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Case Report

Ulcerated cellular benign fibrous histiocytoma: A challenging diagnosis in biopsy practice

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Abstract A biopsy diagnosis of conventional (common) type of benign fibrous histiocytoma (BFH) is usually easy. However, there are many other histopathologic variants, that may cause difficulties to make an accurate diagnosis. The author describes a 53-year old women, who presented with a protuberated ulcerated skin tumor arising on the left shoulder. It consisted of a highly cellular mass of proliferating spindle-shaped cells with a fascicular growth pattern, that was confined to dermis. The cells were relatively uniform with a slightly increased mitotic rate and proliferation activity. Immunohistochemically, the tumor expressed vimentin, Factor XIIIa and alpha-SMA, while it was negative for CK5/6, CK7, BerEP4, p63, EMA, S-100, melan A, HMB-45, MSA, h-caldesmon and CD34. A diagnosis of ulcerated cellular BFH was made. Although BFH is a very frequent cutaneous tumor, its less common cellular variant may result in diagnostic pitfalls. The purpose of this paper was to point out that even such „banal" and prognostically favourable cutaneous lesion sometimes requires a complex differential diagnostic approach in biopsy practice

Key words
Benign fibrous histiocytoma, dermatofibroma, alpha-SMA, factor XIIIa.

Introduction

Benign fibrous histiocytoma (BFH, dermatofibroma) is a frequent diagnosis in routine dermatopathological practice.[1,2] It usually manifests as a slowly growing solitary nodule on the limbs of young to middle-aged adults, with a slight female predominance.[1-3] Histologically, a common (conventional) BFH generally consists of spindled (myo)fibroblasts forming short intersecting fascicles and histiocyte-like cells, admixed with inflammatory cells, multinucleated giant cells, foamy cells and siderophages in the dermis.[1-3] The epidermis above the lesion is usually hyperplastic, accompanied by hyperpigmentation of basal keratinocytes.[1-3] In addition to common BFH, many other variants and subtypes have been reported in the literature **(Table 1)**. They display distinct or overlapping histomorphologic features, that may cause difficulties to make a correct diagnosis. Herein, a cellular variant of BFH with an extensive ulceration is described.

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Case report

A 53-year old women presented with a solitary cutaneous tumor arising on the left shoulder. She claimed that the lesion had been present for a few months, during which it had increased in size. Grossly, it appeared as a well-demarcated, ulcerated nodular skin tumor measuring 1cm in diameter. It was brownish in color and elastic in consistency. The presumptive clinical diagnosis was basal cell carcinoma. A total surgical exstirpation of the lesion was done and a specimen was send for microscopic examination.

Low magnification revealed a protuberated tumor with an extensive central ulceration and a purulent necrotic detritus at the base of ulcer

Table 1 Histopathologic subtypisation of BFH of the skin.[2])

Histopathologic variants and subtypes	
- conventional (common) type	- BFH with osteoclast-like giant cells
- lipidized variant	- BFH with smooth muscle proliferation
- haemosiderotic variant	- BFH with prominent myofibroblastic proliferation
- keloidal variant	- BFH with intracytoplasmic eosinophilic globules
- granular cell variant	- epithelioid BFH
- clear cell and baloon cell variant	- aneurysmal BFH
- signet ring cell variant	- cellular BFH
- palisading variant	- atypical BFH
- atrophic variant	- angiomatoid BFH
- myxoid variant	- plexiform BFH
- lichenoid variant	- atypical fibroxantoma

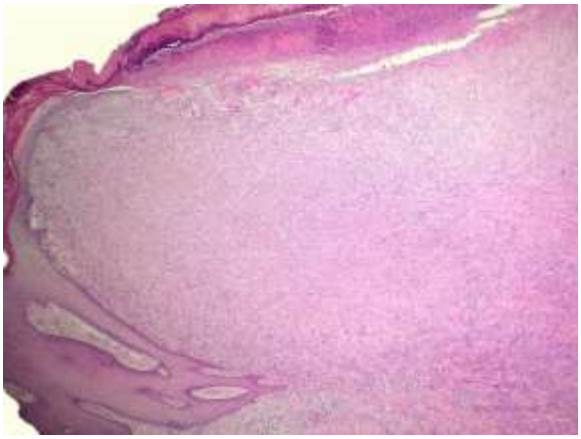

Figure 1 Protuberated skin tumor with an extensive ulceration in the centre. (H&E, magnification 40x).

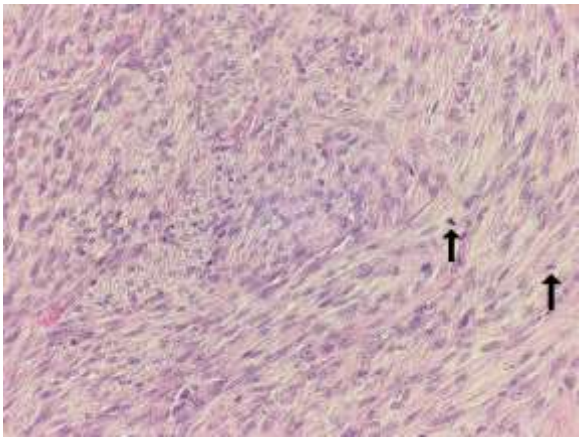

Figure 2 Dense mass of spindle-shaped neoplastic cells with a fascicular growth pattern. Two mitotic figures (arrows) are visible. (H&E, magnification 120x).

