Atypical fibroxanthoma-like amelanotic malignant melanoma: A case report and literature review

Chao-Kai Hsu1,2, Sheau-Chiou Chao1, Shyh-Jou Shieh3, Julia Yu-Yun Lee1,*

1 Department of Dermatology, National Cheng Kung University, College of Medicine and Hospital, Tainan, Taiwan
2 Institute of Clinical Medicine, National Cheng Kung University, College of Medicine and Hospital, Tainan, Taiwan
3 Department of Surgery, National Cheng Kung University, College of Medicine and Hospital, Tainan, Taiwan

Abstract

Atypical fibroxanthoma (AFX)-like malignant melanoma is very rare. Here, we report a case of amelanotic AFX-like melanoma in a 72-year-old Taiwanese woman presenting with two separate, asymptomatic, enlarging erythematous nodules within a large hypopigmented patch on her left cheek. Histologically, both lesions showed cellular nodules in the reticular dermis separated from the overlying flattened epidermis by a zone of solar elastosis or fibrosis. The tumor consisted of sheets of atypical epithelioid cells arranged in a vague nesting pattern, as well as many atypical large or gigantic cells with one or more, large hyperchromatic, vesicular, or pleomorphic nuclei with prominent nucleoli, and moderate-to-abundant eosinophilic or foamy cytoplasm. Focal intraepidermal proliferation of atypical melanocytes with a pagetoid pattern was found only in the periphery of the main tumor. The tumor cells were moderately to strongly positive for S-100, Melan-A, and HMB-45. The pleomorphic giant cells were focally CD68-positive but CD163-negative. The patient underwent tumor excision followed by radiotherapy due to the narrow surgical margins. A sentinel lymph node biopsy revealed no metastasis of the melanoma. This case illustrates the importance of scrutinizing any subtle proliferation of atypical melanocytes in the epidermis in an AFX-like tumor in order to avoid misdiagnosis.

Case report

A 72-year-old Taiwanese woman presented with a 2-year history of two asymptomatic, enlarging nodules on her left cheek. Examination revealed two erythematous, dome-shaped nodules measuring 0.9 × 0.6 cm and 0.6 × 0.5 cm, respectively, within a large hypopigmented patch (Figure 1). Biopsy specimens of both lesions showed well-circumscribed cellular nodules in the reticular dermis separated from the overlying flattened epidermis by a zone of solar elastotic or fibrotic upper dermis (Figure 2A).

The nodules consisted primarily of sheets of atypical epithelioid cells arranged in vague nesting pattern (Figure 2B), as well as giant or gigantic cells with two or more large pleomorphic nuclei (Figure 2C). Both types of atypical cell had large hyperchromatic, and one or more vesicular, nuclei, mostly with a prominent nucleolus, and moderate-to-abundant eosinophilic cytoplasm. Some giant cells also had foamy cytoplasm in places (Figure 2C).

In addition to these two major types of cell, there were also atypical, oval or spindled cells in some foci. Increased mitotic rates...
with atypical mitotic features were present. A patchy dense inflammatory infiltrate, mostly of small lymphocytes, was found at the periphery of the tumors. One of the tumors also showed lymphoid follicles. There was no vascular or perineural invasion, or obvious infiltration of melanophages. The morphology of the dermal tumors resembled AFX.

However, close inspection revealed some atypical melanocytes in the epidermis with pagetoid spread in one small focus away from the dermal nodules (Figure 3). Fontana-Masson staining revealed an absence of melanin in the tumor nodules and reduced pigmentation in the overlying epidermis. The tumor cells showed a moderate-to-strong expression of S-100, Melan-A, and HMB-45 (Figure 4). The pleomorphic giant cells were focally CD68-positive but CD163-negative (not shown). Based on the pathological findings, AFX-like amelanotic malignant melanoma, with a Breslow thickness of 3.4 mm and a Clark level of IV, was diagnosed.

Positron emission tomography revealed hypermetabolic changes in the tumors on the cheek without evidence of distant metastasis. The tumor was excised with a sentinel lymph node biopsy, the latter being negative for metastasis. Because of the narrow surgical margin (less than 1 mm), the patient underwent postoperative radiotherapy. During a 16-month follow-up, there was no evidence of recurrence either clinically on or imaging study.

