A novel de novo variant of LAMA2 contributes to merosin deficient congenital muscular dystrophy type 1A: Case report.

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Abstract

Merosin deficient congenital muscular dystrophy type 1A (MDC1A) is caused by defects in the LAMA2 gene. Patients with MDC1A exhibit severe symptoms, including congenital hypotonia, delayed motor development and contractures. The present case report describes a Vietnamese male child with clinical manifestations of delayed motor development, limb-girdle muscular dystrophy, severe scoliosis and white matter abnormality in the brain. Whole exome sequencing (WES) was performed with subsequent validation using Sanger sequencing, and a de novo missense variant (NM_000426.3:c.1964T>C, p.Leu655Pro) and a splice site variant (NG_008678.1:c.3556-13T>A) in the LAMA2 gene of the proband was detected. The missense variant located in exon 14 and has not been reported previously, to the best of our knowledge; whereas the splice site variant has been previously reported to cause premature termination of transcription in patients with MDC1A. In silico tools predicted that the missense variant was damaging. Phenotype-genotype analysis suggested that this proband was associated with classical early onset MDC1A. The co-existence of a de novo and a heterozygous variant in the LAMA2 gene suggested that the de novo variant contributed to the autosomal recessive manner of the disease. Careful consideration of this event by clinical confirmation of parental carrier status may help to accurately determine the risk of occurrence of this disease in future offspring. Additionally, WES is recommended as a powerful tool to assist in identifying potentially causative variants for heterogeneous diseases such as MDC1A.

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KEYWORDS: LAMA2 gene; de novo; merosin deficient congenital muscular dystrophy type 1A; whole exome sequencing

PMID: 31929873  PMCID: PMC6951223  DOI: 10.3892/br.2019.1260