The antiphospholipid syndrome (APS) is an autoimmune condition characterized by recurrent arterial and venous thrombosis, besides obstetric complications. The pathogenesis is associated with the presence of antiphospholipid and/or anti-b2-glicoprotein I (anti-b2GPI) antibodies that appear to change the anticoagulant activity of b2GPI. Antibody-induced dimerization of b2GPI seems to be related to the induction of platelet aggregation, contributing to the development of thrombosis in APS. The objective of the present study is to demonstrate the influence of antiphospholipid antibodies in platelet aggregation tests with different agonists (ADP, collagen, and adrenaline). We analyzed platelet aggregation tests with different agonists (ADP, collagen, adrenaline) when normal platelets were exposed to serum with different concentrations of antiphospholipid antibodies. Results demonstrated a significant inhibition in adrenaline- and ADP-induced platelet aggregation curves ($P < 0.05$) in all antibody concentrations tested when compared to the control. The paradox between the prothrombotic state and the presence of autoantibodies that show anticoagulant activity in vitro was demonstrated in the literature, making it difficult to understand the pathophysiological mechanism of the antiphospholipid syndrome. Results showed that anticardiolipin and anti-b2GPI antibodies-rich serum, both of which belonging to the IgG class, can interfere with platelet aggregation curves.
Background: Antiphospholipid syndrome (APS) is a disorder that manifests usually clinically with venous or arterial thrombosis and/or fetal loss. APS may occur as primarily or secondary to another systemic autoimmune disease. This study is aimed to evaluate the demographic and clinical characteristics of patients with primer and secondary APS.

Methods

Retrospective chart review of patients seen at the Hacettepe University Rheumatology Department between 2015 and 2016. Demographic data, clinical features, cardiovascular risk factors, antibody status and treatment were collected. Patients were diagnosed APS according to the revised Sapporo criteria.

Results

Thirty three patients were included in the study (28 with secondary APS and 5 with primary APS). There were no statistically significant differences in sex, age, disease duration between primary and secondary APS groups. All of our secondary APS had diagnosis of SLE.

APS diagnosed with thrombosis in 69.6%, with pregnancy morbidity in 18.1%, and with both of these features in 6% patients.

Non-diagnostic clinical features were more frequent in secondary APS 85.7% patients when compared with the primary APS 60% patients but the difference did not reach statistical significance (p=0.17).

60.6% patients were positive any aPL combination, 12.1% patients were positive only for anticardiolipin (aCL), 24.2% patients were only LA, and 3% patient was positive only for Anti beta-2 glycoprotein I (anti-β2GPI).

Conclusion:

In this study, non-criteria APS features and cardiovascular risk factors were found more frequently in secondary APS patients than primary APS. Thrombocytopenia was also more common in secondary APS group.
Phospholipids are the main structural constituents of cell membranes; they form the smooth bilayer matrix that delimits cells in which membrane proteins are located. However, some anionic phospholipids can lead to the formation of non-bilayer phospholipid arrangements (NPA) within the bilayer. NPA are transient but when they are stabilized by the drugs chlorpromazine, procainamide or hydralazine (which produced lupus-like disease in humans) they induce a disease resembling human lupus in mice which form anti-NPA IgG antibodies produced by B cells via germinal centers before others like ANA's and anticardiolipin antibodies. Anti-NPA have been associated with SLE. The aim of this work is to explore the role of anti-NPA antibodies in the development of antiphospholipid syndrome. We measured anti-NPA by the ELISA method and flow cytometry in 100 patients and in 100 healthy controls. We found higher levels (cut point > 3 UA, >$10^{-3}$ respectively) in patients with primary or secondary APS than in the SLE alone suggesting that the recognition of NPA by anti-NPA antibodies may trigger the classical complement pathway, which in turn causes the characteristic clinical symptoms of APS. We also found a significant correlation of anti-NPA with the presence of renal involvement that required hospitalization, regardless of histopathology. We concluded that the presence of anti-NPA might be useful in predicting severity of the disease.
Background: Risk factors for thrombosis are known in antiphospholipid syndrome (APS). Comparative analysis of factors at disease onset vs follow-up is not fully established.

Objective: To analyze the risk factors at APS onset/ during follow-up.

Patients and methods: We studied primary APS patients (PAPS) (Sidney Criteria). Information about risk factors at APS onset and subsequent thrombosis were obtained: pregnancy, puerperium, trauma, infectious process, stay in bed, cardiovascular risk factors (CRF): Smoking, arterial hypertension, obesity, diabetes mellitus. Thrombosis recurrence was considered if ≥2 thrombotic events happened. Descriptive statistics /chi square test were employed.

Results: We included 57 PAPS patients, 45 females, age: 48.8 ± 13.44 years, evolution: 14.7± 7.74 years, median thrombotic events: 2 (Range: 1-4). 37 patients had thrombosis recurrence and 20 without it, with other non-thrombotic manifestations after onset. The most frequent initial manifestations were deep venous thrombosis (33%), stroke(26%) pulmonary embolism (PE) (19%);remaining as the main manifestations on follow-up. At APS onset 36.8% of patients had thrombosis during pregnancy or puerperium, (9 had DVT, 6 stroke,2 venous cerebral thrombosis, 4 PE), 5.3% had recent trauma. 5.3% stay in bed, 1 recent surgery, 26 % had 1 CRF at APS onset. In contrast during follow up only 3.5% of patients had thrombosis recurrence after puerperium, 44 % of patients had 2 or more CRF (p=0.0001).

Conclusions: Pregnancy and puerperium were the principal triggering factors for thrombotic APS at onset, while CRF play a role on the subsequent thrombosis. Close monitoring of pregnant patients with APS suspicion and control of CRF are mandatory.
Background: Digital necrosis can be due to multipies diseases. Connective tissue disease and especially systemic
sclerosis represent one of the most frequent etiology in internal medicine departement. Systemic lupus erythematosus
is involved in 1% of the cases. Its association to antiphospholip antibodies syndrome and/ or cryoglobulinemia
worsen the prognosis. We report a case of a patient diagnosed with systemic lupus erythematosis in which digital
necrosis revealed antiphospholip antibodies syndrome and cuoglobulinemias.

Case: A forty-nine-year-old female diagnosed with a SLE had a palmar erythema. She complained about
paresthesia in her lower limbs and arthralgia. Physical examination showed bilateral palmar erythema, digital and oral
ulcerations and malair rash. Routine laboratory showed pancytopenia. Complement was low. Proteinuria was
negative. The capillaroscopy was normal. Cryoglobulinemia and anti bèta2glycoprotein antibodies were both
positive. Acute Systemic lupus erythematosis was diagnosed associated to a polyclonal cryoglonulinemia and
antiphospholipe antibodies. The patient was treated by 3 pulses of methylprednisone than prednisone at a dose of
1mg per kilogramme per day. Palmar erythem and pancytopenia disappeared but digital necrosis worsened. daily
intraveinous injections of ilomedine were needed. Digital ulcerations improved. Amputation was ovoided.

Conclusion: treatment of digital necrosis must be etiological and symptomatic. Our patient improved with steroids
and prostacyclines.
Background: test predictive role of RF type IgM/Ig A, anti-CCP, anti-MCV, 14-3-3 eta protein and COMP on a group of patients treated with anti-TNF α agents.

Methods: prospective/observational study including 64 patients followed 12 months with active RA, uncontrolled by conventional synthetic DMARDs.

Results: 59 patients (92.2%) were women and 5 (7.9%) men, mean age 57.5 ± 9.4 years.

Following baseline immunological parameters titres and the response at 6 months, tests for identifying differences between the groups showed that lower titres of both RF isotypes, anti-CCP, 14-3-3 eta protein and COMP had predictive value on achieving a good EULAR response at 6 months. Grouping patients in 2 categories, just 14-3-3 eta protein and anti-CCP maintained their predictive value for the response at 6 months (Table 1).
After 12 months, 1 patient was nonresponder, 11 achieved moderate response and 44 good response. Lower baseline titres for RF IgM (92.93±120.22U/ml, p=0.01032) and IgA (49.96±98.08 U/ml, p=0.00247) had predictive value for achieving a good response at 12 months.

The status pretreatment influenced the good response for COMP at 6 months (p=0.0001) and RF IgA at 12 months (p=0.0041).

Using multivariate logistic regression methods we obtained a statistical model for predicting the response at 6 months including normal values for 14-3-3 eta protein, anti-CCP and COMP (Hosmer and Lemeshow according test $\chi^2 = 5.795$, p = 0.670 ≥0.05 with a predictive response accuracy of 89.1%).

**Conclusion:** in the future a version using multiple biomarkers could increase accuracy for identifying pretreatment patients who will respond to anti-TNF therapy.

<table>
<thead>
<tr>
<th></th>
<th>Nonresponder</th>
<th>Moderate response</th>
<th>Good response</th>
<th>p value</th>
<th>Nonresponder</th>
<th>Responder</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>7</td>
<td>38</td>
<td>19</td>
<td></td>
<td>7</td>
<td>57</td>
<td></td>
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<tr>
<td>RF type IgM</td>
<td>132.35±99.602</td>
<td>157.22±131.47</td>
<td>51.36±95.359</td>
<td>0.01629</td>
<td>121.93±129.92</td>
<td>57168</td>
<td></td>
</tr>
<tr>
<td>RF type IgA</td>
<td>122.81±99.876</td>
<td>102.08±128.33</td>
<td>22.45±61.256</td>
<td>0.03336</td>
<td>122.81±99.87</td>
<td>75.54±116.282</td>
<td>0.30787</td>
</tr>
<tr>
<td>Anti-MCV</td>
<td>74.04±47.951</td>
<td>80.06±149.543</td>
<td>33.77±113.069</td>
<td>0.43914</td>
<td>74.04±47.951</td>
<td>64.63±119.174</td>
<td>0.86037</td>
</tr>
<tr>
<td>14-3-3 eta protein</td>
<td>0.99±0.888</td>
<td>0.28±0.469</td>
<td>0.51±0.580</td>
<td>0.04518</td>
<td>0.99±0.888</td>
<td>0.36±0.515</td>
<td>0.04042</td>
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<tr>
<td>Anti-CCP</td>
<td>146.16±41.688</td>
<td>113.65±50.448</td>
<td>60.82±26.331</td>
<td>0.00011</td>
<td>146.16±41.68</td>
<td>96.04±50.355</td>
<td>0.02834</td>
</tr>
<tr>
<td>COMP</td>
<td>1042.2±181.71</td>
<td>1032.8±188.67</td>
<td>746.04±130.09</td>
<td>0.00000</td>
<td>1042.2±181.71</td>
<td>937.27±218.10</td>
<td>0.22727</td>
</tr>
</tbody>
</table>

Table 1. Baseline titres and EULAR/2 groups response to anti-TNF therapy at 6 months
Poster Session

ANTI-TNFs AND AUTOIMMUNITY

An examination of the serum levels of infliximab (IFX) and anti-IFX antibodies in patients with inflammatory bowel disease in a private hospital in Brazil
LACA7-0145
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1Hospital Nossa Senhora das Graças, gastroenterology, Curitiba, Brazil
2Hospital de Clínicas do Paraná, Hepatology, Curitiba, Brazil

Crohn’s Disease (CD) and Ulcerative Colitis (UC) are chronic inflammatory bowel diseases (IBD). There is an increase of the production of the alpha tumor necrosis factor (TNF-α). The presence of anti-drug antibodies (ATI) may be responsible for the adverse events and the reduction of the effectiveness of the drug. There is a need for a method to evaluate the effect of the drug, such as the dosage of the serum level of IFX, as well as antibody research. The study aims to examine the serum levels of IFX and of the anti-IFX antibodies in patients with intestinal inflammatory disease in a maintenance or post-induction therapy, and describe the therapeutic practices that were modified due to the serum levels of IFX and AIT. It is a retrospective study, with the analysis of the dosage of serum levels of IFX and ATI. Fifty-four patients were included, with a total of 97 collections of IFX dosage. Thirty-three patients had an adequate IFX serum level, 42 patients had subtherapeutic levels and 22 patients supratherapeutic levels. Seven patients had their medication suspended due to therapeutic failure or high levels of ATI. In conclusion, only a third of the patients had adequate IFX levels and 43.29% of the patients presented subtherapeutic levels at the end of the induction. In about 66% of the samples, the practice adopted was based on the IFX and ATI levels, demonstrating the importance of having this tool to help the clinical handling of patients with IBD in biologic therapy.
Aim: Aim of the study was to study the effectiveness, toxicity and "survival" of infliximab in patients with persistent psoriatic arthritis (PA) severe psoriasis.

320 patients with PA and severe persistent psoriasis, who received at least two disease-modifying drugs, were included in the study. All patients had active disease with >6 swollen or painful joints, psoriasis area severity index (PASI)>10 and erythrocyte sedimentation rate (ESR)>28mm/h or C-reactive protein (CRP)>10mg/l. Patients were treated with infliximab. 20 patients were taking methotrexate (MTX) and cyclosporine A (CsA), 7 were on MTX and leflunomide (LFN), and 5 patients were taking CsA and LFN. One year after the treatment 81.25% of the patients had achieved the PsARC criteria, 84.4% were meeting ACR20% criteria, 59.4% and 46.9% of the patients had achieved ACR50% and 70% respectively. Two years after the treatment 71.9% of the patients continued to meet PsARC criteria and 75%, 53.1% and 43.75% of the patients had achieved ACR20%, 50% and 20% respectively. At the same time 75% of the patients were meeting PASI70 and 90. This clinical improvement was correlated with ESR and CRP reduction. 8 patients (25.0%) discontinued the study. Hypersensitivity reaction was the main reason for 5 patients (15.6%). The survival of infliximab was 84.4% in the first year of the treatment while in the second it was 75.0%.

Conclusion: Patients with severe persistent PA and severe psoriasis who received infliximab had significant clinical improvement that lasted for two years. The survival of the drug after two years of treatment was 75.0%.
Poster Session

ARBOVIROSIS, ARTHRITIS, AND IMMUNE RESPONSE IN LATIN AMERICA

Early diagnosis of psoriasis arthritis in patients with severe psoriasis: a hospital-based study
LACA7-0021
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¹RUDN University, Dermatovenerology and cosmetology, Moscow, Russia

Objectives: To evaluate and to compare effectiveness, sensitivity, specificity of two psoriatic arthritis (PsA) screening questionnaires (Early Arthritis for Psoriatic patients (EARP), Psoriatic Arthritis Questionnaire (PAQ)) in hospital-based cohort of patients (pts) with severe psoriasis (PsO).

Methods: 40 pts (19 Male(M.)/21 Female(F.)), mean age 50.3±29 years accordingly, mean PASI >10, PsO duration 8±2.8. 7 PsO pts with clinically diagnosed PsA (L 40.5). To diagnose early PsA (ePsA) we have used EARP and PAQ questionnaires in cohort of pts with severe PsO in the Dermatological hospital “Clinica Korolenko” in 2016 year. M±m, t-test, (%) were calculated (55.5±7.7).

Results: 40 pts (100%) with psoriasis were invited to participate and all of them returned the questionnaires. 7 pts (%) were diagnosed with PsA earlier and 33 PsO (%) pts who earlier were not diagnosed PsA, of witch 10 pts increased with the number of positive questionnaires. 10 pts responded positively to the EARP questionnaire, as for PAQ only 3 pts of the same group responded positively all of them have not been previously diagnosed with PsA. The majority of pts with a false positive response had degenerative or osteoarthritis. At the same time in the group of pts who earlier were diagnosed PsA (7pts) we have 4 pts who didn’t respond positively to the PAQ and only 2 pts to the EARP of the same group.

Conclusion: Although the EARP questionnaire performed slightly better than the PAQ questionnaire at identifying PsA, there is a big difference between these instruments.
Background and objective: In Dominican Republic, by February 2014, were reported the first cases of Chikungunya virus (CHIKV). After the acute epidemic, it was reported that one third of the patients continue with chronic manifestation and even they could develop a rheumatic disease.\textsuperscript{1,2} The purpose of this study is to evaluate the clinics characteristics; laboratory findings and treatment received by a Dominican population who develop rheumatic disease after the CHIKV.

Patients and methods: Multicentric, transversal study. This study included 62 patients who met ACR criteria for Rheumatic Disease. The rheumatologists evaluated the patients from June 2014 to June 2016.

Results: Sixty-two patients were included. The mean age (±SD) 47.6 ± 13.5 years, 93.5% were female. The CHIKV diagnostic was made by clinical/epidemiological criteria in 85.4% cases. The mean time between the acute infection and the diagnosis of the rheumatic disease was 9.7 ±6.6 months. The most frequents clinical manifestation: arthralgia (90.3%), arthritis (87%), fatigue (53.2%) and morning stiffness (50%). Rheumatic diseases are described in Table 1. We found elevated ESR (82.2%), and elevated CRP (75.8%), anemia (48.3%), RF+ (48.3%) and ACPA+ (35.4%). The patients need NSAIDs (90.3%), glucocorticoids 92%, antimalarial 84%; cDMARDs in 82.2%, 6.5% need biological DMARDs.

Conclusions: The infection by CHIKV may predispose to develop a rheumatic disease. The virus is a superantigen, can activate the cellular immunity and trigger clinical manifestations in a subject with genetic susceptibility. The rheumatologist in the endemic areas should be aware of this reality to make an early diagnosis and treatment.

<table>
<thead>
<tr>
<th>Table 1. Type of disease (N = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Spondyloarthritis*</td>
</tr>
<tr>
<td>SLE</td>
</tr>
<tr>
<td>Scleroderma</td>
</tr>
<tr>
<td>Inflammatory myopathy</td>
</tr>
</tbody>
</table>

\* Includes: 4 patients with SpA, 1 Psoriatic arthritis, 1 Psoriasis
Introduction

Infection with Zika virus (ZIKV) is usually asymptomatic (75-80%). Those patients with symptoms show a mild and self-limiting disease. These patients are at high risk of developing rare neurological complications. In a series of cases of Guillain-Barré syndrome associated with ZIKV, a high prevalence of dysautonomia has been reported. However, a primary association between dysautonomia and ZIKV infection has not been described.

Objectives

To evaluate the presence of dysautonomia in patients with ZIKV infection.

Methods

Dysautonomia was evaluated in patients with previous ZIKV infection and no evidence of neurological syndromes by using the Composite Autonomic Symptom Score-31 (COMPASS-31) form. All patients were selected from the National System of Public Health Surveillance during the ZIKV outbreak in Cucuta, Colombia. The diagnosis was confirmed by ELISA and immunofluorescence assay.

Results

A total of 36 patients were included (Table 1. Thirty-three patients (91.7%) presented autonomic dysfunction, including orthostatic, vasomotor, secretomotor, gastrointestinal, bladder and pupillomotor symptoms during and after infection. The median COMPASS-31 score was 26.21 (IQR: 4.9-36.7). Patients with dysautonomia were older than those without it, regardless of gender. Orthostatic and bladder symptoms were associated with secretomotor, as well as with pupillomotor and vasomotor symptoms. Patients with orthostatic, secretomotor and bladder symptoms
disclosed the highest scores of total COMPASS-31 score (>31.2).

### Table 1. Demographic and clinical characteristic of 36 patients with ZIKV disease

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>42 (32.7-52)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (66.7)</td>
</tr>
<tr>
<td>Orthostatic intolerance (%)</td>
<td>23 (61.9)</td>
</tr>
<tr>
<td>Vasomotor (%)</td>
<td>5 (13.9)</td>
</tr>
<tr>
<td>Secretomotor (%)</td>
<td>22 (61.1)</td>
</tr>
<tr>
<td>Gastrointestinal (%)</td>
<td>20 (55.6)</td>
</tr>
<tr>
<td>Bladder (%)</td>
<td>15 (41.7)</td>
</tr>
<tr>
<td>Orthostatic intolerance, median (IQR)</td>
<td>16 (9-20)</td>
</tr>
<tr>
<td>Vasomotor (IQR)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Secretomotor, median (IQR)</td>
<td>2.1 (0-8.4)</td>
</tr>
<tr>
<td>Gastrointestinal, median (IQR)</td>
<td>4.0 (0.5-5.5)</td>
</tr>
<tr>
<td>Bladder, median (IQR)</td>
<td>1.1 (0-3.3)</td>
</tr>
<tr>
<td>Pupillomotor, median (IQR)</td>
<td>0 (0-1.8)</td>
</tr>
</tbody>
</table>

### Conclusion

Dysautonomia, as a neurological manifestation of ZIKV infection, is described for the first time. Further research aimed to confirm these findings and to evaluate the mechanism by which ZIKV could induce autonomic dysfunction is warranted.
Background: World Health Organization (WHO) suggested case definitions to suspect and diagnose chikungunya virus infection (CHIKV). Although useful, when applied in practice, its lack definition for specific joint involvement and absence of other systemic symptoms apart from fever, leads to a broad clinical spectrum which increases the need for laboratory tests.

Methods: A group of specialists in rheumatology, epidemiology and bacteriology from different parts of Colombia with experience in diagnosis and treatment of CHIKV patients from the epidemic of 2014-2015 met to reach agreements on clinical characteristics of CHIKV infection. A series of questions were formulated and agreement in percentage was calculated on the following answers: totally agree, agree, not in agree or disagree, disagree and totally disagree. Agreement was set when the sum to the answers totally agree and agree or disagree and totally disagree of was ≥50%. When agreement was not reached, the moderator performed a discussion with the opinions of the confronting members of the group and after that reformulated the question. This procedure was made until agreement was reached. With the results a set of clinical criteria was proposed.

Results: The agreement percentage to the formulated questions are depicted in table 1.

Conclusion: Agreement was achieved in abrupt onset of symptoms, and the presence of fever, rash, myalgia, fatigue, and symmetrical arthritis or arthralgia of wrists, hands, knees, ankles and feet. A set of clinical criteria was proposed (figure 1).
<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Totally Agree</th>
<th>Agree (Not in Agree or Disagree)</th>
<th>Disagree</th>
<th>Totally Disagree</th>
<th>Type of Agreement (Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetrical joint involvement</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Agree (100)</td>
</tr>
<tr>
<td>Abrupt onset of symptoms</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Agree (100)</td>
</tr>
<tr>
<td>Fever</td>
<td>38</td>
<td>50</td>
<td>12</td>
<td>0</td>
<td>Agree (78)</td>
</tr>
<tr>
<td>Rash</td>
<td>13</td>
<td>75</td>
<td>0</td>
<td>12</td>
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<tr>
<td>Mucosal involvement</td>
<td>0</td>
<td>0</td>
<td>63</td>
<td>37</td>
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<tr>
<td>Myalgia</td>
<td>25</td>
<td>75</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Fatigue</td>
<td>63</td>
<td>25</td>
<td>12</td>
<td>0</td>
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<tr>
<td>Gastrointestinal involvement</td>
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<td>12</td>
<td>0</td>
<td>25</td>
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</tr>
<tr>
<td>Arthralgia in shoulders</td>
<td>0</td>
<td>25</td>
<td>12</td>
<td>38</td>
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<tr>
<td>Arthritis in shoulders</td>
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<td>Arthralgia in elbows</td>
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<td>0</td>
<td>0</td>
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<tr>
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<td>0</td>
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<td>63</td>
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<td>0</td>
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<td>Agree (100)</td>
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<tr>
<td>Arthritis in ankles</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Agree (100)</td>
</tr>
<tr>
<td>Arthralgia in feet</td>
<td>50</td>
<td>38</td>
<td>0</td>
<td>12</td>
<td>Agree (88)</td>
</tr>
<tr>
<td>Arthritis in feet</td>
<td>75</td>
<td>13</td>
<td>0</td>
<td>12</td>
<td>Agree (88)</td>
</tr>
</tbody>
</table>

CHIKV: chikungunya virus infection
Background: CHIKV is suspected based on epidemiological and clinical criteria, however confirmation of the disease is only achieved by laboratory tests. Laboratory diagnosis is made by two approaches: the detection of viral RNA and identification of the specific immune response by serological methods. In Colombia, CHIKV’s probable cases are not mandatory to be confirmed, so there is no standardization for laboratory confirmation tests.

Methods: IgM and IgG antibodies against CHIKV were measured by ELISA technique in 604 patients with CHIKV suspicion. A typical case of CHIKV with high sensitivity and specificity obtained from a previous study was used as gold standard for diagnosis of CHIKV. Since CHIKV epidemic of 2014-2015 was the first to be reported in our country (Colombia), no second measurements of IgG were needed to confirmed infection.

Results: Cut off point for IgG was 14,3 SU and for IgM was 11,2 SU. Mean values for IgG was 36,7 SU (±22,7) in patients with CHIKV and 8,6 SU (SD± 6,3) for IgM. Statistical significance was obtained for both IgG and IgM (p<0,0001) when comparing patients with and without CHIKV. Receiver operating characteristic (ROC) curves showed and area under the curve (AUC) of 0,81 for IgG and 0,65 for IgM (figure 1).

Conclusion: Our study revealed a good performance of IgG and regular performance of IgM for the diagnosis of CHIKV in a cohort of CHIKV patients.
from Colombia’s epidemic. Cut off points for both IgG and IgM were measured for future reference.
Background: Host factors like innate and adaptive immune response play an important part in disease susceptibility. Studies have demonstrated HLA class II alleles association to susceptibility or resistance to chikungunya virus infection (CHIKV), however there is no evidence of association studies of HLA class I and II in the Latin-American CHIKV epidemic.

Methods: Characterization of HLA allele A, B, and DR of 62 patients with confirmed CHIKV was compared with 100 unrelated healthy subjects as a control group. The comparison between the different allele frequencies in the patient group and the control population was performed using chi², with Bonferroni correction. A p value <0.05 was considered to be significant. The magnitude of associations was assessed using odds ratio (OR) and confidence intervals (CI) of 95%. To establish the homogeneity of the studied groups, the Hardy-Weinberg disequilibrium was used.

Results: Of the 62 patients studied 46 were female (74.2%). The mean age was 45.0 (SD±16.8) years. Most of the patients were from Barranquilla (64.5%; n: 40). Mean CHIKV immunoglobulin G (IgG) was 38.6 SU (SD±21.7), while IgM was 13.3 SU (SD±7.6). Also C reactive protein levels were high (mean: 14.7 mg/L; SD±8.4). Association alleles of HLA-A, and DR are depicted in table 1. No association was found with HLA-B alleles.

Conclusion: Our study demonstrated the alleles A*28 and A*29 to be associated with resistance to CHIKV, and alleles A*68, DRB1*01, DRB1*04 and DRB1*13 to be associated with susceptibility to CHIKV. No association was found in any HLA-B alleles.

<table>
<thead>
<tr>
<th>Table 1. Associated Alleles with CHIKV</th>
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<tr>
<td><strong>Resistance</strong></td>
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<td>• A*28</td>
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<tr>
<td>0</td>
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<tr>
<td>11</td>
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<td>0.0-INF</td>
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<td>0.002</td>
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<td>0.040</td>
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<td>• A*29</td>
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<td>6</td>
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<td>24</td>
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<td>0.2</td>
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<td>0.0-0.6</td>
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<td>0.002</td>
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<td>0.048</td>
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<td><strong>Susceptibility</strong></td>
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<td>• A*68</td>
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<td>14</td>
</tr>
<tr>
<td>2</td>
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<td>9.9</td>
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<td>2.1-45.1</td>
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<td>0.000</td>
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<td>0.008</td>
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<tr>
<td>• DRB1*01</td>
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<td>21</td>
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<td>5</td>
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<td>6.4</td>
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<td>2.3-17.9</td>
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<tr>
<td>• DRB1*04</td>
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<tr>
<td>26</td>
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<td>• DRB1*13</td>
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CHIKV: chikungunya virus infection; CI: confidence interval 95%; Cp: Bonferroni corrected p value
Demonstrate our indigenous medicines that are made by 1000 years old Herbal & Ayurvedic medicines practicing field in the spectrum of finding remedies for Asthma, Tuberculosis, Cancer and various other ailments.

Allopathic practitioners in India are outnumbered by practitioners of traditional Indian medicine and homeopathy (TIMH), which is used by up to two-thirds of its population to help meet primary health care needs.

Hypertension (HTN) is the medical term for high blood pressure. It is dangerous because it makes the heart work too hard and contributes to atherosclerosis (hardening of arteries), besides increasing the risk of heart disease and stroke. HTN can also lead to other conditions such as congestive heart failure, kidney disease, and blindness. Conventional antihypertensives are usually associated with many side effects. About 75 to 80% of the world population use herbal medicines, mainly in developing countries, for primary health care because of their better acceptability with human body and lesser side effects. In the last three decades, a lot of concerted efforts have been channeled into researching the local plants with hypotensive and antihypertensive therapeutic values.

The hypotensive and antihypertensive effects of some of these medicinal plants have been validated and others disproved. However, ayurvedic knowledge needs to be coupled with modern medicine and more scientific research needs to be done to verify the effectiveness, and elucidate the safety profile of such herbal remedies for their antihypertensive potential.

**Keywords:** Antihypertensive, herbs, hypotensive, hypertension, medicinal plants
Poster Session

CANCER AND AUTOIMMUNITY

Lupus and pulmonary carcinoma: a paraneoplastic lupus like syndrome or and idiopathic lupus?
LAC7-0089
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Background: Variety of solid and hematological tumors showed to be associated with rheumatologic disorders (RD). The most frequently reported paraneoplastic RD are inflammatory myositis, some atypical vasculitis and seronegative rheumatoid arthritis. For systemic lupus erythematosus (SLE), the causal relationship remains uncertain and poorly documented, particularly in case of solid cancer. We report a case of paraneoplastic SLE to lung carcinoma.

Case report: Mrs. NA, aged 57 years, with two years history of joint pain and arthritis, was treated three years ago of a pulmonary carcinoid tumor classified T3N0M0. Physical examination found joint swelling of both knees and both wrists, buccal ulcerations, alopecia plaques and axillar adenopathy. Laboratory exams showed biological inflammatory syndrome, renal insufficiency and positive proteinuria at 1.14g/24hours associated with hematuria. Renal biopsy revealed mesangial proliferation. Anti-nuclear antibodies were positive as well as the native anti-DNA. The diagnosis of SLE in its cutaneous-articular and renal form was retained. The patient was treated by corticosteroid. Two weeks later, she developed a cortico-induced psychosis with an acute delirious state, a disorganization syndrome, and confusion items. Brain imaging was normal with no evidence of vasculitis or metastasis. Corticosteroids were rapidly degreased. Thoracic CT scan showed obstruction of the Nelson bronchus and bronchi and tumor recurrence was confirmed by biopsy. The patient was referred to carcinology. Conclusion: The mechanisms of autoimmunity during solid cancers remain undetermined. The autoimmune pathologies associated with neoplasms do not necessarily behave like an authentic paraneoplastic syndrome, their evolution may not be parallel to that of tumor pathology.
BACKGROUND: The most recognized relationship is hypersensitivity vasculitis (Henoch-Schönlein purpura-PSH) with lymphoreticular neoplasms. OBJECTIVE: To present the case of a PHS as an initial manifestation of Multiple Myeloma (MM). CASE REPORT: Woman of 40 years. She presented generalized palpable purpura, edema and abdominal pain. Initial skin biopsy showed leukocytoclastic vasculitis and documented nephrotic syndrome with proteinuria of 10g / 24h and hematuria. Renal biopsy showed thrombotic microangiopathy, establishing PHS diagnosis. It was treated with 1g of cyclophosphamide and 3g of methylprednisolone monthly (5 cycles); with complete remission of skin lesions and kidney damage. Two weeks after the last cycle: asthenia, vomiting and hypercalcemia of 14mg / dl, acute renal failure with Cr 2.2mg / dl, required hemodialysis. Studies reported: Hb 10.6g / dl, leukocytes 9,800 and platelets 75000. Abdomen Rx and Abdominopelvic CT: left iliac crest lytic lesion. FSP: Roleaux. AMO: Infiltration of > 50% of lymphoplasmocitoid cells, binucleate cells, others with central nucleus and cytoplasmic extensions. Immunoglobulins: IgA 2640mg / dL (100-480), IgG 204mg / dL, IgM 16.9mg / dL. Albumin 2.0g / dL. Total Globulins 4.5g / dL. B2 Microglobulin 17.90mg / L (<2.51mg / L). Proteinogram: Fraction γ 2.57g / dL (0.8-1.6): monoclonal paraproteinemia. Immunofixation: lambda monoclonal protein trace. Guided biopsy of iliac lesion: Insufficient sample. Bone Biopsy: Cellularity 5%, Spinal Aplasia. We diagnosed MM IgA of lambda light chains, clinical stage IIIB with factors of poor prognosis. CONCLUSIONS: Vasculitis as paraneoplastic syndromes are of great importance since they precede a neoplasia susceptible to detection and timely treatment.
SSc is associated with an increased risk of malignancy with variable incidence, the cause has been attributed to the effect of antibodies and immunosuppressive therapy but to date the mechanism of this association is unknown. Risk factors suggest the onset of SSc at older age, Diffuse cutaneous variety (DcSSc) and positivity for anti-RNA polymerase III. It has been associated with lung cancer in 5%, breast, non-Hodgkin's lymphoma and multiple myeloma.

OBJECTIVE: Determine the prevalence of malignancy in patients with SSc, at CMN 20 de Noviembre ISSSTE hospital.

MATERIALS AND METHODS: Cross-sectional study in patients with SSc who attend to the rheumatology service. Descriptive statistics were performed. Calculations were performed using the SPSS software version 20.

RESULTS: 42 women with a mean age of 56 years. 5 (11.9%) had a diagnosis of DcSSc and 37 (88.1%) of limited cutaneous variety (LcSSc). The prevalence of malignancy was 14.4% (6 cases). The 40% presented hematological malignancies and the 60% solid tumor, of these 20% were of the breast. The mean age at diagnosis of the patients presenting with neoplasia was 57 years. 100% LcSSc. 6 patients (50%) had immunosuppressive management with Mycophenolate mofetil and methotrexate.

CONCLUSION: We found an increased prevalence of malignancy in SSc patients (14%), unlike reported in the literature, the main variety was LcSSc and according to what was reported, hematological malignancies were frequent and the age at diagnosis was higher.
Herbal medicine is the use of medicinal plants for prevention and treatment of diseases: it ranges from traditional and popular medicines of every country to the use of standardized and titrated herbal extracts. Generally cultural rootedness enduring and widespread use in a Traditional Medical System may indicate safety, but not efficacy of treatments, especially in herbal medicine where tradition is almost completely based on remedies containing active principles at very low and ultra low concentrations, or relying on magical-energetic principles.

In the age of globalization and of the so-called ‘plate world’, assessing the ‘transferability’ of treatments between different cultures is not a relevant goal for clinical research, while are the assessment of efficacy and safety that should be based on the regular patterns of mainstream clinical medicine.

The other black box of herbal-based treatments is the lack of definite and complete information about the composition of extracts. Herbal derived remedies need a powerful and deep assessment of their pharmacological qualities and safety that actually can be realized by new biologic technologies like pharmacogenomic, metabolomic and microarray mythology. Because of the large and growing use of natural derived substances in all over the world, it is not wise to rely also on the tradition or supposed millenarian beliefs; explanatory and pragmatic studies are useful and should be considered complementary in the acquisition of reliable data both for health caregiver and patients.
Poster Session

CANCER AND AUTOIMMUNITY

PD-L1 EXPRESSION IN 14 BIOPSY TISSUE SAMPLES OF USUAL INTERSTITIAL PNEUMONIA (IDIOPATHIC PULMONARY FIBROSIS)

LACAT-0212

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Introduction: There are striking similarities in the pathobiology and clinical outcomes of IPF and lung cancer. PD-L1 plays a role in controlling inflammatory response to injury in the normal lung tissues and could be critical in the pathogenesis of both IPF and lung cancer. Transforming growth factor-β (TGF-β), recognized as a key GF in the pathogenesis of IPF, is a pleiotropic cytokine with immunosuppressive effects on multiple cell types of the innate and adaptive immune system and one of the potential key factors modulating response to immune checkpoint inhibitors.

Purpose. The aim was to explore fibroblast and myofibroblast membrane Programme cell death-ligand-1 (clone 22C3) expression in formalin-fixed, paraffin-embedded lung fibrosis tissue samples.

Methods. Our study included IHH analysis of tissue samples from fourteen patients with IPF within different fibrotic patterns. Histological criteria comprised fibroblastic foci, as well as hypertrophic myofibroblast fibres. As controls, we have used rare intraalveolar macrophages or other immune cells positivity to PD-L1.

Results: PD-L1 expression was negative in all fourteen cases of IPF.

Conclusion: Based on similarities in the pathobiology of IPF and lung cancer and common expression of a number of GFs, some lung cancer drugs have already been translated into treatment option for IPF (Nintedanib). If findings of PD L1 expression would have been positive, there would have been place to investigate checkpoint inhibitors as a part of treatment modality for IPF as well.
We investigated the regulation of STAT3 in the immunophenotype modulation macrophage from M1 to M2 generate by cell culture supernatant of prostate cancer line PC3.

Supernatant PC3 and macrophages were collected, and cytokines analyzed nitric oxide and cytotoxic tests. Macrophages were evaluated by STAT3 and membrane proteins by flow cytometry. Macrophage cultures were exposed to supernatant PC3 line, with and without Sttatic inhibitor

Epidermal growth factor, fibroblast, granulocyte-monocyte colony, hepatocyte, platelet derivative A and B, cell stimulator, beta transformant, increased p <0.005 in the supernatant obtained from cultures of the macrophages exposed to the supernatant of the Line prostate cancer PC3 without inhibitor, like angiopoietin and erythropoietin. Cytokines IL-6, IL-4, IL-10 increased. IFN-γ and TNF-α decreased to undetectable values. Lactic acid increased 5 more times in both lines; nitric acid decreased p <0.005. Phosphorylated STAT3 increased 3-fold when macrophages were stimulated with PC3 supernatant, but not the total which maintained baseline values.

Cytokines present in the supernatant of the PC3 tumor line favor a change in the immunophenotype of macrophages to M2. Tumor-associated macrophages have been shown to play a key role in proliferation, progression, angiogenesis and metastasis. The results shown so far point to some points through which M2 may be constituted as therapeutic targets such as inhibition of STAT3 phosphorylation and suggest that the decrease in levels of these M2 or the reversion to an M1 phenotype can lead to in a decrease in tumor growth and spread.
Autoimmune encephalitis (AIE) is a disease of subacute presenting and it is mainly associated with autoantibodies anti-N-methyl-D-aspartate receptor (NMDAR). Objectives: to compare, according to autoantibody status, the main clinical characteristics of patients with suspected AIE.

Materials and methods: were evaluated 82 consecutive patients with a request for anti-NMDAR, anti-AMPA, anti-GABAB, anti-LGI1 and anti-CASPR2 antibodies (March 2015-March 2017) in CSF and/or serum (cell-based assays; Euroimmun, Germany); 63 with clinical data were included. The diagnosis of AIE was made based on clinical status, complementary studies, autoantibodies and exclusion of other pathologies.

Results: only anti-NMDAR positive was observed in 10 patients confirming the diagnosis of AIE; 2 female / 8 male, 18 months-36 years; 9 children. In 53 patients the autoantibodies were negative; 27 female / 26 male; 1-81 years; 40 children. In 2/53 patients a probable AIE was diagnosed (both children); 10/53 patients had previous diagnosis of another pathologies; 41/53 with other diseases or without a diagnosis. Anti-NMDAR positive patients presented: behavioral disorders (78%), speech dysfunction (89%); deglutition disorders (67%); insomnia (44%) and movement disorder (78%) which were significantly more prevalent compared to the negative ones; seizures and neuropsychiatric disorders had no significant differences. All patients with anti-NMDAR positive presented in their evolution 4 or more symptoms. Conclusions: patients with positive anti-NMDAR presented with a characteristic clinical picture; only 4% of patients with negative autoantibodies had a probable AIE. There was a lack of selection criteria for the request of autoantibodies in patients without clinical features of AIE or with previous pathologies.
Purpose: Cytokine-induced killer (CIK) cells have a high proliferative rate and anti-tumor activity, and can serve as an alternative cellular immunotherapy. We performed a randomized, phase III clinical trial to assess the safety of autologous CIK cells administration for adoptive immunotherapy combined with the standard temozolomide (TMZ) treatment with newly diagnosed glioblastomas (GBMs).

Methods: In this study, we randomly assigned patients with newly diagnosed GBM to receive CIK cell immunotherapy combined with standard TMZ chemoradiotherapy (CIK immunotherapy group) or standard TMZ chemoradiotherapy alone (control group). Toxic effects were recorded and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0.

Results: A total of 180 patients were randomly assigned to the CIK immunotherapy (n = 91) or control group (n = 89). Treatment-emergent adverse events (TEAEs) of any grade were reported in 84 (98.8%) of patients who received CIK immunotherapy group, and 83 (97.6%) of the control group. The incidences of total and ≥ grade 3 were higher in the CIK immunotherapy group than the control group. However, there was no significant difference between groups.

Conclusions: Our study suggested that adverse events by autologous CIK cells immunotherapy in GBM have been represented minor, self-limiting, and not serious.
An increased level of the protein serum amyloid A was detected by proteomic analysis in Neuropsychiatric Lupus Erythematosus Systemic (NPSLE) patient’s serum.

**Background:** Neuropsychiatric systemic lupus erythematosus (NPSLE) have multiple pathogenic mechanisms that cause its diverse manifestations, implying an additional challenge in diagnosis. A proteomics approach applying two dimensional electrophoresis (2D) and mass spectrometry (MS), allowed comparing the protein profile of the serum samples from NPSLE patients and control groups.

**Methods:** Eighteen patients with SLE were included. Nine of these patients had NPSLE, nine patients with neuropsychiatric syndromes not associated with SLE (NPnoSLE) and nine control subjects (CTRL). Two fractions were obtained, low and high abundance proteins. These fractions were resolved by 2D, and the gels were digitalized and analyzed with the PDQuest software. The statistical analysis of the spots was performed using the non-parametric Kruskal Wallis and the Dunn’s multiple comparison tests. The interest spots were identified by MS.

**Results:** Two spots showed significant differences. Spot 4009 was significantly lower in NPSLE with regards NPnoSLE (p= 0.004) and was identified as apolipoprotein A1 (APOA1) (score 809-1132). Spot 8001 was significantly higher in NPSLE regarding CTRL and NPnoSLE (p= 0.01 y 0.03) respectively and was identified as serum amyloid A (SAA) (score 725 - 2488).

**Discussion:** The inflammatory high density lipoproteins (HDL) have been described in SLE. In this HDL the decrease of APOA1 is followed by an increase in SAA. This has been implicated in the activation of certain proinflammatory pathways and the production of cytokines like IL-1β e IL-23. This cytokines might be involved in the disruption of the hematooencephalic barrier involved in many manifestations of NPSLE.
Background: When using HEP-2 cells for screening anti-nuclear antibodies (ANA), anti-dense speckled (DFS) immunofluorescence pattern could be observed. This fluorescence is due to the presence of nuclear DFS 70 antigen. These antibodies were associated to various chronic inflammatory diseases but also in healthy adults. We report 2 cases of DFS 70 antibodies associated to vasculitis.

Case 1: A 36 year-old female with no medical history was admitted for an etiological assessment of a retinal vasculitis responsible of a decrease in visual acuity. Physical examination was normal. Usual biological tests were normal. Infectious disease were ruled out with negative serologies. Cerebral MRI was normal. Antineutrophile antibodies were negative. ANA were positive at 1:1280 DFS70 positive (ELISA). There were not enough arguments to retain a systemic vasculitis such as the Behçet disease nor Takayasu’s arteritis or a connective tissue disease. Primary retinal vasculitis was diagnosed. The patient was treated by high doses of steroids with an improvement at one of treatment.

Case 2: A 17 year-old female had severe headaches. Physical examination was normal. Routine biological tests showed lymphopenia. Cerebral angio MRI showed multiples frontal demyelination. infections were ruled out. ANA were positive at 1:400 DFS70 positive (ELISA). Primary cerebral vasculitis was diagnosed. Headaches disappeared with high doses of steroids.

Conclusion: the prevalence of DFS 70 antibodies varies from 5 to 40%. ANA does not systematically means connective tissue disease. Although their negative predictive role if not associated to typical ANA is not yet confirmed. Prospective studies are needed.
Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as mineral oil, silicone and vaccines, which act as adjuvants and eliciting chronic stimulation of the immune system. There is little information about fibromyalgia (FM), depression and the deterioration of the quality of life (QL) in ASIA patients.

To determine the prevalence of FM, depression and both in ASIA patients versus systemic sclerosis (SSc) patients.

Patients and methods: A comparative cross-sectional study was performed in patients with ASIA. The prevalence of fibromyalgia according to criteria of ACR, depression by Beck questionnaire and QL with FS36 in patients with ASIA versus patients with systemic sclerosis matched by age were evaluated.

Results: There were 100 women, 50 ASIA patients (mean age 49 ± 9.7 yo) compared to 50 SSc patients (mean age 49 ± 10 years). Depression was found in 72% (Beck score median of 12), FM 66% (median score of 10) and both 56%: median of 12 (RIQ7). ASIA patients had a higher proportion of depression and the combination of depression and fibromyalgia were 72% vs 46% respectively. Fibromyalgia in 66% and both in 56%, (P0.008) and 56% vs 28% (p = 0.005). Patients with ASIA had a worse QL with SF36 and the most affected parameter in ASIA was the emotional role.

Conclusion: ASIA patients had higher prevalence of depression, fibromyalgia and greater deterioration of QL compared to SSc patients. ASIA criteria were fulfilled in all patients eluding the plausible link between ASIA and FM.
Aim: To evaluate the efficacy and safety of anti-tumor necrosis factor-alpha (anti-TNF-α) agents including infliximab (IFX) and adalimumab (ADA) in the treatment of refractory Behçet uveitis.

Results: Prior to anti-TNF treatment, 6 patients had used conventional immunosuppressive (IS) agents including azathioprine and cyclosporine, and 6 other patients had additionally used interferon-alpha 2a treatment. Before switching to anti-TNF agents, screening for latent TB was performed using the local guideline. The majority of the patients (n:10) received only IFX infusions 5 mg/kg at 0., 2nd, 6th weeks and in every 8 weeks thereafter. Among the other two patients, one received only ADA, while the other used both, i.e. later switched from IFX to ADA due to loss of clinical response. Altogether, there were 11 cases who used IFX.

Overall, mean treatment period for anti-TNF agents was 11.6 ± 4.9 (6-21) months, and treatment response was observed in 10 out of 12 patients (80%). Considering the 13 eyes of 8 patients who completed one-year period with these anti-TNF agents, basal uveitis relapse rate of 3.4±1.2/year decreased to 0.8±1.0/year (p<0.05). Overall, potential vision was preserved in all of the 21 eyes and visual acuity with Snellen was increased at least two lines in 6 out of 21 eyes (28.6%). No adverse effect requiring cessation of anti-TNF agents was observed. In 5 patients who completed the first year of anti-TNF treatment without any relapses, anti-TNF treatment could be stopped only in a single case using ADA, while anti-TNF treatment had to be continued in others.
Poster Session

CITRULLINATION AND AUTOIMMUNITY: ACPA

ECONOMIC IMPACT OF CCP TEST MISCLASSIFICATION (FALSE POSITIVES) IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS. A BENCHMARKING SIMULATION STUDY ACROSS SEVERAL LATIN-AMERICAN COUNTRIES.

LAC7-0211
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Introduction

Rheumatoid Arthritis (RA) is a chronic and progressive disease which needs to be diagnosed and treated in the early stages in order to avoid joint destruction. Anti-CCP antibodies are highly specific for RA and can help doctors to make decisions. Although the diagnostic accuracy of the CCP test used is important, the consequences of CCP misclassification have not been investigated. CCP-False Positives (FPs) patients could be managed as RA patients, bringing extra costs until correct diagnosis is made.

Objective

To simulate the economic burden of FPs for CCP across several Latin-American countries, comparing the misclassification results obtained with anti-CCP tests from different manufacturers.

Methods

A 12-months Markov model simulated, from the hospital perspective, 1,000 RA-suspected individuals tested in secondary care with five CCP tests (EliA CCP, Quantalite CCP 3.0, Anti-CCP EDIA, Axis-Shield anti-CCP; Elecsys Anti-CCP).

Sensitivities and specificities were derived from a systematic literature review and meta-analysis. Costs came from the published literature.

Uncertainty was addressed with sensitivity analysis.

Results

Costs for resource and clinical utilization were found to vary conspicuously between countries and studies from the same country (Table 1).

Using a prevalence of 50% in the secondary care setting, FPs ranged from 1.7% (EliA CCP) to 4.3% (Elecsys anti-CCP).

Cost of FPs was lowest when using EliA CCP (2.022 € - 21.559 €), and highest when using Elecsys Anti-CCP (5.055 € - 53.896 €) (Table 2).

Conclusion

EliA CCP test demonstrates superior value from patient, health care provider and payer perspective as a consequence of less false positive results.
CITRULLINATION AND AUTOIMMUNITY: ACPA

MONOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS DON’T HAVE AN INFLAMMATORY RESPONSE TO PLATELET DERIVED MICROPARTICLES FORMING IMMUNE COMPLEXES

LACAT-0077

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Introduction: Platelets are a known source of microparticles (MP). An increase in platelet-derived MP (PMP) positive for citrullinated peptides (CP) has been reported in synovial fluid and circulation of Rheumatoid Arthritis (RA) patients compared to healthy controls (HC). It is proposed that PMP and PMP forming immune complexes (PMP-IC) could activate different leukocytes like monocytes in synovial fluid and circulation, contributing to the inflammatory process in RA.

Methodology: PMP generated from HC platelets after collagen type IV stimulation, were stained for surface CP and opsonized or not with IgG (PMP-IC) obtained from seropositive RA patients. Monocytes from HC and RA patients were cultured under non-adherent conditions with or without PMP and PMP-IC for 6 hours; cytokine levels (IL-1β, TNF-α, and IL-10) in supernatants and membrane molecules associated with activation (HLA-DR, CD69, CD32) were evaluated by flow cytometry.

Results: PMPs generated in vitro contain CP and form IC (PMP-IC). In monocytes from RA patients, PMP and PMP-IC induced lower levels of IL-1β and TNF-α compared with HC; also IL-10 was induced in monocytes from RA patients but not in HC. There was up-regulation of HLA-DR, CD69 and CD32 in phagocytes from HC but not in those from RA patients after PMP-IC treatment. For both HC and RA patients, a higher response was observed with PMP-IC compared with PMP.

