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CASE REPORT

Case report of superior mesenteric artery syndrome that developed in a lean type 2 diabetes patient and was associated with rapid body weight loss after sodium–glucose cotransporter 2 inhibitor administration

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Keywords
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ABSTRACT

A 58-year-old women who was diagnosed with type 2 diabetes 20 years earlier had been treated with antidiabetic medicines since she was aged 40 years. After sodium–glucose cotransporter 2 inhibitors administration, her bodyweight rapidly decreased from 40 to 30 kg over a period of 3 weeks. She had abdominal symptoms, including nausea, especially after a meal. On admission, physical examinations and laboratory data showed euglycemic ketoacidosis, dehydration and low insulin secretion levels. Additionally, abdominal contrast computed tomography showed the finding of superior mesenteric artery syndrome. This case urges caution, including rapid excessive bodyweight loss and euglycemic ketoacidosis, on the use of sodium–glucose cotransporter 2 for lean diabetes patients.

INTRODUCTION

Sodium–glucose cotransporter 2 inhibitors (SGLT2i) have been widely used to treat diabetes patients. Additionally, SGLT2i show a reduction in bodyweight (BW) through energy loss into the urine. There are several warnings, including excessive BW loss, progression of sarcopenia in older adults and euglycemic ketoacidosis, regarding the use of SGLT2i[1].

Superior mesenteric artery (SMA) syndrome is characterized by compression of the third portion of the duodenum as a result of narrowing of the space between the SMA and abdominal aorta[2]. SMA syndrome is primarily attributed to loss of the intervening mesenteric fat pad, which might be induced by rapid BW loss, particularly in lean patients.

Here, we report a case of SMA syndrome and euglycemic ketoacidosis caused by rapid excessive BW loss after SGLT2i administration in a lean middle-aged woman with type 2 diabetes mellitus.

CASE REPORT

A 58-year-old women with type 2 diabetes mellitus presented to the emergency department of Kanazawa Medical University Hospital, Uchinada, Japan. She had been diagnosed with type 2 diabetes mellitus 20 years earlier, and was treated with antidiabetic medicines beginning at the age of 40 years. For a few years, she was taking repaglinide at 1.5 mg, vildagliptin at 100 mg and metformin at 1,500 mg a day. As her hemoglobin A1c level was 8–9%, her family doctor recommended insulin therapy. However, she refused insulin therapy. Three weeks before admission, 100 mg of canagliflozin was provided daily. At that time, her bodyweight (BW) and body mass index were 40 kg and 17.7 kg/m^2, respectively. She had epigastric pain, nausea (especially after a meal) and appetite loss for 3 days before admission. Thereby, she visited her family physician and

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received a drip infusion of 500 mL of saline with vitamin B_1 for 3 days. However, her abdominal symptoms became severe, and she presented to the emergency room of our hospital. Initial laboratory tests in the emergency room showed urine ketone body 3+, although the blood glucose level was 192 mg/dL, suggesting an acute metabolic abnormality. Thereby, the patient was referred to our department, and admitted for detailed examination and treatment.

At admission, her consciousness was alert, and blood pressure, pulse rate, respiratory rate and body temperature were 123/73 mmHg, 95 beats/min, 25/min and 36.7°C, respectively. Her BW and body mass index were 30 kg and 13.3 kg/m^2, respectively. She lost 10 kg of BW over a period of 3 weeks after administration of canagliflozin. On physical examination, she had upper abdominal tenderness, and the bowel sounds disappeared. Her oral cavity was dry, and the capillary refilling time was >2 s. Additionally, abdominal ultrasonography showed that the diameter of the inferior vena cava was 8 mm, without respiratory variability. Thus, the physical examination and results of abdominal ultrasonography showed that dehydration was present.

Laboratory tests showed metabolic ketosis with a pH of 7.385 (arterial blood gas), pCO_2 of 17.9 mmHg, serum bicarbonate level of 10.5 mmol/L, anion gap of 36.5 mmol/L and urine ketone body 3+. These data indicated that this patient was in the state of ketoacidosis with compensative respiratory alkalosis. Her total ketone body, 3-hydroxybutyrate and acetoacetate levels were markedly elevated at 15,130 μmol/L, 11,357 μmol/L and 3,782 μmol/L, with a blood glucose level of 215 mg/dL. Diabetic states data showed hemoglobin A1c of 9.0%, fasting serum C-peptide of 0.55 ng/mL and urinary C-peptide excretion of 15 μg/day, indicating a low insulin secretory capacity. The anti-glutamic acid decarboxylase antibody was negative. Other data and the state of diabetic microvascular complications are shown in Table 1. We diagnosed euglycemic ketoacidosis, and canagliflozin was discontinued as a potential precipitant of euglycemic ketoacidosis and dehydration. Treatment with insulin, and drip infusion with saline and 5% glucose solution was started. Metformin, vildagliptin and repaglinide were suspended as a result of abdominal symptoms.

