Fibrous histiocytomas: histopathologic review of 95 cases

Histiocitomas fibrosos: revisão histopatológica de 95 casos

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Abstract: Fibrous histiocytoma (FH) is a heterogeneous tumor composed of fibroblasts, histiocytes, and blood vessels. We conducted a retrospective histopathologic analysis of 95 biopsies, performed over the last 3.5 years, of fibrous histiocytomas to analyze the location, delimitation, epithelial changes, induction of folliculo-sebaceous structures, cellularity, vascularity, collagen pattern, and types of composite cells of the FH. In the majority of the biopsies, we confirmed the classical histopathologic features of fibrous histiocytomas. The presence of lymphoid nodules, mast cells, and sparse infiltrate of inflammatory cells was an interesting finding observed in our study.

Keywords: Histiocytes; Histiocytoma benign fibrous; Histology

Resumo: O histiocitoma fibroso é tumor heterogêneo composto por fibroblastos, histiócitos e vasos sanguíneos. Efectuamos uma revisão histopatológica retrospectiva de 95 biopsias de histiocitomas fibrosos do nosso arquivo dos últimos 3,5 anos, com o objectivo de avaliar a localização, delimitação, alteração da epiderme, indução folículo-sebácea, celularidade, vascularização, padrão do colagénio e tipo de células constituintes. Na maioria das biopsias, confirmamos as características histopatológicas clássicas dos histiocitomas fibrosos. Achados interessantes observados no nosso estudo foram presença de células nódulos linfoides, mastócitos e infiltrado de células inflamatórias.

Palavras-chave: Histiocitoma fibroso benigno; Histiócitos; Histologia

INTRODUCTION

Fibrous histiocytoma (FH) or dermatofibroma is a proliferation of fusiform cells in the dermis, constituted by a variable combination of fibroblasts, collagen, histiocytes, and blood vessels. Several variants have been described and more than one may be present in the same lesion. 1-15 Cytologically, most cells are fusiform and oval, 1-15 with vesicular nuclei, slightly prominent nucleoli, and scant amphophilic cytoplasm. 1-15 There are small grouped or isolated cells of xanthomatous cytoplasm or cytoplasm filled with hemosiderin in between fusiform cells. 1,2,5-7 The presence of an inflammatory infiltrate typically lymphocytic, of variable intensity, is common. 1,2,4,6 Another typical histopathological finding consists in the encapsulation of collagen bundles, making it hyaline or keloid-like in the periphery of the tumor. 1,2,5-7

Lesions are symmetrical, round 1,2, and non-encapsulated. 1,2,4,6 A typical characteristic of this type of lesion is the absence of clear demarcations, 1,2,4,6 both in their lateral margins and depth. 1,15 In most FH cases there is a zone of relatively normal collagen of variable thickness demarcating the boundary between normal epidermis and a dermal lesion (Grenz zone). 1,4,6 Tumors are located in the medium dermis and sometimes they extend to the hypodermis. 1,2,4,7 This extension is observed throughout the fibrous
septa, separating fat lobules. Peripheral infiltration of fat lobules, in a pattern similar to that of dermatofibrosarcoma protubersans (DFSP), rarely occurs. Occasionally, the FH is located in the hypodermis, without a dermal component, showing tumor relapse in 20% of the cases.

Another very typical characteristic is polymorphism of the proliferative cell and of the relationship between the cellular component, blood vessels, and newly-formed collagen. The cellular component predominates in the cellular dermatofibroma, with an unsystematic arrangement in storiform pattern. Cells often contain intracytoplasmic deposits of lipids (xanthomatous form) or of hemosiderin (hemosiderotic form). Sometimes the vascular component is abundant, and a proliferation of dilated capillaries inside fusiform cells is observed. Pseudovascular spaces filled with red globules or hemosiderin, without endothelial lining, are found in some FH.

Occasionally, in these hemorrhagic variants, multinucleated giant cells - Touton or foreign body - are found. Mitosis may be observed, but the presence of mitotic activity does not indicate malignancy. Mast cells and lymphomononuclear cell infiltrate are sometimes observed. Rarely, cellular pleomorphism may occur in dense cellular areas, with cells that contain a big, bizarre and hyperchromic nucleus, and foamy cytoplasm, atypical, monstrous or pseudosarcomatous.

