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Multifocal epithelioid hemangioendothelioma of the phalanges of the hand

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Abstract Epithelioid hemangioendothelioma (EH) of bone is a rare vascular neoplasm characterized by epithelioid endothelial cells and a variable biologic behaviour. The principal sites of occurrence of this osteolytic tumor are the lower extremity and the axial skeleton. Approximately half of the cases present with multifocal disease. The latter feature can be helpful in suggesting the diagnosis of a vascular tumor; on the other hand, it strengthens the need for a skeletal survey or whole-body MRI/CT. We report on the clinical, histologic and radiologic features—including CT and MRI findings—of EH in a case of multifocal disease of the phalanges of the hand, a very uncommon anatomic site of affliction.

Keywords Hand · Epithelioid hemangioendothelioma · Vascular bone tumors · MRI · Radiography

Introduction

Epithelioid hemangioendothelioma (EH) of bone is a rare borderline malignant neoplasm which belongs to a group of vascular tumors characterized by endothelial cells having an epithelioid appearance. This group also includes benign epithelioid hemangioma and its malignant counterpart, epithelioid angiosarcoma [1]. All share the more or less distinct tendency to develop multifocal disease [2, 3]. Since EH primarily affects the lower extremity and axial skeleton, manifestations in the upper limb, especially distal to the elbow, are rare [4]. We report on a case of EH of bone in which multifocal disease was confined to the phalanges of adjacent fingers.

Case report

A 28-year-old previously healthy man presented with a history of pain and swelling in the right little finger for 2 months. The patient denied any history of trauma or infection. Physical examination revealed swelling and tenderness of the proximal phalanx of the right little finger. The range of motion of the adjacent finger joints was slightly limited due to pain. Further portions of the right hand and arm seemed uninvolved and the axillary lymph nodes were not palpable. Laboratory studies were unremarkable, with the exception of a marginally elevated C-reactive protein equal to 0.7 mg/dl (normal range <0.5 mg/dl) and a mildly elevated erythrocyte sedimentation rate equal to 22 mm/h (normal range <15 mm/h).

Radiographs of the right hand showed an expansile osteolytic lesion involving the cortex and cancellous bone of the diaphysis and metaphyses of the proximal phalanx of the little finger (Fig. 1). The lesion had a coarse trabeculated pattern with poorly defined margins. A distinct soft tissue swelling was present. Furthermore, a small radiolucent, well-defined lesion was seen in the base of the middle phalanx of the ring finger. Our differential diagnosis derived from these radiographic findings primarily included giant cell tumor and a bone tumor of vascular origin. Skeletal metastasis or tuberculous dactylitis were also considered, but due to the unremarkable history of the patient, neither of these diagnoses was likely.



Fig. 1 Dorsovolar radiograph of the right hand demonstrates a large, lytic lesion of the proximal phalanx of the little finger involving the medullary cavity and cortex of almost the entire bone with exception of the juxta-articular epiphyseal areas. Ill-defined lesion margins are accompanied by tiny spicular periosteal reactions. Extensive soft tissue swelling is present. Additionally, there is a small, round, radiolucent lesion in the base of the middle phalanx of the ring finger

Computed tomography (CT) images better demonstrated the aggressive radiologic features of the lesion in the proximal phalanx of the little finger (Fig. 2). Extensive cortical destruction, partly in combination with cortical expansion, and a distinct soft tissue mass were present. The small lytic lesion in the middle phalanx of the ring finger showed no evidence of marginal sclerosis. Thus, an incidental finding of a simple bone cyst was excluded.

At magnetic resonance imaging (MRI), the lesion of the proximal phalanx of the little finger exhibited a nodular, heterogeneous pattern with low signal intensity approximately isointense to muscle on T1-weighted images and high signal intensity on T2-weighted images (Fig. 3). Homogeneous enhancement was seen on post-contrast T1-weighted images. The small lytic lesion in the base of the middle phalanx of the ring finger showed identical signal characteristics. In addition, a similar, tiny lesion was found in

