Early Mycosis Fungoides

S Lessin

Citation

S Lessin. *Early Mycosis Fungoides*. The Internet Journal of Dermatology. 2008 Volume 7 Number 3.

Abstract

Stuart R. Lessin M.D. is an investigative dermatologist with a research and clinical interest in cutaneous oncology. He has investigated the etiologic role of oncogenic viruses in cutaneous T cell lymphoma (CTCL) and the molecular mechanisms underlying oncogene and tumor suppressor gene expression in development and tumor progression of CTCL. He has developed techniques for the molecular diagnosis of lymphoproliferative skin diseases based on T-cell receptor (TCR) gene expression.

Since 2000, Dr. Lessin has served as Director of Dermatology at the Fox Chase Cancer Center (FCCC) in Philadelphia, Pennsylvania, the nation's first cancer hospital. He oversees clinical care and research programs in melanoma, non-melanoma skin cancer, cutaneous lymphoma and skin wellness. Dr. Lessin's clinical trial investigations focus on the development and testing of topical and skin directed therapies for skin cancer treatment and prevention.

INTRODUCTION

A large percentage of cutaneous T-cell lymphomas (CTCL) present as early mycosis fungoides (MF). The prognosis and treatment of early MF differs dramatically from mid to advanced stages of CTCL. A variety of skin-directed therapies has been shown to be active in early MF and is incorporated into treatment guidelines (1). Retrospective cases series have provided a rationale for therapy in early MF (2,3). A complete response to therapy in early MF has important prognostic significance as it is associated with freedom from tumor progression and a normal life span. This case study will emphasize the rationale for treatment of early MF, the practical selection of skin-directed therapies and their implication on prognosis.

INITIAL PRESENTATION

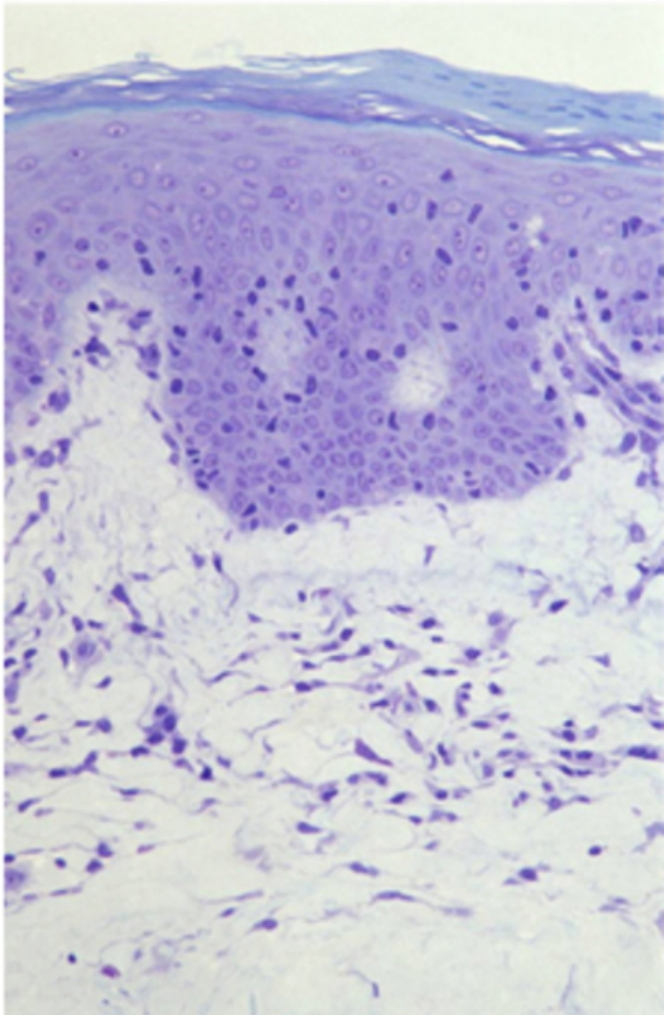
A 55 year old white women developed asymptomatic, erythematous, scaling macules on the trunk in 1983. In 1993, the diagnosis of Stage IA (T1N0M0B0) was established. Her past medical history was only remarkable for a history of breast cancer and bilateral mastectomies. At the time of diagnosis the physical exam revealed erythematous, scaling macules with a digitate configuration about the flanks and hips involving less than ten percent of the body surface area. There was no lymphadenopathy and no organomegaly.

Staging for early MF (T1) includes CBC with Sezary screen and/or flow cytometry, comprehensive metabolic panel and chest x-ray. Staging blood work revealed a normal complete blood count and no Sezary cells detected on Sezary screen. Comprehensive metabolic panel was within normal limits and the chest x-ray revealed no abnormalities.

HISTOLOGY

The diagnostic skin biopsy demonstrated parakeratosis and a superficial, patchy lichenoid infiltrate amid wiry collagen bundles of the papillary dermis. Prominent exocytosis of atypical lymphocytes with cerebriform nuclear contours was present within a non-spongiotic epidermis. Figure 1 shows hematoxilin stained one-micron section, 10 X magnification. Her Stage is IA (T1N0M0B0) CTCL – MF (digitate variant).

Figure 1
Figure 1



THERAPY AND RESPONSE

Her first therapy was topical Nitrogen Mustard 0.01% ointment and resulted in complete response. The patient has had multiple relapses of T1 disease after variable disease free periods (6 – 24 months). She used Clobetasol 0.05% cream for recurrent T1 relapses resulted in complete response. Also, the less potent steroid, triamcinolone 0.1% cream, was used as subsequent therapy for recurrent T1 relapses resulted in complete response. In 2008, Targretin 1% gel in combination with clobetasol 0.05% cream was her most recent therapy for recurrent T1 relapses resulted in complete response. The patient currently has no evidence of disease, 16 years after diagnosis; at age 81.

