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Cardiovascular Response After Isokinetic Power-Endurance Ecercise

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Inclusion Body Myositis — Report of a Case

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A female of age 30 years developed a muscular weakness in proximal extremities during 2 years and responded poorly to steroid treatment. Creatine kinase in isoenzymic MM form was markedly elevated according to a serum muscle enzyme test. Electromyography examination showed a myopathic feature. Histopathological tests in muscle biopsy specimens revealed prominent cytoplasmic vacuoles rimmed by basophilic granules under space optical microscopy, and abundant intranuclear filamentous inclusions in electron microscopy. These clinical features and pathological especially electron microscopic findings are considered to be of paramount importance for the diagnosis of inclusion body myositis.

Key words: inflammatory myopathy, inclusion body myositis.

INTRODUCTION

Inclusion body myositis (IBM) is a rare form of chronic inflammatory myopathy that is characterized histopathologically by nuclear and cytoplasmic filamentous inclusions and vacuoles rimmed by basophilic materials in the muscle fibers [1-5]. A viral etiology was suggested but remains unproven [3,6,7]. In addition to the inflammatory reaction and myopathic changes, IBM patients generally fail to respond to immunosuppressive treatment [6,8,9]; this ailment has emerged as a distinct clinicopathological entity over the past two decades. We report a patient with a clinical picture of progressive chronic inflammatory myopathy and pathological findings of IBM.

CASE REPORT

A 30-year-old female vegetable monger was examined in 1991 for increasing muscular weakness of her upper and lower extremities for two years. There was no complaint of myalgia or arthralgia during the disease course. The muscle power in admission was on MRC (Medical Research Council) scale 3-4 in proximal muscles, and scale 4-5 in distal muscles. Mild muscular atrophy over bilateral gluteal and shoulder girdle muscles was noticed. Deep tendon reflexes were diminished. Sensory disturbances were absent. There was a Cushingoid appearance with moon face, trunkal obesity and acne on face. No definite skin lesion over trunk and extremities was found. Laboratory examinations

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showed an elevation of ACTH (144 μg/dL) but normal cortisol level. T3, T4 and TSH levels were within normal limits. A test of muscular isoenzyme in serum revealed a total creatine kinase (CK) level 1197 mg/dL with MM form 97.22% and MB form 2.78%. Electrophysiological tests showed normal motor and sensory nerve conduction velocities in the upper and lower extremities. Needle electromyography showed increased spontaneous activities including fibrillations and positive waves in the right vastus medialis muscle. There were markedly increased small-amplitude and short-duration motor unit action potentials in right deltoid and vastus medialis muscles, indicative of myopathy.

A computerized tomography (CT) scan of adrenal glands showed no abnormal lesion. Head CT showed a mild decreased content of pituitary fossa which suggested a partially empty sella. No evidence of organic lesion was detected in hypothalamus.

Histopathological Examination

Muscle specimen was taken from left biceps brachii muscle via a needle biopsy. The specimens were frozen in isopentane which had been cooled in liquid nitrogen immediately and cut into slices of sections 8 μm thick for routine stainings of hematoxylin and eosin (H&E), modified Gomori-trichrome, nicotinamide adenine dinucleotide tetrazolium reductase (NADH-TR), periodic-acid-Schiff (PAS) and adenosine triphosphatase (ATPase, PH9.4). For electron microscopy (EM), the muscle specimen was fixed in 3% glutaraldehyde and post-fixed in 1% osmium tetroxide. Ultrathin sections were cut with a diamond knife after dehydrated concentration and were stained with uranyl acetate and lead citrate.

In H & E and modified Gomori-trichrome stains, there was a mild inflitration of mononuclear cells in perimysial areas. Variation of muscle fiber size was prominent. Some fibers were enlarged and partly segmented. There was a proliferation of subsacrolemmal or internal nuclei. Prominent cytoplasmic vacuoles rimmed by basophilic granular materials (Fig. 1) were present in several fibers. Most vacuoles were located beneath the sarcolemma. The vacuoles contained various multilamellate membranous structures and granular materials. According to EM, the granules were seen to contain membranous whorls. Some nuclei contained filamentous tubular structures and these filaments were oriented in varied directions (Fig. 2).

