Lichen planus (LP) is an inflammatory disease of autoimmune origin affecting the skin and mucosa with a population prevalence of 0.5%–1.5%. Esophageal involvement with LP is very rare. Oral LP has been associated with chronic liver disease, particularly Hepatitis C virus (HCV) infection. The treatment of hepatitis C, at present, is based on pegylated interferon (Peg-INF) and ribavirin. The relationship between LP and treatment of HCV remains uncertain. Some case series have indicated a worsening of oral lichen planus lesions during interferon based treatment but this association is not clear.

In this paper, we report the first case in the literature of a patient with esophageal lichen planus related to HCV infection and provide a review of the pertinent world’s literature.

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A CASE TO REMEMBER

Esophageal Lichen Planus and Hepatitis C:
Review of the Literature

INTRODUCTION

Lichen planus (LP) is a T-cell-mediated chronic inflammatory disease of autoimmune origin affecting the skin, nails and mucosa, including the oral cavity and rarely the esophagus. The disease is characterized histologically by a dense lichenoid (band like) lymphocytic infiltrate along the dermal epidermal junction (1). The T-cells induce the overlying keratinocytes to undergo apoptosis. This T-cell induced inflammation causes the characteristic histological findings of multiple civatte (colloid) bodies, “saw tooth” appearance of the rete ridges, and small clefts at the dermal epidermal junction called Caspary-Joseph spaces. LP of the skin clinically shows flat topped, purplish, pruritic, papules. There are a number of other variants of lichen planus of the skin including, bullous, atrophic, hypertrophic, annular, linear and erosive. LP of the nails occurs in about 5% of patients. Wickham’s striae is a term used to describe clinical finding of
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white streaks that are occasionally found on the lesions of LP (2). Lichen planus usually appears in the oral cavity as white striations, white plaques, erythema, erosions, or blisters affecting mostly the buccal mucosa, gingiva and tongue (3) (Figure 1). The oral involvement in LP is the sole presentation of the disease in about half of the patients. LP affects 0.5%–1.5% of the population, with a predilection for women (about 70% of patients are females) (4). Oral involvement is typically chronic in nature, while skin disease will more often than not spontaneously remit after one-to-two years. Three out of four patients are in their early thirties to late fifties. The esophageal involvement of LP is rare (less than 30 case reports of esophageal LP have been published) and in most cases present with dysphagia. Diagnosis of the esophageal LP is often delayed, as the disease is not common. The symptoms are usually attributed to gastroesophageal reflux disease, before the final diagnosis is made by endoscopic appearance and biopsy.

Oral LP has been associated with chronic liver disease particularly Hepatitis C virus (HCV) infection. In a study done by Cribier, et al (5), it was found that the prevalence of HCV in patients with LP was 3.8% versus 2.6% in controls; but several other studies have shown a range of prevalence being 3.4% to 38%. A study done by Bellman, et al (6) in Florida showed that 23 patients out of 30 with LP had HCV infection. From the opposite perspective, in recent studies, it has been shown that up to about 5% of patients with HCV may have LP (7). There is currently no cure for oral LP. Treatment is aimed to reduce symptoms and this is achieved mostly with topical or systemic steroids and more recently with the newer topical immunomodulator tacrolimus. Difficult cases often need systemic therapy with hydroxychloroquine, mycophenolate mofetil or cyclosporine.

The treatment of hepatitis C, at present, is mostly based on pegylated interferon (Peg-INF) and ribavirin. The relationship between LP and treatment of HCV remains uncertain. Some case series have indicated a worsening of oral lichen planus lesions during interferon based treatment (8). Still others have shown histological improvement of oral lichen planus after treatment with interferon (9). The mechanism of exacerbation of these lesions after starting interferon is unknown at present but it is thought to be related to a cell-mediated immune response against HCV that is provoked by the interferon or hypersensitivity to drug treatment (lichenoid drug reaction) (10).

In this paper, we report the first case in the literature of a patient with esophageal lichen planus related to HCV infection. This report discusses the course of her esophageal LP as she was successfully treated with peg-INF and ribavirin achieving a sustained virological response. A review of the pertinent world’s literature is discussed in this report.

