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CASE REPORT

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Acute poisoning of copper sulfate: a case report and review literature

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Abstract

Background: Copper sulfate is a bright blue crystal used primarily for agricultural purposes, as a pesticide, disinfectant, feed, and soil additive. Acute volunteer poisoning of copper sulfate is not common in the world and in Iran.

Case presentation: We reported the case of a 15-year-old girl who presented to the emergency department after ingestion of an unknown amount of copper sulfate following a struggle at school. She had become acquainted with the toxic compound through school textbooks. On admission to the hospital, she had abdominal pain and a sore throat with a normal serum copper level. The patient stated that she had three episodes of bluish vomiting. She underwent symptomatic treatment and was monitored for 3 days. The outcome was favorable, and she had no signs and symptoms of organ failure.

Conclusions: As a result, copper sulfate poisoning depending on the consumed dose can be mild or very severe with a high mortality rate. The authors discuss the various pathogenesis and treatments of this rare poisoning by reviewing the available literature.

Keywords: Copper sulfate, Poisoning, Toxicology

Background

Copper (Cu) is a critical trace element catalyst for heme synthesis and iron absorption. Copper is the third most plentiful trace element found in the human body after zinc and iron [1]. Copper's physical properties include high thermal and electrical conductivity, alloying ability, low corrosion, and malleability [2]. Copper is used in intrauterine contraceptive devices (IUD), and the release of copper is necessary for their critical contraceptive results [3]. A human adult's average daily intake of copper is approximately 0.6 to 1.6 mg Cu, with the diet being a primary source [1, 4, 5].

Copper (II) sulfate is a salt containing copper^{2+} as the metal ion created by treating cupric oxide with sulfuric acid. It is a large, bright blue crystal containing five water molecules ($CuSO_4 \cdot 5H_2O$) and is also named *blue vitriol* or *blue stone.* Copper sulfate was used in burn wound debridement until cases of systemic copper poisoning were reported [6]. It is used primarily for agricultural purposes such as fertilizer, pesticide and disinfectant, fungicide, feed, soil additive, and an emetic [7]. In the 1960s, copper sulfate, a 250-mg dose, containing a 100-mg copper ion, ironically was recommended as an emetic agent, typically for use in children following potentially toxic exposures. It was recognized for its rapidity of onset and effectiveness and compared favorably with syrup of ipecac. However, copper-induced emesis was rapidly identified as an unsafe practice, and this use was generally discontinued. Cases of acute poisoning are rare and usually voluntary with suicidal intent, are infrequent in Iran and over the world, except in India [8], where copper salts are administered in religious rituals as a green-colored *spiritual water* containing 100 to 150 g/L of copper sulfate as an emetic to expel one's sins [9]. We

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report a case of poisoning by ingesting copper sulfate in a young woman who committed suicide, and we discuss the various treatments available through a literature review.

Case presentation

Patient information

On May 27, 2022, a 15-year-old female student was taken to the emergency department following a suicide commission with ingestion of about 200-ml copper sulfate solution with an unknown concentration, after a school struggle. The patient complained of abdominal pain and had experienced three episodes of bluish vomiting. Her past medical history did not include anything relative.

Clinical findings and diagnostic assessment

On arrival in the poisoning ward, she had drawling and complained of sore throat and abdominal pain. She was conscious and oriented with stable vital parameters. Her vital signs included a pulse rate of 100/min, blood pressure of 120/70 mmHg, and SpO_2 of 97%. Periumbilical tenderness was seen in the clinical examination. Routine hematological investigations and contrast CT scans of the abdomen and pelvis were insignificant.

Therapeutic information, outcomes, and follow-up

The treatment was started with an intravenous (IV) injection fluid normal saline, ondansetron, and pantoprazole infusion. On the second day of hospitalization, the general condition of the patient was good; hematological and biochemical investigations were all within normal limits; she had a pH of 7.37, Po_2 of 90 mmHg, Pco_2 of 39.1 mmHg, Hco_3 of 22.2 mEq/L, hemoglobin of 12.9 g/dL, creatine phosphokinase (CPK) of 109 U/L, alanine transaminase (ALT) of 10 U/L, aspartate aminotransferase (AST) of 16 U/L, creatinine of 0.8 mg/dL, urea of 22 mg/dL, and serum copper level of 60 µg/dL. But she was still complaining of consistent sore throat and abdominal pain. An endoscopic examination was requested for the patient. Gastroduodenal endoscopy revealed a grade A of esophagitis and erythematous mucosa. No significant damage was observed in the duodenum. No abnormalities were seen in the patient's laboratory tests. And on the third day of hospitalization, the patient was discharged.

