CASE REPORTS

A RARE CASE OF EPITHELIOID ANGIOSARCOMA

Ana Margarida Correia[1]*, Rafael Ribas Fernandes[2], José Carlos Vidoedo[3], Jorge Guimarães[1], João Almeida Pinto[3]

[1] Surgical Oncology Department, Instituto Português de Oncologia do Porto Francisco Gentil (IPO-Porto), Porto, Portugal
[2] General Surgery Department, Hospital das Forças Armadas – Pólo do Porto, Portugal
[3] Vascular Surgery Department, Centro Hospitalar do Tâmega e Sousa, Penafiel, Portugal

* **Corresponding author**: i2450@ipoporto.min-saude.pt

Abstract

Introduction: *Epithelioid angiosarcoma is a rare high-grade vascular neoplasm with a poor prognosis.*

We present an anticoagulated 77-year-old man with a history of popliteal/soleal vein thrombosis in the previous month, complaining of ipsilateral persistent lower limb pain and claudication. Absent popliteal/distal pulses prompted an arterial Doppler ultrasound (DUS), revealing thrombosis of the distal superficial femoral artery and a popliteal mass. As the arterial wall's integrity could not be appropriately evaluated by DUS, adventitial cystic disease of the popliteal artery was suspected. Computed tomography angiography and magnetic resonance imaging findings were also suggestive. Due to refractory pain, he was submitted to a popliteal mass excision and a femoral-posterior tibial bypass. Pathology revealed an epithelioid angiosarcoma. He was referred to a Sarcoma Center, requiring hospitalization for agitation and fever. A positron emission tomography (PET) scan revealed extensive lower limb disease persistence and distant metastases. He died on the 56th day after surgery.

To our knowledge, only 15 cases of angiosarcoma of the popliteal artery are described in the literature. Ours stands out as the first one unrelated to a popliteal aneurysm.

As it is a highly aggressive tumour, an early diagnosis is challenging but essential to a successful treatment, warranting the need for suspicion of this neoplasm. An early core biopsy or surgical sample may expedite the diagnosis.

Keywords: *Surgical Oncology; Vascular surgery; Diagnosis, Differential; Angiosarcoma*

INTRODUCTION

Angiosarcoma is a rare malignancy of endothelial origin, comprising 1 to 2% of all soft tissue sarcomas[1]. Its histology may vary from well-differentiated to high-grade tumours and this neoplasm may arise anywhere, with the most common locations being the skin, soft tissue, breast, and liver[2]. However, primary arterial angiosarcomas are most frequently found in the pulmonary artery and aorta[3].

Epithelioid angiosarcoma is a subtype of angiosarcoma, constituting a rare high-grade vascular neoplasm with predominantly epithelioid-appearing malignant endothelial cells deriving from vascular or lymphatic cell lines [4]. Given the ubiquity of blood vessels and lymphatics in the body, epithelioid angiosarcoma can occur anywhere but is more commonly found in the deep soft tissues of the extremities (namely intramuscular, corresponding to areas with vast lymphovascular supply) or in other locations such as the thyroid gland, skin, adrenal glands and bone[4,5]. Typically occurring in men around the seventh decade of life, with few described pediatric cases, it is an aggressive tumour that tends to invade locally and metastasize early, either to the lymph nodes or solid organs such as the lungs, soft tissue and skin. Its poor prognosis translates into a 10-15% five-year survival rate[4,5,6,7].

