Lacunar Infarction due to Middle Cerebral Artery Stenosis

To the Editor:

Some cases of lacunar infarction with middle cerebral artery (MCA) stenosis may be explained by the Bernoulli principle. In a constant flow system, the smaller the cross-sectional area, the greater the flow velocity, and the lower the perfusion pressure. If the flow were turbulent, the pressure would be lower still. Thus, if the origin of a lenticulostriate artery were within a stenotic segment of MCA,1–3 the perfusion pressure in this segment would be reduced, compared to that in normal MCA segments, perhaps sufficiently to produce ischemia in the supply territory of the lenticulostriate artery. Such a hemodynamic mechanism might explain progressive lacunar infarction, which until now has not been satisfactorily explained.4

As a limited test of this hypothesis, we have reviewed 62 cases of acute hemiplegia in whom transcranial Doppler was performed within 48 hours of onset. These included 10 cases of lacunar stroke, in five of whom MCA stenosis was presumed by the criterion of mean velocity 20–60% greater on the symptomatic than on the asymptomatic side. In three of these, the hemiplegia evolved progressively over periods of 18–72 hours. In two, the abnormally high MCA velocity was documented during the period of evolution. By contrast, abnormally high velocity was present in only two of 40 cases of MCA territorial stroke, in none of six cases of lacunar stroke in whom the hemiplegia was present, but none were likely to be the etiology of an extracranial internal carotid artery occlusion.

Two additional case histories may help to illustrate the potential significance of stenosis of the MCA bifurcation. Such a mechanism might explain the sudden occurrence of stroke in a patient with no previous history on the asymptomatic side.

**Lupus Anticoagulant Associated With Extracranial Internal Carotid Artery Occlusion**

To the Editor:

Stroke and transient ischemic attacks have been associated with the lupus anticoagulant and antiphospholipid antibodies.1–3 The lupus anticoagulant prolongs the partial thromboplastin time (PTT), but is paradoxically associated with thrombotic events such as deep venous thrombosis, cerebral and extracerebral arterial disease, and cerebral venous thrombosis. Few angiographic results have been reported. We have encountered a patient who gave a history of two spontaneous abortions, the last one 2 months prior to this stroke. There was a history of a pituitary microadenoma for which she was treated with bromocriptine. She smoked one pack of cigarettes per day. There was no history of head or neck trauma, and she had not used birth control pills.

General examination disclosed a blood pressure of 108/64 and a regular heart rate of 68 beats per minute. There were no cardiac murmurs. She had dysarthria, nonfluent speech, poor repetition, and made numerous paraphasias. There was severe dysnomia and acaulca. A right facial weakness, severe spastic right hemiparesis, right hyperreflexia, and Babinski sign were present.

Pertinent laboratory data included a normal complete blood count and platelet count. Fasting blood sugar, electrolytes, renal, liver, and thyroid functions were normal. Cholesterol was 297 mg/dl and triglycerides 150 mg/dl. Plasma reagin test was nonreactive. An erythrocyte sedimentation rate was 21 mm/hr. An antinuclear antibody was 1:8 when performed initially and 1:640 with a speckled pattern at the time of this evaluation. DNA antibody was negative. Electrocardiogram and two-dimensional echocardiogram were normal.

Coagulation studies included anticardiolipin antibodies, which were not elevated. The activated partial thromboplastin time was 41 seconds (23–36 seconds was the normal range). The partial thromboplastin time did not correct with a 1:1 mix with normal plasma. A thromboplastin inhibition test was done and was positive for the lupus anticoagulant at a dilution of 1:500. At that dilution, the control was 105 seconds and the patient 152 seconds for a ratio of 1.45 (a ratio greater than 1.3 is considered a positive result). The platelet neutralization test was also positive for the lupus anticoagulant. The PTT with platelets corrected to 38.5 seconds, but remained elevated with saline alone at 45.5 seconds (test positive when the PTT with platelets is at least 5 seconds shorter than a PTT with saline).

The CT scan showed no evidence of a pituitary adenoma, but rather a partially empty sella. There was a left frontal infarction. A review of digital subtraction angiograms demonstrated a left internal carotid artery occlusion approximately 1 cm above the bifurcation.

A cardiology consultant examined the patient and her cardiac studies and found no basis for cardiogenic embolism. Angiographic studies in patients with the lupus anticoagulant have been summarized by Levine and Welch,1 who reported a total of 17 patients. Six of these patients had an internal carotid artery stenosis or occlusion, but only one was reported to have been an extracranial internal carotid artery occlusion.4 Two additional case reports were found. One patient was a 38-year-old man with a vasculitis who suffered infarctions in the left cerebral hemisphere caused by an intraluminal thrombus in the left internal carotid artery. He improved after surgical excision of the thrombus.5 Another patient was a 38-year-old man with a diagnosis of systemic lupus erythematosus, who was hypertensive and a smoker.6 Angiography disclosed an ulcerated, nearly occluded left internal carotid artery.

Our patient had a characteristic history for stroke associated with the lupus anticoagulant. She was young and suffered two spontaneous previous abortions, the most recent one 2 months before the stroke. There was neither a history of head or neck trauma nor use of birth control pills. She did not have systemic lupus erythematosus nor a cardiac source for embolism. Risk factors of smoking, migraine, and hypercholesterolemia were present, but none were likely to be the etiology of an extracranial internal carotid artery occlusion in a 24-year-old woman.

