

Carcinoma *In situ* arising in the Oral Lichenoid Lesion-An Unusual Case Report

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Abstract

Drug-induced lichenoid reaction is quite common in the oral cavity. Patients with oral lichenoid lesions (OLL) may increase risk of developing epithelial dysplasia and squamous cell carcinoma. Although this subject remains controversial, several studies suggested that the overall rate of malignant transformation of OLL was greater than that of general population or patients with oral lichen planus (OLP). In the present article, we report a 66-year-old female Thai patient with OLL associated with many medications including simvastatin. She also had a history of hypertension, osteoarthritis and hepatitis B virus infection. Her physician treated her with amlodipine, etoricoxib, glucosamine and chondroitin sulfate for more than 20 years. Simvastatin had been prescribed for the treatment of dyslipidemia for 2 years. Notably, the patient reported that oral symptoms and lesions arose after taking this medication. This patient later developed epithelial dysplasia and carcinoma *in situ* within areas of OLL approximately 7 and 8 years, respectively after its initial presentation. This case report will be useful for clinicians to become aware of the possible adverse outcome of long-standing drug-induced OLL.

Keywords: Carcinoma *in situ*; Dysplasia; Lichenoid; Oral lichenoid lesion; Simvastatin

Introduction

Drug-induced oral lichenoid lesion (OLL) is relatively common in the oral cavity and its symptoms can greatly compromise patients' quality-of-life. Many drug groups have been associated with this condition, the most common of which are oral hypoglycemic agents, angiotensin-converting enzyme (ACE) inhibitors, and non-steroidal anti-inflammatory agents (NSAIDs) [1]. Recent reports showed that statins, representing a class of hypolipidemic drugs, can induce lichenoid eruptions involving both skin and mucosa [2,3]. Simvastatin in particular has been reported to induce cheilitis, generalized exanthematous pustulosis, chronic actinic dermatitis and contact dermatitis [4]. In addition, a case of simvastatin-induced lichenoid drug eruption with skin and mucosal involvement was previously reported [5]. In addition to the localized painful oral symptoms associated with the flare-up of lesions, patients with OLL may harbor an increased risk of developing epithelial dysplasia and squamous cell carcinoma. Although this subject remains controversial, several studies suggested that the overall rate of malignant transformation in patients with OLL was greater than those in general population and patients with oral lichen planus (OLP) [6]. In the present article, we report a case of OLL associated with multiple medications including simvastatin. Interestingly, the patient later developed epithelial dysplasia and carcinoma *in situ* during the course of treatment.

Case Report

A 66-year-old female Thai patient was referred to the Oral Medicine clinic at the Faculty of Dentistry, Chulalongkorn University, Bangkok in 2006 with a chief complaint of burning sensation to hot and spicy food, present for 9 months. She was diagnosed with trigeminal

neuralgia 10 years prior and was treated previously with carbamazepine and vitamin B₁₂.

She also had a history of hypertension, osteoarthritis and hepatitis B virus infection. Her physician had treated her with amlodipine, etoricoxib, glucosamine and chondroitin sulfate for more than 20 years.

Simvastatin had been prescribed for the treatment of dyslipidemia for 2 years. Notably, the patient reported that her oral symptoms and lesions arose after taking this medication. Subsequently, she received prednisolone, ketoconazole and triamcinolone acetonide 0.1% in orabase to treat oral lesions, but showed only slight improvement. She denied tobacco or alcohol use.

Upon examination, the extraoral finding was unremarkable. Intraorally, her right buccal mucosa had a small erosive area with faint white patch Figure 1a, and her left buccal mucosa had mild white patch and striae Figure 1b. Her oral hygiene was fair and generalized dental attrition was observed. She was diagnosed clinically with OLL and was treated with fluocinolone acetonide 0.1% in solution and sodium bicarbonate mouthwash.

The lesions were slightly improved. During the follow-up period of every 3-6 months, clobetasol propionate 0.05% and fluocinolone 0.1% with clotrimazole gel were used alternately to control the flare-up of lesions. Pseudomembranous candidiasis erupted during the course of treatment and was treated with miconazole gel.

Simvastatin was continually prescribed by her physician, despite our request for a drug change. The Naranjo algorithm was applied and this case was scored 3, indicating a possible Adverse Drug Reaction-ADR [7].



Figure 1a: The right buccal mucosa on the first visit showed an erosive area with mild white patch.



