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Multifocal Epithelioid Hemangioendothelioma of the Foot and Ankle Developing a Postoperative Infection—Long-term Outcome: A Case Report

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ABSTRACT

A case of rare epithelioid hemangioendothelioma with multiple foot and ankle lytic lesions in a 41-year-old male is reported. The patient presented to our hospital after having received treatment elsewhere and developing a local postoperative infection. After thorough investigations and establishing the diagnosis, we initially treated the local infection and highlighted the potential risk of malignancy. Finally, respecting the patient's wishes, he was treated with consideration mostly of the pending foot and ankle fractures rather than the risk of malignancy. At 9.5 years postoperatively, the patient was clinically well and asymptomatic, without clinical, laboratory, or radiologic signs of malignancy, and the previous infection might have even played a remote role in that outcome. A review of the published data regarding the treatment of this unpredictable neoplasm is also presented.

Epithelioid hemangioendothelioma (EH) of the bone is a rare vascular tumor characterized by endothelial cells with an epithelioid appearance. It has an intermediate malignant potential and it discloses very unpredictable clinical behavior. It also has a tendency to develop into multifocal disease, primarily in the axial skeleton (1,2). This group of vascular tumors also includes benign hemangioma and malignant angiosarcoma. Recently, it has been reported that local infection has a positive effect on skeletal malignancies, improving the tumor prognosis (3–6).

We report a rare case of EH with multiple lesions in the foot and ankle, which developed a postoperative infection. The patient refused the suggested below-the-knee amputation (BKA) and was treated considering mostly the symptoms resulting from the pending fractures in the foot and ankle rather than the risk of potential malignancy. To the best of our knowledge, it is one of the few similar foot and ankle EH cases reported and the only one treated in this fashion and associated with a postoperative infection.

Case Report

A 41-year-old male typographer with a clear medical history had presented first to a district hospital in April 2006 with a 5-month history of left ankle pain. In the beginning, he attributed the pain to the long hours of standing work. The duration of the pain and its worsening prompted him to seek medical help. He had had no previous trauma or surgery in his left lower extremity. Radiographs showed multiple osteolytic lesions in the left foot and ankle (Fig. 1). The laboratory study findings were unremarkable. A magnetic resonance imaging scan below the distal one third of the tibia revealed multiple osteolytic lesions in the distal fibula, tibia, talus, calcaneus, navicular, and first cuneiform (Fig. 2). At that time, a computed tomography scan and bone scan were not considered, and the physicians proceeded to perform open biopsy and curettage of the proximal lesion of the fibula, with internal fixation of the fibula's 2 lesions, 1 distal to the lateral malleolus and 1 more proximally at the mid-shaft, using 2 separate plates (Fig. 3). The result of the biopsy examination was EH. At 3 weeks postoperatively, the patient

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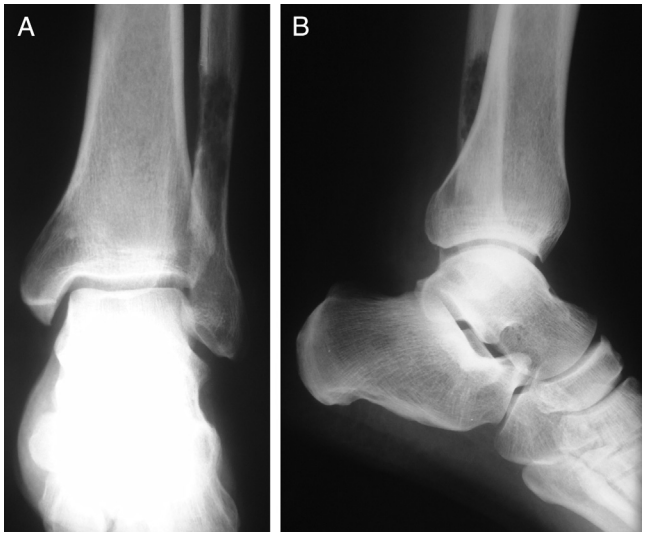

Fig. 1. (*A* and *B*) Plain radiographs of the patient's ankle at his first presentation to the hospital.

developed a discharging sinus in the distal surgical incision. Culture developed *Staphylococcus aureus*, and the patient underwent a 6-week course of antibiotics (amoxicillin and clavulanate).

