Conclusion: This study confirms that PM can now be considered a rare IIM subtype. A thorough examination, complete myositis antibody panel including HMGCR testing and careful interpretation of the biopsy results is recommended to accurately classify these patients.

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SAT0332

ANTIBODIES AGAINST CYTOSOLIC 5'-NUCLEOTIDASE 1A IN SPORADIC INCLUSION BODY MYOSITIS: ASSOCIATION WITH CLINICAL AND MRI FEATURES

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Background: Autoantibodies directed against cytosolic 5'-nucleotidase 1A (cN1A) have been identified in sporadic inclusion body myositis (sIBM) and other connective tissue diseases. Anti-cN1A antibodies may support the diagnostic process for sIBM as well as potentially provide clues for disease pathogenesis. Nevertheless, the utility of anti-cN1A autoantibody testing in clinical practice remains unclear and requires validation.

Objectives: To investigate the association between anti-cN1A antibody status and clinical and MRI features in patients with sIBM.

Methods: Data for patients fulfilling European Neuromuscular Centre (ENMC) 2011 criteria for sIBM were obtained from a natural history study database. Demographic, clinical, functional assessment, and muscle MRI data in patients with sIBM who had anti-cN1A autoantibody testing were collected and analysed. Comparisons between subgroups with anti-cN1A antibody status were performed with the Mann-Whitney or Fisher's exact tests, as appropriate.

Results: Forty-nine patients with sIBM had anti-cN1A autoantibody testing, of whom 17 (34.7%) were positive. Twelve patients had muscle MRI performed (seropositivity=5). Demographics, disease duration at antibody testing and overall disease pattern were closely matched in antibody positive and negative cohorts. Dysphagia was more common in the seropositive subgroup (77% vs 47%, $p=0.070$). Antibody positive patients were more severely affected with a trend to lower IBM functional rating scale (IBMFRS) scores (22.4 ± 8.4 vs 26.7 ± 6.4 , $p=0.09$) with significantly worse ability to climb stairs (0.9 ± 0.9 , 1.7 ± 1.1 , $p=0.02$). On T1-weighted MRI more fatty infiltration was found in seropositive patients (Mercuri score: 3.0 ± 0.8 vs 1.7 ± 0.7 , $p=0.03$). Short tau inversion recovery (STIR) hyperintensity was more conspicuous in seropositive patients (STIR extent score: 2.4 ± 0.6 vs 1.4 ± 0.7 , $p=0.04$).

Conclusion: There was a trend for more dysphagia and severity of dysphagia in seropositive patients. Differences in upper limb involvement were not seen according to IBMFRS and Medical Research Council (MRC) strength grades. Seropositive patients were more severely affected at the lower limb level, in terms of muscle weakness, physical function, MRI fatty infiltration and muscle inflammation. These results suggest positive antibody status is associated with a worse phenotype. These results have potential implications in clinical trials: whether antibody status influences treatment response should be assessed.

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SAT0333

SERUM METABOLITES AS BIOMARKERS IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: In fibrotic diseases, metabolic processes are altered with a tendency towards an anabolic state, which is partially reflected in serum. Circulating biomarkers for interstitial lung disease (ILD), the leading cause of death in systemic sclerosis (SSc), are still sparse and not established in routine care.

Objectives: To assess the potential of serum metabolites as biomarkers for the presence and progression of SSc-ILD.

Methods: Age and sex matched serum samples of SSc patients from the Zurich cohort and of healthy controls (HC) were analyzed. Progressive SSc-ILD was defined as either a relative decrease in forced vital capacity (FVC) >10%, a decrease in FVC of 5-9% and a concomitant decrease of carbon dioxide diffusion capacity >15%, or an increase of the extent of lung fibrosis on computed tomography from <20% to ≥20% compared to the last visit (mean follow-up interval = 14 months (range = 9-26)). Sera of HC, non-ILD SSc and stable vs. progressive SSc-ILD patients ($n = 12$ per group; total $n = 48$) were screened for 110 metabolites by targeted liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). Peak areas were analyzed with R 3.6. For univariate analysis, FDR-corrected one-way ANOVA was used. In multivariate group-wise partial least squares discriminant analysis (PLS-DA), variable importance in the projection (VIP) scores ≥2 were considered significant.