Additionally, we carried out abdominal contrast computed tomography. We found that the patient's stomach and upper

Table 1 | Laboratory data

Urine test		*Biochemistry*		*Arterial blood gas analysis*	
pH	5	Na	143 mEq/L	pH	7.385
Protein	±	K	3.6 mEq/L	pCO_2	17.9 mmHg
Glucose	4+	Cl	96 mEq/L	pO_2	128 mmHg
Ketone	3+	pOsm	319 mOsm/kg	$HCO3^-$	10.5 mmol/L
Blood	–	BUN	53 mg/dL	Anion gap	36.5 mmol/L
		Cr	0.72 mg/dL		
CBC		eGFR	64 mL/min/1.73 m^2	*Glucose metabolism*	
WBC	14,620/μL	TP	6.6 g/dL	Glucose	215 mg/dL
Neutro	85.20%	Alb	3.6 g/dL	CPR	0.55 ng/mL
Lympho	7.50%	T-Bil	0.3 mg/dL	IRI	1.1 μU/mL
RBC	4.68 × 10^6/μL	AST	28 U/L	HbA1c	9%
Hb	13.8 g/dL	ALT	32 U/L	Anti-GAD antibody	<5.0 U/mL
Ht	42.30%	γ-GTP	14 U/L	Total ketone body	15,139 μmol/L
Plt	283 × 10^3/μL	CRP	2.25 mg/dL	3-Hydroxybutyric acid	11,357 μmol/L
		T-cho	130 mg/dL	Acetoacetic acid	3,782 μmol/L
		TG	93 mg/dL	U-CPR	15 μg/day
		HDL-cho	47 mg/dL		
		LDL-cho	64.4 mg/dL		

Diabetic microvascular complications		
Neuropathy	Vibration	Rt 10 s, Lt 10 s
	Achilles tendon reflex	Rt (+), Lt (+)
	CV R-R (at rest time)	1.54%
Retinopathy	Simple diabetic retinopathy	
Nephropathy	UACR 32 mg/gCr	

γ-GTP, γ-glutamyl transpeptidase; Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CBC, complete blood count; CPR, C-peptide immunoreactivity; Cr, creatinine; CRP, C-reactive protein; CV R-R, coefficient of variation of R-R interval; eGFR, estimated glomerular filtration rate; GAD, glutamic acid decarboxylase; Hb, hemoglobin; HbA1c, hemoglobin A1c; HDL-cho, high-density lipoprotein cholesterol; Ht, hematocrit; L, left; LDL-cho, low-density lipoprotein cholesterol; Lympho, lymphocytes; Neutro, neutrophils; NPDR, non-proliferative diabetic retinopathy; Plt, platelets; pOsm, plasma osmolality; R, right; RBC, red blood cells; T-bil, total bilirubin; T-cho, total cholesterol; TG, triglyceride; TP, total protein; UACR, urine albumin-to-creatinine ratio; U-CPR, urinary C-peptide immunoreactivity excretion; WBC, white blood cells.

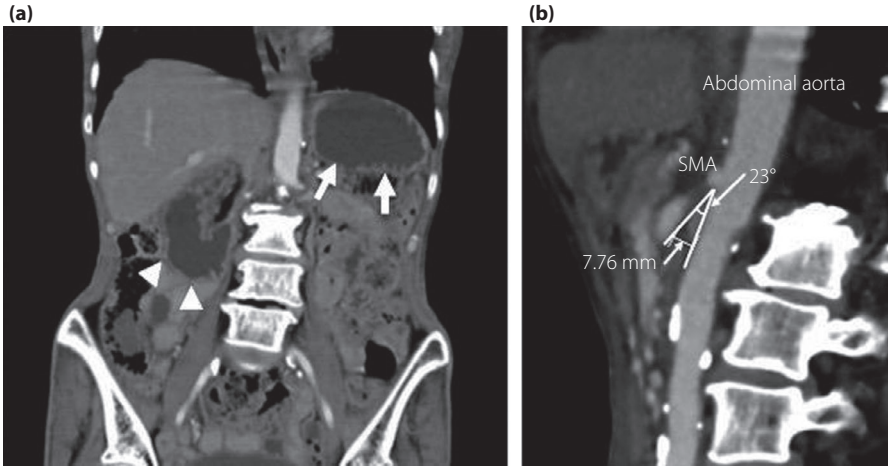

Figure 1 | Finding on abdominal contrast computed tomography. (a) This patient's stomach (white arrow) and upper duodenum (white arrowhead) were filled with residue. (b) The horizontal portion of the duodenum was compressed between the superior mesenteric artery (SMA) and abdominal aorta (the aortomesenteric angle: 23° (diagnostic criteria: <25°) and the distance: 7.76 mm [diagnostic criteria: <8 mm]).