Figure 2b: The left buccal mucosa showed ulceration with white patch and slough covering.



Figure 1b: The left buccal mucosa had a white patch and faint striae.

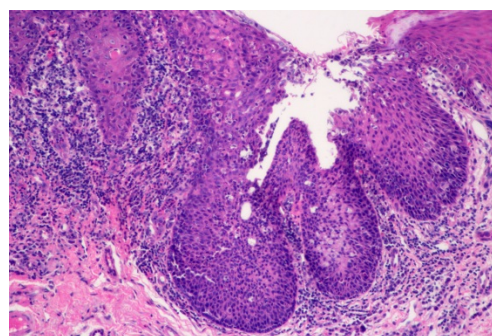


Figure 3a: Microscopic examination of the specimen from right buccal mucosa revealed the acanthotic stratified squamous epithelium with pleomorphism, hyperchromatism and increased mitotic activity throughout the entire epithelial thickness.

In 2013, a small erosive area and white patch still persisted on her right buccal mucosa Figure 2a. Her left buccal mucosa showed an irregular large ulcerative area with white patch and slough covering Figure 2b. The incisional biopsy was performed on the lesions on her right and left buccal mucosa and showed carcinoma *in situ*, Figure 3a and ulcer with moderate epithelial dysplasia, Figure 3b, respectively.

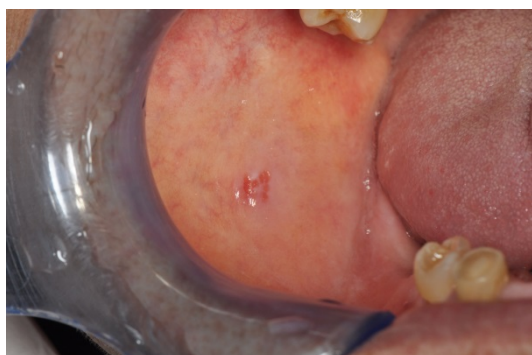


Figure 2a: The right buccal mucosa showed an erosive area and mild white patch.

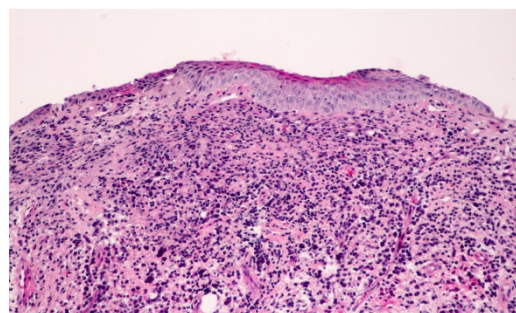


Figure 3b: Microscopic examination of the specimen from left buccal mucosa revealed an ulcer with adjacent atrophic stratified squamous epithelium with atypical keratinocytes involving half of the epithelial layer. Chronic inflammatory cells consisting plasma cells, lymphocytes and macrophages were present in the underlying connective tissue (Magnification X100).

Discussion

This report presented the challenge OLL case with a long-term course of observation and treatment. Although the patient had been

taking multiple medications, she reported that oral symptoms and lesions appeared after taking simvastatin. Nonetheless, due to the fact that simvastatin was not withdrawn in this case, the relationship between OLL and this drug cannot be directly established. With continual administration of probable causative drugs, treatment of oral lesions with topical steroids showed only a slight improvement. The patient later developed oral epithelial dysplasia and carcinoma *in situ* within areas of OLL approximately 7 and 8 years, respectively after the its initial presentation. This case report will be useful for clinicians to become aware of the possible adverse outcome of long-standing drug-induced OLL. At first visit, lesions appeared clinically characteristic for OLL with only mild symptoms and biopsy was not performed. However, after 7-year follow-up, the biopsy specimen was taken, due to the significant change in clinical features with areas of irregular erosive and keratotic patch.

The issue of premalignant potential of OLL and OLP remains debatable. However, it is generally accepted that a percentage of these patients may develop carcinoma during the period of treatment or follow-up. The erosive form of lesions is more prone to transform into malignancy and a predilection for older female patients is noted [8]. Interestingly, one study also showed that OLL may have a higher risk of malignant change than OLP [6]. In summary, we advocate that drug-induced OLL in patients should be closely monitored in a long term and any persistent red and white lesions in the oral cavity particularly in elders have to be biopsied albeit mild or no other symptoms.

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Conflict of Interest

None

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