Mutations in GMPPB Presenting with Pseudometabolic Myopathy.

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Abstract
Mutations in the guanosine diphosphate mannose (GDP-mannose) pyrophosphorylase B (GMPPB) gene encoding a key enzyme of the glycosylation pathway have been described in families with congenital (CMD) and limb girdle (LGMD) muscular dystrophy with reduced alpha-dystroglycan (\(\alpha\)-DG) at muscle biopsy. Patients typically display a combined phenotype of muscular dystrophy, brain malformations, and generalized epilepsy. However, a wide spectrum of clinical severity has been described ranging from classical CMD presentation to children with mild, yet progressive LGMD with or without intellectual disability. Cardiac involvement, including a long QT interval and left ventricular dilatation, has also been described in four cases. Two missense mutations in GMPPB gene, one novel and one already reported, have been identified in a 21-year-old man presenting with elevated CK (38,650 UI/L; normal values <150 UI/L) without overt muscle weakness. Major complaints included limb myalgia, exercise intolerance, and several episodes of myoglobinuria consistent with a form of metabolic myopathy. Muscle biopsy showed only minimal alterations, whereas a marked reduction of glycosylated \(\alpha\)-DG was evident. This case further expands the phenotypic spectrum of GMPPB mutations and highlights the importance of exhaustive molecular characterization of patients with reduced glycosylation of \(\alpha\)-DG at muscle biopsy.

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