A homozygous DPM3 mutation in a patient with alpha-dystroglycan-related limb girdle muscular dystrophy.


Author information

Erratum in

Abstract
Defects of O-linked glycosylation of alpha-dystroglycan cause a wide spectrum of muscular dystrophies ranging from severe congenital muscular dystrophy associated with abnormal brain and eye development to mild limb girdle muscular dystrophy. We report a female patient who developed isolated pelvic girdle muscle weakness and wasting, which became symptomatic at age 42. Exome sequencing uncovered a homozygous c.131T > G (p.Leu44Pro) substitution in DPM3, encoding dolichol-P-mannose (DPM) synthase subunit 3, leading to a 50% reduction of enzymatic activity. Decreased availability of DPM as an essential donor substrate for protein O-mannosyltransferase (POMT) 1 and 2 explains defective skeletal muscle alpha-dystroglycan O-glycosylation. Our findings show that DPM3 mutations may lead to an isolated and mild limb girdle muscular dystrophy phenotype without cardiomyopathy.

KEYWORDS: Alpha-dystroglycan; DPM3; Dolichol-P-mannose synthase; Limb girdle muscular dystrophy

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