# Quiz

## Correct answer to the quiz. check your diagnosis

# Cellular angiofibroma with atypia or sarcomatous transformation – case description with literature review

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Cellular angiofibroma (CAF) is a rare, benign, mesenchymal tumor. It was first described by Nucci *et al.* in 1997 and then in 1998 by Laskin. The tumor occurs predominantly in the vulvo-vaginal or inguino-scrotal region. We present a 71-year-old male, who was referred to the Bielanski Hospital with a three months' history of a slowly growing nodule in the right groin. Gross examination showed a well-circumscribed tumor attached to the spermatic cord and measuring 6 cm in the greatest dimension. Microscopic examination of the tumor showed a spindle cell lesion with a loose, myxoid, partly collagenized stroma with numerous, prominent thick-walled vessels. Scattered atypical cells were present.

**Key words:** cellular angiofibroma, nuclear atypia, spermatic cord.

## Introduction

Cellular angiofibroma (CAF) is a rare, benign, mesenchymal tumor. It occurs equally in men and women and occurs predominantly in the vulvo-vaginal region of middle-aged females or the inguino-scrotal location of older males. Clinically, it can easily be mistaken for a scrotal hernia. Sporadic cases occurring in the chest wall and retroperitoneum have been reported. It was first described by Nucci *et al.* in 1997 and then in 1998 by Laskin [1, 2]. Rare, atypical nuclear features have been reported in the histopathology of cellular angiofibroma [3]. Only one case of the scrotal cellular angiofibroma with prominent nuclear atypia has been reported to date [4]. We present a case of a 71-year-old male with a tumor attached to the spermatic cord showing the appearance of cellular angiofibroma. In addition, multiple scattered atypical cells were present.

## Case report

A 71-year-old male was referred to the Bielanski Hospital in Warsaw, Poland, with a three months' history of a slowly growing nodule in the right groin. The patient had right inguinal hernia repair in his childhood. At the time of admission to the hospital, ultrasound revealed a well-circumscribed, solid, highly vascularized, hypoechoic tumor mass measuring 5.8 cm in the largest dimension, attached to the spermatic cord. In addition, there was a small amount of fluid in the right scrotum. The patient underwent a right orchiectomy with the excision of the tumor together with a segment of the spermatic cord. Gross examination showed a well-circumscribed, solid, grey, glossy tumor measuring $6 \times 4.5 \times 4$ cm which appeared to be attached to the spermatic cord. The testis and epididymis were grossly unremarkable. Microscopic examination