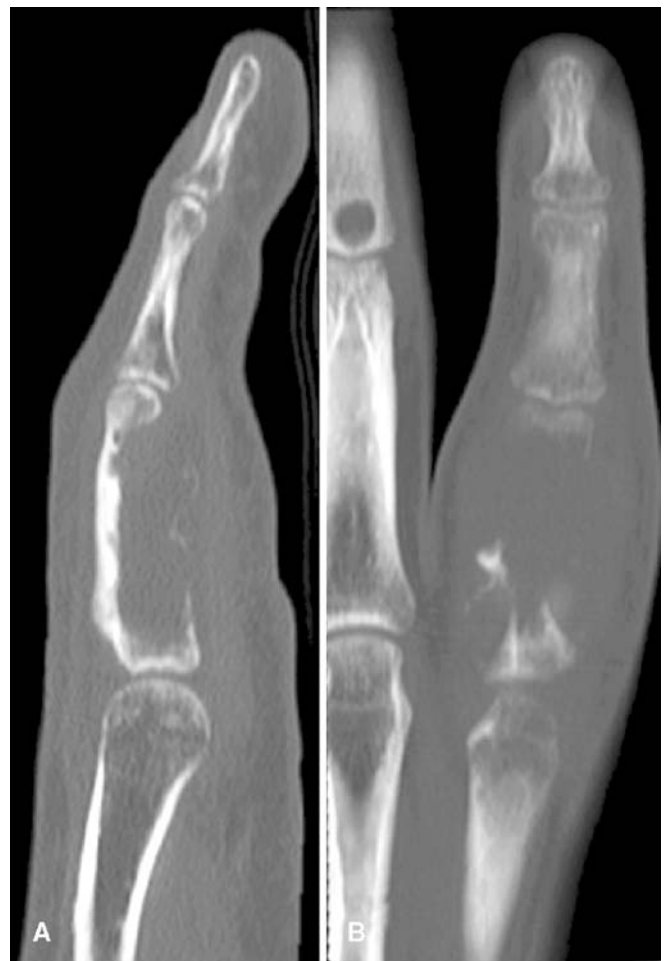
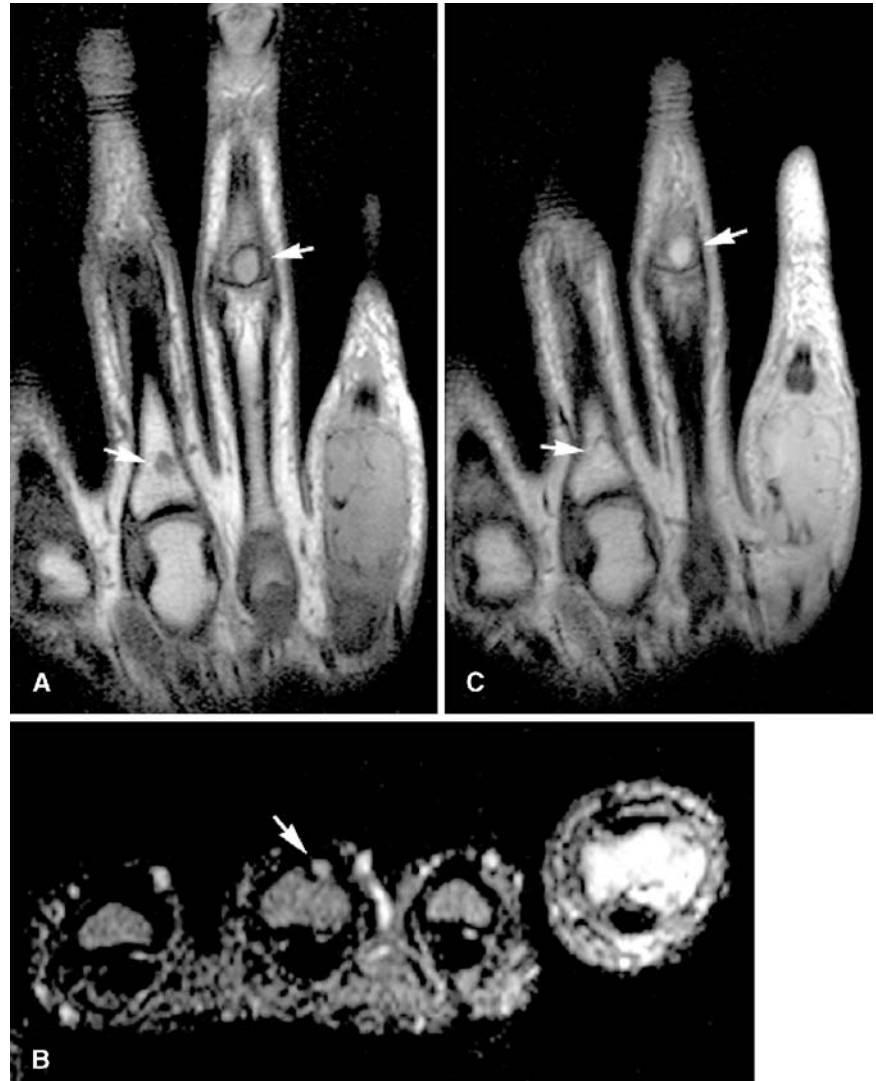


