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## Case Study

### Oncogenous Osteomalacia

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#### Abstract

27 year old male presented to us with the chief complaints of progressive difficulty in walking and proximal myopathy of two years duration. He had been having back pain of six years duration and progressive proximal muscle weakness for past 3 years. On examination he was thin built with a BMI of 19.5kg/m<sup>2</sup> and no palpable soft tissue swellings. Skeletal examination revealed deformity in the chest in the form of pectus carinatum and kyphoscoliosis. He also had deformities in the legs with extreme tenderness in the bones on palpation. Rest of the systemic examination was normal except for proximal myopathy. On biochemical investigations he was found to have a fasting corrected calcium of 8.2 mg%, phosphorous of 1.2 mg%. Alkaline phosphatase was 311 U/L with a vitamin D (25 OH) of 29.38 ng/ml. PTH was 155 pg/ml. TmP/GFR estimated was 1.2 which is suggestive of phosphaturia. MRI of the distal femur showed a relatively well-defined iso to hypointense on T1, iso to hyperintense on T2 lesion of the lateral aspect of the distal metaphysis of the right femur with very thin hypointense peripheral rim causing thinning and areas of the loss of the cortical outline which was suggestive of a vascular tumour. Subsequently the lesion was excised and the biopsy confirmed the same. Following surgery the phosphate requirement decreased and was subsequently normalized after 6 months without any supplementation. His symptoms also improved and was doing well

#### Case Report

27 year old male presented to us with the chief complaints of progressive difficulty in walking and proximal myopathy of two years duration. He had been having back pain of six years duration and progressive proximal muscle weakness for past 3 years. Currently he was able to walk with support only. He also had bone pain and a history of fracture 6 years back with trivial trauma. He noticed weight loss of 10 kgs over past 2 years. His dietary habits were good with poor sunlight exposure past 2 years because of the restricted mobility. There was no history of polyuria, renal stones, epistaxis, steatorrhoea or chronic diarrhoea. There was no significant past medical history. None of the family members had history of similar illness or dental abscess.

On examination he was thin built with a BMI of 19.5kg/m<sup>2</sup> and no palpable soft tissue swellings. Skeletal examination revealed deformity in the chest in the form of pectus carinatum and kyphoscoliosis. He also had deformities in the legs with extreme tenderness in the bones on palpation. Rest of the systemic examination was normal except for proximal myopathy.

On biochemical investigations he was found to have a fasting corrected calcium of 8.2 mg%, phosphorous of 1.2 mg%. Alkaline phosphatase was 311 U/L with a vitamin D (25 OH) of 29.38 ng/ml. PTH was 155 pg/ml. TmP/GFR estimated was 1.2 which is suggestive of phosphaturia. Serum electrolytes were normal showing no acidosis and the Creatinine estimated was normal. Xrays revealed multiple Loosers zones in Femur, tibia and pelvis. Ultrasound of the abdomen was normal. Since the possibility of the Tumour induced osteomalacia was thought of, a Blood pool scintigraphy done by in vivo labeling of RBC with Tc99m pertechnetate after pretinning with stannous pyrophosphate showed an abnormal focal tracer accumulation in the right distal thigh in the lateral aspect suggestive of vascular neoplasm shown in the image below.

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Subsequently the lesion was excised and the biopsy confirmed the same. Histologically, the tumour was composed of interlacing fascicles of spindle shaped cells with oval to elongated, mildly pleomorphic nuclei with coarse chromatin and occasional mitotic figures. Scattered amongst these were osteoclast like giant cells. There was prominence of the vasculature including thick walled, hyalinised and occasional hemangiopericytomatous blood vessels. The above histology was suggestive of phosphaturic mesenchymal tumour (non ossifying fibroma like variant).

Following surgery the phosphate requirement decreased and was subsequently normalized after 6 months without any supplementation. His symptoms also improved and was doing well.

