Customized Oral Night Guard Appliance Loaded with Tacrolimus for Management of Oral Lichen Planus A Case Report

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Abstract

Tacrolimus being a steroid-sparing immunosuppressant has recently replaced the first-line of drugs, i.e., steroids. This report presents a case of a 65-year-old male patient with the chief complaint of a burning sensation in his mouth. On basis of clinical examination and histopathological evaluation confirmed the diagnosis of oral lichen planus. For treatment, topical application of 0.1% tacrolimus powder mixed in orabase, to be applied locally 3-4 times daily using an oral soft splint and intralesional dexamethasone injection, for 2 months. Over a follow-up period of 6 months, the patient showed complete remission of the lesion with no evidence of recurrence. Tacrolimus is a potent and effective drug in the treatment of OLP and can be used either alone or in conjunction with steroids.

Keywords: adjunct therapy, erosive lichen planus, steroid-sparing immunosuppressant, tacrolimus, topical therapy

Key message: Tacrolimus has been proven to be a potent and effective drug of choice in the treatment of Oral Lichen Planus, alone as well as an adjunct to corticosteroids. In addition to the evident benefits of topical application, it also overrides the side effects of steroids.

Introduction

Oral Lichen Planus (OLP) is a chronic mucocutaneous autoimmune disorder arising due to abnormal immunological reactions with a tendency to undergo malignant transfor-mation. Auto-reactive T lymphocytes may be of primary importance for the development of OLP. These cells cannot discriminate between inherent molecules of the body and foreign antigens. Several peptides evoke the inflammatory response depending on the specificity of the auto-reactive T lymphocyte.1

Besides the conventional treatment protocols, newer treatment modalities have shown relatively better results in the remission of the lesions. Among these, Tacrolimus is a newer immunosuppressant that is fairly effective and relatively safer in the treatment of symptomatic OLP. Tacrolimus is almost 10 times

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more effective than other similar drugs such as cyclosporine in inhibiting the IL-2 mRNA synthesis as well as inhibiting the synthesis of chemical mediators from basophils and mast cells. It inhibits the enzyme calcineurin phosphatase activity thereby inhibiting the T cell multiplication.2 For these reasons, tacrolimus plays a major role in the inhibition of the mechanism of lichen planus pathogenesis.

CASE REPORT

A 65-year-old male patient came to the departmental OPD with the chief complaint of a burning sensation in his mouth for the past 1-2 years which was mild to moderate in intensity, intermittent in frequency, initiated on taking hot and spicy food and relieved on its own after some time.

In the intraoral examination, on inspection, there was evidence of erythematous areas surrounded by whitish reticular striations interspersed with pigmented areas, ranging over the right and left buccal mucosa, extending anteroposteriorly from the retromolar area to the retro-commissural area and superoinferiorly extending approximately 1.5 cm above and below the occlusal plane. On palpation, the lesion was slightly tender on palpation, rough in texture, no evidence of bleeding on provocation. Similar erosive lesions were also evident on the gingiva and pigmented predominantly whitish lesions were seen on the bilateral commissural area and lower lip.

The patient was advised to undergo a biopsy and the histopathology report showed the presence of hyperplastic and hyperkeratotic stratified squamous parakeratinized epithet-lium and connective tissue components, diffuse juxtaepithelial inflammatory infiltra-tion. The connective tissue was loosely arranged with a haphazard arrangement of collagen. The photomicrograph of the biopsy specimen has been demonstrated in (Fig 1). Hence, based on the clinical manifestations and the histopathological report, a provisional diagnosis of Erosive Oral Lichen Planus was given.

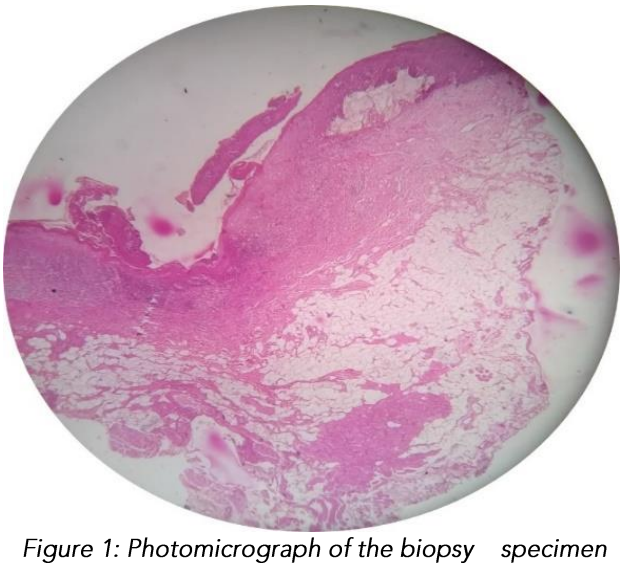

Figure 1: Photomicrograph of the biopsy specimen

The treatment plan included an intralesional injection of dexamethasone 4 mg/ml mixed with 0.5ml lignocaine hydrochloride, to be given once weekly and a topical application of 0.1% tacrolimus powder mixed in orabase, 3-4 times daily, for 2 months. A soft occlusal acrylic splint with extended gingival margins was fabricated using Biostar machine for local drug delivery to the gingival lesions (Fig. 2) which has advantages such as sustained drug release, extended retention of the drug for a longer period and avoiding the clearing effect of saliva.

