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CASE REPORT | ESOPHAGUS

Budesonide Orodispersible Tablet for the Treatment of Refractory Esophageal Lichen Planus

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ABSTRACT

Esophageal lichen planus is an uncommon but highly morbid condition where effective treatments are limited. Diagnosis may be challenging and requires a high degree of clinical suspicion considering endoscopic, histopathological, esophageal, and extra-esophageal manifestations. We describe a severe case of esophageal lichen planus and recurrent esophageal stricture that was refractory to acid suppression, local and systemic steroid formulations, and dilatation. We present the first reported use of budesonide orodispersible tablet for this condition, including the excellent clinical, endoscopic, and histopathological response.

KEYWORDS: esophageal lichen planus; lichen planus; lichenoid esophagitis; budesonide; civatte bodies

INTRODUCTION

Diagnosis of esophageal lichen planus (LP) requires a high index of suspicion. It requires the consideration of esophageal symptoms, compatible but sometimes nonspecific histology, endoscopic findings, and the presence of extraesophageal manifestations of LP. It is an uncommon but highly morbid condition where effective treatments are limited.[1] We present a patient successfully treated with a novel therapy after having failed traditional therapy in an understudied disease process without robust guidelines.

CASE REPORT

A 61-year-old White woman presented to our swallowing clinic complaining of worsening solid food dysphagia, localized to the upper retrosternal region over the course of several years. The medical history was significant for multiple immune diagnoses with no unifying cause, including seronegative rheumatoid arthritis, giant cell arteritis, mild psoriasis, and bronchiectasis. Regular medications included low-dose methotrexate 7.5 mg weekly, prednisolone 10 mg daily, tocilizumab 162 mcg weekly subcutaneously, and rabeprazole 20 mg daily (the latter without relief of her symptoms). She had developed iatrogenic immunodeficiency secondary to immunosuppressive drugs and was receiving intravenous immunoglobulin regularly. Her infective screen had been negative, including hepatitis and HIV.

With regards to her swallowing, she described solid food dysphagia localized to the upper retrosternal region and was presently only able to tolerate a semisolid diet. She was having to chew very carefully and took up to an hour to finish a meal. She also complained of burning pain in the mouth, throat, and esophagus during swallowing. She had been able to maintain a stable weight for some time. There had been no prolonged food bolus impactions. There was no regurgitation, and she denied any typical heartburn.

Endoscopic evaluation 2 years earlier at another center revealed a short upper esophageal stricture, but evaluation including esophageal biopsies had failed to yield a conclusive diagnosis. Endoscopic dilation of the stricture had been performed with modest and very transient relief of her symptoms. She had also empirically been treated with swallowed fluticasone through metered dose inhaler 2 years earlier. Because of lack of symptomatic benefit after 3 months, this was ceased. Esophageal high-resolution manometry 12 months earlier demonstrated esophagogastric junction outflow obstruction, with raised integrated relaxation pressure,

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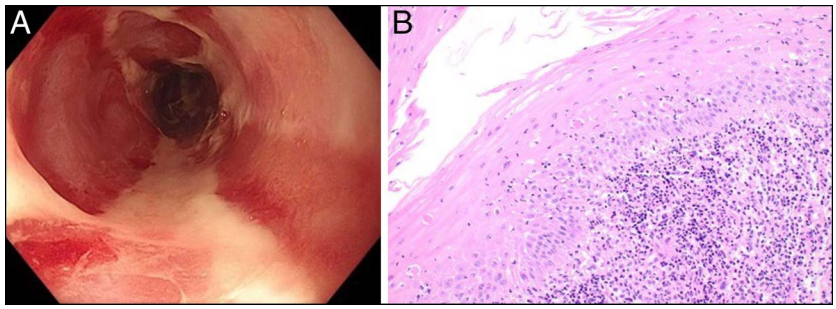

Figure 1. (A) Upper endoscopy before treatment: edematous, linear ulcerations and with white exudate. (B) High-power hematoxylin and eosin stain (200×) histopathology before treatment: lichenoid esophagitis.

intact swallow-induced peristalsis, but raised intrabolus pressure. Twenty-four-hour ambulatory pH monitoring performed at the same time, off acid suppression, showed physiological distal acid exposure time (0.5%; normal <4.2%), and negative symptom association. Thus, all previous endoscopic procedures had provided transient benefits and nonspecific findings.

Physical examination revealed a thin 52-kg woman whose vital signs were stable. Characteristic plaques of psoriasis were noted on the elbows, but no skin thickening was observed. A few small aphthous ulcers were present on the buccal mucosa. There was no supraclavicular lymphadenopathy, and abdominal examination was unremarkable.

At upper endoscopy, the esophagus appeared highly abnormal (Figure 1). There was a short, benign-appearing stricture in the upper esophagus, at 20 cm ab oral, which permitted passage of the standard adult endoscope. The entire esophageal mucosa was edematous with linear ulcerations, and sloughing/peeling of the mucosa was observed to occur with gas insufflation alone (ie, before contact with the endoscope). White exudates were observed.

Histopathological examination demonstrated mildly spongiotic squamous mucosa with a distinct dense band-like infiltrate of predominately lymphocytic cells with associated basal layer vacuolization. Civatte bodies (apoptotic keratinocytes) were seen throughout the full thickness of the squamous mucosa along with an intraepithelial lymphocytosis (Figure 1). Endoscopic and histopathology evaluation leads to a diagnosis of esophageal LP.