In the FH, the cellular component is less abundant and collagen fibers preponderate, among which small groups of fusiform cells interstitially arranged are found. They often show a fascicular, storiform or chaotic pattern or coexistence of various patterns in the same lesion. The presence of nuclear palisade is possible, characterized by a parallel arrangement of the nuclei of cells.

FH is sometimes constituted by a combination of dense cellular areas and other more fibrous areas, with a scant number of cells. In lesions that have evolved, progressive hyalinization and cellularity reduction are detected, leaving residual areas of xanthomatous cells. FH can occasionally show areas of calcification or bone metaplasia or present clear, granular, balloon, or signet-ring cells.

Alterations of the epidermis are also one of the most frequent histopathological characteristics. Acanthosis is observed in most FH cases, and it is of considerable value in the diagnosis of dermatofibroma. Dermal papillae elongation may be associated with hyperpigmentation of the basal layer, mimicking seborrheic keratosis or rarely pseudocarcinomatous hyperplasia. The epidermis may be atrophic or appear ulcerated. In addition to epidermal alterations, basal hyperplasia, with histopathological aspects undistinguishable from basal cell carcinoma, and folliculo-sebaceous induction with follicular or sebaceous rudimentary structures are rarely observed.

The presence of lymphoid nodules is rarely detected, generally in the hypodermis or in the periphery of the lesion, sometimes with formation of germinal centers. Another unusual finding is the presence of abundant eosinophilic infiltrate in the FH stroma.

OBJECTIVES AND METHODS

A retrospective study of 95 skin biopsies of FH, relative to the period from 7/1/2005 to 12/31/2008, was conducted. Selection of the biopsies was performed through a research of the histopathological archive of the Dermatology Service of the University of Coimbra Hospitals.

The following histopathological parameters were evaluated: localization, demarcation, epidermal alterations, folliculo-sebaceous induction, cellularity, types of constituent cells, collagen patterns, sclerosis degree, vascularization, and hemorrhage/hemosiderin deposits. The researchers proceeded to identify other histopathological alterations such as atypia, mitotic activity, nuclear palisade, and focal necrosis.

RESULTS

A total of 82.1% of FH were localized in the dermis and 17.9% extended into the hypodermis, based on septal, radial, and seldom infiltrative patterns. In 54.7% of the cases tumors were poorly demarcated, with an inferior border generally clearer than lateral borders, and superior border separated from the epidermis by a Grenz zone. Clear demarcation of peripheral limits occurred in only 3.2% of the FH cases.

Epidermis hyperplasia was verified in 98.9% of the cases (Figure 1) with predominance of acanthosis (98.1%), followed by hyperpigmentation of the basal layer (80%), basaloïd hyperplasia (12.6%) and pseudocarcinomatous hyperplasia (1%) (Figure 2). In addition to epidermal alterations, folliculo-sebaceous induction was observed in 17.9% of the cases. Regarding the relation cells/collagen, fibrous tumors predominated over cellular tumors – the ratios 1/2 and 1/1 corresponded to 69.5% of the tumors. The presence of multinucleated giant cells was identified in 62.1% of the cases (Figure 3A), with abundant cytoplasm and multiple nuclei, with or without lipid material. Monstrous cells, with xanthomatous cytoplasm and vesicular nucleus were present in 3.1% of the cases (Figure 3B), and Touton giant cells, in 2.1% (Figure 3C). Foci of inflammato-
ry cells were found in 30.5% of the cases, with lymphocytes, plasmocytes, mast cells, and eosinophils in 26.3%, 5.3%, 2.1%, and 1%, respectively (Figure 4). Xanthomatous cells, slightly polygonal, with eccentric nucleus and pale, vacuolated, and lipid cytoplasm, were observed in 12.6% of the cases (Figure 5). Foci of nuclear palisade were identified in 52.6% of the cases of FH. Presence of mitosis was rare, observed in only 2.1% of the cases. The presence of lymphoid aggregates with initial formation of germinal center was detected in 1% of the cases, with deep perivascular localization (Figure 6). Focal necrosis, clear cells, granular cells, balloon cells, calcification or bone metaplasia were not found. Relative to collagen, an irregular storiform pattern was verified in 52.6% of the cases (Figure 7A), and in 3.1% a slightly radial disposition from a central point (cartwheel) was observed. Hyalinization in 76.8% of the cases and sclerosis in 30.5% were associated with cellularity reduction (Figure 7B). Intratumoral foci of increased vascularization, with numerous small blood vessels and vasodilation, were observed in 22.1% of the cases, and pseudovascular spaces filled with red globules, in 3.1%. Hemorrhage areas were present in 8.4% of the cases, with hemosiderin deposits in 16.8% of the biopsies, often adjacent to hemorrhage areas (Figure 8).

