Reversible Acute Renal Failure After Colloidal Bismuth Subcitrate Intoxication: Case Report

Kolloidal Bizmut Subsitrat İntoksikasyonu Sonrası Gelişen Geri Dönüşümlü Akut Böbrek Yetmezliği: Olgu Sunumu

ABSTRACT

Bismuth salts are widely used to treat peptic ulcers. Colloidal bismuth subcitrate has been reported in the literature to be nephrotoxic in humans when taken in high doses. In this case report, we present of acute renal failure on account of colloidal bismuth subcitrate overdose in a 23-year-old young woman. In general, acute renal failure after colloidal bismuth subcitrate intoxication is reversible if appropriately managed. Treatment with the chelating agent dimercaptosuccinic acid particularly in combination with hemodialysis is an effective treatment in reducing serum bismuth levels in the patient with acute renal failure.

KEY WORDS: Acute renal failure, Bismuth salt, Hemodialysis, Intoxication, Nephrotoxicity

INTRODUCTION

Bismuth salts, especially colloidal bismuth subcitrate (CBS) and bismuth subsalicylate are commonly used to treat patients with peptic ulcer and non-ulcer dyspepsia (1,2). Toxic effects are rarely seen with the treatment dose of bismuth salts due to the low amounts of absorption from the gastrointestinal tract (3,4). The most common side effects of high dose bismuth intake have been declared as encephalopathy, nephropathy, osteoarthropathy, gingivostomatitis, and colitis. Chronic exposure to high levels of bismuth salts result in encephalopathy, whereas acute toxicity manifests as nephrotoxicity. In a few case reports, acute renal failure (ARF) was described after an overdose of CBS (5,6,7). In this case report, we present a 23-year-old woman with ARF after CBS intoxication.

CASE PRESENTATION

A 23-year-old woman presented to the emergency department of another hospital one hour after taking 40 tablets (De-nol, Zentiva, Kırklareli, Turkey) (12 g) of CBS in a suicide attempt. Each tablet included 300 mg of CBS. There was no medical history of previous intoxication or any other health problems. On admission, the patient was agitated but other physical examination findings were unremarkable. Her blood pressure was 110/60 mm Hg, pulse rate
was 80 beats/minute, respiratory rate was 16 breaths/minute, and body temperature was 36.5°C. Laboratory investigation revealed white blood cell count (WBC) 8.6 x 10^9/L, hemoglobin (Hb) 14.4 g/dL, platelet count (Plt) 263 x 10^9/L, blood urea nitrogen (BUN) 11.6 mg/dL, blood serum creatinine 1 mg/dL, and normal serum levels of electrolytes and liver enzymes. In the emergency department, the patient underwent gastric lavage with administration of activated charcoal and received intravenous fluid therapy. After consultation with the Turkey National Poison Information Center, they started oral treatment with the chelating agent dimercaptosuccinic acid (DMSA, succimer), using the following regimen: 10 mg/kg/dose every 8 hours for 5 days, followed by 10 mg/kg/dose every 12 hours for 14 days. At the end of the third day, her serum BUN and serum creatinine levels increased to 25 mg/dL and 2.6 mg/dL, respectively. Therefore, she was brought to the intensive care unit in our center.

Evaluation at admission observed that the patient’s blood serum creatinine level increased to 4 mg/dL, while BUN was 25 mg/dL. Other laboratory tests were as follows: WBC, 8.8 x 10^9/L; HB, 11.8 g/dL; Plt, 204 x 10^9/L; serum sodium, 137 mEq/L; serum potassium, 3.3 mEq/L; serum calcium, 9 mg/dL; serum phosphorus, 3 mg/dL; serum uric acid, 2.8 mg/dL; serum glucose, 96 mg/dL; serum aspartate aminotransferase, 25 mg/dL. Other laboratory tests were as follows: WBC, 8.8 x 10^9/L; HB, 11.8 g/dL; Plt, 204 x 10^9/L; serum sodium, 137 mEq/L; serum potassium, 3.3 mEq/L; serum calcium, 9 mg/dL; serum phosphorus, 3 mg/dL; serum uric acid, 2.8 mg/dL; serum glucose, 96 mg/dL; serum aspartate aminotransferase, 25 mg/dL; serum alanine aminotransferase, 23 U/L; serum lactate dehydrogenase, 518 U/L. Urinalysis showed a density of 1012, pH of 5.5, protein of 500 mg/dL, glucose of 150 mg/dL, and 2 leukocytes and 2 erythrocytes per high-power field. Arterial blood gases showed metabolic acidosis with pH 7.27, PCO_2 21.8 mmHg, PO_2 130 mmHg, HCO_3^2 12.6 mmol/L, and BE -15 mmol/L. As the patient remained oliguric (<500 ml/day) and had body temperature was 36.5°C. Laboratory investigation revealed white blood cell count (WBC) 8.6 x 10^9/L, hemoglobin (Hb) 14.4 g/dL, platelet count (Plt) 263 x 10^9/L, blood urea nitrogen (BUN) 11.6 mg/dL, blood serum creatinine 1 mg/dL, and normal serum levels of electrolytes and liver enzymes. In the emergency department, the patient underwent gastric lavage with administration of activated charcoal and received intravenous fluid therapy. After consultation with the Turkey National Poison Information Center, they started oral treatment with the chelating agent dimercaptosuccinic acid (DMSA, succimer), using the following regimen: 10 mg/kg/dose every 8 hours for 5 days, followed by 10 mg/kg/dose every 12 hours for 14 days. At the end of the third day, her serum BUN and serum creatinine levels increased to 25 mg/dL and 2.6 mg/dL, respectively. Therefore, she was brought to the intensive care unit in our center.

