CASE REPORT

Acute Copper Sulfate Poisoning: Case Report and Review of Literature

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Abstract

Background: Copper sulfate ingestion is a relatively popular method for committing suicide in Indian subcontinent. It causes a high mortality rate, and so a growing concern has been raised to identify the severe alarming signs suggestive of poor prognosis and to improve treatment approaches.
Case report: A 22-year-old unmarried man working as a painter was found unconscious at his friend residence. The patient developed hypotension, hemorrhagic gastroenteritis with hematemesis and melena, renal and hepatic failure, severe metabolic acidosis and intravascular hemolysis during admission at hospital. His signs were refractory to treatment with fluid replacement therapy, vasoactive drugs, antiemetic drugs, ranitidine, furosemide, methylene blue and 2,3 dimercaptopropane-1-sulphonate. He died six hours post-admission. In post-mortem examinations, there were multiple sub-pleural and sub-epicardial hemorrhages and the gastrointestinal mucosa was congested, hemorrhagic, and greenish blue in color. The liver, on histological examination, showed sub-massive hepatic necrosis. On toxicological analyses, copper sulfate was detected in preserved viscera and results for other heavy metals were negative.
Conclusion: Hypotension, cyanosis, uremia and jaundice can be considered as signs of poor prognosis in copper sulfate poisoning. Copper sulfate ingestion is life-threatening due to its deleterious effects on the upper GI, kidneys, liver and blood. Having no time to waste, aggressive treatments should be immediately instituted and signs of poor prognosis should be kept in mind.

Keywords: Copper Sulfate; Forensic toxicology; Gastrointestinal Hemorrhage; Hemolysis; Poisoning

How to cite this article: Meena MC, Bansal MK. Acute Copper Sulfate Poisoning: Case Report and Review of Literature. Asia Pac J Med Toxicol 2014;3:130-3.

INTRODUCTION

Copper sulfate occurs in nature as large blue crystals, soluble in water, containing five molecules of water [$CuSO_4$. $5H_2O$]. It is commonly known as "blue vitriol" or "blue stone". It is mainly used for agricultural purposes as a pesticide and in leather and paint industry (1-4). It has metallic taste, and for human, it is rated as moderately toxic. The occurrence of copper sulfate poisoning varies in different regions depending on availability of this toxic agent. In case of poisoning, it is commonly consumed with suicidal intentions; however, accidental poisonings have been reported from children as well (1-3).

Copper sulfate is a powerful oxidizing agent, which is corrosive to mucous membranes (3,4). Concentrated solutions are acidic with pH 4. Cellular damage and cell death may result from excessive copper accumulation through which free reduced copper in the cell binds to sulfhydryl groups and inactivates enzymes such as glucose-6-phosphate dehydrogenase and glutathione reductase (4). Copper sulfate ingestion is a relatively popular method for committing suicide in Indian subcontinent and is able to kill as many as one out of four poisoned patients (2,4,5). This high mortality rate has raised a growing concern to identify the severe alarming signs suggestive of poor prognosis and to improve treatment approaches. In this paper a fatal case of copper sulfate ingestion is presented with a brief review of literature on clinical manifestations, determinants of prognosis and essential treatments.

CASE REPORT

A 22-year-old unmarried man working as a painter in paint industry was found unconscious at his friend residence on April 2012. On admission to the Lady Hardinge Medical College Hospital, he was presented with hemorrhagic gastroenteritis with nausea, hematemesis, melena and dehydration. He was hypotensive (blood pressure = 80/60 mmHg) and tachycardic (pulse rate = 120 bpm). Complete blood test revealed a normocytic normochromic anemia (hemoglobin = 11.2 mg/dL), an increase in leucocyte count with a marked shift to left, and a decrease in platelet count ($82,000/mm^3$). On blood smear, features of hemolysis including presence of microspherocytes, elliptocytes, nucleated red blood cells and polychromatophils were evident. The patient had also a severe metabolic acidosis (pH = 5.2). In liver function tests, increase in aspartate transaminase (189 IU/L) and total bilirubin (4.8 mg/dL) was found, while alanine transaminase (12 IU/L) and direct

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Received 16 February 2014; Accepted 12 August 2014

bilirubin (0.2 mg/dL) were in normal limits. Albumin, prothrombin time and partial thromboplastin time were normal. Renal function was abnormal with a creatinine of 4.9 mg/dL and blood urea nitrogen of 153 mg/dL in biochemical tests. Urine analysis showed presence of 2+ protein, 2-4 WBCs and 1-2 RBCs/HPF. In the police report, it was stated that a copper sulfate container was found inside the house and that the time of ingestion could not be determined.

