Oral Erosive Lichen Planus Treated With Efalizumab

Amy Cheng, MD; Caroline Mann; Washington University, School of Medicine, St Louis, Mo

The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 54-year-old white woman presented with a 3-month history of progressive painful lesions on her tongue and oral mucosa. Her primary care physician initially treated her with nystatin and hydrogen peroxide, followed a few weeks later by acyclovir (Zovirax) ointment and a rapid 5-day prednisone taper, without improvement in her symptoms. Two months after the oral lesions developed, violaceous papules began to appear on her body as well. The week before presentation, she complained of difficulty in swallowing pills because of the pain associated with her oral lesions. She did not have a history of liver disease or hepatitis. A review of systems revealed no recent weight changes, fevers, or chills, and except for the symptoms mentioned above, the findings were otherwise unremarkable.

Physical examination demonstrated excoriated erythematous papules and plaques on the bilateral aspect of the arms and on the chest, back, and lower extremities, a few of which appeared violaceous. Oral erosions were present on the tongue, lips, and buccal mucosa (Figure 1), as was an erosive gingivitis. The neck, eyes and eyelids, abdomen, digits, and nails were otherwise normal in appearance. The initial differential diagnosis included oral erosive lichen planus with cutaneous lichen planus as well as cicatricial pemphigoid and pemphigus vulgaris, which were less likely. Two 4-mm punch biopsy specimens were obtained: one was sent for hematoxylin-eosin staining and the other for direct immunofluorescence. A serum sample was also obtained for indirect immunofluorescence. The patient was started on a regimen of prednisone (60 mg/d tapered over 18 days) and topical tacrolimus ointment (twice daily) for the oral lesions. Laboratory tests revealed a low positive antinuclear antibody titer (<1:40) and a slightly low platelet count (128,000/µL), but the hematocrit, erythrocyte sedimentation rate, complete metabolic profile, and thyrotropin level were normal. Histopathologic examination revealed a lichenoid dermatitis with abundant colloid bodies, which was highlighted by IgG, IgM, and C3 on direct immunofluorescence, findings that were consistent with lichen planus. There were no other abnormalities noted on direct or indirect immunofluorescence. After the steroid taper, the patient experienced a slight (approximately 33%) improvement of the oral lesions, but the painful oral erosions and gingivitis persisted despite the continuation of topical tacrolimus therapy.

THERAPEUTIC CHALLENGE

Oral lichen planus is an autoimmune inflammatory disease with a prevalence ranging from 0.5% to 2%. It is generally divided into 3 clinical subtypes: reticular, atrophic or erythematous, and erosive and/or ulcerative. Unlike cutaneous lichen planus, oral lichen planus has a chronic course, with little chance for spontaneous resolution, and most therapies that are currently available are palliative rather than curative. Patients with the erosive and/or ulcerative form of the disease are typically asymptomatic, with pain being the most common complaint, along with burning, swelling, irritation, and dysgeusia. Many topical and systemic immunomodulative agents are currently available for off-label use in this disorder, but an effective treatment modality remains elusive. We report the first case (to our knowledge) of the successful treatment of oral erosive lichen planus with efalizumab.

SOLUTION

Efalizumab therapy was started with an initial dose of 0.7 mg/kg, followed by a dosage of 1.0 mg/kg per week, approximately 3 weeks after the discontinuation of the ste-
Cell-mediated immunity is thought to play a major role in the development of oral lichen planus, and the nature of the initial stimulatory antigen that activates the autoimmune process is unknown. The majority of lymphocytes in the infiltrate of lichen planus are CD8+ cytotoxic cells, which are usually found adjacent to damaged basal keratinocytes. After recognition of an unknown antigen, either an autoreactive or exogenous peptide in a susceptible individual, CD8+ cytotoxic T cells become activated and undergo clonal expansion. The interactions between affected keratinocytes and activated lymphocytes cause a change in the cytokine milieu, and the secretion of mediators such as interleukin (IL) 2, IL-4, IL-10, interferon gamma, and tumor necrosis factor alpha leads to further up-regulation and migration of inflammatory cells into affected areas. Interferon gamma up-regulates the expression of ICAM-1 (intercellular adhesion molecule 1) and VCAM-1 (vascular cell adhesion molecule 1) by basal keratinocytes, Langerhans cells, and other dendritic cells, and ICAM-1 is a ligand for leukocyte function-associated antigen (LFA)-1, which is expressed on the surface of lymphocytes; their interaction enhances and stabilizes interactions between lymphocytes and antigen-presenting cells. Activated T lymphocytes can subsequently trigger apoptosis or cause direct injury to keratinocytes.

Reports of treatments for oral lichen planus in the literature include topical modalities, such as cyclosporin swish and spit, corticosteroids, retinoids, and tacrolimus, and systemic modalities, such as dapsone, hydroxychloroquine, mycophenolate mofetil, thalidomide, and enoxaparin, but randomized control trials comprise only a limited number of these reports. Efalizumab is a recombinant humanized monoclonal IgG1 antibody that binds to CD11a, the alpha subunit of LFA-1 (lymphocyte function–associated antigen 1). It is currently Food and Drug Administration–approved for the treatment of plaque psoriasis. LFA-1, which is an adhesion molecule that is expressed by most leukocytes, plays an important role in T-cell activation, T-cell trafficking, and T-cell reactivation. In vitro studies of mononuclear cells in oral lichen planus have demonstrated a decrease of 60% in migration by peripheral blood mononuclear cells after pretreatment with anti-CD11a antibodies. Normally, LFA-1 binds ICAM-1, which is expressed on the surface of an antigen-presenting cell, allowing T-cell receptor engagement and signaling, which in turn leads to full T-cell activation and proliferation. ICAM-1 is also up-regulated and expressed on the surface of activated endothelial cells, and interaction with LFA-1 mediates the tight adhesion of T cells to epithelial cells and facilitates the trafficking of activated CD4+ T cells from the circulation into the dermis. The CD4+ cells may then subsequently assist in the activation of CD8+ T cells. Efalizumab, by inhibiting CD11a (LFA-1), can lead to the improvement of oral lichen planus via decreased activation and trafficking of T lymphocytes, which play a vital role in its pathologic development.

To our knowledge, this article represents the first reported case of treatment with efalizumab for oral erosive lichen planus. The results are promising, but double-blind, controlled studies are needed to better evaluate the efficacy of efalizumab therapy for oral erosive lichen planus.

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Correspondence: Amy Cheng, MD, Department of Dermatology, Washington University, School of Medicine, 660 S Euclid, Box 8123, St Louis, MO 63110 (amscheng@hotmail.com).

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REFERENCES

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