ELOVL4 mutation in a case with ichthyosis, spastic quadriplegia, and mental retardation syndrome (ISQMR)

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INTRODUCTION

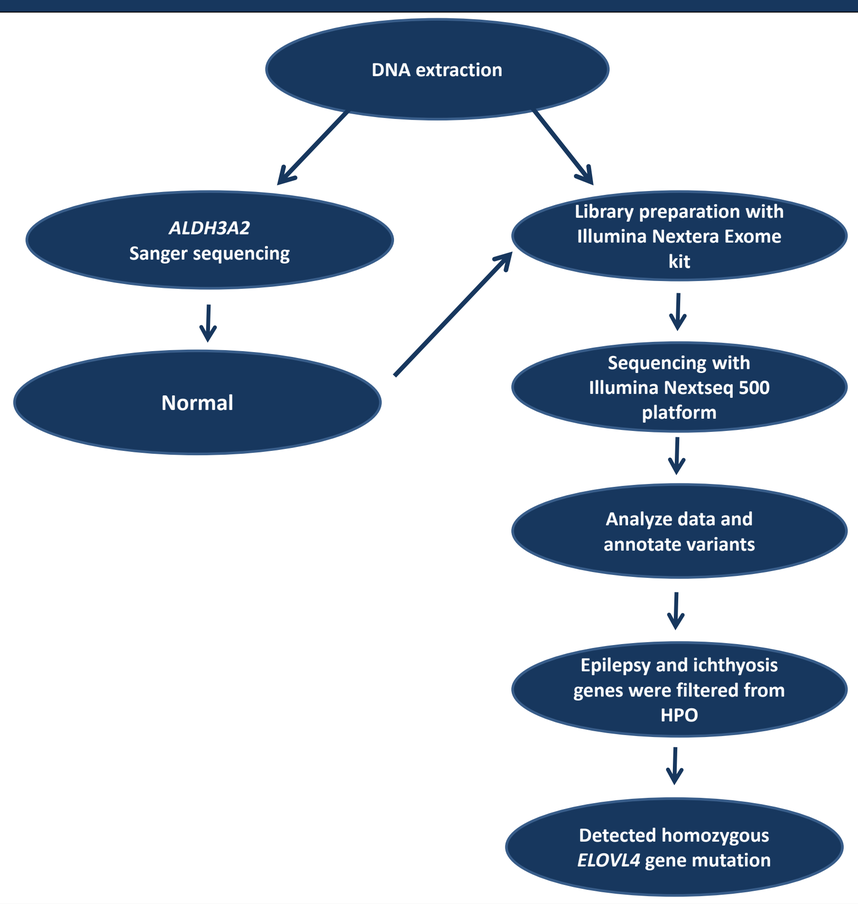
Ichthyosis, spastic quadriplegia and mental retardation syndrome (ISQMR) is a autosomal recessive disorder which is characterized by ichthyosis, profound psychomotor retardation, spastic quadriplegia and seizures[1].

ISQMR syndrome is caused by biallelic mutation in the *ELOVL4* gene on chromosome 6q14[2,3]. Within the retina, the *ELOVL4* protein is produced in specialized light receptor cells (photoreceptors). The *ELOVL4* protein is also found in the brain and skin, but less is known about its activity (expression) in these structures[4].

Sjögren-Larsson syndrome initially comes to mind in cases with ichthyosis and neurological abnormalities including epilepsy. *ALDH3A2* gene have been found to cause Sjögren-Larsson syndrome, a condition characterized by ichthyosis, neurological abnormalities and eye problems. These abnormalities underlie the characteristic signs and symptoms of Sjögren-Larsson syndrome[5,6].

Case with congenital ichthyosis, psychomotor retardation and epilepsy who had consanguinity between her parents was referred to us for evaluation of genetic diseases. Firstly, we performed *ALDH3A2* Sanger sequence analysis but did not detect any mutation. In the second stage, we planned Whole Exome Sequencing (WES) with preliminary diagnosis of epileptic encephalopathy and congenital ichthyosis.

