Eruption of Oral Lichen Planus After Interferon Therapy for Hepatitis C Infection: Case Report

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ABSTRACT

Background: The association between oral lichen planus (LP) and hepatitis C virus infection (HCV) has been discussed in several papers worldwide. The exact pathogenesis of oral LP in HCV-positive patients is still uncertain. There are several studies, which highlight the role of alpha-interferon (INF) being used for treatment of HCV-positive patients, resulting in eruption or exacerbation of oral LP.

Case description: We present a case of erosive LP limited to oral cavity in a 44-year-old Egyptian man with chronic HCV infection who was treated with INF and ribavirin. Despite an extended period of treatment, there was no significant effect on the viral activity (viral load). Interestingly, following five months of termination of anti-hepatitis therapy, there was recurrence of oral LP lesions which was confirmed histopathologically. His condition improved dramatically by Protopic cream 0.1%.

Conclusion: Altered immunogenicity of HCV appears to be the likely explanation, hence understanding the importance of follow-up of the patient post anti-hepatitis C therapy.

KEYWORDS
Oral lichen planus, Hepatitis C infection, Alpha-interferon.

INTRODUCTION

Oral lichen planus (LP) is a relatively common chronic inflammatory condition that affects the oral mucous membrane with variable clinical traits. Since the first description of oral LP associated with hepatitis C infection was reported in 1991, there have been several reports suggesting the association between HCV infection and oral LP. Many studies have showed higher prevalence (1.6-20%) of oral LP in HCV-positive patients. In contrast, some researchers found weak or no correlation between chronic HCV infection and LP. A region-based correlation between HCV infection and LP has been described by some researchers worldwide. However, the possible etiopathogenic mechanism that links the two diseases remains unclear. Immunogenic dysregulation of host infected with HCV, reaction to anti-hepatitis medications particularly alpha-interferon or viral infection are considered to be the current acceptable etiopathogenic factors causing oral LP.

The clinical and histological features of oral LP associated with hepatitis C infection subjects are no different from the control patients. Although, erosive form of oral LP is common clinical phenotype noted in seropositive hepatitis C individuals, the management of oral LP in patients with or without hepatitis remains the same.

CASE REPORT

A 44-year-old Egyptian man was referred from dermatology department at Farwaniya hospital to oral medicine clinic, who presented with painful and swollen ulcerated lower lip on March 2010. On examination, there was apparent swollen lower lip with central erosive areas oozing fresh blood from the eroded surfaces on light palpation, and there were white fine and coarse lace-like mucosal changes abutting the eroded lesions (Fig. 1). Also, there was bilateral lymphadenopathy with mobile, tender lymph nodes palpable in the submandibular triangular region.
lesions were seen on the rest of oral cavity mucosa. The clinical presentation of the lip and oral cavity lesions were consistent with LP.

On reviewing his medical history, he had been diagnosed with hepatitis due to HCV infection (genotype 4) in 2008 for which he received combined therapy of pegylated interferon-alpha (180mcg SC, weekly for 48 weeks) and ribavirin (1000mg PO daily for 48 weeks).

The patient reported an oral soreness and burning sensation after one month of the anti-hepatitis therapy inception for the first time. The exact diagnosis of oral lesion and subsequent therapy provided by dermatology department had not been known to us. Nevertheless, oral condition was quiescent through the period of the therapy. The oral symptoms reappeared five months following discontinuation of anti-hepatitis therapy with increased severity resulting in severe pain, difficulty in eating, swallowing and speaking. In addition, he noticed progressive swelling of the lower lip with bleeding ulcers over the next 6 weeks.

Besides his known medical condition, he is on insulin to manage his diabetes (type II). Furthermore, he is not a cigarette smoker and he does not drink alcohol.

An incision biopsy of lower lip lesion revealed interface dermatitis confirming our clinical provisional diagnosis. Microscopically, the specimen exhibited ortho-keratosis with prominent granular layer, intense band-like lymphohistiocytic infiltrate with plasma cell predominance and hydropic degeneration of basal cell layer with scattered Civatte bodies. (Figs 4-6)

Intra-oral examination revealed bilateral white and red lesions on posterior part of the buccal mucosa. These lesions had striking reticular pattern (reminiscent of LP) centered on erythematous mucosal areas. The lesion on right buccal mucosa was found rubbing against heavily restored molar tooth with amalgam (Figs 2,3). No other lesions were seen on the rest of oral cavity mucosa. The clinical presentation of the lip and oral cavity lesions were consistent with LP.

