En esta edición 23 del Boletín Asoreuma les presentamos algunos de los trabajos presentados por miembros de nuestra asociación aceptados para presentación en eventos internacionales como lo son Eular 2018 y el XI Congreso Internacional de Autoinmunidad, resaltando el gran trabajo realizado por estos especialistas, mostrando el impacto y la importancia de la investigación.
Trabajos presentados por miembros Asoreuma en XI Congreso Internacional de Autoinmunidad

Realizado en Lisboa, Portugal durante Mayo 16 a 20 de 2018.

GENE EXPRESSION OF BAFF, APRIL AND THEIR RECEPTORS IN LUPUS NEPHRITIS

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Background

BAFF and APRIL cytokines are crucial for the survival of B lymphocytes through the receptors BAFF-R, BCMA and TACI. Recent evidence (1, 2) show the importance of BAFF/APRIL in Lupus nephritis (LN) by demonstrating expression in glomeruli and tubular epithelial cells by immunohistochemistry. The aim of this study is to evaluate the relationship between gene expression of BAFF, APRIL, and their receptors in urinary sediment compared with histological characteristics in patients with LN.

Method

Urine samples were collected from patients with SLE before renal biopsy. RNA extraction (High Pure RNA isolation kit–Roche), retrotranscription (Transcriber First Strand cDNA Synthesis –Roche–) and determination of gene expression by real-time PCR (FastStart Essential DNA Green Master–Roche Life Science–) were used for amplification of BAFF, APRIL and the three receptors (BAFF-R, TACI and BCMA).

Results

A total of 11 patients were evaluated. GAPDH was used as housekeeping gene. TACI and BAFF-R expression was found in 4 patients. Two of these patients also expressed APRIL. These patterns were not different according to pathological class (two patients had type IV LN, one patient had LN type I and one patient LN type V). The expression of APRIL was associated with the presence of
cylinders in the sediment. No patient expressed urinary BAFF or BCMA, different to pathological expression.

**Conclusion**

Despite evidence of BAFF expression in the glomeruli by immunohistochemistry, BAFF gene expression was not demonstrated in the urinary sediment. Instead, BAFF-R, TACI and APRIL were found in patients with LN and urinary sediment with cellularity, epithelial cells and cylinders.

**FACTORS RELATED TO MORTALITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background**

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with several complications associated with mortality: cardiovascular, kidney involvement, and infections, among others. Currently it continues to be a challenge to identify the factors that can predict the probability of death [1], [2]. The objective of this study is describe the factors related to death due to SLE.

**Method**

A description was made of a series of patients diagnosed with SLE whom died in a high complexity center in Colombia.

**Results**

After a follow-up of 6 years, 49 patients were included. The average age was 40.6 years (SD ± 17.4) at time of death, 44 were women (89.8%). They had a median of 4.5 years of duration of the disease. At the time of death, 89% of patients presented lymphopenia, 38% had active lupus nephritis and high SLEDAI of 19 (IQR 11-39) (Table 1). The main cause of death was progression of SLE in 22 patients (44.9%), especially associated with catastrophic antiphospholipid syndrome (CAPS), followed by bacterial infections (n = 15, 30.6%) and cardiovascular causes (n = 5, 10.2%) (Table 2). In a subgroup of patients with complete follow-up since diagnosis to death, a tendency to low C3 levels, increase in SLEDAI, use of cyclophosphamide and elevation of the steroid dose prior to the fatal outcome was observed (Table 3).

**Table 1. Characteristics of mortality in patients with SLE.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>49.6 ± 17.4</td>
</tr>
<tr>
<td>Female gender</td>
<td>44 (89.8)</td>
</tr>
<tr>
<td>Years of duration of SLE</td>
<td>4.5 (2-5)</td>
</tr>
<tr>
<td>Previous hospitalizations due to lupus flares</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18 (38.73)</td>
</tr>
<tr>
<td>1</td>
<td>24 (48.98)</td>
</tr>
<tr>
<td>2 or more</td>
<td>7 (14.29)</td>
</tr>
</tbody>
</table>

**Table 2. Causes of death in patients with SLE.**

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>N (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death associated to SLE</td>
<td>22 (44.9)</td>
</tr>
<tr>
<td>CAPS</td>
<td>6 (16.53)</td>
</tr>
<tr>
<td>Lupus activity</td>
<td>6 (16.24)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>3 (6.12)</td>
</tr>
<tr>
<td>Diffuse alveolar hemorrhage</td>
<td>2 (4.08)</td>
</tr>
<tr>
<td>Central nervous system vasculitis</td>
<td>2 (4.08)</td>
</tr>
<tr>
<td>Hemophagocytic syndrome</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Death for other causes</td>
<td>27 (55.1)</td>
</tr>
<tr>
<td>Infection</td>
<td>15 (30.6)</td>
</tr>
<tr>
<td>Sepsis, unspecified origin</td>
<td>9 (18.38)</td>
</tr>
<tr>
<td>Bacterial endocarditis</td>
<td>2 (4.06)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Disseminated histoplasmosis</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Necrotizing fasciis</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>5 (10.2)</td>
</tr>
<tr>
<td>Massive pulmonary thromboembolism</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Acute aortic syndrome</td>
<td>2 (4.06)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Retropertoneal hematoma</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Other causes</td>
<td>4 (8.16)</td>
</tr>
<tr>
<td>Hepatic cirrhosis</td>
<td>2 (4.06)</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>1 (2.04)</td>
</tr>
<tr>
<td>Collapse of unknown origin</td>
<td>3 (6.12)</td>
</tr>
</tbody>
</table>

* Mean ± SD
**Conclusion**

Active SLE and its direct complications continue to be the main cause of death in patients with SLE, especially in young women with lupus nephritis and association with CAPS.

