Background: Autoantibodies permit to classify and subgroup connective tissue diseases (CTD) in homogeneous groups of patients in terms of phenotype and prognosis. Anti PM-ScI antibodies have been associated with different CTD categories such as: idiopathic inflammatory myositis (IIM), systemic sclerosis (SSc), Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD) or undifferentiated connective tissue disease (UCTD).

Objectives: To determine clinical spectrum of anti-PM-ScI associated disease and if it an homogenous condition.

Methods: This multicentric (four hospitals) observational and retrospective study included all consecutive patients with positive testing for anti-PM-ScI antibodies on immunoblot assay and connective tissue disease (2011-2020). Epidemiological, biological, clinical and radiological data were collected in standard form as well as patient's outcome.

Results: One hundred twenty height patients (female n=96;75%) were included. Median [quartiles] age at diagnosis was 50 [18;84] (IQR) and follow-up duration of 7 [3.7-12] years. Seventy-six (59.3%) patients were simple anti-PM-ScI positivity (78.95%) and 40.7% were associated with other antibodies: anti-SSA/SSB (n=13; 10.92%), SSc associated antibodies (n=21; 16.4%), anti-desDNA for (n=9; 7%), anti-RNP (n=6; 4.7%) and anti-CCP antibodies (n=6; 4.7%). Most patients had cutaneous involvement (n=106; 83%) with skin thickening (n=47; 36%), mechanics hands (n=28; 22%), calcinosis (n=26; 20.3%) and subcutaneous edema (n=20; 15.62%). Vascular involvement was frequent with Raynaud phenomenon (n= 89; 69%), telangiectasia (n=36; 28%), skin ulcers (n=27; 21%), pulmonary hypertension (n=8/120; 6.7%) and scleroderma renal crisis (n=2; 1.5%). A majority of patients also displayed an intestinal onset lung disease (ILD) (IDL=38; 63.5%); nonspecific interstitial pneumonia (92.7%) and/or organizing pneumonia (25.3%). ILD was characterized by a subacute onset in 37/81 (45.7%); median [quartiles] forced vital capacity (FVC) and total lung capacity (TLC) at diagnosis of 88% [73-105] and 79.5% [68.9-101] respectively. Sixty patients (47%) had muscular sign including myalgia (47%), elevated CPK (n=51; 40%) and muscular weakness (Medical Research Council score <4) (n=19/124;15%). Finally, fifty-three (41.7%) had gastroesophageal reflux. Thirty-nine patients (30.4%) experienced at least one muscular or ILD relapse and 6 (4.84%) died during follow-up (2 breast cancer, 1 pneumonia, 3 unknown etiology). Concerning patients' prognosis, relapses were associated with skeletal (n=7, 18.4% vs n=2, 2.5%, p<0.007), and subacute ILD (n=19, 65.5% vs n=18, 34.62%, p= 0.05) with organized pneumonia pattern (n=11, 32.3% vs n=10, 13.9%, p=0.05). Strikingly, ILD occurred mainly in men (90.6% vs 57.2%, p= 0.001) and was associated with anti-ScI-70 positivity (n=14, 16.67% vs 0%, p= 0.01). Muscle involvement was associated arthralgia (n=46, 76.67% vs n=34, 50.75%, p=0.005), respiratory signs at diagnosis: dyspnea NYHA ≥3 (n=46, 75.41% vs n=30, 44.78%, p < 0.001), sub-acute ILD (n=24, 61.54% vs n=3, 2.5%, p=0.001), and subacute ILD (n=19, 65.5% vs n=18, 34.62%, p<0.001). Ulcers were associated with Anti-ScI70 positivity (n=9, 33.33% vs n=5, 4.95%, p < 0.001), Raynaud phenomenon (n=27, 100% vs n=62, 61.39%, p < 0.001), digestive involvement (n=20, 74.07% vs n=34, 33.66%, p < 0.001), ILD with chronic onset (n=15, 78.95% vs n=29, 46.77%, p=0.027) and increased incidence of death (n=4, 16% vs n=2, 2.02%, p= 0.01).