### **Discussion**

Oncogenic osteomalacia is an unusual syndrome that is characterized by multiple biochemical abnormalities, such as hypophosphatemia, hyperphosphaturia, and low levels of plasma 1,25-dihydroxyvitamin D. These abnormalities produce osteomalacia in adults and rickets in children, which clinically manifest as muscle weakness, bone pain, and multiple pathologic fractures. In children, it can also lead to skeletal deformities, growth retardation, and gait problems. Tumors producing this syndrome secrete FGF-23 a substance that inhibits the renal tubular reabsorption of phosphorous and inhibits 1 alpha hydroxylase which produces a cascade of biochemical abnormalities. It is interesting that all biochemical and clinical features revert to normal when the tumor is removed.<sup>1</sup>

The majority of these tumors are located in the extremities (skin, muscles, bones) or around the head (paranasal sinuses), but they may occur in almost any part of the body. These tumors are slow growing and often remain hidden or undetected until clinical features reach a fairly advanced stage. In one review of head and neck tumors, the diagnosis of these tumors lasted a mean of 4.7 years from the onset of osteomalacia.<sup>2</sup> Often the clinical presentation mimics X-linked hypophosphatemia (XLH) or hereditary autosomal dominant

hypophosphatemic rickets (ADHR). Excessive paraneoplastic production of phosphatonin(FGF-23) is thought to be involved in the etiology of tumor-induced osteomalacia, whereas impaired degradation and processing of phosphatonin due to endopeptidase mutations (PHEX gene: phosphate-regulating gene with homologies to endopeptidases on the X chromosome) is thought to cause the typical findings in XLH. The fibroblast growth factor (FGF)-23 gene is mutated with ADHR. Both XLH and ADHR typically present in childhood, although ADHR can present with variable or delayed age of onset.

Tumors that cause TIO are often small, slow-growing, vascular, and benign; they are associated with a variety of histologic types and are commonly mesenchymal in origin.<sup>3</sup> Hemangiopericytoma is the most dominant histologic diagnosis noted in TIO. However, malignant tumors have occasionally been reported. Based on their histologic features, they have been sub-divided into 4 types: i) phosphaturic mesenchymal tumor, mixed connective tissue type (PMTMCT); ii) osteoblastoma-like tumors; iii) ossifying fibroma-like tumors; and iv) nonossifying fibroma-like tumors<sup>4</sup>. Hemangiopericytoma is the subtype of PMTMCT that comprises approximately 70% to 80% of all tumors associated with TIO<sup>5</sup>. Fibroblast growth factor 23 belongs to the mesenchymal origin family, and the measurement of serum FGF-23 has been found to be of considerable importance in facilitating early diagnosis.

An important aspect of the management is to identify the tumour and often the resection of the tumour is curative. Nuclear scintigraphy has emerged as a very useful and economical tool to detect and determine the site of these tumors. Once the site is identified, regional CT and/or MRI are performed to further characterize the tumor. If the tumour is not localized the patients need to be started on phosphate along with <sup>1</sup>, 25 OH vitamin D which will control the symptoms and improve the weakness. But it is important to keep on surveillance to localize the tumour as there can be lag period of many years. Once identified surgical resection is curative.

### **Conclusion:**

Unexplained generalized bone pain, proximal weakness and fractures must be tested for calcium and phosphate homeostasis. Detection of renal phosphate wasting indicates the need for further evaluation for possible hereditary and acquired causes. Blood pool scintigraphy can localize the tumour induced osteomalacia which can be confirmed by the CT/MRI. Surgery is potentially curative.

