

CASE REPORTS

Pigmented or Hemosiderotic Atypical Fibroxanthoma

M.A. Pastor-Nieto,^a L.G. Kilmurray,^b and L. Requena^c

^aServicio de Dermatología, Hospital General Universitario de Guadalajara, Guadalajara, Spain

^bServicio de Anatomía Patológica, Hospital del Sureste, Arganda del Rey, Madrid, Spain

^cServicio de Dermatología, Fundación Jiménez Díaz, Madrid, Spain

Abstract. Pigmented atypical fibroxanthoma is a rare variant of atypical fibroxanthoma and is characterized by extensive areas of hemorrhage, erythrophagocytosis, and hemosiderin accumulation in the cytoplasm of the neoplastic cells. It affects elderly individuals and presents as irregularly pigmented, dome-shaped nodules or plaques on areas of skin exposed to the sun. We present a case of pigmented atypical fibroxanthoma on the cheek of an 81-year-old man. Six years after excision of the lesion, the patient remains in complete remission, with no signs of residual tumor or metastasis. The 9 cases of pigmented atypical fibroxanthoma reported in the literature are reviewed, and the histopathological features and differential diagnosis are discussed.

Key words: atypical fibroxanthoma, pigmented, hemosiderotic.

FIBROXANTOMA ATÍPICO PIGMENTADO O HEMOSIDERÓTICO

Resumen. El fibroxantoma atípico pigmentado es una variante rara de fibroxantoma atípico caracterizada por áreas extensas de hemorragia, eritrofagocitosis y depósitos de hemosiderina en el citoplasma de las células neoplásicas. Afecta a pacientes de edad avanzada, y se manifiesta como nódulos cupuliformes o placas pigmentadas, de coloración heterogénea, en áreas de piel fotoexpuesta. Se presenta un caso de fibroxantoma atípico pigmentado de localización malar en un varón de 81 años de edad. Seis años después de la extirpación quirúrgica de la lesión, el paciente permanece en remisión completa, sin que se aprecien signos clínicos de persistencia tumoral o metástasis. Se revisan los 9 casos de fibroxantoma atípico pigmentado publicados en la literatura y se discuten las características histopatológicas y el diagnóstico diferencial de esta rara entidad.

Palabras clave: fibroxantoma atípico, pigmentado, hemosiderótico.

Introduction

Atypical fibroxanthoma, described by Helwig in 1960, is a rare skin tumor. Its histogenesis is a subject of debate, with both fibrohistiocytic and myofibroblastic differentiation being reported. Some authors maintain that it is a superficial form of malignant fibrous histiocytoma, with a better prognosis.^{1,2} The different histopathological variants of atypical fibroxanthoma that have been described in the literature are presented in Table 1.

The pigmented variant of atypical fibroxanthoma was described by Diaz-Cascajo in 1988, with a report of 4 cases. In 2003, the same authors published a series of 9 cases, including the 4 patients from the original article. We present a new case and review the clinicopathological features and the differential diagnosis of this rare condition.

Table 1. Histopathological Variants of Atypical Fibroxanthoma

| |
|---|
| Spindle-cell, nonpleomorphic ³ |
| Clear-cell ⁴ |
| Granular-cell ⁵ |
| With osteoclast-like giant cells ⁶ |
| With prominent sclerosis ⁷ |
| Pigmented (hemosiderotic) ^{8,9} |

Correspondence:
María Antonia Pastor Nieto
Hospital General Universitario de Guadalajara
C/ Donante de Sangre, s/n
19002 Guadalajara, Spain
mapastornieto@gmail.com

