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Inclusion Body Myositis

- A Case Report -

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Inclusion body myositis is a rare myopathy that clinically resembles a chronic polymyositis and histopathologically is characterized by the presence of rimmed vacuoles containing ultrastructural cytoplasmic degradation products with filamentous intranuclear and cytoplasmic inclusions. Since clinical features are not uniform, histopathologic and ultrstructural studies are necessary to confirm the diagnosis. We report a typical case of inclusion body myositis with histopathologic and ultrastructural study. The patient was a 31 year old male who presented with progressive weakness of both forearms, hands and lower exremities for 10 years.

Key Words : *Inclusion body myositis, Ultrastructural study*

INTRODUCTION

Inclusion body myositis(IBM) has been a still poorly understood form of idiopathic inflammatory myopathy since this entity was first described by Yunis and Samaha in 1971. Despite great progress in clinical understanding and various recent report for pathophysiology, the disease has been known to be resistant to all therapeutic trials(Calabrese and chou, 1994; Dalakas, 1994). Clinically IBM shows progressive muscle weakness. Electromyography revealed a mixed neurogenic and myopathic pattern(Hund et al., 1995). Light microscopically, the muscle shows scattered or grouped atrophic fibers with vacuolar changes(Yunis and Samaha, 1971 ; Carpenter et al., 1978 ; Tome et al., 1981 ; Julien, 1982). Ultrastructural rimmed myeloid bodies and filamentous inclusion bodies appear to be the main pathological changes accounting for the progressive muscle fiber degeneration(Adams et al., 1965 ; Carpenter et al., 1978 ; Julien et al., 1982 ; Jongen et al., 1995).

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We report here a typical case of IBM with ultrastructural study and literature review.

MATERIAL AND METHODS

Clinical findings were reviewed from the files of Chung Ang Gil Hospital. Light microscopical and ultrastructural findings were retrospectively reviewed.

Muscle biopsy obtained from vastus lateralis divided into three parts ; one was frozen quickly ; the second one was fixed in 2.5% glutaraldehyde solution for 4 hours and the third one was fixed in 10% formaldehyde solution. The latter one was processed routinely through paraffin, sectioned for 4um, stained with hematoxylin and eosin.

The frozen specimen was stained with Periordic acid and Schiff stain and Masson trichrome stain. Enzyme histochemistry was not done.

For electron microscopic study, the specimen was postfixed in phosphate buffered 1% osmium tetroxide, dehydrated through graded concentration of ethanol and propylene oxide, and embedded in epon. Thin sections were stained with uranyl acetate and lead citrate and examined with a Hitachi H7100 electron microscope.

CASE REPORT

This 39 year old male presented with progressive weakness and atrophy on both forearms, hands and lower extremities for 10 years. Family history and past history were uncontributory. He had no sensory abnormalities. Deep tendon reflexes were relatively normal. On admission day, CPK and LDH were 698/729 IU/L and SALT and SAST were 70/102 IU/L. 5 days after, CPK and LDH lowered to 164/426 IU/L and SALT and SAPT were 27/42 IU/L. Urine creatinine was 96mg/dl. Other laboratory findings were within normal limits. Electromyogram(EMG) revealed fibrillation and myotonic discharge at rest and low amplitude(0.2-0.5mv) motor unit potential with early recruitment. The result of EMG suggested myopathy with inflammation and the neurologist mentioned myotonic dystrophy should be ruled out. Biopsy from the vastus lateralis muscle was done.

PATHOLOGIC FINDINGS

Light microscopically, muscle showed marked size variation with intermixed small angulated atrophic myofibers(Fig. 1). Degenerating myofibers with a few inflammatory cell infiltration were also seen. There were numerous internal nuclei and frequent vacuoles in the center and periphery of the myofibers(Fig. 2). Endomyseal and vascular changes were unremarkable.

Ultrastructurally, the muscle showed size variation with subsarcolemmal and intermyofibrillar deposition of myeloid bodies(Fig. 3). In the perinuclear area, whorled filamentous bodies(Fig. 4) were noted.

