Calcaneal Epithelioid Hemangioendothelioma: A Case Report

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Abstract

The term hemangioendothelioma is the designation for vascular tumors that have a biologic behavior intermediate between a hemangioma and a conventional angiosarcoma; it is associated with a significant risk of recurrence and metastasis.

Epithelioid hemangioendothelioma is a rare vascular tumor; it represents less than 1% of all the vascular tumors. Although it can occur at almost any age, it rarely occurs during childhood, affecting most of the time the liver, the lung, and soft tissues and bones. Because of its heterogeneous presentation, it is often misdiagnosed and not suitably treated.

We report a rare case of hemangioendothelioma epithelioid at the right calcaneus. Through this case and the literature, we will review the problems of differential diagnosis.

Introduction

Epithelioid Hemangioendothelioma (EH) is an intermediate malignant vascular tumor occurring mainly in lung, liver bone and soft tissues. It has a potential for local recurrence, lymph node metastasis and distant metastases [1].

The originality of this case lies in the rarity of this type of bone tumor and even more rare, the location of calcaneus.

Through this case, we will discuss the main differential diagnoses.

Case Report

A 70 year-old man with no previous medical history, which had swelling in the right heel, evolving for 10 years and progressively increasing in size.

The clinical examination revealed a mass measuring 4 cm long, well-limited, non-painful, movable relative to the superficial plane and adhering to the deep plane and the calcaneus.

Radiographic evaluation of the right foot and ankle showed an osteolytic lesion of the calcaneus with cortical expansion and destruction in the cortical bone.

CT scan revealed expansive lytic lesion multilocular with cortical disruption of the calcaneus bone, no calcified matrix. Moderate heterogeneous enhancement of the lesion and of the soft tissues (Figure 1).

Figure 1: Oblique radiograph of the ankle: lytic lesion of the calcaneus multilocular with cortical disruption and invasion of soft tissues.

Figure 2: White-gray appearance of E.H. white gray.

Figure 3: Epithelioid hemangioendothelioma composed of chains and cords of epithelioid endothelial cells in a myxoid background.

Figure 4: Cells of epithelioid hemangioendothelioma with characteristic intracytoplasmic vacuoles containing a red blood cell (arrow) a key diagnosis feature of hemangioendothelioma.

After the patient's informed consent, the surgical indication was retained with wide excision of the tumor (Figure 2) filling with surgical cement and cortico-spongy graft.

The appearance of the lesion is white gray, hence, it, the vascular nature doesn't show on the macroscopic level.

The microscopic study showed a tumor proliferation of nodular architecture. The tumor cells are arranged in clusters and cords in an essentially myxoid stroma (Figure 3).

The tumor cells have a chromatic nucleus showing some mitosis figures, and an abundant eosinophilic vacuolized cytoplasm which occasionally contain red blood cells, thus showing endothelial differentiation (Figure 4).

The radiological extension report showed no pulmonary or hepatic lymph node metastasis.

Discussion

Epithelioid hemangioendothelioma (E.H.) can occur in both children and adults, and affects both sexes about equally [2,3].

The tumor develops as a solitary, slightly painful mass in superficial and deep soft tissue as well as the bone. E.H. also occurs in the liver and lung, although, in rare instances, it can be multicentric, with combinations of soft tissue, lung, liver and bone lesions [4].

At least half of cases are closely associated with or arise from a vessel, usually a vein. Those tumors that arise from vessels usually have a white-red color. Those that do not arise from vessels as our case are white-gray and offer little indication of their vascular nature on macroscopic inspection [5].

E.H. of the bone is rare, with lesions distributed throughout the skeleton with a predilection for involvement of the axial skeleton and long tubular bones [6].

Radiography and CT of E.H. usually reveals a lytic lesion without matrix mineralization that is localized in the medullar to cortical bone. Cortical disruption and joint invasion are also common features of E.H. However, the signal characteristics on MRI are non-specific. Detection of this tumor is difficult due to its rarity and uncharacteristic radiographic appearance [7,8].

On a Histological view, the tumors are composed of short strands or solid nests of rounded to slightly spindled endothelial cells.

