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## LETTER TO THE EDITOR

Male Health

# A rare cellular angiofibroma of the epididymis

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Dear Editor,

Cellular angiofibroma (CAF) is a rare benign mesenchymal lesion, which was first described in 1997 by Nucci *et al.*<sup>1</sup> In previous reports, it has occurred mainly in the superficial soft tissue of the genital region, such as the scrotum, perineal, groin, vaginal introitus, and vulva,<sup>2</sup> and rarely occurs in other locations. Here, we report a cellular angiofibroma in the epididymis; to our knowledge, such an epididymal location has not been reported in the literature so far. In this case, a 63-year-old male presented with a painless and well-circumscribed mass in the right epididymis. Ultrasound revealed a solid homogeneous echo mass lesion measuring 2.6 cm × 3.0 cm in the right cauda epididymidis, suggestive of a benign tumor of the epididymis. Macroscopically, it was of solid to firm consistency, lobulated and appeared homogeneously yellowish gray on the cut surface. Further, microscopical examination of the tumor confirmed the diagnosis of cellular angiofibroma of the epididymis. Owing to its low incidence rate, to our knowledge, such a case has not been previously reported in the literature.

A 63-year-old male presented with a painless mass in the right epididymis that had been growing slowly for 1 year. The result from physical examination showed that the mass was located in the right cauda epididymidis, with 3 cm in the greatest dimension, of a rubbery and smooth mass. It was also found that the mass was fixed, painless, and well circumscribed upon touching. Ultrasonography revealed a solid homogeneous echo mass lesion measuring 2.6 cm × 3.0 cm in the right cauda epididymidis, with a clear border (**Figure 1a**), common configuration, and minimum blood flow signal (**Figure 1b**).

Next, the patient underwent a surgical excision. The tumor was separated along the envelope and excised with a rim of normal tissue. This 3 cm long solid nodule was then found to adherent to the right cauda epididymidis with a well-circumscribed boundary, enveloped by, but not adhered to, the right testicle and scrotum. Macroscopic examination showed a solid to firm consistency, lobulated, appearing homogeneously yellowish gray on the cut surface, and there were no necrotic or hemorrhagic changes (**Figure 2a**). Morphologically, these features were suggestive for CAF.

On microscopical examination, the tumor was composed of two major cellular components: spindle cells and prominent vessels. Tumor cells loosely or densely arranged, short spindle-shaped cells, neither mitotic figures nor nuclear atypia, and proliferating in an edematous to fibrous stroma (**Figure 2b**). Prominent small-to-medium-sized thick-walled vessels were seen (**Figure 2c**) and marked hyalinization of the wall (**Figure 2d**).

Immunohistochemical analysis revealed positive staining of vimentin (**Figure 3a**), cluster of differentiation 34 (CD 34) (**Figure 3b**), partial smooth muscle actin (SMA) (**Figure 3c**), as well as a small proportion of Ki67 positive cells (<5%, not shown) (**Figure 3d**). In addition, desmin, protein s-100, anion exchanger 1/3 (AE1/AE3), estrogen receptor (ER), and progesterone receptor (PR) were negative. The above results are also supportive of the diagnosis of CAF. Currently, at 18 months postoperatively, the patient is doing well with no signs of recurrence.

CAF is a benign mesenchymal tumor occurring mainly in the superficial soft tissue of the genital region, such as the scrotum, perineal, groin, vaginal introitus, and vulva. In recent years, it has also been reported in several rare locations including the prostate, oral mucosa, male pelvis, and subcutaneous tissue of the chest wall.<sup>2–4</sup> CAF occurs with equal chances in both adult women and men. It has been suggested that women are affected most often in their fifth decade, with men mostly in their seventh decade.<sup>5</sup> The symptoms of CAF are usually painless with mild solid mass, slowing growth, and not typical shape; therefore, differential diagnosis is important in clinic.

Ultrasound is often the initial imaging examination, which usually reveals a homogeneous echo, well circumscribed, and nodular lesion. MRI can be used to distinguish different lesions; MRI features of CAF are consistent with the pathological characteristics: a well circumscribed, benign cellular, and fibrous tumor with prominent vascularity.<sup>6</sup> Moreover, ultrasound and MRI can also help improve the surgical approach and excision when completely resecting the tumor.

To confirm the diagnosis, histological examinations including pathological hematoxylin and eosin (H & E) staining and immunohistochemical staining remain a reliable method for diagnosis. In this case, the H & E staining results showed that the tumor was composed of a spindle cell component and abundant small-to-medium-sized thick-walled vessels, which is consistent with CAF cellular characteristic. Immunohistochemically, the positive expression of CD34, vimentin, and partial SMA and the lack of expression of ER and PR was shown in our case, which represented CAF components, therefore indicating the tissue was CAF.

