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CASE REPORT

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Successful treatment using high-dose intravenous immunoglobulin in a patient with rapidly progressive interstitial pneumonia associated with dermatomyositis

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Abstract A 36-year-old male patient with dermatomyositis (DM) associated with rapidly progressive interstitial pneumonia (IP) was successfully treated by high-dose intravenous immunoglobulin (IVIG). He suffered from myopathy, skin lesions, and IP. In spite of the treatment with a high-dose corticosteroid, IP progressed rapidly. Then high-dose intravenous immunoglobulin (20 g/day, 4 days) was administered. The skin lesions, myopathy, and pulmonary lesions improved. High-dose IVIG was considered to be a relatively safe and effective treatment for progressive IP associated with DM.

Key words High-dose intravenous immunoglobulin (IVIG) · Rapidly progressive interstitial pneumonia · Dermatomyositis

Introduction

Interstitial pneumonia (IP) has been reported to be associated with dermatomyositis (DM) in 5% to 10% of cases.[1] It is well recognized that acute-onset IP associated with DM progresses very rapidly. In patients with rapidly progressive IP, the muscle symptoms and the signs of inflammation are often minimal or slight.[2,3] They are often resistant to corticosteroid therapy, and their courses of disease are sometimes fatal. Immunosuppressive agents such as cyclophosphamide (CPM) and cyclosporine were reported to be effective in some of these cases.[4,5] However, these agents were often discontinued because of their severe adverse effects.

The efficacy of treatment using high-dose intravenous immunoglobulin (IVIG) was shown in cases of autoimmune diseases, following the first report of the successful treatment of idiopathic thrombocytopenic purpura.[6] IVIG was also reported to be effective as a treatment for skin lesions and myopathy in patients with DM.[7] Here we report on an adult patient with rapidly progressive IP associated with DM which was treated successfully with IVIG.

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Case report

A 36-year-old man had been suffering from arthralgia of the wrists, shoulders, and knees since December 1995. He visited a nearby hospital and was found to have muscle weakness, fever, and skin lesions, including Gottron's sign. He was diagnosed as having DM in February 1996, and was given prednisolone (PSL) (15–40 mg/day) followed by the administration of mizoribine (150 mg/day). The muscle weakness and fever improved somewhat, although he developed ulceration of the skin on both elbows and dyspnea from August 1996.

He was admitted to Miyazaki Medical College Hospital in November 1996. On admission, edematous erythema on the face, Gottron's sign in the joints of all fingers, and ulcers on both elbows were noted. Fine crackles were audible in both sides of the chest, and muscle weakness was apparent. Laboratory studies showed an accelerated erythrocyte sedimentation rate (21 mm/h), leukocytosis (9100/μl) with a slight shift to the left of the segmented nuclei, and a slight increase in C-reactive protein (0.6 mg/dl). Serum creatine kinase (CK) (30 IU/l) was within normal limits, but levels of aldolase (ALD) (15.4 IU/l) and lactate dehydrogenase (LDH) (536 IU/l) were high. Serum antinuclear antibody, as well as anti-Jo-1 antibody, tested negative. The serum level of KL-6, which is a marker for IP activity, was markedly elevated (2716 U/ml). Chest roentgenography (CXP) and chest computed tomography (CT) revealed a moderate reticulo-nodular shadow, but arterial blood gas analysis (PaO_2 93.0 mmHg) was normal. A bronchoscopic examination revealed telangiectasia of the bilateral bronchial wall. The biopsy specimen from the right B8a revealed thickness

