American Journal of Medical Case Reports, 2021, Vol. 9, No. 7, 345-347
Available online at http://pubs.sciepub.com/ajmcr/9/7/1
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-7-1

Metastatic Epithelioid Angiosarcoma of the Spine, Hip, and Femur

Eman EL-Sawalhy[1,*], Muna Shaaeli[1], Wehbi Hnayni[1], Lubna Alattia[2], Shahina Patel[3]

[1]Department of Internal Medicine, Beaumont Hospital, Dearborn, MI
[2]Department of Clinical Pathology, Beaumont Hospital, Royal Oak, MI
[3]Division of Hematology & Oncology, Internal Medicine Department, Beaumont Hospital, Dearborn, MI
*Corresponding author: Eman.elsawalhy@beaumont.org

Received February 19, 2021; Revised March 22, 2021; Accepted March 31, 2021

Abstract Epithelioid Angiosarcoma (EA) is an extremely rare and highly aggressive malignant tumor. It comprises <1 % of all soft tissue sarcomas and is associated with a poor prognosis. In this case report, we are reporting an 85-years-old male who presented with lower back and left hip pain. A computerized tomography (CT) of the lumbar spine and left hip showed a significant fracture of lumbar spine L3 and osteolytic lesions involving the left hip and femur. The patient underwent L1-L5 fusion with cement augmentation and biopsy of L3. Surgical pathology showed a metastatic undifferentiated tumor of unknown primary origin. Histologic analysis of the specimen and immunohistochemistry confirmed EA. Given extensive diffuse bone involvement, our patient was not a candidate for definitive surgical treatment.

Keywords: *Epithelioid Angiosarcoma, bone, surgical resection, Tazemetostat*

Cite This Article: Eman EL-Sawalhy, Muna Shaaeli, Wehbi Hnayni, Lubna Alattia, and Shahina Patel, "Metastatic Epithelioid Angiosarcoma of the Spine, Hip, and Femur." *American Journal of Medical Case Reports*, vol. 9, no. 7 (2021): 345-347. doi: 10.12691/ajmcr-9-7-1.

1. Introduction

EA is a malignancy of endothelial origin that can arise from a variety of primary sites including the spleen, kidneys, thyroid, adrenal glands, and deep soft tissues of the extremities. Bone is a very rare origin of this malignancy [1,2,3]. EA has a male predilection [3], it can occur at any age but the highest incidence is in the seventh decade. It is associated with a very poor prognosis, with more than 50% of patients dying within two to three years of diagnosis [3,4]. Early diagnosis and treatment improve long-term survival. Treatment plans may vary between individuals. The combination of surgical resection of the primary tumor plus radiotherapy is the main treatment modality [3].

2. Case Presentation

An 85-years-old man with a complex past medical history including Hypertension, Hyperlipidemia, Coronary artery disease with a history of bypass surgery, Pacemaker placement for a second-degree atrioventricular block, abdominal aortic aneurysm repair, chronic kidney disease, and history of prostate cancer, presented to our hospital with a chief complaint of worsening lower back and left hip pain for two months. He described his pain as intractable, localized, and non-radiating. He denied any recent falls or trauma, weakness, numbness, loss of bowel or bladder control. His vitals were stable. However, his labs were significant for normocytic anemia with a hemoglobin of 8.7 g/dl. CT scan of his lumbar spine and hip showed significant pathologic fracture involving the L3 vertebral body, smaller pathologic fracture involving the L2 superior endplate, and multiple lytic destructive bone lesions with adjacent soft tissue lesions involving the left hip and femur without evidence of pathologic fractures (Figure 1). Given these findings, multiple myeloma was in the differential diagnosis. Serum protein electrophoresis and flow cytometry were normal. The patient underwent L1-L5 fusion with instrumentation, open treatment, and reduction of fractures with cement augmentation and biopsy of L3. Later, the pathology result of the L3 specimen showed a small cluster of highly atypical malignant cells most consistent with epithelioid angiosarcoma (Figure 2). Immunohistochemistry of the tumor cells (Figure 3) showed strong diffuse staining for three vascular markers (ERG, CD31, and CD34). Overall findings were consistent with epithelioid angiosarcoma. Claudin-4 marker was negative. Thus, further supporting the diagnosis of EA. As part of the staging workup, he had a CT scan of the chest that did not show any occult masses. Given the patient's anemia, there was an initial concern for a primary gastrointestinal (GI) source. Endoscopic evaluation was held as the patient was too weak and still recovering from recent spinal instrumentation. Multiple tumor markers including CA 19-9, CEA, PSA, and α-fetoprotein were drawn and returned normal. The patient was seen by physical medicine and rehabilitation who recommended inpatient rehabilitation (IPR). After

few days in IPR, our patient became lethargic. His hemoglobin dropped to 6.7 g/dl and he developed sepsis. He was transferred to the general medical floor for further management. Unfortunately, his condition continued to deteriorate. Due to his poor prognosis with epithelioid angiosarcoma, advanced age, declining performance status, and failure to thrive, the patient and his family decided to pursue comfort care and home hospice.

