Risk factors of interstitial lung diseases in clinically amyopathic dermatomyositis

Yu-Zhou Gan[1,2], Li-Hua Zhang[3], Lin Ma[4], Feng Sun[1,2], Yu-Hui Li[1,2], Yuan An[1,2], Zhan-Guo Li[1,2], Hua Ye[1,2]

[1]Department of Rheumatology & Immunology and Beijing Key Laboratory for Rheumatism and Immune Diagnosis (BZ0135), Peking University People's Hospital, Beijing 100044, China;
[2]Center of Clinical Immunology, Peking University, Beijing 100044, China;
[3]Department of Rheumatology, Hulunbeier People's Hospital, Hulunbeier, Inner Mongolia 021008, China;
[4]Department of Rheumatology, Hebei Hospital of Traditional Chinese Medicine, Shijiazhuang, Hebei 050200, China.

Abstract

Background: Clinically amyopathic dermatomyositis (CADM) is a unique sub-type of idiopathic inflammatory myopathies with a high prevalence of interstitial lung disease (ILD). Poor prognosis of the patients was strongly associated with rapid progressive ILD. The aim of this study was to identify risk factors for prediction of different types of ILD in CADM.

Methods: In this study, data of 108 inpatients with CADM were collected, including 87 with ILD. The baseline clinical data and laboratory parameters, including myositis-specific and associated antibodies and tumor-associated antigens were analyzed to identify risk factors for acute or subacute interstitial pneumonitis (A/SIP) and chronic interstitial pneumonitis (CIP).

Results: In 87 patients with CADM-ILD, 39 (36.1%) were A/SIP, and 48 (44.4%) were CIP. There were 22 (20.4%) patients with asymptomatic ILD who were detected by routine high resolution computed tomography. Cytokeratin-19 fragment (CYFRA21-1) was significantly higher in CADM-ILD than that in CADM patients without ILD; carcinoembryonic antigen and neuron-specific enolase were significantly elevated in A/SIP than that in CIP. Patients with A/SIP had a higher positive rate of anti-melanoma differentiation-associated gene 5 (MDA5), while patients with CIP had a higher positive rate of anti PL-12 and anti-Ro-52. Logistic regression analysis indicated that elevation of CYFRA21-1 was a risk factor for ILD, higher titer of anti-MDA5 indicated increased likelihood for A/SIP, and higher titer of anti-Ro-52 was also clearly associated with CIP.

Conclusions: This study indicated that the prevalence of ILD was high in CADM. Asymptomatic ILD has been previously underestimated. Anti-MDA5 was a risk factor for the presence of A/SIP, and CYFRA21-1 was a risk factor for ILD.

Keywords: Clinically amyopathic dermatomyositis; Interstitial lung diseases; Myositis autoantibodies; Tumor-associated antigen

Introduction

Clinically amyopathic dermatomyositis (CADM) is a distinct sub-type of idiopathic inflammatory myopathies. It has typical cutaneous symptoms as classic dermatomyositis with little or no evidence of muscular manifestations.[1-3] CADM was reported to comprise 10% to 20% of all dermatomyositis patients, characterized by an increased risk of interstitial lung disease (ILD), especially rapid progressive ILD (RP-ILD),[4,5] which results in high morbidity and mortality.[6,7] Therefore, it is important to explore key risk biomarkers for different types of ILD, especially acute or subacute ILD, in the management of CADM.

Myositis autoantibodies were found in over 80% patients with idiopathic inflammatory myopathies and traditionally classified into two groups based on their diagnostic accuracy: myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs).[8-10] Previous studies have proved that some MSAs were specifically expressed and serves as a risk factor for RP-ILD in CADM,[4,9,11-13] but recent studies have pointed out that these antibodies alone were insufficient to predict RP-ILD in CADM.[11,14] The predictive factor for chronic ILD was also not fully studied. In addition, other MSAs and MAAs remains elusive in CADM-ILD.

