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Myositis-specific autoantibodies in dermatomyositis/polymyositis with interstitial lung disease

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ABSTRACT

Aim: The prevalence and diagnostic values of myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) in dermatomyositis/polymyositis (DM/PM) were studied.
Method: A commercial immunoblot assay with 16 autoantigens was used to detect MSAs and MAAs in serum samples from 130 DM/PM patients, 100 disease controls, and 50 healthy subjects.
Results: The prevalence of anti-Jo-1, anti-MDA5, anti-TIF1γ, anti-Mi-2α, and anti-Mi-2β was significantly higher in DM/PM than in other connective-tissue diseases (CTDs). Moreover, anti-MDA5 and anti-Ro-52 were significantly higher in DM/PM with interstitial lung disease (ILD) than in DM/PM without ILD, while that of anti-TIF1γ and anti-NXP2 were significantly lower in DM/PM with ILD than in DM/PM without ILD. For distinguishing DM/PM from other CTDs, the sensitivity, specificity, and positive predictive value (PPV) for anti-MDA5 were 28.46, 99.00, and 97.37%, respectively, with a positive likelihood ratio (LR+) of 28.46; they were 46.15, 58.00, and 58.82%, respectively, for anti-Ro-52 with an LR+ of 1.10. For distinguishing DM/PM with ILD from DM/PM without ILD, the sensitivity, specificity, and PPV for anti-MDA5 were 45.57, 100.00, and 100.00%, respectively, and for anti-Ro-52 were 60.76, 73.91, and 80.00%, respectively.
Conclusion: MSAs and MAAs serve as biomarkers for differentiating DM/PM from other CTDs as well as distinguishing DM/PM with ILD from DM/PM without ILD.

1. Introduction

Dermatomyositis (DM) and polymyositis (PM), two of the main diseases in idiopathic inflammatory myopathies (IIM), are characterized by a systemic inflammation of the proximal skeletal muscles and/or the skin [1–4]. DM/PM are considered related to increased morbidity and mortality rates because of severe muscle weakness and organ involvement [5], which can affect the esophagus [6–9], heart [10–13], and especially the lungs [14,15]. Interstitial lung disease (ILD) is the primary pulmonary manifestation in DM/PM and is the most common extramuscular manifestation, with a prevalence ranging from 5.0 to 65.0% [16]. ILD in DM/PM patients is frequently aggressive and refractory to treatment, which results in high morbidity and mortality [14,17,18].

Autoantibodies, important in the diagnosis of DM/PM, help to identify subgroups of IIM as well as different patterns of extramuscular organ involvement [19–21]. There are two groups of autoantibodies in patients with DM/PM—myositis specific (MSAs) and myositis associated (MAAs). MSAs are usually found exclusively in DM/PM, while MAAs are usually found in mixed connective-tissue diseases (CTDs)

Abbreviations: DM, dermatomyositis; PM, polymyositis; IIM, idiopathic inflammatory myopathies; CTDs, connective-tissue diseases; ILD, interstitial lung disease; MSAs, myositis-specific autoantibodies; MAAs, myositis-associated autoantibodies; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio.; LR-, negative likelihood ratio; pSS, primary Sjögren's syndrome; RA, rheumatoid arthritis; EULAR, European League Against Rheumatism; ACR, American College of Rheumatology; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; SD, standard deviation; ARS, aminoacyl-transfer RNA synthetase; HC, healthy controls; NA, not available

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Table 1
Prevalence of autoantibodies in different groups.

