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CASE REPORT

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A case of polymyositis complicated with organizing pneumonia: case report and literature review

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Abstract A 54-year-old man was admitted to hospital with fever, dyspnea, and polyarthralgia. A chest radiograph showed consolidations in the bilateral lungs, and histological examination of transbronchial lung biopsy samples revealed organizing pneumonia. He was also diagnosed with polymyositis because of muscle weakness, elevated muscle enzymes, myogenic findings on the electromyogram, and a positive test for the anti-Jo-1 antibody. Herein, we review 25 cases of organizing pneumonia with polymyositis/dermatomyositis with respect to their clinical features and treatment.

Key words Organizing pneumonia (OP) · Polymyositis · Review

Introduction

Interstitial pneumonia associated with polymyositis/dermatomyositis (PM/DM) is an important complication of some diseases, and acute/subacute interstitial pneumonia is sometimes life-threatening.[1,2] Bronchiolitis obliterans organizing pneumonia (BOOP), which was reported in 1985 as showing a good response to therapy and a favorable prognosis,[3] is often associated with collagen vascular diseases, including PM/DM.[4] In the present report, a case of PM initially presenting as a pulmonary manifestation, organizing pneumonia (OP), is presented with a literature review of 25 OP cases associated with PM/DM.

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Case report

A 54-year-old man was admitted to hospital with fever, sore throat for several days, exertional dyspnea, and polyarthralgia for 1 month. He had no complaints of muscle pain or weakness. He had a 1-year history of diabetes and hypertension, both of which had been well controlled with diet and hypotensive drugs. He had smoked for 24 years but not in the 10 years prior to his admittance to hospital.

On physical examination, his body temperature was 38.5°C, blood pressure was 124/80 mmHg, and pulse rate was 90 beats per minute. Fine crackles were observed in the bilateral lung bases. There were no abnormal skin findings.

Trace proteinuria (±) and occult blood (2+) were detected on urinalysis. A chest radiograph (Fig. 1a) showed bilateral basilar pulmonary infiltrates. Arterial blood gas analysis revealed pH 7.442, PO_2 71.8 mmHg, and PCO_2 37.9 mmHg. Pulmonary function tests demonstrated a moderate restrictive pattern of a reduced vital capacity of 2.41, 66% of predicted value with a normal forced expiratory volume in the first second (FEV_1). Diffusion capacity was not measured. Laboratory studies showed the following: total protein 6.2 g/dl (normal 6.5–8.2 g/dl), albumin 3.4 g/dl (3.7–5.2 g/dl), aspartate aminotransferase (AST) 239 IU/l (8–40 IU/l), alanine aminotransferase (ALT) 161 IU/l (4–45 IU/l), lactic dehydrogenase (LDH) 1091 IU/l (200–470 IU/l), and C-reactive protein 2.05 mg/dl (<0.5 mg/dl). Other laboratory findings, including blood cell counts,

