Carbon monoxide poisoning and nonoliguric acute renal failure

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Carbon monoxide poisoning in a 37-year-old man was complicated by neurologic damage, skin changes, muscle necrosis and nonoliguric renal failure. The relation between nontraumatic rhabdomyolysis and acute renal failure in carbon monoxide poisoning is reviewed. Recognition of the acute renal failure in such cases is important, for this complication can be fatal; the prognosis is excellent, however, if proper medical management is provided.

Chez un homme de 37 ans un empoisonnement au monoxyde de carbone s'est compliqué de dommages neurologiques, de modifications de la peau, de nécrose musculaire et d'insuffisance rénale sans oligurie. On étudie le rapport entre la rhabdomyolyse non traumatique et l'insuffisance rénale aiguë dans l'empoisonnement au monoxyde de carbone. Dans ces cas la reconnaissance de l'insuffisance rénale aiguë est importante car cette complication peut être fatale; le pronostic est néanmoins excellent si un traitement médical adéquat est assuré.

There have recently been a number of reports of acute renal failure resulting from nontraumatic rhabdomyolysis.[1,2] Unlike acute renal failure due to other causes, that arising from rhabdomyolysis appears to have an excellent prognosis. Most reported cases have been associated with drug overdose, myopathy, grand mal seizures or strenuous exercise. Acute renal failure complicating carbon monoxide poisoning has been described, but in most of the reported cases oliguria has developed.[3-6] We present a case of carbon monoxide poisoning resulting in skeletal muscle necrosis and nonoliguric acute renal failure, and discuss the implications of these complications in the management of patients poisoned with carbon monoxide.

Case report

A 37-year-old man drank approximately 2 L of beer and a third of a litre of whisky, then drove his car about 50 km out of the city, closed all the windows, and ran a rubber hose from the exhaust pipe into the left front window. He awoke some time later to find that the hose had fallen out (therefore the duration of exposure to exhaust fumes was unknown); when he tried to get out of the car he felt very weak. He then drove back to the city and presented at our hospital with numbness and weakness of the right arm and weakness of the right leg. There was no headache, visual disturbance, vertigo or dysphasia. His past medical history included surgical removal of a herniated lumbar disc 8 years previously and medical treatment of a duodenal ulcer.

The man was afebrile, the cranial nerves were normal and no nuchal rigidity was detected. There was slight tenderness and swelling of the entire right arm, and a reddish-purple petechial rash extended along the dorsal and volar surfaces of the right forearm; it was most pronounced over the areas of muscle tenderness. The right arm and leg were extremely weak and areflexic. No fasciculations were present. Plantar reflexes were normal bilaterally. Sensation of light touch and pinprick was decreased on the right side of the body.

Over the next 3 days the flexor and extensor compartments of the right arm swelled greatly and the patient experienced a steady severe frontal headache and steady midabdominal pain. Sensation of pinprick was decreased on the dorsum of the right foot and right hand, and he complained of numbness in the fingers of the left hand. On the third hospital day severe abdominal pain and vomiting occurred. Nasogastric suction and meperidine injections relieved the symptoms. Because of elevated serum potassium concentrations a cation exchange resin (sodium polystyrene sulfonate; Kayexalate) was given in an enema twice during the next 2 days. By the seventh hospital day the swelling of the right arm was decreasing, the skin was brawny, the abdominal symptoms had subsided, and the patient was ambulatory with assistance. The output of urine had remained high (Fig. 1).

Both the creatine phosphokinase and the creatinine concentrations in the serum were elevated during the patient's stay in hospital (Fig. 2). Fractionation showed the creatine phosphokinase to