It has been suggested that dermatomyositis is frequently complicated by malignant tumors, and screening malignances is important in clinical practice.[15,16] Recently,

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000691

Correspondence to: Dr. Hua Ye, Department of Rheumatology & Immunology, Peking University People's Hospital, 11 Xizhimen South Street, Beijing 100044, China
E-Mail: yehbmu@126.com

Chinese Medical Journal 2020;133(6)

Received: 23-12-2019 **Edited by:** Li-Shao Guo

several tumor-associated antigens (TAAs) have been reported in dermatomyositis associated ILD in a small group of patients.[17] Therefore, the potential correlation of TAAs with CADM-ILD needs to be further studied.

In this study, we evaluated the prevalence and clinical relevance of myositis autoantibodies and TAAs in patients with CADM, and identified the risk factors for different types of ILD in CADM.

Methods

Ethical approval

The study was approved by the Ethics Committee of Peking University People's Hospital and the study complied with the *Declaration of Helsinki* guidelines. Given the retrospective nature of the study, the requirement of written informed consent was waived.

Patients

Data of 108 inpatients diagnosed with CADM were collected during March 2008 to July 2019, from the Peking University People's Hospital in Beijing. The diagnosis of CADM was based on the Sontheimer criteria[1] or Gerami criteria.[2] Briefly as following: (1) typical rash of classical dermatomyositis, such as Gottron rash or heliotrope rash, occurring for 6 months or longer; (2) no clinical evidence of proximal muscle weakness or only mildly reduced muscle strength; (3) patients might have sub-clinical evidence of myositis upon laboratory, electrophysiologic, and/or radiologic evaluation.[1] The exclusion criteria including: (1) typical muscular manifestations of dermatomyositis occurred within 6 months of being diagnosed with CADM; (2) to eliminate the influence of malignant tumors on TAAs, patients with malignancy at the beginning of diagnosis.

The presence of ILD was defined according to the 2013 statement of the American Thoracic Society and the European Respiratory Society.[18] In general, patients were considered to have ILD if they met the following criteria: (1) restrictive impairments in lung function (total lung capacity and diffusing capacity of the lung for carbon monoxide <80% of predicted), and (2) radiographic signs of ILD on high resolution computed tomography (HRCT) (nodular; reticulonodular; linear or ground-glass opacities; consolidations; irregular interface; honeycombing; or traction bronchiectasis). Patients with ILD were further divided into three subgroups: acute interstitial pneumonitis (AIP) (deterioration within 1 month), subacute interstitial pneumonitis (SIP) (deterioration within 3 months but more than 1 month) and chronic interstitial pneumonitis (CIP) (slowly progressive presentation with gradual deterioration over a period longer than 3 months). The deterioration was defined by two or more of the following: (a) symptomatic exacerbation (dyspnea on exertion), (b) an increase in parenchymal abnormality on HRCT scan, and (c) physiologic change defined by one of the following: >10% decrease in vital capacity or >1.33 kPa decrease in arterial oxygen tension (PaO_2).

Clinical and laboratory findings

The clinical and laboratory data in the study were based on the patients' medical records. TAAs were evaluated, including carcinoembryonic antigen (CEA), alpha-fetoprotein, cytokeratin-19 fragment (CYFRA21-1), neuron-specific enolase (NSE). The cut-off value of TAAs was according to the normal range of the commercial kits. MSAs (anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, anti-OJ, anti-Mi-2α, anti-Mi-2β, anti-signal recognition particle, anti-nuclear matrix protein 2, anti-melanoma differentiation-associated gene 5 [*MDA5*], anti-transcriptional intermediary factor 1γ, and anti-SAE1) and MAAs (anti-Ro-52, anti-polymyositis [PM]-Scl100, anti-PM-Scl75, and anti-Ku) were measured by immunoblotting according to manufacturers' instructions (Euroimmun, Germany). The results were arbitrarily classified as negative (0/3+), weakly (1+/3+), moderately (2+/3+), or strongly (3+/3+) reactive by two independent laboratory technicians who had no knowledge of the diagnostic data from each analyzed case. Besides, weakly, moderately, and strongly reactive were defined as positive.

