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Case Report OMICS International

Cocaine-induced Fulminant Hepatitis

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Abstract

Cocaine abuse and intoxication is a global problem leading to many medical complications that can result in significant morbidity and mortality. We present the clinical case of a young man who presented with a fulminant hepatic failure, renal failure and a duodenal ulcer related to cocaine consumption.

Keywords: Fulminant hepatitis; Cocaine; Clinical case

Case Presentation

A 28-year-old man was admitted to our hospital on November 14, 2016 because of psychomotor agitation with fear delusions after ingesting 0.5 g of cocaine. He had no medical history of interest. As a toxic consumption history, he referred being an excigarette smoker of a pack a day, referred an ex-consumption of 10-12 alcohol units per day, and an ex-consumption of cannabis. Cocaine consumption started at 16 years old but at that time it had become sporadic. On examination in the emergency department, the patient presented a Glasgow Coma Score (GCS) of 12 with bilateral mydriasis, skin and mucous dryness, tachycardia and self- limiting temperature peak of 39.5°C. First blood test analysis showed a 51% hematocrit (43-49), 219 K/mcl platelets (150-450), 13.98 K/mcl leukocytosis (4.4-11.3), a prothrombin time (PT) of 86% (65-100), a 2.67 mg/dl creatinine (0.7-1.2), a 63 mg/dl urea (16.6-48.5), a 0.42 mg/dl total bilirubin (0.1-1.2), a 93 U/L aspartate aminotransferase (AST) (0-40), a 28 U/L alanine transaminase (ALT) (0-41), a 23 U/L gamma-glutamyltransferase (GGT) (0-60), a 97 U/L alkaline phosphatase (ALP) (40-129), a 863 U/L creatine kinase (CK) (0-190) and a high anion gap metabolic acidosis: pH 7.18, 38 mmHg pCO_2, 39 mmHg pO_2 and 14.2 mmol/L bicarbonate. Troponin curve realized at 3 hours was flat. Toxics in urine were tested, being only positive for cocaine. Ethyleneglycol and methanol serum levels were normal and hepatitis A, B and C viruses were negative. Blood test control at 3 hours showed increasing levels of CK to 5.529 U/L and at 6 hours CK levels had arisen to 16.242 U/L, creatinine levels to 3.31 mg/dl and PT had decreased to 52%. At 24 hours, CK levels were 49.162 U/L, creatinine levels had increased to 4.79 mg/dl, platelets had fallen to 39 K/mcl and International Normalized Ratio (INR) had increased to 5.54. Brain computerized tomography (CT) scan was normal. Initial supportive treatment (such as serum therapy and bicarbonate) was initiated in the emergency room.

First diagnostic approach was an acute renal failure AKIN III probably due to microangiopathy and rhabdomyolysis because of cocaine consumption. In the following hours, the patient began with a decreased level of consciousness and oligoanuria. In blood test controls, platelet levels dropped to 18 K/mcl, INR increased to 5.54, total bilirubin increased to 2.03 mg/dl, AST increased to 3.610 U/L, ALT increased to 3.287 U/L, CK levels were about 33.327 U/L and creatinine levels were still increasing to 6.44 mg/dl. A fulminant hepatic failure was diagnosed in addition to an acute renal failure, since previous abdominal ultrasound found in his clinical history showed no abnormalities.

Liver transplant was rejected by our transplant referent center because of active cocaine consumption. The patient was then admitted to Intensive Care Unit (ICU) and progressively developed a complete anuria with top creatinine levels of 10.1 mg/dl accompanied by anasarca. Regarding the hepatic failure, the patient presented jaundice, a top of grade II hepatic encephalopathy, an episode of severe hypoglycemia and, analytically, the lower PT was 8%, top bilirubin total level was 16.95 mg/dl, AST top level of 5.788 U/L, ALT top level of 5.875 U/L and the lower platelet level was 18 K/mcl. The patient started renal replacement therapy with continuous venovenous hemodiafiltration that was changed to standard hemodyalisis when clinical status allowed it, besides vitamin K and plasma transfusions when needed. Low oxygen therapy was also required due to pleural effusion caused by accumulated hypervolemia. The patient was hemodynamically stable and conscious at all times without presenting signs of hepatic insufficiency (except for a short period of encephalopathy grade II presented at the first day). Furthermore, an ultrasound guided evacuator paracentesis was required because of the development of tension ascites that conditioned respiratory difficulty, discarding a bacterial spontaneous peritonitis at that time. During his stay in the ICU, renal function and hepatic function were gradually and progressively improving, thus the patient was transferred to the Gastroenterology Unit. Anasarca and non-tense ascites were still present due to renal and hepatic failure with hypoalbuminemia; therefore, furosemide, spironolactone, intravenous (iv) and albumin was started. Also, a chronic anemia with hemoglobin level of 6.9 mg/dl was developed, which needed transfusion therapy and erythropoietin treatment. During admission, the patient underwent a catheter sepsis for *Staphylococcus epidermidis* successfully treated with piperacillin-tazobactam and the removal of the catheter. Renal and hepatic function progressively improved, so finally hemodialysis was interrupted after 23 days. A follow-up by dietitian was also needed, due to malnutrition that was developed during the admission. Three weeks after admission, the patient started with hematemesis, faeces with

