PAPERS

Heartburn in patients with achalasia

S J Spechler, R F Souza, S J Rosenberg, R A Ruben, R K Goyal

Abstract

Heartburn, the main symptom of gastro-oesophageal reflux disease (GORD), might be expected to occur infrequently in achalasia, a disorder characterised by a hypertensive lower oesophageal sphincter (LOS) that fails to relax. Nevertheless, it is often described by patients with achalasia. The medical records of 32 patients with untreated achalasia who complained of heartburn, and of 35 similar patients who denied the symptom, were reviewed to explore the implications of heartburn in this condition. Data on endoscopic and manometric findings, and on the onset and duration of oesophageal symptoms were collected. Three patterns of heartburn were observed: (1) in 8 patients (25%) the onset of heartburn followed the onset of dysphagia, (2) in 15 patients (47%) heartburn preceded the onset of dysphagia and persisted as dysphagia progressed, and (3) in 9 patients (28%), heartburn preceded the onset of dysphagia and stopped as dysphagia progressed. The mean (SD) basal LOS pressure in the patients with heartburn (38 (16) mm Hg) was significantly lower than that in patients without the symptom (52 (26) mm Hg); the lowest LOS pressure (29 (11) mm Hg) was observed in the subset of patients whose heartburn preceded the onset of dysphagia and then stopped. It is concluded that patients who have achalasia with heartburn have lower basal LOS pressures than patients who have achalasia without this symptom. In some patients with achalasia, the appearance of dysphagia is heralded by the disappearance of longstanding heartburn. For these patients, it is speculated that achalasia develops in the setting of underlying GORD.

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Heartburn, caused by the reflux of gastric acid, is the main symptom of gastro-oesophageal reflux disease (GORD).[1] Abnormal gastro-oesophageal reflux occurs when the lower oesophageal sphincter (LOS) muscle is intrinsically weak, or when it relaxes at inappropriate moments.[2] Achalasia, in contrast, is a disorder characterised by a hypertensive LOS that fails to relax completely, abnormalities that delay oesophageal emptying and result in dysphagia.[3] The same LOS dysfunction that prevents ingested material from leaving the oesophagus in achalasia may also pose a substantial barrier to the reflux of gastric contents, and it might therefore be expected that gastro-oesophageal reflux would not occur frequently in patients with achalasia. Heartburn is described frequently, however, by patients who have untreated achalasia, for reasons that are not clear.[4] To explore the implications of heartburn in achalasia, we compared the clinical features of patients with untreated achalasia who complained of heartburn with those of similar patients who denied heartburn.

Methods

We reviewed the medical records of patients with achalasia whom we had evaluated at the Beth Israel Hospital. The diagnosis of achalasia was accepted for patients who had:

(1) A history of dysphagia, regurgitation, or chest pain;

(2) An endoscopic examination consistent with achalasia;

(3) A manometric examination consistent with achalasia including absent or incomplete LOS relaxation, and aperistalsis. For patients in whom technical difficulties precluded manometric study of the LOS, we required a barium swallow characteristic of achalasia with a dilated oesophagus and 'bird beak' narrowing of the distal oesophagus.

For inclusion in this study, we also required that our medical records mention specifically the presence or absence of heartburn (defined as an uncomfortable burning sensation in the retrosternal area). Data were collected on the presence and duration of symptoms of dysphagia, regurgitation, weight loss, chest pain (other than heartburn), and heartburn. Patients were separated into two groups – those with and those without heartburn. Patients with heartburn were further divided into subgroups depending on the relationship between the onset of heartburn and the onset of dysphagia.

The χ^2 statistic was used to seek differences between groups for dichotomous or multichotomous variables. The unpaired t test was used to compare continuous variables for data that were normally distributed, and the Mann-Whitney rank sum test was used to compare continuous variables for data that were not distributed normally.

TABLE I *Clinical features of patients with achalasia*

Feature	With heartburn (n=32)	Without heartburn (n=35)
Mean (SD) age at diagnosis (y)	49 (21)	53 (20)
Men:women	20:12	13:22
Dysphagia	32 (100%)	34 (97%)
Regurgitation	25 (78%)	22 (63%)
Weight loss	18 (56%)	19 (54%)
Chest pain (other than heartburn)	14 (44%)	21 (60%)
Endoscopic oesophagitis	8 (25%)	4 (11%)
Barrett's oesophagus	3 (9%)	0 (0%)

