P-712 - POLG MUTATION IN A PATIENT WITH RECURRENT MAJOR DEPRESSION, CARDIOMYOPATHY AND ATAXIA

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Introduction: Spinocerebellar ataxias represent a heterogeneous group of neurodegenerative disorders. Over the last decade, novel mitochondrial genetic diseases have been identified in which mutations in DNA polymerase γ (*POLG*) gene are involved. POLG1 is essential for mitochondrial (mt) DNA replication and repair. At present, more than 100 disease mutations in POLG have been indentified that are causally related to an array of multi-system neuropsychiatric diseases.
Objectives: The significance of POLG in the pathophysiology of complex neuropsychiatric disorders.
Aims: Studying the involvement of POLG mutation in major depression.
Methods: Detailed diagnostic evaluation, including genetic analysis, of a middle aged female patient with recurrent psychotic depression, slowly progressive gait instability and dilated cardiomyopathy.
Results: As to psychiatry, major depression with psychotic features was present. The diagnosis of dilatated cardiomyopathy was confirmed. MRI scanning of the brain demonstrated marked cerebellar atrophy. Neuropsychological functioning was characterized by a sub-average disability, lowered speed of information processing and a relatively intact working memory. Extensive genetic and metabolic investigation demonstrated a nucleotide substitution c.2207 A→G in the *POLG* gene resulting in amino acid change Asn 736Ser in exon 13. This mutation was considered to be compatible with a mitochondrial disorder and implicated in the pathophysiology of the neuropsychiatric syndrome.
Conclusions: This novel POLG mutation is considered to be the etiological explanation for the combination of major depression, cardiomyopathy, and ataxia. In patients with complex neuropsychiatric disorders, extensive diagnostic analyses is warranted, including the search for mitochondriopathies.

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