

Boerhaave's syndrome as the primary manifestation of adult eosinophilic esophagitis. Two case reports and a review of the literature

A. J. Lucendo,¹ A. B. Frigal-Ruiz,¹ B. Rodríguez²

Departments of ¹Gastroenterology and ²Allergy, Hospital General de Tomelloso, Tomelloso, Ciudad Real, Spain

SUMMARY. Eosinophilic esophagitis (EoE) has been associated with an increased risk of esophageal mucosal tears induced by vomiting to dislodge impacted food or following endoscopic procedures. However, Boerhaave's syndrome or transmural perforation of the organ resulting from vomiting induced to dislodge impacted food has rarely been reported. In this article, we present two male adult patients with long-term esophageal symptoms who suffered from Boerhaave's syndrome after the impaction of food in the esophagus. Both patients required surgical management because of clinical and radiological signs of perforation. This rare complication of EoE has been documented in 11 other reports, predominantly affecting young men in whom EoE had not been previously diagnosed, despite the majority having esophageal symptoms and a history of atopy. There are only two published cases of esophageal perforation that presented in children, which were managed conservatively. Our two patients and 4 out of the 11 described in literature required surgery because of esophageal perforation. Our two cases involved closure of the perforation, while in three published reports, perforation resulted in a partial or complete esophagectomy. No cases have been published on Boerhaave's syndrome caused by EoE that ended in fatalities. It is important to note that esophageal perforation caused by vomiting is a potentially severe complication of EoE that is being increasingly described in literature. Therefore, patients with non-traumatic Boerhaave's syndrome should be assessed for EoE, especially if they are young men who have a prior history of dysphagia and allergic manifestations.

KEY WORDS: Boerhaave's syndrome, eosinophilic esophagitis, esophageal perforation, esophageal rupture.

INTRODUCTION

Eosinophilic esophagitis (EoE) is a disorder that is becoming increasingly recognized defined by dense eosinophilic infiltration of the esophageal wall.¹ It manifests clinically as dysphagia and frequently includes food impaction that has a chronic or intermittent course. Since EoE was first described, it has been associated with marked fragility of the organ that manifests as frequent mucosal tears produced spontaneously while trying to dislodge impacted food or following endoscopic procedures, especially esophageal dilations.² Perforation of the wall of the esophagus requiring surgery has rarely been reported

in literature. This article presents the cases of two adult patients with EoE who were diagnosed following perforation of the organ as a result of induced vomiting or Boerhaave's syndrome.

CASE REPORTS

Case 1

The first case was of a 36-year-old male with seasonal bronchial asthma and a known sensitivity to mustard, peanuts, grasses, and olive pollen. He had had intermittent esophageal symptoms since childhood and frequent episodes of choking that would usually resolve spontaneously. He frequently felt as though something were obstructing his cervical esophagus that was alleviated by swallowing air. The esophageal symptoms were neither seasonally related nor related to exacerbations of his asthma. At the age of 12, he underwent an emergency endoscopy because

Address correspondence to: Dr Alfredo J. Lucendo, MD, PhD, Department of Gastroenterology, Hospital General de Tomelloso, Vereda de Socuéllamos, s/n, 13700 Tomelloso, Ciudad Real, Spain. Email: alucendo@vodafone.es
Author contribution: All the authors have contributed equally to this work.



Fig. 1 Computed tomography from case 1 obtained before a right thoracotomy to close the esophageal perforation. A bilateral pleural effusion was present (a). After filling the esophageal lumen with gastrografin (b), a slight leak of the contrast media into the mediastinum was observed (c).

of food impaction in the esophagus. In 2008, he presented an episode of meat impaction that was resolved by inducing vomiting followed by intense retrosternal pain and deterioration of his general health for which he sought care at the emergency room. An upper GI endoscopy identified an ulcer in the middle third of the esophagus. Computed tomography using oral and intravenous contrast showed extensive mediastinal emphysema that dissected the thyroid gland in addition to all the structures of the mediastinum evidencing marked subcutaneous emphysema. The wall of the esophagus appeared to be thicker below the carina, a finding that was highly suggestive of perforation (Fig. 1). The patient underwent a right thoracotomy, which led to liberation of the esophagus and closure of the perforation.

