Diagnosis and Management of Eosinophilic Esophagitis

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KEYWORDS

• Eosinophilic esophagitis • Food allergy • Elimination diet • IgG4
• Swallowed steroids

KEY POINTS

- Eosinophilic esophagitis is a chronic inflammatory disease that is commonly food triggered.
- The mainstays of therapy involve the use of proton pump inhibitors, elimination of relevant food triggers, serial esophageal dilations, and topical steroids.
- Contemporary diagnosis and management relies on repeat endoscopy; however, emerging insights hold promise for the development of noninvasive approaches for disease monitoring and novel immune-modulating therapies.

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic, local, immune-mediated esophageal disease, characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.[1] EoE was first defined as a clinicopathologic syndrome in the 1990s,[2,3] and since this time, it has become an increasingly appreciated chronic inflammatory disease. EoE is now estimated to affect 10 to 50 in 100,000 children and adults in the United States, Canada, Europe, and Australia, and like other allergic conditions, the incidence seems to be increasing.[4–9] Although the underlying pathophysiology of EoE remains unknown, it seems to be due to non–immunoglobulin E (IgE)-mediated allergic inflammation to allergens, which have been shown to be predominantly food in both children and adults.[10,11] In this review, we discuss recent advances as they pertain to the diagnosis and management of EoE.

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SYMPTOMS

The presentation of EoE is not uniform across all ages. Young children and toddlers typically present with nausea, vomiting, feeding difficulties, abdominal pain, and failure to thrive.[12,13] In contrast, teenagers and adults with EoE tend to present with dysphagia, esophageal dysmotility, refractory reflux, or other sequelae related to esophageal remodeling, such as food impaction.[14–17]

In addition to the symptoms directly related to EoE, there is a clear association of EoE with other atopic diseases, such as allergic rhinitis, asthma, atopic dermatitis, and IgE-mediated immediate food allergy.[18,19] Recent reports indicate that EoE is also more common in individuals with inflammatory and autoimmune diseases, such as chronic rhinosinusitis, ulcerative colitis, multiple sclerosis, and systemic sclerosis.[20,21] There is also a possible association with connective tissue diseases such as Ehlers-Danlos syndrome, Marfan syndrome, and Loeys-Dietz syndrome.[22] This finding suggests that the suspicion for EoE should be heightened in individuals with such diseases.

PATHOPHYSIOLOGY

EoE shares many immunologic features with other atopic diseases. In addition to local eosinophilia, studies from human and animal models have shown that EoE is characterized by impaired epithelial barrier function[23,24] and infiltration of T helper type 2 (Th2) $CD4^+$ helper T cells,[25,26] mast cells,[27] basophils,[28] plasma cells,[29] and group 2 innate lymphoid cells.[30] Although allergen-specific IgE antibodies are also often detected, elimination diets based solely on IgE sensitization have had mixed success,[31,32] and the use of anti-IgE treatment was not shown to be more efficacious in inducing EoE remission than placebo.[29] It has been shown, in both pediatric and adult populations, however, that food is a key trigger for EoE.[33,34] The strongest such evidence comes from trials with elemental diets, where histologic remission rates of greater than 90% are observed, although focused food elimination diets also often lead to remission.[10,11,34] Taken together, EoE is often considered a non–IgE-mediated, food antigen–driven hypersensitivity,[35] although the exact mechanism remains unclear.

Candidate and unbiased genetic approaches have identified a number of genes associated with EoE. These include the genes that encode for (or are involved in the regulation of) thymic stromal lymphopoietin, filaggrin, desmoglein-1, calpain-14, eotaxin-3, and transforming growth factor-β.[36] Many of these genes are known to be involved in the regulation of barrier function, Th2 induction, and tissue remodeling. Consistent with a Th2-related inflammatory milieu, the cytokines interleukin (IL)-4, IL-5, and IL-13 are also upregulated in EoE.[37] Emerging data also show abundant antigen-specific immunoglobulin G4 (IgG4) in the esophageal mucosa and peripheral blood.[29,38] To date, the relative importance of these different cellular and molecular mediators in the pathogenesis of EoE remains to be established.

DIAGNOSTIC TESTS

EoE is a clinicopathologic disease and, thus, the diagnosis depends on certain pathologic findings in individuals with an appropriate clinical history. As such, an esophagogastroduodenoscopy is a required part of the workup for EoE. At the macroscopic level, a number of findings are associated with EoE, including esophageal rings, linear furrows, plaques, stenosis, and strictures; however, these findings are neither sensitive nor specific for this disease.[39] Histologic evidence of at least 15 eosinophils per