After approximately 4 months of no significant improvement, the patient presented to our department. The physical examination revealed swelling and tenderness all over the distal third of the tibia and ankle joint, with intermittent discharge of the sinus. Laboratory studies revealed a highly elevated C-reactive protein and erythrocyte sedimentation rate. The patient was considered to have a deep infection, which was treated with local surgical debridement and antibiotics for 2 months in accordance with the culture and sensitivity report. Gradually, the wound dried up completely and his C-reactive protein and erythrocyte sedimentation rate returned to normal. However, the patient acknowledged more swelling and pain of the ankle joint during the day on his return to work. It was difficult for him to bear weight and to manage his daily activities. Plain radiographs of his ankle joint demonstrated cortex destruction in the medial malleolus and widening of the calcaneal lesion. A full-body 3-phase 99m-technetium bone scan showed increased uptake throughout the distal tibia and fibula, both the malleoli, and the eighth left rib (Fig. 4). All laboratory studies at this time were unremarkable. We decided to proceed with a second biopsy in the medial malleolus and calcaneus (trucut biopsy). It was again reported as "epithelioid hemangioendothelioma, without any signs of high-grade malignancy" (Fig. 5). The immunohistochemical studies supporting the results of the microscopic examination were positive for vimentin, CD34 antigen, and CD31 antigen. Furthermore, chest computed tomography and abdominal ultrasonography excluded the presence of any other visceral lesions. The unpredictable clinical behavior of the tumor was explained to the patient and because of its potential for malignancy, he was recommended to undergo a left BKA and excision of the middle third of his eighth left rib. However, he wished not to have a BKA. He preferred to take the risk, to receive treatment of the potential fractures in his symptomatic left foot and ankle, and to continue with a close follow-up protocol, considering his disease definitely benign. Finally, the patient underwent removal of the metalwork, excision of the distal fourth of the fibula, intralesional macroscopic curettage of all the remaining lesions, and fusion of the ankle and subtalar joints with a retrograde intramedullary nail (Fig. 6). He refused to have his rib lesion excised, as it was asymptomatic. Postoperatively, the patient started gradual weightbearing without pain, and he was able to return to work, although he changed his employment to a taxi driver from that of a typographer. We continued, initially, with follow-up examinations every 6 months, and later yearly, with radiographs of the foot and ankle, chest radiographs, and laboratory blood tests, including C-reactive protein, erythrocyte sedimentation rate, and alkaline phosphatase. At 9.5 years postoperatively, the patient was clinically well and asymptomatic, without clinical, laboratory, or radiologic signs of malignancy.

Discussion

EH was definitively described as an entity in 1982 by Weiss and Enzinger (7). They presented 41 cases of EH and considered EH to be a neoplasm between a hemangioma and an angiosarcoma (7). Currently, the terminology used to describe malignant vascular tumors in the published data is confusing. Multiple terms have been used interchangeably, including hemangioendothelioma, hemangioendothelial sarcoma, hemangiosarcoma, angiosarcoma, and others (8). These rare tumors constitute approximately 1% of all primary malignancies of the bone. After the first decade, they can occur at any age, with a slight male predominance, and can also coexist with visceral lesions (1,7).

All these tumors have the same tendency to develop multifocal disease, and all have shown very unpredictable clinical behavior often with indolent course and delayed diagnosis. Although not strictly defined, most investigators have used the term EH to describe low-grade malignant vascular tumors and the term angiosarcoma to describe high-grade malignant vascular tumors.

The classic radiographic appearance of EH is a lytic lesion, sometimes with cortical expansion and destruction in the metaphyseal or diaphyseal areas involving both cancellous and cortical bone (1,7). The tumor occurs multifocally in approximately one half of cases, usually in a certain anatomic region (a single bone or the adjoining bones of a single extremity). It frequently involves the long bones such as the tibia, fibula femur, and humerus, followed by the vertebrae and bones of the foot or hand, with nonspecific radiographic findings (9). In addition, the disease can involve the liver, lung, breast, or other soft tissue (1,7,9).

Biopsy and microscopic examination with immunohistochemical studies are necessary to establish a diagnosis. Immunoreactivity to CD34 and CD31 is specific for endothelial cells (8,10). Furthermore, given the multifocality of the osseous lesions, a complete skeletal survey must be performed before definitive treatment is begun. The biologic behavior of EH is unpredictable, with the potential to progress to a stage of higher malignancy. The prognosis is poorer when EH involves the visceral organs (7).

Regarding the clinical effect of a deep postoperative infection in some types of skeletal tumors, such as in osteosarcoma, it has been reported that such an infection has a positive influence on tumor prognosis (3–6). However, either because the latter needs additional clarification or because it is not certain that the same finding applies to different tumors, such as EH, further investigations are needed.

The treatment options and prognosis of EH are controversial issues in the literature owing to the lack of consensus regarding a histologic grading system to predict the prognosis. The type of treatment might depend on the number, size, and location of the tumors. Arteaga et al (11) reported a case of a grade I multifocal EH of the foot in a 24-year-old man treated by large surgical resection of