

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

Histologic Features of Gastroesophageal Reflux Disease and Eosinophilic Esophagitis



Robert D. Odze, MD, FRCP
Chief, Gastrointestinal Pathology
Brigham and Women's Hospital
Professor of Pathology
Harvard Medical School
Boston, Massachusetts

G&H What are the histologic features of eosinophilic esophagitis?

RDO The histologic changes associated with eosinophilic esophagitis often involve multiple segments of the esophagus (ie, the proximal, mid, and distal esophagus) and sometimes occur in a patchy or segmental fashion; they are not always diffuse and continuous. The histologically involved areas show numerous eosinophils, often more than 15 per high-power field in peak areas. Even more importantly, the histologies of patients with eosinophilic esophagitis show clustering of eosinophils and eosinophilic microabscesses, degranulating eosinophils, and, very characteristically, surface layering of eosinophils, often mixed with necroinflammatory debris. Other accompanying features of eosinophilic esophagitis include marked basal cell hyperplasia, intercellular edema, acantholysis, lamina propria fibrosis, occasional ulceration, and elongation and extension of the rete pegs. The mucosa of these patients contains increased chronic inflammatory cells as well.

G&H Does the number of eosinophils in a histologic sample correlate with the severity of disease?

RDO It is not clear whether the number of eosinophils correlates with clinical severity. In some cases, there does appear to be a correlation, but in other cases, there does not. In some studies, eosinophils are a fairly good indicator of response to treatment. However, some patients with only a few eosinophils still remain symptomatic, sometimes as symptomatic as patients with many eosinophils.

G&H Have any studies evaluated the use of different staining techniques for identifying these histologic features?

RDO There are some studies that show various increases in subclasses of inflammatory cells, subclasses of lymphocytes, mast cells, histiocytes, and Langerhans cells. These can all be documented with special stains that highlight each of these different cells; however, none of them are yet clinically useful in this patient population.

G&H Is interobserver variability an issue in terms of examining the histologies of these patients?

RDO There is interobserver variability in terms of enumerating eosinophils and recognizing their location, as well as with many of the other histologic features, such as determining the degree of basal cell hyperplasia and rete peg elongation.

G&H What is the standardized biopsy protocol for patients with suspected eosinophilic esophagitis?

RDO According to the currently recommended biopsy protocol, a total of at least 5 biopsies should be taken. These biopsies should be obtained from all segments of the esophagus and from any endoscopically recognizable pathologic areas, such as ulcers, raised areas, or areas that may correspond to dense aggregates of eosinophils (ie, the biopsies should be targeted toward abnormal areas).

G&H How similar are the histologic features of eosinophilic esophagitis to those associated with gastroesophageal reflux disease?

RDO The histologic features of the 2 conditions are very similar. Although eosinophilic esophagitis often contains more eosinophils, more eosinophilic microabscesses, more layering of the eosinophils at the surface, and more basal cell hyperplasia, patients with gastroesophageal reflux disease can show similar or even the same findings in certain circumstances. In order to distinguish between the 2 conditions, it helps to note the distribution of the disease. Gastroesophageal reflux disease is typically worse in the distal esophagus and gets better as you move proximally up the esophagus; in contrast, eosinophilic esophagitis can affect all portions of the esophagus equally, or it can even be worse proximally (compared to distally).

G&H Are there any other ways to differentiate between the 2 conditions?

RDO Pathologists should never be definitive about differentiating eosinophilic esophagitis from gastroesophageal reflux disease because the former condition is not purely a histologic diagnosis. Eosinophilic esophagitis is a diagnosis that is made clinically and pathologically; it is not a diagnosis that should be established solely by a pathologist.

G&H Could examining different cell types (such as mast cells) help differentiate between the 2 conditions?

RDO There are some papers that show differences in the distribution and number of certain cell types (such as mast cells), but these findings are not yet useful on a clinical basis in individual patients.

G&H Why is it important to differentiate between eosinophilic esophagitis and gastroesophageal reflux disease?

RDO It is very important to differentiate between these 2 conditions because their treatments, outcomes, and prognoses are different.

G&H How often do patients have both of these conditions?

RDO There are reports that a small percentage of patients can have both eosinophilic esophagitis and gastroesophageal reflux disease. The exact percentage of this group of patients is not certain but probably ranges from 5% to 10%.

G&H When examining a patient with suspected eosinophilic esophagitis, are there any conditions other than gastroesophageal reflux disease that should be excluded?

RDO Yes, because eosinophils are not necessarily specific to eosinophilic esophagitis and, as previously mentioned, are also indicative of gastroesophageal reflux disease. Other diseases can show prominent eosinophils in the esophagus as well. Parasitic infections, inflammatory bowel disease, drug reactions, radiation injury, and many other inflammatory disorders can present with esophagitis characterized by prominent eosinophils. However, these conditions often have coexisting histologic variables that help to differentiate them from eosinophilic esophagitis.

G&H What are the most significant challenges when examining the histologies of these patients?

RDO The biggest challenges are recognizing and targeting the areas of highest eosinophil density and differentiating eosinophilic esophagitis from gastroesophageal reflux disease.

G&H Are clinicians usually familiar with the histologic features of eosinophilic esophagitis and gastroesophageal reflux disease?

RDO Most clinicians are aware of the eosinophil prominence and perhaps of the usual numbers of eosinophils in eosinophilic esophagitis patients. However, I am not sure whether most clinicians are familiar with the other histologic manifestations of these conditions. Many clinicians are often not aware that eosinophilic esophagitis is both a clinical and pathologic diagnosis and that they cannot rely exclusively on the pathologist to establish a diagnosis of the condition. These clinicians incorrectly assume that a biopsy with more than 15 eosinophils per high-power field is diagnostic of eosinophilic esophagitis or that a biopsy that does not have 15 eosinophils per high-power field is not diagnostic of the condition.

G&H What are the next steps in research in this area?

RDO More research is needed, particularly in terms of further defining the specific pathologic features of eosinophilic esophagitis compared to gastroesophageal reflux disease, outlining the pathways of the pathogenesis of each condition, determining the association (or lack thereof) between the 2 conditions, and determining the cell types responsible for the inflammatory reaction.

(continued on page 481)