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Lesson of the month (2)

Young man presenting with recurrent food bolus impaction

A young man with recurrent food bolus obstruction presented to the gastroenterology clinic and, after investigation, was found to have eosinophilic oesophagitis. This unusual condition is closely linked to atopy and, in parallel with other atopic conditions, is increasing in incidence. Diagnosis is confirmed on oesophageal biopsy and treatment includes topical steroids and exclusion diet. Eosinophilic oesophagitis is gaining recognition in adult medicine as a cause of dysphagia and is one of the leading causes of recurrent food bolus obstruction. As such, it should be considered as a diagnosis in all young patients presenting with compatible symptoms.

Lesson

A 38-year-old male chartered engineer was admitted to the ear, nose and throat (ENT) ward following food bolus obstruction while eating chicken and potatoes. He underwent rigid oesophagoscopy under general anaesthetic and a piece of chicken was extracted from 23 cm *ab orum*. The oesophagus was noted to appear macroscopically normal. He admitted to an 18-month history of increasing sensation of dysphagia at the mid-chest level and three previous 'near miss' food bolus episodes. Despite this, he was able to eat and drink normally between episodes and had not lost weight.

A barium swallow showed free flow of the barium into the stomach, with no significant hold up or structural abnormality, with some tertiary contractions noted. Routine blood tests were within normal range. The patient was referred for a gastroenterology opinion.

On further questioning, the patient admitted to a fondness for chocolates and volunteered that his oesophageal symptoms were markedly worse after a chocolate binge. He confirmed a personal past history of eczema and allergic rhinitis as well as allergies to fish and penicillin. Furthermore, there was a significant family history of atopy. He denied other oesophageal symptoms of heartburn, odynophagia or vomiting.

A clinical diagnosis of eosinophillic oesophagitis (EoE) was made. A repeat endoscopy was arranged to obtain biopsies from the lower and mid oesophagus. This again confirmed a macroscopically normal oesophagus. All biopsies, as demonstrated by Fig 1, showed squamous cell mucosa with acanthotic and papillomatous epithelium. No ulceration was present. An excess of eosinophils was noted in the epithelium. The lamina propria was unremarkable. These histological features supported the clinically suggested diagnosis of EoE. His serum eosinophil count was normal. Further formal allergy testing revealed a positive skin-prick test to white fish, along with multiple environmental allergens (dust mite, cat dander and grass pollen), and a home allergy kit gave a positive reaction to cow's milk protein.

The patient was referred to the dieticians for an exclusion–reintroduction diet and started treatment with swallowed (rather than inhaled) fluticasone 200 µg twice daily with nystatin lozenges. Following the exclusion of fish, milk and nut products from his diet, his symptoms of dysphagia resolved and his eczema improved dramatically. At a six-month follow - up, he had experienced no further dysphagia or bolus impaction.

Background

EoE was originally described during the 1970s but has only recently gained recognition as a significant diagnosis in the adult population. EoE has been described worldwide, with the exception of Africa and, although the prevalence of this condition is low (0.4–0.7%),[1] it appears to be increasing. The patient group demonstrates a male predominance (70%)[2] and familial clustering has been noted in some studies. There is clearly a link with atopy, with many patients having an extensive personal and family history of atopic conditions, including asthma, seasonal allergic rhinitis and/or eczema.[3] It could be conceptualised as 'Asthma of the oesophagus'.

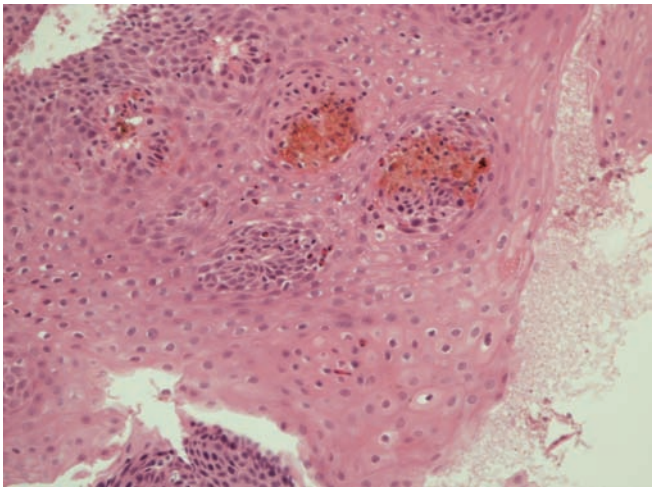

Fig 1. HE stain x100 of mid-oesophageal biopsy demonstrating increased numbers of intraepithelial eosinophils.

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There is no doubt that allergy has a key role in the pathogenesis of this disease. This is evidenced clinically by trials from paediatric practice: children fed with elemental feed, completely devoid of food allergens, have almost 100% resolution of the disease.[4] Supporting evidence also comes from the use of animal models of EoE, which are induced by exposing mice to allergens. EoE is mediated by cytokines, including interleukin (IL-) 5, IL-13 and eotaxin.[5,6] IL-5 and eotaxin released in response to a food allergen stimulate eosinophil infiltration. Over time, several changes occur, including basal cell hyperplasia, prolongation of rete pegs, smooth muscle hypertrophy and/or hyperplasia and lamina propria and/or subepithelial fibrosis.[7] This eventually results in oesophageal remodelling, which is a major factor contributing to solid food dysphagia.

Clinical features

As in our patient's case, recurrent oesophageal food impaction might be a presenting symptom of EoE, particularly in young individuals. It has become the most common cause for food bolus obstruction,[8] with up to 50% of patients with food bolus obstruction in some series being demonstrated to have EoE if biopsies are taken.[9] Other patients present with dysphagia, which can be intermittent, or with symptoms that are typical of gastro-oesophageal reflux refractory to medical treatment.

