

# Proton Pump Inhibitor-Induced Remission of Lymphocytic Esophagitis

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## ABSTRACT

Lymphocytic esophagitis is a chronic condition that has been described in the literature; however, there is little information describing its characteristics and treatment. We present a case of lymphocytic esophagitis that was identified following food impaction. Repeat esophagogastroduodenoscopy (EGD) with biopsy showed a marked decrease in lymphocytic infiltration after a 6-week course of twice-daily high-dose proton pump inhibitor (PPI). After initiation of the high-dose PPI regimen, the patient had no further episodes of dysphagia or food impaction. We propose that treating lymphocytic esophagitis with twice-daily PPI can improve symptoms and show histologic evidence of improvement.

## INTRODUCTION

Lymphocytic esophagitis is a chronic condition that results in intraepithelial lymphocytic infiltration of the esophagus.<sup>1</sup> The diagnosis is made histologically when more than 20 intraepithelial lymphocytes per high-power field are detected in the absence of granulocytic inflammation (neutrophils and eosinophils), after ruling out other clinical entities, most notably reflux esophagitis.<sup>1,2</sup> Presenting symptoms may be similar to those for eosinophilic esophagitis (EoE): dysphagia, food impaction, odynophagia, or heartburn.<sup>3,4</sup> While symptoms are generally similar to that of EoE, there has been a report of esophageal perforation attributed to lymphocytic esophagitis.<sup>5</sup> In one study population, lymphocytic esophagitis was found in 0.1% of patients with esophageal biopsies.<sup>6</sup> Currently, there is a paucity of data regarding the condition and treatment.

## CASE REPORT

A 38-year-old African American male with a history of epilepsy treated with phenytoin presented to the emergency department with a 3-hour history of dysphagia and inability to swallow secretions. The patient stated that he had been eating ribs when he felt as if the food became lodged in his esophagus. A similar episode had occurred approximately 1 year prior, but he was able to regurgitate the food bolus at that time. At baseline, the patient had no dysphagia or odynophagia and had no symptoms of heartburn. The patient underwent an esophagogastroduodenoscopy (EGD) approximately 4 hours after his symptoms began. A large bolus of meat was identified in the proximal esophagus just distal to the upper esophageal sphincter and was removed.

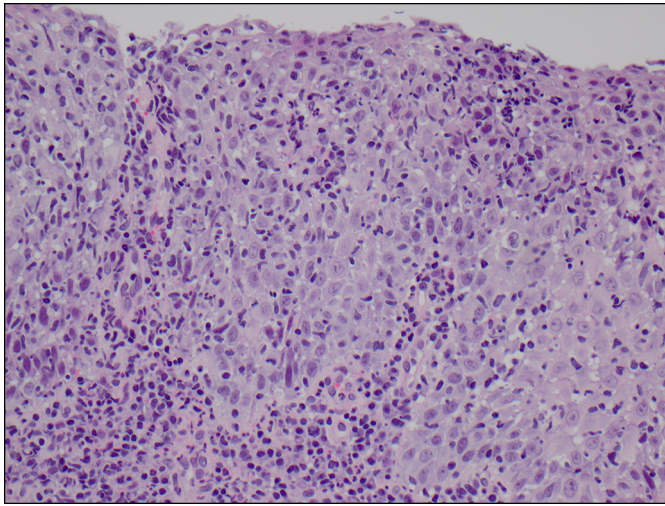
The esophagus was smooth and pink, without furrows, rings, or strictures. There was a small area of irritation at the site where the food impaction had been. Multiple biopsies were obtained in the proximal, mid, and distal esophagus to evaluate for EoE for a total of 7 samples. Following the EGD, the patient had no further dysphagia or odynophagia and was able to tolerate oral liquids without difficulty. He was started on a high-dose proton pump inhibitor

