EXPANDING THE CLINICAL PHENOTYPE OF GBA-ASSOCIATED PARKINSONISM: A CASE REPORT

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OBJECTIVE. Glucocerebrosidase (GBA) is a gene coding for lysosomal enzyme glucocerebrosidase (GCase), whose biallelic mutations cause Gaucher disease. GBA monoallelic mutations are relevant risk factor for development of Parkinson's disease (PD). Clinically, GBA-PD has been associated with a higher prevalence of non-motor symptoms and increased risk of autonomic dysfunction and cognitive impairment over time compared to non-carriers. We report the case of a patient carrying a monoallelic pathogenic GBA mutation and presenting with a corticobasal syndrome (CBS) phenotype.

MATERIALS. This is a 66-years-old male with 3-year history of progressive poorly levodopa responsive right-side akinetic parkinsonism and language/speech difficulties. Over the disease course he also developed postural instability with frequent falls. He also referred rapid eye movement sleep behavioural disorder. No hallucinations nor autonomic dysfunction was reported by the patient/care giver. He has no familiar history of neurological/psychiatric disorders.

METODS. Brain magnetic resonance imaging (MRI), blood tests and neuropsychological assessment were obtained. A massive sequencing of known genes associated with parkinsonism and dementia was also performed.

RESULTS. Neurological examination showed hypomimic face, dysarthria, vertical slow saccades, brisk DTRs in the upper and lower right arms, asymmetric right-side akinetic rigid parkinsonism with flexor dystonia and ideo-motor apraxia in the right arm. Complete blood counts, vitamin B12 and serum levels, thyroid, renal and liver functioning tests, electrolytes, copper metabolism and glucose levels were normal. Neuropsychological assessment revealed the presence of mild cognitive impairment (memory, executive, language and visuospatial domains involved) and mood disturbances (depression). Brain MRI showed midbrain and left parietal cortical severe atrophy. According to clinical and neuroimaging findings, a diagnosis of probable CBS was performed. Genetic testing revealed the presence of a heterozygous c.1226A > G (p.Asn409Ser) variant in the GBA gene, also known as N370S.

DISCUSSION. GBA mutations have been associated to the whole spectrum of atypical parkinsonism and dementia, especially synucleinopathies. A few cases of patients presenting with CBS as well as Progressive Supranuclear Palsy and carrying N370S mutation have also been described in the literature.

CONCLUSION. This case expand the phenotypic expression of GBA variants and highlights that, although rarely, GBA-related atypical parkinsonism may also lie in the spectrum of tauopathies. This may suggest a more complex role of GCcase functioning in neurodegenerative disorders. Genetic screening should be considered in selected cases, with or without clinical signs suggestive of synucleinopathies

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