Fig. 2 **A** Sagittal CT reconstruction image of the little finger precisely demonstrates the extent of cortical destruction of the proximal phalanx and the expansion of the mass into the adjacent soft tissue. **B** The small, round lesion in the middle phalanx of the ring finger shows no evidence of marginal sclerosis

Fig. 3 **A** Coronal T1-weighted SE image (TR 703, TE 20) shows a large mass with lobular margins originating from the proximal phalanx of the little finger. The cortex is destroyed and the tumor extends into the soft-tissues. The signal intensity of the mass is similar to that of muscle. Small, round lesions in the middlephalanx of the ring finger and in the proximal phalanx of the middle finger display identical signal intensity. **B** On transverse T2-weighted SE image (TR 3790, TE 100) the lesions in the proximal phalanges of the middle and little finger exhibit high signal intensity. **C** Coronal contrast-enhanced T1-weighted SE image displays homogeneous enhancement of all lesions



the metaphysis of the proximal phalanx of the middle finger. Thus, multifocal disease was verified, which strongly supported the differential diagnosis of a vascular bone tumor.

Surgical biopsies of the lesion in the proximal phalanx of the little finger disclosed the pathologic diagnosis of EH. Subsequently, further imaging studies for tumor staging were performed. A CT scan of the thorax and sonography of the abdomen excluded pulmonary or hepatic metastatic disease. Whole-body MRI showed no additional sites of bony involvement.

The patient underwent amputation of the little finger, since limb-preserving surgery was not possible due to the extensive tumorous involvement of the proximal phalanx. The small lesions in the middle phalanx of the ring finger and the proximal phalanx of the middle finger were treated with curettage and grafting.

Histopathologic examination of the resected specimens confirmed the diagnosis of EH in all lesions. Gross examination revealed intramedullary well-demarcated soft,

spongy lesions with a hemorrhagic appearance. Areas of cortical erosion and disruption with extension into the soft tissue were found (Fig. 4). Histologically, the lesions consisted of irregularly anastomosing narrow vascular channels lined by epithelioid cells with inconspicuous pleomorphism. Vascular channels were separated by areas of solid strands of epithelioid cells embedded in a myxoid stroma (Fig. 5). Individual cells were rounded or polygonal with prominent nucleoli, and, to some extent, intracytoplasmic vacuolization was present (Fig. 6). Mitoses were rare; approximately 10% of tumor cells showed nuclear immunoreactivity using the proliferation marker MIB-1 (Fig. 7). Epithelioid cells did not react with antibodies against cytokeratins (AE1/3, LU-5). The endothelial nature of the neoplasm was confirmed by the expression of endothelial cell marker proteins. Tumor cells displayed an intense cytoplasmic reactivity with antibodies directed against CD34 (Fig. 8). Immunoreactivity was less intense using anti-CD34 and anti-factor VIII antibodies.



Fig. 4 Gross section of the proximal phalanx of the little finger demonstrates a soft, hemorrhagic lesion with irregular borders. Cortical destruction and soft tissue extension is focally present

At present, 5 months after surgery, the patient is free from symptoms. At latest radiological follow-up, no evidence of residual EH or metastatic disease was found.

Discussion

Endothelial cells may present with an abundant eosinophilic cytoplasm and a rounded or slightly fusiform shape, for which reason they have been designated “epithelioid” or “histiocytoid” endothelial cells. The term “epithelioid hemangioendothelioma” was first introduced by Weiss and Enzinger in 1982 to describe a distinct vascular tumor of soft tissue characterized by epithelioid endothelial cells.

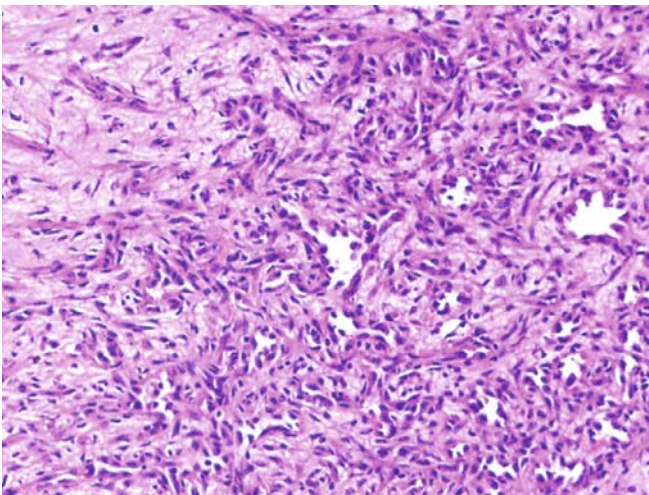


Fig. 5 Anastomosing vascular channels are interspersed with solid strands of epithelioid cells embedded in a myxoid stroma (H&E, $\times 200$)

