MedCrave
Step into the World of Research
International Physical Medicine & Rehabilitation Journal

Case Report

Open Access
CrossMark

Homozygosis variant p.asn115* in the ANO10 gene: a new discovered cause of spinocerebellar Ataxia

Abstract

The spinocerebellar ataxia recessive type 10 is a genetic form associated with ANO10 gene mutations. Affected individuals present with ataxia, hyperreflexia, ocular movement disorders and cerebellar atrophy. The homozygous variant in the ANO10 gene NP_060545.3:p.Asn114* is a 2-nucleotide deletion that would cause the introduction of a premature stop codon at the same position, that has not been previously described in the scientific literature related to disease and it perfectly explains our patient's condition.

Keywords: spinocerebellar ataxia, ANO10 gene, hyperreflexia, polyneuropathy, autosomal recessive

Volume 7 Issue 3 - 2022

Iria Beltrán Rodríguez, Adrián Arés Luque, Laura García-Talavera Casado
Assistance Complex, León University, Spain

Correspondence: Iria Beltrán Rodríguez, León University, Assistance Complex, Spain, Tel 34666640224, Email iriabeltranrodrigue@gmail.com

Received: November 15, 2022 | **Published:** November 28, 2022

Text

Autosomal recessive ataxias are rare genetic diseases primarily characterized by progressive gait and limb cerebellar ataxia, often associated with other neurological or non-neurological symptoms.[1,2] SCAR10: spinocerebellar ataxia recessive type 10 is a genetic form associated with mutations in the ANO10 gene,[1,3] which encodes a transmembrane protein, part of the calcium-activated chloride channels.[1,4] Recent advances in next-generation sequencing have significantly improved the mutation detection rate of inherited ataxia.[5] Particularly suggestive of autosomal recessive inheritance is the presence of similar cases in the sibship or those arising from parental consanguinity even though both parents are healthy.[6]

At least 30 missense, nonsense, frameshift and splicing site variants have been described. Affected individuals present with ataxia associated with hyperreflexia, ocular movement disorders and cerebellar atrophy, with a variable age of onset that is ranged between 27 and 53years old.[1] Additionally, the presence of intellectual disability, motor neuron involvement, bradykinesia and epilepsy has been described in some patients, configuring an expanded phenotypic spectrum. Infrequently, some authors have reported the existence of low levels of coenzyme Q10, pes cavus and tortuosity in the conjunctival vessels, as in the case of the patient under study. Marked cerebellar atrophy with normal supratentorial structures is a typical feature in this patient.[7]

We present the case of a 55-year-old right-handed male with a history of: no known allergies, no alcohol, tobacco or other drugs consumption. No vascular risk factors. Left hip prosthesis. History of family consanguinity (second cousin parents); sister affected by hereditary spinocerebellar ataxia. He begins in the fifth decade of life with clinical signs consisting of increasing dysarthria, poor vision with occasional diplopia, dysphagia that requires thickeners and significant gait disturbances that only allows short trips, at home, and supported. Followed up at "León University Assistance Complex" since 2010 due to suspicion of late-onset hereditary cerebellar ataxia, since then, he has presented clinical progression with severe limitation of his functional motor performance, severe ataxia that makes it difficult for him to walk and requires a wheelchair and worsening of speech articulation and dysphagia with loss weight of about 20kg in 1year. He also presents with urinary urgency and depressive tendency without cognitive impairment.

Physical examination revealed severe scandid dysarthria, inexhaustible multidirectional nystagmus: spontaneous down-beating and nystagmus on lateral gaze. Diplopia at the beginning of the gaze, with normal eye fundus but with conjunctival telangiectasias. No facial or cervical muscle weakness. Difficulty coughing. Decreased gag reflex and decreased soft palate elevation. Atrophy of the shoulder and pelvic girdle muscles. Strength: 4/5 proximal in all four limbs, tetrapendicular ataxia that worsens when visual input is removed. No signs of hyperreflexia. Gait ataxia.

Supplementary tests

Analytics: normal biochemistry including vitamin E, B12, folic acid, thyroid hormones, CK 248, normal blood count and coagulation; normal proteinogram; normal nerve conduction studies and electromyogram, without associated polyneuropathy; Somatosensory evoked potentials: mild axonal involvement of both posterior cords; Magnetic Resonance Imaging: generalized cerebellar atrophy pattern; Auditory and visual evoked potentials: normal; Normal echocardiogram; normal spirometry.

Genetic study

Homozygous variant in the ANO10 gene: NP_060545.3:p.Asn114* related to spinocerebellar ataxia type 10 with autosomal recessive transmission that explains the patient's phenotype.

Discussion

Autosomal recessive cerebellar ataxia is a rare inherited disorder caused by mutations in the ANO10 gene. From our point of view, performing mutational screening is very important to be able to describe new mutations and contribute to the investigation of this disease. According to this, and as far as we have been able to investigate, the homozygous variant in the ANO10 gene NP_060545.3:p.Asn114* has not been previously described in the scientific literature related to this disease, and it does not appear collected in genotyping databases in the general population used as a control population, which suggests that its allelic frequency could be very low in the general population. This variant is a 2-nucleotide deletion that would cause the introduction of a premature stop codon at the same position. In the absence of experimental studies, although it is not possible to determine the functional consequences of this variant, it can be inferred that the abnormal products may not carry out their function correctly.

Conclusion

1. The homozygous variant in the ANO10 gene NP_060545.3:p.Asn114* is a new mutation in this gene which has not been

previously described in the scientific literature related to spinocerebellar ataxia recessive type 10.

2. This variant is a 2-nucleotide deletion that would cause the introduction of a premature stop codon at the same position, causing abnormal products that may not carry out their function correctly.
3. There is a clear need to continue performing mutational screening to the new patients with spinocerebellar ataxia recessive type 10, trying to describe new mutations and contributing to the investigation of this disease.

Acknowledgments

None.

Funding

None.

Conflicts of interest

Author declares that there is no conflict of interest.

References

1. Nanetti L, Sarto E, Castaldo A, et al. ANO10 mutational screening in recessive ataxia: genetic findings and refinement of the clinical phenotype. *J Neurol.* 2019;266(2):378–385.
2. Parodi L, Coarelli G, Stevanin G, et al. Hereditary ataxias and paraparesias: clinical and genetic update. *Curr Opin Neurol*. 2018;31(4):462–471.
3. Beaudin M, Matilla DA, Soong BW, et al. The Classification of Autosomal Recessive Cerebellar Ataxias: a Consensus Statement from the Society for Research on the Cerebellum and Ataxias Task Force. *Cerebellum*. 2019;18(6):1098–1125.
4. Vermeer S, Hoischen A, Meijer RP, et al. Targeted next–generation sequencing of a 12.5 Mb homozygous region reveals ANO10 mutations in patients with autosomal–recessive cerebellar ataxia. *Am J Hum Genet*. 2010;87(6):813–819.
5. Balreira A, Boczonadi V, Barca E, et al. ANO10 mutations cause ataxia and coenzyme Q_{10} deficiency. *J Neurol*. 2014;261(11):2192–2198.
6. Anheim M, Tranchant C, Koenig M. The autosomal recessive cerebellar ataxias. *N Engl J Med*. 2012;366(7):636–646.
7. Renaud M, Anheim M, Kamsteeg EJ, et al. Autosomal recessive cerebellar ataxia type 3 due to ANO10 mutations: delineation and genotype–phenotype correlation study. *JAMA Neurol*. 2014;71(10):1305–1310.