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CASE REPORT

Phosphaturic Mesenchymal Tumor in the Maxillofacial Region: A Diagnostic Dilemma

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Abstract Oncogenic osteomalacia is a rare paraneoplastic syndrome and is associated with the presence of phosphaturic mesenchymal tumor (PMT) which results in renal phosphate wasting with hypophosphatemia. In total, 95% of cases reported in upper and lower extremities and in head and neck are a rare site for these tumors. Besides osteomalacia, the clinical presentation includes bone pain and multiple bone fractures. Only fewer cases of PMT are reported in the oral cavity. The presentation of this rare case in a young patient was palatal swelling mimicking like an abscess which was clinically and by advanced imaging evaluated and histopathological findings confirmed the rare presentation. Following the surgical excision, the serum level of FGF23 rapidly decreased, hypophosphatemia improved, and the clinical symptoms greatly improved. The result suggests that the overexpressed FGF23 primary tumor in the palate was the cause of osteomalacia which is a rare entity.

Keywords Tumor-induced osteomalacia · Oncogenic osteomalacia · Phosphaturic mesenchymal tumor · Hypophosphatemia

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Introduction

Oncogenic osteomalacia (OO) or tumor-induced osteomalacia (TIO) is a rare disorder which results in high levels of renal phosphate wasting leading to hypophosphatemia and osteomalacia [1]. Phosphaturic mesenchymal tumor (PMT) is a mesenchymal neoplasm associated with TIO. PMTs can arise in any soft or bone tissue and has an unpredictable biologic behavior, and the most common location involved is the extremities (95%) followed by maxillofacial sites (5%) [2]. In the head and neck region most of the cases involve the sinonasal tract, and other sites include the pharynx, maxilla, mandible, tongue, floor of mouth and posterior neck. An isolated case in temporomandibular joint was reported by Sandro et al. [3]. PMTs affect both the genders equally and occur most commonly in the fourth or fifth decade, and younger population have also been documented in the literature.

In this report, we present a rare case of PMT seen in the palatal mucosa.

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Case Report

In total, 32-year male patient was referred to Craniofacial unit with a painless swelling in the posterior third of the right hard palate since a year. History revealed attempted root canal treatment of the maxillary molar by the dentist. Patient was apparently alright 2 years back when he started developing severe muscle weakness and pain in the upper and lower extremities which restricted his physical activities. On clinical examination, the patient presented with difficulty in ambulation with severe pain in the upper and lower limbs and a history of pelvic fracture following a simple fall and was managed conservatively. On intraoral examination, a nonulcerated, smooth surface swelling was noted over the right posterolateral aspect of hard palate extending from maxillary right premolar to third molar region anteroposteriorly and mediolaterally from the gingival aspect of the teeth up to the midpalatine raphe (Fig. 1). The swelling was fluctuant, nontender, soft and approximately 3 cm in diameter. There were no signs of odontogenic infection. The differential diagnosis was thought of periapical abscess, odontogenic cyst, salivary gland neoplasm like adenoid cystic carcinoma and mucoepidermoid carcinoma and tumors like schwannoma, odontogenic myxoma and hemangiopericytoma. History revealed that the patient was under the care of endocrinologist and diagnosed with hypophosphatemia and was treated for the same since the 2 years conservatively with calcium and phosphate supplements. A diagnostic F-FDG (f-18 fluorodeoxyglucose) PET scan was performed which revealed an isolated focus of hypermetabolism with high uptake of F-FDG in the right palate. Fine-needle aspiration cytology was performed which appeared swelling was vascular. Computed tomography of the face was performed which revealed a well-defined oval-shaped intra-oral soft tissue density in the submucosal plane of hard palate showing intense postcontrast enhancement (Fig. 2). Digital subtraction angiography (DSA) was not significant without any major feeders to the lesion. Routine laboratory investigations revealed low levels of phosphorus and 1,25 dihydroxyvitamin D, normal levels of serum calcium and parathyroid hormone and high levels of alkaline phosphatase. In view of high vascularity of the lesion, patient was prepared for excisional biopsy surgery under general anesthesia with exposure of the external carotid artery for vessel control during excision. The planned excision was with a margin of 1 cm by staying away from the lesion. An incision was placed around the swelling in the midpalatine raphe extending posteriorly and the lesion was lifted by raising a full thickness mucoperiosteal flap. The lesion was excised in toto (Fig. 1b). The palatal raw area was reconstructed using split thickness skin graft following which a bolster dressing was placed. The surgical site healing was uneventful (Fig. 1c). The histopathology of excised lesion revealed sheets of round to ovoid cells having round nucleus with dispersed chromatin and indistinct cell border intermixed with numerous hemangiopericytoma like blood vessels (Fig. 3a) and scattered osteoclast like multinucleated giant cells (Fig. 3b). The phosphorus levels were normal postoperatively with excellent recovery in 1 month

