Analysis of clinical features and risk factors for patients with idiopathic inflammatory myopathy complicated by *Pneumocystis jirovecii* pneumonia

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Abstract

Objective

To analyse the clinical characteristics and risk factors for Pneumocystis jirovecii pneumonia (PJP) in idiopathic inflammatory myopathy patients (IIM).

Methods

Retrospective analysis was conducted in 432 patients with idiopathic inflammatory myopathy by evaluation of demographic information, clinical characteristics, and treatment data. Receiver operating characteristic curves were used to evaluate the predictive value of (1-3)-β-DG-glucan for diagnosis of PJP. Multiple logistic regression analysis was used to identify independent risk factors for PJP occurrence.

Results

Of the enrolled patients, 34 had PJP and were defined as the PJP+IIM group. The other patients that did not have PJP were defined as the PJP-IIM group. By univariate analysis, dermatomyositis, anti-MDA5 antibodies, rash, concomitant respiratory symptoms, decreased absolute lymphocyte count, increased erythrocyte sedimentation rate, increased ferritin levels and concurrent bacterial or viral infections were found to be risk factors for PJP in these patients. Among these, dermatomyositis, rash, decreased absolute lymphocyte count, and concurrent viral infection were the most important independent risk factors for PJP.

Conclusion

Dermatomyositis, rash, decreased absolute lymphocyte count, and concurrent viral infection are independent risk factors for the occurrence of PJP in idiopathic inflammatory myopathy patients.

Key words

idiopathic inflammatory myopathies, *Pneumocystis jirovecii* pneumonia, dermatomyositis, skin rash, absolute lymphocyte decrease, virus concurrent infection anti-MDA5 antibodies

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Introduction

Idiopathic inflammatory myopathy (IIM) is a group of chronic autoimmune diseases characterised by muscle damage and rash. IIM is separated into five main subgroups: dermatomyositis (DM), antisynthetase syndrome (ASS), polymyositis (PM), immune-mediated necrotising myopathy (IMNM), and inclusion body myositis (IBM) (1). Due to the susceptibility of patients with IIM to interstitial lung disease, combined with the use of glucocorticoids, immunosuppressants, and biologics for treatment, they are prone to pulmonary infections. In recent years, *Pneumocystis jirovecii* pneumonia (PJP) has received increasing attention. PJP is a rare but potentially life-threatening opportunistic infection. In the past, PJP mostly occurred in HIV patients, but with reverse transcriptional treatment of HIV patients, the incidence of PJP has been significantly reduced. However, with a deepening understanding of rheumatic and immune diseases, advances in immunosuppressive therapy, organ transplantation, and tumour chemotherapy, the number of non-HIV patients with PJP has gradually increased (2, 3).

According to reports, PJP in non-HIV but immunosuppressed patients has a more insidious onset, faster progression, and a mortality rate as high as 35–55% (4). The gold standard for diagnosis of PJP is microscopy, but due to its invasive nature and low sensitivity, more effective diagnostic methods have been sought. Measurement of (1-3)-β-DG-glucan (β-DG) is an auxiliary diagnostic method. However, due to the low burden of Pneumocystis jirovecii in non-HIV patients, the value of such measurement is controversial (5). With the absence of a simple and reliable diagnostic method, delays in diagnosis ultimately lead to high mortality rates.

Therefore, the objective of this study was to provide assistance for early identification of high-risk PJP patients with inflammatory myopathy. The objective has been accomplished by presentation of the clinical characteristics of PJP inflammatory myopathy as well as the identification of independent risk factors for the disease.

Materials and methods

Patients and diagnosis

A retrospective analysis was conducted on 432 patients with IIM who had complete data from June 2016 to November 2024. The patients were recruited from the Second Affiliated Hospital of Chongqing Medical University. They were divided into a PJP+IIM group and a PJP-IIM group based on whether they had coexisting PJP. The diagnostic criteria for patients with IIM was based on EULAR/ACR Classification Criteria (6). In this study, diagnosis of PM/DM, IMNM and ASS were based on IIM criteria (7-10). No confirmed cases of IBM were identified among the 432 patients with IIM. All patients at high risk for PJP underwent pulmonary cysticercosis microscopy (Gomori methenamine silver (GMS) staining) for Pneumocystis jirovecii, but the results of all tests were negative. Based on the presence of Pneumocystis jirovecii in the bronchoalveolar lavage fluid (NGS) of the patients, combined with clinical and imaging features, a diagnosis was made, indicating the possibility of PJP (11).

