Letters to the Editor

To the Editor:

We feel that the differences in immunological and histological findings from case to case could reflect clinical heterogeneity, divergences in laboratory methods employed in aPL investigations, or both. These dissimilarities stress the necessity of homogeneity in the study of these patients.

A. Moral, MD
Department of Neurology

References


Sneddon's Syndrome With Antiphospholipid Antibodies and Arteriopathy

The evolution of antiphospholipid antibody levels is shown in Table 1. Although livedo reticularis persisted, no further ischemic cerebrovascular events took place during a 20-month follow-up period.

A noninflammatory arteriopathy, affecting cerebral and cutaneous vessels, has been reported in Sneddon's syndrome. Its pathogenesis is unknown, but there are some reports of Sneddon's syndrome associated with aPL antibodies, suggesting that these antibodies may play a role. Nowadays, it seems clear that the association of livedo reticularis with cerebrovascular lesions could be the result of a wide spectrum of causes, one of which is the "primary" antiphospholipid syndrome.

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Table 1. Evolution of Antiphospholipid Antibody Levels

<table>
<thead>
<tr>
<th>Test</th>
<th>Time of test (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPR</td>
<td>1/2</td>
</tr>
<tr>
<td>ACA</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>30</td>
</tr>
<tr>
<td>IgM</td>
<td>10</td>
</tr>
<tr>
<td>Cephaline Time</td>
<td>Normal</td>
</tr>
<tr>
<td>DPTT</td>
<td>ND</td>
</tr>
<tr>
<td>RVVT</td>
<td>ND</td>
</tr>
</tbody>
</table>

Data in parentheses are normal values.

RPR, rapid plasma reagin; ACA, anticardiolipin antibodies; DPTT, diluted partial thromboplastin time; ND, not done; RVVT, Russell viper venom time.

suggested that the pathogenesis of cerebral ischemia in Sneddon's syndrome differs depending on whether aPL antibodies are present or absent, namely, large-vessel arteriopathy in aPL antibody-positive patients and medium-vessel arteriopathy in aPL antibody-negative patients. In his response, Levine stated that the difference in the size of the vessels affected in Sneddon's syndrome is not so clear cut. We report the case of a patient with typical Sneddon's syndrome, high levels of aPL antibodies, medium-sized arteriopathy, and lack of involvement of large cerebral vessels.

A 44-year-old white man was admitted to the hospital in April 1989 because of left basal pneumonia. His previous history was unremarkable. He was treated with erythromycin with good recovery. Antibody titer for Legionella pneumophila became elevated from 1/1,024 to 1/4,096. One month later livedo reticularis appeared on all four limbs and his trunk. Two months after that, he developed a mild left hemiparesis with sensory impairment, but no other neurological sign. Livedo reticularis was still present. His neurological condition recovered in 4 days. Cranial computed tomography, electrocardiogram, four-vessel angiogram, and routine laboratory tests were normal. The following antibody titers were negative: antinuclear, anti-DNA, anti-ENA, anti-SSA, and anti-SSB. A skin biopsy was normal. Rapid plasma reagin test was positive. High levels of anticardiolipin antibodies were found (30 GPL and 10 MPL). An echocardiogram showed a slightly incompetent and fibrosed aortic valve. Brain magnetic resonance imaging, on the T2-weighted sequences, showed small, hyperintensive lesions on the right frontoparietal white matter, and digital artery biopsy showed focal areas of intimal hyperplasia and a redundant elastic internal layer. Treatment with aspirin was started (500 mg, once a day). The evolution of the different aPL antibody levels is shown in Table 1. Although livedo reticularis persisted, no further ischemic cerebrovascular events took place during a 20-month follow-up period.

A noninflammatory arteriopathy, affecting cerebral and cutaneous vessels, has been reported in Sneddon's syndrome. Its pathogenesis is unknown, but there are some reports of Sneddon's syndrome associated with aPL antibodies, suggesting that these antibodies may play a role. Nowadays, it seems clear that the association of livedo reticularis with cerebrovascular lesions could be the result of a wide spectrum of causes, one of which is the "primary" antiphospholipid syndrome.

We feel that the differences in immunological and histological findings from case to case could reflect clinical heterogeneity, divergences in laboratory methods employed in aPL investigations, or both. These dissimilarities stress the necessity of homogeneity in the study of these patients.

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Recently, Martínez-Menéndez et al reported a patient with Sneddon's syndrome, negative antiphospholipid (aPL) antibody test, and medium-sized arteriopathy. On the basis of these findings, they
References


3. B. Martínez-Menéndez, MD
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The following is in response:

To the Editor:

In our report of a patient with Sneddon's syndrome and negative antiphospholipid antibodies, we said that there were angiographic differences between Sneddon's syndrome and cerebrovascular lesions associated with antiphospholipid syndrome. While cerebral angiography in patients with cerebrovascular disease and antiphospholipid antibody syndrome has either been normal or revealed large-vessel occlusions, middle-sized arteries are involved in Sneddon's syndrome. However, we did not suggest that the pathogenesis of cerebral ischemia in Sneddon's syndrome was different whether antiphospholipid antibodies were present or not.

Moral et al report a patient with Sneddon's syndrome and positive antiphospholipid antibodies with biopsy evidence of medium-sized arteriopathy. Sneddon's syndrome is characterized by the presence of a noninflammatory medium-sized arteriopathy. Digital artery biopsy has shown intimal hyperplasia in nearly all patients in whom this procedure was performed. The case reported by Moral et al supports the hypothesis that this occlusive arteriopathy is the main factor involved in the pathogenesis of cerebrovascular lesions in Sneddon's syndrome.

The significance of antiphospholipid antibodies in Sneddon's syndrome is still unclear although Kalashnikova et al found that their presence is associated with a poorer outcome. Finally, we agree with Moral et al on the need for standardized laboratory methods in the study of antiphospholipid antibodies in patients with Sneddon's syndrome.

The following is in response:

To the Editor:

Moral et al report a patient with Sneddon's syndrome who had antiphospholipid (aPL) antibodies and a digital artery biopsy showing focal areas of intimal hyperplasia and a redundant elastic internal layer: a noninflammatory vasculopathy. Their patient had a normal cerebral angiogram.

It is interesting to note that their patient's syndrome evolved 1 month after pneumonia, presumably Legionella. A single cerebral ischemic event occurred during 14 months of follow-up. Anticardiolipin antibodies were consistently present at 1, 7, and 14 months, and a lupus anticoagulant was probably present as well, based on the single prolonged diluted PTT and Russell viper venom time.

Postinfectious aPL antibodies, probably present in this patient, are not rare. Little, if anything, is known about the antigenic specificities of aPL antibodies in Sneddon's syndrome, making it difficult to know why these immunoglobulins are relatively selective for cerebral and dermal vessels. I agree with Moral and colleagues that Sneddon's syndrome is clinically, immunologically, and histologically heterogeneous, partly because of the nonspecific nature of livedo reticularis and cerebral infarction. Antiphospholipid antibodies represent only one common association between the two clinical phenomena.

I am not sure that inferences about the size of the cerebral arteries involved in Sneddon's syndrome can be drawn from digital biopsy and normal cerebral angiography in a single patient. Perhaps an international Sneddon's syndrome cooperative study group could address some of these aforementioned issues in a more formal, standardized way.

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References


Sneddon's syndrome with antiphospholipid antibodies and arteriopathy.
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