Post-fundoplication late dumping syndrome diagnosis with provocative modified oral glucose tolerance test

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Abstract

We report a case of dumping syndrome, a rare complication of fundoplication in adults, which was diagnosed by a provocative modified oral glucose tolerance test. A 71-year-old woman with a pertinent history of laparoscopic paraesophageal hernia repair and Toupet fundoplication presented for evaluation of post-prandial symptoms such as bloating, nausea, palpitation, dizziness, perspiration, weakness, severe diarrhea and flatulence that were not relieved with Fermentable Oligo-, Di-, Mono-Saccharides And Polyols diet and irritable bowel syndrome medications. A comprehensive work up revealed a rapid gastric emptying on gastric scintigraphy and hypoglycemia on provocative modified oral glucose tolerance test. Late dumping syndrome was diagnosed, and the symptoms were resolved with dietary measures.

Keywords
Dumping syndrome; fundoplication; oral glucose tolerance test

Abbreviations
DS: Dumping syndrome; GERD: Gastroesophageal reflux disease; IBS: Irritable bowel syndrome; FODMAP: Fermentable oligo-, di-, mono-saccharides and polyols; CT: Computerized tomography; VIP: Vasoactive intestinal polypeptide; 5-HIAA: 5-Hydroxyindoleacetic acid; OGGT: Oral glucose tolerance test

Introduction

Dumping Syndrome (DS) in adults is often associated with gastrectomy, Roux-en-Y gastric bypass, and truncal vagotomy. Post-fundoplication DS has been reported predominantly in pediatric population, and only a few has been reported in adult patients. Recently, more cases of post-fundoplication DS in adults are reported in the literature, and DS has recently started to be recognized as a rare complication of fundoplication. A proper diagnosis can be delayed due to the unfamiliar association with fundoplication and shared symptomatology with irritable bowel syndrome. Therefore, utilization of low cost and accessible...
oral glucose tolerance test in post-fundoplication patients may reduce delayed diagnosis of DS.

Case Presentation

A 71-year-old woman with a history of refractory GERD and 3 cm hiatal hernia with Cameron's erosions underwent Toupet fundoplication and laparoscopic paraesophageal hernia repair two years prior to presenting for evaluation of long-standing post-prandial symptoms. The reflux was resolved after undergoing the surgery. However, one month after the surgery, the patient developed severe post-prandial fatigue, abdominal bloating, nauseas, palpitation and dizziness that occurred once in every three to five days. The patient also complained severe diarrhea, burping and flatulence that lasted for several hours after eating.

The patient was evaluated for the symptoms shortly after the surgery, and was treated for dehydration. However, she persistently manifested with the symptoms without any improvements. She further developed signs of malnutrition such as alopecia, onychoschizia, and acholic stools. The initial comprehensive work up performed at post-op six months included unremarkable upper GI series with small bowel follow-through, barium swallow and ultrasound of right upper quadrant abdomen nuclear medicine hepatobiliary scan with ejection fraction. The colonoscopy biopsies were negative for microscopic colitis. The patient was diagnosed with irritable bowel syndrome (IBS) at an outside facility, and denied any symptoms relief from Fermentable Oligo-, Di-, Mono-saccharides And Polyols (FODMAP) diet, dicyclomine, loperamide, and/or amitriptyline.

An extensive work up was performed due to the persistent and severe nature of the symptoms leading to malnutrition and poor quality of life in the patient despite proper IBS treatment. Upper endoscopy, CT abdomen and timed barium esophagram were unremarkable. Celiac, and stool studies, hydrogen breath test, C-peptide, fasting VIP, and gastrin were within the normal limit. 5- HIAA levels was mildly elevated to 6.2 mg/24 hour. Four hour gastric emptying test was significant and revealed a rapid gastric emptying resulting in retention of 37.9% at 30 minutes and 7.7% at 60 minutes (Figure 1).

![Figure 1: The gastric scintigraphy showing very rapid gastric emptying](image-url)
We further performed a provocative modified 50 g oral glucose tolerance test (OGGT). The patient had a blood pressure of 122/85 mmHg, and a pulse of 71 prior to ingesting glucose. During the ingestion, she had a blood pressure of 123/79 mmHg and a pulse of 76 beats per minute. At five minutes after the ingestion, her blood pressure was 107/72 mmHg and pulse was 68 beats per minute. The blood glucose level after two hours of ingestion revealed hypoglycemia of 37 mg/dL (Table 1). The patient complained dizziness, weakness and fatigue after the ingestion. Late DS diagnosis was confirmed by induced post-prandial hypoglycemia and DS symptoms. She reported substantial relief from small frequent meals with high fiber and high glycemic index diet and avoiding simple sugars.

