Recurrence of juvenile dermatomyositis 8 years after remission

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INTRODUCTION

Juvenile dermatomyositis (JDM) is a chronic inflammatory disease characterized by typical skin lesions and muscle weakness, which occurs in children and adolescents younger than 16 years.[1] JDM is classified into 3 clinical types according to the posttreatment course: (1) monocyclic, in which there is one episode with permanent remission within 2 years after diagnosis; (2) polycyclic, with multiple relapses within 2 years; and (3) continuous, with pathologic states persisting for more than 2 years.[2] Early treatment with prednisolone is suggested to limit the disorder to the monocyclic course.[3] Only 2 case reports in which monocyclic JDM recurred more than 3 years after remission have been described in the English-language literature.[4,5] Of these 2 reported cases, 1 patient had no initial treatment and the other had oral prednisolone (PSL) alone.[4,5] Recently a well-designed randomized, controlled trial found that aggressive therapeutic approaches, such as PSL plus methotrexate (MTX) after methylprednisolone (mPSL) pulse therapy, outperform PSL monotherapy after mPSL pulse therapy with respect to clinical remission, treatment failure, and discontinuation of PSL.[6] Here we present a case of monocyclic JDM that recurred 8 years after remission despite initial treatment with PSL plus MTX after mPSL pulse therapy.

Abbreviations used:

CDASI:	Cutaneous Dermatomyositis Area and Severity Index
JDM:	juvenile dermatomyositis
MTX:	methotrexate
mPSL:	methylprednisolone
PSL:	prednisolone

CASE REPORT

A 4-year-old Japanese boy presented with eruptions on the face, ears, elbows, and knees and with muscular weakness. Physical examination found erythema on the cheeks and ears, keratotic papules and purplish erythema on the dorsa of the hands, and scaly erythema on the knees (Fig 1, *A* and *B*). This patient had no symptoms of dysphonia. Cutaneous Dermatomyositis Area and Severity Index (CDASI) was 8. The histopathology of the left knee showed vacuolar changes in the epidermis, deposition of mucin, pigment incontinence, and infiltration of lymphocytes in the papillary dermis (Fig 2, *A*). Biochemical examination found elevated levels of creatine kinase 425 IU/L (normal range, 12−170 IU/L) and aldolase 19.0 IU/L (2.7−7.5 IU/L). Antinuclear antibody and anti-Jo-1 antibody were negative. Magnetic resonance imaging (T2) found diffuse high-intensity areas in the proximal muscles of the extremities, which suggests edema caused by inflammation (Fig 2, *B*). Based on the clinical, histopathologic, and radiologic findings, the diagnosis of JDM was made. According to the recommended regimen at that time,[7] the patient was treated with 2 courses of mPSL pulse therapy (30 mg/kg/d for 3 consecutive days per course) followed by

