Cent. Eur. J. Med. • 7(1) • 2012 • 73-77
DOI: 10.2478/s11536-011-0118-x

VERSITA

Central European Journal of **Medicine**

Metastatic lung angiosarcoma from a femoral subperiosteal origin

Case Report

Evi Vassalou[1], Evangelos Perdikakis[1]*, Elpida Giannikaki[2], Dimitris Mavroudis[3], Pavlos Katonis[4], Nikolaos Karkavitsas[5], Apostolos Karantanas[1]

[1]*Department of Medical Imaging, University Hospital, Heraklion 711 10, Greece*

[2]*Department of Pathology, University Hospital, Heraklion 711 10, Greece*

[3]*Department of Medical Oncology, University Hospital, Heraklion 711 10, Greece*

[4]*Department of Othopaedics, University Hospital, Heraklion 711 10, Greece*

[5]*Department of Nuclear Medicine, University Hospital, Heraklion 711 10, Greece*

Received 12 March 2011; Accepted 30 September 2011

Abstract: Primary malignant vascular bone tumors are unusual and include hemangioendothelioma, epitheloid hemangioendothelioma and angiosarcoma. Although few cases of primary bone angiosarcomas have been reported, those of femoral origin are even more infrequent. Such tumors diagnosis may be challenging due to their radiographic and histologic variety. We present a case of a 24-year-old woman with a subperiosteal diaphyseal angiosarcoma originating from the femoral bone and metastatic to the lung at the time of diagnosis. The clinical, histological and radiological features of this extremely rare lesion are presented.

Keywords: *Angiosarcoma/periosteum • Angiosarcoma/primary bone • Lung metastases • MR imaging/diagnosis*

© Versita Sp. z o.o.

1. Introduction

Malignant vascular bone lesions are rare. They represent a wide spectrum of tumors ranging from hemangioendothelioma at the well differentiated-low grade end to angiosarcoma at the poorly differentiated-high grade end. Epitheloid hemangioendothelioma is described as a histologically distinct endothelial bone malignancy [1]. The usual primary site of angiosarcomas is skin, soft tissues, breast, liver and heart and they metastasize to the lung regardless of their initial location [2-3]. We present a case of a subperiosteal angiosarcoma of the femur metastasizing to the lung, and describe its radiological and histological findings. To the best of our knowledge, this origin has not been previously described to the English literature.

2. Materials and methods

A 24-year-old, previously healthy, woman with a two month history of back pain, presented at the orthopedic department. She also commented on a few week durations soreness of the anterolateral aspect of her left upper thigh, denying any injury, as well as a ten days afternoon habitual fever. General fatigue was mentioned and body weight loss was ongoing.

The physical examination did not show any findings of the respiratory system. A local tenderness of the anterolateral aspect of her left upper femur with no motion restriction was found. No other remarkable signs were obvious. Laboratory tests showed elevated levels of ferritin and an ESR of 116. The additional tests were as follows: Hb:12.7 g/dl, Hct:38%, PTL:588.000 K/ul, WBC:11.500 K/ul, and CRP:18 mg/L.

Chest radiography demonstrated multiple nodules in the lung parenchyma bilaterally, confirmed on chest CT

* *E-mail: perdikakis_ev@yahoo.gr*

as well, which were considered as possible metastatic disease (Figure 1).

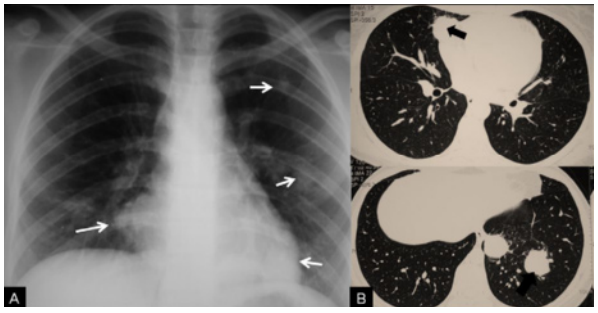


Figure 1. PA (**a**) chest radiograph shows multiple metastatic lesions (arrows). Axial (**b**) CT images demonstrate the two largest lesions (black arrows). The biopsy was performed to the one in the left lower lobe.

