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Sinonasal Phosphaturic Mesenchymal Tumor: A Case Report

Case Report

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Abstract

Phosphaturic mesenchymal tumor (PMT) is a rare mesenchymal neoplasia usually located in the soft tissue and the bone. It is seen in older ages and is most commonly localized in the extremities. Here, we present a rare case of PMT located in the sinonasal region. A 56-year-old male patient was admitted with complaints of congestion in the right nasal cavity and limitation of upward gaze in the right eye. Computed tomography revealed a contrast-enhancing mass with heterogeneous density obliterating the bilateral frontal sinus, the frontoethmoidal recess, the right osteomeatal complex and the right sphenoid sinus, extending to the superior extraconal area in the right orbit. Since the tumor type cannot be determined precisely in the pathological evaluation of incisional biopsy, an excisional biopsy was performed with the preliminary diagnosis of malignancy. But histopathological examination revealed a PMT. PMT is a highly uncommon neoplasm that remains largely unfamiliar to clinicians, surgeons, and pathologists, particularly when arising in rare locations like the sinonasal region. Its histomorphological characteristics can overlap with various other entities, necessitating a broad differential diagnosis.

Keywords: Head and neck surgery, phosphaturic mesenchymal tumor, sinonasal neoplasms, nasal cavity, case report

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Introduction

Phosphaturic mesenchymal tumor (PMT) is a rare neoplasm that is mostly located in the soft tissue and the bone, with the clinic of hyperphosphaturia, hypophosphatemia and osteomalacia (1,2). There is no significant difference between the sexes in terms of incidence rate (3). While the most common locations are the lower and upper extremities, the head and neck region account for approximately 5% of the cases (4). It is most commonly seen in the sinonasal tract in the head and neck region (2,3). In this report, we describe an uncommon case of PMT located in the sinonasal region.

Case Presentation

A 56-year-old male was admitted to the ear, nose and throat clinic with complaints of congestion in the right nasal cavity and limitation of upward gaze in the right eye, which had been going on for about one and a half year. On the examination of the

patient, a polypoid lesion filling the right nasal cavity and extending into the nasopharynx was observed. Computed tomography (CT) revealed a contrast-enhancing mass with heterogeneous density obliterating the bilateral frontal sinus, the frontoethmoidal recess, the right osteomeatal complex, and the right sphenoid sinus. The mass extended to the superior extraconal area in the right orbit, filled the passage up to the lower nasal turbinate on the right, and resulted in secondary exophthalmos in the right eye (Figure 1). In positron emission tomography-CT examination, heterogeneously increased activity was observed in the mass (SUV_{max}: 5.01). Simultaneous biochemical tests revealed hypophosphatemia (1.3 mg/dL; reference range: 2.7-4.5 mg/dL).

Fragmented biopsy material was sent from the mass, and hypercellular spindle cell proliferation was observed microscopically. On immunohistochemical evaluation of the specimen, widespread cyclin D1 and B-cell lymphoma 2 (BCL-2), focal transducin-like enhancer of split 1 and p53 positivity were seen. Pancytokeratin, beta-catenin, S100, smooth muscle actin (SMA), muscle-specific actin, desmin, cluster of differentiation (CD) 68, KP1, CD117, human melanoma black-45 (HMB-45), CD34, signal transducer and activator of transcription 6 (STAT6) epithelial membrane antigen, progesterone receptor, cytokeratin 7 and synaptophysin were negative. Ki-67 proliferation index was evaluated as 2-3%. Histopathological findings supported a spindle cell mesenchymal tumor, but the findings were not sufficient to make further comments about the tumor subtype.

The patient was planned for endoscopic sinus surgery for total excision of the lesion. The surgery was performed under general anesthesia. The right nasal cavity was completely filled by mass which had eroded the anterior wall of the sphenoid sinus. The mass was removed en-bloc with the help of an endoscope, together with the anterior wall of the sphenoid sinus to which it was attached. The minor defect was repaired with oxidized regenerated cellulose (Surgicel) and muscle tissue. The frontal recess was opened. An incision was made under the right eyebrow. The anterior wall of the frontal sinus was defective. The mucocele filling the frontal sinus was totally excised. The superior and medial walls of the orbit were defective due to the mass. Ophthalmologists attended the surgery. It was decided that the eyeball was intact. Bleeders were controlled using bipolar cautery. His postoperative course was unremarkable, and he recovered well.

