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A Mismanaged Case of Hypophosphatemic Rickets

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ABSTRACT

X-linked hypophosphatemic rickets is a common cause of inherited hypophosphatemia and is caused by mutation in the PHEX gene, resulting in excessive expression of FGF23 which causes phosphaturia. Due to its rarity, X linked hypophosphatemic rickets is poorly known and diagnosis is frequently delayed. Conventional treatment is based on oral phosphate salts supplementation and activated vitamin D analogs, which however, cannot cure the disease in most cases.

Keywords: X linked hypophosphatemic rickets, FGF23, PTH

CASE DESCRIPTION

This case report describes the clinical and biochemical features of hypophosphatemic rickets in a 8 years old female child who came to the OPD with a chief complaint of delayed walking and deformity of B/L feet, and delayed eruption of teeth. She had been treated from the age of 3 years for nutritional rickets. There was no genu varum/valgum. There was history of similar complaints of deformities of limb in mother. The child also had H/O delayed dentition, maxillary teeth were absent and there were 7 mandibular teeth. Exposure to sunlight was adequate in the child. The child's linear growth compared to that of other children of her age was less than -3SD. Her pulse rate was 82/min, bp-110/70 mm hg and temperature were normal. Rest of the systemic examination was within normal limits. Laboratory investigations showed normal complete blood counts and normal urine examination, normal serum calcium (Ca++) level of 9.3 mg/dl (8.8-10.8mg/dl) phosphate of 2mg/dl (4-7 mg/dl), while alkaline phosphatase was 300 IU/L(44-147IU/L). Liver and renal functions were within normal limits.

Patient had normal blood gas analysis. The parathyroid hormone (PTH) level was normal 20.80 pg/ml (7-53 pg/ml) ,25 hydroxy vitamin D3 was normal 70.24 ng/l(20-40ng/ml) and 1,25 $(OH)_2D_3$ was low 10pg/ml(18-78pg/ml). 24-hour urine examination showed marked phosphaturia at 26.6 mg/dl (4.5-6.5 mg/dl). Fractional excretion of phosphate 48%. 24-hour urinary creatinine was 20 mg/dl (14-26mg/dl). TMP-GFR for the patient was 1.01(1.11-2.44)

24-hour urinary calcium was 110 mg/dl (100-300mg/dl). Urine routine was normal. TFT and USG neck was normal. Based on history of deformity of extremities, delayed dentition, presence of same complaints in mother and laboratory findings consistent with familial hypophosphatemic rickets with x-linked dominant inheritance. FGF-23 level and genetic study could not be done due to cost constraints. Treatment with tablet calcitriol 0.25 microgram once daily and oral phosphorus 500 milligram thrice daily was started.

