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Aneurysmal Atypical Fibroxanthoma. A Clinical Mimicker of Nodular Malignant Melanoma: Report of Two Cases and Review of the Literature

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Abstract

Background: Atypical Fibroxanthoma (AFX) is a dermal tumor of uncertain histogenesis and presents as irregularly pigmented, dome-shaped nodules or plaques on sun-exposed skin of elderly patients. Several histological variants of AFX have been described. The hemosiderotic and aneurysmal variants are not clearly defined in the literature.

Objectives: Two cases of an uncommon histopathological variant of Atypical Fibroxanthoma (AFX) are described. Were view the literature and the histopathological features and differential diagnosis are discussed.

Material and Methods: Histological features analyzed in both cases were: Cytology, ulceration, size, and growth pattern, depth of invasion and tumor borders, mitotic activity, necrosis, and vascular/Perineural invasion. The antibodies used were CD68, CD10, p63, p40, S100, CD31, CD34, ERG, D2-40, Fli-1, desmin, SMA, CK-AE1/AE3 and HMB45. Clinical features were reviewed for metastases, disease status, treatment, and any other pre-existing conditions.

Results: We present two cases of FXA melanoma diagnosed, with 65 and 94 years old, respectively. Both developed on sun damaged skin. Ulceration was present in one case. Morphological patterns were spindle cells arranged around multiple aneurysmal pseudo cystic spaces with no endothelial lining. Hemosiderin deposits were observed in the cytoplasm of variable numbers of neoplastic cells. An expansile rather than infiltrative growth into superficial subcutis was also noted. No vascular/Perineural invasion was seen. Both cases were consistently negative for S100, CK-AE1/AE3 and desmin. Focal positivity for CD68 and CD10 was seen.

Conclusion: We report here on two cases of an uncommon histological subtype of AFX, for which we advocate use of the term "aneurysmal". Correct identification of this uncommon AFX variant is essential in order to avoid its misdiagnosis as an aggressive neoplasm such as melanoma.

Keywords: Atypical Fibroxanthoma; Immunohistochemistry; Pathology; Tumor; Sarcoma

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Introduction

Many cutaneous tumors of the head and neck area are related to chronic actinic damage; by far the most common are squamous and basal cell carcinomas [1]. Atypical Fibroxanthoma (AFX) is a dermal tumor of uncertain histogenesis most often arising on the sun-exposed skin of elderly patients. The classical histological appearance of AFX is that of a pleomorphic spindle cell and giant cell neoplasm often displaying marked atypia and numerous, sometimes atypical, mitoses [2]. Several histological variants of AFX have been described, differing from each other in terms of the dominant histological component [1,3,4]. Aneurysmal, pseudoangiomatoid or angiomatoid AFX is characterized by the formation of blood-filled pseudo cystic spaces with no endothelial lining, hemorrhagic areas and hemosiderin deposition in the cytoplasm of neoplastic cells [1]. We report on two cases of aneurysmal AFX clinically mimicking nodular melanoma, offering a review of the literature and focusing on several clinical and pathological aspects of this neoplasm.

Material and Methods

Case 1

A 65-year-old Caucasian man with no relevant medical history was seen for a nodular cutaneous tumor mass located in the left temporal region, consisting in a keratotic plaque of maximum diameter 2.8 cm, clinically suggestive of nodular melanoma *vs.* squamous-cell carcinoma (Figure 1A). There was no history of skin lesion or previous damage in this area; nor was there any evidence of systemic disease or previous neoplasms. The tumor was excised with wide surgical margins.

Case 2

A 94-year-old Caucasian woman with a history of atrial fibrillation, dyslipidemia and arterial hypertension consulted with an asymptomatic nodular skin lesion of maximum diameter 0.5 cm. in the left frontal region, which had started to develop 6 to 8 months prior to consultation. Dermoscopy revealed a lacunar pattern, and the clinical diagnosis was nodular melanoma vs. vascular lesion (Figure 1B, 1C). The mass was excised with wide surgical margins.

Results

Histological examination revealed, in both cases, well-circumscribed dermo-hypodermal neoplasms displaying multiple cysts with hemorrhagic content.

