
Dilated cardiomyopathy and limb-girdle muscular dystrophy-dystroglycanopathy due to novel pathogenic variants in the DPM3 gene

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Abstract

Deficiency of Dolichol-P-mannose synthase subunit 3 (DPM3) affects the N-glycosylation and O-mannosylation pathways that are respectively involved in congenital disorders of glycosylation (CDG) and alpha-dystroglycanopathies. Herein, we describe novel pathogenic variants in the DPM3 gene in two unrelated male patients. They developed dilated cardiomyopathy in their late teens, limb-girdle muscular dystrophy - one patient in childhood and the other in adulthood. In both patients, next generation sequencing found in the DPM3 gene a heterozygous deletion and a heterozygous pathogenic missense mutation in exon 2 (c.41T>C, p.Leu14Pro). Electrophoresis of serum transferrin found an abnormal N-glycosylation profile suggestive of CDG type 1 (decreased tetrasialotransferrin, increased disialo- and asialotransferrin). Only two cases of DPM3 gene mutations with limb-girdle muscular dystrophy-dystroglycanopathy have been reported previously. The present study highlights several aspects related to DPM3 gene mutations such as mild to moderately severe limb-girdle muscular dystrophy, dilated cardiomyopathy, and abnormal N-glycosylation profile suggestive of CDG type 1.

Keywords: Alpha-dystroglycanopathies; Congenital disorders of glycosylation; Dilated cardiomyopathy; Dolichol-P-mannose (DPM) synthase subunit 3 (DPM3); Limb-girdle muscular dystrophy.

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