

Charles V. Wetli,¹ M.D. and David A. Fishbain,² M.D.

Cocaine-Induced Psychosis and Sudden Death in Recreational Cocaine Users

REFERENCE: Wetli, C. V. and Fishbain, D. A., "Cocaine-Induced Psychosis and Sudden Death in Recreational Cocaine Users," *Journal of Forensic Sciences*, JFSCA, Vol. 30, No. 3, July 1985, pp. 873-880.

ABSTRACT: Fatal cocaine intoxication presenting as an excited delirium is described in seven recreational cocaine users. Symptoms began with the acute onset of an intense paranoia, followed by bizarre and violent behavior necessitating forcible restraint. The symptoms were frequently accompanied by unexpected strength and hyperthermia. Fatal respiratory collapse occurred suddenly and without warning, generally within a few minutes to an hour after the victim was restrained. Five of the seven died while in police custody. Blood concentration of cocaine averaged 0.6 mg/L, about ten times lower than that seen in fatal cocaine overdoses. Police, rescue personnel, and emergency room physicians should be aware that excited delirium may be the result of a potentially fatal cocaine intoxication; its appearance should prompt immediate transport of the victim to a medical facility. Continuous monitoring, administration of appropriate cocaine antagonists, and respiratory support will hopefully avert a fatal outcome.

KEYWORDS: pathology and biology, toxicology, cocaine, death

Cocaine intoxication with sudden death has been reported in both recreational users of the drug and in cocaine "body packers" [1-3]. Prodromal signs and symptoms often include dysphoria, hyperthermia, tachycardia, mydriasis, stupor, and seizures [3-5]. Fatal cocaine intoxication presenting as an excited delirium is rare, having been described only once previously in a cocaine body packer [2].

This report describes seven recreational users of cocaine who died suddenly and unexpectedly of cocaine intoxication but with a psychiatric presentation of excited delirium [2,6]. The clinical presentation, terminal events, and toxicologic findings are compared to more typical cases of fatal cocaine intoxication. Recognition of the syndrome and treatment recommendations are discussed.

Materials and Methods

The cases selected for this report were ones in which recreational cocaine users presented with a psychotic reaction, died suddenly with respiratory arrest, and had toxic levels of cocaine in their blood. Of nine such cases identified over a thirteen-month period (April 1983 to May 1984), two will not be further discussed; in one the subject died from self-inflicted

Received for publication 1 Aug. 1984; revised manuscript received 18 Oct. 1984; accepted for publication 19 Oct. 1984.

¹Deputy chief medical examiner, Dade County, and clinical associate professor of pathology, University of Miami School of Medicine, Miami, FL.

²Director, Psychiatric Emergency Service, Jackson Memorial Hospital, and associate professor of psychiatry, University of Miami School of Medicine, Miami, FL.

injuries incurred during the psychotic episode, and in the other no blood sample was drawn for toxicologic analysis (although circumstantial evidence indicated recreational use of cocaine before the psychotic episode).

In this report, cocaine refers to illicit street cocaine, which varies in purity and is usually cut or diluted with mannitol. It may also contain lidocaine or procaine.

Terminal and preterminal events, scene descriptions, and background information were provided by investigating police agencies and medical examiner investigators. Medical records and the reports of paramedical (rescue) personnel were also reviewed. Complete autopsies were performed on all cases. Portmortem blood was preserved with sodium fluoride. Gas-liquid chromatography and enzyme-multiplied immunoassay (EMIT,[®] Syva) were utilized to screen urine and blood for alcohol and drugs. Cocaine was detected and quantified by gas-liquid chromatography with a nitrogen-phosphorus detector [7] in a procedure modified from Jatlow and Bailey [8]. Histological sections were reviewed in all cases.