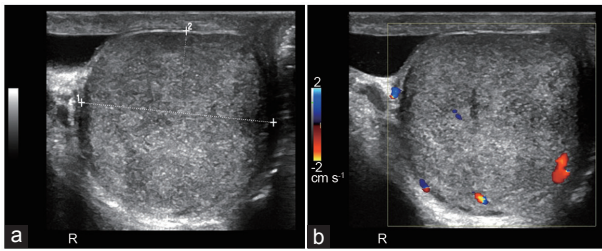
The exact pathogenesis of CAF remains unclear. However, there are three main hypotheses that have been recognized regarding CAF. The first is that CAF cells originate from fiber cells and muscle fiber cells, in which vimentin, CD34, and partial SMA are positively expressed. Second, the estrogen receptor (ER) and progesterone receptor (PR) have been shown to be positive in CAF cells, suggesting a role in the pathogenesis of CAF.<sup>7</sup> However, the direct evidence of ER and PR in the pathogenesis of this peculiar disorder remains yet to be clearly demonstrated. Third, recent cytogenetic and molecular studies of CAF revealed loss of *RBI* and *FOXO1A1* genes owing to the deletion of the 13q14 region, which was also described in spindle cell lipoma and mammary-type myofibroblastoma.<sup>2,8</sup>

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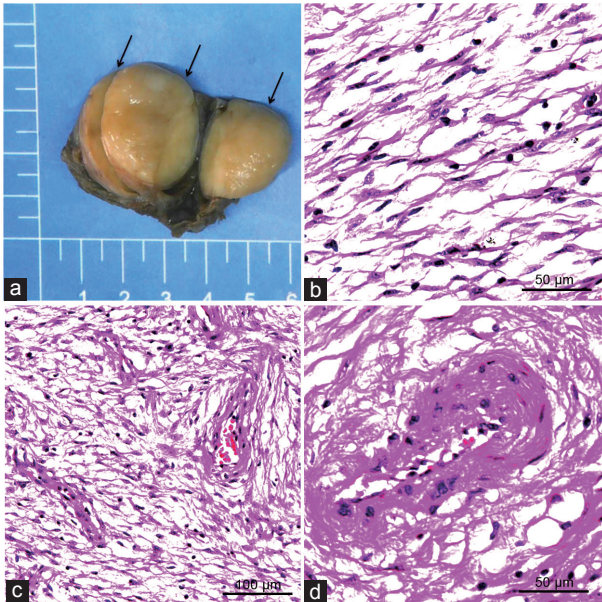
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**Figure 1:** Ultrasonography shows (a) a solid homogeneous echo, mass lesion measuring 2.6 cm × 3.0 cm with a clear border, and (b) minimum blood flow signals (colors in red and blue) in the right cauda epididymidis.

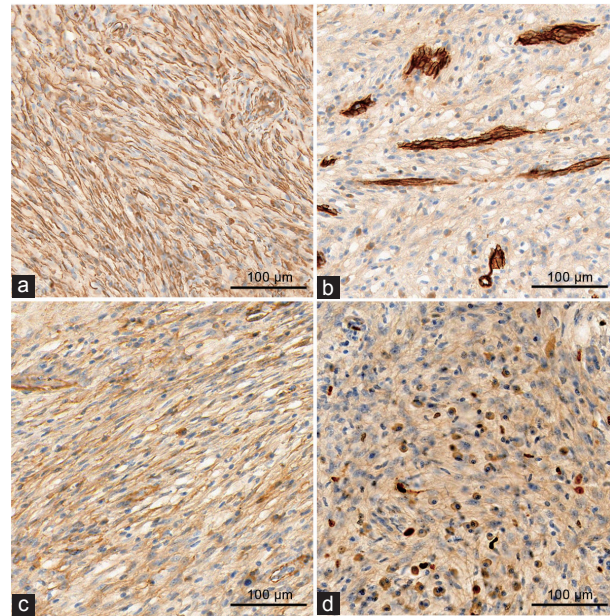


**Figure 2:** Macroscopic examination shows (a) the appearance of the tumor which was cut into 3 pieces; (b) Showing short spindle-shaped cells by hematoxylin and eosin (H & E) staining, scale bar = 50  $\mu$ m; and (c) blood vessels with thick-wall as well as remarked hyalinization of the blood vessel walls in low power, scale bar = 100  $\mu$ m and (d) in higher power, scale bar = 50  $\mu$ m.

Although the diagnosis of CAF can be clarified through H & E staining and immunohistochemical staining, CAF has some similar features to other vascular fibrous tumors that occur in the epididymis, including aggressive angiomyxoma, solitary fibrous, inflammatory myofibroblastic, smooth muscle tumor, angiomyolipoma tumor, spindle cell lipoma, and mammary-type myofibroblastoma, because these tumors show partial overlapping morphological, immunohistochemical, and cytogenetic features, which makes diagnosis of such CAF difficult.

As a benign soft tissue tumor, CAF patients can benefit from local excision with clear margins. This tumor shows no tendency for metastasis or recurrence on the basis of the extremely limited clinical follow-up available. However, there is one case of recurrent CAF, reported by McCluggage *et al.*<sup>9</sup> In addition, Chen and Fletcher<sup>10</sup> reported that CAF may reveal striking atypia or morphologic features of sarcomatous transformation in some cases, not predisposed to recurrence in a short-time clinical follow-up. CAF has a potential risk of recurrence and malignant transformation; therefore, we recommend that patients should be checked 3 months after surgery, including physical and imaging examinations.

To date, the etiology and pathogenesis of CAF remains poorly understood and needs further investigation to define its clinical and pathological features.



**Figure 3:** Immunohistochemistry staining shows positive staining of (a) Vimentin, (b) cluster of differentiation 34 (CD34), (c) smooth muscle actin (SMA), as well as (d) Ki67 in tumor cells. Scale bars = 100  $\mu$ m.

#### AUTHOR CONTRIBUTIONS

QG and JDZ were in charge of the patient, recorded clinical information, and wrote the manuscript. LL carried out histological examination. JPX, DM, and YGZ revised the paper and participated in critical discussion. All authors read and approved the final manuscript.

#### COMPETING INTERESTS

All authors declare no competing interests.

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