Data collection

The basic information of patients was collected retrospectively by reviewing medical records, including gender, age, smoking, diabetes, clinical manifestations, other respiratory diseases, laboratory tests, lung high-resolution computed tomography (HRCT), specific antibodies, non-specific antibodies, and treatment. Concurrent fungal, bacterial, viral, and mycoplasma/chlamydia infections were also analysed. Concurrent infection required sputum culture, faecal culture, urine culture, and next-generation sequencing. Bronchoalveolar lavage and pathogen nucleic acid testing were used to confirm diagnosis. The Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University approved this study, with the ethics number 91.

Statistics

SPSS25 statistical software was used for statistical analysis. Continuous variables with or without a normal distribution are represented as means and

standard deviation (SD) or median and interquartile range (IQR). Categorical variables are represented by numbers and percentages. The Mann Whitney test or t-test were used to analyse continuous variables. The Chi square test or Fisher's exact test were used to analyse categorical variables. Receiver operating characteristic (ROC) curves were used to analyse the predictive value and critical value of β-DG for diagnosis of PJP. Univariate and multivariate logistic regression analysis were used to determine the factors associated with the occurrence of PJP. All regression results are expressed as the odds ratio (OR) with 95% confidence interval (95% CI). A p-value <0.05 was considered significant.

Results

We collected clinical data from a total of 432 patients with a diagnosis of IIM, of whom 7.9% (34/432) had concurrent infection with PJP. Patients with IIM were divided into a PJP+ group and a PJP-IIM group based on whether they were infected with PJP or not. Risk factors for PJP infection were evaluated. Among the 34 patients with PJP+IIM, 27 (79.4%) were females (Table I), with a median age at PJP diagnosis of 53.59±9.36 years. In this study, 270 (67.8%) patients were female. Of the patients, 398 exhibited PJP-IIM, with a median age at PJP diagnosis of 54.43±13.44 years. There was no difference in age between the two groups. In terms of subtype classification of IIM, there were 29 cases (85.3%) of DM in the PJP+IIM group and 210 cases (52.8%) of DM in the PJP-IIM group, with significant clinical difference between the two groups (85.3% *vs*. 52.8%, p<0.001). There were five cases (14.7%) of ASS in the PJP+IIM group and 135 cases (33.9%) of ASS syndrome in the PJP-IIM group. There were no patients with PM or IMNM in the PJP+IIM group. There were 21 cases (5.3%) of PM and 32 cases (8%) of IMNM in the PJP-IIM group. There were no significant differences between the two groups regarding PM and IMNM (p>0.05).

There were no significant differences between the PJP+IIM and PJP-IIM groups in terms of smoking and diabetes mellitus.

In patients with myositis, the primary symptoms of IIM include respiratory (cough, sputum production, fever, dyspnoea), muscle (myalgia, fatigue), and joint (arthralgia, joint swelling), as well as rash (shawl sign, V-shaped sign, gottron sign, heliotrope rash, mechanic's hands, periungual lesions) and other symptoms (dysphagia, difficulty speaking, hoarseness). Among them, PJP+ patients were more likely to have respiratory symptoms (91.2% *vs*. 70.6%, p=0.01) and rash (82.4% *vs*. 49%, p<0.001). There were no significant differences in muscle, joint, and other symptoms between groups.

HRCT identified 25 cases of interstitial lung disease (ILD) in the PJP+IIM group and 247 cases in the PJP-IIM group (73.5% *vs*. 62.1%, p=0.184),

Table I. Demographic and clinical characteristics for PJP among IIM.