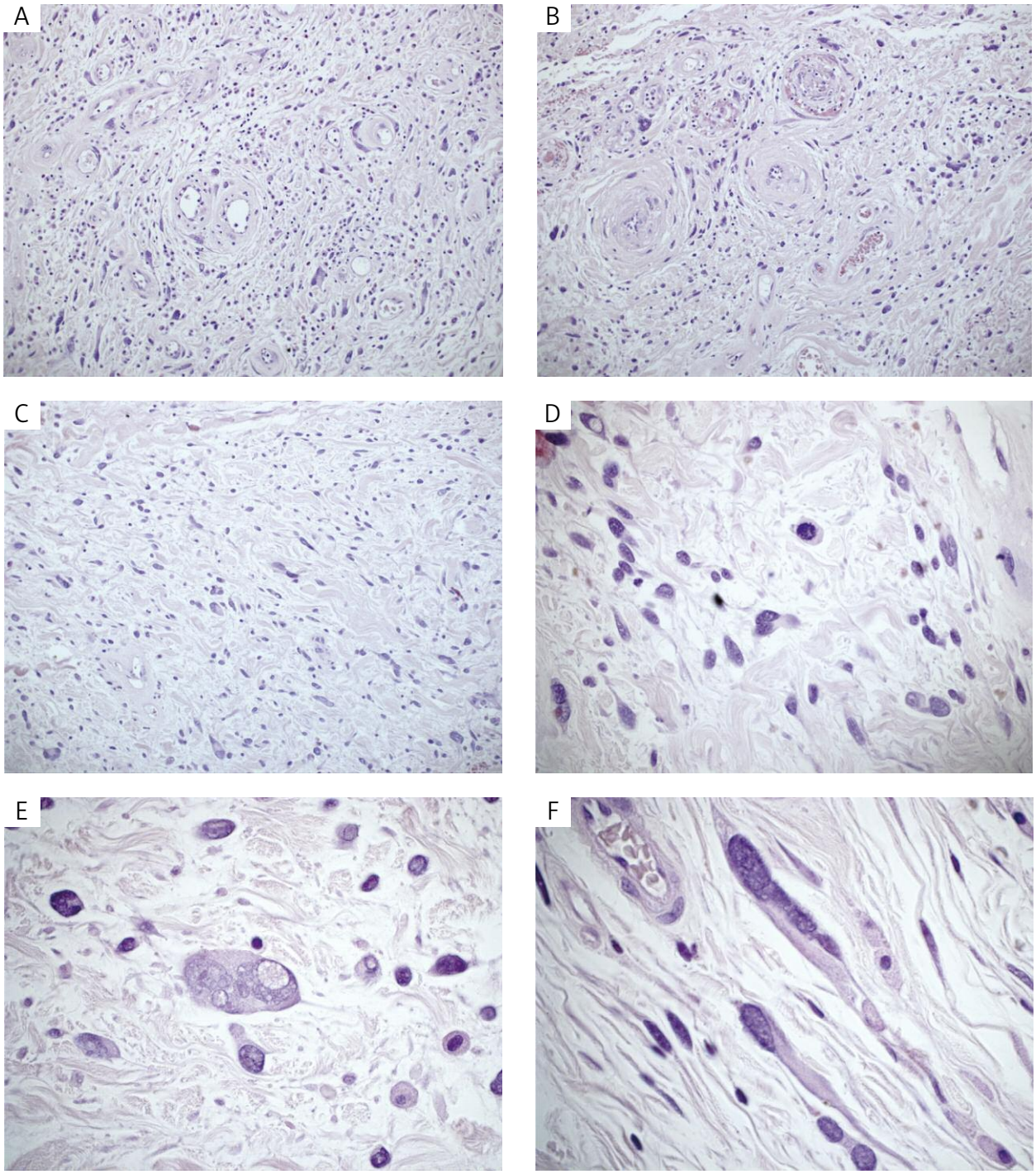


**Fig. 1A-F.** Cellular angiofibroma with spindle cells, prominent vascular channels showing hyalinized walls and scattered atypical cells (HE, A-C 100×, D 200×, E, F 400×)

of the tumor showed a spindle cell lesion with a loose, myxoid, partly collagenized stroma, numerous, prominent vessels with thick, partly hyalinized walls. Scattered atypical mononuclear and multinuclear cells were present. The microscopic images are presented in Figure 1 (A-F). The immunohistochemical studies showed: CD34 (+), desmin (+/–), S100 (–), SMA (–), HHF35 (–), Ki67 (10%).

## Discussion

Cellular angiofibroma occurs equally in men and women in the inguino-scrotal and vulvo-vaginal region, respectively. Histologically, cases of CAF show a heterogeneous appearance. They range from lesions with myxoid stroma to tumors exhibiting collagenized stroma. The tumor cells are usually bland spindle to

**Table I.** Clinical and pathological characteristics of CAF and CAS

| Feature* | Cellular angiofibroma (CAF) | Cellular angiofibroma with atypia or sarcomatous transformation (CAS) |
|---|---|---|
| definition | benign mesenchymal neoplasm composed of bland spindle cells and prominent small to medium-sized vessels with mural hyalinization | |
| etiology/pathogenesis | unknown<br>morphologic and immunophenotypic overlap with mammary-type myofibroblastoma and spindle cell lipoma | unknown |
| incidence | the largest published groups:<br>51 cases; Fletcher *et al*. (2004)[1]<br>25 cases; Flucke *et al*. (2011)[2] | the only published group:<br>13 cases; Fletcher *et al*. (2010)[3] |
| age | 5th-7th decade | 5th decade (range: 25-71; median 46 years) |
| gender (female : male) | F = M | F > M (12 females : 1 male) |
| presentation | well-circumscribed, non-tender, tumors | subcutaneous, well-circumscribed tumors, mostly asymptomatic |
| localization | external genital region, inguino-scrotal or vulvo-vaginal superficial soft tissues | 11 vulva<br>1 paratesticular region<br>1 hip region |
| radiological imaging: ultrasound | well-circumscribed, echogenic mass, sonographic appearance suggestive of fat | not evaluated |
| magnetic resonance imaging | non-lipomatous mass with T1 intermediate signal intensity and T2 diffuse hypointensity | |
| macroscopic image | lobulated, soft, rubbery mass | soft fibrous, firm or rubbery, nodular/lobulated, without necrosis or hemorrhage, morphologically atypical or sarcomatous component was not identified on macroscopic examination |
| size | 1-2.5 cm (females) to 2.5-14 cm (males) | 1.2-7.5 cm (median: 2.7 cm) |
| microscopic image | prominent vessels with perivascular hyalinization and altering less/more cellular areas with tapered, uniform spindle cells separated with collagen fibers | typical CAF image with:<br>– atypia: scattered, discontinuous foci within conventional angiofibroma including: scant cytoplasm, hyperchromatic nuclei, inconspicuous nucleoli<br>– morphologic features of sarcomatous transformation: nodules of pleomorphic liposarcoma (multivacuolated lipoblasts, variably pleomorphic atypical spindle cells), lipoblasts, adipocytes of variable size and hyperchromatic nuclei, atypical hyperchromatic stromal cell, pleomorphic bizarre multinucleated cells |
| immunohistochemistry | mostly positive: CD34, SMA, EMA<br>mostly negative: desmin, h-caldesmon, S-100 protein, pancytokeratin, CD31 | sarcomatous areas (number of cases from total 13 immunostained tumors):<br>(2) negative for CD34, SMA, desmin, S-100 protein<br>(9) positive for p16<br>(1) positive for p53<br>(4) negative for MDM-2 and CDK-4<br>in a component resembling atypical lipomatous tumor |