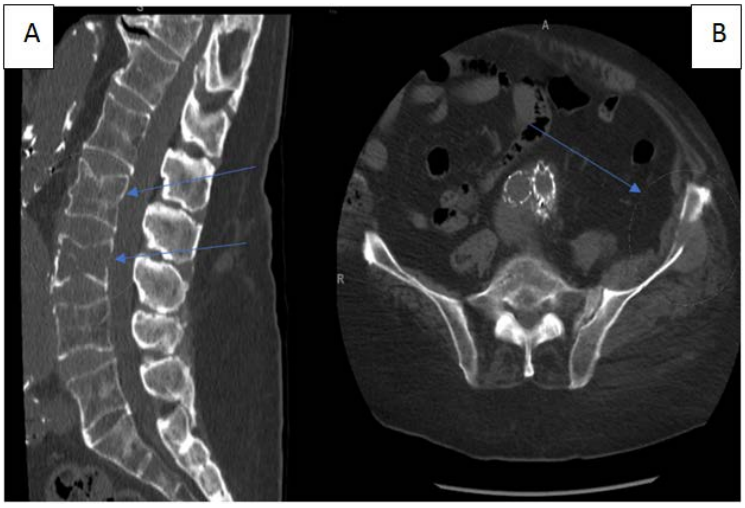

Figure 1. CT scan of the lumbar spine (A) and hip (B) showing pathologic fracture involving the L3 vertebral body, smaller pathologic fracture involving the L2 superior endplate, and multiple lytic destructive bone lesions with adjacent soft tissue lesions involving the left hip and femur without evidence of pathologic fractures

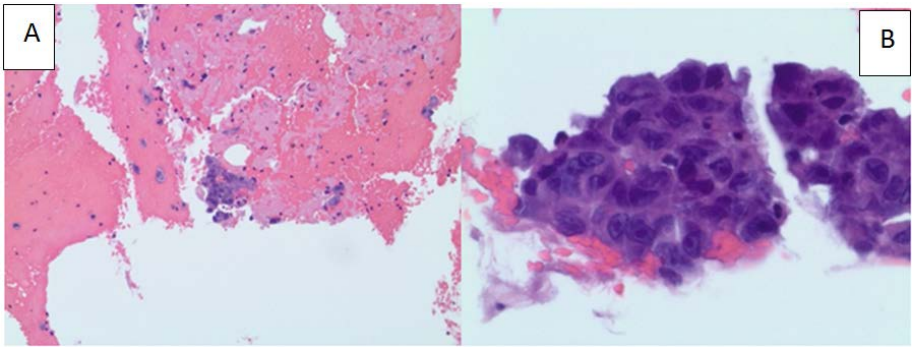

Figure 2. Bone (L3) Biopsy showing small clusters of typical malignant cells, most consistent with epithelioid angiosarcoma. A(H & E stain, ×100 magnification), B(H & E stain, ×400magnification)

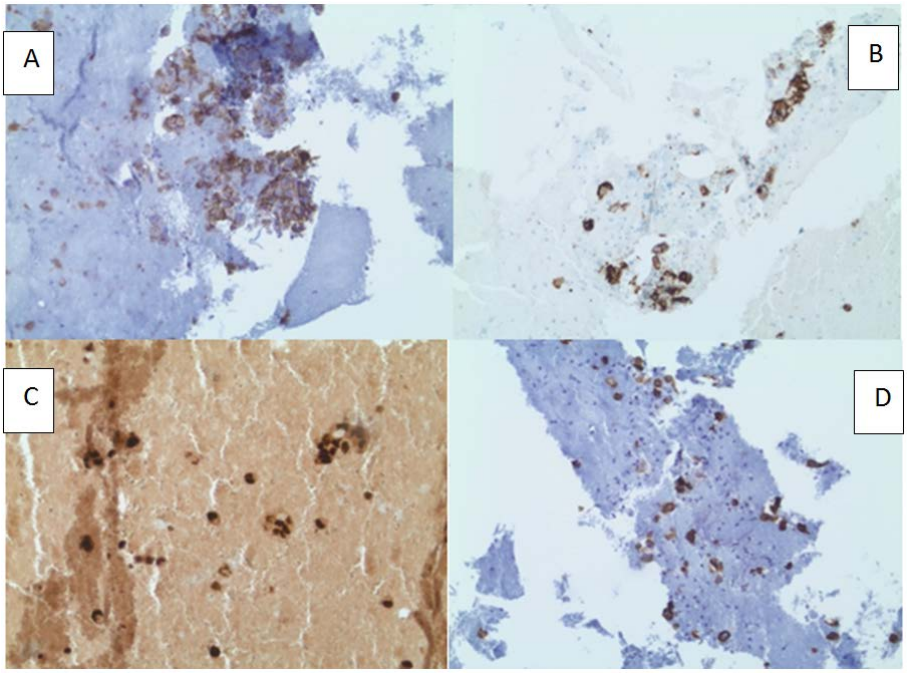

Figure 3. Immunohistochemistry, the tumor cells showing diffuse staining for CD31 (A), CD34 (B), ERG (C) and Pan- cytokeratin (D)

3. Discussion

Epithelioid Angiosarcoma is a variant of angiosarcoma characterized by a poorly differentiated and highly aggressive vascular malignancy of endothelial origin. It mostly affects older males [3]. EA most often arises from deep soft tissues of the extremities but can primarily arise from organs like adrenal glands, kidneys, thyroid, and skin. Primary angiosarcoma of the bone is rare as only 6% of all angiosarcomas originate from bone and only 1% of primary bone malignant neoplasms are primary angiosarcoma [2]. EA is an even more rare subtype of angiosarcoma, comprising <1 % of all soft tissue sarcomas [6].