Conclusion: Monocytes from HC compared to RA patients’ cells respond in a proinflammatory way to PMP and in a more significant manner to PMP-IC.
Autoimmune diseases constitute a heterogeneous group of conditions with variable presentation and severity. About these diseases, the Systemic Lupus Erythematosis, which has one of the most common complications of lupus nephritis, can occur in up to 50% of cases, according to the study population, resulting in high morbidity and mortality. Approximately 20% of patients with lupus nephritis may progress to chronic renal disease at the terminal stage after 10 years of diagnosis of lupus, necessitating for a life-sustaining renal replacement therapy. Defined by the presence of persistent proteinuria ( > 0.5g in 24 hours) or greater than 3+ or by cylindruria (hematic, tubular, granular or mixed cylinders), lupus nephritis has presented advances in diagnostic tests and different immunosuppressive treatments have been developed in the last years. It is known that renal biopsy is the gold standard for the histological classification of nephritis and definition of the ideal treatment. However, because it is an invasive exam, there are limitations in performing it. In this way, new biomarkers of lupus nephritis are of great importance. Currently, the analysis of low molecular weight metabolite concentration profiles in biological fluids has been presented as a useful tool in the identification of new discriminatory biomarkers, allowing a better survival rate and quality of life among the individuals affected by the disease.
DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

PATIENTS WITH NON-AUTOIMMUNE DISEASES PRESENT A DIFFERENT PROFILE OF ANTI-CELL ANTIBODY TEST (INDIRECT IMMUNOFLUORESCENCE ON HEP-2 CELLS) REGARDING PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES

LACAT-0199
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¹Universidade Federal de São Paulo, Rheumatology, São Paulo, Brazil
²Universidade Federal de Pernambuco, Rheumatology, Recife, Brazil

Objectives and Methods: We determined the characteristics of positive indirect immunofluorescence anti-cell (previously named antinuclear) test on HEp-2 cells (HEp-2-IIF test) in 588 non-autoimmune disease (NAD) individuals, 194 systemic autoimmune rheumatic diseases (SARD) patients, and 1,217 healthy individuals (HI). NAD group comprised 4 subgroups: 95 with heterogeneous malignancies; 148 with infectious diseases; 163 with psychiatric diseases; 152 with multiple co-morbidities (diabetes mellitus, arterial hypertension, metabolic syndrome). Sera were tested at 1:80 and diluted to end-titer. Slides were analyzed by two independent blinded examiners at x400 magnification. We followed the anti-cell (AC) pattern nomenclature according to ICAP (International Consensus on ANA Patterns) recommendations. Results: A positive HEp-2-IIF result occurred in 102 (18.3%) NAD patients, 170 (87.6%) SARD patients, and 150 (12.3%) HI (p<0.001). NAD patients had higher titer than HI and these two groups had lower titer than SARD patients (p<0.001). The nuclear dense fine speckled pattern (AC-2) was more frequent in HI than in NAD patients (p=0.029) and was not observed in the SARD group. The nuclear homogeneous (AC-1) and nuclear coarse speckled (AC-5) patterns were more frequent in SARD patients than in the other groups (p<0.001). The most common pattern in all groups was the nuclear fine speckled (AC-4) pattern, which presented a gradient in titer across the three groups (p<0.001): HI and NAD patients had predominantly low and intermediate titer, respectively, and SARD patients had predominantly high titer. Conclusion: The pattern and titer of HEp-2-IIF positive tests in NAD patients clearly differ from SARD patients.
Introduction: Systemic sclerosis (SSc) is an autoimmune disease with multiple manifestations, of which esophageal compromise is frequent. By its characteristics, has a high mortality and morbidity. We did a description of a group of patients who underwent high resolution esophageal manometry for presenting upper digestive symptoms suggestive of compromise by SSc.

Methods: A retrospective analysis was performed in a group of patients with a diagnosis of SSc that required high resolution esophageal manometry in the gastrointestinal physiology unit of the Hospital Universitario San Ignacio during the years 1/2015 - 3/2016

Results: Data were obtained from 23 patients (table 1) of which 21 were women (91.3%), with a mean age of 59.65 (10.63 ±) years, and an average disease time of 7.83 years (± 6.57). The main indication for manometry was dysphagia for solids (69.9%), with aperistalsis finding in 87% of patients.

In addition, it was important to note that the Raynaud phenomenon (91.3%), interstitial lung involvement (17.4%) and diffuse cutaneous involvement (87%) were associated with esophageal compromise, which are being studied recently as predictors of early esophageal involvement.

Conclusions: The results of our study are comparable with those described in the literature regarding the digestive compromise and manometric findings in SSc. Additionally, the role of high resolution esophageal manometry as the best tool for the evaluation of these disorders and the active search for symptomatology that guides the early detection of this compromise is highlighted.
<table>
<thead>
<tr>
<th>Características</th>
<th>N=23</th>
<th>Media (DS) ó n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexo (F)</td>
<td>21 (91,3)</td>
<td></td>
</tr>
<tr>
<td>Edad (años)</td>
<td>59,65 (10,63)</td>
<td></td>
</tr>
<tr>
<td>Poliautoinmunidad</td>
<td>7 (30,4)</td>
<td></td>
</tr>
<tr>
<td>SSc limitada</td>
<td>3 (13)</td>
<td></td>
</tr>
<tr>
<td>SSc difusa</td>
<td>20 (87)</td>
<td></td>
</tr>
<tr>
<td>Tiempo evolución SSc (años) (n=21)</td>
<td>7,83 (6,57)</td>
<td></td>
</tr>
<tr>
<td>Fenómeno de Raynaud</td>
<td>21 (91,3)</td>
<td></td>
</tr>
<tr>
<td>Compromiso intersticial pulmonar</td>
<td>4 (17,4)</td>
<td></td>
</tr>
<tr>
<td>Hipertensión arterial pulmonar</td>
<td>6 (26,1)</td>
<td></td>
</tr>
<tr>
<td><strong>Anticuerpos</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti Centrómero</td>
<td>12 (52,2)</td>
<td></td>
</tr>
<tr>
<td>ScI70</td>
<td>2 (8,7)</td>
<td></td>
</tr>
<tr>
<td><strong>Síntomas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disfagia para sólidos</td>
<td>16 (69,6)</td>
<td></td>
</tr>
<tr>
<td>ERGE</td>
<td>9 (39,1)</td>
<td></td>
</tr>
<tr>
<td><strong>Hallazgos manométricos</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aperistalsis</td>
<td>20 (87)</td>
<td></td>
</tr>
<tr>
<td>Hipotonia EEI</td>
<td>10 (43,5)</td>
<td></td>
</tr>
<tr>
<td>Aclaramiento incompleto</td>
<td>3 (13)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3 (13)</td>
<td></td>
</tr>
<tr>
<td><strong>Hallazgos EVDA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estigmas sangrado</td>
<td>2 (8,7)</td>
<td></td>
</tr>
<tr>
<td>Hemia hiatal</td>
<td>10 (43,5)</td>
<td></td>
</tr>
<tr>
<td>Gastropatía antral</td>
<td>14 (60,9)</td>
<td></td>
</tr>
<tr>
<td>Reflujo gastroesofágico</td>
<td>8 (34,8)</td>
<td></td>
</tr>
</tbody>
</table>

DS: desviación estándar; F: femenino; SSc: Esclerosis sistémica; ERGE: enfermedad por refl ujo gastroesofágico; EEI: esfínter esofágico inferior; Poliautoinmunidad: Presencia de 2 o más enfermedades autoinmunes en un mismo individuo
Poster Session

DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

Inflammatory parameters “TGF-β, Neutrophil/Lymphocyte ratio and Platelet/Lymphocyte ratio” in normovitaminosis vs hypovitaminosis D in systemic sclerosis

LACAT-0177

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⁵Instituto Mexicano del Seguro Social, Jefatura de Investigación en salud, México city, Mexico

Hipovitaminosis D is frequent between 50-80% in systemic Sclerosis (SSc). Vitamin D has the ability to suppress inflammatory cytokines such as TGF-β. SSc is characterized by fibrosis, vasculopathy and autoimmunity. Screening evaluations help to identify complications and rapid progression. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been proposed as biomarkers to assess the inflammation status.

Aim. The aim of this study was to determine the values of peripheral TGF-β, NLR and PLR in adults with SSc (normovitamin or hypovitaminosis D).

Material and Methods. After venous blood collection were measured counts of white blood cells (WBC), neutrophils (NEU), and lymphocytes (LYM), platelets (PLA) and TGF-β. The informed consent was obtained from all participants. X² test, U-Mann Whitney and Spearman's correlation test were used for the analysis. assessed by. A p-value < 0.05 was considered Statistically significant.

Results

We include 101 SSc patients. Only 30 (29.7%) had normal levels of vitamin D(25OHD) and 70.2% had hypovitaminosis D. Twenty-seven cases of hypovitaminosis D, 25 with insufficiency and 19 with deficiency D. The demographics, clinical and laboratory characteristics are summarized in Table 1. There was no difference between two groups (normovitaminosis D vs hypovitaminosis D) with regard to sex, age, disease duration, subtype cutaneous. The correlation analysis between NLR, PLR, TGF-β and 25 OH vitamin D and clinic characteristics are summarized in Table 2.

Conclusions

Hipovitaminosis D is frequent in SSc. PLR and TGF-β values can serve as useful markers of SSc regardless of vitamin D.
Table 1. Sociodemographic attributes and laboratory characteristics of patients with SSc and low levels of vitamin D.

<table>
<thead>
<tr>
<th></th>
<th>SSc+Hypo25OHD</th>
<th>SSc+Norm2OHD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>51 ± 12</td>
<td>50 ± 13</td>
<td>0,537</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>71/3</td>
<td>27/1</td>
<td>1,00</td>
</tr>
<tr>
<td>Subtype cutaneous, (diffuse/limited), p(%)</td>
<td>35/44</td>
<td>10/12</td>
<td>0,889</td>
</tr>
<tr>
<td>Disease duration (years), median (min-max)</td>
<td>12 (1-42)</td>
<td>10 (1-24)</td>
<td>0,605</td>
</tr>
<tr>
<td>25 OH Vitamin D (ng/mL), median (min-max)</td>
<td>16,98 (0,09-44,07)</td>
<td>32,44 (7,38-67,26)</td>
<td>------</td>
</tr>
<tr>
<td>WBC count (x103/μL), mean ± SD</td>
<td>6,85 ± 2,27</td>
<td>6,11 ± 1,93</td>
<td>0,240</td>
</tr>
<tr>
<td>Neutrophil count (x10⁹/μL g/dl), median (min-max)</td>
<td>3,70 (0,39-13,29)</td>
<td>3,70 (0,17-5,88)</td>
<td>0,910</td>
</tr>
<tr>
<td>Lymphocytes, count (x10³/μL g/dl), (min-max)</td>
<td>1,64(0,21-3,33)</td>
<td>1,46(0,10-3,99)</td>
<td>0,077</td>
</tr>
<tr>
<td>PLQ count (x10⁷/μL), mean ± SD</td>
<td>255 ± 66</td>
<td>232 ± 35</td>
<td>0,216</td>
</tr>
<tr>
<td>NLR, median (min-max)</td>
<td>2,14 (0,21-21,35)</td>
<td>2,77 (1,44-4,68)</td>
<td>0,232</td>
</tr>
<tr>
<td>PLR, median (min-max)</td>
<td>142,28 (0,00-975,91)</td>
<td>162,38 (64,57-270,31)</td>
<td>0,309</td>
</tr>
</tbody>
</table>

SSc, Systemic sclerosis, Hypo25OHD, Hypovitaminosis D, Norm25OHD 25 OH vitamin D normal.

Table 2. Correlation analysis between NLR, PLR, TGF-β values and 25 OH vitamin D.

<table>
<thead>
<tr>
<th></th>
<th>NLR (r value; p value)</th>
<th>PLR (r value; p value)</th>
<th>TGF-β (r value; p value)</th>
<th>25 OH VITD (r value; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration (years)</td>
<td>(-0,161; 0,080)</td>
<td>(-0,192; 0,035)*</td>
<td>(0,043; 0,723)</td>
<td>(-0,061; 0,550)</td>
</tr>
<tr>
<td>Body mass index (BMI) (Kg/m²)</td>
<td>(-0,113; 0,287)</td>
<td>(-0,169; 0,111)</td>
<td>(-0,083; 0,502)</td>
<td>(0,247; 0,022)*</td>
</tr>
<tr>
<td>Total score of Rodnao</td>
<td>(-0,051; 0,629)</td>
<td>(-0,028; 0,794)</td>
<td>(0,122; 0,327)</td>
<td>(-0,020; 0,855)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (LVEF)</td>
<td>(0,012; 0,933)</td>
<td>(0,146; 0,323)</td>
<td>(0,287; 0,069)</td>
<td>(0,159; 0,260)</td>
</tr>
<tr>
<td>Forced Vital Capacity (FVC)</td>
<td>(0,775; 0,536)</td>
<td>(0,045; 0,713)</td>
<td>(0,156; 0,328)</td>
<td>(0,150; 0,292)</td>
</tr>
<tr>
<td>Pulmonary artery systolic pressures (PASP)</td>
<td>(0,226; 0,132)</td>
<td>(0,202; 0,177)</td>
<td>(-0,415; 0,009)**</td>
<td>(-0,255; 0,098)</td>
</tr>
<tr>
<td>25 OH D</td>
<td>(0,113; 0,261)</td>
<td>(0,148; 0,138)</td>
<td>(0,034; 0,780)</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>(0,030; 0,763)</td>
<td>(0,021; 0,826)</td>
<td>(0,012; 0,921)</td>
<td>(0,107; 0,311)</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>(-0,585; &lt;0,001)***</td>
<td>(-0,877; 0,000)***</td>
<td>(-0,001; 0,993)</td>
<td>(-0,357; 0,004)**</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>(0,489; &lt;0,001)***</td>
<td>(-0,222; 0,087)</td>
<td>(-0,132; 0,350)</td>
<td>(0,017; 0,894)</td>
</tr>
<tr>
<td>Platelets</td>
<td>(0,026; 0,835)</td>
<td>(0,239; 0,046)*</td>
<td>(-0,046; 0,743)</td>
<td>(0,011; 0,932)</td>
</tr>
<tr>
<td>NLR</td>
<td>-------------------</td>
<td>(0,898; &lt;0,001)***</td>
<td>(0,220; 0,065)</td>
<td>(0,113; 0,261)</td>
</tr>
<tr>
<td>PLR</td>
<td>(0,898; &lt;0,001)***</td>
<td>-------------------</td>
<td>(0,251; 0,035)*</td>
<td>(0,148; 0,138)</td>
</tr>
<tr>
<td>TGF-β</td>
<td>(0,220; 0,065)</td>
<td>(0,251; 0,035)*</td>
<td>-------------------</td>
<td>(0,034; 0,780)</td>
</tr>
</tbody>
</table>
WEAK AGREEMENT BETWEEN 18-FDG PET/CT AND THE INDIAN TAKAYASU ACTIVITY SCORE IN A MEXICAN SINGLE CENTER POPULATION
LACAT-0095
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³Instituto Nacional de Cardiologia Ignacio Chavez, Immunology, Ciudad de Mexico, Mexico

Background:
One of the diagnostic tools employed in Takayasu arteritis is 18-FDG PET/CT. A new clinical score, ITAS2010 (Indian Takayasu Clinical Activity Score), has recently been validated to determine the activity status of the disease, that score can include erythrocyte sedimentation rate and C reactive protein (ITAS-A).

Objective:
To explore the agreement between 18-FDG PET/CT and ITAS2010/ITAS-A in order to measure the activity of Takayasu arteritis.

Methods:
We included the clinical records of patients that had one 18-FDG PET/CT performed and the required information to fulfill the scores ITAS2010 and ITAS-A. The SUVmax cut-off 2.1 was considered. The kappa index was calculated with the cut-off points for ITAS2010 (2) and for ITAS-A (4) previously reported in literature. As an exploratory analysis, we performed ROC to detect new cut-off points for ITAS2010 and ITAS-A, then we calculated new kappa index. We considered p < 0.05 as statistically significant.

Results:
Thirty-six clinical records with 18-FDG PET/CT were available but there was enough information to score ITAS2010 only in 31 patients and for ITAS-A only in 29 patients.

There was no agreement between 18-FDG PET/CT and ITAS2010 and ITAS-A with the previously reported cut-off points. We only observed a weak agreement for ITAS-A with the new 3.5 cut-off point (kappa=0.364, p=0.049).

Conclusions
There was not agreement between 18-FDG PET/CT and ITAS2010/ITAS-A in our population. The retrospective design of the study is the most important limitation.
Autoimmune diseases (AD) are a heterogeneous group of processes, that present in common: autoimmune phenomena, affecting different organs or systems potentially serious, with important repercussions on the economy of the individual, family and health system.

Objective: Determine the frequency of autoimmune disease in hospitalized patients in a third level Hospital in Guatemala City.

METHODS: This is a transversal descriptive study, include all patients hospitalized in Roosevelt Hospital between 2005 and 2014 with an autoimmune disease. The data were included in a ticket for the statistical analysis, made descriptive statistics analysis on the number of cases, percentages of each autoimmune disease and calculation of absolute and relative frequencies.

Results: Of the 1,278 patients hospitalized in the different internal medicine services, the gender of patients: 74.64% (n = 954) women and 25.32% (n = 324) men, the mean age was 33.71 (SD ± 17.24) for male sex and 34.88 (DE+15.72) for female sex, in relation with diagnosis: Systemic Erythematous Lupus 35.36%, Guillian Barre Syndrome 15.49%, Rheumatoid Arthritis 9.62%, for Inflammatory Myopathy 6.24%, Scleroderma 2.73%, Antifosfolipid Syndrome in 2.5%, Vasculitis in 2.58%, Myasthenia Gravis 3.99%, Transverse Myelitis 3.12%, Diabetes Mellitus 1 in 1.33%, Idiopathic Purpura Trombocitopenic in 4.06%, Autoimmune Hemolitic Anemia 1.87%, Pemphigus 1.09%, the principal comorbidities was Arterial Hypertension 6.72% and Diabetes Mellitus 2 in 2.58%. In conclusion the principal causes of autoimmune diseases is same a another reports in the world.
In view of the increasing importance of serological biomarkers for screening and diagnosing celiac disease (CD), lack of back-to-back comparison, and reliability of isolated or combined antibody test systems to reflect intestinal damage in children with CD, their differential performances were evaluated.

95 pediatric CD patients (mean age 8.3), 45 nonspecific abdominal pain children (AP) (mean age 7.3), 99 normal children (NC) (mean age 8.5) were tested with the following ELISAs (detecting IgA, IgG or both, IgA and IgG (check)):

- **AESKULISA® Gliadin (AGA)**, **AESKULISA® DGP (DGP)**, **AESKULISA® tTg “New Generation”** (Neo-epitope tTg complexed to gliadin= tTg-neo), tTg (for in house research purpose only), **AESKULISA® mTg neo-epitope and mTg (RUO)**. Anti-endomysial antibodies (EMA) were checked by immunofluorescence (**AESKUSLIDES® EMA**). The results were compared to the degree of intestinal injury, using the revised Marsh criteria.

Most assays were able to discriminate between patients with low and high degree of intestinal damage. Comparing the different correlations between CD associated IgA and IgG antibodies’ isotypes, the tTg-neo IgA (r=0.6165, p<0.0001) and tTg-neo check (r=0.6492, p<0.0001) stood out, significantly, as the best indicators of the intestinal damage in CD. EMA-IgA, tTg and DGP check and mTg-neo IgG correlated nicely to the mucosal injury.

It is suggested that tTg-neo IgA/IgG antibodies should be used preferably to reflect intestinal damage during screening and diagnosing childhood CD. EMA-IgA, tTg, DGP checks and mTg-neo IgG titers followed the tTg-neo check performance. mTg-neo IgG presents a new serological biomarker for CD.
Poster Session

DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

EPITOPES OF HUMAN AND MICROBIAL TRANSGLUTAMINASES ARE SHARED BY CELIAC DISEASE SERA

LACA7-0028

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Objectives and study: The consumption of microbial transglutaminase (mTg) in Western diet is expanding. mTg shares multiple functional similarities with human endogenous tTg. However, immunogenic comparison of the two enzymes in celiac disease (CD) is lacking.

Methods: Complexing mTg and gliadin results in mTg neo-epitope (mTg neo). The complexes were purified by asymmetric flow field-flow fractionation and confirmed by multi-angle light scattering and SDS-PAGE. Sera of 81 CD patients and 81 healthy controls were analysed using the following ELISAs: AESKULISA® tTg New generation (tTg neo-epitopes) IgA and IgG, AESKULISA® Gliadin IgA and IgG, AESKULISA® DGP IgA and IgG and AESKULISA®s against mTg and mTg neo-epitopes (Research use only (RUO) Kits as IgA and IgG).

Results: Purified mTg-neo IgG and IgA (AUC=0.92, 0.93, respectively) showed an increased immunoreactivity compared to single mTg and gliadin (p<0.001) but similar immunoreactivity to the tTg-neo IgG and IgA ELISA (AUC=0.94, 0.95, respectively). Using a competition ELISA, the mTg neo-epitopes and tTg neo-epitopes have identical outcomes in CD sera both showing a decrease in optical density of 55±6%, (p<0.0002). Sera with high antibody titre [U/ml] against the tTg neo-epitope show also high antibody activities of the mTg neo-epitope and vice versa indicating the presence of similar epitopes within the Tg-gliadin complexes.

Conclusion: mTg and tTg display a comparable immunopotent epitope. mTg neo-epitope IgA and IgG antibodies are immunogenic in CD. If substantiated, it will impact the food industry additive regulation.
Objective and study: Evolution is accompanied by enrichment of gluten content in the wheat and today 80% of the proteins are gluten. In parallel, some unwanted effects induced by gluten consumption in non-celiac affected populations are recently described.

Aims: To summarize the literature for gluten consumption and withdrawal effects on autoimmune diseases in general and rheumatoid arthritis (RA) in particular.

Methods: A systematic review was performed, using Medline, Google, and Cochrane Library databases.

Results: Multiple autoimmune conditions respond to gluten free diet (GFD), including RA. Several pathophysiological avenues were described for the detrimental effects of gluten: breach of intestinal tight junction integrity, decrease in viability and apoptosis induction in human cell lines, induction of neutrophil migration, decrease in NKG2D and ligand expression, increase of Th17 cell population, effect on regulatory T-cell subsets, change of innate immunity, change of dendritic cell functions and change of microbiome diversity. The articular tissue transglutaminase and its inflammatory effects, the intestinal peptidylarginine deiminase, the enterocyte’s origin of citrulline, the beached tight junction integrity, the arthritis in celiac disease, the enteritis in early RA and the partial response to GFD, are several potential pathophysiological pathways, connecting gluten consumption to RA.

Conclusions: Multiple non-celiac autoimmune diseases and conditions respond, to a variable degree to GFD. The protective mechanisms of GFD are constantly unraveled and involve multiple immunoregulatory pathways. Several pathophysiologival pathways can explain the detrimental health effects of gluten consumption in RA.
Introduction

Autoimmune diseases arise from an abnormal immune response, of generally unknown cause; they have been deemed to be in high prevalence among the general population. Environmental factors, viral infections, and genetic factors, have been identified as potential causes that can trigger an abnormal immune response in susceptible individuals. Indirect Immunofluorescent Assay (IFA) on HEp-2 cells is considered to be the gold standard method of ANA detection, making it a useful tool for the diagnosis of many autoimmune diseases.

The International Consensus on Antinuclear Antibody Pattern (ICAP) classifies 28 patterns with the most frequent being homogeneous, granular, centromere and nucleolar. However, there are others that while clinically significant occur less frequently. The objective of this report is to present evidence of 3 low frequency patterns in the population, which are included within the classification of mitotic patterns according to ICAP.

Methodology

Serum specimen were tested using ImmuGlo™ ANA HEp-2 slides (Immco Diagnostics, A Trinity Biotech Company), and subsequently analyzed on the Immco i-Sight IFA system. Images of reacted wells were reviewed by two expert readers who reported immunofluorescence patterns.

Results

Among the samples processed, three patients were observed, 2 men and 1 woman, aged 38 to 54 years old with suspected autoimmune disease and unusual immunofluorescence patterns. These patterns presented characteristics of the typical patterns: centrosome (Fig1), spindle fibers (Fig2) and NuMA-like (Fig3) which conform to what is described by ICAP.

Conclusion

These cases show the importance of adequately differentiate and report mitotic patterns since they provide a useful aid in the diagnosis of many autoimmune diseases.
The aim - to summarize our data on complement components involving in recognition upon autoimmunity diseases. **Methods:** Components of the patient sera were registered by immunochemical methods using microplates (hybrid functional analysis of isotypes C4A and C4B, analysis of functional C1-inhibitor detection). Isoelectrophoresis of the patient sera in the plate of polyacrylamide gel followed by electroblotting on the membrane was developed. Rabbit and goat polyclonal antibodies (conjugated to the horseradish peroxidase) against human complement components (C4, C3, C1-inhibitor, C1q, factor H) and Ig were used. Activity of the antibodies bound peroxidase was detected in the presence of OPD or TMB (microplate) or chemiluminescent substrate (blot) of increased stability and sensitivity (BioWest) in a real time [BioChem System (UVP)]. **Results:** 1. Sera of patients (autoimmune diseases) were characterized on the blot by appearance of aggregated C4B and C4A in the new diagnostic region (pI 4.0-4.7). Target recognition abilities of isotypes were confirmed by analyses in microplate. Amounts of isotypes and their subisotypes as well as ratio of isotypes characterized prognostic-diagnostic patient groups of autoimmune diseases (SLE, antiphospholipid syndrome, rheumatoid arthritis). Appearance and relative intensities of aggregated isotypes and subisotypes of C4 indicated the presence of disease, its initiation, reached phase of disease and/or disease character. 2. Similar localization of the complex C4B and C1-inhibitor of patients on the blot was registered. **Conclusions:** Results reveal relationships between C4B and C1-inhibitor upon disease. New mechanisms of protection involving complement are proposed. Results develop applications in diagnostics of early, progressive and chronic autoimmune diseases.
DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

EVALUATION OF ANTI-DOUBLE STRANDED DNA ANTIBODIES IN THE MONITORING OF SYSTEMIC LUPUS ERYSITEMATOSUS

LACAT-0127

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Background:

Anti-dsDNA antibodies are routinely used to monitor disease activity (DA) and are component of the SELENA-SLEDAI index. Due to the importance of anti-dsDNA antibodies, the choice of anti-dsDNA is crucial in the clinical laboratory. The objective was to compare four anti-dsDNA assays for their performance characteristics of SLE-DA.

Methods:

A cohort of 36 subjects with active SLE presenting with classical complement activation were followed monthly for 1 year. At each study visit serum was obtained resulting in a total of 371. SELENA-SLEDAI was scored on the day of each study visit excluding anti-dsDNA or complement components (non-serological [ns] SELENA-SLEDAI). All specimens were tested using four anti-dsDNA kits (see results section, all Inova Diagnostics). Study visits presenting with inactive disease (ns-SELENA- SLEDAI score=0) were compared to those presenting with active disease (ns-SELENA- SLEDAI>0). The longitudinal data were analyzed using linear mixed effect modeling with the ns-SELENA-SLEDAI as dependent variable and the anti-dsDNA titers as fixed effect predictors. Marginal R² was calculated for each assay.

Results:

The sensitivity of the QUANTA Lite and High Avidity anti-dsDNA both reached 64%; whereas anti-dsDNA positivity was 83% by QUANTA Flash and reached 96% by CLIFT. Study visits with active disease presented with several fold higher anti-dsDNA titers than those with inactive disease status. Linear mixed effect modeling indicated that the decrease in ns-SELENA-SLEDAI scores were associated with significant reduction in titers of all three anti-dsDNA kits (Table 2). QUANTA Flash yielded highest marginal R² (0.112).

Conclusion:

Our data indicate that QUANTA Flash dsDNA has highest value in monitoring SLE-DA.
Background Antibodies targeting carbamylated proteins (anti-CarP antibodies) are present in rheumatoid arthritis (RA) patients and associate with a more severe disease course. In addition, the presence of anti-CarP antibodies is associated with the development of RA in arthralgia patients and healthy blood donors. Carbamylated-fetal calf serum (Ca-FCS), a complex protein mixture, is mostly used as antigen in ELISA to identify the presence of anti-CarP antibodies. Recently, alpha 1 antitrypsin (A1AT) has been identified as a target of autoantibodies in RA patients. The current study aimed to identify B-cell epitopes on 40 mer carbamylated A1AT fragments.

Methods The known protein sequence of human A1AT was used to synthesize 20 synthetic 40 mer peptides with an overlap of 20 amino acids spanning the entire protein sequence. Peptides were then carbamylated using the method described by Shi et al. and tested by ELISA for reactivity with RA patient samples (n=9) and controls (n=6), both in carbamylated and non-carbamylated form. An extended cohort of RA patients (n=71) and disease controls (n=53) was assayed on the three most reactive peptides.

Results The reactivity to A1AT derived peptides significantly increased for most of the peptides when present in carbamylated form (by paired t-test). In the extended testing, the reactivity to the three carbamylated peptides was significantly higher in RA patients compared to controls (by Mann Whitney test; p<0.05).

Conclusion Ca-A1AT derived peptides might represent promising antigens for the detection of anti-CarP antibodies as an aid in the assessment of RA patients.
Introduction:

Primary biliary cholangitis (PBC) is characterized by the presence of anti-mitochondrial type 2 antibodies (AMA-M2). While around 90% of patients have IgG AMA-M2 (often measured as Mit-3), approximately 10% of patients with clinically-proven PBC are consistently serologically negative for IgG AMA-M2. Consequently, a PBC Screen ELISA has been developed measuring both IgG and IgA to Mit-3, SP100 and gp210 antibodies. In addition, antibodies to Kelch-like protein 12 derived peptide (KL-P) and Hexokinase-1 (HK-1) have been described recently in PBC patients. This study aimed to analyze if the two novel antibodies could help to identify more antibody positive PBC patients.

Methods:

The study included 225 samples from patients with PBC which were tested by Mit-3 and PBC Screen ELISA and also for anti-KL-P peptide and anti-HK-1 antibodies using prototype ELISAs (research use only, Inova Diagnostics).

Results:

In our cohort, 30/225 (13.3%) were negative for Mit-3 and 13/225 (5.8%) for PBC Screen antibodies. In the Mit-3 negative group, 3/30 (10%) and 10/30 (33.3%) were positive for anti-KL-P and or anti-HK-1 antibodies, respectively. In the PBC Screen negative group, 0/30 (0%) and 6/13 (46.2%) were positive for anti-KL-P and or anti-HK-1 antibodies, respectively.

**Conclusion:**

In this study a significant proportion of Mit-3 and PBC screen seronegative PBC patients are identified with the detection of KL-P and HK-1 antibodies, supporting their clinical utility.
This study was to aim to determine the microglobulin level of serum B2 in geriatric patient population as an inflammatory marker and to compare with other inflammatory markers in order to determine its effectiveness, reliability and whether it is brittleness marker or not. In order to evaluate the relationship between inflammation and Serum B2 microglobulin level, totally 81 participants were attended as 20 patients with rheumatoid arthritis, 20 patients with osteoarthritis, 22 patients with acute infection and 19 control groups. Serum B2 was compared with other inflammatory makers such as sedime, CRP, procalcitonin, ferritine, IL-1, IL-6, TNF-alpha, D vitamine and routine biochemical tests. To evaluate the touchiness, Quality of Life Measure and Clinical Frailty Scale(cfs) are applied.

29 men and 52 women patients have attended. Average of B2 microglobin level of all groups have been determined as 3.8±1.3 mg/L. Significant difference was determined as statistically between groups and B2 Microglobulin level. B2 microglobulin was determined as high in both acute infection and rheumatoid arthritis. And increased values have been seen in Rheumatoid arthritis, osteoarthritis and healthy individuals. B2 Microglobulin has positive correlation with age, CRP, sedime, procalcitonin, WBC, ferritin, HES, IL-6, TNF alpha, CFS. Beta-2 Microglobulin level is independent from other variables and it has shown positive correlation with age, IL-6, TNF-alfa and CFS scores and it has shown negative correlation with SF-36 score. Serum Beta-2 Mikroglobulin level has shown that it has correlation with CRP in the case of acute infectious.
Background
PBC–AIH overlap syndrome is defined by the simultaneous or consecutive association of at least two of three diagnostic criteria usually recognized in both pathologies. This syndrome is thought to be rare. Its prevalence is of the order of 8-20% of all the CBP and HAI diagnosed as such. Diagnosis is based on the combination of clinical, biologic, immunologic and histological arguments.

Observation
A 49-year-old female with known history of primary sterility presented since 2 years ocular and oral dryness in context of anorexia and weight lost. There was not jaundice or pruritus or fever. The diagnosis of Sjögren's syndrome was confirmed by objective signs of dryness on examination and a characteristic lip biopsy. Hepatic tests gave the following results: elevated serum alkaline phosphatase and gamma-glutamyltransferase with a high level of the other hepatic parameters: aspartate aminotransferase, alanine aminotransferase and bilirubin. The patient denied alcohol and drug use. Serological tests were negative for hepatitis. Liver ultrasound was normal. Immunologic tests showed the presence of anti-mitochondrial antibodies and anti-smooth muscle antibodies. Further biological investigations revealed that she was positive for antinuclear antibodies but negative for cryoglobulinemia. A liver biopsy confirmed the diagnosis of PBC, revealing stage 3 histology according to Ludwig and Scheuer's classification. This led to the diagnosis of PBC associated to AIH. A thoraco-abdomino-pelvic computed tomography showed hepato-splenomegaly and epiploic, mesenteric, mediastinal and axillary lymphadenopathy. Acideursodesoxycholique (UDCA) associated to corticosteroids and Azathiprine induced after 3 months a significant decrease in biochemical cholestasis and cytolysis.

Conclusion
In our case of Overlap syndrome, combination of UDCA, corticosteroids and immunosuppressive treatment led to a significant decrease of biochemical cholestasis and cytolysis.
Background: Zymogen granule glycoprotein 2 (GP2) was demonstrated as the first specific autoimmune target in primary sclerosing cholangitis (PSC) associated with disease severity and/or cholangiocarcinoma. In total, four human GP2 isoforms (GP2\textsubscript{1-4}) were identified and respective autoantibodies were detected in patients with inflammatory bowel disease (IBD) aiding in the serological diagnosis thereof. We wondered whether antibody analysis to all GP2 isoforms can improve the assay performance for PSC serology.

Methods: Antibodies (IgG and IgA) against four GP2 isoforms (GP2\textsubscript{1-4}Abs) were detected by indirect immunofluorescence assay using stable HEp-2 cell-lines expressing membrane-bound GP2 isoforms in 232 patients with PSC of four European gastroenterology centers and 145 controls comprising 95 patients with cystic fibrosis and 45 healthy individuals.

Results: Apart from GP2\textsubscript{2}Ab, all other GP2Abs demonstrated significantly elevated prevalences in PSC patients compared with controls (p<0.05, respectively). Remarkably, IgA GP2\textsubscript{1}Ab (46.6%) and GP2\textsubscript{4}Ab-positives (48.3%) revealed the highest frequencies resulting in an even significantly elevated combined positive rate of 64.7% (IgA GP2\textsubscript{1}and/or GP2\textsubscript{4}Ab, p=0.0001, 0.0004, respectively). Combined IgA GP2\textsubscript{1}Ab/GP2\textsubscript{4}Ab testing with a sensitivity of 65.1% and a specificity of 65.1% and a specificity of 65.1% resulted in the best diagnostic performance (Youden index: 0.63) regarding all GP2Abs and combinations thereof. Apart from significantly higher positive rates of IgG to GP2 isoforms in PSC, we detected a significantly elevated prevalence of IgG GP2\textsubscript{3}Ab in control patients with cystic fibrosis, a bile duct disorder with a different pathogenesis, versus healthy controls (18.9%/4.0%, p=0.0119).

Conclusions: Combined IgA GP2\textsubscript{1}/GP2\textsubscript{4}Ab analysis is required for sensitive PSC-specific autoantibody testing.
Poster Session

DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

LEVELS OF INFLAMMATORY SEROLOGIC BIOMARKERS IN HLA-B27 AND HLA-B15 POSITIVE PATIENTS WITH SPONDYLOARTHRITIS

LACA7-0061

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Background: The main challenge in spondyloarthritis management are the lack of biomarkers that could be associated with disease activity, or that could predict joint damage or response to treatment. With the understanding of SpA pathogenesis, several biomarkers have been proposed including metalloproteinase 3 (MMP-3), interleukin (IL) 1a, IL-6, lipopolysaccharide-binding protein (LBP), tumour necrosis factor α (TNFα), macrophage colony stimulating factor (M-CSF), interferon gamma (INF-γ), IL-17 and IL-23.

Methods: 178 patients with SpA according to ASAS criteria were included in the study. Cytokines levels of TNFα, IL-1a, IL-6, INF-γ and IL-17 were measured by a cytometric bead-array. ELISA was used to determine serum levels of IL-23, M-CSF and MMP-3. CRP and LBP levels were measured by chemiluminescence. Statistical analysis was made for comparison between groups. A P-value < 0.05 was considered statistically significant.

Results: Of the 178 patients, 70 patients were HLA-B27, 34 were HLA-B15 and 74 had other HLA-B. According to ASAS classification criteria, 152 had axial SpA manifestations, 161 had peripheral SpA manifestations, and 148 patients had a mixed axial and peripheral manifestations. Levels of inflammatory serologic biomarkers are shown in figure 1.

Conclusion: High levels of IL-17 and IL-23 were associated with the presence of HLA-B27, which correlates with an axial presentation of the disease, when compared to HLA-B15 patients. With the individualization of patients according to genotype (presence of HLA-B27 or HLA-B15) or phenotype (axial or peripheral involvement) physicians
could be moving towards personalized medicine using targeted therapy with IL-17 inhibition.

Figure 1. A. Disease activity biomarkers (CRP: C-reactive protein; LBP: lipopolysaccharide-binding protein) in axial spondyloarthritis (axSpA) and peripheral spondyloarthritis (pSpA); B. Cytokines (INFγ: interferon gamma; IL: interleukin; M-CSF: macrophage colony-stimulating factor; TNFα: tumour necrosis factor alpha) in axSpA and pSpA; C. Disease activity biomarkers (MMP-3: matrix metalloproteinase 3; ESR: erythrocyte sedimentation rate) in HLA-B27 and HLA-B15 positive SpA patients; D. Cytokines in HLA-B27 and HLA-B15 positive SpA patients.
Introduction: Granulomatosis with polyangiitis (GPA) has been transformed from life-threatening conditions to chronic relapsing long-term diseases as a result of significant advances in immunosuppressive therapy. Structured clinical assessment using Vasculitis Damage Index (VDI) should form the basis of a treatment plan and be used to document progress.

Objective: To investigate the Vasculitis Damage Index in limited and systemic granulomatosis with polyangiitis.

Patients and method: We enrolled 61 (25 female) patients with GP according to ACR criteria at a referral hospital during the period from 2005 to 2015.

Clinical and laboratory data, organ involvement and the Vasculitis Damage Index (VDI) were recorded at baseline. Patients were divide in systemic and limited form.

Results: They were 61 GPA (34 men and 27 women) mean age 42 years old at diagnosis. Systemic form was observed in 53% and localized form 47%. Chronic sinusitis was the most frequent manifestation in 33% followed by otologic in 26%. Subglottic stenosis 4 patients, alveolar hemorrhage 1%. Of the patients with the systemic form 22 presented focal and segmental glomerulonephritis and 10 patients (32%) rapidly progressive glomerulonephritis. Distal-symmetric polyneuropathy and cranial neuropathy were present in 24%, respectively; Scleritis 24.5% and proptosis in 18%, palpable purpura 26.2% and ulcers in 9 patients (14.8%). The VDI score in the systemic form was 3.6 and in the localized 2.55, p NS.

Conclusion: In this cohort of patients with GPA, a high chronic damage was found with similar DVI between the systemic and localized forms of the disease.
Prevalence of severe organic affection according to Medsger scale in a cohort of Mexican patients with early and late systemic sclerosis.

**LANA0163**

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Introduction: Systemic sclerosis SSc is characterized by excessive production of extracellular matrix and vascular and immune system alterations. For evaluation of multiorgan affection in SSc patients, there is the scale of severity of Medsger (SSM) which is the most frequently scale used to assess the severity organic affection.

Objective: To determine the prevalence of severe organic affection according to the SSM in Mexican patients with early and late SSc.

Patients and methods: A retrospective study was performed in tertiary Hospital. Patients with diagnosis of SSc were included and divided into early and late. SSM was applied which consists of 9 items: general symptoms, peripheral vascular, skin, tendon/joints, muscle, gastrointestinal, lung, heart and kidney. Statistical analysis: Ch².

Results: There were 108 patients: 102 women and 6 men, mean age 55±11 years. The prevalence of diffuse SSc (dSSc) was 57.4% (62 patients) and limited SSc (lSSc) was 42.5% (46 patients). A severe organic affection was observed in 36 patients (33.3%): 24 with dSSc, and 12 with lSSc. In the first group the affected organ were: 13 (54.1%), general 3 (12.5%), vascular 3 (12.5%), cardiac 2 (8.3%), renal 2 (8.3%) and gastrointestinal 1 (4.1%). In lSSc were: vascular 9 (75.0%), general 1 (8.3%), cardiac 1 (8.3%) and pulmonar 1 (8.3%). The age and initial manifestations were not associated with a greater severity.

Conclusion: In patients with SSc the severe affection was 33.3% and was manifested in predominantly at lung level in dSSc and at vascular level in lSSc, all patients in late stage.
Introduction: The Multiple autoimmune Syndromes (MAS) was described by Humbert and Dupont in 1988, consists in the presence of three or more well defined autoimmune conditions in a single patient. Objective: To determine the incidence and prevalence of Syndromes (MAS) and Polyautoimmunity (PA) in consultation autoimmune disease (AIDs) of Immunology Institute. Method: The data were processed using descriptive analysis with frequency measurements, chi-square, prevalence, incidence and Clusters analysis. Results: Were reviewed 2,178 records, 1.373 had one or more definitive AIDs. We identified 40 different AIDs 73% were one, 21% had two and 6% AIDs three or more. The MAS-IDI was 69%, while the MAS-HD was 18% Type 3, 13% Type 2 and 0% Type 1. The Capital District had the largest number of patients with MAS and PA. Female gender predominance aged 37 ± 15 years. The ethnic group most affected was of mixed race. The most common phenotype was SLE-APS-AITD followed by SLE-SS-AITD. The time of onset of PA and MAS was five years. The most common auto-antibodies were: ANA, Anti-ds-DNA, Anti-TPO, Anti-SSA, Antithyroglobulin, Anti-cardiolipin IgG, Anti-SSB and anti-SM. The incidences of SLE, AITD and APS were 41.8, 29.4 and 15.4 x100,000 inhabitants/year and prevalence of 27%, 21% and 12% respectively. Conclusions: The PA was more prevalent than MAS, the most common phenotype SLE-APS-AITD, with predominance of the female gender in mixed race, average age of 37 years. The most common auto-antibodies were ANA and Anti-ds-DNA.
Aim: The comparison of detection of anti-CCP antibodies and RF in diagnosis of Rheumatoid Arthritis in patients with multiple articular manifestations.

Material and methods: 282 patients who visited the Rheumatology outpatient department of our Hospital with symptoms of inflammatory arthritis or polyarthralgia were investigated. All patients were tested for anti-CCP antibodies (quantitative Elisa) and RF (Nephelometric method).

Results: 77 patients were diagnosed with RA (ACR criteria) while 205 patients suffered from other rheumatic diseases. 47 from patients with RA had positive anti-CCP test (62%) and 49 (64%) had positive RF test. In the remaining patient groups suffering from spondyloarthritis (v=37), Sjogren syndrome (v=30), undifferentiated inflammatory synovitis (v=29), Polymyalgia rheumatica (v=22), Systemic Lupus Erythematosus (SLE) (v=19) and other diseases (v=15), anti-CCP were detected in 4% and RF in 18% of cases.

Conclusions: In a population of Greek patients who come for investigation of various articular manifestations, the detection of anti-CCP antibodies is accompanied by similar sensitivity (62% against 64%), but greater specialty (96% against 82%), compared to RF for the diagnosis of RA. These results are consistent with international literature and justify the introduction of anti-CCP antibodies detection in daily clinical practice.
Introduction: Systemic Scleroderma is a rare autoimmune disease with a severe impact on patients' health.

Objective: To record the clinical and immunological features of patients with scleroderma who were followed-up by doctors of our division.

Methods: A retrospective study of all medical records of patients with systemic scleroderma who were followed-up in the outpatient department of Rheumatology from 2008, was held.

Results: 39 patients were evaluated. The majority of them were females (95%) with an average age of 57 years. 62% of them suffered from limited scleroderma and the remaining 38% suffered from diffuse scleroderma. Almost all of the patients (93.2%) were positive to antinuclear antibodies while antibodies against topoisomerase (anti-scl-70), anticentromere antibodies (ACA) and antibodies against Ro antigen (anti Ro (SSa)) were positive in 33.3%, 56.4% and 8% of them, respectively. Raynaud’s phenomenon was the most frequent manifestation (97%) of the disease. while sclerodactyly, gastrointestinal disorders, digital ulceration, musculoskeletal symptoms, pulmonary fibrosis and pulmonary hypertension were also present in 71%, 59%, 38%, 35%, 15.3%, 7.6% of them respectively.

Conclusion: The patients manifest similar clinical and laboratory features to the ones of patients in other European countries. It is interesting to note that none of the patients manifested renal disease. These conclusions should be confirmed by a wider polycentric study.
Aim: The investigation of correlation between the presence of aCCP and clinical, laboratory, and social characteristics of patients with early RA.

Material and methods: 135 patients with early RA were diagnosed and followed up in Rheumatology outpatient department of our Hospital. All patients met the RA criteria of the American College of Rheumatology, had disease duration less than 6 months before diagnosis and have been treated with at least one disease-modifying drug. Patients were followed up every 3 months. Demographic, clinical and laboratory characteristics of patients were assessed both at diagnosis of the disease and at the end of the study.

Results: The analysis revealed a statistically significant correlation between αCCP and positive RF test (RF), antinuclear antibodies(ANA), male gender, smoking, erythrocyte sedimentation rate (ESR). No correlation between aCCP, C-Reactive Protein (CRP) and age of patients was found. Analysis showed that positive RF test is the first most important factor and smoking is the second most important factor.

Conclusion: A smoker man with early RA, positive RF test and high disease activity, is very likely to be positive in aCCP.
Objective: To measure the bone mineral density in patients with Ankylosing Spondylitis and associate it with clinical and laboratory markers.

Method: 52 patients and 51 healthy individuals took part in the study. The age, sex and body mass index (BMI) were recorded as well as data with regard to the quality of life, functionality of the hip, the radiographic severity of bone lesions. The levels of ALP, PTH and osteocalcin were also evaluated. Bone mineral density was measured by DEXA on the lumbar vertebral column, on the head of the femur and the heel bone.

Results: There were no differences between male and female individuals with regard to exercise, smoking, the levels of ESR and the level of self-service. Most males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant. 80.5% of males had high levels of CRP but the average levels of PTH were higher in females compared to males and this result was not statistically significant.
Introduction: The ASIA was described in first time in 2011, by now exist more than 300 cases registered in the literature. All associated with exposure to vaccines, silicone implants, mineral oil and others; in genetic predisposed patients. The purpose of this study is to analyze a series of cases, to describe the clinic characteristic in Dominican patients.

Material and methods: Between July 2011-April 2017, 11 patients (all females) were retrospectively enrolled. Clinical information, diagnostic imaging modalities, treatment, and outcomes were evaluated.

Results: The mean age was 44.7±9.7 years, the most common clinical manifestation were arthralgia (90.9%), fatigue (81.8%), inflammatory back pain (54.5%), arthritis (45.5%), adenopathies (45.5%), fever (36.4%) and granulomatous lesion (36.4%). We found anemia 63.6%, neutropenia 18.2%, and thrombocytopenia 18.2%, positive ANA in 4 patients (36.4%), RF in two and ACPA in one. Rheumatic diseases are described in figure 1. The silicone implants were found (63.7%); mineral oil (45.5%). Breast implants were the most common associated. The time between the exposure and the developed of the disease was 2.0±2 years (1-8 years). In four patients the material was remove, with full recovery in all cases. Patients were prescribed with NSAIDs (72.7%), antimalarials (54.5%), Immunosuppressant (18.2%) and Adalimumab to treat SpA HLA-B27+.
Conclusions: ASIA is a condition with high prevalence these days, maybe because of the increment in esthetic procedures in women of this era; most of the time, without the best conditions to be performed; and because we are more aware to diagnostic this syndrome in these days.
ASIA Syndrome comprises a group of entities developed from certain immunological events secondary to the exposure to environmental factors or adjuvants (silicone, silica, solvents, vaccine adjuvants, metals) in a susceptible (MHC DRB101 B4,DQ1) host.

Description of cases of ASIA in a hospital population from Argentina.

Case 1: 83 years-old caucasian female. Worker since 1970 in textile industries and ceramic furnacing and enameling. Twenty years later suffered artrhitis, puffy hands, Raynaud's and pulmonary fibrosis. Diagnosis: Scleroderma and Monoclonal gammapathy of uncertain significance.

Case 2: 57 years-old caucasian male. Worker since 1984 in metal welding for 20 years. Started then with chronic pneumonitis, diarrhea and pancreatitis. Diagnosed as lymphocitc pancreatitis, pneumonitis and enteritis.


Case 5: 32 years-old caucasian male. Military. Received adjuvated flu vaccine in april 2016. Weeks later started with fever, progressive myalgia and muscle weakness, heliotrope erythema and bilateral radial paralysis. Diagnosed as inflammatory myopathy.

Conclusions: ASIA is a recently developed concept, widely studied in animal models, and sustained in case reports in humans. Validation of its criteria would help for specificity and the identification of risk factors for primary prevention in genetically susceptible individuals.
Introduction

The influence of environmental exposure on the risk of developing autoimmune diseases is paramount (i.e., the autoimmune ecology). In fact, environment, more than genetics, shapes immune system.

Objectives

To evaluate the autoimmune ecology in patients with four autoimmune rheumatic diseases (ARD).

Methods

This was an exploratory and self-report study conducted in a focus group of 188 women with ARDs [rheumatoid arthritis (RA, n=51), systemic lupus erythematosus (SLE, n=70), systemic sclerosis (SSc, n=35), and Sjögren’s syndrome (n=32)], and a healthy group (n=30). Data were collected by using a structured questionnaire that sought information about demographic, clinical and immunological characteristics as well as previous and current exposure to possible environmental factors associated with autoimmunity.

Results

General characteristics of the patients and their exposures are shown in Tables 1-3. Among the ARDs, organic solvents exposure was higher in SLE and SS (p=0.01), whereas pesticides exposure was higher in SSc (p=0.02). Cleaning work was more frequent in patients with SLE and SSc (p=0.01). Previous or current work with soot, organic solvent exposure, and hair dye use were associated with all ARDs taken as a group (p<0.01).