Microscopy in Case 1 revealed surface ulceration and an overlying epidermal collarette (Figure 1D, 1E). In both tumors, heterogeneous cell proliferation was observed; tumor cells were arranged in a whorled pattern and in solid nests, extending into the subcutaneous tissues but with no apparent involvement of muscle fascia. The tumors were composed of spindle cells and histiocytic epithelioid cells, numerous osteoclast-like multinucleated giant cells and fibroblasts. Tumor cells tended to be arranged around multiple aneurysmal pseudocystic spaces with no endothelial lining, mimicking those described in aneurysmal fibrous histiocytoma (Figures 2A and 3A, 3B). Close to these pseudocystic spaces, erythrocytes and/or hemosiderin deposits suggestive of intratumoral hemorrhage were observed in the cytoplasm of variable numbers of neoplastic cells (Figure 2A, 3B). Tumor cells were highly pleomorphic, with frequent atypical mitotic figures. There was no evidence of necrosis, vascular or perineural invasion. Solar elastosis was visible in the papillary dermis adjacent to the neoplasm.

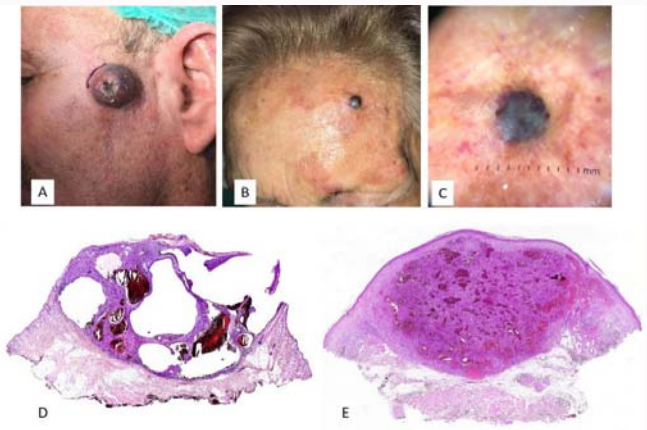

Figure 1: A well-circumscribed dome-shaped nodule with ulceration in the left preauricular area of a 65-year-old-man A). AFX on the forehead of a 94-year-old woman (B), whose dermoscopic features revealed a lacunar pattern C). This low-power photomicrograph shows a nodule mostly confined to the dermis with focal involvement of the subcut is (HE, 10x), case 1 D) and 2 E). The overlying epitheliumisul cerated D).

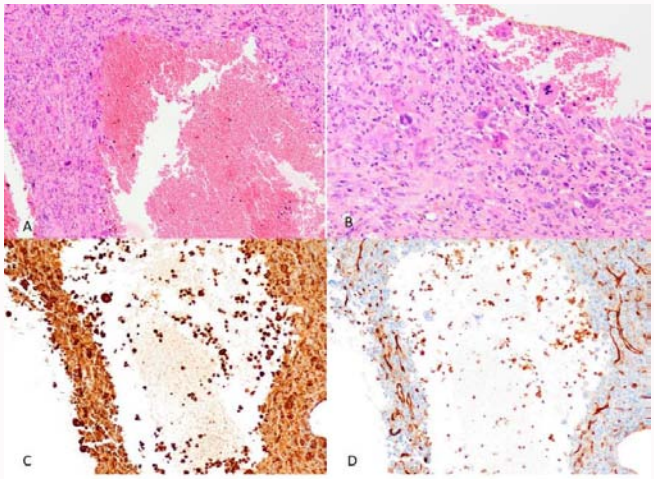

Figure 2: Case 1. (A-B) Aneurismatic spaces devoid of endothelial cells and atypical tumor cells with frequent mitotic activity (HE, x100, HE, 200x). CD68 (C) stain strongly the cytoplasm. Occasional granular cytoplasmic staining for CD31(D) (PAP, 200x).

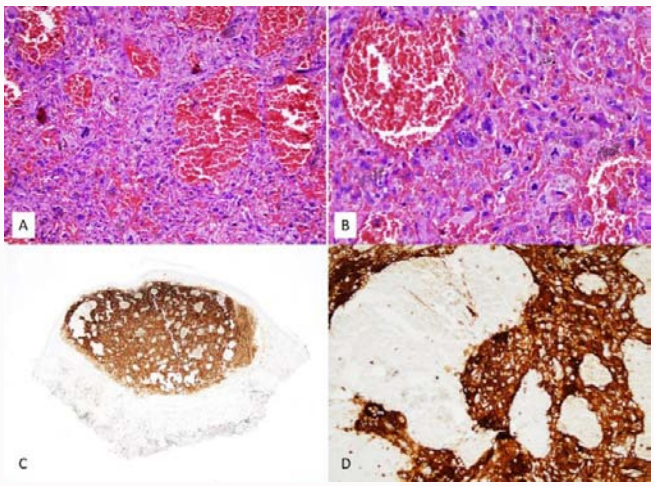

Figure 3: Case 2. (A-B) Dilated blood-filled spaces are prominent, with in tratumoral hemorrhage and hemosiderin. Tumor is composed of pleomorphic epithelioid and spindle cells with admixed multinucleated tumor giant cells. (HE, x100, HE, 200x). (C-D) Diffuse and strong expression of CD10 (PAP, 10x, 200x).

