Milk alkali syndrome: a case of hypercalcemia and acute kidney injury in a previously healthy patient

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Abstract

A previously healthy male presented to the Emergency Department complaining of a three-day history of generalized weakness, fatigue, and nausea. Further investigation into his medical history revealed chronic “reflux,” which he treated with over-the-counter high-dose Tums chewable tablets as needed. The patient endorsed taking at least six to eight tablets per day, often up to 12-15 per day, for the past several months. Laboratory evaluation revealed hypercalcemia to 14.8mg/dL and acute kidney injury with a blood urea nitrogen of 54 mg/dL and creatinine of 6.36 mg/dL. Patient was admitted for intravenous hydration and evaluation by nephrology.

Milk-alkali syndrome is becoming increasingly common as calcium supplementation is easily found over-the-counter, viewed by most as benign with minimal to no side effects, and does not require monitoring by a physician. Many individuals may choose to self-treat heartburn or osteoporosis by taking calcium supplementation without the realization that an overdose of calcium can have serious side effects. Clinically it is important to keep in mind that a conversation about the risks of calcium supplementation may be indicated for certain patients, including those with concerns of osteoporosis or heartburn.

Introduction

We present a case of milk-alkali syndrome, a triad of hypercalcemia, acute kidney injury, and metabolic alkalosis, which recently has emerged as a cause for up to 12 percent of hypercalcemia cases. While throughout the 1980’s-90’s considered a diagnosis of the past, there has more recently been a continual increase in the incidence of milk-alkali syndrome likely due to the easy access and widespread us of calcium carbonate as an antacid and in the prevention and treatment of osteoporosis. It is apparent in this case that the patient’s prolonged excess
intake of the calcium carbonate preparation Tums could likely be the etiology of his acute kidney injury and hypercalcemia found in his lab work. The clinical presentation of milk-alkali syndrome may range from an asymptomatic incidental finding, to acute symptoms such as nausea, vomiting, weakness, altered mental status, and psychosis. Chronic milk alkali syndrome, also known as Burnett’s syndrome, may present with polyuria, polydipsia, myalgias, and pruritis.¹

**Presentation**

A 64-year-old male presented to the Emergency Department with chief complaint of a three-week history of progressively worsening generalized weakness and fatigue. Associated symptoms included progressively worsening heartburn with decreased appetite and nausea. He had been treating his heartburn with over-the-counter Tums as needed. The patient reported a history of gastroesophageal reflux disease and over the past several months had been taking six to eight tablets of Tums per day for symptomatic control, more recently at least 12 tablets per day. He denied any other past medical or surgical history and did not take any other medications. No known allergies to medications. On review of systems the patient endorsed intermittent low-grade fevers and pruritis, and denied any unintentional weight loss, night sweats, abdominal pain, changes in urine output, back pain, cold sensitivity, or any other acute symptoms.

Vital signs revealed elevated blood pressure to 158/98, tachycardia at 106 beats per minute, 20 respirations per minute, oxygen saturation of 97% on room air, temperature of 36.8 degrees Celsius, and body mass index (BMI) of 25.24. Physical exam otherwise grossly normal. Patient well-appearing, alert, and conversive. Head atraumatic and normocephalic with extraocular movements intact, pupils equal, round, and reactive to light, and no scleral icterus or injection. Oropharynx non-injected and mucous membranes pink and slightly dry. No
thyromegaly, nodules, or lymphadenopathy. Lungs clear to auscultation in all fields bilaterally with no wheezes, crackles, or rhonchi. Tachycardia but regular rhythm with no murmurs, rubs, or gallops. Abdomen soft and non-tender with no masses. Pulses 2+ and symmetric with no pedal edema. No paraspinal tenderness, tissue texture changes, Chapman’s points, or CVA tenderness. Skin warm and dry with no rashes or jaundice. Cranial nerves II-XII grossly intact; strength 5/5 in the bilateral upper and lower extremities.