Variables		PJP-IIM (n=398)	PJP+IIM (n=34)	p-value
Age		54.43 ± 13.44	53.59 ± 9.36	0.630
Gender	Female	270 (67.80%)	27 (79.40%)	0.162
subtype classification of IIM	DM	210 (52.80%)	29 (85.30%)	<0.001
	ASS	135 (33.90%)	5 (14.70%)	0.022
	PM	21 (5.30%)	0 (0.00%)	0.338
	IMNM	32 (8.00%)	0 (0.00%)	0.086
Smoking		84 (21.10%)	4 (11.80%)	0.194
Diabetes mellitus		42 (10.60%)	4 (11.80%)	>0.999
Clinical symptoms	Respiratory	281 (70.60%)	31 (91.20%)	0.010
	Muscle	249 (62.60%)	24 (70.60%)	0.352
	Joint	183 (46.00%)	12 (35.30%)	0.229
	Rash	195 (49.00%)	28 (82.40%)	<0.001
	Other symptoms	38 (9.50%)	6 (17.60%)	0.229
Interstitial lung disease		247 (62.10%)	25 (73.50%)	0.184
Respiratory diseases		15 (3.80%)	4 (11.80%)	0.081

DM: dermatomyositis; ASS: antisynthetase syndrome; PM: polymyositis; IMNM; immune-mediated necrotising myopathy; IBM: inclusion body myositis.

Table II. Comparison of experimental data in patients with IIM.

	PJP-IIM (n=398)	PJP+IIM (n=34)	p-value
L	1.30 ± 0.88	0.80 ± 0.51	0.001
N	5.87 ± 3.48	5.98 ± 2.76	0.866
PLT	223.16 ± 89.35	191.92 ± 84.86	0.050
RBC	4.49 ± 6.99	4.00 ± 0.53	0.686
WBC	7.79 ± 3.91	7.34 ± 3.01	0.500
ALB	35.24 ± 5.98	35.03 ± 8.44	0.847
PAB	207.95 ± 83.33	205.18 ± 81.21	0.852
SOD	110.57 ± 31.81	110.64 ± 25.42	0.990
Cr	54.41 ± 21.39	55.04 ± 17.57	0.869
Urea	7.28 ± 23.10	5.84 ± 1.74	0.717
HB	128.00 (26.00)	144.50 (19.25)	0.003
CRP	5.24 (14.83)	14.89 (25.32)	0.001
PCT	0.10 (0.11)	0.07 (0.09)	0.384
ALT	36.00 (66.50)	42.00 (78.00)	0.423
AST	40.00 (85.20)	39.50 (114.50)	0.589
LDH	333.00 (250.25)	312.00 (195.69)	0.822
CK	160.00 (1229.54)	45.50 (340.53)	0.001
CKMB	16.60 (42.43)	12.90 (17.10)	0.043
ESR	29.50 (37.00)	47.50 (34.75)	0.004
Ferritin	610.89 (353.36)	720.10 (999.90)	0.040
β-DG	40.70 (40.70)	59.80 (75.05)	<0.001
GM	0.34 (0.34)	0.00 (0.00)	<0.001

L: lymphocyte; N: neutrophils; PLT: platelets; RBC: red blood cells; WBC: white blood cells; ALB: albumin; PAB: pre-albumin; SOD: superoxide dismutase; Cr: creatinine; HB: haemoglobin; CRP: C reactive protein; PCT: procalcitonin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CK: creatine kinase; CK-MB: creatine kinase-MB; ESR: erythrocyte sedimentation rate; (β-DG): (1-3)-β-DG-glucan; GM: galactomannan.

with no statistical significance between the two groups. Respiratory diseases including asthma, chronic obstructive pulmonary disease, and bronchitis were not statistically significant between the two groups (p=0.081).

In terms of laboratory tests (Table II), haemoglobin (HB), C reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, and β-DG were higher in the PJP+IIM group compared with the PJP-IIM group (HB: 144.50(19.25) *vs*. 128.00(26.00), p=0.003; CRP: 14.89 (25.32), *vs*. 5.24 (14.83), p=0.001; ESR: 47.50 (34.75) *vs*. 29.50 (37.00), p=0.004; ferritin: 720.10 (999.90) *vs*. 610.89 (353.36), p=0.04; and β-DG: 59.80 (75.05) *vs*. 40.70 (40.70), p<0.001). Conversely, lymphocyte (L), creatine kinase (CK), creatine kinase-MB (CK-MB), and the galactomannan (GM) were lower in the PJP+IIM group were lower compared with the PJP-IIM group (L: 0.80±0.51 *vs*. 1.30±0.88, p=0.001, CK: 45.50 (340.53) *vs*. 160.00 (1229.54), p=0.001, CK-MB: 12.90 (17.10) *vs*. 16.60 (42.43), p=0.043, GM: 0.00 (0.00) *vs*. 0.34 (0.34) p<0.001). Neutrophils (N), platelets (PLT), red blood cells (RBC), white blood cells (WBC), albumin (ALB), pre-albumin (PAB), superoxide dismutase (SOD), creatinine (Cr), urea, procalcitonin (PCT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) were not statistically different between groups (all p>0.05).