DISCUSSION

Clinical features of inclusion body myositis(IBM) resemble chronic polymyositis, however, pathologically, unique features of vacuolar changes of muscle are shown. These vacuoles ultrastructurally contain cytoplasmic degradation products and filamentous intranuclear and cytoplsmic inclusions are characteristic in this disease(Julien et al., 1982 ; Jongen et al., 1995).

According to the literatures, IBM showed a male predominance and male to female rato was about 2.5 : 1. The age at onset of symptoms ranged from 16 to 68 years. Clinically IBM showed progressive muscle weakness. Proximal and distal muscles were involved more or less equally(Carpenter et al., 1978 ; Tome et al., 1981). Both upper and lower extremities were involved simultaneously and symmetrically. Scapular, cervical and even facial muscles were occasionally involved (Hudson et al., 1971), but extraocular muscles were always spared. Transient myalgias were noted occasionally at the beginning(Mikol et al., 1982) or during the evolution of the disease(Jerusalem et al., 1972). No sensory abnormalities have been observed and our case did not show them. Atrophy of affected muscles was frequent but not constant. Our case was clinically

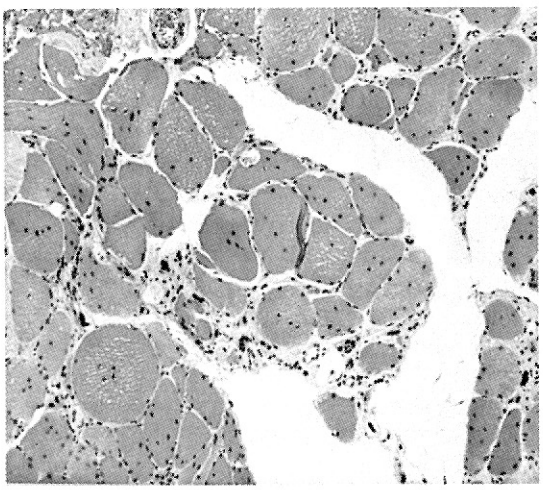

Fig. 1. Muscle shows marked size variation with intermixed small angulated myofibers. There are numerous internal nuclei and occasional vacuoles in the center and periphery of the myofibers. (X 100)

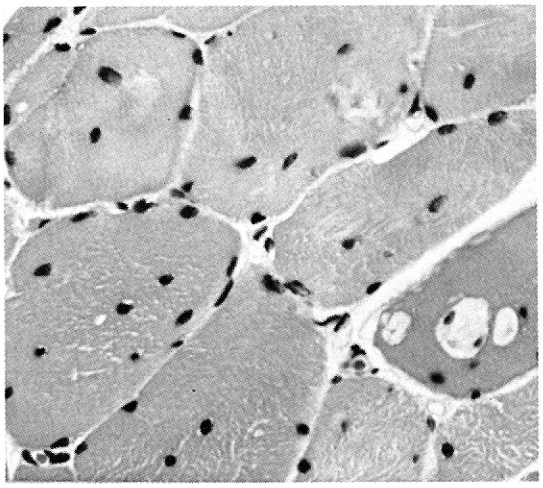

Fig. 2. Endomyseal vacuolar changes and internal nuclei are remarkable. (X 400)

