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

A Novel Missense Mutation (c.215G>A) in Two Iranian Siblings with Combined Oxidative Phosphorylation Defect Type 7: A Case Report

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Background

Combined oxidative phosphorylation defect type 7 is a rare mitochondrial disease resulting from the malfunction of the translational termination factor c12orf65, leading to the disrupted mitochondrial protein synthesis. It is characterized by vision issues and global muscle atrophy. With prevalence of < 1 in 1,000,000 less than ten mutations have been reported to cause the disease.

Materials and Methods

The proband demonstrated intellectual disability, global developmental delay, visual impairment, strabismus and scoliosis. WES and Sanger sequencing were carried out to confirm the mutations in the proband and additional family members, as well as ssessing the variant against various databases namely VarSome and HGMD.

Results

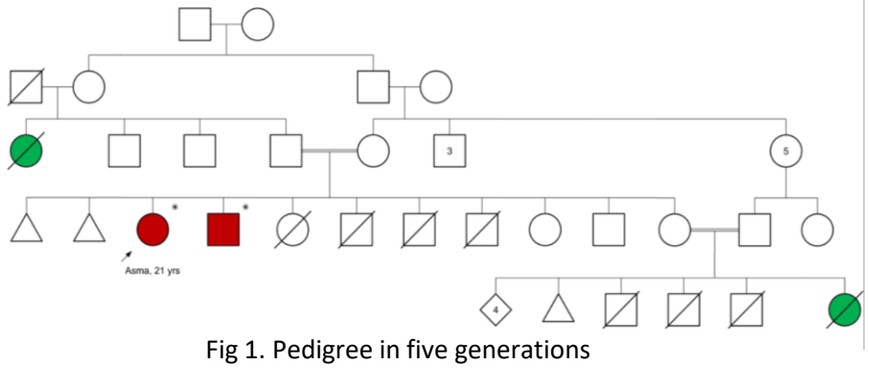

Fig 1. Pedigree in five generations

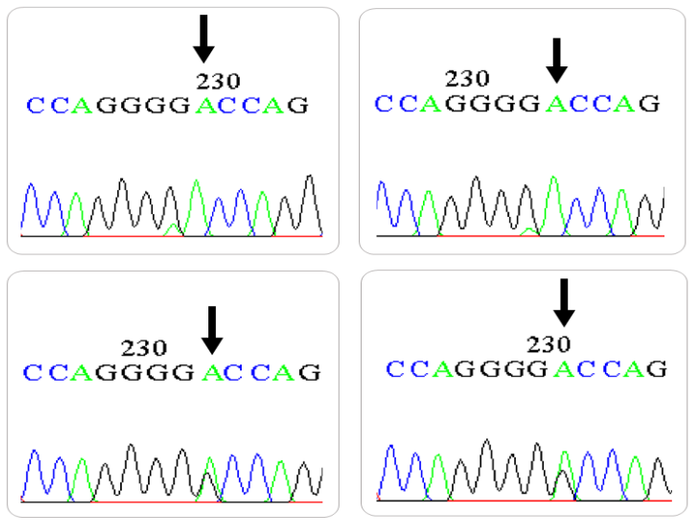

Fig 2. Sanger results indicating the mutation in affected family members

Conclusion

The WES data identified the variant in the proband as likely pathogenic. Sanger results were consistent with WES results, confirming the segregation of c.215G>A with the phenotypes. Here we report c.215G>A as a novel homozygous variant in C12orf65 as the first missense mutation to cause the disease, suggesting a loss of function mechanism might have led to the multisystemic phenotypes.

References

1. Shimazaki, Haruo, et al. "A homozygous mutation of C12orf65 causes spastic paraplegia with optic atrophy and neuropathy (SPG55)." Journal of medical genetics 49.12 (2012): 777-784.

2. Spiegel, Ronen, et al. "Delineation of C12orf65-related phenotypes: a genotype–phenotype relationship." European Journal of Human Genetics 22.8 (2014): 1019-1025.