Common and variable clinical, histological, and imaging findings of recessive RYR1-related centronuclear myopathy patients.


Abstract

Mutations in RYR1 give rise to diverse skeletal muscle phenotypes, ranging from classical central core disease to susceptibility to malignant hyperthermia. Next-generation sequencing has recently shown that RYR1 is implicated in a wide variety of additional myopathies, including centronuclear myopathy. In this work, we established an international cohort of 21 patients from 18 families with autosomal recessive RYR1-related centronuclear myopathy, to better define the clinical, imaging, and histological spectrum of this disorder. Early onset of symptoms with hypotonia, motor developmental delay, proximal muscle weakness, and a stable course were common clinical features in the cohort. Ptosis and/or ophthalmoparesis, facial weakness, thoracic deformities, and spinal involvement were also frequent but variable. A common imaging pattern consisted of selective involvement of the vastus lateralis, adductor magnus, and biceps brachii in comparison to adjacent muscles. In addition to a variable prominence of central nuclei, muscle biopsy from 20 patients showed type 1 fiber predominance and a wide range of intermyofibrillar architecture abnormalities. All families harbored compound heterozygous mutations, most commonly a truncating mutation combined with a missense mutation. This work expands the phenotypic characterization of patients with recessive RYR1-related centronuclear myopathy by highlighting common and variable clinical, histological, and imaging findings in these patients.

KEYWORDS: Centronuclear myopathy; Congenital myopathies; RYR1

PMID: 28818389 DOI: 10.1016/j.nmd.2017.05.016