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Case Report

Acute Cardiovascular Collapse Following Glycerin Retention Enema

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Introduction

Magnesium (Mg^{2+}) is second abundant intracellular cation. It is crucial in maintaining cell viability and involved in regulation of multiple enzymes function, nucleic acid synthesis and energy production [1,2]. Hypermagnesemia is a potentially lethal electrolyte abnormality but has long been considered to be rare. With the increasing use of magnesium in diverse clinical conditions including preeclampsia/eclampisa, arrhythmia, severe acute asthma, migraine, constipation or dyspepsia, the prevalence of hypomagnesemia could possibly be underestimated. It may be caused by that serum Mg^{2+} level is not routinely measured in most cases especially in patients without advanced renal failure in light of high efficacy of renal Mg^{2+} excretion. The delay in the recognition of hypermagnesemia may result in a poor outcome and even mortality. Herein, we presented a case with normal renal function who developed lethal hypermagnesemia following 5-day use of oral magnesium oxide.

Case Presentation

A 59-year-old male presented to the emergency department with worsening abdominal bloating for 2 days. He had a history of diabetes mellitus, hypertension and stroke with residual left hemiparesis on regular medications of sitagliptin and amlodipine. Since he was severely constipated with no defecation, 1500 mg of magnesium oxide daily was consumed for 5 days. On arrival, his blood pressure was 118/70 mmHg, pulse rate 89/minute, respiratory rate 20/minute and body temperature 36.3℃. Physical examinations showed reduced bowel movement and his abdomen being apparently distended, tympanic, diffusely tender with no shifting dullness, rebound tenderness or muscle guarding. The rest of physical examinations were unremarkable. Laboratory investigations demonstrated only mild anemia (Hemoglobin 11.3 g/dL) and his serum biochemistries were within the reference range (Table 1). Plain abdominal radiography demonstrated marked and diffuse dilatation of large intestinal loops with fecal impaction. Computed tomography revealed no abdominal emergencies such as intussusception or hollow organ perforation. Therefore, 20-minute retention glycerin enema was undergone twice with intravenous saline administration but minimal amount of stool was defecated.

Item	Unit	Reference	Admission	12 hours	15 hours	25 hours
Hb	g/dL	14-18	11.3			
WBC	10^3/μL	4-10	9.08			
Platelet	10^3/μL	130-400	178			
BUN	mg/dL	8-25	25	38	42	
Cr	mg/dL	0.63-1.3	1.28	1.98	1.85	
eGFR	mL/min		57.3	38	42	
Na^+	mmol/L	135-145	129	132	133	133
K^+	mmol/L	3.5-5.3	4.3	3.3		3.6
Ca^{2+}	mg/dL	8.5-10	8.5	8.5	8.3	8.8
Phosphate	mg/dL	2.5-4.5	3.2			5.2
Mg^{2+}	mg/dL	1.6-2.3	2.1	10.6	13.7	8.7
pH				7.30		
PCO_2	mmHg	35-45		45.7		
PO_2	mmHg			39.9		
HCO_3^-	mmol/L	22-28		22.0		

Denote: BUN: Blood Urea Nitrogen; Cr: Creatinine; eGFR: Estimated Glomerular Filtration Rate; Hb: Hemoglobin; WBC: White Cell Count

Table 1: A series of laboratory data at emergency department.

Twelve hours later, he became drowsy and blood pressure dropped to 86/58 mmHg acutely with bradycardia (23/minute). Physical examinations showed bilaterally mild basal rales only. Pertinent serological surveys revealed elevated Cr level (1.98 mg/dL), mild mixed metabolic and respiratory acidosis (pH 7.30, PCO2 45.7mmHg and HCO_3 22.0 mmol/L), hypokalemia (K^+ 3.3 mmol/L), and incredible hypermagnesemia (10.6 mg/dL), soon rising to 13.7 mg/dL (Table 2). With serial measurements, serum levels of troponin-T and creatine kinase MB did not elevate. Electrocardiography showed atrial fibrillation with slow ventricular response. Chest radiography revealed slightly increased vascular markings. Cardiac ultrasonography demonstrated ejection fraction rate of 45 % without valvular disorders or pericardial effusion. Saline and calcium gluconate were administered immediately with an implantation of temporary pacemaker, repeated atropine administration as well as continuous vasopressors infusion with dopamine and norepinephrine. However, all those strategies can not correct his bradyarrhythmia with cardiogenic shock. For refusal of transferring to intensive care unit, hemodialysis rather than continuous renal replacement therapy was undergone. Massive saline infusion as replacement solution during hemodialysis, a modality mimicking hemodiafiltration, was performed in our patients. However, poor hemodynamic status caused termination of hemodialysis and Mg^{2+} level was decreased from 13.7 to 8.7 mg/dL post 3-hour hemodialysis with a limited improvement of hemodynamic status. This patient died 10 hours after the first session of hemodialysis.

Patients	Age	Gender	Mg^{2+} salt type	Route	$[Mg^{2+}]_{MAX}$ (mg/dL)		Reference
1	7	Male	$MgSO_4$	Enema	41.2		[3]
2	89	Male	Mg citrate (34g)	Enema	12.6		[4]
3	4	Male	$MgSO_4$ (100mL) (Fletcher's $MgSO_4$ enema)	Enema	14.3		[5]
4	85	Female	$MgSO_4$ (28g)	Enema	18.7		[6]
5	56	Male	$MgSO_4$ (42.5 g)+ Mg citrate (17.45 g)	Oral	23	+ Charcoal	[7]

6	77	Female	Mg citrate (17.5 g)	Oral	10.3	+ Charcoal	[8]
Our case	59	Male	MgO (1.5 g)	Oral	13.7	+ Glycerin enema	

Table 2: Cases with normal renal function but acute fatal hypermagnesemia secondary to a robust Mg^{2+} gut absorption.

