

## Lichen Planus Is an Uncommon Cause of Nonspecific Proximal Esophageal Inflammation

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**Background/Aims:** Esophageal lichen planus (LP) has been described as a cause of nonspecific esophagitis that may cause dysphagia, but its incidence is unknown. We aimed to estimate the incidence of esophageal LP in a defined geographic region and describe the clinical characteristics of affected patients. **Methods:** A histopathology database for a population of 1 million people was searched for all esophageal mucosal biopsy results over an 8-year period. Cases showing inflammation or abnormalities without a diagnosis after three or more biopsies were reviewed for findings of LP.

**Results:** Of 13,589 esophageal biopsies, only one received a diagnosis of LP. Seven patients (four male; mean age, 59 years; range, 39 to 76 years) were identified as having chronic dysphagia and nonspecific proximal esophagitis for which no diagnosis could be made. All patients had proximal inflammation, and six of seven had full-thickness lymphocytic infiltration. Elongation of the lamina propria papillae was noted in all patients, whereas six patients had parakeratosis and ballooning. Only one patient had findings potentially consistent with, but not sufficient for, a diagnosis of esophageal LP. **Conclusions:** Esophageal LP appears to be extremely uncommon in this North American population, and esophageal biopsy alone is likely not sufficient to establish a diagnosis of LP. (*Gut Liver* 2013;7:401-405)

**Key Words:** Esophagus; Inflammation; Esophagitis; Gastroesophageal reflux disease; Lichen planus

### INTRODUCTION

Esophagitis is defined as inflammation of the esophagus, with gastroesophageal reflux disease (GERD) being the most common cause.<sup>1</sup> A wide variety of other identifiable causes of esophagitis

exists, including eosinophilic, infectious, toxic ingestions, radiation effects, and causes related to mucocutaneous disease. The majority of these causes are typically readily diagnosed on the basis of clinical history, esophageal mucosal biopsy, and response to therapy such as proton pump inhibitors (PPIs). However, a small subgroup of patients exists with chronic esophageal inflammation, often proximal, which is not eosinophilic and which does not heal with acid suppressive therapy. These patients represent a difficult diagnostic and management dilemma.

Esophageal lichen planus (LP) has been recently postulated as a cause for chronic proximal esophagitis that can give a wide variety of presentations and may occur without LP involvement elsewhere in the body.<sup>2-4</sup> LP, a mucocutaneous disease of unknown etiology, most often presents in middle-aged adults as a well-defined, pruritic, papular rash. A recent study, however, found that the esophagus was the presenting site for LP in 48% of patients without cutaneous disease.<sup>2</sup> The various presentations of esophageal LP include proximal esophageal stricture formation, mucosal sloughing and/or ulceration, and plaques, among others.<sup>2</sup> A high number of patients with esophageal LP also present with esophagitis consistent with GERD.<sup>2</sup> On histological examination, esophageal LP presents with Civatte bodies and a lymphohistiocytic interface inflammatory infiltrate.<sup>3</sup> However, these findings on their own are nonspecific, and are not sufficient for a diagnosis of LP without corroborating histology from another site such as the skin or oral mucosa. Most larger series of patients with esophageal LP were identified through endoscopy in patients with established diagnoses of LP elsewhere.<sup>2,3</sup>

Other groups have used the term chronic esophagitis disseicans (CED) to describe a form of chronic esophagitis that presents with unique endoscopic and histologic features, including

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Received on August 9, 2012. Accepted on October 5, 2012. Published online on June 11, 2013.

pISSN 1976-2283 eISSN 2005-1212 <http://dx.doi.org/10.5009/gnl.2013.7.4.401>

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chronic dysphagia without reflux, mucosal shedding, localized esophageal strictures, and a lack of concurrent chronic cutaneous-mucous lesions.<sup>5</sup> Although similar in presentation to esophageal LP, one study differentiated this condition by its lack of concomitant chronic cutaneous or oral lesions, esophageal lesions lacking papular elements, and significant inflammatory infiltrates not being seen on histology.<sup>5</sup> This condition has only been reported in a limited number of case reports and case series. It has been seen in both males and females, most often over the age of 60.

Since patients with chronic esophagitis of unknown etiology pose a diagnostic dilemma, and based on a small number of such cases in the clinical practices of the investigators, it was clear that these patients undergo repeated testing with endoscopy and biopsy. Our experience also suggested that these patients typically do not have a pre-existing diagnosis of LP or any other obvious cause for their presentation, and that their esophageal symptoms, especially dysphagia, are their primary concern. We therefore aimed to identify other potential cases in a large, population-based database, and review their clinical and histological presentations.

