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Interstitial lung diseases associated with amyopathic dermatomyositis

Takafumi Suda, Tomoyuki Fujisawa, Noriyuki Enomoto, Yutaro Nakamura, Naoki Inui, Tateaki Naito, Dai Hashimoto, Jun Sato, Mikio Toyoshima, Hideo Hashizume*, Kingo Chida,

Second Division, Department of Internal Medicine, *Dermatology, Hamamatsu University School of Medicine, 1-20-1 Handayama, Hamamatsu, 431-3192, Japan

Corresponding

Author Name: Takafumi Suda

Full Address: 1-20-1 Handayama, Hamamatsu, 431-3192, Japan

Telephone: +81(53)435-2263

Fax: +81(53)435-2354

E-mail: suda@hama-med.ac.jp

Running Head

Lung disease of amyopathic dermatomyositis

ABSTRACT

The aim of the present study was to clarify the clinical characteristics and prognosis of patients with interstitial lung disease associated with amyopathic dermatomyositis (ILD-ADM)

The study subjects consisted of 14 consecutive patients with ILD-ADM. They were classified into two categories, acute/subacute and chronic forms, according to the clinical presentation of ILD. The clinical features, responsiveness to therapy, and prognosis between the two forms were compared.

Nine ILD-ADM patients were categorized as the acute/subacute form, and five as the chronic form. PaO_2 was significantly lower in the acute/subacute ILD than chronic ILD. On high-resolution computed tomography, ground-glass opacities were frequently found in the two forms, but consolidation was more common in acute/subacute ILD than chronic ILD. Bronchoalveolar lavage analysis showed higher numbers of total cells and lymphocytes in acute/subacute ILD than chronic ILD. Histologically, the most common finding was nonspecific interstitial pneumonia in the two forms, while diffuse alveolar damage was found only in acute/subacute ILD. Acute/subacute ILD was generally resistant to therapy, while chronic ILD responded well. Notably, the mortality of acute/subacute ILD was much higher than that of chronic ILD (67% vs. 0%, respectively).

In conclusion, ILD-ADM includes two different forms, acute/subacute and chronic forms, with distinct prognoses.

Key Words

interstitial lung disease, amyopathic dermatomyositis

INTRODUCTION

Amyopathic dermatomyositis (ADM) is recognized as a distinct subgroup of dermatomyositis (DM) with the typical skin rash of classic DM, but without muscle involvement [1-6]. Several studies have demonstrated that rapidly progressive ILD with a poor prognosis occurs in patients with ADM [7-12]. These patients were often resistant to intensive therapy, such as high-dose corticosteroids plus immunosuppressive agents, resulting in fatal respiratory failure. In contrast, a recent report from Europe emphasized a favorable prognosis of ILD associated with ADM (ILD-ADM) among ILD associated with ADM, DM, and polymyositis (PM) [13]. Because ILD-ADM is a rare condition, its characteristics have not been fully clarified. In the present study, therefore, we examined our series of patients with ILD-ADM and attempted to determine its clinical features and prognosis.

METHODS

Patient selection

The study subjects consisted of 14 consecutive patients (one male, 13 females) diagnosed with ILD-ADM. The diagnosis of ADM was confirmed based on modified Euwer's criteria: 1) Characteristic dermatologic manifestations of classic DM, including a heliotrope rash and Gottoron's papules, 2) No muscle weakness, 3) No increases in serum muscle enzymes during the observation period. All the subjects were seen as in-patients or out-patients at our institutions between 1985 and 2005.

ILD Presentations

ILD was diagnosed based on the presence of radiologic abnormalities with respiratory symptoms. According to the clinical presentation, the patients were classified into two

categories. (i) The acute/subacute form was defined as a rapidly progressive ILD showing deterioration within three months. According to the International Consensus Statement of idiopathic pulmonary fibrosis of the American Thoracic Society with modification [14], the deterioration was defined by 2 or more of the followings; (1) Symptomatic exacerbation (dyspnea on exertion): (2) an increase in parenchymal abnormality on HRCT scan; (3) physiological change defined by one of the followings: >10% decrease in vital capacity or >10 Torr decrease in PaO_2. (ii) The chronic form was defined as a slowly progressive ILD that gradually deteriorated over more than three months. Regarding the temporal relationship between the onset of ADM and that of ILD, the interval between them within three months was defined as concomitant onset.