Herein, myositis antibodies are classified into specific antibodies and non-specific antibodies with no statistically difference between the PJP+IIM group and the PJP-IIM group. As previous studies have shown that different antibody types have different effects on whether to combine PJP, this article subdivides specific antibodies and non-specific antibodies (Table III). Among the 432 patients, antibody positivity rates were was as follows: anti-Ro52 antibody was the most common, followed by anti-MDA5 antibody. Within the PJP+IIM group, there were 19 cases positive for anti-MDA5 antibody, accounting for 55.9% of cohort. Anti-MDA 5 autoantibodies were more commonly found in PJP+IIM patients compared with PJP-IIM patients (55.9% *vs*. 23.4%, p<0.001), which was also consistent with previous studies, with 18 (52.9%) cases positive for anti-Ro52 antibodies in the PJP+IIM group and 190 (47.7%) in the PJP-IIM group. The proportion of the PJP+IIM group with anti-Ro52 antibodies was higher than the PJP-IIM group, but not statistically significant (Table III). There were no statistically significant differences between the two groups for the remaining antibodies.

Results for IIM patients with concurrent microbial infections are found in (Fig. 1). Further analysis of the concurrent infection status of the two groups (Table IV) showed that the PJP+IIM

Table III. Classification of myositis antibody subtypes.

	PJP-IIM (n=398)	PJP+IIM (n=34)	p-value
Specific antibodies	326 (81.9%)	29 (85.3%)	0.621
Non-specific antibodies	203 (51.0%)	18 (52.9%)	0.828
Anti-Jo1	77 (19.3%)	4 (11.8%)	0.277
Anti-MDA5	93 (23.4%)	19 (55.9%)	<0.001
Anti-SRP	31 (7.8%)	0 (0.0%)	0.179
Anti-EJ	32 (8.0%)	3 (8.8%)	>0.999
Anti-TIF1γ	25 (6.3%)	0 (0.0%)	0.261
Anti-PL7	28 (7.0%)	1 (2.9%)	0.576
Anti-Mi2	24 (6.0%)	0 (0.0%)	0.279
Anti-NXP2	15 (3.8%)	2 (5.9%)	0.882
Anti-PL12	17 (4.3%)	0 (0.0%)	0.441
Anti-OJ	14 (3.5%)	0 (0.0%)	0.544
Anti-SAE	6 (1.5%)	2 (5.9%)	0.125
Anti-HMGCR	7 (1.8%)	0 (0.0%)	>0.999
Anti-Ro52	190 (47.7%)	18 (52.9%)	0.560

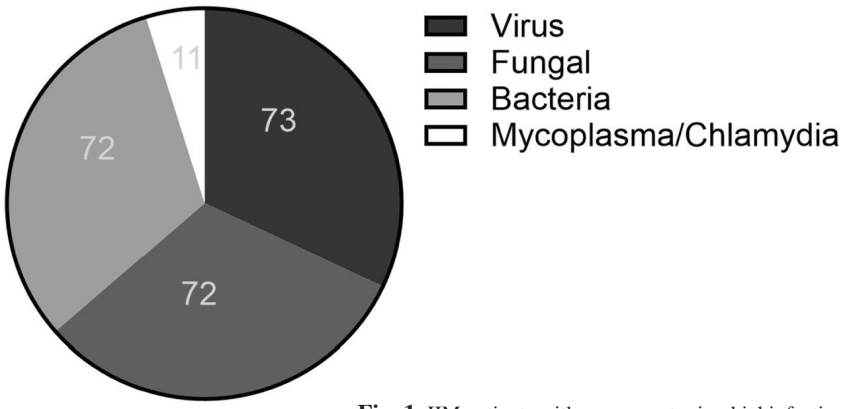

Fig. 1. IIM patients with concurrent microbial infections.

Table IV. IIM patients with concurrent microbial infections.

