

Transverse Myelitis in a Patient with Primary Antiphospholipid Syndrome

Dong Min Lee, Hyun Soon Jeon, and Wan Hee Yoo

Department of Internal Medicine, Chonbuk National University Medical School and Research Institute of Clinical Medicine, Chonju, Korea.

The neurological manifestations of antiphospholipid syndrome (APS) are diverse. Transverse myelitis (TM) is an uncommon, but well-known neurological complication of systemic lupus erythematosus (SLE). On the other hand, the reported cases associated with primary APS are extremely rare. To our knowledge, this is the first report of TM in a patient with primary APS in Korea.

A 32-year-old male patient was admitted with the sudden onset of numbness, a tingling sensation, and weakness in both lower extremities. He had a 19 months history of external iliac and femoral arterial thromboses prior to admission. The laboratory results indicated the presence of anticardiolipin antibodies of the IgG class and lupus anticoagulant. No other autoantibodies were detected and there were no apparent clinical manifestations of SLE or multiple sclerosis. A T2-weighted magnetic resonance (MR) image showed swelling and increased intensity of the cervical and thoracic spinal cord between C6 and T7 with slight enhancement by contrast medium. After steroid pulse therapy, the patient's symptoms were gradually relieved and the abnormal findings on MR imaging disappeared.

Key Words: Antiphospholipid syndrome, transverse myelitis

INTRODUCTION

Transverse myelitis (TM) is a neurological disorder caused by inflammation affecting one or more segments of the spinal cord. The symptoms usually begin with the sudden onset of lower back

pain, muscle weakness or abnormal sensations in the lower legs. These can rapidly progress to more severe symptoms, including paralysis, urinary retention and fecal incontinence. TM in SLE carries a high morbidity with less than 15% of patients walking 3 weeks following diagnosis, and mortality rate of 33%.^{1,2} Therefore, timely diagnosis and management are mandatory for the disease.

The causes of TM are highly variable. Among the many causative diseases that of systemic lupus erythematosus (SLE) is a well-known underlying disease.²⁻⁵ That is, TM may complicate the clinical course of patients with antiphospholipid syndrome (APS) either primary or secondary,⁶⁻⁸ but the reported cases of primary APS complicated with TM are rare.⁹⁻¹¹

CASE REPORT

A 32-year-old male patient visited our hospital with a five-day history of gradually aggravated weakness, tingling sensation, and numbness in both lower legs. He had undergone a stent insertion due to thromboses of the right external iliac and femoral arteries 19 months before, and received anticoagulation therapy during follow-up (Fig. 1). His sister was allegedly suffering from rheumatoid arthritis.

On admission, his blood pressure was 130/80 mm Hg, pulse rate was 84/min, and body temperature was 36.8°C. Neurological examinations revealed a motor weakness of both lower legs, graded as 4/5 in accordance with the 'Medical Research Council's Grading System for Muscle

Received May 10, 2002

Accepted July 29, 2002

Reprint address: requests to Dr. Wan Hee Yoo, M.D., Ph.D., Division of Rheumatology, Department of Internal Medicine, Chonbuk National University Medical School, and Research Institute of Clinical Medicine, #634-18, Keumnam-dong, Duckjin-gu, Chonju, Chonbuk 561-712, Korea. Tel: 82-63-250-1672, Fax: 82-63-254-1609, E-mail: ywhim@moak.chonbuk.ac.kr

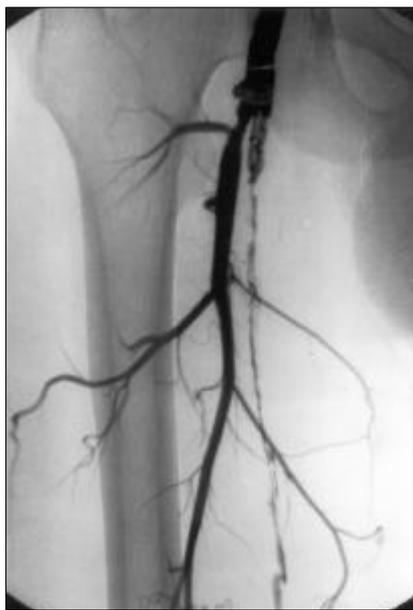


Fig. 1. Peripheral angiography, obtained 19 months before admission, shows thrombotic occlusions of the right iliac and superficial femoral arteries.