Results

The clinical and toxicologic features of the seven cases are summarized in Table 1. The signs of excited delirium most often noted were fear, panic, shouting, physical violence, hyperactivity, and thrashing (particularly after restraints were applied). Six of the seven exhibited unexpected strength, requiring several people to restrain them. Hyperthermia was noted in four of the seven, and mydriasis was noted twice. Physical restraints were required in all but one case.

The blood concentrations of cocaine were from 0.14 to 0.92 mg/L, averaging 0.60 mg/L. Lidocaine was detected in two instances; a review of the medical records indicated this drug was not administered by paramedical or hospital personnel.

Postmortem examination did not reveal any "anatomic cause of death," with the possible exception of Case 4 (peritonitis as a result of a ruptured jejunum). Pulmonary congestion and edema, cerebral edema, and nonlethal self-inflicted injuries were most frequently noted. Specifically excluded by autopsy and witness accounts was death from mechanical asphyxia. This includes asphyxiation because of improper positioning of the restrained patient and the application of law enforcement neck holds such as the "carotid sleeper hold" [9].

A review of the histologic sections did not reveal any occult disease processes such as a myocarditis. Specifically excluded in six cases was myofibrillar degeneration [10], a morphologic hallmark of stress cardiomyopathy associated with sudden death [11]. Histologic sections of heart were not available for review in Case 2.

Case Reports

Case 1

A 33-year-old black male approached a residence (in which he had lived at some time in the past) and began pounding on the door. He was shouting that he wanted to see his wife and daughter. The occupants informed him that nobody by that name resided there, yet he pursued his actions. Four bystanders finally restrained him and assisted police units upon their arrival. The subject was handcuffed and put into a police car, whereupon he began to kick out the windows of the vehicle. The police subsequently restrained his ankles and attached the ankle restraints and handcuffs together. He was then transported to a local hospital. While enroute the police officers noted he became tranquil (about 45 min after the onset of the disturbance). Upon their arrival at the hospital a few minutes later, the subject was discovered to be in a respiratory arrest. Resuscitative attempts were futile. A postmortem examination was performed 1 h and 45 min later (about 3 h after the onset of the disturbance), and a rectal temperature of 41°C (106°F) was recorded. He had needle marks typi-

TABLE 1—Summary of cases.

Case	ARS ^a	Signs of Delirium ^b	Hyper-thermia	Time Interval, ^c min	Custody	Exhibited Increased Strength	Restraints Required	Blood Cocaine, mg/L	Other Toxicology	Comment
1	33 BM	1, 2, 3, 4, 7	yes	50	police	yes	yes	0.80	S2,3-mg/L blood lidocaine	respiratory arrest in police vehicle
2	26 WM	1, 2, 3, 4, 5, 6, 7	yes	120	medical	no	yes	0.80	negative	punched through window sustaining nonfatal laceration; respiratory arrest in hospital; mydriasis; inappropriate disrobing
3	29 WF	1, 2, 3, 4, 5, 7	not noted	20	police	yes	yes	0.92	nasal swabs positive for cocaine	onset of delirium in automobile; respiratory arrest at scene
4	24 WM	1, 2, 3, 4, 5, 7	not noted	240	medical	yes	yes	0.46	0.33-mg/L blood lidocaine	jumped down flight of stairs and ruptured jejunum; respiratory arrest in hospital; inappropriate disrobing
5	37 WM	1, 2, 3, 4, 5, 7	yes	45	police	yes	yes	0.91	nasal swabs positive for cocaine; 0.11% blood ethanol	onset of delirium while driving automobile; respiratory arrest in police vehicle
6	28 WM	1, 2, 3, 4, 5, 7	yes	10	police	yes	yes	0.14	negative	apprehended by police after high speed automobile chase; mydriasis; respiratory arrest in police custody
7	26 WM	1, 2, 3, 4, 5, 7	no	5-10	police	yes	yes	0.18	nasal swabs positive for cocaine	wrestled gun from police officer; onset of disturbance after free-base cocaine usage

^aAge, race, sex.^b1—thrashing, 2—shouting, 3—hyperactive, 4—fearful, 5—panicky, 6—hypervigilant, 7—violent.^cInterval from time taken into custody to time of respiratory arrest.

cal of intravenous drug abuse and pulmonary and cerebral edema. Abrasions and contusions of the ankles and wrists were also evident from his struggling against the restraints. Toxicologic analysis of postmortem blood disclosed 52.3 mg/L of lidocaine and 0.8 mg/L of cocaine. No lidocaine was administered to the victim during the resuscitative attempts.

