Novel KCNA1 Pathogenic Variant Associated Syndrome of Episodic Dystonia and Electrophysiologic Myokymia - A Case Report

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Background:

The KCNA1 gene on chromosome 12p encodes a voltage gated delayed potassium channel, Kv1.1. These potassium channels are found primarily in the central nervous system, and are involved in the regulation of membrane potential and neuronal signaling. Pathogenic variations in KCNA1 have been implicated in a variety of human diseases, and have shown significant clinical heterogeneity. Over 20 variations in KCNA1 have been found to cause episodic ataxia type 1 (EA1), but phenotypes also include isolated myokymia and epilepsy.

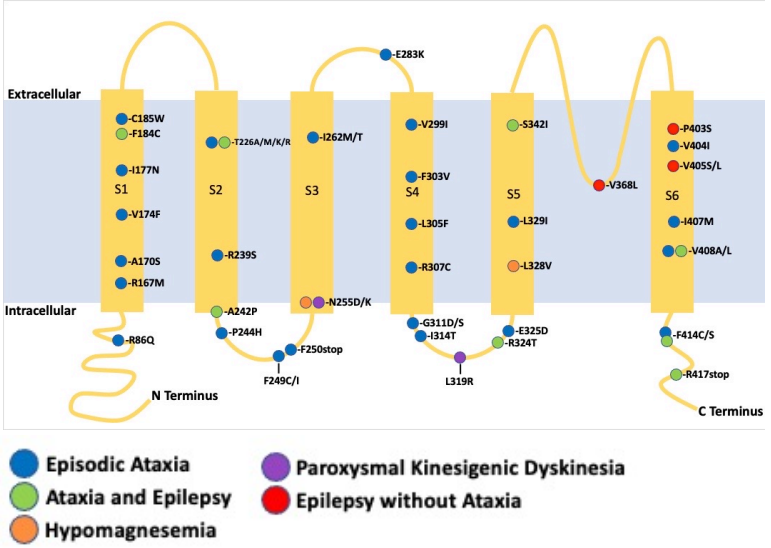

Figure 1. Map of the KCNA1 protein showing the location of different pathogenic mutations and their clinical significance.

Case presentation:

A four-year-old boy presented with painful dystonic episodes involving the lower extremities, lasting hours to days. The onset of symptoms was at two years of age. The dystonic episodes were usually precipitated by illness, and were severe and progressive.

Methods and Results:

Continuous myokymia was noted on electromyography (EMG). A novel KCNA1 pathogenic variant: c.941T>C (p.Ile314Thr), with reference sequence NM000217.2, was revealed by exome sequencing. It was inherited from his father, who reported episodic ataxia and migraine variant. The patient has responded to treatment with carbamazepine daily and lorazepam prn. This case adds to the clinical heterogeneity and associated variant specific phenotype.

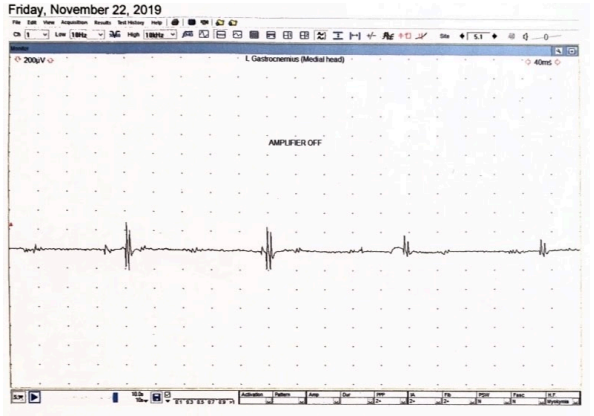

Figure 2. Subclinical myokymia shown by spontaneous semirhythmic slow train of doublets seen in the left gastrocnemius muscle with an extended sweep speed of 40ms.

Conclusions:

- KCNA1 pathogenic variant c.41T>C (p.Ile314Thr) should be considered in patients presenting at an early age with painful dystonic episodes and electrophysiologic myokymia.
- Exome sequencing may be done to confirm the diagnosis for this potentially treatable movement disorder.
- The regimen of scheduled carbamazepine and prn lorazepam should be considered for management.

References:

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- Paulhus K, Ammerman L, Glasscock E. Clinical Spectrum of *KCNA1* Mutations: New Insights into Episodic Ataxia and Epilepsy Comorbidity. *International Journal of Molecular Sciences*. 2020; 21(8):2802. https://doi.org/10.3390/ijms21082802