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Scrotal cellular angiofibroma: A case report and review of the literature

David Buchinsky *, Gaurav Pahouja

Wright State University Boonshoft School of Medicine, Division of Urology, Dayton, OH, USA

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ABSTRACT

Scrotal cellular angiofibroma (CAF) is a rare, benign, soft-tissue paratesticular tumor that has been sporadically reported previously. We present a case of a 55-year old male with a scrotal mass ultimately diagnosed with scrotal CAF. Immunohistochemical analysis stained positively for desmin, CD34, and estrogen receptor. Our series is one of the only published to date demonstrating desmin-positive paratesticular CAF. Diagnosis of CAF remains difficult due to the sparsity of paratesticular CAF, its similar characteristics to spindle cell lipoma (SCL), and variability in immunohistochemical reporting.

1. Background

Paratesticular tumors are a subset of scrotal tumors originating from mesenchymal tissue, connective tissue, or lymphoid tissue.[1] They may derive from the tunica vaginalis, epididymis, spermatic cord, or local supportive tissue.[2] Paratesticular tumors are rare, accounting for approximately 10 % of total scrotal tumors; however, approximately 30 % of these tumors are malignant.[1,3] Sarcomatous tumors account for the majority of malignant paratesticular tumors.[4] Men in their sixth decade of life are at highest risk for paratesticular tumors.[2]

The clinical presentation of paratesticular tumors has been previously described. Typical presentation includes a scrotal mass, which is usually painless.[1] The differential diagnosis for paratesticular tumors includes liposarcoma, rhabdomyosarcoma, leiomyosarcoma, angiomyofibroblastoma, and aggressive angiomyxoma.[5,6] Additionally, inguinal hernia, hydrocele, spermatocele, cyst, or infection may be considered.[1] After a physical exam, ultrasonography is often utilized to better characterize a paratesticular mass.[1] The management of paratesticular tumors includes tumor resection and in some instances, radical inguinal orchiectomy.[3,4]

Cellular angiofibroma (CAF) is a rare, mesenchymal-derived, soft tissue benign neoplasm.[7] Typically, CAF presents within the vulvovaginal region of women in the fifth decade of life.[8] CAF has been sporadically reported in the inguinoscrotal region of men, with men in their seventh decade of life being at highest risk for paratesticular CAF.[9] We present a case of a scrotal CAF in a 55-year old male patient and highlight the aberrant histopathological findings.

2. Case presentation

A 55-year old male presented to clinic with scrotal pain of two months duration. Pain was intermittent in nature. There were no significant exacerbating or relieving factors. His medical history was significant for hypertension, migraines, neuropathy, nephrolithiasis, erectile dysfunction, and depression. His surgical history was significant for gastric bypass, cholecystectomy, and a perforated ulcer repair. He was a non-smoker and had no history of alcohol use. He did not have a family history of any genitourinary malignancies.

Upon examination, he was noted to have an abnormal mass within the midline of the scrotum. Both testicles were separate from the mass and palpably normal. There was no concern for a large hydrocele or varicocele. Overlying skin was within normal limits. Further diagnostic study with imaging was then obtained.

3. Imaging

The patient underwent scrotal ultrasound which was significant for a heterogenous and hypoechoic mass visualized within the midline measuring 4.8cm. There was marked vascularity on color Doppler (Fig. 1). The testicles appeared visually normal with no evidence of abnormal testicular masses.

Given these findings, Computed Tomography (CT) scan of the abdomen and pelvis with intravenous contrast was obtained, which was significant for a midline scrotal mass measuring 3.6cm with marked vascularity (Fig. 2). There was no significant lymphadenopathy, bone lesions, or any other concerns for metastatic disease.

* Corresponding author. 3640 Colonel Glenn Hwy, Fairborn, OH, 45324, USA.
E-mail address: buchinsky.2@wright.edu (D. Buchinsky).

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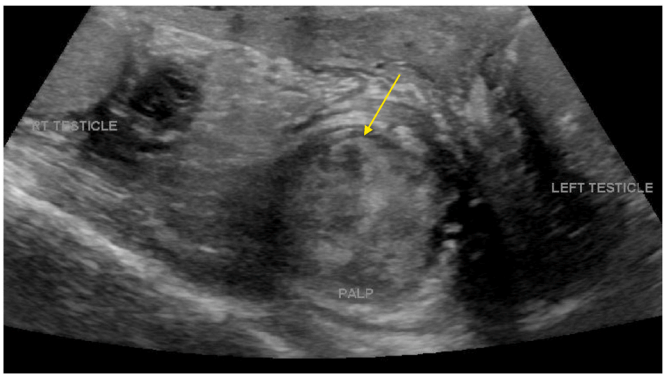

Fig. 1. Scrotal Ultrasound
Ultrasound depicted a heterogenous and mildly hypoechoic midline palpable mass as highlighted by the arrow.

