

Case Report

Oncogenic osteomalacia secondary to hemangiopericytoma: a case report

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ABSTRACT

We are going to present a case of hypo-phosphatemic rickets secondary to phosphaturic mesenchymal tumour who came with complaints of proximal muscle weakness which limited his effort tolerance and activities of daily life like standing from squatting position and rib pain. His FGF-23 levels were very high above normal levels and PET CT revealed a well-defined enhancing lesion abutting femoral neurovascular bundle. After consultation with endocrinologist, we have done complete excision of the mass. Post-surgery all symptoms were relieved, proximal muscle strength improved gradually and serum levels of phosphorus, ALP and FGF-23 came back to normal.

Keywords: Fibroblast growth factor-23, Phosphaturic mesenchymal tumour, Oncogenic osteomalacia

INTRODUCTION

One of the rare paraneoplastic syndromes of osteomalacia is oncogenic osteomalacia (OO) or tumor induced osteomalacia (TIO) where there is phosphate depletion and abnormal vitamin metabolism caused due to small endocrine tumor that secretes phosphaturic hormone, fibroblast growth factor.¹ Phosphaturic mesenchymal tumour is very uncommon and is very difficult to diagnose. Usually, it is misdiagnosed as other mesenchymal tumour due to its heterogeneity.¹ There is inappropriate FGF-23 secretion which causes low phosphate and 1, 25-dihydroxyvitamin D levels.^{2,3}

Osteomalacia (mollities ossium) is a metabolic bone disease which results from inadequate mineralization of osteoid in mature bone in adults. Osteomalacia is a rare inborn error of metabolism. OO is a rare type of osteomalacia in which there is systemic demineralization of bone. Common symptoms of OO are bony pain, muscle wasting and fractures.³ Metabolically there will be renal phosphate wasting, hypophosphatemia, decreased serum-

1, 25 di-hydroxyvitamin levels and resistance to vitamin D supplementation.

TIO like syndrome can also be associated with some other diseases like prostate cancer, hematologic malignancies, neurofibromatosis, epidermal nevus syndrome, and polyostotic fibrous dysplasia of bone.⁴⁻⁶ This disease was first described by Dr. Rober McCane, he observed patient presenting with pain, weakness and abnormal gait with low phosphate levels. He tried to treat patient with high dose of vitamin D but did not succeed. The symptoms were cured by resection of tumor.

OO had association with syndromes such as neurofibromatosis and McCune-Albright syndrome and in patient with carcinomas. It has been reported that OO associated with mesenchymal tumour over expresses FGF-23. This protein inhibits renal tubular epithelial phosphate transport and this is thought to be the mechanism for most cases of OO.

Weidner and Santa Cruz coined the term "phosphaturic mesenchymal tumour, mixed connective tissue variant"

(PMTMCT). Histologically PMTMCT is a mixture of spindle cells, osteoclast like giant cells, prominent blood vessels, cartilage like matrix and metaplastic bone.

CASE REPORT

A 38 years old male presented to neuro-physician with complaint of difficulty in walking, weakness in bilateral lower limb left more than right with waddling gait and pain in ribs. All the symptoms were insidious in onset, gradually progressive limiting his daily routine activities. Patient also complained of difficulty in standing from squatting position and breathlessness after waking for 50-100 meters. Nerve conduction study was within normal limits. Laboratory parameters were Sr. calcium- 9.47 mg/dl, Sr. phosphorus-1.48 IU/L, alkaline phosphatase-175.3 IU/L. Patient was treated symptomatically with phosphorus supplements but he was not relieved rather his symptoms progressed. Patient was then referred to us. On further evaluation we have noticed Sr. phosphorus-1.46 mg% (value) and 1, 25-dihydroxyvitamin value-14.08 ng/ml and was diagnosed to have osteomalacia. X ray femur showed losers zone so patient was primarily diagnosed as hypo-phosphatemic rickets and started on oral calcium and vit D supplements. Symptoms of patient increased in intensity even after the treatment which pinned towards an endocrine pathology.

Endocrinologist's opinion was taken who suggested to get FGF-23 level checked. FGF-23 levels came out to be very high 1117.6 RU/ml (Normal value: 0-150 RU/ml).

PET scan was done which further revealed well defined enhancing lesion involving medial compartment of left upper thigh abutting femoral vein suggestive of hemangiopericytoma.

With this PET CT findings, we subjected patient for excision of the mass.

Intraoperatively it was found that tumour was very vascular and attached to deep femoral vein which was excised in toto and sample was sent for histopathological examination.

