Case Report

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Fatal Hypermagnesemia in Patients Taking Magnesium Hydroxide

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Hypermagnesemia is a rare but potentially fatal electrolyte disorder often overlooked because of its unfamiliarity. Magnesium is regulated through a balance of bone, intestinal absorption, and renal excretion. Hypermagnesemia typically arises from excessive magnesium intake or reduced renal excretion; however, it also occurs in patients with normal kidney function. Herein, we report two cases of hypermagnesemia in patients taking magnesium hydroxide for constipation. The first case involved an 82-year-old woman with end-stage renal disease who developed metabolic encephalopathy due to hypermagnesemia, after taking 3,000 mg of magnesium hydroxide daily for constipation. Her magnesium level was 9.9 mg/dL. Her treatment involved discontinuing magnesium hydroxide and continuing hemodialysis, which led to her recovery. In the second case, a 50-year-old woman with a history of cerebral hemorrhage and mental retardation developed hypermagnesemia despite having normal renal function. She was also taking magnesium hydroxide for constipation, and her magnesium level was 11.0 mg/dL. She experienced cardiac arrest while preparing for continuous renal replacement therapy (CRRT). After achieving return of spontaneous circulation, CRRT was initiated, and her magnesium level showed a decreasing trend. However, vital signs and lactate levels did not recover, leading to death. These cases highlight the importance of prompt diagnosis and intervention for hypermagnesemia and the need to regularly monitor magnesium levels in individuals receiving magnesium-containing preparations, especially those with impaired kidney function.

Key Words: Hypermagnesemia, Magnesium hydroxide, Chronic kidney disease, End stage renal disease

INTRODUCTION

Hypermagnesemia is a rare electrolyte disorder that has received little attention recently. This condition arises when the balance between bone and intestinal absorption and renal excretion of magnesium, similar to that of calcium and phosphorus, is disrupted[1]. Hypermagnesemia typically occurs iatrogenically due to excessive oral or intravenous magnesium intake, especially when renal function is compromised, thereby reducing magnesium excretion[2,3].

The symptoms of hypermagnesemia may vary widely, from nausea and vomiting to altered mental status, hypotension, and hypoventilation. In some cases, it may be fatal[4]. Diagnosis is usually based on laboratory findings during the evaluation process rather than on suspected symptoms.

Treatment strategies include hydration, loop diuretics, hemodialysis, and calcium administration[5]. This paper presents the cases of two patients who were admitted to the hospital with altered mental status and subsequently diagnosed with hypermagnesemia. Both patients had a history

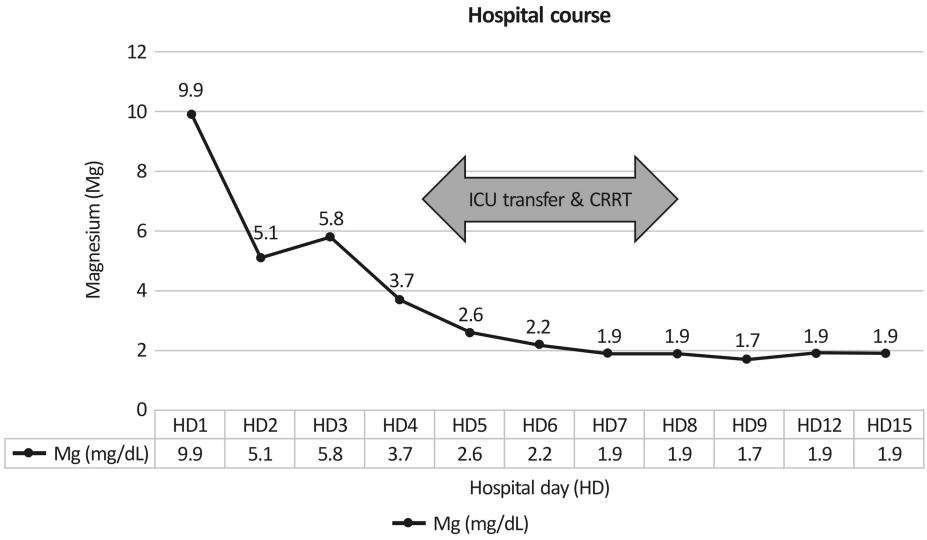

Fig. 1. Changes in magnesium levels during the hospitalization period.

of magnesium-containing laxative use.

CASE REPORT

Case 1.

