Somatic mosaicism represents an underestimated event underlying collagen 6-related disorders.


Abstract

BACKGROUND: Collagen VI-related disorders (COL6-RD) are a group of heterogenous muscular diseases due to mutations in the COL6A1, COL6A2 and COL6A3 genes, encoding for collagen VI, a critical component of the extracellular matrix. Ullrich congenital muscle disorder and Bethlem myopathy represent the ends of a clinical spectrum that includes intermediate phenotypes of variable severity. UCMD are caused by recessive loss of function mutations or de-novo dominant-negative mutations. The intermediate phenotype and BM are more commonly caused by dominantly acting mutations, and less commonly by recessive mutations. Recently parental mosaicism for dominant mutations in COL6 have been reported in four COL6-RD families and germinal mosaicism has been also identified in a family with recurrence of UCMD in two half-sibs.

METHODS AND RESULTS: Here we report three unrelated patients affected by a COL6-RD who carried de novo mosaic mutations in COL6A genes. These mutations, missed by Sanger sequencing, were identified by next generation sequencing.

CONCLUSIONS: This report highlights the importance of a complete diagnostic workup when clinical and histological finding are consistent with a COL6-RD and strengthen the impression that mosaisms are underestimated events underlying COL6-RD.

KEYWORDS: COL6-RD; Collagen 6; Mosaicism; NGS; Ullrich congenital muscular dystrophy

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