

Case Report

A Fatal Case of Hepatic Peliosis in a Cocaine Body Stuffer

Tuccori M¹, Scollo C², Guidi B³, Blandizzi C^{1,2}, Giusiani M⁴, and Di Paolo M^{5*}

¹Unit of Adverse Drug Reactions Monitoring, University Hospital of Pisa, Italy

²Department of Clinical and Experimental Medicine, University of Pisa, Italy

³Unit of Forensic Medicine, Hospital of Lucca, Italy

⁴Unit of forensic Toxicology, University Hospital of Pisa, Italy

⁵Unit of Forensic Medicine, University Hospital of Pisa, Italy

***Corresponding author**

Di Paolo M, Unit of Forensic Medicine, University Hospital of Pisa, S. Chiara Hospital Via Roma 55, 56126, PISA, Italy, Tel: 050-2218500; Fax: 050-2218513; Email: marco.dipaolo@unipi.it

Submitted: 07 February 2017

Accepted: 08 March 2017

Published: 11 March 2017

ISSN: 2333-7079

Copyright

© 2017 Di Paolo et al.

OPEN ACCESS**Keywords**

- Hepatic peliosis
- Cocaine
- Benzoylcegonine

Abstract

Cocaine is a drug commonly involved in severe intoxications associated with body-stuffing, usually characterized by tachycardia, hypertension, abdominal pain, seizures and fever. We report an unusual case of fatal cocaine body stuffing intoxication in a 29-year-old woman, who developed liver peliosis. She was admitted to the Emergency Department, with tachycardia, hypotension and a general malaise. A total body CT scan revealed hepatic injury with perihepatic and perisplenic fluid effusion without evidence of splenic lesions. She became progressively comatose with a score of 3 at the Glasgow Coma Scale. Toxicological tests revealed high levels of cocaine and its metabolite benzoylcegonine in serum and urine. In day 3, the patient clinical picture worsened and she died for cardio-respiratory arrest. At autopsy, a single open plastic bag was found in the gastric lumen. The pathological description of the left hepatic lobe was consistent with a peliosis-like hepatitis. The present case suggests that liver peliosis can occur in chronic cocaine abusers, who stuff cocaine in their body by ingestion of roughly wrapped packages. Therefore, clinicians should consider the possibility of cocaine body stuffing when observing a clinical picture consistent with acute hepatitis in patients potentially involved in illicit drugs trafficking/consumption.

INTRODUCTION

International smuggling of illicit drugs by their concealment within human body has become a widespread practice [1,2]. Transit of illicit drugs by the body as a vehicle usually occurs by ingestion (body packers) or introduction of drug packets into the rectum or vagina (body pushers) [3,4]. The number and size of packets may vary, but each one will usually contain many times the toxic dose of the drug [3]. Furthermore, the concealment of illicit drugs in the body is common in risky situations, when drug carriers need to avoid controls by the authorities and ingest either unwrapped or poorly wrapped drugs (body stuffers) [5,6]. In the latter setting, the risk of leakage or rupture of the package containing the illicit drug in the lumen of gastrointestinal tract is particularly high, with a subsequent poisoning, the clinical picture of which depends on the type of ingested drug. The resulting syndrome has been also defined as “mini packer syndrome” by the authors who described the first fatal case [7].

Cocaine is among the drugs most commonly involved in severe intoxications associated with body concealment [8-13]. The respective syndrome is characterized by tachycardia, hypertension, abdominal pain, agitation, diaphoresis, chest pain, seizures, fever and cardiac dysrhythmia, while liver damage is not usually reported [5,9]. We report an unusual case of fatal cocaine

body stuffing intoxication in a young woman, who developed peliosis of the liver and other complications.

CASE REPORT

A 29-year-old female in custody reported a general malaise with abdominal pain to the police officer. She was then transported to the Emergency Department of the Hospital of Tuscany (Italy), where physical examination revealed a temperature of 36°C, with heart rate of 139 beats/min (tachycardia), blood pressure of 92/45 mmHg (hypotension), breathing frequency of 13/min, mydriasis, areflexia in the lower limbs and hyporeflexia in the upper limbs, right supra-orbital hematoma and right shoulder hematoma. She was placed under mechanical ventilation, rehydration, and colloid infusion for hypotension. ECG confirmed tachycardia, while echocardiogram did not show abnormalities. A total body CT scan revealed subarachnoid hemorrhage, diffuse edema in the peri-ponto-mesencephalic area and diffuse ischemic lesions, hepatic injury with perihepatic and perisplenic fluid effusion without evidence of splenic lesions. No specific evidence of foreign bodies in the gastric lumen was detected. Blood analysis revealed increments of blood glucose levels (315 mg/dl, n.v.: 65-110) and white blood count (13,000/mm³; normal values, n.v.: 5,000-10,000), with normal values for erythrocytes, platelets, haemoglobin and hematocrit.

