THE IMBALANCE OF ACTIVITIES OF PURINE AND PYRIMIDINE METABOLISM ENZYMES IN RED BLOOD CELLS OF SYSTEMIC SCLERODERMA PATIENTS


Background: The systemic sclerosis (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 relationship between changes in ADA activity in red blood cells and pronounced immune disorders [2].

Objectives: to characterize enzymatic patterns of the major purine and pyrimidine metabolic pathways enzymes in lysed red blood cells depending on the SSc activity.

Methods: 51 SSc patients and 30 healthy controls were enrolled in the study. The diagnosis was verified in accordance with the international standards (ACR/EULAR 2013). Disease activity was assessed in accordance with the national classification [3]. Adenosine deaminase (ADA; EC 3.5.4.4); adenosine kinase (AK; EC 2.7.1.20); guanylate kinase (GK; EC 2.7.4.8), dihydroorotate dehydrogenase (DODH; DC 1.3.1.14); IMP dehydrogenase (IMPDH; EC 1.1.1.205); purine nucleoside phosphorylase (PNP; EC 2.4.2.1); thymidine kinase (TK; EC 2.7.1.1); thymidine phosphorylase (TP; EC 2.4.2.4); uracil/thymidine dehydrogenase (UDH; EC 1.17.99.4); cytidine deaminase (CDA; EC 3.5.4.5) activities were measured in lysed red blood cells.

Results: Mean age of patients (MEANS) was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. We revealed substantial changes in enzymatic activities related to both purine and pyrimidine metabolism in lysed red blood cells of SSc patients. The increased ADA (p<0.001), AK (p<0.001), IMPDH (p<0.001), TK (p<0.001), UDH (p<0.001) activities and the decreased DODH (p<0.001), PNP (p<0.001) activities in lysed red blood cells were observed of SSc patients in comparison with healthy controls. AK, IMPDH, TK, UDH activities positively correlated with SSc activity. Negative correlations with SSc activity were revealed for ADA, CDA, DODH, GK, PNP, TP activities.

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


ASSOCIATION OF EUROPEAN SCLERODERMA STUDY GROUP ACTIVITY INDEX (ESCSG-AI) WITH PROGRESSION PULMONARY ALTERATIONS BY HRCT IN PATIENTS WITH SYSTEMIC SCLEROSIS OVER A FIVE YEAR PERIOD

Olga Ovsyannikova, Lidia P. Ananyeva, Olga Koneva, Liudmila Garzanova, Oxana Desinova, Maya Starovoytova, V.A. Nasonova Research Institute of Rheumatology, laboratory of microcirculation and inflammation, Moscow, Russian Federation

Background: Systemic sclerosis (SSc) is a rare connective tissue disease with a heterogeneous clinical course. Interstitial lung disease (ILD) is a common manifestation of SSc and a leading cause of death. Patients with early active SSc are at great risk for progressive ILD.

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 ESCSg-AI score of all pts and in the each groups in first visit and the end of follow up are present in table 1.

Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>First visit</th>
<th>At the end of the study</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=16)</td>
<td>1.9 ± 1.8</td>
<td>1.7 ± 0.9</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Group 2 (n=39)</td>
<td>2.0 ± 1.5</td>
<td>2.1 ± 1.3</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Group 3 (n=22)</td>
<td>2.4 ± 1.5</td>
<td>3.25 ± 2.0</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>All pts (n=77)</td>
<td>2.2 ± 1.6</td>
<td>1.9 ± 1.8</td>
<td>P &gt; 0.05</td>
</tr>
</tbody>
</table>

After 5 years of follow up mean values of ESCSg-AI score increased significantly in group 3 and was more than 3, this actually means the activity of the disease. The mean values of ESCSg-AI score in group 3 is significantly higher than in the other groups.
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 ESScG-AI score associated with and were accompanied by progression pulmonary alterations in pts SSc so ESScG-AI 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 YEAR FOLLOW 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 smokers). The time courses of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients 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. We evaluated the time courses of DLco in anti-Scl-70-positive and anti-Scl-70-negative patients when compared to control.

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). Absolute counts of CD16+ (intermediary and non-classical) monocyte subpopulations were higher in SSc patients compared to HC [79.9 (53.4-103.5)/mm³ vs. 55.9 (26.8-85.8)/mm³, p<0.003]. HLADR-DT expression was significantly higher in all monocyte subsets from ISSc and dSSc patients when compared to control. There was a higher percentage of classical [1.56 (0.84-2.98) vs. 0.68 (0.37-1.88); p=0.003]and intermediate monocytes [15.9 (9.5-29.9) vs. 6.1 (3.7-11.5); p<0.001] with CD206 expression in SSc patients compared to HC, and a higher percentage of CD169 expression in dSSc patients compared to control and ISSc groups (p<0.01).

Table 1. Absolute value (/mm³) about monocyte 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 subpopulations</th>
<th>SSc (n=50)</th>
<th>ISSc (n=48)</th>
<th>dSSc (n=48)</th>
<th>p*</th>
<th>p*</th>
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<tr>
<td>Classical monocytes</td>
<td>346.2 (209.8-699.8)</td>
<td>363.2 (209.8-699.8)</td>
<td>326.5 (209.8-699.8)</td>
<td>0.779</td>
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<td>231.2 (146.1-326.5)</td>
<td>287.1 (146.1-326.5)</td>
<td>245.8 (146.1-326.5)</td>
<td>0.779</td>
<td>&lt;0.001</td>
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<tr>
<td>Non-classical monocytes</td>
<td>36.3 (20.8-52.1)</td>
<td>42.5 (20.8-52.1)</td>
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Data are shown as median (interquartile range - IQR). * Mann-Whitney U test

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

REFERENCES:

Disclosure of Interests: Laiana Schneider: None declared, Natalia Marcondes: None declared, Vanessa Hax: None declared, Isadora Moreira: None declared, Carolina Yuka: None declared, Rafaela Chakr: None declared, Ricardo Xavier Consultant for: Abbvie, Pfizer, Novartis, Janssen, Lilly, Roche, Rafael Chakr: 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 (ISSc) 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 HLA-DR (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 HLA-DR.

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). Absolute counts of CD16+ (intermediary and non-classical) monocyte subpopulations were higher in SSc patients compared to HC [79.9 (53.4-103.5)/mm³ vs. 55.9 (26.8-85.8)/mm³, p<0.003]. HLADR-DT expression was significantly higher in all monocyte subsets from ISSc and dSSc patients when compared to control. There was a higher percentage of classical [1.56 (0.84-2.98) vs. 0.68 (0.37-1.88); p=0.003]and intermediate monocytes [15.9 (9.5-29.9) vs. 6.1 (3.7-11.5); p<0.001] with CD206 expression in SSc patients compared to HC, and a higher percentage of CD169 expression in dSSc patients compared to control and ISSc groups (p<0.01).

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