Spinal cord infarction associated with primary antiphospholipid syndrome in a young child

Case report

MITSUHIRO HASEGAWA, M.D., JUNKOH YAMASHITA, M.D., TETSUMORI YAMASHIMA, M.D., KIYONOBU IREDA, M.D., YOSHI FUSISHIMA, M.D., AND MASAHIDE YAMAZAKI, M.D.

Departments of Neurosurgery and 3rd Internal Medicine, Kanazawa University School of Medicine, Kanazawa, Japan

Antiphospholipid antibodies have been reported to occur in ischemic stroke patients, but there have been no previous reports linking these antibodies to spinal cord infarction. A case of spinal cord infarction associated with primary antiphospholipid syndrome in a 6-year-old boy is reported. Magnetic resonance imaging clearly demonstrated marked swelling of the thoracolumbar spinal cord with gadolinium-diethylenetriamine pentaaetate acid enhancement at an acute stage, followed later by cord atrophy. Serological study disclosed positive lupus anticoagulant and immunoglobulin G anticardiolipin antibody. It is suggested that the role of antiphospholipid antibodies as an etiological factor for spinal cord ischemia should be recognized among causes that might have been categorized as either spontaneous spinal cord infarction or myelitis.

Key Words: spinal cord infarction, antiphospholipid antibody, lupus anticoagulant, anticardiolipin antibody, magnetic resonance imaging

Anticardiolipin antibodies and the lupus anticoagulant are among a population of antiphospholipid antibodies that cross-react against cardiolipin and other phospholipids in the prothrombin activator complex of the coagulation cascade. These antibodies are seen primarily in patients with systemic lupus erythematosus (SLE), but it is now apparent that most antiphospholipid antibody-related stroke occurs in patients without SLE. The gravest clinical feature associated with these antibodies is stroke of multiple organs in young adults, resulting in recurrent venous and arterial thrombosis, central nervous system disease, and recurrent fetal loss.

The role of antiphospholipid antibodies in spinal cord disorders has received little attention; there are two reports of SLE myelopathy associated with antiphospholipid antibodies in the literature. The report by Lavalle, et al.,23 did not include any neuroradiological information, while Markusse, et al.,21 could not visualize any abnormalities in the spinal cord on magnetic resonance (MR) imaging. Since spinal cord infarction manifests cord swelling13 and gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA) enhancement,6,10 difficulties in precise differential diagnosis from intramedullary tumor sometimes force neurosurgeons to perform exploratory laminectomies at an acute stage.5,21,30,33

We describe the first reported case of spinal cord infarction associated with primary antiphospholipid syndrome, and review the MR imaging appearances of spinal cord infarction.

Case Report

This 6-year-old boy had a sudden onset of pain in the knees, radiating down both lower extremities, on August 14, 1991. Paraplegia and sensory loss followed within 1 hour. He was immediately referred to a local hospital and treated with steroids and dextran, but his neurological state remained unchanged. The patient was transferred to our hospital on September 10 for further examination and treatment.

Examination. Physical examination on admission showed complete motor and sensory impairment below the T-10 level, including loss of deep-tendon reflexes, complete sensory loss, and urinary and fecal incontinence. The patient had no history of skin lesions such as lupus rashes and livedo reticularis, but he had suffered at least three episodes of gonalgia and gait disturbance, each lasting a few minutes.

Magnetic resonance imaging performed at the local
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Fig. 1. Magnetic resonance (MR) images obtained 5 days after symptom onset. Upper Left: T₁-weighted MR image (TR 400 msec, TE 13 msec), midsagittal view, depicting severe cord swelling (asterisk). Upper Center: T₂-weighted MR image (TR 400 msec, TE 20 msec, FA 22), midsagittal view, depicting a low-intensity area compatible with deoxyhemoglobin (arrow), probably due to hemorrhagic infarction. Upper Right: Contrast-enhanced MR image, midsagittal view, showing enhancement of the cortical area with gadolinium-diethylenetriamine penta-acetate acid. Lower: T₂-weighted MR image (TR 400 msec, TE 20 msec, FA 22), axial view, depicting the precise location of deoxyhemoglobin.

Gd-DTPA enhancement diminished; the time course for deterioration was consistent with spinal cord infarction rather than with an intramedullary tumor (Fig. 3).