4. Treatment

The patient was counseled on options and elected for surgical extirpation. A skin incision was made over the inferior scrotum in the midline over the palpable mass. The mass was then carefully dissected away from the surrounding tissue using both blunt and sharp dissection with cautery. The mass was freed away from the scrotal contents with a large margin of tissue circumferentially. The mass had a rubbery texture. Hemostasis was obtained and the scrotum was then closed in multiple layers.

5. Histopathology

On pathologic evaluation, there were spindle cells and hyalinized vessels with lymphocytic infiltration (Fig. 3). In addition, on high power stain, analysis revealed wispy collagen, mast cells, and fibrous stoma, which are characteristic of CAF.[10] Notably, spindle cell component of tissue excision were positive for CD34, desmin, and estrogen receptor (ER). CD31, WT1, and ERG stains were also positive in tissue sample endothelial cells. Calretinin staining was negative. Margins were free of neoplasm. Final diagnosis was CAF.

6. Discussion

CAF is a benign, soft tissue tumor that was first characterized in 1997 by Nucci et al.[6] Their morphologic description of CAF in the vulvovaginal and perineal region entailed a small, well-circumscribed, hyalinized vessel tumor containing uniform spindle stromal cells.[6] Their immunohistochemistry analysis showed positive vimentin but negative CD34, desmin, S100, actin, and epithelial membrane antigen.[6] Since Nucci et al.'s original description of vulvovaginal CAF, sporadic case reports of scrotal CAF have been published.[7,10–15]

In 1998, Laskin et al. reported eight cases of an "angiofibroblastoma-like-tumor" in the inguinoscrotal region.[14] In comparison to Nucci et al.'s report, Laskin et al. found collagenous rather than spindled stromal cells.[14] Laskin et al. also noted increased variability of desmin in CAF located within the inguinoscrotal region.[14]

Iwasa et al. further described CAF.[9] Compared to previous CAF literature, they found repeated CD34 positivity in vulvovaginal and inguinoscrotal regions, however, desmin positivity was rare.[9] Iwasa et al. also noted the presence of mast cells were correlated with CAF, as well as the association of desmin with angiomyofibroblastoma.[9] Finally, they observed a larger median CAF tumor size in men (7cm) compared to women (2.8cm).[9]

CAF typically demonstrates spindle-shaped cells, wispy collagen, myxoid stroma, and small-to- medium sized hyalinized vessels.[9] CAF has a well-defined capsular membrane, rubbery texture, and is typically white or yellow in appearance.[9] Our case of paratesticular CAF demonstrated wispy collagen, adipocytes, lymphocytic infiltrate, and mast cells, which are suggestive for CAF.[10] Finally, the absence of tumor-suppressor *RB1* gene is correlated with CAF and may aid in its distinction from other soft-tissue tumors.[16] However, contrary to previous literature, our case of paratesticular CAF demonstrated positivity for desmin, which is reportedly rare. CD34 and ER positivity have been more frequently reported in CAF characterization.[10] Estrogen is hypothesized to contribute to cellular angiofibroma pathogenesis, yet its precise mechanism remains unclear.[15] CD34 is expressed in a variety of benign and malignant soft-tissue tumors, and therefore does not provide definitive diagnosis for CAF.[17]

There is conflicting data regarding desmin staining for CAF in both male and female patients. Prior reports of CAF in both male and female patients are suggestive for negative desmin staining in CAF,[7,12,13,16,18] but there are few reported series with positive desmin staining.[11,14] Desmin is a structural component of both skeletal and smooth muscle and is used to differentiate soft-tissue tumors.[17] Traditionally, its presence in immunohistochemistry staining may be suggestive of myogenic tumors such as rhabdomyosarcoma.[17] Notably, desmin has also been reported in other soft-tissue tumors including aggressive angiomyxoma, Ewing's Sarcoma, and in rare instances, CAF.[17] There is also variability in ER and CD34 staining in CAF. CD34 stain is reportedly positive in approximately 60 % of CAF cases,[8] while ER is positive in approximately 50 %.[19]

Spindle Cell Lipoma (SCL) is closely related to CAF and is considered in the differential diagnosis. SCL presents as a slow growing mass and is treated with complete excision.[8,10] Recurrence is reportedly rare.[10] Microscopically, SCL is characterized by ropey eosinophilic collagen