EA is a highly aggressive tumor and can metastasize early to lymph nodes and solid organs especially lungs, bone, soft tissues, and skin [4]. The etiology of the angiosarcoma is unknown. Multiple proposed risk factors may be associated with the development of the tumor. These risk factors include trauma, foreign body insertion, previous radiotherapy or chemotherapy, orthopedic hardware or prosthesis, or malignant transformation of benign hemangiomas [2,3]. Depending on the location and the size of the tumor, patients may present with different clinical presentations including refractory pain, bone fracture, hemothorax, peritoneal or gastrointestinal bleed, heart failure, and others [3].

Imaging modalities can assist in the diagnosis of the tumor. Pathological exams and immunohistochemistry remain the gold standards for the diagnosis. EA normally presents as a tumor of undifferentiated malignant epithelioid cells. Cytokeratin is expressed in more than 50% of EA cases [1]. General histologic features show well-formed vascular channels and cytoplasmic vacuoles that contain red blood cell fragments which can be mistaken with other vascular tumors; hence Immunohistochemistry is necessary [1,4]. CD31 is highly sensitive and specific for EA. Other vascular markers could be expressed such as CD34 and ERG {1-4}. In our case, the tumor cells expressed CD31, CD34, ERG, and cytokeratin.

EA is associated with a very poor prognosis. Adverse prognostic factors include increased tumor size, advanced age, and high proliferative index (MIB-1 ≥ 10%) [3]. The overall 5-year survival rate of angiosarcomas in general is approximately 20% [2]. In EA, more than 50% of patients die within 2-3 years of the diagnosis [3,4]. Different treatment modalities have been used, but the mainstay of therapy is surgical resection of the primary tumor followed by radiation therapy. Some reports have shown that a paclitaxel-based chemotherapeutic regimen may improve survival, while others have shown that a combination of adjuvant radiation therapy and bevacizumab followed by surgery can be used [3]. Tazemetostat, EZH2 Methyltransferase inhibitor, has been approved as monotherapy for metastatic or local advanced epithelioid Sarcoma who are not candidates for surgery [5]. In addition, a combination of Tazemetostat plus doxorubicin as well as in combination with other immunotherapeutic agents are currently being investigated [5]. Our patient was not a candidate for definitive surgery as he had multiple areas involved. If his performance status was improved through his rehabilitation course, Tazemetostat would have been a consideration.

4. Conclusion

Here, we report a case of metastatic epithelioid angiosarcoma, an extremely rare sarcoma characterized by a very aggressive nature. Pathological examinations and immunohistochemistry are the gold standards for diagnosis. Early diagnosis and treatment improve long-term survival, as the only curative option remains surgical resection for localized disease.

Conflict of Interest

None of the authors have any conflicts of interest to declare.

Disclosure of Funding

None of the authors have any source of funding to declare.

References

[1] Yuanzhou He, Ying Zhou, Min Xie, Xiansheng Liu. *Epitheloid angiosarcoma of the mediastinum: a case report and literature review*. Int J Clin Exp Med 2019; 12(7): 9478-9482.

[2] Houda Boucekkine, BS, David Ying, MD *Primary Epitheloid Angiosarcoma of the Femur and Tibia: A rapidly Aggressive Course.* AMSRJ. Miami. 201.

[3] Hart J, Mandavilli S. *Epithelioid angiosarcoma: a brief diagnostic review and differential diagnosis.* Arch Pathol Lab Med. 2011 Feb; 135(2): 268-72.

[4] 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. Published 2014 Sep 11.

[5] Mrinal Gounder, Patrick Schöffski, Robin L Jones, Mark Agulnik, Gregory M Cote, Victor M Villalobos, Steven Attia, Rashmi Chugh, Tom Wei-Wu Chen, Thierry Jahan, Elizabeth T Loggers, Abha Gupta, Antoine Italiano, George D Demetri, Ravin Ratan, Lara E Davis, Olivier Mir, Palma Dileo, Brian A Van Tine, Joseph G Pressey, Trupti Lingaraj, Anand Rajarethinam, Laura Sierra, Shefali Agarwal, Silvia Stacchiotti. *Tazemetostat in advanced epithelioid sarcoma with loss of INI1/SMARCB1: an international, open-label, phase 2 basket study.*Lancet Oncol.Vol 21 November 2020.

[6] Young RJ, Brown NJ, Reed MW, Hughes D, Woll PJ. *Angiosarcoma*. Lancet Oncol. 2010; 11: 983-991.