Number of subjects	HC		DM/PM		Other CTDs		*p*-value DM/PM vs. other CTDs	DM/PM with ILD		DM/PM without ILD		*p*-value DM/PM with ILD vs. DM/PM without ILD
	50	%	130	%	100	%		79	%	46	%	
Anti-Jo-1	0	0.00	10	7.69	0	0.00	0.012	7	8.86	2	4.35	0.560
Anti-OJ	0	0.00	0	0.00	0	0.00	NA	0	0.00	0	0.00	NA
Anti-EJ	0	0.00	1	0.77	0	0.00	1	1	1.27	0	0.00	1.000
Anti-PL-7	0	0.00	1	0.77	1	1.00	1	1	1.27	0	0.00	1.000
Anti-PL-12	0	0.00	1	0.77	0	0.00	1	0	0.00	1	2.17	0.368
Anti-MDA5	0	0.00	37	28.46	1	1.00	< 0.001	36	45.57	0	0.00	< 0.001
Anti-TIF1γ	0	0.00	12	9.23	0	0.00	0.002	3	3.80	9	19.57	0.010
Anti-Mi-2α	0	0.00	7	5.38	0	0.00	0.049	5	6.33	2	4.35	0.951
Anti-Mi-2β	0	0.00	7	5.38	0	0.00	0.049	6	7.59	0	0.00	0.138
Anti-SAE1	0	0.00	2	1.54	0	0.00	0.506	0	0.00	2	4.35	0.134
Anti-NXP2	0	0.00	6	4.62	0	0.00	0.078	1	1.27	5	10.87	0.047
Anti-SRP	0	0.00	2	1.54	0	0.00	0.506	2	2.53	1	2.17	1.000
Anti-Ku	0	0.00	4	3.08	3	3.00	1	3	3.80	1	2.17	1.000
Anti-PM-Scl75	0	0.00	3	2.31	3	3.00	1	2	2.53	0	0.00	0.531
Anti-PM-Scl100	0	0.00	1	0.77	2	2.00	0.819	1	1.27	0	0.00	1.000
Anti-Ro-52	0	0.00	60	46.15	42	42.00	0.53	48	60.76	12	26.09	< 0.001

Notes: HC = healthy controls; DM/PM = dermatomyositis/polymyositis; CTDs = connective-tissue diseases; ILD = interstitial lung disease.

with myositis. For diagnosing DM/PM, histopathological findings are not always clear, especially in patients with mild muscle involvement and extramuscular manifestations. The noninvasive detection of MSAs and MAAs in serum is another important diagnostic tool that can assist in DM/PM diagnosis and the prediction of clinical complications.

In this study, we evaluated the prevalence of 12 MSAs (anti-Jo-1, anti-OJ, anti-EJ, anti-PL-7, anti-PL-12, anti-MDA5, anti-TIF1γ, anti-Mi-2α, anti-Mi-2β, anti-SAE1, anti-NXP2, and anti-SRP) and 4 MAAs (anti-Ku, anti-PM-Scl75, anti-PM-Scl100, anti-Ro-52) in DM/PM and in DM/PM with/without ILD. In addition, we determined their sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios (LR+ and LR-, respectively). We also investigated their individual diagnostic values in distinguishing DM/PM from other CTDs and distinguishing DM/PM with ILD from those without ILD.

2. Materials and methods

2.1. Study populations

Sera from 280 participants were assessed for autoantibodies. The DM/PM group comprised 112 DM and 18 PM patients diagnosed according to the Bohan and Peter criteria [3,4] and the 2017 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria [22]. The disease controls comprised 25 patients with primary Sjögren's syndrome (pSS) satisfying the classification criteria of the American-European consensus group [23]; 25 with rheumatoid arthritis (RA) satisfying the revised classification criteria of the 1987 ACR [24]; 25 with systemic lupus erythematosus (SLE) fulfilling the revised classification criteria of the 1997 ACR [25]; and 25 with systemic sclerosis (SSc) fulfilling the classification criteria of the 2013 ACR/EULAR [26]. ILD in the DM/PM group and disease controls were identified using high-resolution chest computed tomography. In addition, 50 healthy individuals were recruited for the study. Supported by the Research Special Fund for Public Welfare Industry of Health, 50 patients with DM/PM, 40 with other CTDs, and 20 healthy subjects were recruited through the cooperation of two centers in China. Eighty patients with DM/PM, 60 with other CTDs, and 30 healthy subjects were recruited by Peking Union Medical College Hospital, Beijing, China. All subjects were provided study information and signed an informed consent form. The study was approved by the Ethics Committee of Peking Union Medical College Hospital (NO. JS-1226), Beijing, China.

