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DISEASES OF THE ESOPHAGUS

Case report

Gastroesophageal reflux disease progressing to achalasia

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SUMMARY. **Two achalasia patients with former complaints of heartburn were examined. Antisecretory drugs were used by the patients when dysphagia occured. Barium X-ray and esophageal manometry were performed and achalasia was diagnosed in both patients. Twenty-four-hour pH-metry showed significant and long-lasting acid reflux during supine position. Prolonged reflux episodes can be explained not only by the swallow-unrelated transient relaxation of lower esophageal sphincter (LES) and mechanical damage of the esophageal body, but also by its chemical insensitivity. Thus preoperative detection of reflux should determinate either the operational procedure and the postoperative follow up of the patient.**

KEY WORDS: **achalasia, gastroesophageal reflux disease (GERD).**

INTRODUCTION

Achalasia is defined as selective loss of inhibitory neurons of the lower esophageal sphincter (LES) resulting in an incomplete relaxation of LES during swallow. The normal peristaltic activity of the esophageal body was shown to disappear, and isobaric or 'mirror image' wave forms are generated by the initiation of a swallow. The exact cause of achalasia is not known; however, several reports have shown that motor disorders of the esophagus such as gastroesophageal reflux disease (GERD), and diffuse esophageal spasm may progress to achalasia.[1] Since the LES of achalasia patients was shown to be normo- or hypertensive, and to display absent or impaired relaxation in response to swallowing or gastric distension there is controversy as to whether gastroesophageal reflux disease can occur in these patients prior to treatment. Furthermore, the mild inflammation found in the distal part of the esophagus of achalasia patients was attributed to 'retention esophagitis'.[2] Low pH values recorded in untreated patients were supposed to be the result of degradation of retained food by lactobacilli in the esophagus rather than true gastroesophageal acid reflux.[2]

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However, there are several prospective 24-hour pH studies which have shown that untreated achalasia patients are capable of demonstrating true acid reflux.[1,3–5] Heartburn was described in one-third of patients with achalasia;[3] furthermore, esophagitis and Barrett's esophagus were also found in some patients.[5,6] Barrett's metaplasia is strongly suggested to be an acquired condition produced by severe GERD.[5] It is still not clear whether two coincidental diseases are present or one disease transforms into the other.

Patients with achalasia have been shown more recently to be particularly insensitive to acid in the esophagus,[7] claiming the presence of asymptomatic GERD. Since the medical and surgical treatment is directed at reducing LES resting pressure, it may result in the development of even more severe GERD. In the present study we report two patients documented to progress from GERD to achalasia.

CASE REPORTS

Case 1

A 44-year-old man with a 2-year history of classic heartburn and dysphagia presented in February 1999. Heartburn and symptoms of gastroesophageal reflux started in 1997; heartburn was decreased after meals. These symptoms were transformed into dysphagia within a year. Symptoms were progressive over a 6-months period until dysphagia

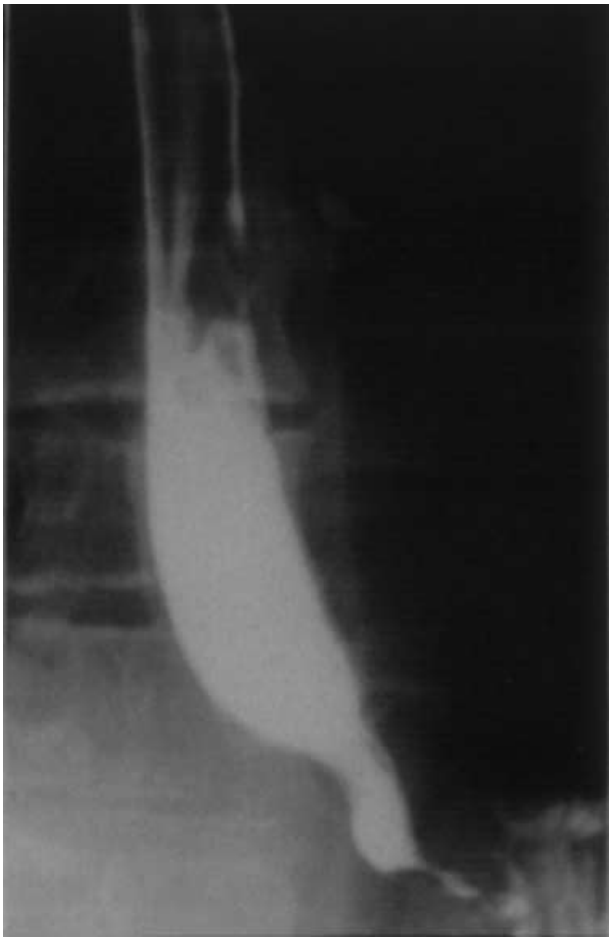

Fig. 1 Barium swallow showing slightly dilated esophageal body with a tapered beak-like esophagogastric junction consistent with achalasia.

