

Phosphaturic Mesenchymal Tumour Involving Nasal Sinus: Case Report with Literature Review

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Abstract

PMT is an unusual mesenchymal tumor of uncertain clinical behavior. We present a case of PMT involving nasal sinus, presenting with uncontrolled epistaxis. We discuss the clinical features, imaging studies and histologic diagnosis with prognosis and treatment options.

Keywords: Phosphaturic Mesenchymal Tumor; Oncogenic Osteomalacia; Tumor Induced Osteomalacia; Fibroblast Growth Factor; Hemangiopericytoma

Abbreviations

PMT: Phosphaturic Mesenchymal Tumor; OO: Oncogenic Osteomalacia, TIO: Tumor Induced Osteomalacia; FGF-23: Fibroblast Growth Factor

Introduction and Case Report

Our patient is a 65 years old woman who was first seen in the ER because of right sided nosebleed of one-week duration. Blood work up was unremarkable with a hemoglobin of 13.6 g/dL. A balloon pack was placed in the right nostril. Because of continued and uncontrolled bleeding, an ENT consult was obtained and a Merocel nasal pack was placed after which the bleeding stopped. A subsequent CT of nasal sinuses showed benign polyps. Her CBC, PT, PTT and platelet counts were normal. Her serum alkaline phosphatase was 64 IU/L (normal 42 - 121 IU/L). Calcium was 8 mg/dl (normal 8.6 - 10 mg/dl). She was later admitted into the hospital for an endoscopic examination and cauterization of bleeding points in her nose. On examination, no polyps or bleeding were noted on the left side, while several polyps with erosions were observed on the right maxillary sinus involving the septum and removed. The procedure was stopped due to continued bleeding despite cauterization of the vessels. Epinephrine pack was applied, and minimal oozing was noted after its removal. Clinical concern for a vascular tumor was high on the list of diagnoses due to excessive bleeding and the specimen was sent to Pathology for evaluation.

On histologic examination, multiple polypoidal lesions with frequent erosions were noted (Figure 1). Focal areas in the stroma showed sheets and groups of spindle cells with capillary network. Several hemosiderophages and scattered multinucleated giant cells were noted. TO multinucleated giant cells were noted (Figure 2). In addition, characteristic grungy calcification was noted (Figure 3). The spindle

cells were positive for ERG, Vimentin while negative with all other antibodies tested against including S100, CD34, CD117, CK and SMA. A working diagnosis of vascular tumor was rendered, and tissue sent for FGF23 mRNA by in-situ hybridization which was diffusely positive (Figure 4 and 5). A diagnosis of PMT was made based on morphology and positive FGF23 staining pattern.

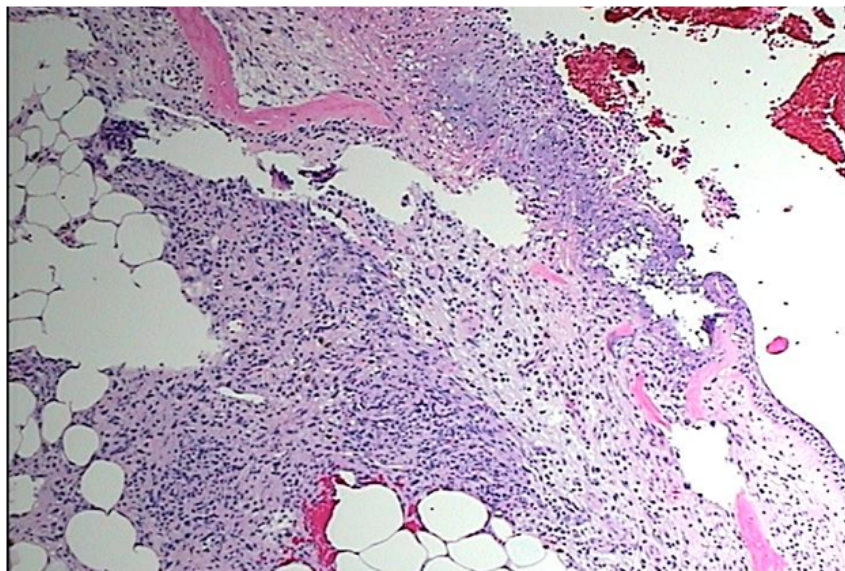


Figure 1: Low magnification (H&E) showing erosion with spindle cell lesion underneath.

