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Case Report

Epithelioid angiosarcoma revealed by livedoid distal vascular emboli

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ABSTRACT

Angiosarcomas are rare malignant mesenchymal tumours with endothelial differentiation, which may arise in any organ. Angiosarcoma of the aorta is even more exceptional. It can be complicated by distal embolization, resulting in suggestive clinical pictures such as cyanotic skin lesions of the extremities or livedo reticularis. We report a case of an epithelioid angiosarcoma revealed by bone metastasis and which caused cutaneous intravascular emboli prior to diagnosis. Intravascular distal embolization arising from a primary malignant vascular tumour of the aorta is extremely rare and this diagnosis can be a challenge for the pathologist, in particular without the clinical context.

Angiosarcomas are a rare type of malignant soft tissue tumour with endothelial differentiation (1–2% of all sarcomas), an aggressive course and poor prognosis [1,2]. Most cases occur in Caucasian men after the age of 60, particularly as a UV-related skin disease of the head or neck, but can be found elsewhere. Some authors have described a cutaneous metastatic onset of the disease [3,4]. As angiosarcomas are often confused with atherosclerotic disease, cutaneous metastatic vascular emboli arising from angiosarcoma are hard to diagnose without histological assessment. Even then, if there is no history of sarcoma, it may be hard to distinguish histologically from benign proliferative or inflammatory lesions. We report a case of cutaneous intravascular metastasis of an epithelioid angiosarcoma diagnosed retrospectively. The patient's next of kin gave written informed consent for publication.

1. Case report

A 63-year-old Caucasian man had been followed for 5 years for an abdominal aortic aneurysm treated with a Zenith-type stent prosthesis. He also presented with obesity, hypertension and hypercholesterolemia. After surgery, the patient experienced three episodes of acute ischaemia of the left lower leg (June and November 2010, November 2012). Two blood clots were histologically analysed but no cytological abnormalities were found. In March 2015, a follow-up abdominal scan showed an increase in size of the pre-existing aneurysm associated with retroperitoneal lymph nodes. Complementary laboratory and radiological investigations were carried out. Screening revealed a persistent biological inflammatory syndrome and marked enhancement of the aortic prosthesis, the iliac bifurcation and the left sacrum on PET scan (Fig. 1). Infection of the prosthesis was later ruled out by LeukoScan and by spontaneous regression of the lymph nodes. A cardiac thrombus and endocarditis were excluded by echocardiography, and lymphoma by clinical and laboratory investigations. The patient was then referred to the department of internal medicine for suspicion of vasculitis. He complained of right ankle joint pain. Physical examination revealed livedo reticularis of the feet, thighs and lower back. A first skin punch biopsy of the left foot identified cholesterol crystal embolism (Fig. 2). A second cutaneous biopsy showed inflammation and granuloma in mid-dermal vessels. The lumens were occluded by fibrin, necrotic tissue and a few atypical cells with increased nuclear-cytoplasmic ratio. These cells were mistakenly considered to be dystrophic due to negative epithelial and melanocytic markers and

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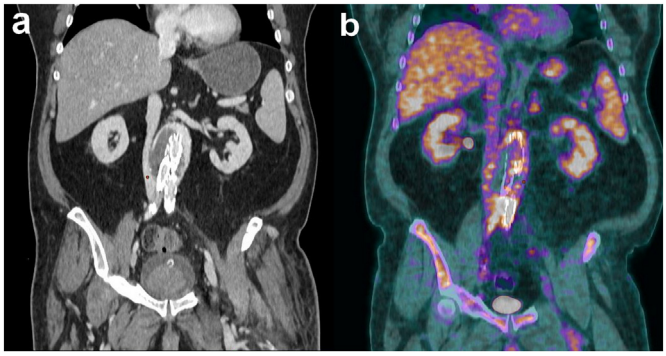

Fig. 1. a) Contrast-enhanced CT. b) 18F-FDG-PET/CT fusion: coronal view of the aneurysm, showing high uptake on the lower neck of the aneurysm and milder uptake on the body and upper neck.

positive endothelial markers. A month later, the patient was admitted for excruciating pain in his left thigh. Two osteolytic left femoral lesions were visible on X-ray, with increased uptake on bone scan. Bone biopsy showed a malignant tumoral proliferation of large epithelioid cells, with abundant eosinophilic cytoplasm and moderate pleomorphism. Vascular differentiation and strong positivity of anti-CD31 and anti-ERG antibodies were also present (Fig. 3). The anti-CD34 antibody was positive only in differentiated areas. The Ki-67 proliferation marker was estimated at 40%. Epithelioid angiosarcoma of bone was diagnosed (French Federation of Cancer Centers (FNCLCC) grade II, score 3 for differentiation, 1 for mitosis, 0 for necrosis). The primary lesion was not definitely identified despite extensive radiological screening, but the abdominal aortic aneurysm was suspected. Disease spread rapidly until the death of the patient in October 2015.

