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CT and MRI Findings of Epithelioid Hemangioma of Bone: A Case Report

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Abstract

Epithelioid hemangioma (EH) of bone is a rare, locally aggressive vascular tumor, classified as an intermediate-grade neoplasm in the WHO classification. This article reports a case of a 15-year-old male patient presenting with left knee pain for over one month. Imaging revealed a well-defined osteolytic lesion in the left tibial metaphysis without a sclerotic border or periosteal reaction. MRI showed the lesion to be markedly hyperintense on T2WI, with progressive heterogeneous enhancement post-contrast. Histopathological examination confirmed epithelioid endothelial cell proliferation, supported by a characteristic immunohistochemical profile (CD31+, ERG+), leading to a diagnosis of EH. This case highlights the atypical presentation of EH in an adolescent and emphasizes the role of multimodal imaging and histopathological correlation in diagnosis.

Keywords

Epithelioid Hemangioma, Bone Tumor, Misdiagnosis, Imaging Diagnosis and Differential Diagnosis

1. Introduction

Epithelioid hemangioma (EH) of bone is a rare vascular tumor. According to the 2020 World Health Organization (WHO) Classification of Soft Tissue and Bone Tumours, it is categorized as an intermediate-grade, locally aggressive neoplasm due to its potential for local recurrence and very rare metastasis [1]. This classification refines the diagnostic criteria established in earlier editions. Although most reported cases occur in adults aged 30 - 60 years, EH can also affect adolescents [2].

Clinically, patients often present with localized pain, which may be chronic or incidentally discovered following minor trauma [3]. Long tubular bones are the most frequently involved sites, although involvement of the spine, flat bones, and

small bones has also been reported [4]. EH is mostly solitary, with approximately 25% of cases being multifocal [3]. In children or adolescents, the lesion may cross the growth plate. Radiologically, EH typically appears on CT as a well-defined osteolytic lesion, usually without a sclerotic rim or periosteal reaction. On MRI, it characteristically shows marked hyperintensity on T2-weighted sequences and prominent, often heterogeneous enhancement after contrast administration.

Histologically, EH is composed of well-formed vascular channels lined by epithelioid endothelial cells with abundant cytoplasm, often accompanied by a mixed inflammatory cell infiltrate [4]. Genetically, recurrent rearrangements involving the FOS gene and, less commonly, the FOSB gene have been identified and serve as valuable diagnostic markers [5].

The non-specific imaging features of EH overlap with several other bone lesions, including epithelioid hemangioendothelioma (EHE), chondroblastoma, and giant cell tumor of bone (GCTB), making preoperative diagnosis challenging and sometimes leading to diagnostic pitfalls [6]-[9]. This report describes a case of tibial EH in an adolescent, detailing its clinical, radiological, and pathological characteristics to aid in recognition and differential diagnosis.

2. Case Presentation

The patient is a 15-year-old male who presented with left knee pain for over one month. The pain began one month prior after his left knee was accidentally pinched by a door. The pain occurred during walking without clicking sounds, worsened with activity, and did not worsen at rest. Physical examination and laboratory tests were unremarkable. CT of the left knee joint showed a roundish osteolytic lesion in the left tibial metaphysis, measuring approximately 3.2 × 3.2 × 4.0 cm in greatest dimensions. The edge showed no sclerotic border or periosteal reaction. Residual bone trabeculae were visible subchondrally. The internal density was relatively uniform, and borders were clear. The lesion was confined to the metaphysis without soft tissue extension. MRI revealed a roundish soft tissue mass in the left tibial metaphysis, crossing the growth plate and involving the articular surface. No sclerotic border was seen at the edge. The lesion appeared isointense to slightly hyperintense on T1WI and markedly hyperintense on T2WI, with clear borders and no surrounding periosteal reaction. Post-contrast scans showed progressive, significant, and heterogeneous enhancement. Patchy and linear non-enhancing low-signal areas were seen within the lesion. Adjacent bone marrow showed irregular patchy areas of prolonged T1 and T2 signals, indicating edema.