## MATERIALS AND METHODS

### 1. Patient population

The Calgary Zone of Alberta Health Services (AHS) covers the urban city of Calgary, Alberta, Canada, and the surrounding rural areas, with a population of 1.25 million in 2008. The ethnic makeup of the region includes approximately 80% Caucasian and 15% Asian ethnicities.<sup>6</sup> All levels of medical and surgical care are provided to residents of the city of Calgary and the nearby small towns and villages. The AHS is the sole provider of upper endoscopy and pathology services in this population.

### 2. Histopathology database

Calgary Laboratory Services (CLS) is the exclusive provider of histopathologic specimen processing and pathological diagnosis in the Calgary Zone of the AHS. All esophageal biopsies taken in the Zone are processed by this provider, regardless of the location of the endoscopic procedure. All histopathology diagnoses are entered into a centralized searchable database that allows corroboration of patient, endoscopist, and pathologist data in addition to diagnosis.

### 3. Search strategy

Consecutive esophageal biopsies taken from January 1, 2001 to December 31, 2008 were identified using the search terms "esophageal" and "esophagus" in the CLS database. Esophageal biopsies reported on surgical specimens were identified and excluded from the analysis. Results were filtered to remove duplicate entries (PASW Statistics software version 18; IBM Co., Armonk, NY, USA).

Initial searching of the database revealed no suggestion of LP or lichenoid features in any of the biopsy results. Additionally, since the patient group of chronic esophagitis of unknown etiology would have no conclusive histopathologic features by definition, we were unable to identify them using specific keywords in the search strategy. Cases were therefore selected for further review if they matched the following criteria: 1) three or more distinct esophageal mucosal biopsies on different dates, 2) repeated biopsies were not for Barrett's esophagus screening or surveillance, and 3) presence of esophagitis or inflammation on at least one biopsy, with none of the biopsies showing cancer, reflux or eosinophilic esophagitis (EoE), postsurgical changes, or biopsies from the gastroesophageal junction only. If the inflammation was present in the distal esophagus only it was presumed to be due to acid reflux. Patients with esophageal infection as the primary cause for their symptoms were also excluded. All esophageal biopsies were then matched to their respective endoscopy information in a separate endoscopy database and their clinic charts and histology were reviewed.

Ethics approval was obtained from the Institutional Review Board of the University of Calgary prior to commencement of this study.

## RESULTS

From 2001 to 2008 there were 13,589 esophageal mucosal biopsies taken in 10,810 unique patients. During the study period, 273 patients had three or more distinct biopsies which were not for Barrett's surveillance. Review of the biopsy reports of these patients revealed a clear or probable cause for the findings in the vast majority, leaving only seven patients with chronic esophagitis of unknown etiology.

Summary of patient characteristics are listed in Table 1. There were four males and three females, with a universal presentation of dysphagia of at least 1 year duration. None had a history of caustic ingestion in the past nor any mucocutaneous disease based on chart review. Patients had a median of four endoscopies (range, three to seven endoscopies), with all patients having an endoscopy in 2005 or later. Endoscopically-visible inflammation was seen in all cases, with proximal stricturing or rings visible in the majority (Table 2). Esophageal manometry was performed in only one patient and the results were normal. Three patients were smokers. All had tried acid inhibition with PPIs. Two had been treated with topical fluticasone similar to published therapies for EoE, and two had required esophageal dilation.<sup>7</sup>

Review of biopsy reports suggested nonspecific lymphocytic inflammation of variable severity found throughout the esophagus in all patients. On repeat histological review, there were no obvious unifying features that would establish a definitive diagnosis in any of the patients, and no previous diagnosis was subsequently revised. All, however, did have elongation of the

**Table 1.** Summary of Patient Characteristics (n=7)

Characteristic	Value
Male gender	4 (57)
Age, mean (range), yr	59 (39-76)
Presenting complaint	
Dysphagia	7 (100)
Odynophagia	4 (57)
No. of gastroscopies during study period, median (range)	4 (3-7)
Endoscopic findings	
Inflammation	7 (100)
Stricture	5 (71)
Rings	4 (57)
Nodularity	3 (43)
Ulceration	3 (43)
Friable/sloughing mucosa	1 (14)
Smoker	
Yes	3 (43)
No	2 (29)
Undocumented	2 (29)
Treatments tried	
Proton pump inhibitor	7 (100)
Dilation	3 (43)
Fluticasone, swallowed	2 (29)
Sucralfate	2 (29)
5-HT4 receptor agonist	1 (14)

Data are presented as number (%).

lamina propria papillae and six of the seven patients had full-thickness lymphocytic infiltration, parakeratosis, and squamous epithelial cell ballooning in the proximal esophagus (Table 3). Civatte bodies, which have been implicated in esophageal LP, were only seen in one patient.