	PJP-IIM (n=398)	PJP+IIM (n=34)	p-value
Virus	50 (12.6%)	23 (67.6%)	<0.001
Fungal	63 (15.8%)	9 (26.5%)	0.110
Bacteria	59 (14.8%)	13 (38.2%)	<0.001
Mycoplasma/Chlamydia	11 (2.8%)	0 (0.0%)	>0.999

Table V. Treatment for IIM patients.

	PJP-IIM(N=398)	PJP+IIM(N=34)	p-value
GC	365 (91.7%)	34 (100.0%)	0.158
GC+DMARDs	294 (73.9%)	23 (67.6%)	0.431
GC+DMARDs+IVIG	65 (16.3%)	7 (20.6%)	0.523

GC: glucocorticoid; DMARDs: disease-modifying anti-rheumatic drugs; IVIG: intravenous immunoglobulin.

Table VI. Univariate and multivariate analysis of PJP occurs.

	Univariable analysis			Multivariable analysis		
	OR	95%CI	*p*-value	OR	95%CI	*p*-value
DM	5.192	1.970-13.687	0.001	4.319	1.438-12.974	0.009
ASS	0.336	0.127-0.887	0.028			
Anti-MDA5	4.154	2.031-8.497	<0.001			
Respiratory	4.302	1.290-14.350	0.018			
Rash	4.858	1.969-11.989	0.001	3.083	1.122-8.471	0.029
L	0.207	0.088-0.488	<0.001	0.368	0.162-0.836	0.017
HB	1.005	0.995-1.015	0.371			
CRP	1.008	0.999-1.017	0.090			
CK	1.000	1.000-1.000	0.166			
CKMB	0.996	0.991-1.002	0.195			
ESR	1.016	1.004-1.028	0.007			
Ferritin	1.001	1.000-1.002	0.005			
GM	0.003	0.000-0.043	<0.001			
Bacteria	3.557	1.689-7.492	0.001			
Virus	14.553	6.689-31.659	<0.001	15.422	6.597-36.054	<0.001

DM: dermatomyositis; ASS: anti synthetase syndrome; L: lymphocyte; HB: haemoglobin; CRP: C reactive protein; CK: creatine kinase; CK-MB: creatine kinase-MB; ESR: erythrocyte sedimentation rate; GM: galactomannan (GM).

group was more prone to concurrent infection with viruses (67.6% *vs*. 12.6%, $p<0.001$) and bacteria (38.2% *vs*. 14.8%, $p<0.001$) than the PJP-IIM group. There were no significant statistical differences in fungal and mycoplasma/chlamydia infection between the two groups.

The treatment regimens were categorised into three groups: glucocorticoid therapy alone, glucocorticoid therapy combined with DMARDs, and glucocorticoid therapy combined with DMARDs and intravenous immunoglobulin. The DMARDs mainly included cyclophosphamide, tacrolimus, methotrexate, cyclosporine, hydroxychloroquine, tofacitinib, iguratimod, leflunomide, tripterygium, mycophenolate mofetil, and azathioprine. We compared the treatment regimens (Table V) between the two groups and the proportion of patients in the PJP+IIM group who received glucocorticoid therapy and DMARDs was similar in both groups. The proportion of patients in the PJP+IIM group who received glucocorticoids + DMARDs + intravenous immunoglobulin, was higher than that in the PJP-IIM group. There was no statistical difference among the three regimens.

Finally, we explored the risk factors for the development of PJP, allowing for identification of patients at high risk. Based on the results of Tables I-V, significant risk factors with *p*-values <0.05 were included in a univariate logistic regression model. The identified factors were analysed in a multivariate logistic regression model (Table VI). β-DG was not included in the risk factor analysis because β-DG is a component of the cell wall of Pneumocystis and increased levels would be a consequence of PJP infection.

Multivariate logistics regression found that absolute lymphocytes decreased (OR 0.368, 95% CI 0.162–0.836, $p=0.017$) with concurrent viral infection (OR 15.422, 95% CI 6.597–36.054, $p<0.001$), dermatomyositis (OR 4.319, 95% CI 1.438–12.974, $p=0.009$), and rash (OR 3.083, 95% CI 1.122–8.471, $p=0.029$), serving as an independent risk factor for a poor prognosis.

