Bangabandhu Sheikh Mujib Med. Coll. J. 2024;3(1):52-55 DOI: https://doi.org/10.3329/bsmmcj.v3i1.72067

Case Report

Familial Hypophosphatemic Rickets: A Case Report and Review of the Literature

LF Zaman[1], MN Sarker[2], GU Ahmed[3], AFM Pervez[4]

Abstract:

Among the genetic disorders causing rickets because of hypophosphatemia, X- X-linked dominant hypophosphatemic rickets (XLH) is the most common, with a prevalence of 1/20,000. The defective gene is on the X chromosome, but female carriers are affected, so it is an X-linked dominant disorder. XLH associated with short stature during childhood are mostly referred to the hospital & diagnosed as vit-D deficiency rickets & received vit D before adulthood. We presented a 2-year-old boy with the complaint of walking difficulties since his 1 year of age. The patient was assessed for sociodemographic, hematological & biochemical parameters. All imaging, Laboratory parameters and positive family history confirmed the diagnosis of XLH. We treated the patient with Di basic sodium phosphate solution and 1, 25 vit D. XLH needs a good assessment, care and follow-up through a complementary medical team.

Key words: Familial, Hypophosphatemic rickets.

Introduction:

Rickets is a systemic disease that occurs during developmental ages. It originates from an abnormal differentiation and maturation of chondrocytes, resulting in a lack of mineralization of the growth plate cartilage and bone deformity[1,2]. The most common form of rickets is secondary to vitamin D deficiency; apart from this, there are rare genetic conditions involving different bone homeostasis pathways, whose clinical presentations are very similar[1,2]. Among the forms of genetically determined rickets, hypophosphatemic rickets (HR) is the most commonly diagnosed[1,3]. HR includes hereditary hypophosphatemic rickets with hypercalciuria, X-linked hypophosphatemic rickets (XLHR, 1 in 20,000 births), autosomal dominant hypophosphatemic rickets (ADHR), and autosomal recessive hypophosphatemic rickets (ARHR).

Familial Hypophosphatemic Rickets (FHR) was found for the first time by Albright in 1937 and is also called vitamin D-resistant rickets[4-6]. It is a disease that can occur through x-linked dominant, autosomal dominant, autosomal recessive and sporadic inheritance[4-7]. Albright found that most FHR is an x-linked dominant type[7]. To distinguish between x-linked dominant and autosomal dominant, the family pedigree cannot be used, because it may look alike. Usually, this disease can be distinguished genetically. The gene that is responsible for the x-linked dominant is located in Xp21 while autosomal dominant is in 12p13[7]. The sporadic type can easily be distinguished from the other two. In the family pedigree, there is no other FHR patient besides the patient himself[6,7]. The case that we are about to report was an X-linked dominant type of FHR.

Case Report:

Rayan, 2-year-old boy, 3rd issue of nonconsanguineous parents, immunized as per EPI schedule, developmentally age-appropriate, hailing from Rajbari got admitted with the complaints of walking difficulty and frequent falls since 1 year of age when he started walking. Raian used to walk keeping the legs wide apart.

1. Dr. Fouzia Zaman, MBBS, FCPS Part II trainee, Bangabandhu Sheikh Mujib Medical College Hospital, Faridpur.
2. Dr. Mst. Naznin Sarker, MBBS, FCPS (Pediatrics), MD (Pediatric gastroenterology), Assistant professor, Department of Pediatric gastroenterology & Nutrition, Bangabandhu Sheikh Mujib Medical College, Faridpur.
3. Dr. Gias Uddin Ahmed, MBBS, FCPS (Pediatrics), MD (Pediatrics), Assistant professor, Department of Pediatrics, Bangabandhu Sheikh Mujib Medical College, Faridpur.
4. Dr. Abu Faisal Md Pervez, MBBS, MD (Neonatology), Associate professor, Department of Neonatology & Head of the Department of Pediatrics, Bangabandhu Sheikh Mujib Medical College, Faridpur.

Address of correspondence:

Dr. Fouzia Zaman, MBBS, FCPS Part II trainee, Bangabandhu Sheikh Mujib Medical College Hospital, Faridpur. Phone: +8801754398818, Email: fouziazaman98@gmail.com.

The mother also noticed that her child was not growing well and there was progressive deformity of legs.

