Severe Esophageal Lichen Planus Treated With Tofacitinib

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PRACTICE **POINTS**

- Patients diagnosed with lichen planus should be informed about the signs of esophageal lichen planus (ELP).
- Twenty-five percent to 50% of patients with oral lichen planus (OLP) have been shown to have concomitant ELP.
- Esophageal lichen planus may be asymptomatic and often is misdiagnosed.
- Tofacitinib should be considered for the treatment of ELP, OLP, and cutaneous lichen planus.

Lichen planus is a chronic inflammatory immune disorder that most commonly affects the skin and mucous membranes. Esophageal lichen planus (ELP) is a frequently misdiagnosed and poorly understood form of lichen planus that can be asymptomatic or present with dysphagia and odynophagia caused by the formation of erosions and strictures in the esophagus. These strictures often reduce a patient's quality of life and may lead to emaciation in more severe cases. We present the case of an 89-year-old woman with a history of cutaneous lichen planus (CLP) and mucosal lichen planus that were successfully managed with topical corticosteroids and oral cyclosporine rinses who presented with an esophageal stricture and erosions that were treated unsuccessfully with surgery. Our patient's condition continued to worsen until she presented in an emaciated state and was treated with tofacitinib, which resulted in complete resolution of oral lichen planus (OLP), ELP, and genital lichen planus.
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To reach early diagnoses and improve outcomes in cases of mucosal and esophageal lichen planus (ELP), patient education along with a multidisciplinary approach centered on collaboration among dermatologists, gastroenterologists, gynecologists, and dental practitioners should be a priority. Tofacitinib therapy should be considered in the treatment of patients presenting with cutaneous lichen planus (CLP), mucosal lichen planus, and ELP.

Lichen planus is a papulosquamous disease of the skin and mucous membranes that is most common on the skin and oral mucosa. Typical lesions of CLP present as purple, pruritic, polygonal papules and plaques on the flexural surfaces of the wrists and ankles as well as areas of friction or trauma due to scratching such as the shins and lower back. Various subtypes of lichen planus can present simultaneously, resulting in extensive involvement that worsens through koebnerization and affects the oral cavity, esophagus, larynx, sclera, genitalia, scalp, and nails.[1,2]

Esophageal lichen planus can develop with or without the presence of CLP, oral lichen planus (OLP), or genital lichen planus.[3] It typically affects women older than 50 years and is linked to OLP and vulvar lichen planus, with 1 study reporting that 87% (63/72) of ELP patients were women with a median age of 61.9 years at the time of diagnosis (range, 22–85 years). Almost all ELP patients in the study had lichen planus symptoms in other locations; 89% (64/72) had OLP, and 42% (30/72) had vulvar lichen planus.[4] Consequently, a diagnosis of ELP should be followed by a thorough full-body examination to check for lichen planus at other sites. Studies that examined lichen planus patients for ELP found that 25% to 50% of patients diagnosed with orocutaneous lichen planus also had ELP, with ELP frequently presenting without symptoms.[3,5] These findings indicate that ELP likely is underdiagnosed and often misdiagnosed, resulting in an underestimation of its prevalence.

Our case highlights a frequently misdiagnosed condition and underscores the importance of close examination of patients presenting with CLP and OLP for signs and symptoms of ELP. Furthermore, we discuss the importance of patient education and collaboration among

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The eTable is available in the Appendix online at www.mdedge.com/dermatology.
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different specialties in attaining an early diagnosis to improve patient outcomes. Finally, we review the clinical presentation, diagnosis, and treatment of CLP, OLP, and ELP, as well as the utility of tofacitinib for ELP.

Case Report

An emaciated 89-year-old woman with an 11-year history of CLP, OLP, and genital lichen planus that had been successfully treated with topicals presented with an OLP recurrence alongside difficulties eating and swallowing. Her symptoms lasted 1 year and would recur when treatment was paused. Her medical history included rheumatoid arthritis, hypothyroidism, and hypertension, and she was taking levothyroxine, olmesartan, and vitamin D supplements. Dentures and olmesartan previously were ruled out as potential triggers following a 2-month elimination. None of her remaining natural teeth had fillings. She also reported that neither she nor her partner had ever smoked or chewed tobacco.

