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Case Report

Rhabdomyolysis with Multiple Electrolyte Imbalances under Proton Pump Inhibitor Treatment after Total Thyroidectomy

Akihiko Yano[a], Ken-ei Sada[a,b,c*], Tsutomu Sawada[a], Hideki Ito[a], Hiroko Yano[a], and Tatsuya Ikeda[a]

[a]*Department of General Medicine, Kochi Health Sciences Center, Kochi 781-8555, Japan,*
[b]*Department of Clinical Epidemiology, Kochi Medical School, Kochi University, Nankoku, Kochi 783-8505, Japan,*
[c]*Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan*

A 90-year-old man presented with muscle weakness, difficulty concentrating, and dysphagia. About eighteen months prior to presentation, lansoprazole had been initiated to prevent stress ulcers; he also had a history of total thyroidectomy due to papillary thyroid cancer ten years prior. Laboratory findings were as follows: K 2.4 mEq/L, Ca 3.7 mg/dL, Mg 1.3 mg/dL, CK 5386 U/L, and intact PTH (iPTH) 14 pg/mL. Rhabdomyolysis with multiple electrolyte imbalances under proton pump inhibitor (PPI) treatment was diagnosed. We initiated intravenous hydration and electrolyte supplementation with discontinuation of PPI. After discontinuing PPI, the patient's serum magnesium, potassium, and calcium levels normalised with oral vitamin D and calcium supplementation. PPIs can cause hypocalcaemia and hypokalaemia via hypomagnesemia; hypocalcaemia is also a common postoperative complication of thyroidectomy. Careful monitoring of electrolyte levels is required in patients with long-term PPI treatment, especially in post-thyroidectomy cases.

Key words: hypocalcaemia, thyroidectomy, proton pump inhibitors, hypomagnesemia, rhabdomyolysis

Proton pump inhibitors (PPIs) are commonly used to treat acid-related diseases, including peptic ulcers and gastroesophageal reflux disease. Although the long-term use of PPIs is considered relatively safe, some adverse effects can occur. Multiple electrolyte imbalances such as hypocalcaemia and hypokalaemia via hypomagnesemia are rare but well-known adverse effects of PPIs [1]. Hypocalcaemia is also a common postoperative complication of total thyroidectomy that sometimes requires calcium replacement therapy [2]. Although two previous case reports have described PPI-related hypocalcaemia in patients after total thyroidectomy, they did not report potassium levels and rhabdomyolysis was not involved as a presenting complication [3, 4].

Herein, we report the case of a patient who developed rhabdomyolysis with hypocalcaemia, hypokalaemia, and hypomagnesemia during PPI treatment after total thyroidectomy.

Case Description

A 90-year-old man presented to a local clinic with muscle weakness and difficulty concentrating in July 2020. He reported a one-month history of fatigue and dysphagia, and had been referred to our hospital because of high creatine kinase (CK) levels. Ten years prior, he had undergone total thyroidectomy due to papillary thyroid cancer. After total thyroidectomy, he

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*Corresponding author. Phone and Fax: +81-88-888-2918
E-mail: sadak@kochi-u.ac.jp (K. Sada)

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exhibited low serum calcium levels of 7.7 mg/dL (8.8-10.2 mg/dL) and intact parathyroid hormone (iPTH) levels of < 5 pg/mL (10-65 pg/mL) but received no specific treatment. One year prior to presentation, after experiencing traffic trauma, he had begun lansoprazole to prevent stress ulcers and had continued its use up to the time of admission. He was also taking levothyroxine, an angiotensin II receptor blocker and warfarin, but no diuretics or statins.