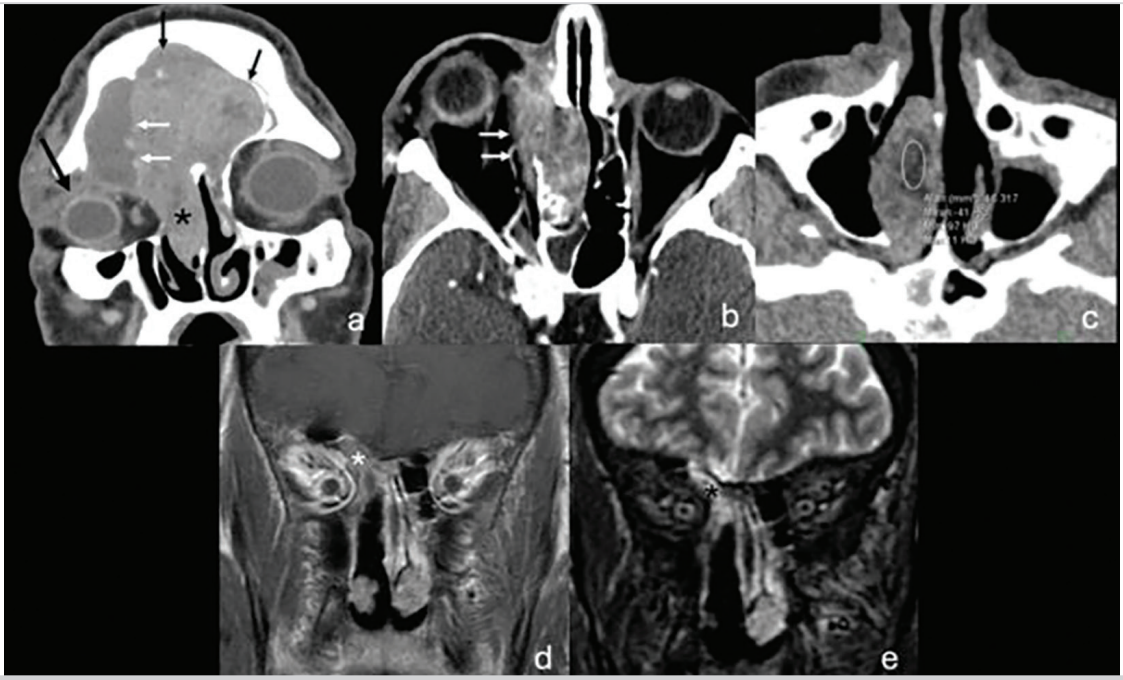

Figure 1. The radiological features and extensions of the right sinonasal lesion are shown in preoperative contrast-enhanced (a and b) and non-contrast (c) CT images. The right sinonasal giant mass extends from the frontal (a, short black arrows) and ethmoid sinuses to the nasal cavity (a, black asterisks) and to the orbit through the lamina papyracea (b, white arrows). Due to the obstruction of frontal sinus drainage, a mucocele (a, white arrows) causing ocular pressure (a, long black arrow) has developed. The density of the adipose component of the mass was measured with an oval ROI (c). Approximately 10 months postoperative MRI (d, contrast-enhanced T1-weighted; e, fat-suppressed T2 weighted) shows the disappearance of sinonasal obstruction and orbital compression, while soft tissue considered radiologically as sinonasal residue is seen near the olfactory fossa (asterisk)

CT: Computed tomography, ROI: Region of interest, MRI: Magnetic resonance imaging