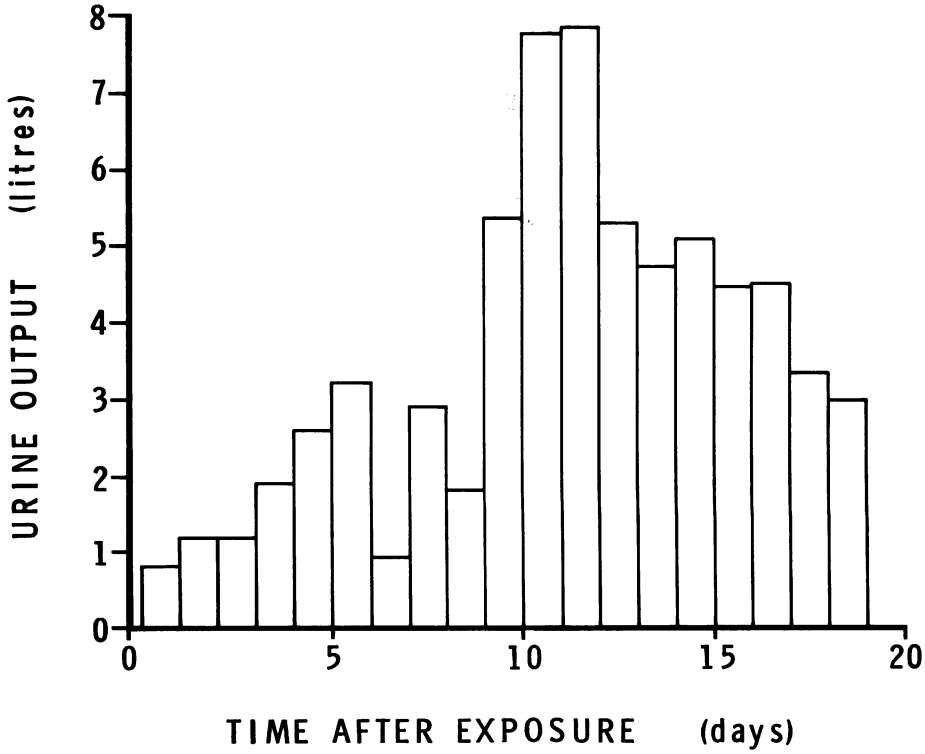

FIG. 1—Urine output during first 18 days of hospitalization of man with carbon monoxide poisoning.

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be primarily of skeletal muscle origin. The serum potassium concentration reached a peak of 6.5 mmol/L on the third hospital day. Although a test for hemoglobin in the urine (Hematest) gave a positive result no erythrocytes were seen. Two or three pigmented granular casts per high-power field were noted in the urine at the time of admission but tests for urinary myoglobin were reported to be negative. Serial electrocardiograms indicated minor, nondiagnostic T-wave changes.

Ten days after admission the patient's urine output increased; it remained elevated for 8 days. Within approximately 3 weeks after admission his muscle strength had returned with the aid of physiotherapy. He was subsequently transferred to a psychiatric treatment centre.

Discussion

Mechanism of carbon monoxide poisoning

Carbon monoxide is produced from the incomplete combustion of organic material. It is found in automobile exhaust, tobacco smoke and exhaust from fuel combustion in industry and the home. In addition, it has been reported to be generated metabolically during the use of paint stripper containing methylene chloride.[7]