2.2. Autoantibody detection

Two hundred eighty sera were tested using the EUROLINE Autoimmune Inflammatory Myopathies 16 Ag (IgG) commercial line blot assay (Euroimmun, Lübeck, Germany) comprising a membrane strip with the 16 autoantigens noted above according to the manufacturer's instructions. Briefly, the serum samples were pipetted into an incubation channel containing the test strips and incubated for 30 min, after which the strips were washed, and an enzyme conjugate was pipetted into the incubation channel. After 30 min, the strips were washed again and a substrate was pipetted into the channel. Finally, the strips were rinsed with distilled water. EUROLineScan (Euroimmun) was used to interpret the assays as negative, borderline, or positive.

2.3. Statistical analyses

SPSS v20.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analyses. Categorical variables were compared using the Chi-squared or Fisher's exact tests. *P*-values < .05 were considered statistically significant.

3. Results

3.1. Demographic profile

The study comprised 130 patients with DM/PM (87 females, 43 males) with a mean age of 46.27 years (standard deviation [SD]: 13.01 years). None of the patients with DM/PM had cancer. Of the 130 patients included in the study, 63.20% (79/125) of the patients had ILD, 36.80% (46/125) did not have ILD, and the remaining 5 patients were not assessed for the disease. In addition, 100 patients with other CTDs (mean age ± SD: 47.27 ± 13.94; 65 females and 35 males) and 50 healthy subjects (mean age ± SD: 48.73 ± 12.99; 33 females and 17 males) were recruited as control groups. Of the 100 patients with other CTDs, 24.00% (6/25) of the pSS patients, 40.00% (10/25) of the RA patients, 12.00% (3/25) of the SLE patients, and 60.00% (15/25) of the SSc patients had ILD.

3.2. The prevalence of anti-Jo-1, anti-MDA5, anti-TIF1γ, anti-Mi-2α, and anti-Mi-2β was significantly higher in DM/PM

The results on the prevalence of MSAs and MAAs are summarized in Table 1. Specifically, no autoantibodies were detected in the sera from

the healthy controls. The prevalence of anti-OJ, anti-EJ, anti-PL-7, and anti-PL-12 in DM/PM was 0.00, 0.77, 0.77, and 0.77%, respectively; the prevalence in the other CTDs was 0.00, 0.00, 1.00, and 0.00%, respectively. The differences were not significant. The prevalence of anti-Jo-1, anti-MDA5, anti-TIF1γ, anti-Mi-2α, and anti-Mi-2β was 7.69, 28.46, 9.23, 5.38, and 5.38%, respectively, in DM/PM, and 0.00, 1.00, 0.00, 0.00, and 0.00%, respectively, in other CTDs; the difference was significant ($p = .012$, $p < .001$, $p = .002$, $p = .049$, and $p = .049$, respectively). No significant differences were observed in anti-SAE1, anti-NXP2, anti-SRP, anti-Ku, anti-PM-Scl75, anti-PM-Scl100, and anti-Ro-52 between DM/PM (1.54, 4.62, 1.54, 3.08, 2.31, 0.77, and 46.15%, respectively) and the controls (0.00, 0.00, 0.00, 3.00, 3.00, 2.00, and 42.00%, respectively).

3.3. The prevalence of anti-MDA5 and anti-Ro-52 was significantly higher in DM/PM with ILD, while the prevalence of anti-TIF1γ and anti-NXP2 was significantly lower

As shown in Table 1, no significant differences were found in the prevalence of anti-Jo-1, anti-OJ, anti-EJ, anti-PL-7, and anti-PL-12 between DM/PM with ILD (8.86, 0.00, 1.27, 1.27, and 0.00%, respectively) and DM/PM without ILD (4.35, 0.00, 0.00, 0.00, and 2.17%, respectively). The prevalence of anti-MDA5 and anti-Ro-52 was significantly higher in DM/PM with ILD than in DM/PM without ILD (anti-MDA5, 45.57 vs. 0.00%, respectively; $p < .001$; anti-Ro-52, 60.76 vs. 26.09%, respectively; $p < .001$).

