Atypical fibroxanthoma of the scalp with recurrent and multiple regional cutaneous metastases

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INTRODUCTION
Atypical fibroxanthoma (AFX) is a neoplastic skin disease that arises from myofibroblasts and most commonly occurs in elderly patients on sun-exposed skin.\(^1\) Immunohistochemistry is commonly used to make the diagnosis of AFX. Findings are positive for vimentin, CD10, CD68, and actin and negative for CAM5.2, CD34, melan-A, S100 protein, HMB45, and cytokeratin A1/A3.\(^2\) AFX is a low-grade malignancy with rare metastases (1% of cases) that usually occur within a short period.\(^3,4\) The risk of metastasis is increased by tumor depth, vascular invasion, and cutaneous tumor recurrence.\(^5\)

In the World Health Organization revised classification of soft tissue tumors in 2013, pleomorphic dermal sarcoma (PDS) was recognized as a distinct diagnostic entity.\(^6\) Previously, PDS was placed in the category of malignant fibrous histiocytoma, a term that has been deleted and replaced by undifferentiated sarcoma. Histologically, AFX cannot be distinguished from a pleomorphic superficial form of PDS.\(^4\) Often the clinical course and involvement of tumor invasion of subcutaneous tissue guides the diagnosis.

This report will (1) show an approach to diagnosing AFX, (2) report a case of AFX with multiple in-transit metastases over a 20-month period, and (3) highlight the updated terminology for fibrohistiocytic tumors of undetermined lineage.

CASE REPORT
In August 2013, an 82-year-old man with a history of chronic lymphocytic leukemia and excisions of multiple squamous cell carcinomas (SCCs) and basal cell carcinomas (BCCs) of the face, scalp, and sun-exposed areas of the arms and hand, presented with recent growth of an erythematous, tender, and hyperkeratotic nodule on the left central frontal scalp measuring 1.7 cm in diameter. Shave biopsy found a dermis-based proliferation of spindle and epithelioid cells arranged in sheets and fascicles. Multinucleated giant cells were scattered throughout the lesion. The entire cellular population showed varying degrees of cytoplasmic vacuolization representing lipidization. Few lymphocytes and mast cells were also present, mostly in the periphery. Marked nuclear pleomorphism and prominent nucleoli were observed. Scattered mitoses were also noted. Focal necrosis and lymphovascular and perineural invasion were not identified (Fig 1).

Immunohistochemistry of the neoplastic cells found absence of staining for keratin, S100, Melan-A, and desmin. Prominent CD68 positivity in all 3 cell types was observed. Based on the immunohistochemical profile, the neoplasm was diagnosed as AFX extending to the deep margin of the shave biopsy specimen. The patient underwent Mohs micrographic surgery, and clear margins were achieved after 2 stages, with no subcutaneous involvement of tumor on either stage. In April 2014, approximately 8 months after the Mohs excision, a 1.1-cm nodule recurred at the center of the previous Mohs excision site. The lesion was excised with single-stage Mohs micrographic surgery.

Abbreviations used:
AFX: atypical fibroxanthoma
BCC: basal cell carcinoma
PDS: pleomorphic dermal sarcoma
SCC: squamous cell carcinoma
A rapidly developing subcutaneous nodular mass, located in the left supra-auricular region 3.0 cm from the previous surgery site, was then observed approximately 6 months after the second Mohs excision at the primary site. The patient underwent wide local excision of the dermal/subcutaneous mass with split-thickness skin graft reconstruction. All margins were clear; however, the tumor was within 0.5 mm of the deep central line of the resection. Final pathology findings showed a dermal tumor extending into the subcutis with epithelioid and pleomorphic cell morphology and no evidence of necrosis or lymphovascular or perineural invasion (Fig 2). Final diagnosis was PDS. Postoperative adjuvant radiation therapy to all intervening areas of the scalp was recommended because of the aggressive nature of this disease. Before beginning radiation, the patient presented with a new nodule on the left vertex scalp. Pathology findings showed a dermal neoplasm composed of atypical spindled and epithelioid cells with highly pleomorphic nuclei, hyperchromatic chromatin, and abundant mitoses, which was consistent with the previously identified lesions, indicating a metastatic AFX. Radiation treatment was then extended to this area. The patient’s postradiation course was remarkable for 2 new regional AFX tumors that were later excised. A subsequent positron emission tomography scan of the brain/skull was performed and results were normal. Microscopic evaluation of the following lesions found morphology similar to that of the initial shave biopsy, and repeat immunostains also showed similar findings indicative of metastatic AFX.

**DISCUSSION**

This clinical presentation of a rapidly growing skin-based nodule in an elderly immunosuppressed patient with a history of multiple prior excisions of SCCs and BCCs leads to a differential diagnosis of SCC, BCC, malignant melanoma, AFX, and PDS.

In considering the differential diagnosis, BCC was excluded because of the absence of typical histologic features. The morphologic features of spindle and epithelioid cells with prominent nuclear atypia suggest the diagnosis of SCC or malignant melanoma; however, immunohistochemical studies were helpful in excluding these diagnoses, as Melan-A and cytokeratin were not found in either initial biopsy. The biopsies were positive for CD68, indicating a histiocytic origin; however, this immunostain is nonspecific for the diagnosis of AFX.

AFX is generally regarded as a low-grade malignancy with a low rate of recurrence after Mohs micrographic surgery, and there have only been rare reports of metastases to regional lymph nodes or other body sites. The previous cases were reported before the distinction of AFX from PDS. PDS recurs frequently and has a significant metastatic potential.

The original excisional lesion was deep seated within the dermis with no subcutaneous involvement or evidence of vascular invasion or necrosis, therefore resulting in a diagnosis of AFX.9 The patient presented with additional diagnoses of AFX after the diagnosis of PDS. Because of the short latency period between the lesions, the 3-cm difference in location, and the deep-seated nature of the initial metastatic lesion, it is highly likely that these subsequent tumors represent in-transit metastatic AFX lesions. Additionally, the relatively short timeframe and varying depth of lesions make...
the possibility of multiple primary lesions highly unlikely, although it cannot be excluded. We report a case of AFX in an actinically damaged, immunosuppressed elderly man, who had multiple nodules likely to represent in-transit metastases. This case highlights that the metastatic potential of AFX may be underestimated and, therefore, requires more aggressive treatment options than originally thought. The case is also especially provocative because having AFX and PDS pathologic findings in the same patient strongly suggests a biologic continuum between AFX and PDS.

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