Discussion

We have described here a rare case of AFX-like malignant melanoma manifesting as two amelanotic nodules on the cheek of an elderly Taiwanese woman. Interestingly, both nodules were located within a large hypopigmented patch, a finding suggestive of the halo phenomenon. Malignant melanoma may have a wide variety of clinicopathological presentations, but the AFX-like variant is very rare. Four cases of this variant have been reported, and their findings are summarized in Table 1.
AFX is a tumor that was first described by Helwig in the 1960s and is believed to be of fibrohistiocytic origin. Most AFX tumors display a rapidly growing, ulcerated or bleeding nodule on the sun-damaged skin of an elderly person. Although AFX has the capacity for local recurrence or even metastasis, it is usually cured by complete excision. AFX-like melanoma, however, has a much worse prognosis. In the three cases of AFX-like melanoma described by Sangueza and Zelger (Table 1), all the lesions were found on the faces of elderly patients, and the diagnosis was delayed due to the unusual clinicopathological presentations. Two of three patients died due to rapid recurrence or metastasis.

Previous reports have highlighted the difficulties in distinguishing malignant melanoma from AFX, and the use of immunohistochemistry is often necessary. Characteristic markers of melanomas such as S-100 protein, Melan-A/MART1, and HMB45 are not expressed in classic AFX. However, melanomas may rarely be S100-protein negative, and not uncommonly Melan-A/MART1-, HMB45-, and/or NKIC3-negative. In one AFX-like melanoma reported by Sangueza and Zelger, the diagnosis was delayed due to the negative results for S-100, Melan-A, and HMB45 in the first excisional specimen.

CD68 expression is variable in AFX and MFH, so is not very useful for distinguishing these tumors from spindle cell

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**Figure 3** Focal proliferation of atypical melanocytes, mostly as solitary units, in the lower epidermis, can be found only in small foci in the epidermis away from the dermal nodule (H&E stain, 20×). Some atypical melanocytes have multiple nuclei and abundant, eosinophilic or pale cytoplasm (inset; H&E stain, 200×).  

**Figure 4** (A, B) Immunohistochemical staining reveals that atypical epithelioid cells and giant cells are moderately to strongly positive for Melan-A and HMB-45. (C) The epithelioid cells are strongly S-100 protein-positive, but the giant cells are mostly S-100 protein-negative. (D) A few pleomorphic giant cells are focally CD68-positive (200×).
melanomas. Smith-Zagone et al showed that the tumor cells of AFX were diffusely CD68-positive, and HMB-45 and Melan-A/MART1 expression was only limited to the large, multinucleated cells with vacuolated cytoplasm.\(^6\)

In our case, the epithelioid tumor cells showed moderate-to-strong positivity for S-100, Melan-A, and HMB-45, while the giant or gigantic cells were mostly S-100-negative but Melan-A- and HMB-45-positive. Although some gigantic cells were CD68-positive, they were negative for CD163, a more specific marker for histiocytes.\(^12\)

Other differential diagnoses of AFX-like melanoma include MFH and a rare example of Merkel cell carcinoma with AFX-like features.\(^13,14\) The tumor cells in MFH were mostly S-100- and HMB-45-negative, although two cases of S-100-positive MFH have been reported.\(^15\) Merkel cell carcinoma, recently found to be associated with clonal integration of the Merkel cell polyomavirus, is usually neuron-specific enolase-positive and shows characteristic paranuclear dot-like positivity for monokeratin.\(^14,16\)

It may be difficult to differentiate epidermotropic metastatic melanoma from primary melanoma, and the importance of distinguishing a local persistence of primary lesions from metastatic lesions has been re-emphasized.\(^17\) With our patient, although the possibility of a metastatic melanoma could not be completely excluded histologically, the finding of an intraepidermal proliferation of atypical melanocytes off to one side of the dermal tumor in conjunction with an absence of dermal scarring favored the diagnosis of primary melanoma. This was further supported by negative findings from the positron emission tomography examination and sentinel lymph node biopsy. The two lesions may represent a primary amelanotic melanoma and a satellite metastasis. The tumor was N2c according to the staging system of the American Joint Committee on Cancer, and should be treated as having nodal metastases.\(^18,19\)

In addition to AFX-like malignant melanoma, collision tumors of AFX and invasive melanoma have also been reported.\(^20,21\) Wilsher reported a 76-year-old male who presented with a 17 mm ulcerated nodule on his scalp.\(^22\) Similarly, McGregor et al reported a 71-year-old male with a 0.6 cm pearly papule on his back.\(^21\) With immunohistochemical staining, both cases were confirmed to contain two distinct but contiguous neoplastic components of AFX and melanoma.

In sum, we have described here a rare case of AFX-like amelanotic melanoma, which may be the fifth such case reported. This melanoma appeared to be a primary one and manifested as two discrete amelanotic nodules in association with a halo-like phenomenon. Our case illustrates the importance of scrutinizing any subtle proliferation of atypical melanocytes in the epidermis in an AFX-like tumor in order to avoid misdiagnosis.

References


