Familial hypophosphatemic rickets: report of a case

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

Nutritional status, both quantity and quality were adequate. Growth seemed to be delayed but development was normal.

Physical examination on admission showed that his body weight was 23 kg (<P5NCHS) and body height was 125 cm (<P5NCHS). He was alert and had no dyspnea or cyanosis. His vital signs were normal. Both legs were unable to straighten up; both knees were increased in size but no signs of inflammation. Other organs were normal.

Laboratory examination, including peripheral blood, urinalysis, renal function, and blood gas analysis revealed normal results. Sodium and blood calcium were normal. Serum potassium and phosphate, urine calcium and phosphate were decreased compared to the normal range. Alkaline phosphatase was increased.

Bone survey showed fractures that is located in the third distal part of both femurs that had already formed calluses (Figure 1), trabeculation in the hip, foot and skull, cupping, fraying, widening metaphysis (Figure 2) and rosary chest (Figure 3), and these findings were compatible with the diagnosis of hypophosphatemia. The swollen knees actually were fractured femur that had already filled with callus formation. The real knee was located 4 cm below this swelling region.

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Based on the above examinations, he was diagnosed as having FHR, treated with half a tablet of Lorinid two times a day, calcitriol 0.25 mg once a day, potassium 500 mg three times a day, and Joulie solution which consists of 2 g of Na$_3$HPO$_4$ and 350 mg of sodium bicarbonate, one capsule three times a day.

After one day of treatment, the patient showed signs of claw hands. Further analysis revealed that the patient suffered from hypocalcemia and was then treated with intravenous calcium and followed by oral calcium. After one month of treatment the patient already tried to walk with support and there was no more pain. The blood calcium decreased and the blood phosphate increased. Right knee circumference was 29 cm and left knee was 30 cm. After two months treatment, the patient could stand up by himself, but still had no balance. Knee circumference showed improvement, 28.5 cm on the right knee and 29 cm on the left knee. After four months of treatment, after we discussed it with an expert from USA, she suggested us to stop the Lorinid and the Potassium.

**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. In FHR, this process is not working. Literature said that a decreased activity of a sodium dependent phosphate transporter might be the one reason responsible for this defect.

Besides a defect in the proximal tubule, there is also a defect in the hydroxylation of 25-hydroxy vitamin D (25(OH)D$_3$) to 1,25-dihydroxy vitamin D (1,25(OH)$_2$D$_3$) that is also located in the kidney. 1,25-dihydroxy vitamin D is useful for increasing calcium absorption in the intestine.

There is a term called classic triad, that consists of hypo-phosphatemia, lower leg deformities and growth retardation in FHR case. Hypo-phosphatemia has already exist since a rickets’ patient was born. Besides hypophosphatemia, there is also a normal or low blood calcium, increased urinary phosphate and alkaline phosphatase and decreased urinary calcium. In our case, all laboratory findings were in accordance with the literature except for urinary phosphate.

Lower leg deformities, bowing and waddling gait usually manifest when a child began to walk around the age of 2 years. In our case, lower leg deformities started to exist at the age of 11 years. 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 on FHR patient is left untreated, his/her final height would only reach 130-165 cm. Normal growth can be maintained if the blood phosphate content is more than 3 mg/dl. There is a research about the usage of recombinant human growth hormone in an FHR patient. But the study concluded that there is no need to treat short stature in an FHR patient.

The height of our patient was only 125 cm and we all know that the 50th percentile of the NCHS curve for 12-year-old boys is 149 cm. It was difficult to conclude that this boy was a short stature because we did not know his previous body height.

The treatment for FHR consists of two kinds of preparations. The first one is called the Joulie solution. It consists of 136 g/dl Na$_3$HPO$_4$ and 58.8 g/dl phosphoric acid. The dose is 0.5-4 g/day, given 5-6 times a day. The side effects are diarrhea and hypocalcemia. Hypocalcemia frequently causes muscular spasm. In our case, we made a modification of Joulie solution by substitution of phosphoric acid with bicarbonate due to its strong acidity. At the first day of treatment, the side effect appeared. The patient got cramps and was treated with calcium immediately and the response was good. The second preparation consisted of vitamin D analog with the dose of 50-65 mg/kg/day. The advantages of this preparation is to increase calcium absorption in the intestine to prevent muscular spasm and stimulate bone recovery. Using only one preparation has no benefit at all. We have to use them in combination. If we use them before the age of 6, the lower leg deformities can spontaneously recover. In our case, a spontaneous recovery should not be expected because we use it when this patient was already 12 years old. Nevertheless, clinical and laboratory findings showed improvement.

Besides the advantages, there are also disadvantages of this combination; they can induce nephrocalcinosis and nephrolithiasis. It is said in some studies that this condition can occur as the cause of...
the increasing secretion of the urinary calcium. To solve the problem, some expert suggested tiazid and amilorid treatment. But the results are still a controversy.\textsuperscript{1,4} Formerly we used two preparations, but after four months of treatment we stopped it, because the treatment did not reveal any improvement.

Surgical intervention can only be performed if radiological finding shows an improvement and alkaline phosphatase turn to normal range.\textsuperscript{8} A long term follow up should be done to assess the effect of Joulie solution on bone recovery. Our goal is to make this patient normal.

\section*{References}