Objective: To summarize the clinical manifestations and determine the molecular etiology for two collagen type VI-related myopathy pedigrees. Methods: Two spontaneous collagen type VI-related myopathy patients were admitted to Department of Neurology, Children's Hospital, Capital Institute of Pediatrics in October 2017. Clinical data of probands and their family members were collected and their genomic DNA was obtained for genetic testing. Next generation sequencing was performed and the variants were verified by the Sanger sequencing in the family members. Results: Target region sequencing indicated that the proband of family 1 has carried a heterozygous variant of COL6A3 gene, c.6229G>C(p.Gly2077Arg), and it was de novo variant confirmed by Sanger sequencing in the family. The patient 1, a 2-year-three-month old boy, was admitted due to motor retardation at birth. He was defined as early severe Ullrich congenital muscular dystrophy. He never achieved independent ambulation, he had onset of symptoms was found at birth, including diffuse muscle weakness, striking distal joint hyperlaxity, proximal contractures, calcaneal protrusion, kyphosis, and hip dislocation. Serum CK level was elevated slightly and EMG showed neurogenic changes. The patient 2, a 7-year-old girl with a limp for 4 years, carried one de novo variant of COL6A3 gene, c.5169_5177del (p.Glu1724_Leu1726del). This variant results in the deletion of amino acids (1724 to 1726) in α3 chain of collagen VI, which may disturb the function of this protein. She was diagnosed as Bethlem myopathy with a mild phenotype. She had delayed motor milestones and presented with walking on tiptoe, hypotonia, and ichthylordosis. The contracture of proximal joints was not very obvious. Serum CK level was normal and EMG showed myogenic changes. Muscle biopsy revealed muscular dystrophy and muscle magnetic resonance imaging of patient 2 showed vastus lateral is a "sandwich" sign. Immunofluorescence staining for COL6A3 chain in the cultured skin fibroblasts from patients 2 showed decreased deposition compared with control. Conclusions: These two patients were...
diagnosed as spontaneous collagen type VI-related myopathy and carried different variants of COL6A3 gene. Different in pathogenetic variants could cause different genetic features and different phenotypes. Collagen type VI- related myopathy patients have various clinical manifestations. Typical phenotypes include muscular dystrophies, proximal contractures, and distal hyperlaxity. Muscle MRI shows diffuse fatty infiltration of gluteus maximus and thigh muscle. The histological staining showed the low level expression of COL6A3 chain. The seventy of phenotype was related to the genotype.

**KEYWORDS:** Genetic diseases, inborn; Genotype; Muscular dystrophies