Clinical Case Report

Successful extracorporeal life support in respiratory failure after copper sulphate ingestion

YONG SOO CHO, JEONG MI MOON, YONG HOON JEONG, DONG HUN LEE, BYEONG JO CHUN

ABSTRACT

A 44-year-old woman intentionally ingested a solution of copper sulphate. She had minimal intravascular haemolysis and methemoglobinaemia but developed acute respiratory distress syndrome (ARDS) 4 hours after acute copper sulphate poisoning. This required extracorporeal membrane oxygenation (ECMO) management in the intensive care unit. Subsequently, she improved clinically and was successfully weaned from ECMO. Acute copper sulphate poisoning can cause severe pulmonary toxicity even in the absence of other serious symptoms. Therefore, a physician treating acute copper sulphate poisoning should look out for respiratory symptoms even in the absence of other common symptoms. We suggest early initiation of venovenous ECMO in those with ARDS following copper sulphate poisoning.

Natl Med J India 2018;31:83–5

INTRODUCTION

Copper is one of the most frequently reported metals to which patients are exposed. Copper sulphate, one of the most abundant salts of copper, is used in various products such as fungicides, algaecides, herbicides and insecticides.[1] The marine blue colour of hydrated copper sulphate crystals is a cause of unintentional poisoning because it is attractive to children. However, copper sulphate poisoning in adults can result from intentional self-harm.[2] The ingestion of large amounts of copper commonly causes intravascular haemolysis, haemolytic anaemia, methemoglobinaemia, acute tubular necrosis, hepatotoxicity and rhabdomyolysis, which can ultimately lead to death. However, few previous reports have described pulmonary toxicity-related copper poisoning.

We describe a patient with copper sulphate poisoning who developed acute respiratory distress syndrome (ARDS) as a major clinical feature.

THE CASE

A 44-year-old female teacher was referred from a primary care hospital to our emergency department approximately 5 hours after intentional ingestion of over 100 g of copper sulphate including as a solution in her science laboratory.

At presentation, her heart rate was 104 per minute, blood pressure was 110/70 mmHg, respiratory rate 26 per minute and her body temperature was 36 °C. She complained of dyspnoea, epigastric pain, nausea and intractable vomiting. Chest X-ray showed diffuse bilateral infiltration (Fig. 1). The echocardiogram and electro-cardiogram were normal. Her arterial blood gas showed pH 7.23, pCO_2 29.7 mmHg, PaO_2 68.8 mmHg, HCO_3^- 12.4 mEq/L and O_2 saturation (SaO_2) of 88.9% (on a 10 L non-rebreather face mask). Her initial methemoglobin levels at the time of presentation and 14 hours post-presentation were 1.7% and 5.7%, respectively. The serum copper levels and 24-hour urine copper tests (inductively coupled plasma mass spectrometry) and other biochemical investigations are shown in Table I.

She received mechanical ventilatory support but her arterial blood gas showed progressive deterioration. After 4 hours, her arterial blood gas showed pH 7.23, pCO_2 31.6 mmHg, PaO_2 56.2 mmHg, HCO_3^- 12.9 mEq/L, SaO_2 80.8% (with FiO_2 1.0) and haemoglobin of 9.9 g/dl. Chest X-ray also showed increased patchy/nodular opacities in both lungs (Fig. 1). She was administered venovenous extracorporeal membrane oxygenation (ECMO) at a flow rate of 3.5 L/minute and a sweep rate of 2 L/minute. Concurrent ventilator settings included a tidal volume of 350 ml (5 ml/kg), a respiratory rate of 12 breaths/minute, a PEEP of 10 mmHg and an FiO_2 of 0.5. Chelation therapy was initiated with penicillamine at a dose of 250 mg every 6 hours because of severe poisoning with more than 100 g of copper sulphate.

Her lung function recovered slowly and the radiological findings also improved by day 7. She could then be weaned from venovenous ECMO and extubated. She was discharged with good clinical recovery.

