Primary pseudomyogenic hemangioendothelioma of right maxilla: a case with immunohistochemistry and *FOSB* rearrangement study

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Objective. Primary pseudomyogenic hemangioendothelioma (PMH) of bone is an extremely rare vascular neoplasm. We present here a case of primary PMH occurring in the maxilla.

Study Design. A 34-year-old man was referred to our hospital for treatment because of possible recurrence after surgery and chemotherapy of a right maxillary malignant tumor. Morphologic features, immunophenotypes, and *FOSB* gene rearrangement status of the surgically sectioned sample were assessed by hematoxylin-eosin staining, immunohistochemistry, and fluorescence in situ hybridization, respectively.

Results. Morphologically, the tumor cells were arranged in a loose fascicular and sheet-like manner, with a large number of reactive woven bones forming. The most striking feature was the presence of epithelioid cells with abundant brightly eosinophilic cytoplasm, which resembled the rhabdomyoblast in appearance. The tumor was diffusely positive for AE1/AE3, CD31, erythroblast transformation-specific transcription factor, and Friend leukemia integration 1; negative for CD34, CAM5.2, epithelial membrane antigen, and desmin; and had retained expression of integrase interactor 1. The tumor harbored *FOSB* rearrangement. No distant metastasis was found during the follow-up period (18 months).

Conclusions. To the best of our knowledge, this case represents the first report of PMH arising in the maxilla. The distinct morphologic features, immunophenotypes, and *FOSB* rearrangement could help achieve precise diagnosis and prevent misdiagnosis of mimics with overlapping features. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:e96–e105)

Pseudomyogenic hemangioendothelioma (PMH) is a rare intermediate vascular tumor. It often occurs in the soft tissues of lower extremities of young people 20 to 40 years old. The 2 reports with the biggest sample size found that the tumor was more common in males, with a male-to-female ratio of 2.85:1 to 4.6:1.[1,2] Pseudomyogenic hemangioendothelioma was first reported by Mirra et al. in 1992,[3] when it was called "fibromatoid epithelioid sarcoma." In 2003, Billings et al.[4] named the tumor "epithelioid sarcoma-like hemangioendothelioma" because it was similar to epithelioid sarcoma-like hemangioendothelioma morphologically but had the characteristics of low-grade tumors in biological behavior, although the immunohistochemistry study suggested endothelial cell differentiation. In 2011, Hornick et al.[1] reported the largest cohort so far, containing 50 cases of PMH. The tumor cells had abundant bright eosinophilic cytoplasm with a striking resemblance to rhabdomyoblasts, but the immunohistochemical detection found that these cells did not have myogenic differentiation, and thus the researchers named it "pseudomyogenic hemangioendothelioma."

Although about 25% of the cases could involve the bone and soft tissue concurrently, primary PMH of bone is extremely rare. Here we report a case of PMH arising in the maxilla, which is the first reported gnathic case. Thirty-eight extragnathic cases arising in bones were documented in the English-language literature and are summarized in Table I.[1,5-21] Clinicopathologic features, immunophenotype, and molecular alteration involving *FOSB* gene arrangement of this case were investigated. We also thoroughly reviewed the literature of primary PMH of bone to achieve a better understanding of this rare tumor, which might help discriminate other histologic mimics.

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Statement of Clinical Relevance

The present study broadens the clinical tumor location spectrum of pseudomyogenic hemangioendothelioma (PMH) and suggests that PMH should be included in the differential diagnosis of tumors of jaw bones. Definitive pathologic confirmation of PMH could help determining the treatment strategy.

Table I. Clinicopathologic features of primary PMH of bone

Case	*Authors (ref)*	*Year*	*Age (y)/sex*	*Sites*	*Multifocal*	*Treatment*	*Molecular abnormalities*	*Recurrence, mo*	*Metastasis, site/mo*	*Follow-up/mo*
1	Hornick et al.[1]	2011	35/M	Finger	No	NA	NA	No	No	ANED/17
2	Sheng et al.[5]	2012	10/F	Left tibia, fibula and distal femur	Yes	Curettage of left tibia and fibula lesions and resection of the distal femur	NA	Yes, 43 and 46	No	AWED/46
3	McGinity et al.[6]	2013	25/M	Thoracic spine and rib	No	Total resection of the tumor	NA	NA	NA	NA
4	Walther et al.[7]	2014	14/M	Foot	No	Curettage of the lesion	*SERPINE1-FOSB*	No	Yes, ramus of the os ischium and abdominal wall/10	AWED/10
5			18/M	Foot	No	NA	*SERPINE1-FOSB*	NA	NA	NA
6	Righi et al. [8]	2014	25/M	Left radius	Yes	Resection of the medium-inferior third of the radius Amputation of the inferior third of the left arm	NA	Yes, 6 and 14	No	ANED/228
7			66/F	Left distal femur, tibia, fibula and foot	Yes	Curettage of the lesion	NA	No	No	ANED/2
8	Shah et al.[9]	2015	82/M	Fibula, patella and distal femur	Yes	Biopsy of the distal femur	NA	No	Yes, pulmonary/ simultaneously	Died of unknown reason/5
9	Joseph et al.[10]	2015	45/M	Right anterior ilium	No	Biopsy, cisplatin, gemcitabine, docetaxel, and paclitaxel	NA	No	No	AWED/16
10	Inyang et al.[11]	2016	74/M	Right iliac crest, spine	Yes	Biopsy of unknown site	NA	No	No	AWED/4
11			20/M	Proximal left femur	Yes	Resection of proximal femur	NA	No	No	ANED/4
12			66/M	Lumbar spine, sacrum, ilium	Yes	Biopsy of sacrum	NA	NA	NA	Died of other disease
13			12/M	Left foot	Yes	Resection of fifth metatarsal Curettage and then below-the-knee amputation Cryoablation of rib lesion	*SERPINE1-FOSB*	Yes, 101 and 102	Yes, rib/103	AWED/103
14			26/M	Skull, spine, pelvis, sacrum, bilateral and proximal femurs	Yes	Biopsy of left ilium and brain	*SERPINE1-FOSB*	No	NA	AWED/8