Case 2

A 26-year-old white man with a history of alcohol, marijuana, and cocaine abuse became involved in an altercation with his homosexual partner. He took off his clothes, began yelling and screaming, and ran about the apartment smashing a variety of objects. Medical rescue units were called when he punched through a window and lacerated his arm. In the emergency room he was noted to have mydriasis and a temperature of 39°C (102°F). His pulse was 200, respirations were 40 per minute, and systolic pressure was 100 mm Hg. Although communicative, he was agitated and combative and had to be restrained. He was in metabolic acidosis. He was administered intravenous fluids and chlorpromazine. About 2 h after admission he became hypotensive and had a respiratory arrest. Although initially resuscitated he died about 6 h after admission. The postmortem examination disclosed a superficial 4-cm laceration of the left arm on its lateral aspect just above the elbow. A blood sample obtained upon admission to the emergency room contained 0.8 mg/L of cocaine. No lidocaine was detected.

Case 3

A 29-year-old white female, with several arrests for cocaine trafficking, was the passenger in an automobile being driven by her boyfriend. She suddenly became violent and paranoid, yelling, "You're trying to kill me. Please don't kill me. I have children." She attempted to exit the vehicle while it was still in motion, and the driver at this point stopped the vehicle. She then tried to run into the traffic, yelling that he was trying to kill her. A passing police officer stopped to render assistance, whereupon the subject became even more violent. With the aid of several police officers she was finally subdued; handcuffs and ankle restraints were applied and then attached to each other. A few minutes later she stopped yelling and screaming and appeared to be choking or aspirating. Medical rescue units arrived at that time to find her in a respiratory arrest from which she could not be resuscitated. The elapsed time was approximately 20 min. By palpation the victim was not hyperthermic when observed by a police officer about an hour after death (the medical records made no mention of body temperature). The autopsy was performed 16 h after death and revealed pulmonary congestion and edema but no evidence of aspiration of gastric contents. The concentration of cocaine in the postmortem blood sample was 0.92 mg/L.

Case 4

A 24-year-old white male with a history of drug abuse became engaged in an altercation in an apartment with two acquaintances. He suddenly disrobed, became abusive, and was forced out of the apartment. He then dove through a window of a neighboring apartment and began to fight with the two residents, biting one on the leg. The apartment manager instructed the two residents to leave the premises and call the police. The victim subsequently ran out of the apartment, jumped down a flight of stairs and began running around the swimming pool area. When police arrived, he was still naked and lying near the pool. He became violent once again upon the approach of the police officers and, with the assistance of several bystanders, the victim was finally subdued. Handcuffs and ankle restraints were placed on the victim and were in turn tied together.

The victim was transported to a local hospital emergency room. His pulse was 92 but he

refused to allow other vital signs to be taken. A peritoneal lavage returned some feculent material (but no blood), and the possibility of iatrogenic bowel perforation was considered. Before an exploratory laparotomy he had a sudden respiratory arrest from which he was resuscitated. This occurred approximately 4 h after the onset of the disturbance. The subsequent laparotomy disclosed two iatrogenic bowel perforations which were oversewn. He became septic and died on the fourth hospital day without ever having regained consciousness. Prior to the respiratory arrest he was not noted to be hyperthermic. A sample of blood drawn upon admission to the hospital contained 0.46 mg/L of cocaine and 0.33 mg/L of lidocaine.