The patient was treated with insulin 50 UI by infusion pump, ranitidine 50 mg i.v. and propranolol 5 mg i.v. On day 2, a further examination revealed metabolic acidosis (pH: 7.174; n.v.: 7.350-7.450), PCO₂ (64.9 mmHg; n.v.: 35-45), PO₂ (144.1 mmHg; n.v.: 80-100). She appeared comatose with a score of 3 at the Glasgow Coma Scale. Toxicological tests revealed high levels of cocaine and its metabolite benzoylecgonine in serum (over 50 g/L and 5.26 g/L, respectively) and urine (22.5 g/L and 76.9 g/L, respectively). The patient, in a comatose areflexic state, was then treated with dopamine 400 mg i.v., insulin 50 UI by infusion pump, pantoprazole 40 mg by intravenous administration and nadroparine 0.4 ml by subcutaneous administration. Further laboratory tests revealed increments of ALT (928 UI/L; 5-40) and AST (733 UI/L; 5-45). In the morning of day 3, the patient clinical picture worsened and she died for cardio-respiratory arrest.

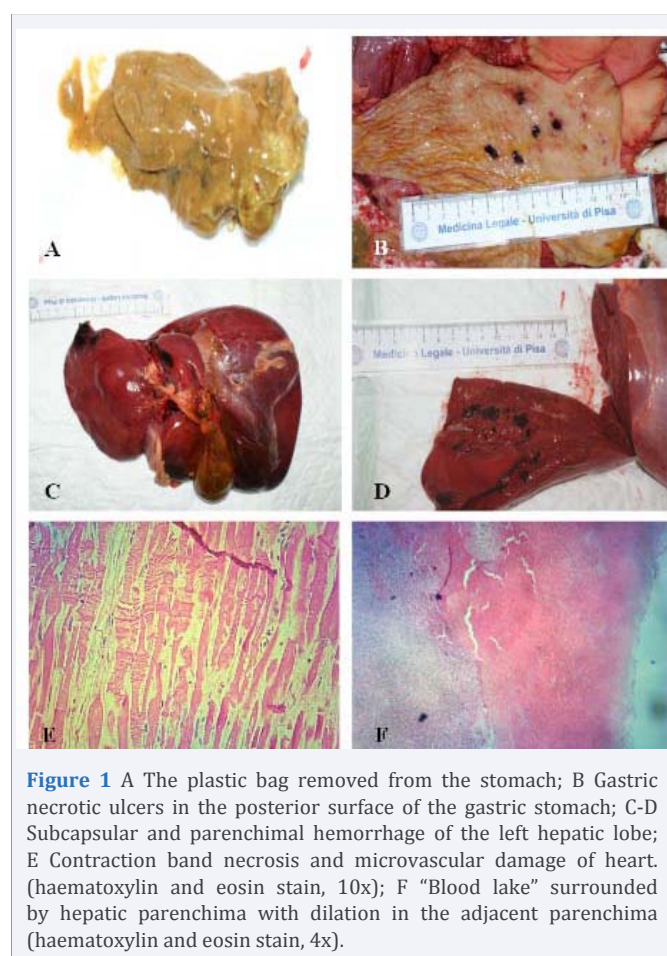
At autopsy, a single open plastic bag of 7x2.5 cm in size (Figure 1A), not detected by the previous CT- scan, and was found in the gastric lumen, on the posterior mucosal surface of the stomach. The plastic bag contained a green-brown fluid. At the interface with the package, the gastric mucosa appeared thinner and presented several deep ulcers with necrotic material (Figure 1B). Subcapsular and parenchymal hemorrhage of the left hepatic lobe and caudatum lobe of the liver (Figure 1 C, D), intracerebral hemorrhage and pulmonary edema were also observed. Histological examination revealed a general circulatory stasis and confirmed the occurrence of hemorrhagic injuries in the

