## **Case Report**

# Phosphaturic Mesenchymal Tumors Involving Skull Bones: Report of Two Rare Cases

#### Abstract

Phosphaturic mesenchymal tumor (PMT) is a rare tumor causing oncogenic osteomalacia (OO). Most such tumors occur in soft tissue and bones of extremities and appendicular skeleton. Intracranial location and involvement of temporal–occipital bone is extremely rare. We report two unusual cases: The first was intracranial, involving the temporal bone, while the other was a skull base tumor arising from the occipital–temporal bone. Both of them presented with paraneoplastic syndrome of OO, resembled a meningioma radiologically, and underwent gross total resection of tumor. Histologically, both of them were diagnosed as PMT, mixed connective tissue variant.

**Keywords:** Fibroblast growth factor-23, intracranial, oncogenic osteomalacia, phosphaturic mesenchymal tumor, temporal–occipital bone

### Introduction

Phosphaturic mesenchymal tumor (PMT) а rare and distinctive is tumor with oncogenic associated frequently osteomalacia (OO). PMT usually occurs in the soft tissue or bones of the extremities and occasionally in the craniofacial area in the mouth, nasopharynx, or one of the paranasal sinuses.<sup>[1]</sup> Occurrence in intracranial and craniovertebral region is very rare, and only a few cases have been reported.<sup>[2-6]</sup> We hereby report two rare cases of PMT, the first case being intracranial involving the temporal bone and the second a skull base tumor originating from the occipital-temporal bone.

#### **Case Report**

#### Case 1

A 46-year-old male came to the outpatient department of our hospital with the complaints of progressive in walking for the difficulty past 5 years. Two years back, he had suffered from a bilateral femoral fracture. His phosphorus was 1.6 serum mg/dl (normal range 2.4–4.5 mg/dl), 1,25-dihydroxy vitamin D was 24 ng/mL (normal range 30-100 ng/mL), and alkaline phosphatase was 942.6U/L (normal range 53-128U/L). hypophosphatemic Α diagnosis of osteomalacia was made clinically. Serum fibroblast growth factor (FGF)-23 was 1023 RU/mL (normal <180 RU/mL). Based on the above clinical and biochemical findings, a diagnosis of OO was suspected. whole-body positron emission А tomography (PET) scan revealed multiple osteolytic lesions in the axial skeleton with no evidence of abnormal FDG uptake. With this clinical history, a somatostatin receptor PET scintigraphy was advised which revealed a somatostatin receptor-positive extra-axial disease in the right temporal lobe with the involvement of adjacent petrous temporal bone, suggestive of malignant meningioma. Subsequent magnetic resonance imaging (MRI) revealed a well-demarcated lobulated dumbbell-shaped heterogeneously enhancing mass lesion in the right temporal region measuring  $1.9 \text{ cm} \times 1.7 \text{ cm} \times 2.6 \text{ cm}$ , involving the mastoid bone, epitympanum with erosions of the bone, especially the tegmen tympanum, and an intracranial epidural component. The mass was hypointense on T1-weighted images and heterogeneously enhancing on T2-weighted and fluid-attenuated inversion recovery images [Figure 1]. The patient underwent right temporal craniotomy and stereotactic gross total excision of the lesion. The postoperative period was uneventful.

Histopathology revealed a cellular tumor composed of sheets of oval-to-short fusiform cells possessing scanty cytoplasm

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and relatively uniform-appearing nuclei [Figure 2a]. osteoclastic giant cells Scattered were focally identified. Foci of "grungy" calcification were also detected [Figure 2a]. Ectatic thin-walled vascular spaces, hemorrhage with hemosiderin pigment deposits, and areas of fibrosis with hyalinization were evident. Few mitoses were noted. No sarcomatous features were detected. On immunohistochemistry, the tumor cells were diffusely positive for vimentin and focally positive for smooth muscle actin, whereas they were negative for S100 and CD34 [Figure 2b-d]. A diagnosis of PMT, mixed connective tissue type (PMTMCT), was confirmed on the basis of the above clinical, biochemical, histopathological, and immunohistochemical features.

#### Case 2

A 52-year-old woman came with the complaints of pain in bilateral hips and thighs and progressive difficulty in walking for the past 2 years. The patient had been investigated outside and was diagnosed as hypophosphatemic osteomalacia and treated with phosphate supplements. Her serum calcium was normal (9.2 mg/dl), phosphorus was low (1.6 mg/dl), parathyroid hormone levels were normal (39.65 pg/ml), 24-h urinary phosphorus was elevated (1005 mg/day), and FGF-23 was elevated (725 RU/mL). With the above clinical and biochemical details, a defect in renal tubular function due to OO was suspected. A whole-body somatostatin receptor PET scan was advised, which revealed a large expansile lesion, involving the left occipital bone including the clivus, and occipital condyle with erosion of mastoid and petrous part of the adjacent temporal bone. Brain MRI revealed a contrast-enhancing left skull base tumor involving the occipital condyle, suggestive of a meningioma or glomus tumor. The patient underwent a left retromastoid craniotomy and complete resection of the tumor.

Histopathology revealed fragments of neoplasm composed of oval-to-short fusiform cells arranged in sheets and fascicles within a vascularized stroma, containing thin-walled vessels and numerous scattered osteoclastic giant cells [Figure 3a]. Areas showing basophilic extracellular matrix were also identified [Figure 3b]. There were no sarcomatous changes. A diagnosis of PMTMCT was given.

