

Hypophosphatemia Dependent Rickets with Failure to Thrive (FTT) in a 4- Years Old Child: a Case Report

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Abstract

Background

Rickets is a disorder due to impaired metabolism of bone mineralization which caused by low concentrations of extra-cellular calcium or phosphate. In children, hypophosphatemic rickets (HR) happen malabsorption of phosphate and increasing of renal tubular loss.

Case Presentation

We present the case of a 4-year-old girl who had medical history of HR with failure to thrive (FTT). Child hospitalized several times due to osteomalacia and leg fractures. In physical examinations, there were obvious signs of rickets such as bow legs and hands, deviations of the wrist and chest pigeon. The results of blood tests showed low level of Phosphorus; but the level of calcium was normal. Radiography showed deformity of wrists and hands.

Conclusion

HR should be considered as one of the childhood disorders which impairs metabolism of bone mineralization and cause osteomalacia and bones fractures. If HR undiagnosed and remedies poor during childhood, in older ages would reveal automatic fractures and mineralization defects.

Key Words: Child, Hypophosphatemia, Hypophosphatemic rickets, FTT.

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1- INTRODUCTION

Rickets is a childhood disorder due to impaired metabolism of bone mineralization in osteoid matrix during growth, which caused by low concentrations of extra-cellular calcium or phosphate. In this disorders, failure of endochondral ossification can cause deformation in the growth plate and make disturbance in compromise both cortical and trabecular bone (1-3).

In early as second century in Roman children, rickets was known. The main cause of rickets was identification by Adolf Windaus in 1930 (4). Study of Shaw (2015) showed, over of 7.5 per 100,000 children under 5 years identified with rickets in the West Midlands region in 2001; also, 38 per 100,000 children in the South Asian (5). The clinical signs of rickets are based on age of appearance. The young infants may show Craniotabes due to softening of the skull bones, delayed tooth growing, bossing of the forehead, and widening of wrists. In the toddlers and young children can be made short stature, bow legs with Genu varum, and delayed walking with waddling gait (4). There are two types of rickets; Nutritional rickets (NR), due to vitamin D deficiency or low calcium concentration and other type of rickets is known as Non-nutritional rickets (NNR), which is revealed with hypophosphatemia and increased vitamin D-resistant rickets (HVDRR)(1, (6). Phosphate is one of the main elements for several physiologic pathways, such as the growth of the skeletal system, bone mineralization, nucleotide structure, and maintenance of plasma pH (7). The majority of phosphate is in bones, but in the kidneys, phosphate effects on homeostasis (8). Hypophosphatemia is determined by low phosphate levels and vitamin D-resistant rickets (6, (9). In children, hypophosphatemia is defined base on the age-related normal ranges. Sever hypophosphatemia can lead respiratory

system failure, neurologic system disorders (irritability, paresthesia, and seizures), cardiovascular dysfunction (arrhythmia, congestive heart disease, and cardiomyopathy), and Osteomalacia (10, 11). Hypophosphatemia dependent rickets due to malabsorption of phosphate, increasing of renal tubular loss, hereditary, and reduction of intestinal absorption (12). The most of reasons of hypophosphatemia rickets (HR) are related to fanconi's syndrome and genetic factors (4). This study aimed to introduce a 4- year-old girl who diagnosed with hypophosphatemic rickets.

2- CASE PRESENTATION

Case was a 4- year-old girl who complained from high- grad fevers for one week before hospitalization to the Imam Ali hospital in Zahedan city, (Province of Sistan and Balouchestan, South East of Iran), in 2015. The fevers of child developed following symptoms of coryza. Medical history of the child, showed history of HR with failure to thrive (FTT). Child hospitalized several times due to osteomalacia and leg fractures. In physical examinations, there are obvious signs of rickets such as pigeon chest (**Figure.1**), bow legs and hands, deformity of pelvic, club foot, deviations of the wrist, and delayed growth (**Figure. 2**).

