

Milk-Alkali Syndrome: A Forgotten Cause of Metabolic Alkalosis

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Abstract

The milk-alkali syndrome is triad of hypercalcemia, metabolic alkalosis, and acute kidney injury associated with the ingestion of large amounts of calcium and alkali. The syndrome was originally described in association with the use of milk and sodium bicarbonate for the treatment of peptic ulcer disease. Once was a classic cause of hypercalcemia, milk-alkali syndrome is now the third leading cause after hyperparathyroidism and malignancy. This is attributed to the development of proton pump inhibitors, antihistamines, and other modalities of treatment for peptic ulcer disease.

Keywords: Milk alkali syndrome; Hypercalcemia; Metabolic alkalosis

Introduction

Milk-alkali syndrome (MAS) consists of hypercalcemia, various degrees of renal failure, and metabolic alkalosis due to ingestion of large amounts of calcium and absorbable alkali. This syndrome was first identified after medical treatment of peptic ulcer disease with milk and alkali was widely adopted at the beginning of the 20th century. With the introduction of histamine 2 blockers and proton pump inhibitors, the occurrence of MAS became rare; however, a resurgence of MAS has been witnessed because of the wide availability and increasing use of calcium carbonate, mostly for osteoporosis prevention. The aim of this review was to determine the incidence, pathogenesis, histologic findings, diagnosis, and clinical course of MAS [1].

Here we present a case of a 54-year-old male who developed hypercalcemia and metabolic alkalosis after ingesting about 70 tablets of Tums and baking soda over a period of 3 days.

Case Report

A 54-year-old male with a past medical history of heavy alcohol use came to the emergency room complaining of abdominal pain for the past 2 days. The pain was in the epigastrium, and non-radiating. It was associated with nausea and multiple episodes of vomiting, which was non-projectile and non-bloody. On further questioning it was found that the patient was taking a large quantity of Tums and baking soda for the past 3 days for his abdominal pain.

On examination the patient was dehydrated and in distress. Initial pertinent lab findings were blood urea nitrogen (BUN) of 17 mg/dL, creatinine of 1.4 mg/dL, calcium of 13.3 mg/dL, and bicarbonate of 49 mEq/L. Arterial blood gas (ABG) showed a pH of 7.61, pCO₂ of 48 mm Hg, and a pO₂ of 53 mm Hg. UDS results were negative. The patient was placed in ICU due to his severe metabolic derangements and was hydrated with intravenous normal saline. The patient's condition improved after 2 days of aggressive hydration. The follow-up labs showed calcium of 7.6 mg/dL, BUN of 13 mg/dL, creatinine of 0.9 mg/dL, and bicarbonate of 26 mEq/L. He was now comfortable and subsequently discharged with outpatient follow-up.

Discussion

In 1915, Bertram Sippy introduced an antacid regimen designed to neutralize gastric acidity and promote the healing of peptic ulcer disease [2]. The regimen included the hourly administration of milk with Sippy powders (a powder containing 600 mg of magnesium carbonate and 600 mg sodium bicarbonate alternating with a powder containing 600 mg of bismuth carbonate and 1,200 to 1,800 mg of sodium bicarbonate) [2]. In 1936, a report associated hypercalcemia with alkalosis and kidney injury in patients treated with the Sippy regimen [2]. The name MAS was first used by Dr. Fuller Albright [2]. The syndrome was originally described in association with the use of milk and sodium bicarbonate for the treatment of peptic ulcer disease [3].

The most common causes of hypercalcemia are hyperparathyroidism and malignancy [4]. MAS is now considered the third most common cause of hypercalcemia with a prevalence of 9% to 12% among hospitalized patients [5]. With the development of non-absorbable alkali and histamine 2 blockers for treatment of peptic ulcer disease, MAS became a rare cause

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of hypercalcemia; however, with the increased use of over the counter calcium carbonate for dyspepsia and supplementation, there is a revival of MAS [5].

In the era of introduction of antacids, MAS was common in patients with peptic ulcer disease. However, modern era calcium-alkali syndrome is now more common in postmenopausal women, pregnant women, transplant recipients, and dialysis patients [6].

Long-term exposure to high calcium levels can result in nephrocalcinosis, tubular necrosis, and other structural changes. Hypercalcemia produces the following effects in the kidney: 1) vasoconstriction, which decreases the glomerular filtration rate (GFR) [7]; 2) activation of the calcium-sensing receptor in the medullary thick ascending limb, which inhibits the Na-K-2Cl cotransporter causing natriuresis and blockade of antidiuretic hormone (ADH)-dependent water reabsorption in the collecting duct [7].

The calcium-induced diuresis results in volume depletion, which stimulates the renal tubular absorption of bicarbonate. The combined effects of increased alkali intake, volume depletion, and decreased GFR lead to metabolic alkalosis.

Alkalosis may contribute to the maintenance of both volume depletion (by enhancing the activity of the calcium-sensing receptor) and hypercalcemia (by increasing calcium reabsorption in the distal tubule via the pH-sensitive calcium channel, the transient receptor potential vanilloid member 5 (TRPV5)). Volume depletion due to vomiting will also worsen the metabolic derangements [7].

Treatment of MAS consists of withdrawing of the offending agent and hydration with intravenous isotonic saline and furosemide. Usually there is rapid clinical improvement and resolution of the metabolic derangements.

Conclusions

Patients who develop MAS have a good prognosis; however,

they are often misdiagnosed. Detailed medication use history, including over the counter medications, should prevent MAS from escaping detection. MAS almost never results in death, but a significant number of patients may be left with permanent renal impairment, in the form of chronic renal disease. Clinicians should be vigilant about MAS, a once common condition, which is now reemerging. Misdiagnosis can lead to invasive investigations and long-term morbidity.

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