The ROC curve constructed for β-DG is shown below (Fig. 2). The AUC was 0.698, the cut-off value for β-DG was 45.05 pg/ml, the sensitivity was 61.8%, and the specificity was 84.2%.

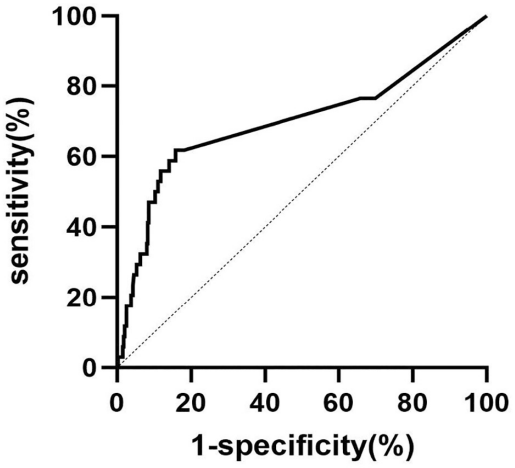

Fig. 2. ROC curve for β-DG. The area under the curve value is 0.698. The cut-off value for β-DG is 45.05 pg/mL. With this cut-off point, the sensitivity and specificity are 61.8% and 84.2% respectively.

Discussion

Due to the susceptibility of patients with IIM disease to interstitial lung disease, combined with the use of glucocorticoids, immunosuppressants, and biologics for treatment, they are prone to pulmonary infections. In recent years, PJP has received increasing attention. However, clinical characteristics of PJP are not obvious and early diagnosis is difficult in that there are no specific indicators to assess risk. Therefore, this study retrospectively analysed the clinical characteristics and risk factors for IIM combined with PJP.

In this study, ASS and DM were the two types of myositis with the great-

est proportion in IIM patients. The typical features of ASS are muscle inflammation, arthritis, interstitial lung disease, mechanic's hand, fever, and Raynaud's phenomenon. The prevalence of ILD was 67%-100% (12). As an important IIM subtype, DM patients with anti-MDA5 antibody positivity are frequently associated with rapidly progressive ILD (RP-ILD) and a poor patient prognosis (13). This study suggests that ASS might be a protective factor for PJP, though further validation is needed; it could also be due to the small sample size of ASS cases causing statistical bias. This study concluded that patients with DM and anti-MDA5 antibodies were more likely to develop PJP, with DM being an independent risk factor. Possible reasons may be as follows: first, the prevalent ILD and other pulmonary pathologies in DM patients not only compromise pulmonary mucosal barrier function but also create a permissive environment for opportunistic pathogen colonisation and infection (14-17). Consequently, we postulate that the coexistence of ILD in anti-MDA5-positive DM patients substantially increases their risk of developing PJP. Second, MDA5+DM patients are prone to acute attacks, which are often accompanied by RP-ILD. Most clinicians use large doses of glucocorticoids and multiple immunosuppressive agents as initial treatments for the disease (18). Glucocorticoids and immunosuppressive agents such as cyclophosphamide, methotrexate, and azathioprine are known risk factors for PJP (19).

Clinically, we often find that rash occurs in the metacarpophalangeal joints, elbows, chest, and back IIM patients, and this study concluded that rash is a risk factor for PJP. The rash also is less responsive to glucocorticoids and immunosuppressants, often requiring prolonged treatment (20, 21). The rash in some patients with anti-MDA5 antibodies can progress to deep ulcers, leading to infection (22). Studies have shown significant lung disease in MDA5+DM patients with extensive skin ulcers (23, 24). Skin ulcers are the strongest predictor of ILD in MDA5+DM patients (21). It is reasonable to assume that rash is more likely to be associated with lung disease and lung damage. Lung biopsy of a patient with DM-ILD and rash showed endothelial cell damage with necrotising capillarities (25), suggesting that the rash was related to vascular lesions. Therefore, physical examination is very important and screening for ILD should be completed for patients with rash.