(*continued on next page*)

Table I. Continued

Case	*Authors (ref)*	*Year*	*Age (y)/sex*	*Sites*	*Multifocal*	*Treatment*	*Molecular abnormalities*	*Recurrence, mo*	*Metastasis, site/mo*	*Follow-up/mo*
15			5/F	Right hip and pelvis	Yes	Biopsy of right proximal femur	NA	NA	NA	NA
16			14/M	Left upper extremity	Yes	Biopsy of unknown site	*SERPINE1-FOSB*	NA	NA	NA
17			47/M	Distal left lower extremity	Yes	Segmental resection of proximal fibula Above-the-knee amputation	NA	No	No	AWED/60
18			19/M	Distal right lower extremity	Yes	Curettage of right foot bones and metatarsal	NA	No	NA	AWED/46
19			59/M	Spine, pelvis, femurs, humeri, scapula, ribs, manubrium, sternum	Yes	Biopsies of L5 vertebral lesion and right iliac bone. Resection of sixth rib	NA	No	NA	AWED/16
20	Ye et al.[12]	2016	14/F	Left distal femur, tibia and calcaneus	No	Ablation of tumor tissue, then amputation of the left thigh	NA	No	No	ANED/3
21	Ozeki et al.[13]	2017	15/M	Left proximal tibia, thoracic vertebra and lumbar vertebra	Yes	mTOR inhibitor, everolimus	Translocation (7;19)	No	No	AWED/10
22	Gabor et al.[14]	2017	9/M	Left femur and the pubic bone	Yes	Resection of pubic and femoral, chemotherapy, mTOR inhibitor, sirolimus	NA	Yes, 2	No	AWED/24
23	Agaram et al.[15]	2018	45/F	Ischium, ankle	Yes	Surgery, chemotherapy, and radiation	*ACTB-FOSB*	NA	NA	AWED/26
24			33/M	Tibia	Yes	Radiofrequency ablation	*SERPINE1-FOSB*	NA	NA	AWED/12
25			44/M	Humerus	No	NA	*ACTB-FOSB*	No	No	ANED/3
26			25/M	Foot	No	NA	*ACTB-FOSB*	NA	NA	NA
27	Pradhan et al.[16]	2018	9/F	Femur head	No	Several biopsies and resection	NA	No	No	ANED/45
28			53/M	Ulna	Yes	Ulna resection	Negative	No	No	ANED/22
29			16/M	tibia	Yes	NA	NA	NA	NA	NA
30	Squillaci et al.[17]	2018	46/F	Right patella	No	Curettage of the lesion	NA	No	No	ANED/12
31	Danforth et al.[18]	2019	6/M	Proximal and distal tibial, fibular metaphyses	Yes	Sirolimus and zoledronic acid	*ACTB-FOSB*	No	No	ANED/37

(*continued on next page*)

Table I. Continued

Case	Authors (ref)	Year	Age (y)/sex	Sites	Multifocal	Treatment	Molecular abnormalities	Recurrence, mo	Metastasis, site/mo	Follow-up/mo
32	Kosemehmetoglu et al.[19]	2019	5/M	Left tibia, femur, fibula, talus and calcaneus	Yes	Curettage of the lesion, chemotherapy	*FOSB* rearrangement	No	No	NA
33			33/M	Right proximal femur	No	Curettage of the lesion	NA	No	No	NA
34			33/M	Distal radius metadiaphysis	Yes	Curettage of the lesion	NA	No	No	ANED/60
35			44/F	T2–3 vertebrae	Yes	Vertebrectomy	NA	No	No	ANED/24
36			25/M	Right femur diaphysis	Yes	Curettage of the lesion	NA	No	No	NA
37	Dianat et al.[20]	2019	63/M	Sacrum	No	S1-S3 partial sacrectomy	NA	No	No	ANED/16
38	Otani et al.[21]	2019	20/F	Left femur, patella, tibia, and talus	Yes	Curettage of the lesion, denosumab	NA	No	No	AWED/48
39	Present case	2019	34/M	Right maxilla	No	Surgical treatment	*FOSB* rearrangement	Yes, 6	No	ANED/18

PMH, pseudomyogenic hemangioendothelioma; *NA*, not applicable; *ANED*, alive with no evidence of disease; *AWED*, alive with evidence of disease.

CASE PRESENTATION

The study design was approved by the Ethical Committee of Shanghai Ninth People's Hospital, College of Stomatology, Shanghai Jiao Tong University School of Medicine, Shanghai, China, according to the Helsinki Declaration.