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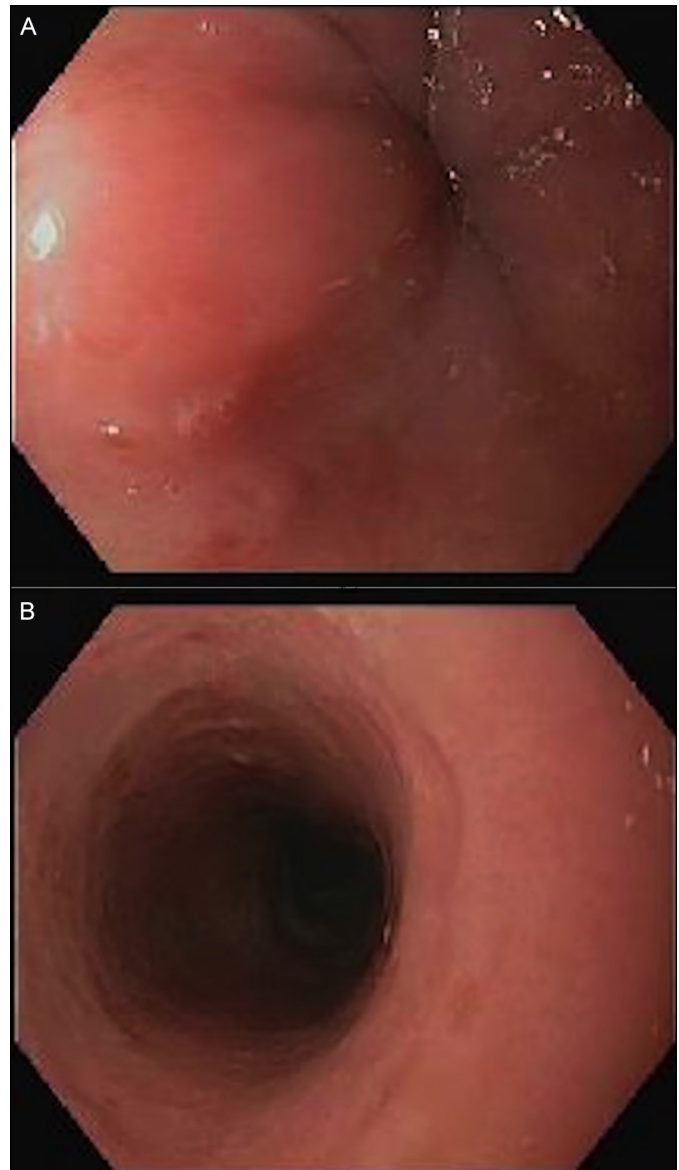
**Figure 1.** Initial biopsy of the esophagus with marked lymphocytic intraepithelial and lamina propria inflammation and reactive squamous epithelium with loss of maturation. Hematoxylin and eosin stain, 400x.

(PPI), pantoprazole (40 mg twice daily) with instructions to take the medication 30-60 minutes before breakfast and dinner.

The esophageal biopsies showed marked esophagitis rich in intraepithelial lymphocytes in all 7 biopsy samples throughout the esophagus (Figure 1). No intraepithelial eosinophils were identified. The lymphocytes were positive for CD3, CD4, CD5, and scattered CD8 by immunohistochemistry, indicating a mixed T-lymphocyte population, consistent with lymphocytic esophagitis. A repeat endoscopy with biopsies of the stomach and duodenum was suggested to evaluate if the lymphocytic infiltration was isolated to the esophagus or if it represented a more diffuse lymphocytosis throughout the gastrointestinal tract.

Prior to his repeat EGD the patient was seen in the gastroenterology clinic to evaluate his symptoms. He stated that he was avoiding meat because of his concern over having another food impaction. A food elimination diet was not explored with the patient as he had symptomatic improvement solely on his PPI regimen.

The patient underwent a repeat EGD with biopsies of the duodenum, stomach, and esophagus approximately 6 weeks after initiating his PPI regimen. At that time, the mucosa again looked normal throughout the extent of the examination (Figure 2). He stated that he had been compliant with his PPI and was also continuing his phenytoin as he had been seizure-free for years. He denied having any symptoms of dysphagia, heartburn, or food impactions. Biopsy results of the repeat EGD showed no lymphocytic infiltration of the duodenum or stomach and showed a markedly decreased lymphocytic

