Case Report: Cerebral Edema and Tonsillar Herniation Leading to Brain Death After Cocaine Use in a Patient with End-Stage Renal Disease

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Abstract

The effect of cocaine use on the cerebral vasculature is well understood, with potential for ischemic or hemorrhagic stroke. The risk of adverse effects can be prolonged and amplified in patients with renal dysfunction and uremia. Uremia-induced osmotic gradients and upregulation of aquaporin channels along with cocaine-induced blood-brain barrier degradation may act synergistically. We present the first known case of a non-compliant dialysis patient who suffers cerebral edema, tonsillar herniation, and brain death following cocaine use. A 32-year-old female with end-stage renal disease presented with shortness of breath and flu-like symptoms for one week and was alert and oriented with no neurologic deficits. The patient had missed her last 5 dialysis treatments and labs revealed hyperkalemia and uremia. Urine drug screen was positive for cocaine, opiates, and tetrahydrocannabinol (THC). Following dialysis and metabolic correction, she developed an irregular respiratory pattern and stridor and received neck computed tomography (CT). The patient became unresponsive with dilated and nonreactive pupils. CT revealed absent intraluminal carotid and vertebral artery flow at the skull base, cerebellar tonsil herniation, and anoxic brain injury. Vital signs were maintained, and cerebral edema was managed with 45-degree head-of-bed elevation and mannitol. Following cerebral edema treatment, the patient had preserved respiratory drive, fixed and dilated pupils, no corneal reflex, no cough or gag reflex, and negative oculocephalic reflex. Repeat cranial CT angiography revealed bilateral hemispheric edema, basal subarachnoid hemorrhage, and confirmed absent intracranial blood flow. Brain death was diagnosed with a radioisotope cerebral blood flow study. The use of cocaine in patients with renal dysfunction may increase the risk of cerebral edema and tonsillar herniation due to synergistic physiologic effects. Physicians should be aware of this interaction to allow for preventative measures.

Keywords: cocaine use, end-stage renal disease, cerebral edema, tonsillar herniation, dialysis disequilibrium syndrome

1. Introduction

Cocaine use accounts for 10% of ischemic and hemorrhagic strokes in the United States (1). The mechanisms of ischemic stroke following cocaine use are

vasospasm, accelerated atherosclerosis, and platelet activation (1). For hemorrhagic stroke, cocaine-induced hypertension leads to rupture of intracerebral vessels. We report a case of a chronically noncompliant dialysis patient who presented to the emergency department feeling ill and short of breath. Labs revealed hyperkalemia, uremia, and recent cocaine use. The patient received a computed tomography (CT) with contrast of the neck for possible airway obstruction but developed neurologic decompensation during imaging. Neck CT revealed bilateral absence of carotid and vertebral blood flow with cerebellar tonsillar herniation. Subsequent brain computed tomography arteriogram (CTA) revealed bilateral hemispheric edema and basal subarachnoid hemorrhage. She never regained her neurological status despite immediate dialysis and subsequent herniation medical management. Brain death was confirmed with a radioisotope cerebral blood flow study. To the best of our knowledge, this is the first case report of cocaine intoxication leading to massive brain edema, tonsillar herniation, and brain death in an end-stage renal disease (ESRD) patient.

2. Case Report

2.1 Patient Information

Age: 32 years old. Gender: Female. Ethnicity: Native American. Related Medical Problems: End-stage renal disease, polysubstance abuse disorder.

2.1.1 Objective for Case Reporting. Our aim is to present a case of tonsillar herniation, cerebral edema, and brain death in an ESRD patient after cocaine use. Physicians should be aware of a potential synergistic effect between cocaine-induced vascular changes and rapid hemodialysis leading to dialysis disequilibrium syndrome. Hemodialysis protocols that more gradually correct for metabolic abnormalities may be instituted in patients with a history of substance use.

