplanin/D2-40 and calretinin, is very helpful in their differential diagnosis. The negativity for vascular endothelial markers (CD31, CD34, Factor VIII related antigen, *Ulex europaeus* agglutinin) and inhibin helps exclude vascular tumors and sex cord-stromal neoplasms [1]. The differential diagnosis with malignant mesothelioma is based on the growth pattern (frequently papillary in malignant mesothelioma), and absence of atypia, mitoses or high proliferative fraction demonstrated by Ki-67 staining.

The exact origin of intratesticular ATs is unclear. Although the tumors show mesothelial differentiation at the histologic, ultrastructural and immunohistochemical level [9,2], and genetic analysis of Wilms Tumor 1 gene expression, their exact origin has been a source of controversy ever since the original description of this tumor under the name "paratesticular adenomyoma" by Sakaguchi in 1916 [22]. The controversy surrounding the mesothelial origin of AT, proposed by Masson et al. in 1942 [23] and supported by Evans in 1943 [24], who referred to the tumors as "benign mesothelioma of the genital sphere" led to the acceptance of the alternative, noncomitant histologically descriptive term "adenomatoid tumor" proposed by Golden and Ash in 1945 [25]. The most commonly accepted origin of ATs is the surface mesothelium, mesothelial inclusions or displaced mesothelial tissue (to explain the occurrence of ATs at extragenital sites). Other possible origins of these tumors include the coelomic epithelium and pluripotent mesenchymal cells that have the potential to differentiate into submesothelial spindled cells and mesothelial cells [26]. The intratesticular location of the tumors may be due to their origin from displaced intratesticular mesothelial or pluripotent mesenchymal cells or to the exclusive intratesticular growth of tumors originating from the tunica albuginea [27].

To conclude, awareness of the possibility that ATs may present as a completely intratesticular mass aids in appropriate diagnosis and patient's management. Histopathologically, ATs should be considered in the differential diagnosis of testicular neoplasms with polygonal, cuboidal, flattened or vacuolated epithelioid cells arranged in tubular/glandular structures or solid cords, embedded in a hypocellular fibrous stroma, interspersed with occasional lymphocytes. Once considered in the differential diagnosis of a testicular tumor, given the characteristic immunoprofile of these tumors, the pathologic diagnosis is usually straightforward after the performance of the appropriate immunostains.

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