The patient was given prednisolone 60 mg daily

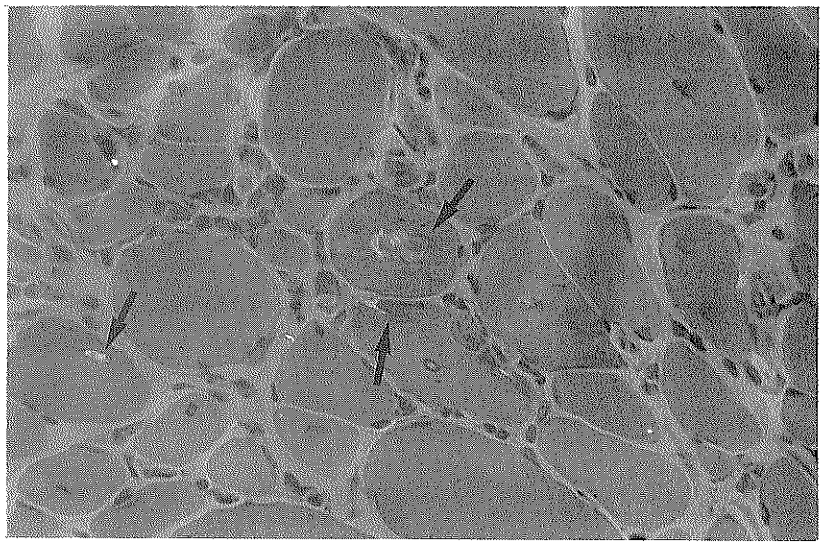

Fig. 1. Cryosection of myofibers showed vacuoles rimmed by small basophilic granular materials (arrows), modified Gomori-trichrome stain (X 400).

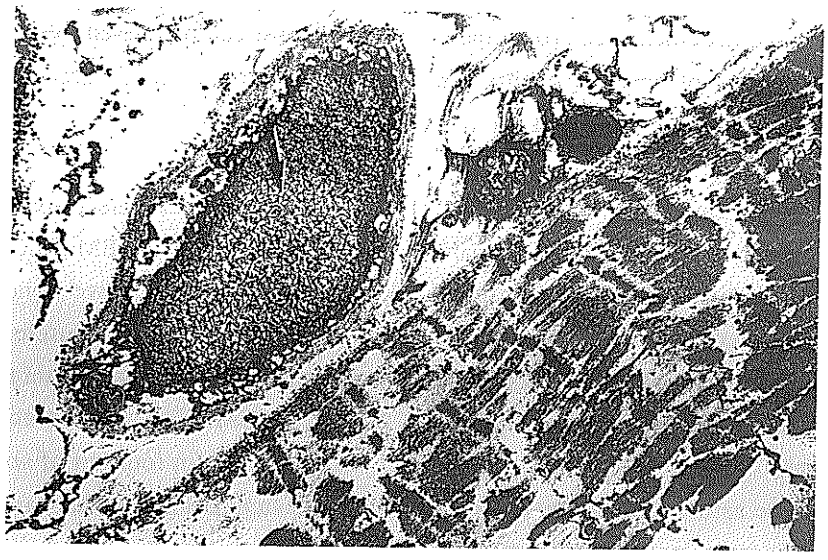

Fig. 2. Electron micrograph of intranuclear filamentous inclusions (arrow) in a muscle fiber (X 7000).

for 2 weeks, but without obvious improvement under the impression of polymyositis in MacKay Memorial Hospital. She was then given dexamethasone 8 mg daily for 4 days during hospitalization in National Taiwan University Hospital and paramethasone 8 mg daily for 15 days after discharge, but there was no definite alteration of clinical pictures. Difficulty in climbing stairs and assisted walking with a waddling gait remained the same as before admission. She discontinued the steroid treatment and took herb drugs in the later course.

DISCUSSION

With the evolution over the past ten years of well defined clinical, demographic, histologic, and immunopathological criteria and the identification of IBM as a distinct type of polymyositis [2], inflammatory myopathies are considered to comprise three major and discrete groups: polymyositis, dermatomyositis, and IBM [5,10,11].

Clinically, IBM has been mostly reported as slowly progressing painless muscular weakness, occurrence in an elderly population, and male predominance. Treatment by corticosteroids or immunosuppressive drugs is ineffective in most cases. Although our reported patient has a typical clinical course, she was afemale and rather young. Demonstration of intranuclear or intracytoplasmic inclusion bodies composed of microtubular filaments in EM confirmed the diagnosis. Although there was circumstantial evidence implicating virus as possible triggering factors or reacting substance forming abnormal filaments in IBM, viruses have not been isolated from the muscle and confirmed. Some evidence of virus antigens in the muscle of IBM patients was reported. Kallajoki [12] and Chou [13] demonstrated that filaments in the inclusion bodies resembled clusters of nucleocapsids in paramyxovirus-infected cells. Chou [3] found muscle biopsies of 8 IBM patients who were tested for the presence of paramyxovirus antigens by immunocytochemistry. Staining with mumps virus antibody was reported to be positive in intranuclear and intracytoplasmic inclusions in the patients [12]. Furthermore, adenovirus type 2 was isolated from muscle biopsy of a patient diagnosed with IBM [15]. The resemblance of the filaments seen in IBM to thick filaments of muscle [1] indicated that they may result from accumulation of contractile proteins in the nucleus through abnormal mitosis or abnormal transport of proteins through the nuclear envelope. This condition might be related to viral infection with a leading biological alteration of muscle cells.