Discussion

Poisoning by copper sulfate is a rare but often fatal intoxication, mainly related to suicide attempts. The route of administration of this substance is usually oral. Our case presents a rare and novel poisoning report as she was the first case of copper sulfate poisoning in Emam Reza hospital of Mashhad, in which the digestive system discomforts and disorders were the only signs and symptoms presented, contrary to our expectations.

Copper physiology and physiopathology

Copper is a trace element crucial for human life. There is 50–150 mg of copper in the body. It is estimated that the daily intake of copper is 2 mg/day. The absorption of copper is mainly through the duodenum and stomach. The serum level reaches the peak concentration after 1–3 h post-ingestion. The distribution of copper is related to sex, age, and diet status in terms of copper content. The heart, muscles, brain, kidneys, and liver are the tissues in which the most copper is distributed [2]. Deficiency and overload of copper cause different pathologies, including Wilson's disease, Alzheimer's disease, and Creutzfeld-Jacob's encephalitis. In the blood, copper binds to ceruloplasmin at close to 90%. Also, albumin is a non-specific transporter that weakly binds to the free form of copper during copper intoxication. Copper has an enterohepatic cycle and is eliminated mainly by the liver through biliary excretion (> 70%). The duodenum function in reabsorbing the bile and pancreatic secretions plays an important role in the complexity of the analysis of copper bioavailability. Elimination through the kidneys only consists of a small part (< 5%) [10].

Copper sulfate is not just known as a toxic substance: it has a long history of use in the debridement of wounds because of its antiseptic properties and as an emetic agent in intoxication. It is still contained in intrauterine devices. Also, in many domestic and industrial products, copper is used. Poisoning with this substance is rare but can be severe and fatal, with up to 23% mortality rates. However, the rates are on the decline, and it is essential that physicians are aware of its lethal complications and management strategies. The most abundant route of poisoning is oral, but intravenous, cutaneous via wounds, and even intra-uterine, for abortion, routes have been reported. In our country, no cases of copper sulfate have been reported so far, and our patient's symptoms were limited to gastrointestinal problems [11]. According to previous studies, acute oral toxicity (LD50) of copper sulfate is about 300 mg/kg in rats [12]. The main complications of copper sulfate ingestion include intravascular hemolysis, methemoglobinemia, acute kidney injury, and rhabdomyolysis which is explained in detail below. Severe gastrointestinal effects may occur with acute overdosage [10]. In extreme or long-term overdosage, symptoms may be similar to those of Wilson's disease, a disease in which the liver does not filter copper adequately and copper accumulates in the liver, brain, eyes, and other organs [13]. Gradually, high copper levels may cause life-threatening organ damage. Ingestion of more than 15 mg of copper has been reported to be toxic to humans [14]. In a survey of human clinical case studies, 5.3 mg/day was

the lowest oral dose at which local gastrointestinal irritation was seen. Ingestion of gram quantities of copper sulfate resulted in death by suicide, whereas less severe effects were reported from estimated copper doses of 40 to 50 mg from ingestion of carbonated beverages in contact with copper containers. Limited data are available on the chronic toxicity of copper. The hazard from dietary intakes of up to 5 mg/day appears to be low [15].

Clinical manifestations

The clinical features of copper sulfate poisoning are summarized in Fig. 1: Clinical features of copper sulfate poisoning.

Cardiovascular effects

Accumulation of copper in myocardial tissue is associated with Cu sulfate cardiomyopathy and arrhythmias. Pathological cardiac examinations have demonstrated interstitial fibrosis, intramyocardial small vessel sclerosis, and focal inflammatory cell infiltration [9].

Methemoglobinemia

As a rare hematologic disorder, methemoglobinemia is the oxidation of divalent ferrous iron [Fe^{2+}] of hemoglobin (Hb) to ferric iron [Fe^{3+}] of methemoglobin. It can result from either inherited or acquired conditions. Acquired forms mainly originate from exposure to substances that cause oxidation of the Hb directly or indirectly [9]. The most common drugs that cause methemoglobinemia are benzocaine and lidocaine. Nitrates and nitrites as water contaminants or food preservatives can also act as trigger factors. Nonetheless, methemoglobinemia originating from Cu sulfate poisoning is rare [16]. Measurement of blood gases, the enzymatic activity of CYB5R, methemoglobin reductase or methemoglobin diaphorase, and molecular testing like DNA analysis are the main tests used in the differential diagnosis of hereditary or acquired methemoglobinemia [17].

Rhabdomyolysis

Like Wilson's disease, rhabdomyolysis is seen in copper sulfate poisoning but occurs less frequently [4]. Na^{+}/K^{+}-ATPase pump inhibition and subsequent increase in myocyte permeability in the skeletal muscle are the known mechanisms for copper sulfate-induced rhabdomyolysis [18].

