Superior Mesenteric Artery Syndrome May Be Overlooked in Women with Functional Dyspepsia

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Abstract:
Objective Superior mesenteric artery (SMA) syndrome is characterized by the compression of the third segment of the duodenum between the SMA and aorta, resulting in duodenal obstruction. Because the symptoms of the syndrome are similar to those of functional dyspepsia (FD), this study aimed to examine whether or not patients with SMA syndrome were present among those diagnosed with FD.

Methods Patients with an FD diagnosis underwent measurement of the angle and distance between the SMA and aorta by ultrasonography or computed tomography. Patients with an angle of ≤22° or with a distance of ≤8 mm between the SMA and aorta were diagnosed with SMA syndrome. Bacterial culture of the duodenal aspirate was also performed.

Results Of the 46 FD patients, 5 (11%) met the criteria. All 5 were women with a body mass index significantly lower than the remaining 41 patients (18.7 vs. 24.0 kg/m², p=0.003). In addition, all 5 patients had 10⁵/mL or more bacteria in the duodenum. The symptoms of these five patients were treated through dietary and postprandial posture counselling with or without medication.

Conclusion Patients with SMA syndrome were observed among underweight women diagnosed with FD. Their symptoms may be associated with bacterial overgrowth.

Key words: functional dyspepsia, postprandial distress syndrome, small intestinal bacterial overgrowth, superior mesenteric artery syndrome

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Introduction

Functional dyspepsia (FD), a relapsing and remitting disorder, is characterized by a constellation of symptoms related to the gastroduodenal region of the upper gastrointestinal tract. The current standard for the diagnosis of FD is based on the Rome III (or recently revised Rome IV) criteria, which define the disease as the presence of one of the following symptoms without any structural diseases: bothersome postprandial fullness, early satiation, epigastric pain, and epigastric burning; the former two symptoms constitute postprandial distress syndrome (PDS), whereas diseases with the latter two are known as epigastric pain syndrome (EPS) (1, 2).

The prevalence of FD in community settings has been reported to range from 5.3-20.4% (3). A number of pathophysiological conditions have been suggested in association with FD, including gastric motility and visceral hypersensitivity, psychosocial factors and acid, *Helicobacter pylori* infection, genetics and a history of abuse in childhood, infectious gastroenteritis, smoking, alcohol intake, sleep disorders, intake of a high-fat diet, and cascade stomach (4). However, no definite treatment strategy has been established for FD, and therefore, to ameliorate symptoms, various therapies, including *Helicobacter pylori* eradication therapy, acid-suppression therapy, prokinetic agents, antidepressants, and psychological therapy as well as placebo or reassurance, are applied to each patient (5).

In this regard, patients with indefinite digestive symptoms...
are likely to be diagnosed with FD. Although structural diseases, including peptic ulcer, gastroparesis, gastroesophageal cancer, as well as the diseases from outside of the gastrointestinal region like gallbladder, pancreas and liver, should be ruled out, proper radiographic and endoscopic scrutiny is sometimes not done prior to a diagnosis of FD (4, 5). Indeed, the Rome III criteria describe upper endoscopy as the only indispensable modality for excluding structural diseases.

Superior mesenteric artery (SMA) syndrome is characterized by the compression of the third segment of the duodenum between the SMA and aorta, causing duodenal obstruction. Its incidence was reported to be between 0.013% and 0.3% (6, 7). The specific symptoms of the syndrome include early satiation, bothersome postprandial fullness, nausea, and vomiting. Thus, the symptoms of SMA syndrome are similar to those of FD, except that SMA syndrome frequently causes vomiting (7-10). Although a diagnosis is usually made radiographically or by ultrasound (US) to determine the compression of the third segment of the duodenum by SMA, those examinations are not always performed appropriately for discrimination of the syndrome from FD (6, 8). Therefore, patients with SMA syndrome may be inappropriately diagnosed with FD due to the similarity in symptoms.

