Clinical lesson: eosinophilic oesophagitis, a new diagnosis to swallow

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See Opinion, p30

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Eosinophilic oesophagitis (EoE) is a recently described condition that has gained increasing recognition over the past 5 years. Despite this, many clinicians remain unaware of EoE, often leading to diagnostic delay and therefore significant morbidity. The diagnosis of EoE should be considered in any patient with a history of intermittent or continuous dysphagia, or oesophageal food impaction. It should be strongly suspected in young patients, particularly men, presenting with dysphagia and a history of atopy. Here, three patients are presented that highlight common features of EoE. In addition, a clinical review of the worldwide literature is provided to heighten physician awareness and understanding of the condition.

Introduction

Eosinophilic oesophagitis (EoE) is a recently described condition that has gained increasing recognition over the past 5 years. Despite this, many clinicians remain unaware of EoE, often leading to diagnostic delay and therefore significant

morbidity. We present three patients that highlight common features of the condition.

Case reports

Patient No 1

A 17-year-old male with a background history of asthma and eczema presented with intermittent dysphagia to solids from the age of 5 years. As a child he had attended his local hospital and underwent an oesophagoastroduodenoscopy (OGD) demonstrating a stricture in the middle third of his oesophagus. A subsequent barium swallow (figure 1A, B) demonstrated concentric oesophageal rings within the stricture and a narrow calibre mid- and distal oesophagus. At age 13 years, on the assumption that his symptoms were reflux induced, he underwent antireflux surgery in the form of a Nissen fundoplication. He received no symptomatic benefit and was unable to tolerate solid foods due to dysphagia. Instead, he survived on a purely liquid diet and could not eat out socially. As such he was referred to our unit at age 17 years where a further OGD revealed persistence of the mid-oesophageal stricture which was 3 mm in diameter and only just allowed passage of a biopsy forceps (figure 2A). pH and manometry studies showed normal oesophageal peristalsis and normal oesophageal acid exposure. Histological examination of biopsies from the stricture revealed a dense eosinophilic infiltration of the oesophageal mucosa, with up to 100 eosinophils per high powered field (eos/hpf). The normal range is ≤ 1 eos/hpf. Full blood count showed a mild eosinophilia of $0.4 \times 10^9/\text{litre}$ (normal $0-0.3 \times 10^9/\text{litre}$). His stricture was dilated endoscopically (figure 2B) prior to commencement of oral prednisolone and later topical beclomethasone ($200 \mu\text{g}$ 3–4 times daily) swallowed from a respiratory inhaler. This and maintenance therapy with montelukast has allowed him to eat

Figure 1 (A) Barium swallow images revealing a mid-oesophageal stricture with concentric rings and (B) a narrow calibre distal oesophagus.

Figure 2 Endoscopic view of tight mid-oesophageal stricture. (A) Pre-dilatation and (B) post-dilatation. (Note also linear furrows and subtle concentric rings on the post-dilatation image.)

a full and varied solid diet, transforming his quality of life.

Patient No 2

A 56-year-old male presented with a history of intermittent dysphagia over the preceding 6 years. His symptoms were typically caused by eating bread. During this time he also presented to the immunology department with facial angio-oedema precipitated by eating egg. Subsequent investigation confirmed his egg allergy and he was provided with an epinephrine auto-injector. Furthermore, he had presented as an emergency during this 6 year period to Ear Nose and Throat services with recurrent food bolus obstruction of his oesophagus. His mother, father and brother all had a history of recurrent dysphagia. Following review in our unit he went on to have an OGD that demonstrated mid-oesophageal concentric mucosal rings (often termed as 'oesophageal trachealisation') shown in figure 3. There was visible hypertrophy and a creamy discolouration to the mucosa.

Figure 3 Concentric oesophageal rings often described as 'trachealisation'.