Diagnosis is challenging due to an insidious and non-specific presentation (an asymptomatic mass, erythematous to violaceous lesions or local symptoms of pain, erythema and swelling) and nonspecific imaging findings[17]. In addition, some patients may exhibit symptoms attributed to a hypocoagulable state (ecchymosis, gastrointestinal bleeding or persistent hematoma)[4]. Although most angiosarcomas occur spontaneously, there are known risk factors that may raise suspicions about the diagnosis, such as previous ther-

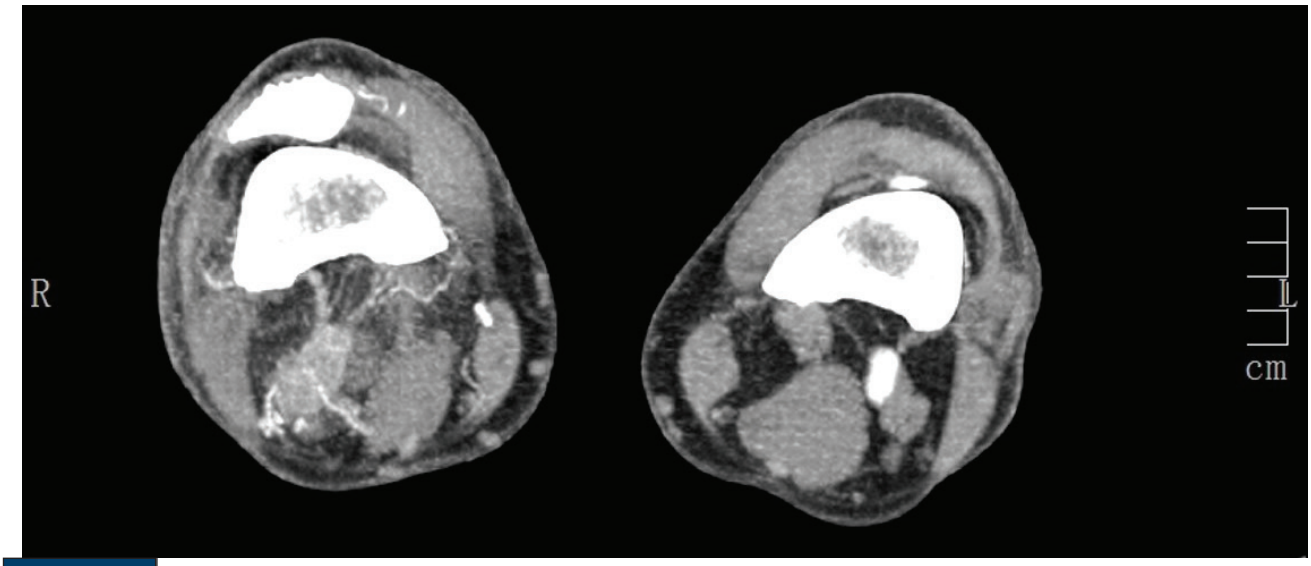

Figure 1

Lower limb CTA showing occlusion of the right popliteal artery with permeabilization of the leg arteries. Images with a vaguely nodular periarterial morphology are observed in the occluded segment, which may correspond to adventitial cystic disease. However, the clinical information of concomitant deep vein thrombosis (not evaluated in this exam, where only arterial phase images were obtained) interprets these images at the popliteal level complex. No other arterial segments of the lower limbs show signs of stenosis or occlusion.

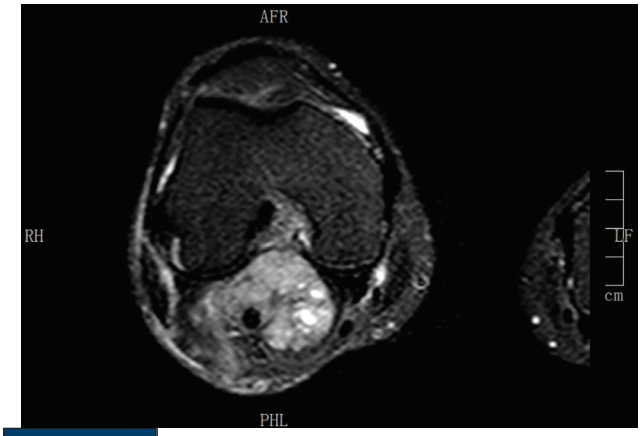

Figure 2 a)

(a) Axial view
Magnetic resonance angiography. The report confirmed thrombosis of the right popliteal artery and vein and identified multiple complex cystic formations with not completely liquefied contents in about 16 cm of a longitudinal extent. These complex cystic formations accompany the distal course of the superficial femoral artery and the popliteal artery, centred in these structures. Contrast uptake is seen only in the cystic wall. No uptake is identified within the lesions. The radiologist found it unlikely to be a neoplastic lesion and diagnosed it as a particularly exuberant form of adventitial cystic disease of the popliteal artery, despite the age group not being the most characteristic. There are no signs of vascular obstruction or adventitial cystic disease in the left lower limb.

