Central Nervous System Infarction Related to Cocaine Abuse

Michael Daras, MD; Alan J. Tuchman, MD; and Stephen Marks, MD

**Background:** Cocaine use in the United States has reached epidemic proportions, and increased availability of "crack" since 1983 has noticeably increased the incidence of neurovascular complications. In this report, we examine the relationship between cocaine use and ischemic infarct.

**Summary of Comment:** This study reports 18 cases of ischemic cerebrovascular events, which occurred among 15 men and three women aged 21-47 years who were evaluated in a 2-year period. Clinical presentations include thirteen cases with hemispheric infarcts, two brain stem strokes, two anterior spinal artery infarcts, and one with both hemispheric and cerebellar infarcts. Nine patients smoked crack, four snorted cocaine, and three injected it intravenously. In two cases, the route of administration could not be determined. Two patients died, but the others survived with various degrees of neurological deficit.

**Conclusions:** Traditional risk factors for strokes were identified in only six patients, suggesting that these factors are not necessary for the occurrence of a cocaine-related infarct. Multiple overlapping mechanisms may be responsible, including vasospasm, sudden onset of hypertension, myocardial infarction with cardiac arrhythmias, increased platelet aggregation, and vasculitis. *(Stroke 1991;22:1320–1325)*

Since the first description by Brust and Richter\(^1\) of a cerebral infarct associated with cocaine use, which was initially accepted with skepticism, the association between cocaine and cerebral infarction is now well established. In particular after 1983, when the use of free base cocaine known as "crack" was introduced and reached epidemic proportions, the number of reports of cocaine-related strokes has been constantly increasing.\(^2\)-\(^{22}\)

Strokes were initially described as isolated case reports\(^1\),\(^3\),\(^4\),\(^6\),\(^7\) or were incorporated in articles describing medical complications of cocaine.\(^5\) As the frequency of cocaine use increased, cocaine-related strokes became part of larger series on neurologic complications of cocaine\(^4\) or series on intracranial hemorrhages or ischemic infarcts,\(^1\),\(^2\),\(^5\),\(^10\),\(^11\),\(^15\),\(^16\),\(^18\),\(^22\) reflecting the continuous increase in their frequency.

We present a series of 18 cases of ischemic infarcts associated with cocaine use, the largest reported collection from a single medical center.

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**Patients and Results**

In a 2-year period we studied a total of 40 patients who developed a neurovascular event (subarachnoid hemorrhage, intracerebral hemorrhage, ischemic infarct, or transient ischemic attack) related to cocaine use. On the basis of clinical and computed tomography (CT) findings we identified a total of 18 patients (15 men and three women, 21–47 years of age) who developed an ischemic event following use of cocaine. The diagnosis of cerebral or spinal cord infarction was made when the patient had an acute focal neurologic deficit persisting longer than 24 hours and corresponding to an arterial territory, and CT or lumbar puncture excluded an intracerebral hemorrhage. Patients with a normal CT scan, whose neurologic deficit lasted less than 24 hours, were classified as having transient ischemic attacks and were not included in the study. Seven patients had a history of intravenous drug abuse, three were frequent cocaine users, and four had a history of alcoholism. Route of administration was not established in two patients because they were severely aphasic and could not give any history. Of the other 16 patients in whom route of administration was established, nine admitted to having smoked crack, four had snorted cocaine, and three had injected it intravenously. In 11 cases, the neurologic deficit occurred less than 3 hours after cocaine use, whereas five patients woke up with a neurologic deficit after heavy cocaine abuse.
the night before; one of them was on a binge of alcohol and crack. All patients had a sudden onset of deficit without progression except one (case 14), who had a slow progression over a week's period. All patients tested positive for cocaine metabolite (benzoylecgonine) in the initial urine toxicology screening on admission but were negative for all other drugs, including alcohol.

Headache preceded the onset of the neurologic deficit in eight cases. One patient, who later developed an anterior spinal artery infarct, had a transient episode of lower limb weakness and numbness following intravenous use of cocaine. One patient (case 18) presented approximately 1 year before her present evaluation with subarachnoid hemorrhage and mild right hemiparesis. A posterior communicating artery aneurysm was found and clipped, and the patient was doing well. She became pregnant, and when she started having labor pains, she smoked crack and subsequently developed aphasia and right hemiplegia. Computed tomography scan of the head demonstrated the presence of a left frontotemporal infarct.