On admission, his consciousness was clear. His vital signs included a body temperature of 36.0°C, blood pressure of 84/58 mmHg, and pulse rate of 88/min. His lungs were clear to auscultation. A pan-systolic murmur (Levine scale grade 4/6) was heard at the left sternal border. Manual muscle testing showed bilateral biceps and iliopsoas weakness but no myalgias. No Trousseau signs of latent tetany were observed. Laboratory findings were as follows: K 2.4 mEq/L, Ca 3.7 mg/dL (corrected Ca 4.6 mg/dL), Mg 1.3 mg/dL, Cr 1.3 mg/dL, CK 5386 U/L, and iPTH 14 pg/mL (other laboratory findings are shown in Table 1). The electrocardiogram showed QT prolongation (QTc = 0.581 sec). The patient was finally diagnosed with rhabdomyolysis due to hypocalcaemia, hypokalaemia, and hypomagnesemia based on physical and laboratory findings. After admission, we initiated intravenous hydration with extracellular fluid for rhabdomyolysis and intravenous potassium, calcium, and magnesium supplementation for electrolyte correction. Serum creatinine and CK levels quickly improved to a normal range after hydration. After discontinuation of lansoprazole, serum magnesium and potassium levels normalised despite discontinuation of magnesium and potassium supplementation. After correction of hypomagnesemia, the serum iPTH level increased to 17.9 pg/ml. The serum calcium level could also be maintained within the normal range with vitamin D and calcium supplementation without any adverse events (Fig. 1). As the magnesium level increased, potassium excretion also decreased (urinary-K: 45.4 mEq/L on admission, 24.4 mEq/L at day 3, and 12.9 mEq/L at day 5, respectively).

Table 1 Laboratory findings on admission

Peripheral blood		
	Hb (g/dL)	9.7
	WBC (/μL)	8,180
	PLT (×10³/μL)	278
Blood chemistry		
	Glucose (mg/dL)	123
	Alb (g/dL)	2.8
	AST (U/L)	61
	ALT (U/L)	20
	T. bil (mg/dL)	0.5
	γ-GTP (U/L)	9
	AMY (U/L)	75
	CK (U/L)	5,386
	Cr (mg/dL)	1.3
	BUN (mg/dL)	11.8
	UA (mg/dL)	4.6
	Na (mEq/L)	143
	K (mEq/L)	2.4
	Cl (mEq/L)	92
	Ca (mg/dL)	3.7
	IP (mg/dL)	2.3
	Mg (mg/dL)	1.3
	CRP (mg/dL)	3.14
Blood gas analysis (veinous)		
	pH	7.496
	PaCO2 (mmHg)	53.9
	HCO3 (mEq/L)	41.3
Endocrinology		
	FT4 (ng/dL)	0.94
	TSH (μIU/mL)	2.629
	intact PTH (pg/mL)	14
	1α-25-vitamin D (pg/mL)	43
	Plasma renin activity (ng/mL/hr)	0.7
	Aldosterone (pg/mL)	< 25
Urinalysis		
	pH	6.5
	Protein	(++)
	Occult blood	(+)
	Cr (mg/dL)	287.49
	K (mEq/L)	45.4
	Ca (mg/dL)	5.0

Discussion

To our knowledge, this is the first reported case with PPI treatment after total thyroidectomy, who developed rhabdomyolysis with hypocalcaemia, hypokalaemia, and hypomagnesemia.

PPIs may promote hypocalcaemia after total thyroidectomy. Although PPIs are widely used to treat acid-related diseases and are considered relatively safe, electrolyte imbalances such as hypomagnesemia, hypocalcaemia, and hypokalaemia do occur on rare occasion [1]. PPIs may inhibit magnesium absorption from the intestinal tract by inhibiting H/K-ATPase in the stomach and colon [5]. A previous report showed diuretics as a risk factor for PPI-induced hypomagnesemia [6], but our patient did not take diuretics. Because

