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Epithelioid Hemangioendothelioma: A Rare Case of an Aggressive Vascular Malignancy

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Patient: Female, 46
Final Diagnosis: Epithelioid hemangioendothelioma
Symptoms: Pain
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Unusual clinical course

Background: Epithelioid hemangioendothelioma (EHE) is a rare vascular malignancy that occurs in multiple organs and tissues with a predilection for the extremities, bone, liver, and lung. It is often characterized by a clinically indolent course, delayed diagnosis, and unestablished standardized treatment options.

Case Report: A 46-year-old female presented with a 2-month history of right shoulder and arm pain. Imaging revealed involvement of the humerus, lung, liver; and brain and biopsies of both the lung and humerus were performed. A diagnosis of epithelioid hemangioendothelioma was confirmed and the patient received radiation therapy to the right humerus and brain stereotactic radiosurgery. She was scheduled to begin palliative chemotherapy with doxorubicin but developed complications and never received chemotherapeutic agents. She died 5.5 months from her first admission with widespread metastasis.

Conclusions: Epithelioid hemangioendothelioma (EHE) is typically a low-to-intermediate grade vascular malignancy, but, as seen in this case, can be aggressive. In the future, diagnosis, prognosis, and treatment may improve using genetic or immune therapy considering a structural chromosomal translocation has been identified.

MeSH Keywords: Bone Diseases • Lung Neoplasms • Vascular Diseases

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Background

Epithelioid hemangioendothelioma (EHE) is a rare, often multifocal, usually intermediate-grade vascular sarcoma originating from endothelial cells. The reported incidence of EHE is less than 1 per 1 million [1]. The primary tumor sites include lung, bone, and liver in over 65% of cases [2]. It is known to metastasize hematogenously and in certain cases can be rapidly fatal. EHE has no standard for treatment and very few therapeutic options are available. We present a case of EHE with an aggressive disease course and grim outcome.

Case Report

A 46-year-old female with a history of migraines, presented with progressive non-radiating, constant, right shoulder and arm pain as well as numbness over a span of 2 months. She denied any chest pain, although was experiencing mild dyspnea on exertion. The patient had a transient cough with minimal clear sputum. She did elicit night sweats, although no elevated temperature or chills along with an unintended 10 pound weight loss within the prior 2 months. She denied any family or personal history of malignancy or autoimmune disease. In addition, the patient reported no use of tobacco or illicit drugs. She also denied any orthopnea or lower extremity edema. The patient recently returned from a vacation to Dubai, but stated her pain began prior to her trip. She tried numerous therapies with a chiropractor as well as anti-inflammatory medications and creams, although all were unsuccessful. On physical examination, the patient had diffuse mild rales bilaterally on auscultation of the chest along with 4/5 strength of the right upper extremity and decreased range of motion, with an otherwise benign examination.

A MRI (magnetic resonance image) of the shoulder and arm was done which showed a right proximal humeral metaphyses intramedullary lesion (Figure 1) and incidentally revealed an abnormal lung parenchyma. As a result a CT (computed tomography) of the chest followed and showed a diffuse reticulonodular process with intraseptal thickening (Figure 2) associated with a soft tissue nodule seen about the anterior chest wall measuring 2.4×2.2 cm. Punctate irregular calcifications were also seen within the areas of nodular infiltrate in the right upper lobe. A focal nodular airspace consolidation was present in the right middle lobe with subjacent pleural thickening. Interferon gamma release assay, ANA (antinuclear antibody), rheumatoid factor, respiratory virus PCR (polymerase chain reaction) panel, angiotensin 1 converting enzyme, Fungitell β-D Glucan assay, histoplasma antigen and coccidioides antibodies panel were performed and were all negative. Subsequently the patient was started on empiric antimicrobial therapy and underwent a bronchoscopy with transbronchial biopsies. The initial