Clinical presentations included signs of cerebral hemispheric dysfunction in 13 cases: right hemiparesis with aphasia, five cases; right hemiparesis without aphasia, four cases; and left hemiparesis, four cases. Computed tomography demonstrated infarction in eight: two had an area of infarction of the main trunk of the middle cerebral artery territory, four involved its anterior branches, two involved the posterior branches, and one involved the penetrating branches to the basal ganglia extending to the subcortical white matter. One patient presented with cerebellar ataxia; his CT scan showed a cerebellar and an occipital infarct. Cerebral angiography was performed in four cases and was normal in three; in one, segmental narrowing of the left middle cerebral artery was present. Two patients had signs of brainstem involvement, and CT demonstrated a low density midbrain lesion in one of them. Finally, two patients presented with sudden paraplegia and anesthesia below the midthoracic level with preservation of posterior column function. After normal thoracic CT scans and myelograms, a clinical diagnosis of anterior spinal artery infarction was made. One of these patients had an unrevealing magnetic resonance imaging study of the spine.

Risk factors for strokes included hypertension in one patient and diabetes mellitus in another. One patient went on a binge of drinking alcohol and snorting cocaine the night before he developed a brain stem infarct. Investigations for collagen vascular disease, including sedimentation rate, antinuclear antibodies, complement, etc., were performed in 11 patients and were negative. Anticardiolipin antibodies were positive in two of four patients who were tested. Electrocardiograms were performed in 12 patients; two patients had thickened mitral valves, but no mural thrombi were demonstrated in any of the patients. Carotid Doppler studies were negative in the two patients on whom they were performed. In case 17, lumbar puncture revealed increased protein, 63 white cells/mm³ (89% lymphocytes). The cerebrospinal fluid was positive for Venereal Disease Research Laboratory (VDRL) serological test. He also had positive serum VDRL and treponemal fluorescent antibody absorbed. This patient experienced headache immediately after he smoked crack, had a generalized convulsion, and developed a "locked-in syndrome." Two of the patients recovered completely; one had a normal CT scan. Fourteen patients were left with moderate to severe neurologic deficit, and two patients died of aspiration pneumonia 3 days after admission. We could not obtain consents for autopsy from their families.

The clinical and laboratory data are summarized in Table 1.

Discussion

The initial skepticism with which the first report of cocaine-related stroke was received seems to have been overcome by the increasing number of reports describing an association between cocaine and strokes, particularly after 1985, when the free base cocaine known as crack hit the street market of the inner cities and has been expanding outwards.

Intracranial hemorrhages following use of cocaine, particularly after 1985, were initially reported more frequently than ischemic strokes. However, Levine et al reported a higher number of ischemic than hemorrhagic strokes in a series from four medical centers. A sudden increase in arterial pressure resulting in rupture of a vessel, often in association with an underlying aneurysm or arteriovenous malformation, has been a rather widely accepted mechanism for the cause of intracranial hemorrhage. Our series include only ischemic infarcts involving the cerebral hemispheres, brain stem, cerebellum, or spinal cord. Case 13 had hemorrhagic changes within the area of the infarct. Cocaine-induced vasconstriction resulting in ischemia and followed by reperfusion has been proposed in hemorrhagic infarcts.

