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Case report

Primary pseudomyogenic hemangioendothelioma of bone: case report and review of the literature

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Key words

Pseudomyogenic hemangioendothelioma • Bone • Vascular tumor • Immunohistochemistry

Summary

Pseudomyogenic hemangioendothelioma (PMH) represents a multicentric recently characterized tumor type, generally presenting in young adults, of postulated vascular origin and intermediate malignancy. This entity tends to arise in the deep-seated dermal-subcutaneous locations, preferentially limited to one anatomic site, and may extend secondary to bone. PMH restricted to the skeletal system is rare. To our knowledge, only 19 cases with description of both histologic and clinical findings have been reported to date. We report the clinicopathological features of a further intraosseous PMH occurring in a 46-year-old woman involving the right patella. Histologic examination showed an infiltrating growth composed of sheets and fascicles of spindled to epithelioid large cells, with ample eosinophilic cytoplasm, large vesicular nuclei and prominent nucleoli, sometimes resembling rhabdomyoblastic tumor cells, without morphologic signs of vascular differentiation. At immunohistochemical examination, neoplastic cells stained diffusely for AE1/AE3 keratins, vimentin, ERG, FLI-1, INI-1, FOSB with only focal CD31 expression.
The morphologic clues leading to the correct diagnosis of intraosseous PMH have been correlated with the data of the literature, and a special emphasis has been given to the differential diagnosis with other neoplasms, particularly epithelioid sarcoma, in order to avoid unnecessary radical surgery and to optimise possible treatment protocols.

Introduction

Mesenchymal tumors that show epithelioid morphological appearance form a heterogeneous group of neoplasms with phenotypic variations and/or histologic similarities, usually representing a diagnostic dilemma for the clinicians as well as the pathologist. Some members of the group tend to share variable immunohistochemical expression of epithelial markers (namely cytokeratins and EMA) that, in inexperienced hands, may be a source of further difficulty. A variety of putative epithelioid sarcomas have subsequently been described until now, with the provision of clear diagnostic criteria and distinctive immunophenotypic and genetic findings [1].
Point of departure in this overview will be a small number of series of a rare tumor type, known by several different names, including pseudomyogenic hemangioendothelioma and epithelioid sarcoma-like hemangioendothelioma that has been published recently in the literature [2 3]. This neoplasm is almost certainly the same lesion as that reported by Mirra et al. [4] in 5 patients in 1992 when it was labeled fibroma-like variant of epithelioid sarcoma. For the purposes of this manuscript we will refer to the tumor as pseudomyogenic hemangioendothelioma (PMH) to remove possible confusion and simplify the technical terms used to name this rare entity. A total of approximately 150 examples has been so far reported with over 75% of cases arising in the skin and soft tissues. PMH limited to the skeletal system is very rare and following the first description by Sheng et al. [5], only further 18 cases have been reported so far.
Here we report the twentieth of these peculiar tumors of the bone, focusing on its histologic and immunohistochemical profile, together with a review of pertinent literature and a discussion of the differential diagnosis.

Case report

In February 2017, a 46 year-old woman, with a past medical history significant of sleeve gastrectomy for reduction of obesity, was admitted to the Orthopoedic Division,

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Hospital of Tortona (AL), Italy for pain, that increased when digital pressure was applied, on right knee, present for several months without a trauma history. At physical examination no lesion in either the skin or the deep soft tissue of the extremity was noticed. Magnetic risonance imaging (MRI) showed a subcortical and intramedullary mass (24 mm x 18 mm) involving the third medium and distal of the right patella. The well delineated lesion was multilobulated, and demonstrated isointense T1 and high T2 signal intensity with consistent and homogenous enhancement post administration of gadolinium. The mass had focally a distinctive pattern of linear growth, with periosteal and subcortical tumor "cloaking" the cortical margin (Fig. 1). One month later, the knee lesion was removed with curettage and filled with bone cement. Grossly, the several submitted fragments of tissue were soft and solid, with a white to grayish colour, gelatinous appearance, and ranged from 13 to 24 mm in aggregate.