Conclusion

These results suggest that the environmental effect on ARDs might well consist of two forms: those common to several ARDs and those specific to a given disorder. Autoimmune ecology seems to be stronger in SSc and SS, followed by SLE and RA. Our results should encourage further studies aimed to explore the role of exposome in autoimmunity.
Table 1. General characteristics of women with autoimmune rheumatic diseases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA n= 51 (%)</th>
<th>SLE n=70 (%)</th>
<th>SSc n=35 (%)</th>
<th>SS n=32 (%)</th>
<th>Controls N=30 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>50 (48.5-63)</td>
<td>50.5 (37.5-57)</td>
<td>56 (51.5-62.5)</td>
<td>64.5 (55.7-68.7)</td>
<td>36.5 (29.42)</td>
</tr>
<tr>
<td>Age at onset of disease (IQR)</td>
<td>36 (26-49)</td>
<td>29 (22-40)</td>
<td>46 (37-53.5)</td>
<td>50.5 (46-58.25)</td>
<td>ND</td>
</tr>
<tr>
<td>Disease duration (IQR)</td>
<td>17 (10.5-26)</td>
<td>13 (9-21.75)</td>
<td>7 (4-13)</td>
<td>12 (9-17)</td>
<td>ND</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Manual exclusive</td>
<td>7/50 (14)</td>
<td>13 (18.6)</td>
<td>6 (17.1)</td>
<td>3/31 (9.7)</td>
</tr>
<tr>
<td></td>
<td>Intellectual exclusive</td>
<td>21/50 (42)</td>
<td>20 (28.6)</td>
<td>14 (40)</td>
<td>5/31 (16.1)</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>2/50 (4)</td>
<td>11 (16)</td>
<td>0 (0)</td>
<td>3/31 (9.7)</td>
</tr>
<tr>
<td></td>
<td>Housewife</td>
<td>13/50 (26)</td>
<td>19 (27.1)</td>
<td>13 (37.1)</td>
<td>9/31 (29)</td>
</tr>
<tr>
<td></td>
<td>Retired</td>
<td>5/50(10)</td>
<td>7 (10)</td>
<td>2 (5.7)</td>
<td>11/31 (35.5)</td>
</tr>
<tr>
<td></td>
<td>Student</td>
<td>2/50 (4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 2. Environmental exposures* of women with autoimmune rheumatic diseases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA n= 51 (%)</th>
<th>SLE n=70 (%)</th>
<th>SSc n=35 (%)</th>
<th>SS n=32 (%)</th>
<th>p-value</th>
<th>Controls N=30 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking habit**</td>
<td>14 (27.45)</td>
<td>25 (35.7)</td>
<td>12 (34.3)</td>
<td>11 (34.4)</td>
<td>0.8</td>
<td>12 (40)</td>
</tr>
<tr>
<td>Coffee intake**</td>
<td>42 (84.1)</td>
<td>65 (90)</td>
<td>34 (97.1)</td>
<td>31 (96.9)</td>
<td>0.74</td>
<td>26 (87)</td>
</tr>
<tr>
<td>Cannabis**</td>
<td>0 (0)</td>
<td>6 (8.6)</td>
<td>1 (2.8)</td>
<td>1 (3.1)</td>
<td>0.12</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Silicone Implants**</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>3 (8.6)</td>
<td>0 (0)</td>
<td>0.2</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Organic Solvent exposure***</td>
<td>27 (53.9)</td>
<td>47 (67)</td>
<td>15 (42.8)</td>
<td>25 (78.1)</td>
<td>0.01</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Hair dye use**</td>
<td>40 (78.4)</td>
<td>61 (87)</td>
<td>30 (85.7)</td>
<td>28 (87.5)</td>
<td>0.55</td>
<td>19 (63.3)</td>
</tr>
<tr>
<td>Asbestos exposure**</td>
<td>2 (3.9)</td>
<td>2 (3)</td>
<td>2 (5.7)</td>
<td>2 (6.25)</td>
<td>0.83</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Heavy metals exposure**</td>
<td>5 (9.8)</td>
<td>2 (3)</td>
<td>1 (2.8)</td>
<td>2 (6.25)</td>
<td>0.33</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pesticides exposure**</td>
<td>4 (7.8)</td>
<td>6 (8.6)</td>
<td>9 (25.7)</td>
<td>2 (6.25)</td>
<td>0.02</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Variable</td>
<td>RA n=51 (%)</td>
<td>SLE n=70 (%)</td>
<td>SSc n=35</td>
<td>SS n=32</td>
<td>p-value</td>
<td>Controls N=30</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-------------</td>
<td>--------------</td>
<td>----------</td>
<td>--------</td>
<td>---------</td>
<td>---------------</td>
</tr>
<tr>
<td>Household close to any organic material storage or warehouse</td>
<td>2 (3.9)</td>
<td>9 (13)</td>
<td>2 (5.7)</td>
<td>3 (9.4)</td>
<td>0.32</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Household close to an airport</td>
<td>2 (3.9)</td>
<td>2 (1)</td>
<td>3 (8.6)</td>
<td>4 (1)</td>
<td>0.29</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Previous or current work with flowers/flowers crops</td>
<td>1 (2)</td>
<td>2 (1)</td>
<td>4 (11.4)</td>
<td>4 (1)</td>
<td>0.05</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Previous or current work with pesticides</td>
<td>0 (0)</td>
<td>2 (1)</td>
<td>3 (8.6)</td>
<td>0 (0)</td>
<td>0.07</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Previous or current work with soot</td>
<td>11 (21.6)</td>
<td>17 (24.3)</td>
<td>13 (37.1)</td>
<td>14 (43.7)</td>
<td>0.08</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Previous or current work in mines/quarters</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (6.2)</td>
<td>0.02</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Previous or current work at plastics factory</td>
<td>1 (2)</td>
<td>1 (1.4)</td>
<td>1 (2.8)</td>
<td>0 (0)</td>
<td>0.81</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Previous or current work at hair salon</td>
<td>3 (5.8)</td>
<td>9 (13)</td>
<td>1 (2.8)</td>
<td>2 (6.2)</td>
<td>0.26</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Previous or current work with stained glass</td>
<td>0 (0)</td>
<td>1 (1.4)</td>
<td>1 (2.8)</td>
<td>2 (6.2)</td>
<td>0.26</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Previous or current work cleaning</td>
<td>1 (2)</td>
<td>8 (12)</td>
<td>6 (17.1)</td>
<td>0 (0)</td>
<td>0.01</td>
<td>1 (3.3)</td>
</tr>
</tbody>
</table>

*Environmental Exposure: exposure to potentially harmful chemical, physical or biological agents in the environment or to environmental factors (as soot) that may include tentorpor toxic exposure at any time in life. **Organic solvent exposure: percentage of people exposed to Alcohol, Acetone, Petroleum ether, aromatic compounds e.g. Benzene and Tol. *Previous or current exposure to home or work with high pollution as biomass fuel used for cooking (i.e. coal or firewood).
Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as silicone implants, which elicit chronic stimulation of the immune system against the prosthetic material, especially in genetically susceptible hosts.

The aim is to describe the prevalence and main autoimmune rheumatic disease (ARD) associated to silicone breast implant (SBI).

We study a cohort of 150 patients with diagnosis of ASIA associated injection of mineral oil and silicone breast implant (SBI), from 2011 to 2017. All patients were evaluated for the fulfillment of ASIA criteria. We only included patients with ASIA criteria associated with SBI plus criteria of a autoimmune rheumatic disease. We excluded patient with ASIA and without ARD.

Results: there were 20 women patients with mean age 43±20 years old, mean disease duration of disease 8±3. The clinical manifestation after de SBI were 8.5 ±2 years. The ARD were systemic sclerosis (SSc), 5; rheumatoid arthritis (RA) 5, systemic lupus erythematosus (SLE) 3, overlap syndrome 3, Sjogren syndrome 1, Takayasu arteritis 1, Still disease 1, antiphospholipid syndrome 1, and 3 patients have fibromyalgia too. Five patients had more than 2 autoantibodies. Four patients had relatives with ARD. All patients are being treated according with the presence of ARD. We also found fibromyalgia in 3 patients.

Conclusion: we found a prevalence of ASIA associated to SBI of 13%. The main ARD were SSc, SLE and RA. In these cases the presence of ASIA associated SBI were related with genetic predisposition in some patients.
FUNCTIONAL POLYMORPHISMS IN PRE-MIR146A AND PRE-MIR499 ARE ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS BUT NOT WITH RHEUMATOID ARTHRITIS AND GRAVES’ DISEASE FROM MEXICO

LACAT-0060
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Recently, some microRNA (miRNA) gene polymorphisms have been associated with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and Graves’ disease (GD) susceptibility. However, other studies have not replicated these findings. This study aimed to determine the role of three single nucleotide polymorphisms (SNPs) located within pre-miR146a (rs2910164G/C), pre-miR196a-2 (rs11614913), and pre-miR499 (rs3746444A/G) genes in a sample of Mexican patients with RA, SLE and GD. This study included 900 patients with RA, SLE and GD as well as 486 controls (healthy individuals with no family history of inflammatory or autoimmune diseases). Genotyping was performed with TaqMan probes in a 5’ exonuclease assay. None of the SNPs located in the miR-146a, miR196a-2, and miR-499 genes were associated with RA and GD susceptibility under any genetic model (i.e., co-dominant, recessive, or dominant). Respect to SLE, the genotype and allele frequencies of the miR-196a-2 rs11614913 polymorphism were similar with the control group, however, the miR-146a rs2910164G/C (OR=1.7, p=0.017) and miR-499 rs3746444A/G (OR=1.5, p=0.033) polymorphisms were associated with SLE susceptibility but not with lupus nephritis (LN). Our results suggest that polymorphisms in miR-146a, miR-196a-2, and miR-499 were not associated with RA and GD susceptibility. However, the miR-146a rs2910164G/C and miR-499 rs3746444 polymorphisms showed association with SLE susceptibility (but not with LN) in the Mexican population.
Autoimmune diseases (ADs), such as systemic lupus erythematosus (SLE), autoimmune thyroid disease (AITDs), which included Graves’ disease (GD) and Hashimoto thyroiditis (HT), rheumatoid arthritis (RA), etc., are a heterogeneous group of pathologies characterized by the loss of immunological tolerance, production of autoantibodies against different autoantigens and the synthesis of several cytokines with autoimmune and inflammatory activity. Tumor necrosis factor alpha (TNF-α) is a key cytokine involved in acute/chronic inflammation and autoimmunity. TNF-α promoter gene contains several single nucleotide polymorphism (SNPs), which are located at the positions -1031T/C, -376G/A, -308G/A and -238G/A of the transcription start site. Some of them have functional implications and affect expression levels. Additionally, these SNPs confer susceptibility to SLE and AITDs. This study aimed to determine whether the TNF-α-1031T/C, -376G/A, -308G/A and -238G/A SNPs confer susceptibility to SLE and AITDs in Mexican population. Nuclear DNA was isolated from PBMCs (300 with SLE and 139 with AITDs, and 502 controls). Genotypes were determined with TaqMan probes (5’ exonuclease assay). Weinberg Equilibrium (H-WE) was evaluated with Finetti software, meanwhile, EPIDAT 3.1 software was used to estimate associations between SLE and AITDs and the TNF-α -1031T/C, -376G/A, -308G/A, -238G/A SNPs. In our study we identified an association between the TNF-α -238GA and -1031CT SNPs and SLE (OR=1.9, p=0.009, and OR=1.3, p=0.035, respectively), meanwhile, the TNF-α -308GA SNP was associated with GD susceptibility (OR=1.91, p=0.028) and the TNF-α -1031CT SNP was associated with HT (OR=3.35, p=0.032). Our results indicate that TNF-α polymorphisms contribute to SLE and AITDs susceptibility in Mexican population.
Introduction: PTPN22 gene encodes LYP protein, a potent inhibitor of T and B cell activation. The PTPN22 1858C>T polymorphism confers rheumatoid arthritis (RA) susceptibility; however, its functional effect on the B and T cells remains unknown. CD40 is an important costimulatory molecule for B cells and CD154 is a marker of activation of CD4+ T cells. The CD40-CD154 interaction promotes pro-inflammatory cytokines secretion and autoantibodies production. Objective: To associate the PTPN22 1858C>T polymorphism with CD40 and CD154 membrane expression in patients with anti-CCP positive early RA. Methods: We included ten control subjects (CS) and ten anti-CCP positive early RA patients, all with known 1858C>T PTPN22 genotype. Membrane CD40 and CD154 expression levels were determined by flow cytometry in B and T cells, respectively. The statistical analysis was performed with SPSS v.20. Results: The B cells (CD19+/CD40+) percentage and mCD40 expression levels were similar between RA and CS (p>0.05) and we not found an association between these variables and the 1858C>T polymorphism. However, CD4+ T cells percentage was higher in RA patients than CS (p=0.003) and in RA, the CD4+ T cells percentage and mCD154 levels were higher in the 1858T allele carriers (p=0.008 and p=0.032, respectively). Conclusions: The PTPN22 1858C>T polymorphism is not associated with the CD40 expression on B cells. However, the PTPN22 1058T allele is associated with increased CD154 expression on T helper cells, which is indicative of a higher activation of these cells and it helps to clarify the role of this polymorphism on the RA susceptibility.
Poster Session

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

GENETIC CONTRIBUTION OF HLA DRB1*08:02 AND HLA DRB1*03:01 IN THE GENETIC SUSCEPTIBILITY TO DEVELOP SYSTEMIC LUPUS ERYTHEMATOSUS IN LOW SOCIOECONOMIC INCOME IN MEXICANS

LACA7-0094


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3Hospital 20 de Noviembre ISSSTE, Coordinación de Investigación, Mexico City, Mexico
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Introduction Systemic Lupus Erythematosus (SLE) is a highly prevalent disease in Mexicans and is particularly influenced by ethnicity; a mixture of Amerindian background with Europeans can be distinguished in most urban centers from Mexico and Mexican-Americans in the United States. The aim of this work is to test if socioeconomic status also has a roll in the susceptibility to develop SLE in Mexicans.

Experimental design

We selected 123 consecutive SLE patients from the outpatient clinic of Rheumatology in a third level hospital form Mexico City, 67 out of 123 were classified as High-income group supported by the social workers department, and 56 out of 123 as Low-income. We also included for comparison a group of 99 healthy Mexican Mestizos from Mexico City.

We performed high resolution HLA typing in all individuals.

Results

We found an increased gene frequency of HLA DRB1*03:01 in the Low-income group of patients as compared to healthy controls (Pc=0.03, OR 2.8 CI 95% 1.1-6.9).

We also found that the genotype HLA DRB1*03:01/DRB1*08:02 was also increased in the Low-income group as compared to High-income group (Pc= 0.02, OR 12, CI 95% 1.3-147).

The roll of HLA DRB1*03:01 in Mexicans and HLA DRB1*08:02 in Mexican-Americans has been previously described, but this is the first time that the genotype including both alleles confers susceptibility on low socioeconomic patients.

This suggests that a mixture of Amerindian genes with Europeans probably include the roll of selective pressure of infectious agents through HLA genes in highly susceptible populations.
POSTER SESSION

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

ANALYSIS OF THE POLYMORPHISMS IN THE PROMOTER REGIONS OF TNF AND IL-10 IN MEXICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

LACA7-0118


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The class III major histocompatibility (MHC) genes including the complement genes C4A, C4B, BF and C2 (Complotypes) and TNF-α, have been associated with systemic lupus erythematosus (SLE) in Mexicans. Here we analyzed the polymorphism of TNF-α promoter in 51 Mexican Mestizo SLE patients and in 56 ethnically matched healthy controls by Real Time Polymerase Chain Reaction method. No statistically significant deviation from normality existed in the frequency of TNFα−308 allele and genotype distribution between patients and healthy controls. However, we found a significant increase in the TNF G/A −238 genotype and in the TNFα −238 allele frequencies in the SLE group when compared with healthy controls (Pc = 0.03, OR = 4.7 and Pc = 0.02, OR = 3.6 respectively). Analysis of promoter IL-10 polymorphism showed a similar distribution in patients and healthy controls. No linkage disequilibrium were obtained between TNF alpha and IL-10 or any other complement polymorphism suggesting an independent association between the TNF-α −238 polymorphism and SLE; it also suggest that patients bearing the susceptibility allele might benefit by using anti-TNF therapy.
Poster Session

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

Effect of the MIF haplotypes on LPS, rhTNF-α and rhMIF response in peripheral blood mononuclear cells from rheumatoid arthritis patients and healthy subjects

LACAT-0119
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¹Instituto de Investigación en Ciencias Biomédicas, Department of physiology, Guadalajara, Mexico
²División de Reumatología, Guadalajara Civil Hospital "Fray Antonio Alcalde", Guadalajara, Mexico

Background: Rheumatoid arthritis (RA) is an autoimmune chronic disease characterized by diarthrodial joint destruction. Macrophage migration inhibitory factor (MIF) plays an important role in RA pathogenesis. It has been shown that tumor necrosis factor α (TNFα) induced the MIF expression. Two functional polymorphisms in MIF promoter have been associated with increased severity of clinical manifestations in RA, however, the effects of MIF haplotypes on cytokines production in peripheral blood mononuclear cells (PBMC) from RA patients are unclear.

Objective: To evaluate the effect of MIF haplotypes on lipopolysaccharide (LPS), rhTNFα and rhMIF response in PBMC from RA patients and healthy subjects (HS).

Methods: MIF polymorphisms genotyping were performed in 230 RA patients and 281 HS. We measure cytokines levels by a microsphere-based ELISA method (Bio-Plex®MAGPIX™) in the supernatant of cell cultures of human PBMC from patients and HS homozygous for each haplotype (5G, 6G and 7C) and stimulated with LPS, rhTNFα and rhMIF.

Results: PBMC from RA and HS with 7C haplotype had higher TNFα, IL-6, IL-17A and IL-17F secretion than non-7C haplotype after LPS stimulation. The rhTNFα stimulation promotes the highest IL-17A and IL-17F levels in PBMC from patients with 7C haplotype. After rhMIF stimulation, we observed similar cytokines levels in 7C and non-7C haplotypes in RA group.

Conclusions: These findings suggest that MIF haplotypes could modified the response of LPS, rhTNFα and rhMIF stimulation in PBMC from RA patients and HS. The 7C haplotype is associated with higher secretion of proinflammatory cytokines than other MIF haplotypes.
Background: Etiology of Behçet’s disease (BD) is still unknown. It was thought that; genetic factors have crucial roles for pathogenesis of BD due to specific geographic distribution and familial inheritance.

Objectives: Vitamin D has a crucial role for immune regulation and genomic function of vitamin D related to vitamin D receptor (VDR).

Methods: In this research, rs1544410 (G>A), rs2228570 (T>C), rs7975232 (G>T) and rs731236 (T>C) polymorphisms of VDR gene were studied in patients with BD in Turkish population. 150 patients with BD and 150 healthy individuals were included and genotyping of each polymorphism was carried out by PCR/RFLP. Patients were evaluated among themselves according to clinical symptoms and activity of BD.

Results: There are significant differences between patients and healthy individuals in rs1544410, rs2228570 and rs731236 genotypes. When rs1544410 polymorphism was determined patients with ocular lesion have higher percentage of A allele than the patients without this clinical symptom and there is significant difference between two groups. When rs2228570 polymorphism was examined with disease activity, it was determined patients with BD in active period have significantly more C allele than patients in remission period. Rs2228570 polymorphism was shown that; patients with oral aphthae, positive pathergy test and arthritis, have more C allele than patients without this clinical symptoms and these results are significant.

Conclusions: It was observed that; vitamin D receptor gene polymorphisms may have possible role in pathogenesis of BD and rs1544410-rs2228570 polymorphisms in VDR gene may lead to increase risk of several clinical symptoms.
Objective The functional PTPN22 R620W polymorphism (rs2476601) is clearly associated with susceptibility to several autoimmune diseases (ADs). However, the PTPN22 R263Q polymorphism (rs33996649) has been scarcely explored in different ADs. Here we aimed to examine the associations of the PTPN22 R620W and R263Q polymorphisms with susceptibility to or protection against rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Graves’ disease (GD) among Mexican patients.

Methods We conducted a case-control study including 876 patients (405 with SLE, 388 with RA, and 83 with GD) and 336 healthy control individuals. PTPN22 genotypes were determined using the TaqMan 5’ allele discrimination assay. Results PTPN22 R620W was associated with GD susceptibility (OR 4.3, \( p = 0.004 \)), but was not associated with SLE (OR 1.8, \( p = 0.19 \)). We previously demonstrated that this polymorphism is associated with RA susceptibility (OR 4.17, \( p = 0.0036 \)). Moreover, PTPN22 R263Q was associated with protection against SLE (OR 0.09, \( p = 0.004 \)) and RA (OR 0.28, \( p = 0.045 \)), but was not associated with GD.

Conclusions Our data provide the first demonstration that PTPN22 R620W confers GD susceptibility among Latin-American patients. Moreover, this is the second report documenting the association of PTPN22 R263Q with protection against SLE and RA.
Background: Systemic Sclerosis (SSc) is a chronic, autoimmune, inflammatory, fibrotic and multisystem disease. An important hallmark is the presence of autoantibodies. The pathogenesis involves various immune cells (T, B, NK cells, and macrophages). Killer-cell Immunoglobulin-like Receptors (KIR) are cell surface receptors expressed on NK cells and some T cell subsets. KIR family consists of 16 genes and according to the gene content of each individual constitutes a genotype, which can be grouped as AA and Bx.

Objective: Evaluate the association between KIR/HLA gene and genotypes with SSc.

Methods: Forty-five SSc patients and 45 healthy subjects (HS) will be included. Peripheral blood will be obtained for DNA extraction. KIR and HLA genotyping was made by PCR-SSP. The differences between KIR/HLA genes and genotypes were analyzed with Fisher test ($p<0.05$). Autoantibodies anti-RNA polymerase III and anti-fibrillarin were performed by ELISA technique.

Results: KIR gene frequencies have been determinate; we found a higher frequency of KIR2DL2 ($p=0.0109$, OR=3.176) and KIR2DS4del ($p=0.0496$, OR=2.551) in SSc, and KIR2DS4full in HS ($p=0.0307$, OR=0.311). Statistically significant combinations of KIR/HLA were found (Table 1). The Bx genotype was the most frequent. We found 2% and 12% positive patients with anti-RNA polymerase III and anti-fibrillarin respectively.

Conclusions: KIR2DL2 and KIR2DS4del could be associated with susceptibility, whereas KIR2DS4full with protection for SS. Compound genotypes could be implicated in the SSc immunopathology. The genotype with ID19 could be associated with autoimmunity. Anti-RNA polymerase III and anti-fibrillarin have a low frequency in our studied group.
Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are systemic autoimmune diseases with unclear etiology but with an important genetic contribution involved in its development. Loci such as TRAF1-C5 and IL-17A could be important factors related with RA and SLE susceptibility. The aim of this study was to determine whether the IL-17A -121G/A and TRAF1-C5 rs3761847G/A polymorphisms confer risk for RA and SLE in Mexican population. Our study included 406 patients with RA, 300 with SLE and 555 healthy controls. Genotypes were determined with TaqMan probes (5’exonuclease assay). Weinberg Equilibrium (H-WE) was evaluated with Finetti software, meanwhile, EPIDAT 3.1 software was used to estimate associations between the IL-17A -121G/A and TRAF1-C5 rs3761847G/A polymorphisms and RA/SLE susceptibility. Our results showed no differences in genotype and allelic frequencies of the IL-17A -121G/A (OR=1.11, p=0.54 for AR, and OR=1.02, p=0.9 for LES) and TRAF1-C5 rs3761847G/A (OR=1.28, p=0.08 for AR and OR=1.19, p=0.24 for LES) polymorphisms and were not associated with RA and SLE susceptibility in Mexican population. However, the TRAF1-C5 rs3761847G/A polymorphism showed a tendency to an association with RA susceptibility (p=0.08). Our results reveled that the IL-17A -121G/A and TRAF1-C5 rs3761847 polymorphisms are not genetic risk factors for RA and SLE in Mexican population.
Poster Session

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

ANALYSIS OF CATALASE GENETIC POLYMORPHISMS AND ENZYMATIC ACTIVITY IN MEXICAN VITILIGO PATIENTS

LACA7-0205

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Introduction. Vitiligo is an acquired pigmentation disorder characterized by melanocyte loss via autoimmune mechanisms which are presumably triggered by the oxidative stress caused due to accumulation of hydrogen peroxide (H₂O₂) and low catalase (CAT) activity. Besides inhibition by its substrate (H₂O₂), low CAT activity might be influenced by allelic variants of CAT gene such as -89A>T (rs7943316) and 389C>T (rs769217), which have been associated to vitiligo in European and Asiatic populations.

Objective. To evaluate the role of CAT activity and CAT -89A>T and 389C>T gene polymorphisms in vitiligo susceptibility in Northwestern Mexican population.

Material and methods. We performed a case-control study including 157 non-segmental vitiligo patients and 159 age/gender matched controls. Serum CAT activity was measured on 39 individuals per group. Differences were analyzed by logistic regression (SPSS), haplotype analysis (SHEsis Plus) and Mann-Whitney test (SPSS).

Results. The 389 TT genotype and AT haplotype conferred 71.2% and 34.3% less risk of developing vitiligo (OR=0.288, CI95%=0.109-0.760 p=0.012 and OR=0.657, CI95%=0.463-0.931 p=0.017, respectively). The -89 A>T polymorphism, and AC and TC haplotypes showed no association with vitiligo. Analysis of serum revealed a decrease in CAT activity of ~30% in vitiligo patients when compared with controls (p=0.002). Neither CAT gene polymorphisms nor CAT activity were associated to clinical characteristics of vitiligo such as clinical type, disease activity and age at onset.

Conclusions. Our results suggest that CAT 389C>T gene polymorphism has a protective effect against vitiligo development in Mexican population and that patients have decreased CAT activity, regardless CAT gene polymorphisms.
GENETIC ANALYSIS OF THE POLYMORPHISM IN THE PROMOTER REGION OF PTPN22 IN MEXICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

LACA7-0171

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The gene protein tyrosine phosphatase nonreceptor type 22 (PTPN22) encodes the lymphoid protein tyrosine phosphatase (LYP) which negatively regulates T-cell activation. PTPN22 has been identified as a major risk factor for developing autoimmune diseases, for instance SLE associates with the functional single nucleotide polymorphism (SNP) rs2476601 that changes a thymidine at nucleotide 1858 (C1858T) in Europeans. Genomic studies have demonstrated that Mexicans have an increased proportion of European ancestry, therefore the aim of this study was to test if the high prevalence of SLE in Mexicans is influenced by the rs2476601 SNP. We genotyped 48 Mexican mestizo SLE patients and compared them to 56 ethnically matched healthy controls by using Real Time Polymerase Chain Reaction. No statistically significant deviation from normality existed in the frequency of allele and genotype distribution between patients and healthy controls. Frequencies of PTPN22 C1858T genotypes in patients were: CC 94%, and CT 6% (gf C: 0.970, T: 0.030); whereas in the control group: CC 96%, and CT 4% (gf C: 0.980, T: 0.020). This data suggest that the polymorphism rs2476601 of PTPN22 do not explain the high prevalence of SLE in Mexicans.
Poster Session

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

Influence of IL1RN VNTR polymorphism on IL-1Ra expression in rheumatoid arthritis
LACA7-0124
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Background

Rheumatoid arthritis (RA) is an autoimmune disease characterized by the production of pro-inflammatory cytokines. IL-1Ra is an anti-inflammatory cytokine codified by IL1RN gene. A VNTR polymorphism of 86 bp in IL1RN gene has been associated with RA risk and regulation of IL-1Ra production. This study was designed to determine mRNA and protein expression of IL-1Ra in RA patients and control subjects (CS).

Patients and methods

This study included 86 RA patients classified according to the ACR/EULAR 2010 criteria and 71 CS. The identification of IL1RN VNTR polymorphism was performed by PCR, the expression of sIL-1Ra (secreted isoform) mRNA was determined by SYBR Green RT-qPCR, and the quantification of soluble IL-1Ra was realized by ELISA test.

Results

RA patients had high soluble levels of IL-1Ra compared to CS (p<0.01), sIL-1Ra (secreted isoform) mRNA expression was 14.33 times higher in RA patients compared to CS (p<0.01). CS carriers of the IL1RN*2/2 homozygous genotype show increased soluble IL-1Ra compared to IL1RN*long/long genotypes and IL1RN*long/2 heterozygous genotypes (p<0.01), whereas mRNA expression in CS carriers of IL1RN*2/2 genotype was 1.2 times higher compared to IL1RN*long/long genotype. RA patients show high expression of sIL-1Ra mRNA on carriers of IL1RN*long/long genotype. Nevertheless, soluble IL-1Ra of RA patients among genotypes did not show significant differences.

Conclusions

IL-1Ra expression is increased in RA patients compared to CS. In CS, IL-1Ra expression was higher in carriers of IL1RN*2/2 genotype compared to all other genotypes. Soluble levels of IL-1Ra in RA patients did not show significant differences among genotypes.
Poster Session

GENETICS AND EPIGENETICS IN AUTOIMMUNITY

KIR GENES AND ANTI-PADI4 LEVELS IN RHEUMATOID ARTHRITIS

LAC7-0213


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BACKGROUND: Rheumatoid arthritis (RA) is an autoimmune disease characterized by inflammation of the diarthrodial joints and production of different autoantibodies such as anti-PAD4. KIR genes encode receptors that regulate the function of NK cells and T cell subpopulations, which may be involved in the activation of B cells.

OBJECTIVE: To identify the association of KIR genes with anti-PADI4 levels in rheumatoid arthritis.

METHODS: Peripheral blood samples were obtained from RA patients (RA, n = 92) and control subjects (CS, n = 70). gDNA was extracted by Miller modified technique and 16 KIR genes were typed by PCR-SSP. Anti-PADI4 was quantified by ELISA test. The data were analyzed with chi-square and t-student tests with a significant p <0.05.

RESULTS: KIR2DL2 was found more frequently in RA than in CS (p <0.0001, OR = 7.0, 95% CI = 3.04 to 16.13), as well as KIR2DS4del (p <0.003, OR = 2.7, 95% CI = 1.4 to 5.2). Anti-PADI4 levels (RA, mean= 4.04 ng/mL; CS, mean= 2.57 ng/mL, p = 0.0001) were higher in RA than in CS. The KIR2DL2+/2DS4del+ genotype showed a tendency to increase anti-PADI4 levels compared to KIR2DL2+/2DS4del+ (p = 0.07).

CONCLUSIONS: KIR2DL2 and KIR2DS4del could act as risk factors in the development of RA. No association was found between KIR genes and anti-PADI4 levels; however, data show a trend towards higher levels of anti-PADI4 in patients with the KIR2DL2+/2DS4del+ genotype.
INTRODUCTION: Rheumatoid Arthritis (RA) is an autoimmune and inflammatory disease characterized by an exacerbated production of proinflammatory cytokines. MYD88 is a Toll-like receptor-activated adapter protein that promotes a central role in transcription of key cytokines involved in immunopathology of RA, via NFκB. OBJECTIVE: The aims of this study were to investigate if a single nucleotide polymorphism (SNP) within MYD88 is associated with RA susceptibility and to evaluate if this SNP are able to modulate the Th1/Th2 cytokine profile in RA patients.

METHODS: A total of 126 RA patients and 189 healthy individuals were recruited at Oswaldo Cruz Hospital. Genotyping was performed using Real Time PCR in ABI 7500 (Applied Biosystems) to evaluate the possible association between SNP rs6853 (located at 3'UTR region of MYD88 gene) and RA susceptibility. Genotype-guided levels of Th1/Th2 cytokines (IL2, IL6, IFN, IL10, TNF, IL4) were measured using CBA (Cytokine Bead Array) in FACSCalibur Flow Cytometry (BD Biosciences). Statistical analyses were performed using Anova Test and Binary Regression Logistic in SPSS Program, considering \( p \text{ value} < 0.05 \).

RESULTS: We found association between GG genotype of rs6853 polymorphism and a lower susceptibility to RA (OR = 0.187; CI = 0.02 0.8; \( p = 0.01 \)). However, we do not found any association between the studied SNP and levels of cytokines of Th1/Th2 profile IL2, IL6, IL4, TNF, IL10, IFN (\( p = 0.351; 0.66; 0.105; 0.713; 0.510; 0.948 \), respectively). CONCLUSION: The studied polymorphism is associated with a lower susceptibility to RA and do not alters Th1/Th2 cytokines profile in RA Brazilian patients.
Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that mainly affects women, characterized by hyperactivity of B lymphocytes and presence of autoantibodies against nuclear antigens. It is a multifactorial disease in which genetic factors are involved. Studies in animal models, as well as in identical families and twins have demonstrated the involvement of several candidate genes with susceptibility to developing SLE. TLR-7 is a receptor for innate immunity that recognizes single stranded RNA, and plays an important role in the production of interferon-alpha (INF-α), central cytokine in the pathogenesis of the disease. IRF5 is a transcription factor that induces the synthesis of IFN-α through the activation of TLR-7. IL-6 is another cytokine with inflammatory properties that has been associated with the development of the disease. The main genetic variations contributing to disease risk include single nucleotide polymorphisms (SNP) and copy number variation, among others. SNP expression of TLR7 (rs197008), IRF5 (rs2004640) and IL-6 (rs1800795) in Mayan women with SLE and their association with the development of the disease were analyzed. No association of rs197008 and rs1800975 was observed with the disease, however the allele and genotype frequencies of rs2004640 showed association. Significant increase of IRF5 mRNA was observed in the patients. The results support the role of IRF5 as a genetic risk factor in the female Maya
population to develop SLE.

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Poster Session

IL17, TH17 AND AUTOIMMUNITY

TH1/TH17 PROFILE INDUCED BY MACROPHAGE MIGRATION INHIBITORY FACTOR IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM RHEUMATOID ARTHRITIS

LACA7-0215

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Background: Macrophage migration inhibitory factor (MIF) is an immunoregulatory cytokine that plays a crucial role as regulator of the innate and adaptive immune responses and takes part in the destructive process of the joint in rheumatoid arthritis (RA) by promoting angiogenesis and inducing proinflammatory cytokines and matrix metalloproteinases (MMP). Several studies have reported that MIF favors the induction of Th1 cytokine profile. However, no studies have investigated the effects of MIF on the Th17 subset of cytokines (e.g. Th17 profile), which are important effectors of inflammatory autoimmune diseases.

Objective: We evaluated if recombinant human MIF (rhMIF) induces the production of TNF-α, IFN-γ, IL-1β, IL-6, IL-10, IL-17A, and IL-17F in peripheral blood mononuclear cells (PBMC) from RA patients and control subjects (CS).

Methods: The PBMC from RA patients and CS were stimulated for 24 hours with combinations of LPS, rhMIF or the MIF antagonist ISO-1. Cytokine profiles were measured using a multiplex immunoassay.

Results: In the supernatants of rhMIF-stimulated PBMC from patients, we found higher levels of TNF-α (538.81 vs 137.90 pg/mL, p<0.001), IFN-γ (721.90 vs 233.97 pg/mL, p<0.001), IL-1β (150.14 vs 40.92 pg/mL, p<0.001), IL-6 (19769.70 vs 4153.73 pg/mL, p<0.001), and IL-17A (31.29 vs 6.38 pg/mL, p<0.001) in comparison with the CS.

Conclusion: Our results indicate that MIF strongly stimulates a Th1 and Th17 profile in RA, favoring the establishment of the chronic inflammatory process which is the principal cause of joint damage in this disease.
**Poster Session**

**IL17, TH17 AND AUTOIMMUNITY**

**ABD-derived protein blockers of human IL-17 receptor A as non-IgG alternatives for modulation of IL-17-dependent pro-inflammatory axis**

**LACA-0051**


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Interleukin 17 (IL-17) and its cognate receptor A (IL-17RA) play a crucial role in Th17 cells-mediated pro-inflammatory pathway and pathogenesis of several autoimmune disorders including psoriasis. IL-17 is mainly produced by activated Th-17 helper cells upon stimulation by IL-23 and, via binding to its receptors, mediates IL-17-driven cell signaling in keratinocytes. Hyperproliferation of keratinocytes belongs to a major clinical manifestation in psoriasis. To interfere with the IL-17-mediated inflammatory cascade, we generated a unique collection of protein binders targeting the IL-17RA that prevent from binding of IL-17A cytokine to its cognate receptor expressed on the surface of keratinocytes. To this goal, we used a high-complex combinatorial library derived from scaffold of albumin-binding domain (ABD) of streptococcal protein G, and ribosome display selection, to yield a collection of ABD-derived high-affinity ligands of human IL-17RA, called ARS binders. From 67 analysed ABD variants, 7 different sequence families were identified. Representatives of these groups competed with human IL-17A for binding to recombinant IL-17RA receptor as well as with IL-17A-IgG chimera, as tested in ELISA. Five ARS variants bind to IL-17RA-expressing THP-1 and Raji cells, as tested by flow cytometry. The four variants exhibited high-affinity binding in nanomolar range to human keratinocyte HaCAT cells, as measured using Ligand Tracer Green Line system. Thus, we identified several ARS inhibitory variants with an immunosuppressive potential which will be further verified.
Rheumatoid arthritis is one of the most common autoimmune diseases in the world. On the other hand, Heat Shock Proteins are stress molecules linked to many effects on autoimmune diseases, such as pro-inflammatory or immunomodulatory mediators. Recent results from our laboratory suggest that heat shock protein 60 from *Klebsiella pneumoniae* (HSP60Kp) may have an immunomodulatory effect in an animal model of arthritis. We investigated the effect of HSP60Kp on the expression of genes associated with Treg and Th17 cells in a collagen-induced arthritis model (CIA).

We used groups of 5 Wistar rats immunized with and without HSP60Kp, ten days before the induction of CIA. Measurements of foot diameter and clinical inflammation score of hind paws were performed every 3 days for 55 days. After that, animals were sacrificed to extract RNA from the knees and spleen. Then, end-point RT-PCR was performed to measure the expression of the genes for molecules related to Th17 and Treg lymphocytes. The pre-immunization with HSP60Kp induced a decrease in the foot diameter and clinical inflammation score in rats with CIA (P <0.05). Rats pre-immunized with HSP60Kp showed a delay in the onset of inflammation when compared with control groups. Also, PCR results showed significant differences in the expression of IL-17 and IL-6 between the same groups. In conclusion HSP60Kp seems to have an immunomodulatory effect on the development of CIA, manifesting itself as a delay in the presence of inflammation, a decrease in its intensity and a decrease in the expression of pro-inflammatory cytokines.
Poster Session

IL17, TH17 AND AUTOIMMUNITY

THE ROLE OF IL-6 AND IL-17 IN PATHOGENESIS OF SYSTEMIC SCLEROSIS AND EVALUATION TO ASSOCIATIONS WITH CLINICAL MANIFESTATIONS
LAC7-0015

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Background: Although the pathogenesis of systemic sclerosis (SSc) remains unknown, cytokine production and release are key events in this autoimmune disease, characterized by T cell activation and auto-antibodies production leading to microvascular damage, inflammation and fibrosis.

Objectives: The aim of this study was to determine the relationship of IL-6 and IL-17 and associations with clinical manifestations in SSc.

Methods: 31 SSc patients, 20 ankylosing spondylitis (AS) patients and 18 healthy controls were included. IL-6 and IL-17 levels of all cases were identified by the ELISA methods. In all cases ESR, CRP and demographic characteristics were recorded. Anti-Scl-70, anticentromere, FVC (force vital capacity), PAB by transthoracic echocardiography, HRCT findings and modified Rodnan Skin Score (mRSS) values were recorded in SSc patients. All these data were statistically compared.

Results: Serum IL-6 and IL-17 levels were not elevated in SSc patients, but IL-17 and CRP levels were elevated in AS patients (p<0.05). There is no association between clinical findings and levels of IL-6 and IL-17 in SSc patients. Additionally, elevated ESR and high values of mRSS were associated with anti-Scl-70 positive SSc patients.

Conclusions: There is no significant difference of IL-6 ve IL-17 levels in SSc patients compared to AS patients and healthy controls. But, significant high serum levels of IL-17 showed in AS patients. In SSc patients, a relationship between IL-6 ve IL-17 levels and other laboratory and/or clinical findings has not been established. Larger multicenter studies are needed to evaluate between cytokine levels and other laboratory and/or clinical findings in early stage of SSc patients.
The immune system reacts very actively to changes in the external and internal environment, which is most often manifested by the emergence of immunosuppressive states. A special place is occupied by the children's organism, which reacts ambiguously to adverse effects due to the immaturity of its structure and functions. In the literature, the results of studying the structure of the immune and endocrine systems under various immunoreactive conditions are widely presented, while other equally important organs, including the reproductive system, have not been studied so thoroughly and extensively. In connection with this, the aim of the study was to establish the features of the structure of the seminal vesicles of experimental animals with artificial immunosuppression. To create a model of immunosuppression, cyclophosphamide was used in the experiment. Cyclophosphamide was administered at a dosage of 1.5 mg/kg body weight for ten days. The animals were carried out from the experiment on days 1, 7, 15, 30 and 60 after the end of the drug administration with observance of all the necessary ethical norms. The absolute and relative masses of the organ significantly decreased in the early observation periods (1, 7 and 15 days) by 8.03%, 10.05%, 17.53% and 9.29%, 11.49%, 13.62% accordingly. The linear parameters of the seminal vesicles underwent similar changes: the length and width of the organ significantly decreased in comparison with the control group by 6.67%, 8.41%, 11.04% and 10.2%, 10.1%, 12.86% accordingly 1, 7 and 15 days.
Metabolic syndrome (MetS) is a clustering of risk factors comprising abdominal obesity, dyslipidemia, elevated blood pressure, and abnormal glucose tolerance. MetS adds an independent risk for developing Cardiovascular Disease (CVD) in the general population. Its prevalence has increased in the last years throughout the world. The prevalence of metabolic syndrome (MetS) is high among rheumatic patients, leading to CVD and consequently to death. Different studies in autoimmune rheumatic diseases, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) ankylosing spondylitis, Sjogren syndrome, systemic sclerosis, psoriatic arthritis, vasculitis and primary antiphospholipid syndrome have shown the presence of MetS in these patients. In RA, CVD is the most common cause of premature mortality, associated to MetS and disease activity. Regarding SLE patients, MetS has been linked to increased cumulative organ damage, accelerated atherogenesis and cardiovascular risk. On one side, studies in humans and experimental models revealed that MetS might contribute to autoimmune rheumatic disease pathogenesis. On the other hand, the participation of chronic inflammation and its mediators, oxidative stress and a direct systemic effect of immunological factors of the disease contribute to modify the natural history of the disease. Both conditions increase cardiovascular risk. Therefore, risk stratification should be a part of the integral care of these patients. Effective management of the inflammatory status as well as control of MetS are mandatory in order to avoid the future development of cardiovascular events especially in the absence of symptoms of cardiovascular disease.
Autoimmune diseases (AID) are burdened by stressful emotional conditions in the past. Experiences related to emotions, sexual experiences, success, frustrations or failures will remain perennial in limbic brain. When they are stressful, will be recorded associated with negative emotion, will be intermittently remembered for years or a lifetime, causing limbic dysfunctions and deregulation of neuropeptides like CRH and other. This leads to immunological dysfunction, which concurrent with other factors, causes AID.

Mind-body therapies decode and reprogram the patient's limbic system, aiding psycho-neuro-immune regulation, demonstrated by molecular and genomic techniques.

Mind-body therapy (emotion release techniques, meditation, and biodance) was applied in four patients with severe AID with high requirement of immunosuppressive drugs. Two patients had dermatomyositis, corticodependents to 1 mg/kg/d of prednisone (PDN) and 3 g/d of mycophenolate mofetil (MMF). One patient with systemic vasculitis with neurological, intestinal, hepatic, pancreatic and dermal involvement in PDN 1 mg/kg/d and cyclophosphamide 100 mg/d. Finally, one SLE patient with dermal, pericardial and active renal type IV compromise in PDN 1mg/kg/d and MMF 3g/d. All patients, for more than 3 years, reactivated the disease in each attempt to lower the PDN to less than 0.5 mg/kg/d. All were individually submitted to mind-body therapies by a certified therapist (SMS).

A decrease in drug requirement was achieved up to 60% of the immunosuppressant with doses of less than 0.5 mg/kg/d of PDN and sustained subsequent decreases, maintaining adequate clinical and laboratory control in a follow-up of more than 5 years. These therapies should be evaluated in controlled studies.
INTRODUCTION: Polyautoimmunity is the association of more than one autoimmune disease (AiD) and Multiple autoimmune syndrome (MAiS) is the association of 3 or more AiDs in a single patient. Identify these associations have an impact on type of treatment and prognosis of the patients.

OBJECTIVES: From the observation of patients who developed more than one AiDs during their follow up at pediatric rheumatology clinics, the members of the GRIP study group developed a registry and analyzed the data obtained to determine demographic features.

METHODS: GRIP study group developed a registry of patients followed at ten pediatric rheumatology clinics in four Colombian cities with association of AiDs according to validated diagnostic criteria. The clinical charts were reviewed and the demographic, family history, clinical and serological and histopathological data were collected in an electronic database. Patients with undefined AiD, overlap syndrome and MCTD were excluded in order to avoid bias. First AiD diagnosed (heralding disease) and following AiDs were reported on a chronologic order. The intervals between them were “simultaneous” (less than 4 weeks) or sequential. The information is updated as needed if the patient develops additional AiDs after was included on the registry. Data was analyzed using a program SSPS 15v.

RESULTS: N= 216 pediatric patients were registered. the sex ratio was female 9,3: male 1 and 96% of them were Colombian mestizo’s. 166/216 had developed two diseases when they were included at the registry and an additional 46 patients developed three and 4/216 four diseases. The age of onset of the heralding disease varies between 2-16 years with a mean of 10,3 years and it was similar in the three groups. 22% developed the first two AiDs simultaneously and the mean interval period of time between heralding disease and additional AiDs was longer for the first two AiDs. 28% developed second and third disease simultaneously and half of the patients developed the third and fourth diseases simultaneously.

32% had a positive family history AiDs with a similar frequency in the 3 groups. The most common AiDs in first degree relatives were: Autoimmune thyroiditis, RA, SLE and SS and were more frequent in female relatives. 22 diseases were identified in different types of associations. SLE was the most common systemic disease and Hashimoto was the first organ-specific disease but uncommon AiDs (Myastenia gravis, Rupus, Kikuchi Fujimoto were also present. The heralding diseases more frequent were: SLE (82), JIA (33) Hashimoto (24), APLS (13), and autoimmune citopenias (16) others (48). Different types of associations were documented during the mean follow up time 4,7 years (12-180 months). The entities that associated another AiDs were: Hashimoto, SLE, JIA and APLS.
CONCLUSIONS: AiDs share genetic backround, pathogenic mechanisms, clinical findings and autoantibody profiles and those factors may predispose to develop polyautoimmunity. Some associations of AiDs are common and well known but others had not been reported on juvenile patients. There are differences with adult polyautoimmunity.

A high index of suspiction and a regular work up of autoantibody profile are needed to confirm polyautoimmunity. Some auto antibodies have predictive value. To perform thyroid profile and APS serology is recommended on all patients with AiDs.

Long term follow up is needed to explore those associations and to define their prognostic impact. Female sex and positive AiDs family history are associated with polyautoimmunity.

REFERENCES:


ROJAS V. INTRODUCING POLYAUTOIMMUNITY. SECONDARY AUTOIMMUNE DISEASES NO LONGER EXIST. AUTOIMMUN DIS 2012;:254319.

LI ET AL. GENETIC SHARING AND HERITABILITY OF PAEDIATRIC AGE OF ONSET AUTOIMMUNE DISEASES. NATURE COMM.DOI 10.1038NATCOMM944210.1038/ncomms9442
FREE COMMUNICATIONS

Free Communications 1 (English)

DEXAMETHASONE AND MONOPHOSPHORYL LIPID A REMOVE DISEASE-ASSOCIATED TRANSCRIPTIONAL SIGNATURES AND INDUCE A DISTINCTIVE REGULATORY PROFILE ON MONOCYTE-DERIVED DENDRITIC CELLS FROM RHEUMATOID ARTHRITIS PATIENTS

LACA7-0063

P. García-González1, K. Schinnerling1, A. Sepúlveda2, J. Maggi1, L. Soto1, O. Neira3, A.M. Mehdi4, H.J. Nel4, D. Catalán1, R. Thomas4, R.A. Verdugo2, J.C. Aguillón1

1Universidad de Chile, Programa Disciplinario de Inmunología, Santiago de Chile, Chile
2Universidad de Chile, Programa de Genética Humana, Santiago de Chile, Chile
3Hospital del Salvador, Departamento de Reumatología, Santiago, Chile
4University of Queensland, Translational Research Institute, Queensland, Australia

Despite their potential use for immunotherapy in autoimmunity, the molecular mechanisms driving differentiation of dendritic cells (DCs) towards a regulatory phenotype are poorly understood. To identify molecular regulators and pathways related with tolerogenicity, we analized the transcriptional pattern of tolDCs from healthy subjects (HC) and rheumatoid arthritis patients (RA), modulated with dexamethasone and activated with monophosphoryl lipid A (DM-DCs).

Methods: Transcriptional profiling of DCs was performed on 76 samples of monocyte-derived DCs. Differentially expressed (DE) genes were determined using a false discovery rate of 0.05 and a 1.5 fold change, compared to untreated DCs. Functional enrichment and pathway overrepresentation was performed using Ingenuity Pathway Analysis. Expression of molecules of interest was confirmed through qPCR and flow cytometry.

Results: Dexamethasone and MPLA exerted a distinctive effect on DCs transcriptional program, similar on RA and HC, removing the disease effect observed on untreated DCs. 653 DE genes were identified in DM-DCs, amongst which several tolerance-related genes were found to be upregulated, whilst maturation/inflammation-associated genes were downregulated. Functional and pathway analysis revealed the enrichment of genes involved in cellular movement, cell-to-cell signaling and interaction, and metabolism, particularly homeostasis of ROS, heavy metals and fatty acids. Analysis of DE genes also predicted the activation of chemotactic responses and the modulation of regulatory populations.

Conclusion: DM-DCs exhibit a particular transcriptional programming in response to Dexamethasone and MPLA, that distinguishes them from other subsets and supports a regulatory profile on these cells, as a result of the modulation of biological processes that help control immune responses.
FREE COMMUNICATIONS

Free Communications 1 (English)

AUTOANTIBODY AND CYTOKINE CLUSTERS IN RHEUMATIC AUTOIMMUNITY
LACA7-0168
N. Molano-Gonzalez¹, Y. Pacheco¹, A. Espejo-Mojica¹, D.M. Monsalve¹, J.E. Barahona-Corra³, M. Rojas¹,
Y. Rodríguez², J. Saavedra³, D. González-Bravo³, M. Rodríguez-Jimenez², R.D. Mantilla¹, C. Ramírez-Santana¹,
J.M. Anaya¹
¹Center for Autoimmune Diseases Research CREA, School of Medicine and Health Sciences, Bogota, Colombia

Introduction

Autoimmune diseases (ADs) disclose similar immunopathogenic mechanisms (autoimmune tautology), which explain
the fact that a single AD may carry several autoantibodies with diverse specificity. Cytokine production is pivotal in
the pathophysiology of ADs and influence the synthesis of autoantibodies.

Objective

To analyze the relationship between autoantibodies and cytokine profiles in patients with four autoimmune rheumatic
diseases (ARDs).

Methods

An exploratory study, 188 women with ARDs [rheumatoid arthritis (RA, n=51), systemic lupus erythematosus (SLE,
n=70), systemic sclerosis (SSc, n=35), and Sjögren’s syndrome (n=32)] were included. Fifteen serum cytokines were
measured by cytometric bead array (Beckton-Dickinson). Simultaneously, 14 autoantibodies were assessed by IFI
and ELISA (Inova). Cluster analysis was performed to define autoantibody profiles. Bivariate analysis was done to
identify associations between autoantibody profiles and related variables.

