

Case Report

A case of epithelioid hemangioma of the right third rib in a 55-year-old man

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Abstract: We report a case of epithelioid hemangioma in a relatively uncommon location but with typical features in a 55-year-old man. A 55-year-old man was referred to our hospital with an asymptomatic mass of the right third rib, after the mass was incidentally found during a health checkup in April 2014. The mass had been gradually growing in size during the previous 1 year and 8 months. On physical examination, the mass was not palpable. On a plain radiograph, a bone tumor with ballooning was identified on the right third rib. Chest computed tomography revealed a mass protruding into the thoracic cavity from the right third rib with cortical destruction. Surgical resection of the tumor was performed because the tumor had been gradually increasing in size. The tumor size was 35×25×20 mm. Histopathologically, the tumor was proliferating within the bone and replacing the marrow cavity. The tumor was composed of small to medium sized arteriolar vessels lined by flat to swollen endothelial cells with prominent nucleoli. The tumor stroma was filled with mixed inflammatory cells with massive eosinophils. The tumor cells did not show apparent nuclear pleomorphism. No necrotic area or mitosis was observed. Immunohistochemically, tumor cells were diffusely positive for CD31 and were focally positive for AE1/AE3, but were negative for CD34, D2-40, and CAM5.2. MIB-1 labeling index was almost 0%. Based on these findings, a final diagnosis of epithelioid hemangioma of the rib was made. The patient is disease-free at 5 months after surgery. However, further long-term follow up is needed.

Keywords: Epithelioid hemangioma, bone, rib

Introduction

Epithelioid hemangioma of the bone is a locally aggressive uncommon vascular neoplasm composed of cells with an endothelial phenotype and morphology [1]. These tumors mostly involve the long tubular bones (40%), distal femur (18%), and flat bones (18%), with only 4% occurring in the ribs [2].

Since it exhibits a wide range of histological features, including an intravascular growth pattern, massive inflammatory infiltration, and solid/cellular pattern, it has been referred to as histiocytoid hemangioma, angiolymphoid hyperplasia with eosinophilia, and hemorrhagic epithelioid and spindle cell hemangioma [1]. Therefore, epithelioid hemangioma can be confused with other conditions, ranging from Kimura disease to malignant epithelioid vascular

tumors such as epithelioid hemangioendothelioma and epithelioid angiosarcoma. Although the tumorigenesis of epithelioid hemangioma remains unknown, a recent study demonstrated frequent FOS rearrangement in this tumor [3], providing evidence of classifying this tumor as a distinctive entity.

Here, we report a rare case of epithelioid hemangioma of the rib, a relatively rare location, in a 55-year-old male patient.

Case report

A 55-year-old man was referred to our hospital with an asymptomatic mass of the right third rib, because the mass was incidentally found during a health checkup in April 2014. The mass had been gradually growing in size during the previous 1 year and 8 months. On physical

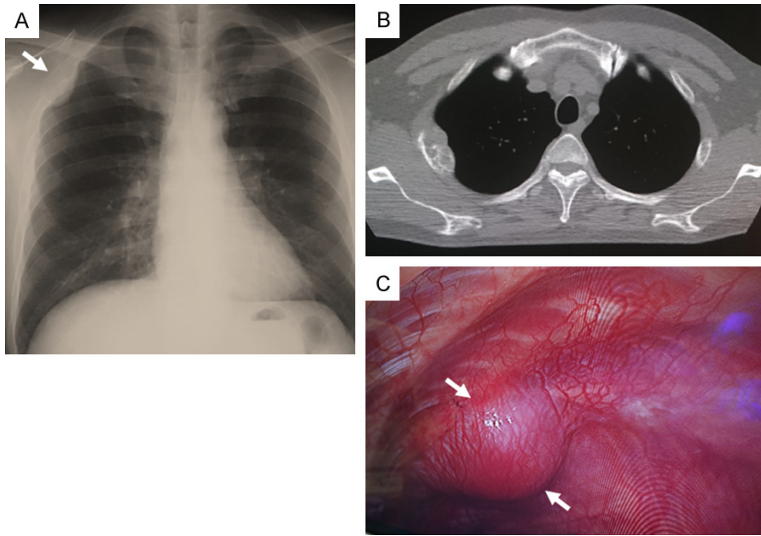


Figure 1. (A) A plain radiograph showing the bone tumor with ballooning on the right third rib. (B) Chest computed tomography (CT) image showing a mass protruding into the thoracic cavity from within the right third rib with cortical destruction. Thin bone trabeculae seemed to separate the interior of the mass. (C) Intraoperative thoracoscopy image showing a protruding tumor originating from the right third rib; the pleura on the side of the chest wall is preserved (C).

