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CASE REPORT

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A case of inclusion body myositis with systemic sclerosis

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Abstract We report a case of systemic sclerosis (SSc) associated with inclusion body myositis (IBM). A 58-year-old man was diagnosed as having SSc at the age of 35 years, and had been suffering from chronic progressive weakness and atrophy of the limb muscles. A diagnosis of IBM was established by muscle biopsy. Although most such patients show a poor response to corticosteroids and immunosupressants, glucocorticoid therapy was effective in the present case.

Key words Autoimmune disease · Corticosteroids · Inclusion body myositis (IBM) · Rimmed vacuoles

Introduction

Inclusion body myositis (IBM) is an uncommon variant of inflammatory myositis that occurs in two forms, i.e., sporadic and hereditary IBM. Sporadic IBM commonly occurs in middle-aged men,[1,2] and it is considered to be the most common muscle disease after the age of 55 years.[3] Clinically, it is characterized by slow progression without fluctuation, and by combined proximal and distal muscle weakness. One-third of patients also have difficulty in swallowing.[4] The serum creatine kinase (CK) concentration tends to be moderately increased, usually to less than four times the upper normal limit. Electromyography shows evidence of myopathy associated with neurogenic changes. Muscle biopsy reveals degenerating and regenerating fibers as well as the presence of inflammatory cells. Characteristic histopathological features of sporadic IBM are rimmed vacuoles, eosinophilic cytoplastic inclusions, endomysial inflammation, amyloid deposits (detected by Congo Red stain), atrophic and nonnecrotic muscle fibers, and 15- to 18-nm tubulofilamentous inclusions and mitochondrial abnormalities on electron microscopy.[5] Interestingly, along with rimmed vacuoles there are similarities between sporadic IBM and neuronal degeneration in Alzheimer's disease, such as the accumulation of β-amyloid and other substances.[6] The response of sporadic IBM to immunotherapy has been controversial. Early reports and reviews emphasized the lack of a therapeutic response, especially to corticosteroids. We encountered a patient with sporadic IBM in late middle age as well as systemic sclerosis (SSc). His slowly progressive muscle weakness was successfully treated with high-dose corticosteroids.

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Case report

A 58-year-old man was admitted to our hospital with muscle weakness. He was diagnosed as having SSc at the age of 35 years from the presence of sclerodactyly, facial skin sclerosis, Raynaud's phenomenon, and interstitial pneumonia. He had not received any specific treatment for at least 22 years prior to this admission. Approximately 10 years ago, he had started to suffer from slowly progressive muscle weakness of the lower extremities. Within 6 months, he experienced difficulty in standing up from a sitting position.

Examination showed that he was 159 cm tall and weighted 39 kg. Sclerosis of the skin was observed on his face and fingers, and limited opening of the mouth was noted. Fine crackles were audible in the bilateral lower lung fields. He had proximal and distal muscle weakness of the bilateral lower limbs and the left upper limb (lower 3/5, left upper 4/5, according to the Medical Research Council scale) without myalgia or sensory disturbance. Furthermore, he had significant atrophy of the deltoid, triceps, and quadriceps muscles. Deep tendon reflexes were decreased in both knees.

On admission, his blood count was within normal limits. The erythrocyte sedimentation rate was 60 mm/h, and there was an increase in CK (738 IU/l; normal range 9–93), LDH (572 IU/l; normal range 280–510), and aldolase (8.9 mU; normally less than 6). The serum IgG level was elevated

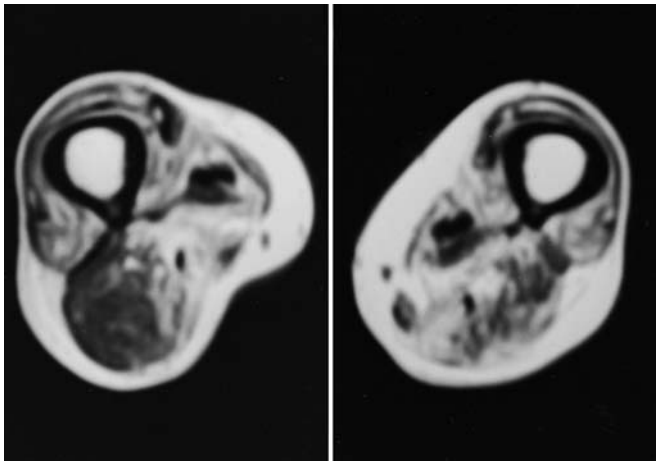

Fig. 1. T1-weighted magnetic resonance image reveals marbled brightness of the bilateral quadriceps, demonstrating muscle atrophy and replacement by fatty tissue

(1940 mg/dl; normal range 870–1700), but IgA and IgM were normal. Antinuclear antibody was positive (homogeneous and speckled pattern) with a titer of 1:80. Anti-Scl 70 antibody was also positive, but rheumatoid factor and antibodies for Jo-1, Sm, SS-A/Ro, SS-B/La, and U1RNP were negative. All other laboratory parameters tested were within normal limits.

