

A Case of Congenital Neuromuscular Disease with Uniform Type 1 Fiber

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Congenital neuromuscular disease with uniform type 1 fiber (CNMDU1) is a rare but distinct form of nonprogressive, congenital myopathy. CNMDU1 is characterized by a type 1 muscle fiber content of more than 99%. This condition has only been previously described in a few reports. The authors report an 11-year-old girl who exhibited delayed developmental milestones, proximal muscle weakness, and bilateral ptosis. Her serum creatine kinase level was normal but an electromyographic study showed myopathic changes. A biopsy specimen from the left deltoid muscle revealed a uniformity of type 1 fibers (greater than 99%) with a moderate variation in fiber size. This is the first case of CNMDU1 reported in Korea.

Key Words: Congenital neuromuscular disease with uniform type 1 fiber (CNMDU1), congenital myopathy

INTRODUCTION

Congenital neuromuscular disease with a uniform type 1 fiber (CNMDU1) was first described by Oh and Danon in 1983. CNMDU1 is a rare but distinct form of congenital myopathy, which is characterized by an early symptom onset, mild proximal weakness, hyporeflexia, a normal serum muscle enzyme level, uniform type 1 fibers, and a non-progression of the disease course.¹ We present a case of an 11-year-old girl with the characteristic clinical features and pathological findings of CNMDU1.

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CASE REPORT

An 11-year-old girl presented with a waddling gait and bilateral ptosis. She was born at full term by cesarean section due to her mother's narrow birth canal. She had no perinatal problem or head trauma history and there was no family history of neuromuscular disease or mental retardation. Her early developmental milestones were unremarkable, and she showed a bilateral ptosis at the age of 8 months. She began walking alone at 18 months of age but her gait was unstable and she fell frequently. Shortly after that time, her parents noted a weakness, particularly when she tried to climb stairs or run. The weakness progressed slowly, and was expressed by a waddling gait and difficulty rising from a sitting position. Her intelligence and speech were normal. In addition, there was no evidence of scoliosis or other skeletal abnormalities. Pseudohypertrophy, winged scapula, muscle atrophy, and fasciculation were absent. She had a large elongated face, a high-arched palate, positive Gowers' sign, and a toe in gait. The neurological examination revealed no abnormalities in her mental status, cranial nerve function, sensation, or coordination. By the MRC (Medical Research Council) grading, she had a mild weakness in her neck (MRC grading 4), both proximal upper extremities (MRC grading 4⁻), both distal upper extremities (MRC grading 4⁺), both proximal lower extremities (MRC grading 4⁻), and both distal lower extremities (MRC grading 4⁺). She had no weakness of facial muscle and no limitations of extraocular muscles. There were no babinski signs or ankle clonus, and her deep tendon reflexes were hypoactive. The EKG and

chest X rays were also normal. Her serum creatine kinase level and nerve conduction studies were normal. A needle electromyography study revealed small brief motor unit action potentials. A biopsy of a specimen from the left deltoid muscle indicated a mild variation in the size and uniformity of the type 1 fibers (greater than 99%), and a severe loss (less than 1%) of type 2 fibers. However, a biopsy showed that there were no nemaline bodies, cores, targetoid structures, or central nuclei.

DISCUSSION

Congenital neuromuscular disease with uniform type 1 fiber (CNMDU1) was proposed by Oh and Danon to be a new congenital myopathy.¹ In their report, CNMDU1 is described to have common

clinical, electrophysiological, and histochemical features: (1) delayed motor developmental milestones, suggesting an early onset; (2) mild proximal weakness; (3) hyporeflexia or areflexia; (4) normal serum muscle enzyme levels; (5) a substantial decrease in the mean duration of motor unit potentials; (6) uniform type 1 fibers; and (7) non-progression of the disease.¹ CNMDU1 shares common clinical aspects with congenital nonprogressive myopathy, but exhibits characteristic histochemical features.^{1,2} In the CNMDU1 cases reported previously,¹⁻³ no nemaline rods, central nuclei or core structures were observed, but more than 99% of the muscle fibers were of type 1 (normally up to 55%). Some patients exhibit severely delayed motor milestones and muscle weakness.^{2,3} It has also been reported that CNMDU1 may be associated with mental retardation^{4,5} or borderline intelligence with brain

