2021 International Conference on Human Genetics and Genomics
1-2 December
Yazd University

A Iranian long chain-3-hydroxyacyl-CoA dehydrogenase deficiency patient with HADHA mutations: Case Report

Maliheh Alimardani[1,2,3] , Reza Ebrahimzadeh-Vesal [5], Mohammad Reza Abbaszadegan[2,4,5]*

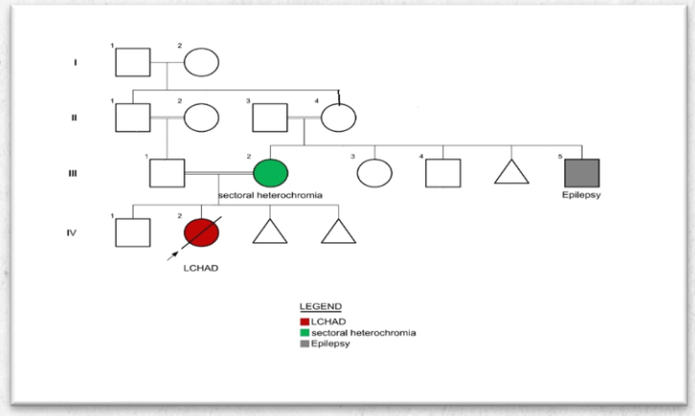
[1]Medical Genetics Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [2]Department of Medical Genetics and Molecular Medicine, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [3] Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [4] Immunology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran [5] Pardis Pathobiology and Genetics laboratory, Mashhad, Iran
*Corresponding author: AbbaszadeganMR@mums.ac.ir, m.r.abbaszadegan@gmail.com

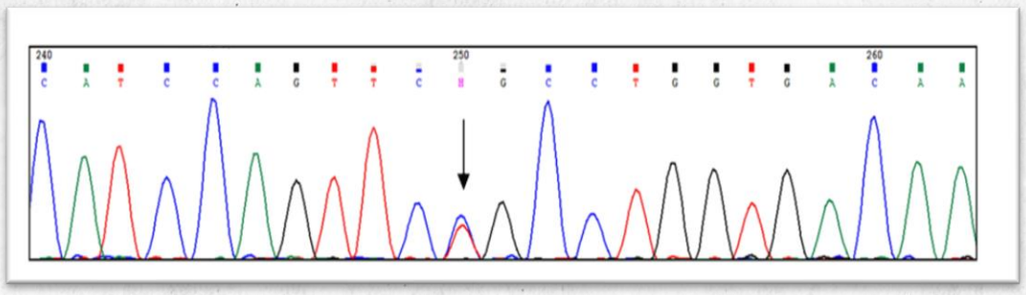
Background

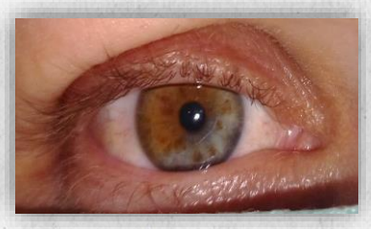
Mitochondrial trifunctional protein (M-FTP) deficiency, as a rare metabolic disorder, classified into three phenotypes including lethal phenotype which begins in the neonatal period. The M-FTP protein catalyzes the oxidation of long chain fatty and composed of 8 subunits such long-chain 2,3-enoyl-CoA hydratase (LCEH) and long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD). LCHAD deficiency inherited as an autosomal recessive trait and associated with HADHA gene mutations (OMIM: 600890). These causes a clinical spectrum of symptoms such as progressive peripheral neuropathy, hypoketotic hypoglycemia, hepatopathy, cardiomyopathy, myopathy and pigmentary retinopathy.

Case presentation

We report an Iranian girl with an initial diagnosis of LCHAD deficiency using tandem mass spectrometry (MS/MS) who unexpectedly died on the 70th day after birth. The parents were first cousins, with one healthy son, and a history of two previous miscarriages (Figure 1).







Results & Conclusion

When an AR disorder occurs in a family without familial history, the whole exome sequencing (WES) is an option to identify the genetic causal mutation in the parents of deceased child and then further confirmed by Sanger sequencing. The mother, with sectoral heterochromia, had heterozygous missense mutation “c.2026C>T (p.Arg676Cys)” mutations in the HADHA gene, diagnosed by WES. According to ACMG guideline and several prediction tools, this mutation is known as likely pathogenic mutation. Furthermore, she had 2 other heterozygous missense mutations in CFTR and PLEKHG2 genes. Then, these 3 mutations were examined in her husband by sanger sequencing and the heterozygosity for “c.2026C>T (p.Arg676Cys)” mutations in the HADHA gene was detected. Due to the validation of carrier state for mutant alleles in both parents and pathogenicity of c.2026C>T mutation in HADHA gene, this is the cause of the disease in deceased affected child. Moreover, it is important to perform genetic counseling and prenatal diagnosis (PND) for next pregnancy to prevent the birth of another affected child.