Two Patients with Polymyositis or Dermatomyositis Complicated with Massive Pleural Effusion

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Two patients with polymyositis (PM) or dermatomyositis (DM) complicated with massive pleural effusion are reported here. Both patients presented a high-grade fever, pleural effusion prominent on the right, and good response to steroid therapy. In a 50-year-old woman with PM, combined process of pleural inflammation, cardiomyopathy and coexisting hypothyroidism were considered to be responsible for the accumulation of the massive pleural effusion. However, in a 34-year-old man with DM, pleural inflammation associated with interstitial pneumonia or pleural microvasculopathy in DM was considered to be responsible for the accumulation of the massive pleural effusion.

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Introduction

The spectrum of pulmonary involvement in polymyositis/dermatomyositis (PM/DM) includes interstitial lung disease, bronchiolitis obliterans, with organizing pneumonia, bronchopneumonia, pulmonary vasculitis, pulmonary edema, primary pulmonary malignancy, diffuse alveolar damage, pulmonary embolism and diaphragmatic atrophy. In contrast to the frequent lung involvement in patients with PM/DM, an accumulation of a massive pleural effusion is very rare. We recently encountered to two patients with PM or DM complicated with massive pleural effusion. The mechanism of an accumulation of the pleural effusion and the therapeutic effect of the medicine in the reduction of the pleural effusion in these patients are discussed here.

Case Report

Case 1 of PM with pleural effusion

A 50-year-old Japanese woman (N.K.) was admitted at Soma Public Hospital in July 1990 because of muscle weakness in the upper arms and thighs, polyarthralgia of both hands and wrists and high-grade fever. Breath sounds were diminished bilaterally, with inspiratory rales at both bases; slight pitting edema was noted over the lower extremities, bilaterally. Chest X-ray and computed-tomography (CT) revealed massive pleural effusion, interstitial edema and pericardial effusion, as shown in Fig. 1 (A) and (B). She had no past history of lung or heart disease. Her serological test was positive for anti-SS-A antibody, but negative for other anti-nuclear antibodies like anti-Jo-1 antibody and anti-U1-RNA antibody. She did not exhibit any symptoms such as erythema, skin sclerosis, dry eye, dry mouth and Raynaud’s phenomenon. Heart disease, bronchopneumonia, pulmonary malignancies and pulmonary embolism were excluded on the basis of the additional examinations.

She had a) prominent muscle weakness, b) elevation of serum creatinine kinase (CK) level: 1,400 IU/l (normal, 40–120 IU/l) and serum myoglobin: >500 ng/ml (normal, <35 ng/ml), c) the characteristic electromyographic triad in anterior tibial muscle: small-amplitude, short-duration polyphasic motor potentials, and increased membrane irritability. Based on these findings, she was diagnosed as having PM according to the criteria of Bohan and Peter (1).

The characteristics of the pleural effusion taken in August 1990 were as follows: specific gravity: 1.017; Rivalta test:
PM/DM with Massive Pleural Effusion

Figure 1. Chest X-ray and computed tomography of the first PM patient showing massive pleural effusion, interstitial edema and pericardial effusion as indicated by arrows (A and B). The pleural effusion disappeared completely as shown in (C), following administration of prednisolone at a dose of 30 mg/day combined with furosemide at a dose of 80 mg/day and thyroid powder at a dose of 100 mg/day.