Data collection

Clinical data, including history, treatment, and laboratory findings, were obtained from patients' medical records at the first encounter, which eventually led to a diagnosis of ILD. Signs and symptoms were also recorded. The following pulmonary function test parameters were assessed: vital capacity (VC), and forced expiratory volume in one second (FEV1.0).

High-resolution computed tomography

High-resolution computed tomography (HRCT) examinations of the lung were performed on 1.0- or 1.5-mm thick sections to evaluate radiographic abnormalities. The HRCT images were reviewed for the presence of each of the following signs: consolidation, ground-glass opacities, traction bronchiectasis, irregular linear opacities, bronchovascular bundle thickening, honeycombing, and pleural effusion.

Bronchoalveolar lavage

Bronchoalveolar lavage (BAL) was performed as described previously [15]. Briefly, a fiberotic bronchoscope was passed transorally and wedged in a segmental or subsegmental bronchus of the middle lobe. Three 50-ml aliquots of sterile 0.9% saline were instilled and the returns gently aspirated through the side channel of the bronchoscope. BAL fluid (BALF) was centrifuged at 800 g for 10 min to obtain the cellular components. The total cell count was determined using a hemocytometer and a differential cell count was taken on Giemsa-stained cytocentrifuged preparations. To characterize the phenotype of the lymphocytes in the BAL fluid, flow cytometric analysis was performed in a flow cytometer (EPICS Profile, Coulter Electronics, Hialeath, France) using mAb OKT3 (anti-CD3; Coulter Electronics), OKT4 (anti-CD4; Coulter Electronics), and OKT8 (anti-CD8, Coulter Electronics).

Lung biopsy

We did not performed surgical lung biopsy in patients with severe respiratory failure. Besides those patients, 6 patients (3 acute/subacute ILD, 3 chronic ILD) underwent surgical lung biopsy, and two patients did autopsy. Lung specimens were obtained from at least two lobes. The specimens were categorized using the following abnormalities consistent with ILD: usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), bronchiolitis obliterans organizing pneumonia (BOOP), and diffuse alveolar damage (DAD), according to the current classification of interstitial pneumonias [16].

Treatment and outcome

During the course of treatment, we assessed respiratory symptoms, chest x-ray/CT findings, VC, and PaO_2. According to the International Consensus Statement of idiopathic pulmonary fibrosis by the American Thoracic Society with a slight modification [16], "improvement", or "favorable (or good) response" was defined by two or more of the following: 1) A decrease in symptoms (dyspnea on exertion), 2) Reduction in parenchymal abnormalities on chest

radiographs or HRCT scans, 3) Physiological improvement defined as one of the following; > 10% increase in VC or total lung capacity, > 10 Torr increase in PaO_2.

Statistical analysis

For two group comparisons involving binary data, we used either the chi-square test or Fisher's exact test, depending on the sample size. Comparisons involving continuous data were made using the Mann-Whitney U test. The cumulative survival rate was calculated using the Kaplan-Meier test. A p value < 0.05 was considered significant. All data are expressed as mean ± SD.

RESULT

Clinical features and laboratory findings

Clinical characteristics of patients with acute/subacute ILD-ADM and chronic ILD-ADM are shown in Table 1. Nine patients (9 females) and 5 patients (one male and 4 females,) were diagnosed as having acute/subacute ILD-ADM and chronic ILD-ADM, respectively. None of our patients had been given any drugs that might have caused ILD. Age and sex did not differ between the two groups. The observation period and duration of respiratory symptoms were shorter in acute/subacute ILD-ADM than chronic ILD-ADM. In most patients (89%) with acute/subacute ILD-ADM, ILD onset was concomitant with a diagnosis of ADM. In contrast, 60% of patients with chronic ILD-ADM developed ILD after an initial diagnosis of ADM (range 6-24 months). There were no patients in whom ILD onset preceded the initial diagnosis of ADM. None of our patients had any malignancies. Dyspnea on effort, fever, and arthralgia were more common in acute/subacute ILD-ADM than chronic ILD-ADM.

