Moyamoya syndrome associated with cocaine abuse

Case report

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The authors report the case of a 30-year-old woman who was a long-term intranasal cocaine abuser and who presented with transient ischemic attacks and multiple cerebral infarctions that were associated with moyamoya syndrome. The authors suggest that, because of its sympathomimetic effects, chronic cocaine use may promote intracranial arterial stenosis, distal ischemia, and subsequent formation of moyamoya-like vessels. The patient has remained clinically stable with no new episodes of stroke 6 years after undergoing "pial synangiosis" (modified encephaloduroarteriosynangiosis) to revascularize both hemispheres. Cocaine abuse may lead to moyamoya syndrome and may represent a chronic effect on the cerebral vasculature.

Key Words * cocaine abuse * moyamoya syndrome * intracranial carotid artery stenosis * pial synangiosis * encephaloduroarteriosynangiosis

The association between cocaine use and cerebrovascular complications is well established, and cocaine abuse has become one of the principal precipitating factors for stroke in young adults in North America.[4,5,7,8,12] Cerebrovascular complications resulting from cocaine use have been related to rupture of vascular anomalies, such as aneurysms and arteriovenous malformations, and to spontaneous intracranial hemorrhage.[4,7] We present a patient who, after a long history of repeated cocaine abuse, suffered bilateral strokes that were shown on angiography to be related to the development of moyamoya syndrome.

CASE REPORT

History. This 30-year-old Caucasian, right-handed woman presented with headache, dysphasia, and right arm and leg weakness. She had a long history of headaches, occurring approximately once every week, which had worsened in frequency and intensity over the previous 2 weeks. She was seen at an outside hospital, and outpatient computerized tomographic scanning was scheduled. Several hours later, however, she developed dysphasia and right-sided weakness, and she underwent reevaluation in the
hospital emergency room.

From age 16 to 27 years, the patient used intranasal cocaine heavily, which led to the need for nasal septum reconstruction. She had not used cocaine in any form for 3 years and denied any intravenous drug use. She had a history of smoking 30 packs of cigarettes a year and had been using birth control pills, which she had ceased to take secondary to hypertension 4 weeks prior to presentation. There was a family history of diabetes and coronary artery disease. Her father had died of a stroke at age 60 years.

**Examination.** Physical examination revealed no carotid artery, ocular, or temporal bruits, and there was no evidence of cyanosis, clubbing, edema, petechiae, or hemorrhage. She was fully alert and oriented but spoke hesitantly and experienced difficulty in finding words and naming objects. It was also difficult for her to draw, and right/left confusion was noted. Findings from cranial nerve examination were normal. She had pronator drift of the right upper extremity, and her grip was slightly weakened. Fine finger movements on the right were slowed, and gait was hemiparetic. Routine laboratory tests, including toxic screening, were negative, and findings on electrocardiogram were normal.

Both computerized tomography and magnetic resonance imaging studies showed multiple small cerebral infarctions, which appeared to be of several different ages and were particularly prominent in the right hemisphere. After admission, cerebral arteriography was performed. The arteriograms revealed evidence of advanced-stage moyamoya syndrome, with virtual occlusion of the supraclinoid carotid arteries bilaterally and extensive moyamoya-like vasculature (Fig. 1). There were extensive numbers of collateral branches from the external circulation. After vertebral injection, the posterior cerebral arteries were narrowed, and there was collateralization to the anterior circulation via prominent dorsal pericallosal arteries.

![Fig. 1. Preoperative left common carotid artery angiogram showing the stenotic segment of the supraclinoid ICA. Moyamoya-like collateral branches can be seen throughout the region of the basal ganglia. The posterior branch of the STA (arrows) can be seen.](image)

**Operation.** The patient improved. However, after experiencing several additional episodes of dysphasia
and hemiparesis despite aspirin therapy, she underwent a modified left encephaloduroarteriosynangiosis (what we term "pial synangiosis"; see Discussion) in hope of improving collateral vasculature in the left hemisphere. This procedure was complicated when the patient suffered a perioperative stroke that caused temporary worsening of her speech disturbance. Follow-up angiography was performed 1 year after initial surgery, which revealed a progressive moyamoya-like process, with increased narrowing of the intracranial carotid arteries, further development of the moyamoya-like vasculature, and extensive new collateralization in the left hemisphere via the external carotid artery in the site at which pial synangiosis was performed (Fig. 2). Pial synangiosis was later performed on the contralateral side. At the present time, the patient remains neurologically stable and has experienced no further progression of her symptoms 66 months after presentation.