The patient underwent two surgical procedures. First, an open biopsy of the left tibial plateau mass was performed under spinal anesthesia on August 13, 2024. During surgery, a large amount of dark red fluid flowed from the lesion. Some fluid was aspirated, and part of the cystic wall tissue was curetted and sent for pathological examination. Microscopically, tumor cells exhibited epithelioid morphology with enlarged nuclei, irregular nuclear membranes, visible nucleoli, and abundant eosinophilic cytoplasm, growing in solid sheets. Vascular formation was observed. The

tumor was accompanied by inflammatory cell infiltration and hemosiderin deposition. Immunohistochemistry: CD31 (+), ERG (+), CD34 (−), MDM2 (+), CDK4 (+), SATB2 (−), S-100 (−), CD1a (−), SMA (−), Desmin (−), CD68 (histiocytes, +), P-CK (−), H3.3G34W (−), H3K36M (−), TFE3 (−), Ki-67 approximately 5% (+). The pathological diagnosis was consistent with epithelioid hemangioma.

Subsequently, on August 19, 2024, the patient underwent curettage of the left tibial lesion, autologous iliac bone graft harvesting, and bone grafting. The previous incision was extended to approximately 4 cm. The cystic wall was curetted, and additional abnormal tissue was sent for pathological examination. The surgical field was irrigated and soaked with distilled water, and exploration revealed no obvious residual abnormal tissue. A mixture of autologous cancellous bone (harvested from the left anterior superior iliac spine) and allograft bone was implanted into the cavity. Microscopic examination again revealed epithelioid tumor cells with similar features, accompanied by necrosis. Combining these findings with the initial biopsy results, the diagnosis remained epithelioid. A follow-up CT scan one month after surgery showed no evidence of residual tumor or recurrence (Figure 1).

Figure 1. (a)-(b): DR and CT show a roundish osteolytic lesion in the metaphysis of the left proximal tibia with clear borders. CT reveals residual bone trabeculae subchondrally. (c)-(f): MRI shows the lesion in the left tibial metaphysis crossing the growth plate and involving the articular surface. It appears isointense to slightly hyperintense on T1WI and hyperintense on T2WI. Post-contrast scans show progressive, significant, and heterogeneous enhancement, with patchy and linear non-enhancing low-signal areas inside. Adjacent bone marrow edema is present.

3. Discussion

Epithelioid hemangioma (EH) of bone is a rare vascular tumor with non-specific imaging features, and definitive diagnosis still relies on pathological examination [10]. The imaging findings in this case primarily manifested as a well-defined osteolytic lesion without a sclerotic border or periosteal reaction, markedly hyperintense on T2WI, with progressive and significant enhancement on post-contrast scans. These findings are largely consistent with the reported imaging characteristics of EH [2].

Regarding differential diagnosis, distinguishing EH from other epithelioid vascular tumors, particularly epithelioid hemangioendothelioma (EHE), is difficult and primarily relies on integrated pathological and molecular evaluation. Well-formed vascular structures are rarely observed in EHE [3], and 94% of EHE cases express WWTR1-CAMTA1 [6], which helps differentiate it from EH. EH also needs to be differentiated from chondroblastoma. Chondroblastoma and EH share similar imaging features. Chondroblastoma typically appears as a well-defined osteolytic lesion with a sclerotic border. Calcification is common, and periosteal reaction and adjacent soft tissue reaction may occur. The presence of calcification is a key differentiating point between chondroblastoma and EH [2]. EH also requires differentiation from giant cell tumor of bone (GCTB). Radiographically and on CT, GCTB mainly presents as an eccentric, expansile osteolytic lesion with indistinct borders, no sclerotic rim, and may break through the cortex to form a soft tissue mass. On MRI, it appears as intermediate signal on T1WI and heterogeneous hyperintensity on T2WI, with marked enhancement. Pathologically, GCTB is characterized by mononuclear stromal cells mixed with numerous osteoclast-like multinucleated giant cells, and is positive for H3.3 G34W immunohistochemistry [11]. The immunohistochemical results in this case (CD31+, ERG+, H3.3G34W-) effectively support the diagnosis of EH and exclude the main differential diagnoses mentioned above.

