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Multicore Myopathy

— A Case Report —

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Multicore myopathy is a rare congenital myopathy. The multicores consist of numerous small areas of decreased oxidative enzyme activity. The long axis of the lesion is perpendicular or parallel to the long axis of the muscle fiber. These cores are usually smaller than central cores. For this reason they are also called minicores. Although the multicores represent a nonspecific change in that they can be observed in malignant hyperthermia, muscular dystrophy, inflammatory myopathy, etc. Muscular weakness dating from early infancy is combined large proportion of the muscle fibers. In about half of the reported cases the muscular weakness has not been progressive, while in the others a slow progression has occurred. This 9-year-old boy presented with congenital nonprogressive myopathy associated with thoracic scoliosis and bilateral equinovarus deformity. The serum creatine phosphokinase and lactic dehydrogenase levels were normal. Electromyography showed "myopathic" features. The biopsy revealed a marked size variation in myofibers, ranging from 10μm to 100μm. A few small angular fibers and slight endomyseal fibrosis were also noted. There was type I fiber predominance. NADH-TR reaction disclosed more well-defined cores with loss of intermyofibrillary mitochondrial activity. These cores were usually located with loss of intermyofibrillary mitochondrial activity. These cores were usually located in the peripheral portions of the myofibers and the core size measured 10-30μm in diameter. Electron microscopic examination revealed circumscribed areas of disintegrated Z band material and disorganized sarcomeric units near the sarcolemma. A decrease in the number of mitochondria and glycogen particles was noted.

Key Words: *Multicore myopathy, Congenital, Mitochondria, NADH-TR stain.*

INTRODUCTION

Multicore myopathy is a benign nonprogressive congenital myopathy assoicated with multifocal degeneration of myofibers. The first case was reported in 1966 by Engel (Engel and Gomez, 1966) and subsequent cases have been reported with strikingly similar findings on histochemical and electron microscopic studies. Clinical symptoms are usually benign and nonprogressive, which is similar to congenital myopathies of other variants. Its common mode of transmission is sporadic rather than autosomal traits. Thereafter cases with aggressive course or variable associated diseases have been further detected in addition to classical findings of the multicore disease.

Recently we experienced a case of multicore myopathy presented with severe musculoskeletal deformity. His muscle biopsy revealed typical light microscopic, histochemical, and electron microscopic findings of multicore myopathy and so we would describe him as the first in the Korean literature.

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CASE REPORT

This case was represented at 9 years of age because of standing difficulty and thoracic scoliosis. He was born to a mother with no special perinatal problems. At about 5 months of age, weakness in both legs was detected by his parents. He was diagnosed as having congenital disolcation of the hip joints and wore a hip spica cast for a short duration. He spent one or two years without it but showed the delay of motor milestones. At 2 years, his thoracic spine revealed left side scoliosis and his legs became spastic, with equinovarus deformity. he underwent a corrective opertion for the equinovarus deformity at 3 years, after which he has worn a brace intermittently for the scoliosis till now, with slight improvement. However, he continued to have difficulty in standing alone and doing exercises. School performance was good and daily life was relatively normal. This time at 9 years of age, he visited the Orthopedic Service of Seoul National University Hospital for a complete and more precise correction of the scoliosis. Famiy and past medical histories were unremarkable. Physical examination revealed a relatively lean body habitus with normocephalic head but not a malformed face. Limping gait and thoracic scoliosis in addition to persistent coxa valga deformity were found. Neurologic examination disclosed muscle atrophy most prominently in the proximal muscles of the upper extremity. The muscle atrophy was also noted in proximal leg and interscapular areas. Nerve conduction velocity was normal but an electromyogram revealed multiple short polyphasic spikes in the deltoid and vatus medialis muscles. Levels of creatine phosphokinase and lactic dehydrogenase were within normal range. He underwent a calf muscle biopsy.

