

Safe and Efficacious Use of a Topical Retinoid Under Occlusion for the Treatment of Mycosis Fungoides

Daniel Aires MD JD,^a Tarek Shaath BS,^c Garth Fraga MD,^b
Anand Rajpara MD,^a Ryan Fischer MD,^a Deede Liu MD,^a

^aUniversity of Kansas Medical Center, Department of Internal Medicine,
Division of Dermatology, Kansas City, KS

^bUniversity of Kansas Medical Center, Department of Pathology, Kansas City, KS

^cUniversity of Kansas School of Medicine, Kansas City, KS

Oral and topical retinoids are widely used for treating Mycosis Fungoides (MF), the most common form of cutaneous t-cell lymphoma (CTCL).^{1,2} While the retinoid-X-receptor-selective bexarotene is the only topical retinoid approved for MF, other retinoids such as tretinoin have also been used.³ As with all topical retinoids, both bexarotene and tretinoin typically cause mild-to-moderate local irritation.^{4,5} This irritation may be reduced by alternating retinoid treatment with mid-potency topical corticosteroid treatment. Use of topical steroids may also bring synergistic benefits in conjunction with retinoids.⁶ An added benefit of combination treatment arises from the fact that steroid-associated skin atrophy can potentially be mitigated by concomitant retinoid usage.⁷

Retinoids under occlusion have been tried used in various settings other than MF. Stam-Posthuma et al attempted unsuccessfully to treat nevi with tretinoin and/or hydrocortisone under occlusion.⁸ Watson et al reported use of 0.025% all-trans retinoic acid under occlusion to treat photoaging.⁹ Fisher et al explored tretinoin under occlusion for prevention of photodamage.¹⁰

We present the first report of MF treated with combined steroid and retinoid wraps. A 76-year-old Caucasian male with folliculotropic MF presented to an academic outpatient dermatology clinic for further management of skin-directed therapy. Physical exam revealed scaly, erythematous papules and plaques with follicular prominence distributed over the trunk and extremities. Fevers, night sweats, and lymphadenopathy were absent. Flow cytometry showed an elevated CD4:CD8 ratio of approximately 30:1. Treatments at time of presentation included topical triamcinolone and clobetasol twice daily to affected areas on the trunk and limbs, as well as interferon alfa 2b three million units subcutaneously biweekly, and extracorporeal photopheresis (ECP) every other week. The systemic treatment regimen did not change during the duration of the case reported here.

At time of presentation most cutaneous lesions were responding to therapy, with the exception of a few resistant raised firm scaly erythematous plaques on the chest, arms

and legs. To address this, a new regimen was tried initially on a single resistant plaque on the right calf (Figure 1). An occlusive Unna wrap was applied to the right calf over a layer of 0.1% tazarotene gel and a layer of 0.1% triamcinolone ointment. The initial wrap stayed in place until the patient's follow up examination two weeks later. At that time the resistant plaque showed decreased erythema and scaling with no local or systemic side effects. Despite the good initial response, the patient chose to switch over to a more convenient and affordable regimen of 0.1% tretinoin and 0.05% clobetasol under plastic-wrap occlusion to be applied at home. Specifically, the patient applied a fresh plastic-wrap dressing each night, alternating tretinoin wraps with clobetasol wraps. Follow up appointments at two-week intervals demonstrated continued improvement in the patient's resistant folliculotropic MF plaque. Treatment was continued for 22 more weeks without any adverse side effects or patient complaints. By that time the patient's right lower extremity plaque had become significantly flatter and smoother, similar in appearance to his non-resistant lesions (Figure 2). Based on this response, other resistant plaques were subsequently treated in the same way.

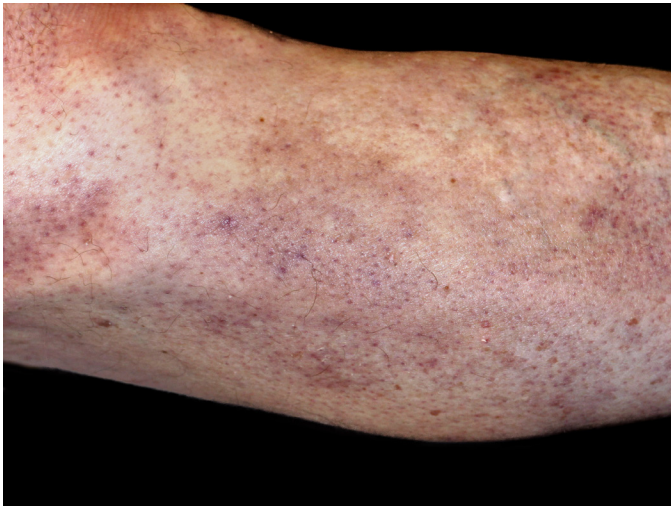
FIGURE 1. Folliculotropic T-cell lymphoma of the right lower leg prior to use of topical retinoids in combination with topical steroids under occlusion.