Laboratory data showed weakly positive antinuclear antibody (× 20, speckled with rat cell line), platelet-associated immunoglobulin (IgG) (49.5 ng/10⁷ cells, normal range 9 to 25 ng/10⁷ cells), and IgG anti-cardiolipin antibody (24 lgG phospholipid antibody (GPL) units measured by enzyme-linked immunosorbent assay (ELISA) [normal < 10 GPL units]). The lupus anticoagulant was confirmed by the kaolin clotting time (125.0 seconds, control 98.5 seconds) and rabbit brain neutralization procedures (ratio of patient:control clotting time 0.84, normal < 0.17). The erythrocyte sedimentation rate was 28 mm in 1 hour and 60 mm in 2 hours. Tests for platelet count, factor VIII, antithrombin III, protein S, and protein C levels, fibrin degradation products, venereal disease, anti-deoxyribonucleic acid antibody, and complement studies were normal. The IgM anticardiolipin antibody level was within normal limits. Analysis of cerebrospinal fluid obtained via lumbar puncture on the day of symptom onset revealed a normal protein level of 47 mg/dl, a sugar level of 50 mg/dl, and a normal cell count. The positive IgG anticardiolipin antibody titer persisted during the follow-up period (24 and 28 GPL units at 3 weeks and 17 months after the first measurement, respectively).

According to the criteria of Harris, the diagnosis of primary antiphospholipid syndrome was made from the symptomatology, persistent positive anticardiolipin antibody, and a positive lupus anticoagulant test.

Course. Treatment with anticoagulant therapy (aspirin, 40 mg daily) was given in order to prevent further ischemic attacks that might affect any other organs. The patient showed no neurological improvement.

Discussion

Antiphospholipid antibodies are members of the IgG and IgM groups with activity against negatively charged phospholipids. Three tests are now available for the detection of antiphospholipid antibodies: the venereal disease test, the lupus anticoagulant test, and solid-phase antiphospholipid immunoassay. The lupus anticoagulant, which was first described by Feinstein and Rapaport, is found in 10% of patients with SLE and is defined as an immunoglobulin that interferes with the in vitro phospholipid-dependent coagulation test without inhibiting the activity of specific coagulation factors; it is not necessarily identical to antiphospholipid antibodies identified by ELISA. Those antibodies are associated with recurrent venous and/or arterial thrombosis, which is clinically paradoxical to the in vitro study. The association of antiphospholipid antibodies with a variety of neurological, obstetric, and thromboembolic complications is well recognized. These complications include thrombosis of the large cerebral arteries (mainly middle cerebral artery branches), giving rise to stroke or transient ischemic attacks (TIA's), myocardial infarction, brachial artery thrombosis, peripheral artery occlusion, retinal artery occlusion, throm-
basis of leg, retinal, and/or hepatic veins, pulmonary hypertension, and recurrent abortion. In our case, clinically repeated TIA's followed by major spinal cord infarction, the presence of several autoantibodies (including IgG anticardiolipin, platelet-associated IgG, and antinuclear antibody) as well as a positive lupus anticoagulant test indicated that the cause of the spinal cord infarction in this young patient was the existence of autoantibodies. The mechanism of this antiphospholipid antibody remains unknown. Several hypotheses have been raised, including inhibition of prostacyclin formation, adhesion and activation of platelets, prekallikrein inhibition, low function of antithrombin III, and inhibition of protein C. However, the appropriate theory for this syndrome remains controversial.

Recently, findings of cerebral ischemia on MR imaging have been reported in patients with primary antiphospholipid syndrome, indicating

![Figure 2](image)

**Figure 2.** *Left and Center:* Magnetic resonance (MR) images. T₁-weighted (TR 500 msec, TE 20 msec, left) and gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA)-enhanced (center), midsagittal view, obtained 27 days after symptom onset. Slight atrophy of the cord can be seen, especially at the T10-11 level, with severe cord enhancement (asterisk). *Right:* Digital subtraction angiography, obtained 29 days after onset, showing no obstruction in the artery of Adamkiewicz (arrow). Note capillary blush compatible with Gd-DTPA-enhanced lesion on MR imaging.

