

Case Report

Rare cause of pathological fracture in adults as hypophosphatemic rickets

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ABSTRACT

Hypophosphatemic rickets is a disorder of defective bone mineralization due to defect in renal phosphate handling process. It is characterised by increased phosphate excretion accompanied by increased phosphatonins like fibroblast growth factor 23. It can be hereditary form of X linked, autosomal dominant, autosomal recessive type of hypophosphatemic rickets. It is associated with low serum phosphorus, normal serum calcium, inappropriately low to normal vitamin D level. Correct identification of these disorders is important for determining therapy. Early diagnosis and management prevent subsequent complication of the disease.

Keywords: Hereditary, FGF 23 - Fibroblast Growth Factor 23, Phosphorus, PTH – Parathyroid Hormone, Rickets

INTRODUCTION

Phosphate plays a critical role in bone mineralization and its homeostasis is maintained by dietary intake, gastrointestinal absorption, renal re-absorption, and renal excretion.^{1,2} Blood phosphate concentration is maintained by these systems, as well as the movement of phosphate in and out of bone and the intracellular space. Hypophosphatemia can occur as a result of low dietary intake, decreased gastrointestinal absorption, or lack of renal conservation. The clinical sequelae of hypophosphatemia results in defective bone mineralization and the rickets phenotype.^{3,4}

Discussion of management

Hypophosphatemic rickets (HR) is a type of hereditary rickets characterized by persistent hypophosphatemia and hyperphosphaturia. Caused by mutation in the gene encoding the phosphate-regulating endopeptidase homolog, X-linked (PHEX), identified in 1995. It is rare

form of rickets causes deficient calcification of mineralized structures such as bones and teeth. The most common mechanism for hypophosphatemic rickets is renal phosphate wasting mediated by increased FGF - Fibroblast Growth Factor 23. Here, we report rare case.

A 44 years old male, born from non-consanguineous marriage presented with history of Low backache, localised, dull aching and non-radiating pain, aggravated by activity, relieved by taking rest since 1 year. Proximal muscle weakness of lower limbs since 1 year. There was no history of distal muscle weakness of lower limb. No history of sensory involvement. No history of bladder & bowel involvement. No history of weakness of upper limb. No history of trauma, no history of fever. No history of co-morbidities. Family history is insignificant. No history of drug intake. No history of weight loss or loss of appetite.

On examination, patient was well built, nourished with height of 160cm, weight 50kgs and BMI of 19.5kg/m².

Vitals were stable. No dental abnormalities. No deformities of chest, deformities of limbs, kyphoscoliosis. Central Nervous system examination revealed higher mental functions normal, cranial nerves intact. Bulk - normal in all 4 limbs. Tone - normal in all 4 limbs. Power at bilateral Hip joint was 4/5, rest of the joint were normal. Reflexes - intact. Bilateral plantar - flexor. Sensory and cerebellar examination normal. Other systemic examination was normal. Lumbar spine tenderness elicited at L4, L5.

We made clinical diagnosis of Lower limb Paraparesis of metabolic cause. Laboratory investigations revealed - Hb 13.9g/dl, WBC - 6730/mm³, Platelet 2.12 lak/mm³. Peripheral smear was normocytic normochromic. ESR - 17mm/hr. Serum total protein - 7.6mg/dl. Serum albumin - 4.5mg/dl. A/G ratio - 1.4. Blood urea - 20mg/dl, Serum creatinine - 0.7mg/dl. Serum sodium - 140meq/l, Serum potassium - 4.2meq/l, Serum 104meq/l. Serum Free T3 - 3.35pg/ml, Serum Free T4 -0.95ng/dl, Serum TSH - 3.35uIU/ml. CRP was negative. Serum Calcium - 8.9mg/dl. Serum phosphorus - 1.7mg/dl, Serum alkaline phosphatase - 353U/L. 24 hour urinary calcium 31mg/24hrs, 24 hour urinary phosphorus 2.6g/24hrs, 24 hour urine protein 21mg/24hrs. Urine for amino acids was negative. Arterial blood gas analysis was normal. Serum 25 hydroxy vit D 33.2ng/ml. Serum PTH 65.70pg/ml. Ratio of tubular maximum reabsorption of phosphate (TmP) to Glomerular Filtration Rate (GFR), TmP/GFR was 0.215. HLA - B 27 negative. USG abdomen - normal study.

