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Review

Is Gastroesophageal Reflux Disease and Achalasia Coincident or Not?

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Achalasia and gastroesophageal reflux disease (GERD) are on opposite ends of the spectrum of lower esophageal sphincter dysfunction. Heartburn is the main symptom of GERD. However, heartburn and regurgitation are frequently observed in patients who have achalasia. The diagnosis of achalasia might be delayed because these symptoms are misinterpreted as gastroesophageal reflux. Here, we reviewed the clinical characteristics of patients with the erroneous diagnosis of GERD who actually had untreated achalasia.
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Key Words
Esophageal achalasia; Gastroesophageal reflux; Heartburn

Introduction

Achalasia is a motility disorder characterized by esophageal aperistalsis and nonrelaxation of the lower esophageal sphincter (LES).[1] Gastroesophageal reflux disease (GERD) is a condition that develops when reflux of gastric contents causes symptoms and complications.[2] Generally, achalasia and GERD are thought to be at opposite ends of the spectrum of LES dysfunction. In achalasia, the LES may be hypertensive and show impaired relaxation in response to swallowing.[3] In GERD, the LES can either be hypotensive or display frequent relaxations. Therefore, LES dysfunction in achalasia may serve as a substantial barrier to the reflux of gastric contents, and GERD may not be expected to appear frequently in patients with achalasia. However, there is a portion of overlap between achalasia and GERD, and it is still controversial whether these conditions co-exist or whether one disease transforms into the other.

Overlap Between Gastroesophageal Reflux Disease and Achalasia

In the early stages of achalasia, chest pain or heartburn, and regurgitation commonly occurs.[4-6] The sensitivity and the specificity of symptoms are poor indicators of the status of esophageal motility disorder.[7] Heartburn and regurgitation is the main symptom of GERD, caused by reflux of gastric acid. However, heartburn and regurgitation is frequently observed in patients who have achalasia (Table). Heartburn was reported in 13.2-68.0% of patients with achalasia. According to a previous report, proton pump inhibitors were prescribed to 53% of achalasia patients, histamine H_2 blockers to 10%, and both to 6% on the assumption that GERD was the cause of heartburn and regurgitation.[8] Dysphagia occurs in patients with achalasia and is not easily recognized by patients and physicians.[9] Spechler et al[10] demonstrated that in some patients, the

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Table. Symptoms of Achalasia

Study ID	Authors	Year	Heartburn (n [%])	Regurgitation (n [%])	Chest pain (n [%])	Participant	Other symptoms (n [%])
1	Patti et al[7]	1997	27 (67.5)	NA	NA	40	Dysphagia (40 [100.0])
2	Fisichella et al[8]	2008	75 (51.7)	110 (75.9)	60 (41.4)	145	Dysphagia (136 [93.8]), weight loss (51 [35.2]), aspiration (18 [12.4])
3	Rosenzweig and Traube[9]	1989	10 (40.0)	16 (64.0)	5 (20.0)	25	Dysphagia (23 [92.0]), nocturnal cough (9 [36.0]), weight loss (12 [48.0])
4	Spechler et al[10]	1995	32 (47.8)	47 (70.1)	35 (52.2)	67	Dysphagia (67 [100.0]), weight loss (37 [55.2])
5	Ponce et al[26]	2011	15 (37.5)	NA	NA	40	NA
6	Howard et al[36]	1992	5 (13.2)	NA	NA	38	Dysphagia (38 [100.0]), weight loss (23 [60.5])

NA, not applicable.

dissolution of heartburn and regurgitation and appearance of dysphagia could be a symptom of achalasia. In particular, they insisted that achalasia could develop in patients with chronic GERD.

Does Gastroesophageal Reflux Disease Really Progress to Achalasia?

Several authors have suggested that a spectrum of related esophageal motor disorders exists and that some patients may progress from one type of motor disorder to another.[11-15] There is no sufficient data to prove whether GERD progresses to achalasia. There are several case reports describing the progression of GERD to achalasia. Smart et al[16] described 5 patients with longstanding GERD that antedated the onset of achalasia. Additionally, Robson et al[17] showed that GERD progressed to diffuse esophageal spasm and then to achalasia.

Are Gastroesophageal Reflux Disease and Achalasia Coincident Diseases?