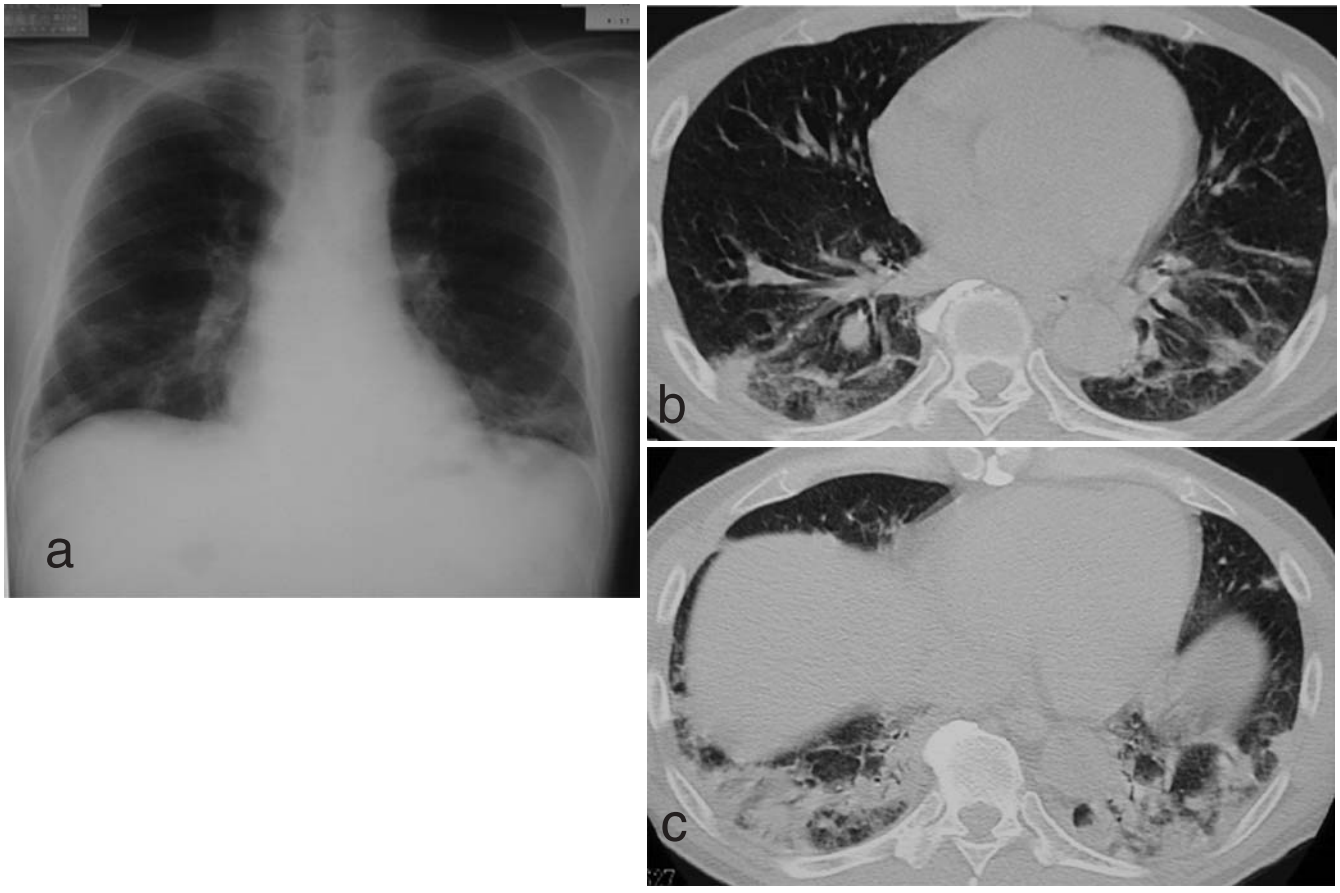

Fig. 1. **a** Chest radiography on admission shows bilateral basilar pulmonary infiltrates. **b** Chest computed tomography (CT) scan at the level of the basal bronchus bifurcation shows bilateral nodular opacities predominantly in peribronchovascular distribution. **c** Chest CT scan at the level of the diaphragm shows patchy air space consolidation in subpleural distribution

renal function, serum levels of lipid, electrolytes, angiotensin-converting enzyme, anti-DNA or anti-RNP antibodies, thyroid hormones, and antibodies to *Mycoplasma* or hepatitis C virus were normal or negative. Creatine kinase (CK) and myoglobin levels were not measured on admission.

