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

Bulent Hacihamdioglu*, Gamze Ozgurhan**, Catarina Pereira***, Emre Tepeli**, Gülşah Acar**, Serdar Cömert**
* Istinye University, Istanbul, Turkey
** University of Health Sciences, Suleymaniye Women Maternity and Child Diseases Training and Research Hospital, Istanbul
*** Centogene AG, Rostock, Germany

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).

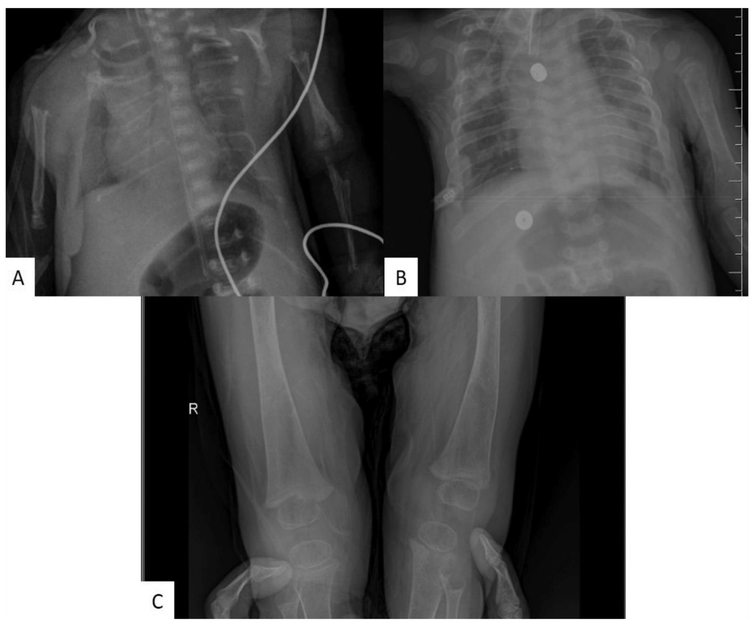

Figure 1. X-ray of the patient; (A) before treatment, (B and C) at 12 months of treatment. Note the general improvement of mineralization and of rachitic changes with asfotase alfa enzyme replacement therapy

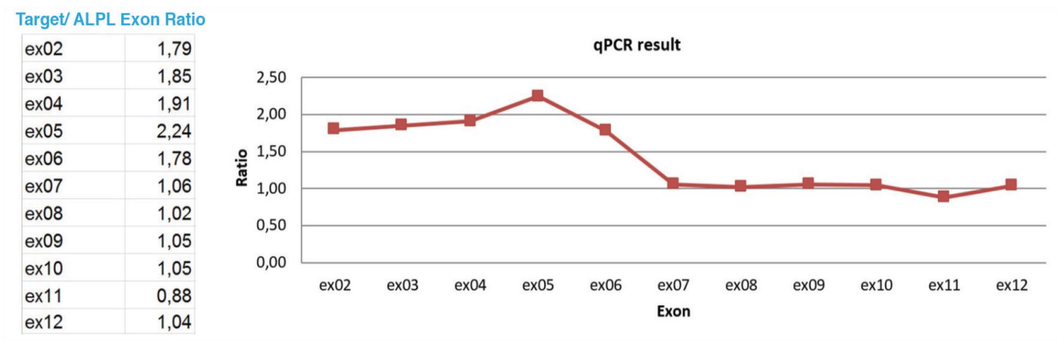

Figure 2. Quantitative polymerase chain reaction (qPCR) assay by using 11 gene-specific amplicons encompassing the coding exons 2 to 12 of the *ALPL* gene. Normalized qPCR ratios are WT (0.70-1.35) and homozygous duplication (4n) (1.75 -2.35)

qPCR: quantitative polymerase chain reaction

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.

58ESPE P2-051
Bone, growth plate and mineral metabolism
Bulent Hacihamdioglu
Poster presented at: ESPE 2019 VIENNA
PosterSessionOnline.com