Bone epithelioid angiosarcoma is rare and generally shows positive immunostaining for epithelial markers. Multicentric bone epithelioid angiosarcoma is easily misdiagnosed as carcinoma, including metastatic carcinoma, multiple myeloma, and multiple lymphoma of bone.

This article describes a case of multicentric bone epithelioid angiosarcoma. The patient was first misdiagnosed as having metastatic carcinoma. Examination showed osteolytic lesions in the bilateral heels and the lower left humerus. The diagnosis was confirmed postoperatively and corrected after immunohistochemical analysis of the biopsy. The immunohistochemical analysis revealed that the tumor mass was strongly positive for CD31, factor VIII, vimentin, and neuron-specific enolase. The patient refused chemotherapy and died of lung metastasis 4 months postoperatively.

Most bone epithelioid angiosarcomas are immunopositive for epithelial markers (ie, keratin, cytokeratin, high-molecular-weight keratin, and epithelial membrane antigen), vascular endothelial markers (ie, CD31, CD34, and von Willebrand factor), and factor VIII–associated antigen. Bone epithelioid angiosarcoma shows a relatively high degree of malignancy. Patients often die of distant metastasis, including those found in the lung and lymph node tissue. A wide excision of epithelioid angiosarcoma should be performed during the operation of the primary tumor. A better understanding of the clinicopathologic features of this disease may help to clarify the confusion, provide better treatment, and improve the clinical prognosis.

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Figure: Magnetic resonance image revealing a large, contrast-enhancing mass in the left heel with surrounding signal abnormality (A). Computed tomography scan revealing that osteolytic lesions were localized in bilateral heels, with the lesion in the left heel being more obvious and infiltrating the surrounding soft tissues (B).
Epithelioid vascular tumors are divided into different subtypes, such as epithelioid hemangioma, epithelioid hemangioendothelioma, and angiosarcoma, according to their architecture, degree of vascular differentiation, and cytonuclear atypia. Epithelioid angiosarcoma, a high-grade sarcoma of vascular origin, is a rare variant of angiosarcoma and is characterized by large cells with an epithelioid morphology. Lines of evidence show that epithelioid angiosarcoma has a wide anatomic distribution. These tumors have been found in the soft tissue, skin, adrenal gland, thyroid gland, vagina, uterus, breast, lung, gallbladder, and bone.

Bone epithelioid angiosarcoma is rare. Due to the epithelioid appearance of the tumor cells, multicentric bone epithelioid angiosarcoma is easily misdiagnosed as a carcinoma, such as metastatic carcinoma, multiple myeloma, or multiple lymphoma of bone. Better understanding of the clinicopathologic features of this disease may help to clarify the confusion, provide better treatment, and improve the clinical prognosis. This article describes a case of bone epithelioid angiosarcoma previously misdiagnosed as a metastatic carcinoma.

CASE REPORT

A 64-year-old woman with no significant medical history was admitted due to a 2-month history of left heel pain and gait dysfunction. Two months previously, the patient had presented with moderate paroxysmal pain in her left heel without rubefaction. Ten days previously, the symptoms had become aggravated and caused walking difficulty. Radiographs obtained by another hospital revealed a left heel tumor, and she presented to the current authors for follow-up treatment. Physical examination showed a tender tumor mass without clear margins that was localized in the lateral side of her left heel. The patient was afebrile.

Radiographs obtained at the other hospital suggested the presence of osteolytic lesions in both of the patient’s heels (Figures 1A, B). Also, emission computed tomography analysis at the other hospital showed that the tumor in the left heel had an abnormally enhanced metabolism. After further examination, an osteolytic lesion with local tumor mass in her left heel was confirmed by magnetic resonance imaging (Figure 1C). Tumor tissues exhibited moderate T1 signals and slightly higher T2 signals. Computed tomography scans confirmed that the osteolytic lesions were present in the bilateral heels (Figure 1D). The lesion was more obvious in the left heel and displayed infiltration of the surrounding soft tissues. No abnormalities were observed in the internal organs after B-ultrasound examination, and the chest computed tomography was normal.

