OBJECTIVES

X-Linked Dominant Hypophosphatemic Rickets

X-linked hypophosphatemic rickets (HR) is a group of rare disorders caused by an excessive renal phosphate wasting. X-linked HR (XLHR) is caused by mutation in PHEX (phosphate-regulating endopeptidase) gene and is characterized mainly by bone deformities, disproportionately short stature, dental anomalies and hypophosphatemia with coexisting low renal phosphate reabsorption. Early treatment with vitamin D and phosphate improves the patient’s growth. Recombinant human growth hormone (rhGH) may also improve growth in XLHR through a direct effect on growth cartilage, and by increasing renal phosphate reabsorption and serum phosphate levels.

AIM OF STUDY

The aim of the study was to investigate the clinical phenotype and molecular background of HR in a family in which XLHR was suspected.

CASE PRESENTATION

2 patients, 0.25 years old girl and 0.75 years old boy were diagnosed with HR at the age of 2.25 years and then treated with alfalcaldiol (73 and 69 mg/kg/d) and phosphate (175 and 39 mg/dl). Due to the diagnosis of growth hormone deficiency, rhGH therapy was initiated at the age of 0.75 years and 4.75 years, respectively (current doses of rhGH are 0.269 and 0.328 mg/kg/d).

METHODS AND RESULTS

DNA was isolated from fresh blood and all exons of PHEX gene were amplified using PCR and directly sequenced. The dominant clinical signs in both patients were bowing of legs and short stature. HtSDS at the time of diagnosis was -3.7 and -2.3, respectively. Current HtSDS is -3.4 and -2.1, respectively and the height gain during rhGH therapy was +0.3 and +1.04 SD. In the patient 1, we found a known c.4716T>T, p.T239M heterozygous polymorphism (rs7955866) in FGF23 gene which was absent in the patient’s affected father. We also found a novel heterozygous mutation c.326_327insCA, N110fs7 in PHEX gene which was also present in the patient’s father. FGF23 in the patient 2 was intact, but we found a known hemizygous mutation c.1801_2250del in PHEX gene covering exon 17 to exon 22.

CONCLUSIONS

- Early clinical and molecular diagnosis of HR, and early implementation of vitamin D and phosphorus is crucial to prevent severe bone deformities and to improve final height.
- rhGH therapy in patients with XHLR may be very effective in those with coexisting growth hormone deficiency.
- Genetic counseling in families with HR patients should be proposed.

References

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