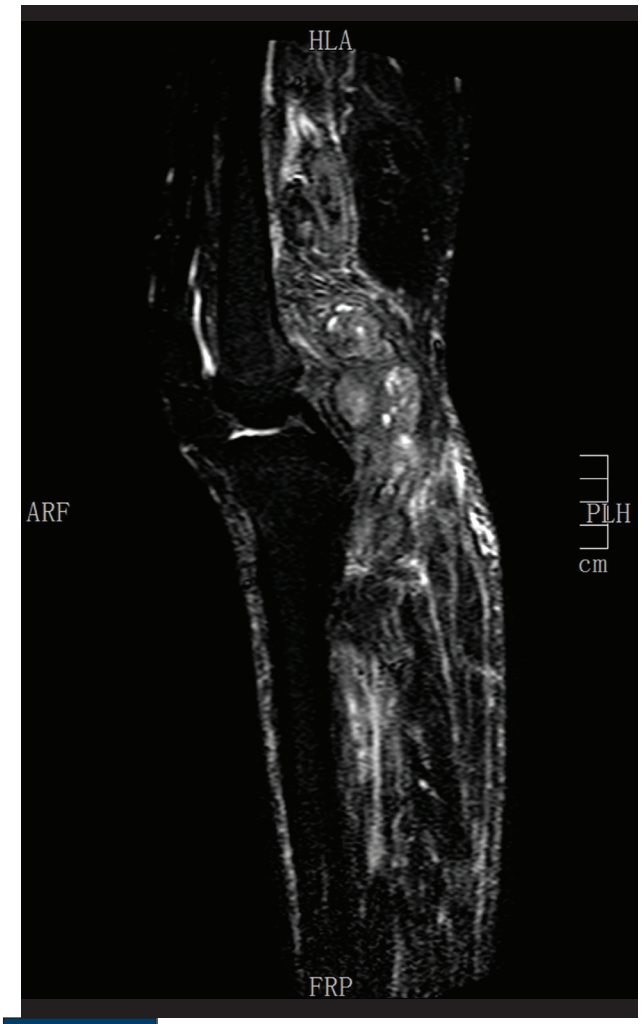

Figure 2 b)

(b) Sagittal view

apeutic radiation, chronic lymphedema (Stewart-Treves syndrome), in association with foreign bodies such as synthetic vascular grafts or orthopedic hardware/prostheses or exposure to toxins (thorotrast, vinyl chlorides, insecticides)[1,4,6,7,8].

Surgery is the mainstay of treatment, but recurrence is common despite adequate resection margins due to occult tumour spread. Adjuvant radiation therapy may be helpful, while adjuvant chemotherapy is controversial, with

reports that paclitaxel-based chemotherapy might improve survival[1,4,7,8].

We describe a case of primary epithelioid angiosarcoma of the popliteal artery. This rare case had an unusual presentation as deep venous thrombosis and suspected adventitial cystic disease of the popliteal artery in a patient without risk factors for angiosarcoma.

CLINICAL CASE

A 77-year-old man was referred to a vascular surgery appointment following complaints of ipsilateral persistent lower limb pain, paraesthesia at rest, and claudication. He had no relevant medical history except for a diagnosis of right popliteal and soleal vein thrombosis in the previous month, treated with apixaban 5mg q12h.