Results

We reviewed the medical records of 107 patients who carried the diagnosis of achalasia. Sixty seven of these patients fulfilled our criteria for study entry; 32 complained of heartburn, and 35 specifically denied this symptom. The clinical features of the study patients are summarised in Table I. The mean age of the patients with heartburn did not differ significantly from that of the patients without heartburn, and the groups did not differ significantly in the frequency and duration of the symptoms of dysphagia, regurgitation, weight loss, and chest pain. Men outnumbered women in the patients with heartburn, whereas women predominated in the group without heartburn; the difference was not statistically significant, however. Oesophagitis (erosions and/or ulcerations in the distal oesophagus) was seen on initial endoscopic examination (before treatment) in 8 of the 32 patients who complained of heartburn, and in 4 of the 35 patients without heartburn; the difference in the frequency of oesophagitis was not statistically significant. Barrett's oesophagus was seen on initial endoscopic examination and confirmed histologically in 3 patients, all of whom had a history of heartburn. All patients had aperistalsis in the body of the oesophagus on manometric examination.

We observed three patterns of heartburn in the 32 patients who complained of this symptom as follows: (1) in 8 patients (25%) the onset of heartburn either accompanied or followed the onset of dysphagia; (2) in 15 patients (47%) heartburn preceded the onset of dysphagia and persisted as dysphagia progressed; and (3) in 9 patients (28%) heartburn preceded the onset of dysphagia and stopped as dysphagia progressed. Mean LOS pressures for the patient groups are shown in Table II. The mean (SD) LOS pressure in the 25 patients with heartburn (38 (16) mm Hg) as well as in the subset of 18 patients whose heartburn preceded the onset of dysphagia (37 (15) mm Hg) was significantly lower than in the patients without heartburn (52 (26) mm Hg). Note that the lowest mean LOS pressure (29 (11) mm Hg) was found in the subgroup of 9 patients whose heartburn preceded the onset of dysphagia and stopped as dysphagia progressed. The duration of heartburn, and the relationship between the cessation of heartburn and the onset of dysphagia in these 9 patients is summarised in Table III. Note that in 8 of the nine patients, the heartburn disappeared within 2 years of the onset of dysphagia.

TABLE II *Basal lower oesophageal sphincter (LOS) pressures in patients with achalasia*

Patient group	Basal LOS pressure (mean (SD)) (mm Hg)
No heartburn (n=26)	52 (16)
Heartburn – all patients (n=25)	38 (16)*
Heartburn followed dysphagia (n=7)	40 (16)
Heartburn preceded dysphagia (n=18)	37 (15)*
Heartburn preceded dysphagia and continued (n=11)	42 (17)
Heartburn preceded dysphagia and stopped (n=7)	29 (11)*

*$p<0.05$ compared with 'no heartburn' group.

Discussion

In typical GORD, heartburn results when the oesophagus is exposed to noxious gastric contents that reflux across an LOS that is weak or inappropriately relaxed.[5] In achalasia, the sensation of heartburn might result from mechanisms other than gastro-oesophageal reflux. For example, retrosternal burning might be due to the disordered oesophageal motor activity of achalasia. Dysmotility can cause oesophageal spasm and distention that might produce sensations indistinguishable from the heartburn of acid reflux.[6] Heartburn also might be caused by ingested irritants that linger in the flaccid oesophagus.[7] Furthermore, ingested food retained in the dysfunctional oesophagus can be metabolised by bacteria into noxious substances such as lactic acid that might cause pain, oesophagitis, or both.[7]

Heartburn also could be due to a form of GORD that results from the dysmotility of achalasia. Although the typical LOS dysfunction in achalasia might be expected to pose a substantial barrier to reflux, some patients do experience occasional episodes of complete LOS relaxation during which gastric contents can enter the oesophagus.[8] Material refluxed in this fashion may be cleared poorly from the aperistaltic oesophagus. Even small quantities of refluxed acid that linger in the dysfunctional oesophagus might cause substantial heartburn, inflammation, or both. In support of such a mechanism, protracted oesophageal acid exposure has been documented by pH monitoring in some patients with achalasia.[7 9] However, it is difficult to determine whether the low oesophageal pH observed in these cases was caused by the retention of ingested acids (for example, fruit juices), by bacterial metabolism of retained food, or by refluxed gastric acid.