remnants of blood and episodes of dizziness with tachycardia but stable arterial tension. Urgent blood test revealed hemoglobin of 2.9 g/dl and 9% hematocrit. Three red blood cell concentrates were administered and a fibro-gastroscopy revealed two duodenal bulb ulcers, Forrest Ib, one on the upper side with fibrin and an attached clot, where 1 ml of etoxiesclerol was injected, and another one on the lower side with venous bleeding in sheet and an attached clot. Adrenaline and etoxiesclerol were injected, which stopped the bleeding, and hemostatic clips were placed.

Proton-pump inhibitor infusion was started. After solving this complication, the patient developed a tense ascites, fever of 38°C and sepsis parameters start to increase again in successive analytical controls. A paracentesis was performed, which revealed a high leukocyte count: 4525/mcl and 82% of neutrophils, so antibiotic treatment was started with piperacillin-tazobactam. Urine and blood cultures were negative and a thoracoabdominal CT scan was performed. A collection adjacent to the second duodenal portion with 4.3 × 3.2 cm major diameters was revealed. It was considered an infected hematoma due to a post endoscopic treatment microperforation with secondary peritonitis. Antibiotic spectrum was again extended to meropenem adjusted to renal function after 48 hours of the piperacillin-tazobactam beginning since fever was persistent. Finally, the ascitic fluid culture revealed a growth of a *Klebsiella pneumoniae* resistant to piperacillin-tazobactam but sensitive to meropenem, so fever disappeared in the following days and sepsis analytical parameters were declining. The patient was finally discharged on December 30, 2016 and is currently recovering.

Discussion and Conclusion

Cocaine is a local anesthetic, vasoconstrictive and sympathomimetic drug found in leaves of the Erythroxylum coca plant. The relationship with its plasma concentrations and its toxic effects has shown a wide variability between patients [1]. Cocaine is well-known for its cardiovascular complications such as stroke and cardiac arrest, and its respiratory problems [2]. Gastrointestinal complications are uncommon and little documented. They include vasoconstriction and ischemia as the most common, which may result in gastrointestinal ulceration (most of times juxtapyloric, or within the first part of the duodenum [3]), infarction, perforation with intra-peritoneal hemorrhage, pancreatitis, and rarer, retroperitoneal fibrosis and ischemic colitis [4-9]. As far as we know, this is the first case of acute liver failure and fulminant hepatitis caused by cocaine. Since 1967, it has been recognized that some cocaine users have mild, transient abnormal liver enzyme levels that can recover spontaneously in absence of continued insult; however, cocaine itself has not been determined to be hepatotoxic in humans. It has been demonstrated that cocaine does cause liver damage in rodents; however, the responsible hepatotoxins are oxidative metabolites such as norcocaine, which are very minor metabolites in humans. Suggested pathogenesis is the following: cocaine is metabolized in liver by CYP450, particularly CYP2E1 and CYP2A, to norcocaine, which is metabolized to free radicals causing oxidative stress and lipid peroxidation in hepatocytes. Despite this, it is believed that liver abnormalities in cocaine users could be also related to viral hepatitis from injection drug use, alcoholic liver disease, concurrent rhabdomyolysis, use of other hepatotoxic drugs, or other consequences of a drug-using lifestyle, rather than cocaine by itself [10-12]. An observational, 8-year period study in the United States identified 39 patients with acute cocaine intoxication and rhabdomyolysis. 23 of the patients (59%) demonstrated biochemical evidence for hepatic dysfunction: 16 patients had severe liver injury as defined by an alanine aminotransferase (ALT) of greater than 400 U/l and 7 had an ALT between 36-399 U/l. The other 16 showed no evidence of liver injury. Among those who had severe liver injury, profound hypotension, hyperpyrexia, rhabdomyolysis, renal failure and disseminated intravascular coagulation was also detected, rising mortality rates up to 45% [10,13]. Either way, the mortality associated with all gastrointestinal and hepatical complications can be as high as 21%, especially in the presence of gangrenous bowel [14,15]. Clinicians must be aware of cocaine induced gastrointestinal and hepatical symptomatology, in order to astutely manage the multiple varied and serious complications affiliated with this substance abuse.

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