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Single Case

Anti-MDA5 Antibody-Positive Dermatomyositis Presenting with Cellulitis-Like Erythema on the Mandible as an Initial Symptom

Yuki Hattori Kanako Matsuyama Tomoko Takahashi En Shu
Hiroyuki Kanoh Mariko Seishima

Department of Dermatology, Gifu University Graduate School of Medicine, Gifu, Japan

Keywords
Anti-MDA5 antibody · Rapidly progressive interstitial lung disease · Cellulitis-like erythema · Dermatomyositis · Panniculitis

Abstract
Panniculitis is an uncommon skin eruption observed in patients with dermatomyositis (DM)/clinically amyopathic dermatomyositis (CADM), especially in anti-melanoma differentiation-associated gene 5 (MDA5) antibody-positive DM. We present here a 51-year-old Japanese woman with an anti-MDA5 antibody-positive DM who initially had cellulitis-like erythema on her right mandible. Histopathological findings showed a subcutaneous lobular infiltration of lymphocytes. The patient developed typical skin eruptions of DM/CADM, rapidly progressive interstitial lung disease, and severe muscle weakness 2 weeks after the first visit. After the diagnosis of anti-MDA5 antibody-positive DM, she was treated with intravenous steroid pulse therapy (methylprednisolone, 1,000 mg/day for 3 days), oral prednisolone at 1.0 mg/kg/day, and tacrolimus at 4.0 mg/day. The lesions of panniculitis associated with DM/CADM typically present on the buttocks, thighs, arms, and abdomen. This is the first DM/CADM case with localized panniculitis on the face. Panniculitis and myositis usually show simultaneous improvement during treatment. Although panniculitis disappeared with steroid and tacrolimus treatment and did not recur, muscle weakness was intractable and recurred in

KARGER

Yuki Hattori, MD
Department of Dermatology, Gifu University Graduate School of Medicine
Yanagido 1-1
Gifu 501-1194 (Japan)
E-Mail yukihgifu@gmail.com

this case. This indicates that the clinical courses of panniculitis and myositis of DM/CADM do not always change in parallel.

Introduction

Clinically amyopathic dermatomyositis (CADM), a subtype of dermatomyositis (DM) with little or no muscle involvement, is frequently complicated by rapidly progressive interstitial lung disease (RP-ILD), which is an intractable and life-threatening complication [1–3]. Recently, several myositis-specific autoantibodies have been identified in DM/CADM patients and are closely associated with the clinical phenotypes [4]. High levels of anti-melanoma differentiation-associated gene 5 (MDA5) antibodies and serum ferritin are strongly associated with high mortality due to RP-ILD development in anti-MDA5 antibody-positive DM/CADM patients [5, 6]. Therefore, rapid diagnosis and treatment are imperative for improving the prognosis of DM/CADM. Skin ulcerations, palmar papules, and oral pain and/or ulcers [7] are often present in anti-MDA5 antibody-positive DM/CADM patients. Herein, we present the rare case of an anti-MDA5 antibody-positive DM patient who initially presented with cellulitis-like erythema on the mandible. Afterwards, the patient developed typical skin eruptions of DM/CADM, ILD, and severe muscle weakness.