Strength, hyperesthesia and impairment of vibration sense below the knee. Despite these he was alert and there was no evidence of cranial nerve involvement, loss of deep tendon reflexes or pathologic reflexes.

Laboratory tests revealed normal blood cell counts and an increased erythrocyte sedimentation rate (23 mm/hr, normal < 9 mm/hr). Coagulation tests showed a prolonged prothrombin time (18.0 sec, normal 11.7 - 13.7 sec, INR 2.2) and an activated partial thromboplastin time (78.3 sec, normal 29.8 - 41.8 sec), but other blood chemistries were within normal limits. The serologic test for lupus anticoagulant was positive. The test for IgG and IgM anticardiolipin antibodies were 34.28 GPU (normal < 15 GPU) and normal (1.25 MPU, normal < 5 MPU), respectively. The test for syphilis was falsely positive. The subsequent tests, including rheumatoid factor, antinuclear antibody, cryoglobulins, anti-Sm, anti-dsDNA and anti-RNP antibodies, were all negative. The blood levels for C3, C4, CH50, factor VIII, antithrombin III, protein S and protein C were all normal. Analysis of the cerebrospinal fluid revealed a clear color, mild lymphocytic pleocytosis and the protein and glucose levels were 0.2 g/l and 64 mg/dl, respectively, but no oligoclonal bands were found and

the VDRL was negative. Viral assays for infectious agents, such as influenza, measles, coxsackievirus, varicella, mumps, Epstein-Barr virus and cytomegalovirus, were all negative. About six months later, the tests for IgG and IgM anticardiolipin antibodies were 46.71 GPU and normal, respectively, and the test for lupus anticoagulant was also positive.

T1- and T2-weighted sagittal and axial Magnetic resonance imaging (MRI) of thoracic spine were obtained. On the T1-weighted image, the cervical and thoracic cord between C6 to T7 levels was slightly enlarged, and gradually tapered to a normal size at the lower thoracic vertebra (Fig. 2A). The T2-weighted MRI demonstrated an increased signal intensity of the involved cord in comparison to the normal area (Fig. 2B and 2C).

Following the diagnosis of acute TM associated with primary APS, intravenous therapy with methylprednisolone (1g/day for 5 days) was started, followed by a gradually tapered oral combination of prednisolone with the anticoagulants, warfarin and a low dose of aspirin.

Three to four days after treatment, the patient experienced an increase in motor strength (grade 5) and was gradually relieved from hyperesthesia. Seventeen days after the initial examination, an MRI showed that the previously enlarged spinal cord had normalized on the T1-weighted images (Fig. 3A). The abnormally increased signal intensity on the T2-weighted images from the previous examination had been completely resolved (Fig. 3B and 3C). At present, he is on our follow-up, with a low dose of oral prednisolone and anticoagulation therapy, as an outpatient.

DISCUSSION

Transverse myelitis (TM) is an uncommon neurological disorder of the spinal cord, with uncertain and variable causes. The inflammation causing such extensive damage to the nerve fibers of the spinal cord, may result from several viral or bacterial infections,¹²⁻¹⁴ insufficient blood flow due to vascular diseases and hemorrhages,¹⁵ or autoimmune diseases, such as SLE.^{2-5,16} The acute, rapidly progressing form of TM can be the manifestation of multiple sclerosis, and is an uncommon manifestation of APS.

