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Atypical fibroxanthoma with dermal amyloid deposit

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Abstract

Atypical fibroxanthoma (AFX) has been associated with several secondary changes, such as keloidal areas, myxoid or chondroid changes, osteoclast-like giant cells, sclerosis, fibrosis, pigmentation, hyalinization, or hemorrhagic areas. We report a case of an AFX 4 cm in diameter on the forehead of a 77-year-old male patient. There were dermal amyloid deposits intermingled with the tumor fascicles on the periphery of the lesion. A moderate inflammatory chronic lymphoplasmacytic infiltrate was found in the periphery of the tumor. The amyloid deposits were positive with Congo red staining (but negative after permanganate-treatment). The deposit was also immunostained with antibodies against CKs (AE1/AE3 and CK5/6). It did not stain with anti-amyloid A, or with antibodies against either kappa light or lambda light chains. Therefore the amyloid deposit was keratinic in nature.

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Introduction

Atypical fibroxanthoma (AFX) is a cell neoplasm occurring mainly (or only, according to some criteria) on sun-exposed skin. It can be spindle, epithelioid, or (the most common) a mixture of spindle and epithelioid. From a morphologic point of view, several secondary changes have been described as being associated with AFX, such as keloidal areas, myxoid or chondroid changes, osteoclast-like giant cells, sclerosis, fibrosis, pigmentation, hyalinization, or hemorrhagic areas (1-3). However, we have not found any reported cases of dermal amyloid deposits related to AFX. Such deposits are very common in other cutaneous tumors and they have often been published in cases of basal cell carcinoma (BCC) (4-10).

This paper reports a case of AFX with amyloid deposits intermingled with the periphery of the tumor.

Methods

The patient, a 77-year-old male, had a 4 cm ulcerated tumor on the forehead that had rapidly grown in the last few months. The lesion was excised and sent to the pathology department for examination.

The lesion was fixed in 10% formaldehyde and embedded in paraffin using conventional methods. After that, 4 µm-thick sections were obtained and routine hematoxylin eosin stained slides were made.

The lesion was also immunostained for the antibodies shown in Table 1. Staining was performed with EnVision/DAB (Dako, Glostrup, Denmark).

Table 1 | Antibodies used in the immunohistochemical study. CK – cytokeratin, MMAH – monoclonal mouse antihuman, EMA – epithelial membrane antigen, SMA – smooth muscle actin.

Antibody	Manufacturer	Type	Clone	Isotype	Code
CK7	Dako	MMAH	OV-TL 12/30	IgG1, kappa	M7018
Desmin	Dako	MMAH	D33	IgG1, kappa	M0760
EMA	Dako	MMAH	E29	IgG2a, kappa	M0613
Melan-A	Dako	MMAH	A103	IgG1, kappa	M7196
S100	Dako	Polyclonal rabbit anti-S100	-	-	Z0311
HMB-45	Dako	MMAH	HMB-45	-	IR05
SMA	Dako	MMAH	1A4	IgG2a, kappa	M0851
Caldesmon	Dako	MMAH	h-CD	IgG1, kappa	M3557
CD34	Dako	MMAH	QBEnd 10	IgG1, kappa	M7165
CD31	Dako	MMAH	JC70A	IgG1, kappa	M0823
Factor VIII	Dako	Polyclonal rabbit anti-human	-	-	IR527
CK20	Dako	MMAH	Ks20.8	IgG2a, kappa	M7019
CK AE1/AE3	Dako	MMAH	AE1/AE3	IgG1, kappa	M3515
CK high molecular weight	Dako	MMAH	34βE12	IgG1, kappa	M0630
CAM5.2	Becton Dickinson	-	-	-	-
CK 5/6	Dako	MMAH	D5/16 B4	IgG1, kappa	M7237
CK 7	Dako	MMAH	OV-TL 12/30	IgG1, kappa	M7018
CK 8	Dako	MMAH	35βH11	-	N1560
CD 10	Dako	MMAH	56C6	IgG1	M7308
CD 68	Dako	MMAH	PG-M1	IgG3, kappa	M0876
CD 117	Dako	Polyclonal rabbit anti-human	-	-	A4502

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Results

The tumor showed a classic atypical fibroxanthoma made of a diffuse spindle cell dermal growth with marked cellular atypias, giant cells, and atypical mitoses (Fig. 1). In some areas, the tumor was ulcerated, although no connection between the tumor and the epidermis was observed (Fig. 2, top left).

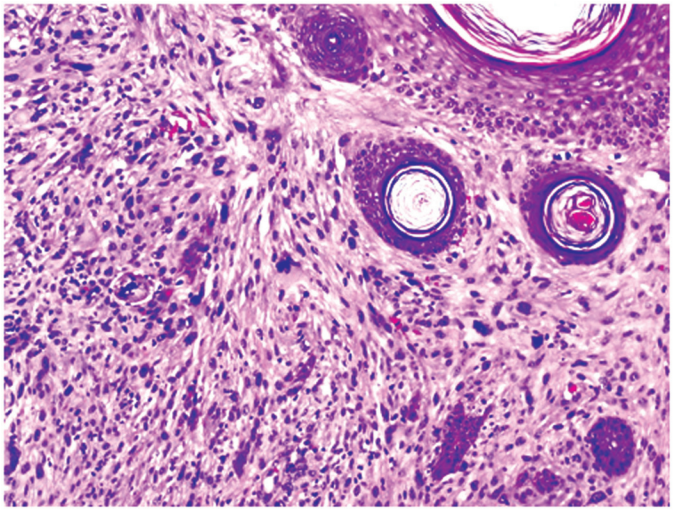

Figure 1 | Classic atypical fibroxanthoma, with cellular atypias and no connection with the epidermis.