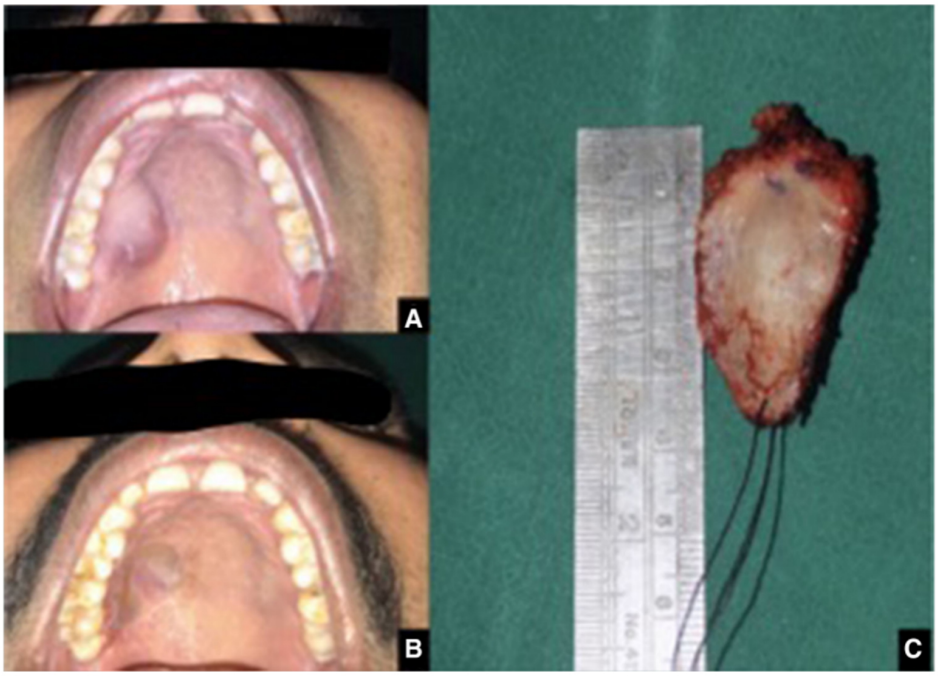

Fig. 1 **a** Preoperative intraoral swelling. **b** Excised lesion. **c** Postoperative intraoral healing

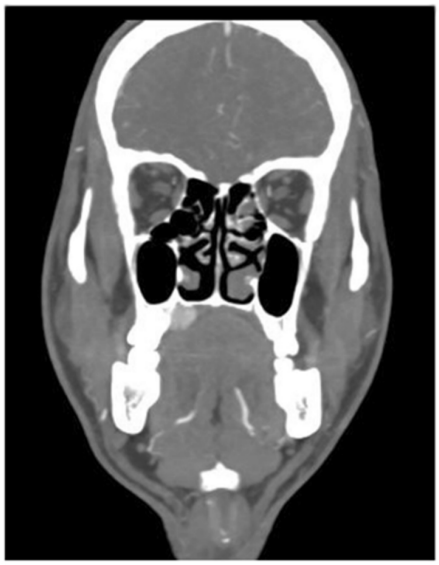

Fig. 2 CT coronal section showing lesion in the right side of palate with no erosion of bone

(Table 1). At 6-month follow-up, patient had no signs of recurrence and the muscle weakness had decreased drastically and the patient was able to perform his normal daily activities.

Discussion

PMT is a rare neoplasm, most commonly occurring in the extremities. It is said to be a strange tumor in strange places [4]. This tumor was first described by McCance in 1947, and a relationship between osteomalacia and tumor was established in 1959 by Prader [2]. Literature review suggests of only few cases of PMT presenting intraorally [2, 5].