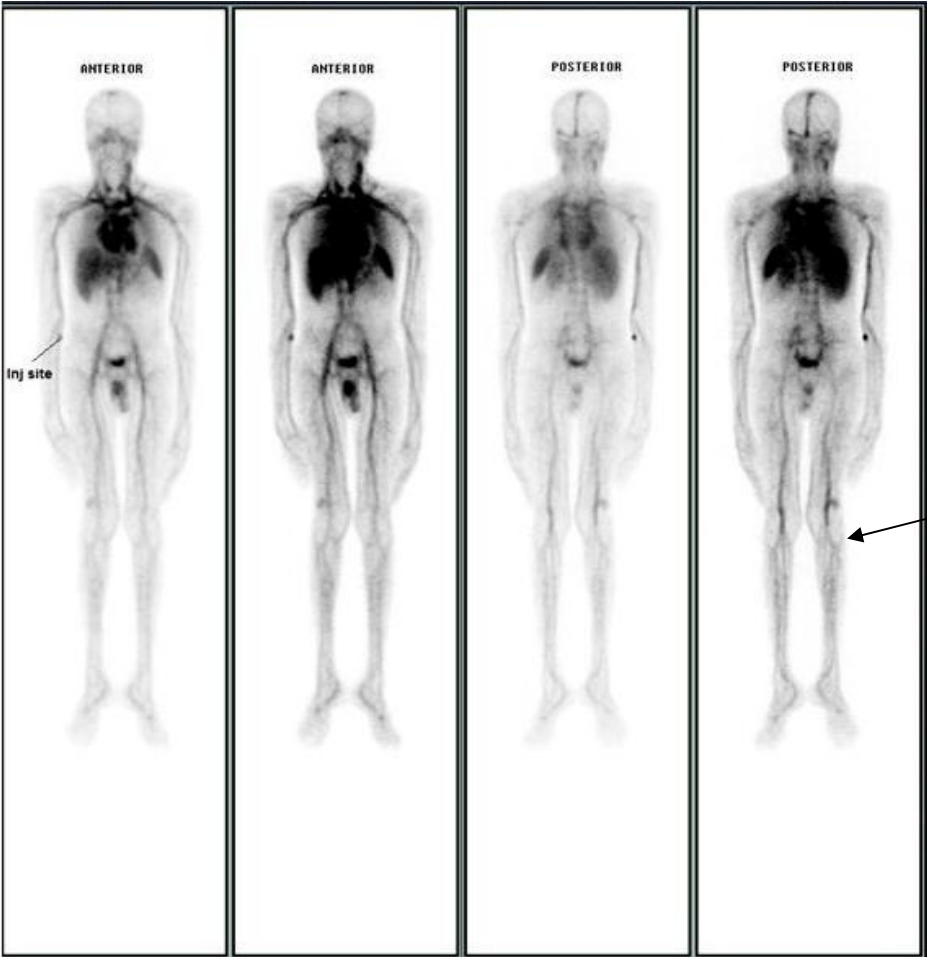
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**Fig. 1: MRI of the distal femur:**

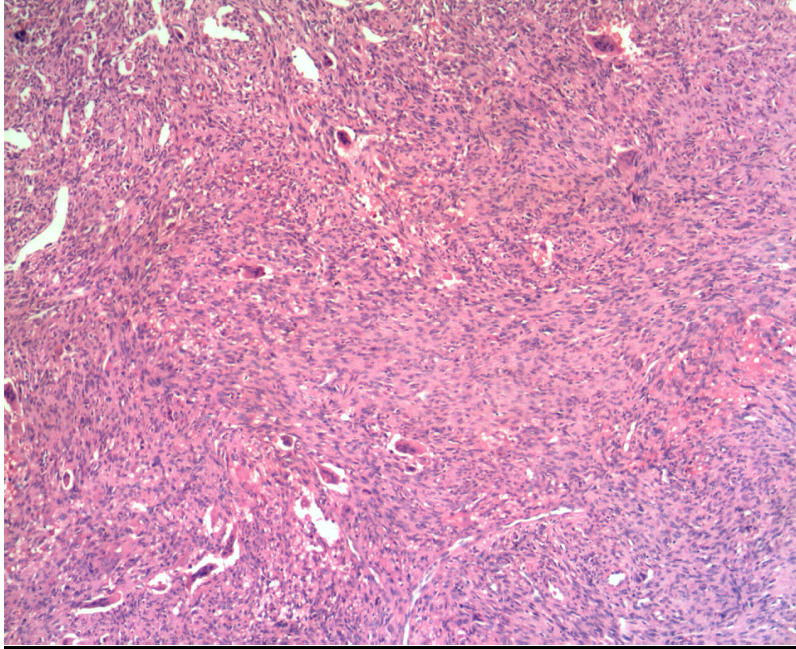


**Fig. 2: Blood Pool Scan:**



**Histopathology:**

**Fig. 3: "H&E section, 100X magnification"**



Interlacing fascicles of spindle shaped cells with scattered osteoclast like giant cells and occasional hemangiopericytomatous blood vessels.