Dear Editors,

A 63-year old man was referred to our outpatient department with an eight-week history of slowly growing, painful skin lesions on his right foot. He also reported a weight loss of 10 kg, occasional fever and excessive spontaneous sweating. He had been experiencing these symptoms for one year. His medical history included arterial hypertension, hyperlipidemia and an operation of an aneurysm of the vena poplitea in his right leg in 2013.

Clinical examination revealed blue-to-blackish papules measuring 5–8 mm that were mainly localized on the sole but also on the toes and back of the right foot (Figure 1). The left foot was unremarkable. Phlebological work-up revealed saphenous vein insufficiency of the right lower leg. Histopathology of a skin biopsy showed a dermal capillary proliferation accompanied by a dense infiltrate consisting of lymphocytes, histiocytes and eosinophils and numerous hemosiderin deposits. Most of the vessels were positive for CD31 and negative for D2-40. Immunostaining for human herpesvirus type 8 (HHV-8) was negative, excluding Kaposi sarcoma. Clinico-pathological correlation was consistent with a diagnosis of Mali-type acroangiodermatitis.

Due to the reported B-symptoms, further diagnostic work-up with abdominal and thoracic computed tomography (CT) was performed, revealing an enlarged, atypical lymph node in the right groin that was then surgically removed. Histopathology revealed dense formations of epithelioid, pleomorphic cells with numerous mitotic figures (Figure 2) The tumor exhibited many small intratumoral vessels, extravasated erythrocytes and necrosis and stained positive for CD31, ERG, pan cytokeratin antibody (AE1/AE3), and factor VIII related antigen but negative for HMB45, Melan A, S100, CD34 and HHV8. The proliferation-index was high (Ki67: 60 %). Finally, metastasis of an epithelioid angiosarcoma (EA) was diagnosed. MRI of the right leg revealed a deep-seated vascular tumor located in the right thigh in close proximity to the knee. An increased blood flow in the cranial part of the tumor was detected by sonography. The lesion was then classified as a primary tumor. Comparing both legs by CT angiography, MRI and sonography did not reveal any differences in functional status and perfusion of the arterial system of the left leg. In particular, neither tumor-induced vascular compressions nor connections between arterial and venous system could be found. After two cycles of neoadjuvant chemotherapy (ifosfamide 2.5 g/m² and doxorubicin 25 mg/m²), the tumor was surgically removed. Histopathology was consistent with formations of the known EA. Further staging by CT showed stable disease. Currently, adjuvant radiotherapy and two further chemotherapy cycles are planned.

There are two types of acroangiodermatitis: one described in 1965 as the Mali type (caused by venous stasis) and one described two years later as Stewart-Bluefarb type (caused by congenital arteriovenous malformation without venous stasis) [1, 2]. Acroangiodermatitis Mali (AM), also known as pseudo-Kaposi sarcoma or acral capillary angiomatosis, is the more common form and represents a reactive angiodysplasia of cutaneous vessels [3]. Cases caused by chronic venous insufficiency, acquired arteriovenous anomalies, paralyzed extremities or amputation stumps have been described [4–8]. The etiology of AM remains elusive, though it has been argued that chronic hypoxia can induce neovascularization and fibroblast proliferation [9]. Skin lesions generally occur on the lower

![Figure 1](image1.png) Clinical pictures of the first presentation in our department; blue-to-blackish papules measuring 5–8 mm plantar right (a), instep right (b), right outer edge of the foot (c).
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distal extremities, especially on the feet and are characterized by angiomatous macules, papules, plaques or nodules [10]. Histologically, AM is composed of a proliferation of small thick-walled vessels with narrow lumina, often in lobular arrangement. A perivascular fibroblastic proliferation, as well as extravasated erythrocytes, spindle cells or hemosiderin deposits are found [5]. The most important differential diagnosis is Kaposi sarcoma. Other differential diagnoses include reactive angioendotheliomatosis, diffuse dermal angiomatosis, glomeruloid angioendotheliomatosis and angiopericytomasis [10, 11]. Kaposi sarcoma resembles AM clinically and histologically, but in Kaposi sarcoma there are also perivascular CD34 positive cells, nuclear atypia and most importantly positivity for HHV8 [10]. The therapeutic gold standard is the treatment of any potential underlying vascular disorder by operative or conservative methods in order to reduce venous stasis [3, 4, 12, 13].

EA is a rare variant of cutaneous angiosarcoma with extremely poor prognosis that metastasizes early (lung, bone, soft tissue, lymph nodes and brain) [14]. It is more common among elderly men. EA has been described in patients with chronic lymphedema, radiation therapy and after sun exposure [15, 16]. Histologically, EA is dominated by dense clusters of atypical epithelioid cells. Although not specific, CD31, factor VIII related antigen, UEA (ulex europaeus agglutinin I), laminin and CD34 are mostly positive [17]. It is known that angiosarcomas can secrete variable levels of VEGF-A (vascular epidermal growth factor type A) into the circulation, and this may be associated with p53 mutations [18]. Because EA is rare and data are scarce, evidence-based therapy recommendations are lacking. The therapeutic standard includes radical excision with regional lymph node dissection, with or without (neo)adjuvant radiotherapy followed by multidrug chemotherapy. Targeted therapies and immune checkpoint inhibition have also been described [14].

In the present case, the diagnosis of AM in combination with B-symptoms provoked further diagnostic measures which revealed, by chance, the much more serious diagnosis of EA. To our knowledge, this is the first reported case of unilateral AM and an associated proximal leg tumor. Whether a causal relationship exists between these diagnoses (AM and EA) remains unclear. We believe that the pre-existing popliteal aneurysm and especially its surgery in 2013 with a femoropopliteal bypass using the saphenous vein contributed to the development of AM due to hemodynamic changes in the right leg. We cannot rule out that additional hemodynamic changes caused by the EA or by elevated serum levels of VEGF may also have contributed to the development of AM.

Cases like this impressively highlight the need to clarify all of a patient’s symptoms (especially when they are not in accordance with the previous diagnosis) and emphasizes the dermatologist’s guiding role.

Figure 2  Histopathology of the lymph node in the right groin (a–d) and Mali-type acroangiodermatitis on the right foot (e–f). Lymph node: Atypical, epithelioid cells and numerous extravasated erythrocytes. Note the small primitive vessels containing a single erythrocyte (hematoxylin-eosin stain [HE], original magnification x 200 (a), x 400 (b)). Lymph node: ERG staining (x 100) (c). Lymph node: AE 1/3 staining (x 100) (d). Acroangiodermatis (HE, x 100) (e). Acroangiodermatis: CD31 staining (x 100) (f).
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Conflict of interest
None.

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