Nonspecific Interstitial Pneumonia with Poor Prognosis Associated with Amyopathic Dermatomyositis

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Abstract

Amyopathic dermatomyositis (ADM) is a clinical subtype of dermatomyositis, characterized by the lack of motor weakness and the presence of normal muscle enzyme levels. ADM is sometimes accompanied by interstitial pneumonia that shows a rapid progressive course associated with a poor prognosis. We report a 49-year-old patient who presented with nonspecific interstitial pneumonia (NSIP) associated with ADM. The patient failed to respond to prednisolone and immunosuppressive therapy and died. Although idiopathic NSIP is known to have a better prognosis, NSIP in ADM could be a fatal disease. Therefore, we should appropriately treat interstitial pneumonia in ADM even if it is NSIP.
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Key words: amyopathic dermatomyositis, nonspecific interstitial pneumonia, diffuse alveolar damage, interstitial pneumonia

Introduction

Interstitial pneumonia is frequently identified in patients with polymyositis and dermatomyositis (1). Amyopathic dermatomyositis (ADM) is a clinical subtype of dermatomyositis, characterized by the lack of motor weakness and the presence of normal muscle enzyme levels (2). It is well known that some patients with ADM develop rapidly progressive interstitial pneumonia (3). We report a fatal case of rapidly progressive nonspecific interstitial pneumonia (NSIP) in ADM resistant to steroid therapy.

Case Report

A 49-year-old Japanese man with no medical history was referred to our hospital in October 2002 because of exertional dyspnea for a month. He worked as a land surveyor and was a current smoker. Physical examination on admission showed a slight fever, scaly erythema on the dorsum of the hands (Gottron's sign), erythema around the nails and eruption in the back, but no muscle weakness. Auscultation of the chest identified audible fine crackles on the lower aspects of both lungs. Results of laboratory findings on admission (Table 1) revealed that the white blood cell count was 7,700/mm^3 with 66% neutrophils. Erythrocyte sedimentation rate and C-reactive protein were mildly elevated. Serum creatine kinase concentration was normal. Anti-nuclear antibody, rheumatoid factor and anti-Jo-1 antibody were negative. Serum concentrations of KL-6 and SP-A were elevated. Arterial blood gas analysis at room air revealed hypoxemia. Pulmonary function tests revealed diffusion disturbance. Examination of bronchoalveolar lavage fluid showed a high total cell count with relative lymphocytosis and the normal ratio of CD4/CD8. Biopsy specimens from the erythematous skin area on the back showed moderate perivascular infiltration of lymphocytes, edema of the dermis, dilatation of capillaries with increased mucin and stromal deposit of myxoid material, which were compatible with dermatomyositis. Since the patient had no muscle weakness and a normal muscle enzyme level, the diagnosis of the skin lesion was amyopathic dermatomyositis. Chest X-ray showed reticular shadows, which were predominant in the lower lobes, bilaterally (Fig. 1). Chest high resolution computed tomographic (HRCT) scans showed subpleural funicular opacities and consolidation (Fig. 2). Lung biopsy was performed from S^5 and S^8 of the left lung by video-assisted thoracoscopic surgery. Histopathologically, the biopsy specimen showed widening of the alveolar

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Table 1. Laboratory Findings on Admission

<Hematology>				<Arterial blood gases>	
WBC	7,700/μl	BUN	12 mg/dl	Room air/at rest	
Ne	66%	Cr	0.8 mg/dl	pH	7.442
Ly	27%	Na	140 mEq/*l*	$PaCO_2$	35.8 Torr
Mo	6%	K	4.1 mEq/*l*	PaO_2	76.0 Torr
Eo	1%	Cl	104 mEq/*l*	HCO3	24.0 mmol/*l*
Ba	0%			$AaDO_2$	30.9 Torr
RBC	455×10^4/μl	<ESR>	41 mm/h		
Hb	13.5 g/dl			<Pulmonary function tests>	
Hct	40.1%	<Serology>		%VC	84.4%
Plt	27.8×10^4/μl	CRP	1.02 mg/dl	$FEV_{1.0\%}$	75.8%
<Blood chemistry>		IgG	1,380 mg/dl	%DLCO	51.7%
TP	7.3 g/dl	IgA	307 mg/dl		
T-Bil	0.6 mg/dl	IgM	77.2 mg/dl	<BAL cell findings>	
AST	38 IU/*l*	ANA	(–)	Cell recovery	52%
ALT	42 IU/*l*	RF	<10.2	Total cell	9.4×10^5 cells/ml
LDH	247 IU/*l*	anti-Jo-1	(–)	Mϕ	78.7%
ALP	241 IU/*l*	KL-6	1,490 U/ml	Ly	19.6%
γ-GTP	37 IU/*l*	SP-A	51.9 ng/ml	Ne	1.3%
CK	250 IU/*l*	SP-D	75.0 ng/ml	Eo	0.3%
				Ba	0%
				CD4/CD8	1.59

