



## Case Report

# Primary angiosarcoma of the femur in a patient with Takayasu arteritis<sup>☆</sup>



Juliane Comunello\*, Suely Akiko Nakagawa, Felipe D'Almeida Costa, Wagner Santana Cerqueira, Wu Tu Chung, Fábio Fernando Eloi Pinto

Hospital AC Camargo Cancer Center, São Paulo, SP, Brazil

### ARTICLE INFO

#### Article history:

Received 28 December 2016

Accepted 2 May 2017

Available online 5 April 2018

#### Keywords:

Primary angiosarcoma

Bone neoplasm

Metastatic neoplasm

Takayasu arteritis

#### Palavras-chave:

Angiossarcoma primário

Neoplasia óssea

Metástase neoplásica

Arterite de Takayasu

### ABSTRACT

Primary osseous angiosarcoma is a rare entity with variable biological behavior and poor prognosis. Little is known about the oncologic treatment and its etiology is still unknown. This study presents a case of lytic lesion in the right femur with dissemination to other bones, such as the vertebral column and skull, and to the lungs and central nervous system. Orthopedic surgery was performed in order to improve quality of life. Surgical specimen confirmed the diagnosis of high-grade malignant osseous angiosarcoma. Despite oncologic and orthopedic treatment, the patient had rapid and aggressive progression with a poor outcome.

© 2017 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### Angiossarcoma primário do fêmur em um paciente com arterite de Takayasu

### RESUMO

O angiossarcoma ósseo (AO) é uma patologia rara de comportamento biológico variável e com prognóstico reservado. Pouco se conhece sobre o seu tratamento oncológico e sua etiologia ainda é desconhecida. Os autores apresentam um caso de lesão lítica em fêmur proximal que se disseminou para outros ossos (tais como coluna e crânio), pulmão e sistema nervoso central. Foi instituído tratamento ortopédico, com vistas a uma melhoria da qualidade de vida e ao conforto do paciente. O diagnóstico de AO maligno de alto grau foi confirmado pelo espécime cirúrgico. Apesar disso e do tratamento oncológico feito, o paciente apresentou uma evolução rápida e agressiva com desfecho desfavorável.

© 2017 Sociedade Brasileira de Ortopedia e Traumatologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<sup>☆</sup> Study conducted at the Hospital AC Camargo Cancer Center, São Paulo, SP, Brazil.

\* Corresponding author.

E-mail: [jucomunello@gmail.com](mailto:jucomunello@gmail.com) (J. Comunello).

<https://doi.org/10.1016/j.rboe.2018.03.014>

2255-4971/© 2017 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Bone angiosarcoma (BA) is a rare entity of unknown etiology that affects long bones. The diagnosis is often challenging, and the disease presents an unpredictable clinical course. The treatment is still controversial, with an unfavorable prognosis. Takayasu arteritis is a primary large vessel vasculitis, affecting vessels such as the aorta and its branches.

This study is aimed at presenting a case of BA in a patient with Takayasu arteritis.