A 34-year-old man was referred to our hospital because of the possible recurrence after surgery and chemotherapy of a right maxillary malignant tumor. Six months before, the patient had received subtotal right maxillary resection and partial left maxillary resection as a result of a right maxillary mass, in an outside hospital. Surgical pathologic examination determined that the tumor was a low-grade osteosarcoma of the right maxilla. Postoperative chemotherapy and apatinib (Aitan, HENGRUI Medicine, Jiangsu, China) treatment were performed. Six months later, hypermetabolic uptake was found around the former surgical areas, including the remaining right maxilla, os nasale, pterygoid process, and infratemporal fossa, by positron emission tomography–computed tomography scanning, conducted to consider the possibility of tumor recurrence. He was subsequently admitted to Shanghai Ninth People's Hospital for further treatment. The preoperative radiographs revealed a radiolucent mass in the right maxilla (Figure 1). Cone beam computed tomography identified an irregular, osteolytic lesion in the right upper alveolar bone involving the right maxillary sinus and hard palate (Figure 2A and 2B). The lesion had no obvious boundary and there was a moth-eaten resorption of the surrounding bones (Figure 2C and 2D).

An intraoral physical examination revealed a postoperative defect in the palate (2.0 × 2.0 cm) covered with gray-yellowish secretions on the surface. Oronasal perforation was present, and no obvious mass was found. The patient had no obvious spontaneous pain or numbness. Maxillofacial enhanced computed tomography suggested that the right maxilla had postoperative alterations, and part of the normal structure of the surgical area was absent. The patient received a complete preoperative examination and was treated with extracranial excision of the right maxillary lesion combined with an anterior external femoral flap repair. The surgical specimens were sent to the Department of Oral Pathology for pathologic examination.

Histologic findings

Grossly, the specimens were composed of 4 pieces of hard and soft tissue, with a total size of 7.0 × 6.0 × 3.5 cm. The cut surface of the lesion was gray-white. Microscopically, a thin, bony shell structure was seen focally around the tumor. Nodules of the tumor cells, a large amount of reactive woven bone, and focal hemorrhage were seen under low-power magnification (Figure 3A). The tumor cells were plump spindled and polygonal epithelioid arranged in a loose fascicular and

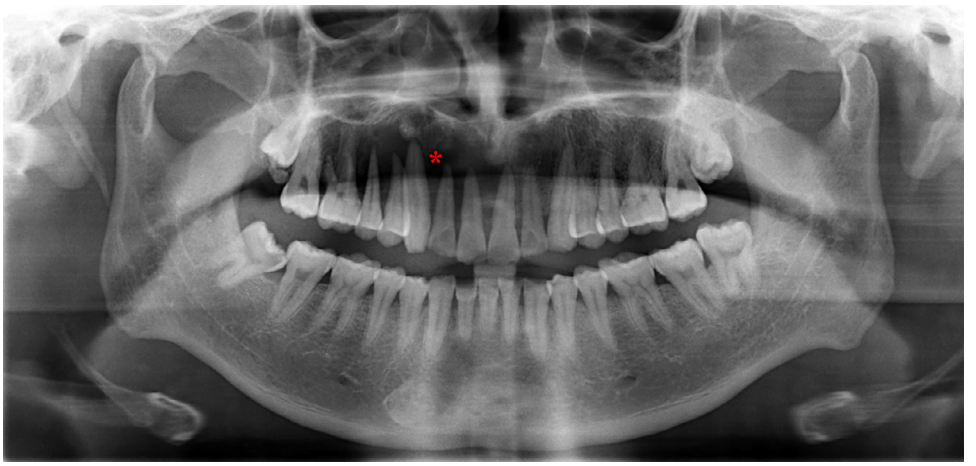

Fig. 1. Orthopantomography revealed a radiolucent mass in the right maxilla (asterisk indicated the tumor location).

sheet-like architecture (Figure 3B and 3C). The tumor cells contained abundant bright eosinophilic cytoplasm and vesicular nuclei with distinct nucleoli. Some cells strikingly resembled rhabdomyoblasts (Figure 3D). Scattered neutrophils and eosinophils were seen in the stroma (Figure 3E). Loosely distributed osteoclast-like