We initially suspected that the patient had atypical pneumonia and started antibiotic therapy with minomycin and clarithromycin. One week later, pulmonary infiltrates on the chest radiograph enlarged, and computed tomography (CT) of the chest (Fig. 1b,c) showed patchy airspace consolidations and multiple nodular opacities that were predominantly subpleural and peribronchovascular. A transbronchial lung biopsy (TBLB) was performed, and histopathological analysis revealed fibroblast plugs in the alveolar space and the peribronchial region as well as thickening of the alveolar septa with mild infiltration of chronic inflammatory cells (Fig. 2). Because these histopathological findings were consistent with OP, our clinical diagnosis of OP was made based on the CT findings.[5]

Two weeks after admission, the patient was unable to squat because of muscle weakness in the lower limbs, which had gradually appeared since admission, although muscle weakness was not apparent on muscle strength testing. His serum levels of creatine kinase at that time were highly elevated at 7853 IU/l (normal 43–272 IU/l) with 96% MM fraction. Aldorase was also elevated, although myoglobulin was not measured. Immunological analysis revealed the following: rheumatoid factor at 36.2 IU/ml (normal 0–10 IU/ml), antinuclear antibody 1:20 (normal <1:20), and anti-Jo-1 antibody 48.4 [normal <10.0, enzyme-linked immunosorbent assay (ELISA)]. An electromyogram of the left deltoid and biceps muscle of the arm showed positive sharp waves at rest and a short duration of motor unit potential, which are characteristic features of a myogenic disorder. The histopathological findings of the biopsied specimens obtained from the left bicep muscle were normal. An additional muscle biopsy was not performed because drug treatment had already been initiated. The diagnosis of "probable" polymyositis was made according to diagnostic criteria.[6,7]

He was diagnosed as having OP complicated by PM. After the administration of prednisolone (60 mg daily), his exertional dyspnea and muscle weakness dramatically diminished and disappeared within 4 weeks (Fig. 3). The serum levels of CK, AST, ALT and LDH gradually decreased and normalized within 10 weeks. Three months after the therapy, vital capacity recovered to 2.83 l, 78% of

the predicted value, and the chest radiographic findings markedly improved. The patient was in good health until he committed suicide 5 months after therapy while he was taking prednisolone (17.5 mg daily). An autopsy was not performed.

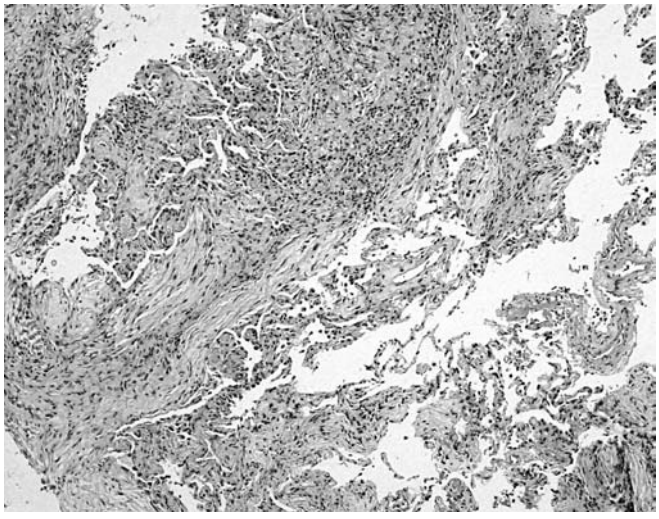

Fig. 2. Fibroblast plugs in the alveolar space and peribronchiolar region are easily visible even at this magnification. The alveolar septa are thickened by mild infiltration of chronic inflammatory cells along with type 2 pneumocytes. HE stain, ×4

Discussion

Interstitial lung disease associated with collagen vascular diseases is a possible predictor of a poor prognosis, which is notable in PM/DM patients.[1,4] Specifically, interstitial pneumonia associated with DM with mild myositis is often refractory and fatal.[2] Cryptogenic organizing pneumonia (COP), originally reported as BOOP in 1985 by Epler et al.,[3] is based on histological analysis and shows a favorable response to corticosteroid therapy and a relatively good prognosis in general; however, it is life-threatening in certain cases.[8,9] The association of OP with collagen vascular diseases, including PM/DM, has recently been reported.[10,11]

Tazelaar et al. retrospectively examined the histological pattern of interstitial lung diseases associated with PM/DM and reported a better prognosis in patients with OP than in those with the usual interstitial pneumonia or diffuse alveolar damage.[12] Nonspecific interstitial pneumonia (NSIP), originally reported in 1994,[13] was not included in the study by Tazelaar et al., but it is remarkable that the histologic pattern of NSIP was found in 18 of 22 cases in their subsequent examination, whereas OP was found in only one case.[14] OP is rarely complicated with PM/DM compared to NSIP.

