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CASE REPORT

Primary intraosseous papillary intralymphatic angioendothelioma of the distal femoral epiphysis: a case report with literature review

J. J. Pozo-Kreilinger[1] · E. M. Pena-Burgos[2] · E. J. Ortiz-Cruz[3] · J. M. Cordero-García[4] · I. Barrientos Ruiz[3] · M. Tapia-Viñe[5] · M. Peleteiro-Pensado[3] · D. Bernabéu-Taboada[5]

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Abstract

Introduction Papillary intralymphatic angioendothelioma (PILA) is an exceptionally rare metastasizing soft tissue tumor. It tends to arise in the subcutaneous tissues of distal extremities in children. Only four intraosseous PILA cases have been reported until now in English language literature.

Case report We present a case of PILA arising in the distal femoral epiphysis of a 50-year-old female patient. It started as a relentless pain in her left knee. A plain radiography revealed a radiolucent area in the left internal femoral condyle. Computerized tomography revealed a 1-cm lytic lesion with a sclerotic rim. Magnetic resonance images showed a significant bone marrow edema signal focused on a 1-cm subchondral lesion suggestive of an intraarticular osteoid osteoma. Histologically, the tumor contained vascular channels covered by a single endothelial layer with intraluminal papillary endothelial structures lined with hobnail cells. Immunohistochemically, the cells were positive for ERG, CD31, and D2-40. The tumor underwent cryoablation and 6 months later, after local recurrence or tumor persistence, a wide tumor resection was referred. After 7 years of follow-up, the patient displayed neither local recurrence nor distant metastases.

Conclusion Primary intraosseous PILAs are exceedingly rare tumors that should be considered in the differential diagnosis of vascular bone tumors.

Keywords Papillary intralymphatic angioendothelioma · Dabska tumor · Vascular tumors · Bone tumors

Introduction

Papillary intralymphatic angioendothelioma (PILA) is a vascular tumor that was first described by Dabska et al. in 1969 [1]. It is also referred to as Dabska tumor and is believed to arise from lymphatic vessels [2]. PILA accounts for less than 1% of all soft tissue tumors [3], with no more than 50 reported cases [3]. PILA most frequently occurs as skin nodules or plaques involving distal extremities in children [4]. Currently, only four primary intraosseous PILAs have been reported [5–8].

The plain radiography appearance of intraosseous PILA consists of a circumscribed radiolucent area [5, 6]. In computerized tomography (CT), these lesions are lytic and well-defined, and a sclerotic rim and periosteal reaction may be present [3]. Magnetic resonance imaging (MRI) reveals hypointense lesions in T1-weighted images (WI) and hyperintense lesions in T2-fat suppressed (FS)-WI, possibly indicating the presence of a bone edema signal. The association of a small peripheral lesion, periosteal reaction, and bone marrow edema signal may suggest an osteoid osteoma [5, 6, 8].

Most cases are benign lesions consisting of lymphatic vascular channels lined by columnar hobnail cells. Variably, intraluminal papillary tufts, proteinaceous material and lymphocytes may be observed [3]. Cells are

✉ E. M. Pena-Burgos
evapenaburgos.ep@gmail.com

1 Pathology Department, La Paz University Hospital, Madrid, Spain

2 Pathology Department, Gregorio Marañón General University Hospital, Madrid, Spain

3 Orthopaedic Surgery and Traumatology Department, La Paz University Hospital, Madrid, Spain

4 Nuclear Medicine Department, La Paz University Hospital, Madrid, Spain

5 Radiology Department, La Paz University Hospital, Madrid, Spain

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immunohistochemically positive for pan-endothelial and lymphatic endothelial markers [2]. Some cases reveal lymph node metastasis [4]. The objective of this article is to present the clinical, radiological, and histopathological features as well as the management of this exceedingly rare vascular bone tumor.

Case report

Clinical findings

A 50-year-old female was referred to our hospital for evaluation of her painful left knee. The pain began 6 months ago and was located in the internal femoral condyle. It was nocturnal, interfering with sleep, and ceased with non-steroidal anti-inflammatory drugs (NSAIDs). She denied any recent local trauma. She had no relevant personal medical history.

