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Phenotypic description of two unreported families with ANO3 dystonia

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Background: ANO3 gene encodes for a Ca2þ-gated chloride channel. DYT24 has an adult onset and usually presents with cranio-cervical dystonia combined with tremor [1,2].

Objective: This is the phenotypic description of two families affected by hereditary dystonia associated to gene ANO3 mutation (DYT24), one with a heterozygous verisimilarly pathogenic variant (hVPV), and the other with a heterozygous variant of uncertain meaning (hVUM).

Methods: Phenomenology description (with related videos), next generation sequencing of dystonia genetic panel, multichannel EMG were performed in both families.

Results: In one family, proband was the mother, who presented a severe axial dystonia associated with tremor at the head and upper limbs, whereas her son had a cranio-cervical dystonia and head jerky movements. Genetic analysis identified a hVPV in ANO3 gene associated to PINK1 gene hVUM mutation in the mother and to PANK2 in the son. Both patients are under deep brain stimulation of internal globus pallidus with benefits. In the other family, proband is a 60 y.o. man who presented cranial dystonia and upper limbs dystonic tremor, whereas his sister shows just dystonic features of Meige syndrome. Our patients were found to be heterozygous for a *de novo* missense variant in ANO3 c.1690C>G which predicts the corresponding protein change of p. (Leu564Val) and which is absent from the GnomAD reference population database and never reported in literature. All patients are under treatment with botulinum toxin with benefits. They all reported dystonia onset before the age of 20 year. Brain MRI scan showed normal findings in all of them.

Conclusions: Dyt24 has heterogeneous clinical aspects [3,4,5], both families here reported have cranio-cervical and upper limb impairment but with different clinical presentation. Patients of the same family are similar but show significant difference with subjects of the other family.

References:

[1] Olschewski L, Jesús S, Kim HJ, et al. Role of ANO3 mutations in dystonia: A large-scale mutational screening study. Parkinsonism and Related Disorders. 2019;62:196-200. doi:10.1016/j.parkreldis.2018.12.030.
[2] Charlesworth G, Plagnol V, Holmström KM, et al. Mutations in ANO3 cause dominant craniocervical dystonia: Ion channel implicated in pathogenesis. American Journal of Human Genetics. 2012;91(6):1041-1050. doi:10.1016/j.ajhg.2012.10.024.
[3] Laurencin C, Broussolle E, Danaila T, Anheim M, Chelly J, Thobois S. A novel heterozygous ANO3 mutation responsible for myoclonic dystonia. Journal of the Neurological Sciences. 2019;403:65-66. doi:10.1016/j.jns.2019.06.014.
[4] Miocinovic S, Vengoechea J, LeDoux MS, Isbaine F, Jinnah HA. Combined occurrence of deleterious TOR1A and ANO3 variants in isolated generalized dystonia. Parkinsonism and Related Disorders. 2020;73:55-56. doi:10.1016/j.parkreldis.2020.03.028.
[5] Stamelou M, Charlesworth G, Cordivari C, et al. The phenotypic spectrum of DYT24 due to ANO3 mutations. Movement Disorders. 2014;29(7):928-934. doi:10.1002/mds.25802.