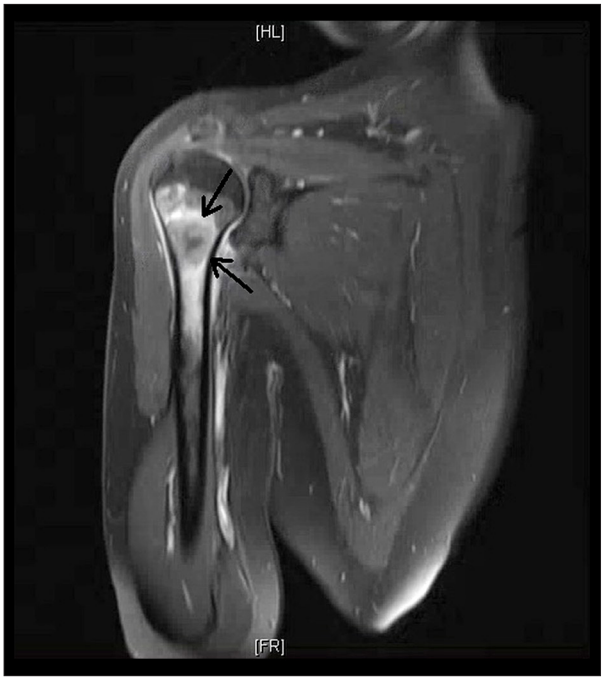

Figure 1. Magnetic resonance imaging of right upper extremity showing a right humeral intramedullary mass.

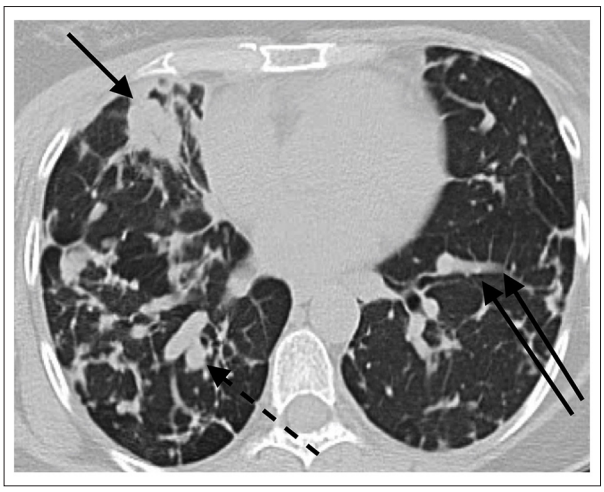

Figure 2. Computed tomography thorax showing a right apical mass (solid arrow) and diffuse reticulonodular infiltrates (dotted arrow) with intraseptal thickening (2 arrows).

pathology showed extensive diffuse fibrosis replacing and destroying the normal pulmonary tissue architecture without an active inflammatory cellular component and was negative for malignancy. A Congo red stain for amyloid was negative. The fibrotic tissue stained blue with trichrome stain, in a manner which was compatible with dense fibrous connective tissue. As no definitive diagnosis was made, the patient underwent a biopsy of her right humerus (Figure 3). In the interim, the initial lung biopsies were reevaluated at a leading histopathology

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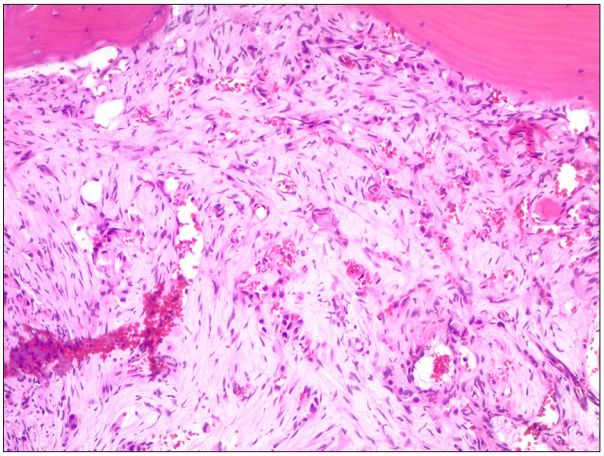

Figure 3. Bone biopsy showing scattered, highly atypical and poorly differentiated cells consistent with epithelioid hemangioendothelioma. Interosseous fibrous and vascular proliferation with epitheloid endothelioma. There is an intraluminal fibrin thrombi. Stained positively for CD31 and CD34.

