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Mobility shift of beta-dystroglycan as a marker of *GMPPB* gene-related muscular dystrophy.

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Abstract

BACKGROUND: Defects in glycosylation of alpha-dystroglycan (α -DG) cause autosomal-recessive disorders with wide clinical and genetic heterogeneity, with phenotypes ranging from congenital muscular dystrophies to milder limb girdle muscular dystrophies. Patients show variable reduction of immunoreactivity to antibodies specific for glycoepitopes of α -DG on a muscle biopsy. Recessive mutations in 18 genes, including guanosine diphosphate mannanose pyrophosphorylase B (*GMPPB*), have been reported to date. With no specific clinical and pathological handles, diagnosis requires parallel or sequential analysis of all known genes.

METHODS: We describe clinical, genetic and biochemical findings of 21 patients with *GMPPB*-associated dystroglycanopathy.

RESULTS: We report eight novel mutations and further expand current knowledge on clinical and muscle MRI features of this condition. In addition, we report a consistent shift in the mobility of beta-dystroglycan (β -DG) on Western blot analysis of all patients analysed by this mean. This was only observed in patients with *GMPPB* in our large dystroglycanopathy cohort. We further demonstrate that this mobility shift in patients with *GMPPB* was due to abnormal *N*-linked glycosylation of β -DG.

CONCLUSIONS: Our data demonstrate that a change in β -DG electrophoretic mobility in patients with dystroglycanopathy is a distinctive marker of the molecular defect in *GMPPB*.

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Conflict of interest statement

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