(Fig. 1) shows a swollen lower lip with central erosive and hemorrhagic areas

(Figs 2-3) Exhibit lichenoid changes “reticular pattern” on right (A) and left (B) buccal mucosae

(Fig. 4) reveals interface dermatitis (Hematoxylin and eosin stain at lower magnification 4X plain)

The patient was treated with protopic cream 0.1% three-four times daily for 2 weeks. The lower lip status improved dramatically. (Fig. 7)
DISCUSSION

Among viruses, human herpes viruses, human papilloma virus and hepatitis viruses have been linked with oral LP, albeit on the basis of equivocal data.\textsuperscript{12}

There have been several studies, which suggest an association between LP and HCV infection.\textsuperscript{3-7} In a recent review the pooled data from all studies revealed a statically significant difference in the population of HCV seropositive subjects among LP patients when compared with the controls.

Interestingly, geographic heterogeneity seems to play an important role in this LP-HCV association. As indicated by studies from the Mediterranean basin showing a significant association whereas studies from Northern Europe did not present any such association. Furthermore, in studies from countries with high prevalence such as Egypt, negative or insignificant association between HCV infection and oral LP has been reported.\textsuperscript{12,14} The discrepancy may be explained by genetic differences among the population studies and this may possibly be the reason for development of LP in our patient.

The exact etiopathogenesis of oral LP in HCV-positive individual is still uncertain. Nonetheless, eruption of oral LP in our case could have resulted from a lichenoid reaction to the medication used in the treatment of hepatitis C, particularly alpha-interferon. This hypothesis (i.e. drug reaction) was plausible in some studies.\textsuperscript{15-20} Most of these case reports demonstrate the aggravating effect of the interferon rather than causative effect for the development of oral LP in patient with HCV infection. Besides, in our case, reappearance of severe erosive oral LP while not receiving INF therapy, suggests that it may not have played a significant role in its pathogenesis. Nonetheless, this may be viewed as it having more aggravating rather than causal effect. Therefore, it would be a good practice to screen the oral cavity of HCV-positive patients prior to initiating antiviral therapy. So, the possible eruption of oral LP can be anticipated and managed appropriately especially in those with quiescent LP.

Besides INF therapy, other confounding factors appeared to have contributed to the possible initiation or aggravating already present of oral LP in our case, such as presence of amalgam on right mandibular molar and chronic rubbing of buccal mucosa. Unfortunately, we are not aware of the intra-oral examination findings of the patient prior to anti-hepatitis treatment.

Also, there is plethora of literature suggesting role of immune dysregulation in the pathogenesis of oral LP involving the cell-mediated immunity. However, viral factors, such as genotypes of HCV and HCV-RNA levels, are less important pathogenic cause.\textsuperscript{12}
Why oral mucosa is most frequently affected is still unknown. Several experimental studies conducted proposing a theory of “compartmentalization of mucosa” that still does not give a clear explanation to this phenomenon.21,22

In HCV seropositive subjects, erosive oral LP is commonly prevalent lesion.23,24 Megat et al.23 noted three types of OLP. He found lymphocytic inflammation deeply infiltrating lamina propria in OLP associated with a HCV infection and that could be associated with the erosive trait, as noted in our case.

Management of HCV associated oral LP lesion is no different from oral LP in HCV-negative subjects. Since there is no cure different therapies are aimed primarily to ameliorate the signs and symptoms of oral LP. Although corticosteroids have been the mainstay of management, other immunosuppressant and immunomodulatory agents have also contributed significantly towards treatment of the disease.12,26-28 A comparative systemic review of 28 randomised controlled clinical trials of therapy for symptomatic oral LP has concluded that there is insufficient evidence to support the effectiveness of any specific treatment as being superior.26,29 A plausible therapeutic approach should be guided by severity of the patient’s condition. In our case, tacrolimus cream (0.1%) was prescribed and used three to four times daily for 2 weeks. Some studies recommend use of tacrolimus as second line of treatment especially in recalcitrant lesion. We preferred to use it due to severity of the lesion, which is found to be effective in other studies.12,26 In order to prevent a flare up of the condition, we avoided use of systemic immunosuppressant therapy.

Up to the time of writing this case report, his oral condition is fairly controlled with topical steroids in addition to tacrolimus. Due to chronicity of LP, relapses of his oral condition did occur but with lesser frequency and severity. The potential for malignant transformation of OLP is still controversial. The frequency ranges from 0.4% to 6.25% with the highest rates in the erythematous and erosive lesions.30-32 Follow up is mandatory not only to control his oral LP but also to detect early malignant transformation.

REFERENCES