The patient underwent a CT guided biopsy. Pleomorphic epithelial and atractoid mesenchymatic cells with plenty of eosinophilic cytosomes, with a high degree of cytological atypia and nuclear pleomorphism, were revealed histopathologically. The neoplasmatic cells were forming occasional lumina combined with solid areas, and revealed an intense reactivity by the use of antibodies directed against CD31 and vimentin, testifying their endothelial origin. A metastatic angiosarcoma was considered as the most probable diagnosis due to the presence of multiple lesions. Due to the reported femoral pain, the patient underwent a radiograph which showed a subcortical, diaphyseal lytic lesion with unilaminal periosteal reaction (Figure 2a). Whole body scintigraphy showed no evidence of multifocal disease (Figure 2b).

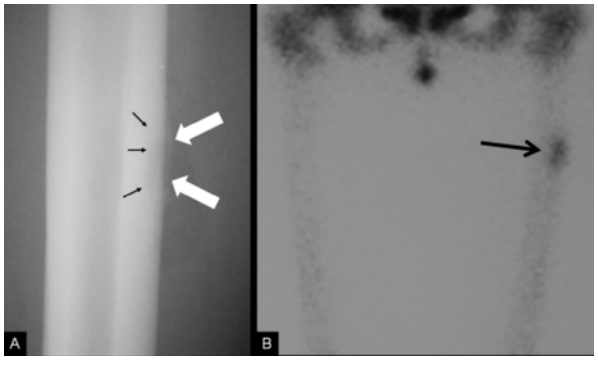


Figure 2. Radiograph (**a**) of the left femoral bone shows a thin periosteal reaction (white arrows) and an underlying lytic lesion (thin black arrows). Bone scan (**b**) shows a focal uptake on the proximal femoral diaphysis (thick black arrow).

A subsequent MR imaging study showed an intensively enhancing lesion which originated from the subperiosteum, surrounded by periosteal reaction (Figure 3).

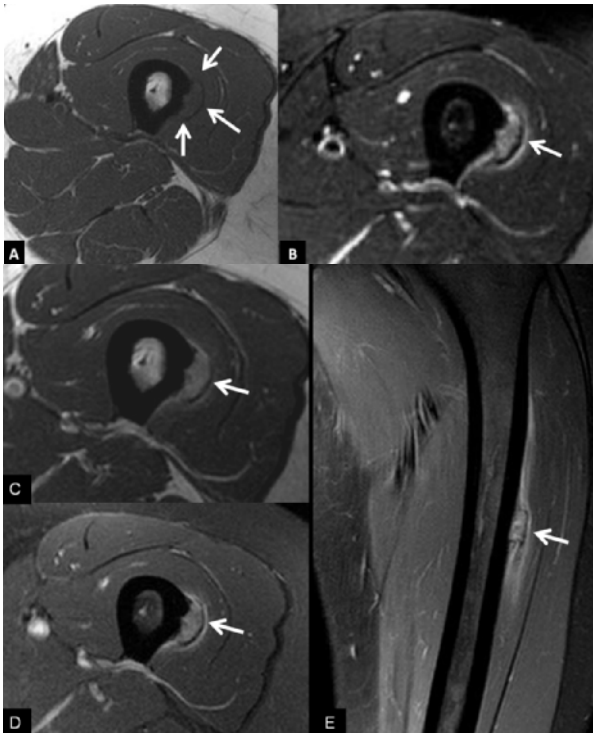
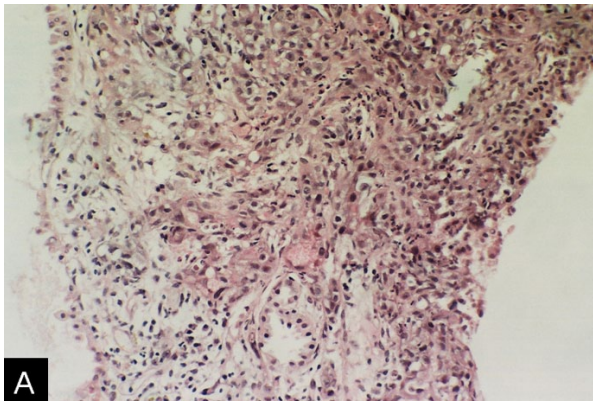