Skin-directed MF therapies typically include steroids,¹¹ retinoids,¹ mechlorethamine,¹² phototherapy,¹³ and radiotherapy.¹⁴ Folliculotropic MF is generally considered to be more resistant to topical therapies.¹⁵ If MF plaques are resistant to these topical therapies, systemic treatment may be considered. Systemic MF / CTCL treatments include photopheresis,¹⁶ oral retinoids,² histone deacetylase inhibitors,¹⁷ denileukin diftitox,¹⁸ and ultimately conventional chemotherapy.

The present case demonstrated tolerability and efficacy of topical retinoids under occlusion combined with topical

FIGURE 2. Significantly smoother and flatter folliculotropic T-cell lymphoma of the right lower leg after 22 weeks of treatment with topical retinoids in combination with topical steroids under occlusion.



steroids under occlusion for treatment of a resistant folliculotropic MF plaque. This may present an alternative for resistant MF. It also points toward the need for further work exploring treatment of MF and other dermatoses with occluded retinoids and steroids.

Disclosures

The authors have no conflicts of interests to declare.

References

- Martin AG. Bexarotene gel: A new skin-directed treatment option for cutaneous T-cell lymphomas. *J Drugs Dermatol.* 2003;2(2):155-167.
- Duvic M, Hymes K, Heald P, et al. Bexarotene is effective and safe for treatment of refractory advanced-stage cutaneous T-cell lymphoma: multinational phase II-III trial results. *J Clinical Oncol.* 2001;19(9):2456-2471.
- Querfeld C, Rosen ST, Guitart J, et al. Comparison of selective retinoic acid receptor- and retinoic X receptor-mediated efficacy, tolerance, and survival in cutaneous t-cell lymphoma. *J Am Acad Dermatol.* 2004;51(1):25-32.
- Heald P, Mehlmauer M, Martin AG, et al. Topical bexarotene therapy for patients with refractory or persistent early-stage cutaneous T-cell lymphoma: results of the phase III clinical trial. *J Am Acad Dermatol.* 2003;49(5):801-815.
- Griffiths CE, Kang S, Ellis CN, et al. Two concentrations of topical tretinoin (retinoic acid) cause similar improvement of photoaging but different degrees of irritation. A double-blind, vehicle-controlled comparison of 0.1% and 0.025% tretinoin creams. *Arch Dermatol.* 1995;131(9):1037-1044.
- Apisarnthanarax N, Talpur R, Ward S, Ni X, Kim HW, Duvic M. Tazarotene 0.1% gel for refractory mycosis fungoides lesions: an open-label pilot study. *J Am Acad Dermatol.* 2004;50(4):600-607.
- McMichael AJ, Griffiths CE, Talwar HS, et al. Concurrent application of tretinoin (retinoic acid) partially protects against corticosteroid-induced epidermal atrophy. *Br J Dermatol.* 1996;135(1):60-64.
- Stam-Posthuma JJ, Vink J, le Cessie S, Bruijn JA, Bergman W, Pavel S. Effect of topical tretinoin under occlusion on atypical naevi. *Melanoma Res.* 1998;8(6):539-548.
- Watson RE, Craven NM, Kang S, Jones CJ, Kietly CM, Griffiths CE. A short-term screening protocol, using fibrillin-1 as a reporter molecule, for photoaging repair agents. *J Invest Dermatol.* 2001;116(5):672-678.
- Fisher GJ, Wang ZQ, Datta SC, Varani J, Kang S, Voorhees JJ. Pathophysiology of premature skin aging induced by ultraviolet light. *New Engl J Med.* 1997;337(20):1419-1428.
- Zackheim HS. Treatment of cutaneous T-cell lymphoma. *Semin Dermatol.* 1994;13(3):207-215.
- Ramsay DL, Meller JA, Zackheim HS. Topical treatment of early cutaneous T-cell lymphoma. *Hematol Oncol Clin N Amer.* 1995;9(5):1031-1056.
- Pothiwala SZ, Baldwin BT, Cherpelis BS, Lien MH, Fenske NA. The role of phototherapy in cutaneous T-cell lymphoma. *J Drugs Dermatol.* 2010;9(7):764-772.
- Micaily B, Vonderheid EC, Brady LW, Andrews C. Total skin electron beam and total nodal irradiation for treatment of patients with cutaneous T-cell lymphoma. *Inter J Radiat Oncol, Biol, Phys.* 1985;11(6):1111-1115.
- Hunzeker CM, Fangman W, Latkowski JA. Folliculotropic mycosis fungoides. *Dermatol Online J.* 2007;13(1):5.
- Heald P, Rook A, Perez M, et al. Treatment of erythrodermic cutaneous T-cell lymphoma with extracorporeal photochemotherapy. *J Am Acad Dermatol.* 1992;27(3):427-433.
- Olsen EA, Kim YH, Kuzel TM, et al. Phase IIb multicenter trial of vorinostat in patients with persistent, progressive, or treatment refractory cutaneous T-cell lymphoma. *J Clin Oncol.* 2007;25(21):3109-3115.
- Olsen E, Duvic M, Frankel A, et al. Pivotal phase III trial of two dose levels of denileukin diftitox for the treatment of cutaneous T-cell lymphoma. *J Clin Oncol.* 2001;19(2):376-388.

AUTHOR CORRESPONDENCE

Deede Liu MD

E-mail:..... dliu@kumc.edu