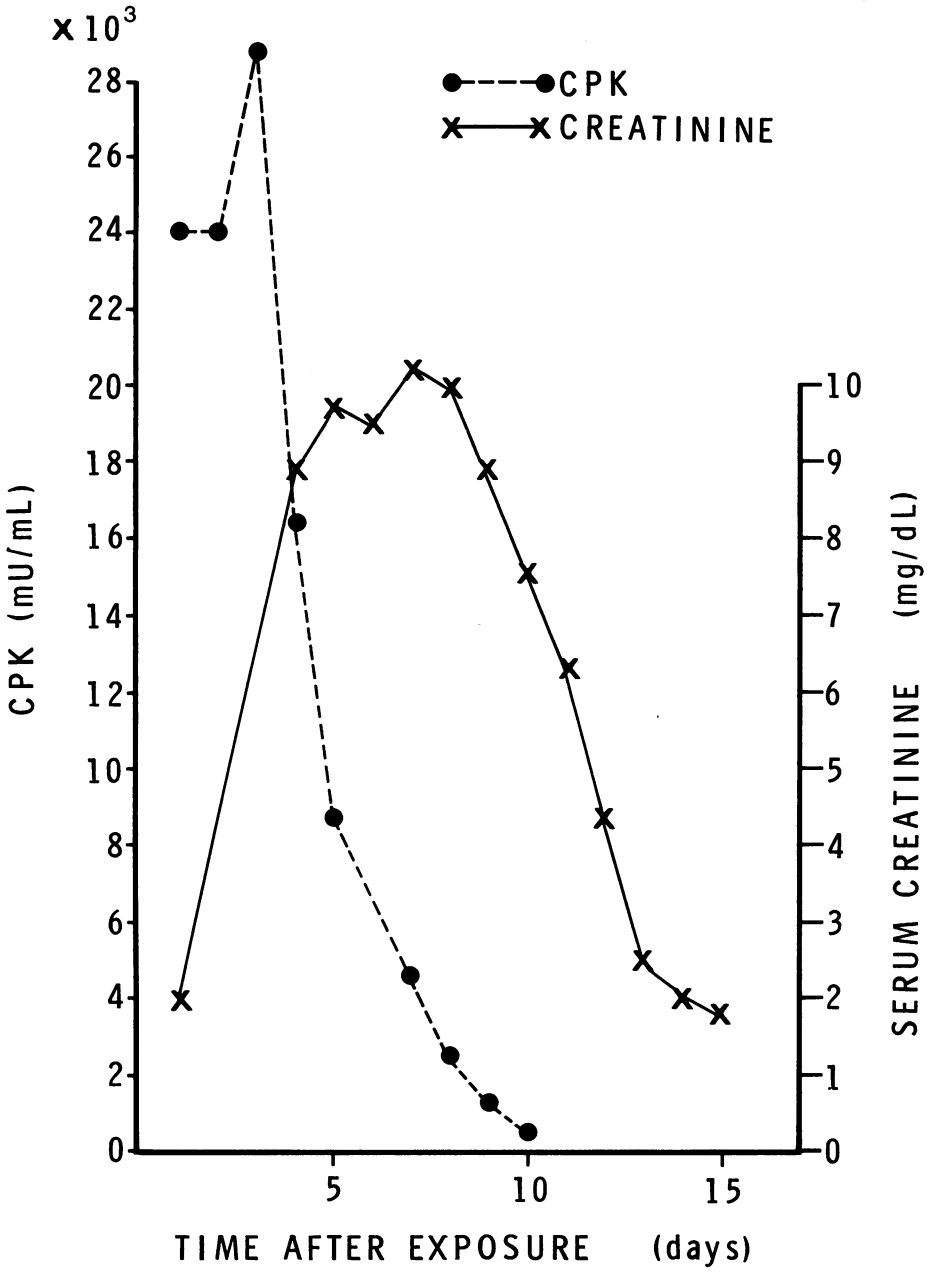

FIG. 2—Serial measurements of creatine phosphokinase (CPK) and creatinine concentrations in the serum after exposure to carbon monoxide.

The toxic effects of carbon monoxide (Table I) are based entirely on its combination with hemoglobin (one to four molecules of carbon monoxide combine with one of hemoglobin), with resulting displacement of oxygen and consequent disruption of the oxygen transport system. Carbon monoxide effectively competes with oxygen for binding sites on the hemoglobin molecule, having an affinity for hemoglobin 200 to 300 times greater than that of oxygen. Not only is carboxyhemoglobin without practical function as a carrier of oxygen, but also its presence shifts the oxyhemoglobin dissociation curve to the left. As a result, tissue oxygen tensions must fall to much lower levels than normal before the oxyhemoglobin can give up its oxygen. This results in a greater tissue oxygen deficiency than would be produced by an equivalent reduction in arterial oxygen tension or in hemoglobin concentration secondary to anemia.[8]

Carbon monoxide is rapidly absorbed through the lungs and most is eliminated unchanged by the same route; less than 1% is oxidized within the body to carbon dioxide. The biologic half-life of carbon monoxide in the healthy sedentary adult is 4 to 5 hours.[7] Oxygen administration hastens the elimination of carbon monoxide and therefore shortens the half-life.

Neurologic damage

Because the central nervous system is extremely sensitive to lack of oxygen, symptoms referable to this system are one of the most frequent and variable manifestations of carbon monoxide poisoning. Symptoms can include throbbing headache, excitability, confusion, dizziness, visual

Table I—Clinical features of acute carbon monoxide poisoning

Mental changes
Headaches
Convulsions
Coma
Sensory and motor paralysis
Respiratory paralysis
Cherry-red colour
Skin lesions
Nausea
Rhabdomyolysis
Myocardial damage
Albuminuria
Glycosuria
Renal failure
Fever

disturbances, nausea, vomiting, fainting, convulsions, coma, respiratory failure and death.[9]

We did not measure carboxyhemoglobin concentrations in the blood, nor did we know the duration of exposure to the gas. By the time the patient arrived at hospital his right arm and leg were weak and numb, and the weakness progressed over the next 3 days; muscle strength returned within the next 3 weeks with the aid of physiotherapy. His headache, nausea and vomiting were of shorter duration.

In general, neurologic damage resolves completely, as in our case, but with profound anoxia there may be persistent neurologic deficits such as impaired memory, vision, hearing or speech; tremors; mental deterioration; or psychotic behaviour. Demyelination of the white matter is frequently found in persons dying after several weeks. The histologic changes are typical of anoxia or ischemia — focal or laminar necrosis of the second and third cortical layers and often of the superficial white matter.[10]

Muscle necrosis and skin lesions

The association of muscle necrosis with carbon monoxide poisoning has been reported previously.[3,4,11,12] Pressure necrosis of the muscles occurs with immobilization and is probably enhanced by the impairment in oxygen delivery due to the accumulation of carboxyhemoglobin.

