Prevalence of the antiphospholipid syndrome in primary systemic vasculitis

J D Rees, S Lancã, P V Marques, J A Gómez-Puerta, R Moco, C Oliveri, M A Khamashta, G R V Hughes, D P D'Cruz

Methods
All attendees at the vasculitis clinic at St Thomas' Hospital over the 12 month period October 2001–October 2002 were reviewed. We also included all inpatients admitted under our care during this time. The case notes were reviewed and only those patients with a definite diagnosis of PSV were included. Patients in whom a diagnosis of systemic lupus erythematosus was suspected were excluded. The 144 patients were classified according to American College of Rheumatology (ACR) criteria14 and for those with microscopic polyangiitis according to the Chapel Hill consensus definition.13 Patients not meeting these criteria were designated unclassified systemic vasculitis.

All patients were tested for anticardiolipin antibodies (aCL) and lupus anticoagulant (LA) on at least one occasion. Of these, nine had definite APS (classified by the Sapporo criteria) and a further four patients had clinical and serological features of APS, although insufficient to satisfy the Sapporo criteria. Twelve had only positive aPL.

Conclusion: The antiphospholipid syndrome, aCL, and the LA may occur in association with PSV.
It has been suggested that aPL are associated with acute vascular inflammation, and their temporary presence in the serum is a reflection of polyclonal globulin secretion. Thus, their presence in vasculitis may simply represent a secondary response. Another hypothesis is that the endothelial cell disruption which occurs in vasculitis reveals cryptic antigens and stimulates antiendothelial cell antibodies that may be part of the spectrum of aPL. In this case, aPL might just be an epiphenomenon of endothelial phospholipid exposure due to vascular inflammation, as proposed by Manna et al. Some authors found positive aPL in patients with acute infections such as mycoplasma, adenovirus, rubella, chicken pox, and mumps. The levels often declined when the infection resolved, were often low, and not associated with thrombosis. This possibility might explain the presence of aPL in some of our patients; particularly the patients with only one weak positive result. However, many of our patients had high titre positive antibody levels which were consistently present over multiple occasions. These patients therefore may have highly pathogenic LA or aCL and thrombosis while other patients, often with high antibody titre levels, do not. Possibly, the pathogenicity of the antibodies is influenced by host genetic factors, antibody isotype, and underlying vessel wall integrity, as proposed by Norden et al.19

In conclusion, our data suggest that aPL can be present in patients with PSV and may influence its clinical course and management. Studies are in progress to assess the possible impact of aPL on morbidity in these patients.

**Table 1** Summary of patients with systemic vasculitis who also had a definite (Sapporo criteria) diagnosis of antiphospholipid syndrome

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Test Results</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>Polyarteritis nodosa</td>
<td>IgG &gt; 160 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>F</td>
<td>Relapsing polyarthritis</td>
<td>IgG &gt; 16 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>M</td>
<td>Wegener’s granulomatosis</td>
<td>IgM up to 70 IU/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>F</td>
<td>Churg-Strauss syndrome</td>
<td>IgG &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>M</td>
<td>Unclassified systemic disease</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>6</td>
<td>71</td>
<td>F</td>
<td>Giant cell arteritis</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>F</td>
<td>Churg-Strauss syndrome</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>M</td>
<td>Limited Wegener’s granulomatosis</td>
<td>IgG 10.4 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>9</td>
<td>39</td>
<td>F</td>
<td>Takayasu’s disease</td>
<td>Multiple positives</td>
<td>Aspirin 75 mg daily</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis; CVA, cardiovascular accident; PE, pulmonary embolism.

**DISCUSSION**

Our results show a prevalence of definite APS of 6% (9/144) in our population of patients with PSV. A further 3% (4/144) have features of APS with positive serology but not enough for the Sapporo criteria (probable or possible APS). A further 12 had positive aPL serology with no significant clinical features; the remaining 119 were completely negative for aPL. Table 1 summarises the patients with definite APS. Of the 12 patients with positive aPL but without clinical features of APS, one had positive serology for both aCL and LA, four were positive for aCL alone, and the remaining seven were LA positive. Of the seven positive for LA alone, four were positive on multiple occasions.

