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Myoglobinuric Acute Renal Failure Associated With Phencyclidine Abuse

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Phencyclidine (also known as PCP, angel dust, crystal and hog) has become an important drug of abuse since it was first introduced as a street drug in San Francisco in 1967. It is manufactured for use as an anesthetic in veterinary medicine but can be easily synthesized in a home laboratory from commercially available precursors. It is sold in a variety of physical forms and can be ingested, smoked, inhaled or injected. It is a frequent ingredient of other drugs of abuse, and in one survey was detected in 184 of 237 samples of illicit drugs.

Phencyclidine is an analgesic which acts primarily on the central nervous system by stimulation or depression. In man, these effects are highly dose-dependent, and consist of some combination of schizophreniform psychosis, analgesia, anesthesia and sympathetic dysfunction. Acute rhabdomyolysis and myoglobinuria not associated with renal dysfunction have recently been reported in association with phencyclidine abuse. We are unaware of any reports of myoglobinuric acute renal failure developing in persons who abuse phencyclidine. Because of this, the following two cases in which phencyclidine toxicity was associated with myoglobinuric acute renal failure are of interest.

Methods

Urine specimens were screened by Laboratory Procedures, Inc. (Woodland Hills, California) for the following groups of toxic substances: barbiturates, amphetamines, narcotics, hypnotics, analgesics, alcohol and phencyclidine. The initial screen was done using thin layer chromatography and positive results were confirmed by gas liquid chromatography.

Reports of Cases

Case 1. A 25-year-old man was admitted to hospital in stupor four hours after smoking cigarettes sprinkled with phencyclidine. He was agitated and was placed in soft restraints to control the purposeless movements of his arms and legs. Blood pressure was 120/80 mm of mercury, pulse 120 per minute, temperature 38.1°C (100.6°F), respiration 18 per minute. Heart, lungs and abdomen were normal. Horizontal nystagmus was present but the remainder of the neurological findings were within normal limits.

Laboratory studies gave the following values: hematocrit was 39 percent; leukocyte count 13,200 per cu mm; serum sodium was 134, potassium 5.2, chloride 98 and bicarbonate 24 mEq per liter; blood urea nitrogen (BUN) was 13, serum creatinine 1.2, glucose 120 and calcium 9.2 mg per dl. Analysis of urine showed the following: specific gravity 1.016, pH 5.5, protein and glucose negative, 1 to 2 leukocytes and 0 to 1 red blood cell per high-power field, and no casts. The urine was positive for phencyclidine but negative for the other substances listed in the Methods section. An X-ray film of the chest and an electrocardiogram showed no abnormalities.

On the following day, BUN was 52 and serum creatinine 4.8 mg per dl. Analysis of urine showed specific gravity 1.007, pH 5.0, trace protein, glucose negative, 6 to 8 leukocytes and 1 to 2 red blood cells per high-power field, and numerous brown-stained granular casts. Spot urine sodium was 46 and potassium 18 mEq per liter. On the tenth day, BUN was 75 and serum creatinine 8.5 mg per dl, and a renal consultation was requested. On that day, serum creatinine phosphokinase was 1,866, lactic dehydrogenase 694, glutamic oxaloacetic transaminase 441 and glu-
tamic pyruvic transaminase (SGOT) 89 IU per liter. Urine excreted on the same day was positive for myoglobin by the immunodiffusion technique. A diagnosis of myoglobinuric acute renal failure was made and the patient was treated conservatively. The serum creatinine level stabilized and declined on the 15th day. On the 26th day, the serum creatinine concentration was 1.3 mg per dl.

CASE 2. A 33-year-old man was brought to the hospital for abnormal behavior four hours after smoking two marijuana cigarettes laced with phencyclidine. He was evaluated by a psychiatrist who prescribed haloperidol. Urine specimens were taken for toxicology studies and the patient was discharged after overnight observation. Restlessness and agitation developed later that night, and he continued to “thash about” periodically for the next two days; he was then readmitted to hospital. The patient had had to be physically restrained at home.

On admission, he complained of aching in the legs and of decreased urination. He was conscious, alert and orientated. Blood pressure was 162/98 mm of mercury, pulse 84 per minute, temperature 37°C (98.7°F) and respiration 16 per minute. The heart, lungs and abdomen were normal. The calf muscles were diffusely tender. Results of the neurological examination were within normal limits.