duodenum were filled with residue (Figure 1a), because the horizontal portion of the duodenum was compressed between the SMA and abdominal aorta (Figure 1b). We diagnosed SMA syndrome by computed tomography scan findings[3,4]. A nasogastric tube was inserted to release the stomach fullness for 2 days. Three days after admission, the urinary ketone bodies disappeared, and the patient's abdominal symptoms improved. Four days after admission, she could eat a meal, and the administration of insulin changed from continuous insulin infusion to insulin intensive therapy by subcutaneous injection. Additionally, she implemented a chest–knee position after a meal; therefore, her abdominal symptoms no longer occurred. She was discharged 2 weeks after admission with only insulin therapy. Her BW increased by 2 kg during admission, and she gained an additional 7 kg by the follow-up visit 28 weeks after discharge.

Written informed consent was obtained from the patient for publication of this report. Formal ethics approval was waived, because this is a case report.

DISCUSSION

In the present case, rapid excessive BW loss might be closely related to the onset of SMA syndrome by possibly reducing the mesenteric fat pad between the SMA and abdominal aorta. BW loss after treatment with SGLT2i has been consistently observed in patients with type 2 diabetes mellitus. However, SGLT2i might promote unexpected excessive BW loss, including sarcopenia in lean patients, particularly those with a low insulin secretory capacity, because insulin plays a crucial role in muscle protein synthesis[5]. SMA syndrome occurs most commonly in lean patients, and loss of BW is one of the causes of the onset of SMA syndrome. In general, the symptom of SMA syndrome is non-specific, but high-pitched bowel sounds are often observed. However, in the present patient, the bowel sounds were decreased on admission because of gastroparesis as a result of diabetic autonomic neuropathy. There are several reports of SMA syndrome in patients with diabetes[6–8]. In some patients with diabetic autonomic neuropathy, it has been reported that it is difficult to distinguish gastroparesis from SMA syndrome on initial diagnosis[6,7].

This is the first report of SMA syndrome developing in a type 2 diabetes mellitus patient and being associated with rapid BW loss after administration of SGLT2i. Euglycemic ketoacidosis in this patient was associated with loss of dietary intake as a

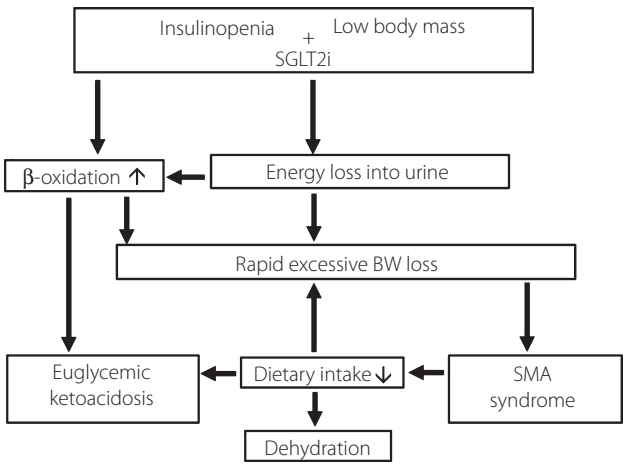

Figure 2 | Schema of pathophysiology in the present case. Administration of sodium–glucose cotransporter 2 inhibitors (SGLT2i) in a lean type 2 diabetes patient with insulinopenia promoted rapid excessive bodyweight (BW) loss through both energy loss into the urine and increased β-oxidation. Rapid excessive BW loss resulted in the development of superior mesenteric artery (SMA) syndrome, and loss of dietary intake induced by SMA syndrome led to euglycemic ketoacidosis and dehydration.

result of SMA syndrome through SGLT2i-induced BW loss in addition to energy loss into the urine (Figure 2). We should be aware of excessive BW loss and the development of ketoacidosis when using SGLT2i, especially in diabetes patients with dehydration and insulinopenia[9]. Additionally, with abdominal symptoms in diabetes patients with a past history of rapid excessive BW loss, SMA syndrome needs to be considered as a differential diagnosis. The present case urges caution in the use of SGLT2i for lean diabetes patients.

DISCLOSURE

The authors declare no conflict of interest.

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