Traditional risk factors for stroke were present in five of our patients. One had hypertension and one had diabetes mellitus. Another went on a binge of drinking alcohol and smoking crack. Although ethanol intoxication per se has been considered a risk factor for cerebral infarction, the combination of alcohol and cocaine has also been reported to be associated with cerebral infarcts. Two patients (cases 14 and 16) tested positive for anticardiolipin antibodies. An association between anticardiolipin antibodies and cerebral infarcts has been encountered with increasing frequency, but only one case of cocaine-related stroke has been previously reported to have anticardiolipin antibodies. We included case 17 in the series because of the clear temporal relation between the use of crack and the onset of the symptoms. In view of the cerebrospinal fluid findings it is safe to speculate that this patient
<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>IVDA</th>
<th>Route and time</th>
<th>Clinical features/ outcome</th>
<th>CT results</th>
<th>Other information</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>47/M</td>
<td>+</td>
<td>Unknown</td>
<td>Coma, left hemiplegia, seizure (BP, 210/110 mm Hg)/ Improvement, residual left hemiparesis</td>
<td>Right MCA infarct</td>
<td>Echo: normal Carotid Doppler: normal LP: normal</td>
</tr>
<tr>
<td>2.</td>
<td>40/M</td>
<td>+</td>
<td>Unknown</td>
<td>Global aphasia, right hemiplegia, aspiration pneumonia/ Died after 2 days</td>
<td>Left MCA infarct</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>31/M</td>
<td>-</td>
<td>Immediately after snorting cocaine</td>
<td>Headache, left hemiparesis/ Improvement, residual left hemiparesis</td>
<td>Normal</td>
<td>Echo: normal CV: negative</td>
</tr>
<tr>
<td>4.</td>
<td>24/M</td>
<td>+</td>
<td>Crack smoking binge previous night</td>
<td>Aphasia, right hemiplegia, hemianesthesia/ Improvement, dysphasia, right hemiparesis</td>
<td>Left subcortical MCA infarct</td>
<td>Echo: normal Carotid Doppler: normal CV: negative Angiogram: segmental narrowing of left MCA Alcoholism</td>
</tr>
<tr>
<td>5.</td>
<td>33/M</td>
<td>-</td>
<td>3 hours after smoking crack</td>
<td>Headache, expressive aphasia, right hemiplegia/ Normal in 4 weeks</td>
<td>Left MCA infarct (anterior branches)</td>
<td>Alcoholism</td>
</tr>
<tr>
<td>6.</td>
<td>39/F</td>
<td>-</td>
<td>Crack smoking binge previous night</td>
<td>Left hemiparesis/ Improvement (left against medical advice)</td>
<td>Right MCA infarct</td>
<td>Alcoholism</td>
</tr>
<tr>
<td>7.</td>
<td>33/M</td>
<td>-</td>
<td>3 hours after intravenous cocaine</td>
<td>Paraplegia, urinary incontinence, T5 sensory level Similar transient episode 5 months before this/ Remained paraplegic</td>
<td>Normal</td>
<td>MRI: normal CV: negative Myelogram: normal</td>
</tr>
<tr>
<td>8.</td>
<td>21/M</td>
<td>-</td>
<td>Crack smoking binge for 24 hours</td>
<td>Dysarthria, quadriplegia, cranial nerve palsies (bilateral 7th, left 3rd, right 6th), absent gag reflex/ Improvement</td>
<td>Midbrain infarct</td>
<td>Angiogram: normal Echo: normal CV: negative</td>
</tr>
<tr>
<td>9.</td>
<td>36/M</td>
<td>+</td>
<td>2 hours after intravenous cocaine</td>
<td>Headache, right hemiparesis/ Improvement within 48 hours</td>
<td>Normal</td>
<td>CV: negative</td>
</tr>
<tr>
<td>10.</td>
<td>25/M</td>
<td>-</td>
<td>2 hours after smoking crack</td>
<td>Paraplegia, anesthesia below T5 level, normal vibration and position sense/ Remained paraplegic</td>
<td>Normal</td>
<td>Myelogram: normal IDDM</td>
</tr>
<tr>
<td>11.</td>
<td>37/M</td>
<td>-</td>
<td>Immediately after smoking crack</td>
<td>Headache, aphasia, right hemiparesis/ Improvement</td>
<td>Left MCA infarct (posterior branches)</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>36/M</td>
<td>-</td>
<td>Immediately after snorting cocaine</td>
<td>Ataxia/ Improvement</td>
<td>Infarct, right cerebellum and left occipital lobe</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>29/M</td>
<td>-</td>
<td>Immediately after smoking crack</td>
<td>Aphasia, right hemiparesis/ Improvement</td>
<td>Hemorrhagic infarct, left basal ganglia</td>
<td>Echo: normal CV: negative ACAB: negative Angiogram: normal</td>
</tr>
</tbody>
</table>
TABLE 1. Continued

<table>
<thead>
<tr>
<th>Case</th>
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<tbody>
<tr>
<td>14.</td>
<td>36/F</td>
<td>-</td>
<td>Cocaine snorting binge previous night</td>
<td>Progressive hemiparesis/Improvement</td>
<td>Left MCA infarct (posterior branches)</td>
<td>Echo: thickened mitral valve&lt;br&gt;Angiogram: normal&lt;br&gt;ACAB: positive</td>
</tr>
<tr>
<td>15.</td>
<td>36/M</td>
<td>+</td>
<td>Immediately after intravenous cocaine</td>
<td>Headache, loss of consciousness, right hemiparesis, hypesthesia/Improvement in 3 days</td>
<td>Normal</td>
<td>CV: negative&lt;br&gt;ACAB: negative</td>
</tr>
<tr>
<td>16.</td>
<td>33/M</td>
<td>+</td>
<td>Alcohol+coke snorting binge</td>
<td>Headache, left hemiparesis, hypesthesia/Improvement with physical therapy</td>
<td>Normal</td>
<td>Echo: thickened mitral and tricuspid valves&lt;br&gt;ACAB: positive&lt;br&gt;CV: negative&lt;br&gt;Alcoholism</td>
</tr>
<tr>
<td>17.</td>
<td>24/M</td>
<td>-</td>
<td>Immediately after smoking crack</td>
<td>Headache, loss of consciousness, seizures</td>
<td>Died 6 weeks later of aspiration pneumonia</td>
<td>Normal</td>
</tr>
<tr>
<td>18.</td>
<td>29/F</td>
<td>-</td>
<td>Immediately after smoking crack</td>
<td>History of SAH, aneurysmal clipping; 1 year later smoked crack, then had headache and right hemiparesis/Improvement with physical therapy</td>
<td>Left MCA infarct</td>
<td>Echo: normal</td>
</tr>
</tbody>
</table>

M, male; F, female; IVDA, intravenous drug abuse; CT, computed tomography; BP, arterial blood pressure; MCA, middle cerebral artery; Echo, echocardiogram; LP, lumbar puncture; CV, collagen vascular disease investigation; MRI, magnetic resonance imaging; IDDM, insulin-dependent diabetes mellitus; ACAB, anticardiolipin antibody; WBC, white blood cells; VDRL, Venereal Disease Research Laboratory; and SAH, subarachnoid hemorrhage.