<table>
<thead>
<tr>
<th>50g glucose ingestion</th>
<th>Before</th>
<th>During</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mmHg)</td>
<td>122/85</td>
<td>123/79</td>
<td>107/72</td>
</tr>
<tr>
<td>Heart rate (beats per minute)</td>
<td>71</td>
<td>76</td>
<td>68</td>
</tr>
<tr>
<td>2 hours glucose (mg/dL)</td>
<td>n/a</td>
<td>n/a</td>
<td>37</td>
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Table 1: 50 g provocative modified oral glucose tolerance test result

Discussion

DS in adult population is well associated in gastrectomy, gastrojejunostomy, vagotomy and early post-operative period of Roux-en-Y gastric bypass [1]. Post-fundoplication DS was exclusively associated in pediatric population in the past [2]. Since the first reported case of DS after an open Nissen fundoplication in 1983 followed by the DS case after laparoscopic Nissen fundoplication in 2006, more post-fundoplication DS cases have been reported in the literature [3-7]. Recently, DS has been recognized as a rare complication of fundoplication in adult population.

Common post-fundoplication side effects are gas bloat syndrome, dysphagia, abnormal gastric motility, gastric hypersensitivity and recurrent heartburn. On the other hand, diarrhea is a less discussed complication of anti-reflux surgery that is frequently associated with DS along with severe abdominal pain [8]. A study by Klaus et al. on post anti-reflux surgery diarrhea revealed that 15 out of 84 patients (18%) after laparoscopic antireflux surgery developed a new onset of diarrhea. Two thirds of these patients developed diarrhea within six weeks after surgery that is worsening after meals, and 13 of 15 patients (85%) continued to manifest with diarrhea even after two years [9]. DS patients often have previous diagnosis of gastroparesis (37.1%) or IBS (14.3%) [10]. These suggests that DS may be an under diagnosed complication in adult population that is often misdiagnosed for IBS and gastroparesis due to shared symptomatology and unfamiliar association with fundoplication [11].

The symptoms of DS are mainly vasomotor and gastrointestinal. Tachycardia, perspiration, palpitation, flushing, hypotension and syncope are known vasomotor symptoms whereas cramping abdominal pain, borborygmi, bloating, nausea and diarrhea are known gastrointestinal symptoms [7]. Uncontrolled longstanding DS can lead to sitophobia, weight loss, and malnutrition from a limited mucosal contact time for absorption [11].

Dumping syndrome is divided into two types: Early (osmotic) or late (hypoglycemic). Patients with
early type DS predominantly complains of flushing, tachycardia and dizziness that occur up to 45 minutes after a meal. These vasomotor symptoms occur in response to vasodilation and hemoconcentration as a large volume of osmotic material pass into the small bowel causing a rapid influx of fluid from intravascular space, and a release of vasoactive GI hormones [7]. Patients with late type predominately presents with diaphoresis, palpitation, weakness and fainting that occurs two to four hours after a meal. The hypoglycemic symptoms are caused by a rapid delivery of sugars into the duodenum and consequent a rapid rise in blood sugars and an excessive serum insulin response leading to reactive hypoglycemia. This response is associated with an enhanced secretion of the insulinotropic hormone GLP-1 and GIP [12].

Gastric emptying is controlled by multiple factors: fundic tone, antropyloric mechanism and duodenal feedback, and these are regulated by enteric nervous system and circulating GI hormones. 1 Current literature suggests that reduction of fundus size from fundoplication decreases fundic relaxation, and thus, leads to acceleration of gastric emptying. Gastric motility studies in post-fundoplication and fundectomy patients revealed less pronounced and shorter relaxation of proximal stomach, and accelerated gastric emptying due to impaired fundal accommodation [13,14]. GI hormone role in late DS was noted by a study by Miholic et al. that revealed rapid and early rise of plasma glucose, increased GLP-1 and GIP concentrations and reactive hypoglycemia after ingesting glucose solution in post-fundoplication patients [12]. These studies both suggest an increased risk of DS in post-fundoplication patients.

