Eosinophilic esophagitis

Abstract

Eosinophilic esophagitis (EoE) is a chronic immune disease that affects children and adults. Dysphagia and food impaction are the main symptoms, but gastroesophageal reflux-like symptoms may also be present. The diagnosis of EoE is performed during endoscopy for the evaluation of dysphagia and it is confirmed by biopsy of the esophagus. Three criteria must be met for diagnosis: 1) clinical symptoms of esophageal dysfunction; 2) an esophageal biopsy with eosinophil count of at least 15 eosinophils per high-power microscopy field 3) exclusion of other possible causes of esophageal eosinophilia. The higher prevalence of EoE patients suffering from atopic diseases that may play a role in development of the disease; however, both the etiology and pathophysiology are not completely understood. Elimination diets are considered the first-line therapy in children, but this approach appears 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.

Keywords: Eosinophilic esophagitis, Dysphagia, cytokines, biopsy, proton pump inhibitors

Introduction

Eosinophilic esophagitis (EoE) is a is a chronic disease of the esophagus. EoE is identified by clinical symptoms such as dysphagia and characteristic histologic finding which is eosinophilic infiltration limited to the esophagus.

In adult patient EoE usually represents by dysphagia ,typical and atypical gastro-esophageal reflux disease (GERD) symptoms, including vomiting, regurgitation and nausea . However in children feeding intolerance and GERD symptoms are the commen symptoms . Esophageal mucosal biopsy disclose diffuse eosinophilic infiltration ,muscle hypertrophy and basal cell hyperplasia (1).

Prevalence

Several studies in united states have sujjested that incidence rate of EoE in cold climate zones is higher than in tropical area ,which indicates a relationship between climate and the disease (2, 3). In addition recent studies estimate the incidence (7/100000) and prevalence

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(43/100000) of EoE (4, 5) ,similar to the studies performed in Minnesota by Olmsted County (6) . It is more common in males than in females with a 3 to 1 ratios (6).In most cases, there is also a history of atopy with EoE (7-10).

Pathogenesis

The EoE and allergic diseases have strong association . About 70% of EoE patients have allergic diseases or positive skin pricks, and 50% of patients are atopic and have food allergy (11).In addition, a recent study shows that the IgG4 play an important role in allergic reaction in patients with EoE (12).

The role of food in the pathogenesis of EoE has become imperative when elimination of some special food was helpful in preventing disease recurrence (13).

EoE is due to high levels of cytokines, eotaxins, particularly eotaxin-3, eosinophils and mast cells that mediate this type-1 hypersensitivity and high level of reactive esophageal epithelial cells, (14).

EoE patients have high levels of cytokines especially IL-3, IL-5, IL-13, eotaxin chemokines CCL11, CCL24 and CCL26 that attract inflammatory cells, especially eosinophils (15, 16). The most significant cytokines in this allergic disease are IL-5, IL-13 and eotaxin-3 (CCL26) (17, 18).

Furthermore, some studies show that mast cells have strong association with EoE disease(19-21).

Clinical presentation of EoE

EoE is common in children and young adults .(22-24) Symptoms of EoE is different in patient.(25-28) In children, symptoms include feeding intolerance , food refusal, poor growth, abdominal pain, nausea, vomiting, or regurgitation . however, in adults dysphagia is the hallmark of EoE (24, 29-31). In 50% of patients who have esophageal food impaction EoE is the leading cause (32, 33). heartburn can be observed in both children and adults with EoE (24, 29-31, 34). Also in 1% to 8% of patients who are thought to have GERD, EoE is the leading cause (25, 26, 31, 34-37).

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In about 50% of EoE patients Atopic diseases, such as asthma, atopic dermatitis, allergic rhinitis/sinusitis, and food allergies are observed frequently (38-41).

Endoscopic findings in EoE

When EoE is suspected , esophagogastroduodenoscopy (EGD) is required to evaluate the esophagus and esophageal biopsies. There are multiple characteristic endoscopic findings in EoE (22) which are not specific for diagnosis of EoE (27, 42).

Esophageal rings can either be fixed (this finding has previously been termed esophageal trachealization or corrugation) or transient (previously termed felinization). Linear or longitudinal furrows are mucosal grooves that run parallel to the long axis of the esophagus, and white plaques or exudates can coat the esophagus and may mimic the appearance of candida. In some cases the mucosa appears pale, congested, or has decreased vascularity. Because the mucosa is fragile it can fracture with passage of the endoscope if the esophagus is narrow in caliber, a phenomenon termed crêpe-paper mucosa .

