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Hypophosphatemic Rickets in Monostotic Fibrous Dysplasia of mandible: A Case Report

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Abstract

Fibrous dysplasia is a genetic non- neoplastic disease affecting the skeleton either in isolation (monostotic and polyostotic forms) or in variable combinations with endocrine and cutaneous abnormalities. Hypophosphatemic rickets is recognised as a rare complication of fibrous dysplasia and the clinical features may mimic tumor induced osteomalacia. We are reporting a rare case of a 14 year old male with features of hypophosphatemic rickets such as hypophosphatemia, bone and muscle pain and lower limb weakness. Further evaluation led to identification of fibrous dysplasia of mandible. The patient showed clinical improvement after surgical resection of the dysplastic bone.

Keywords: Hypophosphatemic Rickets, Monostotic Fibrous Dysplasia, Osteomalacia

Introduction

Fibrous dysplasia (FD) is a genetic, non-inherited disease caused by somatic activating missense mutations of GNAS1 encoding the α subunit of stimulatory G protein Gs[1]. This non-neoplastic disease affect the skeleton either in isolation or in combinations with endocrine and cutaneous abnormalities as like in McCune-Albright syndrome[2,3] .Phosphate-wasting disorders include autosomal dominant hypophosphatemic rickets; X-linked hypophosphatemic rickets, and acquired tumour-induced osteomalacia (TIO)[4].Uncommon associations with fibrous dysplasia include hypophosphatemic rickets and

osteomalacia, that resemble disorders associated with skeletal and non-skeletal tumours[5].It has been proposed that renal phosphate wasting in FD is caused by either renal tubule cells bearing Gs α-mutations or alternatively, to the presence of a circulating phosphaturic factor produced by the dysplastic bone[6,7]Osteomalacia have been reported anecdotally as a rare complication of polyostotic fibrous dysplasia, with approximately 22 cases in the literature[8]. No cases of hypophosphatemic rickets/ osteomalacia were reported in association with fibrous dysplasia of jaw bones.

Case report

A 14 year old Indian male, second born of a non-consanguineous marriage reported to Dept: of Endocrinology, Medical College Hospital, Trivandrum with chief complaint of generalised weakness, pain on lower limbs for one year which slowly progresses to difficulty in walking and difficulty in standing from sitting posture for three months. His nutritional history and exposure to sunlight were adequate. There was no family history of any metabolic bone diseases.

On physical examination, the patient was thin built and moderately nourished with prominent chest wall (Fig 1),proximal myopathy(Fig 2) and waddling gait. On radiological investigations he had rachitic rosary(Fig 3), metaphyseal widening and radiolucency of wrists(Fig 4) suggestive of rickets. Biochemical investigations revealed serum calcium level of 9.4 mg/dl (8.5-10.5), serum phosphorus level of 1.4 mg/dl (2.5-4.5 mg/dl), alkaline phosphatase 1604 IU/L (108-306 IU/L),Vit D 88.6 ng/ml and parathormone level of 48.5pg/ml. Complete blood count, liver function test, renal function test, thyroid function test were normal. 24 hr urinary calcium and phosphorus levels are 43 mg/dl and 555mg/dl respectively with tubular reabsorption of phosphate (TRP) of 75% (normal > 85%). The ratio of tubular reabsorption maximum of phosphate to glomerular filtration was 1.125 mg/dl (normal 2.5-4.2 mg/dl).Ultrasound scan of abdomen was normal with no nephrocalcinosis.Based on the clinical findings, radiological and biochemical investigations, he had beenevaluated for tumor induced osteomalacia and hereditary hypophosphatemic rickets. The Ga Dotate scan performed showed somatostatin avid lesion in left body of mandible (Fig 5& 6). For further detailed evaluation, patient was referred to the Dept of Oral Medicine and Radiology.

On intraoral examination, a bony hard swelling of size 2×2 cm noted over left body of mandible in relation to thebuccal aspect of 33 to 35; anteroposteriorly the lesion extendedfrom distal aspect of 33 to mesial aspect of 35; superoinferiorly extendedfrom the alveolar crest to the buccal vestibule (Fig 7). On mandibular cross sectional occlusal radiograph, the lesion showed periosteal reaction with sun burst appearancewithout any bony expansion (Fig 8). Panoramic view (Fig 9)showed a mixed radioopaque - radiolucent lesion with altered trabecular pattern in relation to the periapical region of 33 and 34 with loss of lamina dura. Pan view also showed incomplete apical closure of multiple teeth. With a radiological diagnosis of osteosarcoma, the patient had been sent for an insicional biopsy which revealed fibrous dysplasia (Fig 10). The patient's symptoms improved after resection of the dysplastic bone and serum phosphorus level returned to normal range after one week.