Statistical analysis

Data analyses were performed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous data with normal distribution were expressed as the mean ± standard deviation and differences between groups were analyzed by one-way analysis of variance. Continuous data with skewed distribution were expressed as median (P25, P75) and differences between groups were analyzed by Kruskal-Wallis test. Dichotomous variables were reported as frequency (percentages) and differences between groups were compared using the Chi-square test (or Fisher exact test when appropriate). Univariate and multivariate logistic regression analysis were adopted to identify risk factors of different types of ILD. The variables assessed in univariate regression analysis were entered as independent variables in multivariate logistic regression analysis when P value <0.1. Two-sided $P < 0.05$ was considered statistically significant. P values were adjusted in multiple tests by the Bonferroni correction.

Results

Clinical characteristics of patients

Demographics and clinical features are shown in Table 1. Most patients were female (80.6%) and the average age at onset was 49.0 ± 12.4 years. For cutaneous manifestations, Gottron sign (80.5%) were the most common, followed by V/Shawl neck sign (52.8%), heliotrope eruption (50.0%), mechanic's hands (38.0%), cutaneous pruritus (30.6%), and perionychia erythma (22.2%). Skin ulceration and cutaneous calcinosis were relatively rare (8.3% and 5.6%, respectively). For systemic symptoms, arthralgia (53.7%) was the most frequent, and non-infectious fever (38.0%) and weight loss (35.2%) were also common at the time of CADM diagnosis. The presence of ILD was observed in 87 (80.5%) patients, 39 (36.1%) with A/SIP and 48 (44.4%) with CIP; and the most common respiratory symptom was dyspnea (55.6%). Remarkably,

Table 1: Comparison of demographics, clinical features, and TAAs in CADM.

Items	Overall ($n=108$)	Without ILD ($n=21$)	A/SIP ($n=39$)	CIP ($n=48$)	F/χ^2	P
Demographic feature						
Age (years), mean ± SD	50.4 ± 12.1	46.3 ± 15.6	51.6 ± 10.7	51.3 ± 11.3	1.536¶	0.220
Female, *n* (%)	87 (80.6)	15 (71.4)	32 (82.1)	40 (83.3)	1.409‖	0.494
Smoking history, *n* (%)	17 (15.7)	4 (19.0)	8 (20.5)	5 (10.4)	1.869‖	0.393
Age of onset (years), mean ± SD	49.0 ± 12.4	44.8 ± 15.6	50.9 ± 11.0	49.3 ± 11.7	1.705¶	0.187
Pulmonary involvement, *n* (%)	87 (80.5)					
Dry cough,	45 (40.7)	–	21 (53.8)	23 (47.9)	–	–
Dyspnea on exertion	60 (55.6)	–	25 (64.1)	35 (72.9)	–	–
Velcro rale	46 (42.6)	–	24 (61.5)	22 (48.8)	–	–
ILD without symptoms	22 (20.4)	–	11 (28.2)	11 (22.9)	–	–
ILD onset before CADM diagnosed	15 (13.9)	–	9 (23.1)	6 (12.5)	–	–
Cutaneous manifestation, *n* (%)						
Gottron sign/papule	87 (80.5)	17 (81.0)	30 (76.9)	30 (62.5)	0.276‖	0.871
Mechanic's hands	41 (38.0)	4 (19.0)	16 (41.0)	21 (43.8)	4.028‖	0.133
Heliotrope eruption	54 (50.0)	13 (61.9)	21 (53.8)	20 (41.7)	2.755‖	0.252
V/shawl neck sign	57 (52.8)	13 (61.9)	22 (56.4)	22 (45.8)	1.837‖	0.399
Skin ulceration	9 (8.3)	1 (4.8)	3 (7.7)	5 (10.4)	0.644‖	0.725
Perionychia erythma	24 (22.2)	3 (14.3)	12 (30.8)	9 (18.8)	2.748‖	0.253
Systemic symptoms, *n* (%)						
Non-infectious fever	41 (38.0)	8 (38.1)	16 (41.0)	17 (35.4)	0.288‖	0.866
Arthralgia	58 (53.7)	10 (47.6)	23 (59.0)	25 (52.1)	0.799‖	0.671
Raynaud phenomenon	11 (10.2)	2 (9.5)	2 (5.1)	7 (14.6)	2.115‖	0.347
Weight loss	38 (35.2)	12 (57.1)	13 (33.3)	13 (27.1)	5.880‖	0.053
Serum TAAs* (ng/mL)						
CEA	2.89 (1.65, 5.47)	2.14 (1.48, 3.52)	5.01 (1.58, 6.40)†	2.45 (1.67, 4.87)§	**6.685**¶	**0.035**
AFP	2.46 (1.93, 3.28)	2.41 (1.64, 3.19)	2.61 (2.07, 3.33)	2.44 (1.88, 3.16)	1.800¶	0.407
CYFRA21-1	3.44 (2.09, 5.11)	2.01 (1.78, 2.73)	4.18 (3.28, 7.02)‡	3.49 (2.31, 5.49)†	**20.310**¶	**<0.001**
NSE	14.41 (11.28, 17.45)	13.29 (10.85, 17.39)	16.18 (13.82, 20.65)†	13.95 (10.97, 16.27)§	**9.004**¶	**0.011**

