Cutaneous fibrohistiocytic/ fibroblastic tumours: an update

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Abstract

Fibrohistiocytic tumours are among the most frequently encountered soft tissue tumours of the skin. "Fibrohistiocytic" is a descriptive term for cells that resemble both normal fibroblasts and histiocytes, rather than a true line of differentiation. This review discusses the clinical, histologic and immunohistochemical findings in benign, intermediate and malignant fibrohistiocytic tumours, including prognostic and molecular findings. Pertinent entities in the differential diagnosis, with discriminating features, are also discussed.

Keywords atypical fibroxanthoma; benign fibrous histiocytoma; cellular neurothekeoma; dermatofibrosarcoma protuberans; epithelioid fibrous histiocytoma; fibrohistiocytic tumours of intermediate malignancy; pleomorphic dermal sarcoma

Introduction

Fibrohistiocytic tumours are among the most frequent soft tissue tumours encountered in the skin.[1] "Fibrohistiocytic" is an entirely descriptive term devised to designate a group of heterogeneous tumours resembling both normal fibroblasts and histiocytes. Unlike most similar designations ("adipocytic, vascular, etc."), it does not cover a definitive line of differentiation. In fact, most tumours in this category are of uncertain histogenesis.[2]

The focus of this review is on the fibrohistiocytic/fibroblastic spectrum of the category, while purely histiocytic neoplasms are beyond the scope of this paper. Based on their histological features, cutaneous fibrohistiocytic tumours fall into benign, intermediate and malignant subcategories.[3] Importantly, diagnostic difficulties carrying potential therapeutic implications are not infrequent in fibrohistiocytic lesions. This is due to the large number of variants/entities and histologic overlap between benign and malignant entities. Malignant cutaneous neoplasms included in this category bear less resemblance to histiocytes than the term "fibrohistiocytic" would suggest, but they are historically included in this category.[4]

Benign fibrohistiocytic tumours

Benign fibrous histiocytoma

Due to its frequency, there is an exhaustive body of literature on benign fibrous histiocytoma of the skin. Therefore, the focus of this paper will be on important variants, other fibrohistiocytic entities in the differential diagnosis and any recent findings, covering only essential information on classical benign fibrous histiocytoma.

Briefly, benign fibrous histiocytoma is a tumour most commonly encountered as a solitary polypoid, flat or depressed lesion in the extremities of young to middle-aged adults, more frequently females.[3] In a proportion of cases it is multiple, occasionally in the setting of immunosupression.[5] Over the course of years it has been debated whether BFH is of neoplastic or inflammatory origin.[6] Recently, recurrent fusions of genes encoding membrane-associated proteins (podoplanin, CD63 and LAMTOR1) with genes encoding certain protein kinase C isoforms have been reported in a proportion of cases, setting a strong argument for the true neoplastic origin of benign fibrous histiocytoma.[7]

Most benign fibrous histiocytomas are located superficially (hence the synonymous term "dermatofibroma"), and centred in the mid dermis. They are composed of a polymorphous population of oval to spindled cells with fibroblastic and histiocytic features, arranged in short, storiform fascicles, intermediate fascicles or sheets, characteristically interdigitating between dermal collagen fibres, so-called "collagen trapping", most apparent at the tumour periphery (Figure 1a). Frequently, the tumours contain hemosiderin pigment and inflammatory cells in varying quantities. Many dermatofibromas induce epidermal hyperplasia and increased melanin production, while some exhibit adnexal induction phenomena such as follicular[8] (Figure 1b), sebaceous[9] or apocrine[10] induction. The list of histological appearances is exhaustive and includes variants such as cellular,[11] aneurysmal,[12] epithelioid,[13] atypical,[14] hemangiopericytoma-like,[15] lipidized,[16] myofibroblastic,[17] sclerotic,[18] palisaded,[19] clear cell,[20] granular cell,[21] balloon cell,[22] myxoid,[23] ossified,[24] giant,[25] metastasizing[26] and other.[27,28] A list of differential diagnoses for all of these variants is as exhaustive and includes equally diverse entities. Nevertheless, nearly all of these variants will show the typical interdigitating collagen pattern (collagen trapping) characteristic of benign fibrous histiocytoma, at least focally. In this review, cellular, aneurysmal, epithelioid, atypical and the rare metastasizing benign fibrous histiocytoma will be discussed in detail.

