Acute renal failure, thrombocytopenia, and elevated liver enzymes after concurrent abuse of alcohol and cocaine

Alireza Hosseinnezhad,[1]
Rajakrishnan Vijayakrishnan,[1]
Mary Jo S. Farmer[1,2]

[1]Department of Medicine, Saint Vincent Hospital; [2]Department of Pulmonary, Critical Care & Sleep Medicine, Fallon Clinic, Worcester, MA, USA

Abstract

Cocaine has been associated with known adverse effects on cardiac, cerebrovascular and pulmonary systems. However, the effect of cocaine on other organs has not been extensively reported. A middle age man presented with abdominal pain and nausea after inhalation of crack cocaine. On admission, he was found to be hypertensive and tachycardic. Physical examination revealed mild abdominal tenderness without rebound. Laboratory investigations were significant for acute kidney failure with elevated serum creatinine (3.72 mg/dL), thrombocytopenia (platelet count 74,000/UL), elevated alanine and aspartate transaminases (ALT 331 U/L; AST 462 U/L) and elevated creatine phosphokinase (CPK 5885 U/L). Urine toxicology screening solely revealed cocaine. A clinical diagnosis of cocaine toxicity was made and patient was admitted to the intensive care unit because of multi organ failure. Despite downward trending of liver enzymes during the hospital course, he continued to have residual renal insufficiency and a low platelet count at the time of discharge. In a patient with history of recent cocaine use presenting with these manifestations, cocaine itself should be considered as a likely cause.

Introduction

Cocaine abuse has been associated with multiple known adverse effects, including myocardial ischemia, cerebrovascular accidents, pulmonary edema, and mesenteric ischemia. However, the effects of cocaine on other organs have not been extensively reported. We present a middle age patient who developed multi organ failure after inhalation of crack cocaine, in order to increase awareness of under-reported cocaine-induced renal, hematologic and hepatic complications.

Case Report

A 51-year-old man with no significant past medical history was brought to the hospital with abdominal pain and nausea. Crack cocaine and half glass of wine were consumed the day prior to admission. Other recreational drug use was denied. Patient admitted to long-standing crack cocaine use but denied cigarette smoking or ethanol abuse. Family history was noncontributory. There was no regular use of prescription medication. Vital signs on admission revealed blood pressure 170/100 mmHg, heart rate 134/min, temperature 98.1°F (36.7°C), respiratory rate 24/min and oxygen saturation 98% on room air. Physical examination revealed an awake, alert, obese middle age patient with no jugular venous distension. Nasal mucosa was normal. The only significant finding on physical examination was mild right upper quadrant abdominal tenderness without rebound.

Laboratory investigations on admission revealed leukocytosis (white cell count 13,500/UL), hyperkalemia (5.8 mEq/L) and normal ionized calcium. Serum creatinine 3.72 mg/dL, creatine phosphokinase (CPK) 5885 U/L, lactate dehydrogenase (LDH) 2964 U/L, elevated alanine and aspartate transaminases (ALT 331 U/L and AST 462 U/L), and thrombocytopenia (platelet count 74,000/UL) were also observed. Hemoglobin, coagulation tests and fibrinogen level were normal ruling out disseminated intravascular coagulation. Peripheral blood smear did not show evidence of Thrombotic Thrombocytopenic Purpura and Hemolytic Uremic Syndrome (TTP/HUS) but confirmed low platelet count. Serum bilirubin, alkaline phosphatase, amylase, and lipase were within normal limits. Troponin was negative on admission but increased to 0.2 ng/mL in 4 hours. Viral hepatitis panel (anti-HAV IgM, HBs Ag, anti-HBc IgM, anti-HCV antibody and HCV RNA) was negative. Urine toxicology screening on admission was positive for cocaine only and the ethanol serum level was undetectable. Urine myoglobin was highly positive. Electrocardiogram showed sinus tachycardia without ischemic changes. Radiographic imaging studies including computed tomography (CT) scan of the abdomen showed no evidence of pathology.

