Scientific papers

Antiphospholipid antibodies: a risk factor for occlusive ocular vascular disease in systemic lupus erythematosus and the 'primary' antiphospholipid syndrome

R A Asherson, P Merry, J F Acheson, E N Harris, and G R V Hughes

SUMMARY Seven cases of occlusive ocular vascular disease affecting retinal and choroidal vessels were found among 84 consecutive patients with raised levels of anticardiolipin antibodies attending the lupus arthritis clinic at St Thomas's Hospital from 1985 to 1987. Six patients with systemic lupus erythematosus (SLE) and one with a 'primary antiphospholipid syndrome' had occlusive ocular vascular disease affecting a variety of vessels. This gives a prevalence of occlusive ocular vascular disease of 8% in this subgroup of patients, significantly higher than the 0.5-2.0% previously reported in patients with SLE. Four of these patients also suffered from cerebrovascular disease, supporting the previously documented association between occlusive ocular vascular disease and central nervous system disease in SLE. Additionally, other features of the antiphospholipid syndrome were frequently present. These findings suggest that patients with SLE and raised anticardiolipin antibodies have a higher risk of developing occlusive ocular vascular disease than has been previously reported.

Key words: anticardiolipin antibodies, lupus anticoagulant, retinal vein/artery thrombosis.

Accepted for publication 21 July 1988.
Correspondence to Dr R A Asherson, Lupus Arthritis Research Unit, The Rayne Institute, St Thomas's Hospital, London SE1 7EH.
Table 1  Oclusive ocular vascular disease and antiphospholipid antibodies

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Manifestations of APL* syndrome</th>
<th>Anticardiolipin antibodies</th>
<th>Antinuclear antibody titre</th>
<th>Ocular lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>53</td>
<td>SLE*</td>
<td>Transient ischaemic attacks</td>
<td>Medium</td>
<td>+</td>
<td>1/320</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Valve lesion (MI)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cerebral infarctions (2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Livedo reticularis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>38</td>
<td>SLE</td>
<td>Transient ischaemic attacks</td>
<td>Medium</td>
<td>+</td>
<td>1/40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cerebral infarctions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Multiple abortions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Livedo reticularis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>33</td>
<td>SLE</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>33</td>
<td>SLE</td>
<td>Left subclavian thrombosis</td>
<td>High</td>
<td>+</td>
<td>1/640</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Guillain-Barré syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Recurrent cerebral infarctions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Multi-infarct dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Deep vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pulmonary emboli</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Livedo reticularis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>49</td>
<td>Primary APL syndrome</td>
<td>Multi-infarct dementia</td>
<td>High</td>
<td>+</td>
<td>1/20</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cortical blindness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>52</td>
<td>SLE</td>
<td>Aortic valve lesion</td>
<td>Medium</td>
<td>+</td>
<td>1/160</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>28</td>
<td>SLE</td>
<td>Thrombocytopenia</td>
<td>Medium</td>
<td>+</td>
<td>1/160</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Miscarriage (1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*APL=antiphospholipid; aCL=anticardiolipin; SLE=systemic lupus erythematosus; MI=mitral incompetence.
†IgG aCL: high=>80 GPL units, medium=20–80 GPL units, low=5–20 GPL units; IgM aCL: high=>50 MPL units, medium=6–50 MPL units, low=3–6 MPL units.
bodies, we identified seven patients with occlusive ocular vascular disease. These seven patients had previously undergone a full ophthalmological examination. Table 1 records their main clinical and serological characteristics. The anticardiolipin antibodies were estimated by a modified enzyme linked immunosorbent assay (ELISA) as described by Gharavi et al.  

Results

Of the 84 patients in the study, seven patients suffered from occlusive ocular vascular disease (six had SLE and one had primary antiphospholipid syndrome). Thus the prevalence of occlusive ocular vascular disease was 8% in this subgroup of patients with raised anticardiolipin antibodies. Table 1 records the ocular lesions of these patients.

Four of these patients also had cerebrovascular disease (three had SLE, one had primary antiphospholipid syndrome). Thus three of six patients (50%) with SLE and occlusive ocular vascular disease had cerebrovascular disease. Table 1 records the neurological lesions of these patients.

