CASE REPORT

Amyopathic Dermatomyositis Complicated with Eosinophilic Pneumonia

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Abstract

A 67-year-old woman was admitted to our hospital due to dyspnea on exertion with lung abnormal shadows. A transbronchial lung biopsy specimen demonstrated eosinophilic pneumonia (EP). The patient also exhibited heliotrope eyelids without muscle weakness, which led to a diagnosis of amyopathic dermatomyositis (ADM). As we were unable to find any other causes of EP, we diagnosed her as having EP associated with ADM. Dermatomyositis (DM) has been reported to be associated with various interstitial lung diseases; however, only one case of EP associated with DM has been reported. We herein report the first case of EP complicated with ADM.

Key words: amyopathic dermatomyositis, eosinophilic pneumonia, interstitial lung disease, interstitial pneumonia


Introduction

Dermatomyositis (DM) is a systemic inflammatory disease of the skeletal muscles and other internal organs. Interstitial lung disease (ILD) and cancer are major complications that affect both the mortality and morbidity of DM. Amyopathic dermatomyositis (ADM), a distinct subgroup of DM, presents with the typical skin rash of classic DM but without muscle involvement. Several reports have documented cases of rapidly progressive ILD with a poor prognosis in patients with ADM. While the features of ILD complicated with ADM have not been fully clarified, the most common histological findings in the literature are nonspecific interstitial pneumonia (NSIP), diffuse alveolar damage (DAD), organizing pneumonia (OP) and usual interstitial pneumonia (UIP). This case report is the first account of a patient with ADM complicated with eosinophilic pneumonia (EP).

Case Report

A 67-year-old Japanese woman with mild bronchial asthma was admitted to our hospital due to dyspnea on exertion. On admission, she had a blood pressure of 123/81 mmHg, a pulse of 110 beats per minute, a temperature of 37.6°C and an oxygen saturation of 96% on room air. Fine crackles were auscultated in the bilateral lower lung fields, with rhonchi in both lungs. The patient had mechanic’s hands on both fingers and Gottron’s papules on the dorsa of the knuckles. The laboratory findings on admission (Table) revealed a white blood cell count of 16,900/mm³ with 55% eosinophils. The serum creatinine kinase concentration was normal; however, the aldolase level was high [7.2 U/L (normal range 1.7-5.1 U/L)]. Anti-asparaginyl (anti-KS) antibodies, a type of anti-aminoacyl-tRNA synthetase antibodies (anti-ARS Abs), were positive. Other autoantibodies to specific antigens, including anti Jo-1 antibodies and anti-CADM140 antibodies, were negative. The serum concentra-
A partial pressure of carbon dioxide in arterial blood gas analysis performed on room air revealed a pH of 7.415, a PaCO₂ of 36.7 Torr. Spirometry showed an obstructive pattern, with FEV₁/FVC of 0.7 and %VC of 87.7%. Chest X-rays and chest computed tomography (CT) performed on admission both demonstrated reticular shadows (Fig. 1) with subpleural non-segmental airspace consolidation in the bilateral lower lungs. CT also disclosed eosinophilic infiltration (Fig. 3B), which supported a diagnosis of EP. Many diseases can present with EP, including parasitic infection or malignancy. Chronic eosinophilic pneumonia can be diagnosed in cases in which no other causes of pulmonary eosinophilia are demonstrated. Chronic eosinophilic pneumonitis, skin lesions or peripheral nerve damage suggestive of microscopic polyangiitis (MPA). There was also no histopathological evidence of angiitis, such as MPA or Churg-Strauss syndrome (CSS), in the TBLB or skin biopsy specimens. After conducting careful whole-body examinations, we were unable to find any evidence suggesting hypereosinophilic syndrome (HES), chronic eosinophilic leukemia (CEL), parasitic infection or malignancy. Chronic eosinophilic pneumonia (CEP) can be diagnosed in cases in which no other causes of pulmonary eosinophilia are demonstrated.

