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Corpus callosum hypoplasia and parkinsonism with poor response to levodopa in DYNC1H1 mutation

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Background: Mutations in the cytoplasmic dynein 1 heavy chain 1 gene (DYNC1H1) are associate with autosomal dominant lower extremity-predominant spinal muscular atrophy [1-2], neuromuscular [3-4] and neurodevelopmental disorders [5], and hereditary spastic paraplegia. To the best of our knowledge, only one case was reported of DYNC1H1 haploinsufficiency with associated parkinsonian features responding to levodopa [6].

Aim and Methods: Case presentation and literature review.

Results: A 58-years-old caucasian man developed progressive motor slowing in right limbs. His medical history revealed diabetes mellitus type 2 and arterial hypertension. His family was non-consanguineous, his brother suffered from intellectual disability, epilepsy and interatrial septum aneurysm. Patient's occipitofrontal circumference was 58,5 cm (>97°c). He presented strabismus, antiverse nares, long philtrum, fleshy lips. The patient was partially cooperative, presented hypomimic face, rest tremor at right hand, rigidity and bradikynesia predominant in right limbs. He walked in shuffling gate with reduced arm swing in both sides. 123I-FP-CIT SPECT imaging showed decreased tracer uptake in both the striatum bilaterally. A brain MRI scan displayed corpus callosum hypoplasia. The neuropsychological evaluation revealed a globally poor cognitive performance at the frontal battery, and cognitive slowing. Routine laboratory work ups were unremarkable. A levodopa challenge test showed no improvement on the Unified Parkinson's Disease Rating Scale motor scores. Poor response to long-term L-dopa therapy was observed. The molecular analysis for fragile -X syndrome (FMR1 gene) and array-CGH resulted normal. Next generation sequencing of customized panel targeting 63 genes associated with neurodevelopmental disorders and macrocephaly detected variant c.13783C>T (p.Gln4595Ter) in heterozygosis of DYNC1H1 gene.

Conclusions: Unlike a previous described case with DYNC1H1 mutation and parkinsonism [6], our patient was unresponsive to the dopaminergic therapy and showed corpus callosum hypoplasia. The mutation found has never been described before. Further studies are required to define the effect of this mutation and its possible causative role in parkinsonism.

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