Fig. 2. Postoperative left external carotid artery angiogram demonstrating the development of cerebral collateralization in the site at which pial synangiosis was performed. The caliber of the STA has enlarged considerably. Spontaneous cortical collateralization is also seen through a burr hole made during the same procedure in which the dura and arachnoid were opened (arrow).

DISCUSSION

The association between cocaine use and cerebrovascular events is well established, with numerous reports of ischemic events, intraparenchymal hemorrhage, and subarachnoid hemorrhage.[5,7,8,12] Temporally removed effects of cocaine abuse, on the other hand, have not been clearly described. Although there have been several reports of vasculitic changes in association with abuse of cocaine, the clinical significance of these findings has been disputed.[4] There has been only one previous, isolated report of stenosis of the supraclinoid ICA.[2]

Several mechanisms for the deleterious effects of cocaine have been proposed. Because cocaine inhibits reuptake of catecholamines at the synaptic junction, hypertension and increased pulse rate occur, which may in turn lead to rupture of occult vascular abnormalities.[11] The adrenergic action of cocaine also
leads specifically to vasoconstriction of the cerebral vasculature.[4,6] Cocaine intake has also been reported to cause platelet activation by stimulating endothelial thromboxane production.[14] The combination of vasoconstriction and hypercoagulability may predispose the cocaine user to ischemic events.[7,8]

Moyamoya disease is characterized by stenosis and occlusion of large intracranial arteries and enlargement of collateral vessels that can be seen on angiography; the disease is most common in those of East Asian descent. A number of associated, and possibly causative, factors have been identified in relation to moyamoya syndrome (or a moyamoya-like syndrome) that affect members of all ethnic and racial groups. Among the most well-established associated factors are sickle-cell anemia, neurofibromatosis, tuberculous meningitis, atherosclerosis, and Down's syndrome, as well as the effects of receiving cranial radiation therapy.[13] The direct pathophysiological causes for the changes seen in moyamoya disease are not well understood. Intimal changes that have been demonstrated intracranially as well as in other vessels suggest the presence of systemic etiological factors.[3]

Authors of recent reports describe moyamoya syndrome in association with cigarette smoking and the use of oral contraceptives.[9] The synergistic association between smoking and oral contraceptive use and cerebrovascular events is well established, and the pathogenesis of moyamoya syndrome in this setting may be related to the generous sympathetic supply to the intracranial arteries together with the hypercoagulable state induced by circulating anti-estrogen antibodies.[9] The sympathomimetic effects of cocaine are very well established and may lead to the development of moyamoya syndrome by these same mechanisms. Its effects may be especially pronounced because cocaine in itself may lead to both vasoconstriction and platelet activation.[7,8]

The characteristic presenting clinical symptoms of moyamoya disease include headache, hemorrhage, infarction, transient ischemic attacks, and seizure.[13] Treatment remains controversial. Because available medical therapy focuses on treatment of symptoms and cannot prevent the inevitable progression of the proximal stenoses, surgical procedures have been devised to enhance the development of collateral vessels in the external carotid system. Direct anastomotic procedures, such as superficial temporal artery (STA) to middle cerebral artery bypass surgery, may produce immediate additional collateral vessels. Encephaloduroarteriosynangiosis, which was initially described by Matsushima, et al.[10] and which we term "pial synangiosis," involves suturing a length of uninterrupted STA into a dural incision in an attempt to induce cortical neovascularization. In our modified method, we open the arachnoid over the brain surface and suture the intact STA adventitia directly to the pia of the underlying brain.[1] Our patient has remained well during a 6-year follow-up period and has shown no new symptoms of transient ischemia or stroke after undergoing pial synangiosis.

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