## Case report

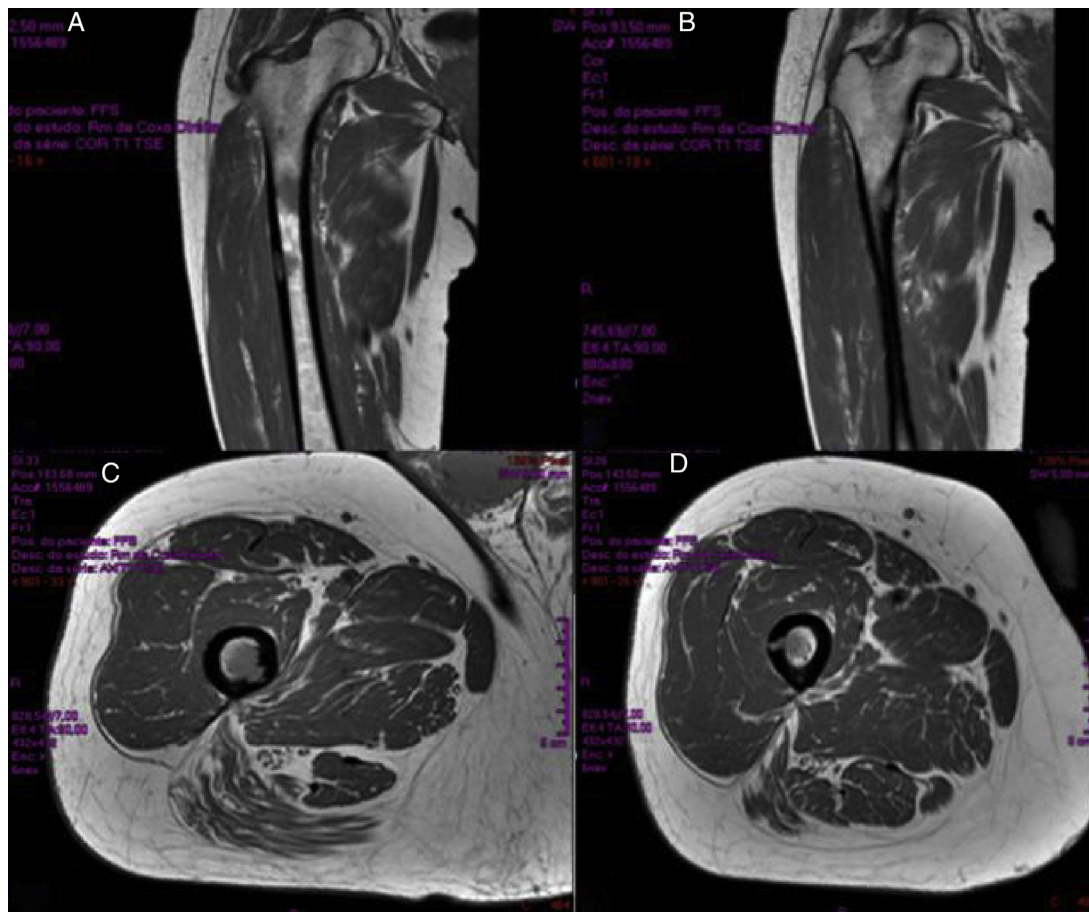
Through a medical record review, the authors present the case of a 57-year-old male white patient who presented with pain in the right thigh. He reported the following comorbidities: Takayasu arteritis with thoracoabdominal aortic aneurysm, upper mesenteric artery, and left subclavian artery obstruction.

In December 2014, simple radiographs were taken, which showed osteolytic lesions in the right proximal femur (Fig. 1).

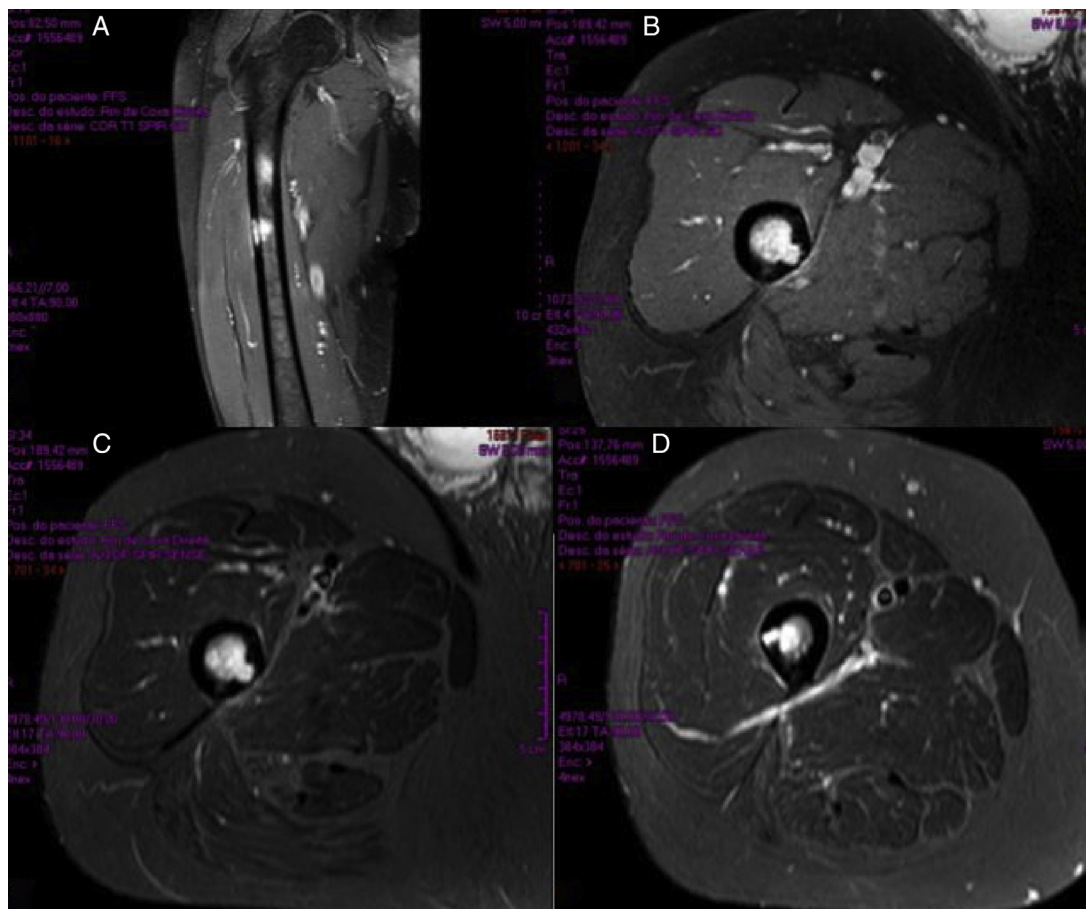
Magnetic resonance imaging of the right thigh was performed (Figs. 2 and 3), as well as total body bone scan, chest



