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MILK-ALKALI-INDUCED PANCREATITIS IN A CHRONICALLY HYPOCALCEMIC PATIENT WITH DIGEORGE SYNDROME

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☐ **Abstract—Background: Pancreatitis is a common diagnosis in the emergency department (ED), and milk-alkali syndrome (MAS) is an uncommon etiology for pancreatitis. MAS is caused by increased calcium and alkali ingestion, causing hypercalcemia accompanied by metabolic alkalosis and renal failure. Once considered rare, MAS is an increasingly common cause of hypercalcemia. Awareness of the resurgence of this syndrome is important for emergency physicians when recalling the causes of renal failure and pancreatitis. We present a case of pancreatitis and acute renal failure (ARF) in a chronically hypocalcemic DiGeorge syndrome patient, resulting from hypercalcemia secondary to excessive ingestion of calcium carbonate tablets. Case Report: A patient with DiGeorge syndrome and chronic abdominal pain due to gastroesophageal reflux disease (GERD) presented to our ED for severe abdominal pain. He reported nausea and vomiting, as well as epigastric pain that seemed worse than his typical pain. Laboratory evaluation revealed pancreatitis and ARF, although the patient had no prior history of these conditions. Upon further questioning, his mother divulged that the patient had been taking large quantities of calcium carbonate tablets for his worsening GERD symptoms. The patient was admitted to the intensive care unit where his pancreatitis and ARF eventually resolved as his calcium levels returned to his baseline. Why Should an Emergency Physician Be Aware of This?: MAS is a relatively uncommon diagnosis, but can lead to serious sequelae such as pancreatitis and ARF. Questioning the patient about calcium ingestion is an important facet to the diagnosis and work-up of pancreatitis and ARF. Recognition of this etiology can improve patient outcomes and prevent recurrences.** © **2015 Elsevier Inc.**

☐ **Keywords—milk-alkali syndrome; pancreatitis; hypercalcemia; hypocalcemia; acute renal failure; calcium carbonate; DiGeorge syndrome**

INTRODUCTION

Milk-alkali syndrome (MAS) is a condition caused by excessive ingestion of calcium and alkali products, causing the classic triad of hypercalcemia, metabolic alkalosis, and acute renal failure (ARF). Once considered uncommon, MAS is increasingly recognized as a major cause of hypercalcemia, with some suggesting that it is the third most common etiology of hypercalcemia (1–3). Although pancreatitis is a fairly common emergency department (ED) presentation and hypercalcemia is a well-known cause, there are few reports of pancreatitis caused by MAS. Here we present the case of a chronically hypocalcemic patient with DiGeorge syndrome who presented to our ED with hypercalcemia-induced pancreatitis, secondary to MAS. To our knowledge, this is the third reported case of acute pancreatitis secondary to MAS, and the first reported in a patient with congenital hypocalcemia.

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CASE REPORT

A 28-year-old man with a medical history of DiGeorge syndrome, gastroesophageal reflux disease (GERD), Nissen fundoplication, tetralogy of Fallot repair, and esophageal dysphagia with stricture presented to the ED in June 2013 with a chief complaint of epigastric pain, nausea, and vomiting. He had been seen in our ED on numerous occasions for epigastric pain related to his esophageal stricture and had undergone several esophageal dilation procedures, with the most recent having been 6 weeks prior. He denied other symptoms, including hematemesis, and reported the nausea was not associated with oral intake. Home medications included ondansetron, docusate sodium, nortriptyline, polyethylene glycol, sucralfate, esomeprazole, aluminum hydroxide-magnesium hydroxide-viscous lidocaine-dicyclomine combination, and calcium carbonate. His mother reported that the symptoms started 2 days prior and that he had been taking many more calcium carbonate tablets than his usual dose of 1000 mg four times daily.

