A new case expanding the mutation and phenotype spectrum of TMEM5-related alpha-dystroglycanopathy.

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Abstract

Dystroglycanopathies are a diverse group of neuromuscular disorders caused by aberrant glycosylation of alpha-dystroglycan. TMEM5 is one of many glycosyltransferases recently described to be associated with alpha-dystroglycanopathies. We report the case of a 15-year-old boy suffering from a congenital muscular dystrophy with elevated serum creatine kinase levels and an almost complete absence of alpha-dystroglycan in muscle biopsy. The clinical course was milder than any previously reported case and did not include brain or eye defects. Standard next-generation sequencing analysis revealed a homozygous mutation in the donor splice site region of exon 5 in TMEM5 (c.914+6 T>G). Available in-silico prediction tools anticipated a reduced efficiency of the splice site. Subsequent cDNA sequencing confirmed the expression of a truncated transcript of TMEM5 lacking exon 5, hence leading to an in-frame deletion in the exostosin domain of the protein. This report expands the clinical and mutation spectrum of alpha-dystroglycanopathies.

KEYWORDS: Alpha-dystroglycan; Dystroglycanopathy; NGS; TMEM5

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