P. multocida was subsequently recovered from the throat of the cat that inflicted the bite (cat A), but the onset of illness antedated the injury. The colonization or infection of the human respiratory tract by P. multocida is most commonly associated with atraumatic animal exposure resulting in airborne or direct transmission. In a recent review of pet-associated illness,8 the hazards and the management of animal bites are described with particular reference to P. multocida as a pathogen, but atraumatic infections are not mentioned. Because P. multocida has a predilection for patients with impaired host defenses, such patients should avoid close contact with domestic pets. Such close contact may involve kissing or nuzzling or being licked by the pets. P. multocida causing subdural empyema has been described in a patient with a history of ethmoid polyectomy who kissed her dog and two cats.10,11 Joint infection associated with rheumatoid arthritis and prostheses may be contracted by pet owners,12,13 as may appendiceal peritonitis14 and spontaneous peritonitis associated with hepatic cirrhosis.15 Where contact is close or a person susceptible, or both, it may not be necessary for puncture or abrasion of the skin to occur.16,17 Thus, a report of a 60-year-old patient with meningitis who regularly kissed her pet mongrel includes a specific warning that pets should not be kissed.18 Further to this point, Clapp and colleagues regard P. multocida meningitis in infants as a disease that may be prevented by advising parents not to allow their infants to be licked by household pets.19 The inoculation of fur by P. multocida in saliva during grooming is a further hazard to infants in close contact with pets and presumably also to susceptible owners who nuzzle their pets.20 Respiratory symptoms develop in only a few patients who have IgA deficiency. Those who have respiratory tract illness appear to be at particular risk for P. multocida infections developing, as is the case with persons with cirrhosis of the liver or chronic joint disease, during infancy, and in pregnancy.21 In general, the benefits of pet ownership far outweigh the disadvantages, but if pets are recommended by physicians as therapeutic aids,22 then due attention and advice should be given regarding the risk and prevention of zoonotic infections including those caused by P. multocida. Patients with IgA deficiency and respiratory tract symptoms should be urged to avoid close contact with cats and dogs. Further, the occurrence of infection in susceptible persons who are pet owners should give rise to the suspicion that zoonotic infectious agents such as P. multocida or the DF-2 bacillus may be responsible.23 Both organisms are commensals in dogs and cats24 and are more likely to cause serious disease in patients with impaired host defenses against infection.5,25 Unless there has been injury, a history of contact with animals may not be volunteered. If there is a suspicion of such zoonotic infection, detailed bacteriologic investigation and prompt treatment with penicillin should be initiated. “Those who’ll play with cats must expect to be scratched” (Cervantes, Don Quixote), but it is clear that even nontraumatic contact with cats may give rise to serious and sometimes fatal illness.

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Fatal Hyperthermia Associated With Cocaine Use

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RECREATIONAL COCAINE USE has been associated with multiple medical complications, particularly cardiovascular and central nervous system dysfunction.1 We report two cases of fatal cocaine-associated hyperthermia.

Report of Cases

Case 1

The patient, a 30-year-old man, presented to the Harborview Medical Center (Seattle) Emergency Department following a witnessed seizure, which occurred three to four hours after the intravenous administration of cocaine. His

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medical history was significant for heroin and cocaine abuse, including cocaine-associated seizures.

On arrival, the patient was agitated, diaphoretic, and alert. His temperature by axilla was 38°C (100.4°F), blood pressure 90/60 mm of mercury, heart rate 155 per minute, and respirations 20. The results of his initial examination were otherwise unremarkable. The initial laboratory values included a serum sodium of 151 mmol per liter, potassium 5.0 mmol per liter, chloride 111 mmol per liter, bicarbonate 23 mmol per liter, blood urea nitrogen 5.4 mmol per liter of urea (15 mg per dl), creatinine 190 μmol per liter (2.1 mg per dl), and glucose 5.1 mmol per liter (92 mg per dl). The hematocrit was 0.52, leukocyte count 7.8 × 10⁹ per liter, and platelet count 281 × 10⁹ per liter. A blood smear showed atypical lymphocytes with budding nuclei, but the findings were otherwise normal. Three hours later a prothrombin time was 15.4 seconds (control 12.0 seconds), partial thromboplastin time 45 seconds (range 26 to 42), fibrin degradation products greater than 2,000 ng per ml (normal <200), fibrinogen 161 mg per dl (normal 150 to 400), and the thrombin time was 35 seconds (normal 18 to 28). The platelet count was not repeated.

