Superior Mesenteric Artery Syndrome Complicated by Diabetic Ketoacidosis and Graves’ Disease in Slowly Progressive Insulin Dependent Diabetes Mellitus (SPIIDDM): A Case Report and a Review of the Literature

Hiroyuki Hirai¹, Naotaro Fukushima¹, Koji Hasegawa¹, Tsuyoshi Watanabe¹, Osamu Hasegawa² and Hiroaki Satoh¹

Abstract

A 48-year-old woman with a history of diabetes was admitted for nausea and vomiting with body weight loss. A blood examination revealed high plasma glucose and thyroid hormone levels and metabolic acidosis. She was therefore diagnosed with both diabetic ketoacidosis (DKA) and hyperthyroidism. Nausea and vomiting continued intermittently despite the administration of saline and insulin. The patient was further diagnosed with superior mesenteric artery syndrome (SMAS) after abdominal computed tomography revealed that a horizontal portion of the duodenum was sandwiched between the aorta and the superior mesenteric artery. Clinicians should be vigilant for SMAS in patients with both DKA and hyperthyroidism who present body weight loss.

Key words: diabetic ketoacidosis, superior mesenteric artery syndrome, slowly progressive insulin dependent diabetes mellitus, Graves’ disease

(Intern Med 55: 2035-2042, 2016)
(DOI: 10.2169/internalmedicine.55.6203)

Introduction

Diabetic ketoacidosis (DKA), which is one of the most serious acute complications of diabetes, can occur in conjunction with acute major illnesses, such as sepsis, pancreatitis, and thrombosis (1-3). In cases of DKA, clinicians should therefore be vigilant in addressing both DKA management and the complicating illness. Superior mesenteric artery syndrome (SMAS) is defined as duodenal obstruction due to the compression of the organ between the aorta and the superior mesenteric artery (4). Although many cases of SMAS have been reported in the recent literature, there are few reports of both SMAS and DKA in patients with hyperthyroidism or Graves’ disease. We herein report a case and review the literature on DKA complicated by SMAS and Graves’ disease.

Case Report

A 48-year-old woman had been suffering from thirst, nausea, and intermittent vomiting for approximately 1 week. Over the 6 months prior to her hospital visit in June 2011, she lost approximately 15 kg of body weight (from 57 kg to 42 kg). The patient had an approximately 13-year history of diabetes and was being treated with sulfonylurea. However, her diabetes was poorly managed, and her HbA1c level had been over 8%. She had stopped visiting the hospital in the year prior to her hospitalization after she became busy with work. The patient was diagnosed with diabetic ketoacidosis after a laboratory examination revealed a high plasma glucose concentration.