Cellular fibrous histiocytoma

Cellular fibrous histiocytoma differs from classical benign fibrous histiocytoma by several key histological features: it is more cellular with a more uniform population of spindled cells with a predominantly fascicular growth pattern (Figure 2a). It is often larger and more deeply located than conventional benign fibrous histiocytoma and frequently shows some infiltration into the subcutis, typically in a limited lace-like pattern (Figure 2b).[11]

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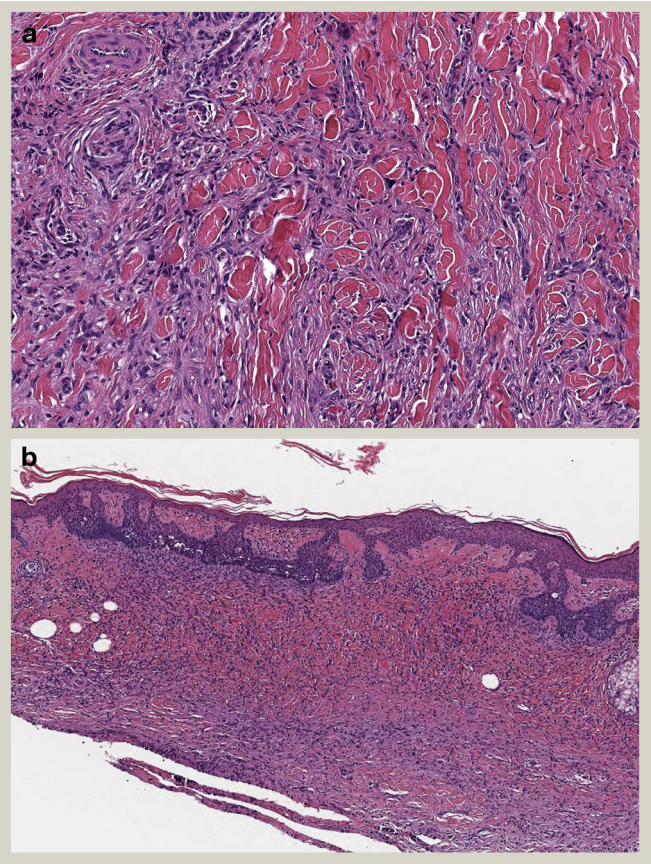

Figure 1 Classical fibrous histiocytoma (dermatofibroma). (**a**) composed of bland spindled cells admixed with histiocytes. At the periphery of the tumour the cells interdigitate around collagen fibres of the reticular dermis; (**b**) follicular induction in the form of elongated basal layers resembling superficial basal cell carcinoma.