Histologically consistent with phosphaturic mesenchymal tumour.

On good successive follow up all features suggestive of mesenchymal and vascular tumor with low grade likely to be associated with hypo-phosphatemic rickets IHC was also done which was positive for S-100P and KL-67 and diagnosed as benign spindle cells tumor lab parameters including FGF-23 levels came within normal limits at the end of 3 weeks and patient was declared free from hypo-phosphatemic rickets. Patient is now symptom free and resumed his all-daily activities. (FGF-23-59.3 RU/L, serum phosphorus-5.60 mg%, alkaline phosphatase-137.2 mg%. Patient is not on phosphorus supplements).

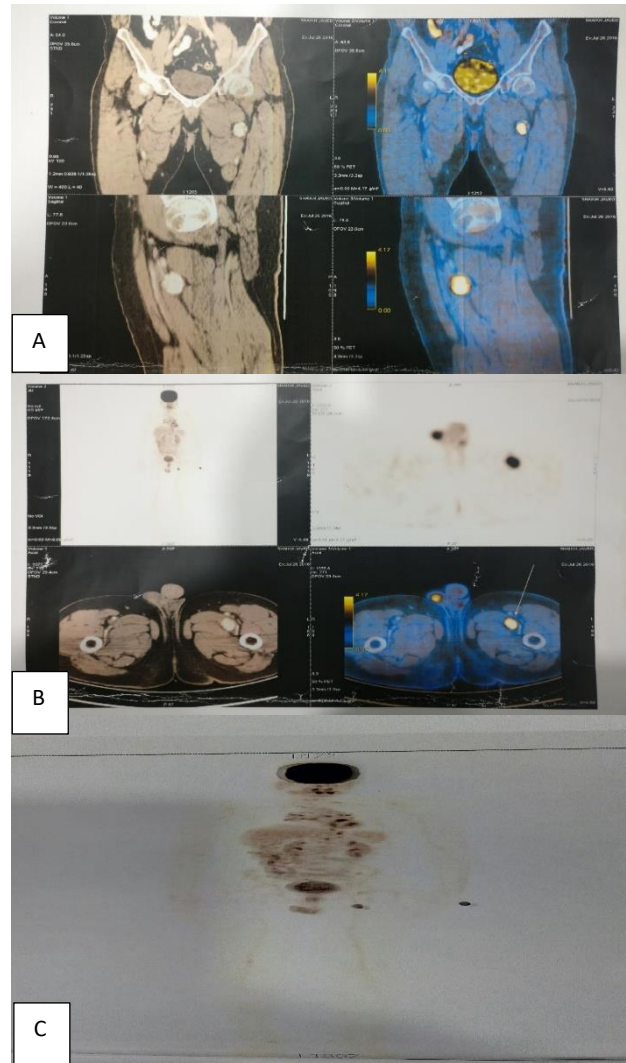


Figure 1 (A-C): MRI coronal image showing lesion, PET scan and MRI showing lesion in left thigh, and PET scan of whole body.

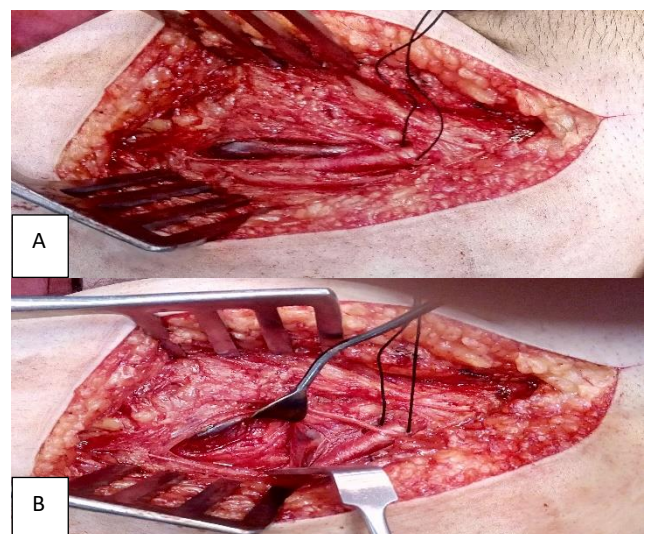


Figure 2 (A and B): Exposure of femoral vessels and lesion abutting femoral vein.