Erdöğmuş Ş et al: Nephrotoxicity of Colloidal Bismuth Subcitrate

Table 1: The patient’s serum bismuth concentration and renal function parameters at different stages after the overdose of CBS.

<table>
<thead>
<tr>
<th>Day after ingestion</th>
<th>Serum BUN (mg/dL)</th>
<th>Serum creatinine (mg/dL)</th>
<th>Serum bismuth (μg/l)</th>
<th>Urine volume (ml/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>25</td>
<td>4</td>
<td></td>
<td>400</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>4.1</td>
<td></td>
<td>2500</td>
</tr>
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<td>10</td>
<td>17</td>
<td>5.2</td>
<td>69</td>
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<td>11</td>
<td>24</td>
<td>6.7</td>
<td>48</td>
<td>2600</td>
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<tr>
<td>13</td>
<td>21</td>
<td>6.6</td>
<td>36</td>
<td>2300</td>
</tr>
<tr>
<td>19</td>
<td>23</td>
<td>5.6</td>
<td>1.8</td>
<td>2450</td>
</tr>
<tr>
<td>25</td>
<td>15</td>
<td>1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>19</td>
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</table>
bismuth concentration was higher before treatment with hemodialysis and chelation with DMSA.

Hruz and colleagues showed that the treatment with the chelating agent sodium 2,3-dimercapto-1-propanesulfonate (DMPS), which is related structurally to 2,3-dimercapto-1-propanol (dimercaprol), combined with hemodialysis is an effective treatment in reducing the serum bismuth levels (6). In another case report, Cengiz et al (7), tried another metal chelator, penicillamine. DMSA (succimer) is an analogue of dimercaprol and has replaced dimercaprol as one of the main antidotes used in the management of poisoning by lead and other heavy metals. The advantages of succimer are that it is effective by oral administration because of its water-soluble pattern, it is well-tolerated, it has relatively low toxicity, and it can be given at the same time as iron supplements to treat iron deficiency anemia (12). In this regard, a study has shown that both DMSA and DMPS effectively increase the elimination of bismuth in the human urine and both chelators may be of benefit in the treatment of patients with bismuth intoxication (13). In our case, ARF occurred despite starting the treatment with DMSA as a chelating agent at the first day of ingestion. We suggest that early treatment with hemodialysis and DMSA helps to prevent the development of ARF in cases of bismuth overdose.

Leussink et al (14,15) developed a rat model for bismuth-induced reversible nephropathy. Histological examinations showed that the necrosis of the epithelial cells of the S3 segment of the proximal tubule occurs as early as 3 hours after CBS administration and is followed by a similar event in the S1/S2 segment 3–12 hours later. When acute tubular necrosis occurs, this lead to defective reabsorption in the proximal tubule. Acute tubular necrosis was the most encountered pathology in several case reports (11,16). Initially, in our case, we observed findings of proximal tubular dysfunction (Fanconi’s syndrome) such as glucosuria (despite normal blood glucose levels), hypouricemia, hypophosphatemia, and metabolic acidosis. Because of the clear history of heavy metal intoxication and recovery of kidney failure, biopsy was not performed.

In summary, bismuth intoxication is a rare cause of ARF and is usually reversible if appropriately managed. Clinicians should be aware that ARF can occur after bismuth intoxication. Treatment with the chelating agent DMSA combined particularly with hemodialysis is an effective treatment in reducing serum bismuth levels.

REFERENCES