The aim of this study was to examine whether or not patients with SMA syndrome were present among those who had been previously diagnosed with FD.

Materials and Methods

Patients

We retrospectively examined the data of patients diagnosed with FD based on the Rome III criteria and requested further examinations with the expectation of finding other comorbid diseases associated with their symptoms. Our criteria for the selected patients included those who had undergone examinations for the discrimination of SMA syndrome with computed tomography (CT) or US and small intestinal bacterial overgrowth (SIBO) by culture of duodenal aspirate during upper endoscopy. Patients were identified consecutively from those who had visited Hashimoto Municipal Hospital and Wakayama Rosai Hospital between April 2015 and April 2016. Forty-six patients met the criteria, and air insufflation were minimized prior to obtaining aspirate in order to avoid contamination and to maintain the intraluminal anaerobic environment. Approximately 2 mL of aspirate were collected in a sterile tube and transferred immediately in order to be plated for both aerobic and anaerobic microorganisms. When growth was detected, organisms in the colonies were counted and identified by standard methods. A total bacteria count of ≥10^7/mL was considered positive for bacterial overgrowth, as previously reported as the definition of SIBO (13-15).

Statistical analyses

Differences between patients with and without SMA syndrome were determined using Wilcoxon’s signed-rank test and the Mann-Whitney U test as appropriate. A p value <0.05 was considered statistically significant. Data were statistically analyzed using the JMP version 12 software program (SAS Institute, Cary, USA).

Results

Table 1 shows the clinical characteristics of all 46 pa-
patients. Twenty-nine patients (63%) were classified into PDS. The median age was 64.5 (21-83) years, and 27 (59%) were women. The median body mass index (BMI) was 23.9 (16.5-29.1). The median body mass index (BMI) was 23.9 (16.5-29.1). Bacterial overgrowth (18.7 (16.6-19.8) vs. 24.0 (16.5-29.1), p=0.003). Bacterial overgrowth (18.7 (16.6-19.8) vs. 24.0 (16.5-29.1), p=0.003). The bacterial species isolated from the two groups were similar (Escherichia coli, Enterococcus species, Klebsiella pneumonia and Proteus mirabilis), and some patients with and without a diagnosis of SMA syndrome obtained transient symptom relief with antibiotics administration [4/5 (80%) and 4/9 (44%), respectively]. The characteristics of the five patients with SMA syndrome are summarized in Table 3. The symptoms of those five patients were resolved through dietary and postprandial posture counselling, with or without medication based on the treatment of SMA syndrome.

**A typical case of SMA syndrome previously diagnosed as FD**

A 35-year-old woman had chronic postprandial discomfort in her epigastrium and had been diagnosed with FD 8 years previously. Her symptoms never disappeared despite continuous administration of a PPI and a prokinetic agent.
Table 1. Baseline Characteristics of Patients with Functional Dyspepsia.

| Patients      |       |
|---------------|-------|
| Total         | 46    |
| Age (years)   | 65 (21-83) |
| Gender        |       |
| Male          | 19 (41%) |
| Female        | 27 (59%) |
| Type of functional dyspepsia |       |
| Postprandial distress syndrome | 29 (63%) |
| Epigastric pain syndrome | 17 (37%) |
| Body mass index (kg/m²) | 23.9 (16.5-29.1) |
| Superior mesenteric artery-aorta |       |
| Angle (degrees) | 34 (18-52) |
| Distance (mm)  | 19 (8-28) |
| Number of bacteria from duodenal aspirate (/mL) |       |
| ≥10⁵ (/mL)    | 14 (30%) |
| Helicobacter pylori infection (current or past) | 20 (43%) |
| Concomitant diseases |       |
| Diabetes mellitus | 10 (22%) |
| Pulmonary diseases | 6 (13%) |
| Liver cirrhosis  | 5 (11%) |
| Heart diseases  | 5 (11%) |
| Stroke         | 4 (10%) |
| Hemodialysis   | 3 (7%) |
| None           | 22 (48%) |
| Medication     |       |
| Proton pump inhibitor | 30 (65%) |
| Histamine type 2 receptor antagonist | 9 (20%) |
| Prokinetic agent | 15 (33%) |