The patient received gastric lavage, fluid replacement therapy, vasoactive drugs, antiemetic drugs, ranitidine and furosemide. The gastric lavage returned fluid appeared dark green in color with no peculiar odor. Based on the history of patient as a paint industry worker, findings on police report, color of gastric lavage returned fluid and clinical picture at hospital, the diagnosis of copper sulfate poisoning was suspected for the patient and specific antidotes including methylene blue (1-2 mg/kg/dose in 5% dextrose intravenously) and 2,3 dimercaptopropane-1-sulphonate (DMPS; 250 mg every four hours intravenously) were administered to the patient. He was also given one transfusion of packed red cells (10 mL/kg/dose) during admission. Despite the treatments, patient's condition deteriorated and he died 6 hours post-admission.

Post-mortem findings

On external examination, cyanosis was present over lips and nail beds (Figure 1). Self-inflicted injury marks were present over flexor aspect of left forearm (Figure 2). A yellowish discoloration was seen all over the body. Internal examination revealed all internal organs were congested. There were multiple sub-pleural and sub-epicardial hemorrhages. The gastrointestinal (GI) mucosa was congested, hemorrhagic, and greenish blue in color (Figure 3). The liver, on histological examination, showed sub-massive hepatic necrosis. On toxicological analyses, copper sulfate was detected in preserved viscera and results for other heavy metals were negative.

DISCUSSION

Copper sulfate poisoning in high-dose ingestions and advanced stages is known to be fatal (2,4,6). In this paper, we presented a patient who died despite early supportive and specific treatments.

Clinical manifestations

Common clinical manifestations of copper sulfate poisoning include erosive gastropathy, intravascular hemolysis, hepatitis, acute kidney injury and hemoglobinuria (2-8). Arrhythmias, pancreatitis, methemoglobinemia, rhabdomyolysis and seizures are also reported in smaller number of cases (2,4,9).

Common GI effects of copper sulfate poisoning (i.e. epigastric pain, hematemesis, and melena) are predominantly due to corrosive injury to mucosal membranes (4). In our patient, GI injuries presented with marked vomiting, hematemesis and melena that contributed to substantial blood loss and hypotension on admission. Blue staining of esophageal and GI mucosa in the post-mortem examinations reveals the direct damages of high amounts of the poison ingested by the patient. However, GI toxicity may also result from parenteral poisoning, suggesting that GI damages are not only caused by the direct contact of copper sulfate with the digestive tract but also the systemic effects of the poison (10).

As the majority of absorbed copper is deposited in liver after being delivered from the portal circulation, severe hepatoxicity and subsequently acute liver failure are predictable consequences (2,7,11). In our patient, we found sub-massive hepatic necrosis in post-mortem examinations.

Two major hematological manifestations of copper sulfate poisoning are intravascular hemolysis and methemoglobinemia (1,2,4,9,11). Intravascular hemolysis can be developed as early as the first 24 hours post-ingestion and is due to the direct oxidative damage to erythrocyte membranes. The hemolysis can be rapid and severe with drastic drops in the hemoglobin level. The Cu^{2+} ion oxidizes the Fe^{2+} ion to Fe^{3+} in hemoglobin resulting in met-hemoglobin formation (7,12,13). This manifests with