**DISCUSSION**

This study evaluated a small group of patients with chronic proximal esophagitis of unknown etiology. Based on our search strategy in a population-based database, it appears that this situation is fortunately uncommon. Due to the ubiquity and power of PPIs to treat reflux esophagitis, it is not felt that acid reflux played a significant role in any of the patients studied here. Similarly, with EoE being increasingly recognized with standardized criteria, this group of patients can now be easily identified.<sup>7</sup> Although EoE was not widely recognized at the early part of the study period, repeat review did not show any evidence or suspicion of this diagnosis. Nonsteroidal anti-inflammatory treatment and other medications similarly can cause pill esophagitis, but this typically occurs at sites of obstruction and no patients had a suspicion of this based on endoscopic or clini-

**Table 2.** Case Data

Patient	Age	Sex	Main symptom	Duration of symptoms, yr	Smoker	Endoscopic findings	Histological findings	Treatment	Treatment success
1	46	M	D	1	Yes	I, Str, ER	Lichenoid reaction	PPI, dilation	Yes
2	61	F	D, O	2	Yes	I, Str, SI, U	Mixed inflammatory infiltrate (eosinophils, neutrophils, lymphocytes) in lamina propria, fungal hyphae, acute and chronic nonspecific inflammation	PPI, oral fluticasone, sulphate suspension	Partial
3	71	F	D, O	>1	No	I, U, Str, N, HH	Mixed inflammatory infiltrate (neutrophils, eosinophils, lymphocytes)	PPI, domperidone	Mild improvement
4	39	M	D	>1	No	I, SR, N, EF, CE, HH	Nonspecific inflammation, intraepithelial lymphocytes, neutrophils	PPI, dilation, oral fluticasone	Yes
5	58	M	D, O	>1	No	I, U, P	Granulation tissue, mucosal ulceration, few eosinophils	PPI, oral fluconazole	?
6	76	M	D, O	>1	No	I, Str, SR, HH, N, ER	Neutrophilic and lymphocytic infiltration of squamous mucosa, superficial microabscesses, acute, and chronic inflammatory cells in submucosa	PPI, 5-HT4 receptor agonist, sulphate suspension, cholestyramine	No
7	61	F	D	3	Yes	I, Str, ER	Mixed inflammatory infiltrate (lymphocytes, neutrophils)	PPI, dilation	?

M, male; I, inflammation; D, dysphagia; Str, stricture; ER, esophageal ring; PPI, proton pump inhibitor; F, female; O, odynophagia; SI, sloughing; U, ulceration; N, nodules; HH, hiatal hernia; SR, Schatzki's ring; EF, esophageal fold; CE, corrugated esophagus; P, plaques.

**Table 3.** Proximal Esophageal Biopsy Results

Finding	No. (%)
Elongation of lamina propria papillae	7 (100)
Parakeratosis	6 (86)
Ballooning of squamous epithelial cells	6 (86)
Lymphocyte infiltration	
Full thickness	6 (86)
Basal prominent	2 (29)
Basal cell hyperplasia	4 (57)
Dilated intracellular spaces	3 (43)
Neutrophil infiltration	3 (43)
Civatte bodies	1 (14)

cal history.

LP is an inflammatory disease diagnosed by the presence of cutaneous shiny, violaceous, flat-topped polygonal papules which retain the skin lines.<sup>8</sup> However, these findings are not expected in the squamous mucosa of the esophagus, where it is typically characterized by a range of subtle findings, including strictures of the proximal esophagus, friable mucosa, papular lesions, and erosive changes to both the proximal and distal esophagus.<sup>9,10</sup> Previous studies of esophageal LP were based on patients with established LP at other body sites, who were then investigated for esophageal involvement. Since the esophageal findings are nonspecific and generally not pathognomonic, the diagnosis rests on an LP diagnosis elsewhere. Only one patient in this group (patient 1) had findings that could clearly be consistent with esophageal LP. This suggests that as a group there may be a variety of causes for this presentation.

Cutaneous LP is routinely treated with steroids, either systemic, topical, or injected, as well as with a variety of other potential alternatives such as retinoids and phototherapy. Many similar therapeutic options are also available for esophageal LP, including systemic corticosteroids, retinoids, cyclosporine, and azathioprine.<sup>11</sup> Since established treatment for LP is available, we suggest referral for a dermatological evaluation in such patients when high suspicion exists.