The patient had two generalized seizures 50 minutes after arrival. His temperature by rectum was 43°C (109°F) 45 minutes after the seizures. Bradycardia and ventricular arrhythmias resulted in hypotension, requiring intubation and the administration of pressors. He was placed on a cooling blanket, and ice packs were placed over his major arteries. An hour later his temperature was 38.6°C (101.5°F). The results of repeat laboratory studies were remarkable for a serum sodium of 159 mmol per liter, a potassium of 6.9 mmol per liter, chloride 104 mmol per liter, bicarbonate 18 mmol per liter, creatinine 265 μmol per liter (3.0 mg per dl), ionized calcium 1.94 mmol per liter (normal 2.32 to 2.58), and phosphate 3.75 mmol per liter (normal 0.97 to 1.45). The creatine kinase level was 14,090 units per liter (normal <100), the lactic dehydrogenase level was 2,170 units per liter (normal <304), and urine myoglobin more than 5,000 ng per ml. A gastric toxicologic screen was positive for nicotine metabolites and cocaine and negative for other drugs such as amphetamines, barbiturates, phenothiazines, phencyclidine hydrochloride (PCP), narcotics, mescaline, and methaqualone. A serum toxicology screen was negative for salicylate, amphetamine, sedatives, hypnotics, and volatiles. An electrocardiogram showed ST segment depression in the inferior leads. A chest x-ray film showed the lungs to be clear.

The patient became anuric, more hypokalemic, and remained hypotensive despite pressor support. Signs of pericardial tamponade developed, and a pericardiocentesis yielded 25 ml of bloody fluid. Five hours after presenting to the emergency department, he died. An autopsy showed 600 ml of bloody pericardial fluid and hemorrhage, congestion, and atelectasis in the lungs. Blood and urine cultures were negative. A drug screen of a serum specimen taken at the time of the autopsy was negative for cocaine but positive for benzoylecgonine, a cocaine metabolite. No drugs, including cocaine metabolites, were detected on an autopsy urine screen.

Case 2

A 38-year-old known cocaine user was brought to the Harborview Emergency Department by police. He had been acting bizarrely and barking like a dog. The patient was agitated, diaphoretic, incoherent, and unresponsive to pain. His blood pressure was 120/69 mm of mercury, his pulse was 150 per minute, respirations 40, and temperature 41.1°C (106°F). The precordium was hyperdynamic and a grade II/VI nonradiating systolic murmur was auscultated. There were old needle marks on the extremities, and a stool specimen was guaiac-positive.

Initial laboratory values were remarkable for a serum sodium of 144 mmol per liter, a potassium of 5.1 mmol per liter, a chloride of 105 mmol per liter, a bicarbonate of 11 mmol per liter, and an anion gap of 18. A blood urea nitrogen level was 6.1 mmol per liter of urea (17 mg per dl), and creatinine was 190 μmol per liter (2.2 mg per dl). Arterial blood gases determined while the patient was breathing room air were a pH of 7.31, a partial oxygen pressure of 61 torr, and a partial carbon dioxide pressure of 26 torr. A leukocyte count was 9 × 10⁹ per liter, hematocrit 0.48, and platelets 145 × 10⁹ per liter. A blood smear showed slight poikilocytosis and hypersegmented polymorphonuclear leukocytes. The prothrombin time was 19.9 seconds, partial thromboplastin time 79 seconds, thrombin time 50 seconds, fibrinogen level 108 mg per dl, and fibrin degradation products more than 2,000 ng per ml. The serum aspartate aminotransferase level was 1,555 units per liter (normal <25), the alanine aminotransferase was 1,155 units per liter (normal <30), lactic dehydrogenase 7,480 units per liter (normal <290), and creatine kinase 17,040 units per liter. A urine myoglobin level was more than 5,000 ng per dl. A lumbar puncture showed an opening pressure of 500 mm of water and 9 erythrocytes. A urine toxicology screen was positive only for cocaine and cocaine metabolites and nicotine and metabolite; a gastric screen was negative for cocaine, as well as for other drugs (those mentioned in case 1).

An endotracheal tube was introduced, and the patient was cooled with gastric lavage to normal body temperature. Broad-spectrum antibiotics were administered. Massive gastrointestinal and nasal bleeding was associated with a partial thromboplastin time of longer than 200 seconds, a fibrinogen level of less than 5 mg per dl, fibrin degradation products of more than 2,000 ng per ml, and a platelet count of 25 × 10⁹ per liter. Hypotension ensued, as did anuric renal failure. The creatine kinase level peaked at 30,000 units per liter, and persistent hypoglycemia required an infusion of a solution of 50% glucose in water. Hemodynamic and hematologic stability was obtained but the patient remained unresponsive, with renal and hepatic failure. On hospital day 7, a total bilirubin level was 422 mmol per liter (24.7 mg per dl) and creatinine 870 μmol per liter (9.8 mg per dl). The patient died after ventilator support was discontinued. Urine and cerebrospinal fluid cultures were negative. One blood culture was positive for coagulase-negative staphylococci (in aerobic broth).

