Recurrent Transient Ischemic Attacks and Stroke in Association With an Internal Carotid Artery Web

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Fibromuscular dysplasia is a nonatherosclerotic vascular disease that most commonly affects cervical carotid arteries at the C1-C2 level when cephalic arteries are involved. Several histopathologic and angiographic subtypes of fibromuscular dysplasia exist; most have a benign natural history. We describe the third reported case of a pathologically proven, symptomatic proximal internal carotid artery web and suggest that patients with this lesion are at a higher risk for stroke. (Stroke 1991;22:94-98)

Fibromuscular dysplasia is a nonatherosclerotic vascular disease characterized by pathologic changes in the smooth muscle and fibrous tissue of small and medium-sized arteries. Cephalic fibromuscular dysplasia most frequently involves the internal carotid artery extracranially at the C1-C2 level. Intracranial fibromuscular dysplasia is less common, and proximal lesions are rare.

Fibromuscular dysplasia has been divided into three histopathologic subtypes based on vessel wall abnormalities. Medial fibromuscular dysplasia (90-95% of cases) is characterized by thickening of the media due to proliferation of fibrous tissue and smooth muscle, with destruction of the elastic lamina. Intimal fibroplasia (5% of cases) involves intimal thickening and destruction of the internal elastic lamina. Periadventitial fibroplasia (1-2% of cases) consists solely of fibrosis of the adventitia. Because of the pathologic abnormalities of the vessel wall, cerebral angiography may demonstrate characteristic changes that suggest the diagnosis of fibromuscular dysplasia. The most frequent angiographic abnormality is the "string of beads" appearance of the cervical carotid artery caused by alternating regions of vessel narrowing and dilatation in patients with medial fibromuscular dysplasia. Tubular stenosis and webs may also be seen.

Proximal internal carotid artery webs have been suggested to be associated with an increased risk of hemodynamic compromise and thromboembolism. However, only two cases of pathologically proven symptomatic proximal internal carotid artery webs have been reported. We describe a patient with recurrent transient ischemic attacks (TIAs) and stroke in association with a pathologically verified proximal internal carotid artery web and no other apparent cause of stroke.

Case Report

A 34-year-old, right-handed, white woman who was in good health experienced a 30-minute episode of light-headedness while doing aerobics. The following day, she became weak and slumped to the floor 20 minutes after starting aerobics. She did not lose consciousness. A nurse who was present noticed slurred speech and a right facial droop.

On admission several hours later, the patient complained of speech difficulty and weakness of her right hand. She did not have a history of headache, diabetes mellitus, hypertension, cardiac disease, or drug abuse or a family history of early stroke. She had a 15 pack-year smoking history and had been taking oral contraceptives (1 mg norethindrone/0.05 mg mestranol) for 3 years.

Her blood pressure was 140/80 mm Hg, her heart rate was 88 beats/min and regular, and she was afebrile. General examination was unremarkable except for a grade II/VI systolic ejection murmur heard at the left sternal border. There were no bruits heard over the head or neck. She was fully oriented but dysarthric. General examination was unremarkable except for a grade II/VI systolic ejection murmur heard at the left sternal border. There were no bruits heard over the head or neck. She was fully oriented but dysarthric. She had decreased spontaneous speech, difficulty finding words, and trouble naming parts of objects. She made occasional paraphasic errors. Repetition was minimally impaired, and comprehension was normal. She had numbness to pinprick on the right side of her face (V1-V3), right upper motor neuron–type facial weakness, and a diminished gag

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response. Her tongue deviated to the right on protrusion. A right pronator drift and right hand weakness were present. Pinprick, stereognosis, and graphesthesia were impaired on the right. Biceps and triceps reflexes were 3+ on the right and 2+ on the left. The plantar responses were flexor. Fine coordination was impaired in the right hand.

Laboratory studies included a normal blood cell count and electrolyte concentration and normal findings on urinalysis and electrocardiography. Sedimentation rate, cholesterol level, and serum viscosity were normal. Prothrombin time, activated prothrombin time, antithrombin III level, plasminogen level, protein C level, protein S level, and reptilase time were normal. Rapid plasma reagin assay was nonreactive, and β-human chorionic gonadotropin level was normal. Lupus anticoagulant level could not be determined due to heparinization. Computed tomography of the brain showed a lucency in the left sylvian and suprasylvian regions consistent with early infarction in the distribution of the left middle cerebral artery. The patient received heparin following review of the brain computed tomogram. Oral contraceptives were stopped.

Results of prolonged cardiac monitoring, echocardiography with microcavitation study, and a cardiac stress test were normal. Cerebral angiography demonstrated a linear filling defect projecting into the proximal left internal carotid artery (Figure 1). The lesion occluded approximately 50% of the lumen. There was slow filling in the left middle cerebral artery territory consistent with recent infarction. There was no evidence of atherosclerosis in the intracranial or extracranial vessels.

Her neurologic deficits improved, and warfarin therapy was started. Six days after admission, she had a single episode of blurred vision and increased word-finding difficulty that lasted 5 minutes. Her prothrombin time was 1.6 times control. During the remainder of her hospitalization no other episodes occurred. She was discharged on warfarin therapy with minimal word-finding difficulty and right facial numbness and weakness.