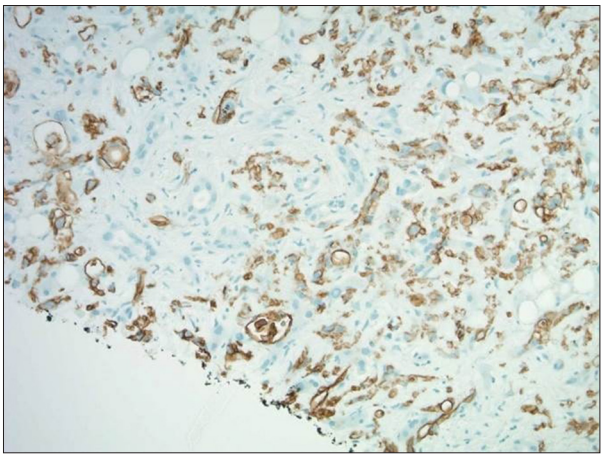

Figure 4. Bone showing CD34 staining.

laboratory and after careful analysis the patient obtained a diagnosis of epithelioid hemangioendothelioma. The patient's right humerus bone lesion biopsy was also consistent with the initial diagnosis of epithelioid hemangioendothelioma. The hematoxylin and eosin stain showed bone involvement by a fibrotic neoplasm containing scattered highly atypical, poorly differentiated cells. Immunostains were performed and showed atypical cells negative for ck (cytokeratin) ae1/3, ck7, ck20, ttf1 (thyroid transcription factor), gata2; but positive for cd31 (cluster of differentiation) and cd34 (Figure 4). Once a definitive diagnosis was made the patient was scheduled for outpatient follow-up with Oncology for further care. After a thorough evaluation which showed disease involvement of not only the lungs and bones, but also the liver and brain, it was determined that the patient would benefit from radiation therapy to the right humerus and brain stereotactic radiosurgery. After receiving successful radiation therapy, the patient was scheduled to begin palliative chemotherapy with doxorubicin. Unfortunately, she was unable to receive chemotherapy as she developed significant dyspnea and required hospitalization during which a CT scan of the chest revealed an obstructive endobronchial mass with suspected post obstructive pneumonia. The patient was started on empiric antimicrobial therapy and palliative bronchoscopy Argon plasma coagulation was performed to maintain her airway while waiting to clear the infection in hopes to initiate chemotherapy. She died of acute hypoxemia and respiratory failure 5.5 months after the initial diagnosis.

Discussion

This case is important for 2 reasons. First it is a case of an extremely rare vascular malignancy. The epidemiology of the tumor even appears unsettled. There is evidence that most patients with this malignancy are males in their second decade [3] and other reports that most cases are in their fifth decade and female [4,5]. One reference even states there is no gender preference [6]. Moreover, the clinical presentation in some reports suggests that the majority of patients present symptomatically with pain [3] or pulmonary symptoms, and other reports suggest most cases are incidental findings in asymptomatic individuals [7]. In all likelihood, these discordant observations probably represent the low incidence of this malignancy combined with both the primary tumor site and metastatic burden at presentation [2]. Nonetheless, because of its rarity, there is limited clinical data to guide treatment choices; consequently very few therapeutic options are available. Current reported treatment options include chemoembolization, radiotherapy, and chemotherapeutic agents such as doxorubicin, vincristine, fluorouracil (5-FU), and Interferon (IF)-alpha 2b [7,8].

As EHE is a vascular malignancy which expresses vascular endothelial growth factor (VEGF), anti-angiogenic therapy together with systemic chemotherapy has been suggested [8]. Interestingly, pegylated liposomal doxorubicin (PLD) is used as first-line or second-line treatment for conditions such as angiosarcoma and HIV-associated and classical Kaposi's sarcoma. As such, considering the vascular cell origin of EHE, a case report of metastatic EHE, discussed PLD as a viable treatment option as possible [9]. Our patient was able to benefit from palliative radiation therapy. Unfortunately due to her aggressive disease course, she was unable to benefit from chemotherapy.