METHODS



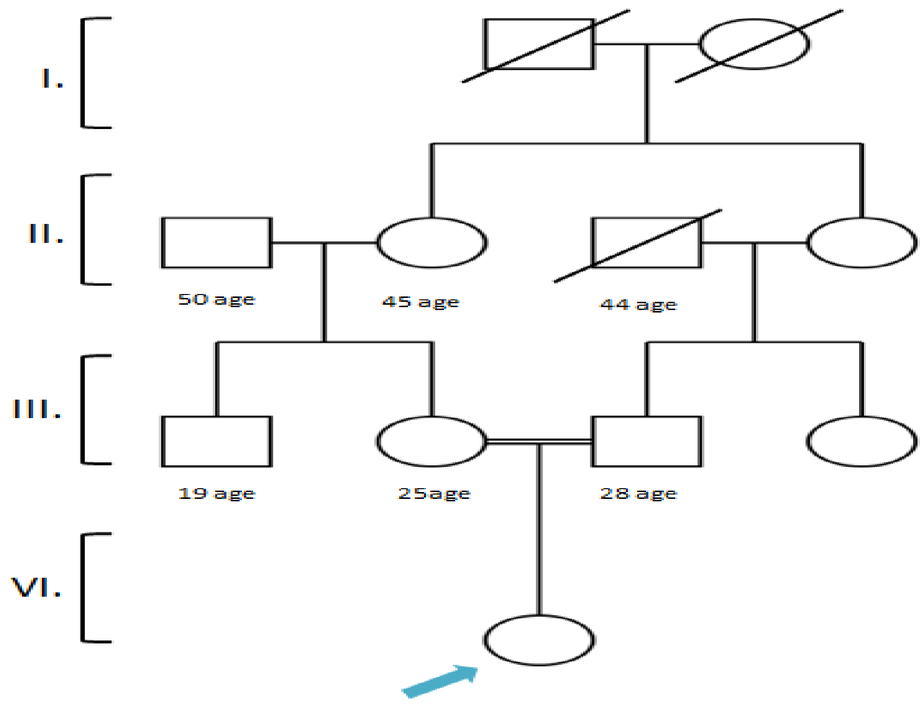


Figure 1. Pedigri chart

Figure 2. IGV Results

DANN Score	MutationTaster	GERP (RS)	SIFT	PROVEAN	GnomAD
0.9982	Disease causing	5.82	Damaging	Damaging	N/A

Table 1. In slico datas of ELOVL4 gene

RESULTS

We examined the *ALDH3A2* gene sequence analysis and found no mutations. As a second step we performed Whole Exom Sequence. Genes associated with epilepsy and ichthyosis phenotypes were filtered from Human Phenotype Ontology (HPO). We detected p.H192R (c.575A>G) homozygous mutation in *ELOVL4* gene which is reported with 'Ichthyosis, underdevelopment and microcephaly' phenotype before.

DISCUSSION & CONCLUSION

- ***ELOVL4* (NM_022726.3) gene p.H192R (c.575A>G) missense variant is classified as 'cause of disease mutation' for 'Ichthyosis, underdevelopment and microcephaly' with access number of CM178648 in Human Genome Database (HGMD). According to American College of Medical Genetics (ACMG) criteria (PM2, PP3) it is classified as ' Uncertain Significance' variant.**
- **In both father and mother, we identified a heterozygous mutation in *ELOVL4* gene. We also determined the same variant as homozygous in their child.**
- **Our results are compatible with ressesive inheritance pattern and familial segregation. As a result we have correlated this variant with the ISQMR phenotype and evaluated it as likely pathogenic.**
- **We aimed to emphasize that we should be kept in mind *ELOVL4* gene together with the *ALDH3A2* gene (was associated with Sjogren-Larsson syndrome) in patients with congenital ichthyosis, psychomotor retardation and seizures.**

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