Nine months after the surgery, the patient was sent to our clinic. He informed us that the most significant symptoms were intermittent dysphagia and a feeling of obstruction in the neck, which persisted despite treatment with 20-mg rabeprazole twice a day. An upper GI endoscopy showed that the esophagus was of normal caliber with a narrowing of the lumen in the middle third because of the presence of simultaneous contraction rings. In the distal third, there were clear longitudinal linear furrows, and the mucosa had a cobblestone appearance similar to EoE. A Schatzki ring and a small hiatus hernia were also observed. The histopathologic study of the biopsies taken from the upper and lower esophageal thirds revealed epithelial infiltration by more than 100 eosinophils per high-power field. The blood test did not show any specific immunoglobulin E (IgE) against food, and the skin prick tests failed to detect any food sensitivity. Following diagnosis of EoE, the patient began treatment with fluticasone propionate. He remained asymptomatic for more than 1 year and did not show any signs of pyrosis, dysphagia, or throat obstruction. He is currently awaiting treatment based on a six-food elimination diet.³

Case 2

A 65-year-old male who presented with a several-year history of intermittent esophageal symptoms that had never required treatment, until 1999, when he suffered from intense abdominal pain after choking on a piece of plum that he tried to dislodge by inducing vomiting. He subsequently sought care at the emergency room. An endoscopy detected a deep ulcer in the distal third of the esophagus, and the chest X-ray showed a left pleural effusion and free air surrounding the gastric fundus (Fig. 2). Because of suspected esophageal perforation, a half-laparotomy was performed, suturing the perforation and covering the lesion with the wall of the gastric fundus.

In 2006, the patient was referred to the gastroenterology department because of distal dysphagia and the frequent sensation of a retrosternal 'knot.' The upper GI endoscopy showed slight stenosis of the distal third of the esophagus that was dilated using a hydropneumatic balloon, and the esophageal mucosa appeared corrugated like in EoE. The biopsies taken during the same procedure diagnosed the aforementioned disease.

The patient was referred to the allergy department where tests did not detect any sensitivity to food or inhalants. Consequently, treatment with oral fluticasone propionate was prescribed, initially on a scheduled basis (400 µg twice a day) and later in accordance with symptoms. Since then, the patient has ceased to have any esophageal complaints and can swallow without any difficulty.

LITERATURE REVIEW

A PubMed-based search was carried out combining the terms 'eosinophilic/allergic esophagitis,' 'esoph-

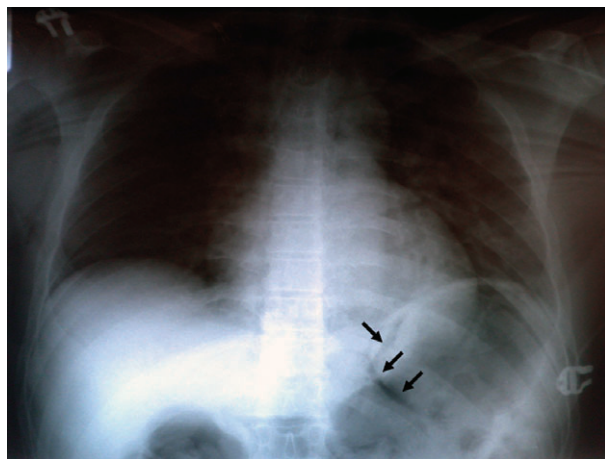


Fig. 2 Chest X-ray image relating to case 2. The arrows point to free air surrounding the fundus or the stomach, supporting the previously suspected perforation of the lower esophagus.

ageal perforation/rupture,' and 'Boerhaave's syndrome.' We found that Boerhaave's syndrome had been previously reported in 11 patients (8 men/3 women) (Table 1). Most of the patients described were young (aged between 9 and 56), and Boerhaave's syndrome frequently arose in the 20s and 30s age groups, which are precisely the most frequent age group in which EoE is initially diagnosed in adult patients.¹⁵ Only 1 of the 11 cases described in literature had been previously diagnosed with EoE.¹³ However, chronic or intermittent esophageal symptoms or a history of allergies were commonly found in literature. It is particularly noteworthy that the history of the esophageal symptoms of 10 of the patients included dysphagia and frequent episodes of food impaction,^{4-6,10,11,14} and that they had not been previously diagnosed with EoE. Similarly, asthma and other allergic symptoms were present in three patients together with esophageal symptoms,^{4,6,10} a finding that should have aroused suspicion of EoE.