On examination, he was in moderate distress due to epigastric pain. Initial vital signs were blood pressure 136/87 mm Hg, pulse 88 beats/min, respirations 18 breaths/min, temperature 36.1°C, and oxygen saturation 98% on room air. His abdomen was diffusely tender to palpation, worse in the epigastric region, and without rigidity or rebound tenderness. His baseline 4/6 holosystolic murmur was noted and the remainder of the physical examination was unremarkable. A normal saline intravenous bolus (1 L) was started and the patient given 4 mg of ondansetron and 4 mg of morphine for symptom control. Abdominal and chest radiographs were unremarkable and without signs of pneumoperitoneum or intestinal obstruction. Hemoglobin was 9.8 g/dL, consistent with his baseline chronic anemia, and the remainder of the complete blood count was otherwise unremarkable. The complete metabolic panel was significant for severe hypercalcemia and signs of ARF (Table 1). Lipase was elevated as well, at 1600 U/L (normal range 14–51 U/L).

The patient was admitted to the adult progressive care unit, where he was started on calcitonin twice daily, continuous normal saline infusion, and given a single dose of pamidronate. All calcium supplementation was ceased. His hospitalization included consultations with Gastroenterology, Nephrology, Urology, and Hematology. A retroperitoneal ultrasound was performed that revealed right-sided hydronephrosis, and a subsequent nuclear medicine flow study showed right-sided partial obstruction secondary to intrarenal calcifications. To assess for other causes of his hypercalcemia, parathyroid hormone (PTH) and 1,25-dihydroxycholecalciferol (1,25[OH]2D) levels were obtained, and were low-normal and low at 15 pg/mL (normal range 12–88 pg/mL), and 11 ng/mL (normal range 30–200 ng/mL), respectively. Over the next several days, the patient's abdominal pain, nausea, and vomiting resolved. He underwent repeat esophageal dilation for his chronic esophageal stricture. His calcium levels returned to his hypocalcemic baseline, his renal function returned to normal, and he was discharged to home on day 11 to follow up with Urology for a planned pyeloplasty.

Table 1. Complete Metabolic Panel

Component	Normal Range	Values
AST	15–41 U/L	15
ALT	17–63 U/L	11
Alkaline phosphatase	32–91 U/L	76
Total bilirubin	0.3–1.2 mg/dL	0.9
Calcium	8.9–10.3 mg/dL	18.2
Total protein	5.9–7.5 g/dL	7.0
Albumin	3.4–4.7 g/dL	3.8
Glucose	70–125 mg/dL	138
BUN	6–20 mg/dL	31
Creatinine	0.64–1.27 mg/dL	3.13
Sodium	136–145 mmol/L	137
Potassium	3.6–5.1 mmol/L	3.1
Chloride	101–111 mmol/L	96
Osmolality	275–295 mOsm/kg	283
CO_2	22–32 mmol/L	34
GFR	> 59	24

AST = aspartate transaminase; ALT = alanine transaminase; BUN = blood urea nitrogen; GFR = glomerular filtration rate.

DISCUSSION

First described in 1923 by Hardt and Rivers, MAS is a condition caused by supratherapeutic ingestion of calcium and alkali (4). They attributed MAS to the Sippy regimen, which was developed in 1915 as one of the first treatments for peptic ulcer disease and consisted of the hourly consumption of milk, cream, and a mixture of alkaline powders (5). Prior to the advent of H2 blockers and proton pump inhibitors, the mainstay of peptic ulcer treatment was the administration of milk and bicarbonate. The introduction of H2 blockers heralded a decline in the incidence of MAS and by the mid-1980s, MAS was considered uncommon (1,2). The reason is unclear, but MAS has made a resurgence in the literature and is now thought to be a more common etiology for hypercalcemia than accounted for (1–3,6). Several studies have attempted to discern the prevalence of MAS. Beall and Scofield found that 7 of 100 patients hospitalized for hypercalcemia had MAS, and with a prevalence of 12%, determined that MAS was the third leading cause of hypercalcemia in hospitalized patients (1). An additional study also established MAS as the third leading cause of hypercalcemia in hospitalized patients, as well as the second leading cause of severe hypercalcemia (2). It is also possible that public awareness regarding osteoporosis prevention