In contrast, the prevalence of anti-TIF1γ and anti-NXP2 was significantly lower in DM/PM with ILD than in DM/PM without ILD (anti-TIF1γ, 3.80 vs. 19.57%, respectively; $p = .01$; anti-NXP2, 1.27 vs. 10.87%, respectively; $p = .047$). No significant difference was observed in the prevalence of anti-Mi-2α, anti-Mi-2β, anti-SAE1, anti-SRP, anti-Ku, anti-PM-Scl75, or anti-PM-Scl100 between DM/PM with ILD and DM/PM without ILD (anti-Mi-2α, 6.33 vs. 4.35%, respectively; anti-Mi-2β, 7.59 vs. 0.00% respectively; anti-SAE1, 0.00 vs. 4.35%, respectively; anti-SRP, 2.53 vs. 2.17% respectively; anti-Ku, 3.80 vs. 2.17%, respectively; anti-PM-Scl75, 2.53 vs. 0.00%, respectively; anti-PM-Scl100, 1.27 vs. 0.00%, respectively).

3.4. Predictive power of multiple autoantibodies in distinguishing DM/PM from other CTDs

The overall predictive power for distinguishing DM/PM from other CTDs is provided in Table 2. Anti-MDA5 and anti-Ro-52 exhibited moderate sensitivities of 28.46 and 46.15%, respectively; however, the specificity of anti-MDA5 (99.00%) was higher than that of anti-Ro-52 (58.00%). The sensitivities of anti-Jo-1, anti-OJ, anti-EJ, anti-PL-7, anti-PL-12, anti-TIF1γ, anti-Mi-2α, anti-Mi-2β, anti-SAE1, anti-NXP2, anti-SRP, anti-Ku, anti-PM-Scl75, and anti-PM-Scl100 were < 10.0%, while the specificities of each were > 97.0%. PPVs of anti-Jo-1, anti-EJ, anti-PL-12, anti-MDA5, anti-TIF1γ, anti-Mi-2α, anti-Mi-2β, anti-SAE1, anti-NXP2, and anti-SRP ranged from 97.37 to 100.0%. In contrast, PPVs of anti-PL-7, anti-Ku, anti-PM-Scl75, anti-PM-Scl100, and anti-Ro-52 were relatively lower, ranging from 33.33 to 58.82%. NPVs of all the autoantibodies were similar, ranging from 43.17 to 51.56%. LR+ was the highest for anti-MDA5 (28.46), and ranged from 0.38 to 1.10 for anti-PL-7, anti-Ku, anti-PM-Scl75, anti-PM-Scl100, and anti-Ro-52. LR- was similar for all autoantibodies, ranging from 0.72 to 1.01.

3.5. Predictive power of multiple autoantibodies in distinguishing DM/PM with ILD from DM/PM without ILD

The predictive power of multiple autoantibodies in distinguishing DM/PM with and without ILD is shown in Table 3. For distinguishing DM/PM with ILD from that without ILD, only anti-MDA5 and anti-Ro-52 exhibited moderate sensitivities of 45.57 and 60.76%, respectively. The sensitivities of the remaining 14 autoantibodies were < 10.0%. All autoantibodies demonstrated high specificities (> 80.0%), except anti-Ro-52, which showed a relatively low specificity (73.91%). PPVs of anti-EJ, anti-PL-7, anti-MDA5, anti-Mi-2β, anti-PM-Scl75, and anti-PM-Scl100 were 100.0%. NPVs of anti-Ro-52 was the highest (52.31%), followed by anti-MDA5 (51.69%). No autoantibody exhibited a high LR + or high LR-.

Table 2
Predictive power of autoantibodies for differentiating dermatomyositis/polymyositis from other connective-tissue diseases.