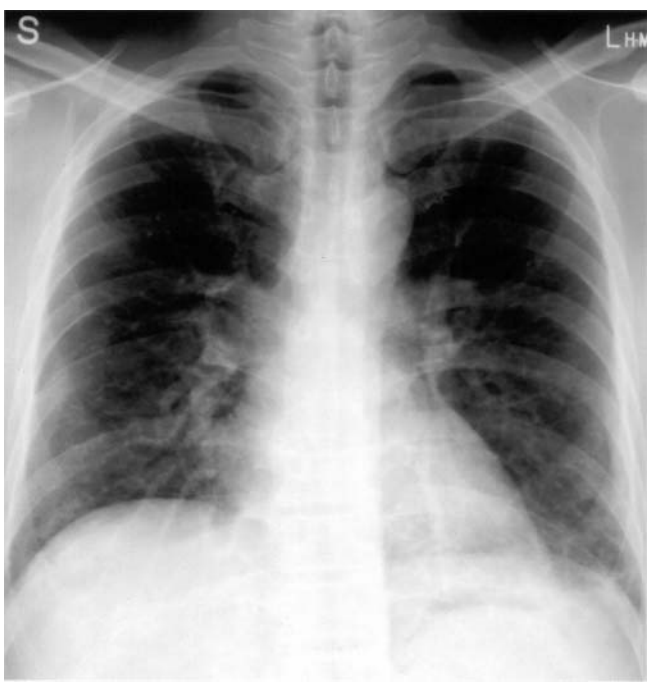

Figure 1. Chest radiograph obtained admission, showing reticular shadows in both lower lung fields.

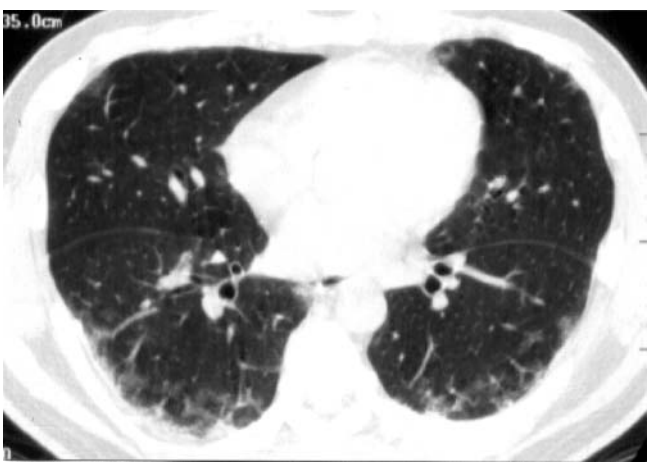

Figure 2. High-resolution CT image of the lungs, showing subpleural funicular opacities and consolidation in both lungs.

septa by loose collagenous fibrosis and active fibrotic lesions without temporal heterogeneity, associated with scattered lymphocytic infiltration. The histopathologic diagnosis was cellular and fibrotic NSIP (Fig. 3).

Although the patient was treated with a high dose of methylprednisolone followed by oral prednisolone, the chest X-ray and clinical condition deteriorated rapidly. Oral cyclosporin A and intravenous cyclophosphamide were added. Furthermore, antibiotics, amphotericin B and ganciclovir were also added in his clinical course because of detection of *Pseudomonas aeruginosa* in sputum culture, *Aspergillus* antigen in the serum, and cytomegalovirus antigenemia in the peripheral blood. However the patient died two months after admission (Fig. 4). An autopsy was performed; which showed diffuse alveolar damage (DAD),

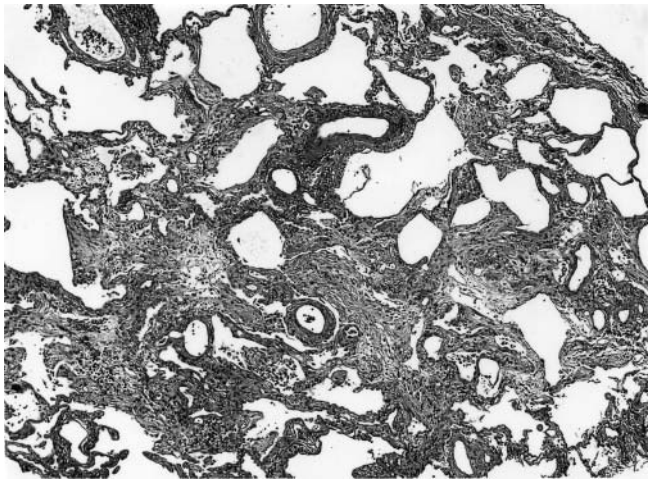

Figure 3. Lung biopsy specimen shows widening of alveolar septa by loose collagenous fibrosis and active fibrotic lesions without temporal heterogeneity, associated with scattered lymphocytic infiltration (HE stain, ×50).

