LMO3-Associated Nemaline Myopathy: Prenatal Ultrasonographic, Pathologic, and Molecular Findings.

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Abstract

To describe the prenatal presentation, including ultrasonographic, histologic, and molecular findings, in 2 fetuses affected with LMO3-related nemaline myopathy. Prenatal ultrasonographic examinations and histopathologic studies were performed on 2 fetuses with evidence of nemaline myopathy. To establish a molecular diagnosis, whole-exome sequencing was pursued for the affected fetuses. Nemaline myopathy is a common form of congenital myopathy manifesting with nonprogressive generalized muscle weakness, hypotonia, and electron-dense protein inclusions in skeletal myofibers. Although clinically, nemaline myopathy can be viewed as a common pathway phenotype, its molecular basis is heterogeneous, with mutations in 11 identified genes implicated in its pathogenesis so far. Whole-exome sequencing revealed that the affected fetuses were compound heterozygous for 2 newly reported pathogenic variants in the LMO3 gene, which encodes leiomodin 3. To our knowledge, this article is the first report of LMO3-related nemaline myopathy since the original reported cohort. We provide a detailed description of the prenatal imaging of these affected fetuses, which we hope, in combination with next-generation sequencing, may contribute to further diagnosis in additional families.

KEYWORDS: LMO3; arthrogryposis; genetics; leiomodin 3; nemaline myopathy; pediatrics

PMID: 29331079 DOI: 10.1002/jum.14520