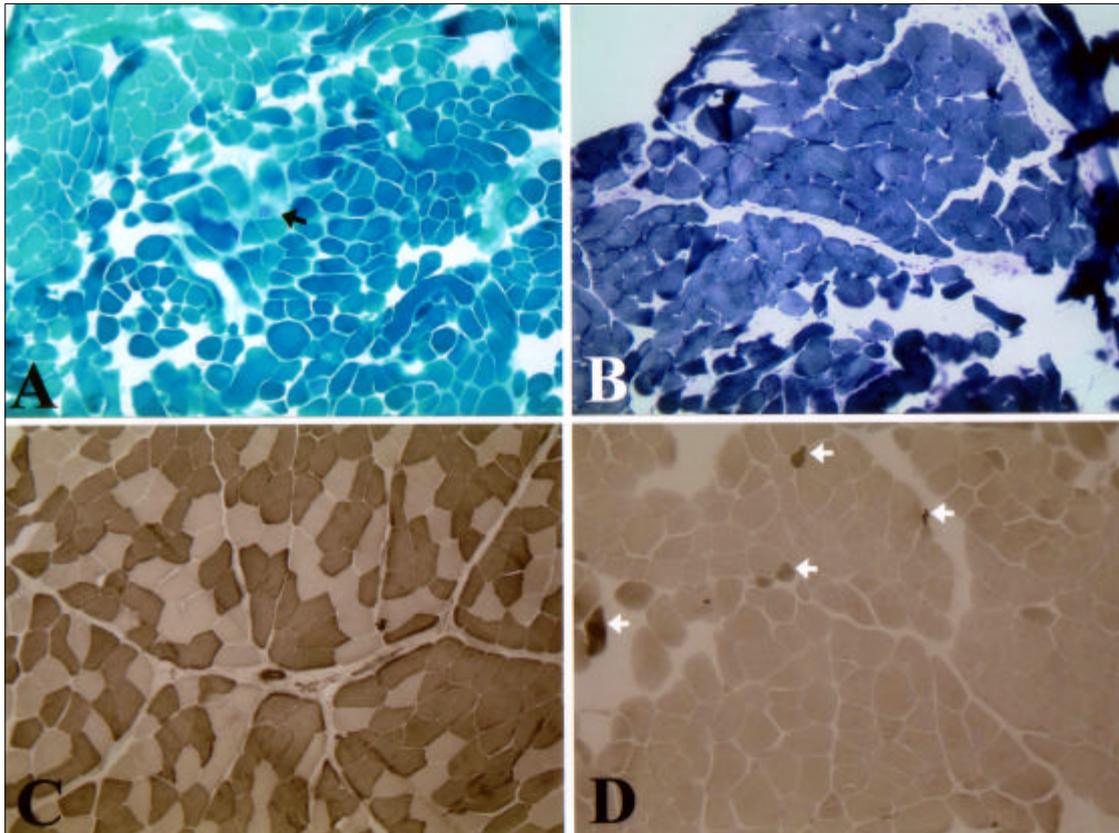


Fig. 1. Pathological findings of a muscle biopsy from the left deltoid muscle. Histochemical staining showed:- a mild variation in the fiber size and a small normal nerve fascicle (indicated by the black arrow) (A), no nemaline bodies, core structures, targetoid structures, or central nuclei (B), a normal proportion of type 1 and 2 fibers in the normal control (C), and over 99% of type 1 fibers in the muscle fibers, with a severe loss of type 2 fibers (indicated by the white arrow) (D). (A; modified Gomori trichrome, B; NADH-TR, C&D; ATPase pH 9.4).

atrophy by brain CT.⁶ In addition, ophthalmoplegia and ptosis have been reported to be absent in CNMDU1, with the exception of one case.⁶ Our patient had only mild weakness and ptosis without mental retardation. The main findings that differentiate CNMDU1 from congenital muscular dystrophy or spinal muscular atrophy are; a normal CK level, no mental retardation, no neurogenic findings on EMG, and no small angulated fibers with normal nerve fascicles on the muscle biopsy. Type 1 fiber predominance is defined when more than 55% of the fibers are type 1,¹ and is a common finding in many non-progressive myopathic disorders: congenital fiber type disproportion⁷ (CFTD), central core disease⁸ (CCD), nemaline myopathy,⁹ myotubular myopathy,¹⁰ multicore disease,¹¹ and in fingerprint body myopathy.¹² However, unlike these congenital myopathies, CNMDU1 lacks their specific diagnostic findings.⁶ It is questionable that CNMDU1 is associated with other congenital myopathy entities, and that formation of central core is associated with age. Tachi, et al. reported a girl with CFTD at 3 years of age, who later showed uniform type 1 fibers with core structures at 12 years of age.¹³ Tojo, et al. reported a family in which the proband (the father) had CCD and his son had CNMDU1.¹⁴ Both father and son had uniform type 1 fibers but only the father had the core structures. Morgan-Hughes, et al. also reported a family in which the mother had central cores with a type 1 fiber predominance (97%), and the daughter and son showed 83% and 92% type 1 fiber predominance, respectively, but with no core structures.¹⁵ The absence of cores in these children may have been due to either the muscle sampling technique, or to the patients being too young to have developed cores, since the number of core structures appears to increase with age.¹⁴ On the other hand, one family showed different core formation frequencies among the family members: the grandmother had cores in 75% of the fibers, the mother in 50%, and the daughter 100%.¹⁶ These findings show that CNMDU1 may be related to CFTD and CCD, but that age is not a definite cause of core formation. Further morphological studies will be needed to explain these phenomena.

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