Discussion

We describe two cases of cocaine-associated hyperthermia that resulted in death. Both patients were known cocaine users whose toxicologic screens were positive only for cocaine and nicotine and negative for other drugs or toxins. The cases are similar in that both presented with fever greater than 40°C (104°F) early in the evaluation, diaphoresis, tachycardia, tachypnea, and altered mental state. The results of laboratory tests were remarkable for metabolic
acidosis, bleeding due to coagulopathy, anuric renal failure with rhabdomyolysis, and a dramatic elevation of muscle and liver enzymes.

The clinical findings are consistent with described cases of heatstroke. In a review of 36 patients, all were young men engaged in physical exercise. There was no description of drug use. Eight of the cases were fatal, characterized by convulsions, prolonged unconsciousness, hypernatremia, oliguric renal failure, evolving disseminated intravascular coagulation, and elevated liver enzymes.

In addition, these patients had manifestations similar to those of other patients with drug-associated hyperthermia. Rosenberg and co-workers described 12 patients with hyperthermia due to anticholinergic agents, central nervous system stimulants, salicylates, or a combination of drugs. Manifestations included coma (11/12), increased muscle activity before hyperthermia (9/12), seizures (5/12), rhabdomyolysis (6/12), hypotension (8/12), coagulopathy (5/12), and acidosis (11/12). Five patients died, and four patients had permanent neurologic sequelae.

While hyperthermia has been associated with a variety of drug intoxications, its association with cocaine use has not been well documented until recently. We found two cases of apparent cocaine-induced hyperthermia previously reported in the literature. Toxicologic screens were negative for cocaine in both, however, and in one case the screen was positive for methadone, amitriptyline, and ethanol. Both patients survived. In addition, fatal malignant hyperthermia has been described in a 20-year-old man after recreational cocaine and ethanol use. This patient had a history of being susceptible to malignant hyperthermia and a family history of the same. Our patients both had a history of known cocaine use, had toxicologic screens positive for cocaine, and were found free of other drugs and metabolites. In addition, no evidence of infection as a possible cause of fever was found despite several cultures. Thus, the hyperthermia was strongly associated with intravenous cocaine use in these patients.

In the past year or two, three cases of hyperthermia, rhabdomyolysis, and acute renal failure associated with cocaine use have been reported. The patients presented with agitation, an altered mental state, and tachycardia. Toxicologic screens confirmed the presence of cocaine (or its metabolite) in all cases. These three patients survived, renal function improved, and they were discharged from hospital.

Our patients, in addition to manifesting hyperthermia, rhabdomyolysis, and renal failure, had coagulopathy and fatal outcome. Patient 2 had hepatic failure and remained unresponsive despite a correction of hemodynamic and laboratory values.

Our two patients had a clinical course similar to that of patients afflicted by heatstroke. We suggest that cocaine-associated hyperthermia may be a primary cause of various clinical toxic reactions associated with cocaine use. These toxic effects include rhabdomyolysis, renal failure, liver enzyme elevation, obtundation, and coagulopathy. Our hypothesis is supported by a study of cocaine intoxication in dogs. Cocaine was administered intravenously to dogs. Hemodynamic, clinical, and metabolic indices were controlled with pharmacologic pretreatment. The effects of hyperthermia on the clinical outcome were evaluated, and it was found to be the most important factor associated with a fatal outcome.

Hyperthermia due to cocaine intoxication is probably multifactorial and includes increased muscle activity, seizures, an increased metabolic rate from increased sympathetic nervous system activity, and impaired heat loss from peripheral vasoconstriction. Therapy is directed at rapidly lowering the body temperature to prevent irreversible cellular injury. Suggested measures to lower the body temperature include a cooling blanket, convection evaporation, intubation with cool air ventilation, and iced saline gastric lavage. As muscular activity is probably a primary cause of hyperthermia, sedation or paralysis may be indicated in certain cases.

Our patients rapidly defervesced without extensive measures. Difficulty in controlling hyperthermia associated with cocaine use may indicate an underlying thermoregulatory dysfunction precipitated by cocaine use or an adulterant. Specifically, findings of muscular rigidity suggest malignant hyperthermia, which might require pharmacologic intervention, such as the use of dantrolene sodium.

Hyperthermia may be a leading contributor to the toxic effects of cocaine use. Aggressive management of this problem is indicated to decrease the toxic effects.

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