Another theory of the etiology of post-fundoplication DS is vagus nerve injury. Hejazi et al. reported that about 10.5% of patients who had a rapid gastric emptying of greater than 50% at 1 hour was identified to be post-fundoplication patients with a confirmed accidental vagotomy from sham meal challenge [11]. However, previously reported cases of adult post-fundoplication DS have confirmed the normal vagal nerve function or identified the vagus nerve intraoperatively [2,14]. In addition, Lindeboom et al. revealed that gastric emptying in patients with signs of postoperative vagus nerve dysfunction did not significantly differ from that of the control group [13]. Paradoxically, accidental vagus nerve injury and/or truncal vagotomy can also result in delayed gastric emptying. Nissen Fundoplication is the major surgery associated with post-surgical gastroparesis and could be attributed to “accidental” vagal nerve injury during surgery. The theory is that the extension of the denervation to the antral area results in delayed gastric emptying, whereas minor vagal injury localized to the fundus results in rapid gastric emptying test by inhibition of receptive relaxation [11].

The diagnosis of dumping syndrome is made by clinical assessment and modified oral glucose tolerance test. Sigstad's scoring system is a symptom-based questionnaire that was developed to help predict DS and assess therapy response in DS patients [15]. Provocative modified OGTT, which was performed in the patient, is a main diagnostic test for both types of DS. A rise in heart rate by 10 beats per minutes or more in the 30 minutes after an OGTT is diagnostic of early type. This test has high sensitivity and specificity for early type, 100% and 94% respectively [16]. Late type patients will present with hypoglycemia of <60 at one to two hours after glucose intake. Elicitation of symptoms after an OGTT is considered more accurate for the diagnosis of late type [16]. Hydrogen breath test after glucose ingestion can also be used to diagnose early type as it indirectly measured gastric emptying [17].
Gastric emptying scintigraphy can reveal a rapid gastric retention, which is considered 70% retention at 30 minutes and 30% retention at one hour [17]. A previous study investigating the gastric-emptying scintigraphy results on suspected DS patients showed questionable utility. A study by Balan et al. revealed 17 normal (24%), 48 rapid (69%) and five delayed (7%) gastric emptying in patients with clinically suspected DS, and a positive predictive value of clinical suspicion for rapid gastric emptying of 62% [18]. Similarly, a study by Sigstad et al. showed no difference in rates of gastric emptying between post-gastrectomy patients with and without dumping symptoms [15]. In conclusion, the scintigraphy may only be used to aid diagnosis of DS as this test has poor sensitivity and specificity [16].

A rare adult post-fundoplication late DS in this patient was confirmed by the positive provocative modified oral glucose tolerance test with elicitation DS symptoms like dizziness, weakness and fatigue and hypoglycemia of < 60 mg/dL after two to three hours of ingestion. The gastric emptying scintigraphy result aided the diagnosis with a retention of 37.9% at 30 minutes and 7.7% at 60 minutes (Figure 1).

Many patients with dumping syndrome respond well to dietary management with small, frequent, high fiber, delayed post-prandial fluid intake, and avoidance of simple carbohydrate and lactose. Small and dry meals target to prevent early type symptoms, and high fiber and complex carbohydrate target to prevent late type symptoms. If patient is refractory to diet management, medications can be used such as beta-blockers for early DS, and acarbose or miglitol for late DS targeting postprandial fluctuation of blood glucose and plasma insulin level [19]. Somatostatin analogs can also be used to inhibit release of insulin and gut derived hormones, and slow the rate of emptying. Efficacy of octeotide and pastiteotide has been well proven by previous studies [3,20]. Surgery is an option for patients who are refractory to both diet management and medications. Mizrahi et al. reported a case of a patient who required partial gastrectomy and Roux-en-Y gastric bypass for post-Nissen fundoplication dumping syndrome [6].

**Conclusion**

This case highlights utilization of low cost and accessible provocative modified OGTT that may reduce delayed diagnosis of DS in post-fundoplication patients. OGTT and gastric emptying scintigraphy should be considered as a part of workup for presumed new onset IBS in post-fundoplication patients. DS work up should be performed especially in patients with predominant post-prandial and systemic symptoms such as dizziness and palpitation that are refractory to standard IBS treatment.
References


19. Hirose S, Iwahashi Y, Seo A, Sumiyoshi M, Takahashi T, Tamori Y. Concurrent therapy with a low-carbohydrate diet and migtol remarkably improved the postprandial blood glucose and insulin levels in a patient with reactive hypoglycemia due to late