Gastric and duodenal examination was normal. Histopathological examination confirmed dense oesophageal eosinophilia at a concentration of >100 eos/hpf (figure 4). His symptoms were adequately controlled on exclusion of precipitating foods and he did not require pharmacological intervention.

Patient No 3

A 48-year-old male presented with recurrent episodes of oesophageal food impaction. Symptoms were typically precipitated by eating chicken, lamb, beef or bananas. He also described dysphagia to potatoes and felt his symptoms could be made worse by milk. He had some degree of heartburn but no nausea or vomiting. He had a background history of contact dermatitis and multiple allergies, including diclofenac, house dust mite and chocolate. A therapeutic trial of proton pump inhibitor (PPI) did not provide symptomatic benefit. OGD demonstrated linear 'tram track' erosions quadrantically, on a background of multiple concentric oesophageal rings (figure 5). There was no evidence of a hiatus hernia or reflux oesophagitis. Histopathological examination confirmed oesophageal eosinophilia at a concentration exceeding 50 eos/hpf. His symptoms have settled significantly on a combination of montelukast and topical beclomethasone.

Discussion

Eosinophilic oesophagitis (EoE) is a chronic relapsing inflammatory condition of the oesophagus characterised by high concentrations of intraepithelial eosinophils.^{1 2} Although initially described

Figure 4 Oesophageal biopsy stained with haematoxylin-eosin E revealing a dense eosinophilic infiltration of the squamous epithelium.

Figure 5 'Tram track' linear furrows and concentric oesophageal rings, both typical in eosinophilic oesophagitis.

in 1993, reports and primary research of the condition were initially very few. However, in the past 5 years, EoE has been more widely appreciated, and there has been a dramatic rise in interest, with almost 200 publications on the disease worldwide in 2007 and 2008 alone. The prevalence of the condition is thought to be around 30–40 per 100 000 in Western populations, rivalling that of Crohn's disease.^{3 4} However, despite this, the condition remains poorly understood by many clinicians and therefore often goes unrecognised in routine practice.⁵

EoE affects both adults and children. The three patients presented demonstrate the predominant typical symptoms of the condition in adults: dysphagia, which is classically intermittent but can be continuous, and oesophageal food impaction.^{6–10} Adults may also present with chest pain and in some cases, for example patient No 3, with heartburn. As a consequence, patients are often mistakenly diagnosed as have gastro-oesophageal reflux disease (GORD). Oesophageal food impaction, or bolus obstruction, is a common presenting symptom in EoE but the condition is often overlooked in the differential diagnosis. Indeed, two recent series have demonstrated that if oesophageal biopsies are taken in patients presenting with food impaction, over half may be due to EoE.^{11 12}

In children, the condition is more diverse and age dependent. In the preschool years, common symptoms are similar to reflux, including nausea, vomiting, dyspepsia and food refusal. As in patient No 1, there are

a large number of cases worldwide where surgical antireflux procedures have been carried out unsuccessfully due the diagnosis having been presumed as GORD.¹³ Adolescents often experience more adult symptoms, predominantly dysphagia.¹⁴ Symptoms can eventually lead to dietary avoidance and social anxiety, thereby impacting adversely on quality of life.

The presented patients also highlight the need for a wide variety of medical disciplines to be aware of EoE, including general practitioners, and specialists in gastroenterology, surgery, endoscopy, cardiology, accident and emergency, acute medicine and ear nose and throat.