The following values were shown on laboratory studies: hematocrit was 42 percent; leukocyte count 10,000 per cu mm; serum sodium 131, chloride 95, potassium 5.6 and bicarbonate 17 mEq per liter; BUN 98, serum creatinine 13.8, calcium 5.7, phosphate 9.0, uric acid 15 and glucose 102 mg per dl. Analysis of urine showed specific gravity 1.008, pH 6.0, protein 1+, glucose 0, 2 to 3 leukocytes and 1 to 2 red blood cells per high-power field, 10 to 12 golden-brown coarsely granular casts per low-power field. On the next day, serum creatine phosphokinase was 2,900, SGOT 450, lactic dehydrogenase 800 and alkaline phosphatase 78 IU per liter. Urine specimens taken during the first but not the second admission were positive for phencyclidine but not for the other toxic substances listed in the Methods section. Myoglobin was detected by immunodiffusion in the second urine specimen. X-ray studies of the chest and an electrocardiogram showed no abnormalities.

Myoglobinuric acute renal failure was diagnosed and peritoneal dialysis was instituted. After 40 exchanges, BUN was 102 and serum creatinine 12.0 mg per dl. Thrice weekly hemodialysis was begun and continued for two weeks. On the 13th day, the serum calcium level rose to 12.9 mg per dl and, therefore, saline infusion and intravenous administration of furosemide were begun. The serum calcium value was normal six days later. Six weeks after the patient's admission, the serum creatinine level was 1.2 mg per dl.

Discussion

In the first patient, urinary abnormalities and rise in serum creatinine were first observed 24 hours after smoking phencyclidine. The second patient had severe renal failure by the time we saw him three days after he used the drug. The development of renal failure in these two patients in close temporal relationship to phencyclidine exposure suggests a causal relationship. We suspected myoglobinuria to be the cause of renal failure in our patients because neither was in shock and urine specimens from both contained pigmented granular casts and were toluidine-positive but free of significant hematuria. Our diagnoses were confirmed by the finding of elevated serum creatine phosphokinase and other muscle enzymes, and of myoglobin in specimens of urine.

The myoglobinuria was presumed to be secondary to acute rhabdomyolysis although muscle biopsies were not done in either of the patients. This result could have been due to a direct toxic effect of phencyclidine on the skeletal muscle or of excessive involuntary muscle activity. In the absence of any evidence for the former, we favor the latter inference. A remote possibility is that myoglobinuria was caused by a reaction to some component drug contained in the phencyclidine used by our patients, although none was detected by analysis of urine. Neither of our patients had a history of alcohol abuse and alcohol was not detected in urine specimens; therefore, acute alcoholic rhabdomyolysis was unlikely to have been the cause of myoglobinuria.

The mechanism leading to rhabdomyolysis and myoglobinuria in our patients is unclear. In both our patients, violent involuntary muscle activities necessitated the use of physical and mechanical restraints. Therefore, dystonic muscle activity was accompanied by isometric muscle contractions. This observation in patients may be relevant when considered in the light of the experimental observations of Kuncl and Meltzer on the effect of phencyclidine in rats. They noted that injection
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of phencyclidine in rats produced severely exaggerated locomotor activity. Pronounced rise in serum creatine phosphokinase was observed when phencyclidine-treated animals were restrained in cages. The serum enzyme level correlated with isometric muscle tension that developed when the animal was under restraints. Nonspecific myopathic changes consisting of scattered necrosis of muscle fibers and myofibrillar disruption were seen. These muscle changes did not occur when phencyclidine-treated animals similarly restrained had the motor nerve to the biopsied muscle area cut before the injection of the drug. Similarly, rhabdomyolysis did not occur in the restrained untreated, or in the unrestrained phencyclidine-treated animals. In support of these observations, Cogen and co-workers have described a dramatic fall in the serum muscle creatine phosphokinase from a level of 40,000 to 9,000 units within 24 hours in a patient with phencyclidine toxicity in whom intentional peripheral motor nerve paralysis was induced with pancuronium. These findings suggest that in phencyclidine toxicity, rhabdomyolysis may be a consequence of vigorous muscle activity against restraint.

In our second patient, renal failure was initially treated with peritoneal dialysis. However, after 40 exchanges, there was remarkably little change in the serum creatinine concentration while the BUN actually rose. Subsequently, intensive hemodialysis was required to control the uremia. Nolph and associates have described a similar experience in patients in whom acute renal failure develops in connection with heat stress and exercise, where the mechanism of renal failure is presumably identical. Therefore, in severe cases, the course of acute renal failure may resemble that in traumatic cases, and may require repeated hemodialysis. Nonetheless, complete recovery of renal function ensued in both our patients, an observation that agrees with the generally good prognosis reported by others in cases of renal failure associated with nontraumatic rhabdomyolysis and myoglobinuria.