**Background**

Primary angiitis of the central nervous system (PACNS) is a rare autoimmune disease characterized by the inflammation of central nervous system arteries without compromising any other organs, and without a primary cause. This disease predominately affects medium to small caliber arteries in the brain parenchyma, the spinal cord and the meninges, causing central nervous system (CNS) dysfunction (1). Its pathophysiology is not yet elucidated, but it appears to be mediated by antigen presentation to the T lymphocytes in the arterial wall (2). The aim of this study is to evaluate the immunological profile in two biopsies of patients with primary angiitis of the central nervous system.

**Method**

We describe a immunological profile in biopsies of primary angiitis of the central nervous system.

**Results**

An immunohistochemical study was done in 2 samples, revealing a leukocytic infiltration (CD45+) constituted almost entirely of T lymphocytes (CD3+) with a clearly higher prevalence of CD4+ cells (Figure 1), with no evidence of plasmatic cells (CD138 and CD38 markers were negative) and an absence of Treg Lymphocytes (negativity for CD25). Class II HLA expression was detected in 50% of the cells in both samples (Figure 2).

**Table 3. Subgroup of patients with SLE with full follow-up in the institution**

<table>
<thead>
<tr>
<th>Complete Follow up in the hospital (n=8)</th>
<th>Diagnosis</th>
<th>1 year before death</th>
<th>6 months before death</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency admissions due to lupus flares</td>
<td>0 (0-1)</td>
<td>0 (0-1.5)</td>
<td>0.5 (0-1.5)</td>
<td>1.5 (0-3.5)</td>
</tr>
<tr>
<td>Complement C3 (mg/dl) **</td>
<td>73.5 (57.8)</td>
<td>70 (48.15 - 77.5)</td>
<td>57.5 (45.76)</td>
<td>53.5 (41.6 - 100.7)</td>
</tr>
<tr>
<td>Complement C4 (mg/dl) **</td>
<td>111.5 (75.61)</td>
<td>11 (6.4 - 17.4)</td>
<td>9 (4.5 - 13)</td>
<td>10.2 (4.5 - 19)</td>
</tr>
<tr>
<td>SLEDAI**</td>
<td>6 (4-11)</td>
<td>8 (5-23)</td>
<td>11 (6-14.5)</td>
<td>19 (12-24.5)</td>
</tr>
<tr>
<td>Oral steroid dose (mg) **</td>
<td>10 (6.2-15)</td>
<td>12.5 (10-25)</td>
<td>15 (10-35)</td>
<td>46 (27.5-50)</td>
</tr>
<tr>
<td>Number of steroid pulses received **</td>
<td>0 (0-1.5)</td>
<td>0 (0-3)</td>
<td>0 (0-4)</td>
<td>3 (0-7)</td>
</tr>
<tr>
<td>Cyclophosphamide pulses, n (%)</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>2 (25)</td>
<td>3 (25.9)</td>
</tr>
<tr>
<td>Days hospitalized in general ward **</td>
<td>0 (0-3.5)</td>
<td>3 (0-11)</td>
<td>0 (0-27)</td>
<td>12.5 (2.5-35.5)</td>
</tr>
<tr>
<td>Days hospitalized in intensive care unit **</td>
<td>0 (0-4)</td>
<td>0 (0-2)</td>
<td>0 (0-4)</td>
<td>11.5 (4.38-5)</td>
</tr>
</tbody>
</table>

**Median (RIC)**

**057 - IMMUNOLOGICAL PROFILE IN BIOPSIES OF PRIMARY ANGIIITIS OF THE CENTRAL NERVOUS SYSTEM**

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J. Naranjo-Escobar 4 - 4Fundación Valle del Lili, Rheumatology, Cali, Colombia
L.A. Escobar 5 - 5Fundación Valle del Lili, Pathology, Cali, Colombia
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G. Tobón 7 - 7Fundación Valle del Lili, Rheumatology, Cali, Colombia
Conclusion

Our study suggests a T lymphocyte (with CD4 predominance) in patients with PACNS. The negligible presence of B lymphocytes and the absence of plasmatic cells implies this is not a humoral immunity mediated entity. Nevertheless, more complex studies are required to understand the pathophysiology of this disease and the cytokine expression pattern.

112 - PLASMAPHERESIS IN SYSTEMIC AUTOIMMUNE DISEASES

Background

Autoimmune diseases correspond to a diverse and complex group of pathologies with a broad clinical spectrum including autoantibodies production. Plasmapheresis is a valid option for the management of critical patients in addition to immunosuppressive treatment. The aim of this study is to describe the main clinical characteristics and outcomes of patients with systemic autoimmune diseases who received management with plasmapheresis.

Method

A descriptive study was carried out, including patients with systemic autoimmune diseases who received plasmapheresis.