In addition, child would not be able to walking from the birth to now due to clubfoot and osteomalacia. The child's family were not following the treatment of child's clubfoot. One considerable point was that the child had history of FTT. As, weight of child was 8,200 grams and the length was 74 cm which these show growing of child was not significant increase. Although, the child would not be able to standing and walking, but specking and mental and cognitive developments of child were appropriate and talked easily. The teeth of child grown, when the child

was two- years old. In blood tests, abnormal parameters of blood were as follows, Phosphorus = 1.2, Ca = 9.7 FBS = 104 ALK = 6981, SGOT = 97, total Bilirubin = 1.2, respectively. FBS at the beginning of hospitalization was 104 and in the latest test, achieve 93.

Also, liver enzymes were high levels. Hgb and MCV levels were low. Other biochemical and hematologic parameters of blood were normal (**Table.1**). The results of liver enzymes showed that her liver is

involved. The mother's child had history of gestational diabetes mellitus (GDM), and hypocalcaemia during his pregnancy.

His mother mentioned that uncle's child had delayed in mental and physical developments and wouldn't be able to walk, that it strengthen the factors of genetic for HR in this child. Radiography showed deformity of wrist, hand, lower limb bones and even knucklebones (**Figure.3**). Her prescribed medications included: Atiten, Rocaltrol and Vitamin AD.



Fig.1: Pigeon chest in a 4- year-old girl with HR



Fig.2: Bow legs and hands, club foot and deviations of the wrist in a 4- year-old girl with HR

Table-1: Results of blood tests in a child with HR

Results of blood tests in child	Normal levels of blood parameters	Results of blood tests in child	Normal levels of blood parameters
*Total Protein=5.8 mg/dl	(6-8mg/dl)	*Hgb=11mg/dl	(11.5-16 g/dl)
BUN=10.1 mg/dl	(10-25 mg/dl)	*MCV=66 fl	(80-100 fl)
Cr=0.4 mg/dl	(0.5-1.5 mg/dl)	PLT=210,000	(150,000 – 400,000)
CPK=61 units/l	(55-250 units/l)	CRP=Negative	Negative
LDH=10 units/l	(240 – 525 iu/l)	ESR=11 mm/h	(0-15mm/ h)
Na=135 mg/l	(135-145 mg/dl)	PT= 13 seconds	(10 – 14 Seconds)
K=3.5 mg/dl	(3.5 – 5 mmol/l)	PTT=42 seconds	(35 – 45 Seconds)
Ca= 9.7 mg/dl	(9-11.5 mg/dl)	*SGOT=97	(10-55U/L)
*Phosphorus=1.2mg/dl	(2.5-5 mg/dl)	*Total, bilirubin =1.2	(0.1-1 mg/dl)
*Alp=6981units/l	(85-300units/l)	*BS = 104	(70-110 mg/dl)
WBC=9500	(4000-10,000)		

*Abnormal levels of blood parameters; BUN: Blood urea index; Cr: Creatinine; CPK: Creatinine phosphokinase; LDH: Lactate dehydrogenase; BS: Blood sugar; ALP: Alkaline phosphatase; SGOT: Serum glutamic oxalo- acetic transaminase; MCV: Mean corpuscular volume; CRP: Creatinine protein; ESR: Erythrocyte sedimentation rate; LDH: Lactate dehydrogenase.