The patient was readmitted 6 weeks later for surgical evaluation. No symptoms had occurred since discharge. Magnetic resonance imaging of the brain disclosed an infarct in the left middle cerebral artery distribution (Figure 2). A repeat cerebral angiogram was unchanged. She underwent surgical resection of the web. A shelf of tissue was found to be nearly obstructing the lumen of the internal carotid artery and encompassing 270° of the circumference of the vessel. Microscopic examination of the surgical specimen demonstrated intimal fibrosis with destruction of the internal elastic lamina, consistent with a diagnosis of intimal fibroplasia (Figure 3). There was no evidence of atherosclerotic plaque. The patient has been asymptomatic for 8 months since surgery while taking 325 mg aspirin/day.

Discussion

The management of patients with fibromuscular dysplasia represents a therapeutic dilemma. A variety of neurologic disorders have been reported in association with fibromuscular dysplasia. These include thromboembolic events, hemodynamic compromise, arterial dissection, and aneurysm and fistula formation.1,2,7-10 In a series of 13,955 cerebral angiograms performed over 17 years for a variety of indications, fibromuscular dysplasia was found in 82 patients (0.6%).11 Only 13 (14%) of 79 patients studied had angiography performed because of a TIA or stroke. Thus, determining which patient with fibromuscular dysplasia will develop symptoms caused by the lesion is difficult.
There have been two prospective studies of neurologic outcome in patients with cephalic fibromuscular dysplasia. In the above-cited series, 79 of the 82 patients with fibromuscular dysplasia were followed up for an average of 5 years. The patients were subdivided into four groups: 13 patients had focal cerebral ischemia, 29 had fibromuscular dysplasia discovered incidentally during the investigation of an intracranial mass lesion, 10 had fibromuscular dysplasia in association with an intracranial aneurysm, and the remaining 27 had fibromuscular dysplasia in association with other disorders. Seven of the 13 patients with focal cerebral ischemia were treated, four medically and the other three surgically. None of these patients had strokes during follow-up. Of the remaining 66 patients, three had strokes during the period of observation; all three were from the second group. None of these patients had undergone treatment of fibromuscular dysplasia, and only one patient had a stroke in the same vascular territory as the fibromuscular dysplastic lesion. This patient was 71 years old, and the stroke occurred 216 months after the original angiography. In a smaller study, a search of three medical centers' radiologic and clinical records disclosed 17 patients with fibromuscular dysplasia. One patient was treated surgically, and the remaining 16 were treated medically or received no specific therapy. During an average follow-up of 3.8 years, two patients (aged 60 and 79 years) with concurrent atherosclerosis had strokes. Thus, the available data suggest a low incidence of stroke in both asymptomatic and symptomatic patients with fibromuscular dysplasia. However, a controlled trial of medical or surgical therapy has not been performed. Several surgical series using endarterectomy, resection, or graduated dilatation for cephalic fibromuscular dysplasia have reported low morbidity, but it is unclear what the outcome would have been without surgery.

In addition to our patient, two other cases of pathologically proven symptomatic cephalic fibromuscular dysplasia in the form of an internal carotid artery web have been reported. The first patient was a 30-year-old woman who had recurrent TIA's upon head turning. A ridge of tissue was resected from the posterior wall of the proximal internal carotid artery. Histologic evaluation of the surgical specimen disclosed subintimal and medial fibrosis (medial fibromuscular dysplasia). The patient was asymptomatic postoperatively. The second patient was a 47-year-old woman who presented with embolic infarction in the right middle cerebral artery territory and was found to have a proximal internal carotid artery web on angiography. She was treated medically, but her symptoms recurred 1 year later. Cerebral angiography demonstrated that the lesion had increased in size and had an associated thrombus. A ring of tissue was surgically removed from the origin of the internal carotid artery. Examination of histologic sections demonstrated fibrous proliferation of the intima, consistent with a diagnosis of intimal fibroplasia. She was asymptomatic after surgical resection of the lesion.

Hormonal influences may be important in the pathogenesis of fibromuscular dysplasia. Our patient was taking oral contraceptives and had a history of cigarette smoking. Stroke rates are increased in women taking oral contraceptives and may be even higher in those who also smoke. However, the vasculopathy found in association with oral contraceptive use differs from that seen in our patient. The vasculopathy of oral contraceptive use consists of intimal thickening with reduplication of the internal elastic lamina. In our patient the internal elastic lamina was absent. While smoking is an independent risk factor for stroke, no atheromatous changes were seen on angiography or histopathologic section of the cervical lesion. Thus, the proximal internal carotid artery web was the only identifiable cause for our patient's stroke. It was likely a consequence of artery-to-artery embolism. Although thrombus was not seen in association with the internal carotid artery web at surgery, the patient had received anticoagulants for 6 weeks prior to resection and thrombolysis may have occurred.

Conservative medical therapy is indicated for asymptomatic, and most cases of symptomatic, fibromuscular dysplasia because the available data suggest a benign natural history for this disease. Our patient is the third reported case of recurrent TIA's and stroke in association with a proximal internal carotid artery web. Of the three reported cases, histologic evaluation of the surgical specimen in two cases demonstrated intimal fibroplasia and in one case medial fibromuscular dysplasia. Patients with internal carotid artery webs may represent a subpopulation of patients with fibromuscular dysplasia in whom the risk of ischemic stroke is higher. In these
FIGURE 3. Photomicrographs of resected web demonstrating intimal fibrous proliferation and absence of internal elastic lamina, without atheromatous deposits. Histologic appearance is consistent with diagnosis of intimal fibroplasia. Hematoxylin and eosin stain. Top: x32; bottom: x400.
patients, surgical treatment should be considered, especially if medical therapy is unsuccessful.

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