negative; fibrin crystals: positive; total protein: 3.6 g/dl; cell count: leucocytes: 8–10/field, erythrocytes: 40–50/field. These data indicated the mixed characteristics of exudate and transudate. Her serum C-reactive protein (CRP) level was 0.3 mg/dl (normal, <0.3 mg/dl). Examination for bacteria and Mycobacterium tuberculosis were negative and the adenosine deaminase level was 3.1 IU/l (normal, 7.7–19.3 IU/l). Thyroid function tests showed the following: thyroid stimulating hormone (TSH): 7.4 μU/ml (normal, 0.6–5.1 μU/ml); triiodothyronine (T3): 0.5 ng/ml (normal, 0.8–1.8 ng/ml), % T3 uptake: 39.9% (normal, 25.0–36.0%), thyronine (T4): 5.0 μg/dl (normal, 4.6–12.6 μg/dl) without any antibodies to thyroid, microsome and TSH receptor. Prednisolone at a dose of 30 mg/day did not improve the muscle weakness, pleuritis and the muscle enzyme levels, therefore, the dose was increased to 60 mg/day. At this point in September 1990, she was referred to the Department of Internal Medicine II, Fukushima Medical University School of Medicine for further management. The serum levels of CK, aldolase and myoglobin on admission to our department were 325 IU/l (normal, 40–150 IU/l), 4.9 U/l (normal, 0.5–3.1 U/l) and 238.5 ng/ml (normal, <50 ng/ml), respectively. Muscle biopsy performed in October 1990 showed non-specific type-2 atrophy.

No evidence of heart block or heart failure such as tachycardia and low voltage was noted in the electrocardiogram, but pericardial effusion and cardiac enlargement was noted on ultrasonic cardiograph, suggesting the presence of heart failure. No evidence of malignancy in the lung was noted on CT and Ga scintigraphy.

Following treatment with prednisolone at a dose of 60 mg/day, a rapid decrease in serum CK level was noted, along with marked improvement in muscle strength. Therefore, the dose of prednisolone was decreased to 30 mg/day. However, the amount of pleural effusion increased further as seen in Fig. 2. The characteristics of the pleural effusion taken in September 1990 were as follows: specific gravity: 1.018, Rivalta test: negative, Runeberg test: negative and total protein: 1.4 g/dl, indicating that it was more likely transudate. Considering that massive pleural effusion in this state is most likely due to cardiomyopathy, we increased the dose of furosemide from 20 mg/day to 80 mg/day along with additional administration of thyroid powder at a dose of 100 mg/day. This regimen combined with prednisolone at a dose of 30 mg/day was effective to reduce the pleural effusion as shown in Fig. 1(C). The patient was discharged on November 10, 1990. She had no recurrence of PM.
until at the time of this writing date on 5 mg/day prednisolone administration.

Case 2 of DM with pleural effusion

A 34-year-old Japanese man (A.Y.) complained of dyspnea along with erythema over his fingers in August 1997. He was admitted at Soma Public Hospital in November 1997 because of muscle weakness in his arms and fingers, along with extended erythema over his neck and high-grade fever. Chest roentgenogram and CT of the lung revealed massive pleural effusion and interstitial pneumonia as shown in Fig. 3 (A) and (B). He did not exhibit any symptoms such as face erythema, skin sclerosis, Raynaud’s phenomenon or arthritis. He had no specific disease history of lung and heart. Heart disease, bronchopneumonia, pulmonary malignancies and pulmonary embolism were excluded on the basis of the additional examinations.

He had a) prominent muscle weakness, b) slight elevation in serum CK level: 272 IU/l (normal, 40–150 IU/l), c) characteristic skin lesions: facial erythema, rash on the both elbows and feet, scaly erythema on both knees, and positive Gottron’s sign, and d) positive reaction for anti-Jo-1 antibody, but negative for other anti-nuclear antibodies such as anti-U1-RNP antibody. He was therefore diagnosed as having DM according to the criteria of Bohan and Peter (1). The characteristics of the pleural fluid taken in November 1997 were as follows: specific gravity: 1.025, Rivalta test: negative, total protein: 6.6 g/dl, cell count: lymphocytes: 60%, monocytes and histiocytes: 38% and neutrophil leucocytes: 2%, indicating that the pleural effusion was exudate. His serum CRP level was 1.44 mg/dl (normal, <0.3 mg/dl). No evidence of heart block or heart failure such as tachycardia, low voltage, pericardial effusion and cardiac enlargement was noted in the electrocardiogram and ultrasonic cardiology. Gas analysis of arterial blood was as follows: PO2: 57.3 mmHg, PCO2: 35.3 mmHg, HCO3: 24.6 mmol/l and O2 saturation: 91.2%.

