A 25-year-old woman with dysphagia and food impaction: A case of asthma of the oesophagus?

Aoife Sweeney *(Fourth Year Medicine, TCD)*

Clinical Points

- Eosinophilic oesophagitis (EO) is a relatively novel inflammatory disease characterized by eosinophilic infiltration of the oesophageal mucosa.
- Symptoms of EO include dysphagia, food impaction, chest pain, heartburn, early satiety and abdominal pain.
- Diagnosis of EO is made histologically by taking a biopsy of oesophageal tissue on endoscopy.
- Various food, environmental and drug allergens are thought to play a role in the pathogenicity of EO.
- The mainstay of treatment of EO includes ingested corticosteroids and identification and avoidance of dietary allergens. Mechanical dilatation of the oesophagus may be carried out in severe cases.

Presentation of Case

RD, a twenty-five year old Irish female, presented to her general practitioner (GP) following a recent episode of food impaction in her oesophagus and associated chest tightening after a meal. Although she admitted to having suffered from swallowing difficulties over the past five years, RD had never sought previous medical attention as she found it difficult to describe her symptoms and felt they would not be recognized as a medical problem.

RD reported that whenever she swallowed food, it 'did not clear properly from her throat.' She also reported feeling 'bloated' and 'over-full' after small meals; however, she did not experience symptoms of heartburn (a burning sensation in the chest or throat) or gastro-oesophageal reflux (regurgitation of gastric acid into the oesophagus). RD further denied any abdominal pain, haematemesis (vomiting of blood) or changes in her appetite or bowel habit. She did, however, admit to eating less at mealtimes to ease the bloating she experienced but denied any weight loss as a result. Moreover, she was unable to identify any other factors that aggravated or relieved her dysphagia (difficulty in swallowing) and bloating.

Aside from additionally noting an itchy rash on her left forearm, RD was healthy, with no other relevant medical or surgical history. She was not taking any medications at the time of presentation and denied any drug allergies. When questioned about her family's medical history, she reported that her father had been diagnosed four years previously with hypertension, and that both her brother and aunt each suffered from asthma and eczema. At the time of consultation, RD was a student living in Dublin. She was a non-smoker, had never taken illicit drugs and consumed approximately eight units of alcohol per week. Review of systems was non-contributing.

On examination, RD was apyrexial with a blood pressure of 115/75 mmHg and a pulse rate of 68 beats per minute. Her abdomen was found to be soft and non-tender. On the anterior surface of her left forearm, her GP noted an erythematous, macular rash. There were no positive findings on physical examination of cardiovascular, respiratory, genitourinary and neurological systems.

Investigations and Diagnosis

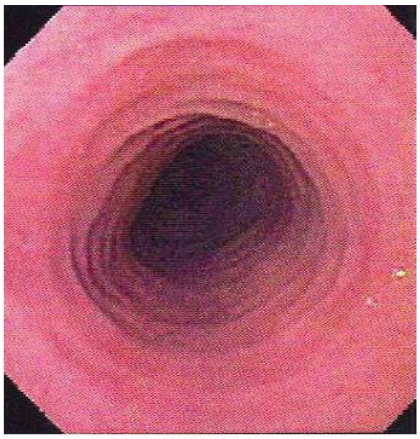
The differential diagnosis for RD's symptoms included both oesophageal and gastric pathologies. Potential oesophageal aetiologies included oesophagitis (inflammation of the oesophagus), oesophageal web (a thin, smooth extension of normal oesophageal tissue into the lumen of the oesophagus causing dysphagia), achalasia (inability of the lower oesophageal sphincter to relax) and oesophageal cancer. Gastric diagnoses considered included gastro-oesophageal reflux disease (GORD), gastritis (inflammation of the gastric mucosa) and infection with Helicobacter pylori (a flagellate organism that causes excess gastric acid secretion and potential ulcer formation). Coeliac disease was also considered as a differential as it is known to cause vague abdominal bloating and indigestion, as well as an itchy, blistering skin rash (dermatitis herpetiformis), and in addition, is a very common condition in Ireland.

Initially, RD's GP ordered a full blood count, as well as ferritin, folate and B12 levels to rule out anaemia since RD was only eating small meals (potentially causing a reduced nutrient intake), in addition to this being a sign of malabsorption. Her GP also