The walking difficulty was not associated with fever, joint pain or any trauma. He had no h/o polyuria, polydipsia, jaundice, chronic diarrhea, taking anticonvulsant or anti-tubercular drug.

Mother has genu vulgum and elder brother has wind-swept deformity and short stature. His feeding history was appropriate and he has proper sunlight exposure.

On examination, he was toxic had a box-shaped head, was mildly pale, febrile, had tachypnoea and tachycardia , was severely underweight, stunted, and moderately wasted.

Figure 1: Our Patient

Musculoskeletal examination revealed there was widening of both wrist and ankle joints, genu varum (Figure 1,2,3). Nervous system examination revealed hypotonia, diminished muscle power (4/5) and waddling gait.

Other systemic examinations revealed no abnormality.

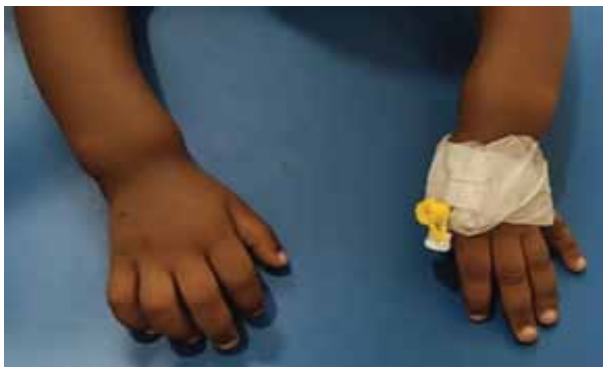

Figure 2: Wrist of the patient

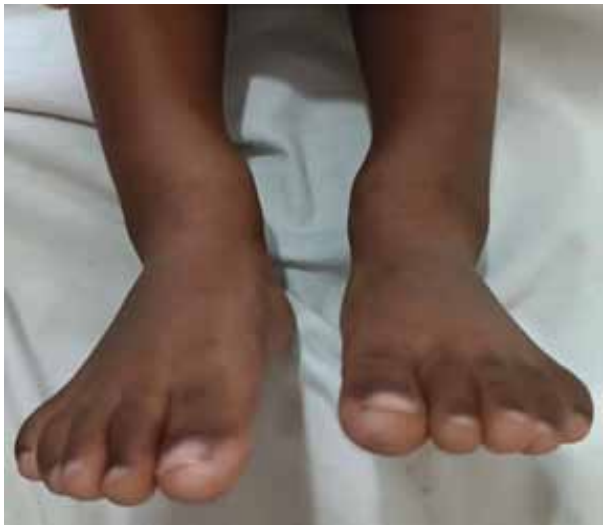

Figure 3: Ankle of the patient

Laboratory analysis showed hypophosphatemia (1.3 mg/dL, normal values 2.5-4.5 mg/dL), increased alkaline phosphatase (ALP) activity (1173 U/L, normal values 140–400 U/L), 24 hr urine phosphate - 2000mg (normal 226 – 1797mg) and normocalcemia (9.2 mg/dL, normal values 8.8–10.8 mg/dL), Vit D3 – 141.0 ng/ml (normal 30 – 100 ng/ml) and serum parathormone (PTH) was 30.70 pg/ml (normal 9.00 – 80.00 pg/ml), serum creatinine – 0.6 mg/dl.

X-ray of long bones showed cupping and fraying of the metaphyseal regions, a diffusely reduced bone mineralization and bowing of long bones (Figure 4, 5).