Microscopic examination of the excision material revealed a well circumscribed spindle cell proliferation with a hypercellular appearance, showing a patternless, diffuse architecture. The tumor consisted of oval and round cells with generally uniform nuclei, eosinophilic cytoplasm, and unclear cytoplasmic boundaries. There was an edematous zone between the neoplastic cells and the epithelium (Figure 2). Generally small-caliber vascular structures with thin- and thick-wall, edematous hypocellular areas, and occasional hemosiderin deposition were observed within the tumor (Figure 3). Adipose tissue was seen at the periphery of the tumor. In focal areas, there was a grungy calcified matrix (Figure 4). Occasional mitosis was observed, but no necrosis was seen. Special AT-rich sequence-binding protein 2 (SATB2), friend leukemia integration 1 (FLI-1), BCL2, cyclin D1, *ETS-related gene (ERG)* and CD56 immunohistochemical markers were diffusely positive in neoplastic cells. D2-40 and melanoma inhibitory activity C2 protein were stained in focal areas. STAT6, S100, HMB-45, keratin, synaptophysin, beta-catenin, SMA and neuron-specific enolase were negative. Ki-67 proliferation index was 4-5%. There was faint nuclear staining with the somatostatin receptor 2A (SSTR2A) marker. fibroblast growth factor-23 (FGF-23) immunohistochemical marker was not performed at the time of diagnosis for technical reasons.

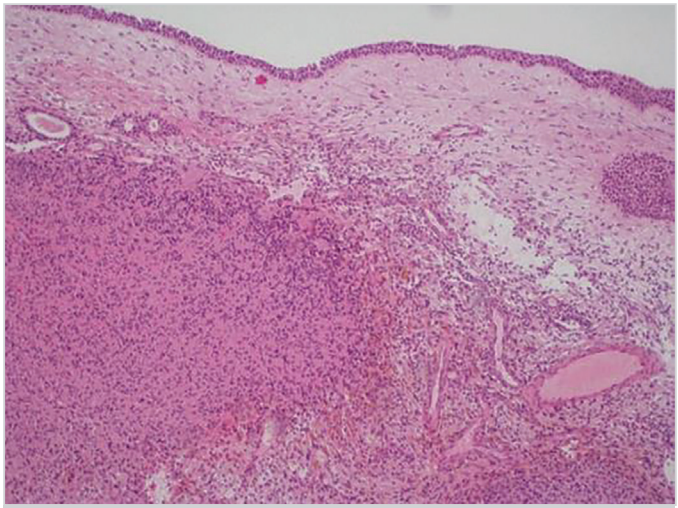

Figure 2. Patternless, hypercellular, well-circumscribed spindle cell proliferation is seen under the edematous respiratory mucosa (hematoxylin and eosin, x100)

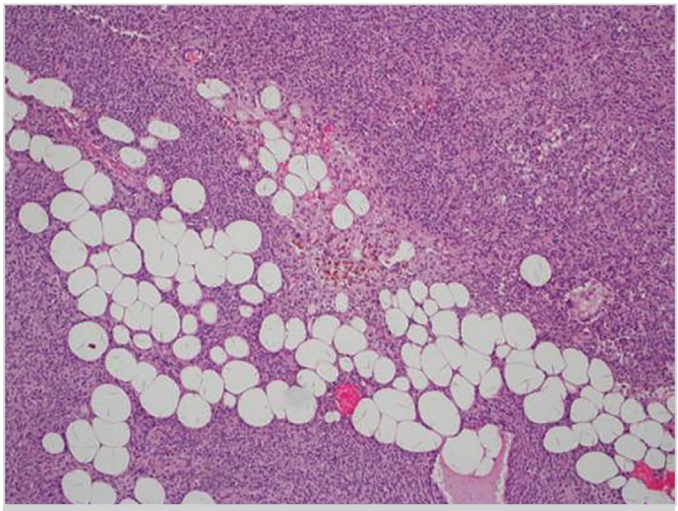

Figure 3. The tumor generally consists of oval and round cells with uniform nuclei, eosinophilic cytoplasm, and unclear cytoplasmic borders. Hemosiderin deposition and fatty tissue are also noted (hematoxylin and eosin, x200)

When clinical, histopathological, and immunohistochemical findings were evaluated together, the final diagnosis was compatible with PMT, and simultaneous biochemical tests revealed hypophosphatemia (1.3 mg/dL; reference range: 2.7-4.5 mg/dL). During the postoperative follow-up, the patient's complaints were resolved, and serum phosphate levels returned to normal limits (3.1 mg/dL; reference range 2.7-4.5 mg/dL). No recurrence was observed in the patient's 3-year follow-up. Informed consent was obtained from the patient for this report.

