

Laryngeal Edema, Rhabdomyolysis and Acute Renal Failure Following Ingestion of “Black Rock”

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Para-phenylenediamine is an organic compound producing a natural color that does not fade readily with washing. It therefore serves as a common ingredient in hair dye and temporary tattoo ink (black henna). The black henna can be purchased as a commercial product in stores, mainly in India but also available in many local markets as “black rock” or powder. Following numerous reports of contact dermatitis and even systemic toxicity from skin exposure, the U.S. Food and Drug Administration approved its use only for hair dye and not for direct application on the skin.

Systemic toxicity from the ingestion of PPD, either intentional or accidental, is frequently reported in India and North Africa but is less common in the developed world [1,2]. Systemic intoxication commonly presents as angioedema, rhabdomyolysis and acute renal failure, with high rates of mortality [1-4]. The medical community must be aware of the potential toxicity of this substance and of the clinical signs of intoxication in order to provide the appropriate medical treatment. We present a case of accidental PPD ingestion and discuss the clinical presentation and treatment approach.

PATIENT DESCRIPTION

A 60 year old woman with a history of diabetes and hypertension presented to the emergency room complaining of dyspnea,

neck edema, blurred vision and weakness, immediately after ingesting “black rock” powder containing unknown ingredients. There was no history of excessive physical activity, febrile illness, muscle trauma or convulsions.

On arrival, she was alert with no signs of dyspnea and stridor. Oxygen saturation was 96% while breathing ambient air. Blood pressure was 176/92 mmHg and pulse 120 beats per minute. While in the emergency room the patient rapidly developed severe dyspnea, agitation and laryngeal angioedema. Otolaryngologic evaluation revealed tongue, pharynx and epiglottis angioedema with airway obstruction. The patient was transferred immediately to the operating room for intubation with an otolaryngology team ready for emergency tracheotomy. Assuming it was an allergic reaction, the medical team administered intramuscular adrenalin, steroids and antihistamine.

After initial treatment in the emergency room the patient was admitted to the intensive care unit. Twelve hours later her urinary output decreased but she remained hemodynamically stable; creatinine rose to 5 mg/dl on the fourth day after admission. Urinary microscopy revealed a few granular casts and red blood cells, which ruled out acute tubular necrosis or glomerular disease.

Laboratory results showed metabolic acidosis with normal anion gap, leukocytosis without eosinophilia, normal hemoglobin and platelet count and normal coagulation. Chemistry analysis showed elevated hepatocellular enzymes: 2167 U/L aspartate aminotransferase and 562U/L alanine aspartate aminotransferase. Creatinine kinase levels rose to 78,250 U/L and myoglobin to 106,117 ng/ml.

The patient was treated with hemodialysis and correction of her acid base and electrolyte disorders. Three days after her

admission she was extubated, and a week later renal function returned with normal creatinine and urinary output.

On the day of her admission the medical team learned from the patient’s family that the substance she had ingested was “black rock” [Figure], but its exact components were not known. Further questioning revealed that the patient routinely took a natural medication called “*sabra mor*” (Hebrew for an *Aloe vera* derivative) for the treatment of hyperglycemia. An online search regarding ingestion of this agent did not show similar adverse effects. An investigation in the local market where it was purchased revealed another substance with a similar appearance and called “black henna,” which is used for hair dye and temporary tattoo ink. The main ingredient of this substance is PPD, which is known to cause renal failure, rhabdomyolysis and angioedema following ingestion – the same presentation as the case described [1-4]. A toxicological investigation of the substance ingested by the patient confirmed our suspicion of PPD toxicity.



Black henna is available in local markets as hair dye containing PPD

PPD = para-phenylenediamine

COMMENT

PPD is an aromatic amine used as a chemical ingredient in hair dye and temporary tattoo ink as well as for fabrics, fur and dark makeup. PPD is also used in printing and photocopying inks, rubber products, oil, gasoline and grease products. Its use as black henna for hair dye and temporary tattoo ink is especially common in India and North Africa. Black henna, which looks like a black powder or a rock, can easily be mistaken for other substances such as *sabra mor* in our case.