Chest auscultation revealed fine crackles in most patients with acute/subacute ILD-ADM as well as in chronic ILD-ADM

Laboratory findings are presented in Table 2. Serum levels of KL-6, a marker of interstitial pneumonia, were elevated in the two forms, but no difference was found between them. Only one patient with chronic ILD-ADM had the anti Jo-1 antibody. PaO_2 was significantly lower in acute/subacute ILD-ADM than chronic ILD-ADM. In addition, %VC tended to be lower in acute/subacute ILD-ADM than chronic ILD-ADM

HRCT findings

HRCT images of the lung were available for 13 patients (8 acute/subacute ILD, 5 chronic ILD) and the findings are summarized in Table 3. Representative HRCT scans are shown in Figure 1. All the patients showed ground-glass opacities. Consolidation was more common in acute/subacute ILD-ADM than chronic ILD-ADM, while the frequency of traction bronchiectasis was higher than in chronic ILD-ADM than acute/subacute ILD-ADM. In acute/subacute ILD-ADM, consolidation was a main finding in patients having this abnormality. Ground-glass opacity was a main finding in those showing no consolidation. No patients had ground-glass opacities and/or consolidation superimposing on honey combing. In terms of histologic patterns, consolidation was more frequently seen in DAD than in NSIP (100% vs. 60%, respectively). Honeycombing was found in only one patient having UIP

BAL analysis

BAL was performed in 7 patients (4 acute/subacute ILD, 3 chronic ILD). Patients with acute/subacute ILD-ADM had a significantly higher number of total cell counts than those with chronic ILD-ADM (Table 3). Higher percentages of lymphocytes and neutrophils were

found in acute/subacute ILD-ADM than chronic ILD-ADM. The ratio of CD4+/CD8+ lymphocytes was higher in acute/subacute ILD-ADM than chronic ILD-ADM, but the difference was not statistically significant.

Pulmonary pathology

Specimens obtained from surgical lung biopsy (3 acute/subacute ILD, 3 chronic ILD) and autopsy (2 acute/subacute ILD) were reviewed. The most common histologic pattern was NSIP (~~0 cellular NSIP and~~ 5 fibrotic NSIP) in ILD-ADM (Table 3). DAD was seen only in acute/subacute ILD-ADM at autopsy, but not in chronic ILD-ADM. UIP was found in one patient with chronic ILD-ADM.

Treatment

All patients, except one patient with chronic ILD-ADM, received corticosteroids in the form of oral prednisolone (0.75-1.0 mg/kg/day), but patients with respiratory failure were treated with intravenous methylprednisolone pulse therapy (1 g/day for 3 days) (Table 4). Immunosuppressive agents such as cyclosporine (2-3 mg/day), cyclophosphamide (daily oral treatment; 1-2 mg/kg/day or monthly intravenous treatment; 500 – 700 mg/month), azathioprine (1-2 mg/kg/day), were added to corticosteroid therapy in 8 patients in whom there was not a favorable response to corticosteroids. Four patients received immunosuppressive agents initially, together with corticosteroids. Intravenous immunogloblins were administered to one patient with acute/subacute ILD-ADM that did not respond to corticosteroids plus immunosuppressive agents.