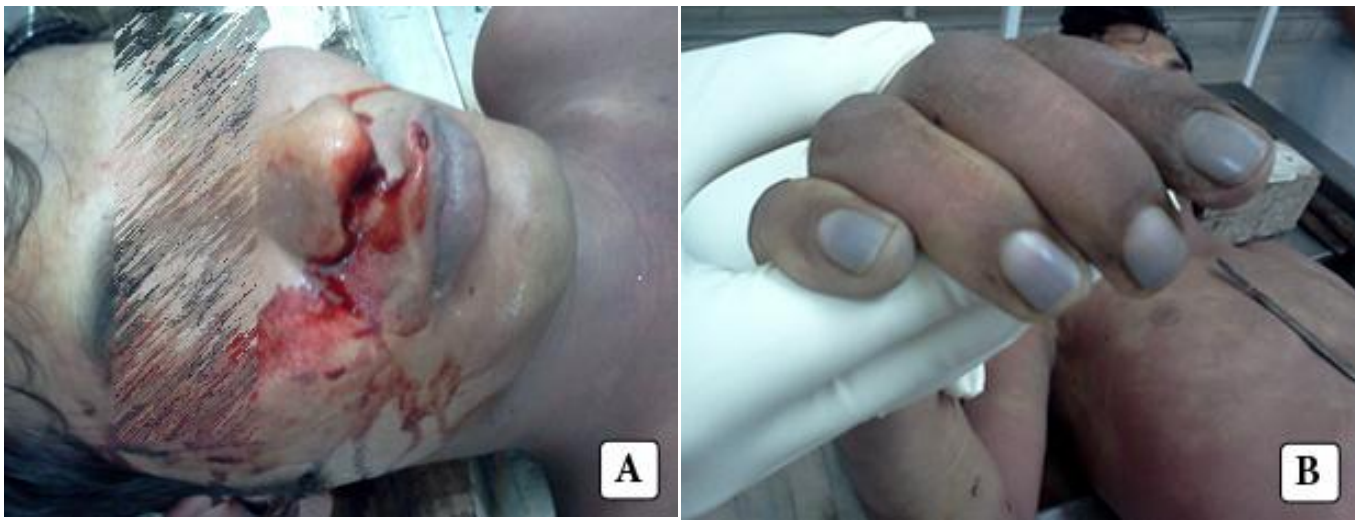

Figure 1. Post-mortem findings of the patient (external examination): A) cyanosis on lips, B) cyanosis on nail beds

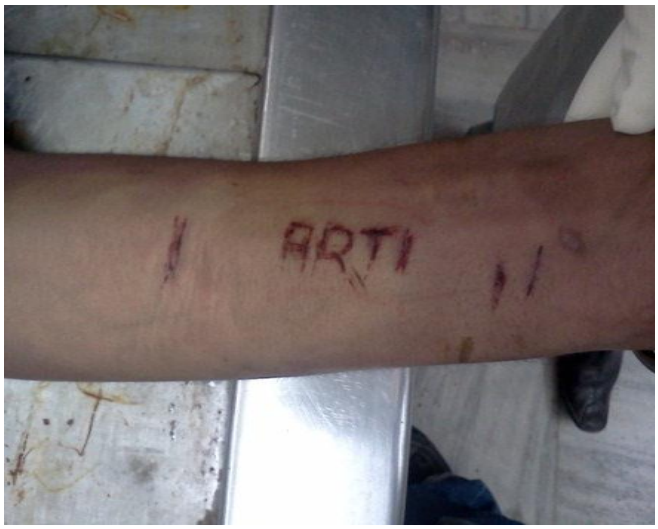

Figure 2. Self-inflicted injury marks over flexor aspect of left forearm of the patient

