論 文 要 旨

A *PRIMPOL* mutation and variants in multiple genes may contribute to phenotypes in a familial case with chronic progressive external ophthalmoplegia symptoms

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Abstract

Chronic progressive external ophthalmoplegia (CPEO) is one of the most common mitochondrial disorders. It is characterized by bilateral, slowly progressing loss of extraocular muscle mobility, orbicularis oculi weakness, ptosis and other neuromuscular symptoms, which are caused by the accumulation of multiple mitochondrial DNA (mtDNA) deletions. Many mutations in different nuclear genes, such as *POLG1*, *POLG2*, *ANT1* and others, have been described as causing autosomal-inherited CPEO with multiple mtDNA deletions. Most causative genes are involved in mtDNA replication impairment. Here, we report a family with CPEO-like symptoms characterized by multiple muscle mtDNA deletions, ptosis, diabetes, hearing loss, mental retardation, and emotional instability. We performed genetic analyses to identify nuclear gene mutations in the family. DNA from the proband was analyzed by whole-exome sequencing. In addition to possible pathogenic mutations, rare variants were prioritized for gene-functional phenotype interpretation. We found possible pathogenetic mutations in the *PRIMPOL*, *BRCA1*, *CPT2*, and *GJB2* genes, and functional polymorphisms in the *CARD8,* and *MEFV* genes. Multiple functional polymorphism and possible pathogenic mutations may contribute to mitochondrial-disease-like phenotypes in a composite manner.