Cluster analysis using anti-aminoacyl-tRNA synthetases and SS-A/Ro52 antibodies in patients with polymyositis/dermatomyositis

Running title: Cluster analysis in polymyositis/dermatomyositis

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CONFLICT OF INTEREST

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ABSTRACT

Objective: Although several autoantibodies have been identified for polymyositis/dermatomyositis (PM/DM) diagnosis, the clinical impact of these antibodies is yet to be elucidated.

Methods: Patients with PM/DM at Okayama University Hospital from 2012 to 2016 were historically enrolled and antibody profiles were analyzed using line immunoassay. Hierarchical cluster analysis was performed based on serological analysis of anti-aminoacyl-tRNA synthetase (ARS) antibodies, including anti-Jo-1, PL-7, PL-12, EJ, OJ and SS-A/Ro-52 antibodies. Clinical symptoms and relapse proportions were compared among these clusters.

Results: Sixty-one patients were enrolled in this study: 28 were diagnosed with PM, and 33 were

diagnosed with DM. The following three clusters were determined: 1 (n = 10), anti-Jo-1 and anti-SS-A/Ro-52 antibodies double positive (10/10, 100%); 2 (n = 24), anti-SS-A/Ro-52 antibody positive (20/24, 83%), anti-Jo-1 antibody negative (24/24, 100%) and anti-ARS antibodies (excluding anti-Jo-1 antibody) positive (15/24, 63%); and 3 (n = 27), anti-Jo-1 and anti-SS-A/Ro52 antibodies double negative (26/27, 96%). The proportion of patients who relapsed was significantly lower in cluster 3 than it was in clusters 1 and 2 (risk ratio [RR], 0.37; 95% confidence interval [CI], 0.17 to 0.83, $p = 0.026$ and RR 0.42; 95% CI, 0.20 to 0.89, $p = 0.019$, respectively). There was no difference in the proportion of relapsed patients between clusters 1 and 2.

Conclusion: Our cluster analysis shows that anti-SS-A/Ro52 or any anti-ARS antibodies or both might be relevant to clinical outcomes.

Keywords: dermatomyositis, polymyositis, line immunoassay, cluster analysis

INTRODUCTION

Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory diseases characterized by proximal skeletal muscle weakness and/or distinctive skin manifestations. Severe organ involvements such as interstitial lung disease (ILD) are complicated frequently in patients with PM/DM, and malignancies are sometimes found.

Various autoantibodies have been identified as myositis-specific autoantibodies (MSAs) or myositis-associated autoantibodies (MAAs) [1]. Among MSAs and MAAs, anti-Jo-1 antibody was discovered in patients with PM in 1980 [2], and histidyl-tRNA synthetase was identified as the specific antigen for anti-Jo-1 antibody in 1983 [3, 4]. Since then, various anti-aminoacyl-tRNA synthetase (ARS) antibodies have been discovered including anti-precipitin line (PL)-7, PL-12, and EJ, OJ, and KS (Patients EJ, OJ, and KS; all full names are unknown) antibodies that recognize threonyl-, alanyl-, glycyl-, isoleucyl- and asparaginyl-tRNA synthetase, respectively [5-8]. Anti-Jo-1 antibody is found in 15-20% of patients with PM/DM [1], while anti-PL-7 and anti-EJ antibodies are found in 5-10 % [1]. Other anti-ARS antibody types are found in less than 5% of patients with PM/DM. Although the clinical features related to each anti-ARS antibody are not completely understood, a recent study showed that muscle involvement in patients with anti-PL-7 antibody is milder than that in the anti-Jo-1 subset [9]. Whereas, other groups reported that patients with non-Jo-1 anti-ARS antibodies (especially anti-PL-7 antibody and anti-PL-12 antibody) have poorer prognosis than patients with anti-Jo-1 antibody [10].

Anti-SS-A/Ro52 antibody is not classified as an MSA or MAA, but is associated with inflammatory

myopathies; a previous report showed that about 20–40% of patients with idiopathic inflammatory myopathy (IIM) were positive for anti-SS-A/Ro52 antibody [11-14]. Dobloug *et al.*, and our own research group, have previously reported that anti-SS-A/Ro52 is a poor prognostic factor for IIM [15, 16], and that patients with IIM who are double positive for anti-Jo-1 and anti-SS-A/Ro52 show poor prognosis due to ILD or malignancy complications [17].