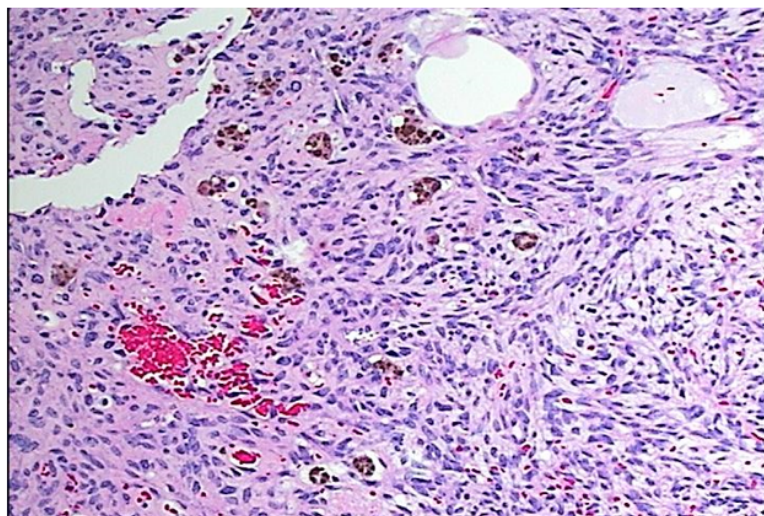


Figure 2: Intermediate magnification (H&E) showing numerous hemosiderophages and rare giant cells.

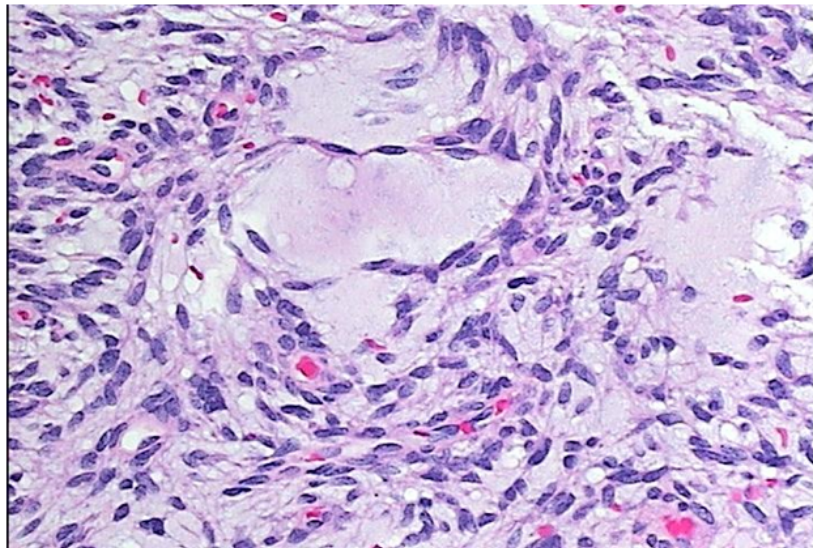


Figure 3: High magnification (H&E) showing stroma with early grungy-type calcification.

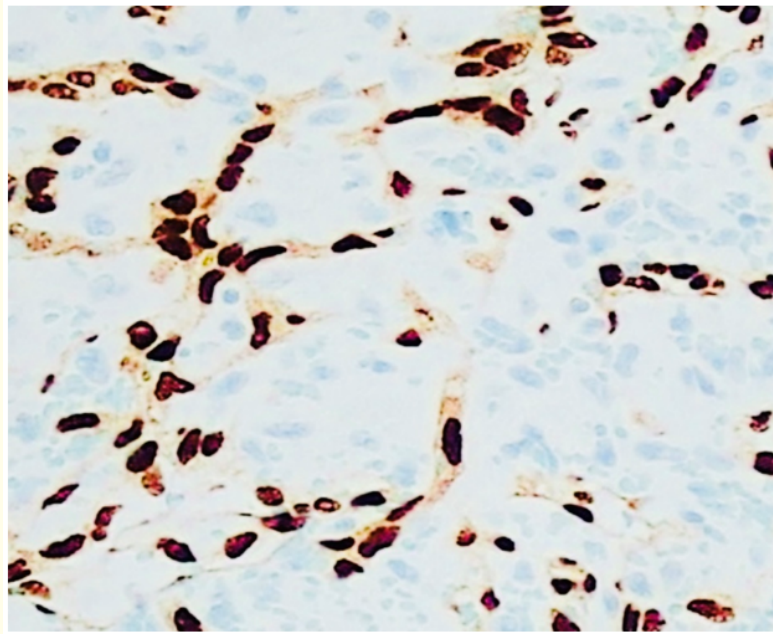


Figure 4: High magnification (IHC) showing ERG positive tumor cells.

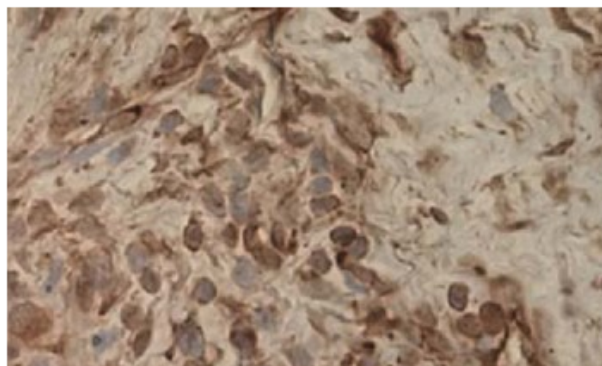


Figure 5: High magnification (in-situ hybridization) showing FGF-23 positive cells.