Results

There were six autoantibody profiles (Figure 1). Associations between these profiles and ARDs were found (Figure
2). IL-1beta, IL-4, IL-13, IL-17A, TNF-alpha and IFN-alpha were more frequent in profiles 2 and 4 (Figure 3). Profile 4
was associated with polyautoimmunity in RA and SS (p-value: 0.025 and 0.037). Significant correlations between the
levels of rheumatoid factor and cytokines were found (Table 1).

Conclusion

Our results highlight the similar pathways involved in autoimmunity and may serve for novel therapeutic approaches.
This analysis will allow to better define subphenotypes within ARDs and it will provide insight for a new taxonomy.
Longitudinal studies are warranted to assess clinical outcomes related to derived profiles.

<table>
<thead>
<tr>
<th>cytokine</th>
<th>Spearman</th>
<th>p-value</th>
</tr>
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<tbody>
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<tr>
<td>TNF</td>
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<td>1.704e-15</td>
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<td>IL17A</td>
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</tr>
<tr>
<td>IL4</td>
<td>0.462</td>
<td>6.582e-11</td>
</tr>
</tbody>
</table>
Introduction
Although infection with Zika virus (ZIKV) is usually asymptomatic (75-80%), the development of autoimmune diseases, mainly Guillain-Barré syndrome (GBS) and autoimmune thrombocytopenia, has been documented. Whether ZIKV infection is related with other autoimmune conditions has not been studied.

Objectives
To evaluate a panel of rheumatic and thyroid autoantibodies in patients with ZIKV infection.

Methods
In this case-control study, the case group consisted in a total of 95 patients (29 with GBS associated with ZIKV infection, 13 with ZIKV and other neurological syndromes, and 53 patients infected with ZIKV without neurological conditions, AD or first-degree relatives with AD). All the patients were selected from the National System of Public Health Surveillance during the ZIKV outbreak in Cucuta, Colombia. The diagnosis was confirmed by ELISA and immunofluorescence assay. The control group consisted of 100 healthy individuals with no ZIKV disease and without clinical evidence of AD, selected by simple random sampling. A total of 14 autoantibodies were evaluated in the sera of cases and controls by ELISA and indirect immunofluorescence assay.

Results
Although some autoantibodies were observed in both Zika patients and controls, significant differences were not observed (Table 1).
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ZIKV (+)</th>
<th>GBS (+)</th>
<th>ZIKV (+)</th>
<th>Other neurological syndromes</th>
<th>ZIKV*</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>29</td>
<td>53</td>
<td>13</td>
<td>95</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Sex, female</td>
<td>14 (48.2)</td>
<td>33 (62.3)</td>
<td>9 (89.23)</td>
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<tr>
<td>Age, years</td>
<td>43.0 (13.8)</td>
<td>39.2 (17.3)</td>
<td>27 (15.4)</td>
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<td>34.3 (8.2)</td>
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<tr>
<td>Rheumatoid factor</td>
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<td>11 (20.7)</td>
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<td>Anti-ds DNA</td>
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<td>6 (12.3)</td>
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<tr>
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<td>0</td>
<td>1 (1.0)</td>
<td>1 (1.0)</td>
<td></td>
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<tr>
<td>Anti-SNP</td>
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<td>0</td>
<td>0</td>
<td>1 (1.0)</td>
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<td>ENA</td>
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<tr>
<td>ACA IgM</td>
<td>1 (3.4)</td>
<td>4 (7.5)</td>
<td>1 (7.7)</td>
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<td></td>
</tr>
<tr>
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<td>0</td>
<td>1 (1.1)</td>
<td>5 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Anti-Si2GP IgM</td>
<td>2 (6.8)</td>
<td>2 (3.7)</td>
<td>1 (7.7)</td>
<td>5 (5.3)</td>
<td>1 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Anti-Si2GP IgG</td>
<td>1 (3.4)</td>
<td>1 (1.8)</td>
<td>0</td>
<td>2 (2.2)</td>
<td>3 (3.0)</td>
<td></td>
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<tr>
<td>Anti-TPO</td>
<td>3 (10.3)</td>
<td>7 (13.7)</td>
<td>3 (23.1)</td>
<td>13 (13.7)</td>
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</tr>
<tr>
<td>Anti-Tg</td>
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<td>3 (5.6)</td>
<td>0</td>
<td>4 (4.2)</td>
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<td></td>
</tr>
</tbody>
</table>

**Conclusion**

ZIKV do not induce rheumatic or thyroid autoimmunity in the population evaluated.
Autoimmune diseases (ADs) represent a heterogeneous group of disorders that affect specific target organs or multiple organ systems. These conditions share common immunopathogenic mechanisms (i.e., the autoimmune tautology), which explain the clinical similarities they have among them as well as their familial clustering (i.e., coaggregation). As part of the autoimmune tautology, the influence of environmental exposure on the risk of developing ADs is paramount (i.e., the autoimmune ecology). In fact, environment, more than genetics, shapes immune system. Autoimmune ecology is akin to exposome that is all the exposures - internal and external - across the lifespan, interacting with hereditary factors (both genetics and epigenetics) to favor or protect against autoimmunity and its outcomes. Herein, we provide an overview of the autoimmune ecology, focusing on the immune response to environmental agents in general, and microbiota, cigarette smoking, alcohol and coffee consumption, socioeconomic status (SES), gender and sex hormones, vitamin D, organic solvents, and vaccines in particular. Inclusion of the autoimmune ecology in disease etiology and health will improve the way personalized medicine is currently conceived and applied.
FREE COMMUNICATIONS

Free Communications 1 (English)

Differentiation between APS patients and antiphospholipid antibody-positive carriers by a novel line immunoassay – Does beta2 glycoprotein I domain 1 reactivity matter?

LACAT-0031

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2Inova Diagnostics, Research and Development, San Diego, USA
3University of Trieste, Department of Life Sciences, Trieste, Italy
4Istituto Auxologico Italiano, Laboratory of Immunorheumatology, Milano, Italy

Background: For assessment of antiphospholipid antibodies (aPL) in the serology of the antiphospholipid syndrome (APS), enzyme-linked immunosorbent assays (ELISAs) have been recommended by consensus guidelines. However, they can detect aPL in apparently healthy subjects (HS), so called aPL-positive (aPL+) asymptomatic carriers, and infectious disease patients (IDP). A novel line immunoassay (LIA) for the multiplex analysis of aPL was developed to address this challenge.

Methods: Sixty-one APS patients (34 primary, 5 secondary, 22 obstetric APS), 146 controls including 24 aPL+ asymptomatic carriers and 73 IDP were analyzed using a novel multiplex line immunoassay (LIA) for the detection of aPL to cardiolipin (CL), phosphatic acid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylylycerol, phosphatidylinositol, phosphatidylserine, beta2-glycoprotein I (β2GPI), prothrombin, and annexin V. Samples were also tested by routine aCL and aβ2GPI ELISAs and Lupus Anticoagulant assay as well as aβ2GPI Domain 1 (D1) and 4-5 assays.

Results: Comparison of LIA with the consensus-aPL assays revealed good agreement for IgG/IgM aβ2GPI and aCL (Cohen’s kappa >0.6, respectively). aCL and aβ2GPI IgG/IgM by LIA were significantly higher in APS patients vs. HS and IDP as detected by ELISA. IgG to CL and β2GPI in LIA was significantly lower in aPL+ carriers and IDP samples than in APS patients. Human monoclonal antibodies against D1 recognized β2GPI bound to anionic PL-complexes on the LIA-matrix (Fig. 1). The novel LIA favors the detection of aβ2GPI-D1 antibodies.

Conclusions: Antibody profiling in APS by the novel LIA exposing β2GPI-D1 can aid in differentiating APS from infectious disease patients and asymptomatic carriers.
Fig. 1 Monoclonal antibodies against domain 1 (aD1) of beta2 glycoprotein I (b2GPI) interact with b2GPI after conformational change thereof due to interaction with immobilized phospholipids (PL) on a polyvinylidene difluoride (PVDF) membrane.
Background: During 2014 and 2015 a Chikungunya (CHIKV) epidemic took place in Colombia concurrently with a study on the prevalence of musculoskeletal (MSK) disorders (COPCORD) across the country.

Methods: World Health Organization (WHO) criteria was used to identify CHIKV patients. Four possible scenarios were established: patients who met or not the criteria for probable case, and patients who met or not the criteria for confirmed case. P values were calculated between patients who met or not met the criteria. Sensibility and specificity was calculated for the WHO criteria.

Results: A total of 604 patients with MSK symptoms were evaluated in 6 different cities in Colombia. 180 met clinical criteria, 424 did not met clinical criteria, 150 met the criteria for confirmed case and 454 did not met the criteria for confirmed case. The sociodemographic, clinical characteristics and joint involvement of the studied population is depicted in tables 1 and 2. Sensibility and specificity of the WHO criteria were 56.2% and 91.1% respectively (PPV: 83.3%, NPV: 74.4%).

Conclusion: Our study shows a clear clinical picture of systemic symptoms (fever, rash and gastrointestinal involvement), high titters of pro-inflammatory markers (hs-CRP), and a defined joint involvement (symmetric arthritis or arthralgia of wrists, hands, knees, ankles and feet), which will help clinicians to identify and differentiate CHIKV infection from other viral infections and other MSK diseases. Also, the sensibility of the WHO criteria applied to our cohort of patients demonstrates the need to improve clinical criteria without the use of laboratory tests.
<table>
<thead>
<tr>
<th></th>
<th>WHO Probable Case Criteria</th>
<th>WHO Confirmed Case Criteria</th>
<th>TOTAL (n: 604)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Met Criteria (n: 180)</td>
<td>Did Not Met Criteria (n: 424)</td>
<td></td>
</tr>
<tr>
<td>Age (mean; SD) in years</td>
<td>46,1±16,2</td>
<td>49,5±17,8</td>
<td>48,5±17,4</td>
</tr>
<tr>
<td>Gender Female (%)</td>
<td>133 (73,9)</td>
<td>285 (67,2)</td>
<td>418 (69,2)</td>
</tr>
<tr>
<td>hs-CRP in mg/L (mean; SD)</td>
<td>14,5±10,4*</td>
<td>6,8±6,1</td>
<td>9,1±8,4</td>
</tr>
<tr>
<td>CHIKV IgG in SU (mean; SD)</td>
<td>36,5±22,9*</td>
<td>16,2±18,3</td>
<td>22,2±21,8</td>
</tr>
<tr>
<td>CHIKV IgM in SU (mean; SD)</td>
<td>9,0±6,9*</td>
<td>6,6±5,1</td>
<td>7,3±5,8</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>180 (100)*</td>
<td>0 (0,0)</td>
<td>180 (29,8)</td>
</tr>
<tr>
<td>Rash (%)</td>
<td>126 (70,0)*</td>
<td>28 (6,6)</td>
<td>154 (25,5)</td>
</tr>
<tr>
<td>Gastrointestinal Symptoms (%)</td>
<td>79 (43,9)*</td>
<td>26 (6,1)</td>
<td>105 (17,4)</td>
</tr>
</tbody>
</table>

*p<0.005; WHO: World Health Organization; hs-CRP: high sensitivity C reactive protein; CHIKV: chikungunya virus infection; IgG: immunoglobulin G; IgM: immunoglobulin M
<table>
<thead>
<tr>
<th></th>
<th>WHO Probable Case Met Criteria (n: 180)</th>
<th>WHO Probable Case Did Not Met Criteria (n: 424)</th>
<th>WHO Confirmed Case Met Criteria (n: 150)</th>
<th>WHO Confirmed Case Did Not Met Criteria (n: 454)</th>
<th>TOTAL (n: 604)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetry (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Arthralgia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>177 (98.3)*</td>
<td>215 (50.7)</td>
<td>147 (98.0)*</td>
<td>245 (54.0)</td>
<td>392 (64.9)</td>
</tr>
<tr>
<td></td>
<td>• Arthritis</td>
<td>85 (47.2)*</td>
<td>14 (3.3)</td>
<td>80 (53.3)*</td>
<td>19 (4.2)</td>
</tr>
<tr>
<td>Arthralgia (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Shoulders</td>
<td>50 (27.8)</td>
<td>106 (25.0)</td>
<td>45 (30.0)</td>
<td>111 (24.4)</td>
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<tr>
<td></td>
<td>• Elbows</td>
<td>58 (32.2)*</td>
<td>60 (14.2)</td>
<td>48 (32.0)*</td>
<td>70 (15.4)</td>
</tr>
<tr>
<td></td>
<td>• Wrists</td>
<td>78 (43.3)*</td>
<td>67 (15.8)</td>
<td>65 (43.3)*</td>
<td>80 (17.6)</td>
</tr>
<tr>
<td></td>
<td>• Hands</td>
<td>120 (66.7)*</td>
<td>126 (29.7)</td>
<td>103 (68.7)*</td>
<td>143 (31.5)</td>
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<tr>
<td></td>
<td>• Knees</td>
<td>128 (71.1)*</td>
<td>200 (47.2)</td>
<td>107 (71.3)*</td>
<td>221 (48.7)</td>
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<tr>
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<td>• Ankles</td>
<td>103 (57.2)*</td>
<td>95 (22.5)</td>
<td>92 (61.3)*</td>
<td>106 (23.4)</td>
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<tr>
<td></td>
<td>• Feet</td>
<td>71 (39.4)*</td>
<td>94 (22.2)</td>
<td>65 (43.3)*</td>
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<tr>
<td>Arthritis (%)</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>• Shoulders</td>
<td>8 (4.4)</td>
<td>2 (0.5)</td>
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<tr>
<td></td>
<td>• Elbows</td>
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<td>2 (0.5)</td>
<td>10 (6.7)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td></td>
<td>• Wrists</td>
<td>17 (9.4)*</td>
<td>4 (0.9)</td>
<td>16 (10.7)*</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td></td>
<td>• Hands</td>
<td>44 (24.4)*</td>
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<td>42 (28.0)*</td>
<td>8 (1.8)</td>
</tr>
<tr>
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<td>21 (11.7)*</td>
<td>4 (0.9)</td>
<td>20 (13.3)*</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td></td>
<td>• Ankles</td>
<td>43 (23.9)*</td>
<td>8 (1.9)</td>
<td>42 (28.0)*</td>
<td>9 (2.0)</td>
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<tr>
<td></td>
<td>• Feet</td>
<td>40 (22.2)*</td>
<td>7 (1.7)</td>
<td>39 (26.0)*</td>
<td>8 (1.8)</td>
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<tr>
<td>Myalgia (%)</td>
<td>130 (72.2)*</td>
<td>35 (8.3)</td>
<td>106 (70.7)*</td>
<td>59 (13.0)</td>
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<tr>
<td>Fatigue (%)</td>
<td>165 (91.7)*</td>
<td>41 (9.7)</td>
<td>137 (91.3)*</td>
<td>69 (15.2)</td>
<td>206 (34.1)</td>
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</table>

*p < 0.005; WHO: World Health Organization; CHIKV: chikungunya virus infection; IgG: immunoglobulin G; IgM: immunoglobulin M
Background: The World Health Organization (WHO) criteria for chikungunya virus infection (CHIKV) have demonstrated poor performance in a cohort of patients from a CHIKV epidemic in Colombia. Because of this issue a group of experts in diagnosing and treating CHIKV patients performed an agreement consensus on the clinical characteristics of CHIKV infection and proposed a set of clinical criteria. A clinical scenario was developed with the agreements from the expert panel and the clinical characteristics with higher odds ratios. Methods: Odds ratios of the clinical features of patients with CHIKV infection were analyzed. A clinical scenario was developed and sensitivity and specificity was calculated.

Results: 37 clinical characteristics were evaluated in a cohort of 604 patients with suspicion of CHIKV. From those, 29 exhibited statistical significance and only 10 had high odds ratios (table 1). A clinical scenario with the following joint involvement (symmetrical arthritis of shoulders or wrists or hands or knees or ankles or feet) or systemic symptoms (fever or rash or myalgia or fatigue) poised a sensitivity of 74.2% (PPV: 83.5%) and a specificity of 88.4% (NPV: 81.2%). The following clinical characteristics extracted from the agreements of the consensus group were added to the clinical picture: origin from an epidemic area and abrupt onset of symptoms.

Conclusion: Our study demonstrated that the proposed clinical scenario for suspicion of CHIKV improves diagnostic sensitivity with a slight decrease in specificity, increasing the chance of diagnosis without the need for laboratory tests.

Table 1. Clinical Characteristics with High Odds Ratios

<table>
<thead>
<tr>
<th>WHO Confirmed Case Criteria</th>
<th>Odds Ratio</th>
<th>Confidence Interval (95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met Criteria (n: 150)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Did Not Met Criteria (n: 454)</td>
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<table>
<thead>
<tr>
<th>Symmetry (%)</th>
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<th></th>
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</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>80 (53.3)</td>
<td>19 (4.2)</td>
<td>24.8</td>
</tr>
<tr>
<td></td>
<td>11.2-54.6</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arthritis (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>16 (10.7)</td>
<td>5 (1.1)</td>
<td>22.2</td>
</tr>
<tr>
<td></td>
<td>3.6-204.1</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hand</td>
<td>42 (28.0)</td>
<td>8 (1.8)</td>
<td>36.7</td>
</tr>
<tr>
<td></td>
<td>8.8-152.6</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Knee</td>
<td>20 (13.3)</td>
<td>5 (1.1)</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>2.8-33.8</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ankle</td>
<td>42 (28.0)</td>
<td>9 (2.0)</td>
<td>24.4</td>
</tr>
<tr>
<td></td>
<td>7.5-79.3</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Foot</td>
<td>39 (26.0)</td>
<td>8 (1.8)</td>
<td>69.3</td>
</tr>
<tr>
<td></td>
<td>9.6-510.8</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Myalgia (%)</td>
<td>106 (70.7)</td>
<td>59 (13.0)</td>
<td>13.0</td>
</tr>
<tr>
<td></td>
<td>8.1-20.7</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fatigue (%)</td>
<td>137 (91.3)</td>
<td>69 (15.2)</td>
<td>16.9</td>
</tr>
<tr>
<td></td>
<td>10.9-26.8</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>150 (100)</td>
<td>30 (6.6)</td>
<td>13.1</td>
</tr>
<tr>
<td></td>
<td>8.4-20.5</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rash (%)</td>
<td>109 (72.7)</td>
<td>45 (9.9)</td>
<td>14.0</td>
</tr>
<tr>
<td></td>
<td>8.5-22.9</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

WHO: World Health Organization
FREE COMMUNICATIONS

Free Communications 1 (English)

ERAP POLYMORPHISMS AND ITS ASSOCIATION WITH HLA-B15 AND HLA-B27 POSITIVE SPONDYLARTHITIS PATIENTS
LACA7-0067
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2Universidad de La Sabana, Grupo Genética Humana, Chía, Colombia
3Universidad Nacional de Colombia, Departamento de Imágenes diagnósticas, Bogotá, Colombia
4Hospital Infantil de México Federico Gomez, Departamento de Investigación de Salud Comunitaria, Mexico DF, Mexico
5Universidad de Navarra y Ciberehd, Departamento de Medicina Interna, Pamplona, Spain

Background: In Colombian population HLA-B27 is present in only 40% of patients and HLA-B15 is present almost in 25%. A mechanism of polygenic mechanism has been proposed as an explanation for the development of SpA. ERAP genes 1 and 2 have been implicated. ERAP1 is strongly associated with HLA-B27 positive patients and ankylosing spondylitis, but not with ERAP2.

Methods: 178 patients with SpA according to ASAS criteria were included in the study. HLA typing was performed by the PCR technique. The polymorphisms were determined by the RT-PCR technique using probes for ERAP1 rs27044, rs17482078, rs10050860, and rs30187. For ERAP2 the probes used were rs2910686, rs2248374 and rs2549782. The allele and genotype frequencies polymorphisms were obtained by direct counting. In each group the Hardy-Weinberg equilibrium was evaluated using the x² test. Associations were assessed using OR. The construction and analysis of haplotypes was performed using Haploview v.4.2.

Results: In total 70 patients were HLA-B27 positive and 34 were HLA-B15 positive. Linkage disequilibrium map of the ERAP gene is depicted in figure 1. When analysed by ERAP2 haplotype it is observed that there is a statistically significant association with the combinations described in table 1. No associations were observed between ERAP1 haplotypes and HLA-B15 or B27.

Conclusion: In the group of patients analysed, a statistically significant association was found between patients with SpA HLA-B15 positive and the haplotype TGT of ERAP2. Also HLA-B27 positive SpA patients were associated with haplotype TGC and CAT of ERAP2 with statistical significance.
Table 1. ERAP2 Haplotypes in HLA-B15 and B27 Patients

<table>
<thead>
<tr>
<th>Haplotypes</th>
<th>HLA B15 n (AF)</th>
<th>HLA B27 n (AF)</th>
<th>OR (CI 95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGT</td>
<td>0.201</td>
<td>0.078</td>
<td>2.943 (1.264-6.585)</td>
<td>0.009*</td>
</tr>
<tr>
<td>TGC</td>
<td>0.055</td>
<td>0.227</td>
<td>4.483 (1.524-13.187)</td>
<td>0.003*</td>
</tr>
<tr>
<td>CAT</td>
<td>0.021</td>
<td>0.119</td>
<td>9.014 (1.181-68.807)</td>
<td>0.009*</td>
</tr>
<tr>
<td>CAC</td>
<td>0.643</td>
<td>0.499</td>
<td>1.750 (0.968-3.162)</td>
<td>0.077</td>
</tr>
<tr>
<td>CGC</td>
<td>0.016</td>
<td>0.035</td>
<td>0.465 (0.053-4.056)</td>
<td>0.672</td>
</tr>
<tr>
<td>CGT</td>
<td>0.031</td>
<td>0.013</td>
<td>2.406 (0.332-17.45)</td>
<td>0.584</td>
</tr>
<tr>
<td>TAT</td>
<td>0.019</td>
<td>0.013</td>
<td>1.185 (0.106-13.29)</td>
<td>1.00</td>
</tr>
<tr>
<td>TAC</td>
<td>0.013</td>
<td>0.015</td>
<td>1.185 (0.106-13.29)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

ERAP: endoplasmic reticulum aminopeptidase; AF: allelic frequency; OR: odds ratio

Figure 1. Linkage disequilibrium (LD) map of the ERAP gene. The value of the LD coefficient in each cell D \( [(\text{values close to 1.0}) \times 100] \) is shown. The colour map of the haplogroups represents the LD relationships, the bright red squares represent evidence of LD (log odds [LOD] score ≥ 2 and D' ≥ 1), the light red squares indicate a slight evidence of LD (log odds [LOD] score ≥ 2 and D' < 1), and white squares mean that there is no LD and independent segregation (log odds [LOD] score < 2 and D' < 1).
Chikungunya virus can induce both seropositive and seronegative rheumatoid arthritis: incident cases from a Mexican cohort of patients with previous chikungunya fever

**Background:** The chikungunya virus (ChikV) causes chronic articular pain and inflammation. Since formal epidemiologic surveillance of ChikV began in 2014, over 11,000 cases have been reported in Mexico. The long-term burden resulting from these infections has yet to be estimated in our country. Measurement of inflammatory biomarkers, activity indexes, and autoantibodies induction in subjects who were free of arthritic symptoms prior to confirmed diagnoses with ChikV allowed us to further elucidate the mechanism and clinical picture of ChikV-induced arthritis.

**Aim:** To describe four cases who meet the 2010 ACR/EULAR criteria for rheumatoid arthritis (RA) following ChikV infection.

**Methods:** Subjects with molecular confirmation of ChikV infection during Mexican outbreak that reported persistence of articular symptoms after 10 days of acute infection were enrolled in a prospective study in a tertiary care center in Chiapas, México, to evaluate clinical profile, activity indexes, inflammatory biomarkers, autoantibodies induction, and RA development.

**Results:** Between 2015-2017, 53 patients with persistent articular symptoms were followed for 24 months. During follow-up, 4 patients fulfilled the 2010 ACR/EULAR criteria for RA and required immunosuppressive therapy. Two cases were categorized as seropositive and 2 seronegative. DAS 28 and biomarkers were higher in subjects who induced autoantibodies. Severity of joint involvement was higher in seropositive RA. After 3 months of immunosuppressive therapy, all cases reported complete remission.

**Conclusion:** ChikV can induce RA, independently of autoantibody profile. Susceptible hosts must be followed closely to determine if chronic articular symptoms are becoming RA. Our findings must be validated with greater sample.
Aim of the study: Self-specific B and T cells play a main role in pathogenesis of Systemic lupus erythematosus (SLE) and are a logical target for a selective therapy. The complement receptor type 1 (CR1) on human B-lymphocytes has suppressive activity and engagement of this receptor inhibits B cell activation.

The protein Annexin A1 (ANXA1), is a modulator of the immune system and abnormal expression was found on activated B and T cells during autoimmunity.

We hypothesize that it may be possible to down-modulate the activity of autoreactive T and B cells from SLE patients in humanized SCID mouse model by treating them with a neutralizing antibody against ANXA1 or by protein engineered molecules, which co-crosslink the BCR and CR1.

Materials and Methods: Protein chimeric molecules construction, Immunodeficient SCID mice transfer with human PBMC from SLE patients, apoptosis and cytokines assay, ELISA, FACS, ELISpot and protein array.

Results: Reconstituted SCID mice showed presence of auto-antibodies, as well as immunoglobulin deposition in the renal glomeruli. Treatment of the transferred SCID mice either with DNA-like chimera and anti-ANXA1 antibody prevented appearance of anti-DNA antibodies and proteinuria, while the PBS-injected animals had high levels after the transfer. The treatment reduced the levels of disease-associated cytokines.

Conclusions: It is possible to down-regulate the activity of pathogenic human T and B cells in humanized SLE-SCID mouse model by targeting Annexin A1 or CR1 with a specific monoclonal antibody or chimeric molecule.
FREE COMMUNICATIONS

Free Communications 1 (English)

ANTI-DOMAIN 1 BETA2 GLYCOPROTEIN I ANTIBODIES PREDICT MULTIPLE AUTOANTIBODY POSITIVITY IN ANTIPHOSPHOLIPID SYNDROME

LACA7-0112

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2ARUP Institute of Clinical and Experimental Pathology, Immunology, Salt Lake City, USA
3ARUP Laboratories, Autoimmune Immunology, Salt Lake City, USA

Antibodies directed to the domain I of beta2 glycoprotein I (aD1) are associated with increased risk for antiphospholipid syndrome (APS). In this study, we investigated the significance of aD1 IgG antibodies in patients under evaluation for APS. Samples from 216 patients referred to ARUP Laboratories for APS antibody evaluation from the University of Utah Clinics were retrospectively tested for aD1 IgG in addition to recommended markers for APS. Following testing, a comprehensive chart review was performed and patients categorized according to their clinical diagnosis as well as the presence of criteria antiphospholipid (aPL) and aD1 antibodies. Of the 216 patients, aD1 IgG was observed in 31 (14.4%) cases. Of these, 74.2% (23/31) had a confirmed diagnosis of APS, a majority with thrombosis 78.3% (18/23). The remaining 8 patients had an underlying autoimmune disease (n=5) or non-criteria APS clinical manifestations (n=3). Presence of aD1 IgG positivity was associated with lupus anticoagulant (LAC), IgG anti-beta2 glycoprotein I (aβ2GPI), and IgG anticardiolipin (aCL) antibodies in 92.6%, 90.3% and 87.1% of the cases respectively. Patients positive for aD1 IgG had triple (71%), double (10%), and single (19%) aPL antibody positivity. The presence of aD1 antibodies was also positively correlated with ‘medium-to-high’ titers of aCL and aβ2GPI IgG antibodies. Overall, IgG aD1 antibodies are found in patients with APS, and are significantly associated with triple aPL antibody positivity and risk for thrombosis. Our data suggest that testing for aD1 IgG antibodies maybe useful in risk assessment of APS patients.
FREE COMMUNICATIONS

Free Communications 1 (English)

Early expression of B7-H3 during progression of hepatocellular preneoplastic lesion in rat model
LACA7-0075
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1Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Departamento de Nanociencia y Nanotecnología- Departamento de Biología Celular, Ciudad de México, Mexico
2Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Departamento de Genética y Biología Molecular, Ciudad de México, Mexico
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4Universidad Autónoma Benito Juárez de Oaxaca, CONACYT- Facultad de Medicina y Cirugía, Oaxaca, Mexico
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The B7 family proteins present in antigen-presenting cells, are recognized by costimulatory receptors of T cells, and are important in T-cell proliferation, tolerance, and activation. B7-H3 is considered as co-stimulatory as well as inhibitory protein. B7-H3 exhibits altered expression in various types of cancers. This study was aimed to determine the correlation between B7-H3, tumor markers and T cells markers in hepatocellular carcinoma in a rat model. We first detected expression of B7-H3 and GSTp as a tumor marker and analyzed its correlations with CD4 and CD8 proteins by immunofluorescence. Next, we determined the soluble B7-H3 expression during the carcinogenesis process by western blot. The results presented here showed B7-H3 was co-expressed with GST in hepatocellular preneoplastic lesion in rat model and not expressed in liver normal tissues. B7-H3 expression level was correlated with ABCC3 a recent tumor marker since the carcinogenesis initiation process. Some altered hepatocytes co-expressed B7-H3 and CD4 marked. We also found positive CD8a cells around the staining of B7-H3. The soluble B7-H3 protein was overexpressed during hepatocellular carcinoma progression and was secreted into the bloodstream of rats with the hepatocarcinogenesis model. Our results suggest that the overexpression of B7-H3 is implicated in the evasion of the immune respond and suggests an essential function during carcinogenesis process and the soluble B7-H3 can be used as new biomarker.
FREE COMMUNICATIONS

Free Communications 2: Barcelona Clinic Autoimmunity- Alumni (Bilingual Session)

CHILEAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS SHOW INCREASED SERUM LEVELS OF IL-21 (SPANISH)
LACAT-0169
D. Hirigoyen¹, A. Alvarez¹, R. Montalva¹, R. Naves², M. Iruretagoyena¹, P. Burgos¹
¹Pontificia Universidad Catolica de Chile, Inmunología Clínica y Reumatología, Santiago, Chile
²Universidad de Chile, Programa de Inmunología- Instituto de Ciencias Biomédicas, Santiago, Chile

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by aberrant B cell signaling. Interleukin 21 (IL-21) signaling pathway is involved in B cell differentiation into plasma cells and antibody production and has been recently suggested to play a role in SLE pathogenesis. Consistently, deficiency of IL-21 receptor (IL-21R) improves clinical symptoms in a SLE mouse model. Reports in SLE patients show variable results, in different ethnicities studied. In this study, we assessed serum IL-21 levels and IL-21R expression in B cells obtained from Chilean SLE patients and healthy controls. Analyses were done by ELISA and flow cytometry, respectively. We found significantly higher levels of IL-21 in serum of SLE patients (226.3 ± 54.11 pg/ml) compared to controls (37.1 ± 22.53 pg/ml) (Mann Whitney, p< 0.005) (Figure 1). We also evaluated IL-21 expression in T helper cells by flow cytometry, finding that SLE patients showed more peripheral blood CD4+ IL-21+ T cells than controls (5.05 ± 2.36% vs. 1.16 ± 0.12%), although the statistical significance was borderline (Figure 2). We observed no differences in IL-21R expression in B cells of patients when compared to controls (MFI 34.04 ± 11.07 vs. 29.83 ± 6.71) (Figure 3).

Overall, Chilean SLE patients present increased expression of IL-21 compared to controls, but IL21R remains equal between groups. Further studies are required to establish the role of the enhanced expression of IL-21 in Chilean SLE patients.
Figure 1
IL-21 levels in SLE patients and healthy controls

Figure 2
IL21+ Th cells in healthy controls and SLE patients

Figure 3
IL21R expression in LES patients and healthy controls
OBJECTIVES: To compare the gestational outcomes of patients who presented deep vein thrombosis (DVT) without APS to those of APS patients with history of vascular thrombosis. METHOD: A cohort study was carried out on the patients treated at our Hospital prenatal care who presented with vascular thrombosis and divided them into two groups. The first group consisted of patients who presented vascular thrombosis without APS; and the second group consisted of patients with APS. RESULTS: Seventy-five patients with vascular thrombosis were included in the present study; 39 with a history of thrombosis with negative antiphospholipid antibodies (aPL) (Group 1), while 36 had positive aPL (Group 2). Group 2 presented an unfavorable obstetric history (13 stillbirths and 27 abortions vs 1 stillbirth and 13 abortions in Group 1). Patients with thrombosis and positive aPL (Group 2) had more restricted intrauterine growth (11 vs 0, p<0.001); preterm birth (10 vs 2, p=0.004); oligohydramnious (7 vs 1, p=0.01) and preeclampsia (10 vs 4, 95% CI, p=0.03). The mean birth weight (2,367.14 + 869 vs 3,451.11 + 502, p<0.001) and gestational age (36.24 + 3.7 vs 38.74 + 1.5, p<0.001) at delivery were significantly lower in group 2. CONCLUSION: Presence of aPL in patients with previous thrombosis is associated with worse gestational results, including preeclampsia, premature delivery and lower birth weight, while the history of DVT with negative aPL presented favorable outcomes.

Table 1: Gestational outcomes
Table 2: Newborn's outcomes
Objective and methods: Our aim was to evaluate the prevalence of Anti-Domain 1 B2GPI antibodies in a cohort of Colombian patients with systemic lupus erythematosus (SLE) with and without thrombosis, primary APS and patients with previous history of recurrent miscarriages (RM) without APS criteria. In this cross-sectional study, Anti-D1 B2GPI antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash B2GPI IgG, Inova Diagnostics).

Results: 177 patients (median age 33.5 ± 12.1 years; 89% women) were included. 138 had SLE (78%), 27 primary APS (15%) and 13 RM (7%). 55 (31%) out of 177 had history of thrombosis and 41 (23%) of pregnancy losses. Anti-D1 B2GPI antibodies were positive in 35 (20%) of patients. Anti-D1 B2GPI were positive in 23%, 17% and 0% of patients with primary APS, SLE and RM, respectively. Overall, serum Anti-D1 B2GPI were significantly higher in patients with than without previous thrombosis (149.1 ± 336.1 vs 16.3 ± 61.8 CU, p <0.0001) and in patients with previous history of pregnancy losses (40.2 ± 123.1 vs 21.0 ± 74.5 CU, p=0.04). Anti-D1 B2GPI were significantly higher in patients with primary APS vs SLE with thrombosis, and in patients with SLE with thrombosis vs SLE without thrombosis.

Conclusions: Serum titers of Anti-D1 B2GPI antibodies were higher in patients with thrombosis and pregnancy losses. Serum titers were significantly higher in patients with primary APS than in SLE patients with thrombosis. Whether Anti D1- B2GPI antibodies titers are useful to differentiate patient with primary and secondary APS requires further analysis.
FREE COMMUNICATIONS

Free Communications 2: Barcelona Clinic Autoimmunity- Alumni (Bilingual Session)

VCAM-1 and TWEAK as biomarkers for membranous lupus nephritis
LACA7-0037

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2Universidad Simón Bolívar, Grupo de investigación Nefrología, Barranquilla, Colombia
3Hospital San Vicente Fundación, Grupo de Reumatología, Medellín, Colombia
4Universidad de Antioquia, Grupo de Reumatología, Medellín, Colombia

Background and objective: Some previous studies (most of them in Caucasian, Afro-American and Asiatic cohorts) have demonstrated clinical utility of urinary vascular cell adhesion molecule-1 (VCAM-1) and TWEAK as biomarkers in patients with systemic lupus erythematosus (SLE). Our objective was to evaluate the diagnostic value of urinary VCAM-1 and TWEAK in a cohort of Latin-American patients with SLE. We included SLE patients from 2 referral centers at Medellín and Baranquilla, Colombia. Urinary levels of VCAM-1 (uVCAM-1) and TWEAK (uTWEK) were measured using an ELISA kit (R&D system, USA).

Results: 158 SLE patients were recruited (89% female) with median age of 32.8 ± 12.1 years and median disease duration of 7.27 ± 6.6 years. Mestizo (77%) and African Latin-American patients (20%) were majority. Mean SLEDAI score was 8.5 ± 8.7. 144 (64%) had lupus nephritis (LN). 76 out of 104 patients had biopsy proven LN, in 62% of cases with proliferative forms. uVCAM-1 and uTWEAK were significantly higher in patients with LN than without LN. uVCAM-1 (581 ± 1197 vs 189 ± 256 ng/ml, p<0.001) and uTWEAK levels (3202 ± 3778 vs 1123 ± 1873 pg/ml, p=0.038) were significantly higher in patients with Class V LN in comparison with other LN classes.

Conclusions: uVCAM-1 and uTWEAK are useful biomarkers in Latin-American patients with SLE for the identification of patients with LN. In addition, urinary levels of VCAM-1 and TWEAK were significantly more elevated in patient with membranous LN.
Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease that is characterized by the production of autoantibodies directed against nuclear antigens, leading to multiple organ pathologies and organ destruction. Studies in murine SLE models have revealed a critical role for Toll-like receptors (TLRs) in the production of autoantibodies and development of other clinical disease manifestations. Vitamin D exerts important regulatory functions on cells from the innate/adaptive immune response and it has been suggested that vitamin D deficiency has an association with SLE disease activity and some clinical manifestations. In this study, SLE patients with hypovitaminosis D (n=20, serum levels below 30 ng/ml) were supplemented with vitamin D (50,000 IU/week) or placebo during twelve weeks. TLR7 expression in B cells was evaluated by flow cytometry and mRNA expression by PCR, before and after vitamin D supplementation. We observed that when SLE patients are supplemented with vitamin D reaching normal values, TLR7 expression in B cells significantly decreases, by flow cytometry and PCR (p = 0.026, t test), compared to placebo. In these patients after a 3 month follow up period, vitamin D levels decrease and concomitantly, TLR7 expression in B cells increases. Chilean SLE patients supplemented with vitamin D have lower TLR7 expression in B lymphocytes after treatment, when compared to placebo. Further studies are required to establish the effect of vitamin D in TLR7 expression.

Supported by Fondecyt 1141211 (PB) and 1140049 (RN).
FREE COMMUNICATIONS

Free Communications 2: Barcelona Clinic Autoimmunity- Alumni (Bilingual Session)

ANTIPHOSPHOLIPID SYNDROME LONG TERM FOLLOW UP: REAL LIFE EXPERIENCE OF A SINGLE CENTRE (SPANISH)
LACA7-0114
R.M. Serrano Morales¹, G. Pons-Estel¹, G. Espinosa¹, R. Quintana¹, R. Cervera¹
¹Hospital Clinic. University of Barcelona., Department of Autoimmune Diseases, Barcelona, Spain

Objective: The aim of this prospective study was to assess the real life prevalence of the main causes of morbidity and mortality of APS during 10 year-follow-up in a single referral center.

Methods: The cohort included 160 consecutive APS patients followed by the Autoimmune Diseases Unit of Hospital Clinic Barcelona from 2003 to 2013. The epidemiological, clinical, immunological and treatment features were analyzed.

Results: The cohort consisted of 126 (79%) female and 34 (21%) male patients. Mean (SD) age at diagnosis was 39 (14) years. The causes of diagnosis were thrombosis (56.3%), obstetric morbidity (26.9%) and association of both (16.9%). 65% were primary APS, 22.5% APS associated with systemic lupus erythematosus (SLE), 8.8% associated with lupus-like syndrome and 3.7% associated with other diseases. Fifty-five patients were lost to follow-up (3.4% every year).
During the study, 6 primary APS patients were reclassified as SLE-associated APS and 3 patients as lupus-like syndrome. 3 episode of catastrophic APS occurred. Table 1 shows the frequencies of the main APS clinical manifestations during the 10-year-follow-up and at baseline. At diagnosis, 97.5% received antithrombotic treatment: low dose antiaggregants (37.5%), oral anticoagulants (62.5%), heparin (2.5%). During the study, 72.7% of recurrences were without antithrombotic treatment and 27.3% were despite it. Eleven major bleeding episodes occurred and 2 were fatal. The global mortality rate was 6.3% and 33.3% in catastrophic APS. Table 2 shows the main causes of death.

Conclusions: This study shows long-term morbidity and mortality of a large APS patient cohort and exposed the real-life experience of a referral unit.
Table 1. Main clinical manifestations related to the antiphospholipid syndrome (APS) that appeared before the entrance into the study (baseline) and during the 10-year follow-up (2003-2013) of the total cohort of 160 patients.

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Baseline(^a) (n=160) No. (%)</th>
<th>0-5 year (n=160) No. (%)</th>
<th>5-10 year (n=118) (^b) No (%)</th>
<th>0-10 year (n=160) No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep vein thrombosis</td>
<td>46 (28.8)</td>
<td>3 (1.9)</td>
<td>0</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Stroke</td>
<td>36 (22.5)</td>
<td>7 (4.3)</td>
<td>2 (1.7)</td>
<td>9 (5.6)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>16 (10.0)</td>
<td>2 (1.3)</td>
<td>0</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>9 (5.6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transient ischaemic attacks</td>
<td>8 (5.0)</td>
<td>2 (1.3)</td>
<td>0</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>8 (5.0)</td>
<td>1 (0.6)</td>
<td>0</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Superior extremity venous thrombosis</td>
<td>6 (3.8)</td>
<td>1 (0.6)</td>
<td>1 (0.9)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Extremity arterial thrombosis</td>
<td>3 (1.9)</td>
<td>1 (0.6)</td>
<td>0</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Valve disease</td>
<td>51 (31.9)</td>
<td>40 (35.0)</td>
<td>32 (48.3)</td>
<td>57 (35.6)</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;100,000/µl)</td>
<td>44 (27.5)</td>
<td>22 (13.7)</td>
<td>17 (14.4)</td>
<td>39 (24.4)</td>
</tr>
<tr>
<td>Catastrophic APS</td>
<td>1 (0.6)</td>
<td>2 (0.6)</td>
<td>1 (0.9)</td>
<td>2 (1.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Obstetric manifestations(^b) (No.=235)</th>
<th>(No.=43)</th>
<th>(No.=1)</th>
<th>(No.=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia/eclampsia</td>
<td>5 (2.1)</td>
<td>1 (2.3)</td>
<td>0</td>
</tr>
<tr>
<td>HELLP</td>
<td>2 (0.8)</td>
<td>2 (4.6)</td>
<td>0</td>
</tr>
<tr>
<td>Early pregnancy loss (&lt;10 weeks)</td>
<td>115 (48.9)</td>
<td>6 (13.9)</td>
<td>0</td>
</tr>
<tr>
<td>Late pregnancy loss (≥10 weeks)</td>
<td>52 (22.1)</td>
<td>1 (2.3)</td>
<td>0</td>
</tr>
<tr>
<td>Live birth</td>
<td>69 (29.4)</td>
<td>35 (81.4)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Live birth with prematurity</td>
<td>12 (17.4)</td>
<td>6 (17.1)</td>
<td>0</td>
</tr>
<tr>
<td>Live birth with intrauterine growth restriction(^c)</td>
<td>1 (1.4)</td>
<td>3 (8.6)</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 2. Causes of death during the 10 years of follow-up (2003-2013) of the total cohort of 160 patients.

<table>
<thead>
<tr>
<th>Causes of death*</th>
<th>0-5 year (n=6) No. (%)</th>
<th>5-10 year (n=4) No. (%)</th>
<th>0-10 year (n=10) No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage</td>
<td>3 (42.9)</td>
<td>0</td>
<td>3 (25)</td>
</tr>
<tr>
<td>Catastrophic APS</td>
<td>0</td>
<td>1 (20)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>0</td>
<td>1 (20)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2 (28.5)</td>
<td>0</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>0</td>
<td>1 (20)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>1 (20)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Intestinal ischemia</td>
<td>0</td>
<td>1 (20)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Infection</td>
<td>1 (14.3)</td>
<td>0</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (14.3)</td>
<td>0</td>
<td>1 (8.3)</td>
</tr>
</tbody>
</table>

n. Number of death.
*Several patients had more than one cause of death.
APS, antiphospholipid syndrome

Scientific progress can be directly measured by the growth of the scientific archive. To our knowledge, there has never been a systematic evaluation of the number of the publications on autoimmune diseases in Latin America. The aims of this study is to compare scientific production in the field of autoimmune diseases between Latin America countries and evaluate the publications.

METHODS. All papers on autoimmune diseases that were published between 2000 and 2017 by at least one latin american author and that were indexed in PubMed were evaluated. The key words used were: Autoimmune diseases and country. If a publication had authors from different countries, it was quantified as an article corresponding to each country.

RESULTS. Original articles were the most common document type. Most of the papers were published in immunology and rheumatology journals. From the point of the number of published papers, the top countries were Brazil (3302 papers) Mexico (1539 papers), Argentina (936), and Chile (408). The countries with less than 200 publications were Cuba (117), Venezuela (117), Peru (87), Uruguay (45), Ecuador (29), Costa Rica (11). The productivity in systemic lupus erythematosus (SLE), the prototype of autoimmune disease, was analyzed and showed the following results: Brazil (833), Mexico (570), Argentina (156), Chile (77), Peru (41), Venezuela (36), Cuba (18), Uruguay (10). The total scientific productivity in Latin America from 2000 to 2017 is: 7,042 (Figure 1). In SLE, the total productivity is: 1512 articles.

CONCLUSIONS. Brazil, Mexico, Argentina, and Colombia clearly dominate the production of scientific publications in autoimmune diseases and SLE. However, some countries have high scientific output relative to their size and the number of specialists in autoimmune diseases. This study consider only quantitative data about publications; new research is required to qualitatively evaluate the data.
Figure 1. Autoimmune Diseases. Latin America scientific productivity
Multiple sclerosis (MS) is an autoimmune, chronic, progressive, inflammatory and demyelinating disease of the central nervous system that affects 2.5 million people worldwide. The experimental autoimmune encephalomyelitis (EAE) is the most accepted model for studying the pathogenesis of MS. MS and EAE are mediated by Th1 and Th17 cells, with production of pro-inflammatory cytokines, such as interferon-gamma (IFN-γ), Tumor Necrosis Factor-alpha (TNF-α) and interleukin 17 (IL-17) and mediated nitric oxide (NO). Currently, due to the high cost and adverse effects of the used medications for MS the search for new drugs, which are capable of modulating the production of these inflammatory mediators, are necessary. Thus, in the present study we investigated the in vitro and in vivo immunomodulatory effects of parthenolide (PAR) on the production of NO, TNF-α, IFN-γ, IL-17 and Interleukin 6 (IL-6) in mice induced with EAE. EAE was induced in female C57Bl/6 mice, which were euthanized on the peak of disease. For in vitro studies, PAR was tested at 1, 5, or 20 µM, while in the in vivo experiments, PAR was used at 2,5 or 5 mg/Kg/day (by gavage). In both in vitro and in vivo studies PAR was able to decrease the production of IL-6, TNF-α, IFN-γ, IL-17 and NO. Results suggest that PAR may modulate the production of inflammatory mediators, demonstrating the great potential of this natural compound as prototype for the development of new drugs to treat in EAE, an animal model of MS.
Immunomodulatory effects of licochalcone A on experimental autoimmune encephalomyelitis

LACA7-0076

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Experimental autoimmune encephalomyelitis (EAE) is a murine autoimmune disease used to study multiple sclerosis. Herein, we have investigated the in vivo and in vitro immunomodulatory effects of licochalcone A (LicoA) on NO, \( \text{H}_2\text{O}_2 \), tumour necrosis factor-alpha (TNF-\( \alpha \)), interferon gamma (IFN-\( \gamma \)) and IL-17 production from EAE-mice. EAE was induced in C57BL/6 mice with myelin oligodendrocyte glycoprotein peptide (MOG\( \text{35-55} \)). For in vitro analysis, splenocytes were obtained from EAE-mice and incubated with LicoA (4, 20 and 40 \( \mu \text{M} \)). For the in vivo study, EAE-mice were treated with LicoA (15 and 30 mg/kg/day by gavage, during 10 days). \( \text{H}_2\text{O}_2 \), NO, IFN-\( \gamma \), TNF-\( \alpha \), and IL-17 production were determined by ELISA method. Histopathological analysis with hematoxylin-eosin and clinical score were used to evaluate severity of EAE disease in mice. LicoA (40 \( \mu \text{M} \)) inhibited \( \text{H}_2\text{O}_2 \), NO, IFN-\( \gamma \), TNF-\( \alpha \), and IL-17 production in vitro. LicoA (30 mg/kg/day) inhibited TNF-\( \alpha \), IFN-\( \gamma \) and IL-17 production in vivo and reduced clinical score and severity of EAE-mice. LicoA displayed in vitro and in vivo immunomodulatory effects on oxygen radicals, cytokines production and severity of disease. It is suggested that LicoA acts on the mechanism of EAE development by inhibiting IFN-\( \gamma \), IL-17, and TNF-\( \alpha \), modulating the immune response on both Th1 and Th17 cells.
Poster Session

IMMUNOMODULATION

Regulation of the response of T regulatory lymphocytes by Interferon (IFN)-gamma in experimental autoimmune encephalomyelitis

LACA7-0109

G. Arellano¹, J. Tichauer¹, E. Acuña¹, C. Castillo¹, R. Naves¹

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The understanding of the Interferon IFN-gamma (IFN-g) role in the pathogenesis of Multiple Sclerosis and experimental autoimmune encephalomyelitis (EAE) still unclear. In this study, we analyzed the less known protective effects of IFN-g on T regulatory lymphocytes (Tregs) during the chronic phase of EAE. Our results showed that IFN-g treatment induces EAE suppression with an amelioration of disease symptoms associated with less CNS inflammation and demyelination determined by histological analysis. Interestingly, IFN-g treatment significantly increased the frequency of Trég (CD4+CD25⁹⁹FOXP3+) in the central nervous system (CNS) of EAE. Assays performed ex vivo showed that CNS-infiltrating cells isolated from EAE mice did not increase the Treg cells frequency upon IFN-g stimulation. Furthermore, purified CD4+CD25- cells or CD4+ naive cells treated with IFN-g were not induced to express FOXP3 and inhibit the FOXP3 expression under inducible Tregs conditions (TGF-beta + IL-2). Instead, IFN-g induced an increase of CD4+FOXP3-LAP+ (TGF-beta) cells from CD4+CD25- cells and CD4+ naive cells. EAE mice treated with a combination of IFN-g and an anti-TGF-beta monoclonal antibody revealed that TGF-beta is necessary for the protective role of IFN-g in EAE. In conclusion, these results indicate that the IFN-g protective effects in EAE depend of expression of TGF-beta and an indirect increase of Tregs.

Supported by FONDECYT 1140049 (RN) and 3150133 (JT), and CONICYT Doctoral fellowship 21130452 (GA).
Rheumatoid arthritis treatment involves immunupression and polipharmacy with partial results. DLE is a heterogenous mixture of peptides <10KDa in size obtained from human leukocytes and has been shown to modify IFNγ, TNFα and IL6 levels and thus may have an immunoregulatory role. DLE may be useful as an adjuvant for uncontrolled autoimmune disease.