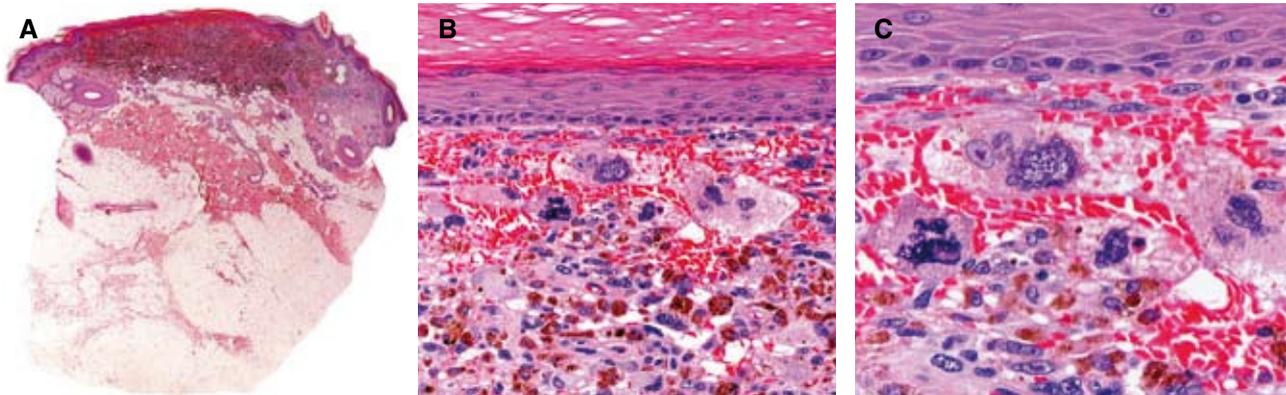


Figure 1. A, Cell proliferation in the form of a well-defined, nonulcerated, asymmetrical plaque situated in the dermis. Uniform distribution of brownish pigment throughout the lesion. B, Proliferation of highly pleomorphic cells with hyperchromatic, atypical nuclei, abundant foamy cytoplasm, and poorly defined cell borders. Extensive hemorrhage within the tumor. C, Atypical multinucleated, neoplastic giant cells, abnormal mitotic figures, and signs of erythrophagocytosis (presence of red blood cells, eosinophilic globules, and hemosiderin deposits in the cytoplasm of the tumor cells) (hematoxylin-eosin, A $\times 16$, B $\times 200$, C $\times 400$).

Case Description

The patient was an 82-year-old man who had undergone surgery in 2001 for an asymmetrical pigmented plaque measuring 0.8 cm across, of heterogeneous color and irregular borders, situated on the left cheek. The clinical suspicion prior to excision was melanoma; histopathological study revealed an asymmetric, nodular neoplastic proliferation of pleomorphic cells situated in the papillary and reticular dermis. The majority of the cells had hyperchromatic nuclei of irregular morphology and a large volume of eosinophilic cytoplasm; there were also multinucleated giant cells with variable degrees of xanthomatization, and a few, more monomorphic spindle-shaped cells. There were extensive areas of hemorrhage within the tumor and at its periphery, and the cytoplasm of the tumor cells was occupied by granular deposits of hemosiderin in large areas of the tumor. There were numerous atypical mitotic figures. No epidermal abnormalities were observed. The diagnosis of pigmented atypical fibroxanthoma was made based on these clinical and pathological findings (Figures 1 and 2).

Now, 7 years after the operation, the patient remains in complete remission, with no clinical signs of persistence of the tumor or lymph node infiltration and no pathological findings on the imaging studies (chest x-ray and abdominal ultrasound).

Discussion

The pigmented variant of atypical fibroxanthoma was described by Diaz-Cascajo in 1998, with a series of 4 patients.⁸ In a later article published in 2003, the same authors extended the series with 5 additional cases.⁹ All

the patients, 6 men and 3 women aged between 59 and 86 years, presented single lesions in the form of nodules or plaques in the skin of areas of the face that had suffered actinic damage. Ulceration was present in 3 cases. The clinical diagnosis was of a melanocytic tumor in 5 cases (3 melanomas, 1 metastatic melanoma, and 1 melanocytic tumor) and squamous cell carcinoma in 2 cases. A preoperative diagnosis of atypical fibroxanthoma had only been made in 1 case. All the lesions were treated by simple excision and no patient developed metastases. The patients were alive and free of disease after a follow-up period that varied between 8 months and 4 years. Local recurrence occurred in 1 case due to inadequate surgical margins; this patient was alive and with no recurrence or metastasis 15 months after the second excision (Table 2).⁹

