Case report

Severe hypercalcaemia due to household cleaner ingestion

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SUMMARY

We report the case of a 59-year-old man with a history of type 2 diabetes, hypertension and chronic kidney disease who presented with symptomatic severe hypercalcaemia (calcium 15.8 mg/dL) and acute kidney injury. Evaluation revealed that the hypercalcaemia was not mediated by parathyroid hormone (PTH), PTH-related peptide or 1,25-hydroxyvitamin D. Adrenal insufficiency was subsequently diagnosed and was initially thought to be the aetiology of the hypercalcaemia. He was treated with intravenous fluid, pamidronate and started on hydrocortisone with resolution of his hypercalcaemia. Over the next several months, despite adherence to hydrocortisone therapy, the patient continued to have recurrent severe hypercalcaemia requiring hospitalisation. Additional laboratory evaluation showed similar results to the initial evaluation. On further questioning, the patient admitted to routinely ingesting the household cleaning product Comet, which contains a large amount of calcium. Psychiatric assessment confirmed the diagnosis of pica. The patient eventually discontinued ingestion of Comet with resolution of his hypercalcaemia.

BACKGROUND

Ingestion of calcium-containing products is traditionally believed to be a rare cause of hypercalcaemia; however, more recent studies suggest that excess calcium ingestion may be the second-most frequent cause of severe hypercalcaemia in hospitalised patient.¹ Although the use of calcium-containing antacids has declined over the years, excess consumption of other products with high calcium content, such as calcium carbonate for osteoporosis prevention, chronic gastritis or chronic kidney disease (CKD), continue to be reported as causes of hypercalcaemia.^{2,3} We describe a case of chronic ingestion of the household cleaning product Comet that led to severe hypercalcaemia.

CASE PRESENTATION

A 59-year-old man presented to the emergency room with nausea, vomiting, headache, fatigue and generalised weakness beginning the day prior to presentation. His medical history was significant for CKD stage III, hypertension, type 2 diabetes, hyperlipidaemia, gastro-oesophageal reflux disease and migraine headaches for which he took losartan, amlodipine, furosemide, atorvastatin, ranitidine, omeprazole and amitriptyline. He denied the use of over-the-counter medication, such as vitamin D,

calcium, non-steroidal anti-inflammatory drug or antacids. The patient also denied a prior history of psychiatric disorders.

On arrival to the emergency room, the patient was hypotensive and tachycardic, which resolved after 2 L of normal saline. On examination, the patient was ill-appearing and showed generalised muscle weakness, but was alert and oriented to time, place and self. Mild gait imbalance and speech slurring were noted. The remainder of the physical examination was unremarkable. The patient underwent a head CT scan which did not reveal any acute intracranial pathology.

Initial laboratory evaluation showed severe hypercalcaemia (serum calcium 15.8 mg/dL), acute kidney injury (serum creatinine 6.01 mg/dL) and metabolic alkalosis (venous CO₂ 37 mmol/L). Intact parathyroid hormone (PTH) level was low normal (8 pg/mL). Hypokalaemia and hypomagnesaemia were also present (table 1). Of note, although the patient was not aware of a previous history of hypercalcaemia, chart review revealed intermittent hypercalcaemia over the past 3 years with previous evaluations consistent with non-PTH-mediated hypercalcaemia with normal 25-hydroxyvitamin D, PTH-related peptide, thyroid-stimulating hormone and serum/urine protein electrophoresis. The patient's previous complete blood count revealed microcytic anaemia with elevated red cell distribution weight and total iron-binding capacity consistent with iron-deficiency anaemia.

He was treated initially with a 2L intravenous bolus of normal saline which was followed by normal saline intravenous infusion at 200 mL/hour resulting in improvement of calcium to 9.7 mg/dL. On discontinuation of the saline infusion, his calcium level increased again to 12.1 mg/dL; thus, pamidronate 30 mg was given intravenously. Pamidronate was used instead of zoledronic acid due to the patient's low GFR. The patient's hypercalcaemia, acute renal failure, metabolic alkalosis and other electrolyte abnormalities subsequently resolved. His presenting symptoms of weakness, headache, nausea, speech slurring and gait imbalance resolved with improvement in calcium level.