Recently, Yamasaki *et al.* reported that patients with anti-ARS antibodies had higher positivity for anti-SS-A/Ro52 antibody than those without the antibodies did [18]. Although anti-ARS and anti-SS-A/Ro52 antibodies play a significant role in PM/DM diagnosis, their clinical significance or mutual relationship has not yet been elucidated.

Therefore, we evaluated the relationship between clinical symptoms, prognosis and positive autoantibody profiles by cluster analysis. Cluster analysis is the grouping of a set of objects in such a way that objects in the same group are more similar to each other than to those in other groups. It is a major task in exploratory data mining. Recently, cluster analysis has frequently been used as a novel approach to classifying connective tissue disease types in clinical research [19].

MATERIALS AND METHODS

Patient selection and study design

Of 296 consecutive patients who were measured for MSAs, MAAs and anti-SS-A/Ro52 antibody at Okayama University Hospital from 2012 to 2016, 79 patients with PM or DM were identified using

medical records. Of these 79 patients, 18 were excluded because of missing clinical symptom information regarding skin or muscle. Ultimately, 61 patients were enrolled in the present study and all enrolled patients fulfilled the Bohan and Peter criteria (possible, probable or definite) for PM/DM [20].

The following data were collected at diagnosis: age at disease onset, sex, history of malignancy, complication of Sjögren's syndrome (SjS), clinical symptoms, laboratory data, histological data, and initial treatment status. Clinical symptoms included upper arm or thigh stiffness, muscle weakness, arthritis, arthralgia, dysphagia, cutaneous signs of DM (*e.g.* Gottron's Papules, heliotrope rash, mechanic's hand, shawl sign, V-sign), cutaneous sclerosis, and dry mouth and eye. Laboratory data included creatine kinase (CK), aldolase (ALD), C-reactive protein (CRP) and sialylated carbohydrate antigen Krebs von den Lungen-6 (KL-6) levels. Muscle electromyography and histology were also collected. ILD was diagnosed using thoracic computed tomography. Treatment status included an initial daily glucocorticoid dose and concomitant immunosuppressant use.

Using the line blot test kit (Myositis Profile Euroline Blot test kit, Euroimmun, Lübeck, Germany), anti- Jo-1, PL-7, PL-12, EJ, OJ, SRP, Ku, Mi-2, PM-Scl75, PM-Scl100, and SS-A/Ro52 antibodies were evaluated semi-quantitatively [21]. The results of this kit are represented as follows: negative, -; positive, + or ++; strong positive, +++.

To identify groups of patients with PM/DM who had a similar autoantibody profile, hierarchical cluster analysis of autoantibodies was performed. For clustering, we used the results of the line blot test kit for anti-Jo-1, PL-7, PL-12, EJ, OJ, and SS-A/Ro52 antibodies as variables.

The primary outcome measure in the present study was the proportion of relapse patients after disease stabilization. Disease stabilization was defined as no exacerbation of clinical symptoms and muscle enzyme laboratory data for at least 4 weeks after treatment initiation. Relapse definition was based on the options of the myositis intention to treat activity index (MITAX) scoring system [22]. Relapse was defined as option ≥ 3 in at least one MITAX item, *e.g.*, exacerbation of muscle weakness, ILD, skin rash, arthritis, and/or elevation of myogenic enzymes, requiring additional treatment or change of treatment. Exacerbation of ILD included new lesion development in patients without ILD.

This study was conducted in accordance with the Declaration of Helsinki and the ethical guidelines for epidemiological research in Japan. This study was approved by the ethics committee of Okayama University Hospital and Graduate School of Medicine, Dentistry and Pharmaceutical Sciences < Committee No.: ken1702-001>. Patient agreements were obtained using opt-out consent forms.

Statistical analysis

We first described the patient's clinical background in its entirety. Next, hierarchical cluster analysis using the Ward method was performed based on the semi-quantitative value of anti- Jo-1, PL-7, PL-12, EJ, OJ and SS-A/Ro52 antibodies to identify characteristics of patient with PM/DM. We investigated differences in each cluster's clinical background, and compared prognosis between the three clusters.

