Table 1.

<table>
<thead>
<tr>
<th>Autoantibody</th>
<th>n</th>
<th>Anti-Ro52 IC</th>
<th>Anti-Ro60 IC</th>
<th>Anti-SSB IC</th>
<th>Anti-Sm IC</th>
<th>Anti-U1RNP IC</th>
<th>Anti-dsDNA IC</th>
<th>Anti-Histone IC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Ro52+ sera n=139</td>
<td>84.9%</td>
<td>90.6%</td>
<td>56.8%</td>
<td>17.9%</td>
<td>23.7%</td>
<td>12.2%</td>
<td>16.5%</td>
<td></td>
</tr>
<tr>
<td>Anti-Ro60+ sera n=192</td>
<td>62.6%</td>
<td>84.3%</td>
<td>49.5%</td>
<td>17.2%</td>
<td>22.4%</td>
<td>13%</td>
<td>17.7%</td>
<td></td>
</tr>
<tr>
<td>Anti-SSB+ sera n=95</td>
<td>74.7%</td>
<td>80.5%</td>
<td>91.6%</td>
<td>13.7%</td>
<td>16.8%</td>
<td>15.8%</td>
<td>17.9%</td>
<td></td>
</tr>
<tr>
<td>Anti-Sm+ sera n=88</td>
<td>39.7%</td>
<td>47.7%</td>
<td>26.1%</td>
<td>45.5%</td>
<td>54.5%</td>
<td>31.8%</td>
<td>32.9%</td>
<td></td>
</tr>
<tr>
<td>Anti-U1RNP+ sera n=99</td>
<td>29.3%</td>
<td>35.4%</td>
<td>17.2%</td>
<td>32.3%</td>
<td>66.7%</td>
<td>17.2%</td>
<td>23.2%</td>
<td></td>
</tr>
<tr>
<td>Anti-dsDNA+ sera n=196</td>
<td>27.6%</td>
<td>38.8%</td>
<td>21.9%</td>
<td>16.8%</td>
<td>28%</td>
<td>20.9%</td>
<td>30.1%</td>
<td></td>
</tr>
<tr>
<td>Anti-Histone+ sera n=160</td>
<td>32.5%</td>
<td>42.5%</td>
<td>23.8%</td>
<td>19.4%</td>
<td>30.6%</td>
<td>21.9%</td>
<td>38.1%</td>
<td></td>
</tr>
</tbody>
</table>

Objectives: To investigate cross-sectionally the IC-derived fraction of SLE specific and associated antibodies, together with the total circulating C1q-binding immune complex (CIC) levels, in a large well-characterized SLE cohort.

Methods: We studied n=530 consecutive SLE patients (≥4 ACR 1982 revised criteria for SLE) who received care at a tertiary referral center for SLE. All participants gave written informed consent for inclusion. The control population consisted of region of residence, age and sex-matched controls (n=192) and n=200 local experimental controls. ACR criteria (at study inclusion), SLEDAI scores, clinical and laboratory variables were obtained at inclusion and through medical file review. At inclusion, fasting blood was drawn from an antecubital vein and was processed to serum, which was stored at -80 °C. To obtain IC-derived antibodies, a novel validated method, described in detail elsewhere,[1] was employed. Briefly, sera were incubated with C1q-coated beads; the C1q-bound ICs were then eluted through two sequential washes with an acidic and alkaline solution respectively, yielding disassembled IC eluates with conserved antibody specificity. Antibody levels of Anti-dsDNA, Anti-Histone, Anti-Sm, Anti-U1RNP, Anti-Ro60, Anti-SSB were measured in IC eluates and in serum with a bead-based multiplex assay. CIC levels were measured with a commercial ELISA according to the manufacturer’s instructions. Parallel analyses of autoantibody levels in serum and in IC eluates were performed on the same day. The results were reported on a standard curve; the 98th percentile of the standard curve values of control sera were set as the threshold for positivity for binary analyses.

Results: CIC levels were higher and more widely dispersed in SLE patients than controls (p<0.0001). A higher CIC load was associated with nephritis, arthritis, and SLEDAI > 6 (p<0.0001). Among autoantibody specificities, Anti-dsDNA in serum was independently associated with a high CIC load (OR 4.8, 95% CI 2.5-9.5, p<0.0001, see also Figure 1). Concordance between serum and IC-eluted positivity varied strongly among autoantibody specificities, being highest for Anti-SSA/SSB, and lowest for Anti-dsDNA (Table 1). Among serum Anti-dsDNA+ patients, carriers of Anti-dsDNA from ICs displayed higher Anti-dsDNA titers, lower complement levels, and higher SLEDAI scores (p<0.01 for all). Conclusion: Different autoantibodies are differentially represented in circulating ICs in SLE. Anti-dsDNA in serum is an independent marker of a higher CIC load, carrying facets of a more IC-mediated disease. Patients with elevated Anti-dsDNA in IC eluates, compared to anti-dsDNA only in serum, are more clinically and biologically active subset, showing promise of IC-derived Anti-dsDNA as a potential SLE biomarker.

REFERENCE:

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AB0126 EXPRESSION OF β2 MICROGLOBULIN IN SALIVARY GLAND EPITHELIAL CELLS OF PATIENTS WITH SJÖGREN SYNDROME

Keywords: Sjögren syndrome, Biomarkers

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Background: Salivary glands epithelial cells (SGECs) activation and loss of homeostasis play a key role in primary Sjögren Syndrome (pSS) [1]. High serum and saliva levels of β2-microglobulin (β2-M) have been described [2] in pSS, however, the exact origin of this molecule is still unclear. Our preliminary data from single cell analysis on pSS salivary glands treated with immunosuppressors show a downregulation of this protein in SGECs following treatment.

Objective: Aim of this study is to evaluate the expression of β2-M in pSS SGECs and to dissect its modulation in inflammatory conditions. Methods: To mimic the inflammatory microenvironment of pSS, a human salivary gland (HSG) cell line was treated (48h) with 1) Poly-I:C (40 μg/ml), 2) LPS (50 μg/ml), 3) culture medium (untreated). The HSG expression of β2-M (Ab anti-β2-M) was evaluated by flow cytometry along with the expression of apoptotic [annexin V (MBL)] and activation [ICAM-1 (Ab anti-CD54)] molecules. Ex vivo expression of β2-M was then assessed in SGECs deriving from both pSS patients (n=3) and sicca controls (n=3). Results: In the HSG cell line treated with both Poly I:C and LPS a significant increase in β2-M was documented [mean fluorescence index (MFI): untreated=1 (1-1), Poly-I:C=2.46 (1.5-3.9), LPS=1.3 (1-1.3); p=0.003]. The increased expression of β2-M was paralleled by an increase in ICAM-1 (MFI: untreated=1 (1-1), Poly-I:C=2.46 (1.5-3.9), LPS=1.3 (1-1.3); p=0.06) and annexin V (mean%: untreated=7.6% (5-9), Poly-I:C=14.3% (9-18), LPS=8% (6-11); p=0.003). In SGECs from pSS a higher expression of β2-M was detected as compared to controls (MFI: pSS=2.5 (2-3) vs sicca=1 (0.5-1.5) (Figure 1).

Conclusion: Our preliminary data suggest that β2-M is actively expressed by SGECs in pSS and that its exposure is driven by the local inflammatory milieu. Such expression is particularly interesting in view of the already demonstrated capacity of β2-M to activate pro-inflammatory pathways and to influence cellular viability and autoantigens exposure [3]. Functional studies are currently ongoing to dissect the potential pathogenic role of β2-M in pSS.

REFERENCES:

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

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