The patient's lichen planus involvement first manifested as red, itchy, polygonal, lichenoid papules on the superior and inferior mid back 11 years prior to the current presentation (Figure 1). Further examination noted erosions on the genitalia, and a subsequent biopsy of the vulva confirmed a diagnosis of lichen planus (Figure 2). Treatment with halobetasol propionate ointment and tacrolimus ointment 0.1% twice daily (BID) resulted in remission of the CLP and vulvar lichen planus. She presented a year later with oral involvement revealing Wickham striae on the buccal mucosa and erosions on the upper palate that resolved after 2 months of treatment with cyclosporine oral solution mixed with a 5-times-daily nystatin swish-and-spit (Figure 3). The CLP did not recur but OLP was punctuated by remissions and recurrences on a yearly basis, often related to the cessation of mouthwash and topical creams. The OLP and vulvar lichen planus were successfully treated with as-needed use of a cyclosporine mouthwash swish-and-spit 3 times daily as well as halobetasol ointment 0.05% 3 times daily, respectively. Six years later, the patient was hospitalized for unrelated causes and was lost to follow-up for 2 years.

The patient experienced worsening dysphagia and odynophagia over a period of 2 years (mild dysphagia was first recorded 7 years prior to the initial presentation) and reported an unintentional weight loss of 20 pounds. An endoscopy was performed 3 years after the initial report of dysphagia and noted esophageal erosions (Figure 4A) and a stricture (Figure 4B), but all abnormal involvement was attributed to active gastroesophageal reflux disease. She underwent 8 esophageal dilations to treat the stricture but noted that the duration of symptomatic relief decreased with every subsequent dilation. An esophageal stent was placed 4 years after the initial concern of dysphagia, but it was not well tolerated and had to be removed soon thereafter. A year later, the patient underwent an esophageal bypass with a substernal gastric conduit that provided relief for 2 months but failed to permanently resolve the condition. In fact, her condition worsened over the next 1.5 years when she presented with extreme emaciation attributed to a low appetite and pain while eating. A review of the slides from a prior hospital esophageal biopsy revealed lichen planus (Figure 5). She

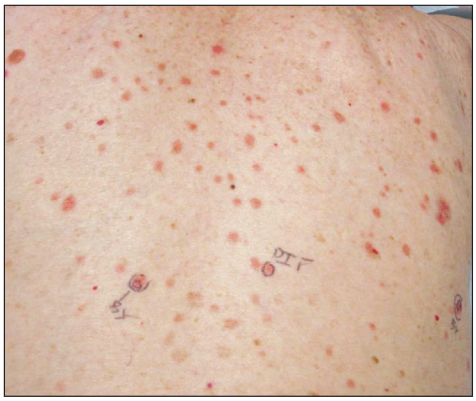

FIGURE 1. Bright and dusky, erythematous, flat-topped papules and plaques of lichen planus located on the superior and inferior mid back.

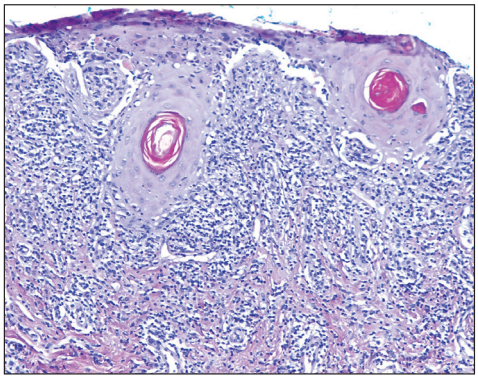

FIGURE 2. Histopathology of a vulvar lesion revealed a bandlike infiltrate of mononuclear cells that "hugged" the overlying epidermis, a feature diagnostic of lichen planus (H&E, original magnification ×10).