including edema, hyaline membranes and acute interstitial inflammation (Fig. 5). Acute bronchopneumonia was shown in rt. S^8 (not shown). There were no findings of the infection in the lung with *Pneumocystis carinii*, cytomegalovirus and *Aspergillus*. Pathologic changes related to the NSIP were inconspicuous at autopsy. Drug-resistant *Pseudomonas aeruginosa* was detected in blood cultures at postmortem examination.

Discussion

Polymyositis/dermatomyositis are frequently accompanied by interstitial pneumonia, which is known as a significant prognostic factor in patients with polymyositis/dermatomyositis (4). Histopathologic subclassification of interstitial pneumonia has proven to be a better predictor of survival of patients with polymyositis/dermatomyositis (5). The concept of NSIP was first described by Katzenstein and Fiorelli in 1994 (6). NSIP helped to identify a group of interstitial pneumonia with a more favorable prognosis and needed to be distinguished from usual interstitial pneumonia. NSIP also differ from desquamative interstitial pneumonia, DAD, and organizing pneumonia by histopathology (7). NSIP was sub-

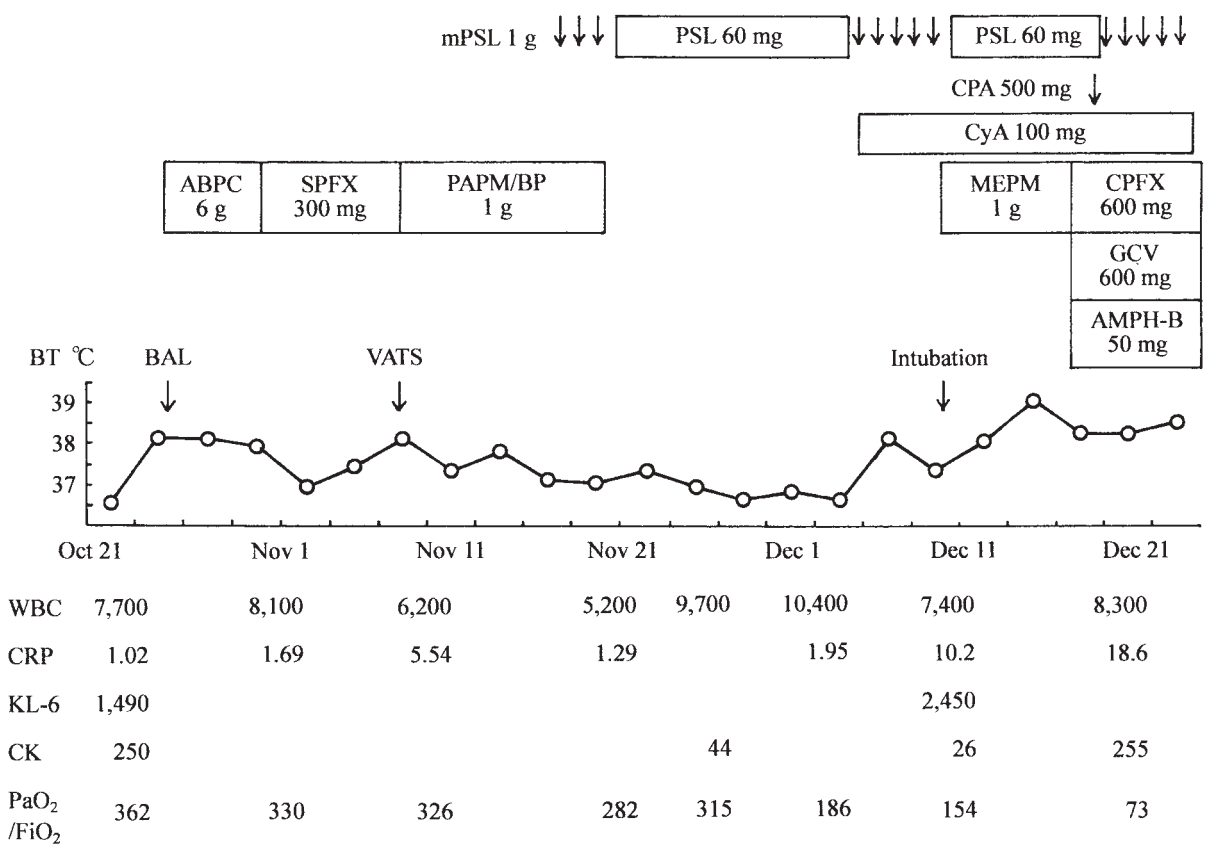

Figure 4. Clinical course.