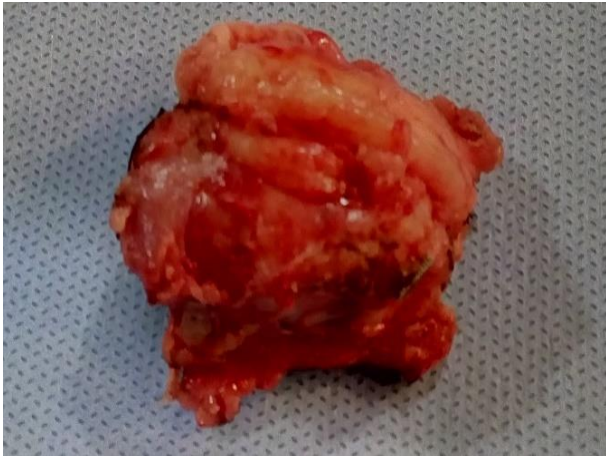


Figure 3: Excised lesion.

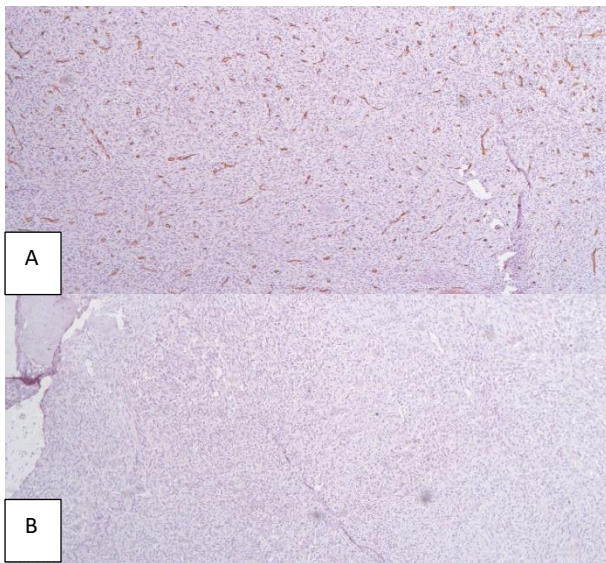


Figure 4 (A and B): CD 34 negative and desmin negative.

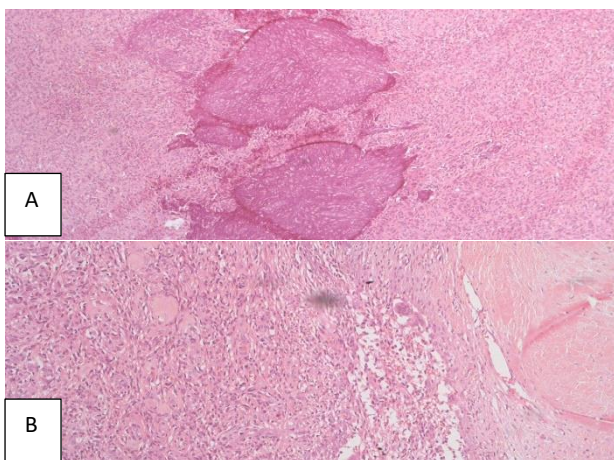


Figure 5 (A and B): Low power field-vascular and vascular components of mesenchymal elements endothelial spindle cell proliferation.

