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Not every tremor is essential: a challenging case of young-onset tremor

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Case description: A 29-year-old girl presented to our clinic with a long-standing diagnosis of essential tremor. However, her history was a 6-year progressive ataxia, appendicular tremor, and neck stiffness. No other relevant history was reported, and no family history of neurological disorders was described by the proband parents. At the neurological examination she was able to walk unaided, at the tandem walk test, despite the presence of a slight unsteadiness. A mild to moderate postural and kinetic dystonic tremor hampered most of the clinical tests, interrupted by frequent myoclonic jerks. Despite she complained of anterior neck stiffness, no clear dystonic features were detected. Her brain magnetic resonance showed only a mild atrophy of the right hippocampus and an enlarged metabolic screening for tremor syndromes (blood cell count with red cell smear analysis, electrolytes, liver and renal function markers, ammonia, thyroid hormones) was unremarkable. In the clinical suspicion of myoclonus-dystonia, an extensive panel of genes for dystonia was performed. Next generation sequencing analysis of a panel of genes test revealed a heterozygous c.592G>A missense variant [p.(Glu198)Lys] of the TUBB4A gene of the proband and of her 64 years old healthy mother and 20 years old sister. Levodopa, benzodiazepines, anticholinergic medications were administered without seeing any major clinical benefit. Low dose clonazepam showed a mild response. The patient was evaluated on regular basis for a two-year period and no substantial changes in clinical picture were observed.

Discussion: TUBB4A mutations can be causative of a variety of neurological disorders, embracing a wide scale of clinical phenotypes such as the hypomyelinating leukodystrophy with basal ganglia and cerebellum atrophy or disabling dystonia syndromes. Missense mutation or deletion of TUBB4A gene segregates mainly with a full autosomal dominant pattern, even if reduced penetrance is described. [1-2] Our case suggests that TUBB4A mutations can express with reduced penetrance and manifest with milder phenotype.

References:

[1] Erro, R., Hersheson, J., Ganos, C., Mencacci, N. E., Stamelou, M., Batla, A., Thust, S. C., Bras, J. M., Guerreiro, R. J., Hardy, J., Quinn, N. P., Houlden, H., & Bhatia, K. P. (2015). H-ABC syndrome and DYT4: Variable expressivity or pleiotropy of TUBB4 mutations? Movement disorders: official journal of the Movement Disorder Society, 30(6), 828–833. https://doi.org/10.1002/mds.26129.

[2] Ferreira, C., Poretti, A., Cohen, J., Hamosh, A., & Naidu, S. (2014). Novel TUBB4A mutations and expansion of the neuroimaging phenotype of hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC). American journal of medical genetics. Part A, 164A (7), 1802–1807. https://doi.org/10.1002/ajmg.a.36526.