Values displayed as *n* (%), mean ± SD, or median (P25, P75) according to their features of distribution. *Fourteen patients did not have the data of serum tumor markers; †Adjusted $P < 0.05$, ‡Adjusted $P < 0.01$, compared with patients without ILD; §Adjusted $P < 0.05$, compared with patients with A/SIP; ‖Differences were analyzed by Chi-square test and the statistics value was χ^2; ¶Differences were analyzed by one-way analysis of variance and the statistics value was *F*. TAA: Tumor-associated antigens; CADM: Clinically amyopathic dermatomyositis; ILD: Interstitial lung disease; A/SIP: Acute or subacute interstitial pneumonitis; CIP: Chronic interstitial pneumonitis; SD: Standard deviation; CEA: Carcinoembryonic antigen; AFP: Alpha-fetoprotein; CYFRA21-1: Cytokeratin-19 fragment; NES: Neuron-specific enolase; –: Not applicable.

22 patients (20.4%) were asymptomatic ILD, only diagnosed after HRCT scan. Besides, 15 patients (13.9%) were initially complained with idiopathic ILD and diagnosed as CADM based on their later appearance of typical cutaneous manifestations. Significant differences were not seen among the three sub-groups (A/SIP, CIP, and without ILD) about demographic figures (age and gender) and clinical features (skin rash and systemic features).

TAAs in CADM-associated ILD

Patients without ILD had lower levels of CYFRA21-1 than patients with A/SIP and patients with CIP (2.01 [1.78, 2.73] *vs.* 4.18 [3.28, 7.02] *vs.* 3.49 [2.31, 5.49] ng/mL; $F = 20.306$, $P < 0.001$). Patients with A/SIP had higher levels of CEA and NSE than patients without ILD and patients with CIP (CEA: 5.01 [1.58, 6.40] *vs.* 2.14 [1.48, 3.52] *vs.* 2.45 [1.67, 4.87] ng/mL; $F = 6.685$, $P = 0.035$; NSE: 16.18 [13.82, 20.65] *vs.* 13.29 [10.85, 17.39] *vs.* 13.95 [10.97, 16.27] ng/mL; $F = 9.004$, $P = 0.011$). TAAs were not measured in 14 patients.