PATHOLOGICAL EXAMINATION

Specimens for paraffin sections were fixed in neutral formalin. Specimens for electron microscopy were fixed with a 3% glutaraldehyde solution, postfixed in 2% osmium tetroxide and embedded in Epon 812. Paraffin sections were stained with hematoxylin and eosin (H&E), and phosphotungstic acid hematoxylin (PTAH). Specimens for enzyme histochemistry were cut at 10 μm in a cryostat at $-160 \sim -170$°C and serial sections were stained with H&E, modified gomori trichrome, myofibrillar adenosine triphosphatase (ATPase) at pH 9.4, and nicotinamide-adenine dinucleotide-tetrazolium reductase (NADH-TR). Ultrathin sections were cut on a Sorval ultramicrotome and

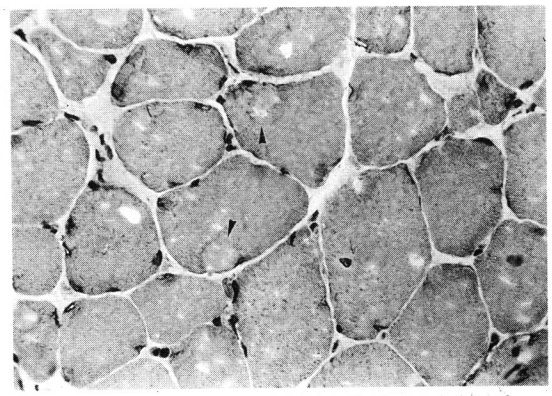

Fig. 1. H&E sections reveal moderate size variation of myofibers due to scattered small atrophic fibers, internal nuclei, and endomyseal fibrosis. A few fibers are suspicious for mini-core lesions (arrowheads) due to pale stainability in comparison to the remaining sarcoplasm.

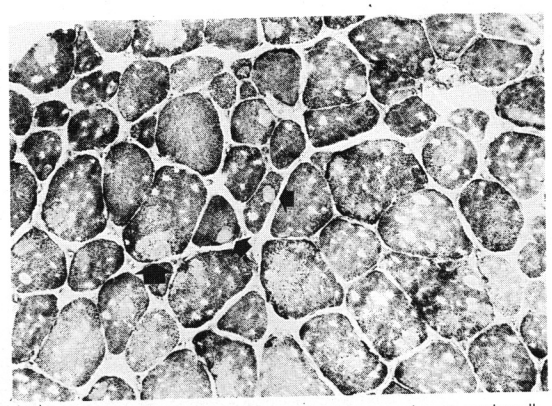

Fig. 2. NADH-TR staining reveals the prominent and well-defined multifocal core lesions (arrows), which were largely peripheral-located (×200).

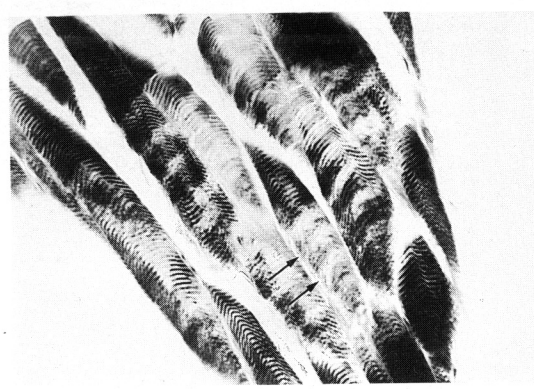

Fig. 3. Longitudinal section reveals discontinuous involvement of the variable length of the myofibrils, sometimes with perpendicular involvement (arrows).

