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CASE REPORT

Severe rhabdomyolysis induced by cocaine contaminated with caffeine: a case report

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Abstract

Background: Global consumption of illicit substances has increased, and cocaine dependence remains an important public health problem. Currently, the use of adulterants can overlap or exacerbate the symptoms of cocaine intoxication hindering the diagnosis. This case shows how the morbidity and mortality of inhaled cocaine consumption adulterated with caffeine can increase by generating unusual severe rhabdomyolysis and rare serious complications.
Case presentation: 31-year-old Hispanic male, single, construction worker, generally healthy except for the past history of inhaled cocaine hydrochloride dependence, who after three days of cocaine snorting presented profound altered state of consciousness and multiple complications, liver damage, kidney failure and severe rhabdomyolysis (CPK=657625 U/L, troponin=3.6, potassium=6 mEq/L). After fourty-five days in the ICU, the patient stayed for two more months hospitalized for the treatment of healthcare-associated infections before being discharged without sequelae. An analysis of the powdered substance consumed by the patient confirms the presence of caffeine as cocaine adulterant. None other additional substance was detected in the sample.
Discussion: This clinical case describes serious complications presented by the excessive consumption of cocaine adulterated with caffeine. Notably, most of the complications herein described were of unexpected severity and duration for an acute cocaine intoxication. This case can suggest that in patients suffering from cocaine who have severe rhabdomyolysis, a simultaneous consumption of adulterants such as caffeine should be considered.

Keywords: Cocaine; cocaine-related disorders; caffeine; rhabdomyolysis; renal insufficiency

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BACKGROUND

Global consumption of illicit substances has increased, and cocaine dependence remains a major public health problem (1, 2).

Cocaine is a norepinephrine, dopamine and serotonin reuptake inhibitor, leading to the accumulation of these neurotransmitters in post-synaptic terminals, inducing an adrenergic toxidrome characterized by increases of blood pressure and heart rate, diaphoresis, hyperventilation, mydriasis, hyperthermia, and euphoria (3, 4). Commonly, acute cocaine intoxication presents with life-threatening conditions such as hypertensive emergency, cardiac arrhythmia, renal failure and toxic hepatitis (3, 4). Moreover, cocaine-induced rhabdomyolysis with secondary renal failure has been reported in up to a third of patients (5).

Currently, the use of adulterants can overlap with or exacerbate the symptoms of cocaine intoxication hindering the diagnosis. In a recent analysis of 116 samples of illicit substances, up to 83% of the products tested were adulterated with compounds such as levamisole (79%), phenacetin (18%), caffeine (12%), hydroxyzine (9%) and benzocaine (5%) (6). However, to our knowledge, there are few clinical case reports describing the changes in clinical manifestations of acute poisoning induced by cocaine adulterated.

Here we present an acute intoxication induced by heavy consumption of cocaine adulterated with caffeine, exhibiting an unexpected severe rhabdomyolysis and other life-threatening complications.

31-year-old Hispanic male, single, construction worker, generally healthy except for the past history of inhaling cocaine hydrochloride dependence, who after three days of continuous cocaine snorting presented a profound altered state of consciousness and generalized tonic-clonic seizures requiring immediate attention in an emergency service. The patient's mother provided the physician in the emergency service with a sample of an off-white powder that she found next to the subject.

At this point of time, the physical exam was normal except for mydriasis, Glasgow Coma Scale of 3, blood pressure of

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220/110 mmHg, heart rate of 190 beats/minute, SaO_2 of 66%. In consequence, he was intubated, and isotonic fluids, labetalol 60 mg single dose IV, bicarbonate 1 mg/kg IV, another IV infusion of midazolam 1 mg/hr and fentanyl 50 mg/hr were initiated, he was transferred to an intensive care unit (ICU).

Laboratory results at the admission time reported: urine cocaine levels=604 ng/mL, CPK=580 U/L, troponin-I=1.03, total bilirubin=1.48 mg/dL, direct bilirubin=1.1 mg/dL, GPT=25 U/L, GOT=43 U/L, hemoglobin=8.6 mg/dL, platelets=566000 mm^3, creatinine=0.37mg/dL, BUN=20 mg/dL, INR=1.22, sodium=149 mEq/L, potassium=3.9 mEq/L, arterial blood gases test reported pH=7.31, HCO_3=18.6 mEq/L, $PaCO_2$=84 mmHg, and serum lactate=71.4 mg/dL. The electrocardiogram showed supraventricular tachycardia and the CT scan of the head was normal.

