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Primary familial brain calcification due to a novel mutation in SLC20A2 gene: a case report

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Introduction: Primary familial brain calcification (PFBC) is a neurodegenerative disorder characterized by extensive intracranial calcium deposition. Patients mostly present with parkinsonism and cognitive impairment. Pathogenic variants in six genes (SLC20A2, PDGFB, PDGFRB, XPR1, MYORG, JAM2) have been associated with PFBC, but genotype-phenotype correlations have not been established [1]. We report the case of a PFBC patient with a novel heterozygous SLC20A2 mutation presenting with postural tremor.

Case report: A 69-year-old man was followed for bilateral arms tremor beginning 10 years earlier. He had a positive family history (tremor and epilepsy in two siblings, tremor and psychiatric disorder in his mother). His first neurological consult at age 62 found bilateral axisymmetric postural and kinetic hands tremor. In the suspect of essential tremor, different pharmacological therapies (propranolol, primidone, valproate) were started unsuccessfully. Levodopa/benserazide 100mg/25mg bid was prescribed with minor improvement. He underwent brain CT and MRI that revealed bilateral calcifications in the cerebellum, thalami and basal ganglia. DAT-scan showed mildly diminished right striatal binding. Serum biochemical parameters of bone and mineral metabolism were unremarkable. Follow-up evaluations documented persistent mild hands tremor with dystonic component on the left side, anticholinergic therapy was added (trihexyphenidyl 4mg daily). At 68 y.o. patient begin to complain craving for sweet food, insomnia and nocturnal hyperactivity. Cognitive evaluation revealed attentive deficits and behavioural disinhibition (MMSE 29/30). Episodic tongue protrusion during stress was described. Right hand rest tremor appeared without bradykinesia or rigidity. Genetic test identified the c.410G>A, p.(Trp137Ter) heterozygous variant of SLC20A2 gene. This is a novel mutation, yet not described on GnomAD database (https://gnomad.broadinstitute.org/), that gives rise to a stop codon and is considered pathogenic by many prediction programs. The patient's sons refused to be tested.

Conclusions: For patients classified as having essential tremor-plus phenotype, PFBC must be considered in the differential diagnosis, especially this novel SLC20A2 variant.

References:

[1] Balck A, Schaake S, Kuhnke NS et al. A. Genotype-Phenotype Relations in Primary Familial Brain Calcification: Systematic MDSGene Review. Mov Disord. 2021 Nov;36(11):2468-2480.