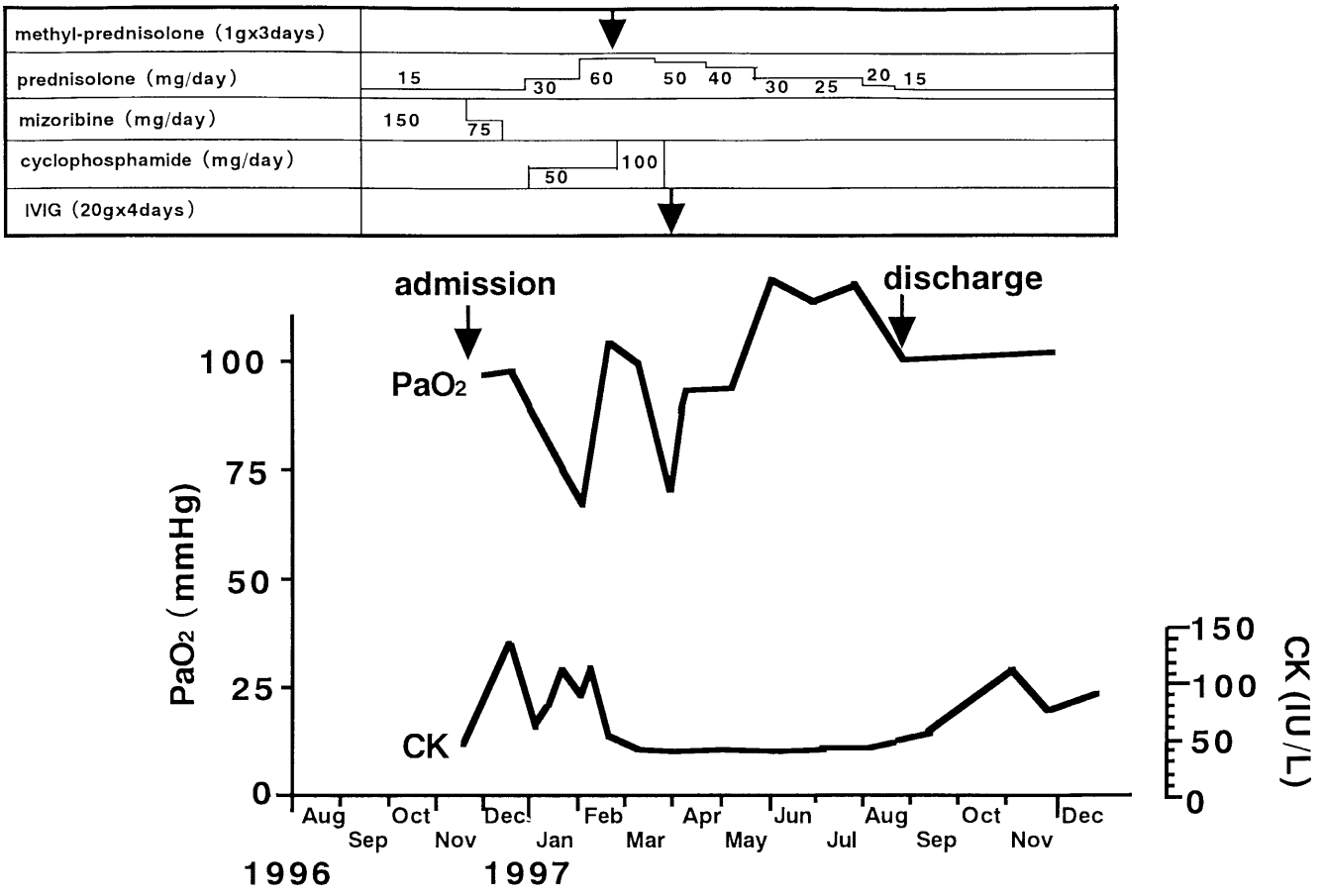

Fig. 1. Clinical course of the patient

of the alveolar septa, infiltration of inflammatory cells in alveoli, and focal organization in the alveolar space.

His symptoms of arthralgia, muscle weakness, skin lesions as edematous erythema on his face, and Gottron's sign strongly suggested that he was suffering from DM, although the CK level did not increase. Because he had active ulceration on both elbows, a muscle biopsy was not performed. In spite of increasing the PSL dosage up to 60 mg/day, he had fever and his skin lesions developed. Moreover, oxygen saturation of the arterial blood decreased, and oxygen was supplied from January 1997 (Fig. 1). Therefore, treatment with CPM (50–100 mg/day) was administered from the beginning of January, and a high-dose corticosteroid (methylprednisolone, 1000 mg/day) was added in February. However, adverse effects of CPM such as myelosuppression and bleeding cystitis appeared, and in the middle of March the administration of CPM could no longer be continued. Then PaO_2 decreased markedly to 63.5 mmHg even with an oxygen supply. In addition, CXP and chest CT on March 6, 1997, revealed diffuse ground-glass-like infiltrations and honeycombing patterns (Fig. 2a). Because the progression of IP was considerable, the patient was treated with IVIG (20 g/day of immunoglobulin, Polyglobin-N, Bayer, Tokyo) for 4 days (March 25–28, 1997) after obtaining informed consent. The levels of PaO_2 increased gradually after IVIG, and the oxygen supply could be decreased gradually. The serum level of KL-6 in April decreased to 1695 U/ml. In July 1997, the oxygen supply was no longer necessary and PaO_2 was 78.0 mmHg. Both CXP and CT examinations revealed a marked improvement of the reticulo-nodular shadows and diffuse ground-glass-like infiltrations on July 8, 1997 (Fig. 2b). Also, the arthralgia of the wrists and knees and the erythema on his face gradually improved. The serum levels of CK, ALD, and LDH in July, 1997, decreased to 22 IU/l, 10.4 IU/l, and 410 IU/l, respectively. The PSL amount was gradually reduced to 15 mg/day and he was discharged from the hospital in August, 1997. He is still (1999) in good condition at home without any oxygen supply.

