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CASE REPORT

Primary angiosarcoma of the fibula : A case report

Yener SAGLIK, Yusuf YILDIZ, Hakan ATALAR, Kerem BASARIR

From Ankara University, Ankara, Turkey

Primary vascular neoplasms of bone are rare and have a poor prognosis. Angiosarcoma of bone originates in vascular endothelial cells within bone tissue. Patients may present with unifocal or multifocal osseous disease. The most commonly involved bones are femur and tibia, followed by pelvis, vertebral column and bones of the upper limb. Here we present a 72-year-old male patient who had primary angiosarcoma of the fibula. He was treated with amputation, and the metastases that later emerged were successfully managed with chemotherapy.

Keywords : angiosarcoma ; bone neoplasms ; vascular tissue neoplasms.

INTRODUCTION

The term angiosarcoma refers to malignant vascular tumours that have many functional and morphologic features of normal endothelium, and is used for all sarcomas showing endothelial differentiation (*18*). Approximately 6% of all angiosarcomas are found in bone (*18*). Primary angiosarcoma arising in bone is very rare, and accounts for less than 1% of malignant bone tumours (*16*).

A variety of terms has been used in the literature regarding bone tumours of vascular origin. The term haemangioendothelioma of bone has been used to describe malignant tumours that arise from endothelial cells in bone (*19*). This term has also been used to describe vascular tumours that are intermediate between haemangioma and conventional angiosarcoma (*10,18*). However, Unni has used the term haemangioendothelioma as a synonym for angiosarcoma (*16*). Campanacci defined haemangioendotheliomas as a class of tumours ranging from high grade malignant to low grade malignant to benign, with the benign type including epitheloid haemangioendothelioma, epitheloid haemangioma, histiocytoid haemangioma and cellular haemangioma (*4*). Campanacci used the term angiosarcoma to refer to high grade haemangioendothelioma (*4*). In this article, Campanacci's definition of angiosarcoma is used.

Skeletal angiosarcoma generally affects young adults and elderly individuals, with a 2/1 male to female ratio (*7*). The bones of the lower limb, particularly the femur and tibia, are most commonly involved, followed by pelvis, vertebral column and bones of the upper limb (*7*). Angiosarcoma of the

■ Yener Saglik, MD, Professor.
■ Yusuf Yildiz, MD, Associate Professor.
Department of Orthopaedic Surgery and Traumatology, Ankara University, Ankara, Turkey.
■ Hakan Atalar, MD, Assistant Professor.
Department of Orthopaedic Surgery and Traumatology, Fatih University, Ankara, Turkey.
■ Kerem Basarir, MD, Consultant.
Department of Orthopaedic Surgery and Traumatology, Hakkari State Hospital Hakkari, Turkey.
Correspondence : Hakan Atalar, Alparslan Turkes Caddesi No : 57 06510 Emek / Ankara, Turkey.
E-mail : atalarhakan@yahoo.com

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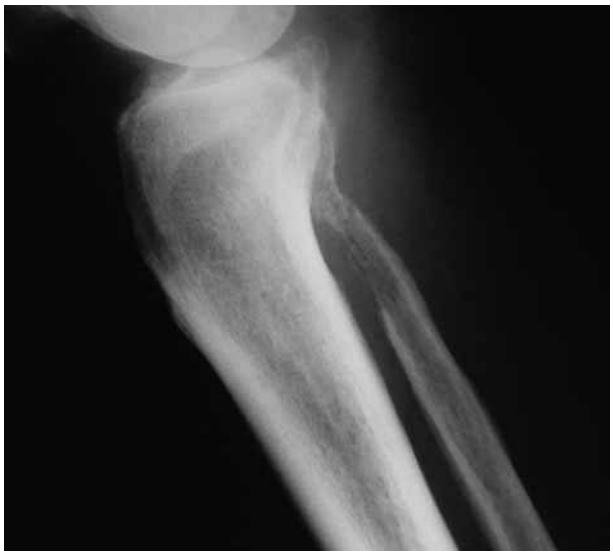

Fig. 1. — This plain lateral radiograph shows an osteolytic mass with irregular borders at the proximal fibula.

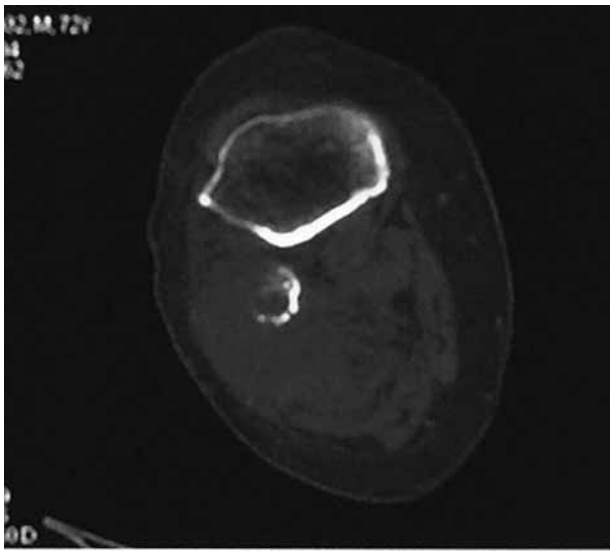

Fig. 2. — Computed tomography demonstrated cortical destruction in the fibula.

fibula is rare, and to our knowledge approximately 10 cases of fibular angiosarcoma have been reported (*4,5,9,13,14*).