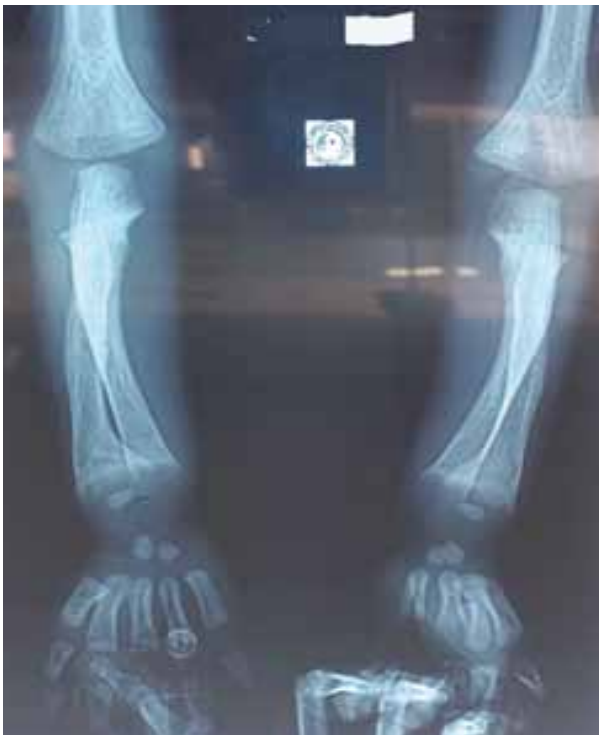

Figure 4: X-ray of upper limbs

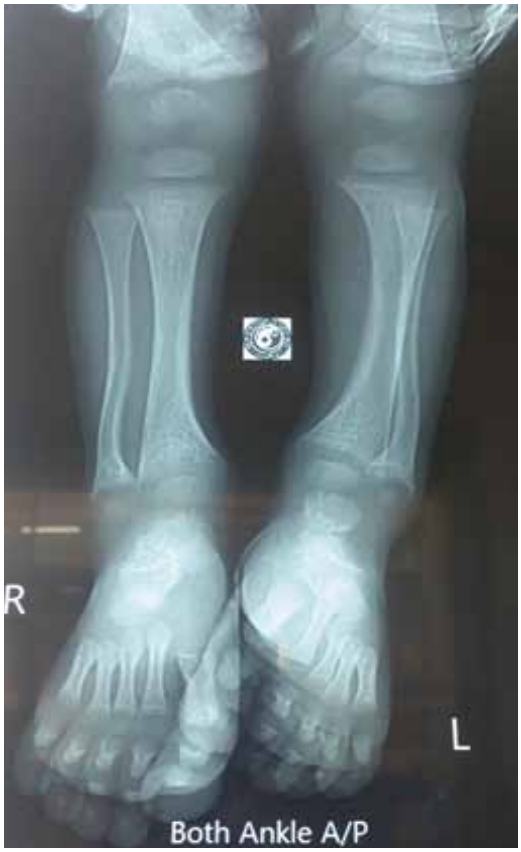

Figure 5: X-ray of lower limbs

Based on the above examinations, he was diagnosed as having FHR, treated with calcitriol 0.25 mcg twice a day and Joulie solution which consists of 30.4mg of dibasic sodium phosphate per ml 2g in 5 divided dose daily.

After one month of treatment, we followed up the patient and there was a significant improvement in general well-being, radiological improvement was also seen.

Discussion:

The main defect in FHR is located in the proximal tubule of the kidney. Phosphate usually enters the tubule cell passively by bonding to sodium. From inside this cell, the two electrolytes were transported actively with the help of sodium/potassium ATPase to the interstitial space and then to the peritubular capillary[8,9]. In FHR, this process is not working. The literature said that a decreased activity of a sodium-dependent phosphate transporter might be the one reason responsible for this defect[10]. Besides a defect in the proximal tubule, there is also a defect in the hydroxylation of 25-hydroxy vitamin D (25(OH)D3) to 1,25-dihydroxy vitamin D (1,25(OH) 2D3) that is also located in the kidney[4,6,10]. 1,25-dihydroxy vitamin D is useful for increasing calcium absorption in the intestine. There is a term called classic triad, which consists of hypo-phosphatemia, lower leg deformities and growth retardation in FHR case[6]. Hypo-phosphatemia has already existed since a rickets patient was born[5,6]. Besides hypophosphatemia, there is also a normal or low blood calcium[6,10], increased urinary phosphate and alkaline phosphatase and decreased urinary calcium [4-6,10]. In our case, all laboratory findings were in accordance with the literature. Lower leg deformities, bowing and waddling gait usually manifest when a child begins to walk around the age of 2 years. In our case, lower leg deformities started to some extent as the child was 2 years old then. However, the bone survey gave the impression that the disease had already started a long time ago. Regarding growth retardation, usually, it is a short stature. If a FHR patient is left untreated, his/her final height would only reach 130-165 cm[10]. Normal growth can be maintained if the blood phosphate content is more than 3 mg/dl[2]. There is research about the usage of recombinant human growth hormone in an FHR patient. However, the study concluded that there is no need to treat short stature in an FHR patient[9]. The height of our patient was only 75 cm and Height for Age Z (HAZ) was -4.9 which indicates severe stunting.