Figure 3. Axial (**a**) T1-weighted and axial (**b**) fat suppressed PD-weighted MR images, show the low and high signal intensity soft tissue lesion respectively, located between the cortex which is irregular and the periosteum which is elevated (arrows). Axial (**c**) non fat saturated, axial (**d**) fat suppressed and coronal (**e**) fat suppressed contrast enhanced T1-weighted MR images demonstrate the intense homogenous enhancement of the lesion (arrows).

Surgical curettage of the lesion was performed and the histopathological examination of periosteum and the soft tissue mass, revealed neoplasmatic cells exhibiting irregular vasoformation, identical to those found in the lung lesion (Figure 4). Neoplasmatic cells displayed high degree of cytologic atypia and pleomorphism as well as numerous mitotic figures. Regarding all the above, the final diagnosis was primary subperiosteal angiosarcoma of the femur metastasizing to the lung.



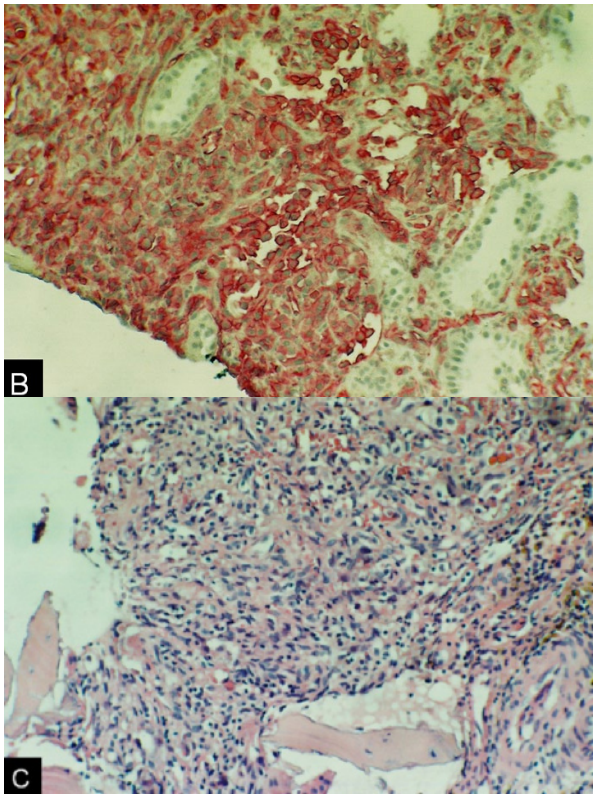


Figure 4. (**a**) High power view (Hematoxylin & Eosin stain) of angiosarcoma, composed of pleomorphic epithelioid endothelial cells forming occasional lumina, tissue sample from metastatic lung lesion. (**b**) Positive immunohistochemical staining for CD31 of the neoplastic cells. (**c**) High power view (Hematoxylin&Eosin stain) of angiosarcoma infiltrating bone tissue, tissue sample from femoral lesion.

The patient received chemotherapy without any significant response and she died of metastatic disease and sepsis 25 months after initial diagnosis.

3. Discussion

Angiosarcoma of bone is a rare primary bone sarcoma. The diagnosis is often delayed because of the non-specific clinical presentation and radiological features. Angiosarcomas represent a high grade form of hemangioendothelioma [1]. They account for 1-3 % of all sarcomas [1-4] and common sites of origin include the skin (33%) and deep soft tissues (24%). It also occurs in breast (8%), liver (8%), bone (6%), spleen (4%), heart, large vessels, and the pericardium (3%), eye sockets (3%), ear, nose, and throat (4%), and other organs including the lungs (7%) [1-5]. They may occur at any age but there is a preference for the third and fourth decades [1-5]. At the time of diagnosis of an angiosarcoma originating in bone, either a single lesion or multifocal disease may be apparent [1-6]. Common symptoms include pain and swelling [1-6]. Advanced stage disease carries unfavourable prognosis as in our patient.