3. Case

A 32-year-old female with a past medical history of ESRD secondary to post-streptococcal glomerulonephritis, hypertension, hypothyroidism, and a history of cocaine use presented to the emergency department (ED) via ambulance. Her chief complaints were progressive shortness of breath and flu-like symptoms for the past week. She received nebulized albuterol in addition to 125 mg of methylprednisolone sodium succinate intramuscularly for

presumed asthma attack. Initial review of systems was negative for fever or chills, and the patient denied recent cocaine use. She was noncompliant with her dialysis regimen (scheduled three days per week) as she had missed her last 5 dialysis sessions due to her malaise.

Initial vital signs revealed a blood pressure of 160/99 mmHg, heart rate of 100 bpm, respiratory rate of 28/min, oxygen saturation of 91% on room air, and oral temperature of 98.5° Fahrenheit. Physical examination revealed an appropriately alert and oriented but slightly distressed female, who was otherwise intact neurologically. Cardiac examination revealed tachycardia with regular rhythm and there was a patent arterio-venous fistula on left lower arm. She was stridorous and tachypneic with rales on auscultation. Emergent arterial blood gas revealed respiratory acidosis with a pH 7.13, PaO_2 72 on room air, and potassium level of 7.3 mmol/L. Her blood chemistries were sodium 129 mmol/L, chloride 96 mmol/L, anion gap of 30, glucose 72 mg/dL, BUN 145 mg/dL, creatinine of 16.7 mg/dL (baseline 6.0), and calculated osmolality of 305 mOsm/kg. Lab findings suggested a mixed respiratory and metabolic acidosis, uremia, and hyperkalemia. CBC revealed anemia with a hemoglobin level of 6.0 g/dL. Urine drug screen was positive for cocaine, opiates, and THC (enzyme immunoassay, Beckman Coulter AU5812, Brea, California, USA). Initial cardiac workup revealed a troponin level of 0.29 ng/mL with an electrocardiogram (ECG) showing sinus tachycardia and peaked T waves.

Management was aimed at correcting her hypoxia, hyperkalemia, and uremia. She received oxygen supplement, calcium gluconate, insulin drip, dextrose, and scheduling for stat dialysis. The patient received 2 hours of dialysis with a 2 K bath and 2 liters of fluid removal but was not able to receive a blood transfusion during dialysis due to antibody incompatibility. Following dialysis her sodium was 134 mmol/L, potassium 3.4 mmol/L, chloride 93 mmol/L, glucose 114 mg/dL, BUN 39 mg/dL, creatinine 6.0 mg/dL, calculated osmolality 279 mOsm/kg, and hemoglobin 4.9 g/dL. Her neurological status had been stable throughout the dialysis session but later declined. She was awake without any focal neurological deficit but continued to have an irregular respiration pattern and mild stridor raising concern for an upper airway obstruction such as retropharyngeal abscess. She was intubated and transported to the CT suite. Upon completion of her cervical CT, she became unresponsive with bilateral nonreactive dilated pupils. The cervical CT with contrast did not show any upper airway obstructive lesions but revealed significant cerebral vascular problems. Both her cervical carotids were patent but absent intracranially (Figure 1A). There was a bilateral absence of intraluminal carotid and vertebral artery flow at the skull base area (Figure 1B). She had a crowded foramen magnum consistent with cerebellar tonsil herniation (Figure 2A).
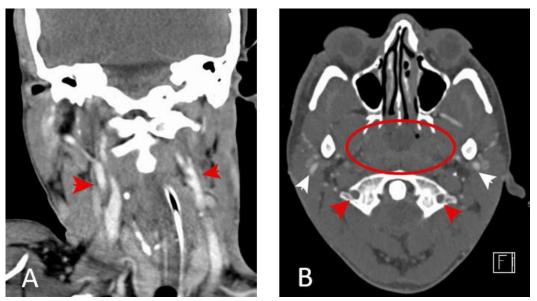
Figure 1. Computed Tomography Angiogram (CTA). A. Red arrows show blood flow through both cervical carotid arteries. B. Red circle shows no flow in the internal carotid artery at skull base level. Red arrows show no flow at the vertebral artery foramen at C1-2.
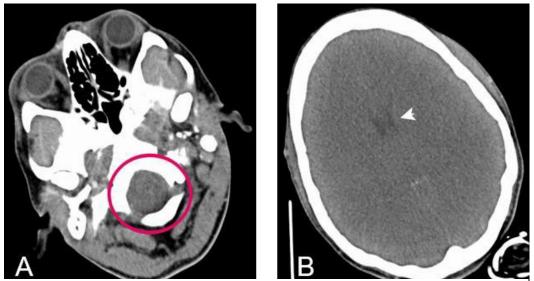