Of these 144 patients, 25 (17%) had some features of the APS: 9 (6%) had classical APS by Sapporo criteria while 4 had features of APS with positive serology but not enough for the Sapporo criteria (probable or possible APS). A further 12 had positive aPL serology with no significant clinical features; the remaining 119 were completely negative for aPL. Table 1 summarises the patients with definite APS. Of the 12 patients with positive aPL but without clinical features of APS, one had positive serology for both aCL and LA, four were positive for aCL alone, and the remaining seven were LA positive. Of the seven positive for LA alone, four were positive on multiple occasions.

**Table 1** Summary of patients with systemic vasculitis who also had a definite (Sapporo criteria) diagnosis of antiphospholipid syndrome

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Test Results</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>Polyarteritis nodosa</td>
<td>IgG &gt; 160 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>F</td>
<td>Relapsing polyarthritis</td>
<td>IgG &gt; 16 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>M</td>
<td>Wegener’s granulomatosis</td>
<td>IgM up to 70 IU/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>F</td>
<td>Churg-Strauss syndrome</td>
<td>IgG &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>M</td>
<td>Unclassified systemic disease</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>6</td>
<td>71</td>
<td>F</td>
<td>Giant cell arteritis</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>F</td>
<td>Churg-Strauss syndrome</td>
<td>IgM &gt; 2</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>M</td>
<td>Limited Wegener’s granulomatosis</td>
<td>IgG 10.4 U/ml</td>
<td>Lifelong warfarin</td>
</tr>
<tr>
<td>9</td>
<td>39</td>
<td>F</td>
<td>Takayasu’s disease</td>
<td>Multiple positives</td>
<td>Aspirin 75 mg daily</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis; CVA, cardiovascular accident; PE, pulmonary embolism.

**DISCUSSION**

Our results show a prevalence of definite APS of 6% (9/144) in our population of patients with PSV. A further 3% (4/144) have features of APS with positive serology but not enough for the Sapporo criteria (probable or possible APS). A further 12 had positive aPL serology with no significant clinical features; the remaining 119 were completely negative for aPL. Table 1 summarises the patients with definite APS. Of the 12 patients with positive aPL but without clinical features of APS, one had positive serology for both aCL and LA, four were positive for aCL alone, and the remaining seven were LA positive. Of the seven positive for LA alone, four were positive on multiple occasions.

As this series is retrospective it is subject to possible left censorship bias in that some patients may have died during the 12 month collection period. We made every effort to include patients who had died and although two patients did die during this period, (definite APS patient 5 and a further patient who was aPL and LA negative) this did not significantly affect our results.

The nine patients with definite APS demonstrate that the APS may occur in association with a PSV, complicating clinical management for these cases. Six of the 12 patients with serological features of APS had persistently positive serology. Of note, although Behçet’s disease was included in our cohort of patients with vasculitis, none of these patients had a thrombosis or positive serology at any time.

**AUTHORS’ AFFILIATIONS**

J D Rees, S Lança, P V Marques, J A Gómez-Puerto, R Maco, C Oliveri, M A Khamashta, G R V Hughes, D P D’Cruz, The Lupus Research Unit, The Rayne Institute, St Thomas’ Hospital, London, UK.

Correspondence to: Dr David D’Cruz, The Lupus Research Unit, The Rayne Institute, St Thomas’ Hospital, London SE1 7EH, UK; david.d.cruz@kcl.ac.uk

Accepted 27 May 2005

**REFERENCES**


Prevalence of the antiphospholipid syndrome in primary systemic vasculitis

J D Rees, S Lança, P V Marques, J A Gómez-Puerta, R Moco, C Oliveri, M A Khamashta, G R V Hughes and D P D'Cruz

doi: 10.1136/ard.2004.034231

Updated information and services can be found at:
http://ard.bmj.com/content/65/1/109

These include:

References
This article cites 19 articles, 1 of which you can access for free at:
http://ard.bmj.com/content/65/1/109#BIBL

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.

Topic Collections
Articles on similar topics can be found in the following collections
- Vascularitis (294)
- Immunology (including allergy) (5144)
- Connective tissue disease (4253)
- Systemic lupus erythematosus (571)

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/