Histopathological examination showed a lesion consisting of loose fascicles and sheets of plump spindle and epithelioid cells separated by a variable background of vascular structures. Vague storiform architecture was focally observed. The cytoplasm of lesional cells was brightly eosinophilic, the cytoplasmic membranes were not clearly delineated and the nuclei appeared elongated in the spindle cells and predominantly round to oval in the epithelioid cells (Fig. 2). The chromatin seemed smudged. The appearance of the nucleoli varied considerably in different areas. On the whole they were rather inconspicuous, but sometimes they were large and deeply basophilic. Tumor cells with a rhabdoid to rhabdomyoblast-like appearance were seen (Fig. 3). There were sprinkled chronic inflammatory cells, neutrophils, osteoclast-like giant cells and reactive osteoid. The stroma was focally myxoid. Mitotic figures were occasionally observed (<1/50 high power field). No necrotic focus was seen.

Fig. 1. A magnetic resonance imaging (MRI) showing a multilobulated subcortical and intramedullary lesion of the right patella.

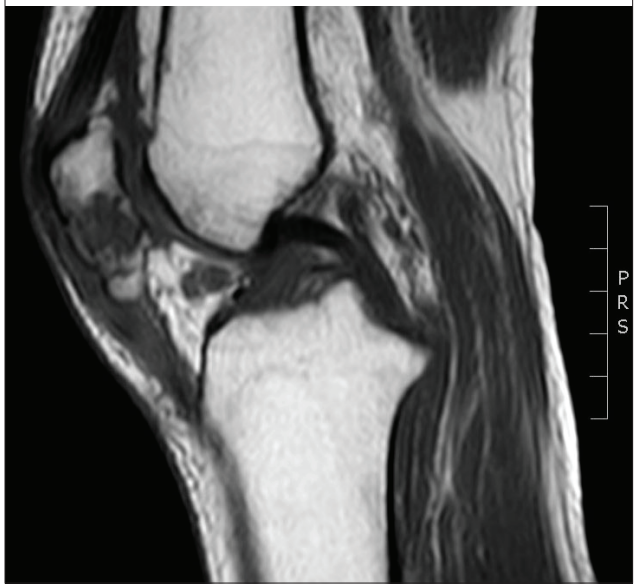


Fig. 2. Tumor proliferation with plump spindle-to-polygonal cells with abundant eosinophilic cytoplasm forming a sheet-like and fascicular architecture.

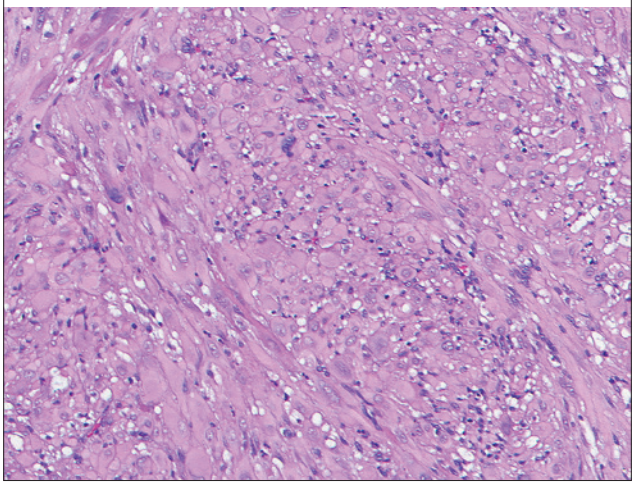
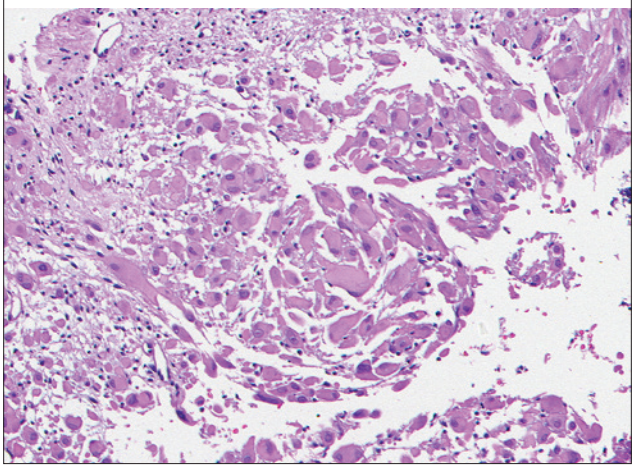