Clinical characteristics were presented as the mean ± standard deviation (SD) of patient numbers. Continuous variables were compared using Student's t-test or the Mann-Whitney U test, depending on

data distribution. Categorical variables were compared between two groups using Fisher's exact probability test. Results comparing multiple groups were analyzed by F-test statistics for continuous variables and Pearson chi-square statistics for categorical variables.

A *p*-value of < 0.05 was considered significant. All statistical analyses were performed using the JMP 11.2.0 software package (SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline characteristics and treatment status

The mean (± SD) age of the enrolled patients at disease onset was 54 (± 14) years, and 44 patients (72%) were female. Twenty-eight (46%) and 33 (54%) patients were classified as PM and DM, respectively. Of the patients classified as PM, 11 were classified as possible, 13 as probable and 4 as definite cases, using the Bohan and Peter criteria. Of the patients classified as DM, 6 were classified as possible, 21 as probable and 6 as definite cases. All patients had clinical muscular symptoms and none had clinical amyopathic dermatomyositis. Malignancy was found in 11 patients (18%), 5 years before or after PM/DM diagnosis. Two patients (3%) were complicated with SjS.

Muscle weakness (evaluated by the attending physician) was found in 41 (67%) patients, and myogenic enzymes (CK, ALD) were elevated in 54 patients (89%). Results of electromyography showed myogenic abnormalities in 12 (40%) out of 30 patients. Muscle biopsy was performed in 43 patients. Histological findings were consistent with myositis in 33 (77%) patients. ILD was complicated in 37

(61%) patients.

All patients were treated with glucocorticoids as induction therapy. The mean (± SD) initial prednisolone (PSL) dose was 46 (± 15) mg/day; 0.8 (± 0.3) mg/kg/day. Concomitant immunosuppressants were used in 31 (51%) of enrolled patients (tacrolimus in 16, azathioprine in 4, cyclosporine in 6, cyclophosphamide in 2, and methotrexate in 3 patients, respectively).

The measured positive antibody rate in enrolled patients is showed in Table 1. Positive rates for other antibodies (anti-OJ, SRP, Mi-2, Ku, PM-scl75, and PM-scl100) were < 5%. Five patients had two kinds of anti-ARS antibodies as follows: anti-Jo-1 and PL-12 antibody positive (one, 2%), anti-Jo-1 and PL-7 antibody positive (two, 3%), and anti-PL-12 and EJ antibody positive (two, 3%).

Cluster analysis

Hierarchical clustering was performed, and three distinct clusters were identified (Figure 1). Patient characteristics among the three clusters are shown in Table 2.

The patients classified into cluster 1 (n =10) were all positive for both anti-Jo-1 (10/10, 100%) and anti-SS-A/Ro52 (10/10, 100%) antibodies, whereas the anti-ARS antibodies (except for anti-Jo-1) were all negative. Joint symptoms in cluster 1 patients (9/10, 90%) were significantly more frequent than those in clusters 2 (10/24, 42%, $p = 0.020$) and 3 (7/27, 26%, $p = 0.0007$) were. Among all the enrolled patients, the joint symptoms were more frequent in patients who were anti-Jo-1 positive (12/13, 92%) than in those who were anti-ARS positive except for Jo-1 (5/15, 33%, $p = 0.0014$) and anti-ARS negative

(9/33, 27%, $p < 0.0001$).

The patients classified into cluster 2 (n = 24) were characterized by high anti-SS-A/Ro52 antibody positivity (20/24, 83%), anti-Jo-1 antibody negativity (0/24, 0%), and high anti-ARS antibodies (excluding anti-Jo-1 antibody) positivity (15/24, 63%). The patients in cluster 3 (n = 27) showed almost total anti-SS-A/Ro52 antibody negativity (1/27, 4%). The ILD complication rate and serum CRP levels in cluster 3 (ILD 9/27; 33%, average CRP levels 0.36 ± 0.40 mg/dl) were significantly lower than those in clusters 1 (9/10; 90%: $p = 0.0030$, 0.98 ± 0.84 mg/dl: $p = 0.0058$) and 2 (19/24; 79%: $p = 0.0017$, 1.98 ± 2.22 mg/dl: $p = 0.0007$).