Radiological findings

Plain radiography revealed a well-defined radiolucent area of 1.5 cm in the left internal femoral condyle having a sclerotic rim. No periosteal reaction was detected (Fig. 1A).

MRI evaluation showed a 1-cm lesion in the subchondral area of the antero-internal femoral condyle with a signal that was hypointense on T1-WI, hyperintense on T2-FS-WI and which had a hypointense peripheral rim in both sequences. Severe bone marrow edema signal spread from the lesion, involving the entire condyle. Homogeneous and intense enhancement of the lesion was achieved using gadolinium (Fig. 1B, C, D). Osteoid osteoma was suggested by MRI findings.

In the CT (Fig. 1E), a lytic lesion of approximately 1 cm in diameter with a sclerotic rim was revealed on the anterior margin of the internal femoral condyle, next to the articular surface. No periosteal reaction was seen. Small punctate calcifications were identified in the tumor, suggestive of a chondral tumor. After MRI and CT findings, the chondroblastoma diagnosis was proposed.

After the intravenous administration of 99mTc-HMDP (Fig. 1G), bone scintigraphy images presented signs of intense hyperemia in the left internal femoral condyle. In the delayed phase, highly increased osteogenic activity was detected. The rest of the scintigraphic study did not reveal any other relevant alterations.

CT-guided biopsy was performed on the lesion, with a histological diagnosis of PILA. The case was presented at the Bone and Soft Tissue Tumors Committee (BSTTC) and the patient underwent cryoablation (Fig. 1G). Given the reduction in size, it was suggested that percutaneous ablation similar as the used in osteoid osteoma cases could be effective.

The epiphyseal lesion continued to be seen in the MRI performed 6 months after cryoablation. It measured 1.6×0.9 cm and was hypointense on T1-WI and hyperintense on T2-FS-WI with homogeneous gadolinium enhancement (Fig. 1H). PET-CT did not reveal distant disease.

Persistence of the lesion was likely to be secondary to technically inadequate cryoablation. In cryotherapy, the "oven effect" did not occur and ice balls were mainly formed behind the needle tip. The needle tip should have been extended beyond the opposite wall of the tumor to obtain adequate results. Furthermore, the patient did not experience significant pain relief after ablation. The case was once again presented to the BSTTC, and wide tumor resection was indicated.

The resection was performed with the aid of intraoperative navigation, and the resulting bone defect created was reconstructed with osteochondral allograft with osteosynthesis using two Acutrak® screws to provide good and headless compression (Fig. 1I).

Histopathological findings

CT-guided biopsy showed an intraosseous vascular tumor without cytological atypia consisting of a vascular proliferation between mature cancellous bone trabeculae (Fig. 2A). These vascular channels were dilated and lined with a single endothelial layer of flat or cuboidal cells. Intraluminal papillary projections were found (Fig. 2B). They were lined with hobnail cells (Fig. 2B, C) and had a central hyaline core consisting of basement membrane material (Fig. 2C). Intraluminal and perivascular lymphocytes were present (Fig. 2B, C). Intraluminal proteinaceous material was observed (Fig. 2B). Neither mitotic figures nor necrosis was identified.

The immunohistochemical study showed CD31 (clone JC70A) (Fig. 2D) and ERG (clone EP111) (Fig. 2E) diffuse positivity. Podoplanin (clone D2-40) was diffusely expressed in the endothelial cells and was very focally expressed only in the intraluminal papillary projections (Fig. 2F). The cell proliferation index (Ki67 [clone MIB-1]) was less than 1%.

The surgical specimen consisted of a partial anterior hemicondylectomy of the left internal femoral condyle. It measured $3 \times 2.5 \times 2$ cm and was partially covered by a synovial membrane (Fig. 2G, H). On sectioning, a well-defined 0.7×0.6 cm subchondral tumor was seen (Fig. 2I). Histologically, the tumor displayed residual PILA and post-treatment alterations. Surgical margins were unaffected.