In acute/subacute ILD-ADM, corticosteroids alone did not achieve a significant improvement. Cyclophosphamide had no therapeutic effect in any of the 7 patients receiving it, and it was replaced with cyclosporine in 5 of them, although 4 subsequently died of

respiratory failure. Cyclosporine was given to 8 patients, but 5 of them died. Several recent studies reported that early administration of cyclosporine might improve the prognosis of acute ILD-ADM [17 11]. Thus, we compared the duration between the start of corticosteroids and addition of cyclosporine, and the duration between onset of respiratory symptoms and the start of cyclosporine among survivors and nonsurvivors. However, no significant differences were found between survivors and nonsurviviors (the duration between the start of corticosteroids and addition of cyclosporine, 26.7 ± 29.0 days vs. 19.0 ± 20.1 days; the duration between onset of respiratory symptoms and the start of cyclosporine, 66.7 ± 55.3 days vs. 42.5 ± 47.6, respectively). Three patients with acute/subacute ILD-ADM were treated with high dose corticosteroids plus cyclosporine very early in the course of ILD, but 2 of them died of respiratory failure. Intravenous immunoglobulin therapy was effective in one patient that showed resistance to corticosteroids plus cyclosporine. In chronic ILD-ADM, corticosteroids alone were given to one patient, who showed improvement. Cyclosporine was given to 3 patients. Two of them received cyclosporine plus corticosteroids initially with a favorable response, while the other one was given cyclosporine as a corticosteroid-sparing agent after the start of corticosteroid therapy. The duration of therapy was longer in chronic ILD-ADM than acute/subacute ILD-ADM.

Mortality and Survival

During the observation period, 6 (67%) of patients with acute/subacute ILD-ADM died (Table 4). Of these, all patients died from respiratory failure due to progression of ILD. In contrast, no patients with chronic ILD-ADM died. A comparison of survival curves in the two groups is shown in Figure 2. Patients with acute/subacute ILD-ADM had a much lower survival rate than those with chronic ILD-ADM (5-year survival, 35% vs. 100%, respectively). Interestingly, 4 of 5 deaths of patients with acute/subacute ILD-ADM

occurred within 2 months, suggesting that the failure of the initial treatment was associated with early death in those patients.

DISCUSSION

In the present study, we retrospectively reviewed consecutive cases of ILD-ADM and attempted to elucidate its clinical characteristics and prognosis. We found that ILD-ADM includes two different forms, acute/subacute and chronic forms, with distinct prognoses. Acute/subacute ILD-ADM, which rapidly progressed with a poor response to therapy, had high mortality. In contrast, chronic ILD-ADM responded well to therapy with a favorable prognosis.

Because ADM is a rare disease, previous studies of ILD-ADM included only one, or a few patients [7-13]. The present study investigated the highest number of patients with ILD-ADM so far. To date, contradictory data have been reported in the prognosis of ILD-ADM. Previous studies mainly from Asia have demonstrated that ILD-ADM generally runs an aggressive course, leading to fatal respiratory failure [7-12]. In contrast, Cottin et al. recently described a benign form of ILD-ADM [13]. They reported 3 patients with chronic ILD-ADM, and corticosteroids alone achieved a favorable response in 2 of them. The other one responded well to corticosteroids plus immunosuppressive agents. None of these 3 patients died during the observation period, leading to the conclusion that ILD-ADM has a good prognosis. In the present study, we demonstrated that ILD-ADM consisted of at least two different forms with distinct outcomes. Acute/subacute ILD, which constituted about two thirds of our ILD-ADM patients, showed a rapid progression that was poorly responsive to therapy, resulting in severe respiratory failure. On the other hand, chronic ILD-ADM showed a mild course and responded well to therapy. Notably, the outcome was completely different between these two forms. The mortality was much higher in patients with

acute/subacute ILD-ADM (67%) than those with chronic ILD-ADM (0%). In acute/subacute ILD-ADM, no patients had chronic respiratory symptoms before ILD diagnosis in our institution. Additionally, in patients developing acute/subacute ILD after ADM diagnosis, no abnormality was found on HRCT at the initial ADM diagnosis. These data suggest that chronic ILD is unlikely to preexist in our patients with acute/subacute ILD. Taken together, these results may account for the contradictory data previously reported in the prognosis of ILD-ADM. Namely, the fatal progressive ILD-ADM described is likely to correspond to the acute/subacute ILD-ADM in the present study, while the ILD-ADM with a favorable prognosis reported by Cottin et al. may be equivalent to chronic ILD-ADM. Although ethnic differences may affect the clinical manifestations of ILD-ADM, it should be noted that ILD-ADM has these two different forms.