Fig. 3. Rhabdomyoblast-like appearance of the neoplastic cells with brightly eosinophilic cytoplasm.

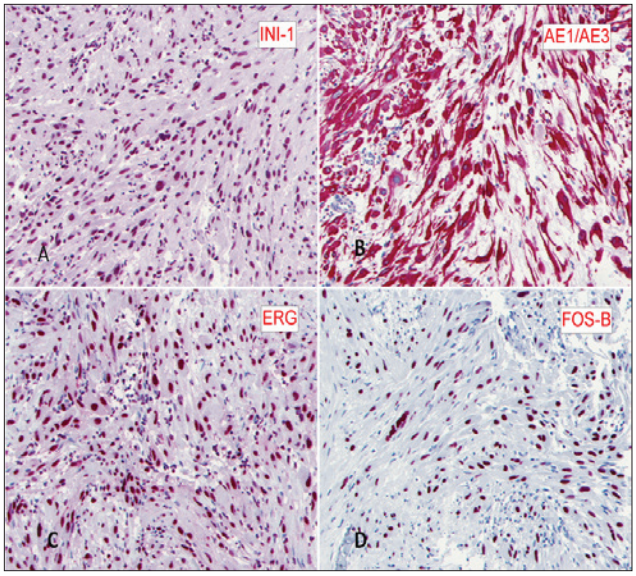


At immunohistochemical examination, tumor cells stained strongly for AE1/AE3 keratins and vimentin, whereas CD31 immunostaining was weaker and irregular, with a focal linear membranous pattern. The neoplastic elements were also diffusely positive for ERG, FLI-1, INI-1, FOSB (Fig. 4). The tumor stained negative for S100 protein, α-smooth-muscle actin, desmin, EMA, HMB-45, MART-1, Cam 5.2 and MNF116 keratins, CAMTA1 and TFE3 confirming the diagnosis of PMH. The patient was alive and free of disease 12 months later.

Discussion

The concept of hemangioendothelioma refers to a family of vascular tumors that have biological behavior inter-

Fig. 4. A: Immunohistochemical staining for INI-1, B: AE1/AE3 keratins, C: ERG and D: FOSB.



mediate between a benign hemangioma and a fully malignant angiosarcoma. Four well-recognized subtypes of haemangioendothelioma are included in the category of intermediate malignancy (rarely metastasizing): retiform hemangioendothelioma, papillary intralymphatic hemangioendothelioma, composite hemangioendothelioma and pseudomyogenic hemangioendothelioma (PMH) [6]. The first well-documented cases of PMH were reported by Mirra et al. [4] who referred to the entity as a "fibroma-like variant of epithelioid sarcoma" [4]. In this, and in subsequent works in which the tumor was given a different name, the authors highlight that neoplasms occurred more frequently in young to middle aged males with strong predilection for the lower extremities and that they often presented as multiple discontinuous nodules involving different tissue planes in an anatomic region [2-5 7-12]. The clinical appearance was non-specific and only rarely a vascular nature of the lesion was suspected. Most cases occurred in deep and superficial soft tissue with secondary bone involvement. PMH of bone without soft tissue lesions is very rare. Previous case reports and small series with illustrations of both histology and clinical findings have described only 19 cases of primary PMH of bone (Tab. I) [3 5 7-9 11 12]. From the published data, including those of our patient, intraosseous primary PMHs, similarly to the clinical behavior of analogous soft tissue tumors, are more often diagnosed in male (male to female ratio = 2,3:1); nearly all patients are between the first and fifth decades (average age = 32 years; median of 25 years); and most tumors (60%) involve the lower extremities often as multifocal disease (70%). Follow-up information was available in 13 patients with PMH of bone for a mean period of 43,23 months (range = 3 months to 19 years). Three patients (15%) developed local recurrences or additional nodules in the same anatomic region after surgical clearance. Reported follow-up revealed that the majority of patients pursued an indolent clinical course [3 7 9 11 12]. Six of 13 patients had early progression of tumors, defined as an increase in size of a known lesion or the development of new nodules, within the first 12 months of follow-up [5 7]. Two of these patients continued to have disease progression, requiring resection of the sixth rib in one of them and knee amputation in the other, with subsequent stabilization of the disease and recovery, respectively [7]. A third patient who also had experienced early progression of disease with stabilized lesions after knee amputation developed a questionable rib metastasis 102 months following the initial diagnosis of the foot tumor [7]. Of the remaining 7 patients without early progression tumor burden, two were submitted to amputation of a limb, one of which also afflicted with fibrous dysplasia [11 12].

