

Alternative treatment using topical tacrolimus for erosive oral lichen planus resistant to steroids

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ABSTRACT

Lichen planus is a T-cell-mediated immunological disorder causing inflammatory lesions on the skin and oral mucosa. The etiology of lichen planus remains unknown, and the current therapeutic strategy is primarily to manage the symptoms. Although topical steroids are commonly used in the treatment of lichen planus, there are lesions refractory to steroids that require different treatment options. This report is of a patient with bilateral erosive oral lichen planus of the buccal mucosa. The lesions did not respond to high-potency topical steroids, so they were treated with topical tacrolimus 0.1% ointment, a potent topical immunosuppressant. All the erosive lesions healed, and the associated pain and bleeding disappeared after 6 weeks of treatment.

Key words: Lichen planus, oral; Steroids; Tacrolimus

Introduction

Lichen planus is a T-cell-mediated immunological disorder causing inflammatory lesions on the skin and oral mucosa. The reported prevalence of oral lichen planus (OLP) varies from 0.5 to 3.0% of the population ^{1,2}. Clinically, OLP can manifest as reticular, papular, plaque-like, erythematous, erosive or bullous subtypes ³. To establish a clinical diagnosis of OLP, reticular or papular textures have to be present.

A biopsy for histopathological examination is usually required for accurate diagnosis and to exclude potential malignancy. As the etiology of OLP remains unknown, the current therapeutic strategy is primarily to manage the symptoms. Although topical steroids are commonly used in the treatment of OLP, there are lesions refractory to steroids that require different medications such as immunosuppressive drugs ^{4,5}.

This report is of a patient with bilateral erosive OLP of the buccal mucosa, which was refractory to high-potency topical steroids and required an alternative treatment approach.

Case report

A 48-year-old woman was referred by a general dental practitioner to the Oral Medicine Consultation Clinic at The Prince Philip Dental Hospital, The University of Hong Kong,

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Hong Kong, in 2010 to manage ulceration occurring at both sides of the buccal mucosa. The patient had had ulceration associated with pain and bleeding, particularly during tooth brushing and eating hard food, for over 6 months. The patient was diagnosed with erosive OLP and treated with triamcinolone prescribed by the general dental practitioner.

Intraoral examination in the clinic revealed two erosive lesions of 1.0 x 1.5 cm and 1.5 x 2.0 cm in size surrounded with white striae at the left (Fig 1a) and right (Fig 1b) buccal mucosa, respectively. Incisional biopsy confirmed the diagnosis of erosive OLP. Topical clobetasol propionate 0.05% ointment, a highly potent topical corticosteroid, was prescribed twice daily, and 4% bicarbonate mouthrinse was prescribed as prophylaxis for oral candidiasis. After 3 weeks of treatment, intraoral examination revealed no improvement of the symptoms. Clobetasol propionate was discontinued and tacrolimus 0.1% ointment twice daily was prescribed. After 3 weeks of treatment, the intensity of the pain and the size of the erosive lesions were remarkably reduced. After 6 weeks, the patient reported that all the pain and bleeding had disappeared. Intraoral examination revealed normal appearance at both the left (Fig 2a) and right (Fig 2b) buccal mucosa. No ulceration or erythematous lesions were found.

Discussion

Various oral lesions such as lichenoid contact reactions, lichenoid drug eruptions, and lichenoid reactions of graft-versus-host disease (GVHD) have similar clinical manifestations as OLP. Histopathological examination cannot distinguish OLP from these lichenoid lesions ⁶. However, trigger factors such as a direct topographic relationship to dental restorative materials, history of taking certain medications, or history of organ transplantation associated with lichenoid reactions can usually be identified ⁶. This patient presented with 'classic' reticular lichen planus, but no risk factors that could trigger lichenoid reactions were identified. Considering the medical/dental history, clinical manifestation and histopathological finding, a diagnosis of OLP was made.

As the etiology behind OLP is not fully understood and no preventive therapies have been developed, currently all treatment strategies are aimed at controlling the symptoms.