DISCUSSION

Copper sulphate is a powerful oxidizing agent that exerts corrosive effects on mucous membranes. Ingestion of more than 1 g of copper sulphate can result in clinical manifestations of toxic symptoms.[3] Although the toxicity varies depending on individual factors, the lethal dose is 10–20 g,[2] and mortality is high, reaching up to 25%.[4,5] Severe vomiting prevents the absorption of the ingested toxicant, which may partially account for the good outcome of our patient despite the ingestion of 100 g of copper sulphate. The most common features of copper sulphate intoxication are gastrointestinal bleeding and irritation (37%), followed by jaundice (58%), intravascular haemolysis (47%–

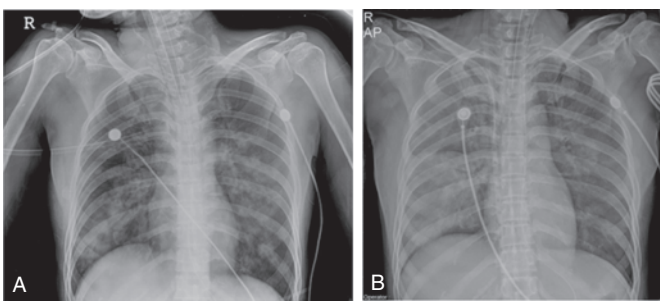

FIG 1. Chest X-rays at the time of admission (A) and after 4 hours (B)

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TABLE I. Blood chemistry values at admission and during hospital stay

Blood chemistry	At admission	Day 2	Day 3	Day 9
Aspartate aminotransferase (U/L)	59	47	92	20
Alanine aminotransferase (U/L)	1	8	6	22
Blood urea nitrogen (mg/dl)	9.9	9.2	24.8	60.5
Creatinine (mg/dl)	0.8	0.7	0.9	1.6
Total bilirubin (mg/dl)	1.34	2.08	2.83	0.75
Direct bilirubin (mg/dl)	–	–	0.92	–
Lactate dehydrogenase (U/L)	808	1280	3250	1450
Creatinine kinase (U/L)	113	80	466	23
Troponin-I (ng/ml)	0.02	0.21	0.18	0.06
Serum copper (µg/dl)	503	–	87	79
24-hour urine copper (µg/dl)	5072.00	–	1816	127

65%), acute renal failure (20%–40%), methemoglobinaemia (3.4%–42%) and hepatic encephalopathy (5%).[6]

Our patient was diagnosed to have ARDS,[7] which is defined as the development of acute, bilateral pulmonary infiltrates (as determined by consensus of two trained physician reviewers) and hypoxaemia ($PaO_2/FIO_2 \leq 300$ mmHg) not primarily due to heart failure or volume overload. Although respiratory alkalosis should occur primarily in ARDS, this patient showed metabolic acidosis. This may be due to differences in the ARDS phenotype. Recent studies on phenotypes of ARDS have shown that phenotype 2 is characterized by metabolic acidosis, shock, sepsis and higher mortality.[8,9]

In copper sulphate poisoning, pulmonary toxicity can occur occasionally and represents an extra-erythrocytic manifestation of the oxidative effects of copper ions.[10] The mechanism underlying pulmonary toxicity induced by copper consists of oxidative effects resulting from the generation of reactive oxygen species (ROS). In addition, copper blocks antioxidant activities in epithelial cells by inhibiting the activity of catalysts and glutathione reductases and by increasing the activity of glutathione peroxidase.[11] Since copper has a high evaporation point (1084 °C), it is difficult to inhale copper at room temperature. In our patient, ARDS might have been caused by aspiration of copper sulphate solution during vomiting.

