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Case report

Lung histopathological pattern in a survivor with rapidly progressive interstitial lung disease and anti-melanoma differentiation-associated gene 5 antibody-positive clinically amyopathic dermatomyositis

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ABSTRACT

Anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are specific indicators of patients with dermatomyositis, particularly clinically amyopathic dermatomyositis (CADM). CADM is occasionally accompanied by fatal, treatment-resistant, rapidly-progressive interstitial lung disease (RP-ILD). All previous reports showed that histopathological findings in RP-ILD with anti-MDA5 antibody-positive CADM indicated diffuse alveolar damage (DAD). This is the first report describing a non-DAD pattern in RP-ILD with anti-MDA5 antibody-positive CADM, which was improved by immunosuppressive therapy. This case may be a milder clinical phenotype than a typical DAD pattern in RP-ILD with anti-MDA5 antibody-positive CADM.

1. Introduction

Anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are specific indicators of patients with dermatomyositis, particularly clinically amyopathic dermatomyositis (CADM) [1–6]. CADM is occasionally accompanied by fatal, treatment-resistant, rapidly-progressive interstitial lung disease (RP-ILD) [7,8]. A few reports have shown that diffuse alveolar damage (DAD) is a histopathological finding in RP-ILD with anti-MDA5 antibody-positive CADM. However, these findings were confirmed only at autopsy [9,10]. To our knowledge, this is the first case report to show a non-DAD pattern in RP-ILD with anti-MDA5 antibody-positive CADM, which was improved by immunosuppressive therapy.

2. Case report

A 32-year-old woman was referred to our hospital with a 4-week history of fever, cough, and erythematous eruptions. She was a never-smoker and had no significant medical history or environmental risk for respiratory disease. Her physical examination revealed a fever (38.3 °C), facial erythema and heliotrope rash (Fig. 1a), erythema over the V area of the neck (Fig. 1b), scaly erythema with ulceration over the elbow (Fig. 1c), knee, and dorsum of her hands (Gottron's sign) (Fig. 1d), and skin thickening on the sides of her fingers (mechanic hands). There were no signs of muscle weakness. Fine crackles were heard in the bilateral lower lung fields. Arterial blood gas analysis showed normal partial pressure of oxygen and carbon dioxide (73.5 and 38.6 Torr, respectively). The alveolar-arterial oxygen difference was 28 mmHg. The serum levels of C-reactive protein and creatine kinase were not elevated. The serum levels of Krebs von den Lungen-6, lactate dehydrogenase,

Abbreviations: MDA5, melanoma differentiation-associated gene 5; CADM, clinically amyopathic dermatomyositis; RP-ILD, rapidly progressive interstitial lung disease; DAD, diffuse alveolar damage; CT, computed tomography; FVC, forced vital capacity; DLco, diffusing capacity of the lung for carbon monoxide; 6MWD, six-min walk distance; MMRC, modified medical research council dyspnea scale; NSIP, nonspecific interstitial pneumonia; IVCY, intravenous cyclophosphamide.

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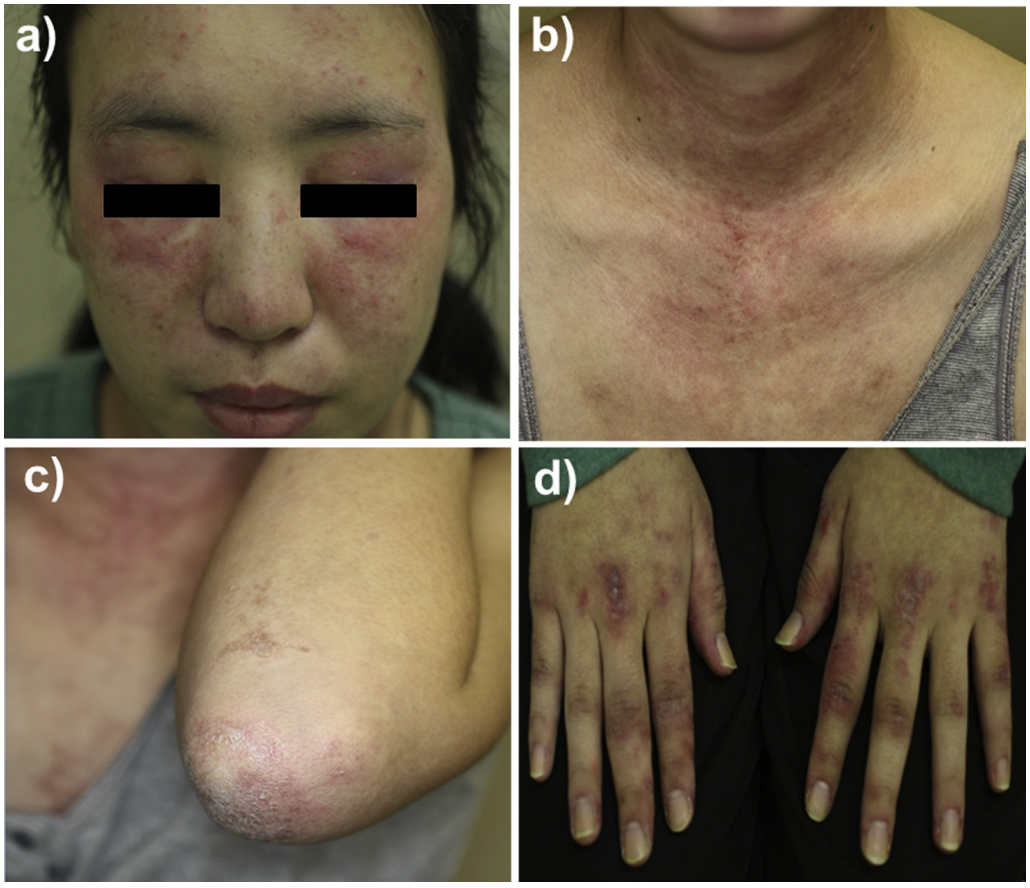