Myositis autoantibodies profiles and their distribution in CADM-associated ILD

Myositis autoantibody testing was performed in 84 of total 108 patients, and their results and the relationship between antibodies profiles and ILD are displayed in Table 2. Among all the MSAs in our study, anti-MDA5 was the most commonly detected autoantibody (29.9%). Anti-aminoacyl-tRNA synthetase antibodies (anti-ARS) were relatively less common in CADM. The positive rate of anti-PL-7 was 12.0%, followed by anti-Jo-1 (10.8%), anti-PL-12 (8.4%), anti-OJ (3.6%), and anti-EJ (1.2%). Intriguingly, anti-Ro-52 had the highest positivity rate (52.4%) among the MAAs. Other MSAs, such as anti-Ku (9.6%), anti-PM-Scl100 (6.0%), and anti-PM-Scl75 (6.0%) were much less frequent in CADM. Chi-square test was used to explore the difference of distribution of myositis autoantibodies in different types of ILD. The positive rate of anti-MDA5 was the highest in patients with A/SIP (44.1%) than patients without ILD (14.3%) and patients with CIP (22.2%). Anti-PL-12 had a higher positive rate in patients with CIP than that in patients with A/SIP (19.4% *vs.* 0, $P = 0.011$). Anti-Ro-52 showed a higher positive rate in patients with CIP than that in patients without ILD (66.7% *vs.* 28.6%, $P = 0.025$).

Risk factors of ILD in patients with CADM

In the overall patients of CADM, the results of univariate models found that elevation of CYFRA21-1 (odds ratio [OR] = 8.571, 95% confidence interval [CI] [2.280–32.225], $P = 0.001$) and CEA (OR = 5.043, 95% CI [1.079–23.565], $P = 0.040$) were positively associated with ILD in CADM, and multivariate logistic models showed elevation of CYFRA21-1 was a risk factor for ILD (OR = 17.838, 95% CI [2.062–154.297], $P = 0.009$) [Table 3].

Table 2: Comparison of myositis autoantibodies in CADM.

Items	Overall ($n = 84$)	Without ILD ($n = 14$)	AIP/SIP ($n = 34$)	CIP ($n = 36$)	χ^2	*P*
MSA						
Anti-Mi-2α	1 (1.2)	0	0	1 (2.8)	1.221	0.269
Anti-Mi-2β	4 (4.8)	2 (14.3)	0	2 (5.6)	7.328	0.120
Anti-TIF-1γ	6 (7.2)	2 (14.3)	3 (8.8)	1 (2.8)	2.256	0.324
Anti-MDA5	25 (29.9)	2 (14.3)	15 (44.1)*	8 (22.2)†	**6.002**	**0.049**
Anti-NXP2	4 (4.8)	2 (14.3)	1 (2.9)	1 (2.8)	3.361	0.186
Anti-SAE1	2 (2.4)	0	1 (2.9)	1 (2.8)	0.412	0.814
Anti-SRP	4 (4.8)	0	2 (5.9)	2 (5.6)	0.844	0.656
Anti-Jo-1	9 (10.8)	0	2 (5.9)	7 (19.4)	6.000	0.051
Anti-PL-7	10 (12.0)	1 (7.1)	5 (14.7)	4 (11.1)	0.579	0.749
Anti-PL-12	7 (8.4)	0	0	7 (19.4)†	**10.182**	**0.006**
Anti-EJ	1 (1.2)	0	0	1 (2.8)	1.349	0.509
Anti-OJ	3 (3.6)	0	0	3 (8.3)	4.148	0.126
MAA						
Anti-Ku	8 (9.6)	2 (14.3)	1 (2.9)	5 (13.9)	2.874	0.238
Anti-PM-Scl100	5 (6.0)	1 (7.1)	2 (5.9)	2 (5.6)	0.046	0.977
Anti-PM-Scl75	5 (6.0)	2 (14.3)	2 (5.9)	1 (2.8)	2.385	0.303
Anti-Ro-52	44 (52.4)	4 (28.6)	16 (47.1)	24 (66.7)*	**6.513**	**0.039**

Values are displayed as *n* (%). *$P < 0.017$ (0.05/3), compared with patients without ILD; †$P < 0.017$ (0.05/3), compared with patients with A/SIP; CADM: Clinically amyopathic dermatomyositis; ILD: Interstitial lung disease; A/SIP: Acute or subacute interstitial pneumonitis; CIP: Chronic interstitial pneumonitis; MAA: Myositis-associated antibodies; MDA5: Melanoma differentiation-associated gene 5; MSA: Myositis-specific antibodies; NXP2: Nuclear matrix protein 2; SRP: Signal recognition particle; PM: Polymyositis; TIF: Transcription intermediary factor.

