CASE REPORT

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Vascular Lesions in Intestinal Ischemia Induced by Cocaine-Alcohol Abuse: Report of a Fatal Case Due to Overdose

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ABSTRACT: Intestinal ischemia induced by cocaine abuse is a rare condition. To this date, only three cases have been described. The diagnosis of bowel ischemia should be suspected whenever a cocaine addict has severe abdominal pain. A pathological examination of the resected bowel segment was performed in one case, and the diagnosis was confirmed microscopically. However, the existence of pathologic alterations of the intestinal vessels was not confirmed. Why the intestinal injury is segmental and whether it is related to the dose ingested, the administration route, or the combination of cocaine with alcohol, caffeine, or marijuana remain unclear. The authors report one fatal case associated with cocaine-alcohol overdose. The postmortem examination demonstrated the existence of segmental intestinal ischemia. Microscopic study failed to demonstrate thrombosis in the mesenteric vessels; however, we found an unusual lesion affecting the arterioles located in the intestinal submucosa of the hemorrhagic areas.

KEYWORDS: pathology and biology, cocaine, alcohol, intestinal ischemia, vascular lesions, death, overdose

Until recently, little information was available about the cardiovascular effects of cocaine. The most well known of its clinical cardiovascular effects are ischemic chest pain syndromes and myocardial infarction occurring anywhere between minutes after cocaine use to hours later [*1–3*].

The pathophysiological basis for myocardial ischemia and infarction remains unknown.

To date, only three cases of intestinal ischemia following ingestion [*4*] or associated with intranasal use [*5*] of cocaine have been described.

The suspected mechanism by which ingested cocaine causes severe bowel ischemia is

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related to the basic pharmacological properties of the drug. The intestinal vasculature contains alpha-adrenergic receptors which are stimulated by norepinephrine, leading to an increase in intestinal vascular resistance. Cocaine-induced catecholamine stimulation of alpha receptors in mesenteric vasculature causes intense vasoconstriction and reduced blood flow, which leads to ischemia [6].

The cocaine facilitates release and inhibits norepinephrine reuptake but also alters neurotransmitter systems involving dopamine and serotonin [7].

A postmortem examination, including histopathological studies, was performed in only one of the three cases previously described [5]. In that case, the diagnosis of intestinal ischemia was confirmed microscopically. However, mesenteric vessel thrombosis or any other alterations of the intestinal intramural vasculature were not described.

This report deals with a fatal case associated with cocaine-alcohol abuse. The postmortem examination revealed many areas of petechial hemorrhages in the mucosa and the serosa of the distal ileum. A histopathological study was performed on the ischemic areas. A special search was made for the existence of thrombi in the mesenteric and intramural vasculature. The existence of thrombi was not confirmed, but we found an unusual lesion affecting the small arterioles located in the intestinal submucosa of the ischemic areas.

Case History

Case Ll., M. A., a 24-year-old bar tender, was taken to the Cruz Roja (Red Cross) Hospital in Barcelona, by a friend, on the night of 16 Oct. (Sunday) 1988. It was noted by the witness that the victim, while lying in the back seat of his car, was "gasping for breath." Emergency rescue personnel found that the victim was unconscious, with his pupils fixed and dilated. The body was pale, cold, and clammy, with an absence of respiration, pulse, or blood pressure. One hour of advanced cardiopulmonary resuscitation proved unsuccessful. A history of cocaine-alcohol abuse during the whole weekend, with an eventual cocaine overdose, 1 or 2 h before his death, was obtained from the friend.

Autopsy Examination

A complete autopsy, including toxicological screening, was performed 24 h after the death and provided the following pathological findings: pulmonary edema and vascular congestion, with a significant amount of hemorrhage, and terminal regurgitation with aspiration of gastric contents. The remaining organs, with the exception of the small intestine, showed moderate to severe congestion. The gastric mucosa presented severe congestion and focal hemorrhages in the mucosa. The small intestine, especially the last 25 cm, showed multiple areas of petechial hemorrhage affecting both the serosa and the intestinal mucosa. A diagnosis of intestinal ischemia was made.