Figure1

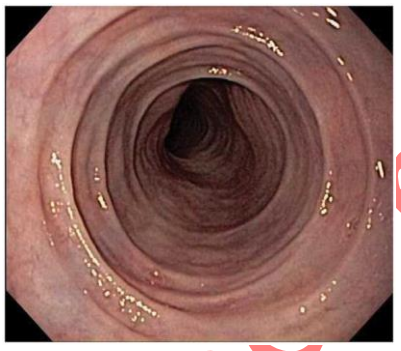

Figure2

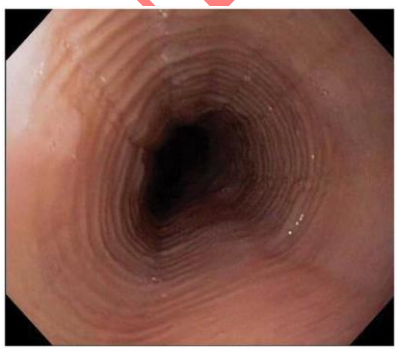

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Figure3

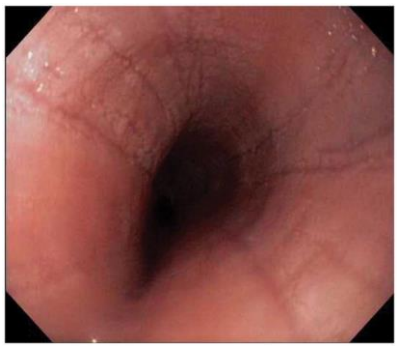


Figure4

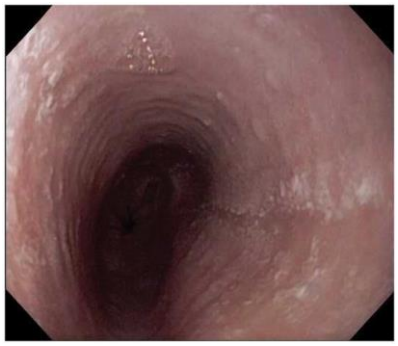
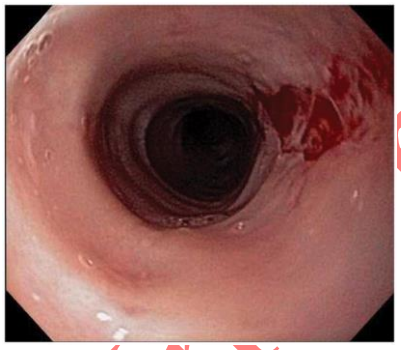


Figure5



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Typical endoscopic findings in EoE is seen in this picture: Figure1 is fixed esophageal rings. Figure2 is Transient esophageal rings. Figure3 is linear furrows, as well as mucosal pallor, congestion, and loss of vascularity. Figure4 is white plaques and exudates, as well as mucosal pallor, congestion, and loss of vascularity. And Figure5 is Crêpe-paper mucosa with a mucosal rent after passage of the endoscope through a narrow caliber esophagus. This occurred without endoscopic dilation.

Esophageal biopsies are currently required to diagnose EoE. Because 10–20% of EoE patients can have an endoscopically normal appearing esophagus,(22, 24) it is recommended that esophageal biopsies should be obtained in all patients suspected of having EoE, including all patients who undergo upper endoscopic evaluation for unexplained dysphagia, regardless of the endoscopic appearance or findings (22).

The approach to obtain esophageal biopsies is informed by studies showing that esophageal eosinophilic infiltrate of EoE is patchy (28) and can vary between the proximal and distal esophagus (43, 44). Because a single esophageal biopsy sample is only a tiny fraction of the mucosal surface, increasing the number of biopsies and including tissue from different esophageal locations improves the sensitivity of diagnosis. Two studies, one in adults and one in children, suggest that sensitivity is maximized when at least 5 biopsies are obtained (43, 45).Therefore, the current recommendation is to take at least 2–4 biopsies from the distal and 2–4 biopsies from the proximal esophagus.

Histologic features of EoE

Hallmark of EoE is the esophageal eosinophilic infiltration (15, 46, 47). This infiltration is diffused through the epithelium, or there can be a surface clustering of eosinophils. Pathological studies in patients with EoE reveal three other abnormalities: eosinophilic microabscesses (which is defined as clusters of at least 4 eosinophils), eosinophil degranulation (where eosinophil granule proteins are observed extracellularly), basal zone hypertrophy, (Figure 2).

Figure6

In this esophageal biopsy specimen, a marked infiltrate of eosinophils is noted in the epithelium. In addition to the increased number of cells, eosinophilic microabscesses are noted (white arrow) and there is eosinophil degranulation (white asterisks). The basal layer is also substantially hypertrophied.

Treatment

The treatment of patients is dependent on the severity of symptoms .

In first line patients are treated with Proton pump inhibitors (PPIs) (10).Although some patients might not respond to PPIs, they should be used as first line therapy(48, 49).

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Patients who don't respond to PPIs are treated with steroid containing local inhalers or with intravenous interleukin blockers and who are complaining about dysphagia due to strictures are treated with esophageal dilation using Savary or Maloney dilators (50).

Topical corticosteroids have become the "gold standard" for the pharmacotherapy of EoE patients . Topical treatment (like fluticasone) is as effective as systemic corticosteroids (like oral prednisone) due to remitting the symptoms. (51)furthermore efficacy of viscous steroids is more than nebulized steroids and it can be used in both children and adults. Remission is usually obtained after 12-weeks treatment (52-55).

Also most patients are responsive to elemental diets restrictions. Although , avoiding pediatric patients from allergenic food like (milk, soy, egg, shellfish, fish, tree nuts and peanuts) might be helpful, no certain dietary restriction has been approved in treatment of EoE (56).

Conclusion

EoE has become one of the main causes of dysphagia, and upper GI symptoms in both children and adults. Since the findings are not specific to EoE making the correct diagnosis due to clinical, endoscopic, and histologic features is important. The first guideline for EoE published in 2007 and it updated in 2011 so it welcomes both the clinician and the researcher to diagnose EoE .

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