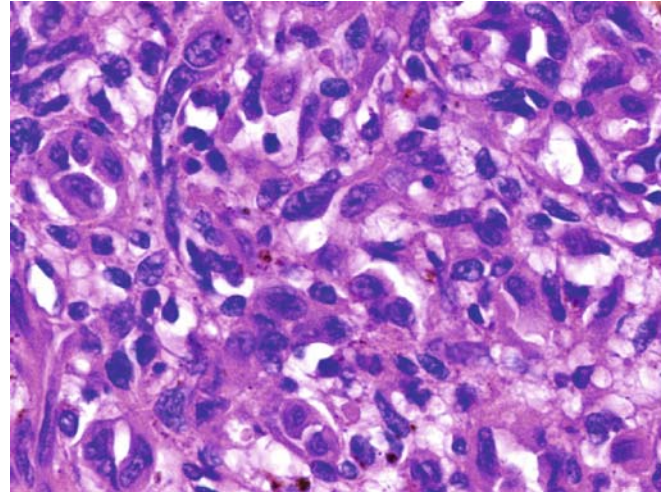


Fig. 6 Rounded nuclei with prominent nucleoli are surrounded by a dense, sometimes vacuolated cytoplasm (H&E, $\times 400$)

Subsequently this tumor entity was recognized in numerous other locations, particularly lung, liver and bone [1, 5, 6].

Epithelioid change may affect the endothelium of a variety of reactive, benign and malignant vascular lesions, and its presence per se does not significantly correspond to the biologic behaviour of the endothelial proliferation. In fact, the latter is determined by the pattern and arrangement of the cells, their degree of cytologic atypia and level of mitotic activity. Accordingly, the primitive vasoformative tendencies and its metastasis in a small percentage of cases distinguish EH from benign epithelioid hemangioma. Epithelioid angiosarcoma, its malignant counterpart, is characterized by its rudimentary vascular differentiation and a rapidly progressive course [1].

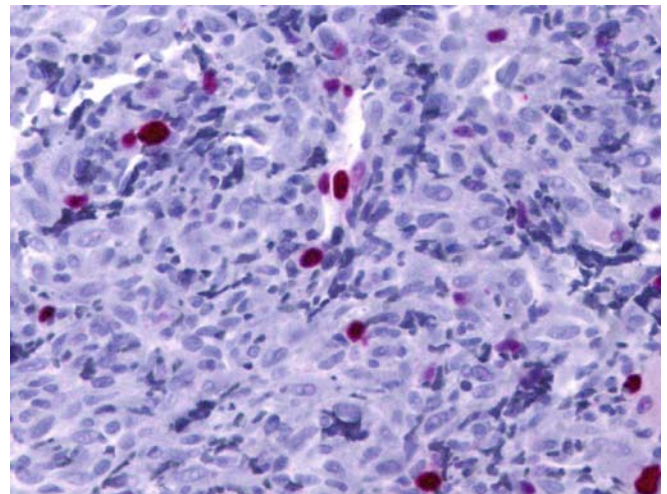


Fig. 7 Immunohistochemical labeling of the proliferation marker MIB-1. Approximately 10% of tumor cells showed immunoreactive nuclei (hemalun counterstain, $\times 400$)

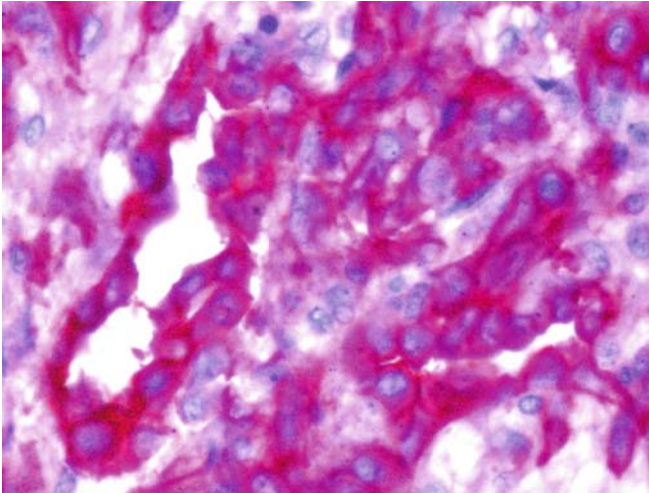


Fig. 8 Immunohistochemical labeling of the endothelial cell marker protein CD34. Tumor cells display intense cytoplasmic staining ($\times 400$)

Due to the rarity of epithelioid vascular tumors of bone and the variety of names assigned to them in previous reports, controversy arose regarding their nomenclature and classification. Meanwhile it has become widely accepted to classify the osseous epithelioid endothelial tumors in a similar manner to their soft tissue counterparts [7].

