Multicentric Prevalence Study of Anti-P Ribosomal Autoantibodies in Juvenile Onset Systemic Lupus Erythematosus Compared With Adult Onset Systemic Lupus Erythematosus

Cecilia N. Pisoni, Sebastián Andrés Muñoz, Carolina Carrizo, Micaela Cosatti, Analía Álvarez, Diana Dubinsky, Eleonora Bresan, Ricardo Russo, Ezequiel Borgia, Mercedes García, Pierina Sansinanea, Maria Cristina Basta, Maria Agustina D’Amico, Juan Carlos Barreir, Eliana Lancioni, Enrique Soriano, Carmen de Cunto, Ana Beron, Alicia Eimon

A R T I C L E   I N F O

Article history:
Received 18 August 2013
Accepted 6 March 2014
Available online 5 June 2014

Keywords:
Systemic lupus erythematosus
Anti-P ribosomal

A B S T R A C T

Objective: To investigate the prevalence and associations with clinical manifestations of anti-P ribosomal antibodies in patients with juvenile-onset and adult-onset systemic lupus erythematosus (SLE).

Methods: Clinical and serological data of 30 patients with juvenile-onset SLE (age at onset younger than 16 years) were compared with data of 92 patients with adult-onset SLE. Symptoms occurring during the entire disease course were considered. Anti-P ribosomal antibodies were tested by ELISA.

Results: Anti-P ribosomal antibodies were found significantly more often in pediatric-onset SLE patients (26.7% vs 6.5%; OR=5.21 [95% CI=1.6–16.5], P=0.03). Alopecia (OR=10.11, 95% CI=1.25–97) and skin rash (non-discoid) (OR=4.1, 95% CI=1.25–13.89) were significantly associated with anti-P ribosomal antibodies.

Conclusion: Anti-ribosomal P antibodies are more often found in patients with juvenile SLE. Alopecia and skin rash were the only clinical manifestations associated with anti-ribosomal P antibodies.

© 2013 Elsevier España, S.L.U. All rights reserved.

Estudio multicéntrico de prevalencia de anticuerpos antirribosomal P en lupus eritematoso sistémico de comienzo juvenil comparado con lupus eritematoso sistémico del adulto

R E S U M E N

Objetivo: Determinar la prevalencia y correlación clínica de los anticuerpos antirribosomal P en lupus eritematoso sistémico (LES) juvenil y compararlo con LES del adulto.

Métodos: Se incluyeron en el estudio 30 pacientes con LES juvenil y 92 pacientes con LES del adulto. Consideramos LES de comienzo juvenil a todos aquellos pacientes que comenzaron su enfermedad antes de los 16 años. Se consideraron las manifestaciones clínicas y serológicas que presentaron los
pacientes desde el diagnóstico hasta el momento de inclusión en el estudio (manifestaciones acumuladas). El anticuerpo antirribosomal P fue evaluado mediante la técnica de enzimo-immunoensayo (ELISA).

**Resultados:** La presencia de antirribosomal P fue significativamente mayor en el grupo de pacientes con LES juvenil comparado con LES del adulto (26,7% vs. 6,5%; OR = 5,21 [95% CI = 1,6–16,5], p = 0,003). Las exacerbaciones (OR = 10,11; 95% CI = 1,25–97) y rash cutáneo (no disconde) (OR = 4,1; 95% CI = 1,25–13,89) fueron las únicas manifestaciones clínicas que se asociaron de forma estadísticamente significativa con la presencia del anticuerpo antirribosomal P.

**Conclusión:** Este estudio confirma un mayor prevalencia de anticuerpos antirribosomal P en pacientes con LES juvenil. La alopecia y el rash cutáneo fueron las únicas manifestaciones clínicas asociadas a la presencia de antirribosomal P.

© 2013 Elsevier España, S.L.U. Todos los derechos reservados.