DM/PM vs. other CTDs	SEN (%)	SPE (%)	PPV (%)	NPV (%)	LR+	LR-
Anti-Jo-1	7.69	100.00	100.00	45.45	NA	0.92
Anti-OJ	0.00	100.00	NA	43.48	NA	1.00
Anti-EJ	0.77	100.00	100.00	43.67	NA	0.99
Anti-PL-7	0.77	99.00	50.00	43.42	0.77	1.00
Anti-PL-12	0.77	100.00	100.00	43.67	NA	0.99
Anti-MDA5	28.46	99.00	97.37	51.56	28.46	0.72
Anti-TIF1γ	9.23	100.00	100.00	45.87	NA	0.91
Anti-Mi-2α	5.38	100.00	100.00	44.84	NA	0.95
Anti-Mi-2β	5.38	100.00	100.00	44.84	NA	0.95
Anti-SAE1	1.54	100.00	100.00	43.86	NA	0.98
Anti-NXP2	4.62	100.00	100.00	44.64	NA	0.95
Anti-SRP	1.54	100.00	100.00	43.86	NA	0.98
Anti-Ku	3.08	97.00	57.14	43.50	1.03	1.00
Anti-PM-Scl75	2.31	97.00	50.00	43.30	0.77	1.01
Anti-PM-Scl100	0.77	98.00	33.33	43.17	0.38	1.01
Anti-Ro-52	46.15	58.00	58.82	45.31	1.10	0.93

Notes: DM/PM = dermatomyositis/polymyositis; CTDs = connective-tissue diseases; SEN = sensitivity; SPE = specificity; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NA = not available.

Table 3
Predictive power of autoantibodies for differentiating dermatomyositis/polymyositis with interstitial lung disease from dermatoyositis/polymyositis without interstitial lung disease.

DM/PM with ILD vs. DM/PM without ILD	SEN (%)	SPE (%)	PPV (%)	NPV (%)	LR+	LR-
Anti-Jo-1	8.86	95.65	77.78	37.93	2.04	0.95
Anti-OJ	0.00	100.00	NA	36.80	NA	1.00
Anti-EJ	1.27	100.00	100.00	37.10	NA	0.99
Anti-PL-7	1.27	100.00	100.00	37.10	NA	0.99
Anti-PL-12	0.00	97.83	0.00	36.29	0.00	1.02
Anti-MDA5	45.57	100.00	100.00	51.69	NA	0.54
Anti-TIF1γ	3.80	80.43	25.00	32.74	0.19	1.20
Anti-Mi-2α	6.33	95.65	71.43	37.29	1.46	0.98
Anti-Mi-2β	7.59	100.00	100.00	38.66	NA	0.92
Anti-SAE1	0.00	95.65	0.00	35.77	0.00	1.05
Anti-NXP2	1.27	89.13	16.67	34.45	0.12	1.11
Anti-SRP	2.53	97.83	66.67	36.89	1.16	1.00
Anti-Ku	3.80	97.83	75.00	37.19	1.75	0.98
Anti-PM-Scl75	2.53	100.00	100.00	37.40	NA	0.97
Anti-PM-Scl100	1.27	100.00	100.00	37.10	NA	0.99
Anti-Ro-52	60.76	73.91	80.00	52.31	2.33	0.53

Notes: DM/PM = dermatomyositis/polymyositis; ILD = interstitial lung disease; SEN = sensitivity; SPE = specificity; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NA = not available.

3.6. Relationships between myositis-specific autoantibodies in DM/PM

We illustrated the distribution of MSAs in patients with DM/PM, with 58.46% (76/130) testing positive for at least one, but 41.54% (54/130) negative for all MSAs. Of note, 13.16% (10/76) of the MSA-positive DM/PM patients were also positive for two autoantibodies (Venn diagram: http://bioinformatics.psb.ugent.be/webtools/Venn/, Fig. 1). Two were positive for anti-Jo-1 and anti-MDA5, two were positive for anti-Jo-1 and anti-Mi-2β, one was positive for anti-MDA5 and anti-Mi-2β, one was positive for anti-MDA5 and anti-SRP, and four were

