The imbalance of activities of purine and pyrimidine metabolism enzymes in red blood cells of systemic scleroderma patients


Background: The systemic scleroderma (SSc) is a connective tissue disease of unknown cause. The key points in development of SSc are the increased number of high collagen-producing fibroblasts in the skin, endothelial dysfunction and immune activation. Recent studies report various metabolic disturbances in SSc patients. Purine and pyrimidine metabolic pathways are underlies the central processes of cellular life. The changes in activity of purine and pyrimidine metabolism enzymes in blood plasma and lysed lymphocytes depending on the SSc activity were described by us earlier [1]. At the same time, there are publications that confirm the enzymatic pattern of purine and pyrimidine enzymes in a regular manner. Activity of the autoimmune inflammation is the factor that underlies the enzymatic pattern of purine and pyrimidine metabolism.

Objectives: To assess the EScSG-AI in patients with systemic sclerosis (SSc) and interstitial lung disease over a five year period.

Methods: It was a longitudinal study involving 77 pts with SSc-ILD (mean age was 46.2±13.4; 69% have limited subset of the disease; 93% were female). The mean duration of follow up was 58.9±11.4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Disease activity was assessed by the 2001 European Scleroderma Study Group Activity Index (ESCSG-AI).

Results: There were no significant differences between groups related to sex, frequency of diffuse form and duration disease. Mean dates of follow up were 58.9±11.4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Disease activity was assessed by the 2001 European Scleroderma Study Group Activity Index (ESCSG-AI).

Conclusion: The progression of SSc goes with the imbalance of the purine and pyrimidine enzymes in a regular manner. Activity of the autoimmune inflammation is the factor that underlies the enzymatic pattern of purine and pyrimidine metabolism.

REFERENCES:

Disclosure of Interests: None declared


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was significantly higher than in groups 1.2 (p < 0.01 and p < 0.04 accordingly) at the end of the study.

Conclusion: Mean values of ESSG-A1 score associated with and were accompanied by progression pulmonary alterations in pts SSc so ESSG-A1 score can be used as valuable tool for long-term follow-up studies.

Disclosure of Interests: None declared

AB0218
CORRELATION BETWEEN IMMUNOLOGICAL PARAMETERS AND PULMONARY FUNCTION PARAMETERS IN THE PATIENTS WITH SSC AND ILD OVER 5 YEARFOLLOW UP STUDY

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Background: Interstitial lung disease (ILD) is related to specific radiographic features in lung imaging and/or the presence of restrictive disorders in pulmonary function tests (PFTs). ILD is one of the leading causes of death in systemic sclerosis patients. Major risk factors of ILD associated with SSc (SSc-ILD) include male sex, diffuse type of cutaneous SSc and presence of anti-Scl-70 antibodies.

Objectives: Taking into account that anti-Scl-70 antibody is an unfavorable predictor of ILD, we have assessed the time course of FVC and DLco in anti-Scl-70-positive and anti-Scl-70-negative patients.

Methods: It was a longitudinal study involving 77 pts with SSc-ILD (mean age was 46.2±13.4; 69% have limited subset of the disease; 93% were female). The mean duration of follow up was 58.9±11.4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes but 3rd group (22 pts) with worsening of fibrosis. We evaluated the forced vital capacity (FVC), diffusing capacity of carbon monoxide (DLCO) in one year and in 5 years and anti-Scl-70 antibodies at the end of the study.

Results: In anti-Scl-70-negative patients the average FVC remained unchanged within a year (91.4 ± 17.4%, 91.6 ± 17% respectively), however, within 5 years FVC significantly increased to 99.1 ± 20% (p < 0.001), while in anti-Scl-70-positive patients the average FVC was lower at the baseline and remained virtually unchanged both 1 year and 5 years later (85.4 ± 17.3%, 85.5 ± 17 and 86 ± 21%, respectively), as a result in 5 years’ time the average FVC in anti-Scl-70-negative patients was significantly higher than in anti-Scl-70-positive patients (p = 0.009).

At the baseline average DLco were below normal and were similar in anti-Scl-70-positive and anti-Scl-70-negative patients: 50 ± 19% and 61.2 ± 14.3% respectively (p 0.05). Within 1 year DLco significantly decreased in all patients, however anti-Scl-70-positive patients demonstrated more pronounced DLco decrease to 53.4 ± 17.2% (p 0.0001), while in anti-Scl-70-negative patients it was less pronounced to 57.2 ± 12.8% (p 0.005), respectively. Within 5 years significant DLco decrease was found only in anti-Scl-70-positive patients: 53.9 ± 16.4% (p<0.001). The time courses of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients by group are shown in Table 1.

Significant DLco decrease over the 5-year period was observed in Group 2 and Group 3, and the lowest DLco (<50%) were observed in Group 3.