CASE REPORT

A 72-year-old man presented with a three-month history of a painless mass below and lateral to his right knee. He had no history of trauma, and his past medical history was unremarkable except for diabetes mellitus. Physical examination revealed a mass in the region of the proximal fibula in the right leg ; the mass was approximately 10×7 cm in size, was non-movable and was tender to palpation. The results of routine laboratory tests were normal. Plain radiographs and computed tomography showed partial destruction of the proximal fibula (figs 1 & 2). Magnetic resonance imaging revealed a lesion with intermediate intensity on T1-weighted images and high intensity on T2-weighted images. Additionally, moderate heterogeneous enhancement was observed following gadolinium DTPA injection (fig 3a, b).

A Tru-cut biopsy was done and a diagnosis of angiosarcoma of bone was made histopathologically (fig 4). Microscopic examination revealed atypical endothelial cells forming dilated vascular channels. Nuclear atypia was prominent and mitotic figures were common. The vascular channels were lined with flat endothelial cells, and intraluminal budding was also observed. Immunohistochemical analysis showed CD-31 positivity which confirmed the vascular origin of the tumour.

At the time of diagnosis, computed tomography images of the thorax and abdomen were normal. Whole-body scintigraphy revealed increased uptake at the right upper fibula. Lower limb amputation (transfemoral) was performed. Postoperative chemotherapy was recommended to the patient, but he declined. He continued in follow-up for potential metastases, and at three months after surgery computerized tomography of the thorax showed nodules which were accepted to be metastases. The patient underwent three courses of chemotherapy including isosfamide 2500 mg/m^2, mesna 2500 mg/m^2 and adriamycin 60 mg/m^2. After chemotherapy the nodules regressed and the patient was free of disease at 29 months after the initial operation.

DISCUSSION

Angiosarcomas arise from vascular endothelium and commonly occur in soft tissue and skin. They

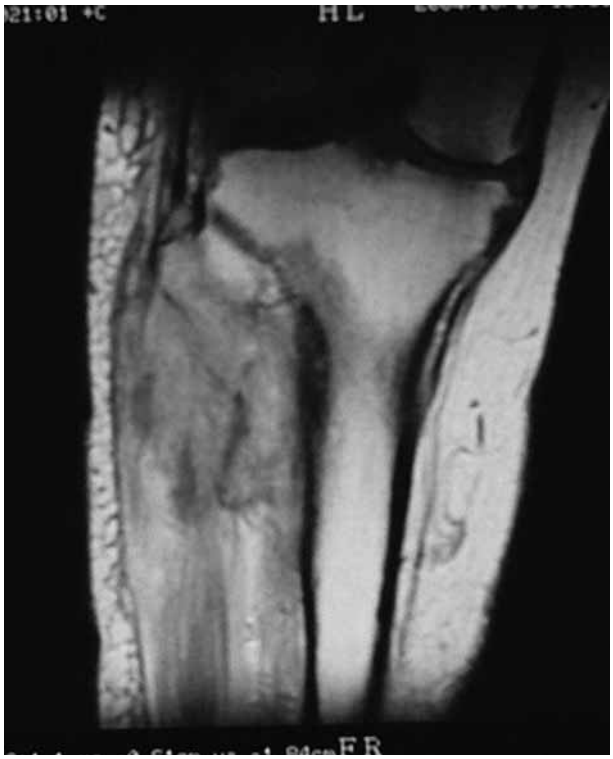

Fig. 3a. — This post-contrast coronal T1-weighted magnetic resonance image shows a contrast-enhancing destructive lesion with soft tissue invasion at the proximal fibula.

