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Tremor and Other Hyperkinetic Movements

Video Abstracts

Paroxysmal Dyskinesias in a *PRRT2* Mutation Carrier

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Abstract

Background: Paroxysmal movement disorders are rare and heterogeneous genetic conditions characterized by the recurrence of transient involuntary movements.

Phenomenology Shown: The phenomenology of a paroxysmal kinesigenic dyskinesia in a young professional athlete.

Educational Value: Providing basic clinical and genetic elements for the early recognition and diagnosis of a rare movement disorder.

Keywords: Paroxysmal dyskinesia, *PRRT2*, dystonia, paroxysmal exercise-induced dyskinesia, paroxysmal kinesigenic dyskinesia, paroxysmal non-kinesigenic dyskinesia

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A 21-year-old male athlete (runner) with a history of infantile seizures presented to our clinic for the recurrence of involuntary sustained and twisting muscular contractions of both hands, grimace, and tightness of limbs during running sessions, with a significant impairment in pace performances (Video 1). Involuntary movements presented quickly after the trigger (physical exercise), showed a stereotyped asymmetric dystonic pattern (forced left clenched fist and twisted posturing of the right hand), and lasted a few seconds (Video 1). Family history was negative for seizures and movement disorders. Brain magnetic resonance imaging, clinical examination, and interictal electroencephalography were unremarkable. Genetic testing showed a heterozygous mutation of *PRRT2* exon 2 (NM_145239.2:c.649dup p.(Arg217Profs*8)), confirming the clinical diagnosis of paroxysmal dyskinesias (PxDs). PxDs are heterogeneous conditions characterized by recurrent episodes of dystonia, chorea, athetosis, ballism, or a combination of these disorders, with normal examination between episodes. PxDs appear spontaneously (paroxysmal non-kinesigenic dyskinesias, PNKDs), triggered by movements (paroxysmal kinesigenic dyskinesias, PKDs), or exercise (paroxysmal exercise-induced dyskinesias, PEDs).[1] Mutations in *PRRT2* are frequently responsible for PKDs with a frequency ranging from 40% to 90% depending on case ascertainment but can also be associated rarely with PNKDs and PEDs.

PRRT2 codes for proline-rich-transmembrane-protein-2, which interacts with SNAP25, a presynaptic membrane protein, in order to promote calcium-dependent vesicular exocytosis; non-sense mutation in *PRRT2* prevents this interaction and perturbates the synaptic function.[2] Autosomal dominant *PRRT2* mutations are associated not only with PxDs but also with episodic ataxia, benign familiar infantile seizures and infantile convulsions plus choreoathetosis.[2,3] The episodic nature, the excellent therapeutic effect of antiepileptic agents and the tight association that some PxDs show with seizures have raised questions about their pathogenesis, with some authors considering PxDs as "basal ganglia epilepsies".[1] Here, the abrupt onset of movement (i.e., due to sprinting from a static position) elicited PKD. In contrast to PKDs, PEDs are typically precipitated by prolonged exercise, show longer duration, and could present with GLUT-1 deficiency syndrome, which is caused by *SLC2A1* mutation.[1]

Differential diagnosis of paroxysmal hyperkinetic disorders cannot fail to include seizures (e.g., frontal and temporal lobe epilepsy, juvenile myoclonic epilepsy), metabolic disorders (e.g., thyrotoxicosis),

Video 1. **Paroxysmal kinesigenic dyskinesias in a professional runner. Segment 1.** Recording of a running session. This segment shows involuntary bilateral hand twisting movements (white arrows) presenting at the end of the sprint of a short running path. The patient complains also facial grimace and leg tightness (not shown). **Segment 2.** Neurological examination and provoking maneuver (running in place). This segment shows an unremarkable finger-tapping test in the beginning of the examination. The exercise provokes after 10 seconds the onset of bilateral hand dystonia with left clenched fist and right hand twisting posture. The finger tapping performances at the end of the segment are impaired by bradykinesia and dystonic jerks.

primary dystonia, Sydenham chorea, tics, hyperekplexia, and functional movement disorders. The number of attacks may decrease over the course of the time, with possible remission after having reached adulthood.[1] In this case, the patient's symptoms receded with carbamazepine (low dose, 200 mg daily) and his running performances improved.

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