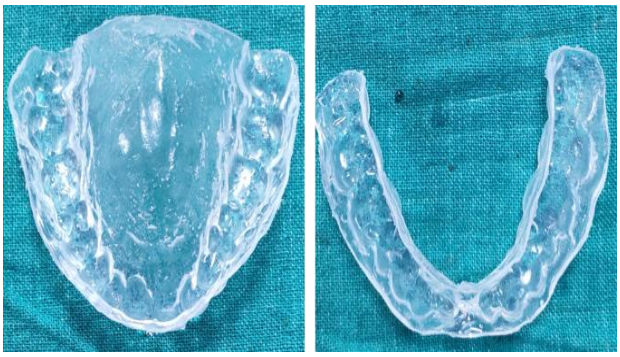

Figure 2: Customized oral acrylic soft splint fabricated for localized drug delivery

The patient was recalled every week for follow-up and subsequent intralesional injections of Dexamethasone 8 mg/2ml solution was administered for two months. After this, the intralesional injections were discontinued and the patient was advised to continue the application of topical Tacrolimus 0.1% w/w for 3 months. The patient was kept on follow-up for 6 months with no evidence of recurrence. The weekly follow-up pictures depicting the remission of the lesion have been demonstrated in Fig 3.

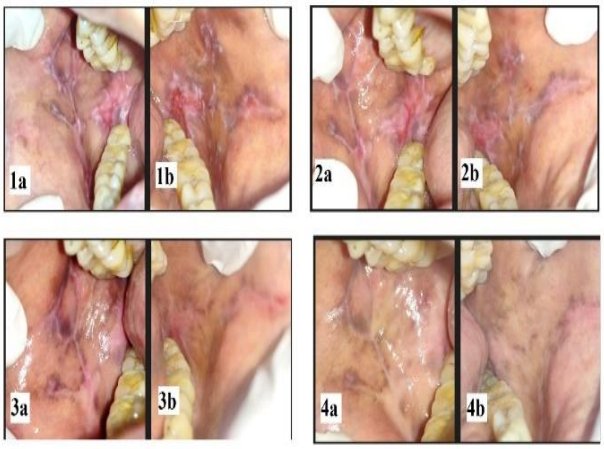

Figure 3(1a and 1b): Day 0 – Lesion before the start of treatment

Figure 3(2a to 2b): Week 1 - 20% remission seen
Figure 3(3a to 3b): Week 2 - 40% remission seen
Figure 3(4a to 4b): Week 5 - 90% remission seen

Discussion

The etiology and pathogenesis of OLP have been proposed by several authors. However, the exact pathogenesis remains to be fully understood.3 Despite successful remission of the lesion initially, the disease continues to show recurrence. Also, several patients have shown resistance to the regularly employed treatment modalities and quite a

few are incapable of tolerating the treatment due to their adverse effects.4

Corticosteroids have largely been used as the first line of treatment for OLP because of their ability to diminish the cell-mediated immune activity and in turn modulate immune function. These drugs can be given topically, intralesionally as well as systemically.3,5 However topical steroid applications very frequently have been associated with secondary candidiasis, thinning of the oral mucosa and local discomfort on application. 5 Also, prolonged use of topical steroids with occlusal dressing can lead to adrenal suppression. 5 Similarly, the use of intralesional steroids, apart from being considerably painful, it can also cause muscular atrophy with prolonged use. 5

Therefore, newer treatment approaches are being implemented. Tacrolimus has been proven to be safe and effective in the treatment management of OLP. The exact mechanism behind the same is still under debate. However, the ability of the drug to inhibit the synthesis of IL-2 seems to be playing a major role in the pathogenesis.

In the etiopathogenesis of OLP, the possible role of Tacrolimus has been demonstrated in Fig 4.