Table 3: Risk factors for ILD in CADM by logistic models ($n = 108$).

	Univariate analysis			Multivariate analysis		
Variables	*B*	OR (95% CI)	*P*	*B*	OR (95% CI)	*P*
CYFRA21-1	2.148	8.571 (2.280–32.225)	**0.001**	2.881	17.838 (2.062–154.297)	**0.009**
NSE	0.847	2.333 (0.700–7.773)	0.168			
CEA	1.618	5.043 (1.079–23.565)	**0.040**	2.115	8.287 (0.844–81.363)	0.070
Anti-Ro-52 (2+ to 3+)	1.304	3.684 (0.959–14.153)	0.058	1.512	4.536 (0.938–21.937)	0.060
Anti-MDA5 (2+ to 3+)	0.492	1.636 (0.330–8.122)	0.547			
Anti-Jo-1 (2+ to 3+)	19.691	356,345,659 (0, ∞)	0.999			
Anti-PL-12 (2+ to 3+)	19.683	353,385,112 (0, ∞)	0.999			

CADM without ILD as control group. ILD: Interstitial lung disease; CADM: Clinically amyopathic dermatomyositis; OR: Odds ratio; CI: Confidence interval; CYFRA21-1: Cytokeratin-19 fragment; NSE: Neuron-specific enolase; CEA: Carcinoembryonic antigen; MDA5: Melanoma differentiation-associated gene 5.

In patients with CADM-ILD, the univariate logistic regression analysis showed that both higher titer of anti-MDA5 and elevation of NSE were positively associated A/SIP, OR = 1.429, 95% CI (1.193–14.598), $P = 0.025$ and OR = 10.000, 95% CI (1.125–88.910), $P = 0.039$, respectively, and higher titer of anti-Ro-52 was negatively associated with A/SIP (OR = 0.332, 95% CI [0.126–0.874], $P = 0.026$). Furthermore, the multivariate logistic models indicated that higher titer of anti-MDA5 was a risk factor for A/SIP (OR = 5.697, 95% CI [1.242–26.130], $P = 0.025$), and higher titer of anti-Ro-52 was a risk factor for CIP (OR = 0.308, 95% CI [0.091–0.922], $P = 0.036$) [Table 4].

Discussion

In this study, we retrospectively reviewed the clinical features of CAMD patients with ILD. By comprehensive analysis on the distribution of myositis autoantibodies and TAAs in CADM-ILD, we found some MSAs, MAAs, and TAAs were might be useful for the prediction of different types of CADM-ILD.

CADM is frequently complicated by ILD, and rapidly progressive ILD are life-threatening in Asian population.[6,19] In our study, more than 80% patients suffered ILD, A/SIP was 36.1%; but one fifth were asymptomatic when diagnosed with CADM, reminding rheumatologists that lung HRCT might be served as a routine test even in patients without respiratory complains.

Previous studies have reported that some MSAs and MAAs were associated with CADM-ILD and anti-MDA5 was related with fatal RP-ILD.[4,12,20-22] In our study, the positive rate of anti-MDA5 was highest in patients with A/SIP, but there were two patients with anti-MDA5

Table 4: Risk factors for A/SIP in CADM-ILD by logistic models ($n = 87$).

