Cocaine use has increased rapidly over the past few years. This has led to an increase in the number and variety of cocaine-related conditions for which medical attention is sought. Among these have been several cases of intracranial hemorrhage. Four cases reported in the literature and 6 from our own institution are presented here. They represent different diagnoses including hemorrhage from aneurysms and arteriovenous malformations, hemorrhage into a tumor, and spontaneous hemorrhage with no underlying lesion with and without preexisting hypertension. Analysis of these cases suggests that the hypertension induced by cocaine secondary to sympathetic stimulation may be the common factor. Cocaine may also cause arterial spasm. Although the pathophysiology has not been entirely resolved, the clinical significance of this association is clear. Intracranial hemorrhage should be considered in the differential diagnosis whenever a patient presents with an acute alteration in neurologic examination associated with cocaine use. (Stroke 1987;18:712-715)

Intracranial Hemorrhage and Cocaine Use

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Cocaine use has increased rapidly over the past few years. This has led to an increase in the number and variety of cocaine-related conditions for which medical attention is sought. Among these have been several cases of intracranial hemorrhage. Four cases reported in the literature and 6 from our own institution are presented here. They represent different diagnoses including hemorrhage from aneurysms and arteriovenous malformations, hemorrhage into a tumor, and spontaneous hemorrhage with no underlying lesion with and without preexisting hypertension. Analysis of these cases suggests that the hypertension induced by cocaine secondary to sympathetic stimulation may be the common factor. Cocaine may also cause arterial spasm. Although the pathophysiology has not been entirely resolved, the clinical significance of this association is clear. Intracranial hemorrhage should be considered in the differential diagnosis whenever a patient presents with an acute alteration in neurologic examination associated with cocaine use. (Stroke 1987;18:712-715)
Case 2
A 29-year-old black woman who was previously in good health and who was a known intranasal cocaine user was found in the bathroom at her place of employment in a confused and noncommunicative state. She was brought to Bellevue Hospital where she was noted to be mildly hypotensive (pressure 90 mm Hg systolic) and tachycardic. On neurologic examination, she was confused, had 3-mm sluggishly reacting pupils, conjugate eye movements, a moderate right hemiparesis, and a right Babinski reflex. Noncontrast CT scan revealed diffuse and massive subarachnoid blood. The patient’s urine toxicology screen was positive for cocaine. The patient was started on routine management for SAH and gradually improved over 12 hours to answer simple questions, but she remained confused and lethargic with a right hemiparesis. Several hours later, she became acutely unresponsive to verbal stimuli and rapidly developed fixed, dilated pupils, dysconjugate gaze, flaccidity in all extremities, and absence of brainstem reflexes. She died shortly thereafter of intractable cardiac arrhythmia. An autopsy was performed and disclosed a ruptured right posterior communicating artery aneurysm.

Case 3
A 34-year-old black man with a history of hypertension but currently on no medication was observed to have an abrupt change in mental status shortly after injecting himself with the contents of a syringe. He was brought to Bellevue Hospital, where he was noted to have a blood pressure of 210/120. On neurologic examination, he was alternately lethargic and agitated, opening his eyes to loud voice. He would mumble and occasionally speak in sentence fragments but would not consistently answer any questions other than to give his name when asked. His examination was otherwise unremarkable. A urine toxicology screen was positive only for cocaine. Noncontrast CT scan demonstrated blood throughout the ventricular system, mild hydrocephalus, and a small left caudate ICH. The patient’s electrocardiogram (ECG) was remarkable for periods of junctional rhythm with retrograde P waves, high voltage, and inverted T waves in Leads III and AVF. Creatine phosphokinase (CPK) isoenzymes were obtained but were normal. The patient’s mental status gradually improved over the following week, and his blood pressure was medically controlled. Cerebral angiography failed to reveal any anatomic lesion. Follow-up CT scans demonstrated resolution of the hematoma, and the patient was discharged on appropriate antihypertensive therapy. He was neurologically intact at that time.