In a comparison of the clinical characteristics between acute/subacute ILD-ADM and chronic ILD-ADM, ILD onset was concomitant with ADM in all the patients with acute/subacute ILD-ADM except one, while more than half of patients with chronic ILD-ADM developed ILD after an ADM diagnosis. In addition, extrapulmonary symptoms, including fever and arthralgia, were more common in acute/subacute ILD-ADM than chronic ILD-ADM. PaO_2 and %VC were significantly lower in acute/subacute ILD-ADM than chronic ILD-ADM. These data suggest that patients with acute/subacute ILD-ADM, which commonly occur simultaneously with ADM onset, have more severe ILD with systemic symptoms at the initial examination than those with chronic ILD. Regarding anti-Jo1 antibody, only one patient with chronic ILD-ADM had this antibody among our ILD-ADM series. To date, several studies have reported a low incidence of anti-Jo1 antibody in ILD-ADM patients [11-13,17-19]. Our results were consistent with those studies.

There have been few reports of the HRCT findings of ILD-ADM [7,13,20]. According to these reports, ground-glass opacities, consolidation, and irregular linear opacities were often

seen in ILD-ADM. Consistently, our patients with ILD-ADM had a high frequency of these findings on HRCT. Notably, ground-glass opacities were found in all the patients. Between the two forms, consolidation was more common in acute/subacute ILD-ADM, while traction bronchiectasis was more frequently found in chronic ILD-ADM. Honeycombing was seen in only one patient with chronic ILD-ADM, who was histologically proven to have UIP. Sixty percentages of ILD-ADM patients with a histologic finding of NSIP had consolidation. Originally, consolidation was reported not to be a common finding in idiopathic NSIP [21,22]. In ILD-PM/DM, however, much higher prevalence of consolidation was demonstrated in NSIP [23,24]. A recent study showed that consolidation was found in 42.9% of NSIP patients associated with PM/DM [23]. In addition, our previous study indicated that 86% of NSIP patients associated with PM/DM showed consolidation [24]. These data suggest that consolidation is more common in NSIP associated with PM/DM/ADM than in idiopathic NSIP.

To date, little is known about the BAL findings of ILD-ADM. Two reports from Japan demonstrated an increase of BALF lymphocytes and neutrophils in acute/subacute ILD-ADM [11,12]. The present study showed that the BAL findings differed between the two forms. Patients with acute/subacute ILD-ADM had an increase in percentages of BALF lymphocytes, as well as neutrophils, while those with chronic ILD-ADM showed only a moderate increase in percentages of BALF neutrophils. In addition, the total cell counts were significantly higher in acute/subacute ILD-ADM than chronic ILD-ADM. Interestingly, the CD4/CD8 ratio of BALF T lymphocytes tended to be higher in acute/subacute ILD-ADM than chronic ILD-ADM. Inconsistent with our data, Yokoyama et al. recently reported a case of fatal acute ILD-ADM with a low CD4/CD8 ratio (0.2) of BALF T lymphocytes [12]. However, none of our patients with acute/subacute ILD-ADM revealed a < 1.0 CD4/CD8

ratio. The reason for this discrepancy is unknown. Further studies including larger numbers of patients will elucidate this point.

