Atypical fibroxanthoma
diagnosed as malignant melanoma

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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.

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 ex-
pression of CD68, lysozyme, alpha-1-antichymotrypsin
and, focally, of muscle-specific actin (HHF-35), as well
as the lack of desmin, CD34 and factor VIII. The immu-
nohistochemical profile justified the diagnosis of mali-
nant fibrohistiocytic proliferation.

The first excised material was obtained from a de-
partment where it had been described as “Epithelioid
and spindle cell nodular melanoma (6.5 mm in depth;
5 mitoses x mm²)”, without performing immunohisto-
chemistry. The histologic features of the lesion - a promi-
nent, ulcerated expansive nodule involving papillary
and reticular dermis, containing elastotic material, and
showing an epidermal collarette (Fig. 3) - were consis-
tent with those previously reported. The staining pat-
terns 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.

Discussion

Atypical fibroxanthoma is a pleomorphic tumor that
usually occurs on the sun-damaged skin of the elderly.
It is histologically indistinguishable from the pleomor-
phic forms of malignant fibrous histiocytoma. However,
from a conceptual point of view, it is classically consid-
ered as a superficial form of malignant fibrous histiocy-
toma, which, by virtue of its superficial location, almost
invariably pursues a benign course, being merely char-
acterized 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 differ-
entiate atypical fibroxanthoma from balloon cell mel-
ana (2) and spindle cell melanoma, including des-
moplastic and neurotropic types (3-4). Furthermore,
although S100 protein stains a majority of these mela-
nomas, 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 fibro-
Xanthoma may mimic melanocytic tumors: epithelioid
histiocytoma, juvenile xanthogranuloma, the adult form

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

Figure 2. Most neoplastic cells are pleomorphic
and very atypical.
of the latter and reticulohistiocytoma. Particularly, Busa-
ni et al. have recently dealt with this problem, describ-
ing three cases of xanthogranulomas with inconspicuous
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 cytoker-
tin) easily resolves the problem. Similarly, atypical
fibroxanthoma can be differentiated from leiomyosar-
coma, using HHF-35 and desmin, and from angiosar-
coma using CD34 and factor VIII, although cutaneous
mesenchymal tumors could show some degree of ex-
pression of CD34 and factor VIII (6). The immunoreac-
tivity pattern of tumor cells positive for vimentin,
lysozyme, alpha1-antichymotrypsin and CD 68 will fi-
nally justify the diagnosis of fibrohistiocytic prolifica-
tion.

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 particu-
larly the categories “fibroxanthomas” and “xanthogranu-
lomas” have a long history of confusion surrounding
them, which has been the source of continued contro-
versy. What is truly needed is an easily understood clas-
sification scheme that allows for precise diagnoses to
be rendered on sections stained by hematoxylin and
eosin; until that is devised, controversy is likely to con-
tinue (7).

Some authors even question the very existence of
this entity, considering atypical fibroxanthoma as a di-
agnosis 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), suppos-
ing 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 repre-
sent a reactive process, while others contend that it is a
true fibrohistiocytic neoplasm, closely related to mal-
gnant fibrous histiocytoma (10).

A review of the literature suggests that atypical
fibroxanthoma can be differentiated from malignant fi-
brous histiocytoma not only because of its superficial
location (dermal), absence of necrosis, vascular inva-
sion, 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 distri-
bution 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 fea-
tures supported the diagnosis of atypical fibroxanthoma,
except the DNA content. Indeed, aneuploid distribu-
tion 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.

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 ma-
lignant melanoma; (II) to order them correctly accord-
ing 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 mel-
noma.
REFERENCES


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