

Successful diagnosis of hyperphosphatasia with mental retardation syndrome type 4 after detecting the c.181+1G>T variant in the PGAP3 gene – using CentoGenome®

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Geographic region

Saudi Arabia, Middle East

Clinical information

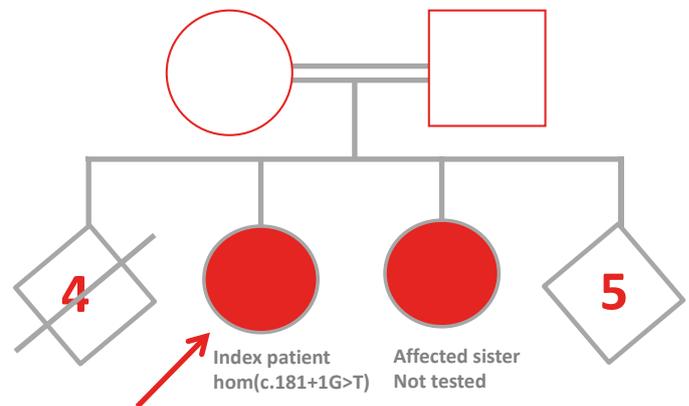
The index patient is a 36 year old female presenting with delayed motor and language development, intellectual disability, muscular hypotonia, generalized seizures, and glaucoma. Parents are consanguineous and healthy; they had 5 healthy children, 1 affected daughter, 4 deceased children (male & female) with a similar phenotype of the index patient, and 1 daughter who was not tested.

Whole exome sequencing (WES) has not shown any variants relevant to the described phenotype for the index patient and the parents.

Diagnostic procedure

Using whole genome sequencing (CentoGenome®), a previously unreported homozygous variant in the PGAP3 gene, c.181+1G>T was detected. This substitution is located in the donor splice site of intron 1. The consequence of this change is not predictable, but a skip of exon 1 is quite probable. This variant was also detected in both parents of the index patient in a heterozygous state.

The homozygous state of the PGAP3 gene c.181+1G>T variant in the index patient was genetically confirmed, which is consistent with the clinical diagnosis of hyperphosphatasia with mental retardation syndrome type 4. This is an autosomal recessive neurologic



disorder characterized by severely delayed psychomotor development, mental retardation, lack of speech acquisition, seizures, and dysmorphic facial features.

Early diagnosis and treatment for seizures and other treatable symptoms could effectively improve the quality of the patient's life.

Due to the lack of complete coverage, this variant could not be identified with WES analysis. CentoGenome® enabled us to identify the genetic cause. In addition genetic counseling for the actual diagnosis was available for the family for an early and effective symptomatic treatment.

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