Anti-SRP, Ku, Mi-2, PM-Scl75, and PM-Scl100 antibody positivity was very low in all clusters. There was no difference in anti-SRP, Ku, Mi-2, PM-Scl75 or PM-Scl100 antibody positivity, serum CK levels, serum KL-6 levels, and cutaneous signs, between the three clusters. Initial glucocorticoid dosage and concomitant immunosuppressant use for remission induction treatment were comparable among the three clusters (Table 1).

Outcomes among the three clusters

Disease stabilization rate in clusters 1, 2 and 3 were 100% (10/10), 100 (24/24) and 92% (23/25), respectively. There was no difference in the disease stabilization rate between whole clusters ($p = 0.24$). Twenty-eight (49%) patients relapsed and their main symptoms were as follows: exacerbation of muscle weakness (11, 39%), exacerbation of ILD (5, 18%), skin rash (2, 7%), arthritis (1, 4%), and only elevation

of myogenic enzymes (9, 32%). Relapse patient proportions in clusters 1, 2 and 3 were 70% (7/10), 63% (15/24) and 26% (6/23), respectively. The relapse patient proportion in cluster 3 was significantly lower than those in clusters 1 and 2 were (risk ratio [RR], 0.37; 95% confidence interval [CI], 0.17 to 0.83, $p = 0.026$ and RR 0.42; 95% CI 0.20 to 0.89, $p = 0.019$, respectively).

DISCUSSION

Positivity of the line blot test kit for IIM was described in a previous report: anti-Jo-1 antibody, 12%; anti-PL-7 antibody, 3%; anti-PL-12 antibody, 0%; and anti-SS-A/Ro52 antibody, 29% [21]. Anti-ARS antibody positivity excluding anti-Jo-1 antibody was too low to investigate the clinical phenotype and prognosis for each antibody [1]. Thus, we divided patients with PM/DM into three groups using an autoantibody profile-based clustering analysis to categorize patients with similar characteristics.

We defined three clusters using autoantibody profiles. Cluster 1 was characterized by double positivity for anti-Jo-1 antibody and anti-SS-A/Ro52 antibody, and more frequent joint symptoms. Cluster 2 was highly positive for anti-SS-A/Ro52 antibody, but negative for anti-Jo-1 antibody. The patients in cluster 3 were almost completely negative for anti-ARS antibodies and anti-SS-A/Ro52 antibody, had lower ILD frequency, and significantly lower serum CRP levels. The proportion of relapse patients in cluster 3 was significantly less than in clusters 1 and 2.

Using cluster analysis, Hervier *et al.* revealed that PM/DM patients with anti-Jo-1 antibody positivity were highly complicated with polyarthritis [19]. Mielnik *et al.* compared patients with and without anti-

Jo-1 antibodies, and determined that patients with anti-Jo-1 antibody had cases of arthritis more frequently [23]. In the present study, patients with PM/DM who had anti-Jo-1 antibody were highly complicated with joint symptoms. Therefore, the anti-Jo-1 antibody might be linked to the development of joint symptoms.

Cluster 3 was characterized by very low autoantibody positivity, with almost total negativity for anti-ARS and anti-SS-A/Ro52 antibody, in particular. The cluster 3 autoantibody profile differed from that of other clusters. Therefore, patients in cluster 3 had fewer complications of ILD, with lower CRP levels at diagnosis, compared to clusters 1 and 2. Zhang *et al.* and Cen *et al.* reported that elevated CRP levels and the presence of anti-Jo-1 antibody were risk factors for developing ILD [24, 25]. Anti-synthetase syndrome is well-known to frequently comprises ILD [26]. Anti-SS-A/Ro52 antibody was associated with ILD complications in PM/DM [27]. Thus, the absence of anti-ARS and anti-SS-A/Ro52 antibody, and lower CRP levels, lead to fewer ILD complications in cluster 3.

In the present study, the proportion of relapse patients in cluster 3 was significantly lower than those in clusters 1 and 2. A common feature in clusters 1 and 2 was high positivity for anti-SS-A/Ro52 antibody, in spite of the fact that almost no patients were complicated with SjS. However, there were few patients with anti-ARS and SS-A/Ro52 antibodies in cluster 3. The presence of anti-SS-A/Ro52 antibody is associated with severe myositis in patients with anti-synthetase syndrome [17]. Anti-SS-A/Ro52 antibody is identified as an independent mortality risk factor in patients with PM [16]. We also previously reported that anti-SS-A/Ro52 antibody positivity may be a useful biomarker for relapse prediction [15].