Chest or epigastric pain following food impaction or choking in the esophagus was the most common symptoms presented, while two patients also had a fever. One patient was undergoing an endoscopy when the complication occurred, induced by a poorly tolerated technique. A computed tomography scan diagnosed perforations in all cases. Four out of 11 patients required surgery to resolve the problem, and in two cases, a total or partial resection of the esophagus was performed, which is a major intervention.

DISCUSSION

This article presents two adult patients with esophageal perforation following the impaction of food, which required surgical intervention.

Food impaction is the most frequent clinical manifestation that leads to diagnosis of EoE in adult patients.¹⁶ According to a retrospective study of 251 Swiss patients with EoE, up to 34.7% at some point required extraction of the impacted bolus by flexible or rigid esophageal endoscopy.¹¹ A high rate of tears and lacerations of the mucosa has been also reported in EoE patients,¹⁷ showing increased fragility of the organ's mucosa.

Various cases of esophageal perforation in patients with EoE have been reported in recent years, most of whom underwent endoscopic procedures.¹⁸⁻²⁴ This implies that these techniques must be performed gently on EoE patients and preferably by experienced endoscopists. Recent studies have not shown that there is a higher risk of perforation than in other causes of esophageal stenosis, provided that the dilation is performed on EoE patients by experts.¹⁷

The mere rub of the endoscope may result in mucosal tears in EoE patients,²⁵ but spontaneous perforations have been also described,⁵ probably second-

ary to the patient's efforts to induce vomiting in order to dislodge impacted food or Boerhaave's syndrome.⁶ This complication has been documented in several articles since 1996 as having affected patients with EoE (Table 1). Like our cases, nine patients registered in our search were men (in fact, males are clearly predisposed to suffering from EoE) in their 20s and 30s.

Only two documented cases were shown to affect children.^{7,10} In this respect, one recent study showed that prolonged EoE symptoms are a risk factor for developing esophageal perforation in addition to a higher density of eosinophilic infiltrate and the presence of esophageal stenosis.²⁶ Consequently, adult EoE patients could be more prone to suffering from Boerhaave's syndrome than children. Both of the children described in literature were managed conservatively, which contrasts with the high rate of complications and the need for surgery shown in a recent review about Boerhaave's syndrome in children under 18 years old, in whom it usually occurs because of trauma or iatrogenesis, and associates with a high mortality rate.²⁷

As shown in our cases, EoE was not suspected when perforation occurred in most of the cases described in literature, and the primary cause of the perforation was diagnosed mainly after the complication arose.

The exact cause of fragility of the esophageal wall has not been clearly established, but it could be directly related to the inflammatory infiltrate and the effect of eosinophils. Eosinophils contain several cytotoxic proteins in their cytoplasmic granules capable of damaging tissues,²⁸ the risk of which is likely to be higher in patients with a high density of eosinophils and long-term symptoms.¹¹ Multiple evidence obtained from patients²⁹ and animal models³⁰ of EoE have shown that the inflammatory infiltrate penetrates deeply into the esophageal wall, reaching the muscle layers. Fibrous remodeling of the esophageal wall has also been described in EoE patients,³¹ which could reduce the elastic properties of their components. In this sense, esophageal distensibility has been shown to be significantly reduced in adult EoE patients compared with controls, which alters the mechanical properties of the esophageal wall.³²

Accordingly, both the resistance and distension of the organ could be impaired in EoE, leading to increased fragility during endoscopic dilation procedures² and in traction movements around the gastroesophageal junction in cases of nausea and vomiting.