The radiographic findings include a purely lytic with indefinite margins lesion or infrequently, a combination of both lytic and sclerotic areas. Intraosseous infiltration combined with cortical disruption and extraosseous tumor extension are occasional manifestations whereas periosteal reaction is quite uncommon [1]. In our case, however, the subperiosteal location provoked an intense periosteal reaction even identifiable on plain X-rays. MR imaging features of bone arising angiosarcomas are non specific [6-7]. High signal intensity on T1-w MR images may also be seen and represents hemorrhage [6-7]. Many reports on angiosarcomas following administration of contrast, describe heterogeneous or homogeneous enhancement [6-9].

Angiosarcomas tend to metastize to lung, bone, liver and lymph nodes regardless of their initial site, with lung representing their most frequent metastatic site [3,8,9]. Similarly in our case a small sized femoral lesion demonstrated a high grade metastatic pattern. The difference in incidence of lung involvement between primary and metastatic angiosarcoma, in combination with the illness course lead us to regard the femoral site as site of origin. Despite the fact that our patient suffered from back pain, fever and weight loss, these symptoms did not contribute to our primary clinical suspicion for an angiosarcoma's diagnosis. The lesions abutting the pleura might be responsible for the back pain due to local irritation. Metastatic pulmonary angiosarcoma encompasses a diversity of radiographic manifestations. Chest radiography may depict a multinodular pattern, often accompanied by perinodular infiltrates, pneumothoraces, and pleural effusions [8,9]. Both intranodular hemorrhagic necrosis and perilesional hemorrhage may be displayed on HRCT exams [3,8,9]. The nodular lesions demonstrate heterogeneous, and only rarely homogeneous enhancement on contrast enhanced CT [3,8,9]. Additional, rather rare CT characteristics include a solitary solid nodule presentation, a miliary pattern, multiple thin-wall cysts and air fluid levels indicating a hemorrhagic process due to neoangiogenesis.

Microscopically the most prominent characteristic of angiosarcomas, is their tendency for irregular vasoformation [1,10-16]. The degree of cytological atypia is remarkable and prominent, while nuclear pleomorphism as well as numerous mitotic figures is predominant. Areas of hemorrhage may be shown. Immunohistochemical staining for factor VIII (von Willebrand Factor), CD31 relative antigen and vimentin testify their endothelial origin [1,3,10-16]. The endothelial cell specific markers CD 31and VIII are by far the most valuable to identify

malignant vascular tumors and to exclude metastatic carcinoma, from the differential diagnosis. This immunohistochemical feature was particularly useful in our case since the initial clinical presentation and the associated X-ray and CT findings, prior to lung biopsy results, were indicative of a metastatic cancer of unknown primary.

A high-grade vascular metastatic neoplasm with a subperiosteal primary origin, not previously reported, is described in the present case report. Gupta A *et. al.* have previously presented a patient with a subperiosteal femoral conventional hemangioendothelioma [13]. A comparison of their imaging findings with our case could support their statement that the radiologic findings of primary bone angiosarcoma with those of hemangioendothelioma are indistinguishable. The lytic pattern, the local extent and the periosteal reaction are remarkably similar. Our findings as well as Gupta *et. al.* are in accordance with data from the already published article by Hisaoka M *et. al.*, who reported a case of spinal epitheliod hemangioendothelioma with epitheliod angiosarcomatous areas [17].

Currently there is no consensus in the literature regarding the exact histological criteria for diagnosing osseous angiosarcomas. A recent paper on a large series showed that 3 or more mitoses per 10 HPF, macronucleoli and fewer than 5 eosinophilic granulocytes per 10 HPF predict an aggressive behavior and poor outcome in primary osteosarcomas of the bones [18]. In our case the metastatic lung disease, the CT guided biopsy together with the excisional biopsy from the primary site and the immunohistochemical staining for CD31 relative antigen and vimentin aided in the correct diagnosis. However, as it was recently stated in a thorough review article upon primary vascular bone tumors by Verbeke SLJ and Bovée JV despite the fact that CD31 and von Willebrand Factor are considered the best diagnostic markers for malignant vascular bone tumors, the use of a panel of endothelial markers is necessary to confirm the diagnosis because a minority of the malignant tumors express only CD34 [19]. For the aforementioned reason relying solely on the expression of the endothelial markers the discrimination between benign and malignant vascular tumors is impossible [19].