Figure 2. Axial CT. A. Red circle showing crowded foramen magnum from tonsillar herniation. B. White arrow shows patent frontal horn without midline shift.

Clinical and radiological findings were consistent with anoxic brain injury and tonsillar herniation.

The patient was transferred to the intensive care unit (ICU) for cerebral edema treatment. Her physical exam now revealed fixed and dilated pupils. She had no corneal reflex, cough/gag reflex, or doll's eye reflex, but a preserved respiratory drive. Vitals and labs were within normal range [sodium 134 mmol/L, potassium 4.1 mmol/L, chloride 96 mmol/L, CO_2 18 mmol/L, glucose 151 mg/dL, BUN 68 mg/dL, creatinine 8.5 mg/dL, measured osmolality 311 A radioisotope cerebral blood flow study was obtained to diagnose brain death, and an absence of intracranial flow was again observed. Vital signs at that time were blood pressure

mOsm/kg, WBC 8.7 K/mm3, and hemoglobin of 8.7 g/dL]. 25 hours after admission, the cranial CTA demonstrated bilateral hemispheric edema (Figure 2B) and basal subarachnoid hemorrhage (Figure 3A). Intracranial blood flow was absent, while extracranial flow at the scalp was preserved (Figure 3B). No improvement in her neurological examination was observed despite normalization of her metabolic parameters. Her PaO2 was higher than 70 with the FiO2 setting at 80%. The decision was made not to perform the apnea test due to her decompensated pulmonary function. of 114/72 mmHg, normal sinus rhythm at 97 bpm, ventilator respiratory rate 24 bpm, and a temperature of 99 degrees
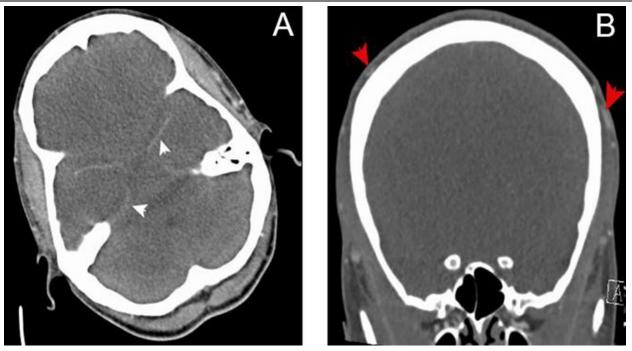
Figure 1. CTA. A. White arrows show basal subarachnoid hemorrhage. B. Red arrows show scalp circulation and absent intracranial circulation.

Fahrenheit. Ventilator settings were volume control/assist control at FiO2 of 80%, tidal volume of 480mL, and PEEP of

5. The patient was later transported to a tertiary medical center per family request. Subsequent electroencephalogram and a second cerebral blood flow study confirmed absence of intracranial circulation. The patient was declared brain dead and underwent organ procurement a few days later.

4. Discussion

Cocaine is notorious for its cardiac toxicity, with ischemic cardiac disease the most common morbidity in chronic cocaine users. Autopsy studies have observed coronary artery disease, myocarditis, and contraction band necrosis in cocaine users (2). Blood cocaine levels can range from 0.1 to 24 mg/L following a single insufflation, demonstrating its wide range of toxicity. Blood levels as low as 0.1 mg/L have been shown to cause myocardial infarction (3). Cocaine and its toxic metabolites can stay in the body longer than usual (2-5 days) in renally impaired patients (4).

