Hereditary spastic paraplegia caused by compound heterozygous mutations outside the motor domain of the KIF1A gene.


Abstract

BACKGROUND AND PURPOSE: Hereditary spastic paraplegia is a clinically and genetically heterogeneous group of rare, inherited disorders causing an upper motor neuron syndrome with (complex) or without (pure) additional neurological symptoms. Mutations in the KIF1A gene have already been associated with recessive and dominant forms of hereditary spastic paraplegia (SPG30) in a few cases.

METHODS: All family members included in the study were examined neurologically. Whole-exome sequencing was used in affected individuals to identify the responsible candidate gene. Conventional Sanger sequencing was conducted to validate familial segregation.

RESULTS: A family of Macedonian origin with two affected siblings, one with slowly progressive and the other one with a more complex and rapidly progressing hereditary spastic paraplegia is reported. In both affected individuals, two novel pathogenic mutations outside the motor domain of the KIF1A gene were found (NM_001244008.1:c.2909G>A, p.Arg970His and c.1214dup, p.As405Lysfs*40) that segregate with the disease within the family establishing the diagnosis of autosomal recessive SPG30.

CONCLUSIONS: This report provides the first evidence that mutations outside the motor domain of the gene can cause (recessive) SPG30 and extends the genotype-phenotype association for KIF1A-related diseases.

© 2017 EAN.

KEYWORDS: KIF1A; SPG30; hereditary spastic paraplegia; spastic paraparesis; whole-exome sequencing

PMID: 28332297 DOI: 10.1111/ene.13279