**Table 1**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Authors &amp; Year</th>
<th>Age (yrs), Sex</th>
<th>Location of Lesion</th>
<th>MR Imaging Findings†</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Brown, et al., 1989</td>
<td>64, M</td>
<td>C4–7</td>
<td>cord swelling high ND</td>
<td>hypertension</td>
</tr>
<tr>
<td>2</td>
<td>Dillon, et al., 1989</td>
<td>37, F</td>
<td>conus</td>
<td>high</td>
<td>low + patch</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>65, M</td>
<td>thoracic</td>
<td>high</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>62, M</td>
<td>thoracic</td>
<td>–</td>
<td>high</td>
</tr>
<tr>
<td>5</td>
<td>Pou Serradell, et al., 1990</td>
<td>77, F</td>
<td>T10–11</td>
<td>normal</td>
<td>high</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>61, M</td>
<td>conus</td>
<td>low, cord swelling high</td>
<td>ND</td>
</tr>
<tr>
<td>7</td>
<td>Dunn &amp; Wiener, 1991</td>
<td>41, M</td>
<td>L2–4</td>
<td>normal</td>
<td>high</td>
</tr>
<tr>
<td>8</td>
<td>Eksnis, et al., 1991</td>
<td>41, F</td>
<td>C7–T3</td>
<td>normal</td>
<td>high</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>56, F</td>
<td>thoraco-lumbar</td>
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<td>high</td>
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<tr>
<td>10</td>
<td></td>
<td>53, F</td>
<td>T6–12</td>
<td>normal</td>
<td>high + T6–12</td>
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<tr>
<td>11</td>
<td>Nagashima, et al., 1991</td>
<td>50, M</td>
<td>T-2</td>
<td>low, cord swelling mixed (6d)</td>
<td>ND</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>52, M</td>
<td>C-4</td>
<td>normal</td>
<td>high (9h)</td>
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<tr>
<td>13</td>
<td>Vandertop, et al., 1991</td>
<td>17, M</td>
<td>C1-T3</td>
<td>slight cord swelling high</td>
<td>ND</td>
</tr>
<tr>
<td>14</td>
<td>Hasegawa, et al., 1993</td>
<td>6, M</td>
<td>T10-conus</td>
<td>cord swelling mixed (5d)</td>
<td>–</td>
</tr>
</tbody>
</table>

* MR = magnetic resonance; AVF = arteriovenous fistula; TIA = transient ischemic attack; ANA = antinuclear antigen; RF = rheumatoid factor; DM = diabetes mellitus; VDRL = venereal disease; HC = hypercholesterolemia; LA = lupus anticoagulant.
† Numbers in parentheses indicate time of study after symptom onset (h = hours, d = days); low = low signal intensity; high = high signal intensity; mixed = high- and low-intensity areas due to hemorrhagic infarction; + = positive enhancement with gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA); – = negative with Gd-DTPA enhancement; ND = not done.
‡ Patients with anterior spinal cord syndrome.
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multiple cerebral white matter infarction or multiple sclerosis mimicry. On the other hand, in regard to spinal cord ischemia, SLE myelopathy associated with antiphospholipid antibody has been described, with no abnormalities detected on MR images. So far, no reports of spinal cord infarction caused by primary antiphospholipid syndrome have been published. This paucity of information might be a reflection of the lack of interest in studying this disease. More careful studies of ischemic disease of the spinal cord, especially in children, should be performed.

The causes of spinal cord ischemia vary widely and are well documented: arteriosclerosis, trauma, especially in children, vasculitis, emboli, aortic surgery, and irradiation. However, the diagnosis of spinal cord infarction depends on clinical evidence, and the radiological manifestation remains unclear. Recently, several reports showing the MR imaging appearance of spinal cord infarction have been published; however, diagnosis of spinal cord infarction at the subacute stage is very difficult, since its MR imaging features sometimes mimic those of an intramedullary tumor. These features, as reported in 14 cases, are summarized in Table 1, and include an anterior spinal artery syndrome in patients who are mainly middle-aged or elderly, a syrinx, and arteriovenous fistula, the risk factors are mainly related to arteriosclerosis. Seven of these patients showed abnormal cord enhancement, and in two (Cases 7 and 12) the time course of Gd-DTPA enhancement is described. Our patient showed a dramatic time course on MR imaging: the lesion was initially enhanced on Day 5 and lasted until Day 59, followed by diminishing enhancement accompanied by progressive cord atrophy. These cases together with ours suggest that, as in the brain, in some cases MR imaging could reveal the cord swelling in the acute stage, Gd-DTPA enhancement in the subacute stage, and diminishing enhancement and cord atrophy later on. To avoid further unnecessary exploratory laminectomy, more reports of spinal cord ischemia should be accumulated.

Conclusions

Our case suggests the necessity of examining the antiphospholipid antibody concentration in spontaneous spinal cord infarction. Recently, Montalban, et al., reported that patients with this antibody were predominantly male and not necessarily young, and that 50% of them had no other vascular factors. Platelet antiaggregating drugs are useful in preventing further cerebrovascular ischemic events. Therefore, measurement of the antiphospholipid antibody concentration might be useful in patients with cerebral and spinal cord ischemia, since those with such antibodies may have a good prognosis when platelet antiaggregating drugs are administered to prevent further ischemic attacks.

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References

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Address reprint requests to: Mitsuhiro Hasegawa, M.D., Department of Neurosurgery, Kanazawa University School of Medicine, 13-1 Takaramachi, Kanazawa 920, Japan.