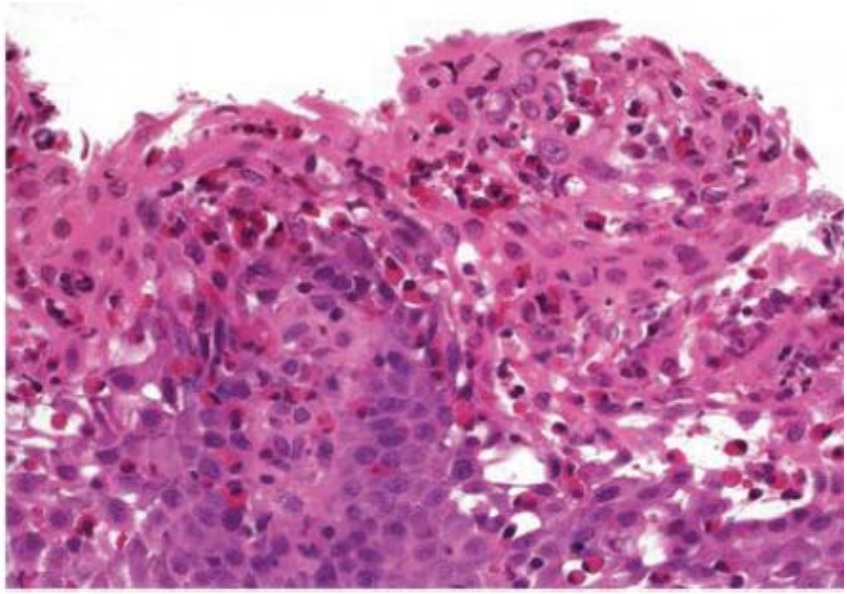
measured her tissue transglutaminase (tTG) autoantibody level, as tTG is a marker for coeliac disease. All were found to be normal. The rash on RD's left forearm was diagnosed by her GP as eczema.

RD was then referred by her GP to a consultant gastroenterologist for an oesophago-gastro-duodenoscopy (OGD), which involves visualizing the oesophagus, stomach and duodenum with a gastroscope, and permits biopsy of the gastrointestinal mucosa. On OGD, inflammatory changes consistent with gastritis were seen in the antrum of RD's stomach. Furthermore, an oesophageal tissue biopsy revealed 'moderate eosinophilic infiltration' which is consistent with current guidelines published by the First International Gastrointestinal Eosinophilic Research Symposium (FIGERS) for a diagnosis of eosinophilic oesophagitis (EO). Refer to Figures 1 and 2 for gross and histological examples, respectively, of EO.

Of note, testing for Helicobacter pylori was undertaken by performing a rapid urease test on a tissue biopsy sample taken during her OGD; this was found to be negative. In addition, RD had also been referred for a barium swallow test. This test involves the oral consumption of a barium sulphate solution that permits the visualization of oesophageal narrowing, hiatal hernias (a defect of the lower oesophageal sphincter causing parts of the stomach to slide into the oesophagus), ulcers and oesophageal tumors on x-ray. No abnormality was detected.



▲ **Figure 1: View of eosinophilic oesophagitis on endoscopy.**



▲ **Figure 2: Histological appearance of eosinophilic oesophagitis. Many eosinophils are present at the luminal surface in this biopsy. Notice the eosinophilic microabscesses and 'moth-eaten' appearance due to intercellular oedema (haematoxylin-eosin, original magnification x400).**

MANAGEMENT

A dual diagnosis of EO and gastritis was established in RD and thus management required targeted treatment of both conditions. To treat her EO, RD was prescribed Fluticasone in inhaler form (200mcg, four puffs twice daily) by her consultant gastroenterologist. In order to target the proximal oesophagus, RD was advised to 'ingest' the Fluticasone, which involved spraying the inhaler into the back of her throat while holding her breath and then swallowing. This technique differs from the inhaler technique used in the treatment of asthma whereby the patient is instructed to 'inhale' deeply after spraying the corticosteroid inhaler.

Fluticasone is a corticosteroid that acts to decrease inflammation of the oesophageal mucosa by reducing the synthesis of the inflammatory mediators IL-5 and eotaxin-3, both of which play a significant role in eosinophil activation and have been shown to be upregulated in EO. A reduction in these inflammatory mediators has been proven to decrease oesophageal mucosal inflammation, thereby alleviating symptoms of dysphagia and food impaction[1].

In addition, RD was prescribed 30 mg of Lansoprazole twice daily, and 10 mls of Gaviscon three times daily for her gastritis. Lansoprazole is a proton pump inhibitor, which reduces the secretion of gastric acid by blocking the hydrogen/potassium ATPase enzyme system of gastric parietal cells. Reduced acid secretion helps to alleviate symptoms of bloating and early satiety. Like Lansoprazole, Gaviscon also has an antacid effect. The combination of calcium carbonate, sodium bicarbonate and magnesium carbonate permits neutralization of gastric acid, and thus provides similar relief of the symptoms of gastritis.

RD was advised to use an over-the-counter hydrocortisone cream for her eczematous rash.

Outcome and Follow Up

RD was followed up one month later with her consultant gastroenterologist at which time she reported a dramatic reduction in her symptoms of dysphagia and bloating. Consequently, the consultant reduced both her Fluticasone and Lansoprazole to maintenance doses of 200mcg two puffs, twice daily and 15mg twice daily, respectively. RD is due to meet her consultant again in six months time for further review of her symptoms and medications. In the long term, RD is likely to be on a maintenance dose of 15mg Lansoprazole twice daily and Fluticasone 200mcg one puff, once daily as symptoms of EO have been found to recur on cessation of corticosteroid therapy[2].

