Missense mutations in LAMA2 causing a new phenotype of mild cognitive impairment, proximal myopathy, seizure, and severe leukoencephalopathy: A case report and protein analysis.


Abstract

Congenital muscular dystrophy with laminin-α2 deficiency, also known as MDC1A, displays an extensive phenotypic and genetic heterogeneity. The combination of clinical, biochemical, and genetic findings must be considered to obtain the precise diagnosis and provide appropriate genetic counseling. Here we report one individual from a family presenting with clinical features including seizure attack, slight weakness of proximal leg muscles, and mild cognitive impairment with increased small angular fibers, decreased expression of α-DG and β-DG, normal expression of laminin-α2, and severe white matter changes. Targeted next-generation sequencing (NGS) revealed two homozygous missense mutations, c.2881G>A (p.Ala961Thr) and c.4406G>A (p.Cys1469Tyr), in LAMA2 in the affected member of the family. Together, these results demonstrate a role for c.2881G>A and c.4406G>A mutations in LAMA2 and show that these two mutations, especially c.4406G>A, may cause mild cognitive impairment, slight motor retardation, seizures, and severe leukoencephalopathy, which extends the clinical spectrum associated with LAMA2 mutations.

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