Macroscopically, resected bone revealed multiple discrete, solid, whitish to tan, tumors generally surrounded by a rim of sclerosis. Tumor sizes ranged from 0,2 to 6,5 cm in greatest dimension, and they were well marginated. Microscopically, our case was similar to the previously reported ones, a tumor with a fascicular, sometimes storiform, architecture composed of spindled to epithelioid tumor cells with a distinctive, intensely eosinophilic, often eccentric, cytoplasm. The rhabdomyoblast-like cells may be sparse, and their identification can suggest the diagnosis. Scattered cells with vacuolated cytoplasm were rarely observed [7 8 12]. Occasional foci of necrosis, sometimes with geographic appearance, were present [7 8]. In the cases of the present review there are some histological features which appear to be unique to those involving the bone. Some tumors contained an exuberant network of interanastomizing reactive woven bone which was proceeded side by side by plump osteoblasts and a rich fibrovascular matrix [7]. These findings resembled the neoplastic bone in osteoblastoma. Besides, the presence of focal to broad areas of hemorrhage and numerous osteoclast-like giant cells in several intraosseous PMHs have also been reported in giant cell tumors of bone [7 8 12]. Again, the presence of the pseudomyogenic cells is helpful in accurately identifying the neoplasm in both conditions.

Almost all the reported cases of intraosseous PMH, including the current case, do not show features of obvious endothelial differentiation, as intracytoplasmic vacuoles and lumen formation, and immunohistochemistry is important to confirm the diagnosis. In our review the neoplastic cells of most primary PMHs of bone, analogously to their counterpart of the soft tissue, expressed CD31, FLI-1, ERG and AE1/AE3 keratin with negativity for CD34 [7 8 11-13]. In a case expression of smooth muscle actin was observed [11]. Only in four cases, including the current case, the positive nuclear results of immunostaining for INI-1 were available [7 8 11].

As in epithelioid hemangioendothelioma, when the specific nuclear expression of CAMTA1 (as evidence of WWTR1-CAMTA1 fusion gene) resulted in a useful immunohistochemistry for diagnosis, a specific genetic feature has diagnostic implications for PMH. The

Tab. I. Clinical and radiologic features of the reported cases of pseudomyogenic haemangioendothelioma of bone.

