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CASE REPORT

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Dermatomyositis associated with autoimmune idiopathic thrombocytopenia and anti-Ku antibody

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Abstract We describe a case of dermatomyositis with concurrent clinical and laboratory features of idiopathic thrombocytopenia associated with anti-Ku antibody. A diagnosis of dermatomyositis was established by the characteristic skin changes together with a muscle biopsy. Scintigraphic studies indicated cardiac involvement. Autoimmune idiopathic thrombocytopenia (AITP) has been described in association with both systemic lupus erythematosus (SLE) and scleroderma, but there are few reports describing AITP associated with myositis. To our knowledge, this is the first report of a case of dermatomyositis associated with AITP and anti-Ku antibody.

Key words Anti-Ku antibody · Autoimmune idiopathic thrombocytopenia (AITP) · Dermatomyositis

Introduction

The clinical entity of dermatomyositis is an idiopathic inflammatory myopathy characterized by proximal muscle weakness, nonsuppurative skeletal muscle inflammation, and cutaneous manifestations. A variety of skin changes may be observed, including Gottron's sign, heliotrope discoloration of the eyelids, and macular erythema of the posterior shoulders and neck.

Cardiac involvement is considered uncommon in patients with polymyositis and dermatomyositis, although there are some reports indicating an association. Autopsy studies have revealed that about one-third of patients with myositis had evidence of myocarditis.[1] Furthermore, scintigraphic studies have demonstrated abnormal technetium-99m pyrophosphate uptake in 57% of patients with polymyositis/dermatomyositis.[2] Autoimmune idiopathic thrombocytopenia (AITP) has been described in association with both systemic lupus erythematosus (SLE) and scleroderma, but few reports have described AITP with myositis.[3–7] Anti-Ku antibodies have been documented in a wide variety of connective tissue diseases, especially in overlapping syndromes with systemic scleroderma (SSc) and myositis.[8] However, there are no reports describing the association of AITP with either anti-Ku antibody or myositis. In this report, we described the first reported case of dermatomyositis associated with AITP and anti-Ku antibody.

Case report

A 30-year-old Japanese woman was evaluated at another hospital following the onset of thrombocytopenia during pregnancy. She successfully delivered a baby by cesarean section with platelet transfusion. However, she developed progressive weakness and atrophy of the limb muscles.

Laboratory investigations included a white blood cell (WBC) count of 6800/μl, a platelet count of 18000/μl, and a markedly elevated creatine kinase (CK) level of 4200 (IU/l). Antinuclear antibody (ANA) testing was positive with a titer of 1:2560 (speckled pattern); antibody assays for Sm, SS-A/Ro, SS-B/La, U1RNP, and Jo-1 were negative.

A muscle biopsy demonstrated features consistent with polymyositis. She continued to deteriorate and was admitted to Tokyo Women's Medical University Hospital in December 2000 with severe thrombocytopenia, progressive muscle weakness, and joint pain. On examination, she was afebrile and normotensive (102/58 mmHg). Muscles were tender to palpation, and nonpitting edema of the lower extremity was present. A heliotropic rash on her face and Gottron's sign on the dorsal aspect of the interphalangeal joints of all fingers and elbows were noted. During the

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course of her disease, she never had evidence of Raynaud's phenomenon, scleroderma, photosensitivity, malar rash, arthritis, or pulmonary involvement such as interstitial pneumonia. The neurological examination demonstrated marked symmetrical proximal weakness.

Laboratory studies revealed the following: WBC count 7600/μl, platelet count 46000/μl, reticulocytes 2.3%, LDH 1101 IU/l (normal 170–370 IU/l), aspartate aminotransferase (AST) 141 IU/l (normal 10–40 IU/l), and alanine aminotransferase (ALT) 89 IU/l (normal 5–45 IU/l). Further investigations included a CK level of 4390 IU/l (normal 10–110 IU/l), creatine kinase mycardial-bound (CK-MB) 196 ng/ml (normal <4.8 ng/ml), aldolase 53.8 ng/ml (normal 2.7–5.9 ng/ml), myoglobin 1700 ng/ml (normal <61 ng/ml), myosin light chain kinase 33.4 ng/ml (normal <2.5 ng/ml), and cardiac muscle troponin T (0.47 ng/ml; normal <0.10 ng/ml). Direct and indirect Coombs' tests were negative.

