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Heterogeneous impact on speech and gait disorders in MYORG gene biallelic mutations: two sides of the same coin or not?

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Introduction: Primary familial brain calcification (PFBC) is a rare inherited neurodegenerative disease characterized by bilateral calcifications in the basal ganglia and other brain regions in the absence of other secondary causes of brain calcification. Affected individuals exhibit a wide range of clinical symptoms, including dystonia, parkinsonism, ataxia, cognitive impairment, and psychiatric symptoms. Pathogenic variants in KIAA1161 (MYORG) gene have been linked to an autosomal recessive form of PFBC.

Case presentation: A 54 years-old woman came to our attention for progressive gait unsteadiness, difficulty in walking with stiffness of right lower limb, subjective deterioration of cognitive performance and anxiety. Neurological examination showed bilateral asymmetrical (right>left) rigidity, bradykinesia, ataxia in the lower limbs together with gait ataxia and postural instability. Blood tests were unremarkable. Brain CT revealed extensive and symmetric calcification of basal ganglia, thalamus, midbrain, pons, and cerebellum. Brain MRI showed high-intensity T2 and FLAIR alterations corresponding to the calcified lesions. PET-FDG showed bilateral hypometabolism in temporal and cerebellar cortex; neuropsychological assessment revealed a mild dysexecutive-visual-spatial impairment. Instrumental gait analysis showed walking at reduced speed, characterized during stance by calf muscle overactivity that impaired the ankle push-off and during swing by a co-contraction of the leg muscles that impaired foot clearance. On the contrary, speech acoustic-perceptual analysis showed a well-preserved speech without ataxic, spastic, or hypokinetic components. A direct search of PFBC genes mutations by NGS was performed revealing biallelic variants in MYORG: p.(Arg441Alafs*65) (class 4 ACMG) and p.(Leu614Pro) (class 3 ACMG).

Conclusion: The deep clinical-instrumental assessment performed in this case allowed to underline the possible heterogeneous impact of MYORG mutations on the different axial functions with a less relevant involvement of speech if compared with gait and balance.