



Case Report on Hypophosphatemic Rickets

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Abstract: In children with rickets, osteoid fails to mineralize. This condition is sometimes accompanied by a vitamin D deficiency or a drop in blood phosphate levels, which causes hypophosphatemia. This case report describes a 4-year-old youngster with persistent respiratory conditions since he was nine months old. At an outpatient tubulopathies clinic, throughout a 24-month study, information on the patient's metabolic profile, creatinine clearance, nutritional status, weight, and body composition was gathered. Clinical and laboratory evidence of hypophosphatemia rickets was present in the patient. The patient's bone metabolism had changed. He had been bedridden for some time and was mechanically ventilated. Our case improved after receiving phosphate, calcium, and calcitriol multiple as treatment. The patient improved, eventually walking alone and breathing on his own. Additionally, weight and structural development are enhanced with transient gallstones. The clearance of creatinine was constant. The medication improved his test results and nutritional status. Following two years of treatment, he fully recovered. Early detection can help kids receive additional support earlier and prevent them from falling behind. All age groups can benefit from multimodality treatment, which is essential for managing the condition. The current example is presented since it is so uncommon.

Keywords: Rickets, metabolic profile, Creatinine clearance, Vitamin D deficiency, hypophosphatemic therapy.

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I. INTRODUCTION

Rickets is a bone disease where blood levels of calcium and phosphate are altered. The clinical picture, which varies depending on the age of onset and cause, is frequently characterized by bowed legs, short stature, and swollen joints.¹ Genetic abnormalities or dietary inadequacies may also contribute to the illness. Mutations have been found in genes that encode proteins involved in bone mineralization, fibroblast growth factor 23 (FGF23) synthesis or degradation, renal phosphate control, or vitamin D metabolism or activity. Nutritional rickets has been returning in several modern nations even though they are far less frequent than they were 200 years ago; preterm infants or those who are breastfed and have dark skin tones are more vulnerable.² main categories of rickets: calcipenic and phosphopenic. Both types of rickets have the common condition of hypophosphatemia. On the hypertrophic cells in the development plate, it inhibits apoptosis.³ The hypertrophic cells assemble in the development plate to produce the rachitic bone without apoptosis. A condition of bone mineralization known as hypophosphatemic rickets is brought on by (inherited or acquired) deficiencies in how the kidneys handle phosphorus. The most prevalent inheritable type of rickets in this category of diseases is X-linked hypophosphatemic rickets.⁴ An X-linked hereditary characteristic, which has a frequency of 1/20,000, is the most prevalent kind of HR.⁵ The pathophysiology of HR has been connected to the discovery of activating mutations in the fibroblast growth factor 23 (FGF-23) gene. Approximately 2-5% of idiopathic short stature (ISS) among males appear to be caused by these mutations. Short stature is a feature of HR development characterized by slower-than-usual skeletal maturation and delayed epiphyseal closure.⁶ Developmental delays are typically noticed in the first year of life, with growth rates of 0.2–0.4 cm/year to 0.4–3 years slower than the average age.⁷ Hypophosphatemic

rickets are the most typical nonatomic, refractory rickets in Indian children. Most hypophosphatemic diseases are inherited while occasionally acquired [for example, drug-induced Fanconi syndrome and tumour-induced osteomalacia (TIO)].⁸ They might be individual defects or a component of a more widespread pattern of proximal tubular dysfunction. A diagnosis is frequently made using a medical history, physical examination, biochemical tests, and radiography. Only nutritional rickets may be avoided with calcium and vitamin D supplements or dietary fortification alone or in conjunction with sun exposure. Calcium and vitamin D supplements can treat conventional nutritional rickets, with phosphate replacement only seldom needed. Treatment for inherited rickets brought on by problems with vitamin D metabolism.⁹ Hence, this study reported a severe case of hypophosphatemic rickets to explain the patient's nutritional and laboratory condition during a follow-up and to show the treatment benefits even in the absence of a molecular diagnosis.

2. CASE REPORT

A 4-year-old boy with a history of chronic respiratory ailments that began when he was nine months old was admitted to the outpatient department of Sree Balaji Medical College and Hospital, a tertiary care facility, on January 21, 2020. The patient's parents provided written consent, and the study was conducted and published with institutional ethics committee approval.

2.1. Medical history

His neuro psychomotor development had gradually regressed, and he had trouble crawling and sitting alone. After a pathological humeral fracture at age three, rickets was first investigated. Skeletal changes were seen in the patient, as shown in Figure: I



Fig: I Clinical feature of the reported patients during initial treatment

2.2. Observation

The patient had a fever and respiratory symptoms when he was examined. Therefore, he was first hospitalized with a chronic respiratory condition diagnosis. He was found to have

extensive rickets symptoms, such as frontal bossing, rachitic rosary, and double malleoli, in addition to his respiratory discoveries. Table I shows additional indications and symptoms of active rickets in the present patient.