The serum immunoglobulin G (IgG) level was elevated (2040 mg/dl; normal 870–1700 mg/dl), but the levels of IgA, IgM, and complements 3 and 4 (C3, C4) were normal. ANA testing was positive with a titer of 1:2560 (speckled pattern), whereas antibodies for Sm, SS-A/Ro, SS-B/La, U1RNP, Scl-70, and Jo-1 were negative. Anti-DNA antibody was 4 IU/ml (normal <6 ng IU/ml), and the anti-ds DNA assay was negative. Anti-Ku antibody was positive with a titer of 1:16. Platelet-associated immunoglobulin G (PaIgG) was elevated (56.1 ng/10^7; normal 5–25 ng/10^7).

Coagulation studies including the prothrombin time and activated partial thromboplastin time were normal. Bone marrow aspirate demonstrated increased megakaryocytes, which is compatible with a diagnosis of AITP. Magnetic resonance imaging (MRI) with fat suppression revealed focal high-intensity and atrophic changes in the quadriceps muscle (Fig. 1A). The right deltoid muscle biopsy demonstrated variation in fiber size with evidence of isolated necrotic muscle fibers. Small basophilic regenerating fibers were scattered throughout the biopsy. A focal lymphocytic and macrophage infiltrate was present in the interstitium and was particularly evident around blood vessels (Fig. 1C). Small basophilic regenerating fibers were scattered throughout the biopsy. Irregularity of the myofibrillar network pattern was noted after NADH staining. ATPase revealed type 2 fiber atrophy. A thallium myocardial scintigram with dipyridamole stress (0.142 mg/kg/min for 4 min) demonstrated focal ischemic changes affecting all areas of the heart (Fig. 2, before treatment). Thrombocytopenia associated with dermatomyositis was diagnosed.

In December 2000, pulse therapy with methylprednisolone was commenced at a dose of 1 g/day for 3 days followed by oral corticosteroids (60 mg/day). The CK level fell, and the platelet count rapidly increased shortly after the initiation of treatment. Thereafter, the corticosteroid dose was reduced to 55 mg/day. After tapering the corticosteroid dosage, the CK gradually increased and the platelet count fell. Therefore, we added intravenous pulse therapy with cyclophosphamide at a dose of 500 mg/month. The CK level decreased thereafter, and muscle strength gradually improved (Fig. 3). Repeated MRI with fat suppression revealed