¹Department of Nephrology, Hypertension, Diabetology, Endocrinology, and Metabolism, Fukushima Medical University, Japan and ²Department of Radiology, Fukushima Medical University, Japan
Received for publication July 17, 2015; Accepted for publication November 19, 2015
Correspondence to Dr. Hiroaki Satoh, hiroakis-tky@umin.ac.jp
Table 1. Laboratory Data on Admission to Previous Hospital.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Unit</th>
<th>Parameter</th>
<th>Result</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>21,000</td>
<td>/μL</td>
<td>TSH</td>
<td>0.01</td>
<td>μIU/mL</td>
</tr>
<tr>
<td>RBC</td>
<td>522 x 10^6</td>
<td>/μL</td>
<td>FT₄</td>
<td>3.41</td>
<td>ng/dL</td>
</tr>
<tr>
<td>Hb</td>
<td>14.9</td>
<td>g/dL</td>
<td>FT₃</td>
<td>10.78</td>
<td>pg/mL</td>
</tr>
<tr>
<td>Hct</td>
<td>44.5 %</td>
<td>%</td>
<td>PG</td>
<td>575</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Pt</td>
<td>28.2 x 10^4</td>
<td>/μL</td>
<td>HbA1c</td>
<td>15.3 %</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>22</td>
<td>IU/L</td>
<td>CPR</td>
<td>0.23</td>
<td>ng/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>31</td>
<td>IU/L</td>
<td>Blood gas analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td>284</td>
<td>IU/L</td>
<td>pH</td>
<td>6.922</td>
<td></td>
</tr>
<tr>
<td>Alp</td>
<td>729</td>
<td>IU/L</td>
<td>PaO₂</td>
<td>127</td>
<td>mmHg</td>
</tr>
<tr>
<td>Na</td>
<td>125</td>
<td>mEq/L</td>
<td>PaCO₂</td>
<td>12.7</td>
<td>mmHg</td>
</tr>
<tr>
<td>K</td>
<td>5.1</td>
<td>mEq/L</td>
<td>HCO₃⁻⁰⁻</td>
<td>2.5</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Cl</td>
<td>85</td>
<td>mEq/L</td>
<td>Blood gas analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cre</td>
<td>0.4</td>
<td>mg/dL</td>
<td>U-Glu</td>
<td>4+</td>
<td></td>
</tr>
<tr>
<td>UA</td>
<td>10.3</td>
<td>mg/dL</td>
<td>U-Pro</td>
<td>2+</td>
<td></td>
</tr>
<tr>
<td>CK</td>
<td>24</td>
<td>IU/L</td>
<td>U-Ket</td>
<td>3+</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>8.01</td>
<td>mg/dL</td>
<td>Urine test</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


level (575 mg/dL) and metabolic acidosis (pH: 6.922, HCO₃⁻⁰⁻: 2.5 mmol/L). Continuous saline and insulin was administered intravenously, and the high plasma glucose level and metabolic acidosis improved by the next day. In addition, a blood examination revealed hyperthyroidism [thyroid-stimulating hormone (TSH): 0.001 μU/mL, free thyroxine (FT₄): 3.41 ng/dL, and free triiodothyronine (FT₃) 10.78 pg/mL] (Table 1). Her severe nausea and vomiting continued intermittently and she was referred to our hospital for further examination.

A physical examination on admission revealed the following results: height, 151.2 cm; body weight, 42.0 kg; body mass index, 18.4 kg/m²; body temperature, 37.2°C; blood pressure, 110/80 mmHg; pulse, 105/min, regular sinus rhythm. Thyroid palpation revealed a slight, diffuse and palpable goiter. Tympanic abdomen and bile-like vomit were observed, and an abdominal X-ray showed a large amount of stomach gas, lower abdominal gas, silent gallstone, and intestinal gas (Fig. 1). An abdominal computed tomography (CT) scan revealed a bloated stomach, duodenal obstruction, and showed that a horizontal portion of the duodenum was sandwiched between the aorta and the superior mesenteric artery. In addition, the location of the SMA seemed to be oppressed by a bloated stomach. The angle between the aorta and the superior mesenteric artery was suspected to be narrower. The patient’s aorta-SMA angle was approximately 13°, while the aorta-SMA distance was approximately 6.44 mm (Fig. 2). Upper gastrointestinal endoscopy on the first day after admission showed the erosion of the entire circumference of the lower esophagus and duodenum and bile-like fluid in the stomach, which was diagnosed as gastroesophageal reflux disease and erosive duodenitis. No stenosis of the duodenum was observed. Based on the above findings, the patient was diagnosed with SMAS.

The patient also showed glutamic acid decarboxylase (GAD) antibody and thyroid stimulating antibody positivity (GAD antibody: 60 U/mL, normal range ≤1.5; TSAb: 940%, normal range ≤120%); she was therefore diagnosed with slowly progressive insulin dependent diabetes mellitus (SPIDDM) and Graves’ disease.