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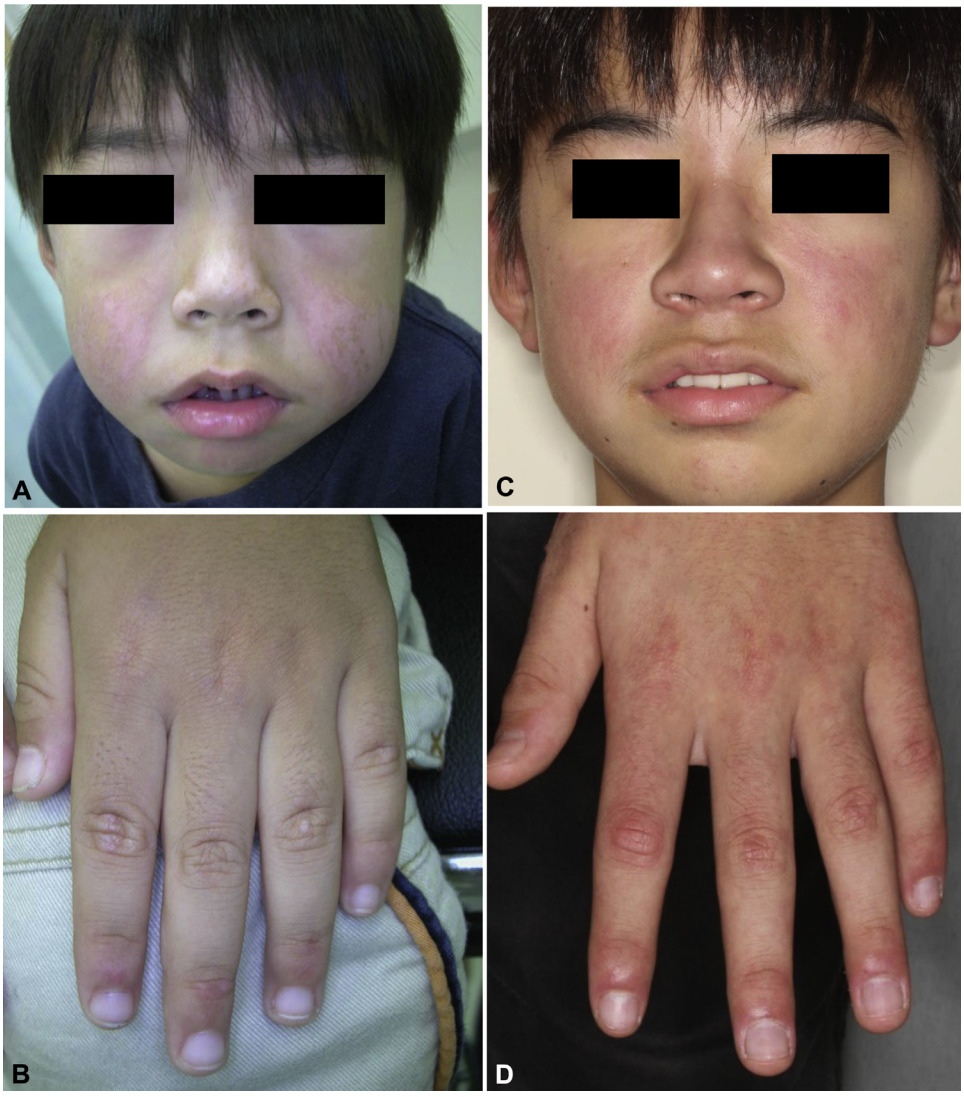

Fig 1. Erythema on the cheeks and ears at initial onset (4 years old) (**A**) and at relapse (12 years old) (**C**). Keratotic papules and purplish erythema on the dorsal of the left hand at initial onset (**B**) and at relapse (**D**).

combination therapy with PSL (1 mg/kg/d) and MTX (0.4 mg/kg/wk), both of which were tapered out in 6 months. Both clinical and biochemical remission was achieved and persisted for 8 years, suggesting a monocyclic course.

At 12 years of age, the patient presented to us with similar symptoms affecting the skin and proximal muscles but without preceding infectious episodes within the previous 3 months (Fig 1, *C* and *D*). Elevated levels of aspartate aminotransferase, 104 IU/L (0−35 IU/L); alanine aminotransferase, 53 IU/L (0−35 IU/L); lactate dehydrogenase, 506 IU/L (80−200 IU/l); creatine kinase, 1930 IU/L (12−170 IU/L), and aldolase 28.6 IU/L (2.7−7.5 IU/L) were observed. Antinuclear, anti-Jo-1, anti-Sm, anti-SS-A, anti-SS-B and anti-RNP antibodies were all negative. The IgM class of antiparvovirus B19 antibodies was not detected. Computed tomography scans showed neither interstitial pneumonia nor visceral malignancy. The clinical, histopathologic, and radiologic findings were virtually identical to those observed 8 years before (Fig 2, *C* and *D*). These findings confirmed the diagnosis of JDM relapse. Both the skin condition and muscle strength improved with 2 courses of mPSL pulse therapy (1 g/d for 3 consecutive days per course) followed by PSL (0.78 mg/kg/d) and MTX (0.20 mg/kg/wk). Serum levels of muscle-derived enzymes also returned to normal ranges. However, when the PSL dose was decreased to 0.29 mg/kg/d, elevation of muscle-derived enzymes and muscle weakness recurred, accompanied by pseudohypertrophy of the gastrocnemius

