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Case presentation

Epithelioid angiosarcoma of the skin. A malignant tumor mimicking many different neoplasms

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Abstract

Epithelioid angiosarcomas are rare malignant mesenchymal tumors. The main problem of these tumors is the complicated clinical and histological diagnosis. We report a case with an immunohistochemical panel. We propose the use of CD31 in the immunohistochemical panel of an undifferentiated tumor with epithelioid features, because it appears to be the only endothelial marker these tumors constantly express.

KEY WORDS: Epithelioid angiosarcoma, angiosarcoma

Introduction

Epithelioid angiosarcomas (EA) are rare malignant mesenchymal tumors, developed from vascular endothelial cells. EA is a subtype or morphologic variant of angiosarcoma, characterized by the epithelioid morphology of tumoral cells. It is recently well known that EA is a different entity with the same bad prognosis as the classic angiosarcoma. The main problem of these tumors is the complicated histological diagnosis, frequently delayed, due to its resemblance with other tumors like melanomas, epithelioid sarcomas, carcinomas or even lymphomas [1]. Its immunohistochemical profile is also confusing because of the co-expression of endothelial and epithelial markers [2,3]. It may also show an aberrant expression of S100 protein and CD30 [3].

Case synopsis

A 67 year-old man presented a rapidly growing, erythematous, skin lesion at the temple measuring 5 cm (Figure 1).



Figure 1. Erythematous infiltrative plaque

Initial biopsy diagnosis was of undifferentiated carcinoma, probably metastatic. Imaging studies and tumoral markers discarded this suspicion. Histological examination revealed dermal and hypodermal tumor, with solid, nested growth pattern, with focal acantholytic areas and pseudoglandular lumens. Tumor cells showed huge, polygonal, eosinophilic cytoplasm, with large vesicular nucleus, and conspicuous nucleoli, some of them had signet-ring cell-like morphology or showed intracytoplasmic lumens with erythrocytes. Necrosis and apoptosis were frequent. Associated inflammatory infiltrate was seen with eosinophils. Mitotic index was 9 mitosis/10 HPF (Fig.2).

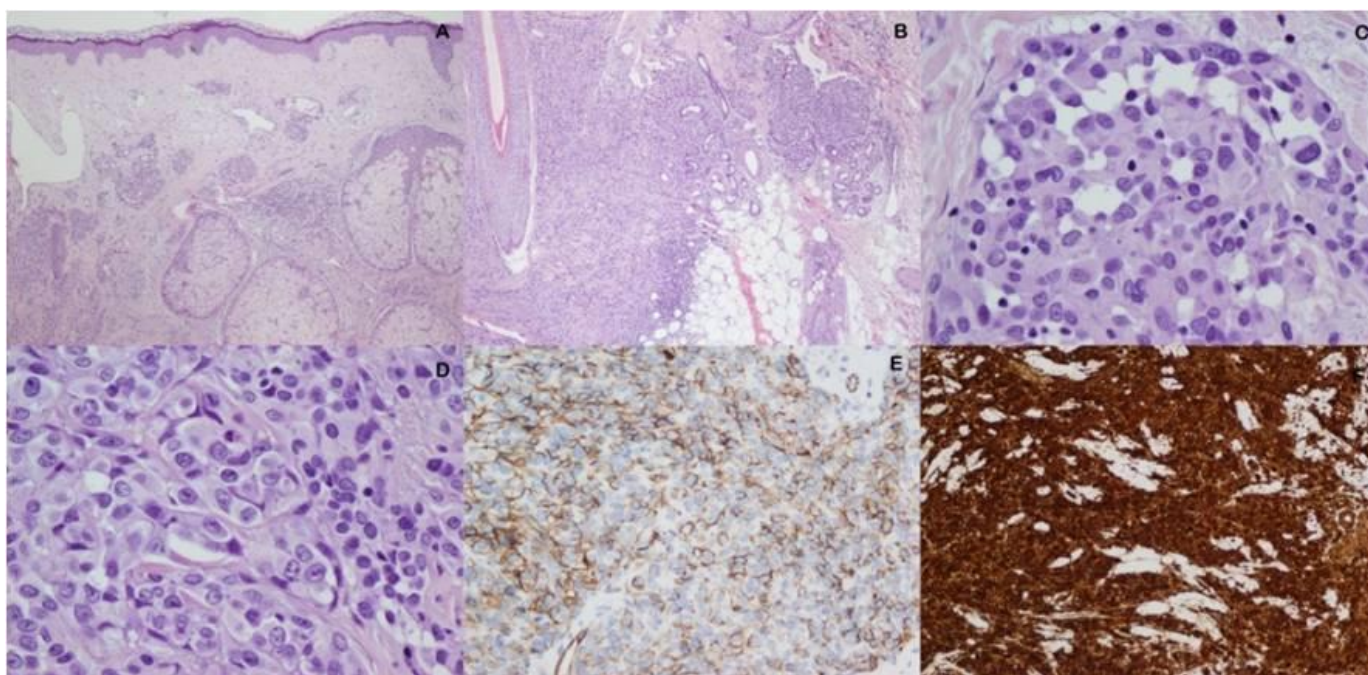


Figure 2. A) Intradermal tumoral nests without epidermal involvement (40x) B) Tumoral cells surround cutaneous adnexal structures (100x) C) Epithelioid cells with focal acantholysis (200x) D) Tumor cells with epithelioid features (400x) E) CD31 (200x) F) Vimentin (200x)

Immunohistochemical profile showed staining for vimentin and CD31; Ki67 proliferation index was 50%. CK AE1/AE3, CK8, Ber-EP4, TAG-72, EMA, CD34, S100, HMB-45, Melan A, CD 10 and D2-40 were negative.