**Table.** Laboratory Findings on Admission. Values Significantly Outside of the Reference Range are Underlined.

<table>
<thead>
<tr>
<th>[Blood examination]</th>
<th>Aldolase (IU/L)</th>
<th>Ferritin (ng/mL)</th>
<th>[Arterial blood gases]</th>
<th>Room air at rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>on admission range</td>
<td>7.2 (2.1-6.1)</td>
<td>106 (3.6-114)</td>
<td>pH 7.415</td>
<td>PaCO₂ (Torr)</td>
</tr>
<tr>
<td>RBCs (×10⁹/μL)</td>
<td>434 (416-552)</td>
<td>C-reactive protein (mg/dL) 0.30 (&lt;0.5)</td>
<td>36.7</td>
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<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.1 (13.2-17.2)</td>
<td>KL-6 (U/mL) 2.000 (&lt;500)</td>
<td>PaO₂ (Torr) 79.3</td>
<td></td>
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<tr>
<td>Hematocrit (%)</td>
<td>39.7 (39.2-49.2)</td>
<td>SP-D (ng/mL) 207 (&lt;110)</td>
<td>HCO₃ (mmol/L) 23.1</td>
<td></td>
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<tr>
<td>WBCs (μL)</td>
<td>169 (34-88)</td>
<td></td>
<td>BE (mmol/L) -0.6</td>
<td></td>
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<tr>
<td>Neutro (%)</td>
<td>33.0 (40-70)</td>
<td>CEA (ng/mL) 3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosino (%)</td>
<td>55.0 (1-7)</td>
<td>CA19-9 (U/mL) 3.8</td>
<td></td>
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<tr>
<td>Baso (%)</td>
<td>0.0 (0-2)</td>
<td>SCC (ng/mL) 1.2</td>
<td></td>
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<tr>
<td>Mono (%)</td>
<td>4.0 (1-10)</td>
<td>CYFRA (ng/mL) 3.1</td>
<td></td>
<td></td>
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<tr>
<td>Lymph (%)</td>
<td>8.0 (18-50)</td>
<td>ProGRP (pg/mL) 29.7</td>
<td></td>
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<tr>
<td>Platelet (×10⁹/μL)</td>
<td>31.1 (11.8-36.4)</td>
<td></td>
<td></td>
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<tr>
<td>Total protein (g/dL)</td>
<td>7.4 (6.8-8.2)</td>
<td>Anti-nuclear antibody (-) (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.6 (3.7-5.2)</td>
<td>Rheumatoid factor (IU/mL) 50 (&lt;19)</td>
<td></td>
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<tr>
<td>BUN (mg/dL)</td>
<td>9.4 (5-22)</td>
<td>anti-CCP antibody(U/mL) 0.6 (&lt;4.4)</td>
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<tr>
<td>Creatinine (mg/dL)</td>
<td>0.64 (0.60-1.30)</td>
<td>anti-DNA antibody(U/mL) 5.0 ≤ 2.0 (0-6)</td>
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<tr>
<td>Na (mEq/L)</td>
<td>141 (134-146)</td>
<td>anti-SS-A antibody (-) (-)</td>
<td></td>
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<tr>
<td>K (mEq/L)</td>
<td>3.7 (3.4-4.3)</td>
<td>anti-SS-B antibody (-) (-)</td>
<td></td>
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<tr>
<td>Cl (mEq/L)</td>
<td>105 (98-108)</td>
<td>anti-Scl-70 antibody (-) (-)</td>
<td></td>
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<tr>
<td>AST (IU/L)</td>
<td>19 (8-40)</td>
<td>MPO-ANCA (EU) &lt;10 (&lt;20)</td>
<td></td>
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<tr>
<td>ALT (IU/L)</td>
<td>12 (5-35)</td>
<td>PR3-ANCA (EU) &lt;10 (&lt;20)</td>
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<tr>
<td>Total bilirubin (mg/dL)</td>
<td>0.5 (0.30-1.10)</td>
<td>anti-Jo-1 antibody(U/mL) ≤ 7.0 (&lt;10)</td>
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<td>LDH (IU/L)</td>
<td>332 (106-220)</td>
<td>anti-KS antibody (+) (+)</td>
<td></td>
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<tr>
<td>CPK (IU/L)</td>
<td>103 (10-180)</td>
<td>anti-CADM antibody (+) (+)</td>
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</tbody>
</table>

tected. We therefore diagnosed the patient with ADM complicated with EP based on positive findings for anti-KS antibodies, as nearly all patients with anti-ARS Abs have ILD, and anti-ARS Abs are regarded to be a marker of ILD (2-7).

The administration of steroid therapy alone failed to improve the EP; therefore, we added the immunosuppressive drug cyclosporine. This combination therapy brought about an improvement in the pulmonary infiltrative shadows (Fig. 4). Renal damage developed during the course of treatment as a side effect of cyclosporine therapy, which necessitated a reduction in the dose of cyclosporine. Over the five years since the initiation of treatment, EP has recurred three times during attempts to taper the therapy (Fig. 5). Overall, the patient’s clinical course also suggests that she had ADM complicated with EP rather than CEP, which usually responds to steroid therapy.