A clinical diagnosis of cocaine toxicity was made and the patient was admitted to the intensive care unit after obtaining written consent. Conservative management included intravenous fluids, vital signs monitoring, and administration of lorazepam for agitation, alpha-blocking agent for elevated blood pressure, and sodium bicarbonate to treat rhabdomyolysis. During a four day course in the intensive care unit, kidney function tests worsened with a peak creatinine of 4.51 mg/dL,

transaminases increased significantly with ALT and AST peaking at 5355 U/L and 4230 U/L respectively and platelets decreased to 47,000/UL. Troponin peaked at 0.2 ng/mL, CPK trended down from a peak value of 7494 U/L, and hemodynamic stability was maintained. After stabilization of clinical status and intense monitoring, the patient was transferred to general medicine ward for three additional days. At the time of discharge, there was residual renal insufficiency (creatinine 2.55 mg/dL) with a low platelet count (97,000/UL) and elevated liver enzymes (ALT 996 U/L and AST 165 of U/L). Unfortunately, the patient missed outpatient follow up appointments due to relocation out of state.

Discussion

Cocaine, a naturally occurring alkaloidal extract of Erythroxylum coca indigenous to South America, is a local anesthetic agent which produces toxicity by activating the sympathetic nervous system.[1] Cocaine is used by more than 14 million people worldwide and approximately 0.3% of the global population of cocaine consumers is aged 15 to 64 years. Cocaine consumption is most prevalent in North America (6.4 million people), Central and South America (2.2 million people), and in Western and Central Europe (3.9 million people).[2] Cocaine is absorbed across all mucosal surfaces, including the oral, nasal, gastrointestinal, and vaginal epithelium; therefore it

can be applied topically, swallowed, or injected intravenously.[1] Intravenous and inhaled use of cocaine result in the fastest onset of action.

Cocaine is an indirect sympathomimetic agent, which enhances the availability of biogenic amines including serotonin and catecholamines (dopamine, norepinephrine, and epinephrine) at adrenergic receptors by blocking their presynaptic reuptake. It also stimulates both alpha and beta adrenergic receptors by increased levels of norepinephrine, and to a lesser extent epinephrine. Cocaine acts as a local anesthetic by slowing or blocking neuronal Na^+ channels and subsequent alteration of nerve conduction. Cocaine can also increase the level of the excitatory amino acids (glutamate and aspartate) in the brain. [3,4]

Pseudocholinesterase deficiency may result in delayed metabolism of cocaine and increased risk to develop toxicity even with low doses. Pseudocholinesterase is a glycoprotein enzyme, produced by the liver, circulating in the plasma.[5]

Cocaine abuse has been associated with multiple known adverse effects, including myocardial ischemia, cerebrovascular accidents, pulmonary edema, and mesenteric ischemia. However, the effects of cocaine on renal, gastrointestinal, and hematologic systems as experienced by our patient have not been extensively reported. Our patient consumed crack cocaine and ethanol simultaneously. A metabolite of cocaine, cocaethylene, has been detected in blood and urine of persons who concurrently abuse alcohol and cocaine. Cocaethylene induces changes in cardiovascular function similar to those of cocaine alone, and the pathophysiologic consequences of alcohol abuse plus cocaine abuse may be additive when both are used together.[6] Cocaine-induced renal injury is multifactorial and involves several mechanisms including renal hemodynamic changes, alteration in glomerular matrix synthesis, rhabdomyolysis, and possibly induction of renal atherogenesis.[7,8] We believe acute kidney injury (AKI) in this case was secondary to intense renal vasoconstriction and rhabdomyolysis. Cocaine-induced acute renal failure (ARF) usually responds to conservative management, however, it may require dialysis.

Rhabdomyolysis can occur following cocaine use with different mechanisms. Severe arterial vasoconstriction can cause skeletal muscle ischemia and infarction in the same manner as cocaine-induced vasospasm causes myocardial infarction. It also may result from markedly increased sympathomimetic activity and hyperthermia induced by cocaine. Inhibition of the reuptake of catecholamines at alpha adrenergic receptors, which leads to high intracellular calcium levels in muscle cells with subsequent cell damage and muscle injury is another mechanism.[9,10]

Association of cocaine abuse with thrombocytopenia has been reported in pregnant women, however, mechanisms behind this pathogenesis have not been well explained.[8,11-13] Possible mechanisms involved in cocaine-induced thrombocytopenia include thrombotic microangiopathy (cocaine-induced TTP/HUS), endothelial damage and subsequent platelet destruction and increased aggregation with thromboxane production.[8] Most of the severe cases were treated successfully with plasma exchange, high doses of intravenous gamma globulin and steroids, while one patient required splenectomy.[8,12]