Several studies on the histopathology of ILD-PM/DM have demonstrated various histologic patterns, such as UIP, NSIP, BOOP, and DAD, and emphasized their prognostic significance [13,25-27]. However, a limited number of data are available on the histopathology of ILD-ADM. Lee et al. recently reported 3 cases of acute ILD-ADM with a histologic finding of DAD, which was associated with poor outcome [7]. In Cottin's study, 3 patients with chronic ILD-ADM showed NSIP with a good prognosis [13]. Based on these observations, acute/subacute ILD-ADM and chronic ILD-ADM might histologically correspond to DAD and NSIP, respectively. In the present study, however, NSIP was found in 3 of 5 patients with acute/subacute ILD-ADM who underwent biopsies. Of these three patents with NSIP, two responded to therapy and survived, while the other one died despite intensive therapy. The remaining two with acute/subacute ILD-ADM had DAD, and all died within 2 months. More recently, Miyazaki et al. reported 3 patients with rapidly progressive ILD-ADM [11]. Of these, NSIP was found in 2, and DAD was seen in one. In addition, Sakamoto et al. described a case of fatal ILD-ADM with a histologic finding of NSIP [10]. Taking together our data with the recent studies, the histologic patterns of acute/subaute ILD-ADM include NSIP in addition to DAD. On the other hand, our patients with chronic ILD-ADM showed UIP and NSIP, but not DAD. Possibly, the favorable prognosis of chronic ILD-ADM was partially associated with the fact that no DAD was found in those patients.

The optimal treatment for patients with ILD-ADM has not been established because of its rarity. Recent studies of rapidly progressive ILD-ADM have highlighted the effectiveness of cyclosporine combined with corticosteroids in the early course of ILD [11,17]. Among our acute/subacute ILD-ADM series, 8 of the 9 patients received cyclosporine, but 5 of them died

of respiratory failure with a poor response to the therapy. Between survivors and nonsurvivors, no difference was found in the duration between the start of corticosteroids and addition of cyclosporine, or the duration between onset of respiratory symptoms and the start of cyclosporine. In addition, two acute/subacute ILD-ADM patients receiving corticosteroids plus cyclosporine together during the very early course of ILD failed to respond. Collectively, these results suggest that early administration of cyclosporine may be beneficial in certain patients with acute/subacute ILD-ADM, but not in all. Interestingly, intravenous immunoglobulin therapy was effective in one patient with acute/subacute ILD that was resistant to corticosteroids plus cyclosporine. More recently, Tsukamoto et al. reported the efficacy of autologous peripheral blood stem cell transplantation (PBSCT) in a patient with ILD-ADM that was unresponsive to corticosteroids plus cyclosporine [28]. To date, however, there is no concrete evidence of treatment for ILD-ADM. Thus, future investigations will be needed to elucidate an effective therapy~~, such as intravenous immunoglobulin and PBSCT,~~ in acute/subacute ILD-ADM. In chronic ILD-ADM, all four of our patients had good outcomes. Interestingly, corticosteroids alone achieved a favorable response in one patient. Three patients received cyclosporine plus corticosteroids, which proved to be effective. However, it remains to be determined whether immunosuppressive therapy is actually required for chronic ILD-ADM patients.

Recently, we reported the characteristics of patients with ILD-PM/DM, and highlighted the differences in clinical features and prognosis between ILD-PM and ILD-DM [24]. ILD-DM was shown to be more refractory to therapy, resulting in poorer prognosis than ILD-PM. Compared to ILD-DM/PM, the survival curve of overall ILD-ADM patients tended to be worse than that of ILD-DM patients without a significant deference, and significantly worse than that of ILD-PM patients (data not shown). In terms of clinical presentation, acute/subacute forms were found in 35% and 47% of ILD-PM and ILD-DM patients,

respectively. Thus, the proportion of acute/subacute form was highest in ILD-ADM patients (64%). Interestingly, none of our patients developed ILD before ADM onset, regardless of acute/subacute or chronic form. To date, only two cases have been reported in which ILD onset preceded ADM [13], while in all of other cases reported ILD onset was concomitant with ADM or followed ADM [7-12]. In ILD-PM/DM, however, 20 – 30% of patients have been reported to develop ILD before PM/DM diagnosis [27,29]. Indeed, our previous study on ILD-DM/PM demonstrated that ILD onset preceded diagnosis of PM/DM in 19% of ILD-PM patients and in 33% of ILD-DM patients [24]. Thus, a low proportion of patients that ILD onset precedes collagen vascular diseases may be one of the clinical characteristics of ILD-ADM. Collectively, these data suggest that ILD-ADM, which is more likely to take acute/subacute course and not to precede ADM, has the poorest prognosis among ILD associated with DM, PM, and ADM.