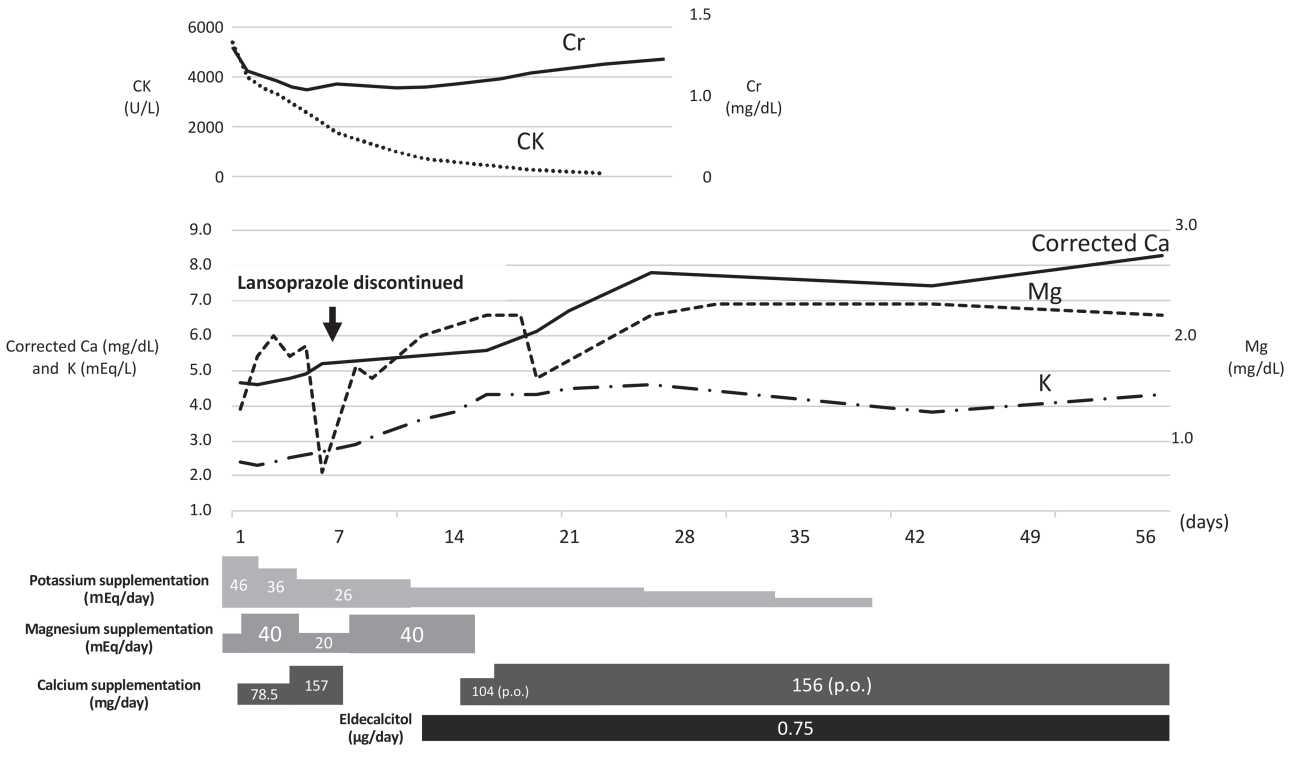

Fig. 1 Clinical course. Mg, serum magnesium; Ca, serum calcium; K, serum potassium; CK, creatine kinase; Cr, creatinine, p.o., Per os.

low serum magnesium levels suppress PTH production/release and bone response to PTH, hypocalcaemia develops due to hypoparathyroidism [7,8]. The increase of the PTH from a previously undetectable level to a measurable level at presentation was considered to have been in response to the patient's severe hypocalcaemia. Considering that the PTH level increased further after Ca correction, Mg correction may have improved PTH secretory production/release. Hypocalcaemia is also a common postoperative complication of total thyroidectomy that sometimes requires calcium replacement therapy [2]. A previous report showed that esomeprazole suppressed calcium absorption and led to hypocalcaemia in a patient after thyroidectomy [4]. The patient in the present case was not begun on vitamin D or calcium supplementation after thyroidectomy. The characteristic hypocalcemic symptoms such as Trousseau signs or muscle spasms may have been absent because of the long duration of this condition [9].

Rhabdomyolysis may develop due to electrolyte imbalances caused by PPIs. Rhabdomyolysis can be caused by exposure to drugs and toxins, electrolyte abnormalities, endocrine abnormalities, and autoimmune myopathy [10]. In this case, there was no autoimmune disease and no suspicious drug except for the PPI.

Hypocalcaemia and hypokalaemia are both well-known causes of rhabdomyolysis [9,10]. Magnesium controls urinary potassium excretion by binding to the renal outer medullary potassium channel; intracellular magnesium deficiency increases urinary potassium excretion [11]. A previous case report showed that omeprazole caused rhabdomyolysis via multiple electrolyte imbalances and renal tubular acidosis [12]. Because renal tubular acidosis could not be found in the present case and the urinary potassium level decreased with the improvement of hypomagnesemia, the hypokalaemia in this case was likely caused by inappropriate potassium excretion.

In conclusion, the long-term administration of PPIs in patients with total thyroidectomy requires careful monitoring of serum calcium, magnesium, and potassium levels.

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