Case Report

Cellular angiofibroma of the inguinoscrotal region with cytologic atypia and abundant adipose tissue simulating liposarcoma: a case report

Abstract

Cellular angiofibroma (CAF) is a rare benign mesenchymal neoplasm of the vulvovaginal or inguinoscrotal regions. We report a case of CAF with abundant intralesional fat and focal cytological atypia that raised the possibility of liposarcoma. We review the literature and discuss the significance of these findings and the differential diagnosis of CAF.

Keywords: angiofibroma, differential diagnosis, sarcoma, spermatic cord

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Abbreviations: CAF, cellular angiofibroma; WDL, well-differentiated liposarcoma; SMA, smooth muscle actin; ER, estrogen receptor; PR, progesterone receptor

Introduction

Cellular angiofibroma is a benign soft tissue neoplasm that occurs almost exclusively in the vulvovaginal region of women or in the inguinal–scrotal region of men. CAF is characterized by bland spindle cells and prominent small to medium-sized vessels with mural hyalinization. Rarely, cellular angiofibromas have been reported to show atypical or sarcomatous features, including foci resembling undifferentiated pleomorphic sarcoma, and pleomorphic liposarcoma.[1,2]

Case report

A 60 year-old man presented with a one month history of a non-tender, painless, and growing lesion in the inguinoscrotal area that progressively became painful before he presented to medical attention. On clinical examination, a trans-illuminating scrotal mass is found in the scrotum that does not appear to be attached to the epididymis or the testicle. A scrotal ultrasound revealed a solid, heterogeneous and hypervascular 2.5cm extra testicular mass in the left lower testicular pole. A scrotal exploration was undertaken with excision of the mass. Grossly, the lesion measured 3x2x1.5cm, was gray-tan, firm, well circumscribed, and attached to the spermatic cord. Cut surface of the mass was pink-tan and firm to solid in consistency.

Microscopically, the lesion was well circumscribed (Figure 1) and there were predominately spindle-shaped cells in an edematous and lightly fibrous stroma interspersed with chronic inflammatory cells consisting of lymphocytes with some plasma cells and occasional mast cells. There were numerous thick-walled blood vessels, many with wall hyalinization (Figures 2 & 3). These findings are typical of cellular angiofibroma, but there were also scattered cells with cytological atypia and abundant intralesional adipose tissue with focal fat necrosis (Figures 1 & 4). These additional findings raised concern for a well-differentiated liposarcoma, and the case was referred to the Joint Pathology Center, the reference laboratory for Veterans Affairs medical Centers, for consultation. The consultant performed immunohistochemical stains for CD34, desmin, and estrogen receptor, which were positive, and MDM-2, which was negative. This immunoprofile, along with the light microscopic appearance supported the diagnosis of cellular angiofibroma with focal cytologic atypia over well-differentiated liposarcoma.

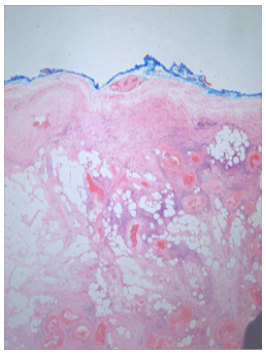

Figure 1 Cellular Angiofibroma showing abundant intralesional adipose tissue and chronic inflammatory cells. Note that the lesion is well-circumscribed. (H&E X40).

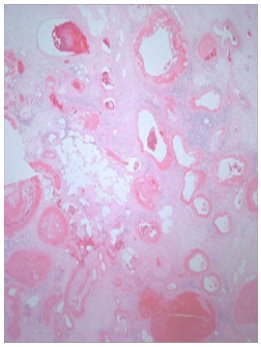

Figure 2 Cellular Angiofibroma with numerous thick-walled blood vessels, many with wall hyalinization (H&E X40).

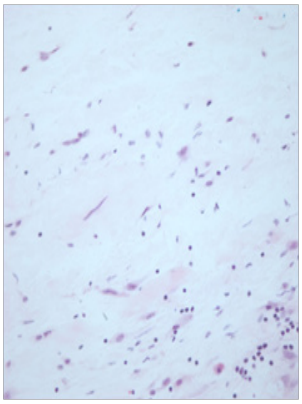

Figure 3 Cellular angiofibroma depicting edematous and slightly myxomatous background with irregular spindle cells and inflammatory cells (H&E X400).