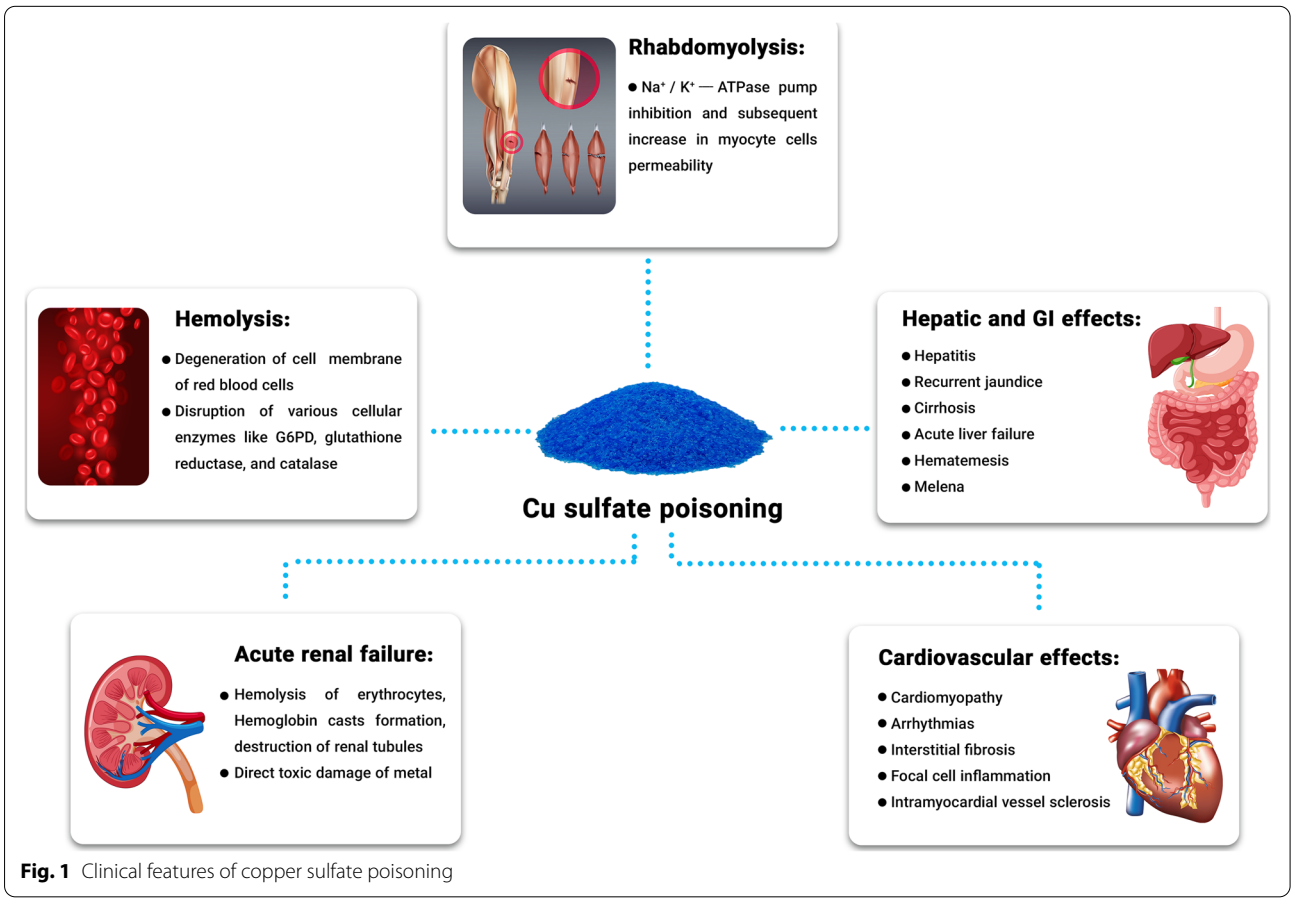

Fig. 1 Clinical features of copper sulfate poisoning

Hemolysis

Copper sulfate can lead to hemolysis by accumulating in red blood cells. It degrades their cell membranes and denatures their hemoglobin content [19]. It may disrupt the activity of various cellular enzymes such as erythrocyte glucose 6-phosphate dehydrogenase (G6PD) [20], glutathione reductase, and catalase [21].

Acute renal failure

Some pathophysiological mechanisms, like intravascular hemolysis as the main factor, may play a role in acute renal failure. Hemoglobin casts can destroy renal tubules, further the hemolysis of red blood cells. The other probable factor can be the direct toxic damage of metal to the kidney tissue. The copper released from the hemolyzed cells could initiate or advance the occurrence of renal lesions leading to acute tubular necrosis [22].