In conclusion, the present study demonstrated two different forms of ILD-ADM, acute/subacute and chronic forms, which were closely related to outcome. To appropriately care for patients with ILD-ADM, these two conditions should be taken into account. Further studies will provide information regarding the optimal treatment for patients with acute/subacute ILD-ADM and chronic ILD-ADM.

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Table 1. Comparison of clinical characteristics between acute/subacute and chronic ILD associated with ADM

	Acute/subacute ILD-ADM N=9	Chronic ILD-ADM N=5
Age, yrs	55.1± 10.4	53.8 ± 8.2
Gender, M/F	0 / 9	1 / 4
Observation period, mo	18.8 ± 30.0	43.3 ± 40.4
Duration of respiratory symptoms, mo	1.2 ± 0.7*	9.0 ± 2.6
Time of ILD diagnosis		
Before ADM diagnosis, %	0	0
Concomitant with ADM diagnosis, %	89	40
After ADM diagnosis, %	11	60
Malignancy, %	0	5
Dyspnea on effort, %	89	20
Cough, %	78	60
Fever, %	78*	0
Arthralgia, %	56	20
Raynaud's phenomenon, %	0	20
Fine crackles, %	89	100

*: $p < 0.05$

Table 2. Comparison of laboratory findings between acute/subacute and chronic ILD associated with ADM

	Acute/subacute ILD-ADM N=9	Chronic ILD-ADM N=5
WBC. mm^3	6436 ± 2092	7286 ± 2090
ESR, mm/h	45 ± 28	39 ± 9
LDH, IU/l	450 ± 211	300 ± 84
CPK, IU/l	73 ± 44	96 ± 48
Aldolase, IU/l	6.1 ± 3.1	5.2 ± 4.0
KL-6, U/ml	851 ± 543	1035 ± 801
IgG, mg/dl	1611± 390	1755 ± 480
Positive ANA, %	38	60
Positive Jo-1, %	0	20
PaO_2, Torr	66 ± 6*	83 ± 12
VC, %	65 ± 16	81 ± 17
FEV1.0, %	85 ± 12	82 ± 8

WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CPK, creatine phosphakinase; LDH, lactate dehydrogenase; ANA, anitinuclear antibody; VC, vital capacity; FEV1.0, forced expiratory volume in one second

*: $p < 0.05$

Table 3. Comparison of HRCT, BAL, and histologic findings between acute/subacute and chronic ILD associated with ADM

	Acute/subacute ADM-ILD	Chronic ADM-ILD
HRCT findings	N=8	N=5
Consolidation,%	75	40
Ground glass opacities, %	100	100
Traction bronchiectasis, %	38	80
Irregular linear opacities, %	50	60
Bronchovascular bundle Thickening, %	20	40
Honeycombing, %	0	20
Pleural effusion, %	0	0
BAL findings	N=4	N=3
Total cell, $X10^5$ml	3.8 ± 1.1*	1.6 ± 1.4
Macrophages, %	76.4 ± 18.1	90.7 ± 9.5
Lymphocytes, %	12.5 ± 3.8*	3.3 ± 0.8
Neutrophils, %	10.4 ± 14.3	5.0 ± 8.5
Eosinophils, %	0.2 ± 0.2	0.9 ± 0.5
CD4/CD8 ratio	3.8 ± 2.7	0.7 ± 0.5
Histologic findings	N=5	N=3
UIP	0	1
NSIP	3	2
DAD	2	0

UIP, usual interstitial pneumonia; NSIP, nonspecific interstitial pneumonia; DAD, diffuse alveolar damage; *: $p < 0.05$

Table 4. Comparison of treatment and outcome between acute/subacute and chronic ILD associated with ADM