Case	Author (Ref)	Age(y)/ sex	Site	Tissue plane (s)	Symptom	Radiologic findings	Size (cm)	Multifocal	Surgery	Recurrence	Follow-up
1	Sheng et al. [5]	10/F	Lower left leg	Bone (tibia,fibula)	Pain, left hip pain during digital pressure	*MRI:* multifocal lesions with homogenous intense enhancement in the left distal tibia; *2nd MRI:* new lesions in the left distal femur and proximal tibia with cortical destruction.	From 0,8 to 1,5	Yes	Curettage of left tibia and fibula lesions and resection of the distal femur	Yes, 4 months and 7 months	NA
2	Righi et al. [11]	25/M	Forearm	Bone (radius)	Left wrist pain	*X-ray:* three well-defined osteolytic areas of the distal left radius without periosteal reaction	6	Yes	Resection of the medium-inferior third of the radius. Amputation of the inferior third of the left arm.	Yes, 6 and 14 months	ANED at 19 years
3	Righi et al. [11]	66/F	Left leg and foot	Bone (distal femur, tibia, fibula,foot)	Swelling and progressively increasing pain during the fourth and fifth toes pressure	*X-ray:* multiple lytic areas without periosteal reaction in the tibia, fibula and almost all foot bones. *MRI:* numerous central and cortical enhancing bone lesions of distal femur and tibia	NA	Yes	Curettage of the lesion.	No	AWED at 2 months
4	Hornick et al. [3]	35/M	Hand	Intraosseous (finger)	NA	NA	NA	No	NA	No	ANED at 17 months
5	Inyang et al. [7]	59/M	Spine, pelvis, femurs, humeri, scapula, ribs, manubrium, sternum	Intraosseous (thoracolumbar spine, right iliac bone, ribs, scapula, right femural head)	Pain	*CT:* multifocal lesions involving thoracolumbar spine, right iliac bone,multiple ribs, scapula and right femural head. *PET scan:* numerous lesions with intense FDG avid uptake in the scapula,manubrium, sternum,rib cage,spine,pelvis,proximal humeri, and femora. *2nd/3end PET-CT:* complete resolution of previously FDG-avide bone lesions.	NA	Yes	Resection of 6th rib.	No	AWED at 16 months. Stable lesions without treatment after resection of an only lesion.
6	Inyang et al. [7]	19/M	Lower right extremity	Intraosseous (femur,tibia,patella,fibula,talus,calcaneus,tarsal and metatarsal bones)	Pain	*MRI:* multiple enhanced tumors involving right distal femoral metaphysis,femoral diaphysis, upper tibia adjacent to the knee, subcondral lesions of the femoral condyles and patella,proximal and distal fibula,talus,calcaneus,tarsals,head of the 5th metatarsal, and 1th metatarsal. Prominent lymph nodes in inguinal and popliteal fossa. *2ndMRI:* other enhanced homogenous lesions in the talus,5th metatarsal, enlargement of the lesions of the 1th metatarsal and calcaneal tumors.	From 1,4 to 1,6	Yes	Curettage of right foot bones and metatarsal.	No	AWED at 46 months
7	Inyang et al. [7]	47/M	Distal left lower extremity	Intraosseous (tibia,fibula,4th metatarsal)	Sprain, tenderness	*x-ray:* numerous lytic lesions in the tibia,fibula, and 4th metatarsal. *Bone scan:* multiple areas with monomelic distribution and avide uptake of isotope	NA	Yes	Segmental resection of proximal fibula. Above the knee amputation.	No	ANED at 60 months
8	Inyang et al. [7]	14/M	Left upper extremity	Intraosseous (humerus, radius, ulna, hand bones)	Pain	*MRI:* multiple enhancing lesions involving the proximal and distal humerus, capitellum,olecranon,trochlea,radial head,ulna,scaphoid,lunate,hook of hamate,metacarpals.*PET-CT:* no significant FDG activity. CT shows lytic lesions surrounded by a rim of sclerotic bone. *Bone survey:* no metastatic disease. Incidental metaphyseal fibrous cortical defects in distal right femur and proximal left tibia,and left calcaneal simple osseous cyst.	From 0,2 to 1,6	Yes	Biopsy of unknown site	No	NA
9	Inyang et al. [7]	74/M	Right iliac crest and spine	Intraosseous (iliac crest, spine)	Incidental finding during staging for urothelial carcinoma	*PET:* lesion involving right iliac crest. Questionable mass in L2. *2nd PET:* new multiple tumors involving the spine	NA	Yes	Biopsy of unknown site	No	AWED at 4 months