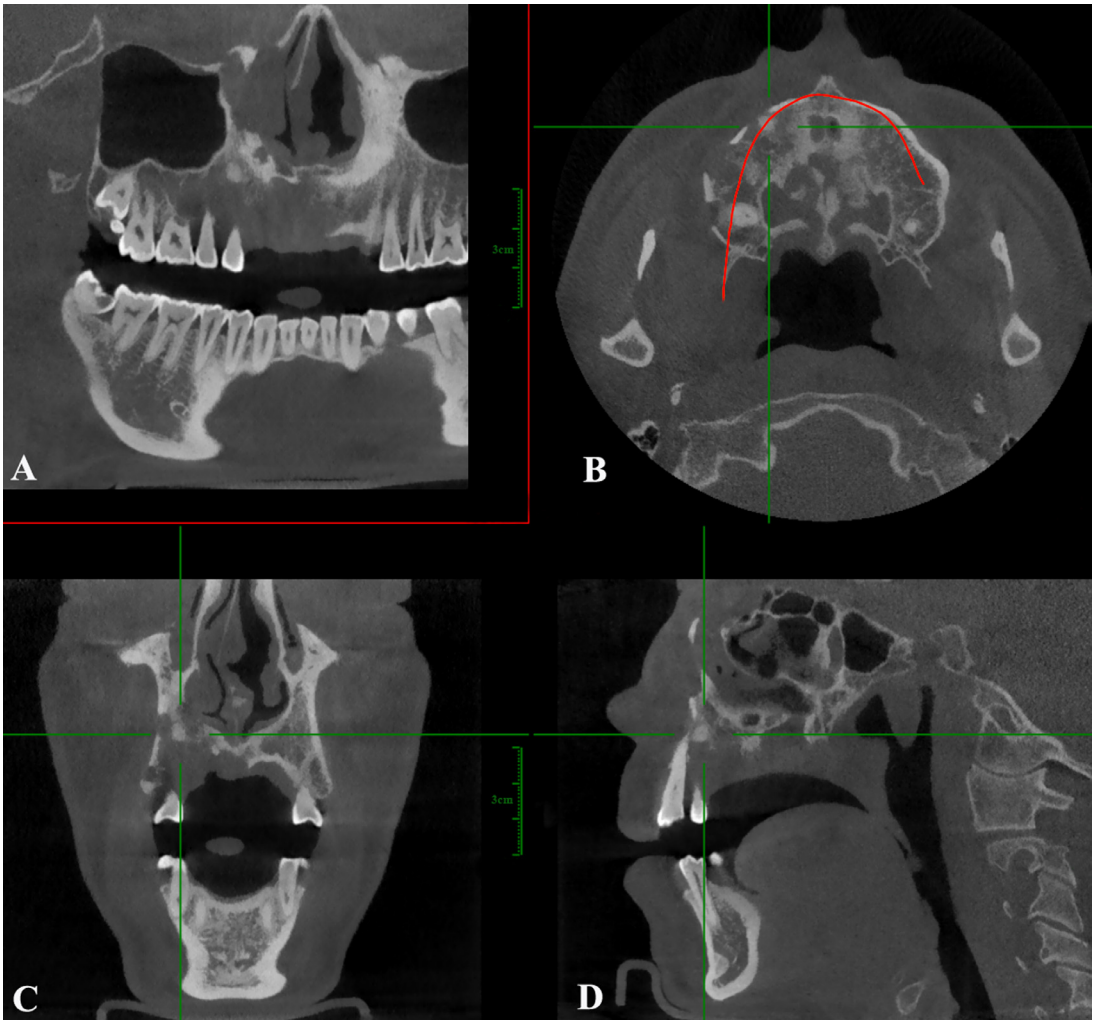

Fig. 2. Cone beam computed tomography imaging identified an irregular, osteolytic lesion in the right upper alveolar bone. **(A, B)** A virtual panoramic radiograph generating from the plane indicated as a red curve **(B)** showed the lesion involving the right maxillary sinus and hard palate. **(C, D)** The lesion had no obvious boundary and there was a moth-eaten resorption of the surrounding bones.