Histological Study

Samples from the different ischemic areas and from the different organs were processed for histopathological study. The samples were included in Paraplast, sectioned at 5 μm, and stained with hematoxylin-eosin-Phloxin B, Masson's trichrome stain, and Verhoeff-van Gieson's elastic stain. Photographs were taken using Kodak Panatomix X film. Some of them were taken using Nomarski's interference.

Microscopical Examination

The presumptive intestinal ischemia was microscopically confirmed. The intestinal ischemia was segmental and a very detailed study of the mesenteric and intramural vasculature failed to demonstrate occlusive thrombosis. However, inside the submucosa from the ischemic areas and among the normal arterioles, we found small-caliber arterioles which showed unusual and atypical obstructive lesions. The internal elastic membrane (Fig. 1) showed multiple protrusions or blebs projecting inside the vascular lumen, which created a drastic and spectacular narrowing of the vascular caliber. Behind the internal elastic membrane, edematous fluid was microscopically detected occupying the insides of the blebs.

Toxicologic Analysis

The objective of the analysis was to detect a fatal reaction to cocaine (which, to date, has been infrequent in Spain) among drug addicts in routine cases of intoxication, so that these cases could, in the future, be investigated immediately by the Section of Histopathology of the National Institute of Toxicology (Barcelona Department).

Samples

Blood (4-mL) and urine (3-mL) samples were submitted for toxicological analysis.

Methods

(a) Extraction—A carbonate buffer of pH 9.6 was added to both samples. The extraction was performed with a Sep-Pak C_{18} cartridge. The solvent used was chloroform and isopropanol at a 9:1 ratio. The extract was evaporated under a stream of nitrogen, just to dryness.

(b) Capillary Gas Chromatography/Mass Spectrometry (GC/MS)—The extracts were analyzed using a Model 5890 A Hewlet-Packard gas chromatograph (GC) with a 5970 B mass selective detector (MSD), with a Supelco 30-m, 0.55-mm inside diameter (ID), 0.25-μm film depth (df) fused silica capillary column. The instrument conditions were as follows: The oven temperature was 260°C; the injector temperature was 275°C. The transfer line temperature was 280°C. Helium was used as the carrier gas at a flow of 0.9 mL/min. The acquisition mode was SCAN and SIM. Selected ion monitoring was used: cocaine *m/z* 82, 182, 198, and 303 and benzoylecgonine *m/z* 82, 196, 272, and 317. The information was processed on an HP 59970 C MS chemstation with a Karl Pflegger Mass Spectral Library of Drugs, Poisons, and Their Metabolites.

(c) Enzyme Immunoassay—The urine was analyzed using a Syva Qst, by means of the urine cocaine metabolite assay.

(d) Widmark Dessication Method for Estimating Alcohol in Body Tissues and Fluids [*8*]—This method was used to determine the alcohol concentration in the blood.

Results

The analysis of urine was done using an enzyme immunoassay, and the result was positive for benzoylecgonine.

The blood alcohol concentration was 2.1 g/L.

The presence of benzoylecgonine was confirmed in the urine and detected in the blood by GC/MS. Cocaine was not detected in either sample.