Neurologically, cocaine intoxication can result in severe agitation, seizure, and stroke (5). An autopsy report of a body packer (a person who smuggles cocaine within their body) who presented with agitation and delirium revealed massive cerebral edema and a cocaine blood level of 0.1 mg/L (6). Animal studies have suggested disruption of the blood-brain barrier and an increase in brain serotonin as a mechanism for cocaine-induced brain edema (7). Increases in heat shock protein as well as marked neuronal and glial damage were also observed in this study.

In our case, the clinical presentation is unique from prior studies in two distinct ways. First, our patient did not have an acute ischemic cardiac event. Her ECG, cardiac enzymes, and echocardiogram were all normal or at baseline. Secondly, the timeline suggests her cocaine use as the sentinel event leading to her cerebral decompensation in the ED, prior to any intervention. To the best of our knowledge, this association after cocaine intoxication has never been reported.

Our patient's coexisting chronic renal failure should be considered in the pathophysiology of her cerebral edema. The rapid correction of uremia has been shown to create a uremic gradient between the brain and plasma, known as the "reverse urea effect", which in turn can lead to dialysis disequilibrium syndrome (8). While rare, this complication can be seen in the neuro ICU. Hemodialysis protocols such as continuous renal replacement therapy and low-efficiency hemodialysis have been designed to minimize this risk (9). Additionally, the degradation of the blood-brain barrier by cocaine and the upregulation of aquaporin channels in uremic states may create a synergistic environment for rapid osmotic shifts and cerebral edema (10). Our patient did not receive a dialysis regimen that accounted for this potentiality.

Common neurological complications from uremia are cognitive decline, asterixis, and restless leg syndrome (11). None of these symptoms, however, were observed in our patient. Diffuse interstitial edema with white matter disruption has been shown to correlate with the elevation of serum urea and cognitive dysfunction (12). Additionally, chronic dialysis patients can develop dementia encephalopathy (11). She never had any prior brain imaging to compare and assess her baseline white matter or interstitial

edema given she was completely neurologically intact in the past.

Even with a history of dialysis noncompliance, it is rare for patients to become comatose from rapidly rising creatinine. An imbalance of neurotransmitters along with secondary hyperparathyroidism are etiologies of coma in uremia patients. Animal studies have shown increased inflammation in the neocortex and hippocampus after kidney injury (13). Specifically, neuron pyknosis and glial fibrillary acidic protein overexpression were found only in uremic animals, which were not seen in liver injury models. In humans, a common finding after renal decompensation is posterior reversible encephalopathy syndrome (PRES) due to high blood pressure (14). In this case, the blood pressure was within normal range and subsequent imaging did not show evidence of PRES. The rapid neurological deterioration within 24 hours resulting from cerebral edema, leading to catastrophic brain death, is a unique finding in this case. The patient never regained any neurological function despite rapid correction of her metabolic abnormality.

5. Conclusion

This case demonstrates the synergistic effects of uremia, dialysis disequilibrium syndrome, and cocaine intoxication as a possible etiology of massive cerebral edema previously unreported in the literature. To the best of our knowledge, there has never been a case report of uremia and cocaine intoxication resulting in severe brain edema and consequential brain death. Our hypothesis is that uremic gradients in addition to cocaine induced vasospasm and blood-brain barrier breakdown acted synergistically in the formation of osmotic gradients and thus cerebral edema, specifically in the setting of dialysis. Renally impaired patients exhibit a decreased clearance of cocaine and its toxic metabolites, and the resulting prolonged disruption of cerebral autoregulation may lead to catastrophic outcomes. Medical providers should be aware of this devastating complication when approaching treatment of cocaine users in the emergency department. Prompt identification, intervention, and resuscitation are needed after patients rapidly decline in this setting. Targeted intracranial pressure treatment algorithms should be initiated as soon as the diagnosis of cerebral edema is established. Hemodialysis protocols should be carefully selected for patients presenting with concurrent ESRD and recent cocaine use.

Conflicts of Interest:

Authors declare no conflicts of interest

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