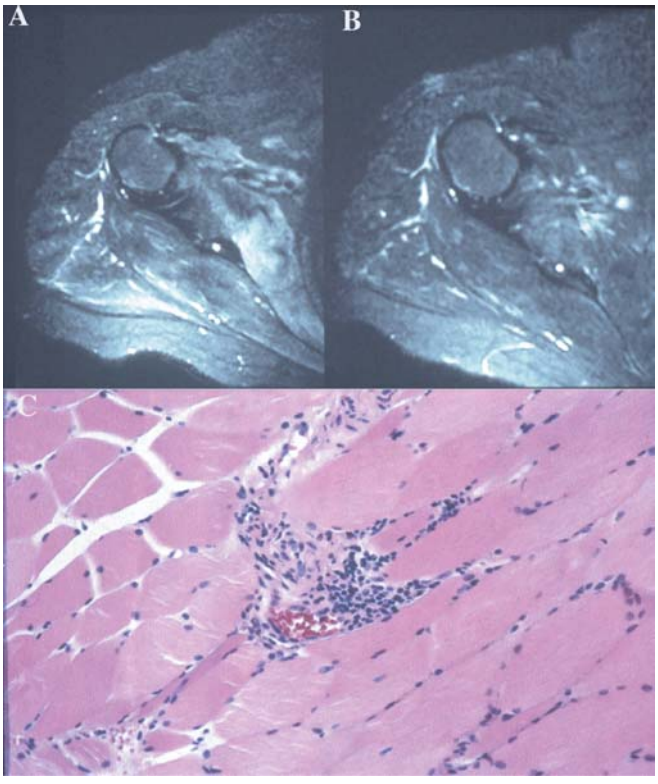

Fig. 1. **A** Magnetic resonance imaging (MRI) scan with fat suppression revealed focal high-intensity, atrophic changes in quadriceps muscle. **B** Repeat MRI with fat suppression revealed improvement of the high-intensity changes. The muscle biopsy demonstrated variations in fiber size. Isolated necrotic muscle fibers were seen, and small basophilic regenerating fibers were scattered through the specimen. Irregularity of the myofibrillar network pattern was noted after NADH tetrazolium reductase staining. ATPase revealed type 2 fiber atrophy. **C** A focal lymphocytic and macrophage infiltrate was present in the interstitium and was particularly evident around blood vessels. H&E, ×100

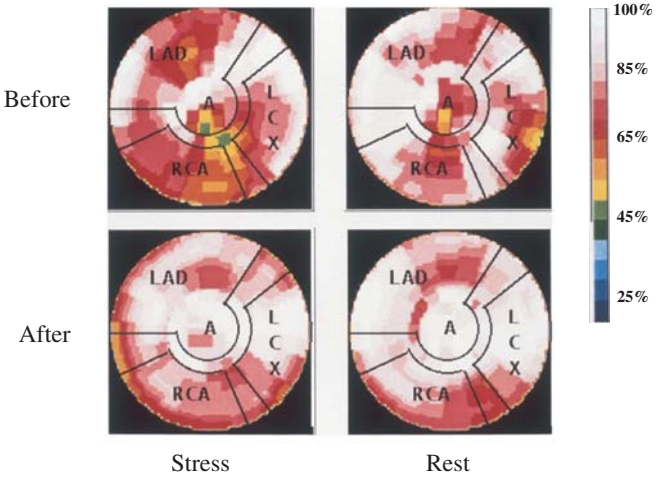

Fig. 2. Thallium myocardial scintigrams with dipyridamole stress (0.142 mg/kg/min for 4 min) demonstrated focal ischemic changes in all areas of the heart before treatment. Repeated scintigraphic cardiac studies after treatment demonstrated improvement of the focal myocardial ischemic changes. *A*, Apex; *LAD*, left anterior descending artery; *LCX*, left circumflex artery; *RCA*, right coronary artery

