Collagen VI-related muscle disorders include severe Ullrich's disease (Ullrich congenital muscular dystrophy: UCMD) and milder Bethlem myopathy. Mutations in the 3 collagen VI genes, namely, COL6A1, COL6A2, and COL6A3, cause both diseases. UCMD is inherited in an autosomal recessive manner, and de novo dominant mutations are also reported. Bethlem myopathy is usually inherited in an autosomal dominant manner, but a rare autosomal recessive inheritance has recently been reported. Patients with UCMD have generalized muscle weakness, multiple contractures of the proximal joints, and hyperextensibility of the distal joints. Bethlem myopathy is characterized by a combination of proximal muscle weakness and contractures of finger, elbow, and ankle joints. Because intermediate phenotypes occur, UCMD and Bethlem myopathy should be considered diseases in a continuous spectrum of collagen VI-related muscle disorders.

Abnormalities of cell adhesion, regeneration, mitochondrial permeability transition pore, and autophagy have been reported in UCMD. Respiratory surveillance for nocturnal hypoventilation and proper respirator implementation are clinical management considerations in UCMD. Orthopedic assessment is necessary if surgery for Achilles tendon contractures is being considered in patient with Bethlem myopathy. We evaluated the role of nonsense-mediated mRNA decay (NMD) in UCMD associated with a premature termination codon in the COL6A2 gene, which caused the loss of collagen VI. A pharmacological block of NMD caused upregulation of the mutant collagen VI and partially functional extracellular matrix formation. Cyclosporin A has been reported to correct mitochondrial dysfunction and muscle apoptosis in patients with collagen VI myopathies, and a pilot trial of cyclosporin A was carried out.

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