Limb girdle muscular dystrophy due to mutations in POMT2.


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Abstract

BACKGROUND: Mutations in the gene coding for protein O-mannosyl-transferase 2 (POMT2) are known to cause severe congenital muscular dystrophy, and recently, mutations in POMT2 have also been linked to a milder limb-girdle muscular dystrophy (LGMD) phenotype, named LGMD type 2N (LGMD2N). Only four cases have been reported so far. ClinicalTrials.gov ID: NCT02759302

METHODS: We report 12 new cases of LGMD2N, aged 18-63 years. Muscle involvement was assessed by MRI, muscle strength testing and muscle biopsy analysis. Other clinical features were also recorded.

RESULTS: Presenting symptoms were difficulties in walking, pain during exercise, delayed motor milestones and learning disabilities at school. All had some degree of cognitive impairment. Brain MRIs were abnormal in 3 of 10 patients, showing ventricular enlargement in one, periventricular hyperintensities in another and frontal atrophy of the left hemisphere in a third patient. Most affected muscle groups were hip and knee flexors and extensors on strength testing. On MRI, most affected muscles were hamstrings followed by paraspinal and gluteal muscles. The 12 patients in our cohort carried 11 alleles with known mutations, whereas 11 novel mutations accounted for the remaining 13 alleles.

CONCLUSION: We describe the first cohort of patients with LGMD2N and show that unlike other LGMD types, all patients had cognitive impairment. Primary muscle involvement was found in hamstring, paraspinal and gluteal muscles on MRI, which correlated well with reduced muscle strength in hip and knee flexors and extensors. The study expands the mutational spectrum for LGMD2N, with the description of 11 novel POMT2 mutations in the association with LGMD2N.

CLINICAL TRIAL REGISTRATION: NCT02759302.