Table 2. Differences between Patients with and without Superior Mesenteric Artery Syndrome.

| Superior mesenteric artery syndrome |       |
|------------------------------------|-------|
| Yes (N=5)                          | No (N=41) | p value |
| Type of functional dyspepsia       |       |
| Postprandial distress syndrome     | 5 (100%) | 24 (59%) | 0.07 |
| Epigastric pain syndrome           | 0 (0%)  | 17 (41%) | 0.07 |
| Body mass index (kg/m²)            | 18.7 (16.6-19.8) | 24.0 (16.5-29.1) | 0.003* |
| Superior mesenteric artery-aorta   |       |
| Angle (degrees)                    | 19 (18-24) | 35 (23-52) | 0.0005* |
| Distance (mm)                      | 9 (8-10) | 19 (9-28) | 0.0007* |
| Number of bacteria from duodenal aspirate |       |
| ≥10⁵ (/mL)                         | 5 (100%) | 9 (22%) | 0.0015* |

*statistically significant

Her BMI was 18.7 at the time of visiting our hospital. The angle and distance between the aorta and SMA, which was measured at the level of passing the duodenum, were 19° (Fig. 1) and 9 mm (Fig. 2), respectively. She was suspected of having SMA syndrome, so counseling on postprandial positions practice (i.e. left lateral decubitus, prone and knee-to-chest positions) and dietary advice (i.e. reduce the amount for each meal and increase the number of meals per day) were provided. Six months later, her symptoms had completely disappeared without any additional medication, and her BMI recovered to 22.1.

Discussion

Symptoms of SMA syndrome, including bothersome postprandial fullness, early satiation, and nausea, are similar...
to those of FD, particularly those of PDS, except that vomiting is rare in FD. Although a diagnosis of FD requires the exclusion of structural diseases, sufficient medical examinations for this purpose are not always performed. Therefore, we suspected that patients with SMA syndrome might have been misdiagnosed with FD. In this study, we examined the positional relationships between the SMA and aorta using CT or US in patients who had previously been diagnosed with FD and found that 5 (11%) out of 46 FD patients were considered to have SMA syndrome. To our knowledge, the discrimination of SMA syndrome from FD has never been reported; therefore, our findings are relevant with respect to the difference in the treatment strategy between these two diseases.

Although the Rome criteria recommend upper endoscopy for discriminating structural diseases, chronic SMA syndrome does not show any specific findings on upper endoscopy (6, 7, 9, 16). In this sense, CT, US, or conventional barium studies is recommended for patients with a diagnosis of FD with PDS, particularly thin women, if their symptoms are not relieved despite conventional FD treatments. They may show characteristic findings, including dilation of the stomach and duodenum and compression of the mucosal folds of the duodenum. However, those studies are rarely performed for patients suspected of having FD. Furthermore, even when those radiologic studies are performed, specific findings can be easily overlooked due to the rarity of SMA syndrome. Therefore, the discrimination of SMA syndrome in prediagnosed FD patients requires suspicion of the syndrome by the attending physicians. Both insufficient examinations for ruling out organic diseases and difficulty in diagnosing SMA syndrome even with imaging modalities may be responsible for the inappropriate diagnosis of SMA syndrome as FD.

An SMA-aorta angle of 22-25° or less and a distance of ≤8 mm have been shown to correlate well with the symptoms of SMA syndrome (12). The criteria we applied to this study were an angle ≤22° or a distance of ≤8 mm, and the specificity of the criteria is based wholly on the improvement of the symptoms by treatments specific for SMA syndrome. The examinations of the correlation between the SMA and aorta were performed with US in most of our patients, although CT is reportedly more accurate than US in determining the criteria of SMA syndrome (11). In the present study, the differences between the two modalities in the angle and distance were 2-4° and 1-5 mm, respectively. The distance discrepancy in 3 patients with SMA syndrome who underwent both US and CT was 0-2 mm, suggesting that US can be used to diagnose the syndrome.