10	Inyang et al. [7]	20/M	Upper left femur	Intraosseous (femur)	Pain	*Xray/MRI:* numerous round focally confluent lytic lesions involving femoral head,neck and proximal diaphysis.	NA	Yes	Resection of proximal femorus	No	ANED at 4 months
11	Inyang et al. [7]	66/M	Lumbar spine, ilium, sacrum	Intraosseous (lumbar spine, sacrum, ileum)	Incidental finding during staging for squamous cell carcinoma of the mouth	*Xray/MRI/bone scan:* multiple oval lytic lesions, surrounded by a rim of sclerotic bone, involving the lumbar spine, sacrum, ileum. No lesion observed on bone scan.	NA	Yes	Biopsy of sacrum	No	Died of complications of squamous cell carcinoma
12	Inyang et al. [7]	12/M	Left foot	Intraosseous (foot bones with cortical destruction and soft tissue extension)	Pain	*MRI:* lytic enhanced lesion in the head of the 5th metatarsal with apparent cortical destruction and soft tissue expansion and lytic area in the calcaneus that destroyed the cortex expanding into adjacent soft tissue	6,5 x 5,5 x 3	Yes	Resection of head of 5th metatarsal. Curettage and repeat curettage, and then below the knee amputation for enlarging calcaneal tumor. Crioablation of rib lesion.	Yes, 101 months and 102 months	AWED at 103 months (rib metastasis)
13	Inyang et al. [7]	26/M	Skull,spine,pelvis,sacrum,bilateral proximal femurs	Intraosseous (vertebrae, bilateral femurs, pelvis, sacrum, skull)	Headaches,dizziness	*Imaging:* multiple ring enhancing lesions in his brain and lytic bone tumors involving multiple sites as vertebrae,bilateral femurs,pelvis,sacrum,skull	NA	Yes	Biopsy of left ilum and brain	No	NA
14	Inyang et al. [7]	5/F	Right hip and pelvis	Intraosseous (femur,ishium)	Pain	*Xray/CT/MRI/bone scan:* multiple lytic lesions with peripheral sclerotic rim involving right upper femur, greater trochanter,right supracetabulum right ishium, dark on T1,hyperintense on stir,enhance with gadolinium, avid on bone scan	NA	Yes	Biopsy of right proximal femur	No	NA
15	McGinity et al. [8]	25/M	Toracic spine	Intraosseous (thoracic spine,rib)	Progressive weakness bilateral of lower extremities	*MRI:* T1-weighed image shows a mass of the fourth thoracic vertebral segment extending into the right thoracic cavity,pedicle and transverse process. *CT:* two pattern of behavior of the tumor respect to bone in coronal and axial images with scalloping of the vertebral body and bone expansion of the lamina and transverse process respectively	4,5 x 3,5 x 3	No	Total resection of the tumor through a posterior approach	No	NA
16	Ye et al. [12]	14/F	Distal left lower extremity	Intraosseous (tibia,calcaneus)	Pain and swelling in her left tibia and calcaneus arising 4 months after diagnosis of fibrous dysplasia of the left distal femur	*Xray:* prominent osteolytic lesion of the tibia and calcaneus with cortical destruction.	NA	No	Ablation of tumor tissue, and then amputation of the left thigh	No	ANED at 3 months
17	Pradan et al. [9]	9/F	Upper thigh	Intraosseous (femur)	Hip pain	Osteolysis and marked osteopenia of femoral head	1,7	No	Several biopsies and resection	No	ANED at 45 months
18	Pradan et al. [9]	53/M	Forearm	Intraosseous (ulna)	Pain	*X-ray:* multiple osteolytic lesions with cortical destruction and periosteal reaction	From 4,3 to 6	Yes	Ulnar resection	No	ANED at 22 months
19	Pradan et al. [9]	16/M	Calf	Intraosseous (tibia)	NA	NA	1,1	Yes	NA	NA	NA
20	Current case	46/F	Patella	Intraosseous (patella)	Pain	*MRI:* a well-delineated lobulated mass with a low-intensity signal in T1 and high-intensity signal in T2, with high and homogeneous enhancement involving the third-medium and inferior of right patella	2,4x1,8	No	Curettage of the lesion	No	ANED at 12 months

