variantyx

Case Study

17 year old male, suspected motor neuropathy

Case background

This study presents a 17-year-old male with history of a healthy birth and no contributory family history. At five years of age he was evaluated for left leg pain. The patient was identified as having abnormal gate, "heavy footprint", muscle weakness and foot drop by age 12. A decline in muscle strength was observed at age 14 and EMG/ NCV studies were probable for demyelinating sensory motor neuropathy at age 15.

Previous testing

The patient had undergone extensive testing including negative MRI studies, negative Charcot-Marie-Tooth panel (42 genes), negative comprehensive neuropathies panel (112 genes), and negative comprehensive hereditary spastic paraplegia panel.

Interpretation and results

The patient presented to Variantyx for testing by Genomic Unity® Exome Plus Analysis, a comprehensive analysis that considers all genes.

The patient was found to be compound heterozygous for a sequence variant and a repeat expansion in the *FXN* gene. Since parental samples were also provided for testing, the variants were identified *in trans*, confirming a diagnosis of Friedreich's Ataxia.

Of note, the "gold standard" method of PCR/Southern blot for detection of repeat expansions was not successful for this case. Orthogonal confirmation by an outside laboratory missed the expansion, likely due to a variant at the restriction enzyme digestion site. However, orthogonal confirmation by a second outside laboratory identified the variant as an 820-repeat expansion of the *FXN* gene.

Test	Detection of sequence variant	Detection of repeat expansion	Result
Panel / Exome	Yes	No	Carrier
PCR / Southern blot	No	Yes*	Carrier
PCR-free whole genome-based testing	Yes	Yes	Compound heterozygous

*Assuming restriction enzyme digestion site is not affected by a variant

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