Results

A total of 66 patients were included. The average age was 33.5 years, the majority of patients were female n=51 (77.27%). Forty (60.61%) patients had Systemic Lupus Erythematosus (SLE) followed by ANCA-associated vasculitis in 12 cases (18%). The main indication for plasmapheresis in SLE was diffuse alveolar hemorrhage (DAH) in 20 (30.3%) cases, followed by neurolupus in 9 (13.6%) (Table 1). Any patient died from plasmapheresis complications. The main adverse event was bleeding, without differences according to the type of plasmapheresis solution. The overall outcomes were improvement in 41 patients (62.12%) (Table 2).

Conclusion

Plasmapheresis is a safe and effective procedure in patients with severe autoimmune diseases, despite this there is a lack of studies that provide more information about the number of sessions and type of plasma exchange that should be used.

Anti–Carbamylated Protein Antibodies Are Present in first-degree relatives of rheumatoid arthritis individuals and they are associated with clinical signs of arthritis

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Background and Objective:

The specific autoimmune response in Rheumatoid Arthritis (RA) mostly targets by post-translationally modified proteins or peptides; one of these modifications is the carbamylation which leads to the generation of anti-carbamylated protein antibodies (anti-CarP). Some evidence shows that anti-CarP antibodies could have an influence on radiological progression in RA. Several studies in RA focused on the pre-clinical phases of the disease in asymptomatic individuals with higher risk to develop RA such as first-degree relatives (FDR). The aim of this study was to determine whether anti-CarP antibodies are already present in healthy individuals and FDR and how the appearance of anti-CarP antibodies relates to adipokines, ACPA, IgM-RF and rheumatological clinical symptoms.

Methodology

In total, 118 FDR and 118 healthy individuals paired by age and gender were included. Rheumatological (clinical and biomarkers) and periodontal assessment was performed. Inclusion criteria for FDR were Colombian individuals first-degree relatives of RA patients, according to EULAR recommendations of 2012. The healthy control group were individuals between 18 and 65 years of age under working or environmental circumstances similar to patients. The exclusion criteria were infectious process, neoplasia, diabetes, antibiotic treatment, periodontal treatment in the last 6 months and pregnant or breastfeeding woman. An Enzyme-linked immunosorbent assay was used to measure anti-CarP antibodies based on fetal calf serum as antigen (Inova Diagnostics), as well as to measure ACPAs levels (QUANTA Lite®CCP3.1 IgG/IgA, Inova Diagnostics). High-sensitivity serum CRP was determined (Siemens®) by chemiluminescence, ESR (Test 1 THL Ali FAX®), Rheumatoid factor (RF-Spinreact®) and HLA-DRB1 (MILLIPLEX® MAP, HADK1MAG61K03on xMAP®) based in Luminex technology were evaluated.

An association analysis was performed to evaluate the relationship between anti-CarP levels and rheumatologic conditions in FDR and a logistic regression model was made to confirm these associations. All the analyses were done with a level of significance of 95%. All individuals signed informed consent approved by institutional ethics committee code 2015-047.

Table 1. Sociodemographic variables in controls and FDR subjects

<table>
<thead>
<tr>
<th></th>
<th>Control (n=118)</th>
<th>FDR (n=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41±12.2</td>
<td>40.2±12.5</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>85 (72.0%)</td>
<td>86 (72.9%)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>37 (31.4%)</td>
<td>48 (40.7%)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>14 (11.9%)</td>
<td>26 (22.2%)</td>
</tr>
<tr>
<td>Former Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>39 (33.1%)</td>
<td>27 (22.9%)</td>
</tr>
<tr>
<td>Passive Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>17 (14.4%)</td>
<td>18 (15.3%)</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal weight</td>
<td>78 (66.1%)</td>
<td>68 (57.6%)</td>
</tr>
<tr>
<td>Overweight*</td>
<td>34 (28.8%)</td>
<td>44 (37.3%)</td>
</tr>
<tr>
<td>Obesity*</td>
<td>6 (5.1%)</td>
<td>6 (5.1%)</td>
</tr>
</tbody>
</table>

Table 2. Anti-CarP antibodies and Rheumatological parameters in Controls and FDR subjects

<table>
<thead>
<tr>
<th></th>
<th>Control (n=118)</th>
<th>FDR (n=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CarP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive*</td>
<td>18 (15.3%)</td>
<td>31 (26.3%)</td>
</tr>
<tr>
<td>Leptin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High level*</td>
<td>15 (12.7%)</td>
<td>31 (26.3%)</td>
</tr>
<tr>
<td>ESR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive hsCRP</td>
<td>19 (16.1%)</td>
<td>16 (13.6%)</td>
</tr>
<tr>
<td>Positive RF</td>
<td>26 (22.0%)</td>
<td>32 (27.1%)</td>
</tr>
<tr>
<td>High Positive</td>
<td>12 (10.2%)</td>
<td>16 (13.6%)</td>
</tr>
<tr>
<td>Painful joint</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence*</td>
<td>28 (23.7%)</td>
<td>46 (39.0%)</td>
</tr>
<tr>
<td>Swollen joint</td>
<td>5 (4.2%)</td>
<td>19 (16.1%)</td>
</tr>
</tbody>
</table>