The autopsy revealed an acute peritonitis from a ruptured jejunum near the ligament of Treitz. The oversewn iatrogenic perforations were intact. It was concluded that the ruptured jejunum was a deceleration type injury sustained when he jumped down the flight of stairs. Also, both ankles were markedly hemorrhagic, but radiologic examination did not disclose any fractures. Abrasions on the wrists and ankles were still evident from his fighting against the restraints.

Case 5

A 37-year-old white male drank some beer with a friend. A short time later he was observed in a van, racing the engine and blowing the horn. He then rammed the vehicle into the front of a residence, jumped out, and began running about the neighborhood jumping over fences and pounding on doors. He was yelling and screaming that people were after him. When the police arrived, they found him hiding in some bushes. They coaxed him out and began a "pat down," whereupon the subject began to violently fight the police. Four officers finally restrained and subdued the victim and he was handcuffed. When placed in the police vehicle he began to kick out the windows. He was removed from the vehicle and his ankles were restrained as well. The ankle and handcuff restraints were then attached to each other. After that, he calmed down and the police interrogated witnesses while the subject remained in the back of the police vehicle. About 45 min later, someone noticed that he appeared to be bleeding from his nose and had difficulty breathing. He was rushed to a hospital and found to be in a respiratory arrest. Resuscitative measures were continued for 30 min to no avail. A rectal temperature approximately 2 h after death was 40°C (104°F). Postmortem examination revealed contusions and abrasions of the wrists and ankles (consistent with fighting against the police restraints) and pulmonary edema and congestion. Nasal swabs were positive for cocaine, and the blood concentration of cocaine was 0.91 mg/L. Ethanol was detected in the blood at 0.11%.

Case 6

A 28-year-old white male was reportedly consuming alcoholic beverages and snorting cocaine with his girlfriend. He suddenly became violent, claimed people were after him, ran to his car, and began driving erratically. When a police unit approached and turned on the red warning lights, the victim accelerated his automobile, commencing a high-speed chase that lasted about 15 or 20 min until the subject stopped his vehicle and ran from the police. He was finally apprehended but it took six police officers to restrain him. He was handcuffed, placed in a police vehicle, and kept under observation while awaiting the arrival of paramedical personnel (which the police requested as a precautionary measure). During this time it was noted that his eyes were dilated. He suddenly developed perioral cyanosis followed by intense facial lividity, and he stopped breathing. Resuscitative efforts were begun by the police and continued by paramedical rescue units. Upon arrival at the hospital emergency room he was noted to have a body temperature of 39°C (102.8°F). Despite supportive measures he died 6 h later. A sample of fluoride-preserved blood taken upon hospital admission had a 0.14-mg/L concentration of cocaine. Tests for alcohol and other drugs were negative.

The postmortem examination revealed pulmonary congestion and edema, cerebral edema, early hypoxic necrosis of the basal ganglia, and a superficial ulceration of the nasal septum. A right periorbital ecchymosis was the result of the struggle with the police.

Case 7

A 26-year-old white male had "free-based" cocaine for an unknown duration. Shortly after he left the residence, while in the same neighborhood, he began running down the street yelling and screaming unintelligibly. Police were summoned and they chased him for some time through backyards and over fences. One officer finally tackled him; during the ensuing struggle, the subject grabbed ahold of the officer's gun and fired it once. Three officers finally subdued the subject after a violent struggle during which the subject was struck twice on the head with a heavy flashlight. He was handcuffed behind his back and placed prone on the ground. He continued to thrash about for a period of time. Upon the arrival of paramedics a few minutes later he was found to be dead. He was not noted to be hyperthermic by the police or paramedics or by the medical examiner who examined him at the scene about 2 h after death.

