Pseudotumor Syndrome Associated With Cerebral Venous Sinus Occlusion and Antiphospholipid Antibodies

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Background and Purpose: Antiphospholipid antibodies are known to be associated with increased risk of venous and arterial thrombotic events, including cerebral venous thromboses. Pseudotumor syndrome can be produced by cerebral venous thrombosis. A patient with cerebral venous thrombosis associated with antiphospholipid antibodies who exhibited pseudotumor syndrome is reported.

Case Description: A 49-year-old man who noted visual blurring and persistent vertical wavy lines in his fields of vision was found to have papilledema. Cerebrospinal fluid values were normal except for an opening pressure increase to 510 mm of fluid. His visual symptoms improved with lumbar puncture and the use of acetazolamide. Imaging studies showed that the transverse sinus was occluded completely on the left and partially on the right and that there was a small left cerebellar cortical venous infarction.

Conclusions: Antiphospholipid syndrome should be considered in the differential diagnosis of pseudotumor syndrome related to cerebral venous thrombosis. (Stroke 1993;24:469–472)

Key Words • cerebrovascular disorders • pseudotumor cerebri • anticoagulants, antiphospholipid antibodies

Antiphospholipid antibodies are associated with increased risk of venous and arterial thrombotic events, including stroke and transient ischemic attacks, and their recurrence, particularly in persons young in terms of stroke age. We describe a patient with antiphospholipid antibodies who exhibited the syndrome of pseudotumor cerebri that was found to be related to cerebral venous occlusion.

Case Report

In July 1989, a 49-year-old man noted vertical wavy lines in the field of vision of both eyes. In August, an ophthalmologist detected papilledema. By this time the patient also had noted pressure pain in the frontal and retroorbital regions bilaterally and visual blurring and light-headedness when he stood up quickly. He had a long-standing history of noise-induced hearing loss. Along with his symptoms, the patient also noted a vague distortion of hearing. Computed tomographic (CT) scan of the head showed no abnormality. Spinal fluid examination revealed the following: opening pressure, 510 mm cerebrospinal fluid (CSF); protein concentration, 42 mg/dL; glucose, 60 mg/dL; no erythrocytes; and one lymphocyte per cubic millimeter. After lumbar puncture, the patient’s bifrontal retroorbital headache and pressure and distortion of hearing resolved, and his light-headedness and visual symptoms improved. Subsequently, the patient was treated with 250 mg acetazolamide three times daily. He took this medication for 2 months, but when he complained about a metallic taste in his mouth he was given 20 mg furosemide (Lasix) once daily instead. After a few months, the visual symptoms again increased: the vertical wavy lines became more prominent, and the patient reported decreased vision in his left eye.

In March 1990, the patient was examined at the Mayo Clinic. The results of the neurological examination were normal except for mild bilateral, preexisting, noise-induced hearing loss and bilateral papilledema, more pronounced on the left. The disc edema appeared to be subacute; there was no surrounding retinopathy. Enlargement of blind spots was found bilaterally on formal visual-field testing.

The findings of the general medical examination were normal. The patient appeared fit and was not obese. Brachial blood pressure was 120/80 mm Hg. No evidence of endocrinopathy was noted on either clinical examination or laboratory testing for total thyroxine, sensitive thyroid-stimulating hormone, prolactin, and cortisol. Digital venous angiography showed nonvisualization of a small part of the proximal right transverse sinus and a large part of the left transverse sinus (Figure 1). Magnetic resonance imaging (MRI) and magnetic resonance (MR) angiography of the head showed nonvisualization of the left transverse sinus. This was thought to be caused by either congenital atresia or an occlusion. The left sigmoid sinus was present. The middle third of the right transverse sinus was partially thrombosed, and there was a small infarct in the posteromedial aspect of the right cerebellar hemisphere (Figure 2). Coagulation profile revealed a normal he-
mostatic survey without evidence of intravascular coagulation or fibrinolysis. Values for platelet count, prothrombin time, plasma clot time, activated partial thromboplastin time, thrombin time, fibrinogen, plasminogen, antithrombin III, protein C, and protein S were all normal. Immunoglobulin (Ig) M anticardiolipin antibody was normal, but IgG anticardiolipin antibody was positive at 1:1,024.

There was no history of venous thrombosis of pulmonary emboli. There was no skin rash or evidence of livedo reticularis. Rheumatological evaluation was normal. Antinuclear antibodies, rheumatoid factor, cryoglobulins, serum protein electrophoresis, and immunoelectrophoresis were within normal limits.

After treatment with 250 mg acetazolamide three times daily, the patient’s visual symptoms improved. Two months later, repeat digital venous angiography showed no change in the stenotic lesions. Anticoagulation therapy with warfarin was started in May 1990 and continued until December 1990, at which time the medication was changed to one tablet aspirin daily and 50 mg dipyridamole three times daily. Since that time, the papilledema has resolved. The patient’s visual fields became normal, and the visual symptoms decreased markedly. Acetazolamide was decreased to 250 mg daily.