Fig. 1. Physical findings suggestive of clinically amyopathic dermatomyositis. a) facial erythema and heliotrope rash; b) erythema over the V area of the neck; c) scaly erythema with ulceration over the elbow; d) Gottron's sign.

aldolase, and ferritin were increased (726 U/ml, 551 U/l, 10.0 IU/l, and 1269 ng/ml, respectively). Anti-MDA5 antibody was detected (40.7 U/ml > 8 U/ml). Other autoantibodies suggesting autoimmune disorders were not detected. A chest computed tomography (CT) scan showed peribronchovascular ground-glass opacities and bilateral subpleural reticular opacities (Fig. 2). A pulmonary function test indicated normal predicted value for forced vital capacity (%FVC) and decreased predicted value for diffusing capacity of the lung for carbon monoxide (%DLco) (%FVC 86.5%; %DLco 71.9%). Bronchoalveolar lavage was performed in right B9. The total cell count was 1.38×10^5 cells m^{-1}, with a normal cellular profile and CD4/CD8 ratio (the percentage of neutrophils and lymphocytes were 2 and 0%, respectively). Microbial culture results from the sputum and bronchoalveolar lavage fluid were negative. Six-min walk distance (6MWD) was 285 m, with 96% of minimum arterial oxygen saturation measured by pulse oximetry. The modified medical research council dyspnea scale (MMRC) was 2. Magnetic resonance imaging of inferior retinaculum of extensor muscles demonstrated muscle edema that was consistent with myositis. In a muscle biopsy, findings of perivascular inflammatory infiltrate and perifascicular muscle fiber atrophy were obtained.

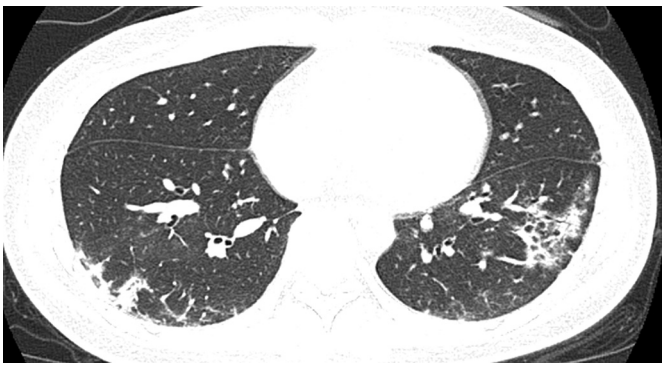

Fig. 2. Chest computed tomography. Peribronchovascular ground-glass opacities and bilateral subpleural reticular opacities.

While the definition of CADM by Sontheimer [5] requires that skin disease be present for 6 months without the development of muscle disease, Sontheimer et al. [6] has also described a subset of patients with CADM in whom fatal ILD developed within the first 6 months of their disease course. Although the disease duration was short in our patient, a presumptive diagnosis of CADM with RP-ILD was made on the basis of the described findings. One week after the first visit, in order to determine the histopathological pattern, we performed video-assisted thoracic surgical lung biopsy (SLB) (right S5, 8, 9).

The lesion was characterized by diffuse mild interstitial fibrosis and inflammatory cell infiltration mostly of lymphocytes, and the changes were homogeneous, as in a nonspecific interstitial pneumonia (NSIP) pattern (Fig. 3a). Meanwhile, mild peripheral accentuation and inflammatory changes around the respiratory bronchioles were also seen. There were accumulations of foamy macrophages and a few neutrophils in the airspace (Fig. 3b), and subacute changes such as scant airspace fibrin and scattered Masson bodies as a minor component of the pathology (Fig. 3c, d).