Patients with IIM who were anti-ARS antibody-positive experienced relapses more frequently than those with IIM without MSAs did [28]. Although the association between each anti-ARS antibody and the relapse rate is yet to be clarified, the coexistence of any anti-ARS and anti-SS-A/Ro52 antibodies could be associated with relapse.

There were several limitations to the present study. First, we did not perform joint X-ray, or rheumatoid factor and anti-cyclic citrullinated peptide antibody measurement, meaning rheumatoid arthritis could not be excluded sufficiently. Second, we investigated PM and DM patients without distinction. The proportion of patients with DM who relapsed tends to be high due to the counting of skin lesion exacerbation. Thus, the DM proportion in clusters may influence relapse patient proportions. Third, previous reports of the association between the anti-SS-A/Ro52 antibody and IIM prognosis only described the relapse rate. The measured outcome of our study was the proportion of relapse patients. Therefore, we must evaluate our results keeping the difference of outcome in mind. Fourth, the anti-ARS antibody positivity in the present study was higher than those previously reported [29]. Moreover, patients who are more likely to have anti-ARS syndrome might be positive for anti-ARS antibodies in the line blot analysis, and detailed difference among clusters might have been overlooked. Fifth, there were four patients positive for multiple anti-ARS antibodies in this study, despite previous reports that the co-existence of multiple anti-ARS antibodies is very rare [30, 31]. Therefore, it might be necessary to reevaluate the performance of this line blot test kit. However, the specificity of the line blot test kit used in this study was very high: Jo-1, 98.7-100%; PL-7, 100%; PL12, 100%; EJ, 100%; OJ, 100%; and

SS-A/Ro52, 96.1% [21, 32-34]. Hence, these results did not affect the evaluation of the relationship between anti-ARS and SS-A/Ro52 antibodies in the present study. Sixth, anti-melanoma differentiation-associated gene 5 (MDA5) antibody was not measured in this study. Anti-MDA5 antibody positivity in classic DM is not very high [35], and no patient had CADM in this study. Thus, not determining MDA-5 might not have affected our results seriously. Finally, since all participants were Japanese in the present study, our results could not be generalized to other racial/ethnic groups.

In conclusion, our cluster analysis showed that anti-SS-A/Ro52 or any anti-ARS antibodies or both might be relevant to clinical outcomes.

KEY POINTS

Anti-SS-A/Ro52 antibody or any anti-ARS antibodies or both might have unique phenotypes and be clinically relevant factors for the outcome in patients with PM/DM.

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FIGURE LEGENDS

Figure 1. Dendrogram of a hierarchical cluster analysis with color map. Each color key shows semi-quantitative value of line immunoassay.