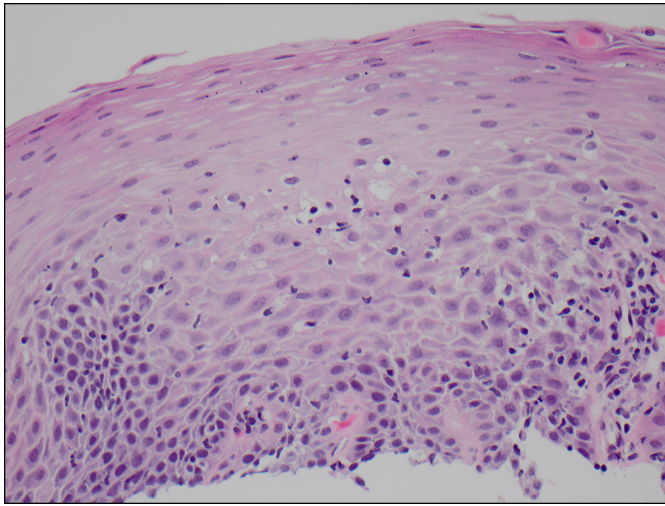


**Figure 2.** (A) Normal appearing mucosa of the gastroesophageal junction. (B) Normal appearing mucosa of the esophagus.

infiltration of the esophagus compared to the prior set of biopsies (Figure 3).

## DISCUSSION

This case of lymphocytic esophagitis following food impaction highlights several important factors. One important finding is that lymphocytic esophagitis can clinically present similar to EoE.<sup>6</sup> Prior studies have shown a significant number of patients with histologic evidence of lymphocytic esophagitis present with dysphagia and have esophageal motility disorders.<sup>3,4</sup> Because of this, it is important to obtain high-quality biopsies to help differentiate the etiology of the esophagitis. Despite differentiating the condition from EoE, the treatment may be similar to PPI-



**Figure 3.** Biopsy after 6 weeks of proton pump inhibitor therapy. Note the marked decrease in lymphocytic inflammation and return of a normal squamous epithelium. Hematoxylin and eosin stain, 400x.

responsive esophageal eosinophilia with high-dose PPI twice daily, although this requires further investigation.<sup>7</sup> Alternatively, in one case report, lymphocytic esophagitis was treated with swallowed fluticasone, which resolved the dysphagia symptoms; however, it is unknown if this resulted in histologic improvement.<sup>8</sup> Other treatment options may include an elimination diet similar to what can be used in EoE.<sup>7</sup> We did not attempt an elimination diet or swallowed fluticasone with our patient due to his response both clinically and histologically to PPI therapy.

On subsequent visits to the office the patient has been symptom-free and has been able to eat meat again without difficulty. It is possible that the patient's lymphocytic esophagitis may be secondary to chronic asymptomatic reflux disease, which might be why the PPI has worked. Alternatively, the PPI may have some pleiotropic effect on the lymphocytic infiltration not previously described.<sup>9</sup> It is possible that the patient's phenytoin caused the esophagitis; however, given the normal appearance of the mucosa it seems less likely to have been pill-induced esophagitis.<sup>10</sup> Additionally, phenytoin is known to cause a drug reaction with eosinophilia and systemic symptoms, which may result in atypical lymphocytosis; however, our patient had none of the systemic findings associated with the condition.<sup>11</sup> Given the patient's response, we intend to continue therapy with PPI twice daily; however, there are no data describing the duration of treatment before attempting to withdraw the PPI. Additionally, there are no data to support repeat EGD off therapy if the patient remains asymptomatic. With that in mind, if the patient does remain asymptomatic, we may consider eventually decreasing the dose

of PPI or discontinuing it entirely. If symptoms return after a dose reduction or discontinuation, it would be a good opportunity to repeat the EGD to evaluate the degree of lymphocytic infiltration. If there is a return of lymphocytic infiltration, this may further strengthen the argument that long-term high-dose PPI therapy can effectively treat these patients. Future studies may be useful in characterizing this condition to develop an evidence-based approach for treatment.

## DISCLOSURES

Author contributions: J. Sloan wrote and edited the manuscript, reviewed the literature, and is the article guarantor. N. Sandhu edited the manuscript and reviewed the literature. R. Miick provided the pathology images and contributed to the manuscript. Y. Govil edited the manuscript and guided the case report.

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Informed consent was obtained for this case report.

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