At clinical examination, he presented swelling of the right leg and absent popliteal and distal pulses. The arterial Doppler ultrasound (DUS) revealed a recent-appearing thrombosis of the distal third of the superficial femoral artery and a bulky mass at the popliteal fossa. As the arterial wall's integrity could not be assessed, the diagnostic hypotheses were a thrombosed popliteal aneurysm or adventitial cystic disease. Further investigation with computed tomography angiography (CTA) (Figure 1) and magnetic resonance imaging (MRI) (Figure 2) suggested adventitial cystic disease of the popliteal artery. It was reported as unlikely to be a neoplastic lesion.

As the patient maintained constant intense and refractory pain, surgery was proposed. With the patient in a prone position, a posterior approach was conducted, and intra-operatively, a popliteal hard elastic mass was dissected, sectioned off of the superficial femoral artery proximally and the crural vessels distally and then thoroughly excised. A femoral-posterior tibial bypass was performed using a composite graft of expanded polytetrafluoroethylene (ePTFE) and a contralateral inverted great saphenous vein graft for revascularization. Surgery and postoperative period were uneventful. The pathology report revealed an epithelioid angiosarcoma and the patient was referred to a Sarcoma Reference Center. While waiting for staging exams, he was hospitalized due to agitation, fever, pain and lower limb swelling. A neurologist observed the patient who performed a lumbar puncture and requested a brain computed tomography (CT) scan, both without relevant findings. Blood and