A transluminal tube was inserted and approximately 2,500 mL of bile-like fluid was aspirated. As a result, the patient’s gastrointestinal symptoms began to improve. After a period of fasting with intravenous drip infusion, the symptoms of nausea and vomiting temporarily decreased. The transluminal tube was removed on the 6th day. However, the symptoms of nausea and vomiting recurred after the start of oral ingestion. The gastrointestinal symptoms persisted. To increase the patient’s body weight, an oral diet, oral nutritional products, and an approximately 5-10% dose of intravenous glucose were administered with basal-bolus insulin therapy. The patient was left in the lateral decubitus position after meals. Metoclopramide and domperidone were administered until the disappearance of nausea and vomiting. After the start of oral ingestion, the oral intake energy was gradually increased. The patient’s approximate energy intake is summarized in Fig. 3. Her energy intake from meals was 85 mEq/L, and the energy intake from carbohydrates, protein, and lipids was approximately 1,000-1,950 kcal during hospitalization. The energy intake from carbohydrates, protein, and lipids were approximately 3-6, 1, and 1.3-1.8, respectively.

An abdominal CT scan on the 24th day revealed that the duodenal obstruction had resolved: the aorta-SMA angle was approximately 21°, and the aorta-SMA distance was approximately 8.74 mm; thus, a wider aorta-SMA angle and a longer aorta-SMA distance were detected (Fig. 4). When the patient’s body weight reached 39 kg, the gastrointestinal symptoms almost disappeared.
Figure 2. Abdominal computed tomography scan. (a) An axial computed tomography scan demonstrating a short aorta-SMA distance, a bloated stomach, duodenal obstruction, and dilatation of the duodenum due to entrapment between the aorta and the SMA. In addition, the location of the SMA seems to be oppressed by the bloated stomach. The top right of the figure demonstrates the measured aorta-SMA distance (6.44 mm). (b) A coronal computed tomography scan demonstrating a bloated stomach and the dilatation of the duodenum. (c) A sagittal computed tomography scan demonstrating a narrow aorta-SMA angle and a bloated stomach. The location of the SMA also seems to be oppressed by the bloated stomach. The top right of the figure demonstrates the measured aorta-SMA angle (13°). SMA: superior mesenteric artery
the dose of insulin (Fig. 3). Furthermore, we evaluated the pathological conditions related to the patient’s diabetes and their complications. A glucagon stimulation test was performed to evaluate the patient’s insulin secretion ability; the patient’s serum C peptide level was from 0.9 to 1.3 ng/mL at 0 and 6 minutes. The low Δ C peptide value suggested that the patient might have a low insulin secretion ability. The results were not inconsistent with SPIDDM. Diabetic microangiopathy, simple retinopathy, excess urine albuminuria, and Achilles tendon reflex attenuation were recognized. In particular, the coefficient of variation of R-R intervals (CVR-R), which was 1.41%, was low. In addition, as orthostatic hypotension was detected, we considered the possibility that the patient’s condition might be complicated with autonomic nerve disorders. There was no evidence of diabetic macroangiopathy. At discharge, the patient’s fasting blood sugar level was 90-150 mg/dL, and her postprandial blood sugar level was 180-250 mg/dL after basal-bolus insulin treatment (insulin aspart: 8-8-8, insulin detemir: 0-0-0-14, total 38 U/day).

Thiamazole (30 mg/day) was administered during hospitalization to treat the patient’s Graves’ disease, and the hyperthyroidism became euthyroid at discharge. A diffuse and blood flow-rich goiter was recognized on ultrasonography. The above-described clinical course is summarized in Fig. 3.

Discussion

The present case illustrates two important issues: first, SMAS occurring with DKA and Graves’ disease is a rare phenomenon. Second, because the symptoms of SMAS symptoms are very similar to diabetic gastroenteropathy, discrimination between these conditions may sometimes be difficult.

