CASE REPORT

Perchloroethylene (PCE; Cl₂C=CCl₂) is an unsaturated chlorinated hydrocarbon in the form of a colorless, volatile liquid that is used extensively as an industrial organic solvent for metal degreasing and for dry cleaning. Although chronic PCE intoxication by inhalation has been relatively well documented, severe acute PCE poisoning by ingestion is reported rarely. Excessive absorption of PCE can produce depression of the central nervous system and hepatic and renal damage. Investigations into its effects on renal function are very limited. Although recent studies have found nephrotoxicity and renal tumors in male rats gavaged with PCE, Lauwerys et al did not find any adverse effects of PCE on the kidneys of workers exposed to PCE. The adverse effects of PCE on renal structure and function remain controversial, so detailed renal histomorphometric analysis and functional studies are required to further characterize the structural changes induced by PCE.

In this report, we describe a patient with acute renal failure requiring hemodialysis after a large quantity of PCE was ingested accidentally. We performed a renal biopsy to assess the clinicopathologic relationship between overexposure to PCE and renal injury. To the best of our knowledge, this is the first report in which we can observe the patient's renal biopsy findings in a patient with acute PCE poisoning.

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ysis values were as follows: pressure, 260 mm HgO; white blood cells, 132/μL (85% polymorphonuclear cells, 10% lymphocytes); protein, 2.45 g/dL (24.5 g/L); and glucose, 72 mg/dL (40 mmol/L). At the local clinic the case was initially misdiagnosed as acute viral meningitis, as a result of insufficient history assessment because of his semicomatose state as well as his cerebrospinal findings. After verbal communication became possible, it was discovered that he had accidentally ingested PCE, and he was transferred to our hospital for the treatment of PCE intoxication and oliguric acute renal failure on the third day after PCE ingestion.

On admission at our hospital he was disoriented, confused, and oliguric (with a urine volume of 390 mL/h). His vital signs were blood pressure, 120/80 mm Hg; pulse, 59 beats per minute; respiration rate, 28 breaths per minute; and temperature, 37°C. The results of physical and neurologic examinations were unremarkable. There was a chloriform-like odor on his breath. Laboratory analysis found the following: white blood cell count, 8,800/μL (8.8 × 10⁹/L); hemoglobin, 16.6 g/dL (166 g/L); hematocrit, 51%; platelets, 442,000/μL (4.42 × 10⁹/L); sodium, 148 mEq/L; potassium, 7.0 mEq/L; chloride, 120 mEq/L (6.246 mmol/L); magnesium, 5.0 mg/dL (2.1 mmol/L); blood urea nitrogen, 81.9 mg/dL (29.2 mmol/L); creatinine, 8.4 mg/dL (742.6 μmol/L); albumin, 3.3 g/dL (33 g/L); total bilirubin, 1.4 mg/dL (23.9 μmol/L); aspartate aminotransferase, 49 U/L; alanine aminotransferase, 28 U/L; prothrombin time, 12.6 seconds; activated partial thromboplastin time, 37.8 seconds; lactate dehydrogenase, 629 U/L; osmolality, 318 mOsm/kg; and osmolar gap, 16 mOsm/kg. Arterial-blood gas analysis values were as follows: pH, 7.397; PaCO₂, 27.7 mm Hg; PaO₂, 106.9 mm Hg; HCO₃, 16.7 mEq/L; base excess, –8.2 mEq/L; O₂ saturation, 97.1%; and anion gap, 11.3 mEq/L.

The amounts of PCE in the blood and urine were not measured. Urine analysis with microscopic examination showed pH, 5.0; specific gravity of 1.010; trace protein, many per high-power field of red blood cells and 20 to 30 per high-power field of white blood cells. A 24-hour urine analysis on the fourth day after ingestion found protein at 102 mg/dL and calcium at 94 mEq/d (23.5 mmol/d). A follow-up analysis showed protein at 90 mg/dL and calcium at 115 mEq/d (28.8 mmol/d). Electrocardiography showed sinus bradycardia (56 beats per min).

Hemodialysis was performed on the day of admission to our hospital (ie, the fourth day after ingestion of PCE), and on the fifth, sixth, eighth, and tenth day after ingestion of PCE. Renal function, as assessed by creatinine clearance by an analysis of urine over 24 hours, gradually recovered during 5 sequential hemodialyses (Fig 1). On the sixth day after ingestion, a follow-up cerebrospinal fluid analysis produced normal findings, and the mental state was completely alert. On the eighth day after ingestion, electron microscopy. The patient had complete recovery of renal function and mental state after 5 hemodialyses and conservative treatment, and his renal function remained normal throughout the 4-month follow-up period after the ingestion of PCE.

**DISCUSSION**

PCE accumulates mainly in the brain and adipose tissue because of its high lipophilicity. High concentrations of the parent compound and metabolites are also found in the liver and kidneys, with lower levels in the heart, lungs, and adrenals. Most of the absorbed compound is eliminated by excretion via the lungs. A minor fraction is metabolized to trichloroacetic acid and trichloroethanol, conjugated with glucuronic acid, and then excreted in the urine.