Clinical evolution

No early postoperative complications developed. The osteochondral allograft was united to the host bone with no complications. Local MRI and thorax CT performed every 6 months after surgery showed no local recurrence or disease

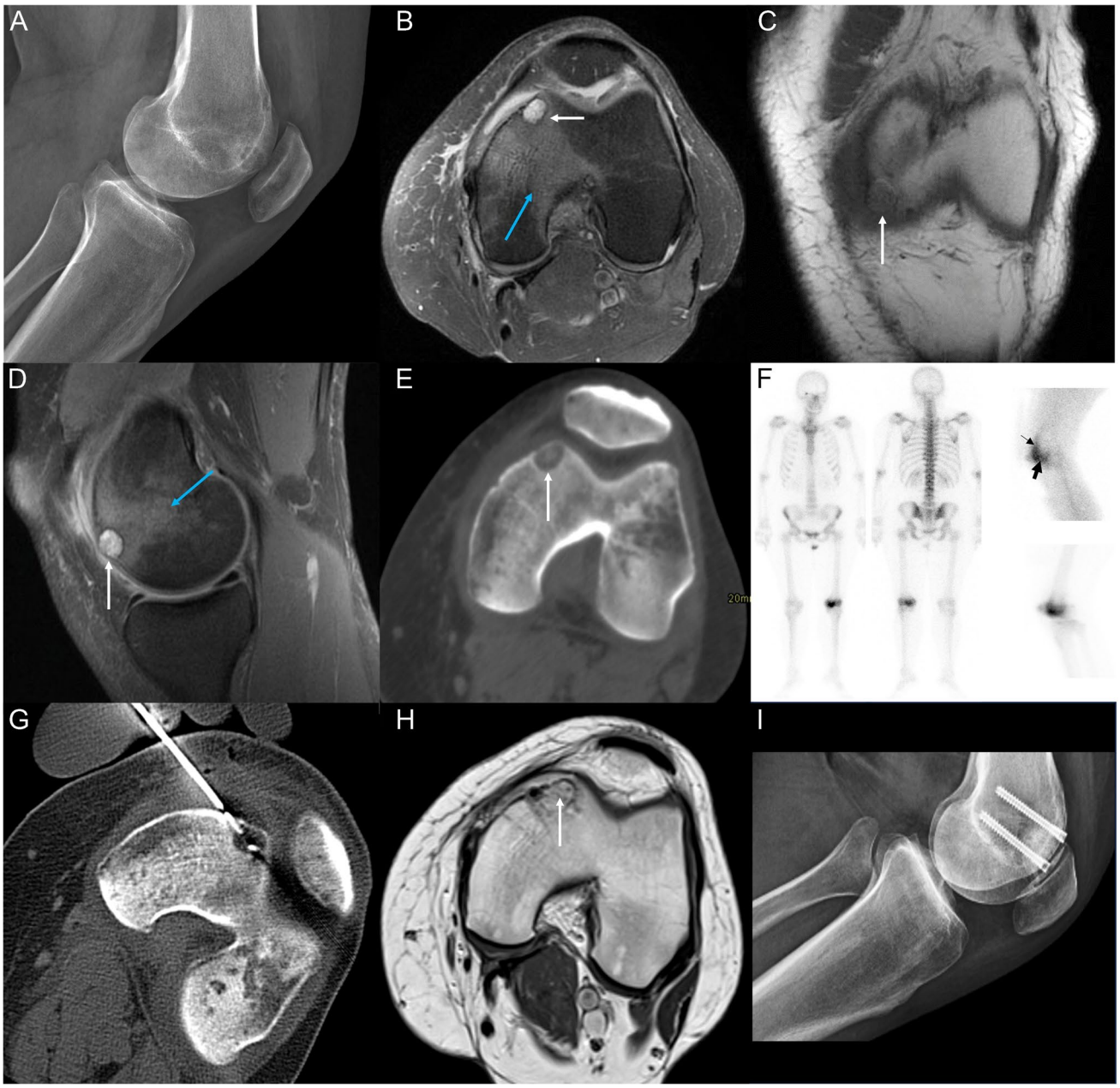

Fig. 1 **A** Lateral plain film: lytic lesion with sclerotic rim in the left antero-internal femoral condyle. **B** Magnetic resonance image (MRI), axial T2 fat suppressed-weighted image (FS-WI): 1-cm hyperintense round lesion (white arrow) with bone marrow (BM) edema signal (blue arrow) and joint effusion. **C** MRI, coronal T1-WI: mild hypointense round lesion (arrow). **D** MRI, sagittal proton density-FS-WI: well-defined round lesion (white arrow) with BM edema signal (blue arrow). **E** Axial computerized tomography (CT): well-defined lytic lesion in the subchondral internal femoral condyle with punctate calcifications (arrow). **F** Bone scintigraphy. Whole body bone scan, selective blood pool (superior right corner) and delayed planar images (inferior right corner), in lateral projection of the left knee: inflammatory changes in the synovial (thin arrow), with hyperemia in the distal epiphysis of the femur (thick arrow), associated with a high increase of the osteogenic activity in the lesion and the surrounding bone tissue, without other findings in the bone. **G** Cryoablation needle tip that did not pass through the opposite wall (inadequate ablation). **H** MRI 6 m later, T1-WI: strong contrast enhancement of the entire lesion suggesting relapse. **I** Post-surgery plain radiography: two screws in the partial anterior hemicondylectomy area

extension. Seven years after tumor resection, the patient is disease-free. The patient does not have a limp or any restrictions on sports activity. Consent for publication has been obtained from the patient.

Discussion

PILAs are exceptional soft tissue tumors originating in the lymphatic vessels [2]. According to the latest World Health