Methods: We added dialyzable leukocyte extract (DLE) to the usual treatment of rheumatoid arthritis patients. We reviewed the changes in the Spanish Stanford Health Assessment Questionnaire 20-item Disability Index Scale scores addressing 8 sections: dressing, arising, eating, walking, hygiene, reach, grip and activities. Scoring within each section is from 0 (without any difficulty) to 3 (unable to do). DLE was added in a weekly oral dose of 2mg/5mL for 4-6 months. Data was analysed using Wilcoxon test due to non normal distribution.

Results: Of 24 patients 23 were female, ages 54±11 yrs. The usual rheumatoid arthritis treatment included methotrexate (67%), azulfidine (42%), oral glucocorticoid (38%), hydroxychloroquine (38%), leflunomide (8%) in various combinations plus non-steroidal antiinflammatory drugs NSAID (88%). 2 patients (17%) used only NSAID due to liver damage. Basal disability scores were 1.69±0.78 (low level disability). After 4-6 months of DLE use, mean disability scores were 1.29±0.75 (low level disability). 18 (72%) patients showed improvement in their disability scores, 11 (46%) decreased the disability level. 83% of patients reported having clinical improvement after 4-6 months of DLE. No serious adverse events were reported.

Conclusions: DLE may be useful as an adjuvant in rheumatoid arthritis patients. Further studies are suggested.
ANTI CD25 TREATMENT OF HUMAN DENDRITIC CELLS MODULATES THEIR CYTOKINE SYNTHESIS PROFILES AND THEIR CAPACITY TO ACTIVATE ALLOGENEIC CD4 T CELLS: A POTENTIAL TOLEROGENIC EFFECT

LACAT-0204
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2Faculté de médecine Université François Rabelais, JE 2448- « Cellules Dendritiques et Greffes », 2 bis Bd Tonnelle- 37032 Tours., France

Background:

Recently attention has been focused on role for dendritic cells DCs, in promotion of peripheral tolerance. It is currently believed that maturation/activation state of DCs might be a control point for induction of graft tolerance through modifications of activation state of T cells. We demonstrated in this study CD25 expression on human DCs upon LPS activation. DCs differentiated from monocytes were exposed to anti CD25 during maturation, this treatment affected abilities of human DCs to induce CD4T cell proliferation in response to alloantigens, maintained endocytic capacity, Anti CD25 treated DCs produce low levels of IL-12 and IFN and high levels of IL-10. All these characteristics suggest that DCs may be used in cellular therapy either to induce allograft tolerance (anti CD25 treated DCs) or to restore immunity against tumors (IL-2 treated DCs).

Methods:

1. DCs generation from monocytes 2. Flow cytometry analysis 3. FITC-dextran uptake Endocytic tracers 4. Isolation of CD4T lymphocytes 5. Allogeneic mixed lymphocyte reaction MLR 6. Cytokine and ELISA

Results:

-Mature human DCs express CD25 - Anti CD25 treated DCs display : reduced intracytoplasmic IL-2 production an impaired IL-12 and IFNγ synthesis and an increased IL-10 production conserved endocytosis capacities impaired allostimulatory properties on CD4Tcells

Conclusions:

Clinical studies have indicated that subtle differences in maturation status of DCs might substantially impact on induced responses and turn T cell immunity into T cell tolerance. Thus, better understanding of factors determining development and function of DCs will be a prerequisite to design strategies for prevention and/or treatment of solid organ allograft rejection. Furthermore, standardized criteria must be developed to investigate DC
Heat shock proteins (HSPs) are molecules produced in response to diverse cellular insults which have immunomodulatory effects. In our group, we have described that patients with ankylosing spondylitis have humoral and lymphoproliferative immune response against the HSP60 from *Klebsiella pneumoniae*, *Yersinia enterocolitica* and other enterobacteria. Also, we found that this enterobacterial HSP60 can induce a decrease in the severity of collagen-induced arthritis in rats, although, this immunomodulatory effect has not yet been demonstrated in humans. So, we aimed to determine if the recombinant HSP60 from *Yersinia enterocolitica* (rHSP60Ye) can modify the production of cytokines in human PBMCs and whether it can affect the polarization of T cells into Treg, Th17, or double positive (IL-17, FoxP3+) cells.

Peripheral blood was taken from ten healthy donors and PBMCs were obtained by density gradient. We cultured one million cells in the presence of anti-CD3/anti-CD28 coated beads, IL-6, IL-23, TGF-b, rHSP60Ye, and LPS alone or in combination for 72 hours. Then, we determined the phenotype of Treg, Th17, and double positive (IL-17, FoxP3+) cells by flow cytometry, and quantified the concentration of cytokines by a multiplex bead array assay.

We did not found any differences in the percentages of the studied cells, nevertheless, cells incubated with the activating beads, the cytokine cocktail, and rHSP60Ye or LPS simultaneously, showed a significant decrease in the expression of FoxP3. Also, the cytokine analysis, resulted in a tendency to the increase of IL-6, and the decrease of TNF, IL-2 and IL-17 concentration in the cultures stimulated with rHSP60Ye.
INTRODUCTION: Disorders in metabolism of osteoblasts cells are frequently associated with bone-related disease such as rheumatoid arthritis and osteoporosis. These diseases are strongly related to immune system and its proteins as interferon gamma (IFN-γ) which may influence in the differentiation, proliferations and survival of these cells. OBJECTIVE: This work aims the role of IFN-γ in calcification and viability of human bone osteosarcoma (SaOs-2) cell line. METHODS: SaOs-2 cell line derived from a human osteosarcoma were cultured in 6-well plates and maintained in hMSC Osteogenic Differentiation BulletKit™ Medium to induce calcification. Subsequently, SaOs-2 cells confluent cultures were seeded at 2 x 10^5 cells/well and then were treated in presence or absence of recombinant human IFN-γ (Peprotech, Germany) with the maximum (1000 U/ml) and minimum (20 U/ml) concentrations. After IFN-γ stimulation, calcification and viability analysis were performed with 24 hours, by Alizarin Red and MTT assays, respectively. RESULTS: The analyses showed that INF-γ increased calcification in vitro in both doses compared with unstimulated controls and 20 U/mL INF-γ exhibited higher calcifications levels than 1000 U/mL INF-γ (69.14% and 19.15%, greater than healthy control respectively). In relation to viability, the 20 U/mL and 1000 U/mL INF-γ increased cell viability (7.23% and 13.61% greater than healthy control, respectively). However, only 20 U/mL showed significantly increased relative to unstimulated control group (p = 0.017). CONCLUSION: We conclude that INF-γ may favor the calcification and viability in the SaOs-2 cells according to used doses.
Poster Session

IMMUNOMODULATION

Tolerogenic activity of IFN-γ on macrophages/microglia in experimental autoimmune encephalomyelitis

LACA7-0144

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¹Universidad de Chile, Immunology, Santiago, Chile

During experimental autoimmune encephalomyelitis (EAE) development, leukocytes are recruited into the CNS mediating a destructive inflammatory response. Resident microglia and infiltrating macrophages present myelin peptides to reactive T cells inducing activation or tolerance. This process is regulated by inflammatory cytokines, such as IFN-γ. Our previous results have shown that IFN-γ treatment during the effector phase of EAE induces amelioration of clinical symptoms. In this study, we evaluated the effect of IFN-γ on the activation of macrophages/microglia during the chronic phase of EAE. Flow cytometry analysis of CNS infiltrating cells revealed that IFN-γ-treated EAE mice had a significantly lower frequency and absolute cell number of CD11b⁺ cells than PBS-treated control mice. Remarkably, IFN-γ-treated EAE mice had a significantly lower frequency of CD11b⁺CD45ʰi (activated) cells and a significantly higher frequency of CD11b⁺CD45ˢʰ (resting) cells associated with higher expression of IL-10, compared with controls. Further analysis performed on the CD45ʰ subpopulation revealed that IFN-γ induced a decrease in macrophages (CD11b⁺CX3CR1ᵐidPD-L1ʰCD45ʰ) expressing high levels of MHC-II molecules and co-stimulatory molecules without affecting activated microglia (CD11b⁺CX3CR1ʰPD-L1ʰCD45ʰ). In addition, CD11b cells obtained from IFN-γ-treated EAE mice and pre-treated ex vivo with low doses IFN-γ/myelin peptide induced an increase on lymphocytes Tregs cells (Foxp3⁺/CD25ʰ) frequency. Overall, our results indicate that IFN-γ treatment induces a tolerogenic phenotype in macrophages/microglia during EAE effector phase.
Poster Session

INFECTION AND AUTOIMMUNITY - MICROBIOME, INFECTOME AND INTERACTOME

VERNEUIL DISEASE: WHAT IS THE ROLE OF INTERNAL MEDICINE?
LACA7-0147
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Introduction- Verneuil Disease or Follicular chronic occlusive disease is an inflammatory process that affects intertriginous areas. This suppurative disorder involving glands, chronic occlusion affecting the sebaceous follicle pilotic, and deregulation of the immune system are involved in this pathogenesis. The possible complications are: anemia and osteomyelitis. Surgery does not work if we do not act on the immune mechanism.

Case-40 year-old man, smoker, diabetes, 20 years of history of axillar skin inflammatory process treated with surgery and antimicrobial therapy, that has been recurrent and has left severe sequels. Up to this moment the suppuration of axillar areas. Biopsy confirmed Hidradenitis Suppurativa phase III. He was treated by surgery, prednisone 0.5 mg/kg and 2-6 mg/kg cyclosporine A and he has improved. Five months later he abandoned immunosuppress therapy and started with axillar supurative processes. A similar treatment was indicated with favorable response.

Discussion- This is an exceptional case because incidence is 6 cases per 100,000. Abscesses, fistulas, suppuration, deformities, diagnosis delay and treatment that look only like an infectious disease. Biopsy was confirmatory. Crohn's disease and anthrax may be differential diagnosis. Diabetes and smoking are associated factors. Surgery is always needed. Prednisone and Cyclosporin A are useful. Biological agents like infliximab may be considered for recurrent chronic stage.

Conclusions- Misdiagnosis Verneuil Disease is the rule and responsible of sequels. Immunosuppresor treatment must be indicated in early stages and eventually biological therapies to prevent recidives, deformities and social impact.
Fig. 1 Hidradenitis suppurativa phase III
Fig. 2 Pre-Treatment
Fig. 3 Post-Treatment with surgery and Cyclosporine A and Prednisone
This study describes three cases with Fever of Unknown Origin (FUO) with definitive diagnosis of rheumatic disease: the first, a 29 years old man with febrile peaks of 40 °C, myalgias and cervical lymphadenopathy; with antecedent of travel to tropical area 30 days prior, suggesting an infectious etiology; however, the fever persisted despite antimicrobial coverage, paraclinical studies with ferritin found in 2208 μg/l suggestive of Adult’s Still Disease at tenth day of stay. The second is a 19 years old man, with an abdominal pain clinic associated with a temperature of 40 °C with no history of importance; abdominal ultrasound evidence hepatomegaly and pleural effusion; during the stay, presented tonic-clonic seizures and pancytopenia with hemolytic anemia, after discarding infectious disease and malignant neoplasia, an immunological profile was requested with ANA and lupic anticoagulant, both positive, and diagnosis was directed towards Systemic Lupus Erythematosus at the eleventh day of hospitalization, with improvement after immunomodulatory management. Finally, a 14-year-old female patient with a history of arthralgia, cervical / submaxillary lymphadenopathy, morbilliform exanthema and fluctuating fevers (38-39.9 °C) of a month of evolution persisting despite negative polycultures and broad spectrum antibiotic therapy. Laboratory studies are expanded finding ferritin of 3156 μg / l at ninth day of stay and is diagnosed Child’s Still Disease. The prevalence of rheumatic diseases in the FUO has been increasing allowing a precise approach to other etiologies previously not considered among its causes. These cases illustrate the importance of a good clinical history.
Rheumatoid arthritis (RA) is a high risk disease for celiac disease (CD), sharing multiple aspects. IgA-tTg autoantibody is a classical marker for CD, however, it has many false positives. Anti neo-epitope tTg complexed to gliadin is a reliable bio-marker for CD, has never been compared to the IgA-tTg performance and false positivity in naïve and treated RA population.

Methods: 135 RA adult patients, mean age 55 ±12.7 years, F/M 1:0.2, respectively, from the ADAPThERA study cohort, where studied in naïve patients and longitudinally at 3 follow up visits. ADAPThERA is a network to improve patient care and to find new bio-markers for RA. Patients were tested using the following ELISAs detecting either IgA, IgG or both (IgA+IgG): tTg (for in house research purpose only) and AESKULISA® tTg New Generation (tTg neo-epitope).

In the naïve patients, on the first visit after diagnosis and along the follow up under pharmaceutical therapy, for 3 consecutive visits, the % positivity of the IgA-tTg (Visit 1, 2, 3, 4 , 6.7 %, 3.1 %, 4.6 %, 7.0 %, respectively) was significantly higher than in the tTg-neo antibodies (Visit 1, 2, 3, 4, 2.2 %, 0.8 %, 1.1 %, 2.8 %, respectively, p<0.05).

Determinations of CD associated autoantibodies in naïve and treated RA groups reveal that IgA-tTg is less specific for CD (mirrored by its higher false positivity) in relation to the lower false positivity of its competitor (anti neo-tTg) in RA patients’ sera.
Innate adaptive protection as glycoconjugates (GC) recognizing system of human organism is important and perspective in respect of infectious and autoimmune diseases. Probiotic protection system is additional component of human protection. The aim was to evaluate probiotic lectin system (PLS) as an important part of the human interactome protection. **Methods:** Probiotic bacteria of human gut origin were from collection of G.N. Gabrichevsky Research Institute for Epidemiology and Microbiology. PLS were identified and isolated using isoelectrofocusing in polyacrylamide gel followed by lectin extraction. PLS were registered on the blot by polymeric glycoconjugate(GC)-biotin (www.lectinity.com) treated with streptavidin-peroxidase conjugate, in the presence chemiluminescent substrate in a real time in *BioChemi System* (UVP). **Results:** The different GC-binding PLS (> 27 kD, pI 4-8) were identified and isolated. The choice of (PLS—GC)-type interactions in human mucosa can be regulated by extended panel of GC. The use of artificial GC creates basis for constructing metabiotic therapeutics of system action. The following activities of strain metabolites can be predicted: antipathogenic activities (the use of GC imitating microbial cell surface and wall structures: peptidoglycans, sialylated glycans, glycoantigens, others); prebiotic/ symbiotic actions (the use of GC imitating prebiotic structures: derivatives of L-fucans; modified D-galactoside oligomers, etc.); increasing human protection (the use of GC regulating peritoneal macrophages and macrophage-like lymphocytes, complement system lectin components: (phospho)mannans and other homopolysaccharides, glycoantigens); on-duty support against cancerogenesis. As a result, PLS effectively imitated activities of cell probiotics. **Conclusions:** Results indicate the prospects of PLS as the new important ingredient of the human mucosal immunity.
Human T lymphocyte virus type I (HTLV-I) is an etiologic agent of several chronic inflammatory diseases from autoimmune origin, as HAM/TSP. It has proposed that by molecular mimicry from virus antigens, autoreactive lymphocytes clones are activated in the host and trigger an inflammatory response, which perpetuates autoimmune and inflammatory phenomenon. Several studies have demonstrated the important role of T and B regulatory lymphocytes in homeostasis maintenance and in inflammatory response control. Previous reports have shown that HAM/TSP patients present a reduction in frequency and function of regulatory T cells (Treg); however, little is known about regulatory B cells (Breg) involvement during this disease. This work quantified, frequency of Treg (CD4+CD25^hiFOXP3+/CD4+CD25^hiCD73+/CD4+CD25^hiCD73^hi), T activated cells (CD4+HLA-DR+/CD4+CD57+/CD8+HLA-DR/CD4+CD57+) and IFN-γ/IL-4 producing CD4+ and CD8+ cells in peripheral blood mononuclear cells from 7 patients and 8 controls. The results show that patients have high Treg frequency (CD4+CD25^hiFOXP3+/CD4+CD25^hiCD73+/CD4+CD25^hiCD73^hi) (median [IQR] 17.1 [6.7-19.3]) as well as high CD4+IFN-γ+ frequency (median [IQR] 21.1 [6.1-29.2]) compared to controls (median [IQR] 4.5 [0.8-7.4] Treg and median [IQR] 4.3 [0.4-6.8] of CD4+IFN-γ+). Strikingly, patients have low Breg percentage (median [IQR] 3.9 [3.4-6]) compared to controls (median [IQR] 6 [5.6-8.5]). No significant differences were found to other parameters. Therefore, these preliminary results confirm previously literature reports regarding the high Treg percentage in patients. However, low Breg percentage in patients suggests that these cells could play an important role in controlling inflammatory response in HAM/TSP, contrasting with high percentages of CD4+IFN-γ cells.
PARVOVIRUS B19 INFECTION IN MAYAN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN MEXICO.
LACA7-0040
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Background. Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that occurs predominantly in women, characterized by the production of autoantibodies. The causative agent of SLE is unknown, but the combination of environmental, hormonal and genetic factors may favor the development of the disease. Parvovirus B19 (PV-B19) has been associated with the development of SLE, since it induces the production of anti-single stranded DNA (anti-ssDNA). The association of infection PV-B19 as environmental factor for developing SLE in the Mayan population of Mexico is unknown.

Aim. We carry out serological and molecular analysis of PV-B19 infection in Mayan women with established SLE.

Methods. IgG and IgM anti PV-B19 were evaluated in 66 SLE patients and 66 control subjects, all women of Mayan origin. Viral DNA and viral load were analyzed by qPCR in patients and controls.

Results. IgM levels no significant were observed in 14.28% (4/28) patients and 11.42% (4/35) controls. IgG was detected in 82.14% (23/28) patients and 82.85% (29/35) controls, but were significantly higher in SLE patients. Viral DNA was found in 86% (57/66) patients and 81% (54/66) controls. Viral load, quantified in 28/66 SLE patients and 31/66 controls which were positive for IgM and IgG, was significantly higher in controls.

Conclusion. The high prevalence of PV-B19 in Yucatan, and the presence of IgM, IgG, and viral load in Maya women with established SLE suggest that PV-B19 infection could be considered as an environmental factor to trigger or reactivate SLE.
Poster Session

MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES

Role of microparticles from patients with systemic lupus erythematosus in the induction of NF-κB dependent inflammatory mediators in mononuclear phagocytes

LACA7-0059
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Background

Microparticles are small vesicles with a wide spectrum of biological activities. Elevated levels of microparticles are reported in systemic lupus erythematous (SLE). In addition, complement and damage-associated molecular patterns (DAMPs) are increased in microparticles from SLE patients. Microparticles could modulate the immune responses, through their recognition and transfer of bioactive molecules following internalization into the cell. These events could induce activation of different signaling pathways like NF-κB, which are overexpressed in SLE patients. We propose microparticles are internalized by different populations of peripheral blood mononuclear cells (PBMC) and are able to induce the production of inflammatory mediators through NF-κB activation.

Methods

Microparticles were isolated from platelet-poor plasma from SLE patients and healthy controls. We evaluated by flow cytometry the union/internalization by PBMC of microparticles labelled with carboxyfluorescein succinimidyl ester. Mononuclear phagocytes pretreated with or without NF-κB inhibitor ammonium pyrrolidinedithiocarbonate (PDTC) were stimulated with microparticles from different source. Interleukin (IL)-6, IL-10 and prostaglandin E2 (PGE2) production were determined by flow cytometry and ELISA, respectively.

Results

Microparticles were mainly internalized by monocytes rather than T and B lymphocytes. Mononuclear phagocytes treated with patients-derived microparticles exhibited high IL-6 and PGE2 levels compared with mononuclear phagocytes treated with control-derived microparticles. Interestingly; PDTC antagonizes the effects of microparticles, suggesting that these vesicles have pro-inflammatory effects which are NF-κB dependent in monocytes

Conclusion

Circulating microparticles from SLE patients could be internalized by mononuclear phagocytes inducing the production of inflammatory mediators in a NF-κB-dependent way, which could contribute to the chronic inflammatory process seen in SLE.
Introduction. In Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA), the vesicles called microparticles (MP) are considered a relevant source of autoantigens. In SLE and AR patients compared to healthy controls, MPs counting as well as their phenotype and composition are altered and they are able to form immune complexes (MP-IC). Monocytes are important players in SLE and RA pathogenesis, and are considered one of the main cells that can remove circulating MP. We propose that circulating MP-IC could activate monocyte subsets contributing to the inflammatory environment present in those patients.

Methods. The classical and non-classical monocytes activation (cytokines and surface markers expression) was evaluated in response to MP and MP-IC from plasma of healthy donors and SLE and RA patients by flow cytometry. Monocyte subsets from healthy donors were isolated and cultured for 24h with MP and MP-IC.

Results. MP and MP-IC from SLE and RA patients induced increase expression of HLA-DR and production of IL-1β, TNF-α, IL-6 and IL-8 in non-classical compared with classical monocytes, without compromise cell viability; these changes were more substantial with MP-IC treatment. These results were related with the fact that non-classical internalized and binded more MP and MP-IC than classical monocytes.

Conclusion. MP and MP-IC recognized by non-classical monocytes could play a role in the proinflammatory status of RA and SLE patients; while classical monocytes respond in a lesser extent suggesting that those phagocytes are more silent removers of MP and MP-IC.
Ankylosing spondylitis (AS) is the prototype of a heterogeneous group of rheumatic diseases known as spondyloarthritis (SpA) characterized by arthritis of the axial skeleton that leads to new bone formation and fusion of the vertebrae. Recently, we found a high number of Th17 and Treg lymphocytes in the synovial fluid of patients with AS that differ from the amounts found in the blood from the same patient and from healthy subjects.

To further analyze the immunopathology of AS, we used the Cytometric Bead Array (CBA) technique to investigate the concentration of the cytokines IL-2, IL-8, IL-10, IL-12, TNF, IL-17 and IFN-γ in the synovial fluid of patients with AS and compared them with serum concentrations of the same patient and samples of serum of 12 healthy subjects as controls.

High concentrations of IL-6, IL-8, IL-12 and TNF were found in the synovial fluid of patients with AS, which significantly differed (p < 0.05) from serum levels of healthy subjects and even from serum of the same patient. We conclude that there are high concentrations of IL-6, IL-8, IL-12 and TNF in the synovial fluid of patients with AS. The alterations in this proinflammatory cytokines in patients with AS are limited to synovial fluid as there are no significant differences in the serum concentrations between patients and controls. The high concentrations of IL-6, IL-8, IL-12 and TNF suggest a chronic inflammatory process in the synovial fluid of patients with ankylosing spondylitis.
Systemic lupus erythematosus is an autoimmune disease characterized by the activation of autoreactive T and B cells, autoantibody production and immune complex deposition in the organs. Although the presence of B cells in the thymus is associated with autoimmune disorders such as myasthenia gravis, no studies have investigated the role of B cells in the thymus of mice with lupus. We investigated in the murine model [NZBxNZW]F1 whether the kinetics of appearance of B cells in the thymus correlates with the onset of lupus.

Our results demonstrate that during the development of the disease there is an increase of B cells in the thymus of diseased mice compared to healthy mice. Moreover, T CD4+ cells from thymus of lupic mice show an effector phenotype compared to T cells from healthy mice. While thymic B cells from healthy and lupic mice show similar expression of costimulatory and antigen-presenting molecules, B cells from lupic mice exhibit a higher capacity to induce proliferation and activation on CD4+ thymocytes than B cells from healthy mice. Finally, thymic B cells from lupic mice can differentiate into anti-DNA autoantibody-secreting cells. This finding suggests that the thymus in autoimmune disease could harbor T-B cell interactions that contribute to the activation of autoreactive CD4+ thymocytes and differentiation to autoantibody-secreting cells.

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Poster Session

MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES

Cysteinyl leukotrienes levels and their receptors expression in colonic mucosa of patients with inflammatory bowel disease.
LACAT-0072

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Cysteinyl leukotrienes are lipid mediators derived from the metabolism of arachidonic acid. They are potent pro-inflammatory mediators associated with asthma, arthritis, psoriasis, ulcerative colitis, etc. Their effects occur through 2 types of membrane receptors: CysLTR1 and II.

Objective: To evaluate the levels of LTC4 and its receptor’s expression in colonic mucosa of patients with inflammatory bowel disease (IBD).

Patients and methods: Colon biopsies of patients with diagnosis of IBD (OMS) were obtained through videocolonoscopy. Samples were analyzed with hematoxylin-eosin and semiquantitatively classified for neutrophil recruitment. CysLTR type 1 y 2 were determined (RT-PCR), and LTC4 and IL-8 (ELISA). Control group were sex and age matched patients undergoing conventional screening for colorectal cancer (OMS). The project was approved by the institutional ethics committee.

Results: Twelve patients (6 women, 6 men) medium aged 49.75 years-old were compared with 12 controls (7 women, 5 men), 50.5 years-old. Significant increase in neutrophil percentages and IL-8 levels at the transversal colon and sigmoid rectum were found (Figure1 A1/A2 - B1/B2) in patients versus controls. This correlated positively with CysLRT1 and LTC4 levels (p=0.01, Fisher’s test). These findings seemed more prominent in patients with extraintestinal manifestations (one patient with ulcerative colitis plus psoriasis, autoimmune hepatitis and type I diabetes, and two other patients, one with ulcerative colitis and other with Crohn’s, both with arthritis).

Conclusion: Our results may indicate that LTC4 plays a central role in the gut's mucosa inflammatory response of our group of patients with IBD, and particularly in those with extraintestinal manifestations.
Poster Session

MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES

Autoimmune Pathophysiology, Physiology to of the Immune system and Biology: the tangled field
LACA7-0009
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How can we understand disease without a clear vision about health? How can we explain immunological mechanisms of diseases if the word ‘physiology’ is virtually absent from immunological texts? Here we present the ‘conservative physiology of the immune system’ observing massive experimental data regarding microbiome, mucosal immune system, and other different systemic and network phenomena of the immune system. We quickly present accumulated evidence that the immunopathological mechanism is associated with ‘Oligoclonal T cell expansions’ published in a huge umber of experimental examples, it is persistent in several immunological diseases syndromes, and may mark severity and progression of disease. We believe this approach may be useful in situating a clearer description of immunological activity based in more physiological and healthy understanding of the organism and nature. Dialoguing with the contemporary debate in biology, namely, evolution, development and cognition, from where new proposals have been published that may aid us in the care for our patients and their health promotion.
Background

Autoimmune diseases tend sometimes to cumulate in the same individual, probably as a consequence of defect in immune regulation with breakdown of self-tolerance. Autoimmune hepatitis and renal vasculitis have been occasionally reported with other autoimmune diseases but the particular association of these both disorders has rarely been previously reported in medical literature.

Case report

A 60-year-old female with history of autoimmune thyroiditis and ANCA negative systemic vasculitis was admitted in department for abdominal pain and urticaria. The diagnosis of systemic vasculitis was made by part of the renal involvement with severe chronic renal failure, hematuria, proteinuria and endocapillar and extracapillar glomerulonephritis at the renal needle biopsy. She was treated by corticosteroid and immunosuppressive treatment (Cyclophosphamide). Physical examination noted homogene hepatomegaly. There was no jaundice or splenomegaly. Hepatic tests revealed an important cytolysis. A liver biopsy showed characteristic features of autoimmune hepatitis (necrosis and inflammation). Serological tests were negative for viral hepatitis B and C. The diagnosis of autoimmune hepatitis (AIH) was retained following detection of high serum gammaglobulin level, significant anti-nuclear antibodies level and the result of liver biopsy with a Score of International Autoimmune Hepatitis Group at 18 points. The patient was treated by corticosteroid at the dose of 1 mg/kg/day and Ursodesoxycholic acid. The patient developed an acute pancreatitis and the evolution was fatal.

Conclusion

This observation is particular by the fact that a renal vasculitis was associated to an AIH. This association is rare. The implicated mechanisms are unknown and lead to difficulties in the choice of a suitable therapeutic management for this particular association.
Poster Session

MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES

THE RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, VEGF AND E-SELECTIN LEVELS AND DISEASE ACTIVITY RELATION IN PATIENTS WITH RHEUMATIC DISEASES

LACA7-0020

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Background: The endothelial damage, changes in vascular permeability and plaque formation are caused by the action of cytokines and chemokines which plays role in chronic inflammation in RA and AS. We aimed to determine the changes in the amount VEGF, E-selectin, arterial stiffness and disease activity with inflammation in RA and AS patients who had active period of disease.

Methods: 13 patients diagnosed with AS, 28 patients diagnosed with RA and 30 healthy controls were enrolled to the study. Arterial stiffness, VEGF and E-selectin, ESR and CRP were evaluated in all patients and control group. BASDAI and DAS28 scores were calculated in patients with rheumatic diseases. The level of serum VEGF and E-selectin were determined by ELISA, and arterial stiffness was measured by oscillometric method. All these data were statistically compared.

Results: DAS28 and BASDAI score, ESR and CRP levels were significantly decreased on the 3th month of treatment in all patients (p<0.001). Increase in VEGF and E-selectin levels and decrease in PWV and Aix parameters was observed with treatment. But these changes were not statistically significant. While the level of PWV was stable, Aix was decreased on the 3th months of treatment in RA patients treated with non-TNF.

Conclusions: Disease activity score, ESR and CRP are decreased with the reduction of inflammation in RA and AS patients with treatment. PWV and Aix of arterial stiffness parameters decreased after 3 months of treatment, but it did not reach to statistical significance. Arterial stiffness and cardiovascular risk is expected to be reduced significantly ongoing treatment process.
POSTER SESSION

MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES

IGA-ANTIENDOMYSIUM ANTIBODY SEROCONVERSION BY SEROLOGICAL FOLLOW-UP OF 1ST DEGREE RELATIVES OF CELIAC DISEASE PATIENTS

LACA7-0178


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CONTEXT: Celiac disease (CD) is an immune-mediated enteropathy of the small intestine triggered by permanent intolerance to gluten in genetically predisposed individuals by the alleles of the Human Leukocyte Antigen (HLA) class II HLA-DQ2 and/or HLA-DQ8, and the serological marker for IgA antibodies IgA-Antiendomysium (IgA-EMA) used for detection and confirmation of new cases of CD to have sensitivity and specificity close to 100% considered positive predictive value.

OBJECTIVE: To determine the incidence rate of IgA-EMA antibodies seroconversion in a cohort of 1st degree relative of celiac patients.

METHOD: Repeat IgA-EMA by serological follow-up of 1st degree relatives of celiac patients that present genetic risk by HLA alleles predisposing to CD at University of Brasília Hospital – Brazil.

RESULTS: 197 patients with predisposing HLA alleles (95 male and 102 female, aged 4-75 years, mean age: 29.9±16.8) participated in the study and was found 11 cases of seroconversion for IgA-EMA. Incidence rate of seroconversion of IgA-EMA within 14 years of follow-up was found in this study, with 95% confidence interval, 1.1±0.2 cases of seroconversion per 100 person-years accompanied by an observation period of 1 to 14 years, average 4±3.7 years.

CONCLUSION: The incidence rate of seroconversion of IgA-EMA suggests serological tests repetition among patients with HLA alleles predisposing to DC belonging to the risk group of developing celiac disease.

Keywords: Celiac disease, seroconversion of IgA-EMA antibodies, genetic predisposition, HLA, follow-up.
Rheumatoid Arthritis (RA) is an autoimmune disease considered a heterogenic clinic syndrome, this variability affects the disease severity and progression. Previously, Killer-cell Immunoglobulin-like Receptors (KIR) genes have been associated with RA pathology and treatment response. Therefore, KIR receptors expression in NK and T CD4+CD28null cells may vary in the pathology and during the therapeutic scheme.

We included 32 individuals: 27 RA patients and 5 healthy subjects; patients were stratified according to the treatment: with no previous DMARD and with previous DMARD treatment. KIR2DL2, KIR2DS2 and KIR2DL3 genes were genotyped using PCR-SSP method. NK and T CD4+CD28null populations and KIR receptors expression were determined by flow cytometry. For statistical analysis, we used r Pearson correlation and T student, with statistically significant at p<0.05.

We compared NK and T CD4+CD28null cell populations frequencies between RA patients and healthy individuals. CD56+CD16+KIR+ and T CD4+CD28null populations were more frequent in RA patients (p=0.015 and 0.025, respectively). In patients with no previous treatment, we found a positive correlation between T CD4+CD28null population with CD56+CD16+KIR+ (r=0.540, p=0.025) and a negative correlation with CD56+CD16+ (r=-0.541, p=0.025). Meanwhile in patients with previous DMARDs treatment, T CD4+CD28null was negatively correlated with NK KIR+ population (r=-0.705, p=0.023).

T CD4+CD28null population was correlated to the NK KIR+ population frequency: positively in patients with no previous treatment and negatively in patients with previous treatment. This suggests that DMARDs treatment may influence the CD56+CD16+KIR+ and T CD4+CD28null populations frequency in RA patients, this ultimately could affect the treatment response.
NOVEL THERAPEUTIC TARGETS IN AUTOIMMUNITY

THERAPEUTIC TARGETING OF CD6 IN AUTOIMMUNE DISEASES: AN UPDATE ON CLINICAL TRIAL DATA WITH ITOLIZUMAB
LACAT-0100
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Background: The CD6 molecule is a pan T cell marker that plays a dual role as a modulator of intracellular signaling. Although CD6 expression has been correlated with human autoimmune diseases (AD), only a few therapeutic approaches are exploring this molecule as target in the clinic. Itolizumab is a humanized anti-CD6 monoclonal antibody that has shown encouraging results in terms of safety and positive clinical effects in patients with rheumatoid arthritis and psoriasis.

Methods: The work provides an overview of the clinical data obtained in patients with autoimmune diseases who have been treated with itolizumab. Furthermore, we discuss the possible mechanism of action of itolizumab basing the analysis on recent site mutagenesis and structural data.

Results: The conducted clinical studies show therapeutic schedules lasting from 8 to 12 weeks induce significant clinical responses that prolong over the treatment periods. Remarkably, itolizumab has a favorable safety profile characterized by a significantly low frequency of treatment-related serious or severe adverse events, a low risk of infection and a low immunogenicity. We observed also that, contrary to previous interpretations, the mechanism of action does involve steric blocking of CD6-ligand interaction in the cellular context. Consequently, it controls inflammation and delays disease progression, without causing immune cell depletion.

Conclusions: Overall, itolizumab is currently the only biological drug targeting the CD6 receptor being used for AD therapy, with increasing information from clinical trials becoming available.
Poster Session

NOVEL THERAPEUTIC TARGETS IN AUTOIMMUNITY

New markers for celiac disease: anti-neo-epitope human and microbial transglutaminases
LACA7-0026

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Objectives: Microbial transglutaminase (mTg) and human tissue Tg (tTg) complexed to gliadin peptides present neo-epitopes. Antibodies against these complexes are called tTg neo-epitope and mTg neo-epitope. Reliability of antibodies against the non-complexed and complexed forms of both transglutaminases to reflect intestinal damage and to diagnose the pediatric Celiac Disease (PCD) was compared.

Methods: 95 PCD patients, 99 normal children (NC) and 79 normal adults (NA) were tested using the following ELISAs detecting IgA, IgG or both IgA+IgG combined: tTg (for in house research use only), AESKULISA® tTg New Generation (tTg neo-epitope (tTg-neo)), AESKULISA® mTg (RUO) and AESKULISA® mTg neo-epitope (mTg-neo, RUO). Marsh criteria were used for the degree of intestinal injury.

Results: All anti-mTg-neo and anti-tTg-neo levels were higher (p<0.001) compared to the single antigens. tTg-neo IgA and IgG+IgA were higher than mTg-neo IgA and IgA+IgG (p<0.0001). The antibody activities reflecting best the increased intestinal damage were: mTg-neo IgA> mTg-neo IgA+IgG > tTg-neo IgG ≥ mTg-neo IgG > tTg-neo IgA> tTg-neo IgA+IgG. Taken together, mTg-neo IgG and tTg-neo IgA & IgA+IgG correlated best with intestinal pathology (r=0.5633, r=0.6165 & r=0.6492; p<0.0001, p<0.0001 & p<0.0001 respectively).

Conclusion: The complexed forms of both transglutaminases exhibited a higher OD activity and better reflected intestinal damage in PCD, compared to the non-complexed forms. mTg is immunogenic in children with CD and by complexing to gliadin its immunogenicity and pathology reflection is enhanced.
Systemic sclerosis (SSc) comes with skin and internal organs fibrosis, constituting a systemic autoimmune disorder, which leads to activating pro-inflammatory cytokines (interleukin, NLRP3, etc), along with vascular conditions and the overexpression of extracellular matrix components, causing systemic fibrosis.

Our goal was to determine the expression of miR-223 as a regulator to NLRP3 by comparing clinical subgroups of SSc patients and a control group in order to establish the relationship between the expression of miR-223 and the severity of SSc.

We recruited 18 SSc patients, whose degree of skin and internal organs fibrosis we measured. We took skin, serum and plasma biopsies to measure the expression of miR-223 by means of real time PCR.

We found an overexpression of miR-223 in the SSc patients, in contrast to the control group (p: 0.007). The clinical subgroup with diffuse SSc showed an overexpression of miR-223, in contrast to the limited SSc patients. The miR-223 levels in both groups were higher in plasma than they were in serum (p: 0.009).

Our group previously showed an overexpression of NLRP3 in SSc patients, which links their clinical severity to pro-inflammatory interleukins very closely. In this paper we prove the relationship between clinical severity and miR-223 in SSc cases. The role of miR-223 as a regulator of NLRP3 becomes evident, which suggests it has a relationship with the modulating of inflammatory processes, therefore modulating fibrosis. Understanding this relationship could shed light on possible therapeutical targets in order to improve the quality of life of these patients.
Fig 1. Relative expression of miR-223 in SSc patients in contrast with control group. SSc: Systemic Sclerosis

Fig 2. Relative expression of miR-223 in SSc patients between samples. SSc: Systemic Sclerosis
Poster Session

NOVEL THERAPEUTIC TARGETS IN AUTOIMMUNITY

Mesenchymal stem cells decrease oxidative stress in bowel of IL-10 knockout mice

LACA7-0223

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Introduction: Inflammatory bowel disease (IBD) is an autoimmune disorder characterized chronic inflammation in large intestine. The interleukin-10 knockout (IL-10 KO) mouse is a well-established murine model of IBD which develops spontaneous intestinal inflammation that resembles Crohn's disease. Mesenchymal stem cells (MSC) evaluated one of promising candidate for treatment of IBD but the main mechanism is still remain to be clear.

In this study, we evaluate effect of MSC on oxidative stress related inflammation in IL-10 KO mice.

Materials and Methods: Human bone marrow derived MSCs were characterized by cell surface CD marks as well as differentiation induction into osteoblasts and adipocytes. Male C57BL/6 mice were divided wild (Wild), control IL-10 KO (CON) and MSC treated IL-10 KO (MSC) groups. At 10 and 11th weeks, 5x10⁵ MSCs were injected through tail vein for MSC. One week after MSCs injection the mice were sacrificed and cecum and colon were harvested for test. Piece of cecum, ascending colon, descending colon were paraffin embedded and morphologic changes were evaluated. Other part was homogenized and uses for molecular analysis.

Results: Inflammatory cell infiltration and thickening of mucosa observed in IL-10 KO mice but such findings attenuated in MSC compared to CON. Superoxide and hydrogen peroxide level was higher in CON than MSC and lipid peroxidation (malondialdehyde) also followed this pattern. Inflammatory cytokine (IL-12, TNF-a, INF-g) expression suppressed in MSC.

Conclusions: MSCs protect progression of chronic bowel inflammation in IL-10 KO mouse by suppression of oxidative stress.
INTRODUCTION: Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis, presenting as an inflammatory and ulcerative disorder of the skin. The most common form is an inflammatory papule or pustule that progresses to a painful ulcer with purulent background and erythematosus-violet halo.

PRESENTATION OF THE CASES: CLINICAL CASE 1. Female 58 years, clinical and histopathological diagnosis compatible with PG in lower limbs. He was treated with glucocorticoids, azathioprine, anti-TNF (infliximab, adalimumab) and mycophenolate mofetil; Resistant to first-line treatment. He received additional management with a hyperbaric chamber, broad spectrum antibiotics and immunoglobulin. Terrible evolution by colonization with Pseudomonas aeruginosa, warranted amputation of affected extremity, however progressed to septic shock and death.

CLINICAL CASE 2. Male 30 years old with dermatosis characterized by pustular, ulcerocrustated lesions in the lower extremities, upper limbs, trunk and facial region, clinical and histopathological diagnosis compatible with PG. He was treated with glucocorticoids at optimal doses, presented relapse and progression of the lesions with data of superinfection (Klebsiella oxytoca, Pseudomonas aeruginosa, Acinetobacter baumannii). It was administered with specific antibiotics, anti-TNF (etanercept, infliximab), immunoglobulin, hyperbaric chamber and wound healing. It is in follow-up with adequate clinical response.

DISCUSSION AND CONCLUSION: There are no definitive guidelines for the management of PG patients, treatment is based on small uncontrolled studies and clinical experience usually requires the use of one or more topical or systemic immunomodulatory agents. The revised current treatment algorithm is shown in Table 1.
<table>
<thead>
<tr>
<th>Treatment 1a. line</th>
<th>Treatment 2a. line</th>
<th>Treatment of refractory disease</th>
<th>Local measures</th>
<th>Surgery</th>
<th>Other Therapies</th>
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<tbody>
<tr>
<td>Systemic glucocorticoids 0.5-1.5 mg/kg/day (oral and intravenous)</td>
<td>Inhibitors of Tumor Necrosis Factor (Infliximab 5 mg/kg)</td>
<td>Intravenous immunoglobulin</td>
<td>Sterile saline solution and antiseptic solutions</td>
<td>Controversial. is only considered in select cases, limited to periods of good control and use of concomitant systemic therapy</td>
<td>Hyperbaric oxygen</td>
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<tr>
<td>Cyclosporin (4-6 mg/kg)</td>
<td>Other anti-TNF (Adalimumab 40 mg/week or 40mg every 2 weeks, Etanercept 25-50mg twice weekly)</td>
<td>Alkylation agents (Cyclophosphamide, chlorambucil)</td>
<td>Absorbent patches (alginates) to prevent maceration of tissues</td>
<td>Gentle debridement</td>
<td>Topical agents: sodium cromoglicate, nicotine, benzoyl peroxide, 5-aminosalicylic acid, nitrogen mustards, platelet-derived growth factor</td>
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<td>Azathioprine (100-300 mg/day)</td>
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<td>Avoid application of caustic substances (silver nitrate)</td>
<td>Skin grafts</td>
<td>Systemic agents: clofazimine, colchicine, doxycycline, imatinib, alpha, mephalan, mercaptopurine, metronidazole, potassium iodide, sulphasalazine, tacrolimus, thalidomide, ustekinumab, carakinumab, ceftriaxone pegol, golimumb</td>
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<tr>
<td>Mycophenolate mofetil (2-3 g/day)</td>
<td></td>
<td>Zinc oxide as protective barrier</td>
<td>Partial-thickness skin grafts with negative pressure</td>
<td>Leukocyte apheresis</td>
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<td>Methotrexate (10-30 mg/week)</td>
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<td>Corticosteroids (clobetasol 0.05%) and calcineurin inhibitors (tacrolimus (0.03-0.3%, pimecrolimus 1%) topical)</td>
<td>Application of keratinocyte autografts obtained by bioengineering</td>
<td>Pleuroperitoneal aspiration</td>
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<td>Dapsone (50-200 mg/day)</td>
<td></td>
<td>Intralemmon triamcinolone</td>
<td>Allogeneic dermal cultures</td>
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<td>Minocycline (100 mg twice daily)</td>
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INTRODUCTION: IgG4-related disease is a fibroinflammatory condition characterized by "pseudotumors" and dense lymphoplasmocytic infiltrate, rich in IgG4-positive plasma cells, fibrosis and elevated serum IgG4. Autoimmune pancreatitis, a type of chronic pancreatitis is characterized by an inflammatory process in which there is abundant lymphocytic infiltrate and fibrosis.

PRESENTATION OF THE CASES:

CLINICAL CASE 1. Male 39 years, diagnosis of Type 2 Diabetes of difficult control. He was hospitalized for weight loss of 8 kg in 2 months without apparent cause, chronic constipation and abdominal pain, with radiological finding of apparent abdominal mass. Pancreas with multiple calcifications and IgG4 elevation (140 mg / dL) were documented; glucocorticoid remission was achieved.

CLINICAL CASE 2. Male 40 years, history of perforation of the nasal septum and hemolytic anemia. He was hospitalized for icteric syndrome and weight loss of 10 kg. Relapse of hemolytic anemia was ruled out, pseudotumor was documented in the head of the pancreas and IgG4 elevation (143.1 mg / dL) was reported; remission was achieved with rituximab and glucocorticoids.

DISCUSSION AND CONCLUSION:
Recommendations for the treatment of IgG4-related disease are limited to retrospective studies and small prospective studies. International guidelines recommend steroid therapy in patients with symptoms. The primary basis for short and long-term treatment is steroids, however, potential adverse effects have led to the investigation of other therapeutic targets for this pathology.
Background/Purpose: Treatment of patients with rheumatoid arthritis (RA) is challenging due to the high heterogeneity. RA synovial genome-scale transcriptomic profiling of different patient cohorts can provide insights on the causal basis of drug responses.

Methods: We have created a normalized compendium that consists of 256 RA synovial samples that cover an intersection of 11,769 genes from 11 datasets. We obtained differentially expression analysis (DEG) that were identified in three independent methods. We then performed functional network analysis, with subsequent grouping of the samples based on a non-negative matrix factorization method. Finally, we built a predictive model for treatment response by using RA-relevant pathway activation scores and four machine learning classification techniques.

Results: We identified 876 up-regulated DEG including 24 known genetic risk factors and 8 drug targets. DEG-based subgrouping revealed 3 distinct RA patient clusters with distinct activity signatures for RA-relevant pathways. We constructed a classifier for the 62 RA samples that were treated with the drug infliximab, where the most informative features were found to be the TCR-, TGFb-, and VEGF signaling pathways. The SVM model showed the best performance in cross validation, with sensitivity of 48.7% and specificity of 91.3% for the test set (p < 0.001).

Conclusion: Construction and analysis of normalized synovial transcriptomic compendia can provide useful insights for understanding RA-related pathway involvement and drug responses for individual patients. The efficacy of a predictive model for personalized drug response has been demonstrated and can be generalized to several drugs, co-morbidities and other relevant features.
Poster Session

PRECISION (PERSONALIZED) MEDICINE IN AUTOIMMUNITY

ARTHITIS AND EXTENSIVE USE OF ANALGESICS AND ANTI-INFLAMMATORY DRUGS. EPIDEMIOLOGICAL STUDY
LACA7-0152
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²General Hospital of Ioannina, Rheumatology Department, Ioannina, Greece
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⁴General Hospital of Preveza, Microbiology Department, Ioannina, Greece
⁵University Hospital of Ioannina, Cardiology Department, Ioannina, Greece

Introduction: Arthritis is a disease that can affect any joint of the body. Due to the fact that there are many joints in the hand, the chances for hand arthritis are many. Arthritis of the hand is usually painful. Hand arthritis may cause many operational problems because of the great importance of hands in daily activities. Osteoarthritis of the hand and rheumatoid arthritis are the most common diseases of the joints affecting the hands. The goals of treatment are to reduce pain and restore the functional ability of hands. The decision of the type and duration of treatment depends on doctor’s final diagnosis. The diagnosis will differentiate osteoarthritis from other forms of arthritis such as rheumatoid arthritis for which the treatment is different. Drugs that can be used are analgesics for pain and anti-inflammatory drugs. Patients should not take drugs on their own without medical advice.

Material and method: Anonymous questionnaire, closed and open-ended questions in survey of 471 patients aged between 52 and 67 years.

Results: The overwhelming majority of respondents made extensive use of drugs especially analgesics to deal with musculoskeletal pain. In addition, they consider chronic pains as symptoms with no treatment, so they do not seek for medical advice. A large percentage of patients turn to alternative medicine.

Conclusion: The extensive use of analgesics and anti-inflammatory drugs will be reduced by educating and informing patients.
Factors that modify the gut microbiota structure to dysbiosis, could contribute to early identification and prevention of celiac disease (CD) or type 1 diabetes (T1D). The objective of the study was to look for association of diet and parasitism with microbiota profile in children with autoantibodies for CD or T1D, as compared with healthy children. Risk haplotypes, family and perinatal factors were evaluated in 614 schoolchildren, to identify high risk. Eleven children were detected with anti-insulin or anti-transglutaminase autoantibodies by ELISA, DNA from feces was analyzed for microbiota by the Illumina MiSeq platform. Parasitism was evaluated by Faust and Kinyoun techniques and diet by 24-h recall. There was no difference in Prevotella and Bacteroides abundance between cases and controls (p>0.05). Other Clostridiales, Proteobacterias and Cyanobacterias had higher abundance in cases (p<0.05), meanwhile other Lachnospiraceae had lower abundance (p<0.05), than in healthy children. Prevotella and Bacteroides proportions were not different according to dietary patterns, but other Cyanobacteria moderately correlated (r=0.66) with high sugars intake. At the species level, there was a trend to higher (p=0.08) abundance of Prevotella stercorea in controls than in cases. Although, there were no differences in parasitism among cases and controls, Cryptosporidium spp. infection correlated with a lower abundance of other Lachnospiraceae (p<0.05). It seems that diet and parasitism induce slightly changes in microbiota profile that could increase the risk of autoimmunity, which could be important for prevention treatments of CD or T1D.
Poster Session

PREDICTING, MONITORING AND PREVENTING EVIDENCE OF INFLAMMATORY/FIBROTIC ACTIVITY IN THE LIVER OF ASYMPTOMATIC AND BIOCHEMICALLY NORMAL INDIVIDUALS WITH ANTI-MITOCHONDRIA ANTIBODIES: OPPORTUNITY FOR EARLY TREATMENT AND PREVENTION IN AUTOIMMUNITY

LACAT-0203

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Background: Anti-mitochondria autoantibodies (AMA) occur in >95% primary biliary cholangitis (PBC) patients. Biochemically normal AMA-positive individuals (BN/AMA+) are identified by indirect immunofluorescence (IIF) on HEp-2 cells, and may represent early stages of PBC. The Enhanced Liver Fibrosis (ELF) score is a surrogate marker for liver fibrosis. This is a prospective study on autoantibody response, serum liver enzymes and ELF score in BN/AMA+ and PBC.

Methods: 327 samples from 35 PBC and 59 BN/AMA+ were prospectively obtained in average 4.09 (range: 0.50–7.40) years apart. Samples were tested by IIF/rat-kidney (IIF-AMA), western-blot and ELISA for antibodies against pyruvate-dehydrogenase (PDC-E2), gp210, sp100 and CENP-A/B. Anti-PDC-E2 avidity was determined by 6M urea-elution ELISA. Alkaline phosphatase (ALP), gamma glutamyl transferase (γGT) and ELF score were measured by automated methods.