	Acute/subacute ADM-ILD N=9, n (%)	Chronic ADM-ILD N=5, n (%)
Treatment		
Corticosteroids alone	0 (0)	1 (20)
Corticosteroids + immunosuppressive agents	9 (100)	3 (60)
Cyclophosphamide	7	0
Cyclosporine	8	3
Azathioprine	1	0
Intravenous immunoglobulins	1	0
Duration of therapy, mo	20 ± 31	46 ± 59
Death due to respiratory failure	6 (67)	0 (0)

Figure legends

Figure 1. HRCT scans of patients with acute/subacute and chronic ILD-ADM. A. HRCT scan of acute/subacute ILD-ADM shows consolidation, ground-glass opacities, and irregular peribronchovascular thickening. B. HRCT scan of chronic ILD-ADM shows the areas of irregular linear and ground glass opacities predominantly in the subpleural region.

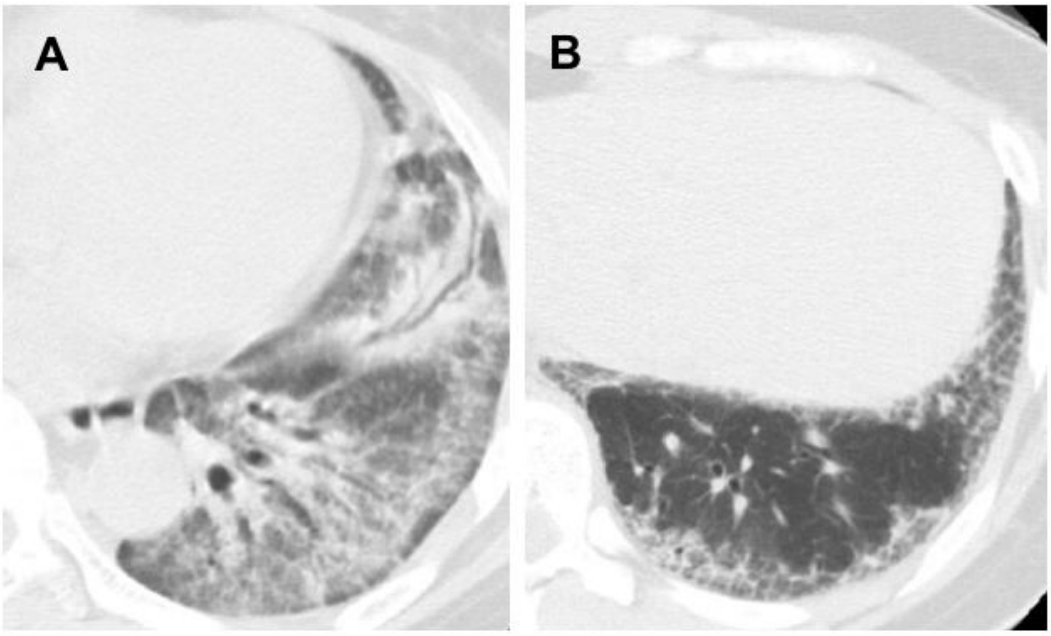
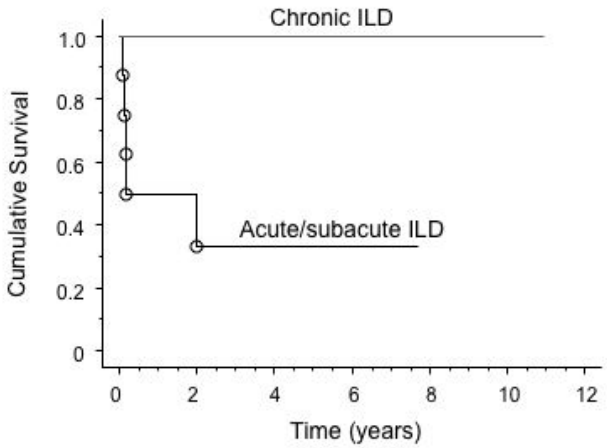


Figure 2. Survival curves of acute/subacute and chronic ILD associated with ADM


Chronic ILD
Acute/subacute ILD
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0
0
2
4
6
8
10
12
Time (years)