Table 1. The time course of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients by group over the 5 years observation period

<table>
<thead>
<tr>
<th>Observation</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>With anti-Scl-70</td>
<td>n = 4</td>
<td>n = 11</td>
<td>n = 3</td>
</tr>
<tr>
<td>Without anti-Scl-70</td>
<td>n = 2</td>
<td>n = 17</td>
<td>n = 13</td>
</tr>
<tr>
<td>In 1 year</td>
<td>78.5±18</td>
<td>61.5±18</td>
<td>62±19</td>
</tr>
<tr>
<td>In 5 years</td>
<td>70±12.5</td>
<td>57±14</td>
<td>56±14</td>
</tr>
<tr>
<td>P</td>
<td>&gt; 0.05</td>
<td>&gt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Conclusion: Therefore, the presence of anti-Scl-70 antibodies was associated with significantly lower pulmonary function parameters specifically in pts with progressive ILD.

Disclosure of Interests: None declared

AB0219
BIOMARKER EXPRESSION IN MONOCYTE SUBPOPULATIONS IN SSc PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by vasculopathy and fibrosis, which can be classified into diffuse cutaneous (dSSc) and limited cutaneous (lSSc) subtypes. Monocytes are key agents in the pathophysiology of systemic autoimmune diseases, including systemic sclerosis (SSc). M1 cells (CD14++CD16-) represent a predominantly pro-inflammatory phenotype and M2 cells (CD14-CD16+++) are more associated to an regulatory/pro-fibrotic phenotype.

Objectives: Our aim was to evaluate circulating blood monocyte subpopulations (classical [M1], intermediate and non-classical [M2]) and analyze the expression of CD163, CD169, and HLADR (function and activation monocytes receptors).

Methods: Fifty consecutive patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were included in a cross-sectional study. Monocyte subpopulations were identified and characterized according to the expression of CD64, CD16, CD14, CD163, CD169, CD206 and HLADR.

Results: SSc patients mean age was 57.2 ± 12.8 years (HC 55.2 ± 11.4) and 94% were female. Limited form of disease was present in 72% of SSc patients and. SSc patients had an increased number of circulating peripheral blood monocytes compared to healthy subjects (table 1).

Table 1. Absolute value (×10^6) about monocytes subpopulations in all systemic sclerosis (SSc) patients compared to healthy controls (HC) and in limited (ISSc) and diffuse (dSSc) systemic sclerosis subtypes.

<table>
<thead>
<tr>
<th>Monocytes</th>
<th>SSc patients</th>
<th>HC</th>
<th>p*</th>
<th>ISSc patients</th>
<th>dSSc patients</th>
<th>p*</th>
<th>p*</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subpopulations</td>
<td>(n=38)</td>
<td>(n=36)</td>
<td>(n=14)</td>
<td>(n=38)</td>
<td>(n=14)</td>
<td>(n=38)</td>
<td>(n=36)</td>
<td>(n=14)</td>
</tr>
<tr>
<td>Classical</td>
<td>346.2</td>
<td>298.9</td>
<td>&lt;0.001</td>
<td>363.2</td>
<td>326.5</td>
<td>0.779</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
<tr>
<td>monocytes</td>
<td>260.9</td>
<td>(146.1)</td>
<td>(262.9)</td>
<td>(231.2)</td>
<td>(450.8)</td>
<td>(287.1)</td>
<td>(451.8)</td>
<td>(461.9)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>38.2</td>
<td>25.4</td>
<td>0.005</td>
<td>38.5</td>
<td>37.1</td>
<td>0.795</td>
<td>0.009</td>
<td>0.069</td>
</tr>
<tr>
<td>monocytes</td>
<td>24.6</td>
<td>(12.6)</td>
<td>(24.7)</td>
<td>(22.1)</td>
<td>(47.1)</td>
<td>41.2</td>
<td>(47.5)</td>
<td>(49.1)</td>
</tr>
<tr>
<td>Non-classical</td>
<td>41.2</td>
<td>28.3</td>
<td>0.006</td>
<td>42.5</td>
<td>37.1</td>
<td>0.310</td>
<td>0.005</td>
<td>0.201</td>
</tr>
<tr>
<td>monocytes</td>
<td>20.8</td>
<td>(11.5)</td>
<td>(20.8)</td>
<td>(20.8)</td>
<td>(58.3)</td>
<td>46.1</td>
<td>(69.0)</td>
<td>(47.3)</td>
</tr>
</tbody>
</table>

Data are shown as median (interquartile range - IQR).” Mann-Whitney U test

Conclusion: In our study, SSc patients show greater monocyte counts than HC with a predominantly regulatory/pro-fibrotic phenotype (M2), dSSc seems to be more associated to CD169 than ISSc.

REFERENCES:

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