Hypermagnesaemia causing mesenteric ischaemia and small bowel infarction

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SUMMARY

We present a case of mesenteric ischaemia caused by hypermagnesaemia after ingestion of a large oral dose of magnesium citrate, which resulted in smooth muscle relaxation, hypotension and bowel infarction. The patient had a history of chronic bowel dysmotility and renal impairment. On operative exploration, the bowel was noted to have a distinct pattern of ischaemia along its antimesenteric border. Small bowel resection was performed, and the patient was left in discontinuity, with definitive repair and anastomosis performed 24 hours later. The patient's magnesium level was 8.39 mg/dL, which was treated with intermittent haemodialysis and eventually normalised over several sessions. Our patient recovered and was discharged after a month-long hospitalisation. She returned shortly after with respiratory failure and died. On review of the literature, we identified similar cases and present a pathophysiological mechanism of hypermagnesaemia causing mesenteric ischaemia, consistent between our cases and those already reported.

BACKGROUND

Magnesium-containing bowel laxatives are widely used for patients with constipation. These are generally not taken in excess by patients; however, when large doses of oral magnesium are ingested, patients are at risk for developing hypermagnesaemia and its clinical sequelae.[1–4] Overall, the incidence of hypermagnesaemia is rare. The cause of hypermagnesaemia is multifactorial, but seems to be more common in patients with impaired bowel motility and can be further exacerbated in patients with existing renal disease, who have more difficulty clearing large doses.[5–7] The symptoms of hypermagnesaemia are widely described and can range from cardiovascular complications, such as arrhythmia and hypotension to neurological dysfunction, and even cardiopulmonary arrest and coma. These are summarised in table 1 for reference.[3 7–9] Given the large number of patients who use magnesium-containing laxatives, and the potential risk for these serious complications, understanding the consequences of hypermagnesaemia is of utmost importance.[8 9]

Currently, there are few reported cases of hypermagnesaemia causing mesenteric ischaemia, and there are even fewer reports of cases that required surgical management.[1–3 10] There is currently no data indicating whether magnesium-containing laxatives are correlated with the need for surgical intervention in a dose-dependent manner. Due to the common use of magnesium-containing laxatives, this potential complication warrants report and discussion so it can be more readily identified in patients. Hypermagnesaemia appears to be seen most often in the elderly, those with delayed bowel transit and those with renal impairment.[2 3 5] The current literature has focused on treating the underlying hypermagnesaemia with intravenous fluid infusion, loop diuretics or haemodialysis.[1–8] Delving deeper into this topic should give opportunities to identify this outcome in future patients and manage it appropriately. The effects of different serum levels of magnesium are outlined below in table 2.[3 11]

We present a case of hypermagnesaemia-induced mesenteric ischaemia which resulted in bowel perforation and required emergent surgery. We propose a mechanism for hypermagnesaemia-induced mesenteric ischaemia and discuss this complication as it pertains to our patient with renal compromise.

CASE PRESENTATION

The patient was a 74-year-old woman who was brought to the emergency department of a secondary care centre overnight with altered mental status and in respiratory distress. Her family reported that she had abdominal pain and nausea/vomiting for 3 days prior to presentation. Medical history was notable for hypertension, chronic kidney disease (with most recent baseline serum creatinine of 1.3 mg/dL), degenerative lumbar disease, chronic obstructive pulmonary disease and coronary artery disease. Prior to her acute illness, she had experienced 3 months of significant constipation, which her primary physician had been working up as an outpatient. Her home bowel regimen consisted of regular fleet enema and oral polyethylene glycol. On the day prior to admission, the patient had ingested three bottles of magnesium citrate, each 1.735 g in 300 mL solution.