On follow-up after 3 months of surgery, the patient's serum phosphorus level (2.3 mg/dL) and FGF-23 (150 RU/mL) levels had normalized, and her strength was improving.

#### Discussion

Impaired mineralization of osteoid matrix in mature bone leads to osteomalacia. FGF-23-secreting mesenchymal tumors and Fanconi's syndrome are acquired causes of osteomalacia; the former is referred as OO.<sup>[7]</sup> The tumor that secretes FGF-23 inhibits the renal reabsorption of phosphorus and downregulates 25-hydroxyvitamin

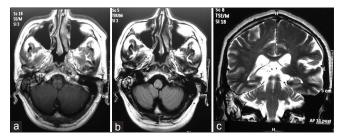


Figure 1: Case 1 (a) Axial T1-weighted, (b) Axial T2-weighted, and (c) coronal fluid-attenuated inversion recovery reveal a well-demarcated lobulated mass in the right temporal region causing bone erosion. It has an intracranial component and is hypointense on T1 and heterogeneously hyperintense on T2 and fluid-attenuated inversion recovery images

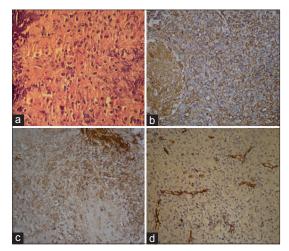


Figure 2: Photomicrograph of Case 1 shows the following: (a) tumor composed of relatively uniform short spindly cells embedded in hyalinized stroma with foci of "grungy" calcification (H and E, ×400); (b-d) tumor cells are diffusely positive for vimentin (×400), focally positive for smooth muscle actin (×400), and negative for CD34 (×200)

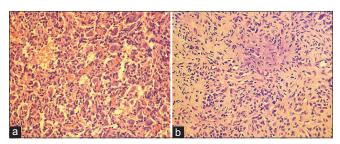


Figure 3: Photomicrograph of Case 2 shows the following: (a) numerous osteoclastic giant cells and a richly vascularized stroma (H and E, ×400); (b) extracellular basophilic matrix (H and E, ×400)

D-1a-hydroxylase.<sup>[1,8]</sup> Patients with OO have hypophosphatemia, normocalcemia, hyperphosphaturia, and increased alkaline phosphatase.<sup>[9]</sup> It is a paraneoplastic syndrome of renal phosphate wasting, leading to weakness, progressive muscle and bone pain, and recurrent fractures in adults.

PMT is usually located in the soft tissue, but the intra-osseous location is also known.<sup>[1]</sup> Occurrence in the extremities or appendicular skeleton is more common than in the trunk or axial skeleton.<sup>[1,2]</sup> Craniofacial sinuses can

be involved in 5% of the cases;<sup>[1]</sup> however, the involvement of the intracranial compartment and temporal–occipital bone is very rare. To the best of our knowledge, <10 cases of intracranial PMT and <5 cases of PMT arising in the temporal–occipital bone have been reported in the English literature.<sup>[2-6,10]</sup>

Histologically, it corresponds to a polymorphous group of neoplastic entities, the most common of which is the so-called "mixed connective tissue type."<sup>[1,9]</sup> Other histological types of PMTs are the osteoblastoma-like tumor, the nonossifying fibroma-like tumor, and the ossifying fibroblastoma-like tumor. Histological features of malignancy are observed in some cases.<sup>[1,9]</sup>

The best treatment for OO is complete removal of the tumor, but because of its unusual location and occult nature, correct diagnosis and resection are delayed for years.<sup>[8,11,12]</sup> This was indeed true for our patients, for whom it took 5 and 3 years, respectively, to find a primary lesion. In such cases, medical management becomes necessary. Medical management comprises phosphorus supplementation to replace the ongoing renal phosphorus loss and calcitriol to supplement insufficient renal production of 1,25-dihydroxy vitamin D. The dosing should be adjusted to improve symptoms, maintain fasting phosphorus in the low normal range, and maintain PTH in the normal range without inducing hypercalcemia or hypercalciuria. Close monitoring of serum calcium and phosphorus, urine calcium, renal function, serum alkaline phosphatase, and PTH is recommended to assess the safety and efficacy of therapy.

Some PMTs express somatostatin receptors that bind octreotide; this has provided the rationale for therapeutic trial of octreotide in patients with TIO and residual tumor. However, due to limited experience with octreotide treatment, it should be reserved for cases refractory to conventional medical treatment.

Thus, PMT should be suspected in older children or adults with hypophosphatemia and osteomalacia who lack a personal or family history of metabolic, renal, or malabsorptive diseases. A thorough workup including a history, physical examination, and biochemical evaluation, followed by radiological search for tumor in the extremities and head, should be done.<sup>[10]</sup> As these tumors are often small, slow-growing, and located in unexpected anatomical regions, imaging techniques such as MRI, computed tomography, or PET scan with particular attention to the brain are recommended.<sup>[2,12]</sup> Somatostatin receptor imaging has been recently proved to improve the detection of such tumors, based on the postulate that these tumors express somatostatin receptors.<sup>[10]</sup> Both meningioma and PMT should be considered as differentials if an extra-axial. well-circumscribed. contrast-enhancing tumor is encountered in such patients. Knowledge of this rare entity at uncommon sites is important to proactively identify,

treat, and prevent associated bony morbidities in affected patients.

#### **Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

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