Rokitansky et al. first reported SMAS in 1842. The main cause of SMAS is considered to be acute body weight loss.
accompanied by a reduction of visceral fat (5). As a result, the third position of the duodenum might be sandwiched between the aorta and the superior mesenteric artery, leading to the obstruction of the duodenum (4). Previous studies on SMAS, have investigated cases with postoperative complications, including bariatric surgery, a cancer-bearing state, and anorexia nervosa (4, 6, 7). Physical stimulus following corrective spinal surgery for scoliosis and the oppression of the duodenum by aneurysm have been reported as other causes (8, 9).

In the present case, because hyperthyroidism due to Graves’ disease was present along with diabetes, the patient’s body weight loss might have been accelerated, thereby leading to DKA and SMAS. Graves’ disease is the main cause of hyperthyroidism and is often complicated by diabetes (10). Although hyperthyroidism is a common cause of weight loss, there are few reports on SMAS due to hyperthyroidism (11). Because SMAS is a rare phenomenon, it is not recognized as a complication of Graves’ disease. Thus clinicians should consider the possibility of SMAS, particularly in patients with DKA and Graves’ disease who show acute body weight loss.

In an upper gastrointestinal contrast study the incidence of SMAS was reported to be approximately 0.2%; however, the actual prevalence of SMAS remains unclear (12-14). To the best of our knowledge, there are only three reports on diabetes complicated by SMAS (14-16). The details from the previous reports on diabetes complicated by SMAS and the present case are summarized in Table 2 and form the basis of much of this discussion [male, 2; female, 3; age, 18-65 years, (median: 41 years); duration of diabetes, 4-25 years (median: 13 years); loss of body weight, 15-50 kg, (median: 22.7 kg)]. Three of the five reported patients had type 1 diabetes (15); two had type 2 diabetes (14, 16). All of the previous cases presented symptoms such as nausea, abdominal discomfort, and vomiting, particularly after meals. Poor glycemic control was observed in four cases, and complications of diabetic neuropathy were observed in three cases, including our own.

According to Table 2, the cases that involve female pa-
Table 2. Characteristics of Five Diabetic Patients Complicated by Superior Mesenteric Artery Syndrome.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Type of Diabetes</th>
<th>Duration of Diabetes</th>
<th>Diabetes Treatment (More recent)</th>
<th>HbA1c (More recent)</th>
<th>Diabetic complications</th>
<th>Duration of SMAS</th>
<th>Body Weight Loss</th>
<th>Complicated Disease</th>
<th>Treatment of SMAS</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>F</td>
<td>Japanese</td>
<td>Type 1</td>
<td>17 years</td>
<td>Intensive insulin therapy</td>
<td>10% over 10 years</td>
<td>Retinopathy/Painful neuropathy</td>
<td>6 years suspected</td>
<td>-16 (56–40) kg (at the age of 16)</td>
<td>-4 kg/2 months (More Recent)</td>
<td>Eating disorder/Autonomic neuropathy/Orthostatic hypotension</td>
<td>Unknown/Unknown</td>
<td>(14)</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>M</td>
<td>Japanese</td>
<td>Type 2</td>
<td>25 years</td>
<td>Conventional insulin therapy</td>
<td>Unknown</td>
<td>Retinopathy/Peripheral neuropathy</td>
<td>10 years suspected</td>
<td>-50 (95–45) kg/27 years</td>
<td>Unknown</td>
<td>Autonomic neuropathy/Orthostatic hypotension</td>
<td>Conservative therapy</td>
<td>Improved</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>F</td>
<td>White</td>
<td>Type 1</td>
<td>12 years</td>
<td>Intensive insulin regimen</td>
<td>11.5%</td>
<td>No diabetic retinopathy and neuropathy</td>
<td>Unknown</td>
<td>-22.7 kg/Unknown duration</td>
<td>Painful sensory peripheral neuropathy</td>
<td>Orthostatic changes</td>
<td>Unknown</td>
<td>(15)</td>
</tr>
<tr>
<td>4</td>
<td>41</td>
<td>M</td>
<td>Unknown</td>
<td>Type 2</td>
<td>4 years</td>
<td>Insulin pump</td>
<td>11.4%</td>
<td>Unknown</td>
<td>1 week</td>
<td>-26 kg/3 months</td>
<td>Albuminuria</td>
<td>Amnorrhea</td>
<td>Conservative therapy</td>
<td>Improved</td>
</tr>
<tr>
<td>5</td>
<td>48</td>
<td>F</td>
<td>Japanese</td>
<td>Type 1 (SPIADD)</td>
<td>13 years</td>
<td>Intensive insulin therapy</td>
<td>15.3%</td>
<td>Retinopathy/Neuropathy</td>
<td>Approximately 1 week</td>
<td>-15 (57–42) kg/6 months</td>
<td>Albuminuria</td>
<td>Graves’ disease/Autonomic neuropathy/Orthostatic hypotension</td>
<td>Conservative therapy</td>
<td>Cured/Our Case</td>
</tr>
</tbody>
</table>