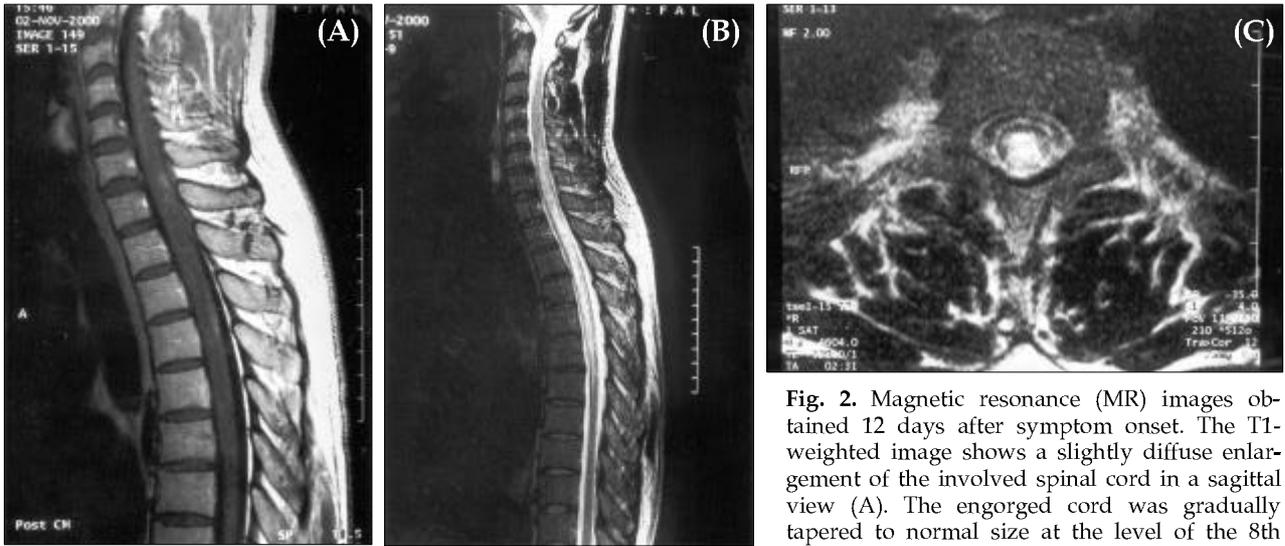


Fig. 2. Magnetic resonance (MR) images obtained 12 days after symptom onset. The T1-weighted image shows a slightly diffuse enlargement of the involved spinal cord in a sagittal view (A). The engorged cord was gradually tapered to normal size at the level of the 8th thoracic vertebrae. The T2-weighted image shows a slightly enhanced patchy lesion in the central portion of the spinal cord (C).

shows increased signal intensity of the same region in a sagittal view (B). A contrast-enhanced T1-weighted image shows a slightly enhanced patchy lesion in the central portion of the spinal cord (C).

