



## **A new missense mutation in FGF23 gene in a male with hyperostosis-hyperphosphatemia syndrome (HHS)**

Farzaneh Abbasi<sup>1</sup>, Soudeh Ghafouri-Fard<sup>2</sup>, Azadeh Ebrahim-Habibi<sup>3,4</sup>

1. Growth and Development Research Center, Children Medical Hospital, Tehran University of Medical Sciences, Tehran, Iran

2. Department of Medical Genetics, Shahid Beheshti University of Medical sciences, Tehran, Iran

3. Biosensor Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

4. Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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Abstract

Background: Hyperostosis-hyperphosphataemia syndrome (HHS) is a rare autosomal recessive metabolic disorder, characterized by recurrent painful swelling of long bones, periosteal new bone formation and cortical hyperostosis or intramedullary sclerosis, hyperphosphatemia and low intact fibroblast growth factor 23 (FGF23) protein levels. It is caused by mutations in 2 genes, N-acetylgalactosaminyltransferase 3 (GalNAc-transferase; GALNT3) and FGF23.

Method: Blood sample was collected from the patient. DNA was isolated using the standard salting out method. All exons and exon-intron boundaries of GALNT3 and FGF23 genes were amplified according to Ichikawa et al and Garringer et al respectively (2, 7). PCR products were sequenced using the ABI Prism3130 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). In order to analyze the effects of observed missense variant PolyPhen-2 was used. This software shows that the mutation leads to substitution of a highly conserved amino acid and is predicted to be probably damaging with a score of 1.000. With this software, values nearer 1 are more confidently predicted to be deleterious.

Results: No nucleotide change was observed in GALNT3 exons and exon-intron boundaries. However, a homozygous mutation was detected in exon 3 of FGF23 gene (NM\_020638.2: c.471C>A) (Figure 1). The nucleotide change results in aminoacid change from phenylalanine 157 to leucin (p.F157L) in receptor interaction site.

Conclusion: Previous researches have proposed that HFTC (Hyperphosphatemic familial tumoral calcinosis )and HHS are clinical variants of the same disease . This study, in accordance with previous studies shows that FGF23 mutations can cause HHS.