The treatment for FHR consists of two kinds of

preparations. The first one is called the Joulie solution. It consists of 30.4mg/ml dibasic sodium phosphate. The side effects are diarrhea and hypocalcemia[5,6,10-12]. Hypocalcemia frequently causes muscular spasms[6,7,9]. In our case, there was no such complication. The second preparation consisted of 1, 25 vitamin D analogs with a dose of 30-70 ng/ kg/ day[5-7,11,12]. The advantage of this preparation is to increase calcium absorption in the intestine to prevent muscular spasms and stimulate bone recovery[7]. Using only one preparation has no benefit at all[6,10]. We have to use them in combination. If we use them before the age of 6, the lower leg deformities can spontaneously recover[3]. In our case, a spontaneous recovery could be expected because we used it when the patient was 2 years old.

Besides the advantages, there are also disadvantages of this combination; they can induce nephrocalcinosis and nephrolithiasis[7,13]. It is said in some studies that this condition can occur as the cause of the increasing secretion of urinary calcium. To solve the problem, some experts suggested thiazide and amiloride treatment. But the results are still controversial[4,7]. A long-term follow-up should be done to assess the effect of the Joulie solution on bone recovery. Our goal is to make this patient normal.

Conclusion:

A family history of short stature, orthopedic abnormality, poor dentition and parental consanguinity may signify familial rickets. The diagnostic criteria of familial hypophosphatemic rickets globally are based on history, clinical examination, biochemical and radiological evaluation. The treatment is done by oral administration of phosphorus and vitamin D. Currently Growth hormone and recombinant human monoclonal antibody targeting FGF-23 are under investigation for treatment of hypophosphatemic rickets. More studies and reports are needed in the future to better understand and treat familial hypophosphatemic rickets, especially in children.

References:

1. Bitzan M, Goodyer PR. Hypophosphatemic Rickets. Pediatr Clin North Am. 2018; 66: 179–207.

2. Carpenter TO, Shaw NJ, Portale AA, Ward LM, Abrams SA, Pettifor JM. Rickets Nat Rev Dis Primers. 2017; 3:17101. doi: 10.1038/nrdp.2017.101.

3. White KE, Evans WE, O'Riordan JL, Speer MC, Econs MJ, Lorenz-Depiereux B, et al. Autosomal dominant hypophosphataemic rickets is associated with mutations in FGF23. Nat Genet. 2000;26: 345–8.

4. Tambunan T, Tubulopati, In: Alatas H, Tambunan T, Trihono PP, editors. Buku ajar nefrologi anak jilid II. Jakarta: BP-FKUI; 1999. p .426-45.

5. Lum GM. Kidney and urinary tract. In: Hay WW, Groothuis JR, Hayward AR, Levin MJ, editors. Current pediatric diagnosis and treatment. 13th ed. Connecticut: Appleton and Lange; 1997. p. 607-30.

6. Glorieux FH, Chabot G, Tau C. Familial hypophosphatemic rickets: pathophysiology and medical management. In: Glorieux FH, editor. Rickets. New York: Raven Press; 1991. p. 185-202.

7. Chesney RW. Familial hypo-phosphatemia. In: Nelson WE, Behrman RE, Kliegman RM, Arvin AM, editors. Textbook of pediatrics. Philadelphia: Saunder; 1996. p. 1986-7.

8. Guyton AC. Human physiology and mechanisms of disease. 3rd ed. Philadelphia: Saunder; 1991. p. 711-27.

9. Alatas H. Anatomi dan fisiologi ginjal. In: Alatas H, Tambunan T, Trihono PP, editors. Buku ajar nefrologi anak jilid I. Jakarta: BP – FKUI; 1993. p. 1-31.

10. Gertner JM. Rickets and other disorder of vitamin D and phosphate metabolism. In: Lifshitz F, editor. Pediatric endocrinology. New York: Marcel Dekker; 1996. p. 507-20.

11. Garg RK, Tandon N. Hypophosphatemic rickets: easy to diagnose, difficult to treat [abstract]. Indian J Pediatr 1999; 6:849-57.

12. Ozuah PO, Adam HM. Planning the treatment of a patient who has rickets. Pediatr Rev 2000; 21:849-6.

13. Seikaly M, Browne R, Baum M. Nephrocalcinosis is associated with renal tubular acidosis in children with x-linked hypophosphatemia. Pediatrics 1996; 97:91-3.