Cocaine use is associated with multiple neurovascular complications, including ischemic and hemorrhagic strokes. Intracerebral hemorrhage is especially prevalent in patients with acute cocaine intoxication as defined by positive urine toxin assays. In addition, intracerebral hemorrhage in patients with cocaine intoxication are more severe, often associated with intraventricular hemorrhage, and have a poorer prognosis than intracerebral hemorrhage from other causes. Still, the majority of patients with cocaine-associated strokes will present with ischemic strokes. Whether intravenous tissue-type plasminogen activator (tPA) can be safely used in patients presenting with ischemic strokes and recent cocaine use is unknown, and their risk toward hemorrhagic conversion is not fully characterized. We describe 2 cases of cocaine-associated ischemic stroke with immediate hemorrhagic transformation after intravenous tPA infusion.

Case 1

A 55-year-old man presented to the emergency department 20 minutes after the sudden onset of left arm weakness while using cocaine. Examination revealed left hemiparesis-hemiataxia and noncontrast head computed tomography (CT) was normal except for bilateral white matter hypointensities suggestive of leukoaraiosis and a nasal septum perforation indicative of chronic intranasal cocaine use (Figure 1). A bolus of intravenous tissue-type plasminogen activator (tPA) was administered for acute ischemic stroke, with a symptom onset to administration time of 45 minutes. During the intravenous tPA infusion, the systolic blood pressure remained below 170 mm Hg. Immediately after the tPA bolus infusion, a CT-angiogram and postcontrast CT were acquired (Figure 1B). While being transported to the neuro-ICU, the patient complained of new headache and right arm weakness before quickly progressing to coma requiring emergent intubation as tPA infusion completed. Review of initial studies revealed multilobar ischemic stroke in the dorsal pons during tPA infusion (Figure 1B, black arrow). A magnetic resonance imaging scan revealed multifocal infarcts and hemorrhages raising suspicion for cocaine-related multifocal vasculopathy. The patient never recovered better than a locked-in state and died 1 month after the stroke.

Case 2

A 68-year-old man with regular cocaine use presented to the hospital after right lower extremity weakness that was presented for 2 hours and resolved completely. His initial neurological examination was unremarkable, but his toxin screen was positive for cocaine. While awaiting admission for a presumed transient ischemic attack, he developed the sudden onset of right hemiplegia and aphasia. A head CT showed no abnormalities except for bilateral white matter hypointensities suggestive of leukoaraiosis (Figure 2A), and he was given intravenous tPA 15 minutes after time last known to be normal. His symptoms began to improve during the infusion. Thirty minutes after completion of tPA, he developed a headache, became nonverbal, and quickly progressed to coma. A repeat CT showed a right caudate hemorrhage with intraventricular extension (Figure 2B). After reversal agents were given, an extraventricular drain (EVD) was placed at bedside with initial flow but subsequent slowing. A repeat head CT showed coagulated blood around the EVD (Figure 2C). One milligram of tPA was administered intrathecally 20 hours after onset of the hemorrhage, with resumption of EVD drainage shortly afterward. Repeat head CT scan showed radiographic improvement of the hemorrhage (Figure 2D), and the EVD was withdrawn on posthemorrhage day 8. A magnetic resonance imaging scan showed multifocal infarcts and hemorrhage raising suspicion for cocaine-related multifocal vasculopathy (Figure 3 shows a magnetic resonance imaging scan for both cases). Three months later, the patient remained bedbound and minimally responsive.
Although hemorrhagic conversion of ischemic stroke is well documented in the era of thrombolysis, we here present 2 cases of ischemic strokes that were thrombolyzed shortly after symptom onset (15 and 45 minutes), but nevertheless had immediate hemorrhagic transformation in the setting of recent cocaine use. These 2 cases raise the question of risk stratification for stroke thrombolysis. Risk of hemorrhagic transformation of ischemic stroke increases by 10-fold after thrombolysis and recognized risk factors include hyperglycemia, high National Institutes of Health Stroke Scale score, and the use of antiplatelet agents, none of which was present here. Leukoaraiosis is also a risk factor that may reflect diffuse cerebrovascular damage and was present in these 2 cases, possibly reflecting chronic cocaine use. Imaging in both of these cases revealed leukoaraiosis, acute ischemia, and hemorrhage in areas distant from the symptomatic lesions, indicative of acute on chronic multifocal vascular injury and suggestive of diffuse central nervous system vasculopathy.

The pathophysiological mechanisms resulting in cocaine-related ischemic stroke are multifactorial and may include vasospasm, microischemia, thrombus formation because of endothelial dysfunction or even vasculitis. Hypertensive surges are also postulated as a potential mechanism for increased risk of intracerebral hemorrhage with cocaine but were not present here.

Although small retrospective data suggest no increased risk of tPA in patients with a urine toxicology screen positive for cocaine, the risk of hemorrhagic conversion with tPA in patients with acute cocaine intoxication and ischemic stroke is unresolved. Conceivably, hemorrhagic transformation of ischemic stroke may not happen more frequently in patients positive for cocaine, but may be more severe when it happens. These 2 cases suggest that further research is needed to ascertain the safety of tPA in active cocaine users with possible multifocal vasculopathy.

In the first case, the first drops of contrast extravasation in the dorsal pons were caught on postcontrast images presaging lethal hemorrhagic transformation. To our knowledge, this is the first report of an immediate spot sign after intravenous thrombolysis.
Intrathecal tPA should be considered for lysis of intraventricular clot even after intravenous tPA as it improves blood clearance.

Furthermore, the management of intravenous tPA-related intracranial hemorrhage is not well established. In these cases, both patients were treated emergently per guidelines with blood pressure reduction to less than systolic of 140 mm Hg, fresh frozen plasma, cryoprecipitate, and synthetic coagulation factors. Unfortunately, data for post-thrombolysis hemorrhage are lacking, and treatment is largely taken from experience with hemorrhage related to other forms of anticoagulation. Although the benefit of intrathecal tPA is increasingly recognized for intracranial hemorrhage with intraventricular extension, our second case is the first report to our knowledge of treatment for intraventricular hemorrhage after intravenous tPA with intraventricular fibrinolysis. The clinical situation may be uniquely advantageous for this therapy: the administration of coagulation factors in the hyperacute setting may lead to prothrombotic complications, including coagulation of intraventricular blood, preventing cerebrospinal fluid drainage via EVD.

**References**


**Key Words:** cocaine  stroke  thrombolytic therapy

**Figure 3.** Brain magnetic resonance imaging (MRI) scan obtained 1 week after admission. **A**, Case 1: axial diffusion-weighted imaging (DWI) MRI revealed not only right corona radiata infarct explaining patient’s initial presentation but also left corona radiata infarct and punctate infarcts in right frontal lobe and left cerebellum (white arrows). Sagittal T1 MRI revealed residual dorsal pontine hemorrhage explaining patient’s coma (black arrow). **B**, Case 2: axial DWI MRI revealed not only left corona radiata explaining patient’s initial presentation but also left splenic infarct (white arrows) and right caudate hemorrhage (black arrow).
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