CENTOGENE
THE RARE DISEASE COMPANY

CentoXome®

CASE STUDY: DIAGNOSIS OF A PRIMARY COENZYME Q10 DEFICIENCY-4

CASE HISTORY

The patient is a 30-year-old male who has presented with dystonia since the age of 12. He has progressive generalized ataxia and axial dystonia. There is no family history of the disease. A diagnosis of hereditary dystonia was considered. Previous genetic testing for the *THAP1* gene, which causes dystonia type 6, was negative.

REASONS FOR TESTING

The patient and his partner are considering having a child. They requested further testing to identify and confirm a genetic diagnosis in order to help determine the risks for their future children. Additionally, depending on the diagnosis, targeted management or treatment options might be available for the patient.

TEST ORDERED

Whole exome sequencing, CentoXome®, was ordered on the patient to target all relevant genes related to the patient's phenotype in one test.

RESULTS

Two pathogenic variants were detected

GENE	VARIANT	ZYGOSITY	CLASSIFICATION	INHERITANCE
COQ8A (*ADCK3*)	c.1399_1408del	Het.	Likely pathogenic	Maternal
	c.901C>T (p.Arg301Trp)	Het.	Variant of uncertain clinical significance (VUS)	Paternal

- **c.13993_1408del** has not been reported in individuals with disease nor in the general population. It affects the acceptor splice site of exon 12, likely resulting in the skipping of exon 12
- **c.901C>T (p.Arg301Trp)** has not been reported in individuals with disease but has been reported in only 4 out of 120,446 alleles in the general population. In-silico tools (PolyPhen-2, SIFT, MutationTaster and Align-GVGD) predict the variant to be probably damaging.
- Parental testing confirmed that the variants are in trans and that each parent is a carrier of one of the variants

POST-TESTING

- The patient was placed on coenzyme Q10 substitution (200 mg tid)
- After starting the coenzyme Q10 supplementation, the patient showed a marked response with almost complete resolution of his neurological symptoms
- Risk counseling for pregnancy planning is now possible

DISEASE INFORMATION

Pathogenic variants in the *COQ8A* gene cause autosomal recessive primary coenzyme Q10 deficiency type 4 (COQ10D4; OMIM: 612016), also known as spinocerebellar ataxia type 9 (*SCAR9*). It is characterized by cerebellar ataxia and exercise intolerance. Affected individuals can also develop seizures, dystonia and spasticity. The clinical presentation is a highly variable spectrum of ataxic phenotypes - presenting as a slowly progressive ataxia or as a severe infantile encephalopathy with cerebellar atrophy.[1] Although oral coenzyme Q10 supplementation has been shown to be ineffective in individuals with *COQ8A*-related primary CoQ10 deficiency, a few individuals had improved neurological outcomes after treatment.[1,2]

CONCLUSION

CentoXome® was able to diagnose the patient are having primary coenzyme Q10 deficiency type 4, ending the diagnostic odyssey. This allowed appropriate treatment and management resulting in mitigation of the patient's symptoms. The confirmed diagnosis also provided risk information to help the patient and his partner with pre-conceptional counseling.

REFERENCES

[1] Mignot *et al.* 2013, PMID: 24164873
[2] Lagier-Tourenne *et al.* 2018, PMID: 18319074

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