**Discussion**

ILD often develops during the clinical course of DM or polymyositis (PM). The prevalence of ILD varies widely (from 23.1% to 65.0%) among the case series of patients with PM and DM reported thus far (8, 9). ILD is a major cause of morbidity and mortality among patients with DM or PM. Histopathologically, the disease manifests as NSIP (33%), DAD (21%), OP (21%) or UIP (14%) (8, 10-15).

ADM is a clinical subtype of DM characterized by elevated muscle enzymes with the absence of motor weakness (16-22). Physicians should be watchful for accompanying ILD or malignant disease, as both can strongly affect the
prognosis. ILD was detected in 15% of the ADM patients reported by Gerami, with a mortality rate of 39%. Another 14% of the ADM patients reported by Gerami suffered from accompanying malignant diseases (17).

A number of studies of patients with DM and ILD (DM-ILD) have been published; however, the coexistence of ADM and ILD (ADM-ILD) is rare and has only been described in a small number of cases. For example, Cottins, Lee and Suda, reported three, three and 14 patients with ADM-ILD, respectively (10-12). Taken together, these studies describe two courses of ADM-ILD: acute/subacute or chronic. The acute/subacute type deteriorates within three months, while the chronic type deteriorates over a period exceeding three months. CT findings, histopathological ob-
observations and the course of treatment all differ between these two types. On imaging studies, for example, the acute/subacute type primarily presents with airspace consolidation and ground-glass opacity (GGO), while the chronic type generally manifests as traction bronchiectasis and GGO. Histopathologically, the acute/subacute type exhibits DAD or NSIP, while the chronic type displays NSIP or UIP. The therapeutic outcomes of the chronic type are superior. For example, among the 13 cases of ADM-ILD reported by Suda (eight acute/subacute type patients and five chronic type patients), the mortality rate due to respiratory failure during the observation period was 67% in the acute/subacute type group versus 0% in the chronic type group (11). The ILD in the present case progressed subacutely with airspace consolidation and GGO, consistent with the course of other ADM-ILD patients reported thus far.

This case is quite remarkable in that the ADM-ILD histopathologically demonstrated EP. EP has not been previously reported in a pure ADM-ILD patient, and, even among cases of DM-ILD, only one patient has been reported to have both EP and OP (23).

We evaluated the levels of serum myositis-specific autoantibodies, and anti-KS antibodies, a type of anti-ARS Abs, was found to be positive. Anti-KS antibodies are highly associated with the presence of ILD alone, without myositis or rashes, similar to that observed in the present patient. Nearly all patients with anti-ARS Abs have ILD (2-7); therefore, the progression and recurrence of cases of EP may be predicted based the titer of anti-KS antibodies.

There is a limitation to this report. There remains the possibility that the CEP was accidentally complicated with ADM. In fact, the patient had experienced asthma attacks, which are frequently associated with CEP (24). CEP is an idiopathic disorder characterized by the abnormal accumulation of eosinophils in the lungs. CEP and cryptogenic organizing pneumonia (COP, idiopathic BOOP) share many features and exhibit overlapping clinical, laboratory and pathological findings (1, 25-27). CEP can be diagnosed in cases in which other causes of pulmonary eosinophilia are not detected. The following is described in the section entitled, “Treatment of chronic eosinophilic pneumonia,” in the UpToDate database (www.uptodate.com): “TREATMENT - Patients with CEP are uniformly responsive to intravenous or oral glucocorticoids. Thus, an alternative diagnosis should be entertained if a patient is steroid-resistant.” We believe that the patient presented with eosinophilic pneumonia (EP) as a pulmonary manifestation of ADM because her overall clinical course was compatible with that of ADM-ILD, not with CEP. If the CEP had been accidentally combined with ADM in the present case, steroid therapy would have been more effective and the serum KL-6 level would have been lower. Moreover, the positive results for anti-KS antibodies strongly suggest the existence of ADM-ILD.

With respect to COP, which shares many features and overlapping characteristics with CEP, only half of affected patients are positive for KL-6 (28, 29).

It is also interesting that the present patient’s spirometry examination showed an obstructive pattern. On the first admission, her chest sounds revealed rhonchi and spirometry demonstrated an obstructive pattern, which we believe indicated worsening of bronchial asthma. Bronchial asthma is associated with lung eosinophilia, which contributes to airway hyperresponsiveness and remodeling, resulting in airflow limitations (30). We believe that the eosinophils observed in patients with ILD and asthma share a similar pathophysiology with respect to airflow limitation.

In conclusion, we experienced a case of ADM-ILD complicated with EP, a condition that has not been previously reported.

The authors state that they have no Conflict of Interest (COI).

References
17. Gerami P. A systematic review of adult-onset clinically