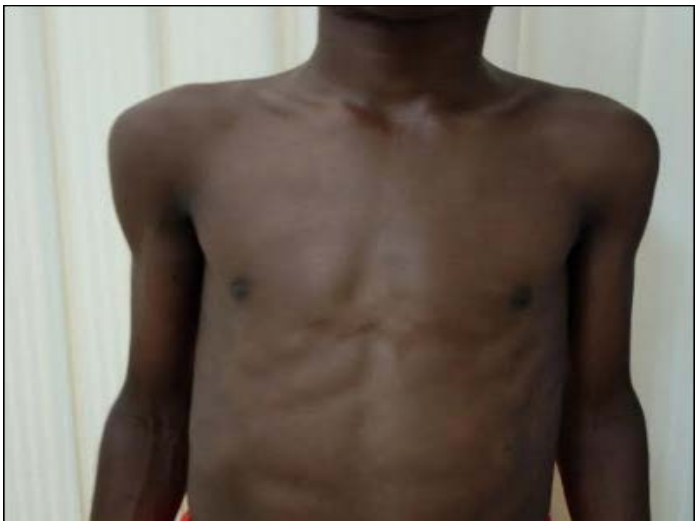

Figure 1: Prominence of chest wall

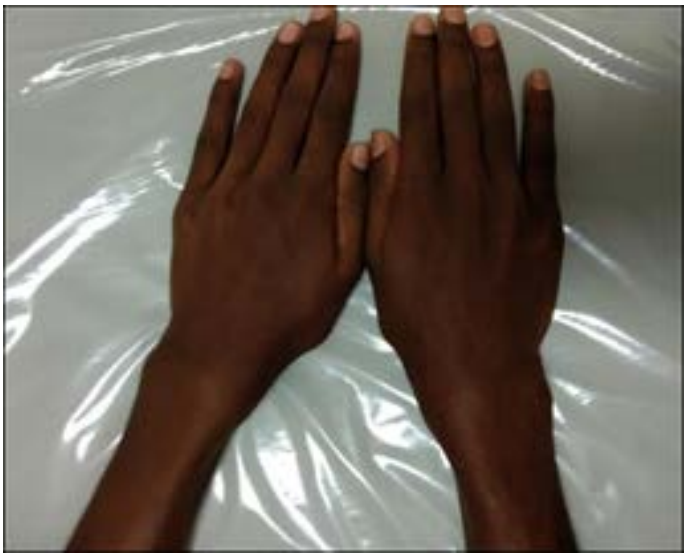

Fig 2: Proximal myopathy

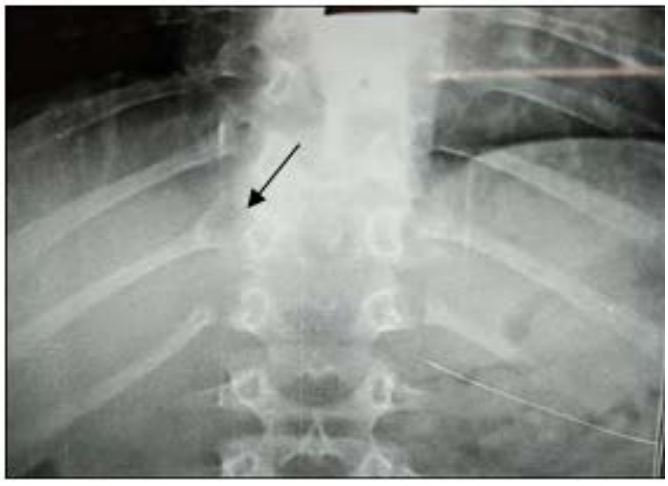

Fig 3:Rachitic rosary

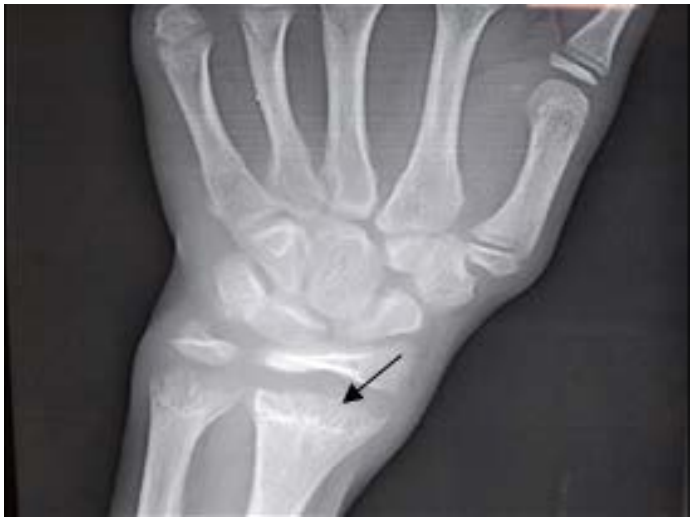

Fig 4: Metaphyseal widening

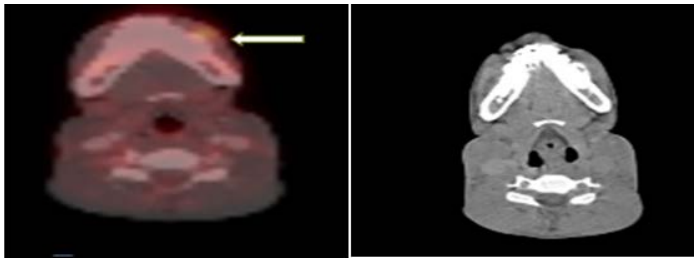

Fig 5 & Fig 6: Ga Dotate Scan

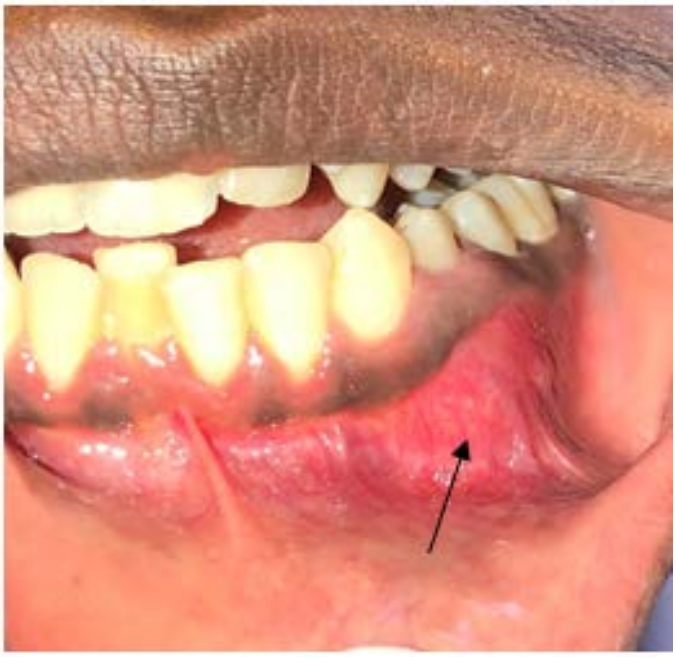

Fig 7: Swelling on the left body of mandible

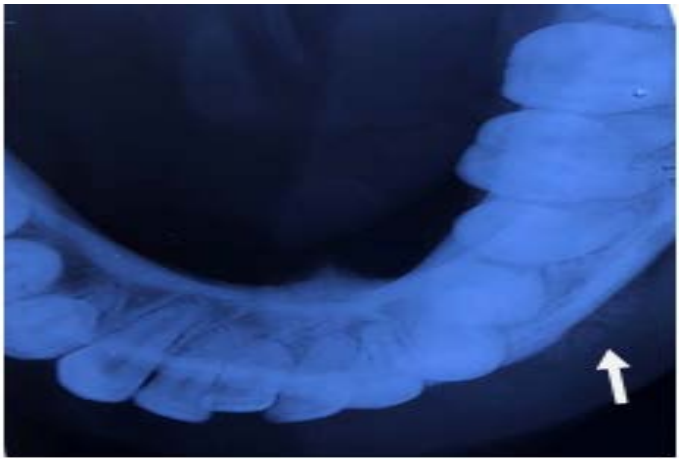

Fig 8: Occlusal radiograph showing periosteal reaction with sun burst appearance

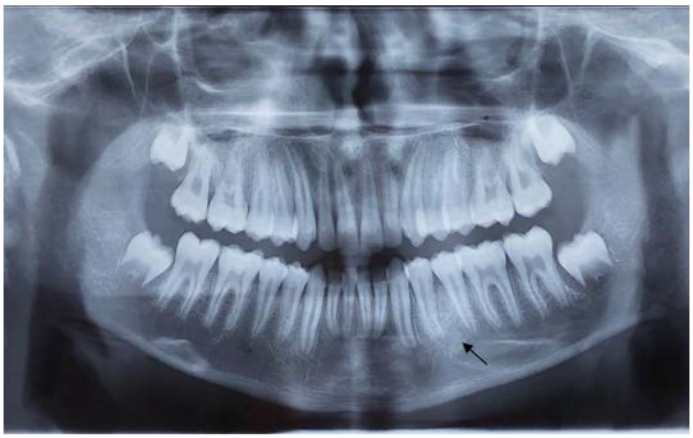

Fig 9: Panoramic view showing mixed radiolucent radio-opaque lesion

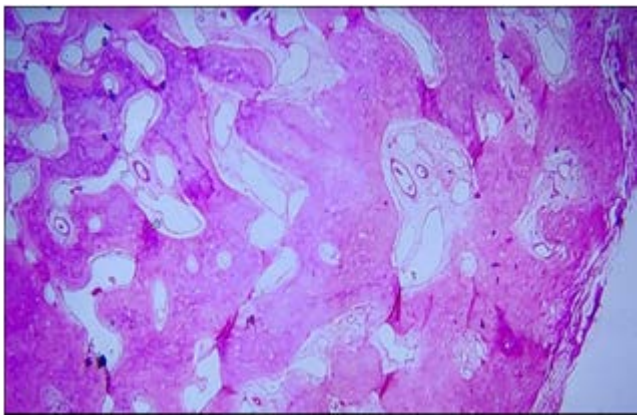

Fig 10: Biopsy showing moderately collagenous connective tissue stroma with sheets of interconnected bony trabeculae with osteoblastic rimming and osteocytes in lacunae.

Discussion

Fibrous dysplasia of bone is characterized by replacement of normal bone and bone marrow by a benign fibro osseous tissue[9].Our case demonstrated the importance of considering the diagnosis of fibrous dysplasia in patients with unusual osteomalacia and persistent musculoskeletal symptoms which may mimic tumour induced osteomalacia.