Results: In total, 85 metabolites were detected. Univariate analysis of all groups were suggestive of changes for 1-methyladenosine, L-tryptophan, L-tyrosine, L-leucine and xanthosine ($p = 0.077$, 0.028 , 0.077 , 0.028 and 0.032 , respectively). In PLS-DA, HCs and SSc patients differed in their levels of L-tyrosine and L-tryptophan, while levels of L-threonine, 3-aminoisobutyric acid, adenosine monophosphate and xanthosine were changed when comparing non-ILD and SSc-ILD patients. Receiver operating curve (ROC) analysis of significant metabolites from uni- and multivariate testing resulted in separation of SSc patients from HCs by L-tyrosine (area under the curve (AUC) = 0.81 , 95% confidence interval (CI): $0.67-0.96$), L-tryptophan (AUC = 0.86 , CI: $0.75-0.97$) and 1-methyladenosine (AUC = 0.82 , CI: $0.71-0.94$). Progressive SSc-ILD patients were separated from stable patients by their levels of L-isoleucine, L-leucine, adenosine monophosphate and xanthosine (AUC = 0.83 , 0.85 , 0.79 and 0.77 ; CI: $0.66-1.00$, $0.70-1.00$, $0.60-0.97$ and $0.55-0.99$, respectively). Validation of increased values of the branched-chain amino acids L-leucine and L-isoleucine in progressive SSc-ILD vs. stable ILD using an enzymatic assay resulted in similar results as LC-MS/MS analysis, with higher values detected in progressive vs. stable patients (mean = 286.5 and 235.5 nM, respectively; $p = 0.005$). In ROC analysis (AUC = 0.81 , CI: $0.62-1.00$), a cut-off value of 250.3 nM separated stable from progressive patients with a sensitivity of 72.7% and a specificity of 83.3% .

Conclusion: This study in SSc-ILD patients suggested alterations in serum metabolite levels corresponding with their current state of disease, indicating the potential use of serum metabolites as discriminating biomarkers upon further confirmation in larger multicenter studies.

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SAT0334

PERICARDIAL INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterized by visceral and skin fibrosis, vascular dysfunction, and immune dysregulation. Regarding cardiac manifestations, pericardial disorder is one of the most frequent but often asymptomatic.

Objectives: To analyze clinical manifestations, diagnostic tools and treatments of a patient cohort with SSc and pericardial involvement associated.

Methods: A descriptive, observational, cross-sectional study was carried out. We included all patients between 1975 and 2019 with diagnosis of SSc. Demographic, clinical and analytical data; imaging tests; treatments; and mortality rate were collected.

Results: 158 patients were included, 142 (89.9%) women and 16 (10.1%) men. 144 (91.1%) were Caucasians. Mean age at diagnosis was 57 years (range: 17-86). Type of scleroderma, clinical manifestations and autoimmunity profile were shown in table 1 and 2, respectively.

Table 1. Clinical manifestations

Clinical manifestations	n (%)
Cutaneous	
- Limited	104 (66.5%)
- Diffuse	40 (25.3%)
- Sine	13 (8.2%)
Raynaud's phenomenon	156 (98.7%)
Digital tip ulcers	63 (39.9%)
Telangiectasia	111 (70.3%)
Calcinosis	29 (18.4%)
Tendon friction rubs	3 (1.9%)
Joint involvement	44 (27.6%)
Muscle involvement	13 (8.2%)
Interstitial Lung Disease	46 (28.9%)
Gastrointestinal	100 (62.9%)
Pulmonary hypertension	22 (13.8%)
Renal	1 (0.6%)