Table: 1 Symptom and Signs of the study patient

Symptoms	Signs
Weakness	Widened wrists
Leg pain with walking	Beading of ribs
Frequent falls	Genu varum
Leg pain at rest	Widened ankles
Inability to walk	Genu valgum
History of fracture	Rib cage deformity
	Anterior tibial bowing
	Humeral bowing

2.3. Family history

The patient in this research had no significant family history of rickets or hypophosphatemic rickets.

2.4. Investigations

Initial tests revealed that the RT PR was 72% (normality value (NV): >80%), serum phosphate was 1.8 mg/dL, and calcium

was 7.1 mg/dL. The serum albumin level and the other electrolyte levels were average. Vitamin D dosage was not achievable. Osteomalacia was detected with a bone biopsy. An X-ray of the long bones revealed widespread osteopenia, epiphyseal dysplasia, many consolidated fractures, and podalic distal phalangeal hypoplasia in addition to hypomineralization and these conditions. [Figure: 2].



Fig: 2 X-ray of forearm and legs during the initial therapy.

Ultrasonography of the kidney revealed abnormal renal parenchymal echotexture. This supported the diagnosis of hypophosphatemic rickets.

2.5. Diagnosis

When the kid was five years old, pneumonia necessitated prolonged care at another hospital. The patient remained bedridden for ten months before the metabolic profile normalized. A tracheostomy was necessary. When he was six

years old, he was checked by a pediatric nephrologist. Clinical and analytical tests revealed a considerable improvement after making these adjustments to the medication regimen. When the patient was four years old, the initial values for their laboratory evolution were recorded. Table 2 demonstrates that the blood's concentrations of calcium, alkaline phosphatase, parathormone, and phosphate rose after three months. He received calcium carbonate, calcitriol, and tricalcium phosphate solution as a substitute for phosphorus.

Table 2: Initial values for the patient's laboratory evolution

Blood parameters with reference value	Initial	Six months	12 months	18 months	24 months	Mean	Median
Calcium [8.6-10.2 mg/dL]	6.8	7.6	8.6	9.5	10.1	8.52	8.6
Phosphorous [4-7 mg/dL]	1.8	3.2	4.8	5.5	6.3	4.32	4.8
Magnesium [1.8-2.5 mg/dL]	0.4	0.8	1.9	2.2	2.4	1.54	1.9
Parathormone [15-65 ng/L]	88.5	75.6	69.5	65.4	64.9	69.8	69.5
Alkaline phosphatase [<300 U/L]	11800	654	524	388	321	2737.4	524
Creatinine clearance [>90]	125	96	85	90	88	96.8	90
Urine Calcium/Creatinine ratio [mg/dL]	0.25	0.22	0.20	0.15	0.14	0.19	0.20
25-Hydroxyvitamin D (ng/mL)	15	15	16	20	25	18.2	14.96

2.6. Treatment

Since learning about it from his companion, he has been a staunch vegan and an advocate of this diet for youngsters. Supplemental dietary phosphorus, oral calcium citrate (1200 mg), and oral vitamin D3 (4000 IU) were begun for the patient 2-3 times per week. As a result, phosphorus, calcium, and calcitriol replacement began. The clinical improvement was noted and reported after a time of stability. When the patient's breathing became regular, it was possible to decannulate the tracheostomy and administer ventilator support. In terms of neuro psychomotor development, the patient, who spent his whole illness in bed, started walking on his own three months after getting medication and more rigorous motor-physical therapy. All three substances—calcium, calcitriol, and phosphorus-replacement therapy-increased progressively.

2.7. Follow up

Throughout the 24 months' follow-up, the patient's height progressively increased, moving from height/age, accounting for the period of the nephrologist's therapy change. The patient's gait was unaltered during the last appointment of the planned visits. However, there were some skeletal changes. The left side of the body loses weight, the left waist widens, and the upper torso reduces height, which is very noticeable. In addition, the patient was receiving calcium, calcitriol, and phosphorus replacement. Blood testing verified the requirement for these vitamins. Hence, 125 and 88 mL/min/1.73 m² were the initial and final creatinine clearances, respectively.

