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A novel compound heterozygous mutation in the POMK gene causing limb-girdle muscular dystrophy-dystroglycanopathy in a sib pair.

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Abstract

We describe two Finnish siblings in whom an incidentally detected elevated creatine kinase activity eventually led to a diagnosis of limb-girdle muscular dystrophy-dystroglycanopathy (Type C12; MDDGC12). When diagnosed at age 10 and 13 years, they were mildly affected with a slow or non-progressive disease course. The main symptoms comprised infrequent hip cramps triggered by flexion, neck cramps triggered by yawning, transient growing pains, calf hypertrophy and mild proximal muscle weakness. Their cognitive and motor developments were unremarkable and they were physically active. Whole-exome sequencing revealed compound heterozygous mutations, both of which were novel, in the protein O-mannosyl kinase (POMK) gene in both siblings; a missense mutation, p.Pro322Leu (c.965C > T), and a nonsense mutation, p.Arg46Ter (c.136C > T). The results were confirmed by Sanger sequencing, showing that the parents were heterozygous carriers of one mutation each. This report adds to the literature by providing phenotype and genotype data on this ultra-rare POMK-related dystroglycanopathy.

KEYWORDS: Dystroglycanopathy; LGMD12C; Limb-girdle muscular dystrophy-dystroglycanopathy type 12 C; MDDGC12; Muscular dystrophy; POMK; Protein-O-mannosyl kinase

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