We prescribed the patient a 3-month course of budesonide orodispersible tablet, 1 mg twice daily, and on review of the patient 10 weeks later, the symptoms had almost completely resolved. In particular, odynophagia had completely resolved, and she had only intermittent mild dysphagia to firm solid foods remaining, but was able to consume a regular diet. Repeat endoscopy 3 months later demonstrated an exquisite response to treatment, with resolution of the inflammatory changes seen previously (Figure 2), and a concomitant marked improvement histopathologically (Figure 2). We endoscopically dilated the stricture to 16 mm, leading to complete resolution of her dysphagia.

DISCUSSION

LP is a multiorgan mucocutaneous inflammatory disorder of unknown origin that predominates in White women aged between 30 and 60 years of age with other comorbid inflammatory and autoimmune conditions.[1–3] LP is reported in 0.5%–2% of the general population, whereas esophageal LP is only diagnosed in approximately 0.19%.[1] Notably 95% of patients with oral LP have signs of esophageal LP.[1]

The typical clinical syndrome of esophageal LP involves dysphagia and odynophagia, although other symptoms such as heartburn, regurgitation, and weight loss may occur.[1,4] Endoscopic findings include edematous, mottled, friable white-lacy, and avascular esophageal mucosa, with sloughing and denuding of epithelium where the entire esophagus is involved. Strictures are common and characteristically located in the proximal esophagus often making intubation difficult.[4]

Orally, LP presents in 2 equally prevalent morphological patterns; as "white forms," they are typically reticular, papular, plaque/lacelike networks, and striae, whereas in "red forms," they may be erosive, atrophic, aphthous-like bullous lesions.[1,3] Cutaneously, LP presents typically as purple, flat-topped, and pruritic papulosquamous lichen lesions. In nails, ridging, splitting, onchylosis, thinning, and nail loss can be present.[1,3] In the genital area, violaceous papules can be found in either sex, with severe disease presenting as vaginal scarring/structuring and phimosis in males.[1,3,5,6]

Histopathological findings may be variable, but classically show a lichenoid esophagitis pattern of injury. There is often a junctional split (unlike in a sloughing esophagitis) with the lamina propria containing the distinctive dense, CD3 positive band-like lymphocytic infiltrates.[1,4,6] Civatte bodies (apoptotic keratinocytes) are evident, often seen through full thickness of the squamous mucosa.[1,4,6] This lichenoid esophagitis pattern of injury is not specific to esophageal LP and can be seen in viral infection (such as HIV or viral hepatitis), Crohn's disease, medications, or pill esophagitis; in many cases where the lamina propria is absent for assessment, other considerations should include gastroesophageal reflux disease and candida esophagitis.

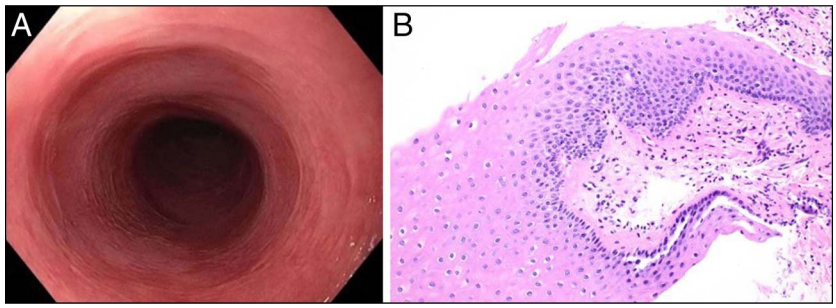

Figure 2. (A) Endoscopic review after 10-week treatment with orodispersible budesonide tablets, 1 mg twice daily. (B) High-power hematoxylin and eosin stain (200×) histopathology after 10 weeks of orodispersible budesonide tablet treatment.

To the best of our knowledge, this is the first report of use of a budesonide orodispersible tablet for this difficult-to-treat condition. Being a rare condition, therapeutic efficacy data in esophageal LP are limited to small retrospective case series. Swallowed topical corticosteroids are an alternative, safer therapeutic option to systemic therapy in esophageal LP. Limited efficacy data report clinical and endoscopic response rates with topical budesonide or fluticasone in 62%–72.5% of patients.[7] Although there are no well-established guidelines for esophageal LP, cases have been reportedly treated with other immunosuppressants including tacrolimus, rituximab, azathioprine, adalimumab, hydroxychloroquine, mycophenolate, and cyclosporines.[8–14] The therapeutic response in the present case seems to be analogous to those well described in eosinophilic esophagitis, and comparison with this more common inflammatory esophageal disease is useful. Previous data in eosinophilic esophagitis emphasized the importance of mucosal contact time of the steroid formulation on histological and endoscopic response,[15,16] and it is reasonable to infer that the same mechanism explains the superior efficacy of the orodispersible budesonide formulation in this case, compared with the repurposed asthma formulations.

Future studies should be performed to more definitively evaluate the efficacy of the budesonide orodispersible tablet in esophageal LP and provide further clarity regarding treatment guidelines in this understudied disease.

DISCLOSURES

Author contributions: T. Skinner: primary author involved in the data analysis, drafting, and is the article guarantor. S. Liang: reviewer, drafter, involved in the data acquisition, analysis, and preparation. S. Sanagapalli: reviewer, drafter, and involved in the data acquisition and analysis. All authors approved the final version to be submitted.

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