Figure

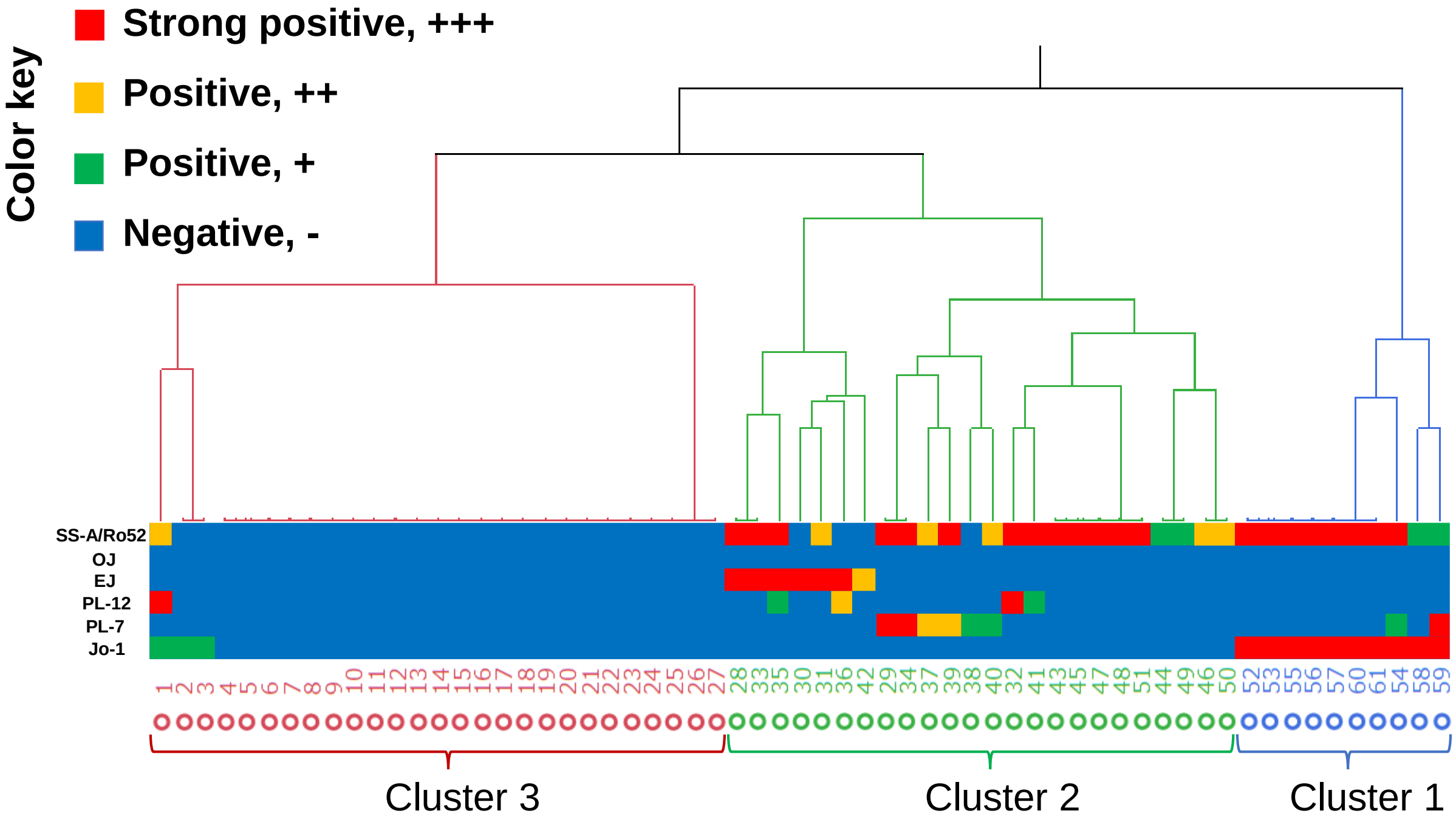
Color key
Strong positive, +++
Positive, ++
Positive, +
Negative, -
SS-A/Ro52
OJ
EJ
PL-12
PL-7
Jo-1
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
28 33 35 30 31 36 42 29 34 37 39 38 40 32 41 43 45 47 48 51 44 49 46 50
52 53 55 56 57 60 61 54 58 59
Cluster 3
Cluster 2
Cluster 1

Table 1. Autoantibody profile of line immunoassay

	-	+	++	+++
Anti-Jo-1, n (%)	48 (79%)	3 (5%)	0 (0%)	10 (16%)
Anti-PL-7, n (%)	53 (87%)	3 (5%)	2 (3%)	3 (5%)
Anti-PL-12, n (%)	56 (92%)	2 (3%)	1 (2%)	2 (3%)
Anti-EJ, n (%)	54 (89%)	0 (0%)	1 (2%)	6 (10%)
Anti-OJ, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anti-SRP, n (%)	58 (95%)	2 (3%)	0 (0%)	1 (2%)
Anti-Mi-2, n (%)	60 (98%)	1 (2%)	0 (0%)	0 (0%)
Anti-Ku, n (%)	58 (95%)	0 (0%)	0 (0%)	3 (5%)
Anti-PM-Scl75, n (%)	59 (97%)	2 (3%)	0 (0%)	0 (0%)

Anti-PM-Scl100, n (%)	60 (98%)	1 (2%)	0 (0%)	0 (0%)
Anti-SS-A/Ro52, n (%)	30 (49%)	4 (7%)	6 (10%)	21 (34%)

