

# Topical Tacrolimus for the Treatment of Oral Lichen Planus

E Stoopler, T Sollecito, S DeRossi

## Citation

E Stoopler, T Sollecito, S DeRossi. *Topical Tacrolimus for the Treatment of Oral Lichen Planus*. The Internet Journal of Dermatology. 2002 Volume 2 Number 1.

DOI: [10.5580/1528](https://doi.org/10.5580/1528)

## Abstract

Lichen planus is a chronic inflammatory mucocutaneous disease that can have both cutaneous and oral involvement. Clinical presentations of oral lichen planus are varied and the erosive form can be the most symptomatic and difficult to treat. New research in cytokine biology may begin to help explain the pathogenesis and chronicity of oral lichen planus. Conventional treatment for oral lichen planus includes topical and intralesional corticosteroids. Tacrolimus, a calcineurin-inhibitor, has been shown to be effective in treating lesions of erosive oral lichen planus that are recalcitrant to topical steroid therapy. We would like to present a case in which a patient with severe erosions of the tongue, due to oral lichen planus, was effectively treated with topical tacrolimus following unsuccessful topical and intralesional steroid therapy.

## INTRODUCTION

Lichen planus is a relatively common dermatologic disorder that occurs on the skin and oral mucous membranes. There are several forms of oral lichen planus (OLP); however, the most common and most readily recognized form is the reticular form, consisting of slightly elevated, fine, whitish lines (Wickham's Striae) that produce a lacelike lesion. Erosive OLP presents as chronic multiple oral mucosal ulcers. Recent studies involving T cells and immunomodulating cytokines, including TNF – alpha, may provide clues as to the pathogenesis and chronic nature of OLP. <sup>1</sup> Patients with reticular OLP frequently are asymptomatic and may not require any treatment. Patients with erosive OLP frequently experience a great deal of discomfort and pain and need to be managed more aggressively. High potency or ultra high potency topical steroids can be used to treat erosive lichen planus and may provide relief to patients. Intralesional steroids can be used for indolent lesions that may not respond to topical steroid therapy. Tacrolimus is a calcineurin-inhibitor initially used to prevent solid organ allograft rejection. Topical formulations of tacrolimus have been developed for use to treat atopic dermatitis. <sup>2</sup> We would like to present a case in which a patient with severe erosions of the tongue, due to OLP, was effectively treated with topical tacrolimus following unsuccessful topical and intralesional steroid therapy.

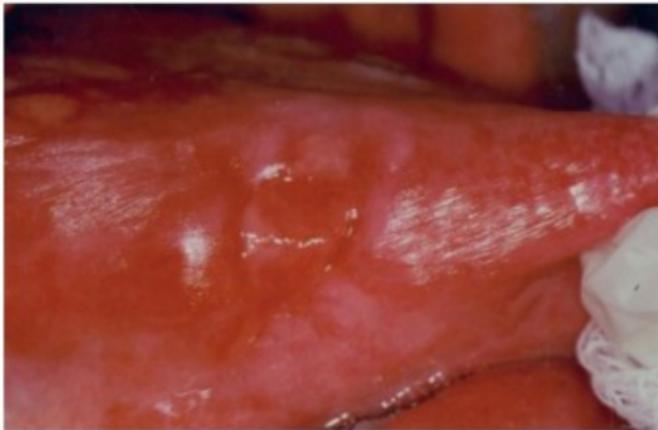
## CASE REPORT

A 56-year-old white female presented to the Oral Medicine Clinic with a chief complaint of sores on her tongue and mouth for the past 13 months. Her symptoms began following an extended trial of antibiotics for sinusitis and bronchitis. A biopsy was performed and confirmed the histopathologic diagnosis of erosive lichen planus.

Her past medical history is significant for hypercholesterolemia, bipolar disorder, asthma, and hypothyroidism. Current medications include amoxicillin, gabapentin, fluoxetine, fexofenadine, ibuprofen, clonazepam, atorvastatin, methylphenidate, levothyroxine, estrogen, and ipratropium. A comprehensive review of systems was significant for some mild heat intolerance and some numbness of her right arm and pain in her lower back. Clinical examination revealed no cervical lymphadenopathy, salivary gland enlargement or lesions on exposed skin surfaces. She had no conjunctivitis. Her oral mucosa was moist with diffuse areas of erythema and desquamation on the buccal mucosa, bilaterally. The tongue had large ulcerations (> 1cm) on the lateral aspects bilaterally (Figure 1).

**Figure 1**

Figure 1: Note the large area of ulceration surrounded by intense erythema on the right lateral border of the tongue.



There were multiple white – yellow small plaques that could easily be removed on the buccal mucosa, confirmed as candidiasis via Gram stain. Initial treatment consisted of clobetasol gel 0.05% applied to the affected areas 3 times per day and Mycelex troches 4 times per day. Clinical exam at one month revealed 10% resolution in the lesions on the buccal mucosa and lateral border of the tongue. The candidiasis had completely resolved. Treatment with intralesional injections of triamcinolone 5mg / cc combined with topical corticosteroids resulted in an additional 15% improvement in signs and symptoms over the next two months. The patient was placed on topical tacrolimus 0.1% 3 times per day and evaluated at 2 months. Subjectively, she noted 50% improvement of symptoms and on 4 month follow up, noted 75% overall improvement. Clinically, there was 90% improvement in erythema and 100% resolution in ulcerations over the same period (Figure 2). The patient is continuing to use topical tacrolimus 2 times per day, and undergoing 6 month follow up.

