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Interstitial lung disease associated with anti-PM-Scl antibody: A single center experience

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Anti-PM-Scl antibody was one of first with nucleolar specificity described as a marker antibody for polymyositis (PM) [1,2]. Due to the low prevalence of anti-PM-Scl antibody, associated clinical features have come from relatively small clinical studies that report its presence in PM, dermatomyositis (DM), or systemic sclerosis (SSc). However, prevalence has been reported to be higher in overlap syndromes of scleroderma with PM or DM, frequently called scleromyositis or sclerodermatomyositis [2–9]. The prevalence of interstitial lung disease (ILD) in patients with anti-PM-Scl antibody varies from 30 to 86% [2,4–10]. We retrospectively reviewed the clinical manifestations, imaging characteristics, and outcomes in patients with ILD associated with anti-PM-Scl antibody (January 2007 through December 2017).

There were 24 patients with scleromyositis spectrum and positive PM-Scl antibody tests out of 244 patients tested during the retrospective period of analysis. The majority were female (19/24, 79%) and mean age at diagnosis was 52 ± 16 years (range 24–84). Thirteen patients (13/24, 54%) had ILD (Table 1). There were no differences in age or smoking status, and the clinical features of skin involvement, arthritis/arthralgia, myositis, GERD or dysmotility, and malignancy between patients with and without ILD.

In the 13 patients with ILD, 5 (39%) had ILD as their first clinical presentation with 1 patient presenting with abnormal capillaroscopy (dilated capillary loops and hemorrhage) at last follow-up. Four patients (31%) presented with ILD simultaneously with scleromyositis features. Four patients (31%) developed pulmonary involvement following myositis, arthritis, and/or skin manifestation.

Patients with the diagnosis of ILD were followed for 9.5 ± 11 years (range 1–44). At the end of follow-up, 1 patient (8%) died at age 71 from progressive respiratory failure after declining transplant evaluation. Mean survival by Kaplan-Meier was 39.8 years (95% CI 31.9–47.6) in patients with ILD, and 12.8 years (95% CI 9.6–15.9) in patients without ILD. There was no statistically significant difference between patients with and without ILD (log rank test p-value 0.30).

In previous series of patients with anti-PM-Scl antibody, most were diagnosed with myositis and/or SSc, but clinical manifestations were highly variable [2–4,7–9,11,12]. The presence of ILD was higher in patients with scleromyositis than in patients with SSc or PM [13]. Lega and colleagues hypothesized that patients with anti-PM-Scl antibody belong to the same clinical diagnostic group as antisynthetase syndrome because they shared the clinical features of myositis, ILD, arthritis, sclerodactyly, sicca syndrome, Raynaud's phenomenon, and mechanic's hands [14]. However, a meta-analysis reported that patients with anti-PM-Scl antibody differed from those with antisynthetase syndrome by a greater prevalence of DM-specific rash, Raynaud's phenomenon, and sclerodactyly without a significant prevalence in ILD [12].

Anti-PM-Scl positive patients can present with ILD without overt extrapulmonary manifestation. While signs of connective tissue disease can develop later in some patients, pulmonary involvement may remain a sole manifestation.

Similar to other cohorts [14,15], the most common radiologic pattern in our patients was nonspecific interstitial pneumonia. In general, the natural course of the disease showed relatively slow progression or stability based on pulmonary physiology. Like others, we did not encounter acute presentations of ILD [9,14,15].

Standard therapy has not been established due to limited evidence. Corticosteroid therapy is the mainstay, which should be used cautiously in patients with scleroderma overlap as there is a risk of renal crisis. Inflammatory features in these patients respond to low to moderate doses of corticosteroids [3,4,16,17]. All patients in the present study also received immunosuppressive agents. Mycophenolate mofetil was frequently used in cases with pulmonary involvement or with myositis which resulted in ILD stability in most patients. Rituximab seems to be an option for more severe or refractory patients with ILD, producing favorable responses in both PFTs and chest imaging in patients who failed other immunosuppressive therapy (Fig. 1). From our observation, long term follow-up is recommended, and immunosuppressive therapy can stabilize or halt progression and thus improve prognosis.

Our cohort showed no difference in survival between anti-PM-Scl antibody positive patients with and without ILD, but this result is limited by the small sample. Esophageal dysmotility was associated with deteriorating pulmonary physiology; the frequency of esophageal dysmotility was lower in anti-PM-Scl patients, which might improve prognosis in patients with ILD associated with anti-PM-Scl antibody [18,19].

Disclosure

None for all authors.

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Table 1
Characteristics and outcomes of patients with ILD associated with anti PM-Scl antibody (N = 13).