1 **Table 2. Clustering analysis results**

2

	Cluster 1 (n = 10)	Cluster 2 (n = 24)	Cluster 3 (n = 27)	*p*-value
Demographic data				
Mean age at onset (years), mean ± SD	52 ± 14	51 ± 13	58 ± 17	0.26
Women, n (%)	9 (90%)	16 (67%)	19 (70%)	0.37
Height (cm), mean ± SD	156 ± 8	160 ± 10	158 ± 8	0.35
Weight (kg), mean ± SD	62 ± 19	53 ± 13	57 ± 11	0.18
Mean follow-up (months), mean ± SD	67 ± 67	49 ± 45	31 ± 60	0.20
History of malignancy, n (%)	2 (20%)	3 (13%)	6 (22%)	0.66
Complication of SjS, n (%)	0 (0%)	2 (8%)	0 (0%)	0.20

Clinical diagnosis	PM, n (%)	4 (40%)	10 (42%)	14 (52%)	0.71
	DM, n (%)	6 (60%)	14 (58%)	13 (48%)	
Phenotype at diagnosis					
ILD, n (%)		9 (90%)	19 (79%)	9 (33%)	0.0004
Joint symptoms (arthralgia or arthritis), n (%)		9 (90%)	10 (42%)	7 (26%)	0.0022
CRP levels at diagnosis, mean ± SD		0.98 ± 0.84	1.98 ± 2.22	0.36 ± 0.40	0.0014
CK levels at diagnosis, mean ± SD		2697 ± 4022	1601 ± 1485	3189 ± 4715	0.30
KL-6 levels at diagnosis, mean ± SD		966 ± 712	578 ± 618	490 ± 623	0.20
Anti-Jo-1, n (%)	+	0 (0%)	0 (0%)	3 (11%)	< 0.0001
	++	0 (0%)	0 (0%)	0 (0%)	
	+++	10 (100%)	0 (0%)	0 (0%)	

Anti-PL-7, n (%)	+	1 (10%)	2 (8%)	0 (0%)	0.18
	++	0 (0%)	2 (8%)	0 (0%)	
	+++	1 (10%)	2 (8%)	0 (0%)	
Anti-PL-12, n (%)	+	0 (0%)	2 (8%)	0 (0%)	0.50
	++	0 (0%)	1 (4%)	0 (0%)	
	+++	0 (0%)	1 (4%)	1 (4%)	
Anti-EJ, n (%)	+	0 (0%)	0 (0%)	0 (0%)	0.016
	++	0 (0%)	1 (4%)	0 (0%)	
	+++	0 (0%)	6 (25%)	0 (0%)	
Anti-OJ, n (%)	+	0 (0%)	0 (0%)	0 (0%)	N/A
	++	0 (0%)	0 (0%)	0 (0%)	

	+++	0 (0%)	0 (0%)	0 (0%)	
Anti-SS-A/Ro52, n (%)	+	2 (20%)	2 (8%)	0 (0%)	< 0.0001
	++	0 (0%)	5 (21%)	1 (4%)	
	+++	8 (80%)	13 (54%)	0 (0%)	
Anti-ARS antibodies, n (%)	+	0 (0%)	3 (13%)	2 (7%)	< 0.0001
	++	0 (0%)	3 (13%)	0 (0%)	
	+++	10 (100%)	9 (38%)	1 (4%)	
Two types of anti-ARS double positivity, n (%)		2 (20%)	2 (8%)	1 (4%)	0.28
Anti-ARS and anti-SS-A/Ro52 double positivity, n (%)		10 (100%)	11 (46%)	1 (4%)	< 0.0001
Treatment					
Initial dosage of PSL (mg/day), mean ± SD		45 ± 13	48 ± 11	44 ± 18	0.71

Concomitant of immunosuppressant, n (%)	5 (50%)	17 (71%)	9 (38%)	0.067

SD, standard deviation; N/A, not available; PM, polymyositis; DM, dermatomyositis; ILD, interstitial lung disease; CRP, C-reactive protein; CK, creatine kinase; KL-6, sialylated carbohydrate antigen Krebs von den Lungen-6; PSL, prednisolone; ARS, aminoacyl-tRNA synthetase