Case Report

Parenteral copper sulfate poisoning causing acute renal failure

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Introduction

Copper is an essential trace metal in humans. It is vital for the function of certain enzymes such as cytochrome c oxidase [1]. It is used commercially in whitewashing, leather manufacture [2], fungicides and insecticides [3], and to bind colours to fabrics. Copper sulfate toxicity is a rare event in the US but is used commonly as a form of suicide in India [4]. In the past, copper sulfate was used as an emetic. It has been replaced by less toxic agents, however, due to reported deaths from copper toxicity. There are case reports of copper-induced haemolysis in patients undergoing chronic haemodialysis when copper-plated tubing was used to deliver the dialysate [4]. A literature search failed to reveal any cases of parenteral copper sulfate poisoning. Here we present a case of intravenous copper sulfate poisoning as a suicide attempt associated with multisystem failure.

Case

GG is a 47-year-old Caucasian male with no significant past medical history who presented at his local emergency department via ambulance. Three days previously, he had tried to kill himself by injecting ~50 mg of copper sulfate both intravenously and subcutaneously. He obtained the copper sulfate from his art supplies. Within 15 min he developed nausea, vomiting, diarrhoea, haematemesis and haematuria. The following day he became anuric and was having diffuse abdominal pain and myalgias. On the third day, GG became jaundiced and confessed the injection to his wife. He was transported by ambulance to his local hospital.

On arrival at the emergency department, he was noted to be hypotensive and to have melena and haematemesis. His haemoglobin was 5 g/dl, haematocrit 9.4%, platelet count 94 000/cm³ and CPK was 2528 U/l. GG received intravenous fluids and was transfused with 3 U of PRBC and 3 U of FFP. He was also given penicillamine 40 mg/kg and dimeracpol 5 mg/kg i.m. on two occasions prior to transfer to the University of Mississippi Medical Center via helicopter.

On arrival at our hospital, his only complaints were dyspnoea and abdominal pain. He had no prior medical problems other than multiple left knee surgeries following a motor vehicle collision. Physical examinations revealed a middle aged white male in no acute distress. He was alert and oriented. His vital signs were as follows: T100.2 F, pulse 88, RR 17, blood pressure 156/88. He was jaundiced and had a diffusely tender and obese abdomen which was soft with normal bowel sounds. There were no peritoneal signs or hepatosplenomegaly. Rectal exam revealed his stools to be occult blood positive but otherwise normal. His neurological exam revealed motor weakness in the right lower extremity but without other abnormalities.

An electrocardiogram and chest X-ray were normal. Laboratory evaluation revealed WBC 20 800 (86% segs; 2% bands), haemoglobin 6.5 g/dl, haematocrit 20.2%, platelets 144 000, room air PaO₂ 76 mmHg/ PaCO₂ 26.5/pH 7.46, methaemoglobin 6.3%, urine insufficient quantity for urinalysis but myoglobin screen was positive, Na 113 mmol/l, K 3.9 mmol/l, Cl 87 mmol/l, HCO₃ 19 mmol/l, BUN 194 mg/dl, creatinine 9.8 mg/dl, glucose 113 mg/dl, alkaline phosphatase 72 U/l; total bilirubin 14.6 mg/dl with 8.2 mg/dl conjugated; ALT <9 U/l; AST 300 U/l; LDH 13 800 U/l; CK 2831 U/l; PT 13.9 s; PTT 25.9 s.

GG was admitted to the Internal Medicine service. The renal service evaluated GG and prepared for haemodialysis on arrival secondary to acute renal failure. GG received 4 U of PRBC during the initial haemodialysis. His serum copper levels were drawn prior and after each of the first two dialyses. The dialysate concentration of copper was also measured prior to and after dialysis (Table 1). EDTA was infused prior to the first two dialyses. There was no marked change in the blood copper levels after dialysis. Copper was detected in dialysate with values of 25 and 20 μg/l at the beginning and end of dialysis, respectively. EDTA was discontinued. On day 3, serum copper was essentially unchanged when comparing pre- and post-
dialysis levels, with values of 165 before and 168 at the end of dialysis. Dialysis results were similar, with 28 μg/l in pre-dialysate fluid and 23 when completing dialysis. By this time, GG was clinically and subjectively better. His hypotension, haemolysis and bleeding were stable. Haemodialysis was continued three times weekly. Before discharge, GG’s urine output had increased to 800 over the previous 24 h period. His creatinine peaked at 14 mg/dl during the hospitalization and was 12.8 at discharge. GG required only one more haemodialysis after discharge. His creatinine 6 weeks after the injection of copper sulfate was 1.7, and GG was doing well.