The common clinical feature of acute PCE overexposure is initial central nervous system depression followed by cardiac dysrhythmias or sudden death, transient hepatic dysfunction, and occasionally renal injury. Acute or subacute PCE poisoning by inhalation has been observed frequently in dry cleaners. After acute inhalation, central nervous system disturbances develop rapidly and are followed by rapid recovery. The
The initial stages of PCE intoxication are similar to those of acute alcohol intoxication, with an early excitatory phase during which patients may experience euphoria, incoordination, a feeling of invulnerability and disinhibition; they also may have a staggering gait. The excitatory phase is followed by central nervous system depression, resulting in stupor, coma (possibly associated with seizures), respiratory depression, and death in severe exposure. The majority of cases of PCE intoxication have been the result of accidental or careless use in dry cleaning establishments. Acute PCE poisoning by ingestion has been reported rarely. Koppel et al described a case of massive poisoning in a 6-year-old boy who drank 12 to 16 g of PCE; 1 hour later he was comatose with a blood PCE concentration of 21.5 mg/L. Hyperventilation therapy and supportive measures allowed a complete recovery within 48 hours. Our patient was discovered in a semicomatose state 5 hours after the ingestion of 75 g of PCE and became completely alert after 6 days of hemodialysis and conservative treatment. His cerebrospinal fluid pressure and polymorphonuclear leukocyte concentration increased, but the follow-up study performed on the sixth day after ingestion found both values to be within normal ranges. The mechanism responsible for the abnormal cerebrospinal finding could not be determined, but we speculate that it was related to direct toxicity of the PCE or its metabolites in the brain.

PCE poisoning patients can experience marked central nervous system depression followed by transient, minimal liver injury. Our patient had normal liver function despite being in a semicoma state as did another case involving a 6-year-old boy who had massive poisoning after ingestion of 12 to 16 g of PCE. We assumed that our result, which is uncommon in animal studies of inhalation intoxication, was caused by differences in absorptivity and toxicokinetics between inhalation and ingestion in humans. Also, these results suggest that the relation between hepatic damage and intensity of exposure, particularly by ingestion, may be related to the renal toxicity of PCE.

The cardiac effects of PCE have been investigated much less than its adverse renal, hepatic, and central nervous system effects. PCE sensitizes the myocardium to the arrhythmogenic effects of catecholamines, which may lead to life-threatening dysrhythmias when catecholamine release is augmented by the euphoria or excitement associated with the early central nervous system effects of PCE or by physical activity. In general, tachyarrhythmias are more common than bradyarrhythmias in the context of PCE intoxication. Although rare, bradycardia has been seen in an animal study. We assumed that bradycardia was exhibited because of blocked impulse transmission caused by the variability of response of individual cells and the complex way in which myocardial electrical impulses are propagated. Our patient’s heart rate showed a tendency to decrease, and he had marked sinus bradycardia (46 beats per minute) without hypotension on the eighth day after ingestion, although it spontane-
ously converted to normal sinus rhythm (88 beats per minute) thereafter.

So far, limited information has been available regarding the effects of PCE on renal structure and function. A recent study reported that 50 dry cleaning workers who were exposed to low levels of PCE over a 10-year period exhibited renal toxicity. In the current study, many urinary and serum markers were measured and compared with unexposed controls for renal tubular and glomerular injury. We found increased release of laminin fragments, fibronectin, and high-molecular-weight proteins resulting from generalized membrane disturbances and increased release of brush-border antigens and Tamm-Horsfall glycoprotein resulting from the shedding of epithelial membrane components from tubular cells at a different location along the nephron. These findings indicate PCE-induced early renal damage, which would need to be monitored for the possible development of chronic renal disease. The lack of association between renal damage or dysfunction and intensity or duration of exposure was consistent with other studies on solvent-exposed workers. A small number of animal and human studies suggest that PCE induces different types of kidney damage. The cytochrome P450 pathway generates tri- and dichloroacetate as metabolites of PCE, and these are associated with renal toxicity and carcinogenicity as well as hepatic toxicity and carcinogenicity. Goldsworthy et al. found nephrotoxicity and renal tumors in male rats gavaged with PCE. Acute renal failure by PCE poisoning probably is a consequence of the shock induced by the collapse of peripheral vessels secondary to central nervous system depression as well as being caused by direct tubular toxicity. Mild renal dysfunction generally returns to normal within days to weeks with appropriate supportive care. Our patient showed severe metabolic acidosis with an increased anion gap and mild azotemia only 5 hours after PCE ingestion. Renal dysfunction with oliguria rapidly progressed, and hemodialysis was performed initially on the fourth day after ingestion. During hemodialyses, the serum creatinine level decreased gradually as urine output increased and reached the normal range (1.3 mg/dL) on the 18th day. Metabolic acidosis also recovered completely.

Green et al undertook renal histology in an animal study and reported that kidney weight was increased, and renal tubules were dilated with proteinaceous materials and cellular debris. In our patient, tubular epithelial cells showed focal marked breakdown with aggregates of rhomboid or triangular crystals in tubular lumens. We used von Kossa stain to show that the crystal deposits were composed mainly of calcium. Our patient did not have hypercalciuria or hypercalcemia, and we could not determine an association between these calcium deposits and PCE toxicity.

The diagnosis of PCE poisoning usually is suggested by the history and supported by the chloroformlike odor of the solvent on the patient’s breath. Quantitative analyses of the PCE concentrations determined by gas chromatographic techniques in serum or urine can be used to confirm an acute exposure. We did not check the blood or urine PCE concentrations of the patient, because the rapid elimination of PCE reduces the correlation between these concentrations and clinical toxicity long after PCE exposure.

Treatment of PCE intoxication consists primarily of supportive care and symptom management. There is no specific antidote for PCE. The patient presenting with respiratory arrest, respiratory depression, or oropharyngeal burns with edema may necessitate aggressive airway management with endotracheal intubation. Severe hypotension may be induced by a combination of central nervous system depression and myocardial anoxia secondary to poor oxygen uptake. Hemodialysis may be indicated for renal failure.

REFERENCES