All five patients with SMA syndrome in this study were women with a low BMI. A low BMI is a significant risk factor for developing SMA syndrome (11, 17-20). In particular, predisposed medical conditions associated with catabolic states and rapid weight loss are known to be a frequent cause of a decrease in the SMA-aorta angle and subsequent duodenal obstruction (18). In addition, anorexia nervosa, which is predominantly observed in women, is known to induce SMA syndrome due to weight loss (21, 22). A lower volume of visceral fat due to a decrease in estrogen may also be correlated (10, 23, 24). Our results therefore appear to be reasonable with regard to the epidemiologic aspects, and close examinations of patients with FD should be considered, particularly for underweight women with complaints of PDS.

The bacterial overgrowth in the duodenum found in this study appeared to be another relevant finding, as some FD patients have been reported to be associated with SIBO (14), and antimicrobial treatment was able to ameliorate the symptoms (14, 15). In this study, 14 (30%) patients, including all 5 SMA syndrome patients, showed bacterial overgrowth (≥10^5/mL) in the duodenal aspirate. Although the amount of bacteria in the duodenal aspirate is considered a diagnostic criterion of SIBO (13-15, 25, 26), this criterion might not be applicable in patients with SMA syndrome due to duodenal obstruction. However, bacterial overgrowth in the duodenum may be correlated with the symptoms and pathophysiology of SMA syndrome. Indeed, the susceptibility to antibiotics appeared to be better in patients with SMA syndrome than in those FD, although no statistical significance was observed (80% vs. 44%, p=0.2), possibly due to the small number of patients. Although there have been few reports on the involvement of SIBO in FD or the effect of antibiotics on FD, the difference in the response to antibiotics may partly reflect the difference in the pathophysiology between FD and SMA syndrome. Further investigations are required on this issue. In this regard, the PPI prescribed for three out of the five SMA syndrome patients might have actually worsened their symptoms. Further investigations are required regarding the correlation between bacterial overgrowth and SMA syndrome.

### Table 3. Characteristics of 5 Patients with Superior Mesenteric Artery Syndrome.

| Age | Sex | BMI (kg/m²) | Angle (degrees) | Distance (mm) | Number of bacteria (10^5/mL) | Treatment |
|-----|-----|-------------|----------------|---------------|-----------------------------|-----------|
| 25  | Female | 19.6 | 20 | 10 | Counseling only |
| 35  | Female | 18.7 | 19 | 9  | Counseling only |
| 48  | Female | 19.8 | 24 | 8  | Counseling and medication |
| 55  | Female | 16.6 | 18 | 8  | Counseling and medication |
| 67  | Female | 17.6 | 19 | 9  | Counseling and medication |

BMI: body mass index
Several limitations associated with the present study warrant mention. First, the number of the examined patients was relatively small, and all of the subjects were Japanese. Reproducibility should be confirmed with large numbers of patients and in other ethnic populations. Second, the diagnosis of FD was based on the Rome III criteria in this study, although the Rome IV criteria were developed in 2016 (27, 28). As the Rome IV criteria of FD are stricter than the Rome III criteria with regard to the frequency and severity of symptoms, some of the 46 FD patients in this study might not have met those criteria. Finally, we provided counseling and medication as the treatment for only five patients with a diagnosis of SMA syndrome. To verify the specificity of our diagnostic criteria, such interventions should have been performed for the remaining 41 patients without SMA syndrome.

In conclusion, we identified several patients with SMA syndrome who had previously been diagnosed with FD—al women with a low BMI. The symptoms of these patients might have been associated with bacterial overgrowth in the duodenum. SMA syndrome should be considered when underweight patients suffer from symptoms associated with FD, as these symptoms may be resolved with appropriate treatment for SMA syndrome.

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

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