Results: There was significant increase in serum anti-PDC-E2 (p<0.001) and IIF-AMA (p<0.001) in BN/AMA+, but not in PBC patients. There was significant increase in anti-PDC-E2 avidity (p<0.001) and ELF score (p<0.001) in both groups. There was positive temporal correlation between ELF and anti-PDC-E2 levels in BN/AMA+ (p<0.001; r=0.239) and PBC (p=0.004; r=0.268); ELF and IIF-AMA in BN/AMA+ (p<0.001; r=0.465); and ELF and anti-PDC-E2 avidity in PBC (p<0.001; r=0.341). Expansion of autoantibody targets along time occurred in 39% BN/AMA+ and 49% PBC patients. The frequency of BN/AMA+ with high probability of having established PBC (≥71.7%) increased from 7% to 14%.

Conclusions: BN/AMA+ individuals present an orchestrated increase in ELF score and humoral autoimmune response over time, indicating an opportunity for early therapeutic intervention and prevention in autoimmunity.
Background: Vogt Koyanagi Harada disease (VKH) is characterized by a systemic and autoimmune pathology, with bilateral granulomatous panuveitis associated with exudative detachment of the retina.

Objectives and Methods: To describe the clinical and epidemiological characteristics of patients with VKH through a descriptive and retrospective study.

Results: In 2016, 5137 consultations were recorded, including 12 patients with VKH, of whom 8/12 (66.6%) were women, with a mean age at diagnosis of 39.75 years. All patients presented altered visual acuity due to bilateral panuveitis, of which 9/12 (75%) had serous bilateral retinal detachment. There were dermatological disorders (vitiligo and poliosis) in 2/12 (16.66%), sensorineural hearing loss in 4/12 (33.33%), general symptoms 1/12 (8.33%), headache on 9/12 (75%) and meningeal symptoms 4/12 (33.33%).

Treatment: All patients received high doses of glucocorticoids, performed in 8/12 (66.66%) induction with cyclophosphamide for 6 months, then maintenance with azathioprine or methotrexate, and 4/12 (58.3%) induction and maintenance with azathioprine. The majority of patients 11/12 presented good evolution of vision and only one case was refractory requiring anti-TNF treatment (Infliximab). The ocular complications were: 5/12 (41.66%) synechiae, 3/12 (25%) Glaucoma, 2/12 (16.66%) cataracts. They presented reactivation of the disease at some point in the evolution 4/12 (33.33%). Currently 1 patient with active disease.

Conclusions: This disease can damage the vision in a severe and permanent way with a significant impact on the quality of life of those affected, it is of paramount importance the diagnosis and early treatment to improve the prognosis.
PREDICTING, MONITORING AND PREVENTING

Pulmonary arterial hypertension in connective tissue disease: About 28 cases
LACA7-0097
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Background

Connective tissue disease is the 2nd cause of pulmonary arterial hypertension (PAH). The aim of our study is to describe the clinical and prognostic characteristics of PAHs during connectivities in the Tunisian population.

Methods

We retrospectively studied 28 cases of patients with connective tissue disease and developed PAH diagnosed by pulmonary pressure measurement by trans-thoracic cardiac ultrasound. PAH is defined by a PAP> 30mmHg. This study was performed in the internal medicine department of the hospital Habib Thameur Tunis over a period of 14 years.

Results

We selected 28 patients, 27 of whom were female. The mean age at diagnosis was 40.1 years (24-76 years). The most frequent manifestation associated with PAH was a Raynaud phenomenon observed in 98% of the cases. Dyspnea was the revealing clinical sign in all cases. PAH was associated with systemic scleroderma (SSc) in 17 cases. In other cases, overlap syndrome was detected in 7 cases, sarcoidosis (n = 2), Sharp syndrome (n = 1), rheumatoid arthritis (n = 1). The mean PAPS was 34 mmHg in SSc and 53 mmHg during the overlap syndrome. All patients were treated with calcium channel blockers and anticoagulants. Specific treatment was prescribed based on prostacyclin (6 cases) and endothelin receptor antagonists (6 cases). Immunosuppressive therapy using corticosteroids in 8 cases and cyclophosphamide in 9 cases were initiated. An improvement in PAP was noted in 22 cases. Aggravation was noted in 6 cases (24%). Only one death was reported following congestive heart failure in a patient with SSc.

Conclusion

Systemic scleroderma was the main connective tissue disease responsible for PAH. The etiological treatment associated with the specific treatment implies a PAP improvement.
Macrophages are related to systemic damage in systemic lupus erythematosus (SLE). CD163 is a marker of activation of macrophages M2c. Some authors have reported elevated levels of soluble CD163 (sCD163) in SLE patients with severe disease. We investigate whether serum levels of sCD163 could discriminate between patients with and without activity among a cohort of Colombian SLE patients.

We included 34 SLE patients who fulfilled 2012 SLICC Criteria, 14 patients with systemic infection (non-HIV) without SLE and 10 healthy volunteers. Active disease was defined if SLEDAI>4. Levels of sCD163 were measured using an ELISA commercial kit (R&D system). We used Mann Whitney test for comparison between non normal data. For correlation, Spearman's rho was used.

We identified 18 patients with active SLE (including 4 with concurrent infection, CI) and 16 inactive patients (2 with CI). Patients with active SLE had significantly higher serum levels of sCD163 than inactive patients (median 719.4 vs 505.3 ng/mL, p = 0.0061) and healthy volunteers, see Table 1. When excluded those 6 SLE patients with CI this difference remained (median 698.1 vs 505.3 ng/mL, p = 0.024). In addition, patients with active SLE had higher but not significant levels of sCD163 than patients with systemic infection (median 719.4 vs 563.4 ng/mL, p = 0.31). sCD163 showed a positive moderate correlation with 24-hours proteinuria (r= 0.51, p= 0.021), and mild correlation with SLEDAI (r=0.35, p= 0.039).

Active SLE patients had significantly higher levels of sCD163 than inactive SLE patients. However, sCD163 levels were similar among patients with systemic infection.

<table>
<thead>
<tr>
<th></th>
<th>SLE active n=18</th>
<th>SLE Inactive n=15</th>
<th>Systemic Infection without SLE n=14</th>
<th>Healthy Volunteers n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>34.5 (20.0-45.0)</td>
<td>28 (24.5-38.0)</td>
<td>57 (49.0-74.0)</td>
<td>32.5 (25.5-42.7)</td>
</tr>
<tr>
<td>Sex female, (%)</td>
<td>17 (94.4)</td>
<td>14 (87.5)</td>
<td>4 (28.4)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>12 (10.7-19.5)</td>
<td>2 (0-4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>sCD163 ng/mL</td>
<td>719.4 (591.5-820.5)</td>
<td>505.3 (387.2-630.9)*</td>
<td>563.4 (380-856.4)¶</td>
<td>348.1 (273.6-425.7)¥</td>
</tr>
<tr>
<td>24 hours proteinuria (mg/dL)</td>
<td>1447 (729-4000)</td>
<td>234 (40-1592)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data are listed as median (IQR). * p = 0.0061, ¶ p = 0.31, ¥ p < 0.0001, in comparison with SLE active group.
Background: Systemic sclerosis (SSc) has been associated with bone loss and increased risk for bone fractures. Objectives: Here we studied osteoporosis in SSc with measurement bone density by DXA, and peripheral forearm quantitative CT (pQCT). Parallel with bone biomarkers.
Methods: 44 SSc patients were randomly recruited. DXA was assessed at the lumbar spine and femoral neck, pQCT (Stratec) is able to assess total, trabecular and cortical density. We determined FRAX, levels of vitamin D, and bone markers and clinical manifestations of SSc.
Results: Vitamin D levels were lower than the normal range. 34 patients (77%) had D-hypovitaminosis. Abnormally increased PTH, P1NP, OC, CTX levels were observed in 10, 7, 2 and 6 patients. Previous fractures occurred in 19 patients. Vertebral and hip FRAX values were 13.5% and 4%. By DXA, osteoporosis of the lumbar spine and hip was detected in 10 and 10 patients, while osteopenia were found in 16 and 20 patients. Total and trabecular bone density with pQCT was significantly lower than in healthy controls. Higher OC levels were associated with the diffuse form of SSc. Longer disease duration correlated with lower pQCT total and trabecular density. Interestingly, P1NP, OC, CTX positively correlated with gastrointestinal manifestations. pQCT total bone density was significantly lower in patients with pulmonary involvement, digital ulcer and anti-Scl70+.
Conclusions: A high proportion of SSc patients have osteopenia or osteoporosis and low vitamin D levels with more common trabecular loss. Bone loss and bone markers may be associated with disease duration, anti-Scl70 and some organ manifestations.
Poster Session

PREDICTING, MONITORING AND PREVENTING

SHORT-TERM ADMINISTRATION OF STEROID DRUGS IN PATIENTS WITH ARTHRITIS
LACA7-0159
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¹General Hospital of Ioannina, Microbiology Department, Ioannina, Greece
²General Hospital of Ioannina, Rheumatology Department, Ioannina, Greece
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⁵University Hospital of Ioannina, Cardiology Department, Ioannina, Greece

Introduction: Non-steroid anti-inflammatory drugs (NSAIDS) and colchicine are the first choice drugs in the treatment of arthritis. A short-term administration of corticosteroids is the safest choice especially when treating certain patient categories.

Objective: To note that the administration of prednisolone or of a similar drug can be efficient and safe when treating gout. Prophylactic administration of colchicine deters relapse.

Methods: 22 patients with polyarticular arthritis were tested. The diagnosis was set by the microscopic identification of uric acid crystals in the synovial fluid with a polarized microscope. The patients were approximately 57 years old, had increased levels markers of inflammation (on average: ESR 71.6 mm, CRP:12.19 mg/dl) and uric acid (on average:10.4 mg/dl) while having estimated the level of pain. All of them were treated with prednisolone (0.5 mg/kg/d) or with a similar drug for 3 days. Subsequently, we reduced the dosage by 10 mg/d every 3 days up until the total termination of the drugs and we administrated a prophylactic dosage of colchicine (0.5mg x2/d)

Results: A significant incline in the levels of pain, an improvement in movement and remission of arthritis were noted. After the end of the treatment (12 days), the patients had a remission of all symptoms while no significant side effects were noted.

Conclusion: The short-term administration of prednisolone or of a similar drug can be used safely as a first-choice treatment in patients with an attack of gout, accompanied by a prophylactic dosage of colchicine for a period of 6 months.
Pregnancy is a critical risk period in autoimmune diseases, increasing morbidity and mortality both for mother and child.

Method: We realized a retrospective study to describe the course and complications of pregnancies in patients with systemic lupus erithematosus (SLE), antiphospholipid syndrome (APS), SLE and APS, and Sjögren syndrome (SS) during a 16 years period (Jan 2000 - Jun 2016). Descriptive statistics was performed.

Results: There were 62 pregnancies in 52 patients: 17 SLE, 18 APS, 11 SLE+APS, 4 SS and 2 healthy women with anti-Ro+. In 2 patients SLE was diagnosed during pregnancy. Mean age was: 30.8±5.8 years. 80% of pregnancies were not planned, and 22 had active disease. 32 patients were taking contraindicated medication. 12 pregnancies were interrupted, 1 was voluntary, 7 because of activity and 5 because of fetal complications.

Maternal adverse outcomes: Hypertension 55.7%, (pre-eclampsia 38.4%, eclampsia 9.6%, HELLP 3.8%). Severe relapse 15.4%, 1 patient had an obstetric bleeding. There were not thrombotic complications. 85% of patients had infections.

Fetal adverse outcomes: Abortions 43.5%. Preterm babies 80% (gestational age 32.3±3.1 weeks), low weight 67% (2.43±0.48 kg). Two obits and 6 neonatal deaths. 70.9% of babies had morbidity (sepsis, respiratory distress, jaundice and fetal malformations). 6 patients had neonatal lupus, all with anti-Ro+ and cardiac disease.

Comment: We found high prevalence of non-planned pregnancies, forbidden medication, relapses and fetal morbidity. There is a great need of better educational efforts for these patients to increase the probability of good outcomes during pregnancies.
Poster Session

RITUXIMAB AND B-CELL DEPLETION THERAPY

RITUXIMAB FOR INTERSTITIAL LUNG DISEASE OF SYSTEMIC SCLEROSIS: A CASE SERIES OF 18 PATIENTS
LACA7-0019
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2Istanbul University - Cerrahpasa Medical Faculty, Pulmonology, Istanbul, Turkey

Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc). Rituximab (RTX) appears to be a promising agent according to case series.

Methods: A chart review revealed 18 patients (16 women, 2 men; mean age 50.3±12.1 SD years (range 30-72), mean disease duration 8.3±9.3 SD years) with SSc and ILD treated with RTX. Efficacy was evaluated according to the criteria of the American Thoracic Society (ATS).

Results: Four patients were treatment naive for ILD when they received RTX (Group 1). The mean duration between the diagnosis of ILD and RTX treatment in Group 1 was 3.5 months. The mean follow-up time after the initiation of RTX in this group was 12.2±6.8 SD months. FVC/DLCO was stable or improved in 2/4 compared to baseline and worsened in 2/4 at the end of follow-up at group 1. Fourteen patients had a 10.2 years-history of SSc and have been treated with immunosupressives for ILD before RTX (Group 2). The mean duration between the diagnosis of ILD and RTX treatment in Group 2 was 71.2 months. One patient died after 3 months following the first RTX cycle (unknown reason) and 1 was unsuitable for spirometry. Of the remaining 12 patients, improvement or stabilisation was seen in 7 and worsening was seen in 5 patients.

Conclusions: RTX seems to be modestly effective for ILD of SSc. The duration of ILD and the presence or absence of previous immunosuppressive therapy do not seem to play a role in response.
Background: Systemic lupus erythematosus (SLE) is a chronic, highly heterogeneous autoimmune disease with a wide spectrum of clinical manifestations and multiple antibodies, as well as a variable course (1).

Objective: To describe a large cohort of patients with SLE followed in a single private center in multiple regions of Colombia.

Methods: A cross-sectional study was conducted in 1374 patients with SLE, in which 88% of patients fulfilled classification criteria for ACR 1997 or SLICC 2012. Clinical and serological characteristics were obtained by interview, physical examination and chart review, and univariate analysis was performed.

Results: Patients included in this analysis were mostly females (91%), with middle-low socioeconomic status. Mean age of the cohort was 43.9 years (SD:13.9), with a mean of 10.7 years of evolution (SD: 8.1). The most frequent involvements were hematologic and mucocutaneous, with a low percentage of CNS compromise (Table 1). Polyautoimmunity was present in 21% of the patients, mainly due to the coexistence of antiphospholipid syndrome and sjögren syndrome. Serum immunological profile is shown in Figure 1.

Conclusions: The definition of epidemiological profiles in autoimmune diseases in the region helps understand differences in disease patterns, that allow the development of personalized interventions and resources optimization.
Table 1. Clinical characteristics of patients with SLE

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucocutaneous compromise</td>
<td>893</td>
<td>73.8</td>
</tr>
<tr>
<td>Serositis</td>
<td>247</td>
<td>20.4</td>
</tr>
<tr>
<td>CNS compromise</td>
<td>66</td>
<td>5.4</td>
</tr>
<tr>
<td>Haematological compromise</td>
<td>984</td>
<td>81.3</td>
</tr>
<tr>
<td>Renal compromise</td>
<td>470</td>
<td>38.8</td>
</tr>
<tr>
<td>Cardiopulmonar and vascular compromise</td>
<td>431</td>
<td>35.6</td>
</tr>
<tr>
<td>Polyautoimmunity</td>
<td>256</td>
<td>21.1</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>377</td>
<td>31.1</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>112</td>
<td>9.2</td>
</tr>
</tbody>
</table>

CNS: Central nervous system
Figure 1. Serum immunological profile in SLE patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA positivity</td>
<td>1062</td>
<td>95.6%</td>
</tr>
<tr>
<td>Low complement</td>
<td>718</td>
<td>60.1%</td>
</tr>
<tr>
<td>Anti-DNA positivity</td>
<td>602</td>
<td>53.3%</td>
</tr>
<tr>
<td>Anti Ro</td>
<td>405</td>
<td>41.8%</td>
</tr>
<tr>
<td>Anti RNP</td>
<td>379</td>
<td>39.1%</td>
</tr>
<tr>
<td>Anti SM</td>
<td>300</td>
<td>31.1%</td>
</tr>
<tr>
<td>Anti La</td>
<td>134</td>
<td>14.2%</td>
</tr>
<tr>
<td>Lupic Anticoagulant</td>
<td>127</td>
<td>24.7%</td>
</tr>
<tr>
<td>AnticardiolipinIgM</td>
<td>86</td>
<td>15.2%</td>
</tr>
<tr>
<td>Anticardiolipin IgG</td>
<td>75</td>
<td>13.1%</td>
</tr>
</tbody>
</table>

References:
Objective: We investigated whether titer and pattern of anti-cell antibody indirect immunofluorescence (IIF) assay on HEp-2 cells (HEp-2-IIF) change according to SLE disease activity. Methods: 269 SLE patients were consecutively retrieved during one-year period and classified into 3 groups: Remission (SLEDAI2K=0); Intermediate (SLEDAI2K=1-5); Active (SLEDAI2K≥6). We determined HEp-2-IIF titer/pattern, serum CH100, C3, C4 and C2, and antibodies to native DNA, denatured DNA, C1q, and nucleosome. 101 of the 269 patients were reassessed after a six-month interval. Results: Active, Intermediate and Remission groups did not differ in age, disease duration and gender. Traditional parameters of disease activity differed significantly among the 3 groups. Nuclear homogeneous pattern (AC-1) was associated with Active Disease and nuclear fine speckled pattern (AC-4) was associated with Remission (Table 1). Patients with AC-1 pattern had higher SLEDAI2K (9.2±7.9) than those with AC-4 pattern (4.8±5.2) (p=0.008). HEp-2-IIF titer was lower in Remission group than in Active and Intermediate groups (Table 1). In the follow-up analysis, 50 patients remained in the same group (SLEDAI2K change ≤3) and 51 changed disease activity status (SLEDAI2K change ≥4). HEp-2-IIF titer decreased in 33 patients that decreased disease activity status (p=0.002) but not in 50 patients with stable SLEDAI2K (p=0.677). ROC curve analysis for determination of disease activity showed equivalent areas under the curve (AUC) for HEp-2-IIF titer and traditional disease activity parameters. Conclusion: HEp-2-IIF pattern and titer are affected by SLE disease activity and can be considered in conjunction with other laboratory and clinical parameters in the assessment of SLE disease activity.
Poster Session

SLE, SJÖGREN’S SYNDROME

CYTOKINE PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND POLYAUTOIMMUNITY
LACA7-0150
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1Center for Autoimmune Diseases Research CREA, Universidad del Rosario, Bogota, Colombia

Introduction

Coexistence of more than one autoimmune disease (AID) in a single patient is known as polyautoimmunity (PAI). Up to 40% of patients with systemic lupus erythematosus (SLE) disclose PAI. Some reports suggest that clinical outcomes of SLE-PAI may differ compared with SLE alone. Cytokine production is pivotal in the pathophysiology of several AIDs. However, their role in SLE-PAI is unclear.

Objectives

To evaluate cytokine profiles in patients with SLE-PAI.

Methods

As an exploratory study, 67 women with SLE (ACR 1997 criteria) were included, of whom 14 (21%) had PAI. Fifteen serum cytokines were measured by cytometric bead array (Beckton-Dickinson). Clinical characteristics including disease activity (by SLAQ) and autoantibodies profile were assessed simultaneously. Data were analyzed by Fisher’s exact and Mann-Whitney’s U tests.

Results

Demographics and disease activity are displayed in Table 1. Significant differences in clinical outcomes were not observed between the two groups (p=0.22). Mean concentration (pg/mL) levels of IL-6 and IL-12/23p40 were higher in SLE-PAI than in SLE [5.3 (13.6) vs. 4.9 (30.9), p=0.037, and 57.2 (92.6) vs. 19.2 (24.2), p=0.057, respectively]. Noteworthy, a few outliers were observed and established (Figure 1).

Conclusion

These results confirm PAI as a frequent subphenotype in SLE and the influence of some cytokines in its occurrence. PAI does not seem to modify significantly the outcome of SLE. Although several common immunopathogenic mechanisms exist among AIDs (i.e., autoimmune tautology), the information obtained from outliers may assist in the practice of personalized medicine and encourage proof of principle studies.
<table>
<thead>
<tr>
<th>Variable</th>
<th>SLE-PAI (n=14)</th>
<th>SLE (n=51)</th>
<th>p-value</th>
</tr>
</thead>
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<td>FA2 (%)</td>
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<td>SLAQ (IQR)</td>
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**Autoimmune serositivity distribution (I):** Sjogren syndrome 6 (6), Antineutrophil cytoplasmic antibodies 4 (4), Anticardiolipin antibodies 1 (1), Sjogren’s 2 (2), Rheumatoid arthritis 1 (1), Systemic lupus erythematosus 1 (1), Myasthenia gravis 1 (1).

**Abbreviations:** FAI: Polymyositis; SLE: Systemic Lupus Erythematosus; MAS: Multiple autoimmune syndrome; FAI: Familial autoimmune disease; SLAQ: Systemic Lupus Activity Questionnaire.
Figure 1. Differences in levels of plasma cytokines in patients with SLE-PAI compared with SLE alone.
**Background:** Neonatal lupus erythematosus (NLE) is an acquired autoimmune disease caused by transplacental passage of anti-SS-A and anti-SS-B antibodies. In this systematic review, it was aimed to examine maternal history traits of patients with NLE.

**Method:** It has been done at August 2015 on Pubmed. Publications are determined by using MeSH term: neonatal lupus. 199 article/case reports has been included in the study.

**Results:** Our study included 755 NLE patients. 249 of them had information on previous maternal history. Among these mothers, 40 (16.0%) of them, had a history of baby with NLE in prior gestations. Among these infants, 30 (75%) of them had congenital heart block (CHB) and 10 (25%) of them had rash, 1 infant had both rash and hematological involvement. Among these 40 mothers, 15 (37.5%) of them had sjogren syndrome, 13 (32.5%) of them had SLE diagnosis and 1 (2.5%) only had Raynaud phenomenon, 11 (27.5%) of the mothers had no connective tissue disease (CTD).

In 21 (52.5%) of these mothers, SS-A and SS-B was both found positive, 10 (25.0%) of patients were solely SS-A positive, 1 (2.5%) patient was solely SS-B positive, and in 2 (5.1%) of patients SS-A and RNP was positive, and in 2 (5.0%) whichever antibody was negative.

**Conclusion:**

Although the mothers with NLE history had no significant difference in diagnosis, sjogren syndrome was seen more frequently, 11 of mothers had no CTD diagnosis. In patients with NLE history, SS-A and SS-B autoantibodies were determined to be found most often significantly.
SLE, SJÖGREN'S SYNDROME

HYPOVITAMINOSIS D AND RELATIONSHIP WITH SLEDAI-2K IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ATTENDED IN TWO RHEUMATOLOGY SERVICES, BOGOTA 2016-2017
LACA7-0034
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Systemic Lupus Erythematosus, (SLE) is a chronic disease that results of recurrent activation of the immune system, with production of antibodies contributing to inflammation and tissue damage. Vitamin D is a hormone with effects on the immune system and is very common to find Vitamin D deficiency in patients with SLE. (ranges from 68.5% to 87%). The prevalence of hypovitaminosis D in worldwide is high and recently in our country we described hypovitaminosis D in more than 70% of the healthy population.
We will evaluate the prevalence of Hypovitaminosis D in patients with SLE and the factors that contribute to this condition.
A cross-sectional study will be conducted with patients with SLE following ACR criteria older than 18 years of age recruited from two specialized clinics of the city. A sample size of 100 patients who wish to participate in the study, will be included.
All of them will be evaluated for a Rheumatology and fill up the chart with emphasis in laboratory test, levels of 25 OH Vitamin D and registry of SLEDAI 2K. Patients with active Lupus nephritis will be analyzed independently.
In Overall population we found high prevalence of hypovitaminosis D and low intake of calcium on diet. We hope find a high prevalence of hypovitaminosis D in patients with SLE.
At the end of the study we would describe the levels o Vitamin D in patients with SLE and its relationship with disease activity. Probably this results will have therapeutic implication for the treatment on patients with SLE.
We report a case of association of five autoimmune disease: primary biliary cholangitis (PBC), autoimmune hepatitis (AIH), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and Sjögren Syndrome (SS) with sarcoidosis.

Case report: Mrs. S.J. 57 year's old, with history of joint pain and generalized pruritus was admitted. Her medical history was unremarkable. She complained of xerostomia, xerophthalmia and dyspnea. Physical examination found cutaneous malar rash, buccal ulcerations, crepitant rales and hepatomegaly. Liver function was disrupted (cytolysis, cholestasis and hepatocellular insufficiency). Polyclonal hypergammaglobulinemia was found with a high level of immunoglobulins (Ig) G type. Diagnosis of overlap syndrome (PBC - AIH) was retained (giant cell granulomas and lymphocytic cholangitis at hepatic biopsy, positive anti mitochondria antibodies type M2 and positive anti-smooth muscle antibodies specific to actine, and high Ig G. SS was retained (sicca syndrome, positive Schirmer test and punctuate keratitis, positive anti SSA and anti SSB antibodies and lymphocytic sialadenitis Chisholm's stage IV). RA was retained in front of joint involvement and anti-CCP positive antibodies with articular destructions on X-ray and synovitis. SLE was confirmed by positive anti-nuclear antibodies with native positive anti-DNA antibodies associated with cutaneous malar rash, buccal ulcerations, pericarditis and hemolytic auto-immune anemia. Thoraco-abdominal CT showed bilateral frosted glass images associated with systemic mediastinal and intra-abdominal adenomegaly. In view of this radiological presentation and the association with a hepatic granuloma, the diagnosis of a systemic sarcoidosis was strongly evoked. Treatment with corticosteroids and immunosuppressive therapy was initiated.

Conclusion: This finding is novel by the association of systemic sarcoidosis with immune perturbations as part of a multiple autoimmune syndrome. Such associations suggest a common immunopathogenic mechanism.
Introduction: Recent reports indicate the involvement a type I Interferon (IFN) regulated genes (IFN signature) in autoimmune diseases such as SLE. Studies have reported the highly-coordinated regulation of Interferon-regulated chemokines in patients with SLE, however, the study of the Interferon-regulated chemokines in Sjögren’s syndrome is understudied. Thus our aim was to investigate the secretion of Interferon-regulated chemokines in PBMCs from patients with Sjögren’s syndrome, SLE and healthy donors.

Methods: Peripheral blood mononuclear cells (PBMCs) from healthy donors (n=13), patients with SLE (n=15) and Sjögren’s syndrome (n=14) were isolated by gradient centrifugation and resuspended in RPMI-1640 medium. PBMCs (1 x 10^6/well) were cultured for 24 h. The PBMC cultured were made in two conditions, with or without human recombinant IFN-α at 1000 U. Supernatant Interferon-regulated chemokines concentrations for MCP-1, MIP-1α, MIG, IP-10 and BLC were determined using Luminex multiplex immunoassay bead array technology.

Results: PBMCs from SLE, Sjögren’s syndrome and healthy donors produced significant amounts of Interferon-regulated chemokines (MCP-1, MIP-1α, IP-10 and BLC) in response to human recombinant IFN-α at 1000 U when were compared with cultured without stimulus, however the chemokine MIG was not detected in supernatant. Interestingly, the level of spontaneous MIP-1α production from SLE patients was higher than in healthy donors. The levels of production of chemokine MIP-1α and BLC were similar in patients with SLE and Sjögren’s syndrome.

Conclusions: PBMC from patients with Sjögren’s syndrome have showed an increased capacity to secrete MIP-1α and BLC. Therapies that block these chemokines could be beneficial in patients with SLE or Sjögren’s syndrome.
Background: Lupus Nephritis (LN) is a frequent and serious manifestation in Systemic Lupus Erythematosus (SLE). Tubulointerstitial (TI) injury in LN has prognostic implications, independently from glomerular lesions, but its impact deserves a better characterisation. A retrospective observational study was performed to describe the incidence, risk factors and clinical impact of TI lesions in the LN cohort at Hospital Clinic of Barcelona, Spain, between the years 2000-2016.

Methods: Data were retrospectively collected from the time of LN diagnosis by systematic review of medical records from 84 patients with renal biopsies recruited from Hospital Clinic of Barcelona, over 10 years. TI injury was divided in acute or chronic lesions, and TI severity was classified according to the percentage of tissue involvement at renal biopsy. Clinical and epidemiological predictors were evaluated, and the end points were renal survival and response to treatment at 1, 5 and 10 years.

Results: Eighty-two patients were studied, with 99 total episodes (including flares). 73% of patients had TI injury, 48% acute and 90% chronic. The presence at presentation of AKI, haematuria, casts, leucocituria or cutaneous lupus predicted more severe TI inflammatory lesions at renal biopsy. Patients with interstitial fibrosis and tubular atrophy (IFTA) >25% had a 62% of survival at 10 years, compared with 100% in patients with IFTA=0 (p=0,049). IFTA >25% increase the risk of developing stage 4 KDOQI-CKD compared with IFTA <25 % (p <0,05). TI acute injury >25% doubles the risk of reaching stage 4 KDOQI-CKD (p=0,02).

Conclusions: TI injury in LN is an independent risk factor for stage 4 KDOQI-CKD. TI injury should be formally included in the current histologic classification of LN, for its prognostic value. Refine the characterisation and clinical impact of TI injury would improve renal survival of lupus patients.

Keywords: Lupus nephritis. Tubulointerstitial inflammation, Systemic erythematosus lupus, Interstitial fibrosis, Tubular atrophy, Chronic kidney disease
C:\Users\...
Poster Session

SLE, SJÖGREN'S SYNDROME

SEVERITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A LATENT TRAIT ANALYSIS
LACA7-0022
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¹Center for Autoimmune Diseases Research CREA, School of Medicine and Health Sciences, Bogota, Colombia

Background: Systemic Lupus Erythematosus (SLE) is a complex disease, which can potentially involve any organ and, therefore, has a wide range of clinical manifestations (i.e., subphenotypes).

Objectives: To propose an item response theory (IRT) model for building an index of severity in patients with SLE and assess its statistical associations with other outcomes.

Methods: A cross-sectional study was done on 319 SLE patients. An IRT model was fitted in order to characterize a severity construct of 17 variables. In addition, the model analyzed possible associations of the severity latent trait with other patient covariates including cardiovascular disease, age at onset of the disease, and expositional factors.

Results: Baseline characteristics of patients were as follows: female gender 91%, median age 37 years, median duration of the disease 5 years, lupus nephritis 37.3%, and central nervous system involvement in 16%. Several symptoms were excluded from the model due to inconsistency. A total of 11 symptoms were included in the final model showing three levels of disease severity (Figure 1). Coffee consumption was associated with severity.

Conclusions: The symptoms excluded share the same pathogenic mechanism in SLE, which corresponds to autoantibody-driven tissue damage, and are associated with high mortality risk. The remaining symptoms are related to inflammation and vasculopathy, and require a less aggressive immunosuppressive treatment. The order of symptoms on the severity scale coincides with clinical experience. The present index of severity could be useful for SLE patients with less severe phenotype.
Poster Session

SLE, SJÖGREN’S SYNDROME

Association of anti-CCP antibodies and arthritis in Primary Sjögren’s syndrome: A systematic review and meta-analysis
LACA7-0035
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2Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Department of Immunology and Rheumatology, Mexico City, Mexico

Aim. To systematically review the literature regarding the association of arthritis and anti-CCP antibodies in primary Sjögren’s Syndrome (SS). Methods. A comprehensive search of MEDLINE, ISI Web of Knowledge and Cochrane Library from inception until June 2016 was undertaken using the keywords: “Primary Sjögren’s syndrome or Sjögren’s syndrome and arthritis or synovitis or arthropathy, and anti-CCP antibodies or anti-citrullinated protein antibody –ACPA–”. No language restriction was used. Studies were included if they: 1) assessed the association of arthritis and anti-CCP antibodies, 2) provided sufficient data to construct a 2-by-2 table and 3) tested IgG anti-CCP antibodies by any method. We used a random effect model and evaluated the heterogeneity and publication bias. Results. Ten studies were included in the meta-analysis (involving 1322 patients). We found a pooled OR=4.42 (IC 95% 1.15-16.94, p=0.03). The test for heterogeneity was I² 0.87, but we did not observe publication bias. Conclusion. Patients with pSS and anti-CCP antibodies are prone to have arthritis as part of the disease clinical spectrum. Clinicians should be aware about the distinction between early RA with secondary SS and primary SS with arthritis.
Background and Aims:

Antimalarials (AMs) have been shown to exert a reduced risk of damage accrual in North American and European SLE patients. We are presenting data from Latin American patients.

Methods:

Patients with a recent SLE diagnosis (≤2 years) from the GLADEL cohort were studied. End-point: Increase in damage (SLICC Damage Index, SDI) since cohort entry. Independent (socio-demographic, clinical laboratory and treatment) variables were included. The effect of AMs use on damage (adjusting for potential confounders) was examined with a multivariable Cox regression model with a stepwise selection algorithm (variables retained in the model α: 0.05). AMs was a time-dependent variable (user: patient receiving AMs during the previous 30 days) in the regression model.

Results:

Of the 1,466 patients included in this analysis 1049 (72%) received AMs during follow-up (as defined); median exposure time: 30 months (Q1-Q3: 11–57 months). Damage accrual occurred in 665 (45%) patients during a median follow-up time of 24 months (Q1-Q3: 8-55) months. After adjusting for potential confounders (SDI at cohort entry, socioeconomic status, disease duration at cohort entry, malar rash, photosensitivity, serositis, oral glucocorticoids, pulse glucocorticoids and SLEDAI at cohort entry) at any time during follow-up, a patient on AMs had a 25% lower risk of damage accrual than a patient not on AMs (adjusted HR 0.75, 95%CI 0.62–0.90).

Conclusions:

After adjustment for possible confounding factors related to AMs use and damage accrual, AMs were independently associated with a reduced risk of damage accrual in this cohort.
SLE, SJÖGREN'S SYNDROME

Unusual variant of acute motor-sensory axonal neuropathy revealing systemic lupus erythematosus
LACA7-0084
I. Rachdi¹, Y. Fekih¹, Z. Aydi¹, F. Daoud¹, B. Ben Dhaou¹, F. Boussema¹
¹Habib Thameur Hospital, Internal Medicine, Tunis, Tunisia

Background

Acute motor-sensory axonal neuropathy (AMSAN) is an axonal variant of Guillain-Barré syndrome (GBS). There are few cases of GBS particularly of atypical variants in association with systemic lupus erythematosus (SLE). Known cases have shown a slow recovery and a poor prognosis. We report a case with evidence of AMSAN in association with active SLE, with a rapid response to steroids combined to immunosuppressants.

Case Report

A 19 years old patient was referred for worsening lower extremity weakness for two months. Motor examination showed Medical Research Council (MRC) 4 strength in both arms, and global weakness of the legs (MCR 3). Reflexes were equal and symmetric in upper extremities but diminished in lower extremities. Magnetic resonance imaging of the brain was normal. A cerebrospinal fluid analysis showed normal cell counts and a protein level of 40mg/dL. Nerve Conduction Studies and needle electromyography of the upper and lower extremities showed severe axonal sensorimotor polyradiculoneuropathy with active denervation and sparing of the sural nerve. Urinalysis showed evidence of an active nephritis. An ANA titer was 1/1600. Serologic testing revealed a strongly positive anti ds-DNA antibody titer. He had a moderately positive IgM-anticardiolipin antibody (aCL) and a positive IgG-aCL. A kidney needle biopsy showed an extra-membranous glomerulonephritis variant of lupus nephritis. A 3-day course of intravenous methylprednisolone, followed by oral prednisone, was administered. A treatment with Mycofenolate Mofetil was initiated to treat the lupus nephritis. A week after, the patient reported an improvement of the motor weakness with recovery of autonomy.

Conclusion

We report an unusual variant of AMSAN in association with active SLE. There was a rapid clinical recovery with immunosuppressant and steroids.
Background

The relation between the implants of silicone and appearance of autoimmune diseases particularly connective tissue disorders was reported in several publications and led to several discussions of scientific and medico-legal order. We report a case of systemic lupus erythematosus (SLE) following the implementation of a gastric banding in silicone.

Case report

A 26-year-old female patient was hospitalized for inflammatory polyarthritis of multiple joints and basic-thoracic pain since 3 months. A gastric banding in silicone, indicated for morbid obesity, was performed 10 months before its admission. Physical examination objectivied morbid obesity, left pleural syndrome and pain at proximal interphalangeal joints and wrists. Diagnosis of pulmonary embolism was evoked in front of hypoxia, hypocapnia and high level of D-dimers. The diagnosis was confirmed by pulmonary angio-scan. The diagnosis of SLE associated to antiphospholipide syndrome was retained in front of polyarthralgia, leucopenia, positive antinuclear antibodies, strongly positive anti-DNA, positive anti-cardiolipine of type IgG and anti Beta-2 GPI antibodies. The evolution under anticoagulants, was marked by the appearance of a fever, right basi-thoracic pain, with dyspnoea and an abdominal pain in front of gastric banding. An extension of the pulmonary embolism was confirmed by a second thoracic angio-scan. On the other hand, the barium swallow with gastro-duodenal follow-up showed indirect signs of banding migration. The patient was then transferred in intensive care units.

Conclusion

Physio-pathological links between implant of silicone and connective tissue disorders remain very controversial. Besides, the relatively short delay of 7 months, between the implementation of gastric ring and the appearance of systemic lupus erythematosus at our patient, would it be in favour of the fortuitous character of this association?
Background: It is thought that increased prevalence of antiphospholipid antibodies in patients with rhupus, this congenital remnant, Chiarì Network will be important for developing formation of thrombosis, cardiac events and stroke. They both may be a severe disease, and cause worse prognosis.

Case report: A 69-year-old female patient admitted to our clinic due to symmetric chronic bilateral arthritis with morning stiffness persisting for 1 hour. Boutonnière, swan-neck deformities, cutaneous vasculitis of lower extremities were observed on physical examination. She had no medical history about taking any drugs. The level of CRP was 18.66 mg/dl, and ESR was 91 mm/hour. We found that ANA (1/1000 homogeneous), anti-RNP, anti-cardiolipin, Rheumatoid factor and anti-CCP antibodies were positive. The patient showed radiological erosion and deformities in the joints. Thoracic CT revealed a mass with a diameter of 51x28x32 mm on the right paracardiac area. Chiarì’s network in the right atrium and interatrial septum patent foramen ovale with normal cardiac motility was achieved on transthoracic and transesophageal echocardiography. She had diagnosed according to ACR/EULAR classification criteria for RA and SLE. According to clinical and laboratuary features, she was diagnosed as rhupus syndrome, and treated with hydroxychloroquine, and prednisolone. The arthritis, vasculitis improved, and the inflammatory markers were decreased to normal values.

Conclusions: The coexistence of connective tissue diseases is rare entite such as Rhupus syndrome. Although Chiarì’s network is an incidental finding, the rheumatologist should be carefull in patients with rhupus syndrome and Chiarì’s network due to complications such as embolic events, thrombus formation, arrhythmias, and worse prognosis.
Objective. Primary Sjogren syndrome (pSS) is a common, systemic autoimmune disease with characteristic manifestation of xerophthalmia and xerostomia. To date, the causes for pSS development is still unknown. There are no affirmative data suggestive of a causal role of HBV in development of pSS. Hence, we examined this association using reimbursement claims data from the Taiwan Longitudinal Health Insurance Database 2005 during a follow-up period of 16 years.

Methods. Analysis of the Taiwan Longitudinal Health Insurance Database 2005 indicated 24237 HBV-infected patients between 1997 and 2012. We used 1:4 propensity score-matching to select 96948 counterparts who did not have HBV infection (control cohort). The cumulative incidence and hazard ratio (HR) for pSS were calculated after adjusting for competing mortality.

Results. This propensity score-matched study of HBV-infected patients indicated the risk of pSS was significantly higher in the HBV-infected cohort (16-year cumulative incidence [CI]: 6.0%; 95% CI: 2.8-10.8%) than in the control cohort (16-year CI: 2.8%; 95% CI: 1.9-3.9%; p<0.0001), with an adjusted HR (aHR) of 1.3 (95% CI: 1.16-1.46; p<0.0001). Multivariable stratified analysis verified the association of HBV infection with enhanced risk of pSS in subgroups of both gender, younger age and without thyroid diseases.

Conclusion. This national cohort study indicates that HBV infection increases pSS risk, especially in patients with younger age or without thyroid disorder. Our results not only suggest the pathogenic role of HBV in pSS, but also imply the benefits of anti-viral treatment for pSS risk reduction in HBV-infected patients. Further research is warranted to better understand the mechanism.
Cumulative Incidence of SS

Modified log-rank \( p < 0.0001 \)

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Poster Session

SLE, SJÖGREN'S SYNDROME

Prevalence and clinical manifestations of pulmonary and extrapulmonary tuberculosis in a cohort of patients with systemic lupus erythematosus

LACAT-0135

O. Vera Lastra1, M. Cameras Orantes2, J. Sepulveda Delgado1, L. Pineda Galindo1

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Objective: To determine the prevalence of pulmonary tuberculosis (TB) - extrapulmonary and associated factor in systemic lupus erythematosus (SLE) patients.

Methods: From a cohort of 328 SLE patients we included SLE patients with TB diagnosis. We investigated associated factors for TB: immunosuppressors (IS) drugs, comorbidities, previous exposure and vaccination for TB, type of TB: pulmonary and extra pulmonary. Time evolution, organ involved and SLEDAI at time of diagnosis of TB were analyzed.

Results: We found 15 SLE patients with TB (mean age 43.5±9.06 years, mean disease evolution of SLE: 6.6±3.2 years). SLE organ involvement: Renal: 7, Neuropsychiatric: 5; hematological: 4 joint -mucocutaneous 6. Active SLE:11 (SLEDAI 11.5 ± 4.9), inactive SLE: 4. Use of IS: mycophenolate mofetil (MM) 6, Azathioprine: 7, Cy: 5, steroid: 15 (prednisone: median 2.5, range 2.5 to 50 mg/day and methylprednisolone pulse 3g bimonthly in 2 patients), Rituximab: 3. Prevalence of TB was 13 of 328 (4%) patients, extrapulmonary:10 (77%) renal: 4, meningeal: 3, cerebral tuberculoma: 1 peritoneal: 1 disseminated: 1, and pulmonary TB: 3 (23%). Manifestation associated with TB: Fever 12 (92%) appetite loss: 3 (23%), weight loss 5 (38%), asthenia 8 (61%) headache: 3 (23%), hematuria: 2 (15%).

Conclusions: The prevalence of TB in SLE patients was about 4.5% and its main form was extrapulmonary. The presence of tuberculosis in SLE patients constitute a challenge and should be identified in promptly in order to initiate an adequate treatment. TB diagnosis in patients with active SLE is difficult because both diseases share clinical and laboratory manifestations.
Poster Session

SLE, SJÖGREN’S SYNDROME

Prevalence and mortality from infections in Systemic Lupus erythematosus patients in a tertiary level hospital
LACAT-0136
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Background: Initial presentation of Systemic lupus erythematosus (SLE) can mimic infections, and in turn infections can mimic disease flares in established SLE.

Aim: To determine the prevalence and mortality from infection in SLE patients as well as to identify etiology, associated factors to severity and site of infection.

Patients and Methods: We performed a retrospective study from 2010 to 2014. We analyzed risk factors (RF) on admission, involved organ, infectious type and etiology.

Results: There were 328 patients, 87% women and 13% men, mean age 32.4±9.9 years. Infections as cause of hospitalizations were 42.2%, prevalence of infections was 49%, and mortality from severe infections was 45%. The RF for severe infections were: renal involvement Odds Ratio (OR) 3.057, P<0.019; hematologic OR 1.9, p <0.001; increased dsAnti-DNA RM 5.1 p<0.001, hypocomplementaemia: OR 2.673, P<0.02, leukolymphopenia OR 2.5, p<0.0001. Type of infections: bacterial 87%, viral: 3.4%, fungal: 8%, mycobacterial: 1.5%. Site of infection: lower respiratory tract 38%, urinary tract: 49% soft tissues: 6.1%, central nervous system: 1.2%, Others: 4.2%. Most frequent etiology agent were: bacterial: S. aureus, E. coli, A. baumanii, E. faecalis. Virales: H. zoster, mycotic: candida albicans and M. tuberculosis.

Conclusions: Infections are an important cause of morbidity, mortality and hospitalization in SLE patients. The lower respiratory tract infections of bacterial origen were most frequent. The renal and hematological involvement, increased dsAnti-DNA, hypocomplementaemia, and leukolymphopenia were the most important factors for severe infections. Infections in active SLE patients constitute a true challenge for the clinician.
Aims: Determine the prevalence of Sjögren's syndrome (SS) and sicca syndrome in Mexican patients with Systemic Sclerosis (SSc).

Methods: 77 patients with SSc were studied. SS and sicca syndrome were investigated according to established criteria. All patients underwent minor salivary gland biopsy, and the results of fibrosis and inflammation were classified according to Tarpley’s classification with a score ≥ 1. Anti-Ro/SSA and Anti-La/SSB antibodies were quantified in 34 patients with positive histological findings for SS. All patients with ocular symptoms were also performed Schirmer’s test to evaluate the ocular manifestations.

Results: 77 patients were studied (mean age 52.7±30 years, with an average SSc diagnosis age of 10 ± 6.5 years. 54 (71%) patients had sicca syndrome, of these 34 patients (44%) were attributed to collagen infiltration characteristic of SSc, and 21 (27%) revealed SS lymphocytic infiltrate. Isolated xerostomia was found in 17 (22%) patients, and isolated xerophthalmia in 5 (7%) patients. Anti-Ro/SSA and/or anti-La/SSB autoantibodies were found in 28.5% (6/21) of SS patients. 21 (27%) patients met the 2002 revised criteria for classification for SS by the AECG, Schirmer’s I test revealed dry eye severity level 2 in 4 (19%) patients, level 3 in 12 (57%) patients and level 4 in 5 (23.8%) patients.

Conclusions: The prevalence of sicca syndrome was 71%, 44 % related to systemic sclerosis’s collagen infiltration, and 27% due to Sjögren’s syndrome’s lymphocytic infiltrate. It is important to give a treatment to improve symptoms in patients with SSc and SS.
Preterm birth is the leading cause of neonatal mortality and sequelae in newborns worldwide. Its incidence in systemic lupus erythematosus (SLE) pregnancies ranges from 17 to 49% and is higher than in general population. Associated risk factors for this increased premature delivery in SLE are multifactorial and still under study. OBJECTIVES: To study the frequency of preterm deliveries and its association with clinical variables in mothers with SLE. METHOD: Retrospective cohort analysis of patients with SLE (≥4 ACR criteria), with single pregnancies and deliveries over 22 weeks, followed from 2011 to 2015. Data were analysed by Student's T test and Chi square. RESULTS: Out of 118 patients, 39 (33%) had preterm births. Their mean gestational age at delivery was 34.2±1.4 weeks; mean birthweight was 2,166±611g and neonatal ICU admission occurred in 45% (p<0.01). All stillbirths (6 cases) were seen among preterm infants (15%, p<0.01). The preterm delivery group presented a higher frequency of active SLE (56%, p=0.01), nephritis (61%, p=0.01), preeclampsia (28%, p=0.05) and use of daily oral prednisone ≥20 mg (48%, p<0.01). CONCLUSION: Active SLE, nephritis (at any time), preeclampsia and steroid use (> 20mg/d) were associated with preterm birth. Further, preterm babies had higher rates of intrauterine fetal death and neonatal ICU admission. The impact of these variables should be taken into account during planning and managing pregnancy in SLE patients. Close fetal surveillance and pregnancy planning may improve gestational outcome of mothers with SLE.
Aim: The aim of the study was to analyze the prevalence and clinical manifestations at diagnosis of SLE in 173 patients. **Material-Methods:** The median age of the patients, at onset of symptoms was 31 years, while the median age at diagnosis of SLE was 33 years. The female/male ratio was 6.5/1. The most common initial symptoms of the disease were arthralgia (joint pain), rash, arthritis and fever. While the frequency of manifestations which are not considered diagnostic for SLE, such as Reynaud syndrome and lymphadenopathy was increased. **Results:** Gender and age-related differences in disease expression were observed. Patients with onset of disease before the age of 14 appeared statistically significant higher prevalence of fever, rash, Reynaud syndrome, arthritis, while those with onset of disease after the age of 50 appeared gastrointestinal symptoms and sicca syndrome more frequently. **Conclusions:** The most frequent initial manifestation of the disease in women was the joint pain while in men were kidney symptoms, thrombosis and strokes. However, the basic question that arises is whether patients with SLE and different types of clinical disease expression also have different prognosis.
Aim: The investigation of factors that affect the severity of systemic lupus erythematosus at diagnosis and those that affect the response to medication.

Method: 121 patients with SLE diagnosis were investigated, were on medication and followed up for 5 years in Rheumatology Department of our Hospital. The disease activity was determined according to the SLEDAI score in all patients, both at diagnosis and at average following up of 25.9 ± 23.2 months.

Results: After statistical analysis including age, smoking habit, presence of positive RF factor test, positive anti-dsDNA antibodies, it was found that SLEDAI at diagnosis depends on smoking to positive anti-DsDNA test in order of importance. In response to the treatment, SLEDAI score showed a greater decrease in smokers with positive RF test smokers and instead of smokers with positive dsDNA antibodies test.

Conclusion: The severity of the disease at diagnosis is statistically significantly affected by smoking and the presence of anti dsDNA, and the
Poster Session

SOCIO-ECONOMIC DETERMINANTS OF HEALTH AND IMMUNOLOGICAL ACTIVITY

EVALUATION OF QUALITY OF LIFE THROUGH THE SHORT HEALTH SCALE (SHS) IN A COLOMBIAN COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

LACAT-0085
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Introduction

Inflammatory Bowel Disease (IBD) is a chronic disease with an increasing incidence in the Colombian population. Due to the impact on the quality of life in this group of patients, an evaluation of the same was made by means of the SHS in 35 patients with IBD.

Methodology

A cross-sectional descriptive study was conducted to evaluate the quality of life of patients diagnosed with IBD in a Colombian population. Quality of life with health status was assessed using the Short Health Scale (SHS).