Discussion

This patient suffered from skin lesions such as Gottron's sign, muscle weakness, fever, arthralgia, and slight elevation of ALD. The diagnosis was considered according to the criteria for DM proposed by the Research Committee on polymyositis and DM of the Ministry of Health and Welfare of the Japanese government in 1993. Histological evidence from the muscle biopsy could not be obtained because of the fear of active skin ulceration. The other observation

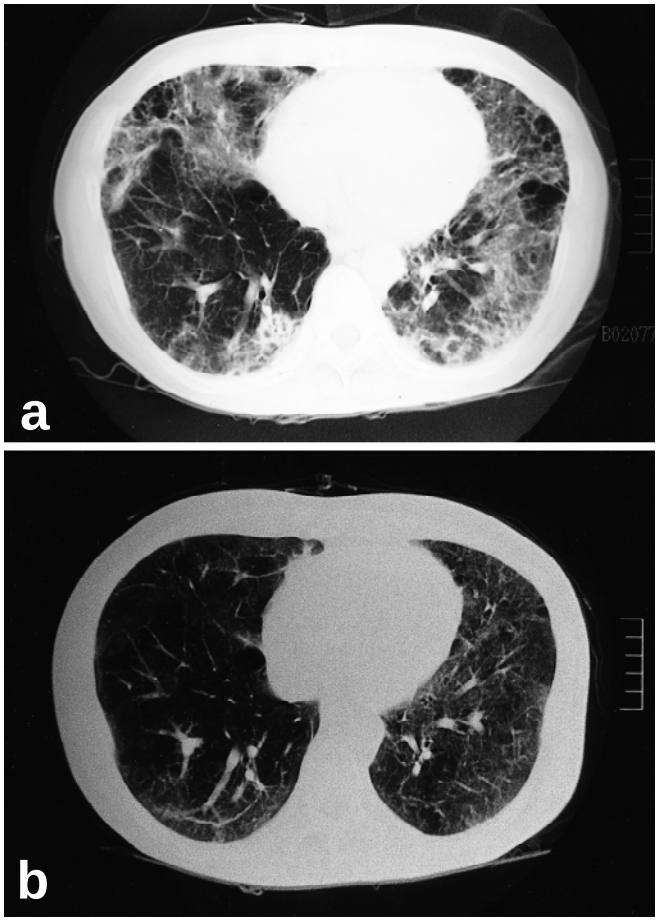

Fig. 2. a Chest CT before intravenous immunoglobulin (IVIG) treatment (March 6, 1997) showing widespread infiltrative shadows, a ground-glass appearance, and honeycombing in both lung fields. **b** Chest CT after IVIG treatment (July 8, 1997) showing a marked improvement of the infiltrative shadows and ground-glass appearance

which did not suggest a diagnosis of DM was the lack of CK elevation in this patient. This may be partly due to the administration of PSL for several months before admission to our hospital. Alternatively, cases of DM without marked elevation of serum muscle-derived enzymes, so called amyopathic DM, have been reported.[3] In fact, amyopathic DM tends to be associated with severe IP,[2] which was true in the present case. At the same time, laboratory studies in reported cases as well as in the present case showed the absence or weakness of inflammatory signs and antinuclear antibodies. Other connective tissue diseases, which showed similar muscle weakness, were ruled out. Taking everything into consideration, this patient was diagnosed as DM associated with IP.

High-dose corticosteroid and immunosuppressive therapies using CPM or cyclosporine have been administered to patients with rapidly progressive DM when they did not respond to conventional treatment with corticosteroids.[4,5] Since PSL administration did not prevent IP progression in the present case, CPM was added. However, the effect of CPM was insufficient, and an adverse effect was noted. Insufficient response to the immunosuppressive treatment was also reported in a case with rapidly progressive IP associated with DM.[2]

Recently, IVIG therapy has been used in DM patients who did not respond to, or could not tolerate, conventional therapies.[7] A double-blind and placebo-controlled study demonstrated that IVIG moderately to dramatically improved the inflammatory myopathy in 75% of the patients with DM.[8] An improvement in skin lesions was also reported.[9] Dalakas[10] reported that the IVIG mechanism was considered to be an inhibition of myotoxic cytokines such as TNF-α and IL-1, blockade of Fc receptors on endomysial macrophages interfering with Fc receptor-mediated phagocytosis, and inhibition of C_3 uptake and interception of the formation and deposition of membranolytic attack complex on the endomysial capillaries. Although the IP mechanism in DM patients is still unknown, its pathogenesis may overlap with those of the skin and muscle lesions. A successful treatment using IVIG in a patient with a severe lung manifestation of DM has also been reported.[11] Therefore, the use of IVIG in this patient was agreed, and an immunoglobulin reagent with a complete Fc portion was chosen.

The present case showed a dramatic improvement in IP as well as skin lesions and myopathy. No adverse reaction which might be specifically associated with IVIG was observed. After IVIG therapy, the corticosteroid was gradually decreased to as low as 15 mg/day. From the outcome of the present case, it is likely that IVIG is a relatively safe and effective treatment for patients with rapidly progressive IP associated with DM, especially when IP does not respond to the conventional therapies. One of the problems with IVIG treatment for patients is its high cost. Moreover, the increased risk of unknown infections should not be ignored because this reagent is derived from human plasma. Therefore, further large-scale evaluation of this treatment for patients with rapidly progressive IP associated with DM is necessary, and then general support for IVIG may be possible in the future.

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