

Optimal approach to obtaining mucosal biopsies for assessment of eosinophilic esophagitis and lymphocytic esophagitis

Abstract

Eosinophilic esophagitis (EoE) and lymphocytic esophagitis (LyE) are inflammatory disorders of esophagus characterized clinically by dysphagia or food impaction. Endoscopic findings like esophageal rings, exudates, furrows and strictures might indicate the presence of these conditions, however, these findings have also been described in other esophageal disorders and endoscopic appearance may be normal in up to 25–30% patients. Inflammation may display a patchy distribution and multiple biopsies from different parts during an endoscopy procedure are required to ensure diagnostic accuracy. Determination of the most appropriate site of the esophagus to obtain a biopsy specimen for diagnosis of EoE or LyE is considered critical. This article highlights issues related to optimal approach to obtaining mucosal biopsies for assessment of EoE and LyE.

Keywords: Eosinophilic esophagitis, Lymphocytic esophagitis, Esophageal biopsies

Volume 5 Issue 3 - 2016

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Received: July 14, 2016 | **Published:** September 08, 2016

Abbreviations: EoE; Eosinophilic Esophagitis, HPF; High Power Field, IPCL; Intrapapillary Capillary Loops, LyE; Lymphocytic Esophagitis, NBI-ME; Narrow-Band Imaging Magnifying Endoscopy

Introduction and discussion

EoE is defined as a chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by an eosinophil-predominant inflammation (≥ 15 eosinophils per high power field (hpf)) in the esophageal mucosa.¹ Endoscopic abnormalities in patients with EoE include esophageal rings, strictures, narrow-caliber esophagus, linear furrows, white plaques or exudates and edema.² However, there are no pathognomonic signs for EoE since these endoscopic findings have also been described in other esophageal disorders. Moreover, endoscopic appearances may be normal in 10–25% of EoE patients.³

Lymphocytic esophagitis (LyE) was first described as an independent entity in 2006 by Rubio et al.⁴ LyE patients clinically present with dysphagia, abdominal pain, heartburn and nausea.⁵ The diagnosis of LyE is considered when more than 40 intraepithelial lymphocytes/hpf are present, and none or only occasional CD15+ intraepithelial granulocytes.^{4,6} Endoscopic features of LyE can be similar to EoE including esophageal rings, furrows, exudates, narrow lumen or stenosis but in one-third of patients the esophageal mucosa appears macroscopically normal.⁵

By consensus, an eosinophilic infiltrate of ≥ 15 eosinophils /hpf suggests the diagnosis of EoE.¹ However the distribution of esophageal eosinophilia is often patchy.^{7,8} There are no studies describing the distribution of lymphocytic infiltration in LyE. Multiple biopsy samples from different parts during an endoscopy procedure are required to ensure diagnostic accuracy.⁷ However, multiple biopsies of the esophagus are not easily carried out during an endoscopy examination in clinical practice. Therefore, determination of the most appropriate site of the esophagus to obtain a biopsy specimen for diagnosis of EoE or LyE is considered critical for gastroenterologists.⁹

Patients with EoE often demonstrate eosinophilic infiltration in both distal and proximal biopsies, although proximal biopsies vary in eosinophil density on a patient-to-patient basis.¹⁰ Gonsalves et al.¹⁰ found that, when the threshold of ≥ 15 eosinophils /hpf was applied, evaluation of a single biopsy specimen yielded a sensitivity rate of only 55% for detection of EoE, compared to 100% when five biopsies were obtained from the proximal, middle and distal esophagus.¹⁰ Nielsen et al.¹¹ demonstrated that four to six biopsy fragments from distal and proximal esophagus should be submitted to optimize the chances of achieving the morphologic criteria for a diagnosis of EoE, and that the field is not increased beyond six biopsy fragments.

An endoscopic feature suggesting EoE (rings, furrows, exudates, narrow lumen and stenosis) does not always represent esophageal eosinophilia although it reminds endoscopist of the presence of EoE.¹² Pooled analysis showed that at least one such feature was detected by endoscopy in up to 93% of patients with EoE.¹³

Endoscopic appearance and location dictate diagnostic yield of biopsies in EoE. However, there are some discrepancies about the suitable biopsy site for detection of eosinophilia. Adachi et al.⁹ reported severe exudates as a significant factor related to a positive finding of eosinophilic infiltration. Salek et al.¹⁴ reported also higher eosinophil counts in biopsies obtained from exudates and furrows although rings alone without associated furrows and exudates did not demonstrate elevated eosinophil counts. In contrary, in a study by Hori et al.¹² diagnostic utility of linear furrows or rings was superior to that of white exudates.

Tanaka et al.¹⁵ recently described narrow-band imaging magnifying endoscopy (NBI-ME) criteria for EoE and LyE. Three abnormal NBI-features were identified:

- i. Beige color of the mucosa,
- ii. Increased and dot-shaped congested intrapapillary capillary loops (IPCL) and
- iii. Invisibility of submucosal vessels. The presence of at least one of the above findings was reported in 100% patients with EoE and 91% of patients with LyE.

In author's own experience NBI–ME criteria are useful to determine the site of inflammation. To this date we have no established guidelines regarding biopsy protocol in LyE. However, the fact that the endoscopic appearances may be normal in up to 25% of EoE patients and 30% of LyE patients supports the recommendation for biopsy acquisition in all patients with dysphagia and/or food bolus impaction.

Conclusion

Esophageal biopsies from the distal, middle and proximal esophagus with assessment of both eosinophils and lymphocytes should be obtained during endoscopy for any patient with a history of dysphagia or food bolus impaction. Endoscopists should probably focus their biopsies towards areas of exudates and furrows, as these areas are likely to represent increased eosinophil infiltrate. NBI–ME may be helpful to identify the site of inflammation and allows targeted biopsies in both EoE and LyE. Additionally, the samples from duodenum and stomach should also be obtained to exclude other causes of eosinophilic and/or lymphocytic infiltration such as eosinophilic gastritis or gastroenteritis, Crohn's or celiac disease.

Financial support

Author was supported by the Stockholm County Council (clinical post doctoral appointment).

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