INVESTIGATIONS

Her abdominal examination was notable for distention and diffuse tenderness with guarding. Her respiratory status worsened, and she was intubated in the emergency department. Vital signs on presentation were notable for a heart rate of 129 beats/min, 22 respirations/min and blood pressure 91/76 mm Hg, with a per cent oxygen saturation in the 80s. Blood work was notable for a white cell count of 20.3 × 10^9/L with bandaemia and neutrophilia, haemoglobin level of 198 g/L and platelet count of 198 × 10^9/L. Chemistry panel was notable for a serum creatinine of 2.42 mg/dL (glomerular filtration rate 20), aspartate aminotransferase 185 U/L,

Table 1 Symptoms of hypermagnesaemia[3 7–9]

Neuromuscular	Confusion
	Lethargy
	Respiratory depression
	Absent tendon reflexes
	Bladder paralysis
	Muscle weakness/paralysis
Cardiovascular	Hypotension
	Bradycardia
	Inhibition of atrioventricular/interventricular conduction
	Heart block
	Cardiac arrest
	Ventricular arrhythmia
Gastrointestinal	Paralytic ileus
	Nausea/vomiting
Electrolyte abnormalities	Hyperkalaemia
	Hypocalcaemia

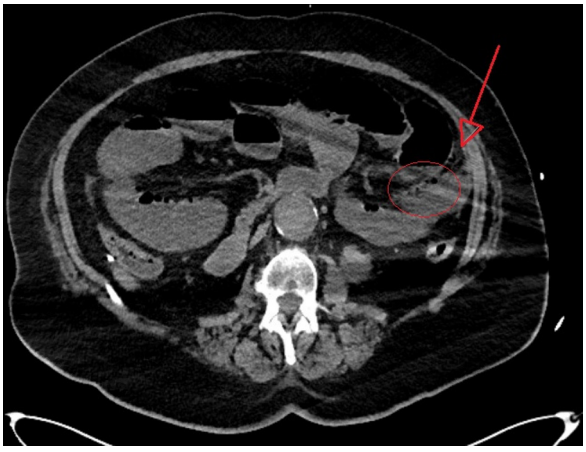

Figure 1 Selected axial CT image demonstrating mesenteric oedema (arrow) and pneumatosis intestinalis in thickened bowel wall (circle) consistent with ischaemic bowel in the left upper abdomen.

alanine aminotransferase 161 U/L and a lactate of 6.5 mmol/L. Serum calcium level was 8.1 mg/dL. Arterial blood gas showed a pH 7.33 and lactate 6.5 mmol/L. CT of the abdomen and pelvis without contrast was performed and was notable for diffuse dilation of the small bowel, with pneumatosis intestinalis and mesenteric oedema identified in a segment of bowel in the left hemiabdomen. Figure 1 demonstrates these findings. These findings were consistent with mesenteric ischaemia and the patient was taken emergently to the operating room for exploratory laparotomy.

TREATMENT

The patient was taken emergently to the operating room. On entry into the abdomen, frank purulence was encountered. Cultures of this fluid were sent and would later grow *Klebsiella pneumoniae*, *Escherichia coli* and *Clostridium perfringens*. The bowel was inspected and approximately 30 cm of midjejunum was noted to be grossly necrotic, with worsened ischaemia noted along the antimesenteric border. This was transected, and due to the patient's tenuous haemodynamic status, the patient was left in discontinuity, closed and transported to the intensive care unit for resuscitation. She was taken back to the operating room 24 hours later for a second-look laparotomy. At that time, an additional 3 cm of bowel at the transected edge was noted to be ischaemic and was transected. A primary anastomosis was performed, and the patient's abdomen was closed and she was returned to the intensive care unit for further resuscitation.