Histopathological study showed that all the tumors were situated in the dermis and were well delimited. In 3 cases, a hyperplastic band of epithelium was identified in the periphery of the tumor. Ulceration was present in 3 cases, making it impossible to evaluate epidermal involvement. In 2 cases, the lesion extended into the hypodermis. The neoplastic cells, grouped together to form solid masses, presented large and atypical nuclei with dense chromatin and abundant, dense or foamy eosinophilic cytoplasm. Atypical multinucleated cells with pleomorphic nuclei and frequent mitotic figures were identified in all cases. In all the lesions, erythrocytes and particles of hemosiderin were observed in the cytoplasm of a variable number of tumor cells in areas of hemorrhage within the tumor. Pseudocystic spaces containing hematic material, similar to those identified in hemosiderotic dermatofibroma (aneurysmal fibrohistiocytoma) were identified in 1 case and there were intracytoplasmic deposits of periodic acid-Schiff-positive, diastase-resistant eosinophilic spheres with diameters of 1 to 10 μm in 2 cases.⁹

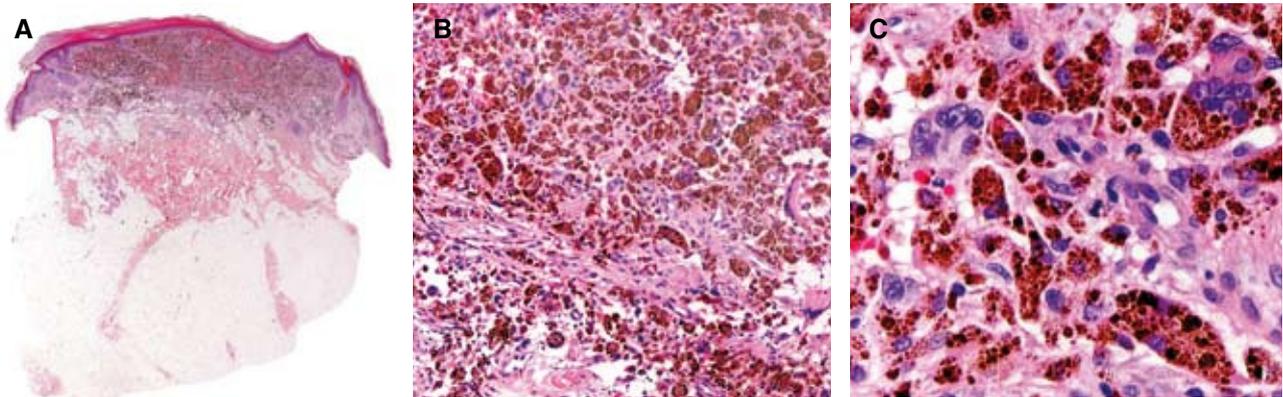


Figure 2. A, Another section from the same lesion, showing a uniformly pigmented, asymmetric, diffuse cell proliferation in the dermis, covered by an intact epidermis. B, Abundant deposits of an ochre pigment corresponding to hemosiderin within the cytoplasm of most of the tumor cells; these cells are organized into solid masses. C, The cytoplasm of the neoplastic cells is full of dark deposits of hemosiderin (hematoxylin-eosin, A $\times 100$, B $\times 200$, C $\times 400$).

Immunohistochemical analysis was intensely positive for vimentin and weakly positive for CD68 and for α -1-antichymotrypsin. Immunologic positivity for factor XIIIa was detected in a large number of neoplastic cells.⁹

Table 3 summarizes the most characteristic histopathological findings of pigmented atypical fibroxanthoma.

The presence of hemosiderin deposits within the tumor caused the lesion to acquire a heterogeneous, brownish color, making it necessary clinically to consider a differential

diagnosis with melanoma. The histopathological differential diagnosis must be established with melanoma, Spitz nevus, and hemosiderotic dermatofibroma (aneurysmal fibrohistiocyoma).