Results

In the FDR-group, 72.9% were female with a mean age of 40.2±12.5 years, 22.2% were current smoker, leptin high in 26.3%, 16.9% APCA and 4.2% IgM-RF positives and 26.3% were anti-CarP positive, 19.5% were single-positive (Only Anti-CarP (+)), 6.8% double-positive (Anti-CarP (+) and RF/APCA (+)) and none were triple positive. In control individuals, 72.0% were women with an average age of 41.0 ± 12.2 years, leptin high in 12.7% (p = 0.004), positive RF in 2.5% (p = 0.710), ACPA 6.8% (p = 0.013) and
anti-CarP 15.3% were positive ($p = 0.027$): 12.7% single-positive, 2.5% double positive, and no one was triple positive. Likewise, in positive individuals, 16.3% had CRP >3mg/L ($p=0.030$), 12.2% had >1 swollen joint ($p= 0.053$), 8.8% had >1 painful joint of which 38.8 and 78.9% were FDR respectively. In FDR, anti-CarP positivity was significantly associated with >1 swollen joint adjusted for increased leptin levels (OR= 2.84, CI 95% 1.20-6.71,$p= 0.017$).

**Figure 1. Anti-Carp antibodies distribution among Controls and FDR subjects**

* $p< 0.05$ among groups and intra-group analysis by Chi Square test

**Figure 2. Painful and swollen joints distribution in positive subjects for anti-CarP antibodies**

* $p< 0.05$ among groups and intra-group analysis by Nested Chi Square test. For this analysis was made only with those subjects who shows positive levels to anti-CarP antibodies ($n=49$, see table 2).

**Conclusions**

The prevalence of anti-CarP antibodies in FDR was similar to previous reports of patients who fulfilled the criteria for RA in their pre-clinical phase. Our data also supports the observation that anti-CarP antibodies are more frequent in FDR compared to healthy individuals and they can be present in both ACPA-positive and ACPA-negative FDRs. The presence of anti-CarP antibodies can have clinical value in the FDR.

Disclosure of Interest: None declared.


Conferencia presentada en Brasil. El impacto potencial de los biosimilares para generar acceso a los pacientes con enfermedades inflamatorias crónicas.

Dr. Carlos Enrique Toro
Mira el vídeo de la conferencia ingresando al link:


Disclosure of Interest: None declared.
Trabajos presentados por miembros Asoreuma en EULAR 2018

Medical or Research Professionals/Clinicians

Topic area: Clinical topics by area of research

Topic: 32. Epidemiology, risk factors for disease or disease progression

Submission N°: EULAR18-3156

ANTI CARBAMYLATED PROTEIN IN HEALTHY SYSTEMIC FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS INDIVIDUALS: RELATION WITH CLINICAL SIGNS OF ARTHRITIS

C. Romero-Sanchez* 1, 2, J. De Avila2, L. Chila2, W. Bautista-Molano1, 2, J. M. Bello-Gualtero1 1Department of Rheumatology and Immunology, Hospital Militar Central, Bogotá, Colombia, 2Unit of Oral Basic Investigation, Universidad El Bosque, Bogotá D.C., Colombia

My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No
Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background:
Association studies in rheumatoid arthritis (RA) have been focused in the pre-clinical phases of the disease in asymptomatic individuals with higher risk to develop RA such as first-degree relatives (FDR). A new group of autoantibodies directed against carbamylated proteins (anti-Carp) have been discover in RA.

Objectives:
To investigate the levels of anti-Carp in FDR and establish their association with the state of rheumatic condition and compare these variables with a control group of healthy individuals from general population.

Methods:
In total, 118 FDR and 118 healthy controls matched by age and gender were included. Rheumatologic (clinical and markers) and periodontal assessment was performed. Individuals selected were over 18 and less than 65 years old were studied in Bogota-Colombia. A complete medical history related to RA was obtained by rheumatologist. They were assessed by two periodontists calibrated. Cancer, autoimmune disease, recent infection, lactation or pregnancy, use of antibiotics in the last three months, diabetes, edentulous, periodontal and orthodontic treatment in the last six months, were exclusion criteria. Anti-carbamylated-fetal calf serum protein by chemiluminescence (Inova Diagnostics, San Diego), RF (Rheumatoid Factor, Spinreact®), ACPAs IgG/IgA (Inova, Diagnosis®), Enzyme-linked immunosorbent assay for leptin, Adiponectin based on Luminex xMAP® technology, high-sensitivity CRP and IL-6 (Siemens®) by chemiluminescence and ESR were evaluated. An association analysis was performed to evaluate the relationship between anti-Carp levels and rheumatologic conditions using Chi square and Fisher test. Logistic regression model was performed to confirm these associations. All the analyzes were performed with a level of significance of 95%.
Results:
In the FDR-group, seventy three percent were female with a mean age of 40.19±12.47 years, 22.2% were current smoker, leptin high in 26.27% and 4.23% and 16.9%, had positive RF and ACPAs respectively. Anti-Carp in 26.3%; Among the controls, 70.97% were women, with an average age of 41.0 ± 12.2 years, leptin high in 12.7% (p=0.004), positive RF in 2.5% (p=0.71), ACPA 6.8% (p= 0.013) and anti-Carp 15.3(p=0.027); in the general group 20.8 % were positive (49/236) for anti-Carp, of which 63.3% are FDR (OR=2.02 IC 95% 1.03-3.96, p=0.04), Likewise, a greater frequency of painful joint (62.2%) p = 0.008 and swollen joint (79.2%) (OR= 4.35 CI 95% 1.5-12.36,p =0.006) were observed. The model designed for FDR showed a significant association between anti-Carp positive with at least 1 swollen joint adjusted to the presence of leptin levels above the moderate range (OR= 2.84, CI 95% 1.20-6.71,p= 0.017).