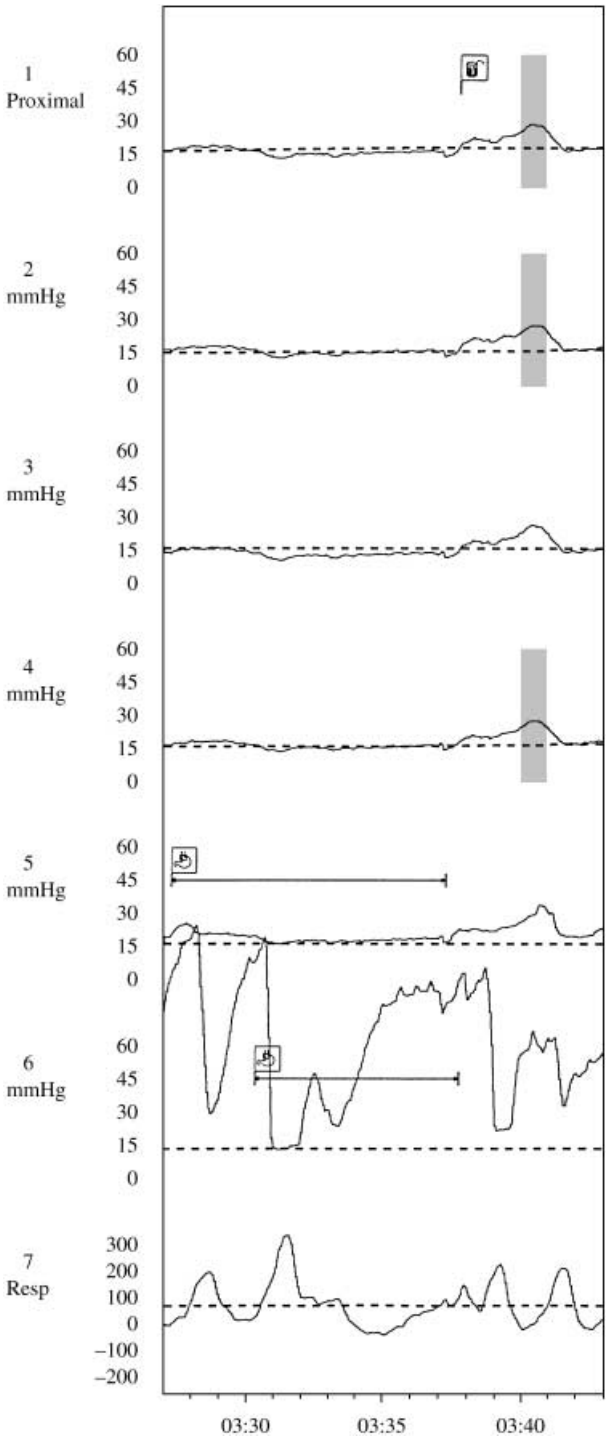

Fig. 2 Representative sample from the esophageal manometry tracing of patient No. 1. Aperistalsis is present in the esophgeal body during wet swallows with increased average pressure (34.4 mmHg) and decreased relaxation of LES (< 90%). These findings are consistent with achalasia.

occurred with every meal, when he stopped to eat, and drank cold water; 15 kg weigh loss was observed in this 2-year period.

Esophagogastroscopy was performed in 1998, showing erosive esophagitis, inflammation was also found in the squamocolumnar junction by histology. The patient was treated with lansoprazole 30 mg daily and cisapride 10 mg three times daily resulting in improvement of the symptoms. Clinically, dysphagia progressed rapidly when re-endoscopy was performed, which revealed dilated esophageal body with intact mucosa. Cardia was closed, but the endoscope could pass through the cardia, suspected to be fibrotic.

Barium swallow showed dilated esophageal body with a short smoothly tapered segment at the esophagogastric junction, decreased peristalsis and retention of barium thought to be consistent with achalasia (Fig. 1) Esophageal manometry demonstrated LES average resting pressure of 34.4 mmHg (Fig. 2). LES did not relax properly (relaxation < 90%). Degluditory waves were of low amplitude, and simultaneous 'mirror image' wave forms were generated by the initiation of a swallow. Twenty-four-hour pH-metry showed acid reflux, with total DeMeester score of 94.9 (Fig. 3). Using pH 3 as a discriminant threshold for GERD, the reflux score was: 62.3. Hypertrophy of LES was found during operation, with the rigidity of the cardia. Esophagocardiomyotomy and anterior fundoplication was performed. The patient's complaints were resolved after the operation.

