Atypical fibroxanthoma diagnosed as malignant melanoma

M. Melato, C. Rizzardi, R. Calacione and G. Trevisan

SUMMARY

An atypical fibroxanthoma characterized by aneuploidy and local aggressive behavior was misdiagnosed as malignant melanoma. The reported case contributes to a better understanding of malignant fibro-histiocytic proliferations. A considered evaluation including immunohistochemistry is needed in diagnosing malignant melanoma.

KEY WORDS

fibroxanthoma, atypical, differential diagnosis, immunohistochemistry, prognosis

Introduction

Poorly differentiated large cell malignancies of the skin frequently pose a diagnostic challenge for pathologists and ultimately many of them are diagnosed as amelanotic malignant melanoma, atypical fibroxanthoma, pseudosarcomatous squamous cell carcinoma, or undifferentiated leiomyosarcoma and angiosarcoma. A precise diagnosis based on morphological features alone is often impossible, and immunohistochemistry is therefore mandatory (1).

An atypical fibroxanthoma, misdiagnosed as malignant melanoma by an experienced pathologist, testifies to the difficulties that may be encountered in differentiating melanoma from the confusing family of fibrohistiocytic tumors. The present case, characterized by an unusually aggressive behavior, contributes to a wider discussion on these tumors.

Case report

In September 2000, a 66-year-old male presented with a mass in the right subclavicular region interpreted as the local recurrence of a malignant melanoma (pT4, sentinel lymph node negative), excised four months earlier. Brain CT, chest X-ray, and abdominal ultrasound scan were negative.

Histological examination showed a dermal infiltration by a densely cellular population of epithelioid and spindle cells with abundant eosinophilic cytoplasm arranged in a diffuse and fascicular pattern (Fig. 1). The cells were amelanotic and exhibited pleomorphism, multinucleation and numerous typical and atypical mitotic figures; a few multinucleated giant cells with irregularly distributed overlapping atypical nuclei were also present (Fig. 2).

By immunohistochemistry, the tumor stained nega-

tive for S-100 and HMB-45. It was therefore tested for cytokeratin and vimentin, resulting negative for the former and strongly positive for the latter. A further panel of antibodies demonstrated in neoplastic cells the expression of CD68, lysozyme, alpha1-antichymotrypsin and, focally, of muscle-specific actin (HHF-35), as well as the lack of desmin, CD34 and factor VIII. The immunophenotypic profile justified the diagnosis of malignant fibrohistiocytic proliferation.

The first excised material was obtained from a department where it had been described as "Epithelioid and spindle cell nodular melanoma (6.5 mm in depth; 5 mitoses x mm^2)", without performing immunohistochemistry. The histologic features of the lesion - a prominent, ulcerated expansive nodule involving papillary and reticular dermis, containing elastotic material, and showing an epidermal collarette (Fig. 3)- were consistent with those previously reported. The staining patterns of the two lesions were identical. DNA ploidy analysis by flow cytometry demonstrated aneuploid distribution of nuclear DNA.

In conclusion, the original diagnosis was revised and both the first excised material and its recurrence were diagnosed as atypical fibroxanthoma.

