Coexistence of digenic mutations in the collagen VI genes (COL6A1 and COL6A3) leads to Bethlem myopathy. - PubMed - NCBI

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Format: Abstract

**INTRODUCTION:** Bethlem myopathy is a kind of collagen VI related myopathy which affects proximal skeletal muscles and leads to gait disturbance and multiple joint contractures with an onset in the first two decades of life. Lung function impairment (respiratory muscle and diaphragmatic weakness, ventilatory restriction, hypoxaemia and hypercapnia) and respiratory failure are part of the clinical spectrum and can occur in ambulatory patients.

**METHODOLOGY:** We carried out whole exome sequencing (WES) in combination with neuromuscular diseases-associated genes-filtering to detect the possible causative mutation(s) in a Korean family with Bethlem myopathy. An electrodiagnostic study showed myopathic pattern (normal nerve conduction study, and early recruitment and short amplitude muscle unit action potentials) in the proband.

**RESULTS:** Coexistence of digenic mutations in the collagen VI genes (COL6A1 and COL6A3) was identified by WES in the proband only: heterozygous missense mutations of the COL6A1 (NM_001848.2: c.823G>T, p.Gly275Trp; rs1556425467) and of the COL6A3 genes (NM_004369.3: c.9349G>A, p.Asp3117Asn; rs1226664855). COL6A3 mutation may be candidate as disease-associated variant, as far as it was found only in the proband harboring another heterozygous
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CONCLUSION: Our findings suggest that the coexistence of these digenic mutations is rare, but it may be used for the risk evaluation of individuals with a possible susceptibility to Bethlem myopathy. Taken together, genetic diagnosis using WES is a useful approach for the identification of pathogenic mutations associated with Bethlem myopathy.

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KEYWORDS: Bethlem myopathy; COL6A1 gene; COL6A3 gene; Digenic mutation; whole exome sequencing

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