An 82-year-old woman was transferred to our hospital due to an altered mental status that occurred 4 hours previously. She had undergone hemodialysis for end-stage renal disease and had a medical history of hypertension, diabetes mellitus, and percutaneous coronary intervention. She had constipation and was taking 3,000 mg of magnesium hydroxide daily for 2 weeks. Her vital signs were stable; however, she presented with stuporous mental status, and we conducted a neurological evaluation. Brain computed tomography (CT), electroencephalography, and cerebrospinal fluid examination showed no specific findings; brain magnetic resonance imaging (MRI) showed small chronic infarctions in the right frontal lobe, thalamus, occipital lobes, and cerebellar hemispheres but these were not associated with decreased consciousness. The laboratory test results were as follows: white blood cell count, 11,200/mm^3; hemoglobin, 14.8 g/dL; platelet count, 145,000/mm^3; blood urea nitrogen, 51.8 mg/dL; serum creatinine, 4.24 mg/dL; sodium, 147 mEq/L; potassium, 4.8 mEq/L; calcium, 9.9 mg/dL; and magnesium, 9.9 mg/dL. Based on these results, we concluded that the metabolic encephalopathy was due to hypermag- nesemia.

We immediately discontinued magnesium hydroxide, performed hemodialysis daily, and monitored magnesium levels. By the 4th day of hospitalization, the magnesium level had decreased to 3.5 mg/dL, and mental status had improved to drowsy. However, the blood pressure decreased to 72/44 mmHg due to septic shock. Consequently, she was promptly transferred to the intensive care unit (ICU), and continuous renal replacement therapy (CRRT) was initiated. The patient's blood pressure was restored through antibiotic treatment for pneumonia and Clostridium difficile infection. Her magnesium level improved to 1.9 mg/dL (Fig. 1), leading to a significant improvement in her consciousness, reaching an alert state. The patient was discharged from the hospital on the 16th day after admission.

Case 2.

A 50-year-old woman was admitted to the hospital with complaints of continuous vomiting and loss of consciousness that occurred 2 hours previously. She had a history of cerebral hemorrhage 2 years before presentation and mental retardation. She resided in a nursing home for care.

The patient was taking magnesium hydroxide for constipation; however, the exact dose was unknown. The initial blood pressure was 80/40 mmHg; heart rate was 124 beats/min; respiratory rate was 24 breaths/min; and oxygen satu-

ration was 74%. The patient was in a stuporous mental state, and intubation was immediately performed. The laboratory test results were as follows: white blood cell count, 8,800/mm^3; hemoglobin, 14.3 g/dL; platelet count, 128,000/mm^3; blood urea nitrogen, 19.9 mg/dL; serum creatinine, 1.07 mg/dL; sodium, 136 mEq/L; potassium, 3.9 mEq/L; total calcium, 9.5 mg/dL; magnesium, 11.0 mg/dL; lactate, 8.49 mmol/L; pH 7.201; and HCO_3- 15.9 mmol/L. Brain CT and brain MRI were performed to evaluate the patient's level of consciousness, and no significant findings were revealed. Abdominal CT revealed fecal impaction and diffuse colorectal dilatation (Fig. 2). Despite a normal renal function, the findings indicated impaired magnesium excretion and enhanced magnesium absorption, raising the possibility of hypermagnesemia. The patient was admitted to the ICU scheduled to undergo CRRT. However, a cardiac arrest occurred during the initiation of CRRT, requiring cardiopulmonary resuscitation (CPR). Return of spontaneous circulation was achieved, and CRRT was subsequently initiated. While the magnesium levels showed improvement, reaching 3.3 mg/dL (Fig. 3), blood pressure did not recover, lactate levels continued to increase, and the patient eventually died.

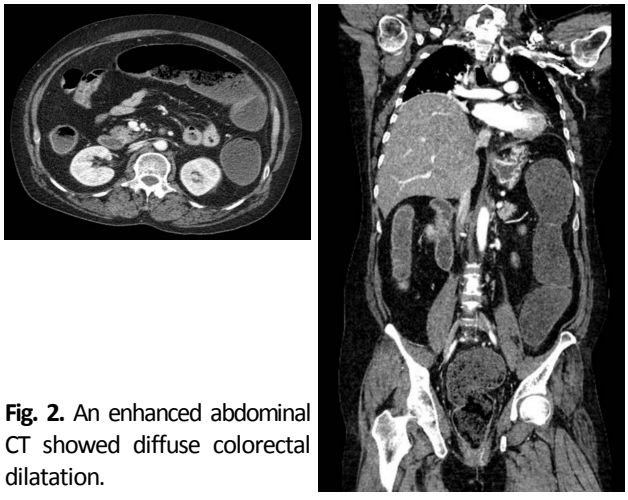

Fig. 2. An enhanced abdominal CT showed diffuse colorectal dilatation.