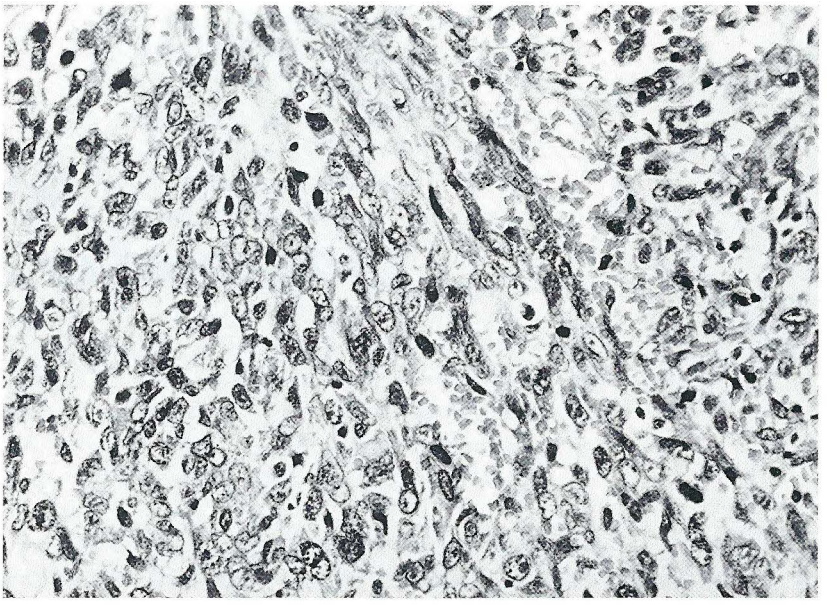


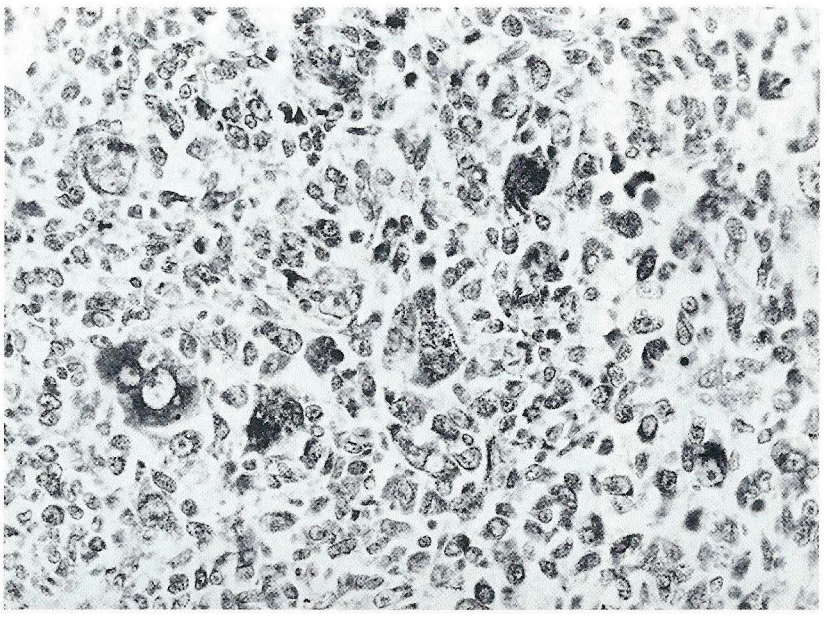
Figure 1. A fascicular pattern was focally evident both in the primary tumor and in the recurrence.

Discussion

Atypical fibroxanthoma is a pleomorphic tumor that usually occurs on the sun-damaged skin of the elderly. It is histologically indistinguishable from the pleomorphic forms of malignant fibrous histiocytoma. However, from a conceptual point of view, it is classically considered as a superficial form of malignant fibrous histiocytoma, which, by virtue of its superficial location, almost invariably pursues a benign course, being merely characterized by a local aggressive behavior. This justifies its accurate recognition and differentiation, especially from malignant melanoma, undifferentiated squamous cell carcinoma, leiomyosarcoma, and angiosarcoma, in which immunohistochemistry plays a key role.

The most common differential diagnosis concerns melanoma, a malignant tumor with a varied histologic appearance, and it can be particularly difficult to differentiate atypical fibroxanthoma from balloon cell melanoma (2) and spindle cell melanoma, including desmoplastic and neurotropic types (3-4). Furthermore, although S100 protein stains a majority of these melanomas, the staining may be weak or focal, and HMB-45, a more specific marker of melanoma, is frequently negative in desmoplastic and neurotropic melanoma. Other histiocytic proliferations than atypical fibroxanthoma may mimic melanocytic tumors: epithelioid histiocytoma, juvenile xanthogranuloma, the adult form

Figure 2. Most neoplastic cells are pleomorphic and very atypical.



of the latter and reticulohistiocytoma. Particularly, Busam et al. have recently dealt with this problem, describing three cases of xanthogranulomas with incospicuous foam cells and giant cells that were misdiagnosed as malignant melanoma (5).

Atypical fibroxanthoma can be misdiagnosed also as a poorly differentiated squamous cell carcinoma but in that case immunohistochemistry (search for cytocheratins) easily resolves the problem. Similarly, atypical fibroxanthoma can be differentiated from leiomyosarcoma, using HHF-35 and desmin, and from angiosarcoma using CD34 and factor VIII, although cutaneous mesenchymal tumors could show some degree of expression of CD34 and factor VIII (6). The immunoreactivity pattern of tumor cells positive for vimentin, lysozyme, alpha1-antichymotrypsin and CD 68 will finally justify the diagnosis of fibrohistiocytic proliferation.

