Data availability statement

The data that support the findings of this case report are available from the corresponding author, upon reasonable request.

Ryosuke Masui, Kosaku Komiya, Ai Tanaka, Hiroyuki Matsumoto, Hiroki Yoshikawa, Shogo Ichihara, Marimu Yamanaka, Atsushi Yokoyama, Kazufumi Hiramatsu and Jun-ichi Kadota
Respiratory Medicine and Infectious Diseases, Oita University Faculty of Medicine, Yufu, Japan

References

1 Devlin JW, Skrobik Y, Gélinas C *et al*. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med* 2018; **46**: e825–e873.
2 Young P, Saxena M, Bellomo R *et al*. Acetaminophen for fever in critically ill patients with suspected infection. *N Engl J Med* 2015; **373**: 2215–2224.
3 Maxwell EN, Johnson B, Cammilleri J, Ferreira JA. Intravenous acetaminophen-induced hypotension: a review of the current literature. *Ann Pharmacother* 2019; **53**: 1033–1041.
4 Young TL. A narrative review of paracetamol-induced hypotension: keeping the patient safe. *Nurs Open* 2021; **9**: 1589–1601.
5 Bae JI, Ahn S, Lee YS *et al*. Clinically significant hemodynamic alterations after propacetamol injection in the emergency department: prevalence and risk factors. *Intern Emerg Med* 2017; **12**: 349–355.
6 Lee HY, Ban GY, Jeong CG *et al*. Propacetamol poses a potential harm of adverse hypotension in male and older patients. *Pharmacoepidemiol Drug Saf* 2017; **26**: 256–264.
7 Saxena MK, Taylor C, Billot L *et al*. The effect of paracetamol on Core body temperature in acute traumatic brain injury: a randomised, controlled clinical trial. *PLoS One* 2015; **10**: e0144740.
8 Chiam E, Bellomo R, Churilov L, Weinberg L. The hemodynamic effects of intravenous paracetamol (acetaminophen) vs normal saline in cardiac surgery patients: a single center placebo controlled randomized study. *PLoS One* 2018; **13**: e0195931.

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A senile case of heart failure associated with hypermagnesemia induced by magnesium-containing laxative agent

Keywords: constipation, heart failure, hypermagnesemia, laxative, renal insufficiency.

Dear Editor,

In the human body, magnesium (Mg) is absorbed by the small intestine and excreted from the kidneys under strict homeostatic regulation.[1,2] Long-term administration of Mg-losing diuretics and Mg-containing agents under impaired Mg homeostasis leads to hypomagnesemia and hypermagnesemia, respectively.[3] Hypermagnesemia in older adults is caused mainly by the long-term administration of Mg-containing laxatives. Yamaguchi *et al*. reported a case series of hypermagnesemia induced by Mg oxide, and speculated that hypermagnesemia occurs more frequently than previously reported.[4] The main symptoms of hypermagnesemia described in their case series are non-specific, including anorexia, weakness and drowsiness. Therefore, this pathological condition has attracted less clinical attention, but many physicians prescribe Mg-containing laxatives without monitoring serum Mg concentrations. Based on such reality, Yamaguchi *et al*. concluded that senescence and renal insufficiency are the risk factors of hypermagnesemia in patients prescribed Mg oxide.[4] However, a cardiovascular manifestation of hypermagnesemia is not described in this literature. Here, we report an older patient with hypermagnesemia leading to heart failure (HF).

A 99-year-old demented, constipated and hypertensive man was introduced to Hara Doi Hospital, Fukuoka, Japan, due to the request for hospitalization by the nursing facility because of gradual hypotension (systolic blood pressure of 70–80 mmHg) and bradycardia (heart rate of 30–40 b.p.m.). On admission, he complained of general fatigue and anorexia, but showed no abnormal physical findings. Amlodipine (5.0 mg/day) and memantine (10 mg/day) were terminated. Blood pressure and heart rate were 110–46 mmHg and 44 b.p.m., respectively. Body temperature and SpO_2 were 36.1°C and 98% at room air. Because blood chemistry showed anemia, renal dysfunction, elevated brain natriuretic peptide and hypermagnesemia, administration of Mg oxide (3000 mg/day, ×3) was terminated, sennoside was started as an alternative laxative, and drip infusion of potassium- and Mg-free solution (500 mL/day) was initiated. The main physical and laboratory findings are shown in Table 1. Chest X-ray showed cardiomegaly (cardiothoracic ratio of 62.0%), but no pulmonary congestion or effusion. Electrocardiogram on admission showed sinus bradycardia associated with second-degree sinoatrial block (longest RR interval 1.8 s, and basic HR 36 b.p.m.), left axis deviation (QRS axis of −34°) and complete right bundle branch block. However, the sinoatrial block disappeared in an electrocardiogram recorded on the next day of admission. Echocardiogram recorded on that day showed an ejection fraction of 68%. The patient was discharged after confirming the restoration of hypermagnesemia.