Conclusions:
The Research effort aimed at the “risk” phases of RA has increased. That is, before the development of clinical signs of arthritis, to identify those individuals and modify environmental factors and pharmacological intervention. The findings show us a significantly higher frequency of anti-Carp in a cohort of FDR of RA patients compared to healthy controls no associations were found with other autoantibodies but a very interesting way with signs of early inflammation.

References:

Acknowledgements:
Disclosure of Interest: None declared

Medical or Research Professionals/Clinicians
Topic area: Clinical topics by area of research

Topic: 32. Epidemiology, risk factors for disease or disease progression

Submission N°: EULAR18-3162

SYSTEMIC FACTORS THAT AFFECT THE PROGRESSION OF PERIODONTAL DISEASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No
Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background:
An association between Rheumatoid arthritis(RA) and Periodontal Disease(PD) has been reported. However, predicting factors of PD progression in patients with eRA are lacking.

Objectives:
To establish the predictive factors for progression of PD in patients with eRA including clinical and serological active scores of RA and status of PD.

Methods:
This cohort study evaluated the progression of PD at 280 inter-proximal dental sites in 28 patients within 2 years of diagnosis with eRA and they were evaluated to establish their progression through one year of follow-up. Adult patients were classified according to the 2010 ACR and the EULAR criteria. Periodontal diagnosis was established based on the AAP and the CDC and Prevention criteria. Serum markers of RA (rheumatoid factor, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and anticitrullinated protein antibodies (APCAs) were evaluated, disease activity was assessed by disease activity score (DAS28ESR) AND the simplified disease activity index (SDAI). Plaque index, gingival index, pocket depth, and clinical attachment loss (CAL) were evaluated at baseline and at one year follow-up. Data were analyzed to establish predictive generalized linear mixed models (GLMM) for clinical attachment loss progression at each site with ≥2 or ≥3mm CAL.

Results:
The patients included had an average age of 47.5±12.69 and 75% were women. The comorbidity given by the
habit of smoking actively occurred only in 1% of patients. The 35.71% had levels of ESR >20 mm/h and 39% APCA positive while in 60.71% had CRP ≥3 mg/L and 67.86% of patients had a positive FR. Regarding the indices of activity of the disease, DAS28-PCR >2.6 was found in 67.86% of the patients and SDAI scale >3.3 in 75%. 71.43% of the patients were being treated with DMARD and corticoid therapy. 71.43% of patients had a diagnosis of periodontitis. CAL ≥ 2 mm and ≥ 3 mm was observed at 15% and 7.5% of dental sites, respectively. Factors associated with CAL in dental sites were: age, ESR, RF, DAS28, treatment with DMARD, corticoids, periodontal pocket, CAL and percentage of CAL >5mm, plaque index, gingival index and hemorrhage. Variables RA associated with activity such as CRP, DAS28, and SDAI showed a similar behavior and they were more frequently associated in periodontal progressive sites. The principal predictive periodontal factors were the percentage of sites with CAL >5mm and high gingival inflammation at baseline. Patients receiving combined treatment with disease-modifying antirheumatic drugs (DMARD) and corticosteroids exhibited less CAL. The predictive values of the GLMM for CAL of ≥3 and ≥2mm were 98% and 82%, respectively.

Conclusions:
Systemic factors as disease activity score and serum biomarkers such as baseline periodontal status are associated with periodontal disease progression in early RA patients. It is known that the very low daily dose prednisolone in combination DMARD therapy substantially decreased radiographic progression and it could influence periodontal disease progression too in patients with RA in early stages of the disease References: Bello-Gualte JM, et al. J Periodontol. 2016;87:346.

References:

Disclosure of Interest: None declared

Medical or Research Professionals/Clinicians

Topic area: Basic and translational research
Topic: 4. Cytokines and inflammatory mediators

Submission N°: EULAR18-3166

LEPTIN LEVELS, OVERWEIGHT AND P GINGIVALIS PRESENCE CONTRIBUTE TO THE MECHANISM OF SYSTEMIC INFLAMMATION IN FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS INDIVIDUALS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No

Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background: Association studies in rheumatoid arthritis (RA) have been focused in the pre-clinical phases of the disease in first-degree relatives (FDR). Data has shown that obesity, ACPA and the periodontal condition may modulate the severity and the clinical presentation of RA.

Objectives: To investigate the levels of adipokines in FDR and establish their association with the state of rheumatic and periodontal condition.