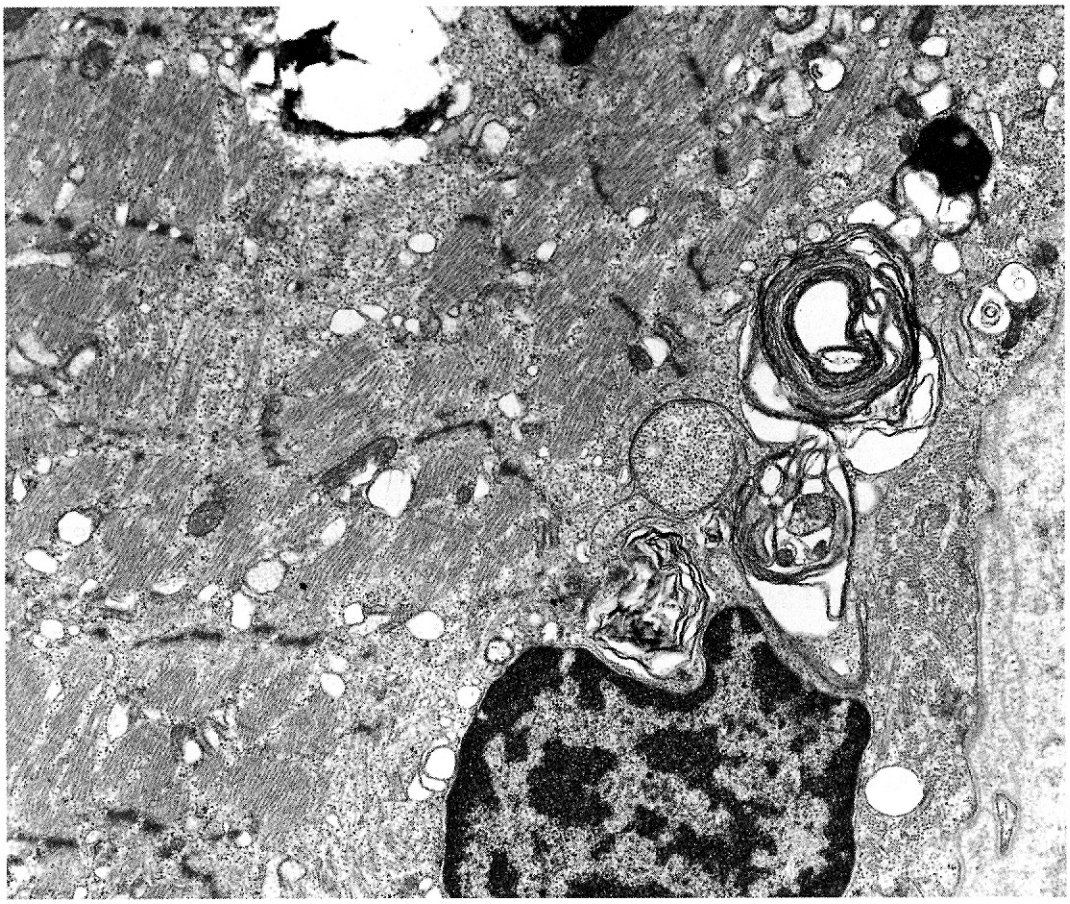

Fig. 3. Ultrastructurally, the muscle shows subsarcolemmal deposition of myeloid bodies. (X 9,000)

compatible with IBM. Our case presented with progressive muscle weakness and atrophy involved both forearms, hands and lower extremities for 10 years. He had no sensory abnormalities.

Electromyogram usually revealed motor unit potentials of short duration with an increased incidence of polyphasic potentials(Engel and Banker,1986). Myotonic dischages were noted very rarely(Julien et al., 1982). Fibrillations in varying number and positive waves were described(Ketelsen et al., 1977). Our case showed typical features of short amplitude motor unit potentials and myotonic discharge as described in the case summary.

The pathology of the muscle in this disease usually shows marked size variation with angulated myofibers, but inflammatory changes are inconsistent. Angular fibers are always present, either randomly scattered or grouped in small or large clusters. Therefore, neurogenic atrophy should be ruled out. There was no perifascicular atrophy which is commonly seen in dermatomyositis. Centrally placed internal nuclei were common. Macrophages invasion into necrotic myofibers was a frequent finding. The infiltrate consisted mostly of lymphocytes and plasma cells and mast cells being rare. Fibrous or fatty connective tissue was increased in most cases. According to the previous reports, the typical vacuoles were seldom recognized in paraffin sections and the vacuolar change, necrosis, regeneration and fibrosis were all clearly displayed in the cryostat sections. However, our case showed vacuoles in paraffin section as well as in cryosection. Enzyme histochemically, the vacuoles were prominent in type 1 fibers, or evenly distributed between type 1 and type 2 fibers (Nonaka et al.,1981). The muscular histopathology was

Fig. 4. In the perinuclear area, whorled filamentous body is seen. (X 15,000)

not specific, but the combined pattern of the histopathologic alterations and the ultrastructural filamentous inclusions were quite typical of the disease(Engel and Banker, 1986).