cerebral truncus, lungs and liver. The pathological description of the left hepatic lobe was consistent with a peliosis-like hepatitis (Figure 1F), with severe sinusoidal dilatation in the absence of endothelial lining. Heart examination showed contraction band necrosis and microvascular damage (Figure 1E). Post-mortem toxicological parameters for cocaine and benzoylecgonine are displayed in Table (1). Toxicological analysis was carried out by means of a Trace GC chromatograph, equipped with a Polaris Q MS detector and a AS2000 autosampler (Thermo Finnigan, USA), using a 15m Rtx® -5MS column (Crossbond® 5% diphenyl/95% polysiloxane, 0.25 mm internal diameter and 0.25 µm film thickness, Restek, USA). The injection port was set at 270 °C (injection volume 1 µl in splitless mode). The initial oven temperature was 100°C held, for 1 min, and then increased at 15°C/min to reach 270°C held for 3 min. The transfer line was set at 280°C and helium at a flow of 1.1 ml/min was used as carrier gas. Electron impact (EI) was used as ionization mode, with temperature of the ion source set at 250°C (emission current 250 µA) and operating both in full scan (from m/z 75 to m/z 430) and SIM mode. Ions monitored in Mass Range and SIM mode for detection of cocaine and benzoylecgonine (PPFA derivative) were: 82, 182 and 303 m/z and 82, 300, 421 m/z, respectively (quantification ion underlined).

DISCUSSION

Peliosis is an uncommon disorder characterized by the appearance of multiple cyst-like, blood-filled cavities within parenchymatous organs. The diameter of cysts may vary from a value less than 1mm to several centimeters. In the liver, the peliotic lesion gives a “swiss cheese” appearance to the organ sections. Microscopically, two types of liver peliosis can be distinguished: parenchymal peliosis, consisting of irregular cavities that are lined neither by sinusoidal cells nor by fibrous tissue; phlebotatic peliosis, characterized by regular, spherical cavities lined by endothelium and/or fibrosis [14]. Rupture of peliotic lesions in the liver may occur, leading to intraperitoneal hemorrhage with potential fatal outcome [15-18]. The present case is consistent with a parenchymal peliosis with an acute clinical picture.

The pathogenesis of hepatic peliosis remains obscure. In particular, it is not clear whether cavities result from a local elevation of intravascular pressure or whether hepatocellular necrosis or apoptosis provides the space for the formation of cystic lesions [14]. Some authors have even hypothesized a neoplastic process, representing the utmost benign end in the spectrum of vascular tumors in the liver [14]. Peliosis has been related to several underlying debilitating diseases, such as tuberculosis, hematological malignancies, acquired immune deficiency



Sample or tissue	Cocaine (g/L)	Benzoylecgonine (g/L)
Urine	5.74	43.23
Blood	1.72	4.31
Liver	2.17	3.95
Kidney	1.74	4.72
Plastic bag	381.2	-

syndrome, and post-transplantation immunodeficiency, as well as intravenous drug abuse and chronic alcoholism [14]. Liver peliosis has been recorded as a rare adverse event complicating treatments with contraceptive or anabolic steroids [19], as a consequence of drug-induced hepatic tumors. Other drugs and toxins involved in the development of liver peliosis includes: arsenic inorganic derivatives, azathioprine, danazol, diethylstilbestrol, estrone, glucocorticoids, vitamin A (overdose), medroxyprogesterone, tamoxifen, thioguanine, and vinyl chloride [20].

To the best of our knowledge, no cases of fatal hepatic peliosis have been described following accidental cocaine intoxication in body stuffers. However, few cases of cocaine-induced liver damage, other than peliosis, have been reported in the medical literature. Wenless et al. (1990), described four cases (one fatal) of patients with liver injury secondary to intravenous cocaine abuse. Liver biopsies from two patients showed a pattern of sharply demarcated zone-3 necrosis, identical to that observed in the set of acetaminophen hepatic intoxication. The patient who died developed necrosis of almost all hepatocytes, as documented at autopsy [21]. One case report described periportal hepatonecrosis associated with cocaine snorting [22], while in another case acute hepatitis developed after intravenous injection of cocaine 1-2 g/week [23]. Overall, in the cases of non-peliotic cocaine-related hepatotoxicity reported in literature, intoxication was associated with chronic cocaine intake by intravenous route or snorting. In the present patient, histological examination of heart tissues was consistent with a chronic use of cocaine. However, the concentration of cocaine and its metabolite in post-mortem tissues/samples and the localization of injuries in specific liver areas as compared to healthy portion of the organ, are likely to exclude a significant contribution of the chronic cocaine intake to the final clinical picture of peliosis.