Discussion

PMT, first described in 1947, is a rare neoplasm that ectopically produces FGF-23, which is secreted by osteocytes and maintains phosphate balance of the body (1,5). FGF-23 reduces the expression of sodium/phosphate transporters and provides phosphate excretion with the urine. It prevents the reuptake of phosphate by the proximal renal tubules and reduces the reabsorption of calcium and phosphate from the intestines. Additionally, it reduces the production of 1,25-dihydroxycholecalciferol by inhibiting the 1α-hydroxylase enzyme. The resulting hyperphosphaturia

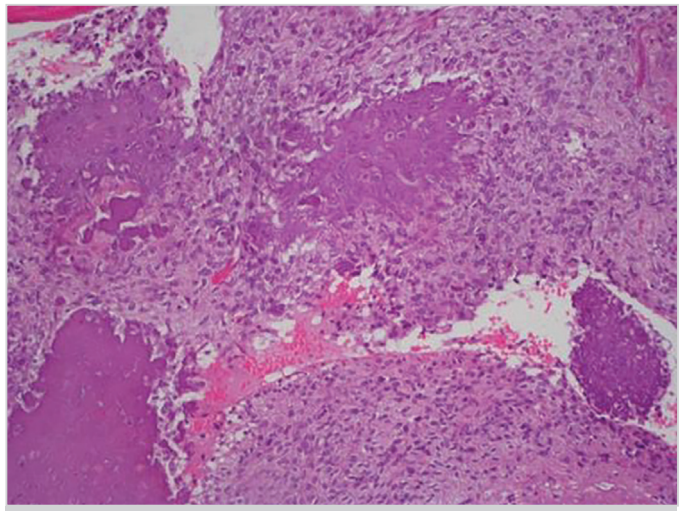

Figure 4. The distinctive and characteristic foci of "grungy" calcification in PMT appear lightly basophilic and granular or flocculent in quality (hematoxylin and eosin, x200)
PMT: Phosphaturic mesenchymal tumor

and hypophosphatemia deflect bone mineralization, and lead to osteomalacia (4,6).

Tumor-induced osteomalacia is extremely rare. Its most common cause are tumors of mesenchymal origin; it is also associated with various syndromes such as McCune Albright syndrome and neurofibromatosis-1. In the last few decades, it has been understood that almost all the cases of tumor-induced osteomalacia are caused by PMT (7).

PMT is mostly located in bone and soft tissue. However, there are few case reports of internal organs and meninges in literature (4). Tumor sizes vary between 1-15 cm but often are smaller than 5 cm. Rare multicentric tumors have been reported (1,8).

In literature, there are 153 cases of PMT described in the sinonasal region, and approximately 80% of the cases were diagnosed between the ages of 30-60 years. The male/female sex ratio is 1:1.05. The most common location is the ethmoid sinus (64.7%), followed by the nasal cavity (50.3%), the maxillary sinus (19.0%), the frontal sinus (16.4%), and the sphenoid sinus (11.8%) (9).

On CT, PMTs appear as round or oval, well-circumscribed, isodense or hypodense soft tissue masses. When the tumor is small, it shows homogenous contrast enhancement (10,11). On magnetic resonance imaging, they are isointense compared to the muscles on T1-weighted imaging, markedly hyperintense on T2-weighted imaging, and markedly enhanced after contrast administration. The increase in tumor size makes the pre- and post-contrast signal properties heterogeneous. Signal-void vascular structures can also be detected in large tumors (12).

In the case presented, the lesion was heterogeneous because of its large size. It has been reported that these lesions may contain adipose tissue pathologically (13). It is noteworthy that adipose tissue was observed in the mass on CT in the presented patient. Other CT features were not different from other sinonasal tumors.

On histopathological examination, the lesion appears hypocellular and consists of round-spindle cells with small nucleoli, indistinct nucleoli, and a calcified-collagenous matrix. Hemangiopericytoma-like vascular structures, hemosiderin pigment, multinucleated giant cells and microcystic changes can be seen in the stroma (3,8). Minimal cytological atypia, low mitotic activity, and absence of necrosis support the benign nature of this neoplasm. Histopathological findings are non-specific in cases seen in the head and neck region, especially in the sinonasal tract. Hypercellular appearance and dense hemangiopericytoma-like vascular structures may be seen. Also, sinonasal PMTs less often contain calcified matrixes and more often mature adipose tissue. Observation of these histomorphological features in cases located in the sinonasal tract causes difficulty in diagnosis (2,7).