Figure 1: Depicting the absence of maxillary teeth in the index child

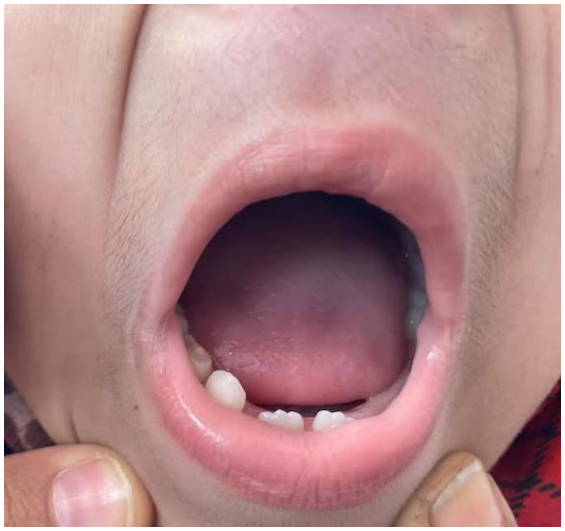

Figure 2: Depicting the delayed eruption of maxillary teeth in the index child

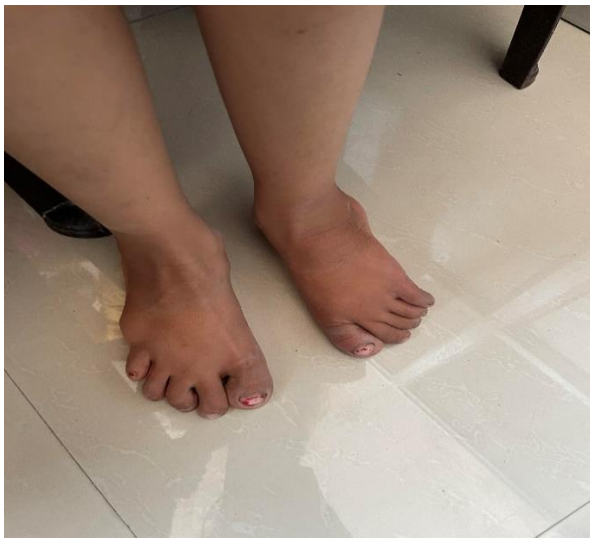

Figure 3: Depicting the skeletal abnormality in bilateral extremities

DISCUSSION

Hypophosphatemic rickets is mostly due to renal wasting of phosphate. X-linked hypophosphatemic rickets (XLHR) is the commonest hypophosphatemic Rickets.

Estimated incidence is 1:20,000 caused by the mutation in the phosphate regulating gene PHEX(**p**hosphate regulating gene with **h**omology to **e**ndopeptidases (PHEX) located on the **X** chromosome (1). It is inherited as X-linked dominant. The physiologic defect in XLHR is impairment in the proximal renal tubular reabsorption of phosphate

For Diagnostic evaluation we need fasting serum and urine phosphate and creatinine to confirm hypophosphatemia, to determine the tubular threshold maximum for phosphate (TMP/GFR). 25-hydroxyvitamin D should be done to exclude vitamin D deficiency which was normal in our patient, while 1,25(OH)2D is inappropriately low or normal. PTH is frequently mildly elevated at diagnosis but it was normal in our patient.The classical laboratory finding in XLHR include Hypophosphatemia, normal Serum calcium and low to normal circulating 1,25(OH)2D levels, normal circulating 25-OHDand high serum alkaline phosphatase as in our patient.The diagnosis of XLHR is made by characteristic findings of low serum phosphate concentration with a reduced tubular reabsorption of phosphate corrected for glomerular filtration rate (TmP/GFR), based on normal values for age. (2)

Treatment of hypophosphatemic rickets includes activated vitamin D (calcitriol or alfacalcidol) and phosphate . Higher doses of calcitriol and phosphate are required to treat XHLR and a recommend doses are phosphate of 20–40 mg/kg/day and calcitriol of 20–30 ng/kg/day(3).

Goal of treatment efficacy should include improvement in height, skeletal deformity, and radiographic evidence for epiphyseal healing and acceptable height velocity We started both one alpha cholecalciferol and phosphate in therapeutic doses and patient was routinely followed up 3 monthly in outpatient clinic for monitoring her growth parameters, serum, calcium, serum

phosphate, alkaline phosphate and serum creatinine.(4)

Biochemical monitoring should be performed in 3 monthly intervals to avoid complications like hypercalcemia, hypercalciuria or hyperparathyroidism (5).

The best biomarker for bone healing is serum alkaline phosphatase activity, which should decreases with treatment suggest optimal bone healing (6). PTH levels should be measured routinely to identify secondary hyperparathyroidism, which can be corrected by increasing the calcitriol dose, or by reducing the dose of phosphate (6)

CONCLUSION

This case highlights the importance of following up a patient who has been diagnosed as nutritional rickets. In the index case doctor shopping was done and there was no proper investigation and follow up record of the index patient since last 5 years. Biochemical parameters not responding to oral vitamin D should be investigated further for vitamin D resistant and vitamin D dependent rickets.

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Conflict of Interest: None

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