Chest X-ray films and chest computed tomography (CT) scans revealed pulmonary fibrosis in the lower lobes of both lungs. On magnetic resonance imaging, muscle atrophy and replacement of the muscles by fatty tissue was seen in both lower extremities, especially the left quadriceps (Fig. 1). Electromyography revealed myopathy together with neurogenic features. Biopsy of the right triceps muscle revealed a number of rimmed vacuoles, numerous fibers with internal nuclei, and a mixture of normal-sized, hypertrophic, and atrophic muscle fibers on hematoxylin and eosin or Gomori trichrome staining (Fig. 2). Electron microscopy revealed twisted cytoplasmic tubulofilaments measuring 16–20 nm in external diameter and 6 nm in internal diameter (not shown).

These findings were consistent with a diagnosis of sporadic IBM. Prednisolone (60 mg/day) therapy was started. Subsequently, the muscle weakness, difficulty in standing up from the sitting position, and restricted opening of the mouth gradually improved, and the serum CK level became normal (Fig. 3). At present (9 months after discharge), although there have been no marked changes in deep tendon reflexes and muscle atrophy, there has been no recurrence of muscle weakness and no increase in muscle-associated enzymes. The dose of prednisolone has been successfully decreased to a maintenance level of 10 mg/day.

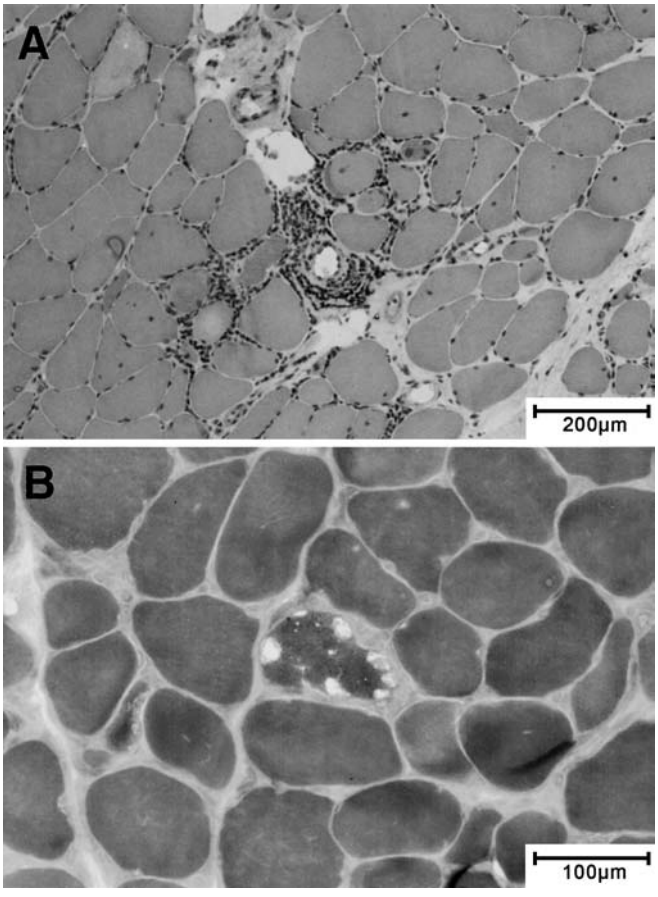

Fig. 2. Representative photomicrographs of the muscle biopsy specimen. Both hematoxylin and eosin-stained (**A**) and Gomori trichrome-stained (**B**) sections revealed centralized nuclei, an extremely wide range of muscle fiber size (including both atrophied and hypertrophied fibers), and typical irregular rimmed vacuoles

Discussion

The 58-year-old man described in this report initially presented with SSc and developed sporadic IBM approximately 20 years later. Clinically, IBM differs from polymyositis because of an increased frequency of distal muscle weakness, a more chronic course, and the rare occurrence of dysphagia, muscle pain, or a response to corticosteroid therapy. The pathological features required for a diagnosis are groups of atrophic fibers, rimmed vacuoles, and nuclear or cytoplasmic filaments.[7] Our patient suffered the insidious onset of slowly progressive, painless, proximal and distal muscle weakness. Additional clinical findings, such as his older age, serum CK less than four times the upper normal limit, a mixed neurogenic and myopathic electromyogram (EMG) pattern, and no evidence of hereditary muscle disease are consistent with the diagnosis of sporadic IBM. Furthermore, all of the characteristic pathological findings described above were observed in the muscle biopsy specimen. Based on these pathological and clinical features, sporadic IBM could be differentiated from other inflammatory myopathies. However, contrary to previous reports, this patient responded well to corticosteroid therapy.

