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A novel de novo ACTA1 variant in a patient with nemaline myopathy and mitochondrial Complex I deficiency.

Pula S[1], Urankar K[2], Norman A[3], Pierre G[1], Langton-Hewer S[4], Selby V[1], Mason F[1], Vijayakumar K[1], McFarland R[5], Taylor RW[5], Majumdar A[6].

Author information

Abstract

We describe the presentation and follow-up of a three-year-old girl with nemaline myopathy due to a de-novo variant in ACTA1 (encoding skeletal alpha actin) and moderately low enzyme level of Complex I of the mitochondrial respiratory chain. She presented in the neonatal period with hypotonia, followed by weakness in the facial, bulbar, respiratory and neck flexors muscles. A biopsy of her quadriceps muscle at the age of one year showed nemaline rods. Based on her clinical presentation of a congenital myopathy and histopathological features on a muscle biopsy, ACTA1 was sequenced, and this revealed a novel sequence variant, c.760 A>C p. (Asn254His). In addition, mitochondrial respiratory chain enzymatic activity of skeletal muscle biopsy showed a moderately low activity of complex I (nicotinamide adenine dinucleotide (NADH): ubiquinone oxidoreductase). Disturbances of Complex I of the respiratory chain have been reported in patients with nemaline myopathy, although the mechanism remains unclear.

KEYWORDS: ACTA1; Mitochondrial dysfunction; Nemaline myopathy

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