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Two novel mutations in TTN of a patient with congenital myopathy: A case report.

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Abstract

BACKGROUND: Early-onset myopathies show a wide spectrum of phenotypes and are composed of various types of inherited neuromuscular diseases, making it difficult to diagnose. TTN mutation-related myopathy is a known cause of early-onset myopathy. Since a next-generation sequencing (NGS) has enabled sequencing of the vast amount of DNA, TTN, which is the longest coding sequence of any human gene, mutations can now be revealed. We report a 10-year-old female with severe congenital muscular weakness and delayed motor development since birth.

METHODS: Next-generation sequencing as well as electromyography and muscle biopsy were performed.

RESULTS: To date, she is incapable of walking alone. Her younger sister had similar but more severe symptoms with respiratory failure. In electromyography, short-duration, small-amplitude motor unit action potential, and early recruitment patterns were observed in the involved proximal muscles, suggesting myopathy. Muscle histopathology showed a specific atrophy of increased fiber size variability, frequent nuclear internalization, as well as degeneration and regeneration of fibers with type I fiber predominance, consistent with the findings of a previous report about congenital titinopathy. A NGS study revealed two different possible pathogenic variants in TTN: (a) canonical splicing mutation in the intron 105 (c. 29963-1G>C) and (b) frameshift and truncating mutation in the exon 339 (c.92812dup/p.Arg30938LysfsTer15). All variants were confirmed by conventional Sanger sequencing.

CONCLUSION: We propose that unbiased genomic sequencing can be helpful in screening patients with early-onset myopathy.

KEYWORDS: TTN ; congenital myopathies; human; next-generation sequencing

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