Perinatal form hypophosphatasia caused by a novel large duplication of ALPL gene and one year follow


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Introduction

• Hypophosphatasia is a rare disease caused by mutations in the gene encoding tissue-nonspecific isoenzyme of alkaline phosphatase. Duplications of the ALPL gene account for fewer than 1% of the mutations causing HPP.
• It has been shown that asfotase alfa treatment mineralizes the skeleton and improves respiratory function and survival in severe forms of hypophosphatasia.

Case report

• The newborn was evaluated for respiratory failure and generalized hypotonia after birth. Diagnosis of HPP was based on low-serum ALP activity, high levels of substrates of tissue-nonspecific isoenzyme of alkaline phosphatase and radiologic findings.
• On day 21 after birth, enzyme replacement therapy using asfotase alfa (2 mg/kg three times per week, subcutaneous injection) was started (Figure 1).
• We were able to discharge our patient when he was 7 months old. His respiratory support was gradually reduced and skeletal mineralization improved during treatment. We increased the dose when we he 13 month-old due to incomplete resolution of radiological rickets findings. He has been no need any respiratuary support after 18 month old.
• He was operated for craniosynostosis at 23 month old.
• No mutation was detected in the ALPL gene by all exon sequencing, and additional analysis was done by quantitative polymerase chain reaction. As a result, a novel homozygote duplication encompassing exons 2 to 6 was detected (Figure 2).

Conclusion

• Early diagnosis and rapid intervention with enzyme replacement therapy is life-saving in the severe form of hypophosphatasia.
• Craniosynostosis can occur these patients although early enzyme replacement treatment.
• Quantitative polymerase chain reaction can detect duplications if a mutation cannot be detected by sequence analysis in patients with hypophosphatasia.