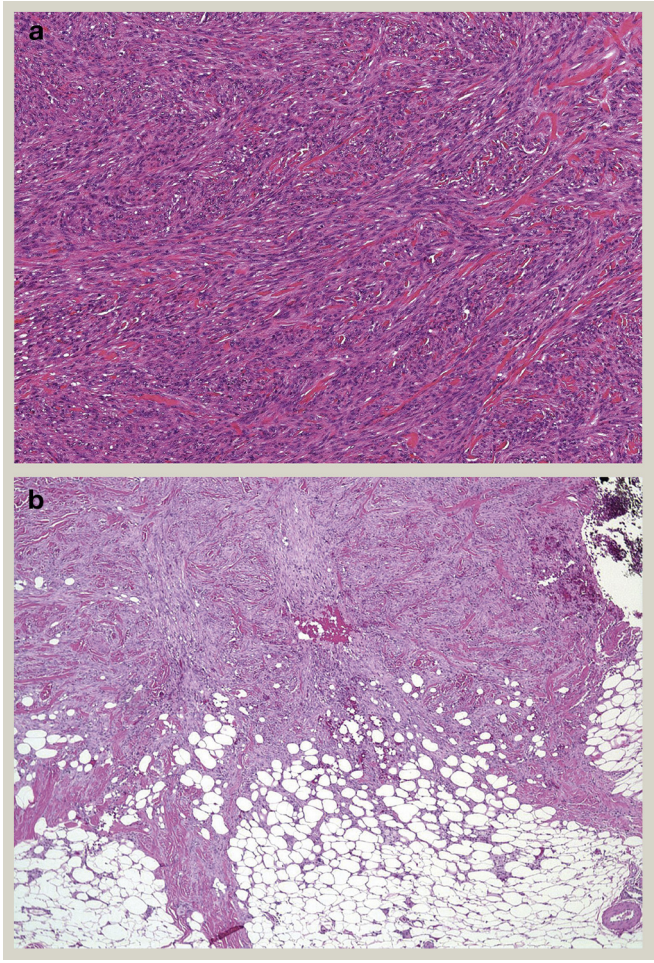

Figure 2 Cellular fibrous histiocytoma. (**a**) spindled cells with a fascicular growth pattern; (**b**) the tumour is centred on the subcutis with lace-like extensions (scanning magnification).

Mitotic activity is common (on average three mitoses/high power field), and tumour necrosis may be seen in up to 10% of cases. Although it typically lacks inflammatory cells and giant cells, it maintains low power features of conventional benign fibrous histiocytoma, including relative circumscription and peripheral collagen trapping. Recognition of this variant is important, as it has greater propensity (up to 25%) for local recurrence.[11] Similar to classical benign fibrous histiocytoma, a proportion of cases shows the aforementioned protein kinase C translocations.[7] Cellular fibrous histiocytoma may show immunoreactivity for SMA and is often negative for Factor XIIIa by immunohistochemistry.[11] Cellular fibrous histiocytoma shows relatively frequent (32%) desmin positivity and some positivity for CD34 in a minority (6%) of cases,[29] the latter being a potential pitfall in the differential diagnosis versus dermatofibrosarcoma protuberans.

Dermatofibrosarcoma protuberans is the entity most frequently confused with cellular fibrous histiocytoma. Recognition of the predominantly fascicular growth pattern, peripheral collagen trapping and relative circumscription allow distinction in most cases. The more limited pattern of subcutaneous fat involvement is distinct from the honeycomb pattern of dermatofibrosarcoma protuberans. The latter also has rearrangement of *PDGFRB*, in contrast to cellular fibrous histiocytoma.[30] Due to its deeper location and frequent immunoreactivity for SMA, cellular fibrous histiocytoma needs to be distinguished from nodular fasciitis. The latter has focal cystic breakdown, extravasation of erythrocytes and a more "tissue culture-like" growth pattern. In difficult cases, detection of the *USP6* gene rearrangement of nodular fasciitis can aid in the differential diagnosis.[31]

Aneurysmal fibrous histiocytoma

A relatively small proportion (1–2%) of benign fibrous histiocytoma develops central cystic haemorrhage. Clinically, they are characterized by rapid growth and blue/black discolouration, being frequently mistaken for a haemangioma or a melanocytic lesion. On histology they contain prominent blood-filled spaces devoid of an endothelial lining, accompanied by abundant siderophages, copious hemosiderin deposition, giant cells and lipidized cells (Figure 3).[12] Protein kinase C translocations are found in some aneurysmal fibrous histiocytomas.[32] Similar to cellular fibrous histiocytoma, aneurysmal fibrous histiocytoma has a higher local recurrence rate (up to 20%)[1] compared with classical benign fibrous histiocytoma. It is quite important to be properly acquainted with the nomenclature, as aneurysmal fibrous histiocytoma is a variant of benign fibrous histiocytoma and entirely different from angiomatoid fibrous histiocytoma,

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