Case 4
A 22-year-old white man with no prior medical history experienced abrupt onset of headache, nausea, vomiting, neck stiffness, and right-sided weakness and numbness while using cocaine intranasally and drinking alcohol. He presented to a local hospital, where a lumbar puncture was performed. The cerebrospinal fluid was found to be bloody, and a CT scan was performed, revealing a left frontal intracerebral hematoma with extension into the lateral ventricle. Angiography was performed, demonstrating a left posterior frontal AVM. The patient was transferred to New York University Hospital. Over the week following his hemorrhage, his hemiparesis gradually improved, but he was left with a moderate cognitive deficit. He underwent a craniectomy for evacuation of the hematoma and resection of the AVM. His postoperative course was uneventful, and he was discharged with a mild residual hemiparesis and a mild memory deficit.

Case 5
A 42-year-old white man was in good health until 1 day before admission, when he experienced the sudden onset of headache while using cocaine. He was brought to the New York University Hospital emergency room, where he was found to have a mild left hemiparesis, homonymous left visual field cut, and confusion. CT scan showed a right posterior temporal intracerebral hematoma with ventricular extension. Angiography failed to demonstrate any lesion. The patient’s hemiparesis and field cut resolved with steroids and conservative management. He was discharged 3 weeks after his hemorrhage, with evidence of clot resolution on repeat CT scans. Six weeks later, he again had acute onset of headache and was admitted to an outside hospital, where CT scan revealed recurrent right temporal hemorrhage with surrounding edema. Angiography was again negative, and the patient remained without focal deficit on steroids. Serial CT scans at New York University Hospital continued to show more hemispheric edema than would be expected surrounding a hematoma, and the possibility of hemorrhage into a tumor was considered. The patient did not tolerate tapering of his steroids, and he developed a hemiparesis. He underwent a craniotomy and right temporal lobectomy 3 months after his initial hemorrhage. The pathologic finding was moderate-to-markedly anaplastic astrocytoma with hemorrhage into the tumor. He required further surgical decompression and drainage of a cyst in the tumor bed 1 week later. Postoperatively, he did well but required maintenance steroids. Progressive tumor growth was seen on CT scans prior to radiation therapy, but significant tumor necrosis was noted after the administration of 4,500 cGy whole brain and 1,720 cGy tumor bed irradiation. After completion of radiation therapy, the patient had recurrent tumor growth and eventually died of his disease.

Case 6
A 51-year-old white man who was well except for mild exertional angina awoke on the day of admission with bifrontal headache and retro-orbital pain. He reportedly had used cocaine intranasally the previous evening. He was admitted to Bellevue Hospital after suffering a grand mal seizure. On admission, the patient had stable vital signs and was without focal neurologic deficit. Noncontrast CT scan disclosed a right thalamoperforator AVM. Creatine phosphokinase (CPK) isoenzymes were obtained but were normal. The patient’s mental status gradually improved over the following week, and his blood pressure was medically controlled. Cerebral angiography failed to reveal any anatomic lesion. Follow-up CT scans demonstrated resolution of the hematoma, and the patient was discharged on appropriate antihypertensive therapy. He was neurologically intact at that time.
frontal intracerebral hematoma. Shortly thereafter, he developed ventricular arrhythmias requiring treatment with i.v. lidocaine. An ECG obtained at this time revealed recent ischemic changes when compared with previous tracings. The relation of this apparently acute myocardial event to the ICH was unclear. After stabilization, cerebral angiography was performed and failed to demonstrate any lesion. One week after his initial hemorrhage, he suffered a right middle cerebral artery infarct, resulting in a dense left hemiparesis and left hemineglect. He was also found to have recurrent atrial fibrillation associated with mildly elevated cardiac enzymes. Echocardiography and gated blood pool study were performed to evaluate the possibility of emboli from a cardiac source and to examine myocardial function. Both studies were normal. There was persistent evidence of recent ischemia on serial ECGs, and this was believed to be consistent with subendocardial MI. The patient was transferred to the rehabilitation service 3 weeks after his initial hemorrhage, but shortly thereafter he developed refractory atrial fibrillation. He had progressively worsening arrhythmias and was believed to have had another MI. He finally died of uncontrollable ventricular tachycardia and fibrillation 1 month after his initial hemorrhage.