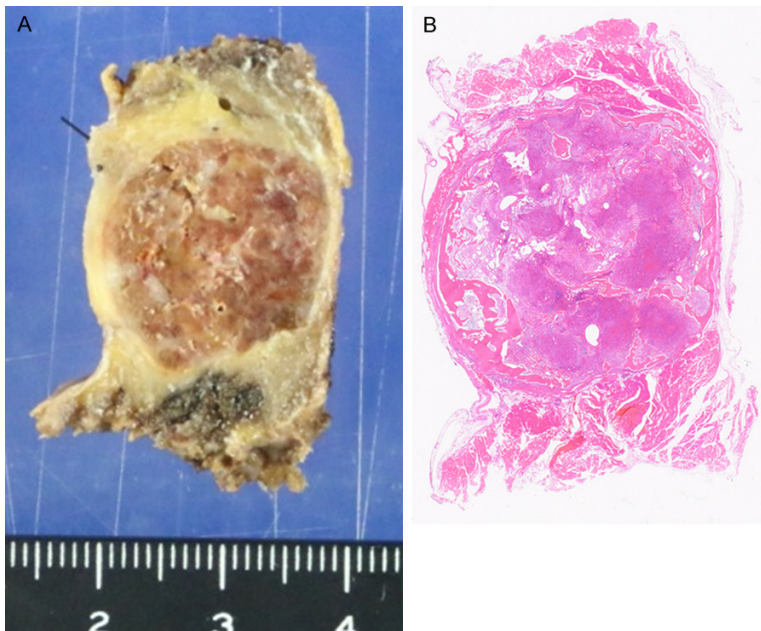


Figure 2. A: The cut surface of a resected specimen showing that the rib was enlarged; a red-brown tumor can be seen occupying the medullary cavity. B: A low-power view image showing that the tumor was multilobulated and separated by thin bony trabeculae. The proliferating tumor cells can be seen replacing the marrow cavity.

examination, the mass was not palpable and lymph node swelling was not noted. The laboratory data did not show any abnormal values,

including tumor markers. A peripheral blood examination taken two months before surgery revealed a total of 7600/ μ L of white blood cells (neutrophils: 54.9%, lymphocytes: 28.8%, monocytes: 7.2%, eosinophils: 7.6%, basophils: 1.5%). The serum IgE level was not examined. On a plain radiograph, a bone tumor with ballooning was identified on the right third rib (**Figure 1A**). Chest computed tomography (CT) revealed a mass protruding into the thoracic cavity from the right third rib with cortical destruction. Thin bone trabeculae seemed to separate the interior of the mass. However, no evidence of pleural effusion, swelling of mediastinal lymph nodes, or invasion into the lung was found (**Figure 1B**). Positron emission tomography (PET)-CT performed 1 year before surgery revealed focal uptake at the right third rib (SUVmax = 6.7). Surgical resection of the tumor was performed because the tumor had been gradually increasing in size, although the clinical diagnosis was a benign to low-grade malignant tumor with possibly secondary aneurysmal bone cyst-like changes. The intraoperative thoracoscopic findings included a protruding tumor that originated from the right third rib, and preserved pleura on the side of the chest wall (**Figure 1C**).