Transient hypercalcemia which complicates the recovery phase of myoglobinuric renal failure in approximately 20 percent to 25 percent of cases did occur in our second patient. Meroney and associates have shown in experiments with animals that acute renal failure facilitates calcium deposition in necrotic muscles. While the calcium content of traumatized muscles in dogs with intact kidneys doubled within six hours of injury, this increase was greater than tenfold after nephrectomy. These changes were not seen in the nontraumatized muscles. Clinically, radiologic and biochemical evidence of calcification involving the affected muscles has been reported in some patients during the oliguric phase of myoglobinuric renal failure. More recently, using the more sensitive technetium-99-diphosphonate scan, Akmal and co-workers were able to detect the presence of calcium deposits in the muscles of all four patients seen with acute renal failure associated with nontraumatic rhabdomyolysis. It has been suggested that hypercalcemia that is seen in some cases during the recovery phase of myoglobinuric acute renal failure may be a consequence of remodelization of these calcium deposits from the damaged muscles into the extracellular space. There is evidence that the appearance of hypercalcemia may be related to the degree and severity of muscle damage and, therefore, the amount of calcium deposited in the injured tissues.

We have been unable to find any report of frank renal failure associated with phencyclidine toxicity in the English language literature. However, in a recent article in French, Dandavino and associates described the development of acute renal failure in an agitated, comatose patient suffering from phencyclidine toxicity. In this patient muscle enzyme values were elevated but a biopsy study of muscle showed no abnormalities. The renal failure was ascribed to a vasculitis and was treated with corticosteroids. It is possible that in their patient, as in ours, there was unrecognized myoglobinuric acute renal failure.

Use of phencyclidine as an illicit drug is becoming a serious problem. Cogen and associates were the first to describe the occurrence of myoglobinuria in association with phencyclidine toxicity. To our knowledge, the two cases reported in our paper are the first in which myoglobinuric acute renal failure developed during the course of phencyclidine abuse. It is necessary that these potentially life-threatening complications of this drug when taken in excess be publicized. Physicians treating such cases should look for the development of myoglobinuria and acute renal failure in their patients.

Summary

Two cases of myoglobinuric acute renal failure associated with phencyclidine abuse are described. Phencyclidine intoxication should be included.
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among the growing list of causes of nontraumatic rhabdomyolysis and myoglobinuria.

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Parenteral administration of antibiotics and appropriate surgical therapy. The literature also is reviewed.

Report of a Case

The patient, a 70-year-old white man, had been treated uneventfully for diabetes mellitus with chlorpropamide for four years. One week before admittance to hospital, the patient presented to a general medical clinic with pain in both ears. Treatment was begun with local administration of drops (polymyxin B, bacitracin, neomycin, hydrocortisone) and orally given phenoxyethyl penicillin for bilateral external otitis. The pain in the right ear resolved but a painful purulent discharge continued from the left ear. Despitewick packings and topical therapy with antibiotics (colistin, neomycin, thonzoniumbromide, hydrocortisone), the condition progressed to ulceration of the floor of the left external canal. This condition was accompanied by a small polypoid mass with the gross appearance of granulation tissue. Pure cultures of Pseudomonas aeruginosa were obtained twice. A biopsy specimen of the polypoid mass showed granulation tissue with no evidence of malignancy. Because of the unresponsiveness of the lesion to treatment, the culture results and the history of diabetes, the patient was admitted to hospital with a diagnosis of malignant Pseudomonas otitis externa so that parenteral administration of antibiotics could begin.

On admission an ulcer was noted on the floor of the canal of the left ear at the juncture of the membranous and cartilaginous portions and there was purulent discharge and pronounced tenderness over the mastoid. An audiogram documented a mild, left sensorineural hearing loss at 2,000 to 8,000 Hz. Findings on x-ray studies of the mastoid showed slight clouding. Probing of the ear dis-

Malignant Pseudomonas External Otitis

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MALIGNANT PSEUDOMONAS EXTERNAL OTITIS is a severe, necrotizing, external ear canal infection most often occurring in elderly persons with diabetes mellitus. It is accompanied by high complication and mortality rates. Early diagnosis and therapy can circumvent the complications of cranial nerve palsies, osteomyelitis of the skull, meningitis, parotitis, vascular thrombosis, septicaemia and death. A primary care physician usually first sees a patient with the disease but, because of few descriptions of the disorder in the general medical literature, he may not be completely familiar with the presentation and complications. Therefore, we report the case of a patient who was cured without complications by

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