In the present case, a pulmonary manifestation appeared almost simultaneously with polymyositis. Although video-

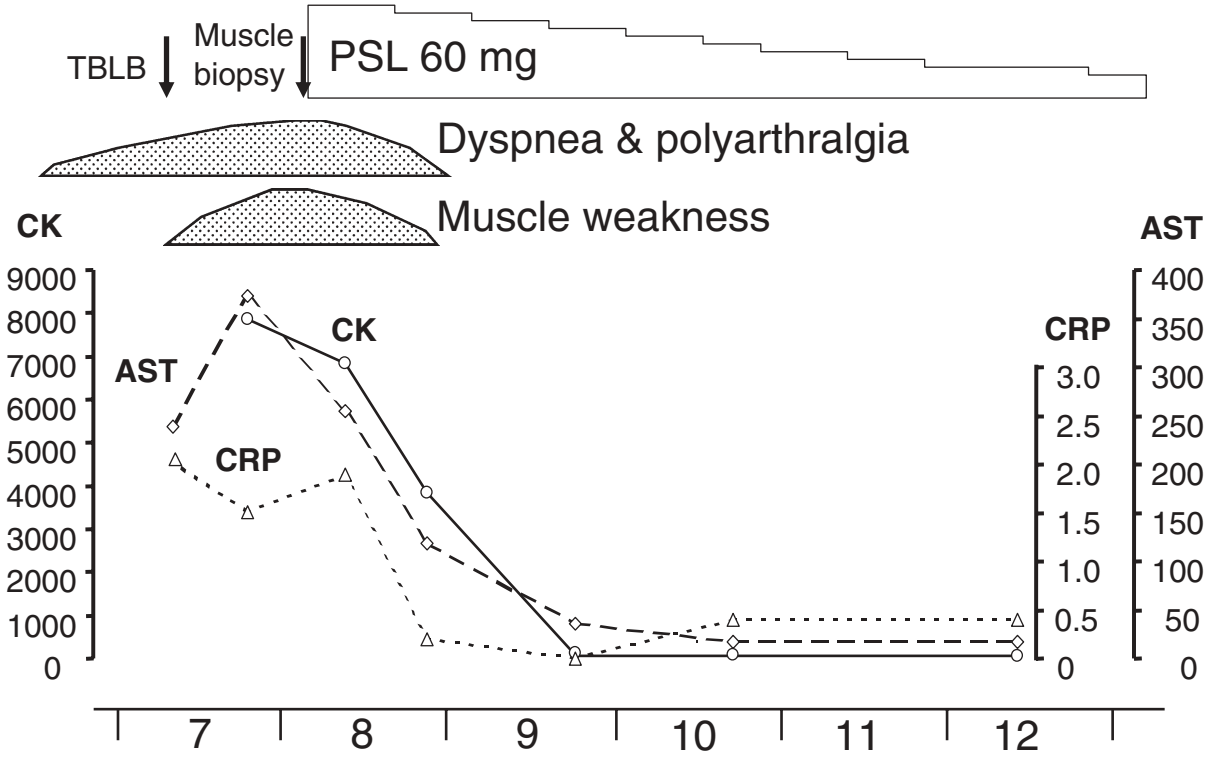

Fig. 3. Clinical course. *TBLB*, transbronchial lung biopsy; *PSL*, prednisolone; *CK*, creatine kinase; *AST*, aspartate aminotransferase; *CRP*, C-reactive protein