Methods: 124 FDR individuals and 124 healthy controls matched by age and gender were included. Rheumatologic (clinical and serological markers) and periodontal assessment was performed. It was quantified the adiponectin, leptin, IL6 levels. HLA-DRB1 was determined. Serum markers of RA (rheumatoid factor, erythrocyte sedimentation rate, C reactive protein (CRP), and APCA. P gingivalis and IgG1/IgG2 P gingivalis were measured. Radiographs of hands and feet were evaluated the Sharp-van der Heijde score. An association analysis was made to evaluate the relationship between adipokines and periodontal, rheumatologic conditions using X2 test, and logistic regression model was performed to confirm this associations.

Results:
In FDR group, 71.77% were women with a mean age of 39.24±12.22 years. 37.09% had overweight and 4.83%...
IMPACT OF SERUM ADIPOKINES IN EARLY STAGES OF RHEUMATOID ARTHRITIS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No
Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background:
Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease. Adipose tissue is regarded as an active endocrine organ producing adipokines such as leptin and adiponectin, and some proinflammatory cytokines which have proinflammatory properties that account for chronic low-grade systemic inflammation.

Objectives:
To investigate the levels of adipokines in eRA and establish their association with the state of rheumatic condition.

Methods:
Cross sectional study was conducted. 51 patients with eRA according to the ACR/EULAR 2010 criteria and 51 healthy controls matched by age and gender, were included. A complete medical history was obtained. Adiponectin levels measured by Luminex technology, IL6 by chemiluminescence and leptin by Enzyme-linked immunosorbent assay. Serum markers of RA such as rheumatoid factor, erythrocyte sedimentation rate(ESR), C reactive protein(CRP), and anticitrullinated protein antibodies-APCA IgG/IgA. Disease activity was evaluated by DAS28CRP, DAS28ESR, CDAI, SDAI and RAPID3, the functional status using Multidimensional health assessment questionnaire(MDHAQ) and radiological status by Simple Erosion Narrowing Score(SENS). An association analysis was made to evaluate the relationship between adipokines levels and rheumatologic conditions using X2 test, Mann Whitney and logistic regression model was performed to confirm this associations. All the results were

Conclusions:
High levels of leptin, the presence of P gingivalis and swollen joints may be relevant conditions associated with the development of RA in FDR. Leptin levels and overweight can modulate the production of acute phase proteins in this group of individuals contributing to the mechanism of systemic inflammation. The clinical implications of our findings propose regulated exercise programs, oral hygiene, and weight control in FDR.


Disclosure of Interest: None declared

Medical or Research Professionals/Clinician

Topic area: Clinical topics by disease
Topic: 12. Rheumatoid arthritis - comorbidity and clinical aspects

Submission N°: EULAR18-3168

had obesity. Among the controls, 70.97% were women, with an average age of 39.31±12.30 years. 27.41% had overweight and 4.83% had obesity. Leptin levels were found in 37.66% vs 18.42% in controls (p=0.002). In FDR, 60.48% had periodontal disease of which 62.66% moderate, P gingivalis in 62.10%. In controls, 55.64% had periodontal disease, of which 63.76% moderate with 42.74% P gingivalis positive (p=0.002). In the FDR, radiography of hands and feet showed in 25.28% of them had some alteration, 68.18% had ≥1 erosion, 45.45% had ≥1 joint space narrowing and in 6.89% juxtaarticular osteopenia. An association of leptin levels with the low economic level was found p=0.006 and high levels of leptin in individuals with BMI≥30 p=0.031. IL6 was found to be associated with severity of periodontal disease, with higher levels being found frequently in mild periodontal disease p=0.039. The condition of FDR was significantly associated with high leptin levels adjusted for presence of swollen joints, presence of P gingivalis and low levels of IL6 OR=2.57, 95% CI (1.14–5.95). In this group, the individual with leptin at moderate levels adjusted with BMI>25, has a lower probability of presenting CRP>3mg/L OR=0.43 95% CI (0.20–0.90).

Conclusions:
High levels of leptin, the presence of P gingivalis and swollen joints may be relevant conditions associated with the development of RA in FDR. Leptin levels and overweight can modulate the production of acute phase proteins in this group of individuals contributing to the mechanism of systemic inflammation. The clinical implications of our findings propose regulated exercise programs, oral hygiene, and weight control in FDR.


Disclosure of Interest: None declared

Medical or Research Professionals/Clinician

Topic area: Clinical topics by disease
Topic: 12. Rheumatoid arthritis - comorbidity and clinical aspects

Submission N°: EULAR18-3168
performed with a level of significance of 95%.

**Results:**
In the eRA group, 80.39% were women, the mean age was 48.54±10.93 years. 37.25% had overweight and 13.72% had obesity. Among the controls, 80.39% were women, with the mean age of 48.55±11.07 years. 27.45% had overweight and 5.88% had obesity. 45.09% had moderate activity and 17.64% had high activity by DAS28ESR. High leptin levels were found in 64.7% vs 23.5% in healthy controls (p=0.001). High adiponectin levels were found associated with BMI<25 (p=0.017) and high leptin level to BMI>25 (p=0.038) and disease activity by RAPID3 (p=0.039). The presence of joint space narrowing in hands was associated with low adiponectin levels (p=0.044). The association of leptin levels >1.67 ng/mL with the diagnosis of RA was maintained in the model adjusted for the presence of P gingivalis, DAS28-ESR, CRP >3 mg/l, economic status and BMI >30, OR = 2.79 (1.54-5.07). The presence of high leptin and IL6 levels and low level adiponectin at the same time were more frequently found in the female gender (p=0.047), primary schooling (p=0.050), BMI >30 (p=0.023), patients with radiological damage SENS >3 (p=0.047) and were found associated at the same time to MDHAQ >3, BMI >25 and RAPID3 >12 (OR 5.03 95% CI 1.05-24) adjusted to clinical variables.