It has originally described four types PMT (mixed connective tissue, osteoblastoma-like, ossifying fibroma-like, non-ossifying fibroma-like types). These are now believed to represent minor morphologic variants. Histopathologic features in our case consisted of the mixed connective tissue type.

Immunohistochemically, the cells are FLI-1, *ERG*, vimentin, CD56, SATB2, SSTR2A, FGF-23, matrix extracellular phosphoglycoprotein, dentin matrix protein 1 positive; and pancytokeratin, CD34, STAT6, HMB-45, nuclear beta-catenin, synaptophysin, S100 and discovered on gastrointestinal stromal tumor 1 negative (1,2). Detection of fibroblast growth factor receptor (FGFR) mRNA by cytokine-inducible SH2-containing protein may help the diagnosis (3,5). In recent years, molecular analyses have shown that fusions of the *fibronectin 1 (FN1)-FGFR1* or *FN1-FGF1* genes play a role in the development of most PMTs (4, 5).

Due to the rarity of this entity and the variability in its histomorphological and immunohistochemical features, establishing a differential diagnosis can be challenging. The differential considerations encompass a broad spectrum of neoplasms (2,3) (Table 1).

Although it is a benign lesion, distant metastasis has been reported in rare cases, and local recurrence is observed in incomplete resected tumors (7). Serum phosphate and FGF-23 levels should be monitored in the postoperative period for the possibility of distant metastasis and local recurrence (8).

Conclusion

PMTs are extremely rare neoplasms with diverse clinical manifestations and histopathological features. Due to the limited awareness among clinicians and pathologists, significant challenges and delays can occur in diagnosis. The variability in biopsy findings further complicates the diagnostic process, especially in small biopsy specimens, where a definitive diagnosis may not always be possible. This, in turn, contributes to diagnostic delays. In this case report, we aim to enhance awareness among clinicians and pathologists by presenting a comprehensive review of the clinical, radiological, and pathological characteristics of PMTs.

Table 1. Differential diagnosis of PMT

Features	PMT	Osteoblastoma/ osteoid osteoma	Chondromyxoid sarcoma	Low-grade osteosarcoma	Hemangiopericytoma/ solitary fibrous tumor
Clinical	Hypophosphatemia, muscle weakness, associated with TIO	Painful, usually in young adults	Painful, common in pelvis and spine	Young adults, slow-growing mass	Painless mass, often asymptomatic
Paraneoplastic effect	✓ (TIO)	✗	✗	✗	✗
Histology	Irregular spindle cells, myxoid stroma, 'grungy' calcification	Bone trabeculae, osteoid formation	Chondroid and myxoid areas	Atypical osteoid production	Vascular pattern, CD34 positivity
Calcification	Characteristic 'grungy' calcification	Possible	Common	Often present	Generally absent
Immunohistochemistry	FGF-23 (+), SMA (+/-), CD34 (+/-)	Osteoblastic markers (+)	S100 (+)	SATB2 (+), MDM2 (+/-)	CD34 (+), STAT6 (+)
FGF-23 expression	✓ (high)	✗	✗	✗	✗

PMT: Phosphaturic mesenchymal tumor, TIO: Tumor-induced osteomalacia, FGF-23: Fibroblast growth factor-23, SMA: Smooth muscle actin, CD34: Cluster of differentiation 34, SATB2: Special AT-rich sequence-binding protein 2, MDM2: Mouse double minute 2, STAT6: Signal transducer and activator of transcription 6

Ethics

Informed Consent: Informed consent was obtained from the patient for this report.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ş.A.İ., H.Ç., Concept: H.T.E., M.F.A., Design: H.T.E., Ö.B., M.F.A., Data Collection and/or Processing: H.T.E., Ö.B., M.F.A., U.T., Analysis and/or Interpretation: H.T.E., M.F.A., Literature Search: H.T.E., U.T., Writing: H.T.E.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- Phosphaturic mesenchymal tumor is a rare benign neoplasm that is mostly located in the soft tissue and the bone.
- The head and neck region accounts for approximately 5% of the cases, and the most common tumor location in this region is the sinonasal tract.
- Clinicians, surgeons, and pathologists often have limited awareness of this condition, particularly when it presents in rare locations like the sinonasal tract.
- Although it is a benign lesion, distant metastasis has been reported in rare cases.
- Total excision of the lesion usually provides effective treatment.

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