In the context of an adolescent patient with a metaphyseal lytic lesion, other entities must be considered. Aneurysmal bone cyst (ABC) often presents with fluid-fluid levels on MRI and an expansile, multiloculated appearance [12]; however, this lesion showed solid enhancement without prominent cystic spaces, making ABC less likely. Brodie abscess, a form of subacute osteomyelitis, typically presents as a lytic lesion with a sclerotic rim on imaging and may exhibit the "penumbra sign" on MRI [13]. In contrast, the current case showed no sclerotic margin or periosteal reaction, and the absence of clinical or laboratory evidence of infection (normal inflammatory markers, negative cultures) argues against this diagnosis. Langerhans cell histiocytosis (LCH) of bone typically affects children and adolescents, with imaging findings that can mimic epithelioid hemangioma. However, LCH is characterized by the presence of CD1a+, S-100+, and CD207 (Langerin)+ dendritic cells on immunohistochemistry, along with the possible detection of Birbeck granules on electron microscopy [14]. In the present case, negative staining for CD1a and S-100 effectively excluded LCH, supporting the diag-

nosis of epithelioid hemangioma.

It is noteworthy that the literature reports the peak incidence of EH to be between 30 - 60 years of age [2], whereas this patient is a 15-year-old adolescent. This aligns with sporadic case reports documenting EH in younger individuals and even in uncommon locations like the spine [15], suggesting that this tumor should be considered in the differential diagnosis for lytic bone lesions across a wider age range. Pathologically, EH is primarily characterized by epithelioid vascular proliferation with inflammatory cell infiltration. Molecular testing shows that some cases harbor *FOS* or *FOSB* gene rearrangements. Although such testing was not performed in this case, this molecular feature provides direction for future diagnosis, especially in challenging cases.

The presence of MDM2 and CDK4 immunopositivity in this case initially raised concern for an MDM2-amplified sarcoma. Immunohistochemical positivity for MDM2 and CDK4 is a valuable tool in distinguishing low-grade osteosarcoma from its benign mimics [16]. However, focal nuclear expression of these markers has been reported in a minority of benign fibro-osseous lesions, and this expression does not necessarily correlate with MDM2 gene amplification [17]. In the present case, the morphological features (epithelioid vascular proliferation) were diagnostic of epithelioid hemangioma, and the MDM2/CDK4 positivity was interpreted as nonspecific expression in this context. Fluorescence in situ hybridization (FISH) for MDM2 amplification was not performed, representing a limitation of this study.

The primary treatment for solitary, symptomatic bone EH is surgical intervention, with curettage or marginal excision being the most common procedures. Complete surgical resection with clear margins is generally curative and associated with a low recurrence rate. However, due to its locally aggressive nature, the reported recurrence rate for bone EH is approximately 11% [4], underscoring the importance of complete initial resection. For multifocal or surgically challenging lesions, treatment strategies may need to be individualized. There is limited but evolving evidence regarding the role of non-surgical modalities. Isolated case reports have described the use of medication for disease control in selected situations, although this is not yet standard practice [18]. Radiotherapy is rarely employed and typically reserved for exceptional circumstances where surgery is not feasible [3].

Given the potential for local recurrence, long-term clinical and imaging follow-up is recommended for patients with bone EH [4]. The follow-up protocol typically involves periodic physical examination and imaging studies, such as MRI or CT, especially within the first few years post-treatment, to monitor for any signs of recurrence or progression. The relatively low proliferative index (Ki-67 ~5% in this case) is consistent with its indolent biological behavior, but does not eliminate the need for surveillance.

This study has limitations. Multifocal disease assessment was not performed in this patient, so the possibility of additional asymptomatic skeletal lesions cannot be completely excluded.

4. Conclusion

In summary, although EH lacks specificity in imaging, combining its predilection site, imaging patterns, and patient demographics can provide important diagnostic clues. Final diagnosis relies on histopathological examination and immunohistochemical analysis. Given its locally aggressive nature and an approximate recurrence rate of 11%[4], regular postoperative imaging follow-up is crucial for monitoring recurrence. This case underscores the importance of a multidisciplinary approach in diagnosing and managing this uncommon bone tumor.

Ethics Statement

Informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. Institutional review board approval was waived due to the retrospective nature of the report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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