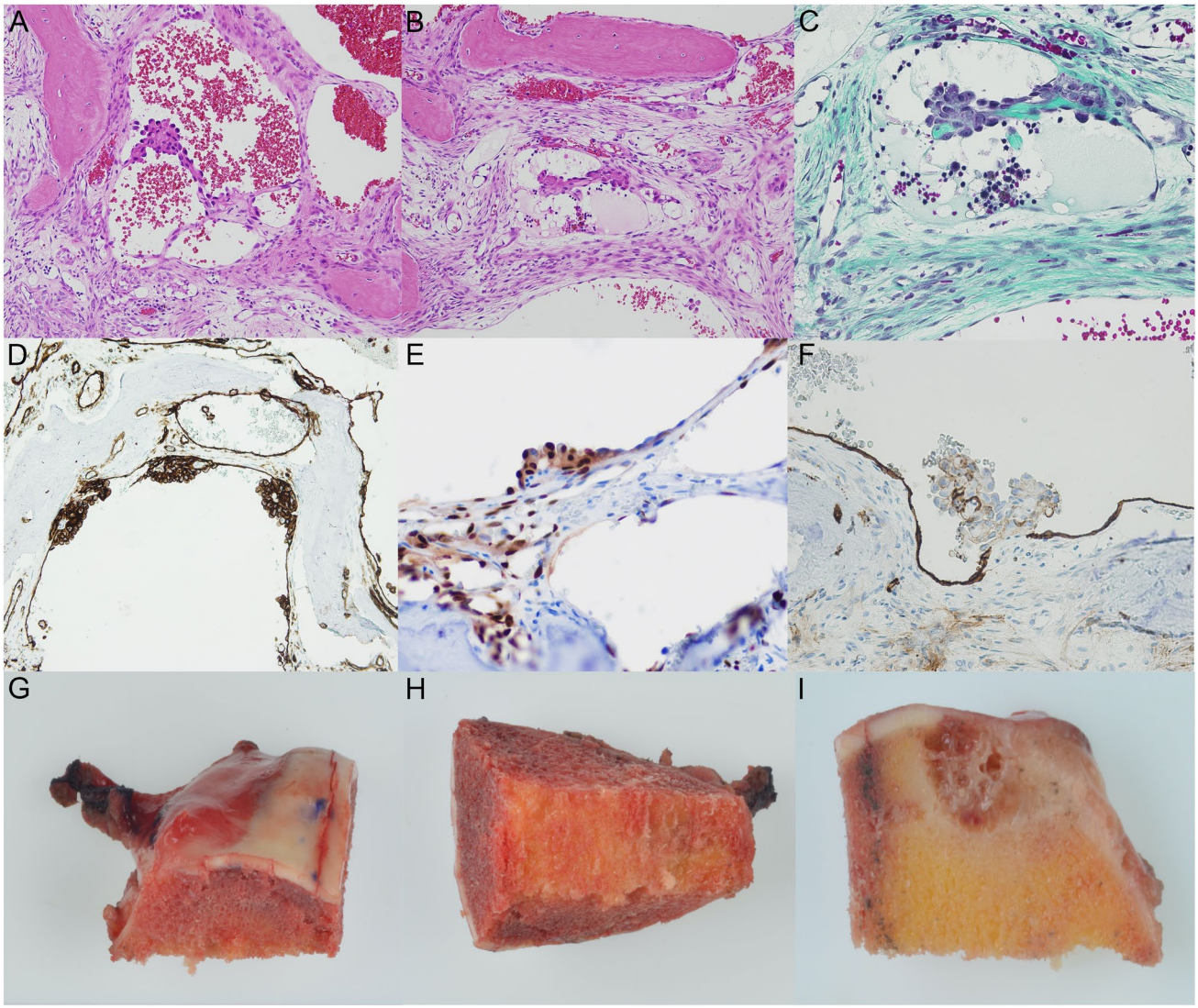

Fig. 2 **A** Dilated vascular channels lined by a single layer and intraluminal papillary projections with hobnail cells (hematoxylin and eosin stain, ×200). **B** Intraluminal lymphocytes and proteinaceous material (hematoxylin and eosin stain, ×200). **C** Central hyaline cores of basement membrane material (Masson ×400). **D** CD31 (×200). **E** ERG (×400). **F** Podoplanin (×400). **G** Antero-internal hemicondylectomy with a reddish nodular lesion. **H** Bone box with wide margins. **I** Subchondral nodular tumor with small cystic cavities

Organization (WHO) tumor classification, they are considered an intermediate (rarely metastasizing) neoplasm [3]. The majority are located in subcutaneous tissue [4], although a few cases have arisen in deeper locations such as the tongue [9], spleen [10], testis [11], or atrium [12]. Only four cases have been reported in bone [5–8]. The main characteristics of our case as compared to prior intraosseous PILA cases are summarized in Table 1.

PILA most commonly occurs in infants, children, and young adults [3]. Four intraosseous cases have been reported in adults aged 39 to 51, with only one case being found in a child. Our case has clinical similarities to prior reports [5, 6] including knee pain, intensified at night and significantly reduced with NSAIDs. In all of these cases, PILA was initially misdiagnosed as osteoid osteoma. Most intraosseous tumors measured between 0.5 and 1 cm. The other epiphyseal case is also a solitary lesion [5]. There have been insufficient cases of bone PILA to offer an accurate differential radiological diagnosis. Osteoid osteoma and chondroblastoma were the radiological diagnoses proposed in our case. Broader differential diagnoses could include eosinophilic granuloma, epithelioid hemangioendothelioma, and clear cell chondrosarcoma [13], in addition to those previously mentioned. In all of these entities, small lytic lesion with a well-defined geographic pattern has been described in meta-epiphyseal locations. The presence of marked perilesional bone marrow edema would favor our diagnostic proposal, along with that of eosinophilic granuloma. Multiple