CASE REPORT

A 39-year-old female was referred to the department of dermatology at our institution (for a second opinion) of severe vaginal and oral lichen planus in 1994. The patient has a past medical history of exposure to hepatitis B virus and oral and vaginal lichen planus. The past surgical history is relevant for knee surgeries and tubal ligations. Social history includes intravenous drug use (IVDU) about 20 years earlier and alcohol abuse in the past with no smoking. The patient reported allergies to aspirin and bronchodilators. She has been using topical steroids for her oral LP. The physical exam was unremarkable except presence in the oral mucosa of erythema including the hard palate and severe gingivitis, also erythematous lesions in the vulva with some fissures with no atrophy. At that time the patient was...
started on an oral regimen of etretinate (a systemic retinoid which comprises a family of polyisoprenoid lipids including vitamin A and its natural and synthetic analogs. Its mechanism of action is not well understood). The patient returned to our institution about a year later for referral to the ophthalmology department regarding acquired nasolacrimal duct obstruction, requiring punctoplasties that was found, after biopsy, to be related to her lichen planus. The patient required stenting of the lacrimal ducts done (in 2000) due to continued symptoms despite medical treatment.

The patient reported having episodes of intermittent dysphagia for the past four years with reported weight loss of about 20 pounds in the past year. An upper endoscopy (EGD) with biopsies (at an outside institution) was performed showing severe esophagitis and the patient was placed on proton pump inhibitors which she did not tolerate due to an allergic reaction. As the symptoms of dysphagia were not improving, a referral to our institution was made. A follow-up EGD showed a stricture of the proximal esophagus and biopsies performed showed reactive changes consistent with LP (no dilation was performed). Figures 2 and 3 show the histology and the endoscopic image of the specific lesions. Due to a past history of IVDU and presence of LP, a hepatitis C antibody test was performed which was positive. She had a liver biopsy which showed chronic hepatitis (Knodell score 7/22). The patient was found to have HCV genotype 2 and abnormal liver function tests. She was started on pegy-

The patient had an EGD done after two months of being on treatment for follow-up on the esophageal LP. At that time, a stricture in the proximal esophagus and inflammation of the distal esophagus due to LP was found. This did not need dilation. Another EGD was performed on the patient after finishing the interferon treatment with no significant changes with respect to previous examinations.

Despite eradication of HCV, the patient developed dysphagia (about three months after finishing the HCV treatment) which required EGD which showed stricture of the proximal esophagus and underwent dilation with savory dilator. The patient continued having complaints of dysphagia in the following months which required dilations (from March 2003 until July 2005 patient needed a total of seven dilations). The patient had her last esophageal dilation on July 2005 and has been symptom free with no need for dilations for the past fifteen months.

Figure 2. Biopsy of lichen planus lesion with dense lymphocytic infiltrates of the epidermis and basal layer degeneration.

Figure 3. Endoscopic picture of the lichen planus lesions of the esophagus showing annular, patchy erythematous lesions with denuded mucosae involving proximal and mid esophagus.
The treatment of HCV infection has been linked to the use of interferons since the late 1980’s (at that time non-A, non-B hepatitis) (11). The cure rate with modifications of regimen has been improving with time. Recently, with the introduction of ribavirin and the PEGylation (the act of covalently coupling a PEG structure to another larger molecule) of interferon, the sustained virological response rates have been as good as 40%–50%.

The effect of interferon in HCV patients with lichen planus is controversial. Most of the cases studied are related to oral involvement of LP. Up until now, there are no reports of the esophageal LP and HCV in the English literature.


There are also case reports that have shown aggravation of LP after starting interferon treatment. Nagao, et al (13), in another publication in 2005, reported an
aggravation of oral LP after treating a patient with interferon alpha-2b and ribavirin for 18 weeks which needed to be discontinued, with partial improvement of oral lesions after eight months of discontinuation of interferon therapy.