Few studies have reported on pulmonary toxicity caused by copper poisoning. Giudice *et al*.[12] reported on dogs exposed to pesticides containing copper sulphate. Acute respiratory failure occurred 3 hours after ingestion, and pulmonary haemorrhage and pneumonia were confirmed by chest X-ray. Pulmonary toxicity was possibly caused by inhalation of copper sulphate. Kim *et al*.[13] reported a 75-year-old man with vomiting after ingestion of a pesticide containing copper sulphate for suicide. The plasma copper concentration was high at 634.7 mg/ml. The patient's PaO_2 showed hypoxaemia of 60.7 mmHg (room air), and he died of respiratory failure 3 hours after admission. His chest X-ray was normal, and his arterial blood gas showed $PaCO_2$ of 85.2 mmHg and PaO_2 of 76.8 mmHg (on 4 L of O_2 given through nasal prongs). Although not consistent with the definition of ARDS, pulmonary toxicity can be estimated from hypoxaemia. This patient also had vomiting and most likely aspirated. However, because death occurred 3 hours after presentation, successful therapeutic strategies were not described. In addition, during chronic occupational exposure to copper, interstitial pulmonary fibrosis and histiocytic granulomas that contain copper have been reported.[14] However, pulmonary toxicity related to acute copper poisoning is no longer reported.

In patients with severe ARDS, venovenous ECMO is recommended. The Extracorporeal Life Support Organization (ELSO) recommends ECMO for patients with a risk of death >80%. For patients with FiO_2 >90%, Murray scores 2–3 and PaO_2/FiO_2 ratio <150, ECMO should be considered.[15,16] In our patient, ECMO was used with a PaO_2/FiO_2 ratio of 56 (FiO_2 1.0) despite the use of a protective ventilation strategy. For optimal oxygenation in venovenous ECMO, the pump blood flow should be ≥60% of the theoretical cardiac output, the sweep gas rate should give a $PaCO_2$ between 30 and 40 mmHg, and the oxygen fraction delivered by the extracorporeal circuit ($FECO_2$) should give an arterial oxygen saturation $SaO_2 \geq 88\%$.[15,16] Our patient was stabilized at a flow rate of 3.5 L/minute and a sweep rate of 2 L/minute. The ventilator was maintained in lung resting mode.

However, we cannot explain the absence of common symptoms of copper poisoning, such as haemolysis and methemoglobinaemia in our patient. Although the patient's indirect bilirubin and lactate dehydrogenase increased for 2–3 days, this increase may be explained by the effects of ECMO rather than intravascular haemolysis due to copper poisoning. Intravascular haemolysis has been reported to occur 12–24 hours post-ingestion.[6] Haemolysis is one of the common complications of ECMO and has been reported to occur in 18% of cases.[8]

Supportive treatment is administered for acute copper sulphate intoxication, including the management of corrosive burns, chelation therapy (D-penicillamine, BAL [British anti lewisite], EDTA [calcium disodium ethylene diamine tetra acetic acid] and dimercaprol) and haemodialysis in those with acute renal failure.[17] Chelation therapy should be initiated when a patient presents with hepatic or haematological complications or other manifestations of poisoning.[10] We started chelation therapy because our patient had ingested more than the reported lethal dose, and ARDS was considered to be a symptom of severe copper poisoning.

Measurements of serum copper concentrations enable a diagnosis of poisoning; however, there is no linear correlation between these values and the clinical features[18] (such as C reactive protein, chest X-ray findings and the PaO_2/FiO_2 ratio), which can be explained in part by the rapid uptake of copper into red blood cells. In contrast to the development of intravascular haemolysis and hepatotoxicity and the description of renal failure in another report of a patient with a serum copper level of 210 mg/dl, our patient with a level of 503 mg/dl did not have any of these symptoms.[5]

In conclusion, acute copper sulphate poisoning can cause pulmonary toxicity without the well-established symptoms of copper poisoning such as intravascular haemolysis, hepatotoxicity

and renal failure. Therefore, a physician treating acute copper poisoning should pay attention to the development of ARDS even in the absence of other common symptoms. In such cases, early initiation of ECMO should be considered for managing respiratory failure.

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