In December 1990, MR angiography demonstrated irregularity of the midportion of the right transverse sinus, consistent with recanalization. The left transverse sinus was absent, with reconstitution of the left sigmoid sinus through the vein of Labbé (Figures 3A and 3B).

Discussion

Pseudotumor cerebri, also referred to as “benign intracranial hypertension,” is defined as a syndrome of increased intracranial pressure without clinical, laboratory, or radiological evidence for focal lesions or hydrocephalus. Four criteria have been proposed for diagnosis of pseudotumor cerebri: 1) increased intracranial pressure, with CSF pressures greater than 200 mm water; 2) normal CSF composition; 3) clinical manifestations related only to the increased intracranial pressure; and 4) normal findings on radiological and imaging studies. The presenting symptoms of pseudotumor cerebri, in decreasing order of frequency, include headache, dizziness, nausea, decreased visual acuity or visual obscurations, and diplopia. Common presenting signs are papilledema, enlarged blind spots, sixth nerve palsy, and visual field defects. The results of the rest of the neurological examination are usually normal.

The major threat to patients with pseudotumor cerebri is loss of vision; therefore, close follow-up of their visual acuity, blind spots, and visual fields is required. Permanent visual deficits have been estimated to occur in about 10–20% of the patients, with severe deficits in 4–12%. Papilledema typically is bilateral but occasionally may be unilateral. Cases of idiopathic intracranial hypertension without papilledema have also been described. In our patient, visual symptoms initially improved significantly with the use of acetazolamide,
deteriorated when acetazolamide administration was discontinued, and again improved significantly when administration was restarted. Our patient had preexisting noise-induced hearing loss. Initially in the course of his disease, he noted further distortion of hearing along with his visual symptoms.

The pathophysiology of pseudotumor cerebri is not clear. However, the weight of the evidence indicates that the disturbed CSF dynamics in these patients are caused by impaired absorption of CSF.

Some of the patients with cerebral venous sinus thrombosis exhibit "pseudotumor syndrome," a syndrome that is clinically identical to pseudotumor cerebri. Although these patients have abnormal angiographic findings, many authors classify them as cases of pseudotumor cerebri. Johnston et al., in proposing a mechanism-based classification of pseudotumor cerebri rather than a strictly clinically based concept, argue that pseudotumor syndrome is in fact a form of pseudotumor cerebri because there is increased intracranial pressure without enlargement of the ventricular system.

Clinically, patients with cerebral venous sinus thrombosis may have manifestations of increased intracranial pressure. The increased pressure is presumably related to disturbed CSF dynamics and decreased CSF reabsorption in connection with disturbed venous drainage. The disruption of venous flow may lead to venous infarcts or ischemic changes and in turn may cause focal neurological deficits or seizures or both. In our patient, the cortical cerebellar infarct was consistent with a small venous infarction. Clinically, however, this occurrence was asymptomatic. Cerebral venous thrombosis has been described in systemic illness with dehydration (particularly in children), infections, and malignancies that either invade the venous sinus or cause a hypercoagulable state, in systemic lupus erythematosus, and in Behçet's disease.

In recent years, attention has been drawn to hypercoagulable states. Cerebral venous thrombosis has been reported in patients with deficiencies of plasminogen, protein S, antithrombin III, and protein C, and in those with lupus anticoagulants.

Antiphospholipid antibodies are heterogeneous groups of antibodies. Two subsets of these antibodies, lupus anticoagulant antibodies and anticardiolipin antibodies, can be associated with a noninflammatory thrombotic endocarditis or with thrombotic venous and arterial occlusions. Arterial occlusions can particularly involve the cerebral circulation.

The data available suggest that antiphospholipid antibodies signify an increased risk of cerebral ischemic events and can therefore be used as markers of increased risk of stroke and transient ischemic attacks, particularly in younger patients. As well summarized by Hess, these patients are often in the fourth or fifth decade of life; there is a slight preponderance of females; and there may be a history of thrombotic events, stroke, or spontaneous abortion. A minority of the patients have systemic lupus erythematosus.

Other neurological manifestations associated with the presence of antiphospholipid antibodies include retinal artery occlusions, acute ischemic encephalopathy, seizures, multi-infarct dementia, chorea, and transverse myelitis. Migraine syndrome frequently complicated by neurological deficits has also been noted. Some but not all patients with Sneddon's syndrome (i.e., cerebral infarction and livedo reticularis) have antiphospholipid antibodies.
To the list of neurological entities associated with antiphospholipid antibodies we add the syndrome of pseudotumor cerebri.

References

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Stroke. 1993;24:469-472
doi: 10.1161/01.STR.24.3.469

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