Extracranial Carotid Artery Disease in Patients With Arterial Limb Embolism

To the Editor:

The relationship between embolism and thrombosis as a cause of ischemic stroke is far from established. Not all ischemic strokes in patients with a cardiac source are caused by cardioembolic embolism since cerebrovascular atherosclerosis often coexists. Thus, the clinical differentiation between thrombotic and embolic infarction is extremely difficult and often impossible. General hallmarks of cerebral embolic events have been outlined, with the presence of atherosclerotic lesions in the appropriate artery considered by most as a feature excluding cerebral embolism.¹⁻³

However, atherosclerotic lesions of the cervical carotid arteries have been found in 23 of 100 asymptomatic men aged 50–69 years,¹ in 34 of 108 patients with familial hypercholesterolemia and coronary artery disease,² and in 21 of 56 elderly adults with isolated systolic hypertension.³ Furthermore, in two different studies, the concomitance of appropriate carotid disease and potential cardiac sources of emboli illustrates the difficulties of diagnosing cardioembolism in an individual patient. In one study,⁴ the appearance together of arterial disease and potential cardiac sources of emboli was evaluated in 205 patients with transient ischemic attacks (TIAs) who underwent both angiography and echocardiography. Fifty patients had a potential source of emboli, and a carotid lesion appropriate to the TIAs was present in 38 of these 50 patients. In the work by Rem et al.,⁵ in which 184 consecutive patients with TIA and stroke were studied, 59 patients with a possible cardiac source for cerebral emboli were detected. After cerebral angiography, 29 of these 59 patients also showed a vascular lesion in the appropriate carotid artery. The authors could not decide definitely which lesion was responsible for the cerebral embolus.

Since carotid atherosclerosis is so frequent in different populations, we must ask what is its frequency in patients with demonstrated cardioembolic emboli? We screened 25 consecutive patients without history of stroke admitted because of an acute arterial limb embolus for atherosclerotic lesions of the cervical carotid arteries using a high-resolution multi-gated pulsed Doppler system. There were nine men and 16 women aged 53–87 (mean 68) years. The anatomic site of lodgement of the arterial embolus was femoral in 10 patients, popliteal in five, upper extremity in five, aortic saddle in three, and iliac in two. The sources of arterial embolism (as determined by two-dimensional echocardiography) were hypertensive heart disease with atrial fibrillation in eight patients, valvular heart disease in seven, dilated cardiomyopathy in two, mitral anulus calcification in one, and lone atrial fibrillation in seven.

Nine of 25 patients (36%) had an abnormal Doppler investigation in the common and/or internal carotid arteries. In two patients multivessel disease was observed. The degree of stenosis was considered to be important (>50% diameter reduction) in three patients.

If any of these nine patients had an arterial embolus lodged in the cerebral arteries, he or she would have been diagnosed for thrombotic stroke and no anticoagulant therapy would have been prescribed. We conclude that asymptomatic carotid artery disease is common in patients with cardioembolic events, and thus its detection should not be used as an argument against cerebral embolism diagnosis.

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References

Multiple Small-Vessel Occlusions in Systemic Lupus Erythematosus

To the Editor:

There has been great interest over the past few years, recently highlighted by the papers of Levine and Welch¹ and Levine et al.,² in the association of cerebrovascular diseases occurring not only in systemic lupus erythematosus (SLE) but also in lupus-like diseases and in the primary antiphospholipid syndrome with antibodies to phospholipids (“lupus anticoagulant,” antibodies to cardiolipin [aCL], and the false-positive VDRL).³,⁴ Multi-infarct dementia accompanied by cerebral atrophy may result,⁵ often with other vascular occlusive events encountered in the same patients. We wish to document one such patient, a young man with SLE, in whom the only serologic evidence of antiphospholipid antibodies was a low positive (1:1) serologic test for syphilis. He had also developed retinal artery occlusions.