Hepatic and gastrointestinal effects

Clinical manifestations of raised copper levels in the liver due to copper sulfate poisoning comprise a wide range of signs and symptoms, including delicate and asymptomatic morphological changes in the hepatic tissue, self-limiting hepatitis-like disease to severe hepatitis, recurrent jaundice, if associated with hemolysis of red blood cells, cirrhosis, and even acute liver failure [23]. Typical manifestations of copper poisoning in the gastrointestinal (GI) tract are generally due to its corrosive feature. Hematemesis and melena have occurred in the reports of massive ingestion of copper salts, due to mucosal damage and subsequent bleeding. Most of the absorbed copper enters the liver through the portal vein and causes hepatoxicity [24].

Diagnosis and treatment

Diagnosis of copper sulfate intoxication is based on the patient's history, with special attention to the patient's occupation, and also via the results of the analysis of the blood copper level. It should be considered that the blood copper level rapidly decreases after ingestion, and it is not correlated to the severity of the prognosis [25]. After diagnosis, management of the patient is based on symptomatic treatment, including correction of fluid-electrolyte imbalance. Hypovolemic shock requires fluid resuscitation and vasoactive treatment. Because copper sulfate is an emetic, gastric lavage is not compulsory, but it can be effective if only done in the early hours. Only in persistent renal failure, renal hemodialysis is indicated. In other cases, renal impairment usually recovers itself. In cases of symptomatic methemoglobinemia, methylene blue and high-dose oxygen should be administrated. Different types of chelators can be used in treating acute copper poisoning, and there is no priority among them. D-penicillamine, dimercaprol, and edentate calcium diphosphate (EDTA) can chelate copper and enhance its elimination by the urinary tract. In our case, because the result of the blood analysis did not reveal copper level in the toxic range, chelation therapy was not performed [7, 10]. Andreja SINKOVIC et al. reported that the use of 2,3-dimercaptopropane-l-sulphonate (DMPS) was beneficial in the treatment of intentional oral poisoning [26]. In another evidence reported, by Manik Chhabra et al., chelation therapy of calcium disodium EDTA prevented further organ involvement [27]. Previous literature reported cases treated adequately with plasmapheresis [28]. Recently, venovenous extracorporeal membrane oxygenation (ECMO) was used in the treatment of acute respiratory distress syndrome, secondary used for treating copper sulfate poisoning [29]. Because copper is mainly eliminated through the bile flow, the kidneys do not play a significant role in removing copper. Therefore, hemodialysis alone has not proven effective in purifying copper sulfate, which early binds to plasma proteins and is then rapidly stored in the liver, erythrocyte cells, and muscle. When the metal is chelated, it is eliminated mainly by the kidneys, which makes hemodialysis theoretically beneficial [11].

Regulation of usage and safety measures should be followed by users

As mentioned earlier, today copper sulfate is used for agricultural purposes, including as fertilizer, pesticide, fungicide, and soil additive. Therefore, it is necessary for people to be familiar with the regulation of usage and safety measures related to this article including the following [15]:

- Wear protective equipment (appropriate gloves, respiratory protective devices, and safety glasses) during usage.
- Don't eat, drink, smoke, or use the personal product during handling.
- Avoid the generation of dust or fine particulate.
- Use it only in a ventilated area.
- Remove contaminated clothing and wash it before reuse.
- Avoid contact with the eyes, skin, and clothing.
- Keep the container tightly closed.
- Avoid ingestion and inhalation.
- Avoid release to the environment

Preventive measures

Copper sulfate is easily available in the Indian and Iranian open markets, similar to other kinds of pesticides.

The relatively unrestricted sale of pesticides is a public health threat in Asia. Devising strict regulations for pesticide sales is crucial to prevent deliberate self-harm by ingestion of these poisons [15].

Conclusions

In conclusion, copper sulfate intoxication is rare but causes mortality and morbidity, so it must be recognized quickly. Treatment of copper poisoning is mainly symptomatic, and besides that detoxification procedures like chelation therapy, hemodialysis, and plasma exchanges might be necessary based on the case.

Abbreviations

Cu: Copper; IUD: Intrauterine contraceptive devices; IV: Intravenous; CPK: Creatine phosphokinase; ALT: Alanine transaminase; AST: Aspartate aminotransferase; Hb: Hemoglobin; G6PD: Glucose 6-phosphate dehydrogenase; GI: Gastrointestinal; EDTA: Edentate calcium diphosphate; DMPS: Dimercaptopropane sulfonate-I-sulphonate; ECMO: Extracorporeal membrane oxygenation.

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Authors' contributions

Conceptualization and supervision: [S. G]. Data collection: [S. H], [V. P], [S. G], [S.R. M], [H. S. I]. Investigation, writing the original draft, and writing review and editing: All authors. The authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

All ethical principles are considered in this article. Written informed consent was obtained from the patient's parents for the publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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