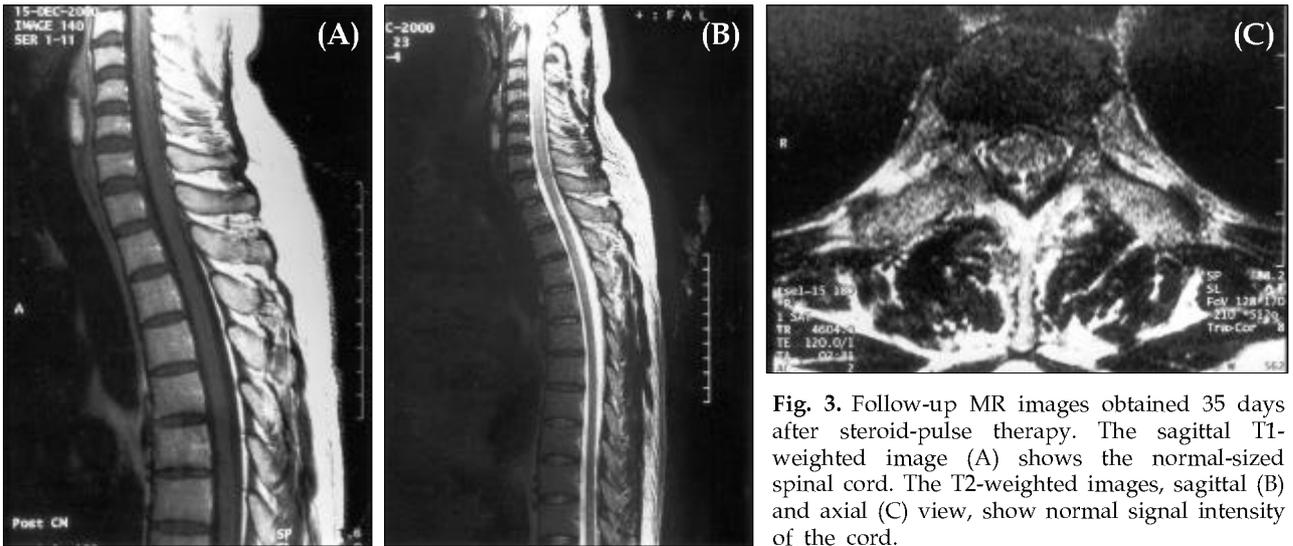


Fig. 3. Follow-up MR images obtained 35 days after steroid-pulse therapy. The sagittal T1-weighted image (A) shows the normal-sized spinal cord. The T2-weighted images, sagittal (B) and axial (C) view, show normal signal intensity of the cord.

APS is a noninflammatory autoimmune disease, and its most critical pathologic process is thrombosis, which may explain most of its clinical features. Any organ and vessels of any size can be affected by this disorder, and the clinical features are extremely variable. The clinical manifestations of APS associated with the central nervous system are diverse, and range from overt manifestations of arterial thrombotic events to psychiatric features, and a variety of other non-thrombotic neurologic syndromes.^{17,18}

Several cases of TM associated with secondary

APS have been reported in Korea.^{19,20} In addition, two cases of dementia and other neurologic manifestations associated with primary APS have been reported.^{21,22} However, our case represents the first description of acute TM in a patient with primary APS in Korea. The patient had a high titer for anticardiolipin antibodies and previous a history of arterial thrombosis without underlying rheumatic diseases, which collectively fulfilled the diagnostic criteria of primary APS.⁶

The exact mechanisms of TM in APS are not clearly known. Vascular changes and ischemic

necrosis, such as widespread microvascular injuries caused by the immune complex-mediated vasculitis, or vascular thrombosis resulting in infarction or hemorrhage, were considered to be the cause of myelitis.³ Some reports explained the pathogenesis as the direct interaction of antiphospholipid antibodies (APA) with spinal cord phospholipids.^{1,5,8} Several studies have confirmed the association of TM with APA,^{6,7} and several cases of TM occurred in primary APS without underlying rheumatic diseases. Hence, APA may have important roles in the pathogenesis of TM in either primary or secondary APS. However, the role of APA in the development of TM is still elusive, and longitudinal studies will be required to reveal the exact relationship.

As with many disorders of the spinal cord, there is no effective cure for patients with TM. TM in SLE shows high morbidity and mortality rates, the remainder being in wheelchair-bound or bed-ridden states, with marked dependence on others for the basic functions of daily living. The outcome of TM in primary APS was not well known. Among 3 cases of TM in primary APS,⁹⁻¹¹ one showed incomplete resolution with sequelae, and the other cases had relapses of TM. Unfortunately, it is difficult to predict outcomes in individual cases, but it has been shown that a rapid onset of symptoms generally implicates a poor recovery outcome. Possibly due to the aggressive steroid treatment, our case showed a relatively good outcome.

In recent years, pulses of methylprednisolone in combination with immunosuppressive drugs, such as cyclophosphamide or plasmapheresis, have gained acceptance by most authors.^{3-5,23,24} In Japan, three cases of TM in primary APS were reported.⁹⁻¹¹ Two of these were treated with steroid pulse therapy; with plasmapheresis being performed in the other to remove the lupus anticoagulant.¹⁰ In our case, the patient improved with the use of steroid pulse therapy combined with an oral anticoagulant and a low dose of aspirin.

In conclusion, acute TM may complicate both primary and secondary APS. Although the prognosis of TM is very poor, early treatment with a high dose of corticosteroid and anticoagulants may improve the clinical outcome.

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