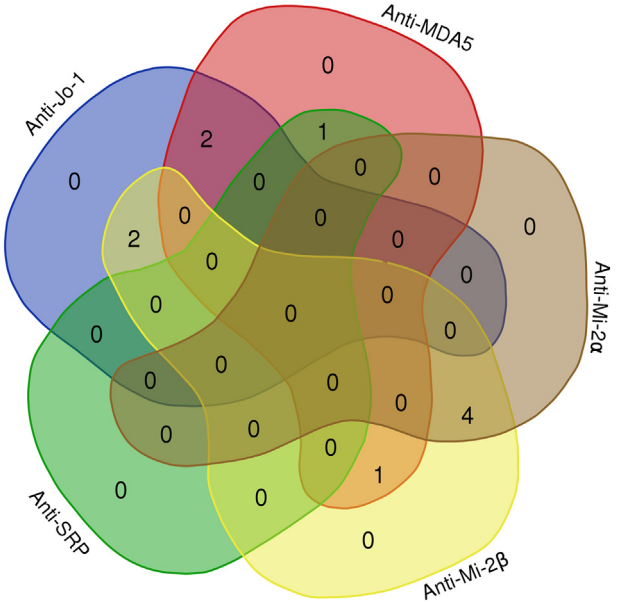

Fig. 1. Venn diagram showing the distribution of myositis-specific autoantibodies in myositis-specific autoantibody-positive patients with dermatomyositis/polymyositis. Two were positive for anti-Jo-1 and anti-MDA5, two were positive for anti-Jo-1 and anti-Mi-2β, one was positive for anti-MDA5 and anti-Mi-2β, one was positive for anti-MDA5 and anti-SRP, and four were positive for anti-Mi-2α and anti-Mi-2β.

positive for anti-Mi-2α and anti-Mi-2β.

4. Discussion

In this study, the prevalence of MSAs and MAAs and their diagnostic potential in evaluating DM/PM and DM/PM with ILD were assessed. The major findings were as follows: (1) The prevalence of anti-Jo-1, anti-MDA5, anti-TIF1γ, anti-Mi-2α and anti-Mi-2β was significantly higher in DM/PM than in other CTDs; (2) the prevalence of anti-MDA5 and anti-Ro-52 was significantly higher in DM/PM with ILD than in DM/PM without ILD; however, anti-TIF1γ and anti-NXP2 were significantly higher in DM/PM without ILD than in DM/PM with ILD; (3) anti-MDA5 and anti-Ro-52 showed moderate sensitivities in differentiating DM/PM from other CTDs, and anti-MDA5 had higher specificity, PPV, and LR+ than anti-Ro-52; (4) anti-MDA5 and anti-Ro-52 demonstrated moderate sensitivities in differentiating DM/PM with ILD from DM/PM without ILD, and the specificity and PPV of anti-MDA5 were higher than those of anti-Ro-52; and (5) the MSAs in DM/PM were not mutually exclusive.

Aminoacyl-transfer RNA synthetases (ARS) are cytoplasmic amino acid–charging enzymes that play a role in catalyzing the ATP-dependent binding of a single amino acid to its specific tRNA during protein synthesis. Anti-ARS are a group of autoantibodies including anti-Jo-1, anti-OJ, anti-EJ, anti-PL-7, and anti-PL-12. A meta-analysis showed that patients with non-anti-Jo-1 ARS had a higher risk of ILD than those with anti-Jo-1 [27]. We found that anti-Jo-1 was associated with DM/PM-related ILD, but no significant difference was observed in the prevalence of anti-ARS between DM/PM with or without ILD, which could be the results of a relatively small sample size in this study.

Components of Mi-2 antigen are identified as a nucleosome remodeling and deacetylase (NuRD) complex that plays a part in regulating gene expression at the chromatin level. Anti-Mi-2α and anti-Mi-2β were considered to be DM-specific autoantibodies, which are significantly correlated with Gottron's papules, heliotrope rash, V-neck sign, shawl sign rashes, and cuticular overgrowth [28]. Our study found that all of the patients with anti-Mi-2α and anti-Mi-2β were diagnosed with DM. This outcome demonstrated that these two autoantibodies are specific markers for DM.