The tumor failed to immunostain with antibodies for cytokeratin (CK)7, desmin, epithelial membrane antigen (EMA), Melan-A, S-100 protein, HMB-45, smooth muscle actin, caldesmon, CD34, CD31, Factor VIII, CK20, CKs AE1/AE3, CK 34betaE12, CAM 5.2, CK 5.6, CK 7, and CK8. It expressed CD10 and also CD68, although focally. CD117 demonstrated abundant mast cells in the tumor.

In the periphery of the lesion, a moderate inflammatory chronic lymphoplasmacytic infiltrate was found. Amyloid deposits were also found in the periphery of the tumor, intermingling with the spindle cell proliferation (Fig. 2, top right). Such deposits were positive with Congo red staining (Fig. 2, left; but negative after permanganate treatment). The deposit was also immunostained with antibodies against CKs (AE1/AE3 and CK5/6; Fig. 2, right). It did not stain with anti-amyloid A, or with antibodies against either kappa light or lambda light chains. Therefore, the amyloid deposit was keratinic in nature.

Discussion

Many secondary changes have been described in atypical fibroxanthoma, such as keloidal areas, myxoid or chondroid changes, osteoclast-like giant cells, sclerosis, fibrosis, pigmentation, hyalinization, or hemorrhagic areas (1-3, 11-19). We have not found any published case of this type of amyloid in an atypical fibroxanthoma. However, the well-known polemic on the nature of atypical fibroxanthoma as a spindle-squamous cell carcinoma (SCC) should be remembered (20) because cases of cutaneous amyloidosis related to common SCC have been reported (5).

Amyloid deposits have been related to other types of cutaneous tumors, including basal cell carcinoma (4-10), syringocystadenoma papilliferum (21), or trichoepithelioma (22). Other cutaneous lesions also related to amyloid deposits are linear verrucous epidermal nevus (23), melanocytic nevus (23, 24), seborrheic keratosis (5), actinic keratosis (6), or Bowen's disease (25).

In our case we wondered whether the amyloid could be related to the tumor or whether it might perhaps be a coincidental finding (i.e., an atypical fibroxanthoma developing on skin already affected by amyloidosis). Arguing against this latter hypothesis, we found the deposits only in the periphery of the tumor, and not in the most peripheral areas of the biopsy, which showed non-tumor skin. In addition, the patient did not present any other lesions clinically suggestive of cutaneous amyloidosis.

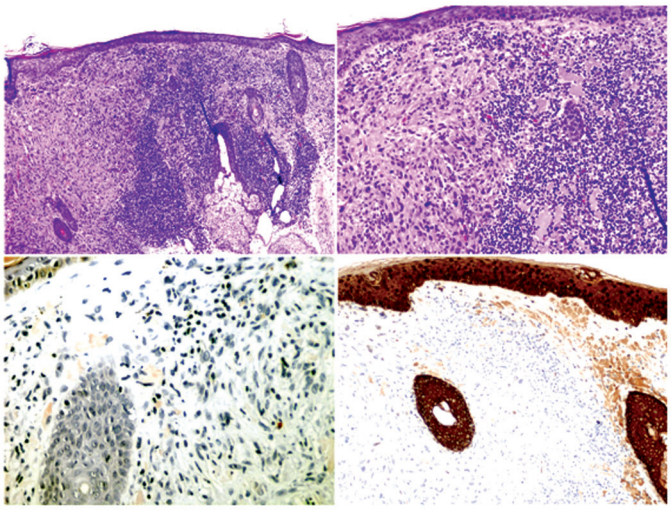

Figure 2 | The tumor was dermal with no epidermal connection (top left). At the periphery, mild deposits of amyloid were found (top right). The deposits were positive with Congo red staining (bottom left) and they were made of keratins (CK AE1/AE3, bottom right).

As shown in the figures for this case, the deposit was close to an area with a marked peritumoral lymphoplasmacytic inflammatory infiltrate. Such an infiltrate could be responsible for the epidermal damage that would have caused the amyloid deposit in a pathogenetic sequence similar to the one observed in lichen planus, for instance (26).

Amyloid deposits should be distinguished from other changes that have been occasionally associated with AFX, such as keloidal collagen (2), or from acellular hyalinization (1). The latter has been described as being associated with lymphoplasmacytic inflammatory infiltrate, as a regressive phenomenon in AFX (3). Both changes can show eosinophilic hyaline areas that mimic amyloid in routine studies. However, such areas will not stain with amyloid techniques (such as Congo red) or with antibodies for CKs. It should be remembered that recently Cassarino reported a case of aberrant expression of CK5/6 in atypical fibrous histiocytoma (27). However, in this case, CK5/6 stained the tumor cells and not any type of hyaline deposit. It is also debatable whether such cases corresponded to AFX or to spindle-cell carcinomas.

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