Patient Information	Specimen Information	Client Information
TEST, TEST3 **DOB: 09/09/1998** **AGE: 25** Gender: M Fasting: Y Phone: NG Patient ID: NG	Specimen: AT062773C Requisition: 0225045 Collected: 05/22/2024 / 09:00 EDT Received: 05/23/2024 / 06:36 EDT Reported: 05/31/2024 / 17:51 EDT	Client #: 97502840 00ATL20 DR WELBY TEST CLIENT (HQ) ATL Attn: JULT11TESTING 100 MAIN ST MADISON, NJ 07940-1813

Test Name	In Range	Out Of Range	Reference Range	Lab
DYSTONIA (DYT1) DNA TEST				WAO

INTERPRETATION

NEGATIVE

This test did not identify any variants associated with early onset generalized torsion dystonia.

TECHNICAL RESULTS

Interpretive Result Table

INTERPRETIVE RESULT: Negative

TEST: DYT1

TECHNICAL RESULT: No deletion detected

CLINICAL RELEVANCE: See Limitations of Analysis

COMMENTS

Comments: While this analysis did not identify any pathogenic or likely pathogenic variants associated with early onset generalized torsion dystonia, the diagnosis cannot be completely ruled out due to variants not detected by this assay or variants in another gene.

Clinical limitations: The c.907_909delGAG mutation in the TOR1A gene associated with myoclonus-dystonia occurs across ethnicities. It accounts for about 80% of early onset cases in the Ashkenazi Jewish population, and 16-53% of early-onset cases non-Jewish populations.

Other testing available: Other disorders may appear clinically similar to those caused by mutations in this gene. Athena Diagnostics recommends additional testing, if not already performed, based on this individual's clinical presentation and family history. Athena Diagnostics currently offers testing for the following gene: THAP1. Please contact the Athena Diagnostics Client Services Department or visit AthenaDiagnostics.com for information regarding additional testing.

Background information: Dystonia is a movement disorder characterized by involuntary muscle contractions that cause abnormal and usually repetitive movements and postures. More than two dozen types of inherited dystonia have been associated with specific genetic loci, and these types vary in terms of their complexity (i.e. aggregate symptoms and comorbidities), severity, onset, therapeutic responsiveness, and persistence. Dystonia is classified along two clinical axes: 1) clinical presentation, which includes age at onset, body distribution, temporal pattern and associated features, and 2) etiology, the underlying nervous system pathology and inheritance. Isolated dystonias, formerly called primary dystonias, are those in which dystonia is the only motor feature with the exception of possible tremor. Dystonia co-occurring with another movement disorder (e.g., myoclonus, parkinsonism) has traditionally been referred to as 'dystonia-plus' but is now referred to as combined dystonia. Complex dystonia (formerly 'secondary dystonia') refers to the co-occurrence of dystonia with other neurologic or systemic manifestations, with dystonia not necessarily the most prominent disease manifestation and

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possibly not even a consistent feature. Dystonia has been found to affect all populations worldwide.
The c.907_909delGAG mutation in the TOR1A gene has been associated with early onset generalized torsion dystonia (DYT1), the most common and potentially severe form of hereditary dystonia. Severity of DYT1 associated with the TOR1A c.907_909delGAG mutation varies considerably even within the same family. Age of onset DYT1 is nearly always before the mid-twenties. DYT1 is inherited in an autosomal dominant manner with reduced penetrance (30%-40% affected).
TOR1A gene information: MIM ID: * 605204; Chromosome Location: 9q34.11; NCBI Reference Sequence: NM_000113.2; In the cDNA, the initiator codon, ATG (methionine), is designated as codon number 1 and the "A" is designated as nucleotide +1. The initiator codon is located in exon 1 and all subsequent numbering is sequential.
Phenotype information: MIM ID: # #128100 for Dystonia 1, torsion, autosomal dominant; DYT1

METHODS

Direct testing for the 3 base pair (GAG) deletion mutation (GAG946) in the TOR1A gene was performed by PCR amplification of genomic DNA followed by electrophoretic separation and size determination. This analysis, as performed here, is greater than 99% accurate.

Limitations of analysis: This test may not detect mutations in patients exhibiting mosaicism or allele dropout. Although rare, false positive or false negative results may occur. All results should be interpreted in the context of clinical findings, relevant history, and other laboratory data.

REFERENCES

1. Ozelius LJ and Ozeliusa and Bressman SB. (2011) Neurobiol Dis.42(2): 127-135. (PMID: 21168499)
2. Albanese A, et al., (2013) Movement Disorders 15:28(7):863-73 (PMID: 23649720)
3. Steeves, T. et al., (2012) Movement Disorders 27:14:1789-1796 (PMID: 23114997)
4. Grundmann K, et al (2003). Arch Neurol. 60:1266-70 (PMID: 12975293)

This test was developed and its analytical performance characteristics have been determined by Athena Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

Laboratory oversight provided by Vivekananda Datta, M.D., Ph.D., CLIA license holder, Athena Diagnostics (CLIA# 22D0069726)
[a portion of testing was performed at CMS00]

Testing performed at:
Athena Diagnostics 200 Forest Street Marlborough, MA 01752

PERFORMING SITE:

WAO ATHENA DIAGNOSTICS,INC, 200 FOREST STREET 2ND FLOOR, MARLBOROUGH, MA 01752-3023 Laboratory Director: VIVEKANANDA DATTA,MD,PHD, CLIA: 22D0069726