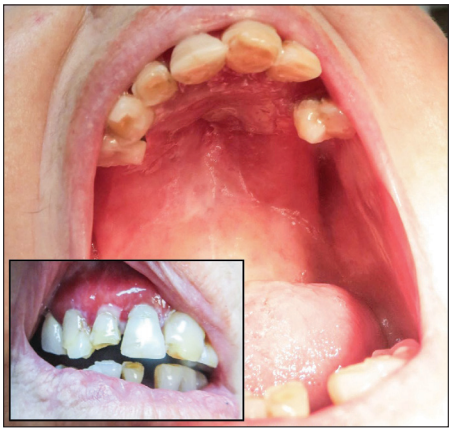

FIGURE 3. Oral involvement of lichen planus progressed to involve skin sloughing with resultant superficial erosions on the hard palate. Wickham striae were present on the left buccal mucosa and right superior gingivae (insert).

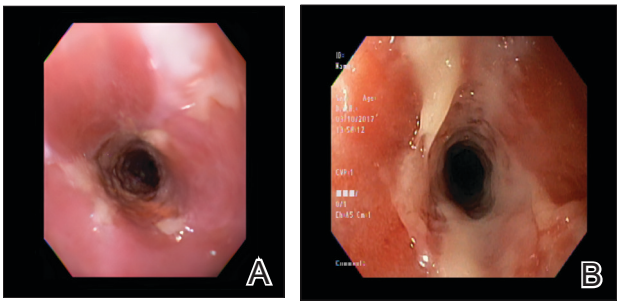

FIGURE 4. A, An endoscopy revealed esophageal erosions in the medial esophagus. B, A refractory esophageal stricture was noted in the medial esophagus.

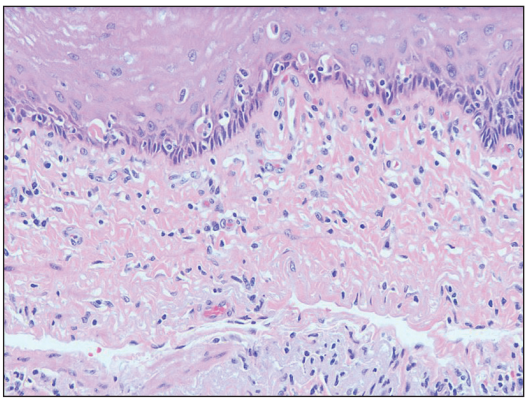

FIGURE 5. An esophageal biopsy revealed necrotic keratinocytes in the lower epithelium and a mononuclear infiltrate, features diagnostic of esophageal lichen planus (H&E, original magnification ×20).

was prescribed tofacitinib 5 mg BID as a dual-purpose treatment for the rheumatoid arthritis and OLP/ELP. At 1-month follow-up she noted that she had only taken one 5-mg pill daily without notable improvement, and after the visit she started the initial recommendation of 5 mg BID. Over the next several months, her condition continued to consistently improve; the odynophagia resolved, and she regained the majority of her lost weight. Tofacitinib was well tolerated across the course of treatment, and no adverse side effects were noted. Furthermore, the patient regained a full range of motion in the previously immobile arthritic right shoulder. She has experienced no recurrence of the genital lichen planus, OLP, or CLP since starting tofacitinib. To date, the patient is still taking only tofacitinib 5 mg BID with no recurrence of the cutaneous, mucosal, or esophageal lichen planus and has experienced no adverse events from the medication.

Comment

Clinical Presentation—Lichen planus—CLP and OLP—most frequently presents between the ages of 40 and 60 years, with a slight female predilection.[1,2] The lesions typically present with the 5 *P*'s—purple, pruritic, polygonal papules and plaques—with some lesions revealing white lacy lines overlying them called Wickham striae.[6] The lesions may be red at first before turning purple. They often present on the flexural surfaces of the wrists and ankles as well as the shins and back but rarely affect the face, perhaps because of increased chronic sun exposure.[2,6] Less common locations include the scalp, nails, and mucosal areas (eg, oral, vulvar, conjunctival, laryngeal, esophageal, anal).[1]