Results

Data from 40 patients were analyzed, of whom 30% had Crohn's disease (CD) and 70% had ulcerative colitis (UC) (Table 1). The mean age was 48.58 years. There were no significant differences in quality of life as a function of the disease. Regarding the Montreal classification, the majority of UC are mild to moderate, with extensive or left-sided colitis, in contrast to CD with a late and severe presentation, with ileocolonic compromise and presence of fistulas and stenoses (Table 2).
<table>
<thead>
<tr>
<th>Características</th>
<th>n =40 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edad (media) (DS)</td>
<td>48,58 (16,48)</td>
</tr>
<tr>
<td>Femenino</td>
<td>21 (52,5)</td>
</tr>
<tr>
<td>Colitis Ulcerativa</td>
<td>28 (70)</td>
</tr>
<tr>
<td>Enfermedad Crohn</td>
<td>12 (30)</td>
</tr>
<tr>
<td>Tiempo de evolución (media) (DS)</td>
<td>8,68 (8,46)</td>
</tr>
<tr>
<td><strong>Escolaridad</strong></td>
<td></td>
</tr>
<tr>
<td>Menos de 10 años</td>
<td>11 (27,5)</td>
</tr>
<tr>
<td>Más de 10 años (media) (DS)</td>
<td>14,21 (2,48)</td>
</tr>
<tr>
<td><strong>Estado civil</strong></td>
<td></td>
</tr>
<tr>
<td>Soltero</td>
<td>14 (35)</td>
</tr>
<tr>
<td>Casado</td>
<td>18 (45)</td>
</tr>
<tr>
<td>Divorciado</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Unión libre</td>
<td>3 (7,5)</td>
</tr>
<tr>
<td><strong>Ocupación</strong></td>
<td></td>
</tr>
<tr>
<td>Manual</td>
<td>9 (22,5)</td>
</tr>
<tr>
<td>Intelectual</td>
<td>13 (32,5)</td>
</tr>
<tr>
<td>Mixto</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Ama de casa</td>
<td>7 (17,5)</td>
</tr>
<tr>
<td>Desempleado</td>
<td>1 (2,5)</td>
</tr>
<tr>
<td>Pensionado</td>
<td>1 (2,5)</td>
</tr>
<tr>
<td>Estudiante</td>
<td>1 (2,5)</td>
</tr>
<tr>
<td>Incapacitado</td>
<td>2 (5)</td>
</tr>
<tr>
<td><strong>Tobaco</strong></td>
<td>19 (47,5)</td>
</tr>
<tr>
<td>Terapia biológica</td>
<td>20 (50)</td>
</tr>
<tr>
<td>Extraintestinal</td>
<td>12 (30)</td>
</tr>
<tr>
<td>Articular</td>
<td>8 (20)</td>
</tr>
<tr>
<td><strong>Short Health Scale</strong></td>
<td></td>
</tr>
<tr>
<td>Síntomas (media) (DS)</td>
<td>3,83 (2,84)</td>
</tr>
<tr>
<td>Funcionalidad (media) (DS)</td>
<td>4,48 (2,96)</td>
</tr>
<tr>
<td>Preocupación (media) (DS)</td>
<td>5,85 (2,97)</td>
</tr>
<tr>
<td>Bienestar (media) (DS)</td>
<td>4,38 (3,02)</td>
</tr>
</tbody>
</table>
Conclusion

In our study population, there are no statistically significant differences between groups, but certain trends are identified since patients with CD have a higher severity score in quality of life, associated with the poor correlation between the perception of severity of the symptoms and the deterioration of its functionality with the concern referred by the patients. The importance of assessing quality of life in these patients and their impact on clinical outcomes and adherence to treatment should be emphasized.
The association of rheumatic disease among individuals in the first degree of inbreeding is widely known, especially in the context of genetics. The objective of the present study is to evaluate the association between variables in patients with rheumatic disease who consult the Roosevelt Hospital Rheumatology Unit.

Methods: Patients with some degree of consanguinity were reviewed who consulted the clinic at some point in the evolution of the disease and the association was searched using variables for clinical and sociodemographic aspects that allowed establishing the relationship.

Results: The total analysis included 78 people, involving 32 family nuclei. With average age 39 years and 31% of family association. The first diagnosis is SLE 70% (55), followed by RA 11% (9). In 50% (39) there was no kinship and in 17% (14) sibling and in 14% (11) maternal. The degree of consanguinity in 50% had none and in 38% (30) first degree relation. There is no correlation (Spearman -0.17) between the first diagnosis and the second diagnosis. The strongest relationship was the first diagnosis with RA, of which 47% (37) had no relatives with autoimmune disease and 33% (26) had RA. Sixty-three percent (49) of their schooling was low and 38% (30) had an association in the first degree of consanguinity and in 50% (39) there was no relationship.

CONCLUSIONS: The correlation between suffering a rheumatic disease and the development of the same or another in relatives is weak, and our data orientate to a first degree of consanguinity and RA. Prospective studies should be conducted.
We examined the consequences of interruptions in healthcare coverage for adults of working age (19-64 years) with type 1 diabetes mellitus. Clinformatics™ Data Mart Database was used, containing 61.8 million Americans, years 2001-2015. Negative binomial regression was used to assess the association between an interruption and services received. Acute care services were compared before and after an interruption with a self-controlled case series design, using fixed Poisson regression. For quality of life measures, tests for trend (variance-weighted least squares) were employed. Overall, 25.3% of the 185,237 subjects had at least one interruption in health insurance over a mean of 2.8 years. Younger individuals were more likely to experience a gap in coverage than older individuals (p<0.001). Men were more likely to experience an interruption than women (p<0.001). There was a 10% increase in the number of different non-facility providers (e.g., physicians, nurse practitioners) seen by those with interruptions versus continuous coverage (Incidence Rate Ratio = 1.10, 95% CI: 1.09, 1.12; p<0.001). There was a 27% increase in the number of mental health visits for those with interrupted versus continuous coverage (p<0.001). The rate of acute care visits after an interruption was greater (3.39/30 person-days) than prior to an interruption (0.51/30 person-days; p<0.001) in those with gaps of <270 days. Perceived health status and current satisfaction with life were lower in individuals with interrupted versus continuous coverage (p=0.002, p=0.010, respectively). Individuals with interruptions were less likely to have a strong network of friends and family than those with continuous coverage (p=0.032).
SOCIO-ECONOMIC DETERMINANTS OF HEALTH AND IMMUNOLOGICAL ACTIVITY

RESILIENCE IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES
LACA7-0129

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¹Center for Autoimmune Diseases Research CREA, Universidad del Rosario, Bogota, Colombia

Introduction
Resilience is the ability of human beings to positively respond to adverse events. Long-term stressors and inflammatory conditions may influence resilience development.

Objectives
To evaluate the relationship between resilience and the clinical and immune responses in 4 autoimmune rheumatic diseases (ARDs)

Methods
Focus groups, individual interviews and chart reviews were conducted to collect data in women with rheumatoid arthritis (RA, n=51), systemic lupus erythematosus (SLE, n=70), systemic sclerosis (SSc, n=35), and Sjögren’s syndrome (SS, n=32). Demographic, clinical and laboratory variables were assessed, including disease activity, by Patient Reported Outcomes (RAPID3, SLAQ, SSPRO, ESSPRI), and a panel of 14 autoantibodies by ELISA and IFI (Inova). Resilience was evaluated by using the Brief Resilience Scale (BRS, 1 to 6). Fifteen serum cytokines were measured by cytometric bead array (BD). Data were analyzed by Spearman correlation and Kruskal-Wallis tests.

Results
Patients with RA, SLE, SSc and SS disclosed similar levels of resilience (Table 1). There was no influence of severity of patients’ symptoms on resilience. Among the ARDs evaluated, significant associations were observed only in SSc, in which patients with higher socioeconomic status and regular physical activity disclosed the higher resilience score (Figure 1). IL-13, IL-5, IL-10, and IL-8 levels were inversely correlated with resilience (Table 2).

Conclusion
Similar resilience (by BRS) was observed in ARDs, regardless of clinical characteristics and patient reported activity of disease. The ways by which exercise and inflammatory process influence coping behavior in SSc deserve future investigation.
Table 1. General characteristics and resilience in women with autoimmune rheumatic diseases.

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA n=51</th>
<th>SLE n=70</th>
<th>SSc n=35</th>
<th>SS n=32</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>58 (48.5-63)</td>
<td>50.5 (37.5-57)</td>
<td>58 (51.5-62.5)</td>
<td>64.5 (55.7-68.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age at onset disease (IQR)</td>
<td>36 (26-49)</td>
<td>29 (22-40)</td>
<td>48 (37-53.5)</td>
<td>50.5 (40-58.25)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Disease duration (IQR)</td>
<td>17 (10.5-26)</td>
<td>13 (9-21.75)</td>
<td>7 (4-13)</td>
<td>12 (9-17)</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>Educational years (IQR)</td>
<td>14 (8-17)</td>
<td>14 (11-16)</td>
<td>11 (9-16)</td>
<td>13.5 (11-16)</td>
<td>0.78</td>
</tr>
<tr>
<td>Socioeconomic status (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0091</td>
</tr>
<tr>
<td>1, 2</td>
<td>18 (36)</td>
<td>19 (27.1)</td>
<td>8/33 (24.2)</td>
<td>3 (9.4)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14 (28)</td>
<td>39 (55.7)</td>
<td>15/33 (45.5)</td>
<td>15 (46.9)</td>
<td></td>
</tr>
<tr>
<td>4, 5, 6</td>
<td>18 (36)</td>
<td>12 (17.14)</td>
<td>10/33 (30.3)</td>
<td>14 (43.7)</td>
<td></td>
</tr>
<tr>
<td>ND</td>
<td>(1.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Employed</td>
<td>30 (59)</td>
<td>44 (63)</td>
<td>20 (57)</td>
<td>11 (34)</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>20 (39)</td>
<td>26 (37)</td>
<td>15 (43)</td>
<td>20 (63)</td>
<td></td>
</tr>
<tr>
<td>ND</td>
<td>1 (1.9)</td>
<td>-</td>
<td>-</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Exercise (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.071</td>
</tr>
<tr>
<td>22 (43.1)</td>
<td>28 (40)</td>
<td>23 (65.7)</td>
<td>17 (53.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyautoimmunity (%)</td>
<td>5 (9.8)</td>
<td>15 (21.42)</td>
<td>2 (5.7)</td>
<td>4 (12.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>Total BRS (IQR)</td>
<td>3.33 (3.1-4.1)</td>
<td>3.42 (3-3.83)</td>
<td>3.33 (2.8-3.7)</td>
<td>3.25 (2.95-4)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 2. Correlations between cytokines levels and BRS.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>RA r</th>
<th>RA p-value</th>
<th>SLE r</th>
<th>SLE p-value</th>
<th>SSc r</th>
<th>SSc p-value</th>
<th>SS r</th>
<th>SS p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL1-β</td>
<td>-0.2</td>
<td>0.33</td>
<td>-</td>
<td>-</td>
<td>-0.18</td>
<td>0.29</td>
<td>-0.14</td>
<td>0.44</td>
</tr>
<tr>
<td>IL4</td>
<td>-0.2</td>
<td>0.24</td>
<td>-</td>
<td>-</td>
<td>-0.22</td>
<td>0.2</td>
<td>0.013</td>
<td>0.94</td>
</tr>
<tr>
<td>IL5</td>
<td>-0.13</td>
<td>0.4</td>
<td>-</td>
<td>-</td>
<td>-0.45</td>
<td>0.0071</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IL6</td>
<td>0.04</td>
<td>0.8</td>
<td>-</td>
<td>-</td>
<td>-0.30</td>
<td>0.077</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IL8</td>
<td>0.21</td>
<td>0.2</td>
<td>-0.29</td>
<td>0.06</td>
<td>-0.38</td>
<td>0.025</td>
<td>-0.12</td>
<td>0.54</td>
</tr>
<tr>
<td>IL10</td>
<td>-0.02</td>
<td>0.9</td>
<td>-</td>
<td>-</td>
<td>-0.41</td>
<td>0.015</td>
<td>-0.24</td>
<td>0.20</td>
</tr>
<tr>
<td>IL12/L23PA4D</td>
<td>-0.09</td>
<td>0.52</td>
<td>-0.07</td>
<td>0.59</td>
<td>-0.15</td>
<td>0.38</td>
<td>-0.11</td>
<td>0.57</td>
</tr>
<tr>
<td>IL13</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.50</td>
<td>0.002</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IL17-α</td>
<td>-0.09</td>
<td>0.6</td>
<td>-</td>
<td>-</td>
<td>-0.06</td>
<td>0.73</td>
<td>-0.11</td>
<td>0.55</td>
</tr>
<tr>
<td>TNF-α</td>
<td>-0.094</td>
<td>0.53</td>
<td>-</td>
<td>-</td>
<td>-0.08</td>
<td>0.65</td>
<td>-0.06</td>
<td>0.75</td>
</tr>
<tr>
<td>G-CSF</td>
<td>-0.09</td>
<td>0.6</td>
<td>-0.14</td>
<td>0.77</td>
<td>-0.23</td>
<td>0.15</td>
<td>-0.14</td>
<td>0.46</td>
</tr>
<tr>
<td>IFN-α</td>
<td>-0.1</td>
<td>0.51</td>
<td>-0.0002</td>
<td>0.1</td>
<td>-0.11</td>
<td>0.54</td>
<td>-0.07</td>
<td>0.72</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.07</td>
<td>0.67</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
**Figure 1.** Resilience differences in patients with SSC according to socioeconomic status (A) and physical activity (B).
Poster Session

SOCIO-ECONOMIC DETERMINANTS OF HEALTH AND IMMUNOLOGICAL ACTIVITY

PREVALENCE OF RHEUMATIC DISEASE IN AN ADULT POPULATION FROM COLOMBIA. A COPCORD METHODOLOGY STUDY.
LACAT-0068
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⁵Asociación Colombiana de Reumatología, Asociación Colombiana de Reumatología, Bogotá, Colombia

Background: In our country there are no data to establish the prevalence of rheumatic diseases. The COPCORD model, constitutes an effective tool in the determination of the prevalence of diseases in countries. This would be the first national study that uses the data collection questionnaire using the COPCORD instrument

Methods: A Cross-sectional analytical study was designed in people older than 18 years. A stratified sampling method using three stages was made. The first stage of sampling was the selection of cartographic sectors in each city. The second stage of sampling was the blocks of each sector. The third stage of sampling was the homes of each block. All household members were surveyed. The sample size was calculated to be 6,528 people. The COPCORD questionnaire was applied in the first stage by standardized interviewers. Positive cases were reviewed by a first year rheumatology fellow. The positive cases for a probable rheumatic disease were reviewed by a second year rheumatology fellow and reviewed again with laboratory and image studies by a certified rheumatologist for definitive diagnosis.

Results: 3,146 men and 3,547 women were included. Pain in the last 7 days not associated with trauma was reported in 3,213 (48%) participants. Table 1 depicts the prevalence of rheumatic diseases in Colombia.

Conclusion: Our study shows a similar prevalence to those worldwide in scleroderma, dermatomyositis, systemic lupus erythematosus, and spondyloarthritis. A lower prevalence was observed in Sjögren Syndrome, fibromyalgia, gout and osteoarthritis. A slightly higher prevalence of rheumatoid arthritis was observed in our population.

<table>
<thead>
<tr>
<th>Table 1. Prevalence of Rheumatic Disease in Colombia</th>
<th>Prevalence (%)</th>
<th>Variation Coefficient</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>10,81</td>
<td>6</td>
<td>9,68-12,06</td>
</tr>
<tr>
<td>Gout</td>
<td>0,56</td>
<td>26</td>
<td>0,33-0,92</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>0,72</td>
<td>22</td>
<td>0,47-1,11</td>
</tr>
<tr>
<td>Soft Tissue Rheumatism</td>
<td>25,82</td>
<td>6</td>
<td>11,60-19,93</td>
</tr>
<tr>
<td>Mechanic Low Back Pain</td>
<td>7,24</td>
<td>7</td>
<td>6,28-8,34</td>
</tr>
<tr>
<td>Inflammatory Low Back Pain</td>
<td>0,65</td>
<td>28</td>
<td>0,38-1,12</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>0,39</td>
<td>51</td>
<td>0,08-0,48</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>1,49</td>
<td>15</td>
<td>1,12-1,98</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>0,05</td>
<td>56</td>
<td>0,02-0,16</td>
</tr>
<tr>
<td>Sjögren Syndrome</td>
<td>0,08</td>
<td>61</td>
<td>0,02-0,27</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>0,03</td>
<td>100</td>
<td>0,00-0,23</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>0,02</td>
<td>100</td>
<td>0,00-14</td>
</tr>
<tr>
<td>CHIKV infection</td>
<td>6,68</td>
<td>8</td>
<td>5,73-7,78</td>
</tr>
</tbody>
</table>

CI: confidence interval; CHIKV: chikungunya virus
Poster Session

SOCIO-ECONOMIC DETERMINANTS OF HEALTH AND IMMUNOLOGICAL ACTIVITY

FUNCTIONAL DISABILITY OF PATIENTS WITH RHEUMATOID ARTHRITIS IN NORTHWESTERN GREECE

LACA7-0156

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Introduction: Rheumatoid Arthritis causes articular damage with a severe impact on functionality. Few data of patients followed-up in Greece have been recorded.

Objective: To estimate the functional disability of patients with R.A in daily activities and the correlation with clinical and laboratory characteristics of the disease.

Method: 173 patients with R.A were evaluated in the outpatient department of the General hospital of Ioannina. We evaluated the correlation between the duration of the disease (DD), extra-articular manifestations, activity according to DAS-28, absence of autoantibodies, RF and/or anti-CCP. The number of co-morbidities and smoking were also estimated.

Results: 73% of the patients were females with an average age of 60 years, an average DD of 10.7 years. 65% of them were ANA positive, 63% were anti-CCP positive and showed an average DAS-28 of 4.6. 42% of them manifested extra-articular manifestations and 82% had >1 co-morbidities. 50% of the patients had a significant functional disability and 20% had severe disability. Disability was more severe in women, in patients with extra-articular manifestations, in patients with positive anti-CCP. The increase in the DD, the activity of the disease and the number of co-morbidities was linearly associated with the HAQ increase. In the multivariate analysis, there was a statistically significant correlation between HAQ and the activity of the disease and the number of co-morbidities.

Conclusion: 50% of the patients with RA show moderate to severe disability and the activity of the disease and the number of co-morbidities are independent adverse factors.
Cardiac involvement in idiopathic inflammatory myopathies (IIMs) attracts more attention than it ever did because of its morbidity and impact on worse prognosis, although the accurate information need further epidemiological studies. Early identification and intervention for diseased heart may help improve the clinical outcomes of IIMs with cardiac involvement. Cardiac troponin assays, allowing for sensitive detection of minor myocardium injury, may provide a new way for early detection for heart involvement in IIMs. While elevated cardiac troponin I (cTnI) specifically indicates cardiomyocyte injury, the elevation of cardiac troponin T (cTnT) levels may not only derive from damaged heart but also diseased adult skeletal muscles in which cTnT could re-express in patients with IIMs. cTnI is the biomarker of choice for diagnosis of cardiac involvement and may also be a prognostic factor in IIMs. Meanwhile, electrocardiography (ECG), cardiac imaging (e.g. echocardiography, cardiac magnetic resonance, etc.) and histopathological techniques (e.g. endomyocardial biopsy) take on different degrees of importance for the diagnosis of cardiac involvement. We propose a diagnostic strategy combining the routine use of cTnI assay with other techniques (routine ECG and echocardiography, cardiac magnetic resonance and or endomyocardial biopsy in necessity) and clinical investigation for early detection of heart involvement in IIMs. Future researches are required to validate the algorithm for performance.
**Poster Session**

**THE HEART AND ATHEROSCLEROSIS AND AUTOIMMUNITY**

**COMORBIDITY IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES**

**LACA7-0140**

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**Introduction:** Comorbidity is associated with worse health outcomes, more complex clinical management, and increased health care costs. Comorbidity has been evaluated in some autoimmune rheumatic diseases (ARDs) separately.

**Objectives:** To evaluate comorbidity in four ARDs simultaneously and to assess associations within them.

**Methods:** Using a focus group approach, self-reported comorbidities (n=19) diagnosed by a physician were evaluated in women with rheumatoid arthritis (RA, n=51), systemic lupus erythematosus (SLE, n=70), systemic sclerosis (SSc, n=35), Sjögren’s syndrome (SS, n=32) and a healthy control group (n=30). Multivariate analysis and a mixed-cluster methodology were performed to summarize sets of related variables.

**Results:** Clinical characteristics are shown in Table 1. Comorbidities were more prevalent in patients with ARDs than in healthy individuals (Table 2). The most frequent comorbidities were cardiovascular disease (CVD), acid peptic disease (APD) and anemia. Stroke, depression and epilepsy were more frequent in SLE, whereas APD was in SS and SSc (Figure 1). CVD was more common in RA and SLE regardless of age at onset (AOR: 1.10, 95%CI 1.03-1.20, p=0.012, and AOR: 1.04, 95%CI 1.00-1.08, p=0.055, respectively), whereas APD was more frequent in SS (AOR: 8.12 95%CI 1.51-65.61, p=0.024).

**Conclusions:** Comorbidity is frequent and significant in patients with ARDs, being more severe in SLE than in RA, SS and SSc. Since comorbidity may affect quality of life, treatment and survival, these results may guide a holistic conception of therapy and assist stakeholders in the policy-making process.
Figure 1. Cluster analysis in autoimmune rheumatic diseases (AIRD). A) Depression, $p=0.0029$. B) Stroke, $p=0.011$. C) Epilepsy, $p=0.048$. D) Acid peptic disorder, $p=0.000024$. 1: Presence of comorbidity; 0: Absence of comorbidity.
Table 1. General characteristics, habits and previous infections in women with autoimmune rheumatic diseases

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA  n=51</th>
<th>SLE n=70</th>
<th>SS  n=35</th>
<th>SS  n=32</th>
<th>p-value</th>
<th>Controls n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>50 (48.5-63)</td>
<td>56.5 (57.5-67)</td>
<td>58 (51.5-62.5)</td>
<td>64.5 (51.7-60.7)</td>
<td>&lt;0.001</td>
<td>36.5 (29-42)</td>
</tr>
<tr>
<td>Age at onset of disease (IQR)</td>
<td>36 (26-49)</td>
<td>29 (22-40)</td>
<td>48 (37-53.5)</td>
<td>50.5 (40-50.25)</td>
<td>&lt;0.001</td>
<td>NO</td>
</tr>
<tr>
<td>Family history of CV disease (%)</td>
<td>3 (5.9)</td>
<td>13 (18.6)</td>
<td>4 (11.4)</td>
<td>8 (25)</td>
<td>0.07</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tuberculosis (%)</td>
<td>5 (9.8)</td>
<td>2 (3)</td>
<td>1 (2.9)</td>
<td>1 (3.1)</td>
<td>0.27</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hepatitis A (%)</td>
<td>8 (15.7)</td>
<td>9 (13)</td>
<td>2 (5.7)</td>
<td>3 (9.4)</td>
<td>0.52</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Malaria (%)</td>
<td>1 (2)</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.75</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Infectious diseases summary (%)</td>
<td>14 (27.4)</td>
<td>12 (17.1)</td>
<td>3 (8.4)</td>
<td>4 (12.5)</td>
<td>0.11</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Polyautoimmunity (%)</td>
<td>5 (9.8)</td>
<td>15 (21.4)</td>
<td>2 (5.7)</td>
<td>4 (12.5)</td>
<td>0.10</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Variable</td>
<td>RA (n=51, %)</td>
<td>SLE (n=70, %)</td>
<td>SSc (n=35, %)</td>
<td>SS (n=32, %)</td>
<td>p-value</td>
<td>Healthy Control (n=30, %)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>---------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (27.4)</td>
<td>23 (32.85)</td>
<td>12 (34.3)</td>
<td>8 (25)</td>
<td>0.77</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0)</td>
<td>12 (17.14)</td>
<td>1 (5.7)</td>
<td>3 (9.4)</td>
<td>0.01</td>
<td>0 (0)</td>
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<tr>
<td>Venous thrombosis</td>
<td>4 (7.8)</td>
<td>8 (11.4)</td>
<td>7 (20)</td>
<td>5 (15.6)</td>
<td>0.07</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Occlusive arterial disease</td>
<td>2 (3.9)</td>
<td>3 (4.3)</td>
<td>2 (5.7)</td>
<td>0 (0)</td>
<td>0.63</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Carotid disease</td>
<td>1 (2)</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>1 (3.1)</td>
<td>0.77</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3 (5.9)</td>
<td>10 (14.3)</td>
<td>6 (17.1)</td>
<td>2 (6.25)</td>
<td>0.24</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cardiovascular diseases(Total)</td>
<td>15 (27.1)</td>
<td>35 (35.7)</td>
<td>14 (40)</td>
<td>13 (40.6)</td>
<td>0.16</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (3.9)</td>
<td>4 (5.7)</td>
<td>1 (2.9)</td>
<td>1 (3.1)</td>
<td>0.68</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>7 (13.7)</td>
<td>5 (7.14)</td>
<td>1 (3.9)</td>
<td>6 (18.75)</td>
<td>0.31</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Depression</td>
<td>4 (7.8)</td>
<td>22 (31.4)</td>
<td>3 (8.6)</td>
<td>8 (25)</td>
<td>0.002</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1 (2)</td>
<td>9 (12.8)</td>
<td>1 (2.9)</td>
<td>1 (3.1)</td>
<td>0.04</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Acid peptic disorder</td>
<td>8 (15.7)</td>
<td>22 (31.4)</td>
<td>18 (51.4)</td>
<td>10 (31.25)</td>
<td>0.002</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>2 (3.9)</td>
<td>35 (50)</td>
<td>6 (17.1)</td>
<td>2 (6.25)</td>
<td>&lt;0.001</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Cutaneous ulcers</td>
<td>3 (5.9)</td>
<td>9 (12.8)</td>
<td>5 (14.3)</td>
<td>3 (9.4)</td>
<td>0.54</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Anemia</td>
<td>11 (21.6)</td>
<td>18 (26)</td>
<td>5 (14.3)</td>
<td>5 (15.6)</td>
<td>0.48</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Neoplasm (any)</td>
<td>3 (5.9)</td>
<td>6 (8.6)</td>
<td>5 (14.3)</td>
<td>7 (21.9)</td>
<td>0.11</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>
Objective: considering cardiomyopathy-scleroderma association

Material and methods: we report the case of a patient diagnosed as having systemic scleroderma since 1975, with cutaneous, pulmonary, digestive involvement, referred to our department for dyspnea on mild exertion, productive cough (mucous sputum), and anterior thoracic pain not related to exertion. All symptoms started about 4 months prior to referral and were very little influenced by corticotherapy and 2 courses of antibiotics administered prior to admission in our department.

Results: Clinical examination reveals telangiectasia over the cheek bones, microstoma, spontaneous amputations of distal phalanges fingers 2-4 right hand, basal bilateral pleural friction rub, apical systolic murmur grade 3. Blood examination shows leukocytosis, polyglobulia, dyslipidemia normal ESR and CRP. ECG: sinus rhythm, HR=96/min, QRS axis at +10, LVH, negative T wave (anterior territory). Respiratory functional evaluation shows obstructive dysfunction (reduction by 30% of FEV1). Cardiac ultrasound reveals interventricular septum of 18mm thickness, posterior wall of left ventricle of 15mm thickness, with an intraventricular pressure gradient of 60mmHg at rest.

Discussion: systemic scleroderma is usually associated with restrictive cardiomyopathy, but our patient has the severe, obstructive form of cardiomyopathy. This was the cause of the respiratory symptoms, despite the interstitial pulmonary disease. As a consequence, we changed diltiazem to verapamil, reduced the vasodilators and the corticosteroid doses, which lead to the net improvement of the symptoms.

Conclusion: respiratory symptoms in systemic scleroderma must not be taken “for granted”, but must be evaluated correctly and completely at each consult.
Prevalence of MS is higher in SLE than in the general population (16-32%). Inflammatory activity and steroids have been associated with the SM. 25% of deaths in SLE have cardiovascular (CV) origin and are associated with dyslipidemia, elevated BMI, insulin resistance and hypertension.

Objective. To determine the prevalence of MS in Mexicans patients with SLE and its association with disease characteristics and inflammatory markers.

Methods: Cross-sectional study of patients with SLE. Demographics, coronary risk, disease activity and inflammatory markers were studied. The diagnosis of MS was established with the NHLBI / AHA criteria. Statistical analysis was performed using SPSS 20.0 software and a P value <0.05 was considered significant.

Result: 126 patients with SLE, 107 women (84%) and 19 men (15%), age 41 ± 13 years and disease duration 9 ± 7 years. The prevalence of MS was 33.3%. No association was found with age, education level, smoking or steroid use in patients wit MS. In multivariate analysis only the erythrocyte sedimentation rate (ESR) had statistical significance (p = 0.012). Positive association was found between higher values of ESR and hypertriglyceridemia (p= 0.0002), body mass index (p= 0.0043) and lower levels of HDL and C3 (p= 0.0152)

Conclusion: The prevalence of MS in our population (33%) was higher than reported in the SLICC registry (15%). The association of metabolic and inflammatory characteristics increases cardiovascular risk by a proinflammatory state. The results suggest the need for early diagnosis and treatment of MS to reduce cardiovascular comorbidity in patients with SLE.
Metabolic syndrome (MS) is caused by insulin resistance and may contribute to increased cardiovascular risk in patients with SLE. The prevalence of MS is higher in SLE patients than in the general population (16-32%). Some SLE characteristics favor the occurrence of MS, including persistent disease activity and corticosteroids.

Objective: Prevalence of MS and insulin resistance in men with SLE and to describe the association with other risk factors and characteristics of SLE

Methods: Cross-sectional study of male with SLE. Demographic characteristics, coronary risk factors, clinical manifestations and biochemical determinations were recorded. The presence of MS was determined according to the NHLBI / AHA criteria. The insulin resistance was assessed with HOMA-IR

Results: Sixteen patients with a mean age of 34.6 years. Only one patient met the criteria for SM (6.3%), while 7 had insulin resistance (43.8%). Measurements of insulin resistance were higher in the presence of anti-La positive (4% vs 2% p=0.04), whereas they were lower in the presence of mucocutaneous activity (0.7 vs 3.5 p=0.003), joint symptoms (1.2 vs 3.4 p=0.045), hematologic activity (0.6 vs 3.3 p=0.002) and in the presence of anti-dsDNA (2.1 vs 4.9 p=0.04). A positive correlation was observed between determinations of insulin resistance and triglyceride levels (r=0.056, p=0.025) and glycated hemoglobin (r=0.616, p=0.011)

Conclusions: In our group of patients there was a lower frequency of metabolic syndrome (6%) compared to the literature that would be explained because the patients were in good control, even for the small sample. However, there was a significant frequency of insulin resistance (44%). The evaluation of MS and other cardiovascular risk factors should be an integral part of the management of these patients
Poster Session

THE HEART AND ATHEROSCLEROSIS AND AUTOIMMUNITY

Use of myocardial perfusion and equilibrium radioisotopic ventriculography in patients with antiphospholipid syndrome as a screening method for the detection of asymptomatic heart disease.

LACA7-0115

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The prevalence of alterations in myocardial perfusion in autoimmune diseases in previous research has been estimated at 40%. To date, there is no consensus regarding the scrutiny of cardiovascular alterations in patients with antiphospholipid syndrome (APS).

Objective: To assess the presence and severity of ischemic heart disease or asymptomatic ventricular dysfunction in a group of patients with primary or secondary APS using 99Tc MIBI Gated-SPECT and equilibrium radioisotopic ventriculography.

Methods: Cross-sectional study. Twelve patients participated in the study and all of them underwent a myocardial perfusion study with 99Tc MIBI Gated-SPECT and a planar equilibrium radioisotope ventriculography and SPECT.

Results: A total of 12 patients were enrolled. There was no evidence of myocardial ischemia in any of the cases studied. Left ventricular systolic and diastolic function were normal in all cases. Alterations were observed in the right ventricle; in one third dilatation, in one of them systolic dysfunction (8%) and in 4 diastolic dysfunction (33%). It emphasizes the association of right ventricular dysfunction and serum positivity of anticardiolipin isotype IgG antibodies, as well as lupus anticoagulant (p = 0.041).

Conclusions: Although APS is associated with accelerated atherosclerosis, in this group of patients there was no evidence of coronary disease or left ventricular dysfunction. The abnormalities found in the right ventricle could be related to alterations in the pulmonary circulation.
THE HEART AND ATHEROSCLEROSIS AND AUTOIMMUNITY

Prevalence of subclinical atherosclerosis in patients with Systemic Lupus Erythematosus determined by Carotid Ultrasound.
LAC7-0117

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Systemic Lupus Erythematosus (SLE) is characterized by a proinflammatory state, which is associated with cardiovascular manifestations including accelerated atherosclerosis and coronary disease, which cause morbidity and early death. A prevalence of carotid atherosclerosis has been observed 37.1% in this group of patients. Although traditional coronary risk factors do not fully explain the increase in cardiovascular risk in SLE

OBJECTIVE: Determine the prevalence of subclinical atherosclerosis in patients with SLE determined by carotid ultrasound.

METHODOLOGY: Patients diagnosed with SLE and control group were obtained from the Internal Medicine consultation. We calculated the prevalence of subclinical atherosclerosis measured by ultrasound in both groups. We studied clinical and laboratory variables. It was considered statistically significant p <0.05.

RESULTS: 130 patients: 50 with SLE and 80 control. 31 Men and 99 Women. 37 patients with subclinical atherosclerosis were distributed in 14 patients (28.0%) with SLE and 23 patients (28.8%) in the control group, with no statistically significant difference between them. Prevalence ratio of subclinical carotid atherosclerosis in patients with SLE compared to the control group was 0.974 (p = 0.92) When comparing the characteristics of patients with SLE and the control group it was found that the subjects in the control group had an older age, DM2 and obesity.

CONCLUSION: The present study support the possibility of an unidentified risk factor related to SLE would compensate for the absence of traditional risk factors. No relationship was found for carotid atherosclerosis in SLE with time of evolution, activity or treatment.
SSc is characterized by endothelial dysfunction of the microvasculature and excessive deposition of connective tissue in the skin and organs. Pulmonary disease is common and manifests mainly as interstitial lung disease and PAH. PAH has been reported in up to 20% of SSc patients and is the leading cause of mortality of 23% with 73% survival at 3 years with current treatment options compared to 52% previously reported.

OBJECTIVE: To determine the prevalence of PAH in patients with SSc at “Centro Medico Nacional 20 de Noviembre ISSSTE”

MATERIAL AND METHODS: Cross-sectional study in SSc patients. Patients with PAH were identified, PSAP was determined with initial and present echocardiography. Treatment was described. Patients with type 1 PAH (Dana Point 2015) were included. Descriptive statistics were performed. SPSS software version 20 was used.

RESULTS: 42 women with a mean age of 56 years. 5 (11.9%) had a diagnosis of Cutaneous-Diffuse variety (DcSSc) and 37 (88.1%) cutaneous-limited variety (LcSSc). The prevalence of PAH was 26.1% of these were 36% DcSSc and 63.7% LcSSc. The mean PASP per echocardiogram was 45.9mmHg and post treatment was 46.4mmHg. 27.5% were management with vasodilators, 18% sildenafil 18% bosentan, 18% combined treatment of sildenafil with bosentan. Mortality was present in 36.3% of the patients.

CONCLUSION: The prevalence of PAH in our population was higher than that reported in the literature (26.1%), according to what was reported, was associated with LcSSc, with response to treatment in 63.7% of patients and higher mortality.
Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) autoantibodies in rheumatoid arthritis (RA), have been used as diagnostic and prognostic tools [1]. This traditional perspective has changed toward a major role in RA pathogenesis. FR and ACPA autoantibodies might influence disease activity, bone erosions and development of comorbidities. Anti-Ro52kDa antibodies have also been associated with disease severity in RA and might influence the development of comorbidities such as insulin resistance (IR).

**Objectives:** To evaluate the association between RF, ACPA and anti-Ro52 kDa and IR in RA patients.

**Methods:** We included 83 RA patients classified according to ACR 1987 and ACR/EULAR 2010 criteria and 90 controls matched for age, gender and body mass index (BMI). Homeostasis Model Assessment-insulin resistance (HOMA-IR), anthropometric parameters and RF, ACPA and anti-Ro52 were evaluated. Multivariate regression analysis was used to assess the contribution of autoantibodies, adiposity and disease activity to insulin resistance in RA.

**Results:** Patients positive for RF or anti-Ro52 kDa showed higher levels of basal insulin (P=0.009, P=0.006) and HOMA-IR. DAS-28 was correlated with basal insulin (r=0.31, P=0.01) and HOMA-IR (r=0.29, P=0.02). Multivariate analysis showed that Triglycerides, HDL-c, DAS-28, RF and anti-Ro52 kDa were independent predictors of basal insulin and HOMA-IR in patients with RA.

**Conclusions:** In RA, RF or anti-Ro52 kDa are independent predictors of IR. This phenomenon might be linked to the network of inflammation, adipokine secretion, since disease activity was also predictive of higher basal insulin.
Multiple sclerosis (MS) is a complex inflammatory, demyelinating and neurodegenerative disease with a heterogeneous pathology and clinical outcomes. Vascular comorbidities, including diabetes, and hyperlipidemia, may adversely affect outcomes in MS. **Objective:** To assess the associations of serum lipid profile with clinical parameters in MS. **Methods:** 50 MS patients classified according to the 2010 McDonald criteria and 50 control subjects (CS), adjusted by age and sex, were included in this study. Serum levels of glucose (Glu), triglycerides (Tg), high and low density lipoproteins (HDL, LDL) and total cholesterol (TC) were determined by spectrophotometer methods. Very low density lipoproteins (VLDL) levels were calculated by Friedwald equation. The data was analyzed with STATA v12 software and \( p<0.05 \) was reported as statistically significant. **Results:** Levels of Glu (\( p=0.003 \)) and TC (\( p<0.001 \)), were more elevated; and Tg (\( p<0.001 \)), HDL (\( p=0.006 \)) and VLDL (\( p<0.001 \)) were more diminuend in MS patients than CS group. Moreover, we found that Glu positively correlates with disease duration (\( p=0.031 \)), EDDS (\( p=0.001 \)), RDRS-2 (\( p<0.001 \)) and FIS (\( p<0.001 \)); TC positively correlates with disease duration (\( p<0.001 \)), EDDS (\( p=0.002 \)), RDRS-2 (\( p<0.001 \)) and FIS (\( p<0.001 \)); LDL positively correlates with disease duration (\( p<0.001 \)), EDDS (\( p<0.001 \)), RDRS-2 (\( p<0.001 \)) and FIS (\( p<0.001 \)); and HDL negatively correlates with EDDS (\( p=0.005 \)), RDRS-2 (\( p=0.004 \)) and FIS (\( p=0.017 \)). **Conclusion:** This study revealed that MS patients altered levels of metabolic profile regarding CS group and these levels correlated with clinical parameters. Our findings indicating the need for future research in the field, to avoiding these preventable comorbidities in MS patients.
Multiple sclerosis (MS) is a complex inflammatory, demyelinating and neurodegenerative disease with a heterogeneous pathology and clinical outcomes. The majority of the treatments for MS are long term mainly suppressing the immune system however, such immune-suppressants pose increased risks for infections, metabolic disorders and cancer.

**Objective**: To assess the effect of treatment on clinical and laboratory parameters in MS.

**Methods**: 50 MS patients classified according to the 2010 McDonald criteria and 50 control subjects (CS), adjusted by age and sex, were included in this study. Treatment were classified as: No treatment, disease-modifying drugs (IFN-β1a, IFN-β1b and glatiramer acetate), low-efficacy treatment (cyclophosphamide and azathioprine) and high-efficacy treatment (teriflunomide, dimethyl fumarate and rituximab). Hematic cytometry was measured by automatic hematology analyzer; and serum levels of metabolic parameters were determined by spectrophotometer methods. Very low density lipoproteins (VLDL) levels were calculated by Friedwald equation. The data was analyzed with STATA v12 software and \( p<0.05 \) was reported as statistically significant.

**Results**: We found a significant difference between the different treatments with ESR \((p=0.031)\), platelets \((p=0.011)\), band neutrophils \((p=0.001)\), mean corpuscular hemoglobin \((p=0.002)\), mean corpuscular hemoglobin concentration \((p=0.004)\) and low-density lipoproteins \((p=0.012)\).

**Conclusion**: Our study indicated that treatment strategy have impact on clinical and laboratory levels in MS.
Poster Session

THE IMMUNE NEURO ENDOCRINE SYSTEM AND AUTOIMMUNE DISEASES

DYSAUTONOMIA IN SJÖGREN’S SYNDROME AND RHEUMATOID ARTHRITIS
LACA7-0139
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Introduction: Autonomic dysfunction occurs in several chronic diseases, including autoimmune diseases (AIDs). Being the third form of neurological involvement in these conditions, a great interindividual variability exists among patients.

Objectives: To evaluate dysautonomia in patients with Sjögren’s syndrome (SS) and rheumatoid arthritis (RA).

Methods: Autonomic dysfunction was assessed in women with SS (N=32) and RA (N=51), by using the Composite Autonomic Symptom Score (COMPASS-31). Demographic, clinical and laboratory variables were collected, including severity of patients' symptoms by Patient Reported Outcomes (ESSPRI and RAPID3, respectively). Previous environmental exposure and a panel of 14 autoantibodies were examined by ELISA and IFI (Inova).

Results: Demographic and clinical characteristics are shown in Table 1. Levels of dysautonomia were higher in SS than in RA [Mean (SD)= 35.6 (17.8) vs. 25 (15.9)], regardless of age at onset of the disease (p=0.018). Table 2 discloses the results of dysautonomia assessment. Severity of symptoms was correlated with dysautonomia in patients with SS but not with RA. In fact, ESSPRI correlated with total COMPASS-31 score (r=0.50, p=0.0035), with secretomotor and with orthostatic symptoms (r=0.43, p=0.012, and r=0.44, p=0.0099, respectively). In addition, a previous exposure to wood smoke was associated with a higher COMPASS-31 in SS (p=0.0005). Evaluated autoantibodies were not associated with dysautonomia.

Conclusion: Dysautonomia is higher in patients with SS than in those with RA. Further investigations aimed at evaluating the relationship of environmental factors and severity of symptoms with dysautonomia in SS are warranted.
<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>RA  n= 51 (%)</th>
<th>SS n= 32 (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>58 (48.5-63)</td>
<td>64.5 (55.7-68.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Age at onset disease (IQR)</td>
<td>36 (26-49)</td>
<td>50.5 (40-58.25)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Disease duration (IQR)</td>
<td>17 (10.5-26)</td>
<td>12 (9-17)</td>
<td>0.038</td>
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<tr>
<td>ESSPRI</td>
<td>-</td>
<td>6 (4.7-6.75)</td>
<td>-</td>
</tr>
<tr>
<td>RAPID3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Near remission</td>
<td>11 (21.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Low severity</td>
<td>3 (5.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate severity</td>
<td>10 (19.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High severity</td>
<td>27 (52.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CLINICAL DOMAINS</td>
<td>SS</td>
<td>RA</td>
<td>p-value</td>
</tr>
<tr>
<td>---------------------</td>
<td>------</td>
<td>------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>Media</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>Orthostatic</td>
<td>14.5</td>
<td>11.8</td>
<td>0.08</td>
</tr>
<tr>
<td>Vasomotor</td>
<td>1.01</td>
<td>1.3</td>
<td>0.17</td>
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<tr>
<td>Secretomotor</td>
<td>7.4</td>
<td>3.6</td>
<td>0.019</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>8.4</td>
<td>4.8</td>
<td>0.047</td>
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<tr>
<td>Urinary</td>
<td>1.5</td>
<td>1.9</td>
<td>0.37</td>
</tr>
<tr>
<td>Pupillomotor</td>
<td>2.8</td>
<td>1.3</td>
<td>0.017</td>
</tr>
</tbody>
</table>
The paradoxical effect of infectious diseases on autoimmunity: main difference between rich and poor countries

J.O. Garcia-Mendez

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Flares in SLE: Predictors and Consequences

**Definition:** Flares in Systemic Lupus Erythematosus (SLE) are defined as a measurable increase in disease activity in one or more organs or systems, which is considered clinically relevant. Flares could be defined using several instruments; according to SLEDAI, flares are defined as an increase of three or four points, and severe flares as an increase of twelve points; and according to BILAG, they are defined as mild flares (BILAG B) or severe flares (BILAG A).

**Incidence:** The reported incidence of flares varies across several cohorts and the instrument used. Using SLEDAI, the incidence of flares range between 7 and 124 per 100 patients-years; in the GLADEL cohort, the incidence of flares was 17 per 100 patients-year; 14 for mild-moderate flares and 3 per 100 patients-year for severe flares.

**Predictors:** Among demographic risk factors, younger patients have a higher risk of flares, male patients experience renal flares more frequently and African descendants have a higher risk than Caucasians. Clinical risk factors include higher disease activity, and neurologic, renal, hematologic involvement, vasculitis and immunological activity. More frequent use of antimalarials are protective of flares, and glucocorticoids and immunosuppressive drugs, in particular azathioprine are predictors of flares; however, they could be reflecting a more severe disease.

**Consequences:** Flares have been associated with more hospitalizations and a worse outcome, including damage accrual and death. Furthermore, it has been associated with higher costs and a diminished quality of life. In the GLADEL cohort, we have reported that flares, regardless of their severity are predictive of damage accrual.

**Conclusions:** Flares are important because they predict a worse prognosis in SLE patients. The risk factors of their occurrence include several non-modifiable conditions (like ethnicity, age, gender, clinical manifestations); but, the use of antimalarials will protect of their occurrence.
ASSOCIATION OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS (JSLE) WITH ANOTHER AUTOIMMUNE DISEASES (AIDs)

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JSLE has been reported associated with another AIDs and provokes a wide spectrum of symptoms that may impacts their treatment and prognosis.

METHODS From a registry developed by GRIP that includes juvenile patients followed at ten pediatric rheumatology clinics in Colombia who associations of AIDs according to validated diagnostic criteria. We developed an electronic database

RESULTS 139 /212 patients with a mean follow up time of 4.7 years developed JSLE. Sex ratio, age of onset, interval between AIDs and family history of AIDs were determined

<table>
<thead>
<tr>
<th>Group A</th>
<th>JSLE preceded by other AIDs</th>
<th>Group B</th>
<th>JSLE heralding disease</th>
<th>Group C</th>
<th>Multiple AIDs heralded by JSLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune cytopenias</td>
<td>12</td>
<td>SLE + APLS</td>
<td>57</td>
<td>SLE + APS + HASHIMOTO</td>
<td></td>
</tr>
<tr>
<td>Hashimoto</td>
<td>12</td>
<td>SLE + HASHIMOTO</td>
<td>22</td>
<td>SLE + APS + GRAVES</td>
<td></td>
</tr>
<tr>
<td>APLS</td>
<td>10</td>
<td>SLE + SIJOREN</td>
<td>3</td>
<td>SLE + APS + Other AIDs</td>
<td></td>
</tr>
<tr>
<td>JIA + JSLE + other AIDs</td>
<td>4</td>
<td>SLE + another AID</td>
<td>5</td>
<td>SLE + Hashimoto + SS</td>
<td></td>
</tr>
<tr>
<td>PTHRUPUS + SIJOREN</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=</td>
<td>39</td>
<td>87</td>
<td>13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

JSLE associated to APs, Hashimoto or Sjogren’s syndrome were the most common. Group B observed the shorter interval between AIDs. All groups observed female predominance. Onset was simultaneous or sequential. 20/ 139 developed multiple auto immune disease

CONCLUSIONS: polyautoimmunity is frequent because AIDs share genetic background, clinical manifestations and autoantibodies profile. An a high index of suspicion and autoantibody profile may help to identify patients.
Introduction: The heterogeneous clinical presentation of Lupus is characterized by the unpredictable appearance of flares and remissions of disease activity associated with severe symptomatology. Various attempts to classify lupus clinically haven’t been successful, still burdened by delayed diagnosis and clinical trial failures. Our aim was to develop and validate a robust method to stratify lupus patients according to longitudinal patterns of disease presentation and gene expression data obtained at several points in time.

Methods: We calculated correlations among expression values of genes and SLEDAI across the different points for each patient. We constructed a bi-dimensional inter-patient matrix and developed a new approach to select genes strongly correlated with SLEDAI in absolute values across all patients as best genes to stratify patients. Finally, we obtain the stratification groups applying consensus clustering that estimates the probability of a patient to belong to a given cluster by random seed permutation.

Results: Longitudinally, lupus patients group into three clusters. They shared the same mean SLEDAI and had no differences in the clinical parameters comprising the score. Functionally however, the clusters had clearly differentiated gene expression profiles and cellular profiles representing three different mechanisms of disease progression. We tested the stability of the clusters by different validation methods and obtained a high reproducibility. Our method could be used in the future to establish and re-design lupus clinical trials and treatment, and may be used in any disease with measurable but variable patterns of disease progression. This work has received support from the EU/EFPIA/Innovative Medicines Initiative Joint Undertaking PRECISESADS grant n°115565.
BACTEROIDES PREDOMINANCE IN FECAL MICROBIOTA OF CELIAC DISEASE AND TYPE 1 DIABETES CHILDREN FROM NORTHWEST MEXICO

FREE COMMUNICATIONS

Background. Celiac disease (CD) and type 1 diabetes (T1D), the two most common autoimmune diseases in children, share genetics and environmental risk factors, as well as intestinal dysbiosis. Bacteroides predominance has been associated with T1D regardless of geographical area, race or age, while there is no consensus about a genus or species in CD dysbiosis, perhaps due to techniques used for microbiota analysis. Additionally, microbiota studies of Latin American autoimmune patients are scarce. Objective. To evaluate the intestinal microbiota composition of children with CD (n = 7) and to compare it with a paired-group of healthy children (n = 7) and newly-diagnosed T1D children (n = 8). Methods. A blood sample was taken for haplotypes and autoantibodies analyses and high-throughput microbial community analysis in DNA from feces was done using the Illumina MiSeq platform. Results. All participants had HLA-DQ2 and/or DQ8 haplotypes. The dominant intestinal phylum in all of the NW Mexican children healthy or ill was Bacteroidetes. Children with CD had a relative abundance of Bacteroides lower than T1D patients (16.97% vs. 44.7%, p = 0.006), but higher than their matched healthy controls (2.76%, p = 0.01) in whom Prevotella was the most abundant genus (Figure 1). In the Linear Discriminatory Analysis (LDA) effect size (LEfSe), Bacteroides fragilis was the most characteristic species in CD children with a 3.8 score. Conclusion. High Bacteroides proportion in microbiota appears to be related to CD and T1D autoimmunity. Bacteroides fragilis could be
used as a new biomarker associated with CD in NW Mexican population.

FIGURE 1. Relative abundance of fecal bacterial genus in healthy, CD and T1D NW Mexican children expressed as percentage. *p < 0.05, t-test.
FREE COMMUNICATIONS

Free Communications 3 (English)

ENDOTHELIAL DYSFUNCTION BY MICROPARTICLES FROM SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS PATIENTS

LACAT-0082

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Introduction. In patients with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) endothelial dysfunction is commonly observed, related with more development of atherosclerosis and cardiovascular diseases. Also, microparticles (MPs) forming immune complexes (IC) could induce microvascular injury. MPs are increased in SLE and RA patients, therefore they could interact and modulate the function of endothelial cells. Hence, the effect of MPs from SLE and RA patients in macrovascular (HUVEC) and microvascular (HMVEC-D and HMVEC-L) endothelial cells was evaluated.

Methods. Endothelial cells were exposed to MP and MP-IC from healthy donors, SLE and RA patients for 24h and were evaluated by ELISA, flow cytometry and epifluorescence microscopy.

Results. Endothelial cells increased their expression of CD54, CD102, HLA-DR as well as CCL2 and RANTES production in response to MP and MP-IC. MP and MP-IC from RA patients decreased the percentage of viable cells, while these structures from SLE patients had the opposite effect. Endothelial cells treated with MP and MP-IC showed increased nuclear condensation, F-actin depolymerization and increased distribution of VE-cadherin in cytosol. These observations were consistent with increased intercellular GAP, suggesting lower cell-cell adhesion and increased endothelial permeability. These changes were more evident with MP-IC. Internalization-binding assay showed that endothelial cells were internalizing MP and MP-IC, and particularly, HUVEC showed more acidic signal.

