

CLINICAL VIGNETTE

Milk-Alkali Syndrome

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Introduction

Milk-alkali syndrome is caused by excessive ingestion of calcium and a base alkaline agent, usually in the form of milk and antacids. It was first described in the 1920's with the advent of a novel treatment for peptic ulcer disease, the Sippy regimen, which involved milk, bicarbonate, and calcium carbonate.¹

Today, due to the availability of over the counter antacid medications, more cases have been reported.^{2,3} Recent studies suggest that milk-alkali syndrome is the third most common cause of hospital admissions for hypercalcemia behind malignancy and hyperparathyroidism.⁴ The syndrome is characterized by hypercalcemia, metabolic alkalosis, and renal failure. The severity can range from mild gastrointestinal disturbance to death. Milk-alkali syndrome should be considered in all patients who present with hypercalcemia.

Case Report

A 67-year-old male with a history of congestive heart failure, hypertension, and gastroesophageal reflux disease presented to Internal Medicine clinic with concerns for 5 months of altered bowel habits. He has noted alternating constipation and diarrhea and admitted to fatigue, polydipsia, polyuria, and nocturia. He denied any nausea, vomiting, abdominal pain, or weight loss. The patient's daily medications included furosemide 40mg, isosorbide mononitrate 20mg twice daily, Lisinopril 20mg, and atorvastatin 10mg. The patient was known to ingest large amounts of over the counter calcium carbonate (equal to 5gm calcium carbonate per day) for indigestion. His social history was significant for rare alcohol use and no tobacco history. Physical examination revealed blood pressure to be 188/104mmHG, pulse 120/min, Temp 98.6°F, and respirations 16/min with O2 sat 98% on RA. EKG revealed a shortened QT and sinus tachycardia. He appeared dehydrated with pale skin and poor hygiene. The patient was transported via EMS to local ED. He was given 10mg labetalol for hypertension and started on aggressive intravenous fluid hydration.

Significant laboratory results included calcium of 15.3 mg/dL, bicarbonate 45mmol/L, BUN 55mg/dL, creatinine 5.4mg/dL, chloride 83mmol/L, and WBC of 18.6 x10E3/uL. ABG revealed a pH of 7.54, PCO2 of 58mmHG, and pO2 of 60mmHG. Parathyroid hormone was undetectable with normal TSH. Liver function, lipase, and coagulations profile were

normal. Chest x-ray showed questionable infiltrate in the right lower lung. Aggressive IV fluids continued in conjunction with IV magnesium, alendronate, and antibiotics for presumed pneumonia.

The patient was hospitalized for a total of 6 days. Once renal function normalized he underwent a malignancy work up with chest and abdominal CT, bone scan, normal prostate exam, PSA, and SPEP/UPEP. He had undergone colonoscopy screening within the year, which was normal. Upon discharge, blood values showed calcium of 8.3mg/dL, bicarbonate 21mmol/L, BUN 19 mg/dL, Creatinine 1.4mg/dL, and WBC 9x10E3/uL. He was placed on pantoprazole for reflux and given instruction to avoid over-the-counter, calcium-based antacids.

Discussion

Milk-alkali syndrome is a hypercalcemic disorder initially described in association with excessive consumption of milk and sodium bicarbonate for the treatment of peptic ulcer disease (Sippy diet).

The syndrome became rare after the introduction of H2 blockers and proton pump inhibitors. Recent data, however, suggests a rising incidence of milk-alkali syndrome as a cause of severe hypercalcemia, probably as a result of increasing use of medications containing calcium carbonate⁵⁻⁹ (over-the-counter antacids and calcium supplementation for osteoporosis prophylaxis or treatment) Other risk factors include hypertension, use of diuretics, chronic kidney disease, osteoporosis, and upper gastrointestinal disease. Excessive calcium carbonate intake is thought to be greater than 4g of calcium carbonate daily; however cases have been reported with doses as low as 2g /day.¹⁰ The diagnosis is based on a history of ingestion of calcium rich compounds, biochemical findings of hypercalcemia, metabolic alkalosis, and renal insufficiency. Exclusion of other causes, the most common being malignancy and primary hyperparathyroidism, must also be considered. Rarer causes include thyrotoxicosis, Addison's disease and sarcoidosis. Management of the syndrome should include correction of the volume depletion, which by itself may correct the majority of metabolic derangements. A bisphosphonate may be added but can take 24-48 hours to take effect and thus are not to be used as first line agents for emergent cases. If a bisphosphonate is chosen, close

observation is warranted to avoid developing hypocalcemia. Calcitriol may decrease calcium levels in as little as 2 hours when used IM or SQ making it better suited in these cases. Once properly hydrated, consideration towards adding a loop diuretic such as furosemide can promote calciuresis.

Early diagnosis and treatment of hypercalcemia is associated with favorable outcomes. A careful history of drug use should always be taken from patients who present with hypercalcemia and confirmed with family or caregivers.

Conclusion

Milk-alkali syndrome can be a difficult diagnosis that requires a high index of suspicion in order to quickly identify the disorder and initiate appropriate therapy. As a common cause of hypercalcemia, it is important for clinicians to keep the syndrome on their list of differential diagnosis.

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