TIO is a paraneoplastic syndrome caused by factors known as phosphatonins. There is multiple phosphatonin, but for this condition there is convincing evidence of presence of FGF23. Clinical presentation is commonly with bone pain, pathologic fractures, gait disturbances, severe muscle weakness and osteopenia [1]. Long-term manifestations such as loss of height, delayed growth and skeletal deformity have also been reported. The classical diagnostic criteria for PMT are hypophosphatemia, hyperphosphaturia, low levels of 1,25 dihydroxyvitamin D, normal levels of serum calcium and parathyroid hormone (PTH) [6, 7]. The overexpression of ectopic hormone like fibroblast growth factor-23 (FGF-23) also known as phosphatonin is secreted by the PMT [8]. These high levels of the hormone lead to phosphate diuresis and inhibit renal phosphate reabsorption which causes hypophosphatemia. These patients will give a long-standing history of symptoms that are related to osteomalacia. There are high chances of delay in diagnosis of the tumor. Patients affected with oncogenic osteomalacia have a clinically

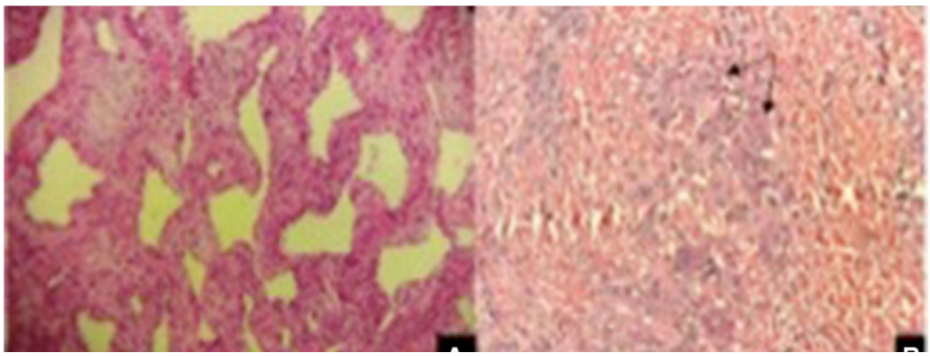

Fig. 3 Photomicrographs showing **a** sheets of round to ovoid cells having round nucleus with dispersed chromatin intermixed with numerous hemangiopericytoma like blood vessels. **b** Scattered osteoclast like multinucleated giant cells (arrow) and hemorrhage

Table 1 Biochemical values of the patient

Biochemical values	Calcium	Phosphate	Parathyroid hormone PTH	Vitamin D	Serum alkaline phosphatase
Normal values	9.3–9.9 mg/dL	2.5–4.5 mg/dL	10–55 pg/mL	40–80 ng/mL	44–147 IU/L
Pre-op	9.5 mg/dL	1.2 mg/dL	32 pg/mL	28 ng/mL	164 IU/L
Immediate post-op	9.4 mg/dL	2.6 mg/dL	34 pg/mL	42 ng/mL	138 IU/L
Follow-up	9.6 mg/dL	3.1 mg/dL	39 pg/mL	48 ng/mL	126 IU/L

palpable primary tumor site. FGF23-mediated disorder should be considered based on the laboratory findings such as hypophosphatemia, hyperphosphaturia and inappropriate normal or low D3 levels. In addition to CT and magnetic resonance imaging (MRI), bone scintigraphy, positron emission tomography (PET) scanning and FDG PET/CT scanning have been used to locate PMTs. Literature suggests that the mesenchymal tumor associated with oncogenic osteomalacia exhibited high F-FDG uptake and was easily detected by PET scans [8].

In two cohort studies done by R Shah et al. wherein TOI was reported in seven patients who were from a single center. In the first study the sites reported were paranasal sinus, intracranial and maxilla. In the second cohort study with systemic review done, 163 patients were identified with a mean age of 46 +—14 years. A PMT mixed epithelial and connective tissue variants were described in 15 patients [5].

Histopathological hematoxylin and eosin stain 10 × magnification of the excised lesion showed round- to spindle-shaped cells intermixed with numerous hemangiopericytoma like blood vessels. The tumor cells have round nucleus with dispersed chromatin and indistinct cell border. Few tumor cells may exhibit nuclear pleomorphism and mitotic figures. The osteoclast like multinucleated giant cells is frequently seen. The tumor stroma can show chondroid or chondromyxoid matrix with "grungy" calcifications. The tumor is usually seen invading into surrounding muscles and adipose tissue.

Complete resection is the treatment of choice and drastically improves the biochemical abnormalities in days or weeks postsurgery (Table 1).

PMT should always be considered in a patient with hypophosphatemia, bone pain and multiple fractures.

Conclusion

PMT is a rare mesenchymal tumor, and its occurrence in palate is not reported. Due to its rare occurrence and nonspecific clinical presentation, it is most commonly missed.

A comprehensive evaluation of systemic, laboratory and radiographic findings in combination with microscopic assessment is crucial for a definitive diagnosis. Diagnosis and management challenges warrant a multidisciplinary team including endocrinologist, maxillofacial surgeon, radiologist, nuclear physicist and pathologist.

Compliance with Ethical Standards

Conflict of interest We the authors have no conflict of interest.

Patient Consent The patient has authorized the publication of the case report and has given his consent for the same.

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