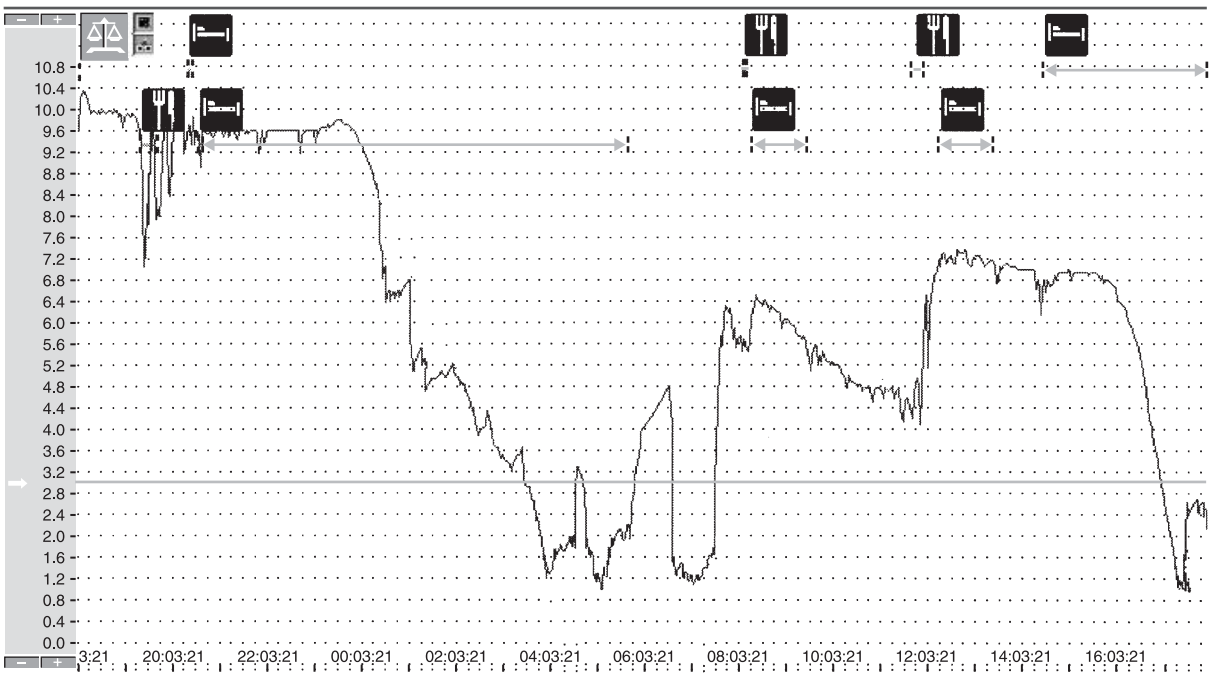

Fig. 3 24-hour pH-study of patient No. 1. 24-hour pH-metry showed acid reflux, with total DeMeester score of 94.9. Using pH 3 as a discriminant threshold for GERD, the reflux score was 62.3.

Case 2

A 42-year-old man presented in September 2000 with the chief complaint of dysphagia. Symptoms were progressive over a 4-month period. The patient felt heartburn, regurgitation, gastroesophageal reflux and at the same time that was inhibited by on-demand taking of the H_2 blocker, nizatidine (150 mg).

Endoscopy revealed dilatation and atony of the esophageal body, closed cardia that did not open during the procedure. Mild inflammation was found in the distal portion of the esophagus; the instrument passed through the sphincter with an increased pressure.

Barium swallow showed dilated esophageal body with non-propulsive contractions, tight, non-relaxing sphincter that allowed contrast material to escape in small quantities from the esophagus.

Sequentially propagated waves transversing the distal esophageal body were absent, low amplitude simultaneous contraction waves were observed. Baseline pressure of the esophageal body was elevated. The resting pressure of the LES was not increased (24.4 mmHg); however, incomplete relaxation could be observed.

Twenty-four-hour pH-metry revealed acid reflux that was not related to meals.

Anterior cardiomyotomy and anterior fundoplication was performed, improving the patient's symptoms.