Table 1 Primary intraosseous PILA published cases

	McCarthy et al., 1999	Nakayama et al., 2004	Li et al., 2013	Gambarotti et al., 2018	Pozo-Kreilinger et al., 2024
Age	45	39	1	51	50
Sex	F	F	M	M	F
Clinical presentation	Pain, worst at night, better with NSAIDs	Pain, worst at night, better with NSAIDs	Pain and swelling	Pain	Pain, worst at night, relieved with NSAIDs
Site	Distal femur (epiphysis)	Distal femur (metaphysis)	Facial bones	Left clavicle, right clavicle, distal femur	Distal femur (epiphysis)
Size (cm)	1.5	1	0.5–1.5	8	1
Single or multiple	Single	Single	Multiple	Multiple	Single
Simple radiography	Solid continuous periosteal reaction on the medial aspect of the distal femoral metaphysis. Intraosseous radiolucency in the epiphysis (in the medial femoral condyle)	Dense, continuous periosteal thickening on the medial distal metaphysis and epiphysis of the femur, with a small radiolucent area	Not mentioned	Not mentioned	Well-defined radiolucent area without periosteal reaction
CT	Not mentioned	Intraosseous radiolucent lesion with a sclerotic margin	Osteolytic lesions	Lytic lesion; cortex destruction and soft tissues invasion	Lytic lesion with a sclerotic edge and narrow transition between the lesion and the healthy bone
MRI T1-WI	Well-defined lesion, hypointense compared to marrow	Hypointense lesion	Not mentioned	Isointense lesion	Hypointense lesion
MRI T2-WI	Mildly hyperintense, lobular pattern	Hyperintense lesion, peritumoral edema	Not mentioned	Heterogeneously hyperintense (fat saturated)	Hyperintense lesion. Significant peritumoral edema
MRI T2-FS-WI	Mild enhancement	Not mentioned	Not mentioned	Not mentioned	Mild enhancement
Bone scintigraphy	Intense tracer uptake in the medial femoral condyle	Not mentioned	Not mentioned	Not mentioned	Hyperemia signs and very intense increase in osteogenic activity in the delayed phase
Pre-biopsy diagnosis	Osteoid osteoma	Osteoid osteoma	Langerhans cell histiocytosis	Not mentioned	Osteoid osteoma, chondroblastoma, complicated benign cystic lesion
Pre-existing vascular lesion	Hemangioma	Not mentioned	Not mentioned	Not mentioned	Not found
Immunohistochemistry	CD31 +	Vimentin +, factor VIII +	CD31 +, CD34 +, D2-40 + endothelial cells, D2-40 − intraluminal cells	CD31 +, D240 +, ERG +	CD31 +, ERG +, D2-40 + endothelial cells, D2-40 + very focally intraluminal cells
Treatment	Complete curettage	Curettage and wide re-excision	Complete curettage	Marginal resection	Radioablation and wide resection
Follow-up (months)	12	50	24	Lost to follow-up	84
Local recurrence or distant metastasis	No	No	No	No	No

lytic lesions in cluster locations have also been described in intraosseous PILAs [4] /4/2024 4:31:00 PM. Epithelioid hemangioendothelioma, Langerhans cell histiocytosis [14], metastases, or even myeloma may be suspected.

Histologically, PILA may be confused with benign, intermediate, or malignant vascular lesions. Some arise from previously benign vascular lesions (hemangioma or lymphangioma) [4, 15] and one case of angiosarcoma developed from PILA has been reported [16]. Hobnail cells and papillary projections may be also observed in retiform hemangioendothelioma (RH) and intravascular papillary endothelial hyperplasia (Masson's hemangioma) [7, 8]. Both lesions have also been described in bones [17, 18]. RH are made up of retiform vessels with perivascular hyalinization and lymphocytes, but without prominent intravascular papillary structures [4]. Masson's hemangioma contains dilated vessels with papillary proliferation of plump endothelial cells without atypia. Fibrous tissue, fibrin deposits, and thrombi are present [8]. Epithelioid hemangioendothelioma (EH) of bone has been reported [17] and it may be confused with PILA since both are formed by vascular endothelial channels. The characteristic myxohyaline stroma of EH is not observed in PILA. Hobnail cells and papillary projections are not found in EH.

Most PILAs are benign lesions that are cured after complete excision. Some cases developed lymph node metastasis [4] and only one reported case resulted in death due to metastasis [15]. None of the primary intraosseous PILA presented neither local recurrence nor distant metastasis [5–8]. Long-term follow-up is recommended for these patients.

Conclusion

Primary intraosseous PILAs are exceedingly rare tumors that may initially be clinically and radiologically misdiagnosed. Knowledge of this unusual location is important to consider PILA in the differential diagnosis of vascular tumors of the bone, especially in epiphyseal location.

Declarations

Conflict of interest The authors declare no competing interests.

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