If CLP is diagnosed, the patient likely will also have oral lesions, which occur in 50% of patients.[2] Once any form of lichen planus is found, it is important to examine all of the most frequently involved locations—mucocutaneous and cutaneous as well as the nails and scalp. Special care should be taken when examining OLP and genital lichen planus, as long-standing lesions have a 2% to 5% chance of transforming into squamous cell carcinoma.[2]

Although cases of traditional OLP and CLP are ubiquitous in the literature, ELP rarely is documented because of frequent misdiagnoses. Esophageal lichen planus has a closer histopathologic resemblance to OLP compared to CLP, and its highly variable presentation often results in an inconclusive diagnosis.[3] A review of 27 patients with lichen planus highlighted the difficult nature of diagnosing ELP; ELP manifested up to 20 years after initial lichen planus diagnosis, and patients underwent an average of 2.5 dilations prior to the successful diagnosis of ELP. Interestingly, 2 patients in the study presented with ELP in isolation, which emphasizes the importance of secondary examination for lichen planus in the presence of esophageal strictures.[7] The eTable provides common patient demographics and symptoms to more effectively identify ELP.

Differential Diagnosis—Because lichen planus can present anywhere on the body, it may be difficult to differentiate it from other skin conditions. Clinical appearance alone often is insufficient for diagnosing lichen planus, and a punch biopsy often is needed.[2,20] Cutaneous lichen planus may resemble eczema, lichen simplex chronicus, pityriasis rosea, prurigo nodularis, and psoriasis, while OLP may resemble bite trauma, leukoplakia, pemphigus, and thrush.[20] Dermoscopy of the tissue makes Wickham striae easier to visualize and assists in the diagnosis of lichen planus. Furthermore, thickening of the stratum granulosum, a prevalence of lymphocytes in the dermoepidermal junction, and vacuolar alteration of the stratum basale help to distinguish between lichen planus and other inflammatory dermatoses.[20] A diagnosis of lichen planus merits a full-body skin examination—hair, nails, eyes, oral mucosa, and genitalia—to rule out additional involvement.

Esophageal lichen planus most frequently presents as dysphagia, odynophagia, and weight loss, but other symptoms including heartburn, hoarseness, choking, and epigastric pain may suggest esophageal involvement.[4] Typically, ELP presents in the proximal and/or central esophagus, assisting in the differentiation between ELP and other esophageal conditions.[3] Special consideration should be taken when both ELP and gastroesophageal

reflux disease are considered in a differential diagnosis, and it is recommended to pair an upper endoscopy with pH monitoring to avoid misdiagnosis.[8] Screening endoscopies also are helpful, as they assist in identifying the characteristic white webs, skin peeling, skin surface erosion, and strictures of ELP.[4] Taken together, dermatologists should encourage patients with cutaneous or mucocutaneous lichen planus to undergo an esophagogastroduodenoscopy, especially in the presence of any of ELP's common symptoms (eTable).

Etiology—Although the exact etiology of lichen planus is not well established, there are several known correlative factors, including hepatitis C; increased stress; dental materials; oral medications, most frequently antihypertensives and nonsteroidal anti-inflammatory drugs; systemic diseases; and tobacco usage.[6,21]

Dental materials used in oral treatments such as silver amalgam, gold, cobalt, palladium, chromium, epoxy resins, and dentures can trigger or exacerbate OLP, and patch testing of a patient's dental materials can help determine if the reaction was caused by the materials.[6,22] The removal of material contributing to lesions often will cause OLP to resolve.[22]

It also has been suggested that the presence of thyroid disorders, autoimmune disease, various cancers, hypertension, type 2 diabetes mellitus, hyperlipidemia, oral sedative usage, and/or vitamin D deficiency may be associated with OLP.[21,23] Although OLP patients who were initially deficient in vitamin D demonstrated marked improvement with supplementation, it is unlikely that vitamin D supplements impacted our patient's presentation of OLP, as she had been consistently taking them for more than 5 years with no change in OLP presentation.[24]