The second reason this case is important is because it took an aggressive course resulting in death within 6 months of initial presentation. In general, the biologic behavior of EHE is typically a more indolent cancer resulting in a mean survival of 4.6 years,

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ranging from 6 months to 24 years [7]. In fact, delayed diagnosis is sometimes reported because the presentation is one of a local tumor rather than a presentation with metastatic potential. Diagnosis requires a clinical awareness and tissue biopsy with proper staining. Immunohistochemical staining with endothelial cell markers is used to help distinguish EHE from other vascular malignancies. Based on current literature, the tumors stain positively for factor VIII-related antigen, CD-31 (platelet endothelial cell adhesion molecule 1 transmembrane glycoprotein), cytokeratin, CD-34, and vimentin [7,10]. One recent development is EHE has been linked to a reciprocal translocation leading to a WWTR1-CAMTA1 fusion gene which drives the proliferation of the malignancy [11]. Unfortunately, a karyotype was not performed on our patient's tumor. However, next gene sequencing was performed and no significant mutations were identified. Nonetheless, if the lung is involved the prognosis worsens. The most characteristic feature of EHE on chest CT is the presence of multiple bilateral perivascular nodules. Although most nodules are approximately 1 cm in size, they can range up to 2 cm and are usually found in relation to small and medium-sized vessels and bronchi. Hilar lymph node metastases have been described, as well as interlobular septal thickening [7,10]. Our patient's most notable chest CT findings showed a diffuse reticulonodular process with intraseptal thickening and interestingly a pulmonary nodule measuring 2.4×2.2 cm. She ultimately died from respiratory failure like most patients who succumb to EHE.

Conclusions

Epithelioid hemangioendothelioma (EHE) is typically a low-to-intermediate grade vascular malignancy, but, as seen in this case, can be aggressive. The diagnosis can be problematic and treatment options are not standardized. Moreover, prognostic elements blend together making it difficult to counsel patients. If there is multiorgan involvement which includes the lung and the patient is symptomatic, then they likely have a worse prognosis. In the future, diagnosis, prognosis, and treatment may improve using genetic or immune therapy considering a structural chromosomal translocation has been identified.

Conflict of interest

None.

References:

1. Yousaf N, Maruzzo M, Judson I et al: Systemic treatment options for epithelioid haemangioendothelioma: The Royal Marsden Hospital experience. Anticancer Res, 2015; 35(1): 473–80
2. Amin RM, Hiroshima K, Kokubo T et al: Risk factors and independent predictors of survival in patients with pulmonary epithelioid hemangioendothelioma. Review of the literature and a case report. Respirology, 2006; 11: 818–25
3. Boutin RD, Spaeth HJ, Mangalik A Sell JJ: Epithelioid hemangioendothelioma of bone. Skeletal Radiol, 1996; 25: 391–95
4. Soo CI, Ng BH, Tan EL et al: Ambiguous presentations of pulmonary epithelioid hemangioendothelioma: Two case reports of a rare pulmonary malignancy. SAGE Open Med Case Rep, 2016; 4: 2050313X16650323
5. Lee CU, Zreik RT, Boland JM, White ML: Radiologic–pathologic correlation: Metastatic pulmonary epithelioid hemangioendothelioma of bone primary. J Clin Imaging Sci, 2015; 5: 50
6. Ignacio EA, Palmer KM, Mathur SC et al: Epithelioid hemangioendothelioma of the lower extremity. Radiographics, 1999; 19: 531–37
7. Sardaro A, Bardoscia L, Petruzzelli MF, Portaluri M: Epithelioid hemangioendothelioma: An overview and update on a rare vascular tumor. Oncol Rev, 2014; 8: 259
8. Semenisty V, Naroditsky I, Keidar Z, Bar-Sela G: Pazopanib for metastatic pulmonary epithelioid hemangioendothelioma-a suitable treatment option: Case report and review of anti-angiogenic treatment options. BMC Cancer, 2015; 15: 402
9. Grenader T, Vernea F, Reinus C, Gabizon A: Malignant epithelioid hemangioendothelioma of liver successfully treated with pegylated liposomal doxorubicin. J Clin Oncol, 2011; 29(25): e722–24
10. Liu K, Xie P, Peng W, Zhou Z: The computed tomographic findings of pulmonary epithelioid hemangioendothelioma. Radiol Med, 2014; 119(9): 705–13
11. Rubin BP, Tanas MR: Towards a proper diagnosis and understanding of the pathogenesis of epithelioid hemangioendothelioma. Electronic Sarcoma Update Newsletter, 2014 *http://sarcomahelp.org/research/epithelioid-hemangioendothelioma.html*

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