Lymphocytes are an important marker of inflammation and tend to be low in patients with more severe lung infections (26). A total lymphocyte counts below 800/mm3 and/or $CD4^{+}$T counts below 200/mm3 are often considered to require PJP prophylaxis. Further, lymphocytopenia has been shown to be a risk factor for PJP according to the previous studies. (27, 28). However, the cause of decreased absolute lymphocyte count remains unclear, but we speculate that lymphocytopenia may be related to glucocorticoid use and lymphocyte escape. For the short term, glucocorticoids can move lymphocytes out of the circulation. Long term, glucocorticoids can reduce lymphocyte production. Thus, a lower absolute lymphocyte count suggests high-dose glucocorticoid therapy, which is strongly associated with the development of PJP (29). Further, the lungs are rich in lymphoid tissue, connective tissue, and blood vessels, creating conditions for lymphocytes to traffic to the lungs to participate in local immunity, resulting in a decrease in lymphocyte numbers (30).

ESR is an inflammatory marker of the body. In this study, the ESR in the PJP+IIM group was higher than that in the PJP-IIM group. Inflammation in patients with IIM increases the ESR, which may be related to tissue necrosis and damage, leading to increased serum ferritin levels (31). It is well known that ferritin is an acute phase reactant, and its level reflect the degree of acute or chronic inflammation. Ferritin is also a marker of macrophage activation and in this study, ferritin levels in the PJP+IIM group were higher than that in the PJP-IIM group. As such, ferritin may play a role in lung injury. The degree of lung involvement in Covid-19 patients has been related to ferritin (32, 33), with ferritin exacerbating acute lung injury through the autophagy-mediated ferritin deposition pathway (34). Ferritin deposition may also trigger inflammation leading to acute lung injury (35). In an autopsy of a patient with MDA5+DM, systemic ferritin-producing macrophages were found in the alveoli (36), suggesting that ferritin can cause lung injury by stimulating macrophage secretion or ferritin deposition in the lungs.

β-DG is a common cell wall antigen of most pathogenic fungi (37). PJP infection can lead to an increase in β-DG, and therefore we did not consider β-DG as a risk factor for PJP and did not include it in the multivariate logistics regression. This study constructed an ROC curve and found that the critical value of β-DG was 45.05 pg/ml, with a sensitivity of 61.8% and specificity of 84.2%. Previous studies have shown that β-DG can be used as a diagnostic aid for PJP, but due to differences in detection accuracy and background, as well as the association between β-DG and low non-HIV fungal burden, the critical value for non-HIV PCR is unclear (5). Although β-DG is not a specific fungal marker for PJP, if efforts are made to exclude patients with other fungal infections, β-DG testing can be used as an auxiliary tool for diagnosing PJP (38). In future studies, the significance of β-DG during infection should be considered.

Patients with autoimmune diseases often receive glucocorticoids and immunosuppressants, which increase infection risk. Bacterial infections, the most common in DM/PM, can exacerbate pulmonary inflammation, a known risk factor for PJP (39). Due to the ubiquitous nature of viruses and their ability to stimulate lymphatic reactions, viral infections have been considered a possible cause of autoimmune diseases (40). Concurrent infection with PJP and cytomegalovirus (CMV) has been widely described in previous studies, especially in anti-MDA5+DM patients, in whom EBV is highly correlated with its development (41). A recent study has shown that herpes virus is an independent risk factor for PJP (42). At present, research mainly focuses on the induction of PJP by EB and herpes viruses.

We consider the mechanism of virus induced PJP as follows: viral infection induces and exacerbates autoimmune disease through molecular simulation mechanisms (40, 43). Alternatively, the virus itself may directly activate antigen-presenting cells, leading to T cell activation, cytokine storm, and ultimately tissue damage.

Based on the above analysis, the risk factors for PJP in IIM patients, as well as the cut-off value, sensitivity, and specificity of β-DG for diagnosis of PJP, this form of pneumonia should be considered when β-DG levels are >45.05.

This study has several limitations, and follow-up confirmatory studies are needed. First, this is a retrospective study with a long follow-up period and possible bias in patient data collection, which is an inherent limitation of such studies. Second, on microscopic examination Pneumocystis was not found and as such was not conclusively confirmed. Third, the study does not thoroughly analyse the treatment protocol and offers limited guidance on PJP risk related to varying drug doses, treatment cycles, and other factors. In addition, pharmacological prophylaxis was not included and we cannot provide recommendations for prophylaxis. Finally, due to the small patient sample size, some of the identified risk factors for PJP have broad compliance.

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