Corticosteroids, retinoids, and calcineurin inhibitors are commonly used in the management of symptomatic OLP. Retinoids are potentially effective for treating OLP, but are probably inferior to topical corticosteroids ⁶. A single-blind randomized study compared a medium-strength topical corticosteroid (triamcinolone acetonide) with ciclosporin and demonstrated no differences in efficacy between the two drugs ⁷. Another randomized, comparative, double-blind study reported that clobetasol, a high-potency topical corticosteroid, is more effective than ciclosporin in inducing clinical improvement ⁸. Triamcinolone has been found to be significantly less effective than clobetasol ⁹. Although numerous studies on the management of OLP have been published, there is a lack of randomized placebo-controlled trials that examine the efficacy of various drug treatments for OLP, and there is insufficient evidence to support the superior effectiveness of any specific treatment. Recommendations for the treatment of OLP are based mainly on clinical experiences.

The choice of drug for treating OLP depends on the severity of discomfort, the site of the lesions, and the general health of the patients ¹⁰. Triamcinolone acetonide 0.1% has been widely used by dental practitioners to manage symptomatic OLP because it is safe and readily available in dental clinics. Triamcinolone acetonide has intermediate potency, and is one of the few topical corticosteroids manufactured in a dental paste formula. Treatment with triamcinolone acetonide is quite effective when lichen planus presents as an erythematous lesion or small erosion. However, for extensive erosive lesions, triamcinolone acetonide is usually not sufficient or takes too long to control the symptoms. Some studies have advocated highly potent topical corticosteroids such as clobetasol propionate in favor of those with intermediate potency ^{4,11}. After the symptoms are controlled using high-potency corticosteroids, either the frequency of administration can be reduced or a medium-potency corticosteroid can be substituted to maintain the effect.

Although topical steroids are commonly used for managing OLP, some refractory lesions do not respond to corticosteroid treatment. Immunosuppressive drugs are an alternative option for treating these refractory lesions. Tacrolimus is a calcineurin inhibitor that shares the same cellular target as ciclosporin. Both ciclosporin and oral

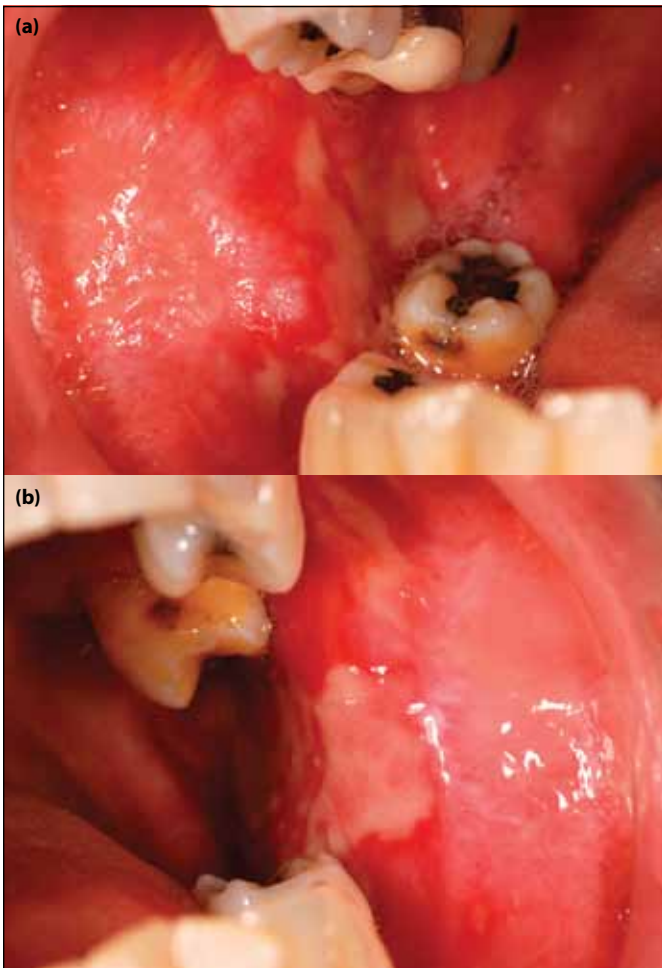


Figure 1 Erosive lichen planus at the (a) left and (b) right buccal mucosa

tacrolimus are approved for use in organ transplantation as part of the immunosuppressive regimen¹². The immunosuppressive action of tacrolimus is 10 to 100 times more potent than ciclosporin¹³. Tacrolimus ointment 0.1% and cream 0.1% have received approval from the US Food and Drug Administration (FDA) on the basis of their demonstrated efficacy in the treatment of atopic dermatitis refractory to conventional treatment¹². Systemic administration of tacrolimus has also been used for prevention of GVHD and for treating psoriasis¹²⁻¹⁵.

