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Case Report

CASE REPORT

Famotidine induced hypomagnesemia leading to hypocalcemia

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Abstract

Fifty-five-year-old female with a past medical history of gastroesophageal reflux disease was admitted to hospital due to increased confusion, and muscle cramps for last 15 days. She was taking famotidine 20 mg twice a day for the last 2 years. She was alert and oriented to person and place only. She had dry skin, positive Chvostek's and Trousseau's sign. Blood work showed 141 mmol/L of sodium, 0.7 mg/dl of creatinine, 5.7 mg/dl of calcium, 0.55 mg/dl of magnesium, low PTH but normal parathyroid related peptide PTHrP, vitamin D (25) and vitamin D (1.25). She was discharged home on electrolyte supplements. She was readmitted with very low calcium and magnesium. Extensive workup including 24 h of urine calcium and magnesium was unimpressive. She was treated with IV therapy and discharged to follow up with nephrology in the clinic, and famotidine was discontinued on second discharge. Her calcium and magnesium levels remained normal, and in a few weeks later, oral electrolyte supplements were discontinued.

INTRODUCTION

Famotidine is a long-acting histamine H2 receptor antagonist that is indicated for the treatment of gastroesophageal reflux disease (GERD), peptic ulcer disease and Zollinger–Ellison syndrome [1]. It is considered to have an excellent safety profile with only a few side effects like constipation, diarrhea and headache. There have been multiple documented cases of proton pump inhibitor-induced hypomagnesemia, but this is the first case of famotidine-induced hypomagnesemia.

CASE REPORT

A 55-year-old female with a past medical history of GERD was admitted to hospital due to increased lethargy, confusion, and muscle cramps for last 15 days. These muscle cramps affected functions of her hands and legs, causing multiple falls. She was not on any medication except famotidine 20 mg twice a day which she was taking for the last two years. She denied nausea, vomiting, diarrhea, and urinary incontinence. Her oral intake was good. Her vital signs were stable. On examination, she was alert and oriented to person and place but not time. She had dry skin, positive Chvostek's, and Trousseau's sign. Initial blood work showed sodium 141 mmol/L, BUN 13 mg/dL, creatinine 0.7 mg/dL, calcium 5.7 mg/dL, magnesium 0.55 mg/dL, phosphorus 3.4 mg/dL, albumin 3.9 g/dL, AST 17 U/L, ALT 12 U/L, alkaline phosphatase 60 U/L, INR 0.8 and bilirubin 0.6 mg/dL. She was treated with multiple doses of intravenous (IV) 2 g magnesium sulfate and 1 g of calcium gluconate.

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Further work showed low PTH but normal PTHrP, vitamin D (25) and vitamin D (1.25). Her calcium (9.5 mg/dl) and magnesium (2.1 mg/dl) level normalized with IV therapy, so she was discharged home on oral electrolyte supplements. She was supposed to follow up with her family doctor in 4 weeks after discharge, but she developed increased lethargy and muscle cramps 2 weeks after discharge; so, she saw her family doctor. Her blood work showed 6.8 mg/dl of calcium and 0.9 mg/dl of magnesium; so, she was directed to the hospital for admission.

She denied missing her calcium and magnesium capsules. Her oral intake was good, and no nausea, vomiting and diarrhea were reported. She had extensive workup including 24 h of urine calcium and magnesium, which was unimpressive. She was suspected to have famotidine-induced hypomagnesemia leading to hypocalcemia. She was treated with IV therapy and discharged to follow-up with nephrology in the clinic with a repeat blood work in 1.0 week. Her famotidine was discontinued on discharge.

She followed up with a nephrologist in 1.0 week and family doctor in 4 weeks, and her calcium and magnesium levels remained normal. Her oral electrolyte supplements were ultimately discontinued.

DISCUSSION

Hypomagnesemia usually presents with neuromuscular disturbances, ventricular arrhythmias, unexplained hypocalcemia and refractory hypokalemia. Hypomagnesemia is induced due to renal or gastrointestinal losses.

Gastrointestinal causes leading to hypomagnesemia include acute or chronic diarrhea, steatorrhea, malabsorption and small bowel bypass surgery [2]. Hypomagnesemia can also be seen in acute pancreatitis due to saponification of magnesium and calcium in necrotic fat [3]. Hypomagnesemia has been described with the chronic use of proton pump inhibitors (PPIs) likely due to impaired intestinal absorption [4–6]. Urinary magnesium loss can be caused by alcohol use [7], diuretics, uncontrolled diabetes mellitus [8–9] and familial renal magnesium wasting, such as with Gitelman syndrome.

Serum calcium is regulated by the coordinated actions of activated vitamin D and PTH [10]. Common causes of hypocalcemia include hypoalbuminemia, hypomagnesemia, hyperphosphatemia, PTH resistance and parathyroid gland destruction. Rare causes include acquired and/or familial autoimmune disorders (such as in polyglandular autoimmune disorder type 1).

Our patient had low calcium level, low PTH and magnesium level. Work up of hypocalcemia showed a normal level of serum albumin, vitamin D (25), vitamin D (1.25), creatinine and phosphorus ruling out PTH resistances, vitamin D deficiency and chronic kidney disease. Low calcium and low PTH are seen in three disorders like hypomagnesemia, hypoparathyroidism and activating mutation calcium-sensing receptor. Hypoparathyroidism and activating mutation calcium-sensing receptor cause high phosphorus and normal magnesium levels. Hypomagnesemia causes normal phosphorus and low magnesium levels, so proving hypomagnesemia as the cause of hypocalcemia in this patient.

In hypomagnesemia workup, she had no alcohol intake history, no acute or chronic diarrhea, gastric surgery, pancreatitis, diuretic use and diabetes mellitus. The 24-h urine magnesium level was normal, ruling out familial renal magnesium wasting. She was taking famotidine for the last 2 years, and stopping it improved her calcium and magnesium levels indicating famotidine as the likely cause of hypomagnesemia. Famotidine is metabolized in the liver (some studies quote 30–35%), and the rest is excreted unchanged via the kidneys. She had no renal or liver disorder to decrease famotidine clearance leading to build-up of the toxic level of famotidine causing complication. It was unclear why she suddenly developed hypomagnesemia after being on famotidine for 2 years. There has been no other case report document; so, it is an area of further research.

Hypomagnesemia is often associated with hypokalemia (due to urinary potassium wasting) and hypocalcemia (due both to lower parathyroid hormone secretion and end-organ resistance to its effect).

The exact underlying pathogenesis for famotidine-induced hypomagnesemia is not unclear, but it could be related to impaired magnesium absorption due to low gastric acid production. Treatment involves stopping the medication. This patient was admitted for the first time with hypocalcemia and hypomagnesemia, but famotidine was continued at the time of discharge. Famotidine was discontinued on second discharge, and ultimately her electrolytes improved.

This is the first reported case of famotidine-induced hypomagnesemia and functional hypoparathyroidism causing hypocalcemia. Famotidine might cause impaired absorption of magnesium, leading to hypomagnesemia and functional hypoparathyroidism. Patients being started on a H2 receptor antagonist for the long-term course should have a baseline serum calcium and magnesium levels and periodic monitoring as well. The optimal timing for monitoring levels is unknown, but annual monitoring (sooner if the patient develops symptoms) may be reasonable. Long-term use of famotidine should be considered in the differential diagnosis for hypomagnesemia and hypocalcemia.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

This is a case report, so no ethical approval is needed.

CONSENT

Written consent was obtained from the patient.

GUARANTOR

Rajesh Essrani MD.
No figure included.

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