Discussion

In view of the difficulty in correcting bradycardia with medications and pacemaker in our patient, arrhythmia secondary to metabolic disturbance especially severe electrolytes imbalance should be considered. For his relatively stationary serum levels of K^+ and Ca^{2+} as well as acid base status, hypermagnesemia related fetal arrhythmia and cardiogenic shock was diagnosed. Magnesium homeostasis is regulated mainly by the balance between intestinal absorption and renal excretion. Although the majority of Mg^{2+} is absorbed by small intestine in a passive paracellular manner, fine-tuning of Mg^{2+} absorption occurs in colon transcellularly via transporters including apical Transient Receptor Potential Channel Melastatin Member 6 (TRPM6) and TRPM7 as well as basolateral CNNM4 Na^+-Mg^{2+} exchanger [9]. In kidney, most filtered Mg^{2+} is absorbed paracellularly via claudin 1, 2 in proximal tubule and via claudin 10, 14, 16, 19 in thick ascending limb, respectively. The final renal Mg^{2+} excretion is determined by fine-tuning of renal Mg^{2+} absorption occurring in distal tubule, the last site of nephron to absorb Mg^{2+} by apical TRPM6 channel and basolateral Na^+-Mg^{2+} exchanger [10,11]. Clinical features of hypermagnesemia usually correlated with serum Mg^{2+} level, varying from asymptomatic, mild gastrointestinal discomforts to conscious change, respiratory depression and fetal arrhythmia. In light of high efficacy of renal Mg^{2+} excretion, Mg^{2+} accumulation in body and lethal hypermagnesemia occurs almost exclusively in patients with advanced renal failure. Other than renal function, the difference in the types of Mg^{2+} salts and the administration routes also contribute to serum Mg^{2+} level. With chronic orally use, almost all types of Mg^{2+} salts have been reported to cause lethal hypermagnesemia progressively but a sudden outset of fatal hypermagnesemia is exclusively caused by an acute large load of Mg^{2+} intravenously, especially in those with normal renal function [12].

Considering the lack of advanced renal failure and intravenous Mg^{2+} administration on admission in our patient, Mg^{2+} responsible for his acute and lethal hypermagnesemia should originate from gut absorption. Several factors have been identified to impact on intestinal Mg^{2+} absorption including gut motility, Mg^{2+} dose, types of Mg^{2+} salt, food constituents and intestinal disorders [13]. To best of our knowledge, only few cases with normal renal function have been reported to have acute lethal hypermagnesemia with Mg^{2+} absorbed from gut following either Mg^{2+}salt retention enema or Mg^{2+} -containing active charcoal ingestion. The robust elevation of serum Mg^{2+} level may be caused by very high electrochemical gradient established by Mg^{2+} containing enema solution or uncontrolled massive Mg^{2+} backleak through intestinal mucosa injured by charcoal. Differently, low bioavailability of inorganic Mg^{2+} salt was used in our patient and no Mg^{2+} salt enema was performed. Chronic use of MgO, despite in recommended dose, in our severely constipated patient may result in a significant accumulation of Mg^{2+} in colon. Glycerin enema has been reported to cause acute colitis or colonic mucosa necrosis via direct toxicity to intestinal mucosa or indirectly resulting in mesenteric vasospasm [14].

Therefore, frequent glycerin enema in our patient may cause colonic mucosal injury to disrupt fine-tuning Mg^{2+} absorption. Accumulated Mg^{2+} in colon of our patient could leak through damaged colonic mucosa wildly and massively, like a large bolus of Mg^{2+} load, to cause an acute life-threatening hypermagnesemia. Whether enema solutions contain Mg^{2+} or not, application of enema should be looked before you leap in severely constipated patients with chronic use of oral Mg^{2+}-based laxatives even in recommended dose because Mg^{2+} accumulation in gut may be massive but underestimated, best illustrated by our case. In those patients chronically using oral Mg^{2+} cathartics regardless of the dose, signs of hypermagnesemia should be assessed frequently with regular measurement of serum Mg^{2+} level no matter how the renal function is. Early recognition with appropriate management is the key to improve outcome of hypermagnesemia. Discontinuing the use of Mg^{2+} salt is always the first step in the management of hypermagnesemia and usually can correct abnormal serum Mg^{2+} level in those with normal renal function. Volume expansion with saline helps renal Mg^{2+} excretion. Calcium should be administrated in symptomatic patients to antagonize the effect of excessive Mg^{2+} [13]. In patients with advanced renal failure, dialysis may be required and continuous venovenous hemodiafiltration (CVVHDF) is usually more effective in Mg^{2+} removal. Almost 40% reduction of serum Mg^{2+} level within three hours in our patient may suggest low efficacy hemodialysis with replacement fluid may mimic CVVHDF while CVVHDF is not available, but longer treatment time may be required.

Conclusion

Acute and lethal hypermagnesemia still should be considered among patients without intravenous administration of Mg^{2+}. Even though enema solution used in severely constipated patients does not comprise Mg^{2+} salt, serum Mg^{2+} level should be closely measured in those with chronic use of Mg^{2+} salt cathartics regardless of renal function and the dose of Mg^{2+} salt.

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