**Fig. 1** – Simple radiograph of the right thigh in the anteroposterior (AP) and lateral (L) views, showing two partially delimited osteolytic lesions in the juxta-cortical bone marrow of the proximal/medial femoral diaphysis, with extension to the adjacent bone cortex, superiorly in the medial portion and inferiorly on the lateral side.



**Fig. 2** – Magnetic resonance imaging (MRI) in the T1 sequence. Coronal juxta-cortical bone marrow lesions with invasion and marked areas of cortical thinning located in the cortical region of the proximal/middle third of the right femur. No extension toward the extra-osseous soft tissue is observed. (A) and (B) Coronal cuts. (C) and (D) Axial cuts.



**Fig. 3 – STIR sequence in magnetic resonance imaging (MRI). (A) Coronal cut. (B)–(D) Axial cuts evidence the high signal and invasion and destruction of the cortical bone.**

tomography, and positron emission tomography–computed tomography (PET–CT; Fig. 4

After imaging, a thick-needle bone biopsy of the right femur guided by tomography was performed. Microscopy revealed small tissue fragments with abundant hemorrhagic material, composed of epithelioid neoplastic cells. These cells showed strong positivity for cytokeratin AE1/AE3 and CAM5.2, as well as for vascular markers (CD31 and FLI1), leading to the diagnosis of high-grade malignant epithelioid angiosarcoma (Fig. 5).

After a multidisciplinary clinical meeting, the treatment decided on was neoadjuvant chemotherapy, extensive resection of the lesion, and replacement with a non-conventional proximal femoral endoprosthesis.

The analysis of the surgical specimen showed a lack of response to chemotherapy. In November 2015, the patient presented disease progression affecting the spine (L2) and lung, also confirmed by biopsy. Chemotherapy with paclitaxel was initiated, followed by radiotherapy (RT 3D) from L1 to L3 ( $10 \times 300$  cGy).

In the course of cancer treatment, in May 2016, the disease progressed again into the lungs and bones, requiring RT 3D in the frontal region ( $10 \times 300$  cGy) and a change of chemotherapy to epirubicin and ifosfamide.

Due to the imminent risk of pathological fracture, prophylactic fixation of the left femur using a long cephalomedullary implant and bilateral acetabular cement was also indicated. One week prior to surgery, the acetabular and femoral lesions were embolized to avoid excessive intraoperative bleeding.

One month later, with advanced bone and lung disease and progression to the central nervous system, he became bedridden, with intense pain and increasingly frequent episodes of mental confusion.

After discussion between clinical oncology and palliative care teams and with the patient's relatives, palliative care was chosen. The patient died in September 2016.

## Discussion

The first malignant vascular bone tumor was described in 1921 by Wells.<sup>1</sup> BA accounts for less than 1% of the primary malignant tumors of bone; it originates in the endothelial cells, but its etiology remains unknown. Among the proposed classifications, the authors consider it to be a high-grade malignant neoplasm, primary or secondary to radiotherapy or bone infarctions.<sup>2–4</sup>

