

Images in Neurology

A Woman With a Novel Mutation of *THAP1* With a Prominent Response to Deep Brain Stimulation of the Globus Pallidus Internus

Jung E. Park, MD; Nora Vanegas-Arroyave, MD; Mark Hallett, MD; Codrin Lungu, MD

A 27-year-old woman presented with generalized dystonia that began at age 15 years as dystonic posturing of the right hand when writing. She was diagnosed with cervical dystonia and botulinum toxin



Video at jamaneurology.com

injections were tried, providing minimal pain relief and no improvement of the dystonia. The cervical dystonia was partially responsive to sensory tricks (Video, A). She was most bothered by her cervical dystonia, and disability was 6 on Part II of the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

On examination, she had increased rate of eye blinking and occasional spasms involving the lower face, mouth, and jaw, and mild dysarthria. Severe right torticollis and an intermittent head tremor were present. Dystonic posturing of the right upper extremity and increased handgrip were observed while writing. Mild left foot inversion was present while walking. The Fahn-Marsden Scale score was 16, and TWSTRS Part I score was 20. A trial of carbidopa/levodopa did not provide benefit.

Deep brain stimulation (DBS) surgery targeting the globus pallidus internus (GPI) was performed, resulting in moderate improvement 1 month after the procedure, prior to initial programming (TWSTRS Part I = 18, Fahn-Marsden = 8.5) (Video, B). She experienced further benefit 2 months after initial programming (TWSTRS Part I = 13, Fahn-Mars-

den = 3). Whole-exome sequencing revealed a frameshift mutation, confirmed as a novel 2-base pair deletion mutation in exon 3 of the *THAP1* gene (heterozygous exon 3 c.377_378delCT, p.Pro126Arg*2) via full sequencing analysis of DYT6.

Discussion

DYT6 dystonia is an autosomal dominant form of isolated dystonia, presenting in adolescence or adulthood.¹ Symptoms are variable, commonly affecting the cranio-cervical region.¹ The locus has been identified on chromosome 8p21-q22 and the gene is designated *THAP1* (Thanatos-associated protein 1).²

Deep brain stimulation of the GPI in patients with primary generalized or segmental dystonia can result in significant improvement during long-term follow-up. Patients with DYT6 dystonia generally have a relatively modest response, but response varies with percentages of improvement of dystonia rating scale scores from 16% to 55%.³

Jech et al⁴ reported a patient with generalized dystonia and a *THAP1* mutation located on exon 2, who had an excellent response to GPI DBS. Our case is another example of a novel *THAP1* mutation expressed as a phenotype that responded well. Different mutations may not only have different clinical presentations, but also variable response patterns to DBS. Sorting this out may help with preoperative decisions.

ARTICLE INFORMATION

Author Affiliations: Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland (Park, Vanegas-Arroyave, Hallett); Office of the Clinical Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland (Vanegas-Arroyave, Lungu).

Corresponding Author: Jung E. Park, MD, Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, 10 Center Dr, Bldg 10, Room 7D42, Bethesda, MD 20892 (junge.park@nih.gov).

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magnetic stimulation and methods for using the same (H-coil); in relation to the latter, he has received license fee payments from the National Institutes of Health (NIH) (from Brainsway) for licensing of this patent. He is on the Editorial Board of 20 journals and received royalties and/or honoraria from publishing from Cambridge University Press, Oxford University Press, John Wiley & Sons, Wolters Kluwer, Springer, and Elsevier. He has received honoraria for lecturing from Columbia University. Dr Hallett's research at the NIH is largely supported by the NIH Intramural Program. Supplemental research funds have been granted by the Kinetics Foundation for studies of instrumental methods to monitor Parkinson disease, BCN Peptides S.A. for treatment studies of blepharospasm, Medtronic Inc for studies of deep brain stimulation, Parkinson Alliance for studies of eye movements in Parkinson disease, Merz for treatment studies of focal hand dystonia, and Allergan for studies of methods to inject botulinum toxins. No other disclosures were reported.

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