INVESTIGATIONS

Further inpatient workup of the patient's PTH-independent hypercalcaemia, including tests for hyperthyroidism, vitamin A intoxication, HIV and multiple myeloma, was negative. Age-appropriate malignancy workup, with CT scans of the chest,

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Table 1 Laboratory evaluation on presentation

Laboratory evaluation	Value	Reference range
Sodium (mmol/L)	139	136–145
Potassium (mmol/L)	2.9	3.5–5.1
Chloride (mmol/L)	89	98–107
CO ₂ (mmol/L)	37	21–30
Glucose (mg/dL)	106	70–99
Creatinine (mg/dL)	6.01	0.66–1.25
BUN (mg/dL)	27	9–20
Magnesium (mg/dL)	1.4	1.6–2.6
Phosphorus (mg/dL)	3.4	2.5–4.5
Calcium (mg/dL)	15.8	8.6–10.2
Albumin (g/dL)	4.6	3.5–5.2
PTH-intact (pg/mL)	8	8–54
PTHrP (pg/mL)	20	14–27
1,25-OH vitamin D (pg/mL)	<5.0	19.9–79.3
TSH (mIU/L)	1.44	0.47–4.68

BUN, blood urea nitrogen; GFR, glomerular filtration rate; OH, hydroxy; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related protein; TSH, thyroid-stimulating hormone.

abdomen and pelvis, as well as bone scintigraphy, and prostate-specific antigen level were also unremarkable. Evaluation for 1,25-hydroxyvitamin D-mediated hypercalcaemia from sarcoidosis and other granulomatous disease was unremarkable. Cosyntropin stimulation test to evaluate for adrenal insufficiency, an uncommon cause of hypercalcaemia, was performed. The results showed an inadequate increase of serum cortisol with a 60 min postcosyntropin of 16.6 µg/dL (normal >18 µg/dL). The patient was discharged on a weight-based maintenance dose of hydrocortisone.

OUTCOME AND FOLLOW-UP

The patient was readmitted to the hospital 3 months later with recurrence of hypercalcaemia (serum calcium 18.5 mg/dL), acute renal failure and metabolic alkalosis despite compliance with hydrocortisone for his adrenal insufficiency. Workup for hypercalcaemia was repeated and was still consistent with PTH-independent hypercalcaemia, with normal level of PTH-related peptide and 1,25-hydroxyvitamin D. Evaluation for rare causes of hypercalcaemia, such as acromegaly and pheochromocytoma, was also negative. He was treated with normal saline, subcutaneous calcitonin and intravenous zoledronic acid with improvement of symptoms and calcium level.

As the workup for the patient's PTH-independent hypercalcaemia was unrevealing, a thorough medical history was repeated and the patient subsequently admitted that he was consuming the household cleaning product, Comet, on a daily basis. He consumed up to two 21 oz. cans of Comet per week. As Comet cleaner contains 60%–100% calcium carbonate,⁴ the patient was consuming 102–170 g of calcium carbonate daily,

which is significantly above the recommended 1 g of calcium daily.² The patient was diagnosed with pica by psychiatry and admitted to the psychiatric unit after hypercalcaemia improved due to concerns for a lack of insight and compulsive self-harming behaviour. In the 12 months since discharge, the patient continues to be asymptomatic with complete resolution of his initial symptoms. The patient denies consumption of Comet and his calcium level continues to be within normal limits without further treatment.

DISCUSSION

Toxicity due to ingestion of calcium-containing products was first described in 1923 with the use of a calcium-containing and alkaline-containing solution known as the Sippy regimen for the treatment of peptic ulcer disease.⁵ The syndrome of hypercalcaemia, metabolic alkalosis and renal failure were subsequently characterised as the major laboratory findings seen in patients with prolonged ingestion of calcium-containing and alkaline-containing solutions.⁶