EH can occur at virtually any age, but the tumor appears to peak during the second and third decades of life. Males seem to be affected more often than females. The most common clinical symptoms are local pain and swelling, which may show a slowly progressive course [4, 8]. If the spine is affected, neurologic disturbances due to pathologic fractures or progressive cord compression can occur [9, 10].

Approximately 50% of EHs are multifocal. In these instances, the tumors are usually clustered in a certain anatomic region, i.e., in a single bone, adjoining bones of a single extremity or contiguous vertebral bodies. In a series of 40 patients from the Mayo Clinic files the most frequent sites of involvement comprised the long tubular bones of the lower limb (38%), the pelvic bones (18%), the vertebral bodies and ribs (16%), the small bones of the feet (10%) and the long tubular bones of the upper limb (10%). Only two lesions (3%) were observed in the bones of the hand [2].

Radiographically, EH presents with a lytic pattern of bone destruction. A coarse trabeculated or honeycomb pattern may be indicative of its vascular nature. Tumor growth most commonly occurs in the metaphyseal and diaphyseal areas and may involve cancellous as well as cortical bone [11]. Lesions may be well defined with or without surrounding sclerosis, but poorly marginated tumors prevail. Areas of cortical destruction and cortical expansion are common. Soft tissue masses, usually less extensive, are identified in approximately 40% of tumors.

Periosteal reaction is rare, and matrix mineralization is usually absent [2, 4].

Since radiographic findings are often nonspecific, the only feature that may be helpful in suggesting the diagnosis of EH is the presence of multiple lesions clustered in the same anatomic region. The radiographic differential diagnosis of multifocal EH includes metastatic carcinoma and multiple myeloma, particularly in middle-aged and older patients. Multifocal EH displaying lesions with a bubble-like appearance and osseous expansion may resemble fibrous dysplasia or adamantinoma. Tumors with a more destructive lytic pattern may mimic tuberculous osteomyelitis. Diffuse cystic angiomatosis should be considered in young patients with multifocal well-circumscribed lytic lesions.

Enchondromas are the most commonly found multiple benign tumors of bone, with a predilection for the small bones of the hand [12]. The small, well-defined osteolytic lesion in the middle phalanx of the ring finger in our case might have been consistent with this differential diagnosis. However, the aggressive features of the lesion in the proximal phalanx of the little finger are contrary to the typical radiographic findings of enchondroma, which is usually well demarcated with varying degrees of cortical expansion, endosteal scalloping and matrix calcification [13].

On MR images, EH presents with heterogeneous masses primarily isointense to muscle on T1-weighted images and hyperintense on T2-weighted images. Compared with hemangioma, fat overgrowth is absent, and more aggressive features, including cortical destruction and infiltration of the surrounding tissues, can be seen. The presence of flow voids, which represent prominent vascular channels, occurring most often in the periphery of the mass, may indicate a tumor of vascular origin. However, this finding is not typical of hemangioendothelioma, but should rather suggest the diagnosis of hemangiopericytoma [11, 14].

The prognosis of EH of bone is hardly predictable. Most cases seem to run an indolent to slowly progressive course, but tumors may also metastasize to parenchymal organs indicating progression to a malignant lesion [1, 15, 16, 17]. Follow-up of patients with EH of bone has been the subject of a study by Kleer et al. [4]. In their series, eight of 40 patients (20%) died of EH during an average follow-up period of 4.3 years. Visceral involvement seemed to be the most important criterion in predicting the outcome.

It is unclear whether unifocal and multifocal disease have a different prognosis [4, 8]. However, the occurrence of multifocal disease in half of the cases and the possible development of metastatic disease emphasize the need for a comprehensive tumor staging, including a skeletal survey or whole-body MRI/CT.

The number, size and location of the tumors frequently determine the type of treatment. For localized disease, wide resection is recommended. Radiation or chemotherapy have been effective in some patients with multicentric tumors [4, 7, 18]. Definitive data regarding the efficacy of

individual therapeutic regimens are not available due to the low number of documented cases.

In summary, our case displays the classic features of multifocal epithelioid hemangioendothelioma, including the young age and male gender of the patient, the typical cli-

nical symptoms, as well as pertinent radiologic findings, i.e., multiple osteolytic lesions of varying aggressiveness clustered in a circumscribed anatomic region. However, this case is atypical and noteworthy due to the uncommon site of manifestation in the phalanges of the hand.

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