Clinical features of collagen VI-related dystrophies: A large Brazilian cohort.

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Abstract

OBJECTIVES: Collagen VI-related dystrophies (COL6-RDs) have a broad clinical spectrum and are caused by mutations in the COL6A1, COL6A2 and COL6A3 genes. Despite the clinical variability, two phenotypes are classically recognized: Bethlem myopathy (BM, milder form) and Ullrich congenital muscular dystrophy (UCMD, more severe form), with many patients presenting an intermediate phenotype. In this work, we present clinical and genetic data from 28 patients (27 families), aged 6-38 years (mean of 16.96 years), with COL6-RDs.

PATIENTS AND METHODS: Clinical, muscle histology and genetic data are presented. COL6A1, COL6A2 and COL6A3 genes were analyzed by next-generation sequencing (NGS).

RESULTS: Homozygous or heterozygous variants were found in COL6A1 (12 families), COL6A2 (12 families) and COL6A3 (3 families). Patients with the severe UCMD phenotype (three cases) had a homogeneous clinical picture characterized by neonatal onset of manifestations, no gait acquisition and a stable course, but with severe respiratory involvement. Most of the patients with the mild UCMD phenotype had neonatal onset of manifestations (88.8 %), delayed motor development (66.6 %), slowly progressive course, pulmonary involvement (55.5 %) and loss of the walking capacity before the age of 10 (66.6 %). In the intermediate group (nine patients), some children had neonatal onset of manifestations (44.5 %) and delayed motor development (88.9 %); but all of them achieved the ability to walk and were still ambulatory. Some patients that had the BM phenotype presented neonatal manifestations (57.1 %); however, all of them had normal motor
development and normal pulmonary function. Only one patient from the group of BM lost the walking capacity during the evolution of the disease. Other frequent findings observed in all groups were joint retractions, spinal deformities, distal hyperextensibility, congenital hip dislocation and keloid formation.

CONCLUSION: COL6-RDs present variable clinical manifestations, but common findings are helpful for the clinical suspicion. NGS is a valuable approach for diagnosis, providing useful information for the genetic counseling of families.

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