---

**Introduction**

Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect virtually any organ or system, manifested clinically by exacerbations and remission periods and serologically characterized by the presence of anticu

**Clinical Data**

A specific questionnaire was designed for the study, where clinical data based on the examination and review of the clinical history of the patient was collected. Clinical manifestations presented by patients from diagnosis to the time of inclusion in the study (cumulative events) were detailed. The following events were considered: Discoid rash, oral ulcers, photosensitivity, alopecia, malar rash, Raynaud’s phenomenon, leukopenia, hemolytic anemia, thrombocytopenia, serositis, arthritis, seizures, neuropathy, transverse myelitis, acute confusional state, glomerulonephritis, vasculitis, dry mouth, dry eyes. Information was obtained on treatments received from the time of diagnosis of the disease to inclusion in the study. Activity was calculated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) at the time of sample collection. Antibody results were also recorded during the patient’s history (ANA, anti-DNA, anti-Ro/SSA, anti-La/SSB, anti-Sm, and anti-nRNP).

All participants signed informed consent; the study was conducted after approval by the ethics committees of each institution.

**Specimen Collection and Laboratory Determinations**

Blood samples for determination of antibodies were taken in the participating centers, and were analyzed centrally in the CEMIC laboratory of Immunology and Rheumatology. Measurement of anti-Ro/SSA, anti-La/SSB, anti-Sm, and anti-nRNP antibodies was performed by double-diffusion technique. The anti-P ribosomal antibodies were evaluated by enzyme-linked immunosorbent assay (ELISA) using as antigen, a purified protein from bovine and/or rabbit thymus (ImmunoVision, Inc.) absorbed at 0.5 μg/well (Maxisorp polystyrene plate; Nunc). Samples were considered positive when ≥ 1 U. Measurement of anti-Ro/SSA, anti-La/SSB, anti-Sm, and anti-P ribosomal antibodies nRNP was performed simultaneously on all samples.

**Statistical Analysis**

Qualitative variables are presented as numbers and percentages, and quantitative variables as mean/median and standard deviation/minimum and maximum values. To determine an association, we employed chi-square ($\chi^2$) or Fisher exact tests. To quantify the strength of association we used odds ratios (OR) and their 95% confidence intervals (95% CI). For analysis of the SLEDAI in patients with positive and negative anti-P ribosomal antibodies and between adult vs juveniles, Wilcoxon and Mann-Whitney’s tests were used. Significance was considered as a P<0.05. Statistical analysis was performed using the Epi Info statistical package™ 7 (Centers for Disease Control and Prevention [CDC]).
Results

Demographics

Twenty-four patients (80%) in the youth group and 81 (88%) adults had Caucasian ethnicity. Two (6.7%) of the patients with juvenile SLE and 6 (6.5%) patients in the adult SLE group were males. The mean age at diagnosis in patients with juvenile SLE was 12.67±3.56 and for adults, 30±11.46 years. The mean age of patients at the time of inclusion in the study was 22.9±8.4 and 39.76±12.37 years for the group of juvenile and adult SLE respectively; the average duration of the disease at the time of inclusion in the study was 10.63±7.16 years in youths and 9.36±7.75 years in adults.

Clinical manifestations and treatment received:

The prevalence of different clinical manifestations in both groups (adults and juveniles) is detailed in Table 1. Malar rash (OR=3.9, 95% CI=1.1–14.25), photosensitivity (OR=2.64, 95% CI=1.03–6.76), vasculitis (OR=5.33, 95% CI=1.7–16.0), non-discoid rash (OR=3.0, 95% CI=1.09–8.4) and neurological involvement; seizures (OR=3.85, 95% CI=1.12–13.22) and psychosis (OR=4, 95% CI=1.15–13.79) were more frequently found in juvenile SLE. Five adult patients developed neurological manifestations (not in the ACR criteria); cognitive impairment in 3 patients, peripheral sensory neuropathy of the lower limbs in 1 patient and 1 patient with acute confusional state. No patient developed transverse myelitis or multiple mononeuropathies.