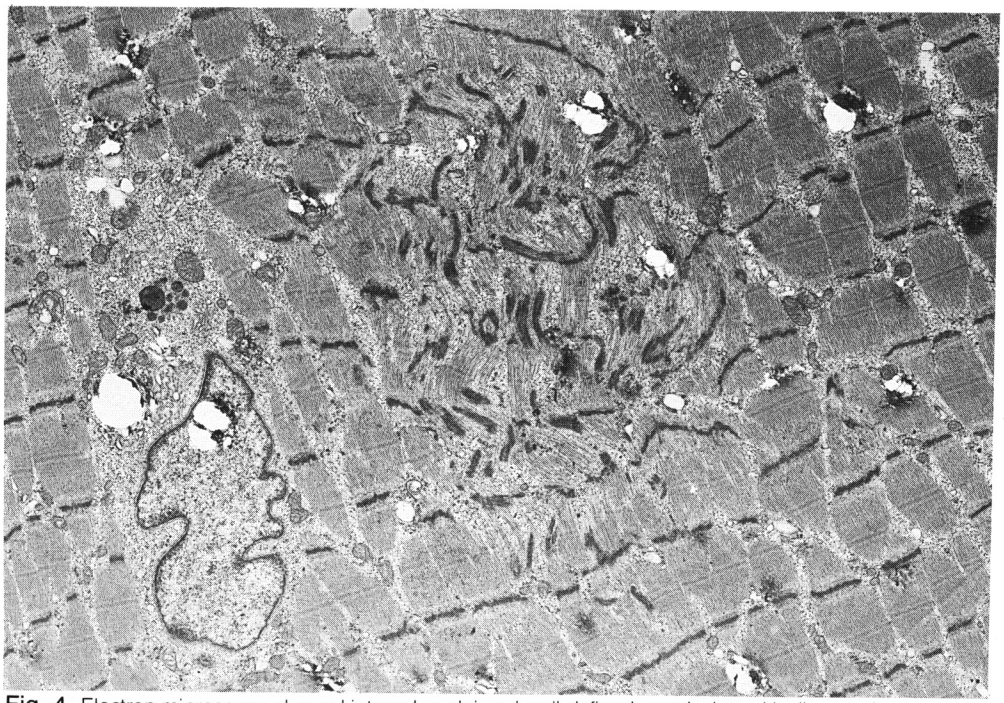

Fig. 4. Electron microscopy showed internal nuclei and well-defined core lesion with disrupted sarcomeric system and severely deformed Z-band materials (×9,200).

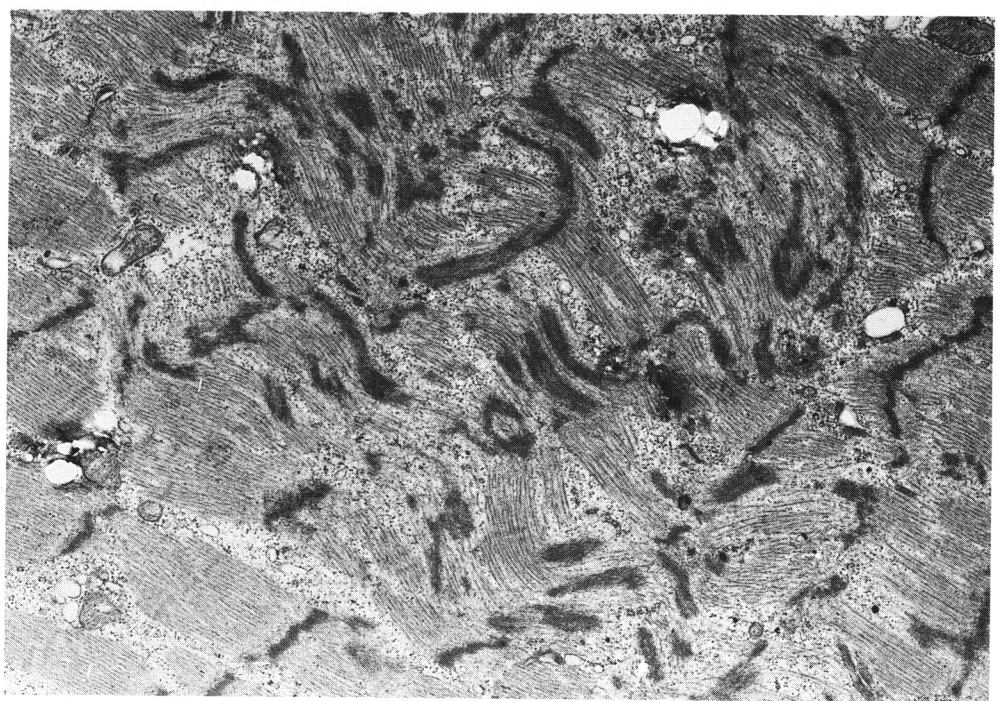

Fig. 5. The more magnified ultrastructural view of the Z-band streaming areas disclosed absence or marked reduction of mitochondria and glycogen particles in contrast to the surrounding interfibrillary areas (×18,400)