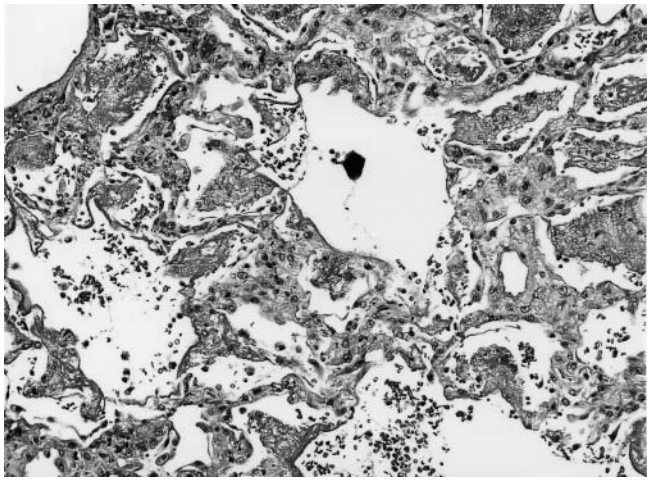

Figure 5. Histopathological examination of the autopsy specimen. Note the presence of hyaline membranes and fibroblastic reaction of interstitum (HE stain, ×130).

divided into cellular and fibrotic patterns, and the cellular pattern was reported to have a favourable response to steroid therapy and a better prognosis than the fibrotic pattern (8, 9). Subsequently studies indicated that NSIP was a major histopathologic finding in interstitial pneumonia associated with polymyositis/dermatomyositis (1, 10). Prognosis of patients with NSIP associated with polymyositis/dermatomyositis is similar to that of patients with idiopathic NSIP and significantly better than that of patients with idiopathic pulmonary fibrosis, which was histopathologically usual interstitial pneumonia, and response to steroid therapy is considered to be satisfactory (10). ADM, which shows lack of motor weakness and presence of normal muscle enzyme level, with dermatomyositis, is associated with fatal interstitial pneumonia (11, 12). In most cases, the accompanying interstitial pneumonia in ADM is histopathologically DAD (13). Idiopathic DAD is regarded as acute interstitial pneumonia in clinical classification, and there is no proven treatment and mortality rates are high (50% or more), most deaths occurring between 1 and 2 months of illness onset (7). Therefore, survival of interstitial pneumonia in ADM is considered to be poor. But several reports showed that there were some cases of steroid-resistant NSIP in ADM (14, 15).

In the present case, histopathological examination of lung biopsy material taken soon after admission showed a NSIP pattern. The patient was resistant to steroid and immunosuppressive therapy, and progressed rapidly to DAD and died. The exact reason for the change of histopathological findings from NSIP to those of DAD is not known at present, but several possible mechanisms could be considered. First, it is possible that acute respiratory distress syndrome developed following acute infection. Infection and sepsis are known to be associated with acute respiratory distress syndrome and the most common histopathological pattern is DAD (16). In support of this argument, drug-resistant *Pseudomonas aeruginosa* was detected in sputum and blood cultures in our the present case. Second, acute exacerbation of interstitial pneumonia caused by surgical lung biopsy could have occurred. Although there are several reports that surgical lung biopsy causes acute exacerbation of interstitial pneumonia (17), the present case did not show the rapid deterioration for one week after surgical lung biopsy. Therefore, it is unlikely that lung biopsy caused DAD. Third, the natural course of interstitial pneumonia with ADM consists of NSIP at the beginning and development of diffuse alveolar damage at the end. Toyoshima et al reported that the surgical lung biopsy specimens of a patient in ADM showed homogeneous cell infiltrations in alveolar septa and regional alveolar damage (13). They speculated that this showed the process of the progression NSIP to DAD. There were also some cases of steroid-resistant NSIP in ADM (14, 15). Although we cannot conclude this problem, based on their reports, we tend to consider the third mechanism as the most likely cause of the clinical course in our case.

Conclusion

We reported a patient with rapidly progressive NSIP in ADM, who showed resistance to steroid therapy and subsequently died. NSIP with dermatomyositis is thought to be associated with a good prognosis, but in some cases, NSIP with ADM subsequently seems to change to the more fatal condition of DAD. Therefore, we should give care to interstitial pneumonia with ADM even if it is NSIP.

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