Serum magnesium level was not checked until routine blood work in the morning following the first operation, and at that time it was 8.39 mg/dL (3.45 mmol/L). Phosphorus was also noted to be elevated at 6.5 mg/dL. Sodium, potassium, chloride and bicarbonate levels were all within normal limits. It was at this time that the patient's family reported her excess intake of magnesium citrate. Intermittent haemodialysis was started via a temporary dialysis catheter. The patient's hypotension, initially present on arrival, was responsive to moderate doses of norepinephrine drip. This pressor requirement would continue until after the patient's first dialysis session. Haemodialysis was performed daily for 2 days until serum magnesium concentration fell below 4 mg/dL, and then proceeded on an every-other-day cycle. Serum magnesium levels would finally return to reference levels by hospital day 13, after several sessions of dialysis. Calcium gluconate was not used as an adjunct treatment for this patient's hypomagnesaemia due to her satisfactory response to intermittent haemodialysis. The patient remained oliguric after the initial physiological insult and would continue dialysis after discharge. The patient developed a prolonged ileus, likely due to a combination of smooth muscle dysfunction from the hypermagnesaemia, as well as a postoperative ileus.

The patient's hospital course was relatively complicated with several further interventions and transfers between the critical care unit and step-down unit, likely due to the physiological insult of her presentation in an already comorbid patient. Non-ST elevation myocardial infarction was found on hospital day 2, with troponin rising to 4.57 ng/mL; cardiac catheterisation did not demonstrate any obstructive lesions and she was treated medically. Large volume of coffee ground fluid was evacuated from her nasogastric tube, and oesophagogastroduodenoscopy did not identify any definitive bleeding.

Table 2 Common symptoms of hypermagnesaemia by serum concentration[3 11]

Serum magnesium	Symptoms
<4 mg/dL	Asymptomatic
4–8 mg/dL	Nausea, vomiting, bradycardia and hypotension
8.5–12 mg/dL	Somnolence, loss of deep tendon reflexes and QT prolongation
>12 mg/dL	Muscle paralysis, complete atrioventricular block, lethargy and decreased breathing rate. Coma and cardiorespiratory arrest at values above 15 mg/dL

OUTCOME AND FOLLOW-UP

The patient would ultimately be discharged from the hospital to a skilled nursing facility. However, she returned less than a week later in respiratory distress due to aspiration pneumonia, requiring intubation. Though she was able to be extubated, her mental status did not meaningfully recover following this physiological insult, and her family ultimately decided for her to be transitioned to comfort care; she would expire shortly thereafter.

DISCUSSION

In this report, we have presented a case of hypermagnesaemia causing mesenteric ischaemia. Prior to presentation, the patient had consumed a large dose of magnesium citrate as an attempted laxative. The diagnosis of mesenteric ischaemia was supported

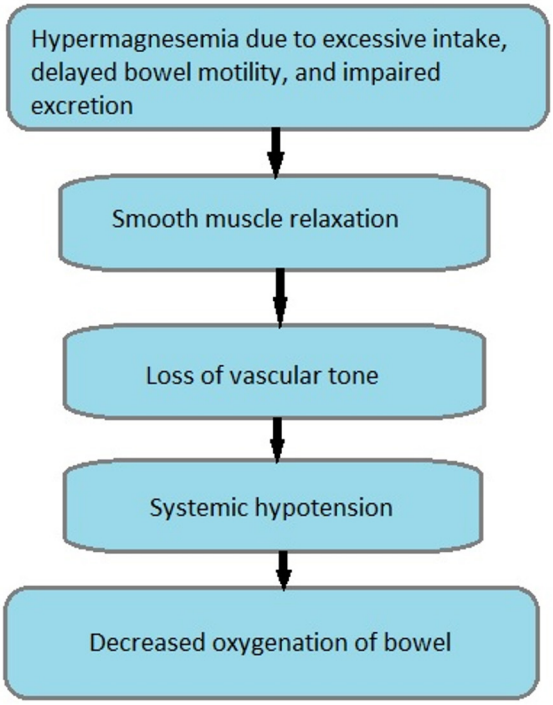

Figure 2 Flow chart demonstrating proposed mechanism for hypermagnesaemia causing mesenteric ischaemia.