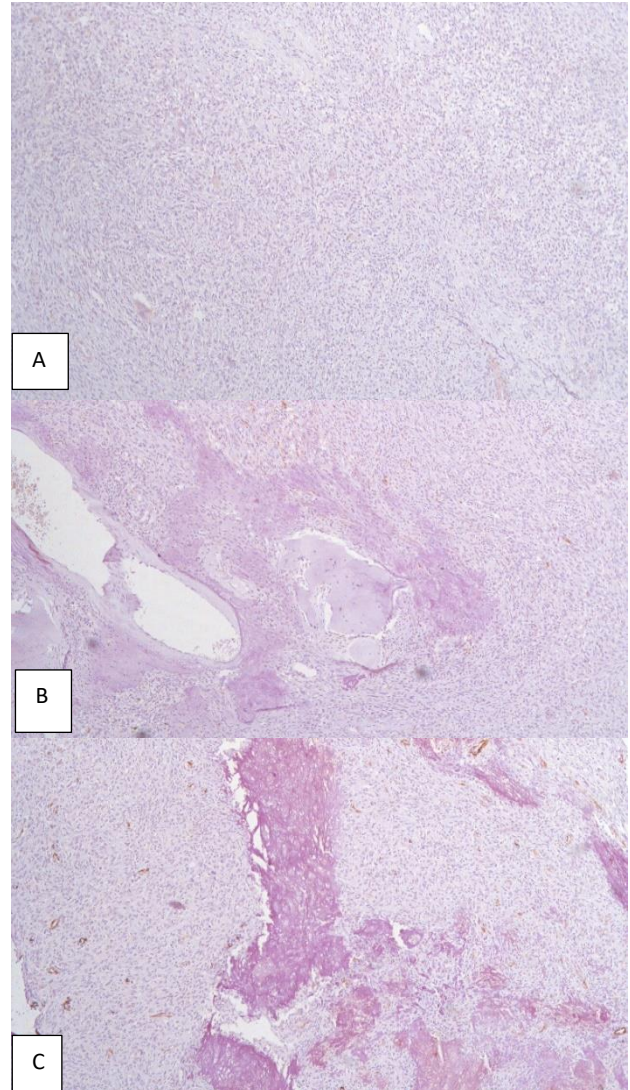


Figure 6 (A-C): KI-67 positive, <01%, s-100 p occasional cells positive and smooth muscle actin negative.

DISCUSSION

Tumour induced osteomalacia is a rare paraneoplastic syndrome with features of hypophosphatemia, myopathy, bone pain and fractures TIO is an acquired form of hypophosphatemia.

Ratio among male and female is 1:1. This disease presents usually at 4th and 5th decade of life. Prevalence of TIO is not known but till now 300 cases have been reported.

Almost all body regions are potentially affected by TIO. TIO presented with features ranging from weakness, difficulty in walking, loss of height, pathologic fractures in femur, vertebra, rounds pseudo-fractures of pubic rami and pelvic deformity. Suspicion of TIO arises when there is hypophosphatemia with hyper-phosphaturia in non-azotemic adult in absence of acidosis. Increased level of FGF-23 produced by the tumor, there is inhibition of

tubular reabsorption of phosphate which leads to hyperphosphaturia in TIO.

Meyer et al and Nebitt et al demonstrated circulating factor that could be responsible in sets of experiments over nice. Miyauchi et al supported this by transplanting human tumor in nude mice which causes hypophosphatemia.⁷ There is increase in vessel size and vascular pattern which leads to increase in microvasculature in these tumors.¹ Differential diagnosis for these tumours are Hemangiopericytoma, hemangioma, sarcoma, ossifying fibroma, granuloma, giant cell tumors and osteoblastoma.^{1,2} Osteocytes releases FGF-23 which is a peptide and it inhibits Na-Pi-11 transporter in intestine and kidneys leading to hypophosphaturia FGF-23 directly inhibits 1 α hydroxylase expression which in turn inhibits activation of 25 hydroxyvitamin D to 1, 25-dihydroxyvitamin D. Decreases level of 1, 25-dihydroxyvitamin D leads to decreased intestinal absorption of phosphate. In the above-mentioned patient very high level of FGF-23 confirmed TIO and patient very high level of FGF-23 confirmed TIO and PET scan localized the tumor. F-18 Fluorodeoxyglucose positron emission tomography with computed tomography is most sensitive for localizing TIO tumors.⁸

Mesenchymal tumour producing FGF-23 are generally benign and very small and difficult to identify. Various imaging modalities have been enjoyed to localize FGF-23 producing tumors including bone scanning, CT, MRI Indium-111 pentreotide or octreotide scintigraphy and PET. Origin of these tumor is either from bone or soft tissue where around 40% arise from bone and 55% arise from soft tissue. 31% of these-tumor are found in head and 56% are found in lower extremities. Since these tumors are found in varied locations so for localization PET scan should be done first followed by conventional CT or MRI. TIO tumors are generally small and often present within bone and are difficult to locate PET/CT with Ga 68-DOTANOC is used for detection of NET (neuroendocrine tumours) is highly sensitive (90%) and specific (82%).⁹ Only solution of TIO to control phosphate wasting and symptoms is to resect the tumor.¹⁰ This tumor recurs locally and can metastasize. Phosphaturic mesenchymal tumour (PMTs) are classified into four types according to morphology 1) primitive aspirations mixed connective tissue tumor (PMTMCT) 2) osteoblastoma like tumors 3) non ossifying findings like tumors and 4) ossifying fibroma like tumors. PMTMCTs typically show Hemangiopericytoma like and aneurysmal come cyst like area.

CONCLUSION

TIO is a rare paraneoplastic tumor and causes hypophosphatemic osteomalacia due to over secretion of FGF-

23. High index of suspicion in non-responsive patients with stepwise approach involving various imaging techniques will help in successful diagnosis in 90% cases. Excision of tumor with wide margin is the treatment of choice.

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