Wide excision of the lesion was practiced and the patient underwent coadjuvant treatment. Nine months after diagnosis he died.

Discussion

We submit a case of cutaneous EA not associated with previous lymphedema nor radiotherapy, both of which are located on the head and neck of elderly people. EA is a rare variant of angiosarcoma, characterized by its epithelioid morphology, and most frequently described on soft tissues as being the most frequent sites, lower extremities, followed by retroperitoneum, mediastinum and mesentery. Exclusively cutaneous instances have also been described [1,3].

Comprehensive histological study usually shows a solid growth pattern of epithelioid cells and some areas of vascular channel formation, where the typical location is the periphery of the tumor. Other typical histological characteristics are the presence of intracytoplasmic vacuoles with or without erythrocytes that sometimes look like signet ring cells, pseudoglandular space formation, inflammatory infiltrate with eosinophils, and absence of desmoplastic reaction [4].

Several EA reports describe erroneous diagnoses. All tumors with epithelioid features enter the differential diagnosis: melanoma, anaplastic lymphoma, breast and lung carcinomas, epithelioid sarcomas, malignant peripheral nerve sheath tumor, histiocytic sarcomas, epithelioid meningiomas, epithelioid monophasic synovial sarcomas and epithelioid hemangioendotheliomas [1]. Our patient showed intracytoplasmic vacuoles, cleft or vascular slits and high mitotic index. The first histological impression was metastatic carcinoma. The main differential diagnosis can be made with immunohistochemistry (Table 1).

Table 1. Main differential diagnostics. EA: Epithelioid angiosarcoma; AL: Anaplastic lymphoma; MEL: Melanoma; ES: Epithelioid sarcoma; CAR: Carcinoma; HS: Histiocytic sarcoma; EMPNST: Epithelioid malignant peripheral nerve sheath tumor; EM: Epithelioid mesothelioma; EMSS: Epithelioid monophasic synovial sarcoma; CLA: Common leucocyte antigen; CK: Cytokeratins; EMA: Epithelial membrane antigen; VIM: Vimentin; V: Variable; +: positive; -: negative; r: rare positivity.

DIFFERENTIAL DIAGNOSTICS	S100	CLA	CK	EMA	CD31	CD34	CD68	VIM
EA	-	-	V	-(r)	+	V	-	+
AL	-	+	-	+	-	-	-	+
MEL	+	-	-	-	-	-(r)	-	+
ES	-(r)	-	+	+	-	+(50%)	-	+
CAR	-	-	+	+	-	-	-	V
HS	-	+	-	-	-	-	+	+
EMPNST	+(80%)	-	-	-(r)	-	+(50%)	-	+
EM	-	-	+	-	-	-	-	+(50%)
EMSS	-	-	+	+	-	-	-	+

Cutaneous EA has an immunohistochemical profile slightly different from EA in other locations. Primary cutaneous tumors generally show intense staining with vimentin, lack of staining for epithelial markers, HMB45, and slight staining or negativity for endothelial markers like CD34, FVIII, D2-40, UEA-I (3-5). CD31 is uniformly positive. Isolated cases with S-100 and CD30 (3) positivity have been described. In general, cutaneous EA rarely stains for epithelial markers, but isolated cases with focal staining for CKAE1/AE3 and high molecular weight keratins have been described, less frequently for cytokeratin CAM 5.2 or EMA [6,7].

Immunohistochemical profiles of soft tissue, bone, and deep solid organ epithelioid angiosarcomas stain with keratins (CK8 and CK18, less frequently with CK7) more often than cutaneous counterparts (4), and almost never express EMA. Other vascular markers (like CD34, Factor VIII, D2-40) show inconsistent results, where expression appears to decrease with dedifferentiation. In summary, all EA expressed CD31 and vimentin.

In our opinion it could be very useful to include CD31 in the immunohistochemical panel of an undifferentiated tumor with epithelioid features, because it appears to be the only endothelial marker these tumors express uniformly.

EA prognosis in any location is poor. Two or three years after diagnosis, around 50% die from this tumor, and 20-30% are alive and free of disease [8]. Based upon the cases we observed, patients are disease-free for less than six months. There is no standard treatment protocol. The recommended treatment is surgical excision with or without adjuvant radiotherapy [9].

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