by the patient's CT scan, elevated lactic acid level and peritoneal abdomen on examination. After thorough review of the literature, there appears to be a logical pathophysiological mechanism.[1–7 10] Underlying bowel dysmotility serves as the precipitant cause of excess magnesium absorption,[1 4 6 10] such as our patient's chronic constipation. Her renal disease caused a decrease in urinary magnesium excretion and clearance.[2 5–7 12 13] This combination of factors facilitated the accumulation of magnesium in her serum. The hypermagnesaemia caused relaxation of smooth muscle in the vessel walls, with resultant vasodilation and hypotension. This then led to a low-flow state in the bowel mesentery and a non-occlusive mesenteric ischaemia (figure 2). The unique pattern of bowel ischaemia noted on operative exploration along the antimesenteric border supports this, as the antimesenteric border is a natural watershed area in the blood supply to the bowel. The timing of vasopressor requirements further supports this theory. After the patient was started on dialysis, and the serum magnesium began to be cleared, she was able to be weaned off vasopressors.

Yamaguchi *et al* describe a similar mechanism in a case series published recently, which we agree with and provide an additional case to support this pathophysiological mechanism.[3] Their study demonstrated hypermagnesaemia in patients with both mild and severely impaired renal function combined with impaired bowel motility. Their patient with the most pronounced hypermagnesaemia (14.28 mg/dL) presented with severe hypotension (78 mm Hg systolic) and with evidence of acute mesenteric ischaemia. The authors describe a mechanism of hypermagnesaemia causing bowel ischaemia: bowel dysmotility or chronic constipation causes increased passive absorption of magnesium, which then induces smooth muscle relaxation and hypotension. Three of their four patients had renal impairment, suggesting that while bowel dysmotility is the primary risk factor for hypermagnesaemia, renal impairment may cause further elevations in serum magnesium. Yoon *et al* reported a case of a patient who developed ischaemic colitis and perforation, again in a patient with acutely worsened chronic constipation, renal insufficiency and excess magnesium ingestion.[5] Their patient presented with normal blood pressure, a mildly elevated serum magnesium (3.0 mg/dL) and without evidence of bowel ischaemia. However, the patient's magnesium level climbed to 6.0 mg/dL on hospital day 3, at which point she developed hypotension and signs of intestinal ischaemia. The findings in these cases form a growing body of evidence that hypermagnesaemia secondary to magnesium laxatives can cause non-occlusive mesenteric ischaemia, potentially resulting in perforation and requiring surgical intervention.

The key limitation of this issue is the rare nature of the problem discussed. Few patients were identified in the literature who required operative intervention with resection of ischaemic bowel. However, hypermagnesaemia is a well-documented issue and we feel that our review of its pathophysiological effects is a complete one. We are confident in our proposed mechanism of bowel ischaemia due to hypermagnesaemia, which agrees with those previously proposed. Laboratory bench studies may be able to confirm our suspicion, or a cross-sectional review for all patients with hypermagnesaemia. Future study may also determine if there is a larger prevalence of this pathology than previously thought, and when it is optimal to choose surgical management versus more conservative medical therapy.

Learning points

- Excessive oral intake of magnesium-containing laxatives can result in hypermagnesaemia, especially in patients with pre-existing renal compromise.
- In elderly patients with delayed bowel transit and renal insufficiency, it is important to limit doses of magnesium and quickly identify the symptoms of hypermagnesaemia.
- Familiarity with the sequelae of hypermagnesaemia is important and our report will help facilitate identification and treatment going forward.
- Mesenteric ischaemia may be induced by hypermagnesaemia, potentially due to smooth muscle relaxation resulting in loss of vascular tone which, in turn, causes systemic hypotension and decreased oxygenation of the bowel.
- The ischaemia develops along the antimesenteric border, suggesting a low-flow state, and that this may also have a propensity to occur at watershed areas of the bowel.

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