Our patient had early motor and sensory impairment of the right arm and leg; severe muscular swelling and pain of the right arm 3 days after exposure to carbon monoxide necessitated frequent injections of analgesic. Creatine phosphokinase concentrations in the serum were elevated even at the time of admission and reached a peak of 28 000 mU/mL (normal range 5 to 35 mU/mL) on the third hospital day (Fig. 1); fractionation showed the isoenzymes to be primarily of skeletal muscle origin. With symptomatic treatment the patient's arm returned to normal in 2 weeks.

Cardiac muscle in this case appeared to be less sensitive than skeletal muscle to the carboxyhemoglobin-induced anoxia since only mild changes were noted on serial electrocardiograms.

A muscle biopsy was not obtained. However, Adams[13] has reported that in the early phase of carbon monoxide intoxication skeletal muscle is yellow-brown or grey. A variety of degenerative changes in the muscle fibres, including necrosis and calcification, are evident microscopically after a few days. The onset of muscle damage has varied from the moment the patient regains consciousness to 10 weeks after the poisoning.

Leavell, Farley and McIntyre[14] described the skin manifestations in one patient: necrosis of the sweat glands, leukonychia, intraepidermal and subepidermal vesicles, intracellular edema, and occlusion of the epidermal portion of the sweat ducts. All these lesions were presumably due to inadequate oxygen supply to the skin.

At the time of admission our patient's skin was not the classical cherry-red; the skin of his arms was reddish-purple, mainly over the areas of muscle tenderness, and in the next few days it became brawny. He had no blisters or necrosis and his body temperature remained normal, so it is unlikely he had generalized necrosis of the sweat glands.

Acute renal failure

There are only a few cases in the literature of acute renal failure complicating carbon monoxide poisoning;[3-6] when urine output was documented, oliguria was often one of the early manifestations.

Our patient's initial renal function was within normal limits, though pigmented casts were detected in the urine. However, within 4 days the serum creatinine concentration had climbed to 10.4 mg/dL. On the third and fourth hospital days marked hyperkalemia necessitated the use of a cation exchange resin administered in an enema. At no time was oliguria recorded.

The occurrence of acute renal failure in cases of carbon monoxide poisoning is thought to be secondary to nontraumatic rhabdomyolysis. The correct diagnosis can be made from the detection of myoglobin in the urine, but myoglobinuria is an early and transient finding and may be absent by the time the acute renal failure is evident. In our case analysis of the urine for myoglobin gave negative results, but the diagnostic triad for myoglobinuria established by Grossman and colleagues[1] was fulfilled: the urine reacted strongly with orthotolidine (Hematest), thus indicating the presence of hemoglobin, the urine sediment contained pigmented granular casts and the serum creatine phosphokinase concentrations were greatly elevated.

Our patient had biochemical abnormalities similar to those in cases of nontraumatic rhabdomyolysis described by Grossman and associates[1] and by Koffler, Friedler and Massry.[2] The abnormalities tend to be more pronounced in such cases than in cases of acute renal failure due to other causes, possibly because of the hypercatabolism of rhabdomyolysis, with hyperkalemia, hyperphosphatemia, hypocalcemia, metabolic acidosis and hyperuricemia present singly or in combination. There are striking elevations in the creatine phosphokinase and the aldolase concentrations of the blood, and the serum creatinine concentration increases daily by more than 2.5 mg/dL. In persons with severe and extensive muscle damage hypercalcemia may develop during diuresis, a finding attributed to transitory hyperparathyroidism.[15]

The asymptomatic hypocalcemia in our patient was probably due to a combination of hyperphosphatemia and skeletal resistance to the calcemic action of parathyroid hormone, as has been described in persons with acute renal failure.[15] Our patient did not experience the transient hypercalcemia of the recovery phase described by Grossman and Koffler and their colleagues.[1,2]

Another explanation for the occurrence of acute renal failure in persons with carbon monoxide poisoning may be that carbon monoxide has a direct anoxic effect on the renal tubular cells, but so far there has been no report of acute renal failure in persons with carbon monoxide poisoning without muscle necrosis. Our patient did not require dialysis, in contrast to the subjects of other case reports,[7,14] for his urinary output remained adequate.

Conclusions

Acute renal failure is a serious complication of carbon monoxide poisoning, for rapid deterioration in renal function associated with hypercatabolism can be fatal. Serum electrolyte concentrations should be measured twice daily, and if rapid

deterioration in renal function occurs dialysis should be instituted. Properly managed, nonoliguric acute renal failure secondary to nontraumatic rhabdomyolysis has a favourable prognosis,[1,2,16] as our case report has illustrated.

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