Several lines of evidence suggest that reactive cocaine metabolites can be responsible for cytotoxic effects of cocaine on hepatocytes. Two main mechanisms have been proposed to account for hepatic adverse events. First, lipid peroxidation was suggested to mediate cocaine-induced hepatotoxicity by impairment of key enzymatic activities leading to injury of cellular membranes [24]. Second, liver damage has been related to covalent interactions of chemically reactive cocaine intermediates with critical tissue proteins [25,26]. Although the above-mentioned mechanisms cannot be excluded as sources of damage in the liver peliosis observed in the present case, other mechanisms were likely to contribute to its pathogenesis. In this regard, it is worth mentioning that peliosis in experimental setting has been elicited by means of phalloidin. Since this toxin is known for its ability in injuring cell membranes, the induction of peliosis by phalloidin is thought to reflect a weakening of membranes supporting the architecture of sinusoids. Moreover, necrosis has been suggested as the initial step in the pathophysiological sequence leading to the clinical picture of peliosis [20]. Consistently with this knowledge, it is conceivable that necrosis, resulting from cocaine-induced vasoconstriction, may have triggered the hepatic peliosis observed in the present case. Such an adverse event was probably facilitated by the lack of early drug package detection in the stomach. Thus, following a continued and sustained leakage from the package into the gastric lumen, cocaine likely underwent a

massive absorption from the intestine into the portal circulation, with a progressive accumulation in the liver, where it induced an abnormal intraparenchymal vasoconstriction, with consequent ischemic necrosis and development of peliosis. The hypothesis of a mechanism based on the vessel-sealing effect of cocaine is consistent with the observation that the hepatic damage selectively localized mainly in the left lobe, while the remaining part of the organ was healthy. Indeed, left lobe is likely to receive a lower fraction of blood stream from portal circulation, due to the peculiar anatomical features of the hepatic blood supply mechanics [27] and, as a consequence, it is more likely to be injured by pathological conditions associated with severe portal-ischemia.

CONCLUSIONS

A massive exposure of the liver to cocaine can be associated with hepatic injury. The present case suggests that liver peliosis can occur in chronic cocaine abusers, who stuff cocaine in their body by ingestion of roughly wrapped packages. Therefore, clinicians should consider the possibility of cocaine body stuffing when observing a clinical picture consistent with acute hepatitis in patients potentially involved in illicit drugs trafficking/consumption, and eventually undertake early interventions aimed at removing the drug package from the body.

REFERENCES

1. Beckley I, Ansari NA, Khwaja HA, Mohsen Y. Clinical management of cocaine body packers: the Hillingdon experience. *Can J Surg.* 2009; 52: 417-421.
2. Robinson T, Birrer R, Mandava N, Pizzi WF. Body smuggling of illicit drugs: two cases requiring surgical intervention. *Surgery.* 1993; 113: 709-711.
3. Booker RJ, Smith JE, Rodger MP. Packers, pushers and stuffers--managing patients with concealed drugs in UK emergency departments: a clinical and medicolegal review. *Emerg Med J.* 2009; 26: 316-320.
4. Bulstrode N, Banks F, Shrotria S. The outcome of drug smuggling by 'body packers'--the British experience. *Ann R Coll Surg Engl.* 2002; 84: 35-38.
5. Sporer KA, Firestone J. Clinical course of crack cocaine body stuffers. *Ann Emerg Med.* 1997; 29: 596-601.
6. Roberts JR, Price D, Goldfrank L, Hartnett L. The bodystuffer syndrome: a clandestine form of drug overdose. *Am J Emerg Med.* 1986; 4: 24-27.
7. Intronza F Jr, Smialek JE. The "mini-packer" syndrome. Fatal ingestion of drug containers in Baltimore, Maryland. *Am J Forensic Med Pathol.* 1989; 10: 21-24.
8. Püschel K, Stein S, Stobbe S, Heinemann A. Analysis of 683 drug packages seized from "body stuffers". *Forensic Sci Int.* 2004; 140: 109-111.
9. June R, Aks SE, Keys N, Wahl M. Medical outcome of cocaine bodystuffers. *J Emerg Med.* 2000; 18: 221-224.
10. Fineschi V, Centini F, Monciotti F, Turillazzi E. The cocaine "body stuffer" syndrome: a fatal case. *Forensic Sci Int.* 2002; 126: 7-10.
11. Norfolk GA. The fatal case of a cocaine body-stuffer and a literature review - towards evidence based management. *J Forensic Leg Med.* 2007; 14: 49-52.
12. Wilcher G. Drug-related deaths with evidence of intracorporeal drug