Finally, some patients might have heartburn due to chronic GORD that antedates the onset of achalasia. In these cases, achalasia develops in the setting of the chronic LOS

TABLE III *Relationship between cessation of heartburn and onset of dysphagia*

Patient	Total duration of heartburn (mth)	When heartburn ceased
1	360	12 mth *before* onset of dysphagia
2	>24	24 mth *before* onset of dysphagia
3	144	59 mth *before* onset of dysphagia
4	24	*With* onset of dysphagia
5	180	*With* onset of dysphagia
6	240	*With* onset of dysphagia
7	42	6 mth *after* onset of dysphagia
8	96	23 mth *after* onset of dysphagia
9	48	23 mth *after* onset of dysphagia

dysfunction that accompanies GORD. Achalasia is a disease of unknown origin that is characterised pathologically by the degeneration of neurons both in the wall of the oesophagus and in the dorsal motor nucleus of the vagus.[10] The degenerative process seems to affect inhibitory neurons primarily.[11] The loss of inhibitory neurons in the LOS causes the basal sphincter pressure to rise, often to levels that are considered hypertensive, and renders the sphincter incapable of normal relaxation.[3 11] In contrast, patients with severe GORD tend to have low basal LOS pressures due to one or a combination of three proposed mechanisms: (1) excessive neural inhibition of LOS muscle mediated by inhibitory neurons, (2) inadequate neural excitation of LOS muscle mediated by cholinergic neurons, or (3) intrinsic weakness of the LOS muscle itself.[5 12] For patients who have GORD and LOS hypotension due to the latter two mechanisms, the acquisition of achalasia might not result in LOS hypertension because the underlying, inadequate cholinergic excitation, and intrinsic sphincter muscle weakness would persist despite the loss of inhibitory neurons. In such cases, basal LOS pressures might remain low or rise only to normal levels, even though the defect in LOS relaxation contributes to dysphagia. Our study supports this hypothesis. Patients with symptoms of chronic GORD who developed achalasia had lower basal LOS pressures than patients without antecedent heartburn.

In 9 of our patients, longstanding heartburn preceded the onset of dysphagia, and the heartburn disappeared as the dysphagia progressed. This group had the lowest mean basal LOS pressure, and this is the group most likely to have developed achalasia in the setting of chronic GORD. Progression of the LOS dysfunction of achalasia would be expected to prevent gastro-oesophageal reflux, and this phenomenon seems to have been heralded clinically by the cessation of chronic heartburn. For patients in the other two heartburn subgroups (those whose heartburn accompanied or followed the onset of dysphagia, and those whose heartburn preceded the onset of dysphagia and persisted as dysphagia progressed), it is difficult to determine which of the possible mechanisms for heartburn were operative.

Further evidence that achalasia can develop in the setting of chronic GORD is provided by the observation that 3 of our patients who complained of chronic heartburn had Barrett's oesophagus on their initial endoscopic examination.[13] Barrett's oesophagus has been well described as a consequence of the severe GORD that can accompany the surgical treatment of achalasia, but has been described rarely in untreated patients.[14 15] Although we cannot exclude the possibility that oesophageal irritation from retained material caused the columnar metaplasia in these patients, it seems more likely that achalasia appeared after Barrett's oesophagus had developed in the typical setting of chronic GORD.

The retrospective nature of our study limits the conclusions that can be drawn regarding the frequency of heartburn in patients with achalasia. We analysed data on 67 patients for whom the presence or absence of heartburn was recorded specifically in the medical record; 40 patients with achalasia were excluded from the study because their medical records contained no specific information about heartburn. Although the precise frequency of heartburn cannot be determined from these data, it is clear that heartburn is not a rare symptom in patients with achalasia. Furthermore, the study shows that achalasia can appear in patients who have longstanding symptoms of GORD, and that cessation of chronic heartburn can be a symptom of achalasia.

Smart *et al* described 5 patients with longstanding, verified GORD that antedated the onset of classic achalasia.[16] The investigators proposed that the same neural dysfunction that eventuated in achalasia initially caused gastro-oesophageal reflux. Achalasia is characterised by a loss of inhibitory neurons, however, a disease process that, even in an early stage, should not cause LOS relaxation and gastro-oesophageal reflux. Although unlikely, it is possible that early gastro-oesophageal reflux could result if the achalasia disease process initially causes excessive discharge of the inhibitory neurons that eventually are destroyed. Such a process would not explain the lack of LOS hypertension in patients with established achalasia who have a history of chronic heartburn, however. It is more likely that GORD and achalasia are the outcomes of two independent disease processes. GORD is a common disorder that does not appear to protect patients from acquiring achalasia.

In summary, we have found that patients who have achalasia with heartburn have lower basal LOS pressures than patients who have achalasia without heartburn. In some patients, the disappearance of longstanding heartburn heralds the appearance of achalasia. We speculate that when achalasia develops in patients with underlying LOS hypotension, the resulting LOS pressures may be normal or low because the weak LOS cannot generate high pressures even when the acquisition of achalasia releases the sphincter muscle from its normal neural inhibition.

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