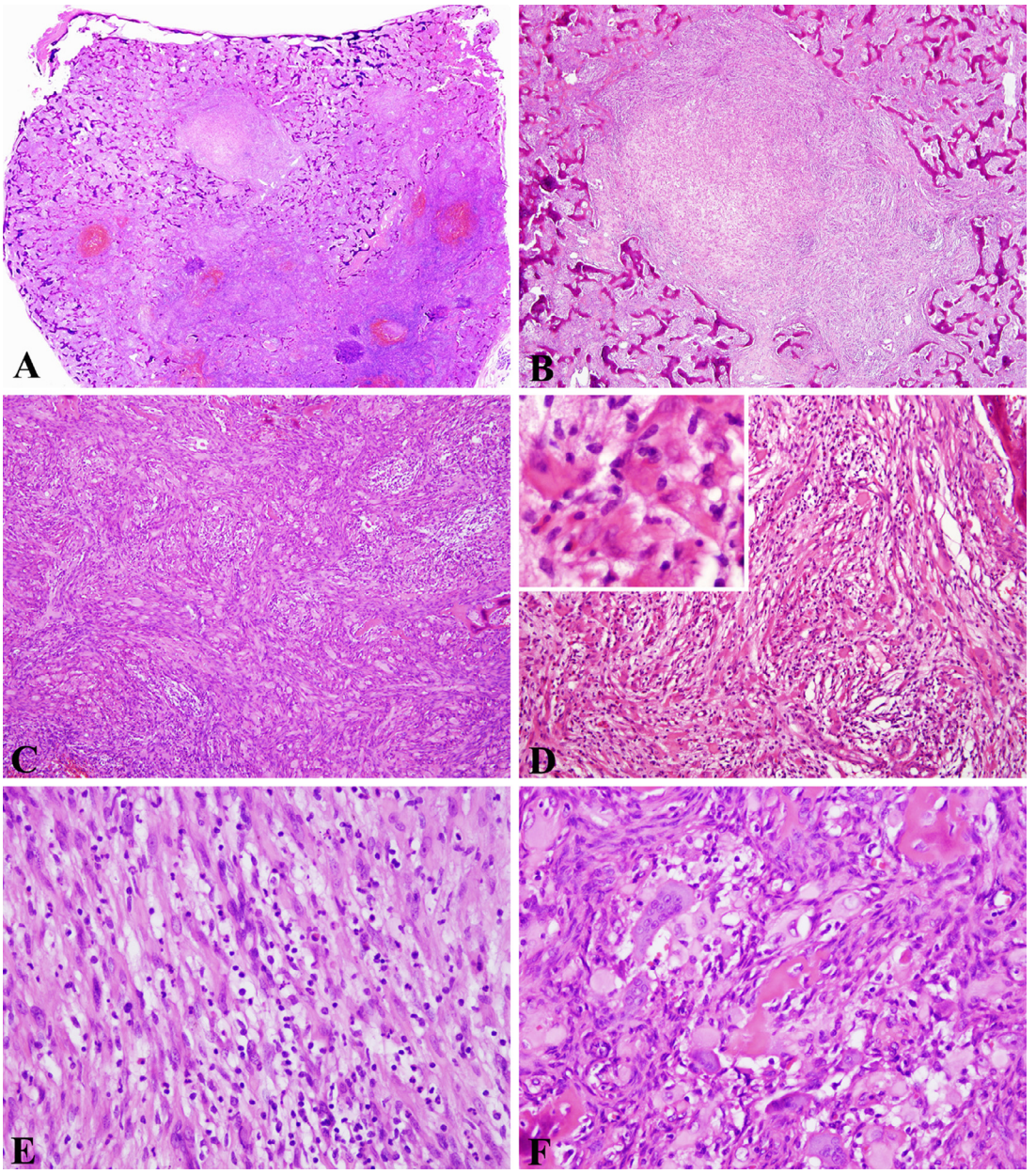

Fig. 3. Photomicrographs of primary pseudomyogenic hemangioendothelioma of the maxilla. A focal bony shell structure was identified around the tumor. The nodular and sheet-like tumor contained reactive woven bone and hemorrhage under super-low-power magnification (**A,** hematoxylin and eosin [H&E]). **(B, C)** The plump spindle and epithelioid cells were arranged in a loose fascicular and sheet-like architecture (B, H&E × 40; C, H&E × 100). **(D)** The tumor cells had abundant bright eosinophilic cytoplasm and strikingly resembled the rhabdomyoblasts (H&E × 200; an inset with higher magnification revealed clearer features of rhabdomyoblast-like cell). **(E)** Scattered neutrophils and eosinophils were seen in the stroma (H&E × 400). **(F)** Loosely distributed osteoclast-like giant cells were seen within reactive woven bones and tumor stroma (H&E × 400). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM05729.*

multinucleated giant cells were intermixed with reactive woven bone and tumor stroma (Figure 3F). The tumor cells had mild cytologic atypia with fewer than 1 mitosis per 10 high-power fields.

Immunohistochemical analysis revealed that the tumor cells were diffusely reactive with AE1/AE3 (Figure 4A), CD31 (Figure 4B), erythroblast transformation-specific transcription factor (ERG) (Figure 4C), and Friend leukemia integration 1 (Fli-1) (Figure 4D). The staining of CD31 had a unique linear membranous expression pattern. The tumor cells were negative for CD34 (Figure 4E), CAM5.2, epithelial membrane antigen (EMA) (Figure 4F), and desmin (Figure 4G) and had retained expression of integrase