Despite the decreasing use of calcium-containing and alkaline-containing solutions for the treatment of peptic ulcer disease, hypercalcaemia due to calcium-containing product ingestion for other indications, such as osteoporosis prevention and phosphate binder, continues to be reported. A 2005 study¹ evaluated the aetiology of hypercalcaemia in 611 hospitalised patients whose admission or discharge diagnosis had hypercalcaemia or related diagnosis documented. After excluding renal transplant, CKD stage 5 and patients who were admitted for elective parathyroidectomy, 125 patients were confirmed to have hypercalcaemia in which 8.8% were attributed to milk-alkali syndrome from calcium carbonate use. The concomitant use of medications, such as thiazide and vitamin D preparations, is frequently reported to cause or worsen hypercalcaemia in combination with calcium carbonate preparations.^{7,8}

Several other substance ingestions have been associated with hypercalcaemia. These include nicotine-replacement gum, carbonated water, enteric feeding formula, commercial moisture absorber, hot packs, liquid calcium fertiliser, oyster shell powder used with betel nuts and massive quantities of cheese.^{3,9–13} The amount of calcium ingested and peak serum calcium level of these cases are presented in table 2. Our case is the first to describe a patient with pica developing severe hypercalcaemia due to household cleaner ingestion.

Hypercalcaemia due to ingestion of calcium-containing substances has also been reported in patients with eating disorders, such as pica. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, defined pica as the persistent eating of non-nutritive, non-food substances. The eating of non-nutritive, non-food substance has to last for at least 1 month, is inappropriate to the individual's level of mental development and is not part of a culturally supported practice.¹⁴

Table 2 Case reports on uncommon calcium-containing substance ingestion

References	Type and amount of ingested substance	Amount of calcium ingested	Peak serum calcium
Swanson <i>et al</i> ⁹	30 pieces of nicotine-substitute gum daily >3 L of carbonated water daily	2.8 g per day for several years 0.48 g per day for several years	17.7 mg/dL
Kleinig and Torpy ¹⁰	Enteric tube feeding (Nutrison Energy, Nutricia, Macquarie Park, Australia)	2.1 g per day for 12 days	1.78 mmol/L (ionised Ca)
Cho <i>et al</i> ¹¹	300 mL of commercial moisture absorber	300 g as a single ingestion	20.7 mg/dL
Padmanabhan <i>et al</i> ¹²	Three commercial instant hot packs	90%–97% calcium carbonate as a single ingestion	21.1 mg/dL
Kim <i>et al</i> ¹³	250 mL of liquid calcium fertiliser	237 g of calcium carbonate as a single ingestion	20.5 mg/dL

The prevalence of pica in the general population is unclear. A recent meta-analysis that evaluated the prevalence of pica in the pregnant and post-partum population found that the heterogeneity among studies is high, ranging from 1.7% to 92.5%, suggesting multiple factors, such as geographic region and education level, may be associated with the differences in prevalence in these studies.^{14 15}

The diagnosis of hypercalcaemia due to ingestion of calcium-containing products is challenging. Picosol *et al*¹ reported that in the inpatient setting, less than half of these cases were accurately diagnosed as milk-alkali syndrome, indicating that this condition is often misdiagnosed. The misleading name of milk-alkali syndrome may incorrectly lead clinicians to believe that co-ingestion of milk needs to be present in a patient's history to establish the diagnosis. Furthermore, this condition along with a broad range of disorders, including adrenal insufficiency, PTH-related peptide and 1,25-hydroxyvitamin D-mediated hypercalcaemia, and malignancy-related hypercalcaemia, are all classified as non-PTH-mediated hypercalcaemia, thus making an accurate diagnosis is more challenging. Performing a thorough history, including patient's diet history, prescription and over-the-counter medication use, as well as presence of an eating disorder, such as pica, is important to establish an accurate diagnosis.^{2 16}

Learning points

- Hypercalcaemia due to ingestion of calcium-containing products is a common yet underdiagnosed cause of severe hypercalcaemia.
- Ingestion of calcium-containing products, such as household cleaners, should be suspected in patients with non-parathyroid hormone-mediated hypercalcaemia.
- A thorough history including dietary intake and a complete medication reconciliation should be performed especially in populations at risk for pica, such as those with iron-deficiency anaemia, pregnancy or chronic dialysis.

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