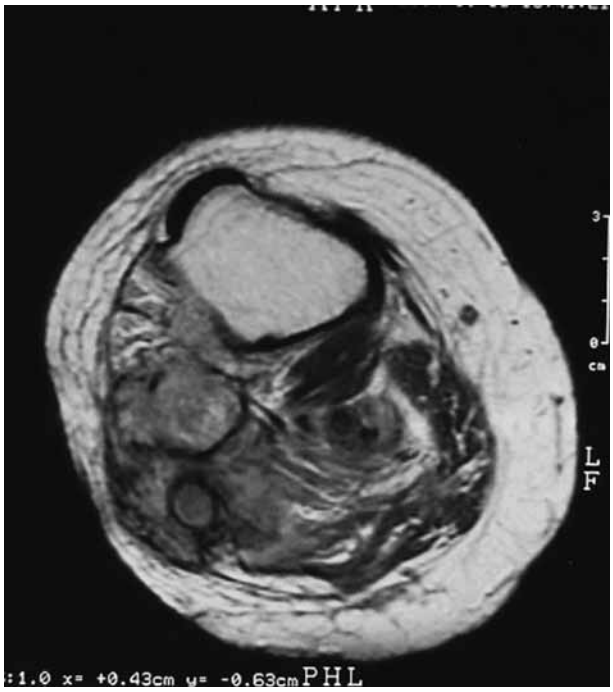

Fig. 3b. — This post-contrast axial T1-weighted magnetic resonance image reveals invasion of anterior, lateral and deep posterior compartments and involvement of the local neurovascular structures. Contrast enhancement of the tumour is also apparent.

can also originate in breast, spleen, liver, heart, and bone (*2,7,10*). Primary angiosarcoma in bone is very rare. It may occur in patients of any age but more commonly it occurs in middle age and later life (*4*). The clinical appearance of malignant vascular bone tumours can be variable, depending on the grade of the tumour (*19*). Pain and swelling are the predominant clinical features. On imaging studies, angiosarcoma of bone is generally a nonspecific, malignant-appearing lesion with ill-defined borders (*7,19*). A permeative and destructive pattern may also be seen. Given the degree of bone destruction seen with the tumour, periosteal reaction and pathologic fractures are relatively uncommon (*4,19*). Some lesions may show a mixed lytic and sclerotic pattern, but purely sclerotic lesions are rare. Computed tomography and magnetic resonance imaging are useful in determining the extent of the lesion and soft tissue involvement.

The aetiology of primary angiosarcoma of bone may be multifactorial. External beam radiation has been mentioned as a risk factor for the development of sarcomas in bone and soft tissue (*3*). Bone angiosarcoma developing in association with benign haemangiomas in bone in an atomic bomb survivor has been described (*20*). Angiosarcomas developing in bone adjacent to orthopaedic implants (*12*) and in bone infarcts (*1,6,11*) have been reported. Malignant haemangioendothelioma occurring in the tibia at the site of chronic non-fistulous osteomyelitis has also been reported (*9*).

When an angiosarcoma of bone is identified, a skeletal survey is recommended to evaluate whether the patient has multicentric disease. Multicentric skeletal angiosarcoma has been reported (*7,14*). Radiologically these lesions are osteolytic and involve the metaphysis with secondary extension to the epiphysis (*6*). Approximately 25% of patients

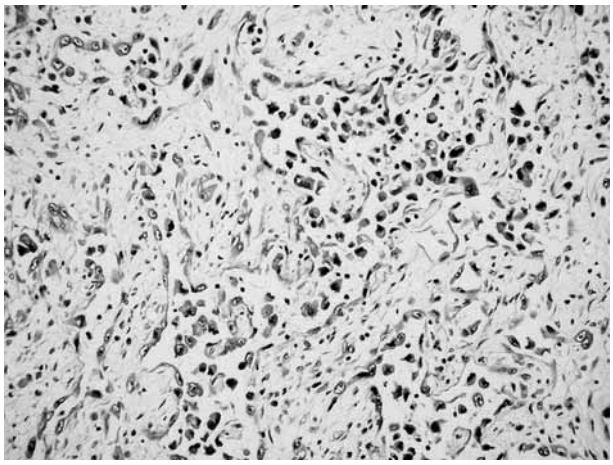

Fig. 4. — Microscopic examination revealed complex, irregular vascular structures containing endothelial cells with nuclear atypia and mitoses (haematoxylin-eosin, 200 ×).

who have angiosarcoma of bone present with multicentric disease (*19*). Multiple lesions can develop in a single bone or in multiple bones (*19*).

Since the majority of angiosarcomas of bone occur in adults, the differential diagnosis includes malignant diseases that produce bone lesions in this age group, such as metastases, myeloma, lymphoma, osteosarcoma and fibrosarcoma (*14,17,19*). Histologically, angiosarcoma of bone has an aggressive and variable appearance. Solid cellular sheets and spindling of the cells may be seen. Large, pleomorphic nuclei with clumped chromatin are common, as are frequent and atypical mitoses, and necrosis (*4*). Other histologic signs include anastomotic vascular channels with reticulum staining, proliferating endothelial cells in the basement membrane, the presence of embryonal-like vessels and Weibel-Palade bodies, and positivity for endothelial markers such as CD31, CD34, factor VIII related antigen and *Ulex Europeus* (*4,7*).

Malignant vascular tumours have a poor prognosis. Therapeutic alternatives for patients with angiosarcoma of bone are similar to those available for patients with other types of bone sarcomas, and involve radical resection or amputation. The role of radiation therapy and chemotherapy is being investigated (*8,15,19*). In our patient, amputation was necessary because of the extent of the tumour and its involvement of neurovascular structures. Our patient's metastases to lung, which emerged after amputation, were successfully treated with chemotherapy.

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