BACKGROUND: Ullrich congenital muscular dystrophy (UCMD) is a form of merosin-positive congenital muscular dystrophy characterized by proximal contractures, distal laxity, rigidity of the spine, and respiratory complications. Recently, a deficiency of collagen VI on muscle and skin biopsy together with recessive mutations in the collagen 6A2 gene were reported in three families with UCMD. However, the clinical spectrum, frequency, and level of heterogeneity of this disorder are not known.

SUBJECTS AND METHODS: The authors studied 15 patients (aged 3 to 23.6 years) with a clinical diagnosis of UCMD. Linkage analysis to the three collagen VI genes was performed in all informative families (n = 7), whereas immunohistochemical analysis of collagen VI expression in muscle was performed in the remaining cases.

RESULTS: An immunocytochemical reduction of collagen VI was observed in six patients. Three of the six patients belonged to informative families, and haplotype analysis clearly suggested linkage to the COL6A1/2 locus in two cases and to the COL6A3 loci in the third case. In the remaining nine patients, primary collagen VI involvement was excluded based on either the linkage analysis (four families) or considered unlikely based on normal immunolabeling of collagen VI. Age and presentation at onset, the distribution and severity of weakness and contractures, and the frequency of nonambulant patients were similar in the patients with and without collagen VI involvement. Distal laxity, rigidity of the spine, scoliosis, failure to thrive, and early and severe respiratory impairment were found in all patients by the end of the first decade of life, irrespective of...
their maximum motor functional ability or their collagen status.

**CONCLUSIONS:** These results suggest that collagen VI involvement is relatively common in UCMD (40%); however, the role of this molecule was excluded in a number of cases, suggesting genetic heterogeneity of this condition.

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