Patients used the following immunosuppressive therapy: methotrexate (MTX), mycophenolate mofetil (MMF), azathioprine (AZA), cyclophosphamide (CF), glucocorticoids (prednisone or equivalent) >20mg; there were no statistically significant differences between adult and juvenile patients or between the patients positive or negative anti-P ribosomal antibodies (data not shown). Adult patients received hydroxychloroquine more frequently than juveniles (95.6% vs 83.3%; P=0.025).

The SLEDAI score in the total population (adults and juveniles) was mean 3.89 (SD 4.68) in patients with juvenile SLE and 5.11 (SD 5.33) and 3.56 in adults (SD 4.44; P=0.09).

Prevalence of Antibodies

The prevalence of antibodies is detailed in Table 2. The antibodies determined, the presence of anti-P ribosomal antibodies (OR=5.21, 95% CI=1.6–16.5) was significantly higher in the group of patients with juvenile SLE.

Relationship of Anti-P Ribosomal Antibodies With Other Antibodies

Table 3 shows the prevalence of other autoantibodies in patients with adult and juvenile SLE, according to whether they were positive or negative for anti-P ribosomal antibodies. The prevalence of all other autoantibodies was similar in both groups.

Relationship Between Anti-P Ribosomal Antibodies With Clinical Manifestations

Table 4 shows the prevalence of anti-P ribosomal antibodies detailed according to the clinical manifestations. Alopecia (OR=10.11, 95% CI=1.25–97) and skin rash (non-discoid) (OR=4.1, 95% CI=1.25–13.89) were the only clinical manifestations that were significantly associated with the presence of anti-P ribosomal antibodies.

The SLEDAI score in the population with negative anti-P ribosomal antibodies was, on average 3.93 (SD 4.76) and, in patients with positive anti-P ribosomal antibodies, on average 3.58 (SD 4.12; P=97).

Discussion

In our study we analyzed the clinical and laboratory characteristics of SLE patients who presented their disease onset before age 16 (young) and compared them with adult SLE patients. The presence of malar rash, photosensitivity, vasculitis, skin rash and neurological involvement (seizures and psychosis) was more frequent in patients with juvenile SLE. When we compared the profile...
of autoantibodies between the 2 groups of patients, we found that anti-P ribosomal antibodies were significantly more prevalent in juvenile SLE (27% vs 5.62%). We found no association of anti-P ribosomal antibodies with other autoantibodies. Alopecia and rash (non-discoid) were the only clinical manifestations that were significantly associated with the presence of anti-P ribosomal antibodies.

Most of the studies reported above agree that there is a higher prevalence of anti-P ribosomal antibodies in juvenile SLE; our study confirmed these findings. It is known that certain characteristics of the study population, such as ethnicity, disease status (higher prevalence of anti-P ribosomal antibodies in active SLE) and treatment intensity makes the prevalence of this autoantibody variable and differs between different studies. Reichlin et al. reported a prevalence of anti-P ribosomal antibodies in 42% of patients with juvenile SLE where a large percentage of them had active SLE. Hoffman et al., unlike previous authors, found a prevalence of 25%, and Press et al. in a previously published study reported a prevalence of 20%. These last 2 studies showed no detail on the activity of the disease and had a prevalence of anti-P ribosomal antibodies similar to that of our study. There is considerable discrepancy in the literature regarding the association between anti-P ribosomal antibodies and different clinical manifestations in juvenile SLE. Reichlin et al. found that anti-P ribosomal antibodies were associated with renal involvement. Quite the opposite was reported by Hoffman et al., who described that the presence of anti-P ribosomal antibodies in the absence of anti-DNA acted as a protector from kidney involvement. In the adult SLE population, other authors found no association between anti-P ribosomal antibodies and the presence of membranous nephropathy. Like us, Press et al. found no association between this autoantibody and kidney involvement.

