# Histopathologic Features of Eosinophilic Esophagitis and Eosinophilic Gastrointestinal Diseases

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#### **KEYWORDS**

- Eosinophilic esophagitis
   Pathology
   Pediatric
   Gastroesophageal reflux disease
- Proton pump inhibitor
   Eosinophilic gastrointestinal disease

#### **KEY POINTS**

- Esophageal biopsies from patients who have eosinophilic esophagitis differ significantly from normal esophageal biopsies, and by definition exhibit eosinophil-rich inflammation, often with additional pathologic changes in the epithelium and lamina propria.
- Biopsy pathology is a specific but not sensitive marker for allergic disease affecting the esophagus.
- Eosinophilic esophagitis biopsy pathology correlates with genetic abnormalities.
- A schema is provided to evaluate mucosal biopsies from the remainder of the gastrointestinal tract, and it may provide the basis for eosinophilic gastrointestinal disease diagnosis and entry criteria for research studies.

#### INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic immune antigen-mediated disease (Box 1). 1-3 Patients who have EoE respond to antigen elimination, especially elimination of food antigens, consistent with disease associated with a T helper cell type 2 (Th2) reaction to swallowed antigen. The definition of EoE does not differ with patient age or gender, esophageal biopsy pathology does not vary with patient age or gender, and response to antigen elimination occurs in both children and adults of both genders. However, symptoms of EoE differ according to patient age: vomiting and failure to thrive are common among young children, and dysphagia is more typically the predominant symptom among affected adolescents and adults.

Disclosures: The author is a consultant for Meritage Pharma, Receptos Inc, and Aptalis Pharma; a TIGER Executive Committee member; and APFED Medical Advisory Panel president. Division of Pathology and Laboratory Medicine, Cincinnati Children's Hospital Medical Center, ML1035, 3333 Burnet Avenue, Cincinnati, OH 45229, USA E-mail address: margaret.collins@cchmc.org

Gastroenterol Clin N Am 43 (2014) 257–268 http://dx.doi.org/10.1016/j.gtc.2014.02.007

#### Box 1

Criteria for biopsy evaluation for eosinophilic gastrointestinal disease. At least one feature should be present for diagnosis in at least one biopsy from each site

#### Eosinophilic esophagitis

- Greater than or equal to 15 intraepithelial eosinophils per HPF in at least one esophageal site<sup>1–3</sup>; additional sections should be obtained from nondiagnostic but highly suggestive biopsies, and fewer eosinophils than the recommended threshold value may not eliminate the diagnosis in patients who otherwise would qualify for the diagnosis
- Altered eosinophil character manifest as surface layering and abscesses
- Epithelial changes such as basal layer hyperplasia, dilated intercellular spaces
- Thickened lamina propria fibers

#### Eosinophilic gastritis

- Greater than or equal to 30 eosinophils per HPF in 5 HPF<sup>43</sup>
- Altered eosinophil behavior manifest as lamina propria sheets, eosinophilic glandulitis, eosinophilic gland abscesses
- Epithelial changes such as reduced mucin, increased nuclear/cytoplasmic ratio, increased epithelial mitotic activity
- Altered eosinophil distribution such as one or more per HPF in surface epithelium, or more
  than one per HPF in gland epithelium<sup>4</sup>; excess eosinophils in muscularis mucosa or
  submucosa; concentration of eosinophils in the subepithelial superficial lamina propria
  instead of deep lamina propria

#### Eosinophilic enteritis (eosinophilic duodenitis, jejunitis, or ileitis)

- More than twice the normal number of eosinophils in the lamina propria per HPF:
  - o More than 52 eosinophils per HPF in duodenum
  - o More than 56 per HPF in ileum
- Altered eosinophil behavior manifest as lamina propria sheets, eosinophilic cryptitis, eosinophilic crypt abscesses
- Epithelial changes such as reduced mucin, increased nuclear/cytoplasmic ratio, increased epithelial mitotic activity
- Altered eosinophil distribution such as:
  - More than 2 per HPF and more than 4 per HPF in surface epithelium in duodenum and ileum respectively
  - More than 6 per HPF and more than 4 per HPF in crypt epithelium in duodenum and ileum respectively<sup>4</sup>
  - o Excess eosinophils in muscularis mucosa or submucosa
  - Concentration of eosinophils in the subepithelial superficial lamina propria instead of deep lamina propria
- · Acute inflammatory cells are not present

#### Eosinophilic colitis

- More than twice the normal number of eosinophils in the lamina propria per HPF:
  - More than 100 per HPF in right colon
  - o More than 84 per HPF in transverse and descending colon
  - o More than 64 per HPF in rectosigmoid colon
- Altered eosinophil behavior manifest as lamina propria sheets, eosinophilic cryptitis, eosinophilic crypt abscesses

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