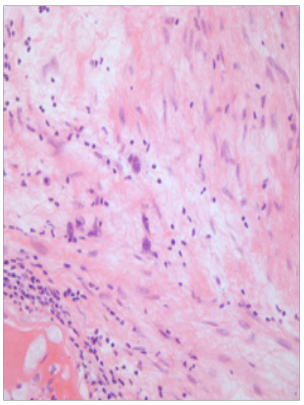

Figure 4 High power field showing atypical and hyper chromatic spindle cells along with mononuclear inflammatory infiltrate (H&E X400).

Discussion

Cellular angiofibroma (CAF) is an uncommon benign mesenchymal neoplasm of the genital tract with a prominent spindle cell component and very prominent stromal vasculatures. Adipose tissue was present in 24% of cases from one of the largest published series. Adipose tissue was usually located in the periphery of the lesion as small clusters with few cases showing large nests or lobules comprising 30-50% of the tumor area.[1] CAF tends to occur in the inguinoscrotal region in males and vulvovaginal region in females. CAF occurs in men and women in equal proportions. It tends to occur in the fifth decade in women and the seventh decade in men.[1]

In addition to the well-differentiated liposarcoma (WDL) which was included in the differential diagnosis because of some of unusual features of this lesion, the entities that are typically considered in the differential diagnosis of CAF are listed in (Table 1), along with the most useful histologic features that help in differentiating them. Fletcher et al.[1] reported immunohistochemical studies on 48 of their study cases. The tumor cells showed multifocal to strong and diffuse positivity for CD34 in 29cases (60%) (11/24, 46% for female and 18/24, 75% for male cases). Immunoreactivity for smooth muscle actin (SMA) was present in 10tumors (21%) and for desmin in 4tumors (8%). The tumor cells were consistently negative for S-100 protein in all cases. Immunoreactivity for estrogen receptor (ER) and progesterone receptor (PR) was examined in 20 randomly selected cases (10 female and 10 male cases). Strong nuclear positivity for ER was present in 7 tumors (35%) (5/10, 50% for female and 2/10, 20% for male cases) and for PR in 11tumors (55%) (9/10, 90% for female and 2/10, 20% for male cases). (Table 2) summarizes the immunohistochemical profile of the lesions considered in the differential diagnosis of CAF, based on published literature. There is limited genetic data suggesting that CAF appear to be closely related to spindle cell lipoma and mammary-type myofibroblastoma.[3,4]

Atypical cellular features and sarcomatous transformation of CAF have been reported.[2] CAF with atypical (bizarre) cells shows scattered, noncontiguous foci of severely atypical cells within conventional CAF. The sarcomatous transformation is characterized by abrupt transition to a discrete sarcomatous component that may form a solitary nodule. This sarcomatous component can resemble well-differentiate liposarcoma atypical lipomatous tumor, pleomorphic liposarcoma, or pleomorphic sarcoma NOS.[2,5] Chenet al.,[2] reviewed 154 usual cellular angiofibromas identified between 1993 and 2009 from their consultation files and identified 13cases of CAF with atypia or sarcomatous change, 12patients were female and one was male suggesting that atypia and sarcomatous changes are more common in vulvar lesions. Nonetheless, based on limited clinical follow-up data, these changes did not seem to predispose to recurrence or metastasis.[2] In that study, three cases of CAF contained areas with features indistinguishable from well-differentiated liposarcoma/atypical lipomatous tumor, but these were negative for MDM2 and CDK4 by immunohistochemistry, suggesting that these two genes are not the underlying alteration when this lesion develops in association with CAF.[2] Table 3 summarizes the cases of CAF we identified in our literature search and highlights those that reported atypia.