The association of anti-P ribosomal antibodies with neurological manifestations in patients with juvenile SLE is also controversial. Aldar et al. observed autoantibody more frequently in patients with juvenile SLE and anxiety, but not with more severe clinical manifestations of the central nervous system. Reichlin et al. and Hoffman et al. do not mention the association between anti-P ribosomal antibodies and neurological compromise. In our study, although we found a higher prevalence of neurological manifestations (psychosis and seizures) in juvenile SLE, we did not find

---

### Table 2
Prevalence of Autoantibodies in Patients With Juvenile SLE Compared to Adult SLE.

<table>
<thead>
<tr>
<th>Autoantibody</th>
<th>Juvenile SLE (n=30)</th>
<th>Adult SLE (n=92)</th>
<th>OR; 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-P ribosomal antibodies; n (%)</td>
<td>8 (26.7)</td>
<td>6 (6.5)</td>
<td>5.21; 1.6–16.5</td>
<td>.003</td>
</tr>
<tr>
<td>Anti-La/SSB; n (%)</td>
<td>0</td>
<td>6 (6.5)</td>
<td>0.23; 0.01–4.3</td>
<td>.33</td>
</tr>
<tr>
<td>Anti-Sm; n (%)</td>
<td>5 (16.6)</td>
<td>29 (31.5)</td>
<td>0.47; 0.16–1.38</td>
<td>.17</td>
</tr>
<tr>
<td>Anti-Ro/SSA; n (%)</td>
<td>3 (10)</td>
<td>5 (5.4)</td>
<td>2.1; 0.47–9.5</td>
<td>.32</td>
</tr>
<tr>
<td>Anti-nRNP; n (%)</td>
<td>7 (23.3)</td>
<td>20 (21.7)</td>
<td>1.22; 0.45–3.3</td>
<td>.68</td>
</tr>
</tbody>
</table>

### Table 3
Prevalence of Other Autoantibodies in Patients With Positive and Negative Anti-P Ribosomal Antibodies.

<table>
<thead>
<tr>
<th>Autoantibody</th>
<th>Anti-P ribosomal antibodies (+)/n=14</th>
<th>Anti-P ribosomal antibodies (−)/n=108</th>
<th>OR; 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-La/SSB; n (%)</td>
<td>0</td>
<td>6 (5.5)</td>
<td>0.61; 0.03–11.6</td>
<td>.74</td>
</tr>
<tr>
<td>Anti-Ro/SSA; n (%)</td>
<td>3 (21)</td>
<td>31 (29)</td>
<td>0.80; 0.20–3.1</td>
<td>.75</td>
</tr>
<tr>
<td>Anti-Sm; n (%)</td>
<td>2 (14)</td>
<td>6 (5.5)</td>
<td>3.33; 0.59–18.7</td>
<td>.17</td>
</tr>
<tr>
<td>Anti-nRNP; n (%)</td>
<td>3 (21)</td>
<td>24 (22)</td>
<td>1.13; 0.28–4.54</td>
<td>.85</td>
</tr>
</tbody>
</table>