HF is defined as a pathological state in which cardiac output is insufficient to meet the oxygen demands and metabolic needs of vital organs. The clinical events exacerbating HF are

Table 1 Serial physical and laboratory findings in a 99-year-old male patient with heart failure

		Day X	Day X + 3	Day X + 7	Day X + 17	Day X + 23
	Normal range					
BP		110–46	126–60	120–66	120–62	124–80
HR		44	52	64	60	56
RBC	435–555	305	307	287	322	349
Hb	13.7–16.8	9.1	9.6	8.9	9.9	10.8
Ht	40.7–50.1	30.4	29.9	28	31.7	34.5
WBC	3300–8600	5700	6200	5200	5100	5400
Plt	15.8–34.8	15.4	17.5	17.8	16.5	16.3
TP	6.6–8.1	6.9		6.7	7	7.1
Alb	4.1–5.1	3.7		3.5	3.5	3.7
FBG	73–109	107		94	94	
T. Chol	142–248	138			148	
HDL	38–90	48				
LDL	65–163	75				
TG	40–234	76			83	
UA	3.7–7.8	6.4	5.2	6	6.6	8.4
CK	59–248	72		37	26	36
BUN	8.0–20.0	33.2	26.5	39.6	53.2	56.3
Cr	0.65–1.07	3.02	2.32	2.44	2.48	2.79
T. Bil	0.4–1.5	0.6	0.7	0.6	0.5	0.6
AST	13–30	42	22	16	19	20
ALT	10–30	29	17	8	8	7
ALP	38–113	89		76	78	78
LDH	124–222	215		166	151	158
CHE	240–486	170				
eGFR	>90	15.5	20.7	19.6	19.2	16.9
eCCR	>90	7.8	10.7	10.2	9.3	7.9
BNP	0–18.4	1105.3				
CRP	0–0.14	0.05	0.21			
Na	138–145	139	143	144	144	145
K	3.6–4.8	4.5	4.1	4.5	4.6	4.4
Cl	101–108	102	109	111	108	107
Ca	8.8–10.1	8.5				
Mg	1.8–2.4	5.1	4	2.6		3.1
Fe	40–188	66				
Zn	80–130	69				

Day X means the day of admission, and this patient was discharged on day X + 24.

Alb, albumin (g/dL); ALP, alkaline phosphatase (U/L); ALT, alanine aminotransferase (U/L); AST, aspartate aminotransferase (U/L); BNP, brain natriuretic peptide (pg/mL); BP, blood pressure (mmHg); BUN, blood urea nitrogen (mg/dL); Ca, serum calcium concentration (mg/dL); CHE, choline esterase (U/L); CK, creatine kinase (U/L); Cl, serum chloride concentration (mmol/L); Cr, creatinine (mg/dL); CRP, C-reactive protein (mg/dL); eCCR, estimated creatinine clearance calculated by Cockcroft–Gault equation (mL/min); eGFR, estimated glomerular filtration rate calculated by creatinine-based equation modified for Japanese patients with chronic kidney disease (mL/min/1.73m^2); FBG, fasting blood glucose (mg/dL); Fe, serum iron concentration (μg/dL); Hb, hemoglobin concentration (g/dL); HDL, high-density lipoprotein cholesterol (mg/dL); HR, heart rate (bpm); Ht, hematocrit (%); K, serum potassium concentration (mmol/L); LDH, lactate dehydrogenase (U/L); LDL, low-density lipoprotein cholesterol (mg/dL); Mg, serum magnesium concentration (mg/dL); Na, serum sodium concentration (mmol/L); Plt, platelet (×10^4/μL); RBC, red blood cells (×10^4/μL); T. Bil, total bilirubin (mg/dL); T. Chol, total cholesterol (mg/dL); TG, triglyceride (mg/dL); TP, total protein (g/dL); UA, uric acid (mg/dL); WBC, white blood cells (/μL); Zn, serum zinc concentration (μg/dL).

(i) sustained reduction of cardiac function; (ii) augmentation of cardiac workload; or (iii) the combination of both. The augmented cardiac workload is common, whereas cardiac dysfunction induced by electrolyte imbalance is rare as a practical etiology of HF. The present case was a senile patient with hypermagnesemia underlying HF. On admission, the serum Mg concentration was 5.1 mg/dL, and Mg oxide was replaced with sennoside immediately. Memantine might have exacerbated constipation and bradycardia. Mg acts as a natural calcium antagonist, exerting negative chronotropic and vasodilating actions. Bradyarrhythmia and hypotension under hypermagnesemia disappeared after the cessation of amlodipine, memantine and Mg oxide. This case strongly suggests that monitoring electrolytes and reviewing prescription are important for treating HF disclosed by bradyarrhythmia and hypotension.