**Figure 2**

Figure 2: Note the absence of ulceration and significantly decreased erythema of the previously ulcerated lesion on the right lateral border of the tongue after treatment with 0.1% topical tacrolimus.



## **DISCUSSION**

Lichen planus is a chronic inflammatory mucocutaneous disease affecting 0.5 to 1% of the adult population. <sup>3, 4</sup> Patients can have both cutaneous and oral involvement. <sup>5</sup> Clinical presentations of OLP are varied and are frequently reported as reticulated, plaque – like, erosive, papular, atrophic, and bullous. The reticular form is the most common; however, the erosive, atrophic, and bullous forms are the most symptomatic and most difficult to treat. All regions of the oral cavity may be affected; however, most commonly, lesions are found on the posterior buccal mucosa and, in order of decreasing frequency, the gingiva, tongue, palate, lip, and floor of the mouth. <sup>6</sup>

Cell mediated immunity seems to play a critical role in the pathogenesis of lichen planus. Though the specific antigen(s) responsible for the activation of T cells has not been identified, studies have demonstrated the interaction of T cells and mast cells in a cyclical nature via the production of cytokines, such as RANTES (regulated on activation, normal T-cell expressed, and secreted) and TNF alpha, which may explain the chronicity of this disease. <sup>7</sup> Investigations have demonstrated the production of RANTES and the presence of specific RANTES receptors, such as CCR1, on T cells and mast cells in OLP lesions. <sup>1</sup> TNF – alpha, an inflammatory mediator, has been shown to up-regulate expression of CCR1. This suggests that RANTES, CCR1, and TNF – alpha interact and may be involved in the accumulation of inflammatory cells in OLP. <sup>8</sup> Dental

amalgam has been shown to increase TNF – alpha concentration in peripheral blood mononuclear cells , and may be a causative agent of OLP eruptions. Medications, flavoring agents, and viruses have also been reported to be associated with OLP eruptions. <sup>10</sup>

Treatment for OLP includes topical and intralesional high – potency corticosteroids, retinoids, cyclosporine, and most recently, topical tacrolimus. Recent evidence – based reviews showed topical corticosteroids were the most effective treatment. <sup>11</sup> Topically, both 0.1% tretinoin and 0.1% isotretinoin (retinoids) have been used for the plaque – like form of the disease. Topical cyclosporine has not demonstrated superior efficacy compared to topical corticosteroids alone. <sup>12</sup>

Tacrolimus, a member of the immunosuppressive macrolide family, suppresses T-cell activation by binding to cytosolic FK – binding proteins, which, in turn, interferes with the calcium / calmodulin – dependent phosphatase calcineurin. <sup>13, 14</sup> This ultimately results in the inhibition of cytokine gene transcription, including Interleukin 2 and TNF – alpha. <sup>15</sup> Topical tacrolimus was shown to be efficacious in atopic and contact dermatitis. <sup>14, 16,17,18</sup> Initial anecdotal evidence reported patients with recalcitrant erosive OLP were treated with topical tacrolimus and either substantial resolution or complete resolution of the lichen planus was noted over a period of time. <sup>19</sup> More recent studies have also demonstrated the efficacy of tacrolimus in treating erosive OLP. <sup>20,21,22</sup> Topical tacrolimus has been shown to produce significantly less skin atrophy than topical corticosteroids. <sup>15</sup> Although tacrolimus ointment is available in 2 strengths, 0.1% and 0.03%, the 0.1% formulation has been shown to be more effective in treating erosive lesions of OLP. <sup>15</sup> The major adverse reaction reported with topical tacrolimus is local irritation at the site of application. <sup>15</sup> Pimecrolimus, a second generation calcineurin – inhibitor, has been developed to treat atopic dermatitis. The major advantage reported when using topical pimecrolimus is significantly less irritation at the site of application in comparison to topical tacrolimus <sup>15</sup> Pimecrolimus is available in a cream vehicle only, making it extremely difficult to use intraorally due to its inability to adhere to moist oral tissues. Therefore, there have been no reports of using pimecrolimus, thus far, to treat erosive OLP.

### CONCLUSION

Topical use of tacrolimus is a safe, well tolerated, and effective therapy for oral lichen planus lesions recalcitrant to traditional therapies. New research in the areas of

immunomodulation and cytokine biology may elucidate the molecular milieu attributed to the pathogenesis and chronic nature of OLP.