Cocaine-induced liver damage has been well-reported, with a clinical spectrum ranging from minimal elevation of transaminases in chronic users, to acute hepatitis associated with rhabdomyolysis.[11,14,15] Liver biopsy usually shows hepatic necrosis and microvesicular steatosis. The zonality of the necrosis varies according to the activity of cytochrome P450 enzymes.[14,16] Several toxic metabolites of cocaine including N-hydroxynorcocaine and norcocaine produced by the cytochromes P450, are responsible for the acute hepatitis. Ethanol consumption increases hepatotoxicity by inducing these enzymes and increasing free radical activity and hepatic lipid peroxidation.[11,16]

Conclusions

Cocaine abuse has been associated with acute renal failure, thrombocytopenia, and acute hepatitis in discrete patients, however, to our best knowledge, we are not aware of prior case reports of simultaneous occurrence of all three in one patient. This case illustrates these complications pertaining to cocaine toxicity which are not well reported in the literature. Physicians should be aware of these potentially life threatening effects of cocaine abuse.

References

1. Perrone J, Hoffman RS. Cocaine, Amphetamines, Caffeine, and Nicotine. Chapter 168. In: Tintinalli JE, Kelen GD, Stapczynski JS, eds. Emergency Medicine - A Comprehensive Study Guide. 6th edition. New York: McGraw Hill; 2004, pp. 1075-1079.
2. United Nations Office on Drugs and Crime. 2007 World Drug Report. United Nations Publication. E.07.XI.5. Wien, Austria: 2007.
3. Tella SR, Schindler CW, Goldberg SR. Cocaine: cardiovascular effects in relation to Inhibition of peripheral neuronal monoamine uptake and central stimulation of the sympathoadrenal system. J Pharmacol Exp Ther 1993;267:153-62.
4. Smith JA, Mo Q, Guo H, et al. Cocaine increases extraneuronal levels of aspartate and glutamate in the nucleus accumbens. Brain Res 1995;683:264-9.
5. Duysen EG, Li B, Carlson M, et al. Increased hepatotoxicity and cardiac fibrosis in cocaine-treated butyrylcholinesterase knockout mice. Basic Clin Pharmacol Toxicol 2008;103:514-21.
6. Mendelson JH, Mello NK. Cocaine and Other Commonly Abused Drugs. Chapter 389. In: Fauci AS, Braunwald E, Kasper KL, et al., eds. Harrison's Principles of Internal Medicine. 17th edition. New York: McGraw Hill; 2008, pp. 2733-2736.
7. Bemanian S, Motallebi M, Nosrati SM. Cocaine-induced renal infarction: report of a case and review of the literature. BMC Nephrology 2005;6:10.
8. Volcy J, Nzerue CM, Oderinde A, Hewan-Iowe K. Cocaine-induced acute renal failure, hemolysis, and thrombocytopenia mimicking thrombotic thrombocytopenic purpura. Am J Kidney Dis 2000;35:E3.
9. Zamora-Quezada JC, Dinerman H, Stadecker MJ, Kelly JJ. Muscle and skin infarction after free-basing cocaine (crack). Ann Intern Med 1988;108:564-6.
10. Parks JM, Reed G, Knochel JP. Cocaine-associated rhabdomyolysis. Am J Med Sci 1989;297:334-6.
11. Balaguer F, Fernández J, Lozano M, et al. Cocaine-induced acute hepatitis and thrombotic microangiopathy. JAMA 2005;293:797-8.
12. Burday MJ, Martin SE. Cocaine-associated thrombocytopenia. Am J Med 1991;91:656-60.
13. Kain ZN, Mayes LC, Pakes J, et al. Thrombocytopenia in pregnant women who use cocaine. Am J Obstet Gynecol 1995;173:885-90.
14. Miscellaneous drugs and diagnostic chemicals. In: Zimmerman HJ, ed. Hepatotoxicity: the adverse effects of drugs and other chemicals on the Liver. 2nd ed. Philadelphia, PA: Lippincott Williams& Wilkins; 1999, pp.709-742.
15. Silva MO, Roth D, Reddy KR, et al. Hepatic dysfunction accompanying acute cocaine intoxication. J Hepatol 1991;12:312-5.
16. Powel CJ, Charles SJ, Mullervy J. Cocaine hepatotoxicity: a study on the pathogenesis of periportal necrosis. Int J Exp Pathol 1994;75:415-24.