Discussion

PMT is a mesenchymal tumor that occurs in middle aged adults with roughly equal gender distribution. Rare examples of PMT have been reported in infants and children. Majority of these tumors (~ 95%) arise in soft tissues of extremities, bone. Head and Neck region including sinuses are involved in ~ 5% of the cases. On microscopic examination, these tumors are typically bland with spindle to stellate shaped cells embedded in a smudgy matrix. Grungy calcifications and hemangiopericytoma like capillary network are common. Though osteomalacia is present in most patients at the time of clinical presentation, this is not required for diagnosis. These tumors produce a phosphaturic factor, a peptide like protein called phosphatonin that causes decreased proximal tubular reabsorption of phosphates. Fibroblast Growth Factor 23, a bone derived hormone is the key phosphatonin and plays an important role in phosphate homeostasis. PMTs are known to produce this factor with resultant abnormalities in phosphate metabolism. Mutations in FGF-23 render the protein resistant to proteolytic deactivation leading to increased activation. Tumor Induced Osteomalacia (TIO) is the most common cause of hypophosphatemic phosphaturia in adults, while vitamin D deficiency as a result of limited sun exposure or inadequate dietary intake is the main cause of Rickets or childhood osteomalacia. TIO occurs due to phosphate loss in urine, hypophosphatemia and concomitant decrease in vitamin D3 levels due to inhibition of alpha 1 hydroxylase. This in turn leads to mobilization of calcium and phosphates from bones and reduction of osteoblastic activity and widespread osteomalacia. Hypophosphatemia can be acute or chronic and symptoms are oftentimes non-specific including general weakness, malaise, chronic fatigue and fractures, hence delay in making a correct diagnosis.

Prader, *et al.* [1] was the first to describe association between neoplasm and osteomalacia in a child with rickets in 1959, However, Weidner and Santa Cruz [2] in 1987 first coined the term 'Phosphaturic Mesenchymal Tumor (PMT) mixed connective tissue type' for a group of mesenchymal tumors occurring in the soft tissue and bone. The current terminology recommended by WHO is simply Phosphaturic Mesenchymal Tumor [3]. In their landmark study, Weidner and Santa Cruz reported 17 mesenchymal tumors causing secondary osteomalacia or rickets. They grouped these tumors into 4 categories based on the morphology. Most of the tumors (11 of 17) exhibited a characteristic morphology of prominent vascular network with osteoclast-like giant cell component, microcystic changes with areas of dystrophic calcification. Of the 11 tumors, 10 occurred in soft tissues and 1 occurred in bone. The one tumor which occurred in bone recurred locally and showed metastases in lung. The other 6 out of 17 tumors comprised the remaining three groups, and all occurred in bone and demonstrated a benign clinical course on long term follow-up. Folpe, *et al.* [4] and Bahrami, *et al.* [5] in their comprehensive analysis of a large series of cases, showed that most cases of TIO can be attributed to PMT. In their study, Folpe, *et al.* observed Osteogenic Osteomalacia in 29 of 32 patients with a histologic diagnosis of PMT in 15 cases. The others were hemangiopericytoma (3), osteosarcoma

(3), giant cell tumor (2) and others (9). FGF-23 was observed in 17 of 21 cases by IHC and by RT-PCR in 2 cases. Most patients (84%) were alive with no evidence of disease in the follow-up period of up to 348 months. Carter JM., *et al.* [6] showed RNA scope CISH for FGF-23 mRNA to be highly sensitive, detected in 22/23 patients (96%) and specific (100%) for the diagnosis of PMT. Alternatively, measurement of serum FGF-23 levels can aid in the diagnosis and follow-up of patients. Deep., *et al.* [7] comprehensively reviewed literature on PMT from 1970-2013 and found 33 individual case reports of head and neck PMTs. Of these, ~50% were found in sinonasal location and the other half in areas of head and neck including mandible, floor of the mouth, pharynx, larynx, thyroid and temporal bone. TIO is observed in 28 out of 33 patients in their study. Differential diagnosis for PMT includes angiosarcoma, solitary fibrous tumor, giant cell tumors and rarely osteosarcoma.

Conclusion

PMTs are benign tumors which can be cured including resolution of TIO with surgical resection with clear margins. Incomplete resection can result in local recurrences and very rarely, these tumors can metastasize to distant sites. Awareness of this entity with accurate diagnosis is crucial to mitigate bone loss and fractures. Our patient underwent successful endoscopic resection with clear margins and is well and alive at 36-month follow-up. She did not have clinical or radiologic manifestations of osteomalacia at the time of her initial presentation and this could be due to early detection of her tumor.

Conflict of Interest

None.

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