Distal myopathy with coexisting heterozygous TIA1 and MYH7 Variants.

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Abstract

TIA1 mutations cause Welander distal myopathy. MYH7 mutations result in various clinical phenotypes, including Laing distal myopathy and cardiomyopathy. We describe a family with coexisting TIA1 and MYH7 variants. The proband is a 67-year-old woman with easy tripping since childhood and progressive asymmetric distal limb weakness, but no cardiac involvement. Muscle biopsy showed rare rimmed vacuoles, minicore-like structures and congophilic inclusions. Her 66-year-old sister has a mild distal myopathy, supraventricular tachycardia and hypertrophic cardiomyopathy. Both sisters carry the only known pathogenic TIA1 mutation and a heterozygous MYH7 variant (c.5459G>A; p.Arg1820Gln). Another sibling with isolated distal myopathy carries only the TIA1 mutation. MYH7 p.Arg1820Gln involves a highly conserved residue and is predicted to be deleterious. Furthermore, the proband's childhood-onset distal leg weakness and sister's cardiomyopathy suggest that MYH7 p.Arg1820Gln likely affects function, favoring a digenic etiology of the myopathy.

KEYWORDS: Digenic myopathy; Distal myopathy; Hypertrophic cardiomyopathy; MYH7; TIA1

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