The aetiology of EoE is not fully understood but allergy appears to be a key factor, mediated by cytokines, including interleukin 5 and interleukin 13.^{16 17} Although EoE may coexist with GORD, the conditions appear to be distinct, and although the exact relationship between the conditions remains controversial, there is currently little evidence to suggest an aetiological link.¹⁸ As demonstrated in all three of the presented patients, asthma and allergies are common (seen in 50%).¹⁰ The condition appears to have a male predilection in up to three quarters of cases.¹⁹ In adults, the peak onset of symptoms is the third and fourth decade but presentation can be considerably later, into the eighth and ninth decades.^{7 19 20} As in patient No 1, peripheral eosinophilia may be seen on full blood count analysis.²¹

Endoscopic features are variable in EoE. Classical signs, demonstrated in figures 2, 3 and 5, include concentric rings caused by contraction of the deep muscle layer, linear furrows (so-called tram track lesions), diffuse inflammation and stipple-like eosinophil rich exudates often mislabelled clinically as candidiasis. However, in up to 25%, the oesophagus appears normal, particularly to those unfamiliar with the condition, and appreciation of this is essential to avoid diagnostic failure. Changes are often, but not exclusively, seen in the middle third of the oesophagus whereas signs of reflux predominantly affect the distal third. Barium studies may also show typical features of oesophageal rings or a narrow calibre oesophagus (often difficult to distinguish endoscopically), as seen in patient No 1.²²

The histological criteria for diagnosis is widely recognised as ≥ 15 eosinophils per

high powered field on microscopy,²³ and in order to maximise diagnostic sensitivity, at least five biopsies should be taken, sampling each third of the oesophagus.⁷ Typical patterns seen include eosinophilic microabscess formation, superficial layering of eosinophils and epithelial hyperplasia.

Treatment regimens in EoE are varied and must be tailored to the individual patient. There are three broad categories: pharmacological treatment, dietary modification and oesophageal dilatation of strictures. Pharmacological treatment is principally the use of corticosteroids in the form of oral prednisolone, topical beclomethasone, as used in patient Nos 1 and 3, topical fluticasone swallowed from a respiratory inhaler (220 µg, up to four puffs twice daily) or swallowed viscous budesonide suspension.^{9 24–26} All have demonstrated an improvement in both clinical symptoms and histopathological changes. While using topical steroids, patients should be advised to rinse their mouths following administration in order to minimise the risk of oral candidiasis. They should also avoid eating or drinking for 30 min following administration, allowing the medication time to coat and be absorbed by the oesophagus. The leukotriene receptor antagonist montelukast has also been shown to successfully improve symptoms in the condition but its effect on histopathology has yet to be clarified.²⁷ The role of PPIs in EoE is primarily diagnostic, to exclude acid reflux as the cause of oesophageal eosinophilia.²⁸ Despite this, a proportion of patients with EoE will receive symptomatic benefit from PPI and so a trial of this drug is recommended prior to the use of steroids. Dietary modification is of particular benefit in children and involves the use of elemental diets or dietary restriction of common food allergens that have been suggested as linked to the aetiology of the condition, including cow's milk protein, peanuts, soy, wheat, seafood and egg, as seen in patient No 2.²⁹

Key lesson point

The diagnosis of eosinophilic oesophagitis should be considered in any patient with a history of intermittent or continuous dysphagia, or oesophageal food impaction. It should be strongly suspected in young male patients with dysphagia and a history of atopy.

The natural history of EoE is unravelling as more patients are recognised with the condition and the length of follow-up is increasing. Its course may be persistent or fluctuating, and activity is likely mediated by exogenous inhaled or ingested allergens. In time this may lead to 'remodelling' of the oesophagus, principally through interleukin 5 mediated subepithelial fibrosis, and ultimately to a loss of oesophageal function.³⁰ As suggested by patient No 3, a possible familial association of EoE is being recognised more frequently.³¹ There are also a number of complications of the condition being identified, including a friable oesophageal mucosa prone to tearing or even perforation during dilatation,³² and spontaneous oesophageal rupture.^{33 34}

Although there is no evidence that EoE has an impact on mortality, symptoms can have a major impact on the quality of life of patients, who often go for several years without diagnosis and institution of correct therapy. The key to successful diagnosis is optimal education regarding the common clinical, endoscopic and histological findings, and an appreciation of the need to biopsy the oesophagus in any patient presenting with unexplained dysphagia.

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