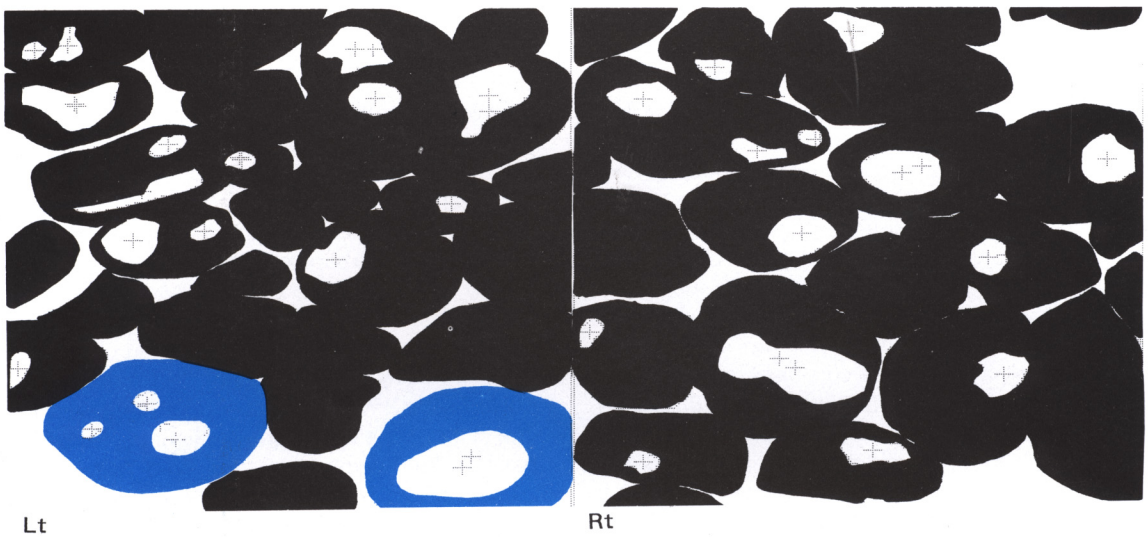

Fig. 6. Morphometric studies on NADH-TR (right) and ATPase 9.4 (left) stains revealed that the stain-defective cores had the larger diameter on the former stain (19μm) than on the latter (16μm).

examined with a H-600 electron microscope. Measurement of the core size was performed by morphometric analysis using Leitz ASM 68K in 2D operating mode.

On light microscopy a moderate size-variability of muscle fibers was observed, which ranged from 10 to 90 μm in diameter. There were small atrophic fibers and some internal nuclei (Fig. 1). A few whorled fibers were also noted. In some places slight endomyseal fibrosis was found but there was no inflammatory cell infiltration. Sections statined by ATPase at pH 9.4 revealed type 1 fiber predominance up to 95%. Multifocal round defects of myofibrillar ATPase activity appeared in many fibers, and they the diameters ranged from 5 to 20μm on NADH-TR stained sections. Many type 1 and 2 fibers contained characteristic unstained round areas due to loss of interfibrillary mitochondrial activity. These cores were usually eccentrically located near the sarcolemma, ranging from 10 to 30 μm in diameter (Fig. 2). Longitudinal revealed multifocal discontinuous stain-defective cores, which are different from the central cores with longitudinal continuity. They could be also variably located in parallel or perpendicular orientation to the longitudinal axis (Fig. 3). Electron microscopy disclosed well-circumscribed areas of disarrayed myofibrls with Z band streaming and sarcomeric disintegration, bordered by normally arranged portions (Fig. 4). Mitochondria and glycogen particles were markedly decreased or absent in these lesions (Fig. 5). Morphometrically, NADH-TR stained sections revealed the larger size of defective areas than ATPase 9.4, respectively measuring 19 and 16 μm in average diameter (Fig. 6).

DISCUSSION

Since Shy and Magee's description of central core disease in 1966, other benign congenital nonprogressive myopathies have been identified. Histochemical and electron microscopic techniques contributed to the recognition and definition of these new entities of congenital myopathy. One of them, multicore myopathy is noted for a decrease in the mitochondrial population as its basic pathologic alteration. The myofibrillar alteration is less widespread, occurs in confines of the mitochondrial lesion, and begins with disintegration of Z-disk. There are also decrease or absence of glycogen granules and sarcotubular profiles in the core lesions in comparison to the adjacent normal myofibrils (Engel et al., 1971). All of these characteristic findings were found in our case. When we first examined this biopsy specimen we thought that we were dealing with the second case of central core disease in Korea, since we have experienced a case recently (Myong et al., 1992). However, as the cores were too small and multiple on H&E sections, we had to suspect another entity namely minicore disease and examined more carefully the lesions. After all, we interpreted it as multicore myopathy.

The pathogenetic aspects of the multicores have major interests in dysfunction of mitochondria and my-