The tumor size was 35×25×20 mm. The cut surface of the resected specimen showed that the rib was enlarged and a red-brown tumor was occupying the medullary cavity (**Figure 2A**). Histopathologically, the lobular tumor was proliferating within the bone and replacing the marrow cavity (**Figure 2B**). Al-

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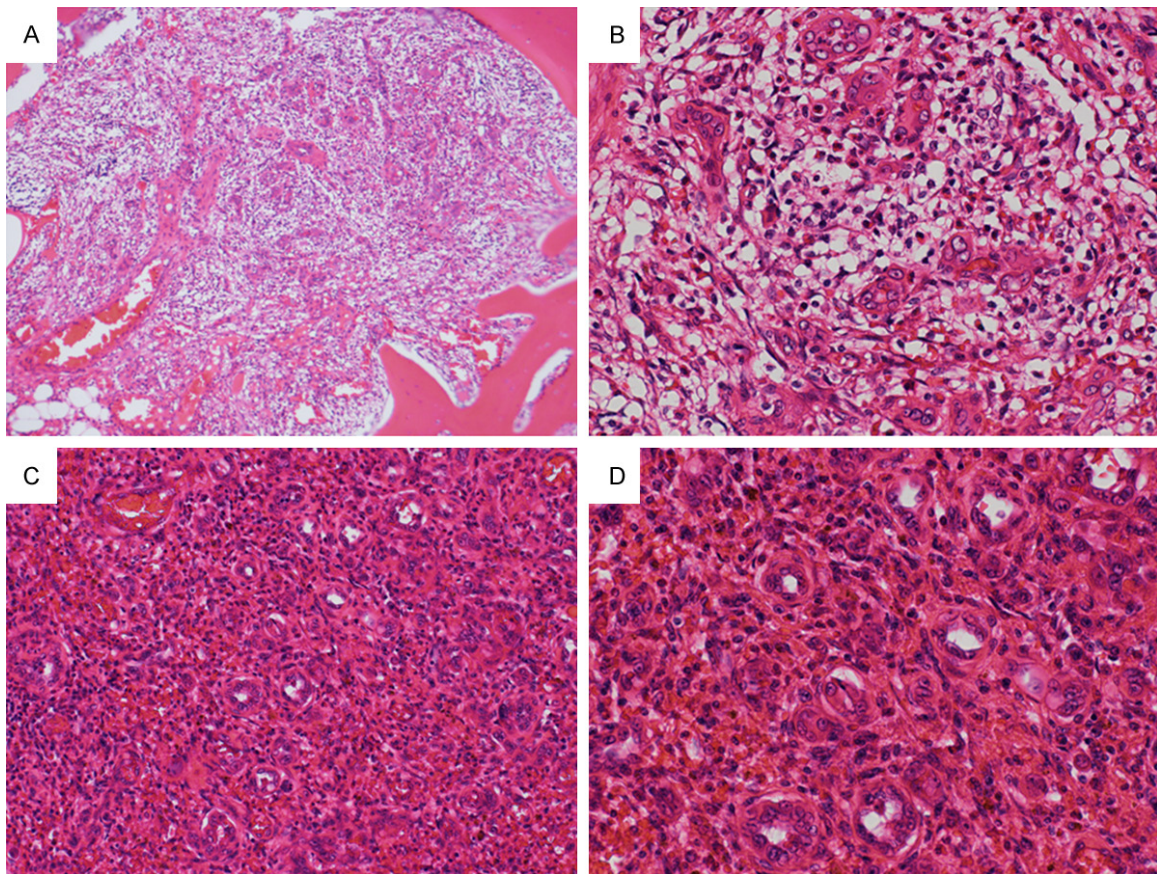


Figure 3. (A, B) Within the tumor, a slightly hypocellular area (A) composed of rather large-sized vessels and cellular areas (B) are noted; however, the latter is rather prominent. (C) The tumor was composed of small- to medium-sized arteriolar vessels lined by flat to swollen endothelial cells with prominent nucleoli. The vessels were filled with erythrocytes. The tumor stroma was filled with mixed inflammatory cells with massive eosinophils. (D) The tumor cells did not show apparent nuclear pleomorphism.