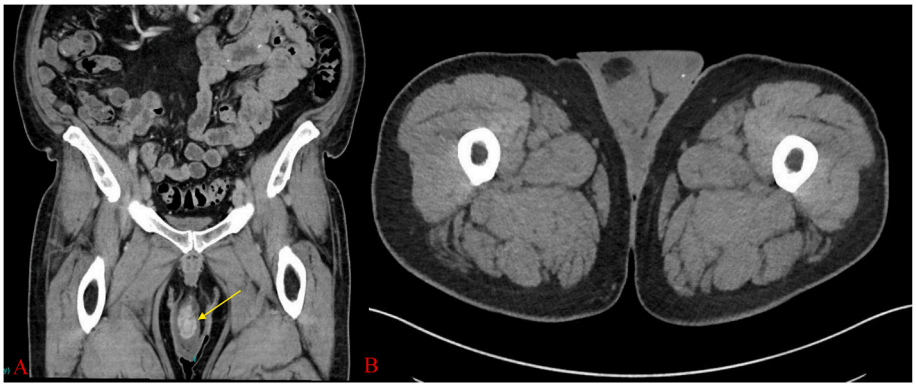

Fig. 2. Computer Tomography Imaging
A) Coronal view of the Abdomen and Pelvis with intravenous contrast. Yellow arrow denotes the vascularized mass at midline of scrotum. **B)** Axial view of Abdomen and Pelvis with intravenous contrast visualizing the scrotal mass.

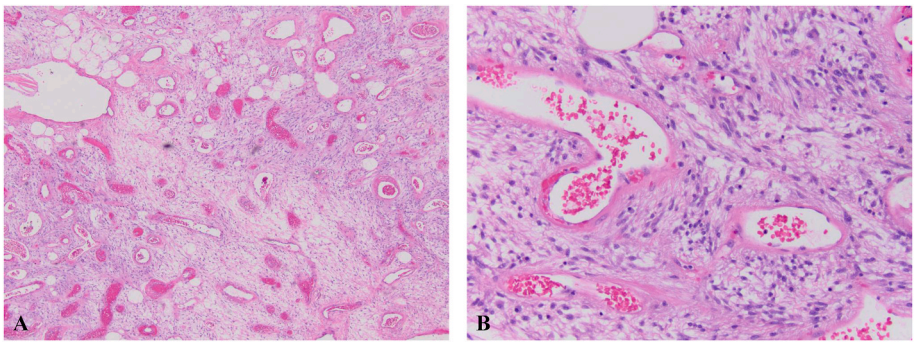

Fig. 3. Pathologic Tissue Stains of Cellular Angiofibroma
A) Low power view showing spindle cells and hyalinized small-medium vessels with general lymphocytic infiltration which are characteristic of cellular angiofibroma. **B)** High power view highlighting wispy collagen, mast cells, lymphocytic infiltrate, and fibrous stroma.

bundles, low-mitotic rates, bland spindle cells, adipocytes and mast cells.[8,10] Immunohistochemistry analysis for SCL shows variable CD34, negative desmin, and variable S100.[10] Genetically both SCL and CAF are characterized by loss in 13q14 chromosome, which contains the *RB1* gene.[10] *RB1* encodes Retinoblastoma Protein (*Rb*), a potent tumor suppressor protein, which is hypothesized to play a role in tumorigenesis of SCL, CAF, and a variety of other cancers.[16]

Morphologically both SCL and CAF contain spindle cells, however; CAF's characteristic hyalinized blood vessels may aid in a differential diagnosis in its favor. Since desmin is typically negative for SCL and has been reported in a minority of CAF cases, this may be an additional differentiating factor. Progesterone is also typically associated with CAF rather than SCL.[10] Nucci et al. note that SCL is predominant to males and typically localizes to the cervical region.[6]

Excision of paratesticular CAF has positive long term outcomes with low recurrence rates and no need for additional systemic therapy.[6,8] Our case demonstrates the significance of the diagnostic process of paratesticular CAF, as immunohistochemistry staining may vary among paratesticular CAF. Further research is warranted to better understand the variable expression of desmin, CD34, and ER in paratesticular CAF to more accurately characterize CAF and aid in its distinction from other soft-tissue tumors. In addition, future investigation is needed to enhance the current understanding of estrogen's role in CAF pathogenesis.

7. Conclusion

We describe a case of paratesticular CAF. Although the tumor contained morphological and immunological markers suggestive of CAF, our case of paratesticular CAF also demonstrated positivity for ER, CD34, and desmin stains. Positive desmin, CD34, and ER staining has been variably reported in paratesticular CAF.[11,14] In order to enhance the understanding of CAF, future research is warranted to investigate paratesticular CAF pathogenesis and its immunohistochemistry markers.

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CRediT authorship contribution statement

David Buchinsky: Formal analysis, Investigation, Writing – original draft. **Gaurav Pahouja:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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