Assigning our lesion into the family of fibrohistiocytic tumors is a further challenge. In fact, the nosology of these neoplasms has been long debated and particularly the categories "fibroxanthomas" and "xanthogranulomas" have a long history of confusion surrounding them, which has been the source of continued controversy. What is truly needed is an easily understood classification scheme that allows for precise diagnoses to be rendered on sections stained by hematoxylin and eosin; until that is devised, controversy is likely to continue (7).

Some authors even question the very existence of this entity, considering atypical fibroxanthoma as a diagnosis of exclusion after ruling out other neoplasms (8). They believe that atypical fibroxanthoma (similarly to its deeply located counterpart, malignant fibrous histiocytoma) represents a potpourri of histogenetically different, dedifferentiated tumors including sarcomas, carcinomas, melanomas, and lymphomas (9), supposing that one-day this enigmatic entity will disappear from the textbooks because of a more sophisticated and considerate approach to this lesion (8). Many investigators have proposed that atypical fibroxanthoma may represent a reactive process, while others contend that it is a true fibrohistiocytic neoplasm, closely related to malignant fibrous histiocytoma (10).

A review of the literature suggests that atypical fibroxanthoma can be differentiated from malignant fibrous histiocytoma not only because of its superficial location (dermal), absence of necrosis, vascular invasion, involvement of hypoderm, fascia and muscle, and no distant metastasis, but also for an absent or just slight expression of LN2 (CD74) (11), and the diploid distribution of nuclear DNA, is considered by some authors as significant in understanding the biological behavior of the neoplasm (10).

In the reported case, all histological and clinical features supported the diagnosis of atypical fibroxanthoma, except the DNA content. Indeed, aneuploid distribution of DNA demonstrated by flow cytometry could be considered as indicative of a more aggressive behavior of the tumor that, in fact, recurred locally after surgical excision.

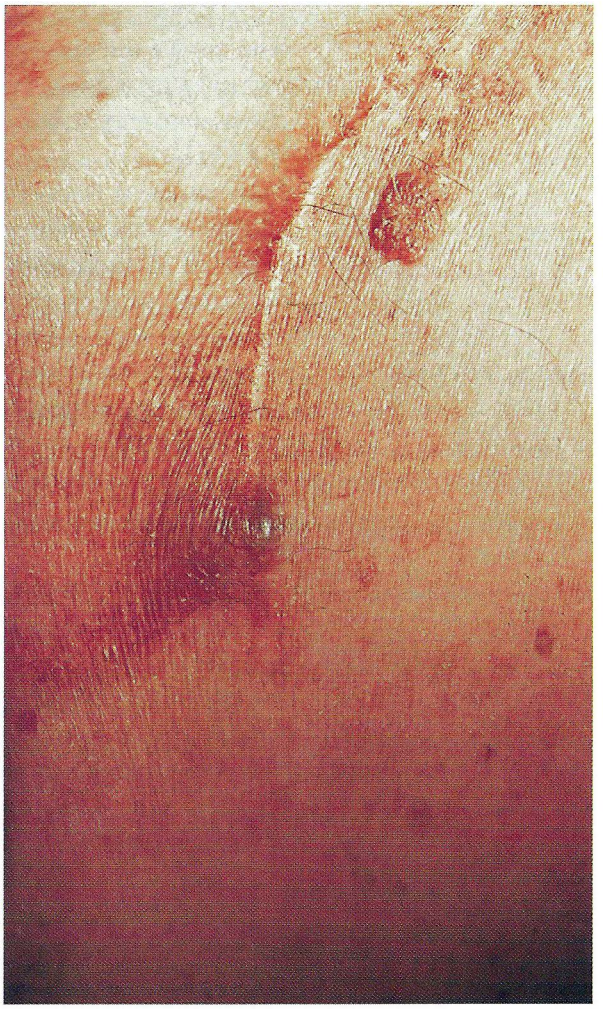


Figure 3. Primary tumor misdiagnosed as malignant melanoma.

In conclusion, we can confirm that fibrohistiocytic tumors of the skin must occasionally be evaluated and treated by a dermatologist and pathologist considering three categories of problems: (I) to distinguish them from other neoplastic processes, particularly from malignant melanoma; (II) to order them correctly according to nosology, and (III) to evaluate appropriately their biologic behavior. We hope that the reported case will contribute to a better recognition of fibrohistiocytic neoplasms and to differentiation from malignant melanoma.

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