Case Report

A 51-year-old woman visited our hospital with a 3-month history of painful erythema on her right mandible. Erythema was observed with tender induration only on her right mandible and neck (Fig. 1a), but no other eruptions were seen. Histopathology of a skin biopsy specimen showed a subcutaneous lobular infiltration of lymphocytes without vasculitis (Fig. 1b). Laboratory data were within normal ranges. Approximately 2 weeks after her initial visit, she visited our hospital again due to continuous fever up to 39.0°C, fatigue, and muscle weakness. At that time, we observed Gottron papules on her elbows and dorsolateral aspects of proximal and distal interphalangeal joints, and papules overlying the palms (Fig. 1c). She complained of dyspnea, and high-resolution computerized tomography demonstrated interstitial changes with ground-glass opacity of the bilateral lower lung fields. Laboratory data of serum revealed the following: creatinine kinase (CK), 406 IU/L (normal, 41–153); C-reactive protein, 0.28 mg/dL; KL-6, 311 IU/L (normal, <500), and ferritin, 410.6 ng/mL (normal, 4.6–204). Anti-MDA5 antibody was positive (titer, 193.4 index value, normal, <32.0, determined using enzyme-linked immunosorbent assay). A diagnosis of anti-MDA5 antibody-positive DM was made based on the above clinical features and laboratory data. She was treated with oral prednisolone at 45 mg/day (1.0 mg/kg/day) accompanied with oral tacrolimus at 4.0 mg/day after intravenous steroid pulse therapy (methylprednisolone, 1,000 mg/day for 3 days). Since the serum ferritin level rapidly increased, though the eruptions disappeared, intravenous cyclophosphamide (IVCY) was administered. However, serum ferritin and CK levels continued to increase accompanied by dysarthria. Accordingly, a second course of steroid pulse therapy and intravenous immunoglobulin (IVIg) (400 mg/kg/day for 5 days) were administered. Although the ground-glass opacity of her bilateral lower lung gradually improved, serum CK and myoglobin levels increased again, while muscle weakness of the lower extremities and dysarthria aggravated. After IVCY and IVIg therapy was reintroduced, the symptoms disappeared and the clinical data improved (Fig. 2).

Discussion

It is well known that skin eruptions sometimes precede the internal organ involvement in DM/CADM. Anti-MDA5 antibody-positive DM/CADM patients are characterized by not only typical eruptions, such as heliotrope rash, Gottron papules, and mechanic's hands, but also skin ulcerations, palmar papules (inverse Gottron), and oral pain and/or ulcers [7]. The present case showed painful erythema with tender induration similar to cellulitis on her mandible and neck, which is a rare cutaneous manifestation of DM/CADM as an initial symptom. Histological findings showed lobular lymphocyte infiltration in the subcutaneous tissue, but not vasculitis.

More than 30 cases of panniculitis in DM/CADM have been reported, including several juvenile DM cases [8]. Panniculitis is significantly associated with anti-MDA5 antibody-positive DM cases (35.7%) compared to anti-MDA5 antibody-negative DM cases (12.6%) [9]. Panniculitis may present prior to, concurrent with, or subsequent to symptoms of DM/CADM. In the current literature, the date of onset ranges from 14 months preceding to 5 years following DM diagnosis [10, 11]. In the present case, a diagnosis of DM was made 3 and a half months after the onset of panniculitis. A histopathological study demonstrated that 9% of skin biopsy specimens of patients with DM showed subclinical panniculitis, suggesting that microscopic panniculitis might be more common than clinically recognized panniculitis [12].

The lesions of panniculitis associated with DM/CADM typically present on the buttocks, thighs, arms, and abdomen [13, 14], while lupus erythematosus panniculitis appears on the proximal extremities, shoulders, buttocks, trunk, breast, face, and scalp [10]. This is the first case report showing panniculitis only on the mandible in DM/CADM, as far as we know. DM/CADM should be included as a possible differential diagnosis in patients presenting with cellulitis-like erythema not only on the extremities, buttocks, or abdomen, but also on the face. Histopathological study is necessary for the diagnosis of panniculitis in DM/CADM, which shows mainly lobular panniculitis with a lymphocytic infiltrate, fat necrosis, and consequent fibrosis [8].

As the prognosis of RP-ILD in DM/CADM patients with anti-MDA-5 antibody is poor, they need rapid and intensive treatment. DM/CADM should be considered, particularly when intractable panniculitis is noted. Panniculitis and myositis have shown simultaneous improvement during treatments [14, 15] and a parallel flare and remission. In the present case, although panniculitis disappeared by steroid and tacrolimus treatment and did not recur, muscle weakness recurred with an increase in CK and myoglobin levels. Therefore, totally, 2 courses of IVCY and IVIg were administered (Fig. 2). The clinical courses of panniculitis and myositis of DM/CADM may not always change in parallel.