HbA1c: glycated hemoglobin, SMAS: superior mesenteric artery syndrome, SPIADD: slowly progressive insulin-dependent diabetes mellitus.

Patients with type 1 diabetes that is complicated by SMA might be complicated by psychosomatic disease. Jones et al. reported that the prevalence of eating disorders was approximately twice as high among diabetic females aged 12-19 as it was among age-matched controls (17). In the present case, however, the patient had SPIADD and there was no evidence of psychosomatic disease at the onset of diabetes, which occurred in middle age. Consequently, the characteristics of the diabetic clinical course, including the onset of Graves’ disease, are clearly different from the previous cases of diabetic female patients with psychosomatic disease. To the best of our knowledge, this is the first report on SMAS occurring with DKA and Graves’ disease.

Although SMAS is considered to have a good prognosis, there are reports of fatal cases where patients died due to gastric perforation or electrolyte imbalance (18). Some cases required emergency surgery due to gastric perforation (19, 20). Although the number is small, fatal SMAS cases have certainly been reported; however, the exact prognosis of SMAS has not been fully elucidated. A rapid and accurate diagnosis of SMAS is therefore very important; however, there are no diagnostic criteria for SMAS. In the present case, a rapid diagnosis prevented gastric perforation.

At present, because the precise diagnostic criteria for SMAS remain to be established, SMAS is often diagnosed based on a combination of findings, including a classical upper gastrointestinal contrast study, enhancement on a CT scan, or an abdominal ultrasound examination. Previous reports suggested that CT was very useful for diagnosing SMAS. In particular, the measurements of the aorta-SMA angle and aorta-SMA distance at the point of duodenal crossing are considered to be important for diagnosing SMAS. Konen et al. reported that the aorta-SMA angle in patients with SMAS was from 6° to 22° and that the aorta-
SMA distance was 2-8 mm; in contrast, they reported that the aorta-SMA angle and aorta-SMA distance in healthy controls were 25-60° and 10-28 mm, respectively (21).

Unfortunately, only a plain CT scan and upper gastrointestinal endoscopy were conducted during the acute period in the present case. In the acute phase, an upper gastrointestinal contrast study might have risked the dilatation of the stomach. In addition, it was not known whether the patient had a history of contrast agent use. Therefore, a non-invasive plain CT scan was conducted. However, Agrawal et al. reported that 16-slice multidetector row computed tomography with 3-dimensional rendering provides sagittal reconstructions that can be useful for measuring aorta-mesenteric angle and distance in SMAS (22). In the present case, we used 16-slice multidetector row computed tomography, and 3-dimensional rendering, including sagittal reconstructions could be conducted. The aorta-SMA angle was approximately 13° (narrow), and the aorta-SMA distance was approximately 6.44 mm (short). The values were not inconsistent with the values of Konen’s reports. Furthermore, abdominal enhanced computed tomography on the 24th day indicated that the aorta-SMA angle was approximately 22°, and that the aorta-SMA distance was approximately 8.74 mm. These changes suggested that the improvement of both the aorta-SMA angle and the aorta-SMA distance had occurred in response to the conservative treatment for SMAS.