Retrospectively, a second serial microscopic examination of the skin biopsies showed similar atypical cells in the lumen of the skin vessels. Carcinomatous emboli were excluded by negative anti-EMA and anti-pan cytokeratin antibodies. Melanocytic markers (HMB45 and anti-PS100) were also negative. These intravascular cells with nuclear-cytoplasmic atypia expressed CD31 and ERG. Finally, these results were in favour of cutaneous embolic metastases of an angiosarcoma, presenting as livedo reticularis.

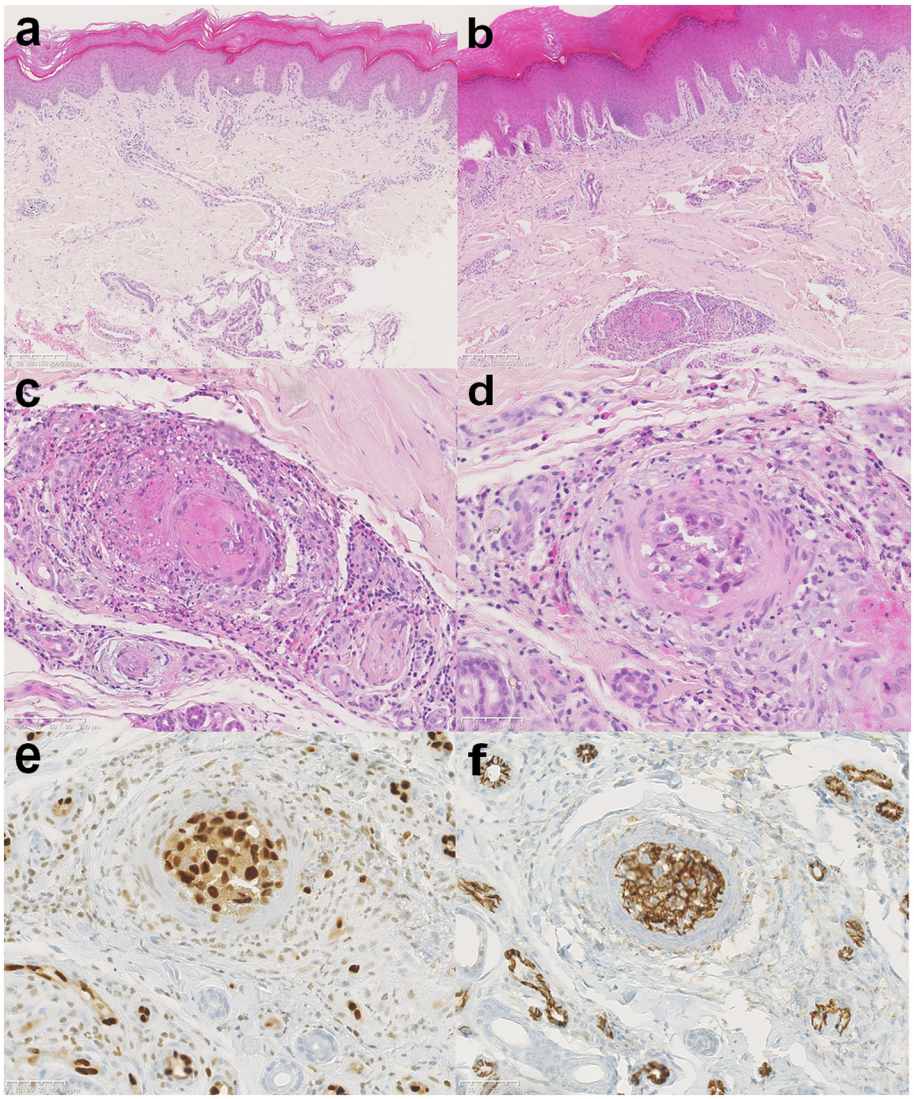

Fig. 2. a) First cutaneous punch biopsy, which was considered normal (hematoxylin and eosin, magnification ×60). b) Second skin biopsy of the left foot with a few atypical cells with increased nuclear-cytoplasmic ratio, considered to be of dystrophic nature at the first examination (hematoxylin and eosin, magnification ×60). c, d) Atypical cells in the lumen of the skin vessels corresponding to distal embolization of the angiosarcoma (hematoxylin and eosin, magnification ×200 and ×300, respectively). e, f) strong nuclear expression of ERG and cytoplasmic expression of CD31 by the atypical cells (anti-ERG antibody and anti-CD31 antibodies, respectively, magnification ×300).