15 (9.4%) patients developed a pericardial disorder, 3 of them (1.8%) an acute pericarditis. In the majority of the patients (11, 73.3%) pericardial involvement appeared later than diagnosis of SSc with a mean time of 8 years (maximum period of time: 20 years), and the remaining 4 (2.5%) presented the pericardial involvement prior to SSc onset (up to 4 years before). Regarding to cutaneous involvement, limited SSc was the most frequent (13 patients, 86.6%), followed by diffuse SSc (3 patients, 13.4%). In relation to antibody profile, 11 (73.3%) patients were AC positive and 4 (26.6%) AT positive. Seven (46.6%) of the 15 patients with pericardial involvement had a prior pulmonary hypertension associated. Eleven (73.3%) were asymptomatic, 4 (26.6%) referred chest pain and 4 (26.6%) dyspnea. 100% of the pericardial effusions were detected through the performance of an echocardiogram, 3 of them (13.4%) with signs of diastolic dysfunction. Regarding to electrocardiographical findings, 2 (13.3%) showed low voltages. The size of the pericardial effusion was described as: mild in 9 (60%) patients, moderate in 5 (33.3%) and severe in 1 (6.7%). One Cardiac-Magnetic Resonance Imaging was performed which showed constriction data. None of the patients suffered cardiac tamponade or hemodynamic compromise, due to invasive therapies were not necessary. A spontaneous resolution of the pericardial effusion was registered in 6 (40%) patients, with a mean time of 8 months (range: 2-36 months); and 1 (6.7%) patient after an increment in immunosuppressive dose, without improvement of pulmonary hypertension. No renal crisis or deaths were recorded in these patients.

Conclusion: In our cohort patient with SSc, 9.5% developed a pericardial involvement. This kind of disorder could be the first manifestation of the disease. Pulmonary hypertension is the most frequent underlying pathway, however serositis must also be taken into account. Most part of the pericardial effusions were mild. No hemodynamic compromise was registered, due to an invasive treatment was not required.

Table 2. Antibody profile

Antibodies	n (%)
Anticentromere (AC) +	92 (58.2%)
Anti-topoisomerase I (AT) +	36 (22.8%)
Antinuclear (ANA) +	155 (97.5%)

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SAT0335

SERUM AND BALF-DERIVED ANTI-JO1 AUTOANTIBODIES EXHIBIT HIGH REACTIVITY TO DISTINCT HISRS DOMAINS AND ASSOCIATE WITH LUNG AND JOINT INVOLVEMENT IN PATIENTS WITH IIM/ASS

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Background: Autoantibodies that target aminoacyl transfer(t) RNA synthetases (aaRS) represent the serological marker of the anti-synthetase syndrome (ASS), a major subgroup of the idiopathic inflammatory myopathies (IIM) (1). Among the anti-aaRS, anti-histidyl tRNA synthetase (HisRS) autoantibodies (anti-Jo1) are the most common. Up to 90% of IIM/ASS patients diagnosed with interstitial lung disease (ILD) harbor anti-Jo1 autoantibodies (2).

Objectives: Reactivity and affinity of anti-Jo1 autoantibodies from serum and bronchoalveolar lavage fluid (BALF) were investigated against HisRS autoantigen. Associations with clinical data from patients IIM/ASS were addressed.

Methods: Total IgGs were purified by affinity chromatography. Samples and clinical data were obtained from: i) 26 anti-Jo1⁺ patients (19 at diagnosis, 16/19 at follow-up, 7 BALF/matching serum at baseline); ii) 29 anti-Jo1⁻ (25 serum at diagnosis, 4 BALF/matching serum at baseline); iii) 24 age/gender matched healthy controls. Anti-Jo1 IgG and IgA response against HisRS was evaluated by ELISA and western blot. Affinity was measured by surface plasmon resonance. HisRS full-length (HisRS-FL), two HisRS domains (ABD and CD), and two HisRS splice variants (WHEP and WHEP + ABD splice variant (SV)) were tested. Correlations between autoantibody reactivity and clinical data, at baseline and over disease course, were evaluated.

Results: Anti-Jo1 autoantibodies from serum and lung bound HisRS-FL, WHEP and SV with high reactivity and affinity already at diagnosis and recognized both conformational and linear HisRS epitopes (Fig. 1). Levels of autoantibodies (against HisRS-FL, -domains and -splice variants) varied among patients and overtime. Patients with ILD, arthritis and less skin involvement presented higher anti-Jo1 titers compared to those with lower anti-Jo1 titers and to the anti-Jo1 negative group (Fig. 2). Anti-WHEP reactivity in BALF strongly correlated with poor pulmonary function.

Conclusion: High reactivity and affinity at time of diagnosis indicates that autoimmunity against HisRS is most likely initiated before IIM/ASS diagnosis. Reactivity to specific splice variants of HisRS may be employed as diagnostic and prognostic markers.

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Fig. 1. Anti-Jo1 reactivity in total IgG purified from the first available serum sample