Tacrolimus has been used successfully for managing inflammatory diseases of the skin, and has been used alternatively in the treatment of severe erosive OLP that does not respond to corticosteroids^{14,15}. This patient had been treated with triamcinolone, but the symptoms failed to

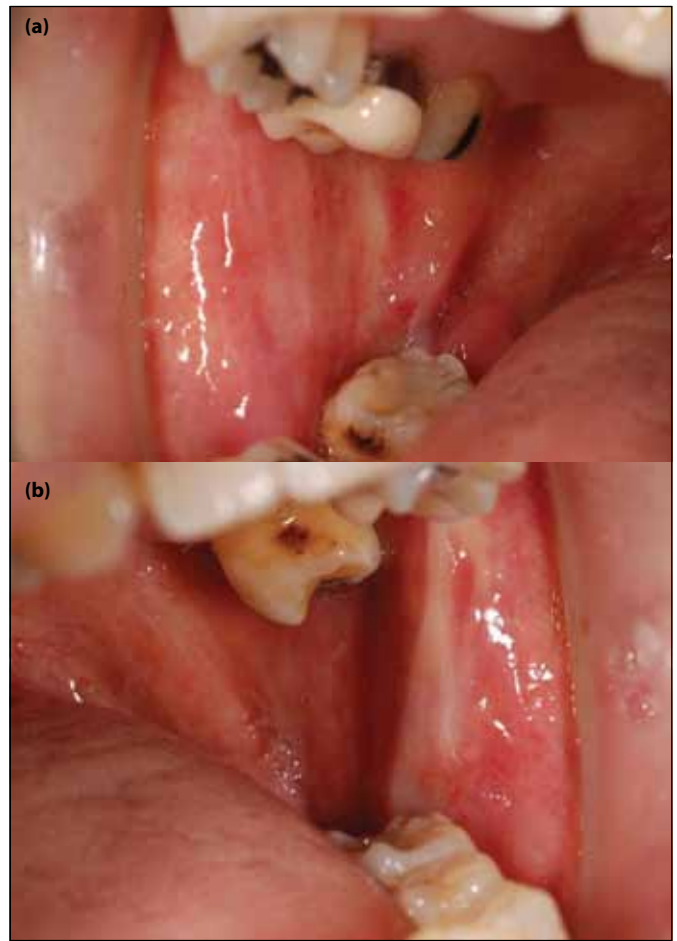


Figure 2 After 6 weeks of treatment with tacrolimus, intraoral examination revealed normal appearance at both the (a) left and (b) right buccal mucosa

improve before she attended the Oral Medicine Consultation Clinic. After a diagnosis of OLP was confirmed by incisional biopsy, treatment with clobetasol propionate 0.05% ointment, a highly potent topical corticosteroid, was started. There was no improvement after 3 weeks of treatment, so clobetasol propionate was replaced by tacrolimus 0.1% ointment. After 3 weeks, the intensity of the pain and the size of the ulceration were remarkably reduced, and all the lesions and associated symptoms disappeared after 8 weeks of treatment. This patient provides evidence that tacrolimus could be used as an alternative treatment for managing severe erosive OLP refractory to potent steroids.

Some studies have shown that tacrolimus has a lower risk for development of oral candidiasis than potent topical steroids¹⁶. However, some reports have raised a concern

that long-term use of tacrolimus may induce squamous cell carcinoma of the skin and oral mucosa¹⁷. The US FDA issued a public health advisory to inform health care professionals and patients of the potential cancer risk based on animal experiments and case reports of a small number of patients in 2005¹⁸. The FDA requested that the labeling of tacrolimus include a boxed warning about the potential cancer risk, and recommended that: (1) continuous long-term use of tacrolimus, in any age-group, should be avoided; (2) application should be limited to the areas of the lesions; (3) treatment is not indicated for use in children younger than 2 years; and (4) only tacrolimus 0.03% is indicated for use in children aged 2 to 15 years¹⁸. Currently, the potential for

tacrolimus to cause cancer remains theoretical and unknown. The American Academy of Dermatology Association Task Force Committee stated that there is no solid proof that tacrolimus causes skin cancer, and recommended that tacrolimus should remain as treatment for inflammatory diseases¹⁹. The European Dermatology Forum concurs with this advice²⁰.

In summary, tacrolimus 0.1% is an effective drug for treating severe erosive OLP. Tacrolimus should only be used as second-line treatment for lesions that are refractory to potent steroids. Continuous application should not exceed 8 weeks.

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