The association of HF with Mg alteration is controversial. Large clinical trials showed the relationship between the serum Mg concentration and the prognosis in HF patients. The prospective randomized milrinone survival evaluation (PROMISE) study clarified that serum Mg is not an independent risk factor of all-cause mortality in HF patients after adjustment of cofounders.[5] The Epleronone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) study showed that Mg alterations have no association with

clinical outcomes in patients with myocardial infarction complicated by HF.[6] However, hypermagnesemia, but not hypomagnesemia, was associated with cardiovascular and all-cause mortalities in HF patients in the meta-analysis.[7] These conflicting results are partly attributable to extents of Mg alterations; that is, the EPHESUS study defined hypomagnesemia and hypermagnesemia as serum Mg concentrations <0.66 mmol/L (1.58 mg/dL) and >1.10 mmol/L (2.64 mg/dL), respectively,[6] whereas these alterations were defined as serum Mg ≤1.5 mEq/L (1. 8 mg/dL) and ≥1.9 mEq/L (2.28 mg/dL) in the PROMISE study.[5]

In conclusion, a senile hypertensive patient presented HF caused by bradyarrhythmia and hypotension under hypermagnesemia. Mg-containing laxative in the gut acts as a reservoir of Mg in constipated patients.[8] Hypermagnesemia exacerbates HF by: (i) negative inotropic and chronotropic actions of Mg; and (ii) hypoperfusion of multiple organs induced by Mg-induced excessive vasodilation. It is of clinical importance to monitor electrolytes, and to review prescription for prevention of hypermagnesemia worsening hemodynamics in senile patients with constipation and renal insufficiency.

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Disclosure statement

The authors declare no conflict of interest.

Data availability statement

The data supporting the findings of this case report are available from the corresponding author upon reasonable request (tmaruyama@haradoi-hospital.com).

Kunimitsu Eiraku, Yuki Uozumi, Michinari Hieda, Toru Maruyama and Hideyuki Nomura
Hara Doi Hospital, Fukuoka, Japan

References

1 Swaminathan R. Magnesium metabolism and its disorders. *Clin Biochem Rev* 2003; **24**: 47–66.
2 Barbagallo M, Belvedere M, Dominguez LJ. Magnesium homeostasis and aging. *Magnes Res* 2009; **22**: 235–246. https://doi.org/10.1684/mrh.2009.0187.
3 William JH, Richards K, Danziger J. Magnesium and drugs commonly used in chronic kidney disease. *Adv Chronic Kidney Dis* 2018; **25**: 267–273. https://doi.org/10.1053/j.ackd.2018.01.005.
4 Yamaguchi H, Shimada H, Yoshita K *et al*. Severe hypermagnesemia induced by magnesium oxide ingestion: a case series. *CEN Case Rep* 2019; **8**: 31–37. https://doi.org/10.1007/s13730-018-0359-5.
5 Eichhorn EJ, Tandon PK, DiBianco R *et al*. Clinical and prognostic significance of serum magnesium concentration in patients with severe chronic congestive heart failure: the PROMISE study. *J Am Coll Cardiol* 1993; **21**: 634–640. https://doi.org/10.1016/0735-1097(93)90095-i.
6 Martens P, Ferreira JP, Vincent J *et al*. Prognostic relevance of magnesium alterations in patients with a myocardial infarction and left ventricular dysfunction: insight from the EPHESUS trial. *Eur Heart J Acute Cardiovasc Care* 2022; **11**: 148–159. https://doi.org/10.1093/ehjacc/zuab111.
7 Angkananard T, Anothaisintawee T, Eursiriwan S *et al*. The association of serum magnesium and mortality outcomes in heart failure patients: a systematic review and meta-analysis. *Medicine* 2016; **95**: e5406. https://doi.org/10.1097/MD.0000000000005406.
8 Bokhari SR, Siriki R, Teran FJ, Batuman V. Fatal hypermagnesemia due to laxative use. *Am J Med Sci* 2018; **355**: 390–395. https://doi.org/10.1016/j.amjms.2017.08.013.

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RESEARCH STUDIES

Frailty screening index and atrial fibrillation outcomes in the All Nippon AF In the Elderly registry

Dear Editor,

As the adverse outcomes of atrial fibrillation (AF) increase with age and comorbidities,[1] and AF is highly associated with frailty,[2] the association of frailty and AF outcomes is a major concern. Previous studies mostly from Western countries, including a systematic review[2] and a subanalysis of clinical trial,[3] showed conflicting results on the association of frailty and AF outcomes. Recently, we reported that frailty was associated with cardiovascular and all-cause death, net clinical outcomes (a composite of stroke/systemic embolic events, major bleeding and all-cause death), and major bleeding, but not stroke or intracranial hemorrhage in a 3000-patient subcohort of the All Nippon AF In the Elderly (ANAFIE) Registry, a nationwide registry with older Japanese adults with non-valvular AF.[4] In that study, we analyzed the frailty status using the Kihon Checklist, a deficit accumulation model of frailty assessment. Here, we report the additional analysis of the ANAFIE Registry on the association of frailty with AF outcomes using the Frailty Screening Index, a phenotype model of frailty assessment.[5]

The ANAFIE Registry is a multicenter Japanese registry of >30 000 AF patients aged ≥75 years, and basic data including 2-year outcomes have been published.[6] The study was carried out according to the ethical principles of the Declaration of Helsinki, and Japanese regulatory and legal requirements for registries (trial registration: UMIN000024006). The study outcomes, statistical analyses and other methods are as described previously.[4]