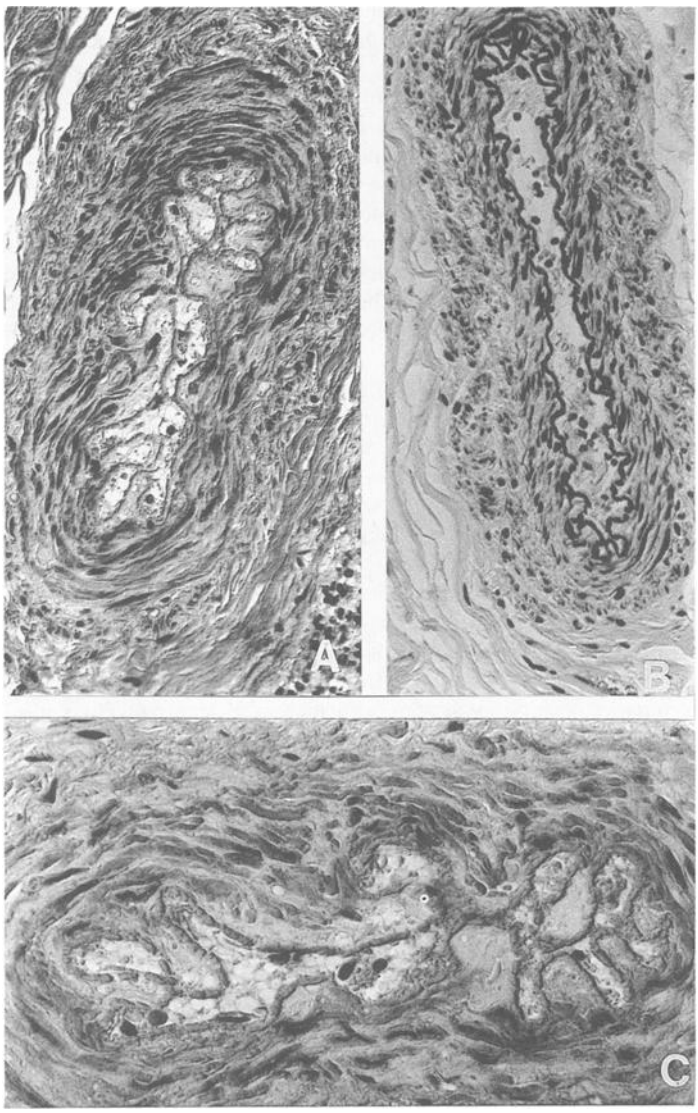

FIG. 1—*Intestinal submucosa from the ischemic areas:* (a) *arteriole showing numerous protrusions of the elastic membrane (note the severe narrowing of the arteriolar lumen and the edematous fluid inside the blebs); stain, hematoxylin-eosin-Phloxin B; magnification,* ×*300;* (b) *normal arteriole; Verhoeff-Van Gieson's elastic stain; magnification,* ×*300;* (c) *detail of the* (a) *showing the fragmentation of the elastic membrane and the subelastic edema; magnification,* ×*480.*

Discussion

Intestinal ischemia, or gangrene, is one of the rare adverse effects of cocaine abuse [6]. To date, only three cases have been reported: two associated with ingestion [4], and the third with intranasal use of the drug [5]. However, the existence of thrombosis or vascular pathology in the intestinal vasculature has never been described.

Cardiovascular effects of cocaine, including ischemia and myocardial infarction, are well documented [3]. In an autopsy study of 40 patients with cocaine detected in the body fluids, histologically demonstrable myocarditis was found in 20% of the victims, and contraction band necrosis in 25% of the victims. One patient in that series had platelet thrombus of the left anterior descending coronary artery superimposed on a 40% eccentric atherosclerotic plaque [3]. In one case that was reported of the existence of a coronary thrombus in a 21-year-old man, no underlying atherosclerotic coronary plaque was found, although the victim had coronary fibrointimal proliferation. The thrombosis was attributed to a coronary artery spasm that caused focal endothelial injury and platelet adherence and aggregation [1]. The hypothesis that the cocaine-induced spasm resulted in endothelial disruption, which induces a cycle of platelet aggregation, is also maintained by other authors [3].

We believe this is the first time a description has been made of an arteriolar lesion which could support the hypothesis previously advanced about the endothelial injury depending on an arteriolar cocaine-induced spasm. The severe narrowing of the arteriolar lumen could explain the intestinal ischemia. The intraluminal blebs, depending on protusions and subendoelastic edema, along with fragmentation of the elastic membrane, can produce a drastic reduction of the blood flow. This lesion was not found in the vasculature of the other organs studied, such as the heart and the lungs.

With regard to the history of the deceased, we do not know whether the last dose of cocaine was sniffed or ingested. The analytical investigation also demonstrated the presence of 2.1 g/L of ethanol in the blood. It is known that sudden cardiac deaths are often associated with recent ethanol intake in drug abusers. Ethanol, cocaine, and cannabis activate the sympathetic nervous system with increased levels of circulating catecholamines, an increased heart rate, and elevated blood pressure. These additive or synergistic effects might increase the likelihood of adverse cardiovascular events [7].

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