Congenital myopathies (CM) are a group of inherited neuromuscular disorders, and they are classified based on the histopathological features encountered in the muscle biopsy. The electrophysiological findings reported in the literature are normal nerve conduction velocities, and a tendency to myopathic pattern in the electromyography. To describe the electrophysiological findings in patients with congenital myopathies, we report on the clinical, histopathological and electrophysiological characterization of 9 patients with CM. Nemaline myopathy was observed in 44.4% (4 cases) (15 yrs average), followed by multiminicore in 33.3% (3 cases) (12 yrs average), central core in 11.1% (1 case) (14 yrs) and centronuclear in 11.1% (1 case) (47 yr). Electrophysiological findings: CMAP was abnormal in 56.8% (5 cases) with alterations in the amplitude of the peroneal nerve (nemaline myopathy), and the SNAP was normal in 100% (9 cases). In electromyography, the analysis of the motor unit demonstrated decreased amplitude in 62.5%, but duration was normal in 100% of cases. In the interference pattern, the relationship of turns and amplitude was analyzed and showed a ratio less than the unit (1) in 60% of cases (indicating a neurogenic pattern) and a ratio greater than the unit in the other 40% of cases (indicating a myopathic pattern). The amplitude of the CMAP of the peroneal nerve may be altered due to muscular hypotrophy. The characteristic myopathic pattern was not observed in all patients, instead neuropathic and nonspecific patterns were found. Clinical characterization in association with histopathological and electrophysiological studies are helpful to complement the diagnosis in congenital myopathies

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Three cases of SEPN1-related myopathy

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The *SEPN1* related myopathy, caused by pathogenic variants in *SEPN1,* is a genetic myopathy characterized by early axial onset, spinal rigidity, respiratory failure, and histopathological findings associated with dystrophic changes and congenital myopathy patterns. Here, we report three cases of *SEPN1*-related myopathy. Case 1: A 19-year-old man was referred due to unsteady gait and spinal rigidity with scoliosis since early infancy. He has had respiratory failure since he was 13 years old and has been using a non-invasive ventilator. His family history was unremarkable. The needle electromyography showed generalized myopathy. Muscle biopsy showed moderate fiber size variation. Targeted next-generation sequencing identified compound heterozygous variants in *SEPN1* (NM_020451.2: c.619del and c.1574T>G). Case 2: A 29-year-old woman complained of a ten-year history of progressive muscle weakness. She showed long face and high arched soft palate. Muscle biopsy showed increased size variability with suspicious area of multi-minicore. Targeted next-generation sequencing revealed compound heterozygous variants in *SEPN1* (c.234del and c.565C>T). Case 3: A 14-year-old woman admitted with pulmonary insufficiency from 5 years of age. Her brother presented pulmonary insufficiency and muscle weakness, and was previously diagnosed with muscular dystrophy. At ten years of age, spinal rigidity with scoliosis was noticed. Neurological examination showed muscle weakness and atrophy of proximal and axial muscles. Muscle biopsy showed moderate size variation of myofibers with some degeneration. Molecular diagnosis revealed compound heterozygous variants in *SEPN1* (c.619del and c.1574T>G). This report underlines the clinical diagnostic clues of early axial weakness or unexplained respiratory failure to suspect a *SEPN1* related myopathy. Moreover, our cases expand the clinical and genetic spectrum of *SEPN1* related myopathy as the first report in Korea.

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Diagnosing pathogenic mutations for congenital myopathy and cardiomyopathy patients

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We performed exome sequencing panel analysis including 43 genes in a cohort of 87 patients with diagnoses of congenital myopathy (CM), muscular dystrophy, or cardiomyopathy. Congenital myopathies are characterized by generalized muscle hypotonia and weakness of varying severity usually beginning at birth. Myopathies cannot be definitely distinguished from each other nor from other congenital muscle disorders on clinical grounds alone; diagnosis depends on characteristic muscle biopsy findings. Cardiomyopathy can present in varied phenotypes including dilated, hypertrophic, and restrictive patterns. In addition to history and physical examination, diagnosis of cardiomyopathy includes electrocardiography and echocardiography testing. More accurate diagnosis includes mutation detection. Our study identifies insertions, deletions, duplications, and single nucleotide missense mutations in cohort of 87 individuals. We detected 51 pathogenic mutations, 29 variants of unknown significance and in 16 patients the panel test did not find any mutations. Diagnostic rate in our panel was 29%. We also validated four large deletions in nebulin (*NEB*), titin (*TTN*), ryanodine receptor 1 (*RYR1*) and dynamin 2 (*DNM2*) using droplet digital PCR. We report the first case of Congenital Fibre Type Disproportion (CFTD, OMIM# 255310) caused by *TTN* and *NEB* mutations.

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A novel compound heterozygous mutation in the PYROXD1 gene in a patient with congenital myopathy

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Congenital myopathies (CMs) are a heterogeneous subgroup of muscle diseases usually characterized by muscle weakness and hypotonia at birth. Cases with *PYROXD1* gene mutations can present with slowly progressive congenital myopathy or limb girdle muscular dystrophy (LGMD). We present a case of an 11-year-old boy who presented with motor developmental delay and inability to walk. He was born after an uneventful pregnancy and delivery, with non-consanguineous marriage of his parents. Motor milestones were delayed, walking without support at the age of 3. He developed inability to walk without support from the age of 9. On physical and neurological examination at the age of 10, his weight was below the 3rd percentile, height and head circumference were normal. He had facial weakness, nasal speech, difficulty swallowing, pes planus, globally absent deep tendon reflexes, and proximal muscle weakness. His maximum muscle strength was sitting without support. Cardiological evaluation was unremarkable. Serum creatine kinase (CK) levels were normal (62 UI/L). At the age of 4, muscle biopsy revealed fiber size variation, internalized nuclei, and fatty replacement. We identified a novel compound heterozygous mutation of *PYROXD1* gene [c.52G>C (p.Gly18Arg) in exon 1, maternal and c.464A>G (p.Asn155Ser) in exon 5, paternal] with whole exome sequencing. Here we describe a case presenting with late-onset congenital myopathy and compound heterozygous *PYROXD1* gene mutation expanding the disease genotypes of PYROXD1-associated myopathy.

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