**Conclusions:** The role of adipokines as the leptin could be considered to be the bridge between immune tolerance, metabolic function, and autoimmunity and suggests the possibility to use circulating levels of adipokines as potential biomarkers of disease activity and functional status in early stage of rheumatoid arthritis.


**Disclosure of Interest:** None declared

**Medical or Research Professionals/Clinicians**
**Topic area:** Basic and translational research
**Topic:** 6. Rheumatoid arthritis - etiology, pathogenesis and animal models

**Submission N°:** EULAR18-3169

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**ADIPONECTIN COULD BE A MEDIATOR OF THE PRESENCE OF P GINGIVALIS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No

Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

**Background:** Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease characterized by joint destruction, deformity, lower functional status and decrease in life expectancy. The Porphyromonas gingivalis (P. gingivalis) has been reported to be significantly associated with RA. The adipokines are suggested to be a common link between periodontitis and RA.

**Objectives:** To determine the association between serum adipokines levels and presence of P gingivalis in patients with early rheumatoid arthritis (eRA) compared to healthy individuals.

**Methods:** A cross sectional study was conducted. Patients with the diagnosis of (eRA) according to the ACR/EULAR 2010 criteria were studied in Bogota-Colombia. A complete medical history related to RA was obtained. Adiponectin levels measured by Luminex technology (MILLIPLEX® MAP®, IL6 by chemiluminescence (Immulite 1000, Siemens®) and leptin quantification by ELISA (Diasource®, high-sensitivity CRP (hs-CRP) (Immulite 1000, Siemens®) and ESR (Test 1 THL Ali FAX®), and the detection of periodontopathic bacteria was carried out by qPCR from subgingival plaque samples. Cancer, autoimmune disease, infection, antibiotic use, diabetes, orthodontics treatment were exclusion criteria. An association analysis was made to evaluate the relationship between
adipokines levels and periodontal, rheumatologic conditions using X2 test, Mann Whitney test and logistic regression model was performed to confirm this associations. All the results were performed with a level of significance of 95%.

Results:
A total of 51 patients with eRA and 51 healthy individuals were matched by age and gender. The mean age in RA patients was 48.54±10.93 years, 80.39% were female, between RA patients, 17.64% were in high activity and 27.45% in remission by DAS 28-ESR. 45.1% had APCA> 20UE. 37.25% were overweight and 13.72% were obese. 82.35% of patients had treatment, of which 80.39% received treatment with conventional disease modifying therapy, being methotrexate the most frequent one in 86.8%. In turn, 64.7% and 51% had high leptin and adiponectin levels respectively. An association of high adiponectin levels was found with Body Mass Index-BMI <25 (p = 0.017). The presence of P Gingivalis in RA patients was 78.4% and in healthy individuals was 45.09% p=0.001. The adiponectin levels >47755pg/ml were found associated with the absence of P gingivalis (OR=0.078 95% CI 0.01-0.62) adjusted an ever smoking history of cigarette smoking, Body Mass Index >30 and high level of leptin and IL6.

Conclusions:
The adiponectin plays an anti-inflammatory role in the pathophysiology of several chronic inflammatory diseases and it has been reported to inhibit LPS-induced NFκB nuclear translocation and to affect other LPS-triggered pathways. To promote the weight control in eRA could be to prevent the oral infection.


Disclosure of Interest: None declared

Medical or Research Professionals/Clinicians

Topic area: Basic and translational research
Topic: 1. Genomics, genetic basis of disease and antigen presentation

Submission N°: EULAR18-3171

LOCATION AND INTERACTION OF IGG HYPERVERSITABLE REGIONS WITH PORPHYROMONAS GINGIVALIS PEPTIDYLARGININE DEIMINASE CITRULLINATED PEPTIDES, A HIGHLIGHT TO UNDERSTAND THE ASSOCIATION MODEL OF RHEUMATOID ARTHRITIS AND PERIODONTAL DISEASE: IN SILICO ANALYSIS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No
Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background:
IgG antibodies against citrullinated peptides are one of the most specific biomarkers used in the classification of the disease. The relationship between RA and periodontal disease is based on the process of citrullination. The enzyme in the most important bacteria related with periodontitis ( Porphyromonas gingivalis) the Peptidylarginine Deiminase (PPAD) modify arginine residues to citrulline.

Objectives:
To model in silico the binding of PPAD peptides with the hypervariable regions of IgG.

Methods: One PPAD peptide with 15 residues was selected in silico by its recognition by B cells (Bcepred y ABCpred) and T lymphocytes (ProPred, MHCPred). The peptide arginines were changed in silico by citrulline (Cit) with the ACD/ChemSketch software, obtaining four different peptides, natural, Arg1 changed, Arg1-Arg8 changed and a random sequence. The 3D peptide modeling was obtained using PEP-FOLD Server and the 3D structure of
variable domains of the heavy and light chain of IgG was obtained with the SwissModel. The amino acids of the hypervariable regions capable of interacting were defined using ConSurf Server. The peptides and variable domains were prepared using Openbabel. Docking models were performed by Patchdock and PyMOL tool was used to rendering the structural complexes obtained.