3. DISCUSSION

The patient had the typical phenotypic of vitamin D insufficiency, including enlarged, malformed long bones and growth retardation, leading to the diagnosis of hypophosphatemic rickets and determining whether the therapy effectively improved the patient's overall condition, bone health, and metabolomics. It is critical to highlight that after two years of no follow-up, motor skills declined, and bone abnormalities worsened. Rickets is defined as an abnormality of differentiation and maturation of chondrocytes resulting in complete disruption of chondrocyte columns and lack of mineralization of the growth plate¹⁸. The proximal tubule absorbs approximately 88% of the filtered phosphate, while the remaining 12% is transported to the distal tubule¹⁰. The inability to release phosphate into the renal tubule lumen is one cause of hypophosphatemia. Because tubule cells are phosphate-impermeable, hyperparathyroidism is a common cause of decreased urine excretion.¹¹ Prolonged hypophosphatemia produced the patient's bone abnormalities because keeping intracellular and extracellular phosphate levels within a specified range is critical for numerous biological functions¹². Furthermore, a lack of phosphorus can affect chondrocyte maintenance, inhibiting bone production and resulting in rickets and delayed development. As indicated by the patient, correct hypophosphatemia is not required for the beginning of bone deformities. Because bone abnormalities are not usually associated with extrarenal hypophosphatemia¹³. An important recent development is the introduction of burosumab (KRN23), a human monoclonal antibody against FGF-23 that is effective in children with X-linked hypophosphatemia⁰⁹. hypophosphatemic rickets with hypercalciuria differs because the former does not require calcitriol, which may worsen hypercalciuria and increases the

predisposition for nephrocalcinosis. Supplementation with phosphate forms the mainstay of its treatment^{05,18,19}. Additionally, Phosphate is essential for the development of bone mineralization, and its lack may result in the onset of osteomalacia, as observed in this patient's biopsy. Serum calcium levels in these conditions are frequently normal or slightly lower.¹⁴ Other variables, such as vitamin D insufficiency due to the patient's bed rest, lack of sun exposure, and protracted immobility, may have altered bone metabolism in this specific case. Hypophosphatemic rickets is one of the rickets diagnoses in children, and its first treatment consists of phosphorus and calcitriol supplementation. Usually, the course of therapy is prolonged until the growth rate is close to normal. In the first year of therapy, the prepubescent child's development can be noticed to be improving. There is a gradual increase in height without a markedly greater body mass index (BMI). As a result of the medicine, the patient experienced transient renal lithiasis during follow-up. Calcium, phosphate, and calcitriol supplements may result in renal lithiasis. When utilizing active vitamin D, it's important to monitor calciuria since, due to temporary hyperphosphatemia, it can cause hypercalcemia, hypercalciuria, and hyperparathyroidism. Furthermore, hypophosphatemia may be followed with lithiasis and nephrocalcinosis if the patient has hyperphosphaturia or hypercalciuria. The patient did not take in the appropriate amount of phosphate since renal lithiasis had already started. The two most important differential diagnoses are Fanconi syndrome [FS] and nutritional rickets. The FS also includes episodes of prolonged dehydration, metabolic acidosis, hypouricemia, proteinuria, and abnormalities in other electrolytes in the blood and urine.¹⁵ Despite nutritional rickets' alteration of bone metabolism, tubular phosphate reabsorption is approximately 100%. The ratio of 1:1 between the inorganic phosphate in urine and the inorganic phosphate in tubular fluid shows how effectively vitamin D works. Proteinuria or irregularities in the patient's acid-base balance were disregarded because neither illness existed. But hypophosphatemia was found to cause urinary phosphate loss. Proteinuria, metabolic acidosis, and hypouricemia are other electrolyte problems.¹⁵ Without molecular identification, hypophosphatemic rickets can be identified and initially treated; nevertheless, the thorough diagnosis obtained from the genetic analysis is important, especially for genetic counselling²⁰. The endopeptidase that the PHEX gene in a cell generates breaks down and renders hormone-like phosphatonin molecules inactive. People who believe there is a substantial genetic correlation between IQ and race continue to make this claim despite evidence to the contrary. FGF is less likely to be inactivated and broken down when the PHEX gene is altered, which raises phosphate excretion and jeopardizes bone mineralization.¹⁶ Mutations in the salt and phosphorus co-transporter gene cause significant dysfunctions in people with familial hypophosphatemic rickets with hypercalciuria. The increased intestinal calcium absorption caused by the high amount of calcitriol is likely the cause of hypercalciuria.^{17,21,22}

4. CONCLUSION

As a result, even if calculi are likely to form, the severity of the effects brought on by the lack of these minerals is less severe the earlier the diagnosis. Maintaining follow-up with acceptable drug use is necessary to sustain obtained gains. Lowering the morbidity of patients with chronic, incurable diseases whose clinical signs first appeared in infancy depends on early diagnosis and effective treatment. The child is already

bedridden for pneumonia, and the proper usage of drugs should modify another comorbidity. The child's follow-up with a suitable treatment plan helps the child's growth. Our work is to follow up with the child till age and closely monitor the comorbidities and current stage for betterment. More studies have been continued in future perspectives.

5. ETHICAL APPROVAL STATEMENT

The parents of the patients provided written consent, and the study was conducted and published with institutional approval.

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6. AUTHOR'S CONTRIBUTION STATEMENT

As I am the author of this research work, Mr N. Bragadeeswaran, Vindhya, Somasekar, Department of Pediatrics, Sree Balaji Medical College and Hospital, Chromepet, Chennai-600044. I am thankful to our department and hospital authority for providing me with such a way to do research work. The manuscript was revised by myself.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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