Immunohistochemistry identified the presence of the marker CD68 (Figure 2C), confirming the histiocytic nature of mononucleated and multinucleated cells. A number of tumor cells were also CD31-positive (Figure 2D) and showed strong and diffuse staining for CD10 (Figure 3C, 3D). Staining for other antibodies (p63, p40, S100, CD34, ERG, D2-40, Fli-1, desmin, SMA, CK-AE1/AE3 and HMB45) was negative. Numerous S-100 positive dendritic cells were observed, sometimes forming clusters.

Morphological and histochemical findings pointed in both cases to a diagnosis of AFX. During follow-up, neither patient displayed local recurrence or metastases; both are alive and disease-free 24 and 18 months, respectively, after diagnosis.

Discussion

The term AFX was first coined by Helwig [5] in 1961, to describe a malignant spindle-cell neoplasm arising on the sun-damaged skin of elderly patients. The neoplasm was previously termed pseudosarcoma, paradoxical fibrosarcoma, pseudosarcomatous dermatofibrosarcoma and pseudosarcomatous reticulohistiocytoma [6]. Although AFX tends to pursue a benign clinical course, recurrence and metastasis have been reported [7,8]. Clinically, it is characterized by nodular or plaque-shaped lesions arising on skin with actinic damage in the head and neck area. According to the current World Health Organization (WHO) classification of tumors of soft tissue [9], AFX is limited to the dermis with no more than minimal extension into adjacent subcutaneous fat. The presence of significant subcutaneous infiltration as well as of coagulative necrosis and vascular invasion warrant the diagnosis of pleomorphic dermal sarcoma [10]. In the two cases presented here, and in several reported by Wang et al. [8], expansive/circumscribed growth of the tumor into the hypodermis prompted no modification of the diagnosis, in the complete absence of other histological findings indicative of malignancy.

For histological purposes, differential diagnosis of AFX includes other cutaneous spindle-cell malignancies, among them desmoplastic malignant melanoma, spindle-cell squamous carcinoma, dermatofibrosarcoma protuberans and leiomyosarcoma. Immunohistochemistry is an indispensable tool for differential diagnosis. Staining for Melan-A, HMB-45, cytokeratins, epithelial membrane antigen, desmin and S-100 protein is invariably negative. While tumor cells in AFX are always negative for S100, numerous S-100-positive Langerhans cells may be observed. In such cases, detection of CD1a antibody may aid identification [1,7,11]. Although CD31 expression has been reported in AFX, it tends to be focal and cytoplasmic, as opposed to the diffuse strong membrane staining found in angiosarcoma [12].

Several histological variants of AFX have been described: clear-cell, granular-cell, myxoid, keloidal, sclerosing, osteoclastic giant-cell and osteoid or chondroid. The hemosiderotic (pigmented) and aneurysmal (angiomatoid) variants are not clearly defined in the literature, and we believe that they lie on the same morphological spectrum, with hemosiderin deposition predominating in the former and blood-filled cystic spaces in the latter [1,3,4,13-17]. While the observation of hemorrhagic/angiomatous histological features is by no means uncommon in AFX, the predominance of pseudovascular spaces is an unusual finding [1,12]. We would therefore propose that, just as the aneurysmal (angiomatoid) variant of fibrous histiocytoma is an accepted entity, this histological subtype should be included in future classifications of AFX.

One striking feature of the cases reported here was the presence of multiple aneurysmal spaces, which in case were considerably larger than those described in the literature [1,3,11,12]. Both lesions were clinically diagnosed as possible nodular melanomas due to the dark appearance caused by hemosiderin deposition [16,17].

To summarize, AFX is a mesenchymal neoplasm of uncertain histogenesis and indolent clinical behavior, often arising in sun-damaged skin-generally of the head and neck-in elderly patients. AFX is a diagnosis of exclusion. At histological examination, morphological features may be highly atypical and alarming; numerous AFX subtypes have been described. We report here on two cases of an uncommon histological subtype of AFX, for which we advocate use of the term “aneurysmal”, and highlight its potential as a clinical mimicker of other neoplasms including nodular malignant melanoma.

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