Conclusion. MPs promote endothelial activation, an increase in adhesion molecules that participate in leukocyte rolling, chemokine production, and structural alterations in macro and microvascular endothelial cells that can partially explain the endothelial dysfunction observed in these patients.
FREE COMMUNICATIONS

Free Communications 3 (English)

ANALYSIS OF THE REGULATORY FUNCTION OF NK CELLS FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

LACA7-0048

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Objective: The interactions of NK:DC in SLE patients have not been studied. The aim of this study is to evaluate the regulatory function of NK cells and to identify a possible new subset of NK cells involved in the pathogenesis of SLE.

Methods: Sixty patients and fifty-five controls were included. The expression of NKG2A, ILT2, NKG2D, NKG2C, NKp30, NKp46, CD161, CD134, CD80, CD86, HLA-DR, CD11c+ was evaluated in peripheral NK cells (CD3−CD56+). NK cell function was assessed by the recognition of monocyte derived DC by NK cells.

Results: Reduced levels of NK cells were found in SLE patients compared to controls (p=0.04). In addition, lupus NK cells showed higher levels of ILT2+, CD86+, CD134+ and HLA-DR+. Importantly, higher levels of atypical NK cells (CD11c+HLA-DR+) were found in SLE patients vs controls. Furthermore, we found that SLE patients showed an increased level of DC lysis by NK cells.

Conclusion: This is the first study demonstrating that NK cells in SLE patients have an altered phenotype and express a different set of receptors, which are characteristic of dendritic cells (CD134, CD86 and HLA-DR). Furthermore, we identified a new subset of NK cells, CD11c+ HLA-DR+. This atypical NK cells are increased in SLE patients and together with the increased of costimulatory molecules expression suggest that NK cells with DC-like phenotype could be crucial in SLE. We propose that the lysis of DC mediated by NK cells could be important to modulate the disease activity in SLE patients.
BACKGROUND:

Systemic Lupus Erythematosus (SLE) is characterized by uncontrollable B lymphocyte activity with over-production of autoantibodies. Alterations in autophagy, apoptosis, T lymphocytes and adverse hormonal environment may contribute to these alterations.

OBJECTIVE

To analyze the relationship between autophagy in Treg lymphocytes and expression of prolactin receptors (PRL-R) in B lymphocytes of patients with SLE.

PATIENTS AND METHODS

We included patients diagnosed with SLE and a control group of healthy individuals. The activity of SLE was determined by SLEDAI-2K. Information was obtained about the organs affected and the treatments used. Patients and controls were given a blood sample to obtain Treg lymphocytes, CD25 + FOXP3 + and B lymphocytes, CD19 +. Autophagy was identified with the anti-ATG14 antibody and PRL-R using the anti-PRL-R. The labeled cells were identified by flow cytometry. The results were analyzed by T of student’s and Anova.

RESULTS

We included 40 patients with SLE, 20 active, 20 in remission and 20 healthy controls. A significant increase of autophagy was observed in CD25 + FOXP3 + Treg cells (Fig. 1) and PRL-R in CD19 + B lymphocytes in patients with active SLE compared to patients in clinical remission and controls (Fig. 2). Autophagy and PRL-R were increased in patients with active lupus glomerulonephritis (Fig. 3).

CONCLUSIONS

1. The increase of autophagy in Treg and PRL-R lymphocytes is involved in the activity of SLE, especially in active lupus glomerulonephritis.

2. Autophagy and PRL-R may be new therapeutic targets in SLE.
Fig. 1 Autophagy in Treg cells in patients and healthy controls:
A: Healthy controls vs. Inactive SLE: 7.44 vs 8.74 $p=0.9999$
B: Healthy controls vs. Active SLE: 7.44 vs 12.11 $p<0.05$
Fig. 2 Prolactin receptors in B cells in patients and healthy controls
A: Healthy controls vs. Inactive SLE: 0.62 vs 5.56 p = 0.7463
B: Healthy controls vs. Active SLE: 0.62 vs 50.79 p < 0.0001
Fig. 3 Autophagy and prolactin receptors in lupus glomerulonephritis

Autophagy marker ATG-14 (red color)
A: Healthy control vs. active SLE: 7.44 vs. 13.63 p = 0.0003
Prolactin receptors PRL-R (black color)
B: Healthy control vs. active SLE: 0.62 vs. 51.22 p = 0.0001
Background: When compared with clinical trials, disease registry data is more close to clinical practice. We use an android-based application, TRA Clinical Electronic Registry (TRACER), for recording rheumatoid arthritis (RA) patients' disease activity, daily medication and biological agents. Through this app, the clinical data of RA patients can be easily exported and merged for further analysis. In this report, we presented the merged data of RA patients, intended to evaluate the biological agent effects and the correlation between disease activity and weather changes.

Method: 567 patients with rheumatoid arthritis from 2013 to 2015 in Chiayi Chang Gung Memorial Hospital and Far Eastern Memorial Hospital were enrolled. Demographic information, disease activity (daily activity scores in 28 joints, DAS28) and medications were recorded by TRACER. Weather data was collected from Taiwan central weather bureau observation data inquiring system.

Results: There are 567 patients with rheumatoid arthritis, the proportion of women was 75 %. Age of diagnosis was 52 (15 to 84) years. Average DAS28-ESR was 3.8 (0.2 to 8.0) in biology user (after treatment) and 3.6 (0.2 to 7.8) in non-biologic user. RA disease activity is associated with pressure and temperature changes but not with sun shine.
and relative humidity.
Conclusion: TRACER is valuable in recording data in daily practice and can be exported for further statistics analysis. Merging personal registry data is useful for increasing data size and decreasing single site bias in clinical research. Similar method can be applied on other autoimmune diseases.
FREE COMMUNICATIONS

Free Communications 3 (English)

Art and medicine: using Shakespeare to treat mental illness in Brazil and Canada
LACA7-0010
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“We are made of the matter dreams are made of” “Violent sorrow now seems to be a modern ecstasy.” “The play is the thing, where in we'll catch the consciousness of the king.” The amplitude of the thinking of the English actor and poet William Shakespeare still crosses generations and disciplinary fields. Here we report the two year experience of playing Hamlet, written in 1601 when Shakespeare was 37 years old, in the oldest Brazilian Psychiatric Hospital Centro Psiquiátrico Pedro II in Rio de Janeiro, and also the more recent experience of playing Macbeth in Montreal, Canada in the last year in a Community Mental Health Organism PRISE II, the theatrical process involves the training of actors freely accepted from the local communities that frequently involved people who had been diagnosed as Schizophrenics and Psychotics, in the Brazilian experience very severe cases got involved in the theater group. During the presentation we’ll show pictures and short movies demonstrating the performance of those actors who became active protagonists of this process, gaining performance and autonomy in persistent commitment to the DyoNises Theater groups in Brazil and Canada.
Brazilian pemphigus foliaceus, also known as Fogo Selvagem (FS), is an endemic autoimmune skin blistering disease associated with pathogenic IgG4 autoantibodies against desmoglein 1 (Dsg1), a desmosomal cell adhesion glycoprotein. Environmental factors, such as insect bites, have been linked to the etiology of FS. We have demonstrated that IgG4 autoantibodies cross-react with an indigenous environmental antigen, LJM11 sand fly saliva protein, suggesting that LJM11 may be one of the environmental antigens that trigger the autoantibody responses in FS. In addition, FS patients possess autoantibodies directed against other desmosomal adhesion proteins (desmogleins and desmocollins). Thus, this investigation aimed to dissect whether these autoantibody responses are linked and associated with immune response to LJM11 environmental antigen. Monoclonal IgG1 and IgG4 autoantibodies were generated from FS patients and their specificity to LJM11 environmental antigen and keratinocyte adhesion molecules determined. Our study found that these autoantibodies cross-react with a conformational epitope on LJM11 and bind to linear epitopes on all tested adhesion molecules, which share high primary sequence homology, especially in regions adjacent to their calcium binding domains. Our investigation indicates that the complex autoimmune responses in FS against diverse desmosomal adhesion molecules are due to the cross-reactivity among these autoantibodies, which also cross-react with LJM11. It suggests that the generation of these autoantibodies results from antigen-specific immune responses which are associated with environmental antigens, such as LJM11. Importantly, FS provides an invaluable model to study the environmental contributions to the development of autoantibodies in autoimmune diseases.
FREE COMMUNICATIONS

Free Communications 3 (English)

SERUM CXCL16 LEVELS IN SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS BEFORE AND AFTER TREATMENT WITH DMARDS

LAC07-0123

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BACKGROUND

Rheumatoid arthritis (RA) is characterized by profound mononuclear cell (MNC) recruitment into synovial tissue (ST) with CXCL16 being the prime MNC recruiter. Hence, changes in serum CXCL16 levels can be used as a prognostic marker in RA.

AIM

To study the levels of serum CXCL16 in seropositive RA patients (either RF+ or ACPA+) before and after treatment with DMARD (Disease Modifying Anti Rheumatic Drug) -both conventional synthetic and biologic

MATERIALS AND METHODS

After obtaining Institutional ethical clearance and written informed consent from patients, a prospective observational study was conducted among 31 RA patients. All patients were initially treated with Hydroxychloroquine, methotrexate and sulfasalazine for 3 months, failing which, they were shifted to anti TNF biologics (n=5). Serum CXCL16 levels were measured using ELISA at baseline and after 6 months. 18 age and sex matched controls was taken.

RESULTS

26 patients showed a lowering of mean serum CXCL16 levels from 56.07 pg/ml to 21.79 pg/ml (62% reduction) after 6 months of conventional synthetic DMARDs. Of the 5 patients who were treated with TNF-α blocker had their CXCL16 levels reduced from 63.81 pg/ml to 12.36 pg/ml (80.6% reduction) at 6 months. There was a corresponding improvement in the disease activity of RA. Lowering of CXCL16 was found to correlate positively with clinical symptoms and lowering of disease activity.

CONCLUSION

DMARDs treatment significantly lowered the serum levels of CXCL16 in patients with RA (more with biologics than csDMARDs) which correlates with clinical improvement. Hence, CXCL16 can be used as a marker for response to treatment in RA patients.
Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by the presence of anti-DNA antibodies which form immune complexes causing lesions in skin, kidneys, joints, and multiple organs. It has been speculated that in SLE patients, the extracellular traps emitted by neutrophils (NETs) might be taken up by plasmacytoid dendritic cells which in turn would induce the production of anti-DNA antibodies by plasma cells. In this work we evaluated the susceptibility of neutrophils from SLE patients (purified by percoll gradient) to produce NETs by image analysis of fluorescence microscopy dyeing DNA with ethidium bromide and spectrophotometric quantification after cocultured with pseudohyphae from Candida albicans, as well as the activation state of their plasmacytoid dendritic cells (purified by negative selection with magnetic cell sorting) measuring CD40 expression and IFN-α secretion by flow cytometry in BDCA-2 positive cells, and their capability to stimulate lymphocytes in a mixed leucocyte reaction. All these parameters were analyzed in comparison to healthy individuals in a gender and age paired study.

The results obtained up today, analyzing 20 SLE patients show statistical significant leukopenia and hypochromic anemia in SLE patients, with decreased absolute numbers of neutrophils and higher susceptibility to produce extracellular traps, which correlate with higher CD40 expression, IFN-α secretion and stimulatory capability of their plasmacytoid dendritic cells.

These results provide scientific information to support the contribution of plasmacytoid dendritic cells activated by a high concentration of DNA derived from NETs as part of the pathological process to produce anti-DNA antibodies in SLE patients.
Biological rhythms are fundamental for homeostasis and have recently been involved in the regulatory processes of various organs and systems. Circadian cycle proteins and hormones have a direct effect on the inflammatory response, and have shown pro or anti-inflammatory effects in animal models of autoimmune diseases. The immune system cells have their own circadian rhythm and the light-dark cycle directly influences the inflammatory response. On the other hand, patients with autoimmune diseases characteristically have sleep disorders and fatigue and in certain disease such as rheumatoid arthritis (RA) a frank periodicity in the signs and symptoms is recognized. The joint symptoms predominate in the morning and apparently subjects with RA have relative adrenal insufficiency, with a cortisol peak unable to control the late night load of pro-inflammatory cytokines. Transatlantic flights represent a challenge in the adjustment of biological rhythms, since they imply sleep deprivation, time zone changes and potential difficulties for drug administration. In patients with autoimmune diseases the use of DMARDs and prednisone at night is probably best suited to lessen morning symptoms. It is also essential to sleep during the trip to improve adaptation to the new time zone and to avoid, as far as possible, works involving flexible or nocturnal shifts. The study of proteins and hormones related to biological rhythms, will demonstrate new pathophysiological pathways of autoimmune diseases, which will emphasize the use of general measures for sleep respect and methods for drug administration at key daily times to optimize their anti-inflammatory and immune modulatory effects.
Ten to 30% of newborns of women with SLE are small for gestational age (SGA - birthweight below the 10th percentile). History of lupus nephritis, antiphospholipid antibody syndrome (APS), arterial hypertension and active SLE have been associated with SGA newborns. Their neonatal mortality is 10 times higher than controls, with an increased risk of neuro-developmental retardation and metabolic syndrome in adult life. OBJECTIVE: To study the frequency of SGA infants and its association with clinical variables in mothers with SLE. METHOD: We analysed retrospectively a cohort of SLE patients (≥ 4 ACR criteria), with single pregnancies and deliveries after 22 weeks, followed from 2011 to 2015. Groups were compared with T Student and Chi Square tests. RESULTS: Out of 118 patients, 23 (19%) had SGA infants. In this group, the mean age at delivery was of 36.4±0.7 weeks, with a mean birthweight of 2,019±53g and neonatal ICU admission in 60% (p<0.01). Stillbirth was 4-fold higher in SGA infants (p=0.05) and 65% of the mothers with SGA newborns had a history of nephritis (versus 42%, p=0.02). We observed a higher frequency of obstetric APS (p=0.06) and preeclampsia (p=0.08) in SGA. CONCLUSION: Lupus nephritis was statistically associated with SGA, with a trend towards obstetric APS and preeclampsia. Neonatal morbidity with ICU admission was higher 60% (p<0.01) as also was lower birthweight among SGA infants. Despite advances in SLE care before and during pregnancy, we still found SGA in one fifth of the offsprings.
A role for the CXCL17/CXCR8 axis in gastrointestinal inflammation, autoimmunity and obesity

LACA7-0102
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1University of California Irvine, Physiology and Biophysics, Irvine, USA

CXCL17 is a chemokine that attracts dendritic cells and monocytes. CXCL17 is mainly expressed in the respiratory and gastrointestinal mucosa. We recently identified its receptor, GPR35/CXCR8, which is a GPCR that is expressed in the mucosa and subpopulations of macrophages. Given that macrophages are known to be involved in fat tissue homeostasis and autoimmunity, we studied a possible role of the CXCL17/CXCR8 axis in gut physiology.

We compared Cxcl17−/− mice to wild type (WT) C57BL/6 mice in a model of diet induced obesity. Mice were fed a high fat diet for four months. Under homeostatic conditions CXCL17 is highly expressed in the upper gastrointestinal tract (oral cavity, esophagus and stomach) in WT mice. Cxcl17−/− mice fed a 60% fat diet gained significantly more weight than WT mice. Obese Cxcl17−/− mice exhibited impaired responses to glucose in an insulin tolerance test. Adipokine assay results revealed differences in FGF-21 levels and in other obesity-associated molecules between WT and Cxcl17−/− mice. Cxcl17−/− mice fed a high fat diet also exhibited signs of inflammation, including higher serum TNFα and IL1b. Importantly, Cxcl17 expresses a homeostatic expression pattern in the upper gastrointestinal (GI) tract, but an inflammatory pattern in the lower GI (including the intestines). The latter observation is important because GPR35/CXCR8 has been associated through genome wide-association studies with ulcerative colitis and Crohn’s disease. We conclude that the CXCL17/CXCR8 axis plays an important role in the recruitment of macrophages to the GI tract and likely participates in controlling the inflammatory state of the intestines.
FREE COMMUNICATIONS

Free Communications 4 (Bilingual)

DIFFERENCES IN CLINICAL PRESENTATION BY GENDER IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
LACA7-0056
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¹Artmedica-IPS, Rheumatology division, Medellín, Colombia
²Artmedica-IPS, Clinical information group, Medellín, Colombia
³School of Statistics, Faculty of Sciences- National University of Colombia, Medellín, Colombia

Background: Gender differences have been reported in various Systemic Lupus Erythematosus (SLE) cohorts (1–3). It has been proposed that males might have more serious manifestations and poorer prognosis (4).

Objective: To analyze the influence of gender on disease patterns in Colombian patients with SLE.

Methods: A cross-sectional study was conducted in 1169 patients with SLE that fulfilled classification criteria for ACR 1997 or SLICC 2012, in whom clinical characteristics were analyzed based on gender. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses (to adjust for possible confounders).

Results: Female-to-male ratio was 10.3:1 with 8.8% of the cohort being males, with a mean age at diagnosis of 32.9 years for women and 33.3 for men. Longer duration of disease was found in females, and a positive association to mucocutaneous compromise (i.e., photosensitivity, oral ulcers, and alopecia), articular involvement, and Raynaud phenomenon. Male gender was associated with more severe compromise, including serositis, renal compromise, alveolar hemorrhage and anticardiolipin antibodies positivity (Tables 1, 2).

Conclusions: In a large Colombian cohort with SLE, male gender was found to be associated with more severe manifestations of disease, despite shorter duration. We did not find differences in discoid lupus, neuropsychiatric compromise, hemolytic anemia and antiDNA antibodies, as reported in other SLE cohorts (5-8).
<table>
<thead>
<tr>
<th>Condition</th>
<th>All N=1169</th>
<th>Female N=1066</th>
<th>Male N=103</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucocutaneous compromise</td>
<td>880 75.2</td>
<td>818 76.7</td>
<td>62 60.2</td>
<td>2.18</td>
<td>1.43-3.31</td>
<td>0.0002</td>
</tr>
<tr>
<td>Malar rash</td>
<td>315 26.9</td>
<td>287 26.9</td>
<td>28 27.2</td>
<td>0.98</td>
<td>0.62-1.55</td>
<td>0.65</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>465 39.7</td>
<td>436 40.9</td>
<td>29 28.2</td>
<td>1.76</td>
<td>1.13-2.76</td>
<td>0.0116</td>
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<tr>
<td>Discoid lupus</td>
<td>97 8.3</td>
<td>90 8.4</td>
<td>7 6.8</td>
<td>1.26</td>
<td>0.57-2.80</td>
<td>0.562</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>307 26.2</td>
<td>294 27.6</td>
<td>13 12.6</td>
<td>2.6</td>
<td>1.45-4.78</td>
<td>0.0010</td>
</tr>
<tr>
<td>Alopecia</td>
<td>449 38.4</td>
<td>424 39.8</td>
<td>25 24.3</td>
<td>2.06</td>
<td>1.29-3.28</td>
<td>0.0024</td>
</tr>
<tr>
<td>Articular compromise</td>
<td>947 81.2</td>
<td>871 81.7</td>
<td>76 73.8</td>
<td>1.58</td>
<td>0.99-2.52</td>
<td>0.0503</td>
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<tr>
<td>Serositis</td>
<td>234 20.0</td>
<td>204 19.1</td>
<td>30 29.1</td>
<td>0.57</td>
<td>0.36-0.9</td>
<td>0.016</td>
</tr>
<tr>
<td>CNS compromise</td>
<td>66 5.6</td>
<td>58 5.4</td>
<td>8 7.8</td>
<td>0.68</td>
<td>0.31-1.47</td>
<td>0.3287</td>
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<td>Hematological compromise</td>
<td>950 81.2</td>
<td>867 81.3</td>
<td>83 80.6</td>
<td>1.05</td>
<td>0.62-1.75</td>
<td>0.8523</td>
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<td>Renal compromise</td>
<td>457 39.1</td>
<td>406 38.1</td>
<td>51 49.5</td>
<td>0.62</td>
<td>0.41-0.94</td>
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<td>Cardiopulmonary and vascular compromise</td>
<td>416 35.5</td>
<td>390 36.6</td>
<td>26 25.2</td>
<td>1.70</td>
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<td>0.0217</td>
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<td>Raynaud phenomenon</td>
<td>324 27.7</td>
<td>308 28.9</td>
<td>16 15.5</td>
<td>2.20</td>
<td>1.27-3.23</td>
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<td>Vascularitis</td>
<td>83 7.1</td>
<td>76 7.1</td>
<td>7 6.8</td>
<td>1.05</td>
<td>0.47-2.34</td>
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<td>Alveolar hemorrhage</td>
<td>12 1.03</td>
<td>9 0.8</td>
<td>3 2.9</td>
<td>0.28</td>
<td>0.07-1.06</td>
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<td>Pulmonary hypertension</td>
<td>20 1.71</td>
<td>19 1.8</td>
<td>1 1</td>
<td>1.85</td>
<td>0.24-13.96</td>
<td>0.5442</td>
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<tr>
<td>Pulmonary fibrosis</td>
<td>10 0.86</td>
<td>10 0.9</td>
<td>0 0</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>Lupus pneumonitis</td>
<td>31 2.65</td>
<td>30 2.8</td>
<td>1 1</td>
<td>2.94</td>
<td>0.39-21.82</td>
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<td>SLEDAI (Moderate/severe activity)</td>
<td>230 19.6</td>
<td>214 20.1</td>
<td>16 15.5</td>
<td>1.36</td>
<td>0.78-2.37</td>
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<td></td>
<td>All</td>
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<td>Male</td>
<td>OR</td>
<td>95%CI</td>
<td>p-value</td>
</tr>
<tr>
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</tr>
<tr>
<td></td>
<td>n/N</td>
<td>(%)</td>
<td>n/N</td>
<td>(%)</td>
<td></td>
<td></td>
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<tr>
<td>ANA positivity</td>
<td>1044/10</td>
<td>97,3</td>
<td>957/9</td>
<td>97,3</td>
<td>0,84</td>
<td>0,19-3,62</td>
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<tr>
<td></td>
<td>72</td>
<td></td>
<td>83</td>
<td>3</td>
<td></td>
<td>0,821</td>
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<tr>
<td>Anti-DNA positivity</td>
<td>588/109</td>
<td>53,9</td>
<td>545/9</td>
<td>53,6</td>
<td>46,2</td>
<td>0,91-2,14</td>
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<td>0</td>
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<td>97</td>
<td>6</td>
<td></td>
<td>0,1189</td>
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<tr>
<td>Lupic Anticoagulant</td>
<td>124/502</td>
<td>24,7</td>
<td>110/4</td>
<td>24,1</td>
<td>30,4</td>
<td>0,37-1,41</td>
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<td></td>
<td>56</td>
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<td>56</td>
<td>1</td>
<td></td>
<td>0,344</td>
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<tr>
<td>Anticardiolipin IgG</td>
<td>73/556</td>
<td>13,1</td>
<td>62/51</td>
<td>12,1</td>
<td>23,9</td>
<td>0,440</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>50</td>
<td>1</td>
<td></td>
<td>0,21-0,91</td>
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<tr>
<td>Anticardiolipin IgM</td>
<td>83/551</td>
<td>15,1</td>
<td>71/50</td>
<td>14,1</td>
<td>26,1</td>
<td>0,463</td>
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<td></td>
<td></td>
<td></td>
<td>5</td>
<td>1</td>
<td></td>
<td>0,22-0,93</td>
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<td>Low complement</td>
<td>696/115</td>
<td>60,2</td>
<td>631/103</td>
<td>59,9</td>
<td>63,7</td>
<td>0,851</td>
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<tr>
<td></td>
<td>5</td>
<td></td>
<td>953</td>
<td>2</td>
<td></td>
<td>0,55-1,29</td>
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FREE COMMUNICATIONS

Free Communications 4 (Bilingual)

CLINICAL AND SEROLOGICAL DIFFERENCES BETWEEN EARLY AND LATE ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

LACAT-0058

S. Herrera1, M.A. Alzate2, D. Hernandez-Parra2, D. Echeverry2, J.C. Salazar-Uribe3, P. Ortiz-Salazar2, R. Pineda2

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3School of Statistics, Faculty of Sciences- National University of Colombia, Medellin, Colombia

Background: Patients with Late Onset Systemic Lupus Erythematosus (LOSLE) are considered as being 50 years or older at onset (1). Different cohorts have suggested a milder disease but a higher burden of comorbidities that cause more damage accrual and mortality (2–5).

Objective: To analyze disease patterns in a large cohort of Colombian patients with SLE regarding LOSLE.

Methods: A cross-sectional study was conducted in 1209 patients with SLE that fulfilled classification criteria for ACR 1997 or SLICC 2012, in whom clinical characteristics were analyzed based on age at onset. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses (to adjust for possible confounders).

Results: In this cohort, 12% had LOSLE, with less years of disease duration. No gender differences between early and late onset were found. Patients with LOSLE had less alopecia, renal and articular involvement, and lower SLEDAI scores (Table 1). Also, a higher burden of comorbidities, with cardiovascular disease and osteoporosis, was found. Additionally, LOSLE had less antiDNA and anti RNP positivity, and less hypocomplementemia (Table 2). We found no statistical differences in anti-SM positivity and SLICC damage score.

Conclusions: In this study, LOSLE in Colombian population was associated with a less severe clinical presentation of disease, less clinical and serological activity, but stronger association with comorbidities such as cardiovascular disease and osteoporosis.
Table 1. Clinical characteristics of patients with SLE by age at onset

<table>
<thead>
<tr>
<th></th>
<th>All N=1209</th>
<th>Early onset N=1062</th>
<th>Late onset N=147</th>
<th>OR</th>
<th>95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alopecia</td>
<td>454 37.5</td>
<td>416 39.2</td>
<td>38 25.9</td>
<td>0.541</td>
<td>0.36-0.79</td>
<td>0.0020</td>
</tr>
<tr>
<td>Articular compromise</td>
<td>970 80.2</td>
<td>863 81.3</td>
<td>107 72.8</td>
<td>0.617</td>
<td>0.41-0.91</td>
<td>0.0156</td>
</tr>
<tr>
<td>Renal compromise</td>
<td>470 38.8</td>
<td>435 41</td>
<td>35 23.8</td>
<td>0.450</td>
<td>0.30-0.67</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>SLEDAI (Moderate/severe activity)</td>
<td>235 19.4</td>
<td>217 20.4</td>
<td>18 12.2</td>
<td>0.543</td>
<td>0.32-0.91</td>
<td>0.0203</td>
</tr>
<tr>
<td>Cardiovascular diseases (CVD)</td>
<td>377 31.1</td>
<td>295 27.8</td>
<td>82 55.8</td>
<td>3.280</td>
<td>2.30-4.66</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Arterial hypertension (AHT)</td>
<td>328 27.1</td>
<td>253 23.8</td>
<td>75 51</td>
<td>3.331</td>
<td>2.34-4.74</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>112 9.2</td>
<td>72 6.8</td>
<td>40 27.2</td>
<td>5.140</td>
<td>3.32-7.94</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
Table 2. Serum immunological profile in SLE patients by age at onset

<table>
<thead>
<tr>
<th></th>
<th>All N=1209 (%)</th>
<th>Early onset N=1062 (%)</th>
<th>Late onset N=147 (%)</th>
<th>OR</th>
<th>95%CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-DNA positivity</td>
<td>602/1129 53.3%</td>
<td>540/992 54.4%</td>
<td>62/137 45.2%</td>
<td>0.692</td>
<td>0.48-0.99</td>
<td>0.0435</td>
</tr>
<tr>
<td>Anti RNP</td>
<td>379/968 39.1%</td>
<td>343/851 40.3%</td>
<td>39/117 33.3%</td>
<td>0.658</td>
<td>0.43-0.99</td>
<td>0.0475</td>
</tr>
<tr>
<td>Anti Ro</td>
<td>405/968 41.8%</td>
<td>350/849 41.5%</td>
<td>55/119 46.2%</td>
<td>1.225</td>
<td>0.83-1.80</td>
<td>0.3011</td>
</tr>
<tr>
<td>Anti La</td>
<td>134/943 14.2%</td>
<td>114/828 13.7%</td>
<td>20/115 17.3%</td>
<td>1.319</td>
<td>0.78-2.22</td>
<td>0.2971</td>
</tr>
<tr>
<td>Lupic Anticoagulant</td>
<td>127/514 24.7%</td>
<td>112/471 23.7%</td>
<td>15/43 34.8%</td>
<td>1.717</td>
<td>0.88-3.32</td>
<td>0.1061</td>
</tr>
<tr>
<td>Anticardiolipin IgG</td>
<td>75/573 13.1%</td>
<td>69/524 13.1%</td>
<td>6/49 12.2%</td>
<td>0.920</td>
<td>0.37-2.24</td>
<td>0.8546</td>
</tr>
<tr>
<td>Anticardiolipin IgM</td>
<td>86/567 15.2%</td>
<td>74/518 14.2%</td>
<td>12/49 24.8%</td>
<td>1.946</td>
<td>0.97-3.90</td>
<td>0.0570</td>
</tr>
<tr>
<td>Low complement</td>
<td>718/1195 60.1%</td>
<td>643/1049 61.2%</td>
<td>75/146 51.5%</td>
<td>0.667</td>
<td>0.47-0.94</td>
<td>0.0217</td>
</tr>
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</table>
FREE COMMUNICATIONS

Free Communications 4 (Bilingual)

Probiotic Saccharomyces boulardii plus metronidazole in small intestinal bacterial overgrowth and gastrointestinal symptoms in Systemic Sclerosis
LACA7-0179
1Instituto Mexicano del Seguro Social-Hospital de Especialidades Centro Medico La Raza, Sección de Estudios de Posgrado e Investigación-Instituto Politécnico Nacional, Mexico, Mexico
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5Instituto Mexicano del Seguro Social-Hospital de Especialidades Centro Medico La Raza, Direction of Education and Research, Mexico, Mexico

Introduction. Small intestinal bacterial overgrowth (SIBO) affects up to 60% of patients with Systemic Sclerosis (SSc). SIBO is associated with severe gastrointestinal symptoms (GIS), malabsorption and malnutrition. The treatment is based on antibiotics; however, probiotics are an alternative by restoring the microbiota.

Aim. To evaluate the efficacy of probiotic Saccharomyces boulardii (SB) in combination with metronidazole for 2 months for GIS and SIBO versus the standard treatment in patients with SSc.

Method. Controlled clinical trial conduct in 39 with SIBO SSc patients (ACR-EULAR 2013) who signed informed consent and divided into Metronidazole(M), SB and Metronidazole plus SB(M+SB) for 2 months. We used NIH PROMIS® questionnaire to assess GIS, Lactulose hydrogen breath test (HBT) for SIBO.

Results. All groups had similar basal characteristics (Table1). A reduction in HBT(ppmH+) were observed in all groups SB (58.3%), MSB(54.5%) and M(50%)(table2). SB decreased reflux/heartburn and gas/bloating(p<0.05). After 2 month of metronidazole plus one month of SB, HBT and constipation decreased (p<0.05). Xerostomia decreased in 60% with SB vs none of metronidazole (0.009). Metronidazole had more adverse events (53%,table3).

Conclusion. SB was more effective in decreasing gastrointestinal symptoms, hydrogen levels in breath and improving xerostomia with fewer adverse effects.
Systemic sclerosis (SSc) is associated to increased mortality. Factors are different around the world. Design. We follow for 10 years a cohort to investigate these factors.

Methods. Patients ≥16 years of age with SSc (ACR/EULAR 2013) were included. Demographic, clinical characteristics and causes of mortality were recorded. We calculated Crude and standardized Mortality Rate, and Kaplan-Meier survival curve, Log-rank analysis and Cox proportional hazard (HR) regression analysis were performed.

Results. Patients with SSc (n=220) were included 199 females and 21 males. During follow-up, 28 deaths occurred. Follow-up time was 1074 years-person, CMR 12.72%. Survival rate at 5 years was 83%. The causes of death were definitively attributed to SSc in 21.4% of the cases, probably in 28.7%, unrelated in 35.6%, and unknown in 14.3%. The direct cause of death of the patients was infection in 25% of cases, cardiovascular disease in 14%, lung involvement in 14%, pulmonary embolism in 11%, and neoplasia in 11%. The Cox regression analysis showed that the factors associated with mortality were: male gender (HR 5.84, CI95% 1.31-26, p=0.013), severe Medsger’s score for general symptoms (HR 5.12, IC95% 1.74-14.97, p=0.021) and severe malnutrition (HR 3.77, CI95% 1.23- 11.06, p=0.008).

Conclusions. Infections, cardiovascular disease, and lung Blinded Manuscript Click here to view linked References 2 involvement were the leading cause of death. Male gender and severe general affection and malnutrition were associated with a poorer prognosis of SSc.
FREE COMMUNICATIONS
Free Communications 4 (Bilingual)

DIFFERENCES IN MORTALITY BETWEEN PRIMARY AND SECONDARY ANTIPHOSPHOLIPID SYNDROME ACCORDING DAMAGE INDEX IN ANTIPHOSPHOLIPID SYNDROME: NESTED CASE-CONTROL STUDY.

LACAT-0101

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Background

The thrombotic cumulative organ damage can be measured by the Damage Index in AntiPhospholipid Syndrome (DIAPS) (Amigo MC, et al. Lupus. 2015 Aug;24(9):927-34). Hypothetically, patients with secondary antiphospholipid syndrome (SAPS) may have more other sources of thrombosis or cumulative organ damage than primary antiphospholipid syndrome (PAPS). The differences in mortality according DIAPS at the moment of diagnosis of antiphospholipid syndrome (DIAPS_Dx) has not been studied.

Objective

Explore the mortality between PAPS and SAPS according DIAPS_Dx in a nested case-control study in a long term retrospective cohort of one single center.

Methodology

This nested case-control study design includes patients with rheumatologic assessment in the last 6 months. Patients with more than 6 months without clinical visit received a phone call to assess the survival status. Patients with no confirmed survival status were not included.

Association of demographic and clinical variables with survival status between PAPS and SAPS were assessed with Fisher’s exact test. Unadjusted exploratory odds ratio for dead were calculated according DIAPS_Dx.

Results

Whole cohort includes 50 patients but survival status at 2017, April was confirmed only in 40 patients. The mean age was 45 ± 12 years-old, 30 patients were females, 21 had PAPS and 13 had died during follow-up (13 ± 5 years of follow).

In PAPS group DIAPS_Dx ≥ 4 was associated with dead (p = 0.029), in SAPS group that was not observed (p=0.614). The odds ratio within PAPS was 13.75 (CI 95% 1.2-156.64).

Conclusions

These preliminary results suggest that DIAPS has a better performance for PAPS.
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TH1, TH2 and TH17 Lymphoid subpopulations in primary antiphospholipid syndrome
LAC7-0044

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OBJECTIVE: To analyze the lymphoid subpopulations, Th1, Th2 and Th17 immune response in patients with PAPS and long term evolution.

PATIENTS AND METHODS: We included PAPS patients, without recent thrombosis > 18 years of age, matched with healthy blood donors for age and sex. Peripheral blood was obtained and lymphoid subpopulations were determined by flow cytometry using specific immunological markers: For Treg cells: CD4+ / CD25+ / FoxP3+ and CD8+ / CD25+ / FoxP3+. Dendritic cells analyzed were: type 1: Lin1- HLA-DR+ / CD11c+; Type 2: Lin-HLA-DR+ / CD123+; B lymphocytes with antiCD19-APC; NK: CD3- / CD16+ 56+; NKT: CD3+ / CD16+ 56+ lymphocytes. Th1 cells were identified by IFN-g+ positivity; Th2: positivity for IL-4+; Th17: positivity for IL-17+. Parametric statistics and Mann-Whitney U-test were used.

RESULTS: A total of 39 patients with PAPS were included, age: 51.9 ± 12.8, evolution time: 12.8 ± 8.9 years and 35 healthy controls. In PAPS patients there was a decrease in the total CD8 count (p <0.05) in iNKT (p <0.005), DC1 (p <0.005) and DC2 (p <0.0005) cells compared to the control group. We found significant decrease in Th1, Th2 and Th17 cytokines basal and after activation compared to healthy controls.

CONCLUSIONS: This study shows profound alterations in innate/adaptive immunity in patients with long-term PAPS, characterized by a decrease in certain lymphocyte subpopulations. These abnormalities can become new therapeutic targets in order to restore immune imbalance.
Multiple sclerosis (MS) is an autoimmune disease that is characterized by demyelinating lesions affecting the central nervous system and spinal cord which leads to progressive neurological deterioration. Previous studies have associated high serum sCTLA4 with the clinical course of MS and other autoimmune diseases, which contribute to the development of the disease. **Objective:** To assess the association of sCTLA4 with clinical and hematological parameters in MS. **Methods:** MS patients classified according to the 2010 McDonald criteria and control subjects (CS), adjusted by age and sex. Hematocytometry was measured by automatic hematology analyzer; and serum levels of sCTLA4 were determined by ELISA method. The data was analyzed with STATA v12 software and *p*<0.05 was reported as statistically significant. **Results:** Levels of hemoglobin (*p=*0.004), ESR (*p=*0.001), lymphocytes (*p=*0.013) and banded neutrophils (*p*=<0.001), were more elevated in MS patients than CS group. In addition, levels of sCTLA4 in MS group were higher than CS group (13.44 pg/mL vs 8.94 pg/mL *p*=<0.001). Also, we found an increase of serum levels of sCTLA4 in MS patients with an EDSS of 6-6.5 that MS patients with an EDSS of 0-3.5 (15.45 vs 12.92 pg/dL, *p*=0.031). Moreover, we found that sCTLA4 is positively correlated with hemoglobin (*p=*0.005) and banded neutrophils (*p*=<0.001). **Conclusion:** This study revealed that MS patients have high levels of sCTLA4 regarding CS group and these increments correlated with hematological parameters and associated with EDSS. These suggest that sCTLA4 can be used as a new serological marker of diagnostic and progression in MS.
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ANTI DFS-70 ANTIBODIES: CONFIRMATION OF THE ANTINUCLEAR ANTIBODIES (ANA) DENSE FINE SPECKLED PATTERN (DFS)

LACAT-0120

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INTRODUCTION: The DFS pattern has particular nuclear characteristics. The autoantigen is a 70kD molecule (DFS70/LEDGFp75). Several studies showed that anti-DFS70 Ab (DFS70Ab) were common among healthy versus systemic autoimmune rheumatic diseases (SARD) individuals. Aims: Determine the frequency of anti-DFS70 Ab by Chemiluminiscence immunoassay method (CIA) in samples showing DFS pattern, and the agreement between three commercially kits for DFS70Ab detection. METHODS: Serum samples with ≥1/80 titers and DFS pattern results were selected, and assessed at the laboratory-Immunology*Dr. Manuel Quintela”Hospital (MQH) and at a private health center laboratory (CASMU), in a 6 month period in 2016. ANA was tested by IIF in HEP-2 substrate (Kallestad-BIORAD) and DFS-70Ab by CIA (Quanta flash DFS70 INOVA). In addition, MQH samples were treated with a specimen diluent containing DFS70 antigen and retested by IIF HEP-2 substrate (NOVA Lite Hep-2 Select Kit with DAPI Kallestad-BIO RAD) and assessed by an Immunoblot assay (NOVA Dot INOVA) searching DFS70Ab. Agreement between Quanta flash DFS70 INOVA/NOVA Dot INOVA, and NOVA Lite Hep-2 Select/NOVA Dot INOVA was determined by Kappa coefficient. RESULTS: 27 sera (26 patients: 5,8 female/male ratio and a 52,6 age average) were selected, 17 (63,0%) from MQH and 10 (37,0%) from CASMU, 18/27 (67%) with 1/80 titers, and 9/27 (33%) with >1/80 titers. 3/27 (11,1%) were DFS70Ab positive by CIA (all 1/80 titers). Kappa between Quanta flash DFS70 INOVA/NOVA Dot INOVA was 1 (IC: 0.5246-1.475), and between NOVA Lite Hep-2 Select/NOVA Dot INOVA was 0.32 (IC: -0.02855-0.6685). CONCLUSIONS: We found a low frequency of DFS70Ab. Recognition of DFS pattern is difficult. Agreement between Quanta flash DFS70 INOVA/NOVA Dot INOVA was excellent while discrete between NOVA Lite Hep-2 Select/NOVA Dot INOVA. We believe it is important to recognize and to confirm DFS pattern, to include DFS70Ab tests into diagnostic algorithms as well as visual training of laboratory specialist.
Objectives. Kawasaki disease (KD) is an acute, self-limited, systemic vasculitis of unknown etiology that occurs predominantly in infants and young children. An increased prevalence of celiac disease (CD), the highest prevalence ever reported (5.5%), has previously been described among KD patients. The present study’s aim was to describe the prevalence of CD in a group of previously diagnosed KD from Brasilia, Brazil.

Methods. Samples from 101 KD patients (60 male and 41 female, mean age at diagnosis 3.7 years, age range 1-9 yr.) were tested to determine IgA-tTG levels by enzyme-linked immunosorbent assay, IgA-EMA by indirect immunofluorescence assay and CD predisposing genotypes (HLA-DQ2 and -DQ8) by Real Time PCR. Duodenal biopsies were performed in patients that tested positive for both serologic exams.

Results and Conclusions. Only one KD patient (0.9%, male; diagnosed at age 5) showed significantly elevated titers of anti-transglutaminase antibodies (47.15 U; cut off value: 20 U). This prevalence does not differ from the prevalence reported for general population which is estimated in 1% nor significantly with previous studies performed in Brazilian general population. Genetic analyses of CD predisposing variants showed a total frequency of 29.7% which is also inside the expected prevalence range found in general population (25-50%). This suggests that KD patients may not have an increased risk of developing celiac disease.
The early identification of patients in the pre-clinical phase of rheumatoid arthritis (RA) is of high importance as it became evident during the last decade that early intervention can prevent joint damage in patients with RA. Several ongoing studies are focused on the prevention of RA based on the treatment of individuals at high risk to develop RA showing promising results. Based on all the findings about the possible treatment in the pre-clinical phase of RA, reliable biomarkers are needed to identify patients who are on the trajectory to develop RA.

In this context, recently, the combination of Anti-citrullinated protein/peptide antibodies (ACPA), rheumatoid factor (RF) and anti-CarP (Carbamylated Peptide) autoantibodies has been shown to provide a very high Odds Ratio for RA. In addition, several studies have now repeatedly shown that ACPA and other biomarkers (e.g. autoantibodies, inflammatory proteins, cytokines, micro RNA) can antedate the development of RA by many years. Although these data are intriguing, it would be more valuable to have biomarkers that are able to provide insights into the evolution of RA within the next 6-12 months, corresponding to the so-called ‘window of opportunity’. In this presentation, we summarize ongoing studies for the prevention of RA and provide an update on future plans for the selection of healthy individuals at risk to develop RA.
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AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IMPROVES THE NEUROLOGICAL CONDITION OF PERSONS WITH MULTIPLE SCLEROSIS (MS): THE MEXICAN EXPERIENCE.

LACAT-0200

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Background: In an effort to reset of the immune system, patients with (MS) have been autografted stem cells; we have shown that grafts can be conducted on an outpatient basis employing non-frozen hematopoietic stem cells and a conditioning regimen with cyclophosphamide (Cy) and rituximab, the so-called “Mexican method”.

Material and methods: Along 132 months patients with MS were autografted in two centers in México employing the “Mexican method” (ClinicalTrials.gov identifier NCT02674217). Peripheral blood stem cell mobilization was accomplished with Cy and filgrastim (G-CSF). Cumulative dose of Cy was 200 mg/kg; after recovery of granulocytes, patients were given rituximab (375 mg/m2) and subsequently (100 mg) every two months along a 12-mo. period. The extended disability status scale (EDSS) score was assessed every 3 mos. after transplant

Results and Conclusions: 392 MS were autografted; median age was 47 years; time to recover > 0.5 x10⁹/L granulocytes was 7 days (0-12), and transplant related mortality was 0%. In 140 patients, EDSS values decreased significantly from 5.05 ± 0.1316 to 4.78 ± 0.1562 three mos after grafting (p = 0.0078). In 28 cases EDSS was measured 12 months after grafting and compared to baseline. Although the mean EDSS value at 12 mos was even smaller (4.67 ± 0.370), the statistical difference was borderline (p = 0.545) probably reflecting the small number of subjects in this subgroup. Improvement or stabilization in the EDSS score at 12 mos. was observed in 75, 72 and 60% of patients with RR, SP or PP forms of the disease.
Systemic autoimmune diseases are a group of chronic inflammatory conditions with autoimmune aetiology and many common clinical features, leading to a difficult diagnosis or deciding the appropriate treatment. Finding new treatments or applying the existing ones in a more effective way is especially hard in SADs due to the heterogeneity of molecular mechanisms within the same disease class. Based on this premise, the first step towards establishing a precision medicine strategy for SADs is to reclassify these conditions at the molecular level, which might result in a more homogenous stratification in terms of pathological molecular pathways.

It is well known that the interplay of DNA methylation patterns and environmental factors, and between these, is determinant in the regulation of the immune system. This, along with the fact that the genetic contribution to disease is dependent on regulatory variants with very small effects, and the low concordance for autoimmunity in monozygotic twins suggests that epigenetic regulation may play an important role in the development of these diseases. Thus, DNA methylation information might be a valuable marker to reclassify the autoimmune disorders molecularly.

We performed an unsupervised clustering analysis of genome-wide DNA methylation profiling of 437 cases distributed across 7 different clinical entities (rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, primary Sjögren's syndrome, primary antiphospholipid antibody syndrome, mixed connective tissue disease and undifferentiated connective tissue disease) and 115 healthy individuals. In this analysis we were able to identify new groups of patients composed of the different clinical diagnoses but with common biological features.
PLENARY SESSION IN ENGLISH (translation into Spanish)

Plenary Session 5: The Environment in Autoimmunity

Sex, Genetics and the Environment
LACA7-0182
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The evolution of the immune system was dependent on developing a diversified and promiscuous response in order to fulfill the important function of host protection from environmental and, particularly, infectious agents. A major failure in this development of immunity is the appearance of autoimmune diseases in which a breach or a loss of tolerance has occurred. Although autoimmunity was once felt to be a relatively rare disorder, there are now nearly 100 distinct autoimmune diseases and, collectively, autoimmunity, whether a flaw in innate or of adaptive immunity, may affect up to 11% of the population. There is strong epidemiological data that supports a genetic basis for loss of tolerance and indeed there is an increased frequency of autoimmune diseases within members of the same family. However, the concordance of autoimmunity in identical twins is in the range of 25-50%, often even lower, suggesting that genetics alone are not the only driver in developing reactions to self. In fact, recent research efforts have strongly implicated stochastic events, i.e. epigenetic modifications of DNA that will be additional mechanisms that lead to the failure to distinguish self from non-self. The classic examples of these epigenetic alterations are changes in DNA methylation, but it is likely that other mechanisms will be involved as well. These concepts are very well illustrated by the human autoimmune biliary disease, coined primary biliary cirrhosis (PBC), in which there is a female predominant disease that leads to high titer and very highly directed autoantibodies to mitochondrial enzymes and specific biliary destruction. Our laboratory has focused on the thesis that epigenetic alterations will account not only for susceptibility to disease, but possibly also modify effector mechanisms that will lead to biliary inflammation and destruction. Our data reflects that patients with primary biliary cirrhosis undergo significant DNA methylations that involve the X-chromosome as well as specific chemokines. One of the great disappointments in immunology has been the failure of genome-wide association studies (GWAS) to identify “smoking guns” or specific and well recapitulated genes that lead to disease induction. The concept that epigenetics are a major player in this paradigm helps explain the relative disappointing data from GWAS, not only in primary biliary cirrhosis, but in other human autoimmune diseases as well. More importantly, there is now significant data on why females develop autoimmunity, which includes not only estrogens, but now also potential influences of the microbiome. Our data will be presented within the framework of the mechaniss in the kaleidoscope of immunological dysfunction that lead to the specific targeting of self molecules, cells and tissues
PLENARY SESSION IN ENGLISH (translation into Spanish)

Plenary Session 5: The Environment in Autoimmunity

Emerging Autoimmunity in Domestic Animals
LACA7-0192
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The etiology of human lupus remains enigmatic. Indeed, it has been nearly 60 years since the discovery of New Zealand Black (NZB) mice and the subsequent development of NZB x NZW F1 hybrids. It has been nearly 40 years since the discovery of MRL mice. Indeed, there are now multiple strains and variations of mice that develop lupus. However, despite enormous efforts and major contributions in our understanding of loss of tolerance, the specific mechanisms that lead to human lupus remain enigmatic. Indeed, genome-wide association studies have been largely disappointing and there is still no specific genetic test that can be applied to human patients. It is therefore of significant interest to note that as enthusiasm for pet ownership has increased, and development of further inbreeding of large numbers of canine breeds, we have seen the emergence of increasing incidence of autoimmune disease. The appearance of lupus in dogs was first noted in the 1970s and appeared before the rapid improvements in veterinary immunology and including the use of the Veterinary Clinical Immunology Laboratory. It is now not unusual to see lupus in dogs, but also in a variety of other species. The clinical manifestations are generally similar to humans and including dermal and renal pathology and the characteristic appearance of autoantibodies. There are valuable lessons which can be learned from the study of outbred animals with their broad similarities to humans. Herein I will review the clinical manifestations of lupus in a variety of animal species as well as discussion of the natural history of disease with clinical comparisons to humans, both diagnostically and treatment regimens.
Systemic lupus erythematosus (SLE) is an autoimmune disease that affects different end organs, including skin and brain. We and others have previously shown the importance of macrophages in the pathogenesis of both cutaneous and neuropsychiatric lupus. Additionally, autoantibodies produced by autoreactive B cells are thought to play a role in both the cutaneous and central nervous system pathologies associated with SLE. In this study we used a novel inhibitor of Bruton’s tyrosine kinase (BTK), BI-BTK-1, to target both macrophage and B cell function in the MRL/lpr murine model of SLE.

We found that treatment with BI-BTK-1 significantly attenuated the skin and neuropsychiatric disease characteristic of MRL/lpr mice. Specifically, BI-BTK-1 treated mice had less macroscopic and microscopic skin lesions, reduced cutaneous cellular infiltration, and diminished inflammatory cytokine expression compared to control mice. BTK inhibition also significantly improved cognitive function, and decreased accumulation of T cells, B cells, and macrophages within the central nervous system.

Directed therapies may improve the response rate in lupus driven target organ involvement, and decrease the dangerous side effects associated with global immunosuppression. Overall, our results suggest that inhibition of BTK with BI-BTK-1 may be a promising therapeutic option for cutaneous and neuropsychiatric disease associated with SLE.
Neuropsychiatric manifestations (NPM) are frequently observed in systemic lupus erythematosus (SLE). The heterogeneity of manifestations and the different degrees of severities suggest that different pathophysiological mechanisms are involved. Studies have shown that both cytokines and autoantibodies are associated with NPSLE. In addition, cardiovascular risk factors and infections may contribute and mimic NPSLE. In this session the main mechanism of NPSLE and mimickers will be discussed.