- concealment at autopsy: five case reports. *Am J Forensic Med Pathol.* 2011; 32: 314-318.
13. Malbrain ML, Neels H, Vissers K, Demedts P, Verbraeken H, Daelemans R, et al. A massive, near-fatal cocaine intoxication in a body-stuffer. Case report and review of the literature. *Acta Clin Belg.* 1994; 49: 12-18.
14. Tsokos M, Erbersdobler A. Peliosis of the liver and spleen. Pathological features and forensic pathological relevance of two rare diseases with potentially fatal outcome. *Foren Pathol Rev.* 2006; 4: 143-156.
15. Wang SY, Ruggles S, Vade A, Newman BM, Borge MA. Hepatic rupture caused by peliosis hepatis. *J Pediatr Surg.* 2001; 36: 1456-1459.
16. Baer PA, Meagher T, Pal JM, Vilorio J. Severe weight loss and fatal intra-abdominal hemorrhage in an elderly man. *Can Med Assoc J.* 1984; 131: 319-324.
17. Tóth P, Takács I, Kerekes L, Sápy P. [Surgical treatment of intraabdominal hemorrhage in peliosis hepatis]. *Chirurg.* 2002; 73: 83-85.
18. Jacquemin E, Pariente D, Fabre M, Huault G, Valayer J, Bernard O. Peliosis hepatis with initial presentation as acute hepatic failure and intraperitoneal hemorrhage in children. *J Hepatol.* 1999; 30: 1146-1150.
19. Bagheri SA, Boyer JL. Peliosis hepatis associated with androgenic-anabolic steroid therapy. A severe form of hepatic injury. *Ann Intern Med.* 1974; 81: 610-618.
20. Zimmerman HJ. Hepatotoxicity. Adverse Effects of Drugs and Other Chemicals on the Liver. ed 2. Philadelphia Lippincott-Williams-Wilkins, 1999.
21. Wanless IR, Dore S, Gopinath N, Tan J, Cameron R, Heathcote EJ, et al. Histopathology of cocaine hepatotoxicity. Report of four patients. *Gastroenterology.* 1990; 98: 497-501.
22. Perino LE, Warren GH, Levine JS. Cocaine-induced hepatotoxicity in humans. *Gastroenterol.* 1987; 93: 176-180.
23. Balaguer F, Fernández J, Lozano M, Miquel R, Mas A. Cocaine-induced acute hepatitis and thrombotic microangiopathy. *JAMA.* 2005; 293: 797-798.
24. Kloss MW, Rosen GM, Rauckman EJ. Acute cocaine-induced hepatotoxicity in DBA/2Ha male mice. *Toxicol Appl Pharmacol.* 1982; 65: 75-83.
25. Evans MA. Role of protein binding in cocaine-induced hepatic necrosis. *J Pharmacol Exp Ther.* 1983; 224: 73-79.
26. Bouis P, Boelsterli UA. Modulation of cocaine metabolism in primary rat hepatocyte cultures: effect on irreversible binding and protein biosynthesis. *Toxicol Appl Pharmacol.* 1990; 104: 429-439.
27. Lutt WW. *Hepatic Circulation - Physiology and Pathophysiology.* Morgan & Claypool Life Sciences; San Rafael (CA), 2009.

Cite this article

Tuccori M, Scollo C, Guidi B, Blandizzi C, Giusiani M, et al. (2017) A Fatal Case of Hepatic Peliosis in a Cocaine Body Stuffer. *J Pharmacol Clin Toxicol* 5(1):1068.