The precise etiology of IBM remains unknown, although similarities between the accumulated proteins in IBM myofibers and Alzheimer's disease neurons have been characterized, as have immunological, mitochondrial, and other factors.[8] The presence of suppressor/cytotoxic $CD8^+$

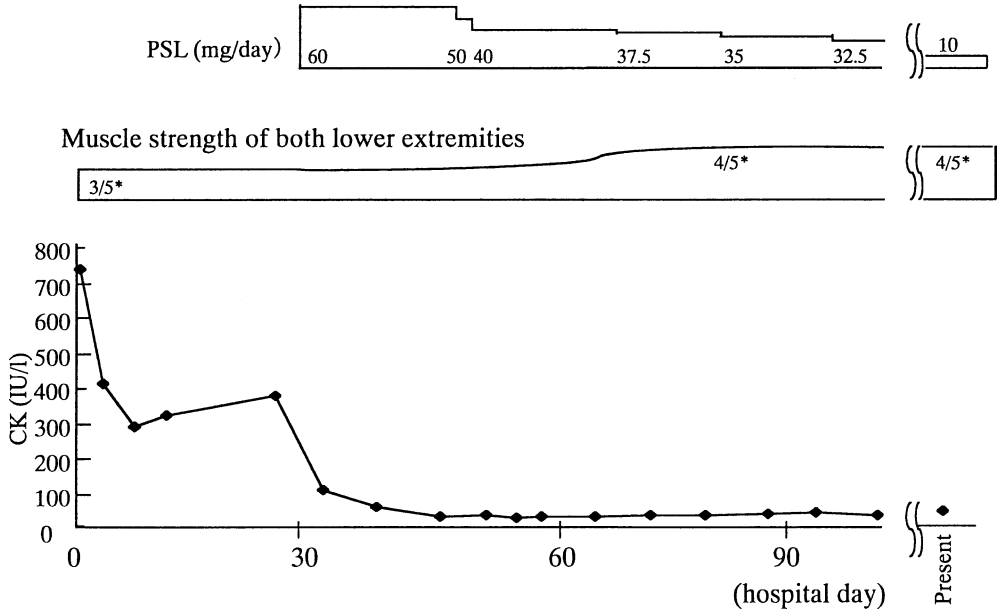

Fig. 3. Summary of the patient's clinical course. *PSL*, prednisolone; *muscle strength according to the Medical Research Council scale; *CK*, serum creatine kinase

T cells, as well as macrophages in and around the affected muscle fibers in sporadic IBM, suggests that the immune system is involved in the pathogenesis.[9] Previous studies have shown that 13%–15% of IBM patients have associated autoimmune diseases such as idiopathic interstitial pneumonia, psoriasis, Hashimoto's thyroiditis, dermatomyositis, Sjögren's syndrome, systemic lupus erythematosus, or SSc. However, it is not yet clear whether the association between inclusion body myositis and autoimmune disease is etiological or pure coincidence.[5,10]

Because of the rarity and clinical heterogeneity of these diseases, little is known about the optimum therapy or the factors that influence the response to treatment. Early reports on sporadic IBM emphasized the lack of response to treatment, especially corticosteroids. However, a few of these patients have been reported to respond to steroid therapy with or without immunosuppressants.[11] In addition, Yamanishi et al.[12] reported that scleroderma–polymyositis overlap syndrome associated with rimmed vacuoles and filamentous inclusions showed a good response to glucocorticoid therapy (although IBM was not diagnosed).

A common finding in many of the patients who respond to steroid therapy is the existence of some features of autoimmunity. Trials of immunosuppressants (including azathioprine, cyclophosphamide, and cyclosporine) or plasmapharesis have been unsuccessful, but there are some reports about a beneficial effect of intravenous immunoglobulin.[13]

The presence of autoimmune features in IBM patients is supported by various findings such as the up-regulation of endomysial cytokines and endomysial inflammatory infiltrates containing $CD8^+$ cells.[10] One possible reason why high-dose steroid therapy was effective for our IBM patient, who has an associated autoimmune disease, is that his primary SSc may have enhanced the autoimmune features of IBM.

In this patient who had IBM associated with SSc, high-dose steroid therapy achieved an improvement in muscle symptoms and there was no exacerbation of SSc during or after steroid therapy. In conclusion, high-dose steroid therapy should be considered for the treatment of IBM associated with autoimmune disease.

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