

Oral Lichen Planus Treated With Apremilast

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ABSTRACT

Oral lichen planus is a very difficult condition to treat and causes patients to experience pain and difficulty eating. Therapeutic approaches focus on minimizing flares and relieving pain and discomfort to improve patient quality of life. Topical preparations are the mainstay of therapy, but they are often insufficiently efficacious for more severe cases. The use of systemic agents can be complicated by potentially serious adverse effects, the need for regular monitoring, suboptimal efficacy, and cost. Reported here are 3 recalcitrant cases of oral lichen planus that were effectively treated with apremilast, a drug recently approved for psoriasis and psoriatic arthritis.

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BACKGROUND

Lichen planus is a chronic, mucocutaneous disease of unknown etiology that has no definitive cure.[1,2] It is characterized by nonspecific inflammation, commonly affecting the oral and genital mucosa, nails, skin, and scalp.[2,3] Oral lichen planus (OLP) occurs more frequently than the cutaneous form and is the most common cutaneous disease of the oral mucosa.[2,3] OLP tends to be more persistent and resistant to therapy, posing a management challenge to dentists and dermatologists.[1,2] OLP presents clinically as reticular, erosive, or ulcerative lesions with whitish streaks, producing pain and sensitivity to spicy foods.[4]

Although high quality evidence for the treatment of lichen planus is sparse,[1] management typically involves topical corticosteroids, immunomodulators, and retinoids, as well as systemic hydroxychloroquine, methotrexate, thalidomide, and griseofulvin.[2] Apremilast is an oral phosphodiesterase 4 (PDE4) inhibitor recently approved for the treatment of moderate-to-severe plaque psoriasis, a condition that involves a cell-mediated immune response with some similarities to OLP.[5]

CASE PRESENTATION 1

A 73-year-old female presented with a 12-year history of open mouth sores that made eating uncomfortable. Her condition was initially identified in 2002 by her dentist, who suspected OLP, and she was referred to a maxillofacial specialist. She was told to avoid citrus and spicy foods and was prescribed lidocaine 2% solution to alleviate the burning sensation. A biopsy of the oral mucosa performed in 2003 confirmed the diagnosis of OLP, with no evidence of malignancy. Topical treatments, including corticosteroids, mouthwash formulations, and tacrolimus ointment, provided little relief.

In 2006, the patient was prescribed hydroxychloroquine 200 mg twice daily, with topical tacrolimus 0.1% as needed for flares. She continued to experience frequent flares over the next 1.5 years before discontinuing the oral therapy due to lack of efficacy, the need for regular blood monitoring, and safety concerns. In 2009, she was prescribed methotrexate, which partially controlled her condition over the next year, but she still experienced periodic flares and difficulty with certain foods. Additional treatment options for her recalcitrant condition were discussed, including tumor necrosis factor inhibitors. However, due to problems with insurance coverage for biologic agents, she was prescribed the immunosuppressant mycophenolate mofetil, at 500 mg twice daily to start, and 2 g daily by the second month. After 8 months, she once again discontinued oral therapy due to lack of efficacy and the need for regular blood tests. She maintained treatment with topical dapsone gel and topical corticosteroids, although with limited benefit, for the next 10 months.

When the patient returned to my clinic in early 2015, she had oral mucosal blisters, inflammation, pain, and difficulty eating (Figure 1). She was given a 2-week supply of apremilast and instructed to follow the 5-day titration schedule, to reach a dose of 30 mg twice daily. At the 2-week follow-up visit, the patient reported that she was free of pain and open sores, and was able to eat whatever she desired for the first time in a very long time. In her words, her mouth had "never felt so good." After 1 month of apremilast therapy, the patient experienced a mild flare, for which an oral prednisone (40 mg) taper was added while she maintained the apremilast therapy. Two months later, a short course of prednisone (20 mg for 3 days) was added to control another mild flare (Figure 2). The patient has now been taking apremilast 30 mg twice daily for more than 5 months and is very satisfied with the control of her condition. Her mouth sores have healed, and she continues to take a low dose of prednisone (5 mg daily) to prevent flares (Figure 3). She is able to eat citrus and spicy foods without restriction, and appreciates that no blood monitoring is required. She has not experienced any side effects that were observed in clinical trials of apremilast, such as diarrhea, headaches, or depression.

FIGURE 1. Case 1 patient photographs at visit when apremilast was first prescribed.

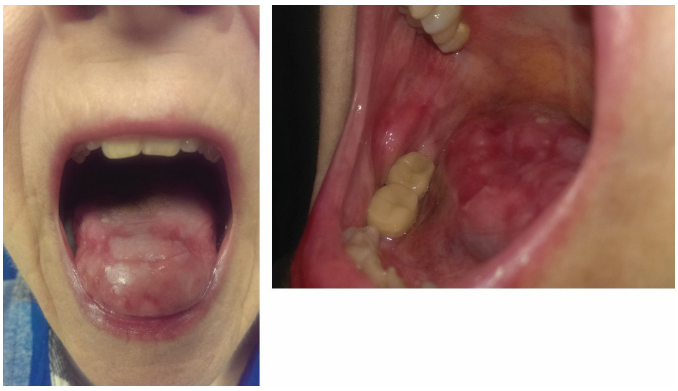


FIGURE 2. Case 1 after 3 months of apremilast treatment.