Discussion

The cases of intracranial hemorrhage associated with cocaine use that we have reported here represent a diverse group of diagnoses. To attribute these hemorrhages to one pathophysiologic process is difficult. What is apparent in reviewing our cases and those reported in the literature is that the majority of patients have had an underlying vascular lesion. It would appear that some physiologic change that occurs after cocaine use places increased stress on these lesions.

The transient elevation in systemic blood pressure that occurs following cocaine use is the most likely common factor. This might also explain the occurrence of ICH without an underlying vascular lesion in at least 1 patient who was known to be hypertensive. Cocaine blocks norepinephrine reuptake by neurons, leading to sympathetic hyperactivity and subsequent transient hypertension similar to that seen following amphetamine use. The reported cases of MI following cocaine use in patients with underlying coronary artery disease are believed to be due to a similar mechanism. Decreased reuptake of norepinephrine leads to sensitization of the heart to catecholamines. This in turn leads to increased myocardial oxygen demand, which may outstrip supply.

The etiology of the hemorrhage in our patient with an underlying glioma is less certain. Spontaneous hemorrhages associated with the abnormal vessels found within malignant astrocytomas are not uncommon, and this patient's second hemorrhage was apparently of this nature. Whether cocaine played a role in the initial hemorrhage by causing transient hypertension in the already weak vessels of the tumor bed is unclear.

The finding of narrowed and occluded vessels on angiography in the patients who suffered acute cerebral vascular occlusion following cocaine use suggests that there may be a direct vasospastic effect of cocaine on the blood vessels. This is supported by reports of patients with no underlying coronary artery disease on angiography who suffer MIs following cocaine use. The pattern and progression of these infarcts has suggested a transient occlusion of one or more major coronary arteries by spasm. There is no evidence to date that cocaine causes an actual vasculitis such as that believed to be at least partially responsible for the well-known entity of intracranial hemorrhage following recreational amphetamine use in the absence of a preexisting vascular lesion.

In addition to directly precipitating MI, cocaine may contribute to the cardiac complication associated with SAH. Recent articles have suggested that the ECG changes and dysrhythmias frequently associated with SAH may be due to irritation of the posterior hypothalamus and subsequent hyperactivity of the sympathetic nervous system. In patients who have died after SAH and who exhibited cardiac dysrhythmias and/or ECG changes, subendocardial myonecrosis and elevated serum CKP-MB isoenzymes have regularly been found. The combined effects of cocaine and the subarachnoid blood itself on the adrenergic system may increase the likelihood of cardiac injury in patients suffering SAH following cocaine use. Indeed, 1 of our patients succumbed to refractory arrhythmias shortly after her hemorrhage, and another was noted to have suffered an acute MI.

Up to 25% of all sudden deaths following cocaine use are from undetermined causes, and these deaths are often associated with preterminal seizures and respiratory arrest. What percent of these deaths might be due to intracranial hemorrhage and/or cardiac arrhythmia demands serious consideration.

Another concern is the recent increase in popularity of highly purified free-base forms of cocaine, such as that referred to as "crack." With the exception of the case reported above, no specific conditions related to the use of this substance have been reported, but as its use spreads, more will be learned about potential side effects.

With cocaine use continuing to spread, there will almost certainly be more patients seeking medical assistance for use-related conditions. It has become apparent that intracranial hemorrhage from a variety of causes must be considered in the differential diagnosis of patients who present with sudden alteration in neurologic function following cocaine use.

References

5. Schachne JS, Roberts BH, Thompson PD: Coronary artery...

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