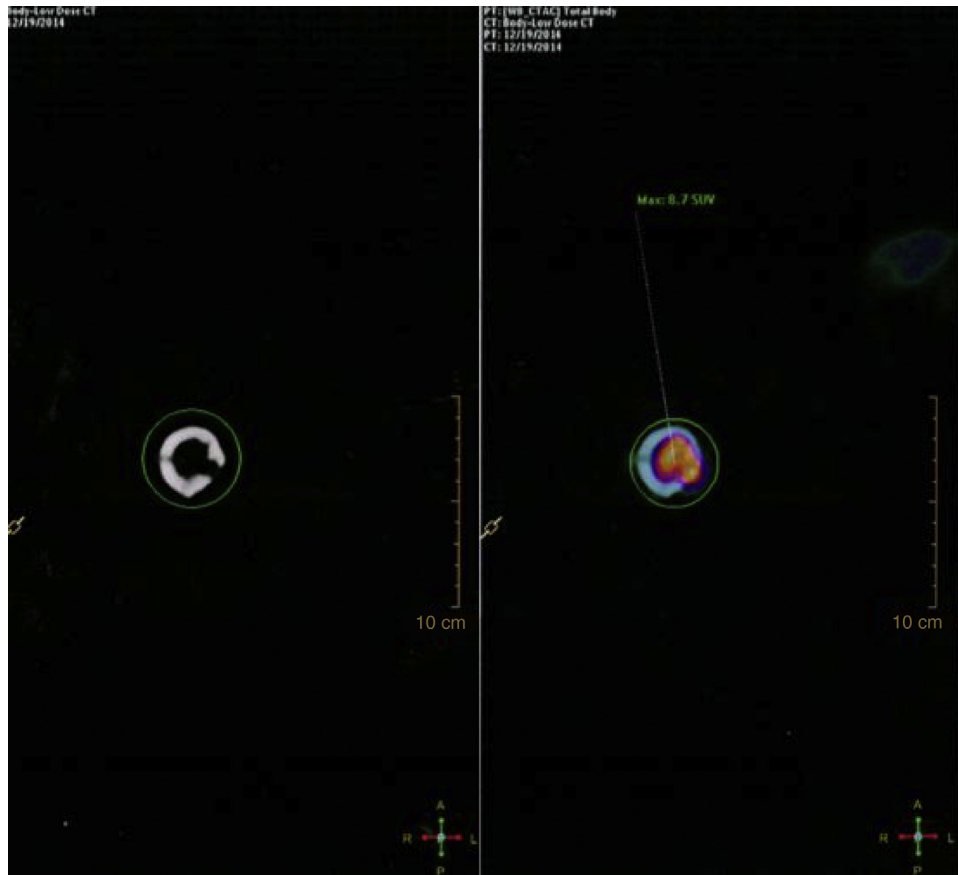


Fig. 4 – PET-CT with 18-FDG concentration/anomalous glycolytic metabolic activity in projection of the proximal/medial femoral diaphysis, with invasion/rupture of the cortex, corresponding to the bone lesions described in the previous studies.

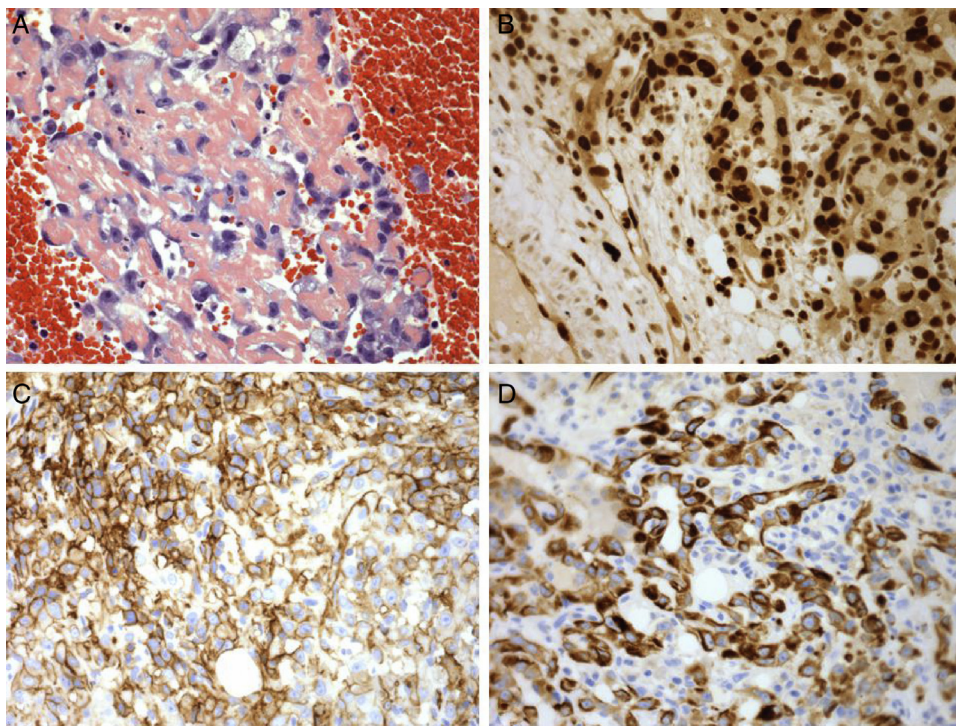


Fig. 5 – (A) Biopsy showing epithelioid cells and formation of vascular spaces (hematoxylin-eosin stain, 400 $\times$ ). (B) Expression of CD31 membrane marker. (C) Nuclear expression of FLI-1. (D) Cytoplasmic expression of CAM5.2.