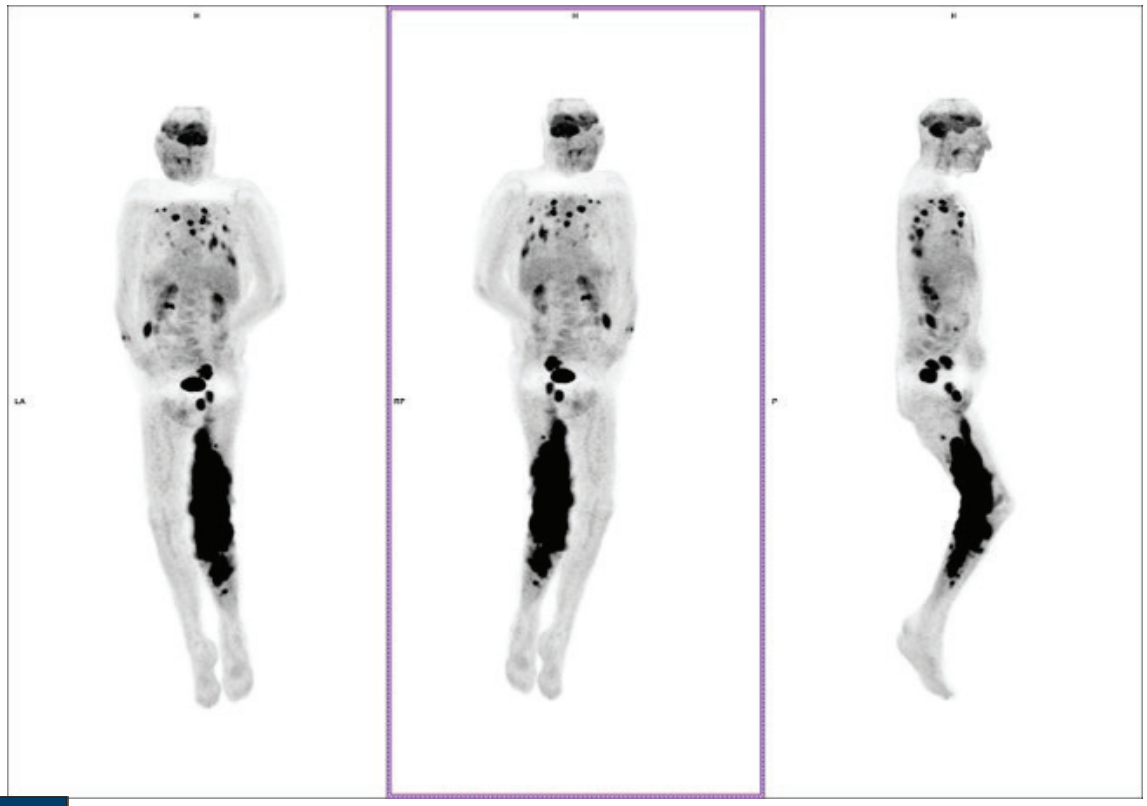

Figure 3

Whole body 18F-FDG PET/CT. Sensitivity and anatomical recording of the scan are impaired by the patient's inability to cooperate (agitation). Extensive and high 18F-FDG metabolism in voluminous coalescing lesion/lesions of the medial and posterior surfaces of the right thigh and proximal half of the ipsilateral leg; focal 18F-FDG uptakes in the vicinity of the posterior surface of the middle third of the ipsilateral tibia and the proximal region of the posterior surface of the right thigh. These findings are suggestive of malignant involvement. Radiopharmaceutical uptake in right inguinal lymph nodes, right external and internal iliac lymph nodes, and bilateral pulmonary lesions compatible with metastases. Additionally, there are foci/areas of 18F-FDG hypermetabolism at the thoracic level, apparently on bilateral costal arches and the right scapula, suspected of secondary bone involvement.

Table 1 **Review of cases of angiosarcoma of the popliteal artery (F, female; M, male; yo, years-old; AS, angiosarcoma)**

Author, year	Gender, age	Presentation	Previous surgery	Time from surgery to AS	Pathology	Metastases at diagnosis	Treatment	Outcome
Croft et al., 1890	M, 71yo	Popliteal aneurysm	Femoral ligation	3 months	Sarcoma	Unknown	Limb amputation	Dead after 1 year
Di Saviero et al., 1995	M, 69yo	Popliteal aneurysm expansion	Venous bypass	1 year	Angiosarcoma	No	Local resection + Radiotherapy	Unknown
Kogon et al., 1998	M, 70yo	Occluded popliteal artery, pseudoaneurysm	Prosthetic bypass	Unknown	Epithelioid angiosarcoma	No	Hip disarticulation + Radiotherapy	Unknown
Nocturne et al., 2010	M, 81yo	Popliteal aneurysm expansion	Venous bypass	15 years	Angiosarcoma	No	Radiotherapy	Dead after 7 months
Cristaudo et al., 2012	M, 79yo	Popliteal aneurysm expansion	Bypass (not detailed)	18 months	Epithelioid angiossarcoma	Lung/nodes	Refused treatment	Dead after 2 months
Bader et al., 2016	M, 72yo	Knee pain	Bypass (not detailed)	7 years	Epithelioid angiossarcoma	No	Unknown	Unknown
Cherchi et al., 2017	F, 64yo	Popliteal aneurysm expansion	Prosthetic bypass	4 years	Angiosarcoma	Unknown	Unknown	Dead 17 days after diagnosis
Chetouani et al., 2017	M, 81yo	Inflammatory syndrome of unknown origin	Prosthetic bypass	1 year	Intimal angiosarcoma	Lung	Unknown	Unknown
Garg et al., 2018	F, 8 months	Primary thick walled aneurysm	Primary AS (no previous surgery)	-	Intimal sarcoma	No	Complete resection	Lost in follow-up after 1 year
Morris et al., 2018	M, 69 yo	Occluded bypass, pseudoaneurysm	Venous bypass	2 years	Angiosarcoma	Lung	Radiotherapy	Died 3 months after surgery
Catalan et al., 2019	M, 74 yo	Popliteal aneurysm expansion	Venous bypass	8 years	Angiosarcoma	Lung	Hip disarticulation	Dead after 3 months
Fabian et al., 2019	M, 74 yo	Thrombosed popliteal aneurysm	Primary AS (no previous surgery)	-	Angiosarcoma	Lung/nodes	Limb amputation	Dead a few days after surgery
Werra et al., 2021	M, 83 yo	Popliteal aneurysm expansion	Venous bypass	3 years	Epithelioid angiosarcoma	No	Limb amputation	Dead after 1 month
Arts et al., 2022	F, 79 yo	Popliteal aneurysm expansion	Venous bypass	9 years	Epithelioid angiosarcoma	Lung	Limb amputation	Dead after 8 months
Our case, 2022	M, 77 yo	Deep venous thrombosis, suspected adventitial cystic disease	Primary AS (no previous surgery)	-	Epithelioid angiosarcoma	Lung/nodes/ bone	Palliative treatment	Dead after 2 months