Based on these observations, the patient was diagnosed with metastatic carcinoma in both heels.

The patient underwent an amputation between the middle and distal part of the left leg. The right heel received curettage and cement reconstruction. An intraoperative frozen section biopsy was performed, revealing a poorly differentiated metastatic carcinoma. Three days postoperatively, the patient felt pain near her left elbow. Radiographs showed an osteolytic lesion in the lower region of the humerus (Figures 1E, F). The local widespread destruction of the lesion increased the pathologic fracture risk.

The patient underwent curettage and cement reconstruction in her lower left humerus and recovered well postoperatively.
Pathological examination with hematoxylin-eosin staining indicated that the tumor cells had typical characteristics of epithelioid angiosarcoma with round to oval nuclei, prominent nucleoli, vesicular chromatin pattern, and abundant amphophilic or eosinophilic cytoplasms (Figure 2). Immunohistochemical analysis revealed that the tumor mass was strongly positive for CD31, factor VIII, vimentin, and neuron-specific enolase (Figure 3). The patient refused chemotherapy and died of lung metastasis 4 months postoperatively.

**Discussion**

Epithelioid angiosarcoma is a unique subtype of angiosarcoma in which the malignant endothelial cells have a predominantly epithelioid appearance. Bone epithelioid angiosarcoma is rare and shows positive immunostaining for epithelial markers. Therefore, multicentric bone epithelioid angiosarcoma is easily misdiagnosed as multiple myeloma, multiple lymphoma, or metastatic carcinoma (from gastrointestinal adenocarcinoma, breast cancer, thyroid cancer, lung adenocarcinoma, or prostatic cancer). The current patient was first misdiagnosed with metastatic carcinoma, which was confirmed postoperatively and later corrected to bone epithelioid angiosarcoma after immunohistochemical analysis of a biopsy. The authors recommend performing the biopsy preoperatively and caution against the diagnoses of bone metastatic carcinoma in patients with multicentric bone lesions before identifying the primary lesion.

Radiographs of the bone lesions reflected no specific features of bone epithelioid angiosarcoma, whereas bone lesion biopsy and histological examination were informative. Deshpande et al detected the foci containing prominent neutrophilic infiltrate (not associated with necrosis) in bone epithelioid angiosarcomas. In addition, the assessment of bone marrow angiogenesis with specific antibodies is important for diagnosis because most bone epithelioid angiosarcomas are immunopositive for epithelial markers (ie, keratin, cytokeratin, high-molecular-weight keratin, and epithelial membrane antigen), vascular endothelial markers (ie, CD31, CD34, and von Willebrand factor), and factor VIII–associated antigen. Among these markers, CD31 is regarded as a marker with relatively high specificity and sensitivity for vascular tumors because it is expressed in approximately 90% of angiosarcomas but in less than 1% of carcinomas. CD34 is reported to be expressed in more than 90% of vascular tumors, but this marker has poor specificity, with noted expression in several other soft tissue tumors. Also, the immunoreactivity of factor VIII–associated antigen can be informative for the diagnosis of bone epithelioid angiosarcoma.

Bone epithelioid angiosarcoma has a relatively high degree of malignancy. Patients often die of distant metastasis, including those found in the lung and lymph node tissue. A wide resection of epithelioid angiosarcoma should be performed during the operation of the primary tumor. If epithelioid angiosarcoma is accompanied by a pathologic fracture, resection needs to be performed immediately, and amputation is sometimes necessary to save the patient’s life. The incision margin, adjuvant chemotherapy, radiotherapy, and distant metastasis should be considered postoperatively. The current patient died from lung metastasis 4 months postoperatively. It is possible that wide resection of epithelioid angiosarcoma accompanied by chemotherapy and radiotherapy would have provided a better outcome for this patient.

**Conclusion**

Bone epithelioid angiosarcoma is rare and should be carefully distinguished from metastatic carcinoma, multiple myeloma, and multiple lymphoma of the bone. This article may provide a better understanding of the pathology of bone epithelioid angiosarcoma and valuable insights for the accurate diagnosis, treatment, and prognosis for patients with this deceptive disease.

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