Conclusion: Conducted on the largest cohort of Anti-PM-ScI patients, this study highlights two main phenotypes that determine different outcome and prognosis. One was associated with muscular disease and subacute onset ILD with more frequent relapses. The second with a vascular phenotype associated with chronic ILD, digestive involvement, chronic evolution and increased incidence of death. This could lead to a reclassification of PM-ScI associated autoimmune diseases.

Disclosure of Interests: None declared

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Systemic sclerosis, myositis - etiology, pathogenesis and animal models

**POS0326** ROLE OF THE IL-25 / IL-17RB AXIS IN THH POLARIZATION IN PATIENTS WITH PROGRESSIVE SYSTEMIC SCLEROSIS

L. La Barbera1, M. Lo Pizzo2, D. Di Liberto2, C. Schinocca3, P. Ruscitti3, R. Giacomelli4, F. Dieli2, F. Ciccia5, G. Guggino6,7. 1University of Palermo, Biomedicine, Neuroscience and Child Care, Internal Medicine and Medical Specialties, Rheumatology Unit, Palermo, Italy; 2University of Campania “Luigi Vanvitelli”; 3Department of Precision Medicine, Napoli, Italy

**Background:** Systemic sclerosis (SSc) is an inflammatory connective tissue disease leading to chronic and progressive fibrosis, typically affecting the skin and internal organs. The alteration of both innate and adaptive immune responses plays a pivotal role in SSc pathophysiology, although it has not yet been fully elucidated [1]. Recent findings have demonstrated interleukin (IL)-9 overexpression and significant group 2 innate lymphoid cells (ILC2) expansion in patients with SSc. Th9-ILC2-mast cells axis seems to be involved in SSc tissue damage and in the induction of fibrosis [2]. Activation and production of IL-9 by Th9 cells are promoted by transforming growth factor (TGF)-β, thymic stromal lymphopoietin (TSLP), IL-25 and IL-33. Thus, the IL-25 / IL-17RB pathway would act as a key player in SSc.

**Objectives:** To determine the role of the IL-25 / IL-17RB axis as a driver in Th9 polarization and ILC2 expansion and polarization in SSc patients.

**Methods:** 26 patients were enrolled in this study. Peripheral blood and skin biopsy specimens were obtained from SSc patients. PBMCs were isolated and incubated with and without recombinant (r)IL-25 for 24-48-72 hours and the frequencies of Th9 cells, Th17 cells and ILC2 were assessed by flow cytometry analysis. Moreover, the ex vivo expression of IL-17RB in ILC2 was also assessed.

**Results:** In SSc samples, Th9 cells frequency progressively increased after stimulation with rIL-25, compared to healthy controls in which IL-9 frequency decreased over time regardless of rIL-25. Simultaneously, we evaluated the role of the IL-25 / IL-17RB axis in Th17 cells. In the SSc pool, the initially low rate of IL-17 increased at 72 hours after stimulation with rIL-25. In unstimulated SSc samples, the initially higher IL-17 rate decreased at 72 hours; conversely, it was consistently low in healthy controls, at both baseline and stimulated conditions.

Our results confirmed the presence of IL-25-dependent clonal ILC2 expansion, suggesting a greater and progressive expansion over time in patients with SSc, compared to controls.

Interestingly, increased IL-17RB expression was found in circulating ILC2 from SSc patients supporting the characterization of ILC2 inflammatory phenotype. Consistently, immunofluorescence on the skin of SSc patients showed a marked infiltrate of CD3+GATA3+ IL-17RB+ cells, confirming the presence of the activated inflammatory phenotype ILC2, absent in skin biopsies of healthy controls (Figure 1).

**Conclusion:** These preliminary data suggest an active role of the IL-25/IL-17RB axis in SSc. It results in Th9 polarization and Th17 clonal expansion, inducing the production of IL-9 and, to a lesser extent, IL-17. Moreover, in addition to promoting Th9-mediated ILC2 differentiation, IL-25 directs the polarization of ILC2 towards the inflammatory phenotype.

**REFERENCES:**


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