The postmortem examination, performed about 13 h after death, revealed superficial scalp and body lacerations, pulmonary congestion and pulmonary edema. No lethal injuries were observed. The concentration of cocaine in the blood was 0.18 mg/L. Nasal swabs were positive for cocaine. No other drugs or alcohol were detected.

Discussion

Depending on the ingested dose and the chronicity of use, cocaine may cause a variety of psychiatric syndromes [5,12]. These include euphoria, dysphoria, paranoid schizophreniform psychosis, and delirium. Delirium is an acute organic mental disorder characterized by a disturbance of attention and perception, impaired thinking, disorientation for individuals around the patient, visual hallucinations, and illusions [6]. The cases reported here are best characterized as an excited delirium secondary to cocaine intoxication. Although this syndrome has been reported once previously in a cocaine body packer [2], all the cases in this report were recreational users of cocaine.

Excited delirium is usually regarded as a medical emergency but with a psychiatric presentation. The prognosis depends on the underlying cause of the delirium [6] and, as these seven cases illustrate, the outcome may be fatal. Cocaine toxicity should be considered as possibly etiologic whenever there is any historical evidence of recent cocaine ingestion or physical signs suggesting cocaine intoxication (namely, hyperthermia, mydriasis reactive to light, or fresh intravenous injection marks). Consideration should then be given to the intravenous administration of propranolol (antagonistic to the sympathomimetic effects of cocaine) or intravenous diazepam to control the agitation and anxiety [13]. The patient should also be given adequate respiratory support and be continuously monitored until the delirium abates. However, sudden tranquility should prompt immediate evaluation of the cardiorespiratory status.

Although the deaths in this series were attributed to cocaine intoxication, they differ in several ways from the more typical cocaine overdose fatality. Generally, a fatal cocaine overdose is quite sudden and frequently preceded by generalized seizures followed by respiratory collapse [3,4]. Prodromal symptoms of dysphoria or hyperthermia may also be present. Death following intravenous administration is generally due to a sudden respiratory collapse with no prodromal symptoms. None of the cases presented here had preterminal seizures, and the prodromal symptoms were those of excited delirium, not dysphoria. The average blood cocaine concentration in this series was 0.60 mg/L, as compared to an average peak therapeutic concentration of 0.31 mg/L in surgical patients [14] and 6 mg/L in fatal cocaine

overdoses [5]. Hence, the exact mechanism of death in these cases of excited delirium is unknown. One may thereby speculate on the possible role of autonomic reflexes [15], a toxic cardiac dysrhythmia [16], or "restraint stress," as has been postulated for the sudden death associated with acute exhaustive mania [17]. Thus far a review of the toxicologic data has failed to identify any common cocaine congeners (contaminants) in these victims. However, the relative purity of street cocaine has increased from about 10% to nearly 35% over the time when these cases were identified (personal communication, Miami Field Office, Drug Enforcement Administration). It is possible that this recent increased purity and availability may have played a role in engendering the psychotic state.

Police and emergency paramedical personnel should be aware of the potential for sudden death in association with excited delirium. As such, there should be no delay in transporting such patients to a nearby medical facility, and the cardiorespiratory status should be constantly observed. Should cocaine be considered a possible cause of the excited delirium, emergency room physicians should be prepared to provide appropriate medication for sedation and control of sympathomimetic symptoms and provide adequate ventilatory support. It is hoped that prompt diagnosis and therapy may prevent sudden respiratory collapse and death in these recreational cocaine users.

Acknowledgment

Dr. James Benz, chief medical examiner of Palm Beach County, Florida, provided the data for Case 7.