Table 1. Clinical features of 25 reported cases

Case no.	Ref.	PM/DM	Age (years)	Sex	Preceding disease	Preceding time (months)	FUP (months)	Outcome	Antibody to Jo-1
1	19	ADM	46	F	DM	2	24	Alive	−
2	20	ADM	42	M	Sim.	–	46	Alive	−
3	21	DM	44	F	OP	2	>5	Alive	+
4	22	PM	56	M	OP	3	>9	Alive	+
5	23	DM	56	F	NA	NA	17	Alive	−
6	24	PM	53	M	Sim.	–	12	Alive	+
7	25	PM	51	M	OP	>2	>8	Alive	−
8	26	PM	61	F	Sim.	–	13	Alive	+
9	27	PM	53	F	Sim.	–	7	Alive	−
10	28	PM	69	F	Sim.	–	>1.5	Alive	+
11	29	PM	50	F	Sim.	–	4	Alive	+
12	8	DM	79	F	NA	NA	3	Died 1 month after admission	NA
13	30	PM	36	F	OP	5	216	Alive	NA
14	31	DM	60	F	NA	NA	10	Alive	−
15	32	PM	58	F	OP	4	7	Alive	+
16	33	PM	65	F	Sim.	–	>5	Alive	NA
17	34	PM	57	F	OP	NA	NA	Alive	NA
18	34	DM	42	F	NA	NA	8	Alive	NA
19	12	PM	47	F	NA	NA	84	Alive	NA
20	12	PM	53	F	NA	NA	24	Alive	NA
21	12	DM	19	F	NA	NA	>1	Died 8 days after OLB	NA
22	12	PM	31	M	NA	NA	216	Alive	NA
23	12	DM	32	F	DM	NA	>3	Died 4 weeks after OLB	NA
24	12	DM	73	M	NA	NA	14	Alive	NA
25	ours	PM	55	M	Sim.	–	7	Died 5 months after Tx	+

ADM, amyopathic dermatomyositis; DM, dermatomyositis; PM, polymyositis; Sim, simultaneous onset; OP, organizing pneumonia; NA, not available; FUP, follow-up period from onset; OLB, open lung biopsy; Tx, treatment

assisted thoracoscopic surgery or open lung biopsy was not performed, we made the clinical diagnosis of OP based on the CT findings as well as the TBLB findings, by which we could exclude eosinophilic pneumonia, sarcoidosis, and idiopathic pulmonary fibrosis. In addition, a marked improvement with corticosteroid therapy, following ineffective antibiotic therapy, supported this diagnosis. Although OP is based on histological findings from specimens obtained by surgical lung biopsy, some investigators suggest that transbronchial biopsy may be adequate to establish a working diagnosis of OP.[15] In our case, pathological evidence of myositis was not obtained, and we cannot exclude the possibility of other myopathies such as inclusion body myositis or muscular dystrophy. We definitively diagnosed our case as PM based on a positive anti-jo-1 antibody test, which is exclusively found in PM/DM.[16] Retrospectively, it was confirmed by the disappearance of muscle weakness after corticosteroid therapy, which is consistent with PM.

To our knowledge, 25 cases of OP associated with PM/DM including the present case have been reported (Table 1). According to these published cases, the mean ± SD age of onset is 51.5 ± 13.5 years, and the ratio of affected males/females is 7:18. The PM and DM cases numbered 15 and 10, respectively, including two cases of amyopathic dermatomyositis (ADM). We cannot find any characteristic clinical features of PM/DM with OP, in contrast to PM/DM.[17] The incidence of a positive anti-Jo-1 antibody test in 14 evaluable cases was 57.1% (8/14), which was similar to that of PM/DM with interstitial lung disease (9/14; 64.3%).[16] In only 2 of 16 cases for which chronological assessment was available did PM/DM precede OP by more than 1 month, although it is likely that OP may precede PM/DM or occur simultaneously.