It can be multicentric in up to one-third of the cases; the differential diagnosis with metastatic carcinoma is paramount.<sup>5,6</sup> It can affect any age group without gender preference, affecting primarily long tubular bones.<sup>7</sup>

Most BA originate in deep soft tissues of the extremities; however, other primary sites have been described, such as the thyroid gland, the adrenal gland, and the skin.<sup>7</sup>

Different studies have sought to describe vascular lesions that arise in the bone, creating several nomenclatures. Even today, it is not easy to define whether there are different pathologies with similar characteristics or if it is a single entity with different clinical presentations.<sup>1</sup>

Many cases of BA described in the literature present an aggressive clinical course; they are initially investigated as metastatic lesions of an unknown primary site. Patients usually have severe pain at the bone lesion site, whether or not associated with the tumor mass. Radiologically, these are purely lytic and eccentric lesions, which rupture the cortex and may have associated soft tissue components. Lacunar and multifocal bone lesions suggest lesions of vascular origin, which ought to draw attention to this diagnostic hypothesis.<sup>8</sup>

An immunohistochemical analysis is important for the diagnosis; it is positive for AE1/AE3 and CAM5.2 cytokeratins, as well as for vascular markers (CD31, FLI1). Factor VIII, epithelial membrane antigen (EMA), and CD68 may also be positive. In contrast, CD1a, HBMB45, CD45, desmin, smooth muscle actin, and lysozyme are negative.<sup>9,10</sup>

Only a few biomolecular studies on BA have been conducted. Cytogenetic studies have documented chromosomal alterations and diverse amplifications, suggesting a wide genetic heterogeneity.

The treatment is similar to that of bone sarcomas, and includes neoadjuvant chemotherapy and wide excision; adjuvant radiotherapy may be associated. The prognosis is poor, with a one-year survival rate of 55% and a five-year survival of approximately 33%.<sup>2,3</sup>

The authors believe that this is the first report of bone BA in a patient with Takayasu arteritis. No correlation between these pathologies has been described in the literature.

## Conflicts of interest

The authors declare no conflicts of interest.

## REFERENCES

1. Wells HG. Relation of multiple vascular tumors of bone to myeloma. *Arch Surg.* 1921;2(3):435-42.
2. Weiss SW, Goldblum JR. *Enzinger and Weiss's soft tissue tumors.* 5th ed. Philadelphia: Mosby; 2008. p. 703-20.
3. Bovée JV, Rosenberg AE. *WHO classification of tumours of Soft Tissue and Bone.* 4th ed. Lyon, France: IARC; 2013. p. 337-8.
4. Abdelwahab IF, Klein MJ, Hermann G, Springfield D. Angiosarcomas associated with bone infarcts. *Skeletal Radiol.* 1998;27(10):546-51.
5. Mitsuhashi T, Shimizu Y, Ban S, Ogawa F, Hirose T, Tanaka J, et al. Multicentric contiguous variant of epithelioid angiosarcoma of the bone. A rare variant showing angiotropic spread. *Ann Diagn Pathol.* 2005;9(1):33-7.
6. Santeusano G, Bombonati A, Tarantino U, Craboledda P, Marino B, Birbe R, et al. Multifocal epithelioid angiosarcoma of bone: a potential pitfall in the differential diagnosis with metastatic carcinoma. *Appl Immunohistochem Mol Morphol.* 2003;11(4):359-63.
7. Sakamoto A, Takahashi Y, Oda Y, Iwamoto Y. Aggressive clinical course of epithelioid angiosarcoma in the femur: a case report. *World J Surg Oncol.* 2014;12:281.
8. Wenger DE, Wold LE. Malignant vascular lesions of bone: radiologic and pathologic features. *Skeletal Radiol.* 2000;29(11):619-31.
9. Verbeke SL, Bertoni F, Bacchini P, Sciò R, Fletcher CD, Kroon HM, et al. Distinct histological features characterize primary angiosarcoma of bone. *Histopathology.* 2011;58(2): 254-64.
10. Chen Y, Shen D, Sun K, Bao D, Song Q, Wang G, et al. Epithelioid angiosarcoma of bone and soft tissue: a report of seven cases with emphasis on morphologic diversity, immunohistochemical features and clinical outcome. *Tumori.* 2011;97(5):585-9.