(Figure 1). It consisted of a highly cellular mass of proliferating, gently eosinophilic spindle-shaped cells with a fascicular growth pattern and less abundant stroma. The cells were relatively uniform with a slightly increased mitotic rate (in hot spots 4 mitoses per 10 HPF) **(Figure 2)**. Atypical mitotic figures were not found. The lesion was confined to dermis with a vague border between tumor tissue and surrounding dermal stroma. A definite diagnosis could not be done without using an immunohistochemistry. In the first step, the goal was to define a histogenetic origin of tumor. A diffuse immunohistochemical positivity for vimentin and negativity for CK5/6, CK7, BerEP4, p63, EMA, S-100, melan A and HMB-45 confirmed mesenchymal, while excluded epithelial and neurocytic origin. In the second step, the focus was to classify the tumor exactly. There was a diffuse weak immunoreactivity for Factor XIIIa **(Figure 3)** and a focal intense expression of alpha-smooth muscle actin (SMA) **(Figure 4)**. Muscle specific actin (MSA), h-caldesmon and CD34 were negative. Proliferation activity (Ki-67 index) did not exceed 10% **(Figure 5)**. Based on the histopathological findings and immunophenotype, a final diagnosis of ulcerated cellular BHF (dermatofibroma) was made. Resection margins were free of tumor.

Discussion

Skin neoplasms composed of spindle cells constitute a very heterogeneous group of mesenchymal and nonmesenchymal tumors.[2,4] They are often diagnostically challenging

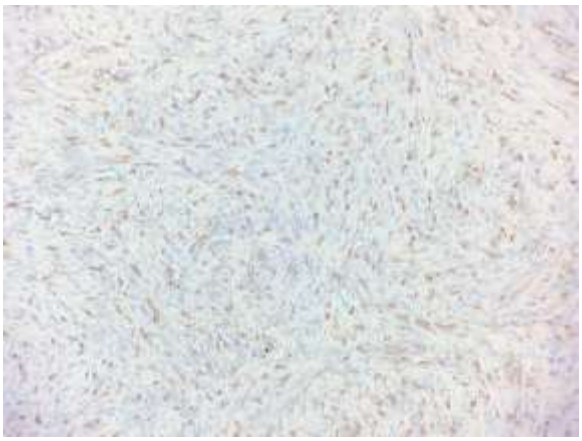

Figure 3 Diffuse weak cytoplasmic expression of Factor XIIIa in the tumor cells. (magnification 100x).

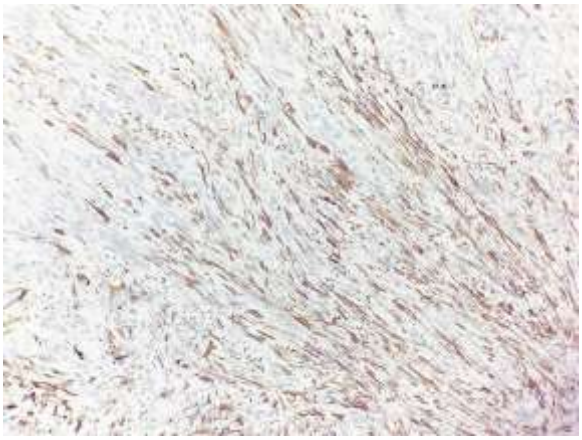

Figure 4 Focal strong cytoplasmic expression of alpha-SMA in the tumor cells. (magnification 100x).

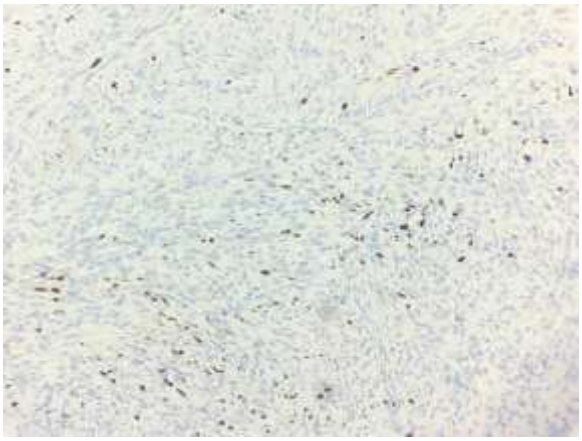

Figure 5 Slightly increased nuclear expression of Ki-67 antigen in the tumor cells. (magnification 100x).

because of considerable morphologic overlap among the various tumor types that compose this group.[2] A detailed description of all neoplasias with a predominant spindle cell histomorphology would go far beyond the scope of this article. This topic is well written in another papers.[2,4] In biopsy practice, the most important diagnostic issues include distinguishing true spindle cell mesenchymal tumors from spindle cell squamous cell carcinoma and malignant melanoma, discriminating between benign and malignant lesions, and classifying their histologic types.[2] Within this group, one of the tumor type that may cause diagnostic difficulties is a cellular variant of BFH.