Sabra mor, an aloe vera derivative, is used as a natural medication for the treatment of hyperglycemia and as a laxative if ingested in powder form. This natural plant is considered to be safe when ingested, although it has several side effects: diarrhea, abdominal pain and hypokalemia secondary to the laxative effect. Prolonged use can cause worsening of constipation after the treatment is stopped.

The clinical presentation of PPD poisoning resembles the case described here, with angioedema, rhabdomyolysis and acute renal failure developing sometimes prior to muscle injury, with high rates of mortality [1,3]. The toxicity is dose dependent with a lethal dose estimated at 7–10 g [5]. A study by Kallel et al. [4] of 19 patients with PPD intoxication in Tunisia over a 6 year period showed clinical symptoms of cervical-facial edema (79%), chocolate-brown colored urine (74%), upper airway tract edema (68.4%), oliguria (36.8%), muscular edema (26.3%), and shock (26.3%). Rhabdomyolysis and metabolic acidosis were seen in all the patients. Acute renal failure occurred in 47.4% and hyperkalemia in 26.3% [4].

The presentation of angioedema is often severe, with orofacial and neck swelling necessitating intubation for airway protection. The mechanism of PPD-induced rhabdomyolysis involves leakage of calcium from smooth endoplasmic reticulum. This results in prolonged contraction and damage to the muscle. The release of intracellular components follows, leading to

electrolyte imbalance [2]. Rhabdomyolysis by itself can cause acute kidney injury; however, direct PPD toxicity to the renal tubules occurs, as demonstrated by histological examination of rats exposed to high levels of topical PPD. The histological findings showed severe damage to the proximal tubule cells, as well as to the vascular bed [5]. Similar results were seen in renal biopsies of 15 patients with acute renal failure secondary to PPD ingestion admitted to a nephrology department in Pakistan. Eight patients had acute tubular necrosis on histological examination and seven had acute interstitial nephritis. The oliguric phase lasted from 1 to 3 weeks, and serum creatinine normalized in 73% of patients [3].

Other factors that contribute to renal impairment are hypovolemia and hemoglobinuria in cases of hemolysis. In the case presented here the toxicity was a result of direct ingestion. Although PPD is a common ingredient in hair dye and temporary tattoo ink, there have been reports of contact dermatitis, asthma and even severe angioedema following such use. Systemic toxicity from topical PPD was demonstrated in a study of rats with the same clinical toxic presentation [5].

The treatment of acute PPD intoxication is mainly supportive. There is no antidote, but a high index of suspicion may warrant an early gastric lavage. In a retrospective study in India of 13 patients suffering from hair dye poisoning after orally ingesting the dye, it was found that a poor prognosis was associated with late presentation to the hospital, when gastric lavage was not performed on admission, in patients with severe angioedema requiring intubation, in patients presenting with low Glasgow Coma Score or seizures, and in patients who required dialysis [1].

Given that systemic PPD intoxication is quite rare in the developed world, presentation of the clinical signs mentioned in this case must raise the suspicion of PPD toxicity. A gastric lavage must be performed as soon as possible to reduce

systemic absorption. When signs of toxicity present, the management is mostly supportive, including intubation, and mechanical ventilation for airway protection in cases of severe angioedema. Early hydration can prevent kidney injury secondary to rhabdomyolysis but not due to direct tubular injury. The fluid composition for repletion has not been established. For patients with acute renal failure, persistent hyperkalemia, fluid overload or severe metabolic acidosis, hemodialysis should be considered. The use of renal replacement therapy is mostly supportive. The toxin itself is not dialyzable [1]. Treatment with steroids and antihistamines are common practice, although their benefit has not been proven by therapeutic trials.

In conclusion, PPD is a common ingredient in hair dye and temporary tattoo ink in the developing world, less so in the developed world. Most of the severe cases of PPD intoxication are the result of toxin ingestion, which presents as angioedema, rhabdomyolysis and acute renal failure. Physicians must be aware of the potential toxicity of this chemical and of the clinical signs of systemic poisoning, since early intervention is crucial for improving prognosis.

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“Life is not about avoiding the storm. It is about learning to dance in the rain”

Anonymous