There are several reports that GERD and achalasia are the outcomes of 2 independent disease processes. Heartburn is the form of GERD that results from dysmotility of achalasia. The LES dysfunction in achalasia might be a substantial barrier to reflux. However, some patients occasionally experience episodes of complete LES relaxation, during which gastric contents can enter the esophagus.[18] The refluxed gastric contents may be poorly cleared from such a dysfunctional esophagus, causing substantial heartburn. This mechanism is supported by previous reports that esophageal acid exposure was documented by pH monitoring in some patients with achalasia.[19,20] However, whether the low esophageal pH in these patients is caused by retention of lactic acid from bacterial fermentation of retained food or true refluxed gastric acid is controversial. Spechler et al[10] showed that patients who have achalasia with heartburn have lower basal LES pressure than patients without heartburn. Because GERD and achalasia are 2 coincidental diseases, patients with heartburn have lower basal LES pressure due to GERD. Therefore, patients with heartburn cannot have higher LES pressure when achalasia develops.

Does Reflux Occur in Achalasia?

Several studies utilizing 24-hour pH monitoring show that untreated achalasia patients experience true acid reflux.[10,17,21,22] Conversely, patients with achalasia are insensitive to acid in the esophagus.[23] Fisichella et al[8] reported data from 145 untreated achalasia patients. Among them, ambulatory pH monitoring was performed for 54 patients. Abnormal DeMeester scores were reported for seven patients. However, the analysis of pH monitoring tracings in all seven patients showed that the abnormal scores were induced by false reflux.[8] Otherwise, among those with a normal reflux profile, a primary esophageal motility disorder such as achalasia or diffuse esophageal spasm occurred in 18% of patients.[24] Patti et al[7] demonstrated that DeMeester scores were abnormal in 14 out of 40 achalasia patients for whom preoperative ambulatory pH was performed. However, true gastroesophageal reflux occurred in 8 patients, and pseudo-gastroesophageal reflux occurred in 6.[7]

Pathophysiology/Pathogenesis of Heartburn in Achalasia

In GERD, heartburn results when the esophagus is exposed to gastric contents that reflux across an weak or inappropriate LES relaxation.[25] In achalasia, heartburn might result from other

mechanisms. Ponce et al[26] demonstrated that patients with achalasia have lower esophageal sensitivity to acid than patients with GERD. Therefore, heartburn does not arise from acid in achalasia. Other possible reasons are as follows. First, retrosternal burning might be due to the esophageal dysmotility of achalasia. Esophageal spasm and distention caused by achalasia might produce sensations like heartburn.[10] Secondly, ingested irritants that remain in the aperistaltic esophagus might cause heartburn.[19] In addition, retained food in the flaccid esophagus can be fermented by bacteria into lactic acid.[19] Crookes et al[27] reported that food and saliva at body temperature were fermented to lactic acid by lactobacilli.

Attributing Factors for Diagnostic Delay in Achalasia

Most patients with achalasia suffer from their symptoms for a prolonged period before receiving a correct diagnosis.[28] The mean delay in diagnosis is 5 years (range, 2-7 years).[29-35] Howard et al[36] reported that 36.8% of achalasia patients had been treated for GERD. Additionally, Rosenzweig and Traube[9] showed that the initial diagnosis was achalasia in only 12 of out 25 achalasia patients, whereas the other 13 patients were diagnosed incorrectly. The most common misdiagnosis in this study was GERD.[9] Eckardt et al[28] demonstrated that the diagnostic delay in achalasia is not significantly associated with atypical symptoms or misleading clinical findings. However, the frequent delay in the diagnosis of achalasia is due to misinterpretation by the physician. Therefore, physician education is important for improving the correct diagnosis.[9,28,37] Rosenzweig and Traube[9] insists that patients who complain of dysphagia should be thoroughly evaluated by manometry when obstruction is excluded by barium studies and endoscopic examinations.

Endoscopic Findings in Achalasia

Esophagitis and Barrett's esophagus were also found in some achalasia patients.[22,38] Howard et al[36] reported that of 34 achalasia patients who underwent endoscopy before manometry, 3 patients showed esophagitis, and one showed esophagitis and stricture. Ponce et al[26] showed that esophagitis was present in three out of 40 achalasia patients. Chronic retention of food in patients with achalasia leads to "stagnation" or "retention" esophagitis.[39-41] By endoscopy, "retention esophagitis" may appear as a mucosal whitish discoloration, mucosal thickening, and nodularity.[42] Therefore, retention of food that leads to esophagitis, called retention esophagitis, may be clues to avoid erroneous diagnosis of GERD in patients with achalasia.

Conclusions

Symptoms of GERD are often observed in patients with untreated achalasia. For those patients who do not respond to proton pump inhibitor treatment, esophageal manometry should be performed to exclude esophageal motility disorders including achalasia.

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