



Diagnosis and Treatment of Eosinophilic Esophagitis in Adults

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ABSTRACT

Eosinophilic esophagitis is a relatively recently discovered disease of increasing incidence and prevalence and is a common cause of dysphagia and food bolus impaction. The definition of eosinophilic esophagitis continues to evolve, most recently with the characterization of proton pump inhibitor-responsive esophageal eosinophilia. The number of high-quality prospective, controlled trials guiding therapeutic decisions in eosinophilic esophagitis has increased steadily over the past several years. Treatment options at present focus on dietary therapy, particularly implementation of a 6-food elimination diet, and medical therapy, primarily the use of swallowed, topical corticosteroids. Proton pump inhibitors play an important role in current management. Conservative esophageal dilation is effective at ameliorating dysphagia in symptomatic patients with esophageal strictures. We conducted an evidence-based review of the diagnosis and treatment options in adults with eosinophilic esophagitis. The understanding of eosinophilic esophagitis continues to be refined. Continued validation of appropriate endpoints, however, is essential to establish the efficacy of existing and novel therapeutic approaches.

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The esophagus is an immunologically active organ normally devoid of eosinophils. Esophageal eosinophilia was initially associated with gastroesophageal reflux disease; however, isolated case reports were published in the 1970s and 1980s highlighting clinical features distinct from gastroesophageal reflux disease.¹ Eosinophilic esophagitis was not fully appreciated as a distinct clinical entity until the 1990s, when reports emerged characterizing patients with dysphagia with esophageal mucosal eosinophilia without gastroesophageal reflux disease.^{2,3} Over the past 2 decades, eosinophilic esophagitis has rapidly emerged as a leading cause of esophageal morbidity among both children and adults. This

review highlights the diagnosis and treatment of adults with this disease.

LITERATURE SEARCH AND RESULTS

PubMed was searched from January 1970 through March 2016 to identify English-language articles published to date. Medical subject heading terms included eosinophilic esophagitis, diagnosis, biopsy, therapeutics, disease management, adrenal cortex hormones, steroids, prednisone, and adult. Keywords searched included: eosinophilic esophagitis, eosinophilic oesophagitis, EoE, esophageal eosinophilia, and oesophageal eosinophilia. Additional keywords searched included: diagnosis, diagnoses, diagnostic, clinical features, presentation, biopsy, biopsies, treatment, treatments, therapy, therapies, therapeutic, therapeutics, intervention, interventions, management, food, diet, diets, dietary, steroid, steroids, corticosteroid, corticosteroids, prednisone, budesonide, fluticasone, dilation, and adult.

We identified a total of 1017 articles. We limited our search to articles published in peer-reviewed journals and excluded reports having only abstracts or presentations at

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scientific meetings. The bibliographies of selected articles were reviewed to find any studies missed using our search strategy. A total of 65 articles were included in this review, with a focus on the highest quality prospective studies where available.

DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS

Epidemiology and Pathogenesis

Eosinophilic esophagitis is reported worldwide; the highest burden of disease is recognized in North America, Western Europe, and Australia.⁴ The prevalence of eosinophilic esophagitis in the United States is estimated to range from 40 to 90 cases per 100,000 persons.⁴ Among patients undergoing upper endoscopy for evaluation of dysphagia, the prevalence of eosinophilic esophagitis ranges from 12% to 22%. Eosinophilic esophagitis is the most frequent etiology of esophageal food bolus impaction requiring an emergency room visit and urgent endoscopy in the United States.⁴ Increasing incidence and prevalence of eosinophilic esophagitis may be attributed to increasing recognition as well as an increase in atopic diseases over the past several decades.

Genetic, environmental, and host immune factors contribute to the pathogenesis of eosinophilic esophagitis. Antigens in food and the environment lead to an adaptive T-helper type 2 cell-mediated response yielding cytokines including interleukin (IL)-5 and IL-13. Interleukin-13 leads to the triggering of esophageal epithelial cells; the eotaxin-3 gene is induced and serves as an eosinophil chemoattractant. Interleukin-13 also leads to the induction of an esophageal transcriptome specific to eosinophilic esophagitis.⁵ Interleukin-5 serves as a factor for eosinophil growth and activation and plays a role in esophageal remodeling and deposition of collagen.⁶ Acid reflux may increase esophageal epithelial permeability and lead to increased exposure to dietary and environmental antigens.

Clinical Presentation and Diagnostic Features

Patients may present at any age, though the majority of patients are diagnosed in the second through fifth decade. There is a male predominance, with a male/female ratio of 3:1.^{7,8} Dysphagia to solid foods is the most common presenting symptom among adults. Food impaction requiring endoscopic management is reported to occur in 33%-54% of

adults with eosinophilic esophagitis.⁹ Among adults with eosinophilic esophagitis, 30%-60% report heartburn and 8%-44% present with noncardiac chest pain.¹⁰ Many patients modify their diet to compensate for narrowing of the esophageal lumen and report taking a long time to eat their meals, chewing their food meticulously and avoiding

foods such as meats or bread, which may be more difficult to swallow. Patients may have concurrent allergic diatheses, including asthma, eczema, rhinitis, atopic dermatitis, or seasonal or food allergies.¹¹ Up to 80% of adults with eosinophilic esophagitis may have comorbid atopic conditions.¹² The chronic nature of the disease, including the need for long-term therapy and social implications, significantly impacts patients' quality of life.^{13,14}

Eosinophilic esophagitis is defined as a chronic immune/antigen-mediated esophageal disease characterized clinically by symptoms of esophageal dysfunction and histologically by eosinophil-predominant inflammation.¹⁵ The diagnosis accounts for both clinical findings and pathologic findings on esophageal biopsies. Recent guidelines define these criteria as symptoms related

to esophageal dysfunction, esophageal biopsies with ≥ 15 eosinophils per high-power field, and persistence of esophageal eosinophilia after a proton pump inhibitor (PPI) trial, with exclusion of secondary causes of esophageal eosinophilia.¹⁶ Although the identification of esophageal eosinophilia is abnormal, numerous potential etiologies exist, including gastroesophageal reflux, eosinophilic gastrointestinal diseases, Crohn's disease, celiac disease, achalasia, hypereosinophilic syndrome, and infection, among other causes.

One of the challenges in diagnosing eosinophilic esophagitis is differentiating this disease from gastroesophageal reflux disease, another condition that may involve esophageal eosinophilia and produce symptoms of esophageal dysfunction.¹⁷ In prior years, a response to PPI therapy was used to exclude reflux in patients with esophageal eosinophilia. Recent studies, however, have demonstrated that 23%-61% of patients with clinical and histologic features of eosinophilic esophagitis respond to PPI therapy.^{18,19} The diagnosis of PPI-responsive esophageal eosinophilia is currently recommended, to acknowledge limitations to our understanding as to whether such patients have gastroesophageal reflux, eosinophilic esophagitis, or both disorders.²⁰ The benefit conferred by PPIs may be due to both acid-suppressive effects as well as anti-inflammatory

CLINICAL SIGNIFICANCE

- Eosinophilic esophagitis in adult patients usually presents as dysphagia or food impaction, with a high incidence in young atopic males.
- Proton pump inhibitor-responsive esophageal eosinophilia must be ruled out with an 8-week course of proton pump inhibitor followed by repeat esophageal biopsies before confirming the diagnosis of eosinophilic esophagitis.
- Endpoints of treatment include improvements in both symptoms and histology.
- Treatment options include elimination diet and topical corticosteroids. Conservative esophageal dilation may be used in selected symptomatic patients.

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