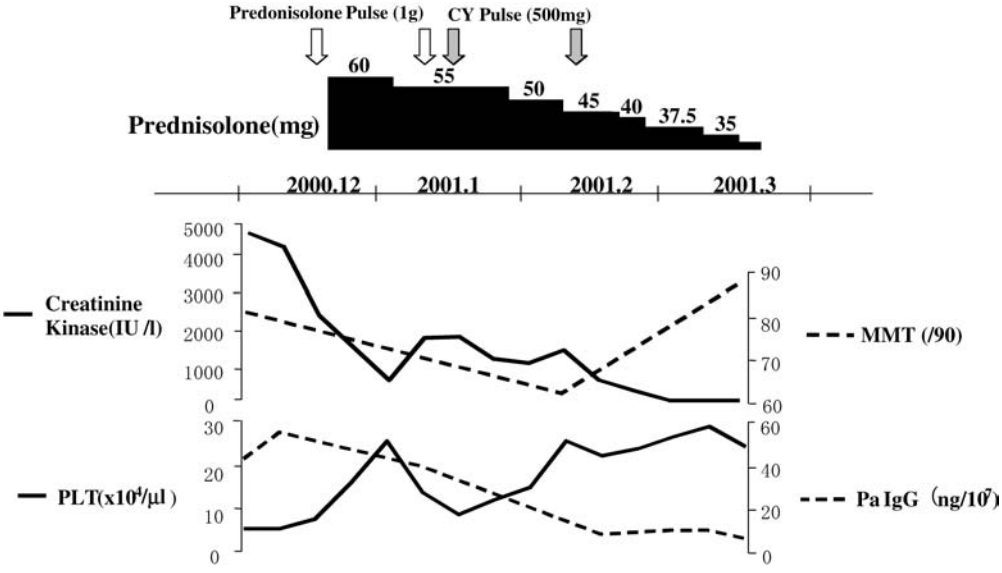

Fig. 3. Pulse therapy with methylprednisolone was started at a dose of 1 g/day for 3 days in December 2000 followed by oral corticosteroids (60 mg/day). Treatment rapidly induced a fall in creatinine kinase (CK) levels and an increase in platelet counts. The corticosteroid dosage was tapered to 55 mg/day, after which the CK level gradually increased and the platelet count decreased. Therefore, intravenous pulse therapy with cyclophosphamide (500 mg/month) was added. Following this treatment, CK levels fell and muscle strength gradually improved. *CY*, cyclophosphamide; *MMT*, manual muscle testing; *Pa IgG*, platelet-associated immunoglobulin; *PLT*, platelet count

improvement of the high-intensity changes (Fig. 1B). In addition, repeated scintigraphic cardiac studies demonstrated improvement in the focal ischemic changes (Fig. 2, after treatment). The patient has been followed for 2 years with no detectable proximal muscle weakness and almost complete resolution of the heliotropic rash.

Discussion

Dermatomyositis is a heterogeneous disorder defined by five criteria: girdle myopathy, muscle biopsy evidence of myositis with necrosis of type 1 and 2 fibers, elevation of circulating skeletal muscle enzymes, typical electromyographic (EMG) findings, and skin involvement.[9] Patients may be categorized into four groups on the basis of the pathogenesis and clinical features: (1) primary idiopathic dermatomyositis; (2) dermatomyositis associated with neoplasia; (3) childhood dermatomyositis associated with vasculitis; and (4) dermatomyositis associated with collagen-vascular disease.[10]

Autoimmune thrombocytopenia is a primary condition of adults characterized by immunological platelet destruction. Although AITP has been described in association with other connective tissue diseases such as SLE and scleroderma, few reports have linked it with myositis.[3–8] In two reports, dermatomyositis was associated with AITP, with one of the patients being positive for hepatitis C virus (HCV) antibody.[5–7] Another patient had polymyositis with AITP and was positive for hepatitis B virus (HBV) antibody.[7] One rare case was reported as scleroderma-dermatomyositis overlapping syndrome; the patient also had Graves' disease and AITP and was positive for anti-Ku antibody.[8] Prednisolone was clinically effective in these reported cases, with no relapses being observed.

It is noteworthy that all of the reported patients, including ours, were negative for anti-Jo-1 autoantibody. Anti-Ku antibodies have been documented, especially in SLE and overlapping syndromes with SSc and myositis.[9] However, there were no clinical or serological findings to indicate a diagnosis of SSc or SLE. To our knowledge, no one has described the presence of anti-Ku antibody in patients with myositis and AITP not associated with SSc. Therefore, this is the first report of a patient with dermatomyositis associated with AITP and anti-Ku antibody.

It is not yet clear whether the association between dermatomyositis and AITP was etiological or occurred by coincidence. A recent report indicated that acute ITP presenting during childhood was associated with a pattern of helper T cells type 1 (Th1) or the absence of vivo cytokine gene expression; they also indicated that stable clinical remission of the disease was associated with the Th2 pattern or the absence of cytokine expression.[11] In addition, analysis of cytokine gene expression in the muscle tissues of patients with idiopathic inflammatory myositis (including dermatomyositis) demonstrated a predominantly Th1 cytokine expression pattern.[12] Thus, AITP and dermatomyositis may have mutual triggering factors that skew the cytokine expression pattern of helper T cells to a Th1 pattern. Such factors could be environmental agents such as viral infections. Further clinical and experimental studies are needed to determine the role of environmental factors in the development of both AITP and myositis.

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