Variables	Univariate analysis			Multivariate analysis		
	B	OR (95% CI)	*P*	*B*	OR (95% CI)	*P*
CYFRA21-1	0.680	1.974 (0.682–5.715)	0.210			
NSE	2.303	10.000 (1.125–88.910)	**0.039**	1.159	3.184 (0.967–10.526)	0.057
CEA	0.879	2.407 (0.831–6.976)	0.106			
Anti-Ro-52 (2+ to 3+)	–1.103	0.332 (0.126–0.874)	**0.026**	–1.176	0.308 (0.091–0.922)	**0.036**
Anti-MDA5 (2+ to 3+)	1.429	4.174 (1.193–14.598)	**0.025**	1.740	5.697 (1.242–26.130)	**0.025**
Anti-Jo-1 (2+ to 3+)	–1.272	0.280 (0.030 –2.636)	0.266			
Anti-PL-12 (2+ to 3+)	0.121	1.129 (0.150–8.500)	0.906			

CADM with CIP as control group. A/SIP: Acute or subacute interstitial pneumonitis; CADM: Clinically amyopathic dermatomyositis; OR: Odds ratio; CI: Confidence interval; ILD: Interstitial lung disease; CIP: Chronic interstitial pneumonitis; CYFRA21-1: Cytokeratin-19 fragment; NSE: Neuron-specific enolase; CEA: Carcinoembryonic antigen. MDA5: Melanoma differentiation-associated gene 5.

positivity who did not suffer ILD at the time of diagnosis. These two patients had been followed up for 1 to 3 years without developing ILD, suggesting that not all anti-MDA5 positive patients would definitely suffer A/SIP in the disease course. This suggested that the relationship between anti-MDA5 and CADM associated ILD needs further exploration.

Anti-ARS-positive patients were reported to have a chronic progressive and repetitive tendency in dermatomyositis,[23,24] which is consistent with our results. We found that anti-Jo-1 and anti PL-12 were associated with CADM-ILD, especially CIP. Anti-Ro-52 is usually found in more than 30% of PM/dermatomyositis patients, and the positive rate is even higher in PM/dermatomyositis-ILD patients.[9,11,12,25] Patients with isolated anti-Ro-52 in dermatomyositis could develop RP-ILD, but had good prognosis in dermatomyositis.[17] We demonstrated that anti-Ro-52 were significant higher in CADM-ILD and was effective in predicting CIP.

Serum tumor markers were reported to be elevated in ILD, including connective tissue diseases associated ILD and idiopathic pulmonary fibrosis,[15,17,26] but the precise mechanisms of elevation of tumor markers in ILD are still unknown, partially because of pneumocytes proliferation.[15] We found that CYFRA21-1 was a predictor for CADM-ILD, and NSE was positively associated with A/SIP, which suggested that elevated tumor markers should be evaluated to check whether there is a potential of A/SIP.

Some limitations of our study should also be considered. First, this study was retrospective cross-sectional and conducted among inpatients at single-center, so selection bias could not be excluded. Second, due to the commercial immunoblotting kits, the myositis autoantibodies were measured by immunoblotting, so it cannot reflect the exact concentration even though the results were classified as 0, 1+, 2+, 3+, and we neither did not detect part of MSAs (anti-KS, anti-ZO, anti-YRS) and MAAs (anti-cN-1A, anti-fibrillarin). Therefore, utilizing a prospective cohort or multi-center studies, are needed to confirm the distribution and clinical association of myositis antibodies in further studies.

In conclusion, our study revealed the clinical significance of serum tumor markers and myositis antibodies in CADM-ILD. CYFRA21-1 was a predictor for ILD. In CADM-ILD patients, anti-MDA5 might serve as a predictive biomarker for A/SIP. Anti-Ro-52, the most common MAAs, was a risk factor for CIP. Further researches might verify our findings by multi-center studies and explore the prognostic value for myositis antibodies by a prospective cohort.

Acknowledgements

The authors thank Dr. Hui-Xin Liu for support in the statistics of the project.

Funding

This work was supported by grants from the National Natural Science Foundation of China (Nos. 81801615 and 81871289).

Conflicts of interest

None.

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How to cite this article: Gan YZ, Zhang LH, Ma L, Sun F, Li YH, An Y, Li ZG, Ye H. Risk factors of interstitial lung diseases in clinically amyopathic dermatomyositis. Chin Med J 2020;133:644–649. doi: 10.1097/CM9.0000000000000691