though a slightly hypocellular area composed of rather large-sized vessels was also noted (**Figure 3A**), cellular areas were rather prominent (**Figure 3B**). The tumor was composed of small- to medium-sized arteriolar vessels lined by flat to swollen endothelial cells with prominent nucleoli. The vessels were filled with erythrocytes. The tumor stroma was filled with mixed inflammatory cells, including massive eosinophils, which obscured the vascular structure (**Figure 3C**). The tumor cells did not show apparent nuclear pleomorphism (**Figure 3D**). The vacuoles within tumor cells containing erythrocytes were not evident. No necrotic area or mitosis was observed. There was a focal defect of the peripheral area of the bone cortex and the tumor expanded into the surrounding soft tissue. The surgical margin was negative for tumor cells. Immunohistochemically, tumor cells were diffusely positive for CD31 and were

focally positive for AE1/AE3, but were negative for CD34, D2-40, CAM5.2 (**Figure 4A-C**). MIB-1 LI was almost 0% (**Figure 4D**). Based on these findings, a final diagnosis of epithelioid hemangioma of the rib was made. Five months after diagnosis, the patient was alive with no evidence of the disease.

Discussion

The term epithelioid hemangioma of the bone has been controversial, and an early study demonstrated that epithelioid hemangioma of the bone represents a variant of epithelioid hemangioendothelioma with metastatic potential [4]. However, it has now been accepted as a benign bone tumor with a low recurrence rate [1]. Epithelioid hemangioma of the bone is often difficult to distinguish from malignant tumors, because of the aggressive and destruc-

Epithelioid hemangioma of the rib

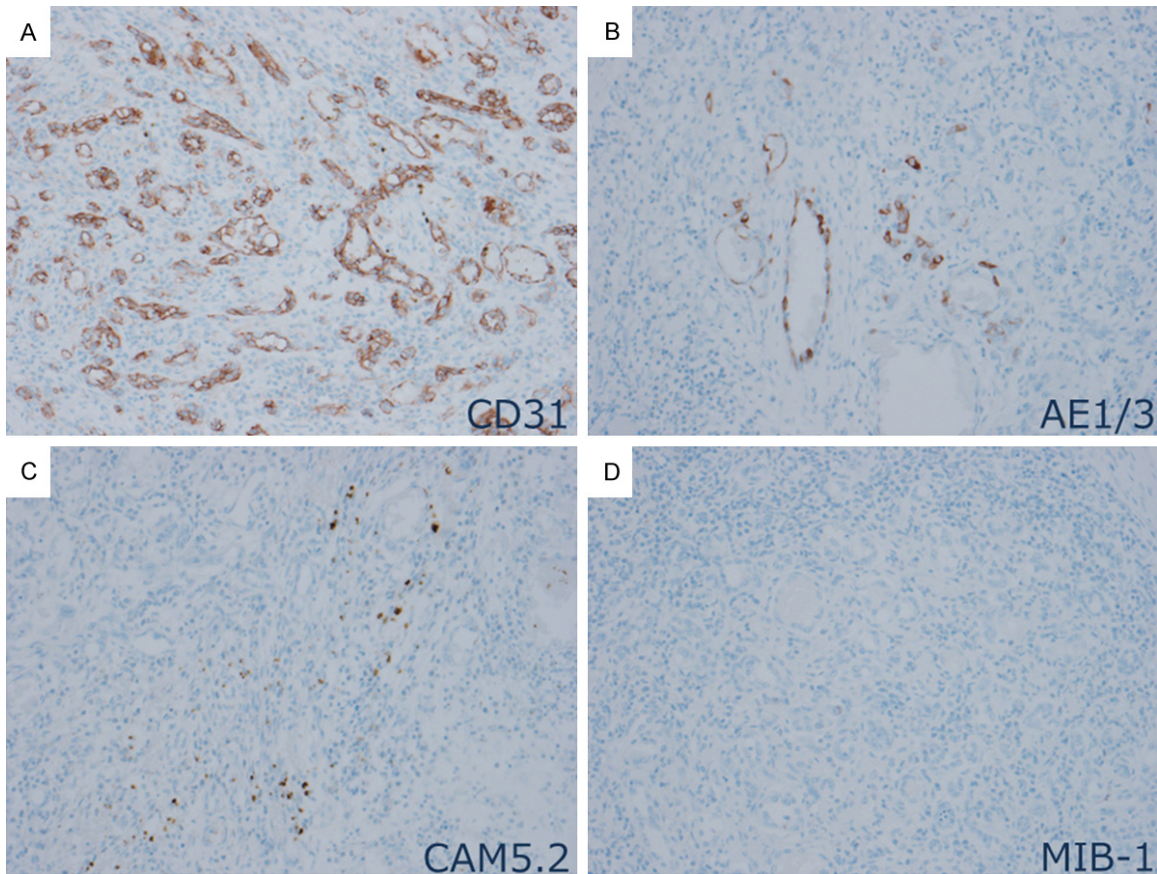


Figure 4. (D) Immunohistochemically, tumor cells were diffusely positive for CD31 (A) and were focally positive for AE1/AE3 (B), but were negative for CAM5.2 (C). MIB-1 LI was almost 0% (D).