MRI Lumbar spine revealed no significant neural compression. MRI Pelvis and Bilateral Hip joint suggestive of pathologic fracture neck of Right femur with surrounding marrow edema. Bone Scan revealed increased Osteoblastic activity and Osteoporotic changes in Head of both femorae, Sacral ala, Condylar region of both tibia, Right 9,10,12th ribs posteriorly and bilateral Scapulae.

Fibroblast Growth Factor 23 - 308.2 RU/ml. FDG - PET CT scan revealed -mild osteopenia, No focal lesion identified to suggest primary neoplastic lesion. Other findings normal. Hypophosphatemic rickets is hereditary form of rickets due to renal wasting of phosphate. Estimated incidence is 1:20,000 caused by the mutation in the phosphate regulating gene Phosphate regulating gene with Homology to endopeptidases (PHEX) located on the X chromosome.^{5,6} It is inherited as X linked dominant. The physiologic defect in XLHR (X Linked dominant hereditary form rickets) is impaired proximal renal tubular reabsorption of phosphate.⁷ Inactivating mutations in PHEX result in increase synthesis and secretion of FGF23.⁸ The increased circulating concentrations of FGF23 is responsible for the biochemical phenotype of XLH like phosphaturia, hypophosphatemia and inappropriately low or normal 1,25(OH)₂D concentrations.⁹ FGF23 is a protein synthesized by osteoblasts and osteocytes which inhibits

phosphate reabsorption by the renal tubule and if secreted in excess leads to hyperphosphaturia and subsequent hypophosphatemia. Serum concentrations of FGF23 are usually high in patients with XLHR.¹⁰ Biochemical features include hypophosphatemia, high serum alkaline phosphatase, reduced TmP/GFR, and suppressed to normal 1,25(OH)₂D concentrations. Usually serum calcium is normal, but secondary hyperparathyroidism is common, both before and after treatment with phosphate.¹¹⁻¹³ Diagnostic evaluation should include fasting serum and urine phosphate and creatinine to determine the tubular threshold maximum for phosphate (TmP/GFR). 25-hydroxyvitamin D should be done to exclude vitamin D deficiency, while 1,25(OH)₂D in XLHR is inappropriately low or normal and Parathyroid hormone (PTH) is frequently mildly elevated or normal.

Our patient had normal serum calcium, lower limit of normal 25(OH)₂D, normal PTH level, hypophosphatemia and hyperphosphaturia, elevated fibroblast growth factor 23 and TmP/GFR was low suggestive of Renal phosphate wasting disorder, hence hypophosphatemic rickets of hereditary form was diagnosed.

The medical management aimed at supplementing oral phosphate up to 2gm/day, Vit D analogs 1-1.5microgm/day.¹⁴ Our patient was started oral phosphate 1gm BD dose daily and calcitriol of 1microgm daily. Patient improved symptomatically over period of 2 weeks. Hypophosphatemic rickets patients will not improve only by supplementing vit D, oral phosphate should also be supplemented. Patients should undergo monitoring of serum alkaline phosphatase, serum calcium, serum PTH, Serum creatinine, and 24hour urine phosphorus for every 6 months and visit OPDs for follow up.

Final diagnosis

Hypophosphatemic Rickets of hereditary form.

CONCLUSION

Phosphorus plays an important role in bone mineralization. Even though, hypophosphatemic rickets is rare cause of pathological fracture in adults, it requires high index of suspicion. Early diagnosis and immediate treatment of hypophosphatemic rickets is of utmost importance, as it prevent subsequent sequel.

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