DISCUSSION

Magnesium is the fourth most abundant cation in the body[6] and is vital for numerous biological processes. Its balance is maintained through bone storage, intestinal absorption, and renal excretion. Disruption of magnesium balance may lead to hypermagnesemia, a rare but potentially fatal condition. Magnesium predominantly exists intracellularly within the bone, muscle, and soft tissue[1]. Approximately 50-60% of magnesium is sequestered in the bone as hydroxyapatite crystal[7]. Only a small fraction of magnesium is stored in the extracellular compartment, approximately 60% of which exists in the biologically active, free form[8]. The normal serum magnesium concentration is 1.7-2.4 mg/dL[6]. Magnesium plays a crucial role in preserving the normal

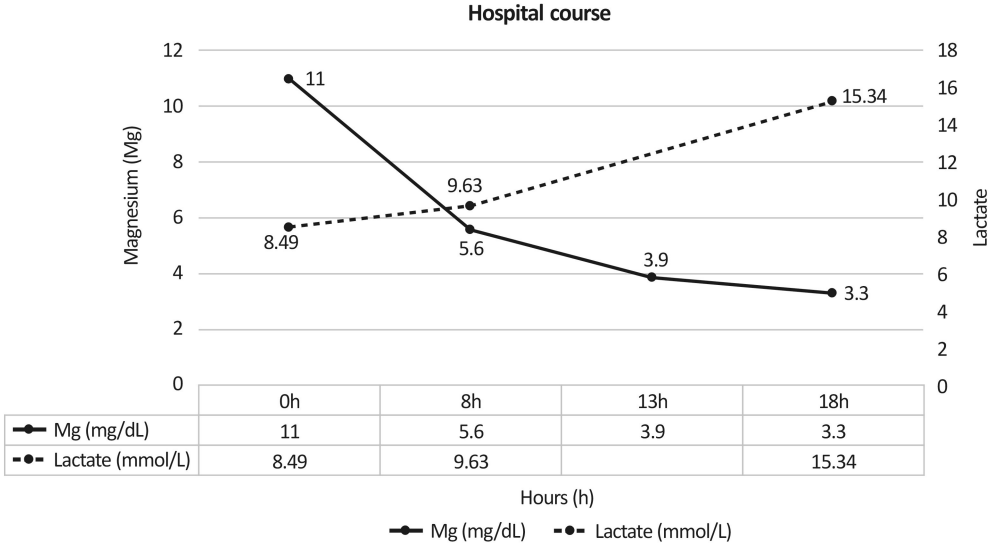

Fig. 3. Changes in magnesium and lactate levels during the hospitalization period.

Table 1. Case reports of hypermagnesemia

	Patient information	Symptoms & Signs	Peak Mg level (mg/dL)	Cause	Treatment	Outcome
Yamaguchi et al.[2]	88-year-old female	Appetite loss, progressive general weakness	6.9	Magnesium oxide in a patient with chronic kidney disease	Hydration, IV loop diuretics, IV Ca gluconate	Survived
	95-year-old female	Altered mental state	6.1	Magnesium oxide in a patient with chronic kidney disease	Hydration, IV loop diuretics	Survived
	87-year-old female	Appetite loss, lethargy	7.6	Magnesium oxide in a patient with chronic kidney disease	Hydration	Survived
	66-year-old female	Altered mental state, hypotension	11.9	Magnesium oxide in a patient with acute colonic ischemia and intestinal perforation	Hydration (Refuse invasive therapy, hemodialysis)	Died
Ishida et al.[14]	56-year-old female	Vomiting, abdomen distension → Altered mental state, hypotension	13.5	Magnesium oxide intake in a patient with intestinal obstruction	Hydration, IV loop diuretics, IV calcium	Survived
Bokhari et al.[15]	53-year-old female	Altered mental state, hypotension, respiratory distress	10.8	Magnesium oxide and magnesium citrate intake in a patient with prolonged colonic retention	Hemodialysis	Died
Weng et al.[16]	72-year-old female	Altered mental state, general weakness → cardiac, respiratory arrest	6.2	Magnesium oxide intake in a patient with chronic constipation and prolonged colonic retention	Hemodialysis, IV calcium, GI decontamination (lactulose, Fleet enema)	Died
Sawalha et al.[17]	73-year-old male	Flaccid paralysis, respiratory distress	9.2	Magnesium citrate and Maalox intake in a patient with pyloric perforation which allowed for increased uptake of magnesium through the inflamed peritoneum	Hydration, IV loop diuretics, Hemodialysis	Survived
Premkumar et al.[18]	42-year-old male	Respiratory distress	8.9 (3.66 mmol/L)	Post-bypass ventricular tachyarrhythmia treated with 1 g IV magnesium sulphate, following earlier 2 g dose post-cross clamp release	Hydration IV loop diuretics IV Ca gluconate Hemodialysis	Survived
Case 1	82-year-old female	Altered mental state	9.9	Excessive magnesium hydroxide intake in ESRD patient	Hemodialysis	Survived
Case 2	50-year-old female	Altered mental state, vomiting, hypotension, respiratory distress → cardiac, respiratory arrest	11.0	Magnesium hydroxide intake in a patient with prolonged gastrointestinal transit time	Hemodialysis	Died