**DISCUSSION**

In general, the results obtained in this work were in agreement with data from the literature. Classical aspects of FH were confirmed. Corroborating other studies, most FH were located exclusively in the dermis, with rare extension into the hypodermis. They corresponded to round lesions, non-encapsulated and often poorly demarcated. Epidermal alterations, referred as one of the most frequent histopathological characteristics of FH, were also identified. Acanthosis predominated, followed by hyperpigmentation of the basal layer and basaloid hyperplasia. Folliculo-sebaceous induction, represented by rudimentary folliculo-sebaceous structures, was observed less frequently. Fibrous lesions...
predominated compared to cellular lesions, in accordance with the literature. \textsuperscript{1,2,4-6} Presence of increased cellularity associated with peripheral infiltration of fat lobules may suggest the diagnosis of DFSP. However, epidermal hyperplasia, cellular polymorphism, xanthomization, collagen encapsulation in the periphery of the lesion, and absence of atypia and/or ulceration, observed in all cases of FH with lobular adipose infiltration in our sample, distinguish them from DFSP. Variations of FH in relation to the types of constituent cells, vascularization, sclerosis degree, and inflammatory infiltrate were identified. In the fusocellular population, multinucleated giant cells and xanthomatous cells - occasionally of Touton and monstrous types - were observed in variable proportions, in agreement with other studies. \textsuperscript{1,2,4-7} If xanthomatous cells without hemosiderin deposits and significant fibroblastic proliferation predominate, the aspect may be undistinguishable from tuberous xanthoma with prominent fibrosis. \textsuperscript{1} In all the cases evaluated in the present work, the number of cells with xanthomization was low and coexisted with apparent fibroblastic population. Copper thread or keloid-like collagen disposition, typical of lipidized FH (“ankle type”), was not observed in this study. \textsuperscript{11} Observations of monstrous cells corresponded to relatively small and circumscribed lesions without atypical mitotic activity or necrotic cells, easily distinguishable from malignant FH. \textsuperscript{10} Intralesional foci of increased vascularization were identified in a few cases, a well-known fact. \textsuperscript{1,2,4-7} In a minority of FH, pseudovascular spaces filled with red globules were detected. FH with pseudovascular spaces are distinguished from neoplasias of vascular origin, particularly Kaposi’s sarcoma, in which fusocellular proliferation is atypically eosinophilic and CD34 positive. The proliferation is accompanied by clefts not covered by endothelial cells that dissect collagen. \textsuperscript{1,2,4-7} These aspects were not observed in the FH with pseudovascular spaces in our sample. Predominance of a storiform pattern and hyalinization/sclerosis was detected in the less cellular FH. In contrast, a fascicular arrangement was seen in more cellular FH, which is in agreement with the literature. \textsuperscript{1,2,4-6} Occasionally, a central palisade disposition was identified, as in the palisade variant of FH. \textsuperscript{11}

Evidence of pseudocarcinomatous hyperpla-

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\includegraphics[width=\textwidth]{figure4.png}
\caption{Plasmocytes; mast cells; neutrophils}
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\includegraphics[width=\textwidth]{figure5.png}
\caption{Xanthomatous cells}
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\begin{figure}
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\includegraphics[width=\textwidth]{figure6.png}
\caption{Lymphoid aggregates with deep localization}
\end{figure}
The existence of lymphoadenoid aggregates was confirmed in identical proportion, and this has not been referred to in the literature. These aspects are often interpreted as evidence of altered immune reaction of the host. Likewise, infiltration of the lesion by plasmocytes, mast cells, and eosinophils was also observed in our sample, but this is a rare occurrence in FH cases.

REFERENCES

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