EKG showed sinus tachycardia of 100 beats per minute with first degree AV block. Complete blood count (CBC) within normal limits. Comprehensive metabolic panel with blood urea nitrogen (BUN) elevated to 54, creatinine (Cr) elevated to 6.36, BUN:Cr of 8.5, calcium elevated to 14.8, albumin low to 3.2, and corrected calcium of 15.44; all other values within normal limits. Troponin, chest x-ray, and non-contrast CT of the chest, abdomen, and pelvis within normal limits. Retroperitoneal ultrasound showed a left renal cyst but otherwise unremarkable with no hydronephrosis.

Patient was diagnosed with acute kidney injury and hypercalcemia most likely secondary to a subacute milk-alkali syndrome due to excessive antacid ingestion. He was admitted to telemetry for continuous monitoring, intravenous hydration with isotonic saline, and nephrology consultation. Following three days of hospitalization and conservative management by nephrology including continued IV hydration, patient was discharged home with renal function returned to his baseline.

Discussion

This case demonstrates that excessive intake of calcium carbonate preparations may lead to a hypercalcemia that triggers the development of further metabolic derangement including metabolic alkalosis.\textsuperscript{1,2,3} Hypercalcemia also causes a decrease in glomerular filtration rate
secondary to vasoconstriction, natriuresis secondary to the activation of the Na-K-2Cl co-transporter of the thick ascending limb of the renal medulla, and blockage of water reabsorption in the antidiuretic hormone-dependent collecting duct. These factors together create a state of hypovolemia, further exacerbating the alkalemia and eventuating in acute kidney injury, thus establishing the triad of milk-alkali syndrome.

Milk-alkali syndrome diagnosis is based on a thorough history, elimination of other causes of hypercalcemia and renal failure, and laboratory evaluation displaying the classic triad: metabolic acidosis (alkalemia on arterial blood gas and increase in bicarbonate), hypercalcemia (serum calcium greater than 10.5mg/dL), and acute kidney injury (increase in serum creatinine of at least 0.3mg/dL or 1.5-fold from baseline). Diagnostic evaluation may be augmented by osteopathic findings such as an anterior or posterior Chapman’s point or a viscerosomatic reflex in the paraspinal musculature of T9-L1, any of which could indicate renal pathology.

Differential diagnosis for milk alkali syndrome is essentially similar to a hypercalcemia differential, including hyperthyroidism, hyperparathyroidism, hypophosphatasia, familial or acquired hypocalciuric hypercalcemia, malignancy, multiple myeloma, PTHrP-releasing paraneoplastic syndrome, vitamin D excess, and lithium. In fact, essential to the diagnosis of milk alkali syndrome is first ruling these other causes of hypercalcemia.

Treatment for milk alkali syndrome includes discontinuation of calcium bicarbonate and the administration of isotonic saline and furosemide. Typically, there is rapid improvement in both the patient’s clinical appearance and in their hypercalcemia and metabolic alkalosis with this therapy regimen alone. It is important to note that while calcitonin and/or bisphosphonates are often used to treat other forms of hypercalcemia, they should be avoided in milk alkali syndrome. This is because the cessation of calcium carbonate intake equates to the immediate
and permanent removal of the hypercalcemic stimulus; conversely, in other etiologies there is a hypercalcemic nidus that must be suppressed acutely by calcitonin and chronically by bisphosphonates to achieve reduction in serum calcium.\textsuperscript{1} Thus, while beneficial in most etiologies of hypercalcemia, treatment with calcitonin or a bisphosphate could quickly push a milk-alkali patient into hypocalcemia.

With the ever-increasing number of patients utilizing over-the-counter calcium carbonate as calcium supplementation or treatment of heartburn, it is important to keep milk-alkali syndrome in the differential when a patient presents with hypercalcemia, particularly because the treatment of hypercalcemia in milk-alkali syndrome differs from that of other etiologies. In addition, the other derangements of this syndrome including metabolic alkalosis and acute kidney injury could have severe and life-long consequences if not identified and treated quickly and appropriately.

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References