Abbreviations: Mg, magnesium; GI, gastrointestinal; Ca, calcium; ESRD, end stage renal disease

functioning of various biological processes, including protein synthesis, DNA and RNA synthesis, energy production, cardiovascular, and neuromuscular system functioning, and bone formation[9].

Magnesium is predominantly absorbed in the small intestine, particularly in the distal parts of the jejunum and ileum, whereas a portion is absorbed through the large intestine[7]. In general, magnesium is absorbed via the passive paracellular pathway, and the amount absorbed increases with increasing intake concentrations. The transcellular active pathway for magnesium absorption occurs through the transient receptor potential melastatin (TRPM) channels, TRPM6 and TRPM7. However, even with increased magnesium intake, absorption does not occur beyond a certain threshold concentration[9,10].

While the reabsorption of calcium and phosphorus primarily occurs in the proximal convoluted tubule, magnesium reabsorption occurs significantly (40-70%) in the thick

ascending limb of Henle[7,11]. Reabsorption generally occurs via the paracellular pathway, facilitated by tight junctions composed mainly of claudins 16 and 19[12]. Approximately 10-30% of magnesium is reabsorbed through the paracellular pathway in the proximal tubule. The remaining 5-10% is reabsorbed in the distal convoluted tubule predominantly through active transport mediated by TRPM6/7[13]. Hypermagnesemia may occur when this balance is disrupted, such as during increased intake or impaired intestinal elimination, leading to increased absorption or reduced excretion from the kidneys.

In the present cases, both patients developed hypermagnesemia owing to the intake of magnesium-containing laxatives. The first patient was undergoing dialysis and the administration of magnesium hydroxide was initiated for the first time. Typically, magnesium hydroxide is used up to a maximum of 2,000 mg daily. However, this patient consumed 3,000 mg daily for 2 weeks. Given the compromised renal excretion in dialysis patients, it is believed that the extended and excessive use of magnesium hydroxide led to the development of hypermagnesemia. In the second case, the patient was presumed to have been on continuous magnesium hydroxide therapy, but hypermagnesemia occurred despite a relatively preserved renal function, possibly due to a prolonged gastrointestinal transit time, leading to increased absorption. Table 1 summarizes other case reports of hypermagnesemia.

When magnesium levels increase above 5 mg/dL, symptoms such as nausea, vomiting, and dizziness may occur. When magnesium levels exceed 9 mg/dL, deep tendon reflexes diminish, and manifestations may progress to bradycardia, hypotension, hypoventilation, mental changes, respiratory arrest, and even cardiac arrest[14,15]. In the first case, although the other vital signs were stable, there was a change in consciousness. In the second case, the patient experienced hypotension, respiratory failure, and altered consciousness, leading to cardiac arrest during the planned CRRT procedure. Eventually, the magnesium levels showed a downward trend, but the patient succumbed to lactic acidosis and deceased. This highlights the potentially fatal nature of hypermagnesemia and emphasizes the importance of prompt diagnosis and intervention.

The treatment of hypermagnesemia depends on kidney dysfunction and symptom severity. It includes discontinuing causative medications, promoting magnesium excretion through hydration and loop diuretics, or dialysis in severe cases[14]. Calcium administration is necessary to address symptoms, such as hypotension, respiratory depression, and arrhythmias. Caution must be exercised during intermittent hemodialysis to prevent rebound hypermagnesemia. In these situations, CRRT may be beneficial[15]. In the present cases, as both patients had impaired kidney function and severe symptoms, dialysis was performed for both.

In conclusion, although uncommon, hypermagnesemia may be fatal, emphasizing the importance of an early diagnosis and prompt intervention. Regular monitoring of magnesium levels is crucial in patients receiving magnesium-containing preparations, especially in those with impaired kidney function.

Disclosure

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