Our patient, a 25-year-old man, presented in 1981 with myalgias, Raynaud’s phenomenon, and generalized lymphadenopathy. Following a lymph node biopsy, his condition deteriorated and he developed pleurisy, fever, and a malar rash. SLE was diagnosed and he was started on prednisolone therapy (5 mg/
day). In 1983 he developed a flare-up of disease activity with vasculitic rash, myalgias, headaches, and fever. He was admitted for tests and within 24 hours had become comatose with a right upper motor neuron lesion. A computed tomogram (CT scan) showed cerebral atrophy with enlarged ventricles and multiple low-density areas in both hemispheres. He was treated with dexamethasone and antibiotics for a possible superimposed infection. He made a good recovery and was discharged 6 weeks later on prednisolone (30 mg/day), which was slowly decreased over the following months in response to a serologic settling of disease activity.

Reduction of steroid dosage to 17.5 mg resulted in a disease flare-up in October 1984, which was again treated with an increase in his steroid dose. Despite an initial response, he had a series of seizures in December 1984, followed by drowsiness. On recovery he was found to be persistently dysphasic. A repeat CT scan showed patches of low density in both hemispheres with further ventricular enlargement, which represented a deterioration from the previous scan. At this time he complained of some visual deterioration, and bilateral retinal infarcts were recorded. He was started on azathioprine and, despite some problems with concentration, he was able to return to work as a chef.

In December 1987, despite immunosuppression therapy (150 mg azathioprine + 17.5 mg prednisolone/day), he deteriorated further with drowsiness and increasing vagueness. A vasculitic rash was noted with ischemic ulceration of his fingertips. Prednisolone dosage was again increased to 30 mg/day, and a slow improvement was achieved. Serologic testing at that time revealed an antinuclear antibody titer of 1:320 (diffuse), positive DNA antibodies, and a false-positive VDRL titer (1:1). The erythrocyte sedimentation rate was elevated at 36 mm/hr, and the white blood cell count was reduced at 3.1 x 10^9/L with a relative lymphocytosis. The platelet count and hemoglobin content were within normal limits. Tests for the "lupus anticoagulant" and aCl were negative.

There are a number of points of interest in our patient. The cerebral events occurred several years before testing for antiphospholipid antibodies. He had been receiving systemic steroids as well as immunosuppressive therapy, which might have abolished "lupus anticoagulant" activity. The effect of steroid therapy on the "lupus anticoagulant" is well documented, although the effect on aCl antibodies is unpredictable.

One of the more interesting aspects of the recent description of this disease in SLE patients with antiphospholipid antibodies (as well as in systemic lupus erythematosus associated with antiphospholipid antibodies) is the emergence of a "seronegative" group of patients with similar clinical features in whom these antibodies have not been detectable. Had our patient been aCl-negative, this would have meant an absence of detectable lupus anticoagulant (LA) and anticardiolipin (aCl) antibodies. These authors, who are recognized experts in the antiphospholipid antibody syndromes, make several important points. Therapy directed against active SLE may suppress LA activity and thus mask its presence. Although the aCl titer is not consistently lowered with therapy, high-dose corticosteroids may moderately suppress the aCl in patients with SLE or SLE-like disease. Two may have been the case in the above patient. A false-positive VDRL (did the positivity of their patient's VDRL change on repeated testing?) and negative aCl assay may suggest differences in the antiphospholipid antibody to "recognize" and bind cardiolipin in two different structural conformations since the three-dimensional conformation of phospholipid in the membrane may be critical to the antibody's recognizing it.

Apart from antiphospholipid antibodies, patients with SLE have many reasons for ischemic stroke, including accelerated atherosclerosis, dyslipidemia, steroid-induced diabetes mellitus, abnormalities of fibrinolysis, cigarette smoking, drug abuse, hypertension, cardiac emboli (Libman-Sacks endocarditis), and thrombotic thrombocytopenic purpura. Vasculitis is distinctly rare. The false-positive VDRL may have been coincidental. The "seronegative" group proposed by Asherson et al may represent patients with these other causes of thrombosis independent of antiphospholipid antibodies.

The recognition of visual disturbances including retinal artery disease in SLE patients with antiphospholipid antibodies (as well as non-SLE patients) is becoming more widespread. Despite frequent use of the term "lupus vasculitis" in clinical practice and the literature, pathologic examination has not confirmed inflammation in the vessel wall in SLE retinopathy. Instead, pathologic studies have generally shown thrombosed arterioles with thickened intima in the absence of "true" vasculitis or foci

References

The following is in reply:
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