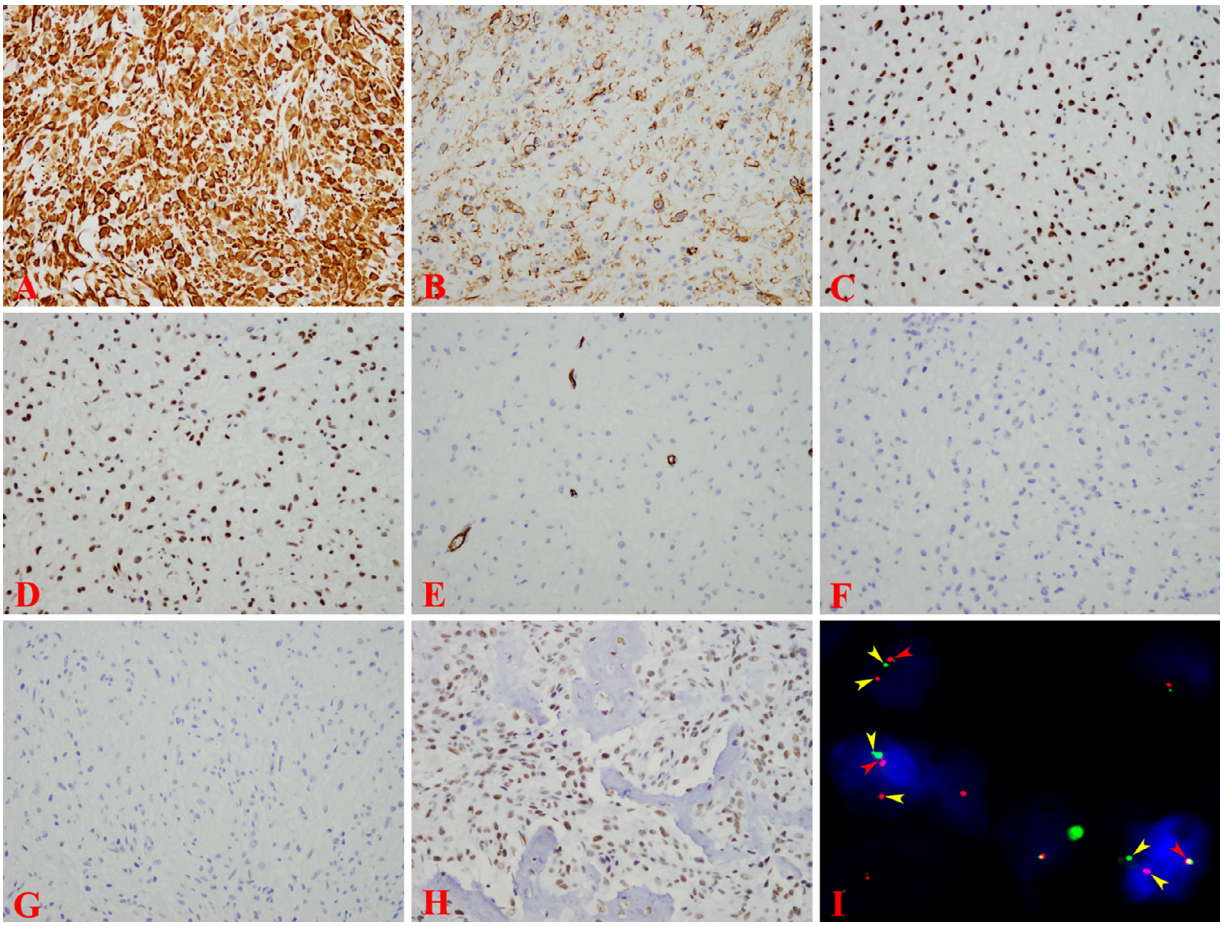

Fig. 4. Immunophenotype and *FOSB* gene rearrangement in pseudomyogenic hemangioendothelioma. The tumor cells diffusely reactivated with AE1/AE3 (**A**, immunohistochemistry [IHC] × 400) and endothelial markers CD31 (**B**, IHC × 400), erythroblast transformation-specific transcription factor (**C**, IHC × 400), and Friend leukemia integration 1 (**D**, IHC × 400) but were negative for CD34 (**E**, IHC × 400), epithelial membrane antigen (**F**, IHC × 400), and desmin (**G**, IHC × 400) and had retained expression of integrase interactor 1 (**H**, IHC × 400). *FOSB* rearrangement status determined by fluorescence in situ hybridization (FISH); red arrows indicate fusion signals and yellow arrows indicate break-apart signals (I, FISH, × 1000).

interactor 1 (INI-1) (Figure 4H). The Ki-67 labeling index was less than 5% (not shown). Break-apart fluorescence in situ hybridization for *FOSB* rearrangement was performed, and 20% of the tumor cells had *FOSB* gene break-apart signals, which was considered positive for *FOSB* gene rearrangement (Figure 4I). Based on the cumulative findings, a diagnosis of PMH was rendered. The patient was routinely followed up after his secondary surgery and had no evidence of tumor recurrence or metastasis during the follow-up period (18 months).

DISCUSSION

PMH of soft tissue is a rare vascular tumor with intermediate biological behaviors, distinctive clinical features, morphologic characterization, and immunophenotype and molecular alterations.[1] It usually involves the soft tissues of the lower extremities of young men. It has been reported that in approximately one-quarter of the cases concurrent bone was affected.[11]

Primary PMH of bone is extremely rare. A total of 39 cases (including the present case) have been described in the English-language literature, details of which are shown in Table I. Among them, 30 patients were male and 9 were female, with a male-to-female ratio of 3.3:1. The age ranged from 5 to 82 years old, with a mean of 31.6 years, and 27 out of 39 of the patients (69.2%) were between the second and fifth decades. In a total of 29 out of 39 cases (74.4%), PMH arose in the lower extremities, and most of these instances were polyostotic (26 out of 39, 66.7%). Thirty cases included follow-up information, 14 patients were alive with evidence of disease, 14 patients were alive with no evidence of disease, 1 patient had died of another disease, and 1 patient had died of unknown causes. Five patients had recurrent tumors, and 3 patients had metastatic lesions. The current case was a 34-year-old male patient with a solitary lesion presenting in the right maxilla. The tumor was recurrent 6

months after primary surgery. In summary, primary PMH of bone occurred in patients with similar demographic characteristics as those with disease arising in soft tissue, as reported by Hornick et al.[1]

Macroscopically, the tumor size of primary PMH of bone was generally less than 6.5 cm in its largest dimension, and the cut surface of the tumor was gray-white or gray-yellow. Microscopically, the morphology of the tumor cells was similar to its soft tissue counterpart, with the cells arranged in a loose fascicular and sheet-like architecture. The tumor cells were plump spindled and sometimes epithelioid with abundant, brightly eosinophilic cytoplasm and vesicular nuclei with distinct nucleoli strikingly resembling rhabdomyoblasts. The tumor cells had mild nuclear atypia and infrequent mitotic activity. Besides these, primary PMH of bone has some other unique histologic features, including reactive woven bone formation, focal hemorrhage, and scattered osteoclast-like giant cells. The current case in the maxilla presented with histologic manifestations similar to PMH presenting in other bone sites. The tumor cells that resembled rhabdomyoblasts are the most important clue for diagnosis of primary PMH of bone.[11,19]

PMH has no features of obvious endothelial differentiation; therefore immunohistochemical analysis is quite important in confirming the diagnosis. The present case had an identical immunophenotype with most cases reported in the literature, which diffusely expressed AE1/AE3, CD31, ERG, and Fli-1, whereas the tumor cells were negative for CD34, CAM5.2, EMA, and desmin and had retained expression of INI-1. This immunoprofile panel could be used to distinguish other histologic mimics with overlapping features. Hung et al.[2] reported that FOSB was a specific and sensitive diagnostic marker for PMH. Importantly, the immunophenotype is unique for PMH regardless of whether the primary tumor arises in bone or soft tissue.