Ref = reference; F = female; M = male; NA= not available; ANED = alive with no evidence of disease; AWED = alive with evidence of disease.

identification of the chromosomal translocation t (7:19) (q22;q23) leading to SERPINE1-FOSB gene fusion is a recurrent alteration and has a pathogenic significance and the recent detection of intense nuclear expression of FOSB by a specific antibody, as notable in the current case, is a highly sensitive and diagnostically useful marker for PMH [14-16]. Also SERPINE1 encodes a serine protease inhibitor family protein, known as plasminogen activator inhibitor-1 (PAI-1). In fibroblasts PAI-1 promotes proliferation, myofibroblastic differentiation, collagen synthesis and inhibition of apoptosis by activating Ca^{+} and Akt signaling pathways. Akt signal causes upstream of mTOR and everolimus (inhibitor of mTOR) could be useful in future therapeutic protocols to treat rare cases of metastatic PMH [15].

The differential diagnosis for osseous primary PMH is broad and includes other epithelioid vascular lesions, nonossifying fibroma, epithelioid sarcoma, and metastatic sarcomatoid carcinoma. Epithelioid hemangioma of the bone generally shows a lobular architecture with well formed vascular lumens and intracellular vacuoles but occasional examples exhibit spindle cell areas with intratumoral haemorrage and scattered osteoclastic-like giant cells intermixed with reactive woven bone formation, features also seen in PMH. In such cases, the presence of rhabdomyoblast-like cells supports the diagnosis of PMH [7 9]. Epithelioid hemangioendothelioma may contain spindle cells but it is usually composed of cords, strands and solid sheets of CAMTA1 and occasionally TFE3 positive polygonal to round cells embedded in a fibromyxoid to chondroid stroma that helps distinguish it from PMH [1 6 7 9]. Epithelioid angiosarcoma can be separated from PMH, because it is usually variably vasoformative with intracellular lumens and severe cytologic atypias, features not seen in PMH [1 9]. Nonossifying fibroma consists of fascicles of spindle cells with a vague storiform pattern, without evidence of elements with brightly eosinophilic cytoplasm and rhabdomyoblastic-like appearance characteristic of PMH [7]. The lack of a history of a previous carcinoma, no evidence of pulmonary and visceral disease, the limited cytologic atypia, immunoreactivity to endothelial markers would strongly argue against osseous metastasis of sarcomatoid carcinoma. One of the most important differential diagnosis of osseous PMH is with the epithelioid sarcoma. These two tumor types have some clinical and histopathological similarities but distinguishing features include the paucity of necrosis and distinctive myoid appearance in PMH, the expression of CD31, INI1 and FOSB in PMH, and the different molecular derangements. Despite frequently presenting in the same manner, epithelioid sarcoma and PMH have different clinic-biological behavior, with PMH, locally recurrent or multifocal, that rarely metastasizes to distal sites. Indeed, in the report by Hornick and Fletcher, only one tumor metastasized to the lungs, and this event occurred 16 years following the presentation [3]. Another case reported as "fibroma-like variant of epithelioid sarcoma" by Mirra et al. [4] presented with multiple nodules in the forearm and pulmonary metastasis radiographically diagnosed after 6 years. An interesting observation in our review was the presence in a case of epithelioid hemangioendothelioma-like features in the calcaneal tumor left untreated for several years [7]. This tumor also contained greater cytologic atypia, mitosis and necrosis than the other cases of our review and was also the only one with a questionable distant metastasis [7]. The diagnosis of this case was molecularly confirmed by FISH [7]. Whether this outlier represents another pathway in the spectrum of PMH or progression of disease with ominous significance remains unknown.

