Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

Eosinophilic Esophagitis

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ARTICLE INFO

Article type
Review article

Article history
Received: 5 Aug 2017
Revised: 12 Sep 2017
Accepted: 29 Sep 2017

Keywords
Cytokines
Dysphagia
Proton pump inhibitors

ABSTRACT

Eosinophilic esophagitis (EoE) is a chronic immune condition affecting children and adults. Dysphagia and food impaction are the main symptoms; however, reflux-like symptoms may also be present. The diagnosis of EoE is made with endoscopic evaluation for dysphagia, and its definitive diagnosis requires biopsy confirmation. The criteria for active EoE are defined as the symptoms of esophageal dysfunction, eosinophilic tissue infiltration (eosinophil count of at least 15 eosinophils per high-power field), and exclusion of other possible causes of esophageal eosinophilia. EoE is more prevalent in patients suffering from atopic conditions; therefore, allergic conditions may play an important role in the development of the disease. However, the etiology and pathophysiology of the disease are not completely understood. Elimination diets are considered as the first-line therapy in children; nevertheless, this approach appears to be less effective in adults, who often require steroids. Despite medical treatments, EoE is complicated in some cases by esophageal stricture and stenosis that require additional endoscopic treatments.

Please cite this paper as:
Ahadi M, Masoudifar N. Eosinophilic Eaophagitis. Rev Clin Med. 2018;5(1):8-11.

Introduction

Eosinophilic esophagitis (EoE) is a chronic inflammation of the esophagus, which is identified by clinical symptoms such as dysphagia and histologic findings including eosinophilic infiltration of the esophageal epithelium. Adult patients with EoE usually present with dysphagia and typical and atypical symptoms of gastroesophageal reflux disease (GERD) entailing nausea, vomiting, and regurgitation.

Nonetheless, in children, EoE typically manifests by feeding intolerance and GERD symptoms. Esophageal mucosal biopsy discloses diffuse eosinophilic infiltration, smooth muscle hypertrophy, and basal cell hyperplasia (1).

Prevalence

According to the results of several studies conducted in United States, the incidence rate of EoE in polar and temperate zones was higher than tropical area, which indicated a significant relationship between climate and the incidence of the disease (2,3). Consistent to the studies performed in Minnesota by Olmsted County, recent studies estimated the incidence and prevalence of EoE to be 7/100,000 and 43/100,000, respectively (4,5). This condition is more common in males than in females with a 3:1 ratio, and most of the cases had a history of atopy (6).

Pathogenesis

The allergic component of EoE is apparent from its strong association with allergic diseases. About 70% of patients with EoE have other allergic diseases or positive skin prick test, and food allergy is documented in 50% of patients (7). In addition, given the results of a recent study, EoE is an IgG4-associated allergy (8). The role of food in the pathogenesis of EoE is confirmed by observing

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the response of the disease activity to elimination diets (9).

EoE is associated with high levels of cytokines, eotaxins, particularly eotaxin-3, eosinophils, and mast cells that mediate type 1 hypersensitivity and increased intraepithelial lymphocytes (10). Patients with EoE have high levels of cytokines, especially interleukins (ILs) such as IL-3, IL-5, and IL-13, as well as eotaxins entailing chemokine ligand (CCL) CCL11, CCL24, and CCL26. These chemokines are responsible for recruitment of inflammatory cells, especially eosinophils (11,12).

Cytokines that are important in the pathophysiology of EoE are IL-5, IL-13, and eotaxin-3 (CCL26) (13,14). Furthermore, several studies demonstrated the presence and possible role of mast cells in EoE (15-17).

Clinical Presentations of EoE

EoE is common in children and young adults (18-20). This disease can have different symptoms depending on the patient . In children, symptoms include feeding intolerance, food refusal, growth failure, abdominal pain, nausea, vomiting, and regurgitation. However, dysphagia is the hallmark of EoE in adults (20-23). The leading cause of food impaction in 50% of patients is EoE (24,25).

Heartburn and GERD symptoms can be observed in both children and adults with EoE (20-23,26). Additionally, EoE is the main cause of reflux-like symptoms in 1-8% of patients with clinical suspicious for GERD (23,26-31). About 50% of patients with EoE suffer from other atopic diseases such as asthma, atopic dermatitis, allergic rhinitis, and food allergies (32-35).

Endoscopic Findings in EoE

If EoE is clinically suspected, esophagogastroduodenoscopy is required to evaluate the esophagus; furthermore, it is essential to obtain esophageal biopsies. There are multiple characteristic endoscopic findings in EoE, which are not specified for the diagnosis of EoE (36,37). Esophageal rings can either be fixed or transient, which are previously named as trachealization or corrugated esophagus and felinization, respectively (Figures 1,2).

Linear or longitudinal furrows are mucosal grooves that run in a direction parallel with the long axis of the esophagus, and white plaques or exudates can coat the esophagus mimicking the appearance of candida esophagitis. In some cases, the mucosa appears pale and congested with decreased vascularity (Figures 3,4). Crêpe-paper mucosa is defined as mucosal rent because of its fragility after the passage of endoscope through a narrow caliber esophagus (Figure 5).