**Table I.** Cont.

| FEATURE* | CELLULAR ANGIOFIBROMA (CAF) | CELLULAR ANGIOFIBROMA WITH ATYPIA OR SARCOMATOUS TRANSFORMATION (CAS) |
|---|---|---|
| genetics | monoallelic loss of RB1 and FOXO1 (13q14) | not evaluated |
| differential diagnosis | aggressive angiomyxoma<br>angiomyofibroblastoma<br>solitary fibrous tumor<br>spindle-cell lipoma<br>leiomyoma | atypical lipomatous tumor<br>pleomorphic/spindle cell liposarcoma<br>pleomorphic sarcoma NOS |
| treatment | surgical excision | surgical excision and reexcision |
| prognosis | benign, without any tendency for recurrence | follow-up for 7 patients available (2-75 months; median 14 months):<br>(6) did not develop recurrence or metastasis<br>(1) died of metastatic carcinoma of an unknown primary site 27 months after diagnosis of CAS |

**Data presented in Table I are based on a review of the following publications 1-15*

oval and epithelioid cells. Prominent vascular channels with thick hyalinized walls are characteristically present in all lesions. Interestingly, there is a morphologic, immunohistochemical and cytogenetic similarity between three lesions described as separate entities: cellular angiofibroma, spindle cell lipoma and extra-mammary myofibroblastoma. It is postulated that these three entities can be in fact a morphological spectrum of one type of neoplasm [5, 6]. Occasionally, the tumor shows scattered atypical cells with nuclear hyperchromasia, nuclear irregularity as well as multinuclear atypical cells. There are single cases with sarcomatous nodules in the otherwise typical cellular angiofibroma. The cases with atypical or sarcomatous features are designated as cellular angiofibroma with atypia or sarcomatous transformation (CAS). There has been only one series of 13 cases of CAS published to date [4]. The series included 11 females with lesions of the vulva, 1 female with a hip lesion and one 26-year-old male with a paratesticular tumor. We present in this article the case of a 71-year-old man with the tumor attached to the spermatic cord. The tumor shows an appearance of cellular angiofibroma with atypia as part of the spectrum of CAS morphology. The age of our patient is in the age range of CAF.

Immunohistochemistry of CAF has been evaluated in several studies. The tumor shows frequently CD34 positive staining. It is variably positive for smooth muscle actin and desmin. There is a negative staining with S100, caldesmon, pancytokeratin and CD31 [7, 8]. Our case showed a positive staining with CD34, focal positive staining with smooth muscle actin and was negative for desmin and S100.

Recent cytogenetic and molecular studies of CAF revealed, in a few reported cases, the loss of RB1 and FOXO1A1 genes due to the deletion of the 13q14 region [9-11].

Differential diagnosis of CAF includes aggressive angiomyxoma, angiomyofibroblastoma, solitary fibrous tumor and schwannoma. Aggressive angiomyxoma shows a less prominent vascular pattern than CAF and exhibits positive desmin staining. Solitary fibrous tumor has areas with the staghorn vascular pattern and dense collagenous stroma. Schwannoma shows characteristic nuclear palisading and is immunohistochemically S100 positive. Well-differentiated liposarcoma (WD-LPS) is the main differential diagnosis of cellular angiofibroma with atypia or sarcomatous transformation (CAS). Moreover, the inguino-scrotal region is one of the most common locations where WD-LPS can occur. It is difficult to distinguish CAS and WD-LPS or another type of sarcoma due to the presence of cells with prominent nuclear atypia. It appears that histological features characteristic of CAF in the lesion next to the CAS nodules or presence of scattered atypical cells among characteristic cellular angiofibroma appearance might help to reach the final diagnosis.

Cellular angiofibroma behaves in a benign fashion and the surgical excision is a treatment of choice. All cases of CAS published by Chen *et al.* had a favorable prognosis according to follow-up information [4]. There were no cases of metastatic disease; no evidence of recurrence has been noted. One patient died of the metastatic carcinoma of unknown primary origin. In our case, six months after diagnosis, there have not been any signs and symptoms of the recurrence or metastasis in our case.

Table I presents a summary of the literature review which includes a presentation of all cases of CAS reported to date [1-15].

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