### Table 4
Differences in Clinical Manifestations Between Positive and Negative Anti-P Ribosomal Antibody-Patients.

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Anti-P ribosomal antibodies (+)/n=14</th>
<th>Anti-P ribosomal antibodies (−)/n=108</th>
<th>OR; 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin and appendages; n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malar erythema</td>
<td>13 (92.8)</td>
<td>76 (70.3)</td>
<td>5.4; 0.68–43.6</td>
<td>.10</td>
</tr>
<tr>
<td>Discoid</td>
<td>0</td>
<td>4 (4.2)</td>
<td>0.72; 0.03–14.1</td>
<td>.83</td>
</tr>
<tr>
<td>Skin rash (other)</td>
<td>6 (42)</td>
<td>14 (13)</td>
<td>4.1; 1.25–13.89</td>
<td>.01</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>11 (78.6)</td>
<td>63 (58.3)</td>
<td>2.6; 0.69–9.9</td>
<td>.07</td>
</tr>
<tr>
<td>Alopecia</td>
<td>7 (50)</td>
<td>9 (8)</td>
<td>10.1; 1.25–97</td>
<td>.04</td>
</tr>
<tr>
<td>Raynaud; n (%)</td>
<td>4 (28.5)</td>
<td>47 (43.5)</td>
<td>0.64; 0.18–2.2</td>
<td>.48</td>
</tr>
<tr>
<td>Oral ulcers; n (%)</td>
<td>5 (35.7)</td>
<td>42 (38.9)</td>
<td>0.87; 0.27–2.7</td>
<td>.41</td>
</tr>
<tr>
<td>Arthritis; n (%)</td>
<td>13 (92.9)</td>
<td>91 (84.3)</td>
<td>2.4; 0.29–19</td>
<td>.22</td>
</tr>
<tr>
<td>Serositis; n (%)</td>
<td>5 (46)</td>
<td>25 (27)</td>
<td>2.22; 0.64–7.64</td>
<td>.20</td>
</tr>
<tr>
<td>Pleuritis</td>
<td>1 (0.90)</td>
<td>22 (24)</td>
<td>0.33; 0.04–2.7</td>
<td>.30</td>
</tr>
<tr>
<td>Glomerulonephritis; n (%)</td>
<td>7 (50)</td>
<td>61 (56.5)</td>
<td>0.77; 0.25–2.3</td>
<td>.32</td>
</tr>
<tr>
<td>Neurological; n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>1 (7.1)</td>
<td>11 (10.1)</td>
<td>0.79; 0.09–6.7</td>
<td>.83</td>
</tr>
<tr>
<td>Psychosis</td>
<td>2 (14.2)</td>
<td>10 (9.2)</td>
<td>1.9; 0.36–10.11</td>
<td>.44</td>
</tr>
<tr>
<td>Hematology; n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>8 (57.1)</td>
<td>49 (45.3)</td>
<td>1.38; 0.44–4.29</td>
<td>.56</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>3 (21.4)</td>
<td>14 (12.9)</td>
<td>1.67; 0.41–6.76</td>
<td>.46</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0</td>
<td>20 (18.5)</td>
<td>0.13; 0.00–2.42</td>
<td>.17</td>
</tr>
<tr>
<td>Vasculitis; n (%)</td>
<td>4 (28.5)</td>
<td>13 (12)</td>
<td>2.86; 0.78–10.46</td>
<td>.11</td>
</tr>
<tr>
<td>Sicca syndrome; n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry eye</td>
<td>0</td>
<td>15 (16)</td>
<td>0.20; 0.01–3.5</td>
<td>.27</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>0</td>
<td>4 (4)</td>
<td>0.77; 0.03–15.2</td>
<td>.86</td>
</tr>
</tbody>
</table>
a statistically significant association between the anti-P ribosomal antibodies and such events, either in the analysis of the total patient population studied or in juvenile SLE.

It has been reported the anti-P ribosomal antibodies correlate with disease activity as measured by SLEDAI and with the presence of anti-DNA. In our study no relationship between disease activity measured by SLEDAI and anti-P ribosomal antibodies was found.

One of the major limitations of our study is the small number of patients with juvenile SLE due to difficulties in recruitment. The anti-P ribosomal antibodies were measured in a single determination, so we could not have detected their presence in patients who were inactive at the time of sampling. On the other hand, in the sample there are only 14 patients with positive anti-P ribosomal antibodies; this may have limited the possibility of finding statistically significant associations between antibody presence and clinical manifestations.

Despite the limitations, this study confirms the increased prevalence of anti-P ribosomal antibodies in patients with juvenile SLE and found no association of their presence with renal and CNS manifestations. Alopecia and rash (non-discoid) were the only clinical manifestations that were statistically associated with the presence of anti-P ribosomal antibodies.

Ethical Responsibilities

Protection of people and animals. The authors declare that this research has not performed experiments on humans or animals.

Data confidentiality. The authors declare that they have followed the protocols of their workplace on the publication of data from patients and all patients included in the study have received sufficient information and gave written informed consent to participate in the study.

Right to privacy and informed consent. The authors have obtained informed consent from patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Conflict of Interest

The authors have no conflicts of interest.

References