E.H. tumor cells have an epithelioid shape with abundant eosinophilic cytoplasm. Cytoplasmic vacuolization results in large intracytoplasmic "microlumens," which are a distinctive feature of E.H.

Frequently confused with the mucin vacuoles of adenocarcinoma, these miniature lumens occasionally contain erythrocytes. The stroma varies from highly myxoid to hyaline [9].

Occasional tumors contain eosinophils and lymphocytes, this feature is rarely as pronounced as it is in the epithelioid hemangioma.

Tumor nuclei may demonstrate mild nuclear atypia. The presence of marked atypia, in addition to tumor necrosis, foci of spindle cell morphology, or solid growth pattern, and high mitotic rate (>2 mitoses per 10 high power field) are features that are associated with an "aggressive" variant of E.H. It has been the practice to designate tumors with cytologic features of malignancy as malignant epithelioid hemangioendothelioma [5].

The differential diagnoses of E.H. of the bone must include melanoma, metastatic carcinoma and various sarcomas, which can assume an epithelioid appearance.

In general, carcinomas and melanomas metastatic to soft tissue display far more nuclear atypia and mitotic activity than the epithelioid hemangioendothelioma and are rarely angiocentric.

Sometimes E.H. of bone needs to be differentiated from chordoma, chondromyxoid fibroma and myxoid chondrosarcoma, which are more voluminous and positive for S-100 protein [6].

The distinction between E.H. and epithelioid angiosarcoma is often difficult. In general, angiosarcoma shows more cytologic atypia and has a higher mitotic rate than E.H. Another helpful feature is that the epithelioid angiosarcoma tends to lack the myxoid or myxohyaline matrix that is a recurrent feature of E.H.

Epithelioid sarcoma is perhaps the closest mimic of this tumor. In ambiguous cases, immunohistochemistry may provide the most reliable clues for differentiation. With appropriate cocktails of monoclonal antibodies directed against a broad spectrum of cytokeratins, immunostaining is positive in virtually all carcinomas and epithelioid sarcomas.

About one-fourth of epithelioid hemangioendotheliomas express cytokeratine [10] but usually the staining is less intense and focal compared to epithelioid sarcoma. The cells of epithelioid hemangioendothelioma express CD31 and CD34, markers that are absent in epithelioid sarcoma and carcinoma [11].

This tumor is capable of producing regional and distant metastasis but at a reduced frequency compared to soft tissue angiosarcomas. Deyrup et al. reported a disease-specific survival of 81% at 5 years compared to a 1-year mortality of approximately 50% for soft tissue angiosarcomas [12].

Lung and lymph nodes are the two most common metastatic sites [3]. Similar data have been reported by others [13].

The etiology of E.H. is still a dilemma. Errani et al. focused on the t (1;3) (p36.3;q25) mutation: a molecular analysis revealed that CAMTA1 on chromosome 1p36.23 and WWTR1 on chromosome 3q25 are the involved genes. This is the first evidence that these genes participate together in a disease process and that this fusion is specific to epithelioid hemangioendothelioma and to no other vascular lesion, in particular, epithelioid angiosarcoma [14,15].

Treatment depends on the number, size, and location of the tumors.

Several therapeutic options have been proposed including surgery, systemic corticosteroids, cryotherapy, laser destruction, radiotherapy, chemotherapy and selective embolization. Surgical treatment is particularly difficult because of the poor peripheral delimitation of the lesion and the diffuse infiltration of the adjacent structures; the resection should be as wide as possible [16]. Adjuvant radiotherapy is mainly indicated in multicentric forms and appears to be effective [17].

Treatment of high-grade forms of malignancy requires more radical surgery.

The poly-chemotherapy used in aggressive multifocal forms, has no clearly demonstrated efficacy [18]. Nevertheless, one study reported the success of a cisplatin cure with low dose and moderate radiotherapy without surgery [19].

However, radiotherapy should be discouraged because of its incrimination in the sarcomatous transformation of the tumor with increased risk of metastasis [20, 21].

Conclusion

Epithelioid hemangioendothelioma is a rare bone tumor, often misdiagnosed and not suitably treated. The treatment options, prognosis, and histological grading of E.H. remain controversial.

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