In the ICU, his clinical condition worsened after 24 hours due to a sustained hypotension with tachycardia (162 beats/minute), requiring vasopressor support for 3 days using norepinephrine and vasopressin.

During the first week, the patient developed toxic hepatitis (GPT=10236 U/L, GOT=19080 U/L, total bilirubin=9.2 mg/dL, direct bilirubin 6.8 mg/dL), severe rhabdomyolysis (CPK=657625 U/L, troponin=3.6, potassium=6 mEq/L), secondary renal failure (creatinine=9.2 mg/dL, ammonium=228 µg/dL, D-dimer=7198 ng/mL, INR=3.86) and the platelets as low as 12000 per mm^3. The electrocardiogram showed signs of sodium channel blockage such as prolonged PR, QRS widening and secondary QT effects. The tests for hepatotropic viruses, Portal system/vein Doppler Ultrasound, and transthoracic echocardiography were normal. An intravenous infusion of N-acetylcysteine was administered for three days (10 g for 1 hour, 900 mg/hour for 6 hours and 450 mg/h for 67 more hours) as hepatoprotective. In addition, calcium gluconate intravenous infusion and polarizing insulin infusion were started for the treatment of hyperkalemia. After the second day in the ICU, the patient required continuous venovenous hemodiafiltration for three days, followed by hemodialysis for two days and ended with an intermittent hemodialysis for one month before being transferred to the general ward, where he stayed for two more months due to treatment for healthcare-associated infections before being discharged without sequelae.

Figure 1 shows the result of the analysis of the powder substance analyzed by gas chromatography mass spectrometry (ISQ 7000 Single Quadrupole GC-MS System), confirming the presence of caffeine as the only adulterant of the cocaine.

For this report the CARE guideline was adopted and the patient's informed consent was obtained.

DISCUSSION

This clinical case describes serious complications presented by the excessive consumption of cocaine adulterated with caffeine. Notably, most of the complications herein described were of unexpected severity and duration for an acute cocaine intoxication.

Rhabdomyolysis, is the massive breakdown of skeletal muscle, that induces an increase of at least five-times of the upper normal limit of CPK level, and is commonly expected after the administration of intravenous or crack-shaped

