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Pulmonary manifestations of anti-ARS antibody positive interstitial pneumonia — With or without PM/DM

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KEYWORDS
Interstital lung disease;
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Summary
Background: Autoantibodies against aminoacyl-tRNA synthetases (ARS) have been found to be highly specific for polymyositis and dermatomyositis (PM/DM) and to correlate strongly with complicating interstitial pneumonia (IP). The aim of the present study was to compare the clinical presentations of anti-ARS antibody-positive IP patients with or without manifestations of PM/DM.
Methods: We retrospectively examined 36 IP patients with anti-ARS antibodies. Sixteen patients presented with and 20 without the features of PM/DM. They were divided into PM/DM-IP and idiopathic-IP (IIP) groups. Clinical symptoms, findings on physical examination, laboratory data, pulmonary function, computed tomography (CT), and bronchoalveolar lavage fluid (BALF) cell counts were compared.
Results: Skin findings, myalgia, and elevation of serum creatinine kinase were found in the PM/DM-IP group. Features common to both groups included: volume loss in lower bilateral lobes; ground-glass opacities, reticular shadows and traction bronchiectasis on chest CT; high percentage of lymphocytes (IIP: 44.0% ± 21.0% (mean ± SD), PM/DM-IP: 50.5% ± 23.5%) and low CD4/8 ratios (IIP: 0.36 ± 0.34, PM/DM-IP: 0.44 ± 0.42) in BALF; decreased pulmonary function, including percentage of predicted vital capacity (VC) (IIP: 80.1% ± 15.4%, PM/DM-IP: 73.6% ± 16.4%), residual volume (RV) (IIP: 70.7% ± 21.7%, PM/DM-IP: 71.5% ± 17.1%), total lung

Abbreviations: anti-ARS antibodies, autoantibodies against aminoacyl-tRNA synthetases; PM/DM, polymyositis and dermatomyositis; IIP, idiopathic interstitial pneumonia; fNSIP, fibrotic nonspecific interstitial pneumonia.

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capacity (TLC) (IIP: 73.4% ± 13.6%, PM/DM-IP: 71.6% ± 13.0%), and diffusing capacity DLco (IIP: 57.5% ± 26.7%, PM/DM-IP: 46.4% ± 10.3%). Both groups achieved good responses to initial corticosteroid or immunosuppressant therapy.
Conclusion: Patients with anti-ARS antibody-positive IP have common pulmonary manifestations regardless of the presence of PM/DM.

Background

Autoantibodies against aminoacyl-tRNA synthetases (ARS), a group of cytoplasmic enzymes, have been found to be highly specific for polymyositis and dermatomyositis (PM/DM), and to strongly correlate with complicating interstitial pneumonia (IP). Eight anti-ARS autoantibodies have been identified. These include anti-Jo-1, anti-PL-7, anti-PL-12, anti-OJ, anti-EJ, anti-KS, anti-Zo, and anti-Ha.[1–3]

Patients with anti-ARS antibodies often present with the following features: myositis, IP, inflammatory arthritis, Raynaud's phenomenon, mechanic's hands, and fever. These features and symptoms have been termed the "antisynthetase syndrome". However, some cases of IP with anti-ARS-antibody have no symptoms of myositis. Yoshimizu et al. have reported that there are common clinical and pathological findings and computed tomography (CT) findings in patients with interstitial lung disease and anti-ARS antibodies.[4] We conducted a retrospective, observational study to compare the clinical features of anti-ARS antibody-positive patients with either idiopathic IP (IIP) or with PM/DM-associated IP (PM/DM-IP).

Patients and methods

We identified 36 anti-ARS-antibody-positive patients with IP at Kanazawa University Hospital and our related facilities from January 2005 to December 2010. The patients in the present study are all Japanese. Anti-ARS antibody analysis was performed at the Department of Dermatology in Kanazawa University Hospital by immunoprecipitation using ^{35}S-methionine-labeled extracts of K562 cells.

The patients were divided into 2 groups, those with and without the features of PM/DM. There were 16 patients with the features of PM/DM, and their IP was designated as PM/DM-IP. The remaining 20 patients did not have any features of collagen vascular diseases, and their IP was designated as IIP. There were 14 women and 6 men in the IIP group (mean ± SD age at onset was 59.1 ± 13.0 years; range, 21–72 years), and 12 women and 4 men in the PM/DM-IP group (mean ± SD age at onset was 58.5 ± 7.9 years; range, 43–69 years). One woman in the PM/DM-IP group also had systemic scleroderma. We extracted and evaluated the following from the patients' medical records: clinical symptoms, physical examination, laboratory data, pulmonary function tests, CT findings, and bronchoalveolar lavage fluid (BALF) cell counts. Two pulmonologist (at least) and one radiologist examined the chest CT scan. Bronchoalveolar lavage was performed with 50 ml of saline for 3 times at the same site where bronchoscope was wedged. We analyzed cell differentiation of the third fraction by counting at least 300 cells on a smear prepared with a cytospin and Wright–Giemsa staining. Skin symptoms such as eruptions, nailfold bleeding, Gottron papules, mechanic's hands, and heliotrope rash were diagnosed by dermatologists specializing in collagen vascular diseases.

Statistical analysis

Variables are expressed as the mean ± SD unless otherwise stated. To detect differences between groups, Student's *t*-test was used for parametric data and the χ^2 square test was employed for categorical data. Analyses were performed using a statistical software package (StatView; SAS Institute Inc; Cary, NC). A *P*-value <0.05 was considered to be statistically significant.

Results

The types of anti-ARS antibodies detected are shown in Table 1. Anti-Jo-1 antibody was detected in 10 patients (27.8%), anti-KS in 3 patients (8.3%), anti-OJ in 2 patients (5.5%), anti-PL-12 in 4 patients (11.1%), anti-PL-7 in 4 patients (11.1%), and anti-EJ in 13 patients (36.1%).

Table 2A shows the clinical symptoms of each patient group. Nonproductive cough and dyspnea on exertion were frequently seen in both groups. Fever was noticed in 3 (16%) IIP patients and 7 (47%) PM/DM-IP patients ($P < 0.05$). Myalgia was seen in 7 (47%) PM/DM-IP patients but was not seen in the IIP patients ($P < 0.05$). Arthralgia was seen in 1 (5%) IIP patient and 3 (20%) PM/DM-IP patients. Raynaud's phenomenon was seen in 4 (21%) IIP patients and 2 (13%) PM/DM-IP patients. Fever and myalgia were more frequently investigated in the PM/DM-IP group than in the IIP group ($P < 0.05$).

Table 2B summarizes the findings on physical examination. Erythema and heliotrope were seen only in the PM/

Table 1 Types of anti-ARS antibodies.

	IIP	PM/DM-IP	Total (%)
Jo-1	4	6	10 (27.8)
KS	2	1	3 (8.3)
OJ	2	0	2 (5.5)
PL-12	4	0	4 (11.1)
PL-7	3	1	4 (11.1)
EJ	5	8	13 (36.1)
Total	20	16	36

IIP group; women $n = 14$, men $n = 6$, (median age 63 yrs, range 21–72 yrs) PM/DM group; women $n = 12$, men $n = 4$, (median age 60.5 yrs, range 43–69 yrs).