### CORRESPONDENCE TO

Eric T. Stoopler, D.M.D. Department of Oral Medicine  
University of Pennsylvania School of Dental Medicine 240  
S 40<sup>th</sup> St., Philadelphia, PA 19104 Phone: 215.746.0112 Fax:  
215.898.7853 Email: ets@pobox.upenn.edu

### References

1. Zhao ZZ, Savage NW, Sugerman PB, Walsh LJ. Mast cell / T cell interactions in oral lichen planus. *J Oral Pathol Med* 2002; 31:189-195.
2. Cheer SM, Plosker GL. Tacrolimus ointment. A review of its therapeutic potential as a topical therapy in atopic dermatitis. *Am J of Clin Dermatol* 2001; 2:389-406.
3. Axell T, Rundquist L. Oral Lichen Planus - a demographic study. *Community Dent Oral Epidemiol* 1987;15:52-56.
4. Buoquot JE, Gorlin RJ. Leukoplakia, lichen planus, and other oral keratoses in 23,616 white Americans over the age of 35 years. *Oral Surg Oral Med Oral Pathol* 1986; 61:373-381.
5. Bricker SL. Oral lichen planus: a review. *Semin Dermatology* 1994; 13:87-90.
6. Lozada - Nur F, Miranda C. Oral lichen planus: epidemiology, clinical characteristics, and associated diseases. *Semin Cut Med Surg* 1997;16:273-277.
7. Zhao ZZ, Sugerman PB, Zhou XJ, Walsh LJ, Savage NW. Mast cell degranulation and the role of T cell RANTES in oral lichen planus. *Oral Maxillofac Pathol* 2001; 7:246-251.
8. Zhao ZZ, Sugerman PB, Walsh LJ, Savage NW. Expression of RANTES and CCR1 in oral lichen planus and association with mast cell migration. *J Oral Pathol Med* 2002; 31: 158 - 162.
9. Schedle A, Rausch-Fan XH, Samorapoompichit P, Franz A, Leutmezer F, Spittler A, Baghestanian M, Lucas T, Valent P, Slavicek R, Boltx-Nitulescu G. Effects of dental amalgam and heavy metal cations on cytokine production by peripheral blood mononuclear cells in vitro. *J Biomed Materials Res* 1998; 42: 76-84.
10. Daoud MS, Pittlekow MR Lichen Planus. In: Freedburg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, Fitzpatrick TB. Eds. *Fitzpatrick's Dermatology in General Medicine*. 5th ed. New York, NY: McGraw Hill; 1999:561 - 577.
11. Cribier B, Frances C, Chosidow O. Treatment of lichen planus: an evidence - based medicine analysis of efficacy. *Arch Dermatol* 1998; 134:1521 - 1530.
12. Lener E, Brieva J, Schacter M, West LE, West DP, el-Azhary RA. Successful treatment of erosive lichen planus with topical tacrolimus. *Arch Dermatol* 2001; 137:419 - 422.
13. Ruzicka T, Assmann T, Homey B. Tacrolimus: the drug for the turn of the millennium? *Arch Dermatol* 1999; 135:574 - 580.
14. Cooper KD. Atopic Dermatitis: recent trends in pathogenesis and therapy. *J Invest Dermatol* 1994; 102: 128 - 137.
15. Nghiem P, Pearson G, Langley RG. Tacrolimus and pimecrolimus: from clever prokaryotes to inhibiting calcineurin and treating atopic dermatitis. *J Am Acad Dermatol* 2002;46:228-41.
16. Aoyama H, Tabata N, Tanaka M, Uesugi Y, Tagami H.

Successful treatment of resistant facial lesions of atopic dermatitis with 0.1% FK 506 ointment. *Br J Derm* 1995; 133: 494-496.

17. Nakagawa H, Etoh T, Ishibashi Y, Higaki Y, Kawashima M, Torii H, Harada S. Tacrolimus ointment for atopic dermatitis. *Lancet* 1994; 344: 883.

18. Jegasothy BV, Ackerman CD, Todo S, Fung JJ, Abu-Elmagd K, Starzl TE. Tacrolimus (FK 506): a new therapeutic agent for severe recalcitrant psoriasis. *Arch Dermatol* 1992; 128:781 - 785.

19. Vente C, Reich K, Ruppert R, Neumann C. Erosive mucosal lichen planus: response to topical treatment with tacrolimus. *Br J Derm* 1999; 140: 338 - 342.

20. Rozycki TW, Rogers III RS, Pittelkow MR, McEvoy MT, el-Azhary RA, Bruce AJ, Fiore JP, Davis MD. Topical tacrolimus in the treatment of symptomatic oral lichen planus: a series of 13 patients. *J Am Acad Dermatol* 2002;46:27-34.

21. Kaliakatsou F, Hodgson TA, Lewsey JD, Hegarty AM, Murphy AG, Porter SR. Management of recalcitrant ulcerative oral lichen planus with topical tacrolimus. *J Am Acad Dermatol* 2002;46:35-41.

22. Morrison L, Kratochvil FJ 3rd, Gorman A. An open trial of topical tacrolimus for erosive lichen planus. *J Am Acad Dermatol* 2002;47:617-620.

**Author Information**

**Eric T. Stoopler, D.M.D.**

Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine

**Thomas P. Sollecito, D.M.D.**

Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine

**Scott S. DeRossi, D.M.D.**

Assistant Professor of Oral Medicine, University of Pennsylvania School of Dental Medicine