Methylprednisolone pulse therapy (methylprednisolone at doses of 500 mg/day for 1 day and 1,000 mg/day for the following two days) was administered against interstitial pneumonia and pleural effusion. For further management, he was referred to the Department of Internal Medicine II, Fukushima Medical University School of Medicine in November 1997. The clinical course of this patient is shown in Fig. 4. He had elevated serum asparate aminotransferase (AST) and alanine aminotransaminase (ALT) levels and the ALT levels appeared to be correlated with the levels of serum CK and lactate dehydrogenase (LDH) levels. Therefore, liver biopsy was performed in December 1997. Histopathology of the liver revealed a severe fatty degeneration. The serum CK levels remained relatively within the normal range, but serum levels of aldolase:
PM/DM with Massive Pleural Effusion

Figure 3. Chest X-ray and computed tomography of the second DM patient showing massive pleural effusion, as indicated by the arrows in the right thorax, with interstitial pneumonia (A and B). Following treatment with prednisolone, the pleural effusion disappeared, but there was only minor improvement of interstitial pneumonia as shown by the arrows (C).

4.6 U/l (0.5–3.1 U/l) and myoglobin: 91.3 ng/ml (<50 ng/ml) were elevated. Prednisolone at 60 mg/day combined with cyclosporin at 200 mg/day was administered following the methylprednisolone pulse therapy. A CT scan of the lung taken in November 1997 (Fig. 3C) revealed the disappearance of pleural effusion with a minor improvement of interstitial pneumonia.

The interstitial pneumonia worsened along with the increased serum levels of CK and LDH levels, but there was no recurrence of pleural effusion; he died of pulmonary insufficiency in March, 1998.

Discussion

Radiographic and autopsy studies have confirmed the high prevalence of pleuritis in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). A study of chest roentgenograms revealed that 33 out of 111 SLE patients (30%) had pleural effusion (2). In autopsy studies, histopathologic changes in the pleura and pleural fluid in the thoracic cavity were found in 93% and 57% of 58 SLE patients, respectively (3). Five percent of a series of 180 RA patients demonstrated radiographic evidence of pleural effusion (4). Autopsy of a series of 30 patients with RA revealed evidence of pleuritis in 22 patients (73%) (5). Although the incidence of pleural lesion is high in patients with RA or SLE as described above, the incidence of prominent pleural effusion in patients with PM/DM is quite low.

Plural reactions in PM/DM had not been reported prior to 1976. However, Schwarz et al, although not able to demonstrate radiographic evidence of pleural lesions, presented histologic changes in pleura involved in 50% of their patients with PM/DM (6). A large amount of pleural effusion demonstrated radiographically in PM, was first reported by Donald et al (7). They also reported massive transudative pleural effusion, called hydrothorax, in DM. The mechanism for the accumulation of pleural effusion in PM/DM was not elucidated in these reports.

Regarding the change from exudate to transudate (hydrothorax) observed in the first patient, it is of interest to find the report of Lakhanpal et al in which out of 65 autopsy cases, 16 patients, 3 PM and 13 DM had hydrothorax, and 15 of these had pulmonary edema/heart failure (8). Therefore, hydrothorax has close relation to the heart muscle weakness which is occasionally observed in PM/DM patients. In fact, the isozyme profile of CK, at 2,370 IU/l, determined in August 1990 in the first patient was as follows; BB: 0% (<1.0%), MB: 26% (1–4%) and MM: 74% (88–96%), indicating the involvement of heart muscle.
Miyata et al

Figure 4. Clinical course and laboratory data of the second DM patient. Pulse therapy with methylprednisolone (500, 1,000 and 1,000 mg/day) followed by administration of prednisolone at a dose of 60 mg/day reduced the pleural effusion completely without any recurrence. However, the interstitial pneumonia become worse along with increased serum levels of CK and LDH in spite of the additional administration of cyclosporin at a dose of 200–150 mg/day. The patient died of pulmonary insufficiency due to interstitial pneumonia in March 1998.