urine cultures were negative and empiric broad-spectrum antibiotics were instituted considering the inflammatory signs and aggravated lower limb swelling. An MRI of the lower limb was also scheduled, but impossible to perform due to the patient's agitation. The following positron emission tomography (PET) scan revealed extensive persistence of disease in the lower limb and nodal, pulmonary and possibly bone metastases (Figure 3). Following an unfavourable clinical evolution, the patient was observed in a Multidisciplinary Team Meeting and was considered unfit for systemic treatment. He died on the 56th day after surgery.

DISCUSSION

Epithelioid angiosarcoma is a rare and highly aggressive tumour. As previously described, preoperative diagnosis is challenging due to a nonspecific and insidious presentation and nonspecific imaging findings[1], as we could observe in this case in which the patient had no risk factors for angiosarcoma and presented with the typical signs of pain and swelling that were interpreted in light of the recent deep venous thrombosis diagnosis and the imaging findings suggestive of adventitial cystic disease of the popliteal artery.

To our knowledge, only 14 additional cases of angiosarcoma of the popliteal artery are described in the literature[1,3,5,6,9,10,11]. Patients were predominantly male (n=11) with a median age of 73 (8 months – 83 years). Two of these were cases of primary angiosarcoma (without previous vascular surgery) initially diagnosed as popliteal artery aneurysm; the remaining 12 were secondary angiosarcoma in popliteal aneurysms/pseudoaneurysms, diagnosed at a median of 3 years after the initial surgery (3 months – 15 years)[3, 9]. Our case stands out as there were no descriptions of a primary popliteal artery angiosarcoma unrelated to a popliteal aneurysm (Table 1). A diagnostic preoperative fine needle aspiration was performed in one case[1], and a core biopsy was performed in two patients following radiological suspicion[5,10]. Two patients underwent surgical biopsies during revision procedures as highly suspicious lesions were found[3,9], and two other patients had surgical biopsies performed in the setting of emergent interventions due to hemorrhage mimicking a ruptured popliteal aneurysm[6,11]. Despite the bleeding risk, several studies advocate for a preoperative core biopsy to obtain a definitive diagnosis. Considering the risk factors already described, a core biopsy or surgical sample should be obtained for suspicious masses in the popliteal fossa (heterogeneous lesions, ill-defined margins, atypical enhancement of arterial wall, invasion of surrounding tissues, disorganized vasculature or neovascularization), and for aneurysms requiring revision surgery (due to aneurysm sac expansion or symptoms needing surgical decompression).

Additionally, in asymptomatic secondary aneurysmal growth without surgical indication, a CTA, MRI or PET scan should be performed, followed by a core needle biopsy if suspicious findings are encountered, especially in constitutional symptoms[1,3,6,9]. In 7 of these 15 cases (including ours), patients had lung metastases at the diagnosis and 4 developed local recurrence or distant metastases after the initial treatment. Regarding treatment, six patients were submitted to surgical resection (either amputation or local resection), 2 had surgery followed by adjuvant radiotherapy, two only received radiotherapy and the remaining were offered palliative or unknown treatment. Unfortunately, every patient described in this information (10 out of 15) died within one year after the diagnosis[3,9].

CONCLUSION

Given the poor prognosis of epithelioid angiosarcoma, clinical and radiological suspicion is paramount to an early diagnosis. To increase the likelihood of a successful treatment, we advocate that a preoperative core biopsy should be considered for every atypical, ill-defined cystic mass in the popliteal fossa.

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