CASE REPORT

An unusual case of acute kidney injury due to poisoning with blue stone

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KEYWORDS
acute kidney injury; copper sulfate; poisoning

Abstract
Blue stone (neela thotha, in local terms) is dehydrated copper sulfate and is commonly used as a pesticide, in the leather industry, and in homemade glue. It results in a rare form of poisoning limited to the Asian continent, with a high incidence in India and Sri Lanka prior to the 1980s. Poisoning due to copper sulfate results in multiorgan involvement. Here, we present a case of poisoning due to copper sulfate with acute kidney injury and intravascular hemolysis.

Case Report
A 30-year-old woman with a history of psychiatric disorder and suicide attempts was admitted to the emergency room following alleged consumption of 30–40 g neela thotha. She experienced multiple episodes of bluish-green vomiting and there was history of loose bowel movements resulting in bluish-green stool. There was no history of cyanosis or greenish discoloration of the skin. She also experienced breathlessness and anuria. At admission, she was irritable, with a blood pressure of 100/70 mmHg, and the presence of pallor and pedal edema. There was no focal neurological deficit or bluish-green fingertip discoloration. Her hemoglobin was 3.3 gm/dL, total leukocyte count was 47,000/mm³, and platelet count was 68,000/mm³. A peripheral smear indicated teardrop cells, schistocytes, and hypochromic red blood cells (RBCs) suggestive of hemolysis. The lactate dehydrogenase level was 1500 IU/mL. Liver function tests showed total bilirubin of 30.78 μmol/L and direct bilirubin of 8.55 μmol/L. Liver enzymes were normal. Blood urea nitrogen was 32.98 mmol/L and serum creatinine was 795.6 μmol/L. She was started on hemodialysis. Urine analysis showed traces of albumin and bland sediment. Abdomen ultrasound was normal. After 2 weeks, urine output improved to 2 L/d and serum creatinine had decreased to 132.6 μmol/L at the time of discharge.

Discussion
Neela thotha, also known as blue vitriol or blue stone, is dehydrated copper sulfate (CuSO₄·5H₂O). Copper sulfate poisoning has been reported in Asian countries, including India, Bangladesh, and Sri Lanka, with incidence rates of 30–60% from 1960 to 1970 and this decreased to 3% by 1980.¹ A study from India reported 118 cases of copper

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sulfate poisoning in a 4-year period in the 1970s. A 10-year study from Manipal, India, reported 37 cases in 2008. There has been a sharp decline in the number of cases since the 1980s.

A lethal dose of copper is 10 g, with clinical symptoms being severe if consumption is > 30–40 g. Following ingestion, copper (2 mg constitutes the average daily consumption) is absorbed from the gastric mucosa, with absorption enhanced when there is a breach in the mucosa. Copper binds to ceruloplasmin (95%) and albumin (5%). In cases of poisoning, this process is reversed and excess amounts bind to albumin and is deposited in various tissues, with the liver being the major site for copper deposition. If deposition exceeds 50 mg/g of liver tissue, liver necrosis occurs, followed by the release of copper into the serum and rapid uptake by RBCs, resulting in oxidative damage to the cell membrane and hemolysis.

Copper sulfate is a strong oxidizing agent. Mechanisms of copper poisoning include binding to the sulfhydryl group of glutathione and glucose-6-phosphodehydrogenase, resulting in inhibition of free-radical scavenging activity, hemolysis through oxidation of hemoglobin sulfhydryl groups, inhibition of Na-K ATPase activity, which increases cell permeability, and possibly direct damage to skeletal muscle.

Copper is excreted in urine (5%) and stool (25%), with 25% incorporated into ceruloplasmin and excreted in bile and 50% forming a complex with metallothionein, which is excreted in the stool. The remaining 5% constitutes free copper in serum. Total serum copper ranges from 60 μg/dL to 140 μg/dL and free copper ranges from 10 μg/dL to 15 μg/dL. Twenty-four-hour urinary copper ranges from 20 μg/dL to 50 μg/dL. The levels of serum copper do not correlate with the toxicity of symptoms because over a period of time, copper is deposited in tissues, such as brain, liver, and kidney. Hence, estimation of serum copper levels was found to be useful between 17 hours and 7 days of consumption.

Clinical manifestations of copper poisoning include gastrointestinal, hematological, cardiovascular, musculoskeletal, hepatic, renal, and neurological involvement. Gastrointestinal manifestations are bluish-green vomit, corrosive gastropathy, pancreatitis, hepatitis, hematemesis, malena, and, rarely, acute liver necrosis. Hematological manifestations include intravascular hemolysis and methemoglobinemia. Rapid onset of intravascular hemolysis, methemoglobinemia, and onset of cyanosis is also observed. Cardiovascular symptoms include tachycardia, hypotension, and arrhythmias. Musculoskeletal manifestation includes rhabdomyolysis. Renal involvement occurs in 50–60% of cases. Presence of dialysis-dependent acute kidney injury (AKI) may increase the risk of mortality by between 30% and 60%.

AKI can manifest as prerenal azotemia, intrinsic renal injury, or postrenal injury. Prerenal AKI occurs with vomiting and diarrhea, while intrinsic AKI occurs due to severe dehydration, rhabdomyolysis, myoglobinuria, direct deposition of copper in proximal tubules, acute tubular necrosis, sepsis, or due to multiorgan dysfunction. Heme pigment released due to intravascular hemolysis and direct effects of copper on proximal tubules are the predominant mechanisms of AKI. Mehta et al. studied renal biopsies from eight patients, which showed acute tubular necrosis in seven cases and interstitial granuloma in one.

Management includes detoxification, supportive measures, and chelation therapy. Detoxification measures include gastric lavage. While the role of activated charcoal is doubtful, it may be administered as 50 g dissolved in 100 mL water at 6-hour intervals. Repeated gastric lavage is not recommended, as it may enhance incidence of erosive gastropathy. Chelating agents include penicillamine, dimercaprol (British anti-Lewisite), and edetate calcium disodium. Penicillamine may be given in a dose of 3–5 mg/kg every 4 hours and then tapered slowly over 7–10 days. Duration of treatment with chelating agents is unclear, though it may be prudent to continue therapy until serum copper levels normalize. Penicillamine and edetate calcium disodium are contraindicated in renal failure.

Our patient consumed ~50 g blue stone that was being used as glue (mixed with maida). Immediately after consumption, she experienced bluish-green vomit and had intravascular hemolysis and hepatic manifestations intrinsic to AKI. She showed signs of renal recovery, normalization of hemoglobin levels, and stable liver function within 2 weeks and experienced complete renal recovery 4 weeks after admission. We did not use chelation therapy due to severe renal insufficiency. Renal recovery was late, although improvement in other organs occurred early. Our patient did not exhibit features of methemoglobinemia.

The clinical indicators suggesting copper sulfate poisoning include consumption of blue stone, bluish-green vomit, and occurrence of intravascular hemolysis. There are three differential diagnoses for bluish-green vomit in emergency departments: copper sulfate poisoning, boric acid poisoning, and paraquat poisoning.

There are two points of interest in this case: copper sulfate poisoning is associated with high morbidity and multiorgan involvement and copper sulfate usage should be licensed in the community with a caution label explaining toxicities.

Conflicts of interest

The authors declare no conflicts of interest.

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