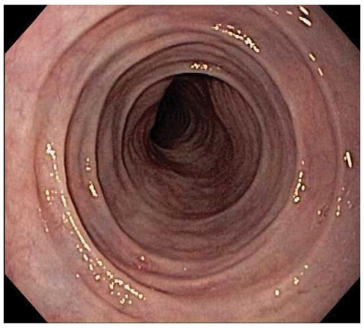

Figure 1. Fixed esophageal rings

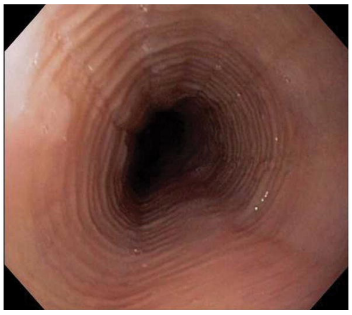

Figure 2. Transient esophageal ring

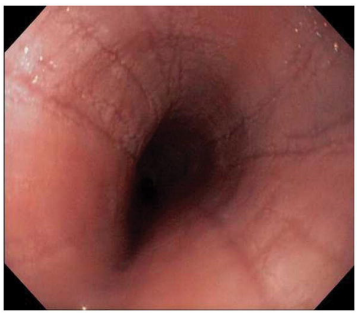

Figure 3. Linear furrows, mucosal pallor, congestion, and decreased vascularity

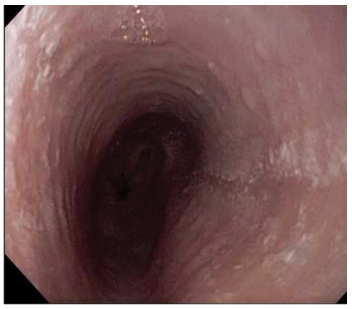

Figure 4. White plaques and exudates, mucosal pallor, congestion, and decreased vascularity

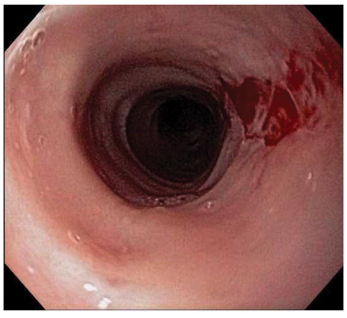

Figure 5. Crêpe-paper mucosa

About 10-20% of patients with EoE can have an endoscopically normal appearing esophagus (18,20). Accordingly, obtaining esophageal biopsies is recommended in all patients suspected of having EoE including all patients undergoing upper endoscopic evaluation for unexplained dysphagia, regardless of endoscopic findings (18).

According to the literature, the distribution of esophageal eosinophilia is often patchy and can vary between the proximal and distal esophagus (38,39). A single esophageal biopsy sample is only a small fraction of the total mucosal surface area; therefore, the sensitivity of diagnosis improves by obtaining more biopsies from different locations. Two studies were conducted separately on adults and children and suggested that the sensitivity of diagnosis increases when at least five specimens are obtained (38,40). Accordingly, the current recommendation is to take at least two to four biopsies from the distal esophagus and two to four biopsies from the proximal esophagus.

Histologic Features of EoE

The hallmark of EoE is diffused or surface clustering eosinophilic infiltration of the esophageal epithelium (11,41,42). Pathological studies carried out on patients with EoE revealed three other abnormalities including eosinophilic microabscesses, which is defined as the clusters of four or more eosinophils, eosinophil degranulation (eosinophils release their granule proteins extracellularly), and basal zone hypertrophy (Figure 6).

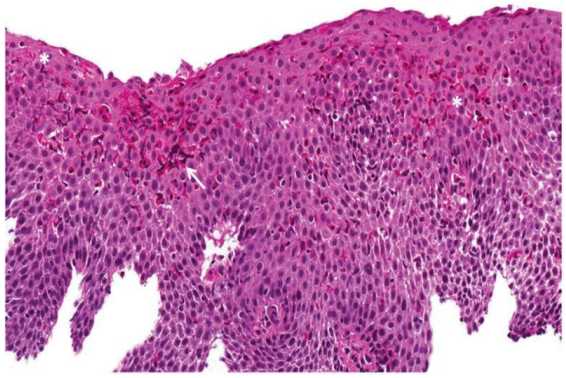

Figure 6. In this esophageal biopsy specimen, a marked infiltration of eosinophils is noted in the epithelium. In addition to the increased number of cells, eosinophilic microabscesses (white arrow), eosinophil degranulation (white asterisks), and basal layer hypertrophy are demonstrated.

Esophageal biopsy specimen, a marked infiltration of eosinophils is noted in the epithelium. In addition to the increased number of cells, eosinophilic microabscesses (white arrow), eosinophil degranulation (white asterisks), and basal layer hypertrophy are demonstrated.

Treatment

The treatment of patients is dependent on the severity of the symptoms. The PPIs are considered as the first-line therapy; however, several patients did not respond to this treatment (43). This group of patients might be treated with inhaled corticosteroids or intravenously administered interleukin antagonists. Moreover, esophageal dilation using Savary or Maloney dilators is a therapeutic technique for those patients who complain of dysphagia due to strictures (44).

Topical corticosteroids such as fluticasone are as effective as systemic corticosteroids such as prednisolone and have become the gold standard for the pharmacotherapy of EoE (45). Furthermore, the efficacy of viscous budesonide is more than nebulized corticosteroids, and it can be used in both children and adults. Remission is usually obtained after a 12-week treatment (46-49).

In addition, most of the patients are responsive to elimination diets. Although elimination diets and avoidance of the food allergens entailing milk, soy, egg, shellfish, fish, tree nuts, and peanuts might be helpful in pediatric patients, there is no certain dietary restriction for the treatment of EoE (50).

Conclusion

EoE is one of the main causes of dysphagia and reflux-like symptoms in both children and adults. These findings are not specific to EoE; therefore, making a correct diagnosis with respect to the clinical, endoscopical, and histological features is of paramount importance. The first guideline for EoE was published in 2007 and it was updated in 2011. This guideline helps both clinicians and the researchers to diagnose EoE.

Conflict of Interest

The authors declare no conflict of interest.

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