Oral lichen planus development has been reported in several cases after starting a patient on interferon therapy. Guijarro Guijarro, et al (14) reported a case of oral lichen planus in a patient with HCV after one month of treatment with interferon alpha. Also Varela, et al (10) reported a similar situation. The mechanism of induction of these lesions in relation to interferon is not clear.

In conclusion, LP has an unpredictable course in the setting of HCV and interferon treatment. Informed consent, when using interferons in the setting of lichen planus, should include possible worsening of condition.

The approach to the problem of esophageal LP has been mainly focused on the reduction of its main symptomatology which is dysphagia. Temporary relief of this symptom is achieved by mechanical dilation of the esophagus. Mechanical dilation is not a risk free procedure; not only the complication of esophageal tear should be considered, but also the possibility of development, in these patients, of what is known as Koebner-like phenomenon (after injury to the mucosa, new plaques can flare up at the site of injury, or old ones spread). Pharmacological approaches have been considered to reduce dysphagia (mostly systemic or topical immuno-suppresion therapy) with variable results. The best way of quantifying improvement in these patients is the number of esophageal dilation needed in a period of time.

The most widely used treatment of LP of the esophagus has been systemic steroids with variable results. A summary of published studies with subsequent results can be seen in Table 1. In recent years, there has been a tendency to use intralesional corticosteroid injections to improve symptoms of dysphagia. The reasons behind usage of intra-lesional steroid are mainly based on:


<table>
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<tr>
<th>Publication—year</th>
<th>Presenting symptoms</th>
<th>Treatment received</th>
<th>Clinical course</th>
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<tr>
<td>Van Maercke, et al—1988 (one, 27)</td>
<td>Swallowing problems and inflammation of the bucal mucosa</td>
<td>Systemic retinoid therapy</td>
<td>Lesions disappeared at 3 month follow up</td>
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<tr>
<td>Bobadilla, et al—1999 (one, 28)</td>
<td>Substernal pain on swallowing for several weeks</td>
<td>Started on oral cyclosporine</td>
<td>Remission for one year with recurrence of symptoms which disappeared with increasing the cyclosporine dose</td>
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<tr>
<td>Abraham, et al—2000 (one, 29)</td>
<td>Progressive dysphagia for solids</td>
<td>High dose etretinate</td>
<td>Patient did not tolerate treatment</td>
</tr>
<tr>
<td>Keate, et al—2003 (three, 30)</td>
<td>Case 1 progressive dysphagia Case 2 erythematoid rash and dysphagia Case 3 presented with history of esophageal stenosis</td>
<td>Case 1. Intralvesional injections of triamcinolone. Case 2. Oral prednisone, intralvesional injections of triamcinolone with oral tacrolimus in Aquaphor 0.1% Case 3. Intralvesional injections of triamcinolone</td>
<td>Case 1. Did not require further esophageal dilatation Case 2. Improved symptomatology Case 3. Improvement of swallowing</td>
</tr>
<tr>
<td>Reissmann, et al—2006 (one, 31)</td>
<td>Progressive dysphagia for solids for 18 months</td>
<td>Intralvesional injections of triamcinolone</td>
<td>Free of symptoms at six month follow up</td>
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2. LP lesions are produced by locally activated T-lymphocytes.
3. And the first choice in treating the cutaneous LP being topical immunosuppression.

The use of topical steroids has been mostly effective in order to reduce the use of systematic route or to taper down the dose of systemic steroids.

Other drugs have been used for this condition. Systemic use of retinoids (a keratolytic drug) has been tried for treatment of esophageal LP with variable results. Cyclosporine is another oral medication that has been used for this condition. Table 2 shows a summary of publications using topical steroids and non-steroid medications.

The malignant transformation of oral LP has been documented in the past by Sigurgeirsson, et al (15) with the risk being close to 1%. Calabrese, et al (16) reported a case showing the development of Squamous cell carcinoma (SCC) in a patient with LP of the esophagus after treatment with several cycles of cyclosporine. This is the first case of esophageal LP and SCC; therefore, surveillance in patients with esophageal LP for possible malignant transformation is of uncertain benefit.

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