Cellular BFH of the skin was first described as a histopathologic entity by Calonje *et al*.[5] in 1994. They reported seventy-four cases of a distinctive variant of BFH, which had been often mistaken histologically for sarcoma.[5] It has been estimated to represents about 5% of all BFHs.[6] Cellular BFH occurs most commonly in young or middle-aged adults (mean age 32-33 years),[5,7] showing a mild predominance in women.[5] It mainly arises on the upper limb/limb girdle (34%), followed by lower limb/limb girdle (27%), head and neck (20%) and trunk (12%).[5] In contrast to conventional BFH, it is usually not recognized clinically and even a biopsy diagnosis may be problematic. The main histologic features, that distinguish this tumor from common BFH are as follows: high cellularity with a predominance of eosinophilic spindle cells with tapering nuclei, fascicular rather than storiform growth pattern, increased mitotic rate up to 10 mitoses per 10 high-power fields (mean 3/10 HPF), and frequent extension into the subcutaneous fat.[5] Foci of necrosis may be found in 12%, while ulceration is less frequent.[5] In biopsy practice, the spectrum of findings mentioned above often result in pitfalls in diagnosis. In our case, the worrisome features were an extensive ulceration and a marked cellularity of lesion with mitoses, that were suspected for malignancy.

Table 2 Clinicopathological and immunohistochemical features of cellular BFH, DFSP and LMS. (summarized from ref.[1-11]).

	Cellular BFH	*DFSP*	*LMS*
Clinical features			
common location	upper limb/upper girdle	trunk/proximal extremities	trunk/lower limb
female/male ratio	1.9 : 1	1 : 1	1 : 3-4
gross appearance	solitary nodule	solitary plaque or nodule	solitary nodule
mean age	32 - 33 y.	43 y.	56 y.
Histopathology			
cell population	eosinophilic spindle cell	uniform elongate cells	eosinophilic spindle cells
atypia	mild	mild	mild to moderate
growth pattern	usually fascicular	usually storiform	usually fascicular
typical mitoses	common	common	common
extension into subcutis	quite frequent	frequent	frequent
Immunoprofile	SMA (may be focally +)	SMA (may be focally +)	SMA (+ in 100%)
	CD163 (+ in 100%)	CD163 (+ in 17%)	MSA (+ in 100%)
	CD68 (+ in 83%)	CD68 (+ in 6%)	h-caldesmon (+ in 100%)
	CD34 (may be focally +)	CD34 (+ in 100%)	desmin (+ in 92.3%)
	Faktor XIIIa (+ in 48%)	Faktor XIIIa (negative)	calponin (+ in 92.3%)

In general, an ulceration in cutaneous BFH is very unusual finding. In a study of Sánchez *et al*.[8] among a total of 484 tumors, only six erosive and two ulcerated cases were found. They concluded, in the presence of an otherwise histopathologically typical BFH, erosion and ulceration should not be considered as suspicious of malignancy.

Cellular BFH must be be particularly distinguished from dermatofibrosarcoma protuberans (DFSP) and cutaneous leiomyosarcoma (LMS).[2,3,5] These tumor entities have a similar histomorphology and compose of proliferating, spindle-shaped (myo) fibroblasts or myocytes in a fascicular or storiform pattern. Therefore, an immunohistochemistry is an essential method to make a correct diagnosis. Briefly, except for vimentin positivity,[5] a cellular BFH is immunoreactive for CD163 and CD68,[9] and may be focally reactive for SMA[5,7] and CD34.[7,9] In one study,[9] factor XIIIa was positive in 48% of the cases, but another author[5] did not show any case positive for this marker. Another antigen, such as cytokeratin, desmin, h-caldesmon, and S-100 are negative.[5,7] DFSP is constantly positive for CD34,[9,10] may be focally positive for SMA[1] and CD163[9] and is negative for factor XIIIa.[9] Cutaneous LMS almost constantly express all myogenic markers, such as MSA,[11] SMA,[3,11] h-caldesmon,[2,11] desmin,[2,3,11] and calponin.[11] It should be noted, although an immunohistochemistry is very useful, the observations must be carefully interpreted in the context with other findings. A summary of the basic clinicopathological and immunohistochemical features of cellular BFH, DFSP and LMS of the skin is illustrated in **Table 2**.

Conclusion

Although BFH is a frequent skin tumor and a histopathologic diagnosis of its conventional type is usually easy, a much less common cellular variant may result in diagnostic pitfalls. The purpose of this paper was to point out that even such banal and prognostically favourable cutaneous lesion sometimes requires a complex differential diagnostic approach in biopsy practice.

Consent The examination of the patient was conducted according to the Declaration of Helsinki principles.

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