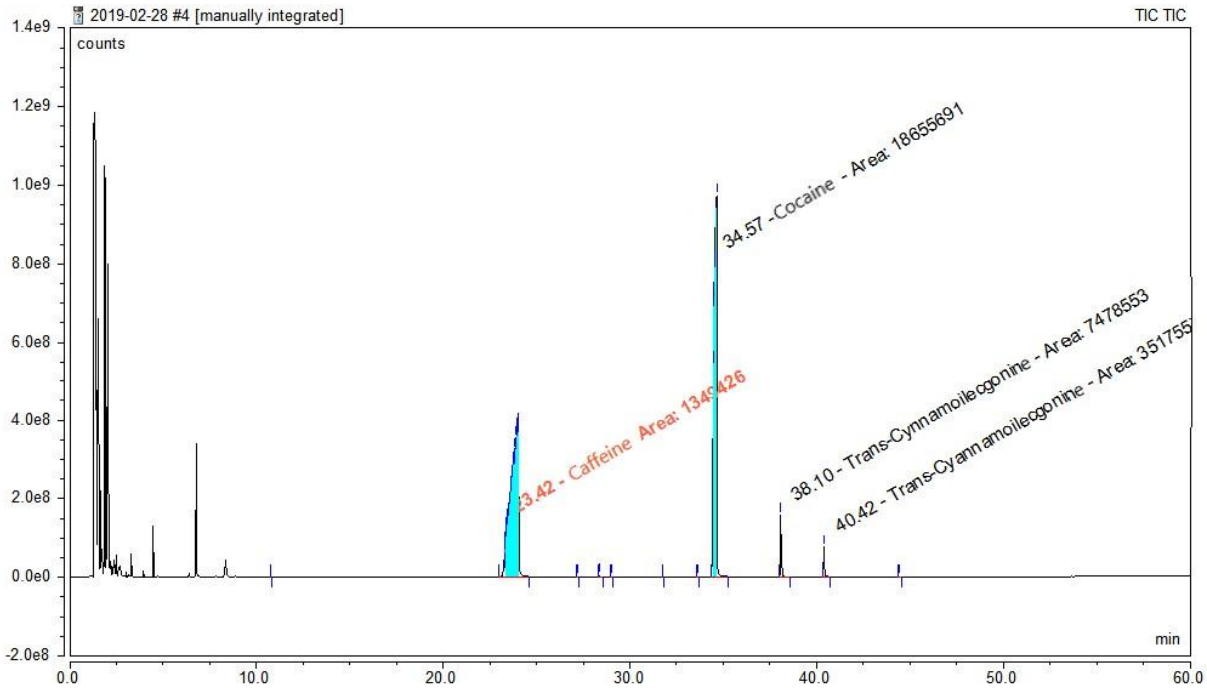

Figure 1. Analysis of the powder substance by gas chromatography mass spectrometry (GC–MS). The compound identification was achieved by quering and comparing the mass spectrum obtained (EI mass spectra, MS/MS spectra, and GC data with retention index) with reference mass spectra reported by NIST/EPA/NIH version 11. Caffeine and cocaine were the products obtained and both are marked in blue.

cocaine, which was not the route of administration in our patient (7). Counselman and colleagues calculate a mean CPK of 1,071 U/L in patients presenting to an urban emergency department with any complaint related to cocaine use within the preceding 24 hours (8). In contrast, here the patient's CPK level reached a peak of 657625 U/L, a value rarely described in literature (5, 9, 10) even considering other possible causes of rhabdomyolysis such as hypocalcemia, hypokalemia, prolonged tonic-clonic seizures (11), multiple wasp stings (12) or the abuse of tobacco, alcohol, heroin, amphetamines and phencyclidine (13). Caffeine is one of the psychoactive substances most widely used as an adulterant of cocaine because enhances the reinforcing effect of cocaine and its motivational value (14). Animal studies have demonstrated that caffeine is able to potentiate several cocaine actions including its acute toxicity, for example the incidence of cocaine-induced death in rats was increased after administration of caffeine from 10% to 90% at the 70 mg/kg cocaine dose (14, 15). While intake under 400 mg per day of caffeine is safe in healthy adults, overdoses higher than three grams are potentially lethal (16). An increase in levels of CPK has been described after excessive coffee drinking (17). Rhabdomyolysis and acute renal failure were described in a male who ingested 3.6 g of caffeine (18). Here, our patient consumed a high but unquantified dose of caffeine by inhalation, a route of administration more prone to be toxic. In studies of healthy subjects, the pharmacokinetics of caffeine after inhalation and intravenous administration were to largely extent similar (19). Then, a plausible explanation to this extremely high level of CPK could be severe rhabdomyolysis potentiated by overdose of the caffeine as adulterant. A retrospective study published by O'Connor et al compared the prevalence of rhabdomyolysis under sympathomimetic toxicity induced by different agents (20). In 89 patients with a single stimulant exposure, the order of occurrence of severe rhabdomyolysis (CPK > 10000 U/L) was synthetic cathinone (26%), methamphetamine with (4%), cocaine (11%, maximal CPK level detected 25614 U/L) (20). It is interesting that in two-thirds of these patients the caffeine was detected during the comprehensive urine drug screen, although it may associated with dietary consumption, in the context of sympathomimetic toxicity they argued that, "it cannot be reliably distinguished whether caffeine contributed to clinical manifestations of sympathomimetic toxicity or not". Even more, it is well known that individuals are at risk of significant caffeine toxicity related to the high caffeine content found in novel psychoactive substances, as synthetic cathinones, according to several reports that analyzed the content of these products describing that some contain only caffeine (20-22).

Cocaine and caffeine share a similar mechanism of muscular damage secondary to vascular spasm and the excessive increase of calcium inside the muscle fibers, with its consequent destruction (5, 16). The passage of the products of muscle destruction into the blood stream can cause hypotension, disseminated intravascular coagulation, massive myoglobinuria with tubular necrosis and renal insufficiency, increase in transaminases and troponins (13), which were all present in our patient.

This case can suggest that in patients suffering from cocaine abuse who have severe rhabdomyolysis, a simultaneous consumption of adulterants such as caffeine should be considered.

A limitation in our case is the lack of confirmation of caffeine levels in the patient, although GC-MS confirms the caffeine was the only adulterant found and if other undetected adulterants were present, caffeine contamination was significantly higher in quantity (analyte abundance of 1349426 in mass spectrometry).

Authorship

MAMG and AFZ conceived the report. MAMG, ECCh, LFD participated in the case management. All authors joined during the acquisition of additional information, interpretation of the results, or in the writing of the text, or during the revisions of the document, and approved the final version.

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