Table 1 Entities that are typically considered in the differential diagnosis of cellular angiofibroma

Differential diagnoses of CAF	Gender	Distinguishing histologic features	Most common site
Aggressive Angiomyxoma	F:M=9:1	Poorly circumscribed with infiltrative borders	Genital. Perineal and pelvic region
Angiomyofibroblastoma	F:M=20:1	Prominent ectatic vessels surrounded by eosinophilic epithelioid cells, usually in vulva	Genital area
Spindle cell lipoma	F:M=1:20	Mature adipocytes and bland spindle cells. Ropy, loosely arranged collagen	Posterior neck, upper back and shoulder
Solitary fibrous tumor	F=M	Benign tumor of spindle cells separated by thick bands of collagen with hyalinization. Large branching (staghorn) vessels	Anywhere in the body, especially body cavity sites, including pleura, peritoneum, and meninges
Neurofibroma	F=M	Non-encapsulated. Spindle cells with wavy or comma-shaped nuclei in a wire-like collagenous stroma. Intralesional nerve fibers	Cutaneous, and anywhere in the body, from the peripheral nervous system

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Table 2 Immunohistochemical profile of cellular angiofibroma and entities considered in its differential diagnosis

	Vimentin	CD34	SMA	Desmin	ER	PR	S100
Cellular angiofibroma	+	+	+/-	+/-	+/-	+/-	-
Aggressive Angiomyxoma	+	+	+/-	+/-	+/-	+/-	-
Angiomyofibroblastoma	+	+/-	+	+	+	+	-
Spindle cell lipoma (CD99 and bcl2 positive)	No data	+	No data	-	No data	No data	+(in Adipocytes)
Solitary fibrous tumor (CD99 positive)	No data	+	-	-	No data	No data	-
Neurofibroma	+	+	No data	No data	No data	No data	+
Well differentiated liposarcoma (MDM2 and CDK4 positive)	+	+	-	-	No data	No data	

Table 3 Summary of cases of cellular angiofibroma reported in the literature with focus on those showing cytological atypia

Case study/report	Number of cases	Cases showing atypia or sarcomatous transformation
Iwasa et al.[1]	51(26 Female, 25 Male)	Mild cytologic atypia characterized by slight nuclear enlargement and hyperchromasia was present in 5tumors (all males), all of which were associated with stromal edema and a prominent chronic inflammatory cell infiltrate, suggesting that this represented reactive/degenerative atypia. One case (female) showed a focus of a microscopic intralesional nodule of pleomorphic liposarcoma
Chen et al.[2]	154(13 cases with atypia described in detail. 12 female, 1 male)	13 total cases with atypia or sarcomatous transformation. 4cases of CAF with atypia 9cases showed morphologic features of sarcomatous transformation including pleomorphic liposarcoma (2cases), and atypical lipomatous tumor/well-differentiated liposarcoma (3cases)
Hameed et al.[3]	1(male)	No
Maggiani et a.[4]	2(1 male, 1 female)	No
Dikaiakos et al.[7]	1(male)	No
Val Bernal et al.[8]	1(male	CAF showed atypical (bizarre) cells
Canales et al.[9]	2(males)	No
Ptaszynski et al.[10]	1(male)	CAF showed atypical cells

Although rare, well-differentiated liposarcoma of the spermatic cord is the most common sarcoma of the paratesticular region in adults.[6] The lesion is characterized by scattered, bizarre cells with irregular, hyperchromatic nuclei present in the fibrous stroma or among the adipocytes, or both. These atypical cells may be numerous, or rare and difficult to identify. Typically, adipose tissue predominates (lipoma-like variant), but the adipocytes show more variability in size than mature fat. Lipoblasts may not be seen and are not required for diagnosis. The sclerosing variant, more common in the retroperitoneum, contains predominantly atypical spindle cells in a fine fibrillary collagenous stroma and only scant adipose tissue. Mitoses are rare. Immunohistochemical staining demonstrates nuclear staining for MDM2 (95% of cases) and CDK4 (78% of cases).[5,6]

In conclusion, the case we present had morphology and immunohistochemical profile consistent with CAF. There were unusual features that included abundant intralesional adipose tissue, in addition to the expected adipose tissue at the periphery. There were also atypical cells that were scattered within the lesion. These atypical cells did not form a discrete nodule, therefore, this lesion is best regarded as cellular angiofibroma.[7–10] with focal atypia. Iwasa et al.[1] suggested that the atypia may be reactive, since most of the lesions, as in our case, had a prominent chronic inflammatory infiltrate. Complete local excision is the optimal treatment for CAF with atypical cells as the lesion shows no tendency to recur based on the current literature. Pathologists should be aware of the morphological variation of CAF and its differentials to avoid misdiagnosis and potential overtreatment.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

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