Serum phosphorus, calcium, alkaline phosphatase, vitamin D3 and parathyroid hormone, should be evaluated to distinguish the causes of hypophosphatemia and osteomalacia. Our patient had low phosphorus level, elevated alkaline phosphatase which indicated hypophosphatemia. The level of Vit D in the patient was also high which may be because of supplemental Vit D given to patient for the treatment of rickets. A 24 hour urine sample was collected. The tubular maximum reabsorption of phosphate per glomerular filtration rate (TMP/GFR) calculated by normogram is a reliable tool for evaluation of hypophosphatemia. In our patient, TMP/GFR was low despite hypophosphatemia which indicated renal phosphorus wasting. The clinical symptoms of TIO which include gradual onset of muscle weakness, fatigue and bone pain especially from ankle, legs, hips and back was almost similar to that in our patient.

Two theories have been proposed for the mechanism of occurrence of hypophosphatemia in patients with skeletal fibrous dysplasia – the production of a circulating phosphaturic substance by the fibrous dysplastic lesions or an intrinsic defect in proximal renal convoluted tubular reabsorption of phosphate[10].In addition to this, activating mutations of GSα have been identified in the kidneys of the patient with fibrous dysplasia and could result in excess generation of cAMP in proximal convoluted tubule[7].

By its nature, fibrous dysplasia is not normally amenable to surgical treatment[5] In our patient, however, surgery was carried out to remove the dysplastic bone. Metabolic studies carried out since surgical intervention strongly suggest that hypophosphatemia and features of rickets have gradually disappeared and the renal phosphate clearance has fallen. Over the next few months, bone and muscle pain was subsided and he was able to walk with normal gait.

Conclusion

Hypophosphatemic rickets/ osteomalacia can occur as a rare complication of monostotic fibrous dysplasia with symptoms mimicking TIO. Clinical symptoms of muscle weakness, gait change, bone pain and proximal myopathy if left undiagnosed and untreated may lead the patient bed ridden. This case highlights the importance of considering fibrous dysplasia among diseases that can induce phosphate wasting disorders and surgical resection of the same can lead to total cure without any morbidity.

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