In conclusion, a malignant vascular tumor of primary subperiosteal femoral origin is presented herein. Further studies are needed to elucidate the possible cytogenetics that may determine the course of primary vascular bone tumors from a benign lesion to the more aggressive counterparts.

References

[1] Wenger DE, Wold LE. Malignant vascular lesions of bone: radiologic and pathologic features. Skeletal Radiol 2000; 29:619-631

[2] Meis-Kindblom JM, Kindblom LG. Angiosarcoma of soft tissue: a study of 80 cases. Am J Surg Pathol 1998; 22:683-697

[3] Patel AM, Ryu JH. Angiosarcoma in the lung. Chest 1993; 103:1531-1535

[4] Murphey MD, Fairbairn KJ, Parman LM, Baxter KG, Parsa MB, Smith WS. Musculoskeletal angiomatous lesions: radiologic-pathologic correlation. Radiographics 1995; 15:893-917

[5] Scholsem M, Raket D, Flandroy P, Sciot R, Deprez M. Primary temporal bone angiosarcoma: a case report. J Neurooncol 2005; 75:121-125

[6] Thananopavarn P, Smith JK, Castillo M. MRI of angiosarcoma of the calvaria. AJR Am J Roentgenol 2003; 181:1432–433

[7] Chou YC, Chang YL, Harnod T et al. Primary angiosarcoma of the cranial vault: a case report and review of the literature. Surg Neurol 2004; 61:575-579

[8] Tateishi U, Hasegawa T, Kusumoto M et al. Metastatic angiosarcoma of the lung: spectrum of CT findings. AJR Am J Roentgenol 2003; 180:1671-1674

[9] Adem C, Aubry MC, Tazelaar HD, Myers JL. Metastatic angiosarcoma masquerading as diffuse pulmonary hemorrhage: clinicopathologic analysis of 7 new patients. Arch Pathol Lab Med 2001; 125:1562-1565

[10] Evans HL, Raymond AK, Ayala AG. Vascular tumors of bone: A study of 17 cases other than ordinary hemangioma, with an evaluation of the relationship of hemangioendothelioma of bone to epithelioid hemangioma, epithelioid hemangioendothelioma, and high-grade angiosarcoma. Hum Pathol 2003; 34:680-689

[11] Abraham JA, Hornicek FJ, Kaufman AM et al. Treatment and outcome of 82 patients with angiosarcoma. Ann Surg Oncol 2007; 14:1953-1967

[12] Wenger DE, Wold LE. Benign vascular lesions of bone: radiologic and pathologic features. Skeletal Radiol 2000; 29:63-74

[13] Gupta A, Saifuddin A, Briggs TW, Flanagan AM. Subperiosteal hemangioendothelioma of the femur. Skeletal Radiol 2006; 35:793-796

[14] Larochelle O, Perigny M, Lagace R, et al. Epithelioid hemangioendothelioma of bone. Radiographics 2006; 26:265-270

[15] Maclean FM, Schatz J, McCarthy SW, et al. Epithelioid and spindle cell haemangioma of bone. Skeletal Radiol 2007; 36:S50-57

[16] Weiss SW, Lasota J, Miettinen MM. Angiosarcoma of soft tissue. World Heath Organization Classification of Tumours. Pathology and genetics of tumours of soft tissue and bone. Lyon: IARC Press, 2002; 175-177

[17] Hisaoka M, Okamoto S, Aoki T, Yokoyama K, Hashimoto H. Spinal epitheliod hemangioendothelioma with epitheliod angiosarcomatous areas. Skelet Radiol 2005; 34:745-749

[18] Verbeke SLJ, Bertoni F, Bacchini P, et. al. Distinct histological features characterize primary angiosarcoma of bone. Histopathology 2011; 58:254-264

[19] Verbeke SLJ, Bovée JV. Primary vascular tumors of bone: a spectrum of entities? Int J Clin Exp Pathol 2011; 4:541-51