References

- [1] Wetli, C. V. and Mittleman, R. E., "The 'Body Packer Syndrome'—Toxicity Following Ingestion of Illicit Drugs Packaged for Transportation," *Journal of Forensic Sciences*, Vol. 26, No. 3, July 1981, pp. 492-500.
- [2] Fishbain, D. A. and Wetli, C. V., "Cocaine Intoxication, Delirium, and Death in a Body Packer," *Annals of Emergency Medicine*, Vol. 10, No. 10, Oct. 1981, pp. 531-532.
- [3] Wetli, C. V. and Wright, R. K., "Death Caused by Recreational Cocaine Use," *Journal of the American Medical Association*, Vol. 241, No. 23, June 1979, pp. 2519-2522.
- [4] Mittleman, R. E. and Wetli, C. V., "Death Caused by Recreational Cocaine Use—An Update," *Journal of the American Medical Association*, Vol. 252, No. 14, Oct. 1984, pp. 1889-1893.
- [5] Van Dyke, C. and Byck, R., "Cocaine: 1884-1974," in *Cocaine and Other Stimulants*, E. H. Ellinwood and M. M. Kilby, Eds., Plenum Press, New York, 1976, pp. 1-30.
- [6] Lipowsky, Z. J., "Organic Mental Disorders: Introduction and Review of Syndromes," in *Comprehensive Textbook of Psychiatry*, 3rd ed., H. F. Kaplan, A. M. Freedman, and B. M. Sodock, Eds., Williams and Wilkins, Baltimore, 1979, pp. 1359-1392.
- [7] Bednarczyk, L. R., Gressman, E. A., and Wymer, R. L., "Two Cocaine-induced Fatalities," *Journal of Analytical Toxicology*, Vol. 4, No. 5, Sept./Oct. 1980, pp. 263-265.
- [8] Jatlow, P. I. and Bailey, D. N., "Gas Chromatographic Analysis for Cocaine in Human Plasma with Use of a Nitrogen Detector," *Clinical Chemistry*, Vol. 21, No. 13, Dec. 1975, pp. 1918-1921.
- [9] Reay, D. T. and Eisle, J. W., "Death from Law Enforcement Neck Holds," *American Journal of Forensic Medicine and Pathology*, Vol. 3, No. 3, Sept. 1982, pp. 253-258.
- [10] Reichenbach, D. D. and Benditt, E. P., "Catecholamines and Cardiomyopathy. The Pathogenesis and Potential Importance of Myofibrillar Degeneration," *Human Pathology*, Vol. 1, No. 1, March 1970, pp. 125-150.
- [11] Cebelin, M. S. and Hirsch, C. S., "Human Stress Cardiomyopathy—Myocardial Lesion in Victims of Homicidal Assaults Without Internal Injuries," *Human Pathology*, Vol. 11, No. 2, March 1980, pp. 123-132.
- [12] Post, R. M., "Cocaine Psychoses: A Continuum Model," *American Journal of Psychiatry*, Vol. 132, No. 3, March 1975, pp. 225-231.
- [13] Rappolt, R. T., Gay, G. R., and Inaba, D. S., "Propranolol: A Specific Antagonist to Cocaine," *Clinical Toxicology*, Vol. 10, No. 3, March 1977, pp. 265-267.
- [14] Baselt, R. C., *Disposition of Toxic Drugs and Chemicals in Man*, 2d ed., Biomedical Publications, Davis, CA, 1982, pp. 193-198.

- [15] Pruitt, R. D., "Death as an Expression of Functional Disease," *Mayo Clinic Proceedings*, Vol. 49, No. 9, Sept. 1974, pp. 627-634.
- [16] Liberatore, M. A. and Robinson, D. S., "Torsade de Pointes: A Mechanism for Sudden Death Associated with Neuroleptic Drug Therapy?," *Journal of Clinical Psychopharmacology*, Vol. 4, No. 3, June 1984, pp. 143-146.
- [17] Wendkos, M. H., "Acute Exhaustive Mania," in *Sudden Death and Psychiatric Illness*, Chap. 10, Spectrum Publications, New York/London, 1979, pp. 165-175.

Address requests for reprints or additional information to
Charles V. Wetli, M.D.
Dade County Medical Examiner Department
1050 N.W. 19th St.
Miami, FL 33136