Recently, Mendell and his colleagues [16] demonstrated a prominent evidence of amyloid deposits in filaments of IBM. The association of amyloid deposits with autophagic vacuoles in IBM raises the possibility that the filaments represent a modification of a normal protein within an acidic degradative vacuolar compartment. An alternative possibility, the intracellular deposition of amyloid also altered muscle proteins that accumulate within the cytoplasm because of the resistance to the usual intracellular digestive process. This pathogenesis is unclear.

IBM is reported to be associated with several conditions like collagen diseases including Sjogren disease, systemic lupus erythematosus and scleroderma [4]. Clinical pictures of progressing muscular weakness, myalgia, arthralgia and skin lesions may commonly mimic non-specific inflammatory myopathy. Awareness of this disease and of its refractoriness to treatment spares patients the risks associated with prolonged, and potentially hazardous therapy with corticosteroid and/or immunosuppressive medications [7,8,17]. Although our patient was treated with corticosteroid for a short period during hospitalization and in discharge, her clinical picture of Cushingoid syndrome revealed that she might have taken a long-term steroid medication. Her progressing deterioration of physical activities reflected the fact of poor response to steroid treatment during the past course. This condition is compatible with Dalakas's finding [5] that patients with IBM account for almost one third of adults with "polymyositis unresponsive to therapy" who are referred to his institution.

The diagnosis of IBM requires rigorous evaluation of muscle specimens by optical microscopy of both cryostat and paraffin sections, and by EM measurements. The presence of more than one rimmed vacuole and more than one group of atrophic fibers in each low-power field, as well as of endomysial inflammatory inflitrates, is predictive of the presence of filamentous inclusions at the ultrastructural level in 93% of IBM patients [9]. If the muscle biopsy specimen is examined only in paraffin-embedded sections, the diagnosis of IBM can be missed, because paraffin processing dissolves the basophilic granules of the rimmed vacuoles [5,18].

Eisen and coworkers [19] suggested a neuropathic origin from clinical, electrophysiologic and morphologic features in some IBM patients. They found slowed motor and sensory nerve conduction velocities and reduced amplitudes of muscle action potentials and sensory nerve potentials in three of six IBM patients. A needle EMG test showed abundant fibrillations or positive waves in four out of six patients. Single-fiber EMG examination revealed an increased mean fiber density and neuromuscular jitter in one patient. In morphological studies, they also found grouped fiber atrophy and angular fibers in all six cases. Target fibers, thought to occur only with neurogenic disease, were seen in one of their cases. These findings indicated that IBM is probably an entity with a bimodal distribution involving muscle fibers or parts of the motor unit. Our patient showed a typically myopathic finding in the needle EMG test and normal conduction measurements of peripheral nerves. No evidence of neuropathy was found.

In conclusion, IBM exhibits considerable clinical heterogeneity; recognition of this disorder as a distinct form of inflammatory myopathy is important. Poor response to steroid therapy is highly suspicious of IBM accompanying chronic myositis clinically. Rigorous evaluation of muscle histopathology including EM measurements is recommended.

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包涵體肌炎——一病例報告

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包涵體肌炎是一種少見的慢性發炎性肌肉病變，其特徵是臨床上以類固醇藥物治療無效，在肌肉組織病理學檢查上肌細胞呈現空泡及絲狀包涵物。本文報告一位30歲婦女，二年來發現有漸進性四肢無力現象，經類固醇藥物治療無效，住院理學檢查發現病人上下肢近端肌肉無力(MRC 3-4/5)，遠端肌力MRC 4-5/5，且臀部及肩肌肉稍有萎縮現象，除了外觀有庫欣氏類似症狀外，無其他皮膚及關節病變，生化檢查發現病人肌氨酸酵素血中濃度為1197 mg/dl, MM型佔97.22%，促腎上腺皮質激素及甲狀腺荷爾蒙檢查正常，神經傳導檢查正常，針肌電圖在右側三角肌及四頭肌都呈現肌肉病變之變化。左側肱二頭肌肉切片檢查，在一般光學顯微鏡下肌細胞大小差異大，單核細胞浸潤稍增加，有些細胞出現明顯空泡其外包圍嗜鹼性顆粒物質，大多數空泡位於纖維肌膜下；電子顯微鏡檢查，發現空泡內含多層膜狀及顆粒物質，有些細胞核中含有許多絲及管狀物質且呈不同方向排列。

由病人的臨床表徵及治療上的效果，配合肌肉細胞組織病理學檢查尤其以電子顯微鏡下的重要發現證實此一少見的包涵體肌炎，在發炎性肌肉病變中需作鑑別診斷，以作為治療及預防評估上的參考。

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