In conclusion, EoE is a well-known cause of esophageal perforation, which occurs after inducing vomiting. Therefore, patients with non-traumatic Boerhaave's syndrome should be assessed for EoE, especially if they are young men who have a prior history of dysphagia and allergic manifestations.

Table 1 Cases of esophageal perforation after vomiting induced by patients diagnosed with eosinophilic esophagitis (EoE) described in literature

Reference	Patient age (years)	Gender	Previously diagnosed with EoE	Prior symptoms	Presentation	Techniques for diagnosing perforation	Findings	Surgery required	Treatment
Riou <i>et al.</i> ⁴	26	Male	No	Chronic history of allergy and swallowing difficulties	1-h history of constant epigastric pain following food impaction	CT scan, contrast swallow study, endoscopy	Esophageal perforation extending 3 cm above the cardia, pneumomediastinum, and mediastinitis	Yes	Left thoracotomy with subtotal esophagectomy and cervical esophago-gastric anastomosis
Prasad and Arora ⁵	54	Male	No	Long history of intermittent solid food dysphagia without impaction	Chest pain after food impaction while eating a roast beef sandwich	Endoscopy and CT scan	A large esophageal tear. Free air in mediastinum, pleural effusion, and inflammatory changes around distal esophagus	No	Intravenous antibiotics and rest
Cohen <i>et al.</i> ⁶	56	Male	No	History of asthma, seasonal allergies, and heartburn	Nausea and vomiting that evolved into severe epigastric and chest pain	CT scan	Air and fluid surrounding the esophagus between the bronchial bifurcation and the gastroesophageal junction	Yes	Closure of the perforation
Giles <i>et al.</i> ⁷	12	Male	No	N/A	Choked on a piece of corn	Contrast esophagram and thoracic CT scan	Contained perforation of the esophagus below the carina	No	Not specified
Gómez-Senent <i>et al.</i> ⁸	35	Male	No	N/A	Dysphagia, repeated vomiting, and epigastric pain	Endoscopy and CT scan	Impacted bean that was removed and a deep 5-cm long tear in the distal esophagus. Free liquid around the esophagus and pneumomediastinum	No	Absolute diet and antibiotics
Liguori <i>et al.</i> ⁹	32	Male	No	Mild solid food dysphagia in the past	Food impaction	Endoscopy and CT scan	Extensive disruption of the mucosal layer in distal esophagus. Intramural circumferential dissection, pneumomediastinum, and subcutaneous emphysema	Yes	Right thoracotomy, total esophagectomy with esophago-gastroplasty and jejunostomy
Robles-Medrandá <i>et al.</i> ¹⁰	9	Female	No	History of asthma, intermittent solid food dysphagia, and blockage	Chest pain pyrosis and fever	Analysis and CT chest scan	Leukocytosis with neutrophilia, high C-reactive protein, and erythrocyte sedimentation rate. Retroesophageal perforation with fluid collection	No	Fasting, antibiotics, and proton pump inhibitors
Straumann <i>et al.</i> ¹¹	28	Female	No	10-year history of dysphagia	Gastroenteritis with severe vomiting followed by hematemesis	CT scan	Pneumomediastinum	Yes	Surgery and installation of multiple mediastinal drainages
Nantes <i>et al.</i> ¹²	28	Male	No	Intermittent dysphagia and episodes of food impaction	Mallory-Weiss tear after a poorly tolerated gastroscopy	Chest CT scan	Peri-esophageal gas collection indicating perforation	No	Not specified
Quiroga <i>et al.</i> ¹³	24	Male	Yes	Treatment with endoscopic dilation 8 years later	Progressive chest pain, nausea, vomiting, and fever	CT scan and contrast swallow study	Intramural circumferential dissection of thoracic esophagus and peri-esophageal abscess formation. Extraluminal pool of contrast in a tubular false lumen	No	Broad spectrum antibiotics and parenteral nutrition
Spahn <i>et al.</i> ¹⁴	41	Female	No	Multiple episodes of dysphagia	Dysphagia after ingesting an acetaminophen pill	Endoscopy and CT scan	Membranous structure behind the impacted pill. Mediastinal air consistent with perforation	No	Not specified

CT, computed tomography; N/A, not available.

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