In summary, we report a case of pseudomyogenic hemangioendothelioma of bone. This neoplasm has a propensity to present with multiple lesions in the long and small bones of the distal extremities of young men and often mimics other epithelioid osseous neoplasms morphologically. The main clinical presentation is skeletal pain, which might be associated with restriction of limb functionality. The awareness of the existence of this tumor type, and clinical behavior has relevance for multiple medical specialists. Surveillance of these patients to determine the presence of local recurrence or development of new nodules is mandatory for at least 24-36 months and longer if new or rapidly growing nodules are present. However, the reports of this tumor are limited and further studies on more cases are in need for fully understanding and appropriate diagnosis of it.

References

1 Cacciatore M, Dei Tos AP. *Challenging epithelioid mesenchymal neoplasms: mimics and traps.* Pathology 2014;46:126-34.

2 Billings SD, Folpe AL, Weiss SW. *Epithelioid sarcoma-like hemangioendothelioma.* Am J Surg Pathol 2003;27:48-57.

3 Hornick JL, Fletcher CDM. *Pseudomyogenic hemangioendothelioma: a distinctive, often multicentric tumor with indolent behavior.* Am J Surg Pathol 2011;35:190-201.

4 Mirra JM, Kessler S, Bhuta S, Eckardt J. *The fibroma-like variant of epithelioid sarcoma.* Cancer 1992;69:1382-95.

5 Sheng WQ, Wang J. *Primary pseudomyogenic hemangioendothelioma of bone.* Histopathology 2012;61:1219-24.

6 Requena L, Kutzner H. *Hemangioendothelioma*. Sem Diagn Pathol 2013;30:29-44.

7 Inyang A, Mertens F, Puls F, et al. *Primary pseudomyogenic hemangioendothelioma of bone.* Am J Surg Pathol 2016;40:587-98.

8 McGinity M, Bartanusz V, Dengler B, et al. *Pseudomyogenic hemangioendothelioma (epithelioid sarcoma-like hemangioendothelioma, fibroma-like variant of epithelioid sarcoma) of the thoracic spine.* Eur Spine J 2013;22 (suppl. 3):s506-s511.

9 Pradhan D, Schoedel K, McGough RL, et al. *Pseudomyogenic hemangioendothelioma of skin, bone and soft tissue - a clinicopathological, immunohistochemical, and fluorescence in situ hybridization study.* Hum Pathol 2018;71:126-34.

10 Requena L, Santonja C, Martinez-Amo JL, et al. *Cutaneous epithelioid sarcomalike (pseudomyogenic) hemangioendothelioma.* JAMA Dermatol 2013;149:459-65.

11 Righi A, Gambarotti M, Picci P, et al. *Primary pseudomyogenic hemangioendothelioma of bone: report of two cases.* Skeletal Radiol 2015;44:727-31.

12 Ye C, Yu X, Zeng J, Liu H, et al. *Pseudomyogenic hemangioendo-*

thelioma secondary to fibrous dysplasia of the left lower extremity in a 14-year-old female: a case report. World J Surg Oncol 2016;14:198-202.

[13] Stockman DL, Hornick JL, Deavers MT, et al. *ERG and FLI1 protein expression in epithelioid sarcoma.* Mod Pathol 2014;27:496-501.

[14] Hung YP, Fletcher CDM, Hornick JL. *FOSB is a useful diagnostic marker for pseudomyogenic hemangioendothelioma.* Am J Surg Pathol 2017;41:596-606.

[15] Ozeki M, Nozawa A, Kanda K, et al. *Everolimus for treatment of pseudomyogenic hemangioendothelioma.* J Pediatr Hematol Oncol 2017;39:e328-e331.

[16] Walther C, Tayebwa J, Lilljebjörn H, et al. *A novel SERPINE1-FOSB fusion gene results in transcriptional up-regulation of FOSB in pseudomyogenic haemangioendothelioma.* J Pathol 2014:232:534-40.