Language and motor function improved slowly up until the time of this evaluation.

The patient gave a history of classic migraine and one episode of prolonged amnesia associated with migraine. She had had two spontaneous abortions, the last one 2 months prior to this stroke. There was a history of a pituitary microadenoma for which she was treated with bromocriptine. She smoked one pack of cigarettes per day. There was no history of head or neck trauma, and she had not used birth control pills.

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Coagulation studies included antiphospholipid antibodies, which were not elevated. The activated partial thromboplastin time was 41 seconds (23–36 seconds was the normal range). The partial thromboplastin time did not correct with a 1:1 mix with normal plasma. A thromboplastin inhibition test was done and was positive for the lupus anticoagulant at a dilution of 1:500. At that dilution, the control was 105 seconds and the patient 152 seconds for a ratio of 1.45 (a ratio greater than 1.3 is considered a positive result). The platelet neutralization test was also positive for the lupus anticoagulant. The PTT with platelets corrected to 38.5 seconds, but remained elevated with saline alone at 45.5 seconds (test positive when the PTT with platelets is at least 5 seconds shorter than a PTT with saline).

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Cerebral Infarction and Familial Protein S Deficiency

To the Editor:

Protein S is an antithrombotic plasma protein that serves as a cofactor of activated protein C anticoagulant activity.1 Hereditary protein S deficiency, inherited as an autosomal dominant disorder,2 predisposes individuals to recurrent venous thrombosis,3 but is not yet currently associated with stroke.4 We report the case of a young patient whose stroke was associated with familial protein S deficiency.

This 33-year-old right-handed man was admitted to our hospital a few hours after stroke of acute onset. While working, he experienced inability to speak and write properly. On admission, he was severely aphasic with a nonfluent paraphasic language. Blood pressure, pulse rate, and electrocardiogram (ECG) were all normal. A computed tomographic scan 12 hours after admission demonstrated a low-density area involving the left posterior temporal region. The carotid arteriogram showed a distal occlusion of the sylvian axis. Further investigation, including chest x-ray, ECG, echocardiogram, Holter ECG recording, and routine laboratory and hematologic studies were normal. Smoking was the only risk factor for arterial disease. The patient was treated with heparin and his condition gradually improved. When discharged, he had fluent paraphasic speech, normal comprehension, and repetition disability suggestive of conduction aphasias.

Family history was significant for venous thrombosis. One member died after thrombophlebitis associated with a protein S deficiency, and six other members of the family had been identified as having a protein S deficiency associated with venous thrombotic events (Figure 1). The mother of the patient was probably affected because she died after pregnancy from pulmonary embolism.

Protein S levels of the patient were measured twice, 3 and 4 months after the stroke, when he was not treated with oral anticoagulants. Total and free protein S antigen levels were 62% and 20%, respectively (n = 70–120%). The concentrations of fibrinogen, antithrombin III, protein C, and plasminogen were within normal ranges. Plasma samples were obtained from two other maternal family members determined to have an asymptomatic protein S deficit. No arterial stroke occurred in the relatives of our patient.

Stroke has rarely been reported to be associated with protein S deficiency. Girolami et al5 reported a familial case of protein S deficiency in which the patient, a 44-year-old woman, was admitted with a left-side hemiplegia and a right carotid angiography showing partial obstruction of the sylvian axis. She had a markedly reduced level of free protein S. Family history was positive for thrombotic conditions, and two members had a protein S defect. Sie et al6 studied 23 patients from 17 families who fulfilled the criteria of isolated protein S deficiency. Among these, six had arterial thrombosis, but only three had involvement of the cerebral vessels.

In the present case, it is likely that there is a relationship between the cerebral infarction and protein S deficiency because no other cause was demonstrated after extensive cardiac and vascular investigations. In this family, some members partially deficient in protein S activity were asymptomatic while others were severely affected. It is possible that individual factors trigger the initial clotting process, some of them precipitating arterial rather than venous thrombosis. This kind of inherited deficit must be distinguished from acquired deficits, which occur in inflammatory states, are usually reversible, and are not proven to cause cerebral infarction.

In an attempt to evaluate an association between stroke and protein S deficiency, one should probably first determine the incidence of cerebral infarction in patients with the inherited form of the disease. If the 26% frequency of arterial thrombosis reported by Sie et al7 is confirmed, a routine investigation of protein S levels in young patients affected by stroke of unknown etiology could be of interest, in conjunction with testing for deficiencies for antithrombin III and protein C.

Patrick Davous, MD
Service de Neurologie
CIR Victor-Dupouy
Argenteuil, France

Marie-Hélène Horellou, MD
Jacqueline Conard, MD
Meyer Samama, MD
Laboratoire d’Hématologie
Hôpital-Dieu
Paris, France

References

FIGURE 1. Family pedigree of patient with stroke associated with familial protein S deficiency. a, Male, deceased. b, Female, venous thrombotic events. c, Female, protein S deficiency; ratio of total versus free protein S levels (%). d, Male, thrombotic event(s) associated with protein S deficiency. e, Patient.
Lacunar infarction due to middle cerebral artery stenosis.
M J Tan and J H Halsey

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