Trombetta et al.[22] found a balanced t(7;19)(q22;q13) as the sole anomaly in 1 case, and Walther et al.[7] reported *SERPINE1-FOSB* rearrangement because of this t(7;19) translocation. More recently, *ACTB-FOSB* and *WWTR1-FOSB* rearrangement were also identified in a subset of PMH.[15,23] Primary PMH of bone harbors the same gene rearrangements. As summarized in Table I, 10 cases had detailed fusion gene data, of which 6 cases had *SERPINE1-FOSB* and 4 cases had *ACTB-FOSB* rearrangement. Another 2 cases, including the present case, had *FOSB* rearrangement. The decalcified tissues might have been of poor quality, which may impede the use of *FOSB* gene rearrangement fluorescence in situ hybridization detection as a useful ancillary method of confirming diagnosis of primary PMH of bone. More importantly, it should be noted that a small portion of osteoblastomas (2/28, 7.1%) also harbor *FOSB* rearrangement.[24]

The differential diagnosis for primary PMH of bone mainly includes epithelioid tumors and other tumors arising in bones. The most important differential diagnosis is epithelioid sarcoma arising in bone, which is composed of predominantly epithelioid cells arranged in nodular architecture rather than in fascicular or sheet-like fashion. Epithelioid sarcoma always presents with focal necrosis and positive for CAM5.2, EMA, and CD34 and almost always has loss of INI-1 expression. Another differential diagnosis is epithelioid hemangioendothelioma, which is mainly composed of cords of epithelioid and spindle cells with occasional intracytoplasmic vesicles that mimic the histologic features of PMH. However, myxoid or hyalinized stroma and genetic analysis help distinguish it from PMH. In contrast to PMH, epithelioid angiosarcoma is usually vasoformative with intracellular lumina and always has prominent cellular atypia and frequent mitosis. Microscopic and immunophenotypic features of PMH and the previously mentioned tumors are summarized in Table II.

Primary PMH of bone has some unique features, including reactive woven bone formation, focal hemorrhage, and osteoclast-like giant cells, which can be shared with other tumors arising in bones like osteoblastoma, low-grade osteosarcoma, and giant cell tumors. Osteoblastomas may have abundant reactive woven bone, and the tumor cells have eosinophilic cytoplasm. Occasional multinucleated giant cells may be present.[25] Immunohistochemical analysis could help separate osteoblastomas from PMH. Furthermore, immunohistochemical and genetic analysis could be used to distinguish low-grade osteosarcoma and giant cell tumors from PMH. Small foci of rhabdomyoblast-like cells could be a characteristic feature in distinguishing those tumors from PMH. The expression of myogenic markers, such as desmin, MyoD1, and myogenin, could help distinguish PMH from rhabdomyosarcoma. The present patient underwent an operation in an outside hospital and was subsequently diagnosed as having a low-grade osteosarcoma. The distinction of PMH from other malignant tumors, including epithelioid sarcoma, rhabdomyosarcoma, and low-grade osteosarcoma, is very important, because misdiagnosis may lead to inappropriate treatment and unnecessary damage to the patient.

Most PMHs were treated by local excision only. For patients with primary PMH of bone, some of them received several biopsies and others were mostly treated by curettage.[11] Mammalian target of rapamycin (mTOR) inhibitors, including everolimus and sirolimus, were considered as alternative treatment options.[13-14,18] PMHs have intermediate biological behavior and may be locally aggressive. A small portion of the tumors may be stable even without any treatment, with some patients living with the disease

Table II. Comparison of the microscopic and immunophenotypic features of PMH and histologic mimics

	PMH	*Epithelioid sarcoma*	*Epithelioid hemangioendothelioma*	*Epithelioid angiosarcoma*
Growth pattern	Nodular, loose fascicular and sheet-like	Nodular	Cords of epithelioid and spindle cells with myxoid or hyalinized stroma	Sheet-like
Vasoformative structure	Absent or present with occasional intracytoplasmic vacuoles	No vascular lumen formation	Always present with intracytoplasmic vacuoles	Always present with vascular channels and intracellular lumens
Necrosis	No	Yes	No	Maybe present
Cellular atypia	Mild to moderate	Moderate	Mild to moderate	Moderate to severe
Neutrophil Infiltrate	Always present	Absent	Absent	Absent
Immunophenotype	AE1/AE3+, CD31+, Fli-1+, ERG+, INI-1+, CD34−, Des-	EMA+, CAM5.2 focally positive, CD34+, CD31−, INI-1-	CD31+, ERG+, Fli-1+, CD34+	CD31+, ERG+, Fli-1+, CD34+

PMH, pseudomyogenic hemangioendothelioma; *ERG,* erythroblast transformation-specific transcription factor; *Fli-1,* Friend leukemia integration 1; *INI-1,* integrase interactor 1, *Des,* desmin.

for a relatively long time (Table I, maximum 103 months). Local recurrence of the tumor is common, and distant metastasis is extremely rare.

In summary, to the best of our knowledge we present a unique case of primary PMH of maxilla for the first time broadening the clinical tumor location spectrum of PMH. PMH should be included in the differential diagnosis of jaw bone tumors. Recognition of the histologic characterization, immunophenotype, and unique genetic alterations of primary PMH of bone is essential in arriving at the conclusive diagnosis and avoiding misdiagnosis.