Pathogenesis—Lichen planus is thought to be a cytotoxic $CD8^+$ T cell–mediated autoimmune disease to a virally modified epidermal self-antigen on keratinocytes. The cytotoxic T cells target the modified self-antigens on basal keratinocytes and induce apoptosis.[25] The cytokine-mediated lymphocyte homing mechanism is human leukocyte antigen dependent and involves tumor necrosis factor α as well as IFN-γ and IL-1. The latter cytokines lead to upregulation of vascular adhesion molecules on endothelial vessels of subepithelial vascular plexus as well as a cascade of nonspecific mechanisms such as mast cell degranulation and matrix metalloproteinase activation, resulting in increased basement membrane disruption.[6]

Shao et al[19] underscored the role of IFN-γ in $CD8^+$ T cell–mediated cytotoxic cellular responses, noting that the Janus kinase (JAK)–signal transducer and activator of transcription pathway may play a key role in the pathogenesis of lichen planus. They proposed using JAK inhibitors for the treatment of lichen planus, specifically tofacitinib, a JAK1/JAK3 inhibitor, and baricitinib, a JAK1/JAK2 inhibitor, as top therapeutic agents for lichen planus (eTable).[19] Tofacitinib has been reported to successfully treat conditions such as psoriasis, psoriatic arthritis, alopecia areata, vitiligo, atopic dermatitis, sarcoidosis, pyoderma gangrenosum, and lichen planopilaris.[26] Additionally, the efficacy of tofacitinib has been established in patients with erosive lichen planus; tofacitinib resulted in marked improvement while prednisone, acitretin, methotrexate, mycophenolate mofetil, and cyclosporine treatment failed.[27] Although more studies on tofacitinib's long-term efficacy, cost, and safety are necessary, tofacitinib may soon play an integral role in the battle against inflammatory dermatoses.

Conclusion

Esophageal lichen planus is an underreported form of lichen planus that often is misdiagnosed. It frequently causes dysphagia and odynophagia, resulting in a major decrease in a patient's quality of life. We present the case of an 89-year-old woman who underwent procedures to dilate her esophagus that worsened her condition. We emphasize the importance of considering ELP in the differential diagnosis of patients presenting with lichen planus in another region. In our patient, tofacitinib 5 mg BID resolved her condition without any adverse effects.

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APPENDIX

eTABLE. Guidelines for the Diagnosis and Treatment of ELP

Category	Finding in patients with ELP
Patient demographics	Age range, 22–85 y; median age, 61.9 y; female to male ratio, 9:1[4]
Symptoms	Common: dysphagia, odynophagia, weight loss; uncommon: heartburn, hoarseness, choking, epigastric pain[4]
Differential diagnosis	Functional disorders (gastroesophageal reflux disease)[8]; inflammatory disorders (eosinophilic esophagitis)[4]; iatrogenic disease (pill esophagitis, radiation induced)[4,9]; fungal infections (esophageal candidiasis)[4]; viral infections (Epstein-Barr virus, herpes simplex virus, cytomegalovirus, HHV-8 [Kaposi sarcoma])[4,10,11]; parasitic infection (Chagas disease)[4]; autoimmune disease (Crohn disease, Behçet disease, pemphigus vulgaris, graft-vs-host disease)[4,12-16]; cancers and mutations (squamous cell carcinoma, palmoplantar keratoderma [Howel-Evans syndrome])[2,17,18]
Presence of other LP area involvement	89% of patients with ELP have OLP involvement; 42% have vulvar LP involvement; 38% have cutaneous LP involvement[4,5]
Treatments	Systemic corticosteroids, systemic retinoids, cyclosporine, mycophenolate mofetil,[3,19] tofacitinib[a]
Recommendations	Refer to gastroenterologist for esophagogastroduodenoscopy
Findings on endoscopy	White webs, skin peeling, skin surface erosion, strictures[4]; most often present in the proximal and/or central esophagus[3]

Abbreviations: ELP, esophageal lichen planus; HHV-8, human herpesvirus 8; LP, lichen planus; OLP, oral lichen planus.

[a]Current report documents a case of ELP successfully treated with tofacitinib.