tive growth and/or multifocality, or by the presence of atypical histological features such as an increased number of mitosis and necrosis. Epithelioid hemangioma often affects separate bone and can be multifocal in up to 20% of cases [2]. However, systemic examination revealed no evidence of other lesions in this case. Furthermore, pleomorphism of tumor cells was not evident, and mitosis/necrosis was not observed. In addition, expansion of the tumor into the surrounding soft tissue was minimal, although the tumor showed an expanding growth pattern. Based on these clinical, radiological, and pathological findings, a diagnosis of epithelioid hemangioma was made.

Recent studies have demonstrated recurrent gene rearrangements in vascular neoplasms such as epithelioid hemangioma [3, 5, 6], epithelioid hemangioendothelioma [7], and angiosarcoma [8, 9]. Furthermore, epithelioid hemangioendothelioma has been shown to be

characterized by recurrent translocations involving chromosomal regions 1p36.3 and 3q25, resulting in the formation of a *WWTR1-CAMTA1* fusion gene in approximately 90% of cases, and a small subset (<5%) have a *YAP1-TFE3* fusion gene [7]. In addition, the diagnostic utility of CAMTA1 immunohistochemical staining has also been shown [10]. Furthermore, subcutaneous implantation of *NUP160-SLC43A3*-expressing fibroblasts induced tumors resembling human angiosarcoma [8]. Although the tumorigenesis of epithelioid hemangioma remains unknown, a recent study demonstrated frequent *FOS* rearrangement in this tumor [3]. A diagnosis of epithelioid hemangioma is often difficult and challenging because of the wide range of histological features in this tumor. However, these studies provide evidence that these tumors have different pathogenesis and are distinctive entities. Unfortunately, we have not examined the formation of these fusion genes in this case.

Histologically, epithelioid hemangioma tends to show well-formed vascular channels, whereas epithelioid hemangioendothelioma contains so-called blister cells with intracytoplasmic lumina reminiscent of their angiogenic properties [2]. A previous study showed that mitoses were relatively infrequent, even in the cellular area, and that small foci of necrosis were present in minority cases [2]. The presence of these features therefore indicates a necessity to carefully distinguish tumors from epithelioid hemangioendothelioma and epithelioid angiosarcoma. Low-power magnification of this tumor revealed a lobulated growth pattern that would favor epithelioid hemangioma. Cytological atypia with hyperchromasia and marked nuclear pleomorphism was absent in this case, and mitosis and necrosis could not be detected. In addition, massive infiltration of eosinophils was noted. These findings led us to reach the diagnosis of epithelioid hemangioma of the bone.

In our case, an osteolytic and expansive lesion was observed on plain radiograph. Previous studies reported that epithelioid hemangioma could show either osteolytic with/without sclerotic changes or even both changes [11, 12]. Differential diagnoses such as fibrous dysplasia with aneurysmal bone cyst-like change and chondroid tumor were considered clinically, because these tumors can appear as osteolytic expanding lesions. The CT findings of epithelioid hemangioma of the bone were also described as lesions that could show a thin ossification rim at the extraosseous periphery and also contain scattered calcifications and residual trabeculae [12, 13]. Our case also demonstrated residual bone trabeculae with a thin peripheral rim, consistent with the previous findings [12, 13]. The massive stromal bleeding and inflammatory cells led us to a clinical diagnosis of fibrous dysplasia with secondary aneurysmal bone cyst-like change.

In summary, we report a case of epithelioid hemangioma in a relatively uncommon location but with typical feature in a 55-year-old man. The patient is disease-free at 5 months after surgery. However, further long-term follow up is needed.

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Disclosure of conflict of interest

None.

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