CONSIDERATIONS FOR DERMATOLOGIST/ONCOLOGIST FROM REFERRING PHYSICIAN

The diagnosis of early MF usually involves issues of interpretation of the skin biopsy and is best addressed by dermatopathologists and clinicians with expertise and experience in CTCL and who have a close working relationship, typically seen in a multidisciplinary team. Early MF is best managed by dermatologists who have the most training and expertise in skin-directed therapies.

MANAGEMENT ISSUES

Rationale for treatment: The first priority of initial therapy of early MF is to induce a complete response with skin-directed therapies. Complete responses are associated with long term survival and freedom from progression. Initial complete responses can be used as an additional prognostic factor to define outcome. After an initial complete response is achieved, any subsequent recurrences of early MF should treated be with further skin-directed therapies with the goal of either inducing a complete response or minimizing clinical involvement.

Multidisciplinary Team considerations: Dermatologists are best trained and experienced in skin-directed therapies including topical and phototherapies and therefore should manage early MF. In rare cases in which electron beam radiation therapy is employed, radiation oncologists are a required.

Clinical evidence: Long term retrospective case-control studies have shown that complete responses to skin-directed therapies (topical mechlorethamine, topical carmustine or total skin electron beam radiation therapy) of early MF is associated with freedom from progression and long term survival (2,3). Additionally, freedom from relapse and overall survival did not differ in patients with stage Ia disease who achieved complete responses (2). Smaller retrospective case series have documented the effectiveness of UVB and PUVA in inducing complete responses in early MF (4,5). Small prospective single arm studies have demonstrated that class I topical steroids and topical retinoids (1% bexarotene gel) are active in early MF (6,7).

TEACHING POINTS

This case highlights that digitate morphology is a part of the MF spectrum of clinical presentations. Patients with early MF can survive multiple decades with chronically relapsing disease and rarely progress to more advanced stages. This case illustrates the rationale for treatment of early MF, i.e., after an initial complete response, subsequent recurrences can be managed conservatively with skin-directed therapies aimed at either inducing a complete response or reduction of

clinical involvement.

Treatment guidelines: The National Comprehensive Cancer Network treatment guidelines for CTCL list a variety of staged based therapies (1). Selection of initial treatment of early MF should be tailored to the individual and may be influenced by age, co-morbidities, access to medication/therapy and compliance issues. Total skin electron beam radiation therapy is considered a second line therapy for early MF.

Skin-directed therapies should be initiated and titrated to maximize clinical response and minimize side effects. The timeframe for observing a clinical response can be tailored to individual needs since time to response and time to relapse have not been shown to influence long term outcomes. For this reason, maintenance therapy for complete responders in early MF is not necessary and can be individualized.

SAFETY CONSIDERATIONS

Skin toxicities can be seen with topical therapies for early MF. Topical mechlorethamine is complicated by irritant and/or allergic contact dermatitis usually seen three to six weeks after initiation of therapy. Topical carmustine is complicated by the formation of telangectasias in treated areas. Bexarotene 1% gel produces an irritant dermatitis and pruritus shortly after initiation of therapy. Topical steroids are often combined with other skin-directed therapies to reduce their side effects.

CONCLUSIONS

Patients with early MF have an excellent prognosis. Skin-directed therapy induced complete responses are associated with long term survival and freedom from disease progression. The goal of initial therapy is to achieve a complete response.

PATIENT FOLLOW-UP

The patient remains alive and well sixteen years after diagnosis with occasionally relapses of T1 disease that remains responsive to topical therapies.

References

1. Horwitz SM, Olsen EA, Duvic M, Porcu P, Kim YH. Review of the treatment of mycosis fungoides and Sézary syndrome: a stage-based approach. J Natl Compr Canc Netw. 2008 Apr;6(4):436-42.
2. Kim YH, Jensen RA, Watanabe GL, Varghese A, Hoppe RT. Clinical stage IA (limited patch and plaque) mycosis fungoides. A long-term outcome analysis. Arch Dermatol. 1996 Nov;132(11):1309-13.
3. Zackheim HS, Amin S, Kashani-Sabet M, McMillan A. Prognosis in cutaneous T-cell lymphoma by skin stage: long-term survival in 489 patients. J Am Acad Dermatol. 1999 Mar;40(3):418-25.
4. Resnik KS, Vonderheid EC. Home UV phototherapy of early mycosis fungoides: long-term follow-up observations in thirty-one patients. J Am Acad Dermatol. 1993 Jul;29(1):73-7.
5. Querfeld C, Rosen ST, Kuzel TM, Kirby KA, Roenigk HH Jr, Prinz BM, Guitart J. Long-term follow-up of patients with early-stage cutaneous T-cell lymphoma who achieved complete remission with psoralen plus UV-A monotherapy. Arch Dermatol. 2005 Mar;141(3):305-11.
6. Zackheim HS, Kashani-Sabet M, Amin S. Topical corticosteroids for mycosis fungoides. Experience in 79 patients. Arch Dermatol. 1998 Aug;134(8):949-54.
7. Breneman D, Duvic M, Kuzel T, Yocum R, Truglia J, Stevens VJ. Phase 1 and 2 trial of bexarotene gel for skin-directed treatment of patients with cutaneous T-cell lymphoma. Arch Dermatol. 2002 Mar;138(3):325-32. Erratum in: Arch Dermatol 2002 Oct;138(10):1386.

Author Information

Stuart R. Lessin, MD
Fox Chase Cancer Center