Statement of Ethics

The patient has given informed consent and the study was done according to the Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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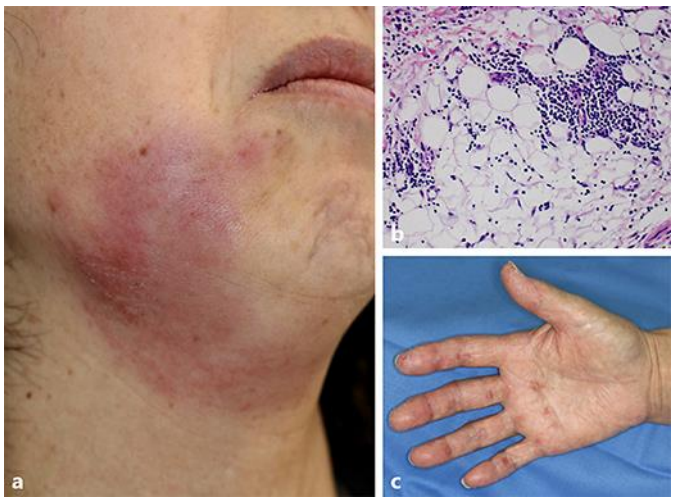

Fig. 1. Clinical features of the right mandible (**a**) and histopathological findings of this eruption (**b**) at the first visit. The clinical findings on the right palm at the second visit (**c**).

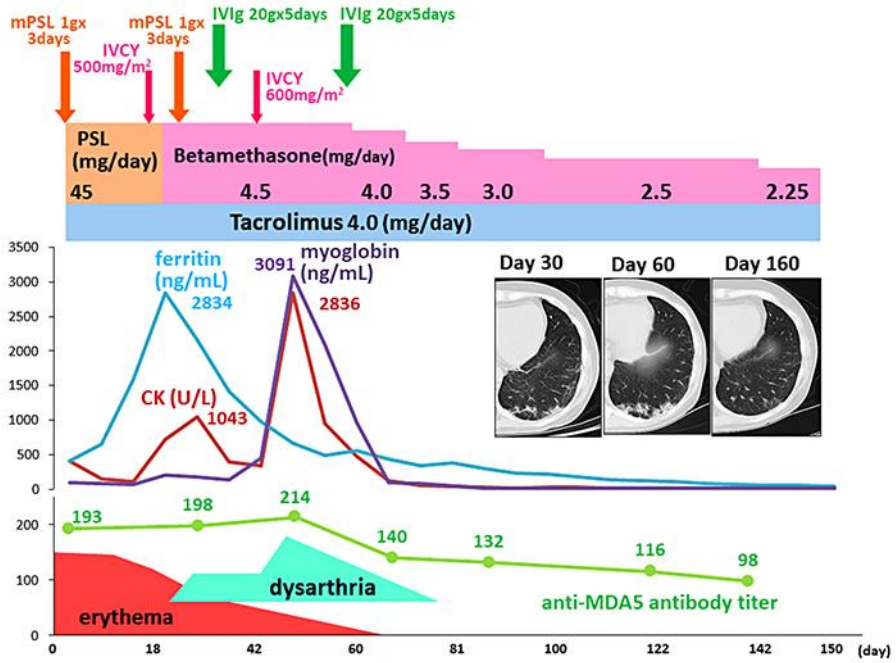

Fig. 2. Graphical presentation of the treatments and the time course for the serum CK, ferritin, and myoglobin levels, as well as the anti-MDA5 antibody titer. CK, creatinine kinase; IVCY, intravenous cyclophosphamide; IVIg, intravenous immunoglobulin; PSL, prednisolone.