Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Paroxysmal Kinesigenic Dystonia in a Lesch-Nyhan Disease Variant

Beatriz De La Casa-Fages, MD, PhD,[1] Javier R. Pérez-Sánchez, MD,[1] Francisco Grandas, MD, PhD[1,]*

Lesch-Nyhan disease (LND) variants are caused by partial deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT). Patients with LND variants have hyperuricemia and varying degrees of motor, cognitive, and behavioral abnormalities that are usually milder than those observed in classical LND.[1,2] The absence of self-injurious behavior is considered an additional diagnostic criterion.[1,2]

Dystonia is the most common motor disorder in both classic LND and LND variants.[2,3] Although a variety of dystonic movements and postures have been associated with LND, paroxysmal dystonia has not been reported. We describe a patient with LND variant who developed paroxysmal dystonia induced by voluntary movements.

A 24-year-old man was diagnosed with LND variant in early childhood (point mutation 212 G>T in the HPRT gene; HPRT activity in erythrocytes <0.01 nmol/h/mg of hemoglobin). This mutation was reported elsewhere.[4] During his first year of life, the patient had hyperuricemia and delayed motor milestones, followed by nephrolithiasis, generalized dystonia, signs of corticospinal tract dysfunction, and severe gait impairment that progressed over the first decade. His intelligence was borderline (IQ, 83), and no self-injurious behavior was observed. His family history was negative for neurological disorders. He was treated with allopurinol and clonazepam and remained clinically stable for years. Although the patient used a wheelchair, he could walk short distances with assistance.

At the age of 20 years, he began to experience paroxysmal spasms of the lower limbs. The sudden muscle spasms were precipitated by voluntary movements of the legs, particularly when walking, and provoked bizarre abnormal postures of the lower extremities (right, left, or both). These episodes occurred up to 50 times a day, lasting from seconds to a few minutes.

The spasms interrupted the patient's gait and often caused him to fall. Consciousness was always preserved during episodes.

Examination revealed dysarthria, generalized dystonia, hyperreflexia, and bilateral Babinski sign, with no significant spasticity in the limbs. In fact, the patient had mild hypotonia when he was fully relaxed, seated on his wheelchair. When the patient tried to walk, helped by another person, his gait was dystonic and stiff. After a few steps, he experienced brief dystonic muscle spasms involving usually one leg, causing abnormal postures with marked hip and knee flexion (see Video). Sometimes the upper limbs were also involved.

A brain MRI was normal. An EEG performed during the spasms was also normal. 18-fluorodeoxyglucose PET of the brain showed bilateral basal ganglia hypometabolism. Therapeutic trials with carbamazepine (600 mg/day), gabapentin (900 mg/day), levetiracetam (1000 mg/day), baclofen (30 mg/day), and pregabalin (100 mg/day) were ineffective.

The dystonic spasms were triggered by voluntary movements, which is consistent with paroxysmal kinesigenic dystonia (PKD), as well as their duration and frequency.[5,6] To our knowledge, this is the first report of PKD in a patient with LND variant; our findings expand the spectrum of its motor symptoms. PKD may be related to the basal ganglia dysfunction observed in functional neuroimaging.

It is noteworthy that PKD appeared after years of stable generalized dystonia, suggesting that, in LND variants, the clinical pattern of dystonia may evolve along the course of the disease. In addition, in this patient, treatment with antiepileptic drugs was ineffective, in contrast to primary PKD. LND variant should be considered in the differential diagnosis of symptomatic PKD.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the First Draft, B. Review and Critique.

B.C.-F.: 3A
J.R.P.-S.: 3A
F.G.: 3B

[1]Movement Disorders Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain

[*]**Correspondence to:** Dr. Francisco Grandas, Servicio de Neurologia, Hospital General Universitario Gregorio Marañón, c/o Doctor Esquerdo 46, Madrid 28007, Spain; E-mail: fgrandas.hgugm@salud.madrid.org
Keywords: kinesigenic dystonia, paroxysmal, Lesch-Nyhan disease, variant, HPRT gene.
Relevant disclosures and conflicts of interest are listed at the end of this article.
Received 28 January 2014; revised 25 March 2014; accepted 8 April 2014.
Published online 23 May 2014 in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/mdc3.12034

doi:10.1002/mdc3.12034

Disclosures

Funding Sources and Conflicts of Interest: The authors report no sources of funding and no conflicts of interest.

Financial Disclosures for previous 12 months: F.G. received honoraria for lecturing from Abbot, Italfarmaco, UCB, and Medtronic and for consultancies from Abbvie.

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Supporting Information

A video accompanying this article is available in the supporting information here.

Video. Three short-lasting paroxysmal dystonic spasms involving one or both legs are shown. In one of the episodes, the right arm is also involved. They appear after walking a few steps with the assistance of a relative.

doi:10.1002/mdc3.12034