Eosinophils in Gastrointestinal Disorders

Eosinophilic Gastrointestinal Diseases, Celiac Disease, Inflammatory Bowel Diseases, and Parasitic Infections

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KEYWORDS

• Eosinophil • Esophagitis • Eosinophilic esophagitis • Eosinophilic gastritis
• Eosinophilic gastroenteritis • Eosinophilic colitis • Parasitic infection

KEY POINTS

- Eosinophilic gastrointestinal diseases (EGIDs) describe a group of diseases occurring in children and adults and are characterized by symptoms related to gastrointestinal (GI) dysfunction and inflammation consistent with increased intestinal eosinophilia.
- Eosinophilic esophagitis, the most common EGID, presents in children with feeding problems, abdominal pain, and symptoms recalcitrant to acid inhibition, and in adults with food impaction and dysphagia.
- Eosinophilic gastritis, gastroenteritis, and colitis are uncommon and present with abdominal pain, vomiting, diarrhea, and bleeding.
- The association of celiac disease with eosinophils in the small intestinal and esophageal mucosa is increasingly recognized and requires individualized assessment and treatment.
- The association of inflammatory bowel diseases (IBDs) with mucosal eosinophilia and its secreted products is increasing, but the role of eosinophils in the pathogenesis of IBD remains uncertain.
- Intestinal helminth infection can produce a clinical picture indistinguishable from eosinophilic gastroenteritis.

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INTRODUCTION

The gastrointestinal (GI) tract possesses the greatest surface area of any organ in the body and contains the largest number of immune cells and products. Functionally, the gut must maintain critical functions of nutrition absorption and of oral tolerance. How this latter process occurs in such a fine-tuned and regulated fashion remains an area of active investigation.

Over the past few decades, the identification of eosinophils in the GI tract has begun to arouse suspicion that they play a role in GI health and/or disease.[1,2] In contrast to the neutrophil, which is typically absent in the healthy GI tract, eosinophils reside in varying quantities in the mucosa. During disease states, eosinophils increase and have been implicated in the pathogenesis of ongoing inflammatory processes (**Table 1**). These observations are typically limited to enumerating eosinophils in the epithelium or mucosal surface; the exact depth, distribution, and state of activation in these circumstances are still undergoing definition.

This article focuses on 4 diseases in which mucosal eosinophils are clearly associated, eosinophilic gastrointestinal diseases (EGIDs), celiac disease, inflammatory bowel diseases (IBDs), and parasitic infections. Here we will provide an overview of their clinical features and summarize the association of eosinophils with each inflammatory state.

EOSINOPHILIC GASTROINTESTINAL DISEASES

Eosinophilic Esophagitis

Epidemiology

Eosinophilic esophagitis (EoE) has been reported in all continents, except Africa, and consistently has been shown to occur more commonly in male individuals with a 3:1 ratio.[3–6] Because this is an emerging disease, the exact incidence is difficult to predict, but estimates range from 1 to 4 in 10,000 in North America. There does not appear to be a clear predilection toward one ethnicity.

Risk factors

Recent studies and clinical experiences provide some insights into potential risk factors but these are difficult to identify completely because the exact pathogenesis is uncertain. A recent twin study revealed that if a sibling has EoE, there exists a risk of 2.4% of subsequent children developing EoE.[7] A variety of EoE genes provides clues to dysfunction of the epithelial barrier (filaggrin),[8] immune system (thymic stromal lymphopoietin, eotaxin-3)[9–11] and other yet to be identified areas (calpain-14).[12,13]

Pathophysiology

Within the epithelia, the prominence of eosinophils, interleukin (IL)-5–expressing T cells, B cells, and increased mast cells suggests an immunologically mediated Th2-type inflammatory disease.[14] In further support, clinical characterization of children and adults reveals many highly atopic patients posses a Th2-type inflammatory profile. Basic studies in experimental models of EoE reveal that T-cell–deficient mice, but not B-cell–deficient mice, were protected from esophageal inflammation and esophageal inflammation induced by aero-allergens and food allergens, IL-13, and IL-5.[15–20] Together, these clinical and basic studies provide strong support for allergy as a pathogenic etiology for EoE. In contrast, some patients do not exhibit the same degree of atopy and thus may indicate alternative mechanisms and EoE phenotypes.[21]

Pathologic remodeling represents the likely underlying mechanism of problematic EoE complications, such as esophageal stricture and food impaction.[22–25] A number of basic and translational studies suggest a wide variety of mechanisms related to