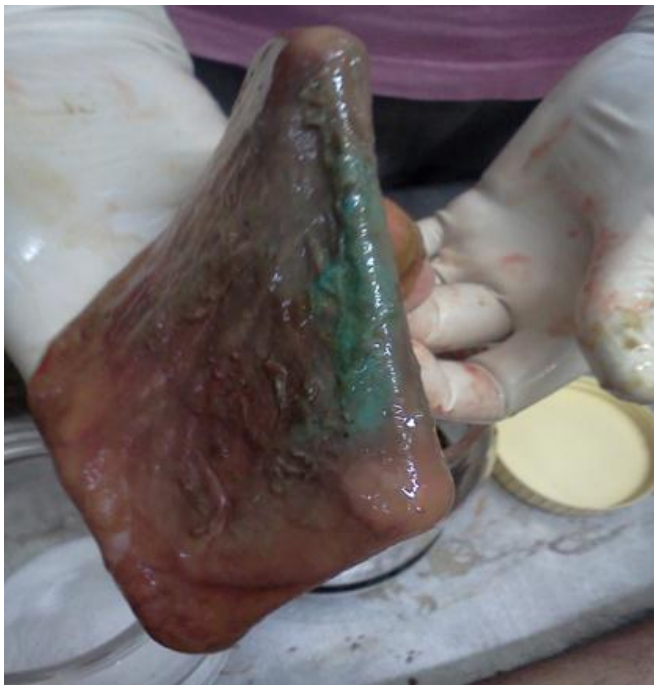

Figure 3. Post-mortem findings of the patient: hemorrhagic and greenish-blue stained mucosa of stomach

cyanosis and loss of oxygen carrying capacity of blood.

Acute kidney injury is a much more common manifestation of copper sulfate toxicity with an incidence rate as high as 40 to 60% (2,7,9,14,15). The possible mechanisms of kidney damage in copper sulfate poisoning include pre-renal failure due to dehydration (vomiting, diarrhea, and reduced fluid intake), hemoglobinuria, rhabdomyolysis, direct copper toxicity on proximal tubules and secondary effects of multi-organ dysfunction (2,5,16).

Signs of poor prognosis

Hypotension, cyanosis, uremia and jaundice can be considered as signs of poor prognosis in copper sulfate poisoning. Immediate cause of death in copper sulfate toxicity include severe shock secondary to hemorrhagic gastroenteritis while death in later stages is attributed to hepatic and renal failure (2,10,11). The dose of copper sulfate ingested by the patient has a crucial role on the prognosis (2,8,9). However, the ingested dose by our patient was unknown; tough it had to be substantial judging by very early signs of gastrointestinal injury and multi-organ dysfunction. There was also conspicuous blue staining of esophagial and gastrointestinal mucosal membranes in post-mortem examinations that proves ingestion of considerable amount of poison by the patient. It has been proposed that ingestion of greater than 1 gram of copper sulfate results in systemic toxicity (7); however, this is only a rough threshold and depends on individual factors. The lethal dose of ingested copper sulfate is estimated to be between 10-20 grams (2,8,9).

Treatments

In case of ingestion, the contact damage to GI mucosa can be minimized by drinking large quantities of milk and water (4). Anemia from hemolysis or bleeding must be corrected with transfusion of packed red blood cells. Methemoglobinemia should be treated with methylene blue (intravenous injection of 1-2 mg/kg/dose and repeated if cyanosis persists after an hour) (4,7,9). As high doses of methylene blue can itself induce hemolysis, and it is also contraindicated in G6PD deficiency, hyperbaric oxygen and ascorbic acid can be alternatively used (4,9). In addition, exchange transfusion was shown to be effective when methemoglobinemia is poorly responsive to methylene blue (17). Renal failure must be identified early by careful monitoring of serum creatinine and urine output. Although hemodialysis has been shown to be ineffective in clearing copper from the body (4,10,17,18), it is essential to reduce serum creatinine and save the patient's life.

For enhanced detoxification of copper from the body, chelation therapy with d-penicillamine, dimercaprol, DMPS and zinc acetate has been recommended (18,19). Based on experimental information, DMPS is probably the best chelator (18).

Preventive measures

Pulverized powdered form of copper sulfate is easily available in Indian open market, similar to other kinds of pesticide. The relatively unrestricted sale of pesticides is a public health threat in Southeast Asia (20). Devising strict regulations for pesticide sale is crucial to prevent deliberate self-harm by ingestion of these poisons.

CONCLUSION

Copper sulfate ingestion can be life-threatening with high mortality due to its deleterious effects on the upper GI, kidneys, liver and blood. Having no time to waste, aggressive treatments should be immediately instituted and signs of poor prognosis should be kept in mind.

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