Discussion

Acute copper sulfate poisoning is a rare event in the US and uncommon worldwide. A literature search failed to reveal any case reports of parenteral copper sulfate poisoning. Clinical features after ingestion of copper sulfate are reported to include a metallic taste, nausea, vomiting, epigastric pain and, in severe cases, diarrhoea, haemoglobinuria and/or haematuria, renal failure, liver failure, hypotension, coma and melena. Anuria usually occurs within 24–48 h and lasts 12–36 h. Agarwal et al. [7] described a case series of acute poisoning requiring haemodialysis over a 17 year period. During that time, there were 19 cases of copper sulfate poisoning presenting to this tertiary care hospital in India. This was the second most frequent poisoning but had the highest mortality rate. The overall mortality rate was 24.2%; the highest mortality (37%) was in the copper sulfate group [5].

This case of parenteral copper sulfate toxicity resulted in the same clinical features as reported for oral ingestion, but at a much lower dose. Most reports of copper toxicity occur with ingestions of at least 1 g [5]. Our patient injected a much smaller dose (50 mg). Therapy for copper toxicity is primarily supportive whether the route of toxicity is enteral or parenteral [1]. There does not appear to be a correlation between serum copper levels and severity of symptoms. This is felt to be due to the rapid influx of copper into red blood cells. In the human body, 98% of copper in the serum is bound to the α-2-globulin ceruloplasmin; the remaining portion is bound to albumin. However, in acute intoxication this is reversed, with copper being bound primarily to albumin. Following ingestion of copper, most copper is taken up by the liver where it induces the production of ceruloplasmin. Copper is then incorporated into the protein structure. This metal—protein product is released from the hepatocytes into the serum and bile, thus explaining the secondary rise of serum copper in acute intoxication.

As the protein complex is degraded, copper is released and associates with taurocholateorycholic acid. Excretion is primarily through the bile [3]. Serum levels of copper are unreliable predictors of severity of symptoms. Whole blood copper levels correlate with severity of symptoms and may predict prognosis more accurately [2].

Treatment is supportive. Chelation therapy is sometimes recommended with dimercaprol, and penacillamine, the treatment of choice for Wilson’s disease, may be useful as well. There is apparently insufficient evidence to suggest a definite role for EDTA in the treatment of copper toxicity. Walsh et al. [3] reported a case of acute copper intoxication treated successfully with dimercaprol and edetic acid followed by penacillamine as an outpatient [3]. In addition to chelating agents, blood products, intravenous fluids, vasopressors and dialysis may be required. Dialysis is recommended only in cases of acute renal failure. Most literature suggests that haemodialysis is ineffective in removing copper from the body [1,5,6]. In a series of 48 cases reported from India [4], anuria and oliguria occurred in 27 and 10.3% of cases, respectively. This is consistent with the minimal changes seen in both serum and dialysate copper observed in our patient (Table 1). It is of interest that our patient developed the well described gastrointestinal manifestations of oral copper sulfate poisoning very early on despite a parenteral route of ingestion. This may indicate that the pathogenesis of the gastrointestinal manifestations is not due to the direct contact effect of the poison on the gastrointestinal mucosa. Schistocytosis was present. LDH was 10 658 U/l on admission and started to decrease on the second day. CK was 4620 U/l and decreased rapidly. Ceruloplasmin was 61 mg/dl (normal 25–63). The renal lesion is usually an acute tubular necrosis related to direct copper toxicity plus haemoglobin nephrotoxicity and the effects of hypotension. Early death is often related to hypotension, while late death is related to renal and hepatic failure.

In summary, copper sulfate is a readily available agent which has a high mortality rate compared with other heavy metal toxicities. Whole blood copper levels should be drawn. Treatment is primarily supportive but almost always requires chelating agents as well. The most proven methods are dimercaprol and penacillamine, although our case is the second known to us

Table 1. Serum and dialysate copper levels before and after haemodialysis

<table>
<thead>
<tr>
<th>Time</th>
<th>Serum copper</th>
<th>Dialysate copper</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-dialysis (µg/dl)</td>
<td>Post-dialysis (µg/dl)</td>
</tr>
<tr>
<td>Day 1</td>
<td>180</td>
<td>165</td>
</tr>
<tr>
<td>Day 3</td>
<td>165</td>
<td>168</td>
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where EDTA was used with success. Our case with intravenous and subcutaneous injection of copper sulfate illustrates the greater toxicity at lower doses compared with enteral toxicity of copper. With treatment, however, the sequelae were reversible, as with ingestion.

References