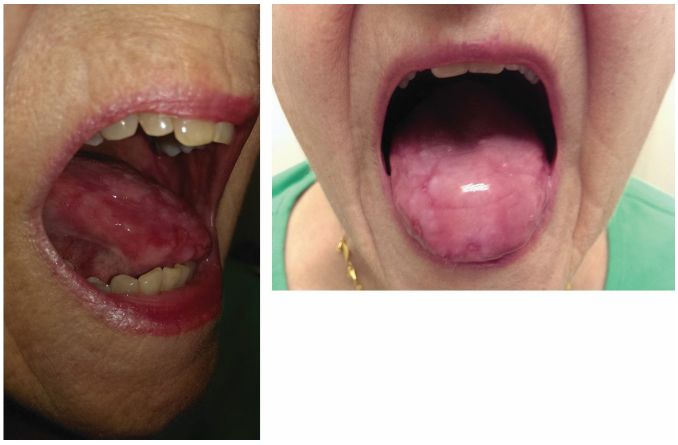
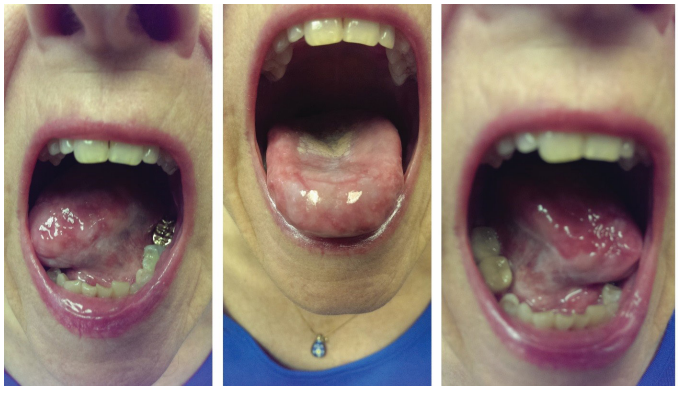


FIGURE 3. Case 1 after 5 months of apremilast treatment.



CASE PRESENTATION 2

A second case involved a 71-year-old female with OLP, confirmed by biopsy 4 years prior to presenting to my practice. She had been treated with topical steroids but remained symptomatic. She had also been prescribed methylprednisolone, which she used intermittently for several months, followed by 40 days of hydroxychloroquine. She continued to experience persistent flares of her mouth sores, and discontinued these oral therapies due to concern over safety and inadequate efficacy. At the time I saw her, her mouth sores were worsening on topical therapy alone.

Upon starting apremilast 30 mg twice daily, she experienced mild nausea and diarrhea following the titration phase. During her 2-week follow-up visit, she was instructed to reduce the dose to 30 mg once daily for the next 2 weeks to minimize the likelihood of side effects. At her next follow-up visit at 4 weeks after initiating apremilast, her mouth sores had cleared and she was no longer experiencing nausea. She wished to remain on once-daily dosing but was instructed to increase the dosage to twice daily if she experienced flares. At present, she has been taking 30 mg apremilast once daily for 6 months and remains in good control, with only minimal erythema of the oral mucosa and no oral discomfort. She has not needed to increase the dose due to flares.

CASE PRESENTATION 3

A 66-year-old female presented to my practice with erythematous and lichenoid papules on her arms and legs. A biopsy taken from her wrist confirmed a diagnosis of lichen planus, and the patient was prescribed a Class II topical corticosteroid. Upon her return to the clinic 2 months later, her skin lesions showed substantial improvement, but she mentioned that she had visited an oral surgeon due to soreness in her mouth. This physician had diagnosed OLP and recommended triamcinolone paste. The topical corticosteroid did not provide relief from the discomfort of eating. A physical examination revealed moderate erythema of the lateral oral mucosa and erosions.

I prescribed apremilast, and the patient has been taking the full 30 mg twice-daily dose for 3 months. During her most recent visit, her mouth was completely clear and free of sores, and she had no pain upon eating. She is extremely happy with her results. The treatment plan is to continue apremilast indefinitely, in view of the chronic nature of lichen planus, but perhaps tapering the dose to once daily.

DISCUSSION

OLP can be refractory to treatment and adversely affects patients' quality of life. The primary aims of therapy for this chronic condition are resolution of painful symptoms, healing of oral mucosal lesions, and maintenance of good oral hygiene. Although there is no specific treatment, topical preparations, including corticosteroids and immunosuppressives, are typically used first-line to provide symptomatic relief. Systemic therapies are used for more difficult cases, although flares can be anticipated, even with systemic treatments. Apremilast, an immunomodulator used for psoriasis, was effective in treating

several patients with OLP, including those with severe cases that were refractory to a variety of approaches. Dosed orally, apremilast had an acceptable safety profile and good tolerability. Additional research will be necessary to fully understand its clinical efficacy and safety in OLP.

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DISCLOSURES

The study was sponsored by Celgene Corporation, Summit, NJ. Dr. Bettencourt has no conflicts of interest to declare.

REFERENCES

1. Davari P, Hsiao HH, Fazel N. Mucosal lichen planus: an evidence-based treatment update. *Am J Clin Dermatol.* 2014;15(3):181-195.
2. Gupta S, Jawanda MK. Oral lichen planus: an update on etiology, pathogenesis, clinical presentation, diagnosis and management. *Indian J Dermatol.* 2015;60(3):222-229.
3. Werneck JT, Costa TO, Stibich CA, Leite CA, Dias EP, Silva JA. Oral lichen planus: study of 21 cases. *An Bras Dermatol.* 2015;90(3):321-326.
4. Krupaa RJ, Sankari SL, Masthan KM, Rajesh E. Oral lichen planus: an overview. *J Pharm Bioallied Sci.* 2015;7(suppl 1):s158-s161.
5. Papp K, Cather JC, Rosoph L, et al. Efficacy of apremilast in the treatment of moderate to severe psoriasis: a randomised controlled trial. *Lancet.* 2012;380(9843):738-746.

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