In the present case, the diagnosis of SMAS was difficult for a number of reasons. First, the common symptoms of SMAS include nausea, vomiting, and body weight loss; however, there are no particular symptoms of SMAS. Second, the digestive symptoms were caused not only by SMAS but also by DKA and hyperthyroidism. Third, because the present patient might have had diabetic neuropathy, diabetic gastroenteropathy could have coexisted.

In the present case, the proof of diabetic neuropathy was the low CVR-R value (1.41%), Achilles tendon reflex attenuation, and orthostatic hypotension. Kageyama et al. reported that a CVR-R value of 2% can be considered as the critical level, which determines whether or not the symptoms of diabetic autonomic neuropathy will appear (23). Because the symptoms of diabetic gastroenteropathy mimic those of SMAS, the detection of SMAS might be delayed (14-16). In the present case, an autonomic nervous disorder due to diabetic neuropathy might have occurred due to the decreased peristalsis of the digestive tract, which might worsen the digestive symptoms of SMAS. Unfortunately, we could not conduct a stomach excretion test; however, Asakawa et al. reported that CVR-R was related to stomach excretion. In the present case, we recognized a low CVR-R value (24). In addition, the persistent residual digestive symptoms which occurred after the treatment of DKA suggested the possibility of SMAS.

SMAS is predominantly treated by conservative medical management, including nutritional support; however, several reports have described the application of surgical therapies (4, 15, 20). However, there are no guidelines on the treatment of SMAS. In the present case, the patient’s digestive symptoms, such as nausea and abdominal discomfort, continued until the patient reached a body weight of approximately 38 kg. Although the patient’s body weight was at its lowest on the 17th to 25th days of hospitalization, the symptoms of nausea and vomiting temporarily subsided. The main reason was thought to be that the physical oppression from the intestinal tract to the SMA was resolved by the aspiration of the intestinal fluid. As a result, both the aorta-SMA angle and the aorta-SMA distance showed improvement, and oral food could be easily pass to a horizontal portion of the duodenum. In fact, the reassessment of the abdominal CT scan on the 24th day indicated that a bloated stomach, duodenal obstruction, and both aorta-SMA angle and aorta-SMA distance had improved, even though the patient’s body weight had decreased (Fig. 4). In present case, although the loss of body weight was major reason of SMAS in the long period, the physical oppression from the intestinal tract to the SMA might have worsened the patient’s SMAS over a short period of time. In addition, as previously described, the patient’s condition might have been complicated by diabetic autonomic neuropathy. Thus, the interaction of high glucose, dehydration, DKA and diabetic autonomic neuropathy might have induce the bloating of the intestinal tract over a short period of time. Table 2 shows that conservative medical management was conducted in three cases, and that duodenoejunostomy was performed in one case. Welsch et al. noted that acute SMAS with a history of up to one month might be better suited to conservative treatment (25, 26). With regard to this viewpoint, our patient had a brief history of symptoms and was cured by conservative management alone over a relatively short period of time.

In addition to the patient’s body weight gain, we calculated the total energy intake and nitrogen content ratio. Calloway et al. reported that even if large amounts of protein are administered, in cases where the total energy intake is insufficient, most of the protein utilized by the body as an energy source (27). To restore protein in the body, we maintained a total energy intake and nitrogen content ratio of approximately 150-200.

In summary, we demonstrated a case of SMAS that occurred in a patient with DKA and Graves’ disease. The present case suggests that clinicians should be vigilant for the occurrence of SMAS when patients with both DKA and Graves’ disease present rapid weight loss. Further reports are need to clarify the pathogenesis of SMAS.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement
We thank Dr. Yoshinori Satoh for introducing us to the present patient.

References
1. Tully GT, Lowenthal JJ. The diabetic coma of acute pancreatitis.