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REFERENCES

1. Hornick JL, Fletcher CD. Pseudomyogenic hemangioendothelioma: a distinctive, often multicentric tumor with indolent behavior. *Am J Surg Pathol*. 2011;35:190-201.
2. Hung YP, Fletcher CD, Hornick JL. FOSB is a useful diagnostic marker for pseudomyogenic hemangioendothelioma. *Am J Surg Pathol*. 2017;41:596-606.
3. Mirra JM, Kessler S, Bhuta S, Eckardt J. The fibroma-like variant of epithelioid sarcoma. A fibrohistiocytic/myoid cell lesion often confused with benign and malignant spindle cell tumors. *Cancer*. 1992;69:1382-1395.
4. Billings SD, Folpe AL, Weiss SW. Epithelioid sarcoma-like hemangioendothelioma. *Am J Surg Pathol*. 2003;27:48-57.
5. Sheng WQ, Wang J. Primary pseudomyogenic haemangioendothelioma of bone. *Histopathology*. 2012;61:1219-1224.
6. McGinity M, Bartanusz V, Dengler B, Birnbaum L, Henry J. 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.
7. Walther C, Tayebwa J, Lilljebjorn H, et al. A novel SERPINE1-FOSB fusion gene results in transcriptional up-regulation of FOSB in pseudomyogenic haemangioendothelioma. *J Pathol*. 2014;232:534-540.
8. Righi A, Gambarotti M, Picci P, Dei Tos AP, Vanel D. Primary pseudomyogenic haemangioendothelioma of bone: report of two cases. *Skeletal Radiol*. 2015;44:727-731.
9. Shah AR, Fernando M, Musson R, Kotnis N. An aggressive case of pseudomyogenic haemangioendothelioma of bone with pathologic fracture and rapidly progressive pulmonary metastatic disease: case report and review of the literature. *Skeletal Radiol*. 2015;44:1381-1386.
10. Joseph J, Wang WL, Patnana M, et al. Cytotoxic and targeted therapy for treatment of pseudomyogenic hemangioendothelioma. *Clin Sarcoma Res*. 2015;5:22.
11. Inyang A, Mertens F, Puls F, et al. Primary pseudomyogenic hemangioendothelioma of bone. *Am J Surg Pathol*. 2016;40:587-598.
12. Ye C, Yu X, Zeng J, Liu H, Dai M. Pseudomyogenic hemangioendothelioma 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.
13. Ozeki M, Nozawa A, Kanda K, et al. Everolimus for treatment of pseudomyogenic hemangioendothelioma. *J Pediatr Hematol Oncol*. 2017;39:e328-e331.
14. Gabor KM, Sapi Z, Tiszlavicz LG, Fige A, Bereczki C, Bartyik K. Sirolimus therapy in the treatment of pseudomyogenic hemangioendothelioma. *Pediatr Blood Cancer*. 2018;65:E26781-e26784.
15. Agaram NP, Zhang L, Cotzia P, Antonescu CR. Expanding the spectrum of genetic alterations in pseudomyogenic hemangioendothelioma with recurrent novel ACTB-FOSB gene fusions. *Am J Surg Pathol*. 2018;42:1653-1661.
16. Pradhan D, Schoedel K, McGough RL, Ranganathan S, Rao UNM. Pseudomyogenic hemangioendothelioma of skin, bone and soft tissue—a clinicopathological, immunohistochemical, and fluorescence *in situ* hybridization study. *Hum Pathol*. 2018;71:126-134.

17. Squillaci S, Pitino A, Spairani C, Rassu PC, Chiapuzzo E, Kutzner H. Primary pseudomyogenic hemangioendothelioma of bone: case report and review of the literature. *Pathologica*. 2018;110:96-101.
18. Danforth OM, Tamulonis K, Vavra K, et al. Effective use of sirolimus and zoledronic acid for multiosteotic pseudomyogenic hemangioendothelioma of the bone in a child: case report and review of literature. *J Pediatr Hematol Oncol*. 2019;41:382-387.
19. Kosemehmetoglu K, Rekhi B, Wakely P.E. Jr., Pant V, Dervisoglu S, Aydingoz U. Pseudomyogenic (epithelioid sarcoma-like) hemangioendothelioma of bone: clinicopathologic features of 5 cases. *Ann Diagn Pathol*. 2019;41:116-123.
20. Dianat S, Yousaf H, Murugan P, Marette S. Pseudomyogenic hemangioendothelioma—a case report and review of the literature. *Radiol Case Rep*. 2019;14:1228-1232.
21. Otani S, Nakayama R, Sekita T, et al. Pseudomyogenic hemangioendothelioma of bone treated with denosumab: a case report. *BMC Cancer*. 2019;19:872.
22. Trombetta D, Magnusson L, von Steyern FV, Hornick JL, Fletcher CD, Mertens F. Translocation t(7;19)(q22;q13)-a recurrent chromosome aberration in pseudomyogenic hemangioendothelioma. *Cancer Genet*. 2011;204:211-215.
23. Panagopoulos I, Lobmaier I, Gorunova L, Heim S. Fusion of the genes WWTR1 and FOSB in pseudomyogenic hemangioendothelioma. *Cancer Genom Proteom*. 2019;16:293-298.
24. Fittall MW, Mifsud W, Pillay N, et al. Recurrent rearrangements of FOS and FOSB define osteoblastoma. *Nat Commun*. 2018;9:2150.
25. Kashikar S, Steinle M, Reich R, Freedman P. Epithelioid multinodular osteoblastoma of the mandible: a case report and review of literature. *Head Neck Pathol*. 2016;10:182-187.

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