Several of the histological findings noted in these patients can be found in cases of GERD, including basal cell hyperplasia, papilla elongation, inflammatory cell infiltrates, and dilated intracellular spaces.<sup>12</sup> Five of the seven patients had no history of reflux and were not symptomatic of reflux at the time of their presentation. Although all patients were given trials of PPIs, minimal improvement was seen with these medications. The proximal nature of our findings also leads us away from a diagnosis of reflux esophagitis, as many of the typical histology findings for GERD are often found near the squamocolumnar junction.<sup>12</sup>

These patients were unified by their clinical presentation of

dysphagia due to presumed inflammatory causes, and which was unresponsive to treatment. A number of histological abnormalities in common were seen, but none of which are sufficient to establish a known diagnosis. A diagnosis of CED was considered, but these patients did not satisfy the diagnostic criteria which includes shedding of mucosal fragments and histologic evidence of mucosal blistering in the absence of significant inflammatory lesions.<sup>5</sup> Ingestion of a toxic material such as cigarette smoke was also considered due to the proximal nature of the inflammation. However, this could not be ascertained from a retrospective chart review as only three of the seven patients were confirmed to be smokers and no other ingestions were documented.

The seven patients reviewed could not be placed into a known diagnostic grouping based on their clinical and histologic findings. Furthermore, due to the diagnostic uncertainty in establishing a diagnosis of LP based on esophageal biopsy alone, a reliable incidence estimate could not be calculated. Given the size of the population, it is likely that the presumed incidence would be very low. For patients with a finding of chronic nonspecific proximal esophagitis, we suggest that management strategies would include a trial of high-dose PPIs, a referral to dermatology for LP, then topical steroid and/or dilation therapy similar to that recommended for EoE.<sup>7</sup>

This study has several limitations. Firstly, as it is a retrospective chart review, data collection was limited to information documented in the patient charts. Variation existed in the thoroughness of patient information available, including areas such as response to therapy and smoking history. Information from all available sources was used to ensure completeness. Secondly, multiple pathologists were initially involved in reviewing biopsies as they were retrieved over several years. To minimize variability in reporting of the histology, a single gastrointestinal pathologist reanalyzed all seven retrieved biopsies as part of this study. Thirdly, again due to the retrospective nature, many endoscopists were involved which may have lead to variable reporting of endoscopic findings. However, the investigators reviewed all available image documentation to confirm described mucosal abnormalities.

In summary, this case series presents a number of patients with chronic proximal esophagitis for which no clear diagnosis can be made. The majority of these cases had findings not suggestive of esophageal LP. Further studies of this uncommon clinical scenario are needed to determine effective treatments and standard approaches to disease management.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

## REFERENCES

1. Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet* 2006;367:2086-2100.
2. Katzka DA, Smyrk TC, Bruce AJ, Romero Y, Alexander JA, Murray JA. Variations in presentations of esophageal involvement in lichen planus. *Clin Gastroenterol Hepatol* 2010;8:777-782.
3. Quispel R, van Boxel OS, Schipper ME, et al. High prevalence of esophageal involvement in lichen planus: a study using magnification chromoendoscopy. *Endoscopy* 2009;41:187-193.
4. Storr M, Gao ZH, Hershfield N. Nonprogressive, long-term dysphagia in a patient with esophageal lichen planus. *Clin Gastroenterol Hepatol* 2009;7:A24.
5. Ponsot P, Molas G, Scoazec JY, Ruzniewski P, Hénin D, Bernades P. Chronic esophagitis dissecans: an unrecognized clinicopathologic entity? *Gastrointest Endosc* 1997;45:38-45.
6. Statistics Canada. 2006 Community Profiles [Internet]. Ottawa: Statistics Canada; 2011 [cited 2011 Jun 20]. Available from: <http://www12.statcan.gc.ca/census-recensement/2006/dp-pd/prof/92-591/index.cfm?Lang=E>.
7. Gonzalez-Castillo S, Arias A, Lucendo AJ. Treatment of eosinophilic esophagitis: how should we manage the disease? *J Clin Gastroenterol* 2010;44:663-671.
8. Mohammed AR, Sherwood P. Oesophageal lichen planus: a missed diagnosis. *J R Soc Med* 2006;99:318-320.
9. Dickens CM, Heseltine D, Walton S, Bennett JR. The oesophagus in lichen planus: an endoscopic study. *BMJ* 1990;300:84.
10. Westbrook R, Riley S. Esophageal lichen planus: case report and literature review. *Dysphagia* 2008;23:331-334.
11. Chandan VS, Murray JA, Abraham SC. Esophageal lichen planus. *Arch Pathol Lab Med* 2008;132:1026-1029.
12. Allende DS, Yerian LM. Diagnosing gastroesophageal reflux disease: the pathologist's perspective. *Adv Anat Pathol* 2009;16:161-165.