Study about the association between anticardiolipin antibodies and peripheral vascular phenomena in patients suffering from systemic scleroderma

Estudo de associação entre anticorpos anticardiolipinas e fenômenos vasculares periféricos em pacientes com esclerodermia sistêmica

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Abstract: Ischemia is common in systemic scleroderma and it is caused by vasospasm and thrombosis. In the present study we analyzed the association of peripheral vascular events and anticardiolipin (aCl) antibodies in 54 patients suffering from systemic scleroderma. The results showed that 100% of the patients presented Raynaud; 59.2% presented digital micro scars; 43.3%, presented teleangiectasies and 14.8%, presented peripheral thromboembolism. ACl IgG were positive in 9.2% and IgM, in 7.4%. Peripheral thromboembolic phenomena had a positive association with aCl IgG (p=0.03). No other associations were found.

Keywords: Scleroderma, diffuse; limited; Skin ulcer.

Resumo: Isquemia é comum em esclerodermia sistêmica e é causada por vasoespasmo e trombose. As autoras analisaram a associação de eventos vasculares periféricos e anticorpos anticardiolipinas (aCl) em 54 esclerodérmicos. Em 100% deles existia Raynaud; 59,2% apresentaram cicatrizes estelares; 43,3%, telangiec-tasias; 14,8%, fenômenos tromboembólicos periféricos. ACl IgG foram positivos em 9,2% dos casos e o IgM, em 7,4%. Fenômenos embólicos periféricos estão associados a aCl IgG (p=0,03), não se encontrando associação com demais manifestações.

Palavras-chave: Esclerodermia difusa; Esclerodermia limitada; Úlcera cutânea

Systemic scleroderma (ES) is an autoimmune disease of unknown etiology. Endothelial disfuction plays a fundamental etiopathogenetic role in it. It is characterized by an increase in the synthesis and deposition of collagen fibers on the skin and internal organs causing structural and functional damage to small arteries and capillaries apart from perivascular infiltration by inflammatory mononuclear cells. The excess of Endothelin-1(ET-1) is associated with the fisiopathologic mechanism of esclerodermic. The ET-1, a potent endogenous vasoconstrictor, is mitogen for fibroblasts, smooth muscle cells and endothelial cells.

Various auto-antibodies have been found in ES, among them, the antiphospholipids (AAF). Marie and cols, studying 69 patients suffering from ES, found positiveness for these auto-antibodies in 19% of them. Assous and cols, in 108 pacients, found anticardiolipin antibodies (aCl) in 14% of the cases.

The AAF are responsible for trombotic phenomena of macro and microcirculation that can superpose the vascular damage of scleroderma, aggravating ischemic lesions. In some studies the presence of aCls was associated with the appearing of digital micro scars.

The present analysis was carried out to verify the prevalance of aCLs in the local population with...
ES and such auto-antibodies are associated with peripheral vascular disorders such as ulcers and digital necrosis, digital micro scars, telangiectasies and peripheral thrombosis.

After being approved by the Ethics in Research Committee and the consent agreements were signed it was carried out a transversal study with 54 patients with ES (5 men and 49 women) with an average age of 51,5±11,7 (maximum of 79 and minimum of 26 years of age ) and an average length of time of the disease of 12,3±8,9 years (maximum of 40 years; minimum of 2 years). All them fulfilled the criteria of the American College of Rheumatology for such disease.7 This sample was formed by patients with ES that agreed in taking part in the study and that had attended the service in the last 12 months of the research. All them presented the systemic form of the disease being divided according to the cutaneous expressions of the disease in 11 (20,3%) with the diffuse form, one (1,8%) with the sine scleroderma form and 33 (61,1%) with the limited or CREST form. Nine (16,6%) presented the overjet form with other collagenosis. It was sought the presence of digital ulcers, digital necrosis, micro digital scars, Raynaud, phenomenon, telangiectasies, peripheral trombosis, of aCl IgG and IgM. The clinical data indexed are part of a list rated regularly in patients of the service with ES. From an immunological point of view, 50/54 (92,5%) patients were FAN positive, 17/51 (33,3%) presented anticentromere and 6/50 (12%) had Scl-70 positive. Around 10/54 (18,5%) were using cyclophosphamide and 5/54 (9,2%), methotrexate. For control, 150 patients with osteoarthritis and without any other comorbidades were included in the study. Neither of the patients or controls were taking drugs that would imply positiviness for aCLs such as propranolol, chlorpromazine, γ interferon, amoxacillin, procainamide, anti TNF-α and cocaine in the moment of the dosage.8 ACls were surveyed by the ELISA technic (Euroimmun®, Lübeck, Germany) being considered positive values above 15 UI/ml. Data was collected in frequency and contingency charts and the Fisher test was calculated for associations with the support of the Graph Pad Prism software, version 4. The adopted significance was 5%.

It was found Raynaud in 100% of the cases, (n=54); digital micro scars in 59,2% (n=32); telangiectasies in 44,4% (n=24); digital pulp ulcers in 18,5% (n=10), peripheral tromboembolic phenomena in 14,8% (n=8); digital necrosis in 7,4% (n=4), other digital ulcers in 3,7% (n=2), other sites ulcers in 1,8% (n=1).

The ACls in patients with ES were positive in 5 (9,25%) for IgG and in 4 (7,4%) for IgM. Among the control patients only 2 (1,3%) were positive for IgG. Comparing the prevalence of ACls among patients and controls it was found p=0,05 for ACls IgG and p=0,01 for IgM (Fisher).

The study of the association between ACls and peripheral vascular manifestations in ES can be found in table 1.

Results show that the ACls are not associated with vascular phenomena in the extremities of patients with ES, except for cases of thrombosis.

<table>
<thead>
<tr>
<th>Positive aCl IgG</th>
<th>Positive aCl IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital micro scars (n=31)</td>
<td>4/31 (12,9)</td>
</tr>
<tr>
<td>Telangiectasies (n=24)</td>
<td>0/24 (0)</td>
</tr>
<tr>
<td>Peripheral tromboembolic phenomena (n=8)</td>
<td>3/8 (37,5)</td>
</tr>
<tr>
<td>Digital pulp ulcers (n=10)</td>
<td>1/10 (10)</td>
</tr>
<tr>
<td>Digital necrosis (n=4)</td>
<td>1/4 (25)</td>
</tr>
<tr>
<td>Digital ulcers (n=2)</td>
<td>0/2 (0)</td>
</tr>
</tbody>
</table>

(*) inverted association; n= sample number

Table 1: Association between anticardiolipin (aCl) antibodies and peripheral vascular phenomena
REFERENCES

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