Six of the patients recorded displayed additional features of the antiphospholipid syndrome.

Discussion

The 8% prevalence of occlusive ocular vascular disease in the subgroup of patients we studied is significantly higher than the 0.5–2.0% previously reported in SLE.  

This study also supports the finding in SLE of a strong association between occlusive ocular vascular disease and central nervous system involvement.

The subject of occlusive ocular vascular disease in SLE was extensively reviewed recently by Jabs et al, who documented 11 of their own patients and reviewed the studies of 21 patients previously published.  

Of their own patients, seven had severe generalised retinal vaso-occlusive disease, while four had more focal vascular occlusions (central retinal artery occlusion (one), branch retinal artery occlusions (two), and central retinal vein occlusion (one)). They found that eight of their 11 patients (73%) also suffered from central nervous system lupus, which was a significantly higher prevalence than in the other publications reviewed, where the figure was 37%. No reference to antiphospholipid antibodies was made in their paper, though one of their patients was subsequently found to have anticardiolipin antibodies on testing by our laboratory. This patient had recurrent deep vein thromboses, pulmonary emboli, transient ischaemic attacks, hemiparesis, and thrombocytopenia.

The antiphospholipid antibodies (antibodies to cardiolipin, the ‘lupus anticoagulant’, and the antibodies responsible for the false positive serological test for syphilis—Venereal Disease Research Laboratory (test) have been associated with arterial and venous thrombosis occurring at various sites.  

This association, originally called the ‘anticardiolipin syndrome’ and subsequently referred to as the antiphospholipid syndrome, has been expanded to include recurrent fetal loss, a variety of neurological syndromes, and thrombocytopenia. Livedo reticularis has also been associated. In comparison with the general SLE population an increased prevalence of heart valve lesions, particularly affecting the mitral and aortic valves, has recently been recorded in patients with these antibodies. This subject has recently been extensively reviewed. The antiphospholipid syndrome may manifest as a primary entity in the absence of any specific autoimmune disease but is more commonly seen in association with SLE, or lupus-like disease (where less than four of the 1982 American Rheumatism Association criteria for the classification of SLE are met).  

In a previous study of an unselected group of 40 patients with occlusive ocular vascular disease and no underlying connective tissue disease antiphospholipid antibodies were not found. There have been few reports linking occlusive ocular vascular disease with antiphospholipid antibodies in SLE. The two patients reported by Hall et al, both of whom demonstrated the lupus anticoagulant, represented the first definitive documentation of this association. One of their patients had thrombocytopenia. One patient recorded by Silverman et al, with a central retinal vein occlusion complicating SLE, had a prolonged partial thromboplastin time, suggesting the presence of the lupus anticoagulant. The patient recorded by Ford et al also suffered a retinal artery occlusion. Retinal vein thrombosis is also mentioned in several reviews on the lupus anticoagulant. A recent interesting paper described a woman with Sneddon’s syndrome, who developed a central retinal artery occlusion in association with antibodies to phosphatidyl-ethanolamine. Sneddon’s syndrome comprises livedo reticularis, variable cerebrovascular symptoms, and labile hypertension. The original patients described by Sneddon did not show any evidence of autoimmune disease, though immunological testing was limited in 1965. In a recent study from our unit, however, three of 35 patients with cerebrovascular disease and livedo reticularis were found to have antiphospholipid antibodies in the absence of SLE, and would conform to the same group of patients as described by Sneddon.
We therefore conclude that patients with SLE and raised levels of antiphospholipid antibodies have a higher risk of developing occlusive ocular vascular disease than previously reported. In our group of patients features of the antiphospholipid syndrome were frequently present and in addition there was a high prevalence of central nervous system disease, particularly stroke.

This work was supported by the British SLE Foundation and the Jean Shanks Foundation.

References
Antiphospholipid antibodies: a risk factor for occlusive ocular vascular disease in systemic lupus erythematosus and the 'primary' antiphospholipid syndrome.

R A Asherson, P Merry, J F Acheson, E N Harris and G R Hughes

doi: 10.1136/ard.48.5.358

Updated information and services can be found at:
http://ard.bmj.com/content/48/5/358

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/