Additionally, pitting edema over the lower extremities, and pericardial effusion in addition to pleural effusion, was observed.

In the first PM patient, prednisolone was effective for muscle weakness and a decrease in serum CK level was noted, but the level of pleural effusion somehow increased, in changing the characteristics of the pleural fluid from exudative to transudative. This would suggest that prednisolone was effective for pleural inflammation, but other causes for accumulation of pleural effusion existed.

We considered the hypothyroidism observed in this patient as a possible cause for the pleural effusion, and started to administer thyroid powder at a dose of 100 mg/day in September 1990; however, the drug was stopped on October 29, 1990 because of side effects such as tachycardia and facial flushes. Some response to administration of thyroid powder in the reduction of the amount of pleural effusion was observed as seen in Fig. 2. Additionally, the dose of furosemide was increased from 20 mg/day to 80 mg/day, resulting in complete disappearance of pleural effusion. Thyroid function in November 1990, after she quit taking thyroid powder, was within normal limits: TSH; 1.5 μU/ml, T3; 0.8 ng/ml and T4; 6.6 μg/dl, suggesting that the evidence of hypothyroidism seen during her clinical course was probably transient, due to a syndrome such as low T3 syndrome. Therefore, the pleural effusion noted in this patient might have been caused by a combined process of pleural inflammation, hypothyroidism and cardiomyopathy.

In the second DM patient, the prominent pleural effusion at presentation was associated with interstitial pneumonia, suggesting the participation of interstitial pneumonia for the accumulation of pleural effusion. However, the pleural effusion disappeared rapidly on methylprednisolone pulse therapy. Despite of the worsening of interstitial pneumonia, pleural effusion did not recur during the clinical course. We consider that continuous administration of prednisolone was effective in preventing the recurrence of accumulation of pleural effusion, consistent with reports of good response of the pleural effusion in PM/DM to steroid therapy by Donald et al (7). It has been reported that complement system is deposited, bound, and activated to completion within the intramuscular microvasculature of patients with DM (9). If the same pathogenic change occurs in the pleural microvasculature, it could cause pleuritis.

We presented two patients with PM or DM complicated with massive pleural effusion. As shown in Table 1, both had high-grade fever at presentation, the pleural effusion was more prominent on the right side and the response to prednisolone
PM/DM with Massive Pleural Effusion

Table 1. Comparison of Characteristic Features of PM/DM Patients Complicated with Massive Pleural Effusion

<table>
<thead>
<tr>
<th>Characteristic features</th>
<th>Patient 1</th>
<th>Patient 2</th>
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<tbody>
<tr>
<td>Diagnosis</td>
<td>Polymyositis</td>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Onset to admission</td>
<td>15 days</td>
<td>30 days</td>
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<tr>
<td>Serum CK</td>
<td>Increase (+++)</td>
<td>Increase (+)</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Antinuclear antibody</td>
<td>Jo-1(-), anti-SS-A antibody (+)</td>
<td>Jo-1(+), other antinuclear antibodies (-)</td>
</tr>
<tr>
<td>Character of pleural effusion</td>
<td>Intermediate to transudate</td>
<td>Exudate</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Lung field</td>
<td>Interstitial pneumonia (-)</td>
<td>Interstitial pneumonia (+)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Outcome</td>
<td>Alive</td>
<td>Died of interstitial pneumonia</td>
</tr>
<tr>
<td>Fever</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>Location of pleural effusion</td>
<td>Right&gt;Left</td>
<td>Right&gt;&gt;Left</td>
</tr>
<tr>
<td>Response to steroid therapy</td>
<td>Good</td>
<td>Good</td>
</tr>
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therapy was good. These observations indicate that in patients with PM/DM complicated with massive pleural effusion, causes of pleural effusion other than the pleuritis caused by the disease itself, such as cardiomyopathy, interstitial pneumonia and hypothyroidism, in addition to pulmonary malignancies, must also be considered.

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References