Infiltration of the superficial dermis by a proliferation of atypical cells, the presence of multinucleated cells, and mitotic figures are histopathological findings that are common to pigmented atypical fibroxanthoma, melanoma, and Spitz nevus. However, the melanocytes in melanocytic lesions usually present intraepidermal

Table 2. Published Cases of Pigmented Atypical Fibroxanthoma

| Authors/Name Used | Case No. | Age | Sex | Site | Clinical Diagnosis | Treatment | Recurrence | Months of follow-up |
|--|----------|-----|-----|-----------------|-------------------------|-----------|------------|---------------------|
| Díaz-Cascajo ^{8,9} / Pigmented atypical fibroxanthoma | 1 | 59 | M | Face | Melanoma | Excision | 0 | 20 |
| | 2 | 63 | M | Face | Unknown | Excision | 0 | 13 |
| | 3 | 78 | M | Face | Metastatic melanoma | Excision | 1 | 23 |
| | 4 | 75 | M | Face | Melanocytic tumor | Excision | 0 | 8 |
| | 5 | 86 | F | Temporal region | Squamous cell carcinoma | Excision | 0 | 48 |
| | 6 | 81 | F | Face | Melanoma | Excision | 0 | 36 |
| | 7 | 75 | M | Ear | Atypical fibroxanthoma | Excision | 0 | 15 |
| | 8 | 84 | F | Face | Melanoma | Excision | 0 | 20 |
| | 9 | 78 | M | Cheek | Squamous cell carcinoma | Excision | 0 | 31 |
| Pastor-Nieto/ Pigmented or hemosiderotic atypical fibroxanthoma | 10 | 76 | M | Malar region | Melanoma | Excision | 0 | 65 |

Abbreviations: F: female; M: male.

Table 3. Histopathological Characteristics of Pigmented or Hemosiderotic Atypical Fibroxanthoma

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|---|
| Dome-shaped nodule or plaque located in the dermis, with occasional extension into the hypodermis |
| Band of hyperplastic epithelium in the periphery of the tumor |
| Neoplastic cells arranged in solid masses |
| Atypical pleomorphic cells with histiocytoid appearance, characterized by a nucleus with a variegate morphology and large volume of dense or foamy eosinophilic cytoplasm, and a few multinucleated cells |
| Numerous mitotic figures |
| Areas of hemorrhage within the tumor |
| Intracytoplasmic collections of erythrocytes or hemosiderin in a variable number of neoplastic cells |

spread with a tendency to aggregate in sheets, and the pigmentation arises as a consequence of melanin deposition. In addition, specific immunohistochemical stains for melanocytic lesions (S100, HMB45, NKI-C3) are negative in pigmented atypical fibroxanthoma.⁹

Hemosiderotic dermatofibroma (aneurysmal fibrohistiocytoma) is characterized by monomorphic, eosinophilic, spindle-shaped cells grouped into short bundles in a storiform arrangement, and pseudovascular spaces (not lined by endothelium). This lesion usually arises on the limbs of middle-aged patients, whereas pigmented atypical fibroxanthoma is most commonly found in elderly patients on areas of the head and neck exposed to sunlight. In addition, atypical fibroxanthoma does not show epidermal hyperplasia, collagen sclerosis, or the lymphocyte infiltrate characteristic of hemosiderotic dermatofibroma. In contrast, the nuclear polymorphism and atypical mitotic figures specific to pigmented atypical fibroxanthoma are not seen in hemosiderotic dermatofibroma.^{10,11}

In general, the term pigmented is used in medical literature to refer to lesions with a dark color (brown or black). However, it is probably more correct to restrict its use to lesions with melanocytic differentiation (nevus or melanoma) or nonmelanocytic tumors in which there is melanin deposition (for example, pigmented basal cell carcinoma or pigmented seborrheic keratosis). The term hemosiderotic has been used to refer to those lesions or tumors in which hemosiderin deposits are typically present, such as hemosiderotic dermatofibroma,¹² targetoid hemosiderotic hemangioma,¹³ hemosiderotic fibrolipomatous tumor,¹⁴ and targetoid hemosiderotic nevus.¹⁵ In pigmented atypical fibroxanthoma, the clinically apparent dark color is due exclusively to hemosiderin

deposition and not to any increase in the quantity of melanin. The term hemosiderotic rather than pigmented atypical fibroxanthoma would therefore possibly be more accurate when referring to this rare condition.

Conflicts of interest

The authors declare no conflicts of interest.

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