The target autoantigen of MDA5 is a cytoplasmic viral sensor that participates in the recognition of viral RNA in the cytoplasm and triggers innate antiviral responses. A European study reported that anti-MDA5 was found in 7.0% of DM/PM patients, with a higher prevalence in Asian DM/PM patients (from 15.8 to 40.6%) [29,30]. In addition, anti-MDA5 was related to DM, clinically amyopathic DM in particular, and not to PM [31]. In our study, of the 37 anti-MDA5–positive DM/PM patients, 36 were DM patients and 1 was a PM patient. The prevalence of anti-MDA5 (28.46%) in DM/PM was consistent with the results of previous studies [29,30]. Previous studies have shown that anti-MDA5 was one of the major MSAs in DM/PM with ILD, ranging from 25.0 to 42.0% [20,32,33]. In our study, the prevalence of anti-MDA5 in DM/PM with ILD (45.57%) was in accordance with that found in previous studies [20,33].

The autoantigen of anti-TIF1γ belongs to the transcription intermediary factor 1 (TIF1) family, part of the tripartite motif (TRIM) superfamily, and is involved in carcinogenesis. Lu et al. [34] investigated 211 adult Chinese patients with DM/PM and found that anti-TIF1γ was observed in DM but not in PM and other CTDs. In addition, Fiorentino et al. [35] revealed that DM patients who tested positive for anti-TIF1γ were less likely to also have ILD. Similarly, in our study, 12 patients who tested positive for anti-TIF1γ were diagnosed with DM but not with PM or other CTDs. In addition, the prevalence of anti-TIF1γ in DM/PM with ILD was significantly lower than that in DM/PM without ILD.

Nuclear matrix protein 2 (NXP2) localizes in the promyelocytic leukemia (PML) nuclear bodies and is involved in the activation of p53 to induce cellular senescence. Some American studies have shown that anti-NXP2 was detected in 11.0–17.0% of DM patients [36–38]. A Japanese study has shown that 1.6% of DM patients tested positive for anti-NXP2. In our study, anti-NXP2 was present in 5.36% of DM patients, but not in PM patients. It appears that the prevalence of anti-NXP2 was lower in Asian than in Western patients, and this could be a result of different ethnic backgrounds or the influence of environmental factors. Ceribelli et al. found that none of those who tested positive for anti-NXP2 had any lung involvement. In our study, except for a small percentage (1.27%), the majority of DM/PM patients who tested positive for anti-NXP2 also had no ILD.

Anti-Ro-52 is not disease specific and is found frequently in pSS, SLE, SSc, and other diseases [39,40]. Dugar et al. [39] have shown that anti-Ro-52 was the most common serological marker in IIM. We found no significant difference in its prevalence between DM/PM and other CTDs in our study; however, we did find a significant difference between DM/PM with ILD and DM/PM without ILD.

Because MSAs and MAAs support the diagnosis of DM/PM [41], we also investigated the diagnostic value of these autoantibodies. Overall, anti-MDA5 and anti-Ro-52 exhibited high value in the diagnosis of DM/PM with and without ILD. Anti-Ro-52 showed the highest sensitivity among the antibodies we investigated, but a low specificity, PPV, and LR+. Assays of both anti-MDA5 with anti-Ro-52 should be performed when attempting to diagnose DM/PM.

Some studies have suggested that MSAs are mutually exclusive [42,43]; therefore, we explored the prevalence of MSAs in the same patients. Notably, our study showed that anti-MDA5 coexists with anti-Jo-1, anti-Mi-2β, or anti-SRP, and that anti-Mi-2β antibody coexists with either anti-Jo-1 or anti-Mi-2α. This result demonstrated that MSAs were not mutually exclusive, which is consistent with the findings of previous studies [44,45]. It is worth mentioning that this finding could most likely also be attributed to the false-positive results introduced by the line blot system. Thus, other experimental methods, such as enzyme-linked immunoabsorbent assay, Western blotting, and immunoprecipitation, could be used to verify this result.

In conclusion, MSAs and MAAs are helpful in diagnosing DM/PM and DM/PM with ILD; however, additional biomarkers to improve sensitivity and accuracy in the diagnosis of both conditions are still needed. Our study also indicated that MSAs in patients with DM/PM

were not mutually exclusive; however, the coexistence of two or more MSAs in the same DM/PM patient should be studied further.

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Conflicts of interest

The authors declare that they have no competing financial interests.

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