The American Gastroenterology Association (AGA) consensus suggests that diagnosis of EoE should be based on a combination of a typical clinical history in a patient with compatible histological findings, provided other causes of oesophageal eosinophilia have been excluded.[8] The presence of any eosinophils in oesophageal biopsies should be considered pathological and there are several differential diagnoses of eosinophilic infiltration of the oesophagus (Box 1), of which the most common cause is gastro-oesophageal reflux disease (GORD). For this reason, a trial of a high-dose proton pump inhibitor (PPI) for 8–12 weeks is advocated and oesophageal pH monitoring might be helpful in situations of diagnostic uncertainty.

Upper gastrointestinal endoscopy is crucial and it can be macroscopically normal in 25% of patients.[8] Other features described include linear furrowing, concentric ring formation, white spots (eosinophil-rich exudates) and 'crepe paper' mucosa. The development of narrow calibre oesophagus and stricture suggests more severe disease. Two biopsies should be taken from each third of the oesophagus (ie six in total), giving a sensitivity of 100%. The classic histopathological finding is of >15 eosinophils per high power field,[8] although other features might be noted, including superficial layering of eosinophils, basal zone hyperplasia and eosinophil microabscesses. It should be emphasised that none of these findings is pathognomic of EoE and must be taken in context with the clinical situation.

Box 1. Differential diagnosis of oesophageal eosinophilia.

1. Gastro-oesophageal reflux disease
2. Eosinophilic oesophagitis
3. Eosinophilic gastroenteritis
4. Crohn's disease
5. Connective tissue disease
6. Hypereosinophilic syndrome
7. Infection (herpes, candida)
8. Drug hypersensitivity reaction

Management

Proton pump inhibitors

A trial of high-dose oral PPI for eight weeks is advocated to exclude GORD or to treat any coexisting GORD. There is also an emerging entity termed 'PPI responsive fully oesophageal eosinophilia'. This is oesophageal eosinophilia that, despite 'normal' pH monitoring, responds to PPI. Realistically, this is likely to reflect insensitivity in current pH monitoring methods.

Corticosteroids

Topical or systemic steroids typically induce remission, but up to 90% of patients will relapse within 12 months of cessation of treatment.[10] Swallowed topical steroids are generally prescribed as fluticasone inhaler (440–480 µg/d for children, 880–1760 µg/d in adults), which is sprayed directly into the mouth and swallowed. Patients are advised not to eat or drink for 30 minutes following treatment and to continue therapy for 6–8 weeks. An alternative topical treatment is viscous suspension of budesonide. Owing to potential adverse effects, systemic high-dose steroids are generally reserved for individuals with severe disease, who require hospitalisation and nutritional support.

Other medications

Currently, there is not enough evidence to support the routine use of sodium chromoglycate, leukotriene receptor antagonists or immunosuppressants, but these have all been anecdotally used in the paediatric population. There are ongoing trials involving monoclonal antibodies to IL-5 and early results from open-labelled studies are encouraging.[11]

Nutritional therapy

Probably the mainstay of management for these patients is dietary manipulation with the aim of eliminating the offending allergen(s), however elusive these might be. There are several ways of approaching this. The most dramatic is to institute an elemental diet. This has proven very effective in the paediatric population, with an almost 100% remission rate.[4] However, this regime is challenging for adult patients to adhere to as the preparation is unpalatable, expensive and inevitably socially isolating. An alternative approach is the six-food elimination diet, where the six most common culprits (wheat, milk, egg, soya, seafood and nuts) are eliminated from the diet and reintroduced one by one to identify the offending allergen. Finally,

targeted elimination of allergens from the diet based on allergy testing can be attempted.

Allergy evaluation

The AGA recommends that all patients are referred on to an allergist for further assessment and for skin-prick and patch testing.[8] In adults, positive skin pricks to food allergens are difficult to elicit and positive results to environmental allergens are more frequently found. However, in children, two-thirds have a positive skin prick to at least one food allergen. Atopy patch testing has primarily been studied in atopic dermatitis. One study examining food allergens in children in this way demonstrated a 77% resolution of symptoms on avoidance of allergens identified.[12] Although these results might help guide management, currently there are not enough data to use this as part of the diagnostic pathway.

Endoscopic therapy

Endoscopic therapy is reserved for the management of complications of EoE, namely for the dilatation of strictures or the diffusely narrowed oesophagus. Although there was some initial concern that the rate of oesophageal perforation in these patients is higher, this has been disproved in observational studies. The rate of perforation remains <0.1%,[10] which is comparable to that of dilatation of any stricture. However, the incidence of mucosal tears and post-procedure chest pain is much higher, and should be emphasised to patients pre-procedure.

Conclusion

Much uncertainly remains for adult gastroenterologists: the natural history of EoE is uncertain and treatment aims are unclear. What treatment endpoints should one aim for: histological or symptomatic resolution? Even if they are asymptomatic, should patients undergo repeat endoscopy, with the attendant risks, to obtain biopsies? The issue of maintenance treatment has not yet been resolved and the best method of identifying allergens is not clear. Concurrent with a general rise in the incidence of allergy-related disorders, it is likely that adult patients who develop EoE will increasingly present to the general practitioner with oesophageal symptoms and to the emergency department with food bolus impaction. Therefore, EoE must be considered as a differential diagnosis in all younger patients presenting with recurrent food bolus impaction and referred appropriately.

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