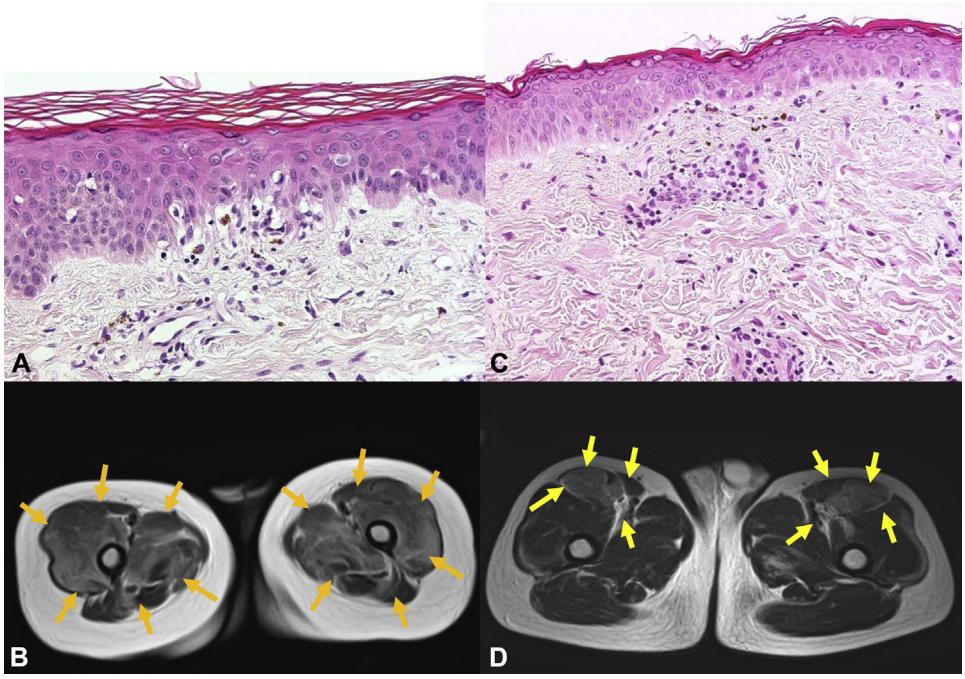

Fig 2. Vacuolar changes at the dermoepidermal junction of the epidermis, and deposition of mucin, pigment incontinence, and infiltration of lymphocytes in the papillary dermis are observed in the biopsy specimen of the left cheek at initial onset (4 years old) (**A**) and of the right knee at relapse (12 years old) (**C**). At the initial onset (T2) (**B**) (*orange arrows*) and at relapse (STIR) (**D**) (*yellow arrows*), magnetic resonance imaging shows high-intensity areas in the proximal muscles of the thighs, which suggests edema caused by inflammation. (**C**, Hematoxylin-eosin stain; original magnification: ×200.)

muscles. Erythema on the cheeks and keratotic papules on the dorsal hands also reappeared. Although his muscle strength and serum levels of muscle-derived enzymes returned to normal levels after the addition of cyclosporine (0.20 mg/kg/d) and an increase of PSL dose (to 0.78 mg/kg/d), the pseudohypertrophy and the eruptions persisted. The change of cyclosporine to tacrolimus (0.04 mg/kg/d) and decrease of MTX (to 0.08 mg/kg/wk) maintained the normal levels of muscle-derived enzymes and muscle strength. There were no sequelae such as calcinosis, muscular contracture, or cutaneous or gastric ulcers during his course. This patient will continue monthly follow-up, with a gradual PSL dose reduction planned for a minimum of 2 years unless a relapse of JDM occurs.

DISCUSSION

There are no established methods for predicting the clinical course of JDM. JDM is usually treated with corticosteroid therapy alone or in combination with immunosuppressive agents such as MTX.[8] It is suggested that early and intensive corticosteroid-based therapy leads to a monocyclic course.[3] Although clinical remission was achieved by early intensive treatment with mPSL pulse therapy followed by oral PSL and weekly MTX in the initial episode of JDM in our case, the maintenance therapy was discontinued at 6 months to prevent adverse events associated with long-term corticosteroid use. Because the treatment for JDM is usually continued for at least 2 years,[6,8] the duration of the initial treatment seems short. However, premature cessation of treatment usually leads to early relapse of JDM. Thus, the short duration of treatment may not have been associated with the relapse 8 years after the initial onset in our patient. Although infections often trigger the onset or relapse of JDM,[9,10] there were no infectious episodes in our patient within 3 months before the relapse of JDM. Recently, 2 possible factors, dysphonia and high CDASI[11] score (CDASI >20), have been associated with relapse in a population of dermatomyositis and JDM.[12] However, this patient did not have dysphonia, and CDASI was less than 20.

The prognosis of late recurrent JDM is not fully understood. Of the 2 previously reported cases, one had been successfully treated with PSL monotherapy until the relapse, whereas the other showed

spontaneous remission.[4,5] Although the initial episode of JDM was completely cured by short-term corticosteroid-based treatment, additional intensive immunosuppressive therapy with tacrolimus was required to control the prolonged skin lesions in the relapse. Thus, the late recurrence of monocyclic JDM could be intractable and require attention.

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