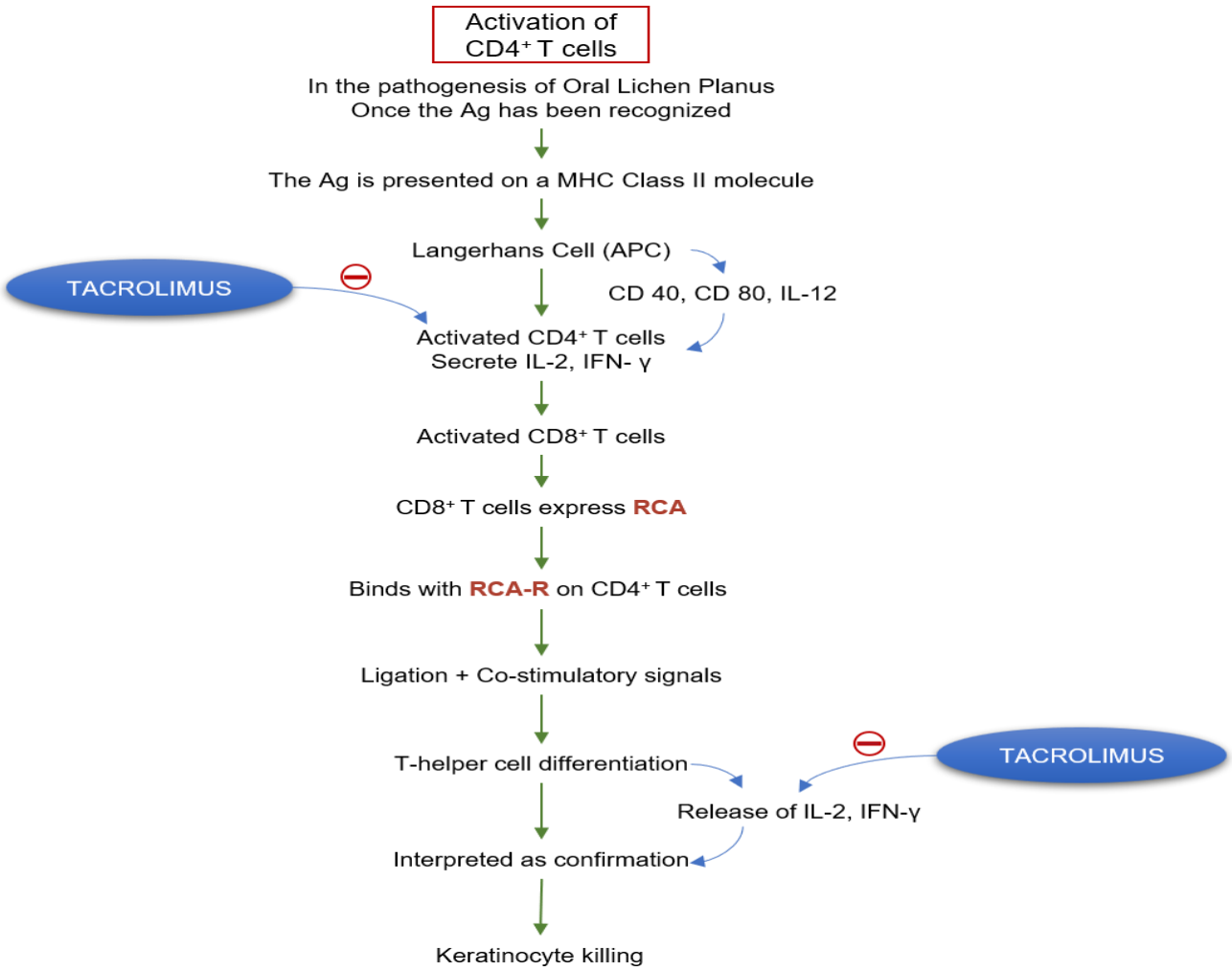

Figure 4: Mode of action of Tacrolimus in the etiopathogenesis of oral lichen planus

Tacrolimus is a steroid-sparing immunosup-pressant and is rapidly replacing the use of steroids in the treatment of OLP. It does not have side effects such as HPA-axis suppression and superadded candidal infections (seen in steroids), there is a faster rate of recovery and fewer number of recurrences. Tacrolimus has been specifically more effective in recalcitrant cases, where the patients have developed resistance to other topical and systemic therapies.6 In a study conducted by Resende et al 3, they found that topical application of 0.1% tacrolimus over 8 weeks showed 80% remission in the lesion. Similar results were also observed by Johnson et al 7, Byrd et al 4 where they observed that 84% of patients reported partial to complete remission of the lesion and Malik et al 2 where 70% of patients showed complete healing of the lesions. In another study conducted by Laeijendecker et al 8, they compared the outcomes of tacrolimus against clobetasol propionate and observed better results with the former drug. Although there were cases of recurrences in both groups.

Conclusion

Thus, it can be concluded that Tacrolimus is a potent and effective drug in the treatment of OLP and can be used either alone or in conjunction with steroids. Not only does it have a better outcome it has also shown fewer recurrences.

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