Fig.3: Deformity of wrist and hand in radiography in a 4- year-old girl with HR

4- DISCUSSION

Phosphate is a basic mineral for multiple functions, such as ossification, keep of the plasma pH, bone mineralization, tooth development, the growth of the skeletal system and nucleotide structure. The dominant of phosphate is in bones, but in

kidneys, phosphate homeostasis occurs with two important hormones included parathyroid hormone (PTH), and fibroblast growth factor 23 (FGF-23), and 1, 25-dihydroxyvitamin D (1,25(OH)₂ D), which increase phosphate intestinal absorption (7). The sources of phosphate in children

are consisted of egg, meat, poultry and legumes (13). The causes of hypophosphatemia are phosphate wasting through defects in tubular reabsorption of phosphorus, reduction of calcitriol and deficit in function of osteoblasts (7, (14). But the most reasons of hypophosphatemia is phosphate wasting. Reasons of phosphate wasting are mostly due to genetic defects in required factors for phosphate handling, so the most important factors which leading to phosphate wasting are congenital (6). There are two different types of phosphate wasting, first, secondary phosphate wasting is related to increased fibroblast growth factor 23 (FGF23), which is secreted by osteoblasts, and osteocytes, Second, phosphate wasting is related to a defect in primary renal tubular (15).

In hypophosphatemia achieves serum phosphate level $<2.5\text{mg/dL}$ and in severe hypophosphatemia achieves serum phosphate level $<1\text{mg/dL}$. Although, in hypophosphatemia serum phosphate level is low, but calcium concentration, vitamin D and parathyroid levels are normal (7). HR is known as a group of hereditary disorders and acquired conditions which, characterized by renal phosphate wasting, hypophosphatemia and abnormal level of vitamin D serum concentration (16).

In HR increases renal phosphate wasting and make disturbance in absorption of the sodium-phosphate co-transporter in the renal proximal tubules, so can lead to increasing urinary excretion of phosphate and resulted to hypophosphatemia (4, 12, 16). As well as, due to increasing of vitamin D-resistant with phosphate wasting, observed delayed walking, leg bowing, waddling gait, greater cartilages, bone pain, craniostenosis, and FTT obviously (6, 9). The treatment of HR was advanced since the availability of vitamin D analogs, such as calcitriol and 1-alpha-hydroxy vitamin D3 (Alfacalcidol).

In the mid-1970s started evolution in surgical procedures for leg deformities.

Also, other treatments are administrated for preventing the phosphate wasting, restoring serum alkaline phosphatase and keeping bone, such as oral phosphorus and Alphacalcidol (6). One of the clinical signs of HR is failure to thrive; Failure to thrive (FTT), is defined as lack of normal physical growth and weight loss below the third percentile for age on the growth chart. In study by Lay Hoon et al. (2016), were reported 5-10% of children in primary care settings and 3-5% of children hospitalization in hospitals diagnosed with FTT in the United States (17).

The main reasons of FTT in Iran, included, poverty, low educations of couple, lack of knowledge on nutrition and lack of accessibility on health services (18). The main signs of FTT is weight loss that weight-for-age is the simplest indexes for FTT diagnosis. Other indexes for FTT assessment are weight-for-height and height-for-age. FTT diagnosis requires growth measurements for over period of time (17).

5- CONCLUSION

Hypophosphatemia depended rickets should be considered as one of the childhood disorder which impairs metabolism of bone mineralization and cause osteomalacia and bones fractures. In HR increases renal phosphate wasting with increasing urinary excretion of phosphate, so can resulted to hypophosphatemia.

In hypophosphatemia observed delayed walking, leg bowing, waddling gait, greater cartilages, bone pain, and Craniostenosis in patients. If HR undiagnosed and remedies poor during childhood, in older ages would reveal bone pain, automatic fractures, mineralization defects such as osteomalacia, severe dental deformities, hearing loss, and fatigue. Our case describes a girl child with HR and FTT who had clinical and chemical signs of HR and she was on maintenance therapy with Atiten, Rocaltrol and Vitamin AD.

5- ABBREVIATION

- Ca: Calcium.
- Na: Sodium.
- K: Potassium.
- Hgb: Hemoglobin.
- PLT: Platelets.
- WBC: White blood cell.
- PT: Prothrombin time.
- PTT: Partial thromboplastin time.

6- CONFLICT OF INTEREST: None.

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