Discussion

Eosinophilic oesophagitis (EO) is defined as an inflammatory disease of the oesophagus and is characterized by eosinophilic infiltration of the oesophageal mucosa[3]. An American gastroenterologist, Robert Landres, first described the condition in 1978[4]; but it was not until the late 1990s that EO was established as a clinical condition[5]. Until approximately ten years ago, EO was considered to be a rare disease and patients were often misdiagnosed as having GORD[5]. Its prevalence, however, is now on the rise as it becomes more widely recognized among physicians. A study carried out in Ohio in 2003 described a prevalence rate of four in ten thousand children in the United States[6]. Exact figures for the Republic of Ireland are currently unknown.

As EO is a relatively new condition, its exact pathophysiology is not well understood. Currently, however, the eosinophilic inflammation seen in patients with EO is thought to represent an allergic process and many food (wheat, eggs, milk, soy)[7] and drug (carbamazepine)[8] allergens have been implicated. These allergens are believed to induce T helper cells to produce inflammatory mediators IL-5 and IL-13, which are thought to play a key role in eosinophil activation. IL-13 appears to cause epithelial cells of the oesophagus to overexpress eotaxin-3 (an eosinophil chemoattractant), while IL-5 appears to regulate eosinophil numbers and their response to eotaxin-3[5]. This eosinophilic allergic response results in impaired smooth muscle function of the oesophagus giving rise to the typical clinical symptoms of EO such as dysphagia, food impaction and chest tightening[5], all of which were experienced by the patient in this particular case. Other common symptoms of EO not experienced by RD include reflux and heartburn[9]. It is this hypersensitivity response to various allergens in association with eosinophilic infiltration of the oesophageal mucosa by which EO receives the title 'asthma of the oesophagus'[10].

Given that EO is an atopic condition, patients commonly present with co-morbid eosinophil-mediated allergic diseases such as eczema, allergic rhinitis, asthma or various food allergies[9]. If food allergens are implicated, dietary alterations in conjunction with corticosteroids may provide maximal symptom relief[9]. Interestingly, after a diagnosis of EO was established, RD underwent skin prick testing and was found to have a wheat allergy, a common allergen associated with EO[11]. RD has thus since been observing a wheat-free diet which, in combination with the use of Fluticasone, has alleviated her symptoms of dysphagia, chest tightening and food impaction.

It is important to distinguish between coeliac disease and wheat allergies, as either condition can co-exist with EO[11,12]. Although these diseases share some similar symptomatic features (such as abdominal pain, cramping and bloating), they differ in their underlying pathophysiology. A wheat allergy is an allergy to the albumin protein of wheat, and involves an IgE-mediated inflammatory response[12]. Coeliac disease, on the other hand, is a T cell-mediated inflammatory disorder that results from hypersensitivity to the gluten protein of wheat[12]. In this particular case, the patient was found to have a wheat allergy and not coeliac disease. Nevertheless, physicians should be acutely aware of the link between EO and coeliac disease given that approximately 1% of the Irish population suffers from coeliac disease[13]. Moreover, a study of an Australian paediatric population undergoing endoscopy for coeliac disease found that approximately 4% of the study group had co-existing EO[14]. Therefore, in light of the high prevalence of coeliac disease in Ireland and it's co-existence with EO, it would be prudent for doctors to bear this in mind in the clinical setting.

A final point of clinical interest is that patients suffering with EO commonly present with dysphagia, which is also a prominent symptom of oesophageal cancer[15]. Although there are no known links between EO and oesophageal cancer at this time, it is of utmost importance that any patient with symptoms of dysphagia and food impaction seek immediate medical attention to rule out the possibility of an underlying malignancy. What is alarming about this particular case is that the patient experienced symptoms of dysphagia for five years before seeking medical attention. This highlights the importance of patient education and the current need for health promotion campaigns to avoid such a lengthy delay in the presentation of patients with dysphagia in the future.

CONCLUSION

EO is a relatively new condition that is currently under-diagnosed in the medical community. Its prevalence, however, is on the rise as more cases are reported from various parts of the world due to an increasing awareness of the condition among clinicians. Since the clinical presentation mimics other gastrointestinal diseases, especially GORD, patients may be misdiagnosed, making endoscopic examination and histological evaluation of oesophageal mucosal biopsies crucial for accurate diagnosis of the disease. In addition, awareness and treatment of co-morbid allergic conditions may permit optimal management of affected individuals. In RD's case, diligent and prudent medical practitioners resulted in a prompt and accurate diagnosis of her condition, thereby permitting the development of an appropriate and effective management plan and an overall improvement in her quality of life.

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