DISCUSSION

Achalasia is a rare disorder of unknown etiology causing aperistalsis and impaired deglutitive LES relaxation. The primary abnormality seems to be the degeneration of esophageal myenteric plexus causing the selective loss of inhibitory nitrinergic innervation of the LES.[8] Since the increased tone and loss of swallow-related relaxation of the LES are present in achalasia patients, there is still controversy as to whether GERD can occur in these patients. Shoenut *et al*. reported approximately 20% of untreated achalasia patients demonstrated abnormal esophageal pH results that clearly showed acid reflux.[7] Crookes *et al*. found almost the same ratio of incidence of GERD in achalasia patients.[2] GERD has been well documented to occur in patients prior to their developing achalasia.[9] Symptomatic GERD patients were shown to develop achalasia over a period of 2–10 years. A progressive autonomic nervous system dysfunction was supposed in these patients to be the primary etiology of both diseases.[8,9] It is not clear weather two coincidental diseases are present or one disease transforms into the other. Spechler *et al*. recently demonstrated that the unique feature of the two coincidental diseases was the lower basal pressure of LES compared to that of pure achalasia patients.[3] Interestingly the prevalence of GERD in patients having Heller myotomy without antireflux procedure was found to be 6–11% by several authors.[10] This prevalence is comparable to that of achalasia patients showing acid reflux before any procedure.[7] Furthermore, Barrett's esophagus has been described in untreated achalasia patients, and adenocarcinoma in the esophagogastric junction was shown to have also the same (6–7%) incidence

in this population.[5] One can conclude that there is a distinct population of achalasia patients where GERD precedes the onset of achalasia. This is the group of patients where even more severe GERD may develop after surgery. Since the medical and surgical treatment of achalasia is directed at reducing LES pressure, it would be tempting to recommend routine esophagoscopy, 24-hour pH-metry and esophageal manometry prior and regular controls, after the treatment of achalasia.

Heartburn is a classic symptom of GERD. This sensation can be explained by different etiologies in achalasia patients: GERD, esophageal dysmotility, distension and ingested irritants. Heartburn preceded the dysphagia and stopped as dysphagia progressed in our both patients claiming the possibility that GERD antedated achalasia. This notion is supported by the first endoscopy of both patients when esophagitis was diagnosed. Recently Crookes *et al.* demonstrated that food and saliva at body temperature undergoes a fermentation to lactic acid by lactobacilli, causing a downward drift of esophageal pH below pH 4 where the conventional acid analysis reports reflux.[2] Furthermore, lactic acid may irritate the esophagus causing internal inflammation. We do not believe that this is the case in our patients. First, both cases showed Sievert 2-stage achalasia where no retained food can be observed in the esophagus. Neither the esophagoscopy, nor the barium X-ray found retained material in the esophagus in these two patients. Second, sudden sharp drops of pH characteristic of true acid reflux was found in both patients' pH-metry. Third, the appearance of acid episodes was not related to feeding. Fourth, the use of pH 3 as a discriminant threshold was offered as a simple objective method to discriminate between acid reflux from food fermentation. Even if the lower threshold was used, both patients' data were in the abnormal range. Taken together, the presence of true acid reflux was clearly shown in both cases. Interestingly some prolonged reflux episodes appeared during the night, when the patients were in recumbent positions. Thus, we hypothesized that the transient complete relaxation of the LES caused acid regurgitation from the stomach, and poor clearance of the aperistaltic esophagus could be the origin of such prolonged acidification. This hypothesis is supported by the fact that the complaint of heartburn was inhibited by the use of proton pump inhibitors (first case) or H_2 blockers (second case). Recently Hirano *et al.* demonstrated that transient lower esophageal sphincter relaxation can be observed in achalasia patients,[8] which might be the etiology for heartburn that has been reported in up to 34% of untreated achalasics.[8,11,12]

The regurgitated gastric acid activates esophageal chemoreceptors, which in turn initiates secondary peristalsis and clearance of the bolus from the esophagus through vagally-mediated pathways.[13,14] Electron microscopy studies showed that not only the degeneration of vagal fibres[14] but also fragmentation and dissolution of nuclear material of the dorsal motor nucleus of the vagus, can be observed in the brainstem.[14] Functional studies have confirmed that vagal functions such as hypoglycaemia-induced gastric acid secretion, gastric emptying, and intestinal transit, are also disturbed in patients with achalasia.[14] Furthermore, decreased chemical sensitivity of the esophagus was also described.[13,14] The incidence of asymptomatic reflux in achalasia patients was found to be increased (70%) compared to that of the normal population.[12–14] Thus, the impaired sensory function of esophageal chemoreceptors must be supposed in achalasia.

In summary, prolonged reflux episodes can be observed in achalasia patients. Prolonged GERD episodes can be explained not only by the swallow-unrelated transient relaxation of LES and mechanical damage of the esophageal body, but also by its chemical insensitivity. Thus, preoperative detection of reflux should determine the operational procedure and the postoperative follow-up of the patient.

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