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# Novel compound heterozygous TTN variants as a cause of severe neonatal congenital contracture syndrome without cardiac involvement diagnosed with rapid trio exome sequencing

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## Abstract

This report focuses on a case of severe congenital myopathy with arthrogryposis without cardiac involvement due to compound heterozygous variants in the TTN gene. The proband presented with severe axial hypotonia, arthrogryposis and severe respiratory insufficiency with ventilator dependence. Electromyogram was abnormal with absent motor responses but preserved sensory nerve responses. Rapid gene-agnostic trio exome sequencing detected novel compound heterozygous variants in the TTN gene. One variant is a truncating frameshift located in the meta-transcript only exon 195. The other variant is a nonsense variant in exon 327 which affects all recognised post-natal transcripts apart from one. This case presents with a severe phenotype and adds to the expanding known variants associated with autosomal recessive titinopathy. It also demonstrates the utility of rapid trio exome sequencing when used early in the clinical course.

**Keywords:** Arthrogryposis; Cardiomyopathy; Exome sequencing; Inferred complete transcript; Respiratory failure; TTN.



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