Pt.	Age	Sex	Smoker	Skin	Myositis	Joint	GI	Positive serology	CT	PFT: initial visit	Follow-up (years)	Treatment	Outcome
1	43	F	Yes	+	+	+	+	ANA 1:160, Jo1, SSA, SSB	NSIP	FVC: 3.28, 96% DLCO: 14.6, 66%	17	Prednisone, methotrexate	Stable PFT, imaging
2	73	F	No	+	+	−	+	ANA 1:2560, SSA, SSB	NSIP	NA	1	Prednisone, mycophenolate	Stable respiratory symptoms; no initial PFT, imaging to compare
3	59	F	No	+	+	−	+	ANA 1:2560	NSIP	FVC: 1.6, 52% DLCO: 7.5, 36%	4	Prednisone, mycophenolate	Stable PFT; improving imaging
4	54	M	No	+	+	+	−	ANA 1:1280, SSA	OP	NA	Single evaluation	Prednisone, methotrexate	No respiratory symptoms; no initial PFT, imaging to compare
5	50	F	No	+	+	+	−	ANA 1:1280	NSIP	FVC: 2.25, 57% DLCO: 10.9, 46%	8	Prednisone monotherapy; mycophenolate, azathioprine, leflunomide, methotrexate, and cyclophosphamide intolerance; rituximab 2 infusions for myositis	Stable FVC with improving DLCO; improving imaging
6	84	F	No	+	−	+	−	ANA 1:320	NSIP	FVC: 2.62, 103% DLCO: 8.8, 45%	1	Mycophenolate, off prednisone	Stable PFT, imaging
7	56	M	No	−	−	−	−	ANA 1:1280	NSIP	FVC: 3.38, 61% DLCO: 17.3, 56%	5	Mycophenolate, off prednisone	Stable PFT, imaging
8	61	F	Yes	+	−	+	+	ANA 1:2560, SSA	NSIP	FVC: 2.25, 61% DLCO: 12.6, 55%	6	Methotrexate, off prednisone	Improving FVC with stable DLCO; improving imaging
9	65	M	Yes	−	−	+	+	ANA 1:160	NSIP	FVC: 2.87, 67% DLCO: 12.8, 48%	6	Mycophenolate, off prednisone	Improving FVC with stable DLCO; stable imaging
10	50	M	No	+	+	+	+	ANA 1:320, SSA	NSIP	FVC: 3.4, 67% DLCO: 19, 61%	11	Prednisone, methotrexate	Stable PFT, imaging
11	65	M	Yes	+	+	−	+	ANA 1:1280	NSIP	FVC: 2.6, 67% DLCO: 7.3, 34%	6	Azathioprine, off prednisone	Deceased at 71; progressive respiratory failure
12	24	F	No	−	−	+	−	ANA 1:160	UIP	FVC: 1.71, 60% DLCO: 6.4, 30%	44	Prednisone, mycophenolate rituximab	Declined in FVC and DLCO; no follow-up chest CT
13	45	F	Yes	+	+	−	+	ANA 1:2560	NSIP	FVC: 2.48, 62% DLCO: 7.7, 31%	7	Prednisone, mycophenolate, rituximab	Declined in FVC but stable DLCO; improving imaging

ANA: antinuclear antibodies; CT: computed tomography; DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; NA: not available; NSIP: nonspecific interstitial pneumonia; OP: organizing pneumonia; PFT: pulmonary function test; SSA: anti SSA autoantibody; SSB: anti SSB autoantibody; UIP: usual interstitial pneumonia.

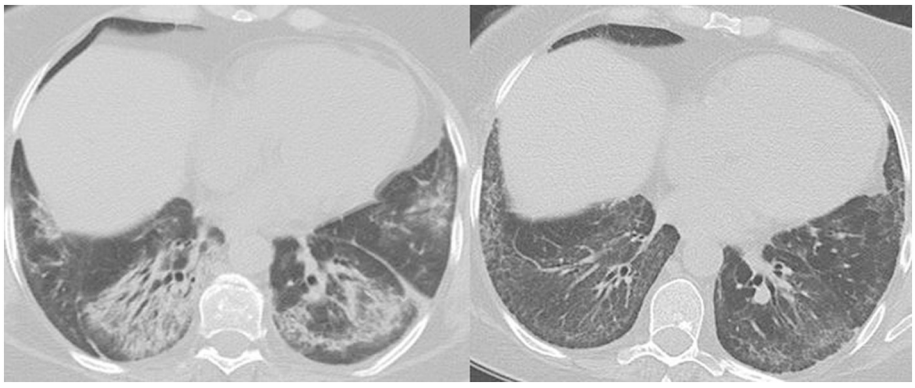

Fig. 1. (A) Axial transverse CT image of lower lung zones in a 45-year-old woman positive for anti-PM-Scl antibody who presented with ILD is consistent with a non-specific interstitial pneumonia (NSIP) pattern, biopsy proven a year prior to the development of myositis, Raynaud's phenomenon and sclerodactyly. (B) Same patient 2 years later after rituximab infusion.

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