...may have been suffering from meningovascular syphilis, and the stroke was triggered by the use of cocaine. Of the four patients subjected to an angiogram, one had evidence of segmental narrowing of the middle cerebral artery on the side of the infarct.

The temporal relation between the administration of cocaine and the onset of the neurologic deficit was established by history in 15 cases. In some cases, however, the patient’s neurologic deficit (aphasia or depressed level of consciousness) interfered with the ability to give any history. Reliable histories of the amount of cocaine were also difficult to elicit. In addition, patients who are able to give a history may be reluctant to admit to drug abuse out of fear that this may interfere with their treatment. Urine toxicology has been a useful tool in evaluating these patients. All our patients had positive urine toxicology for cocaine or its metabolite, benzoylecgonine.

The mechanisms by which ischémic infarcts are induced following use of cocaine may be multiple and overlapping in view of the complicated pharmacologic effects of cocaine on the vascular system. Cocaine prevents the uptake of sympathomimetic neurotransmitters by nerve terminals. This may result in sensitization to epinephrine and norepinephrine and produce vasoconstriction. At the same time, a sudden increase in arterial pressure may alter cerebral autoregulation. Hypertensive opening of the blood–brain barrier may cause catecholamines to enter the brain parenchyma and further increase vasoconstriction. Cocaine may also block the re-uptake of serotonin and thereby increase synaptic levels. Serotonin seems to be the most potent vasoconstrictor amine in the brain, especially for large- and medium-sized vessels. Only one of our cases had high blood pressure in the initial emergency room examination. However, the short half-life of cocaine (less than 1 hour) is probably the reason arterial blood pressure elevation was not found. This widely accepted notion of cocaine-induced vasoconstriction as a major mechanism for ischemic strokes has been recently challenged by the observation that cocaine produces vasodilation of pial vessels in cats.

Cocaine in vitro enhances the response of platelets to arachidonic acid, leading to increased production of thromboxane and platelet aggregation, thus providing another mechanism for infarction. None of our patients had coagulation abnormalities on routine testing, nor did those of Levine et al., who were subjected to extensive studies. The possibility of vasculitis has also been demonstrated in isolated cases. Vasculitis has been documented in other drug-induced strokes such as those caused by amphetamines, which may be an adulterant in intra-
venous or intranasal cocaine use. Additionally, vasculitis may be caused by the innoxious ingredients. The latter is less likely in patients using the smokable alkaloid form and possibly crack, both of which may provide purer cocaine compared with cocaine HCI administered intravenously or by nasal insufflation. None of the four patients who had angiography had findings of arteritis, which is in agreement with the data from other large series. Krendel et al., however, claim that arteritis can be missed by the angiogram and that only a brain biopsy, as they demonstrated in their two cases, can reveal its presence.

Myocardial infarction or ventricular fibrillation leading to cardiogenic emboli or decreased cardiac output resulting in hyperperfusion ischemia have also been proposed as a potential mechanism. We were not able to demonstrate electrocardiographic abnormalities or the presence of mural thrombi in the hearts of the patients who had an echocardiogram. However, only one embolic stroke has been reported after use of crack.

Decreased cerebral blood flow, especially in the frontal and temporal cortex, has been demonstrated after cocaine use. The significance of this observation is not clear. It seems that the effect of cocaine on the cerebral circulation is so complex that several mechanisms may be responsible for causing strokes in cocaine users. Clearly, our series indicates that traditional neurologic community will continue to evaluate young users. Experimental studies on laboratory animals may provide further insight into the pathophysiology of cocaine-induced cerebral infarction.44 The significance of this observation is not clear. It seems that the effect of cocaine on the cerebral circulation is so complex that several mechanisms may be responsible for causing strokes in cocaine users. Clearly, our series indicates that traditional risk factors for stroke are not needed for central nervous system infarctions associated with cocaine use. Experimental studies on laboratory animals may elucidate the exact mechanism or may add more confusion, as is the case with the report by Dohi et al. In the meantime, unless the widespread use of cocaine and particularly crack is reduced, the neurologic community will continue to evaluate young patients with strokes caused by cocaine, leading to serious disability or death.

References


**KEY WORDS** • cocaine • cerebrovascular disorders • cerebral infarction
Central nervous system infarction related to cocaine abuse.
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