Results:
The 3D structure of IgG variable domains had a QMEN6 z-score <1. Modeling of the topological disposition of the amino acids was obtained and the interaction scores between the four peptides and light and heavy chain hypervariable regions were high, although the better score was in the natural peptide and light chain interaction. The heavy chain showed also a high score during the in silico interaction with the Cit1-Cit8 modified peptide. The approximate interface area of the receptor-ligand complex and the contact atomic energy (ACE) between the ligand and the receptor revealed the energy required for the interaction allowing its stability. The PPAD-IgG complexes showed the atomic contact maps in which the heavy chain hypervariable region contacted seven amino acids in all four peptides while only six contacts occurred between light chain and the peptides. The model showed the interactions between light chain and natural peptide (Arg1 with Gly100, Arg8 with Glu1) and for Cit1-Cit8 peptide, Cit8 interact with Thr10 (Cit1 has no contact). Regarding the heavy chain, Arg1 of natural peptide interacted with Trp47 while for Cit1-Cit8 peptide were Cit1 with Lys43 and Cit8 with Pro40.

Conclusions:
The in silico model shows bacterial PPAD peptides with and without citrullination interact with the hypervariable regions of human IgG. The citrulline residues modify the 3D structure influencing the contact area with the heavy and light chain variable regions. Peptide with modifications of two arginine residues by citrulline presented a high interaction score indicating that may have an effective recognition for IgG.

Disclosure of Interest: None declared

Medical or Research Professionals/Clinicians

Topic area: Basic and translational research
Topic: 1. Genomics, genetic basis of disease and antigen presentation

Submission N°: EULAR18-3174
ASSOCIATION OF DICKKOPF1-1 POLYMORPHISMS WITH RADIOLOGICAL DAMAGE AND PERIODONTAL DISEASE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2018: No
Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

Background: Rheumatoid arthritis (RA) is an autoimmune disease that primarily affects the joints but also has extra-articular manifestations such as Periodontal Disease (PD). The Dickkopf-1 (DKK-1) may have an active role in the regulation of bone biology and patients with RA that carry genetic variants of DKK-1 have greater bone damage.

Objectives:
To investigate the polymorphisms of DKK-1 in patients with early RA (eRA) and its association with some rheumatic, radiological and periodontal variables.

Methods:
A cross-sectional study in 63 patients with eRA according to the ACR/EULAR 2010 criteria and PD based on the AAP/CDC and Prevention criteria. Serum markers rheumatoid factor (RF), erythrocyte
sedimentation rate (ESR), C reactive protein (CRP) and anticitrullinated peptide antibodies (APCAs) were evaluated. Patients selected were over 18 and less than 65 years old and were on treatment with conventional disease modifying antirheumatic drugs. Rheumatic activity was assessed by scales disease activity score 28 and simplified disease activity index. Radiographs of hands and feet were evaluated using the Sharp-van der Heijde (SvH) and Simple Erosion Narrowing Scores (SENS). DKK-1 polymorphisms as rs1896368, rs1896367 and rs1528873 were determined using the High resolution Melting technique (Bio-Rad®). A bivariate analysis was performed to determine the variables associated between polymorphism to the presence of radiological and activity scores, diagnosis and severity of PD. A regression model was performed to confirm these associations.

Results:
The mean age was 48.57 ± 11.35 years, and 76.7% were female. 11.7% had a body mass index >30 kg/m². 35% had an ESR>20 mm/h, and 56.7% had elevated CRP. RF>20 was observed in 61.7% of patients as were ACPAs>20 in 43.3% of them. 30%, 42% and 1.6% of patients were homozygous for polymorphism rs1896367, rs1896368 and rs1528873 respectively. Individuals heterozygous for polymorphism rs1896367 had more frequent erosions (p=0.026) and joint space narrowing (JSN) (p=0.005) in the feet, and consequently higher SHS scores (p=0.016). These patients also had higher SENS scores (p=0.001) and more frequent erosions (p=0.02). In contrast, patients homozygous for polymorphism rs1896368 had less frequent JSN in hands and feet as assessed by SHS, as well as less presence of erosions based on the SENS scale. These findings were validated in the regression model (OR: 0.04, 95% CI:0.00–0.93;p<0.05).

Finally, the presence of PD was associated with the homozygous expression of polymorphism rs 1896367 (p=0.009) and the heterozygous expression of polymorphism rs1696368 (p=0.033).

Conclusions:
DKK-1 polymorphisms can be associated with the presence of bone damage in patients with eRA and it could affect periodontal outcomes. While polymorphism rs1696367 seems to be associated with greater radiological compromise, polymorphism rs1696368 confers protection against bone damage in Colombian eRA patients.


Disclosure of Interest: None declared

De los Trabajos presentados en EULAR 2018 destacamos la aceptación para presentación oral (3166) el cual fue el único por Colombia y en esa modalidad y otros dos en formato poster (3168 y 23171) como destacados los demás fueron aceptados en formato online.