Of the 25 patients, 21 were alive during the follow-up period; the others died. The mean ± SD follow-up period was 36.5 ± 64.1 months for the survivors and 3.5 ± 2.5 months for the deceased. Although the PM patient reported here committed suicide, the remaining three DM patients died of respiratory failure in the following manner: (1) acute respiratory distress syndrome 8 days after open lung biopsy; (2) fever and air leak 4 weeks after open lung biopsy; and (3) respiratory failure 1 month after admission.

Some investigators have indicated that OP associated with collagen vascular diseases has a poorer prognosis than COP.[3,18] In a large series of 74 patients with OP, death was observed in 10 of 37 (27%) patients with COP and in 6 of 10 (60%) patients with OP secondary to collagen vascular disease (CVD-OP) after 10.5 years of follow-up. The incidence of pulmonary-related death was 13.5% (5/37) for COP and 30% (3/10) for CVD-OP.[18] The death rate for the published cases was 0% (0/15) for PM and 30% (3/10) for DM. The prognosis of OP complicated with polymyositis (PM-OP) might be similar to that of COP, whereas that of OP with DM (DM-OP) might be worse than that of COP or PM-OP.

To determine if PM-OP and DM-OP behave differently with regard to treatment, we examined 22 cases in which this question could be evaluated (Fig. 4). Resistance to corticosteroid treatment was observed more frequently in DM-OP patients (6/9) than in PM-OP patients (2/13)

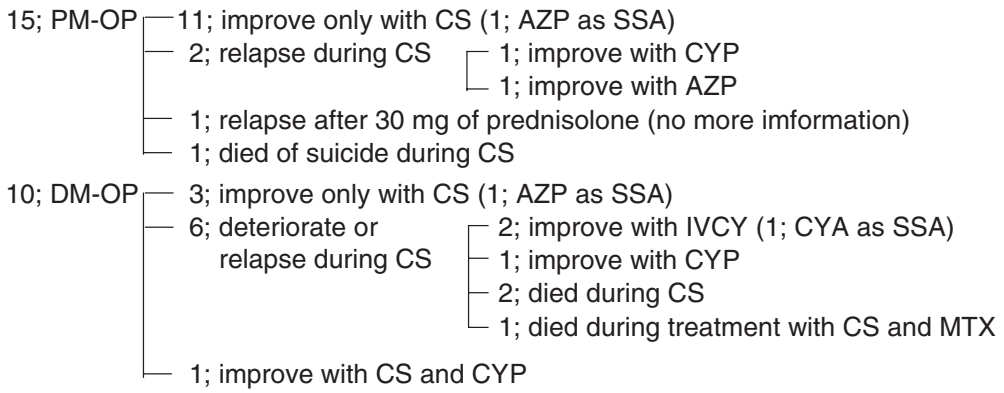

Fig. 4. Treatment and responses in 25 reported cases. *PM-OP*, organizing pneumonia with polymyositis; *DM-OP*, organizing pneumonia with dermatomyositis; *CS*, corticosteroid; *AZP*, azathioprine; *SSA*, steroid-sparing agent; *CYP*, cyclophosphamide; *IVCY*, intravenous cyclophosphamide; *CYA*, cyclosporine A; *MTX*, methotrexate

($P = 0.026$, Fisher's exact test). DM-OP may therefore be more refractory than PM-OP. In five of nine patients who relapsed or whose condition deteriorated during corticosteroid administration, additional immunosuppressants were effective as a second-line treatment, including intravenous cyclophosphamide (two cases), oral cyclophosphamide (two cases), and azathioprine (one case).

It should be noted that there was significant improvement in all five of the patients treated with oral or intravenous cyclophosphamide; in one case, cyclophosphamide was used as a first treatment and in four cases as a second-line treatment. The steroid-sparing agents azathioprine (two cases) and cyclosporine A (one case) were used successfully.

Conclusions

After a review of OP with PM/DM, we conclude that OP may likely precede PM/DM or occur simultaneously, that DM-OP may be refractory compared to PM-OP, and that cyclophosphamide might be beneficial in relapsing cases. Our observations are limited to published cases and should be verified in a prospective examination with a large number of patients with these associations.

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