Ultrastructural studies showed abnormal filaments in all biopsy specimens. The filaments were in the nucleus, the cytoplasm or both. The length of the filaments had a rectilinear course and in some cases were decorated with striations along the long axis(Chou, 1967 ; Chou, 1968). Intranuclear filaments were arranged in parallel or randomly oriented like bundles of sticks. Some of the nuclear filaments perforated the nuclear envelope and were extruded into the cytoplasm. Intranuclear filaments sometimes proved difficult to find and identify. In most cases the cytoplasmic and nuclear filaments were identical in size, but the former were larger in Chou's first case(Chou, 1967). Some nuclei had two types of nuclear inclusions. The first type were a clusters of thin, 7-nm wide filaments. The second type consisted of irregular single or multiple vacuoles encircled by a membrane(Chou,1968 ; Fukuhara et al.,1980). The cytoplasmic filaments were parallel or concentric or randomly dispersed.

Myofiber regions containing cytoplasmic degradation products corresponded to the vacuoles observed by a light microscope. Most of the vacuoles were located at the subsarcolemmal area, but some were deeper in the intermyofibrillar area. The membranous whorls or myeloid structures in IBM were autophasic vacuoles and also nonspecific(Schroder and Adams, 1968 ; Spiro, 1979). They have been described in chloroquine myopathy(Macdonald and Engel, 1970), colchicine myopathy(Markand and D'gostino, 1971), vincristine myopathy(Clarke et al., 1978), acid maltase deficiency(Engel, 1970), primary hypokalemic periodic paralysis(Engel, 1970), juvenile Batten disease, muscular dystrophies and various neuromuscular disease. Focal myofilament loss occurred in the damaged fibers(Nonaka, 1995).

Occasional cytoplasmic bodies, Z-band streaming, or T-tubule system honey combs were observed. Carpenter et el.(1978) described that there was a significant increase in the number of capillaries in IBM in contrast to the capillary loss in dermatomyositis(Carpenter et al. 1978).

The diseases for differential diagnosis are neurogenic atrophy, ordinary polymyositis or dermatomyositis, oculopharyngeal dystrophy(Victor et al.,1962 ; Schmitt and Krause, 1981), and sporadic or familial types of distal myopathy(Nonaka et al.,1981; Miller,1979 ; Markesbery., 1974). To study the incidence of rimmed basophilic vacuoles(RBV) and 15-21nm filamentous inclusions in neuromuscular disorders other than IBM, Jongen et al. (1995) reviewed 1600 muscle biopsies for rimmed basophilic vacuoles and 750 biopsies for filamentous inclusions. The incidence of RBV in non-IBM biopsies was 8.8 per 1000. Major diseases were neurogenic disorders (n=7) and limb girdle muscular dystrophies(LGMO) (n=3). In IBM(n=7), the RBV-fiber density ranged from 10.4 to 63.1 and was significantly higher than in neurogenic disorders(0.9-4.4) and LGMD(1.1-2.7). Filamentous inclusions were seen in 2.7 per 1000 non-IBM biopsies, including familial oculopharyngeal muscular dystrphy with distal myopathy(OPMD-DM), rigid spine syndrome, acid malatase deficinecy and amyloid neuropathy. Both RBV and filamentous inclusions coexisted in rigid spine syndrome and in familial OPMD-DM. However, they had a very low incidence in non-IBM neuromuscular disorders and the RBV-fiber density may help to discriminate neurogenic disorders and LGMD from IBM.

Several reports(Barohn et al., 1995; Hida et al., 1995; Nonaka, 1995) suggested that IBM is not a uniform disorder but the characteristic pathology of IBM might be an ultimate feature of several diverse degenerative and/or inflammatory muscle disorders. Barohn et al. (1995) insisted that the inflammatory response in IBM might play a secondary role in the pathogenesis of IBM and suppression of inflammation had no effect on the clinical course.

For treatment and prognosis, until now all regimens including corticosteroids, immunosuppressive drug and total body irradiation have had no beneficial effect(Engel and Banker,1986 ; Dalakas, 1994) on the course of IBM. In general, the disease is slowly progressive and patients usually remain ambulatory for many years after the onset of symptoms with or without supportive care.

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