

CLINICAL VIGNETTE

A Case of Mycosis Fungoides

Jenna Borok¹; G. Peter Sarantopoulos², M.D.; and Veena Vanchinathan³, M.D., FAAD

¹UCLA David Geffen School of Medicine

²Department of Pathology and Laboratory Medicine, UCLA Medical Center

³Division of Dermatology, UCLA David Geffen School of Medicine

Case Presentation

A 69-year-old male with hypertension, hypercholesterolemia, and glucose intolerance presented with a three month history of an intermittent pruritic untreated rash that primarily affected his arms, trunk, and lower legs. The pruritus was exacerbated by heat but was otherwise asymptomatic. He had no prior history of similar rashes. Medical history was negative for skin cancer, tanning, or excessive sun exposure.

Physical examination revealed multiple coalescing pink scaly, occasionally ovoid, patches on the bilateral upper extremities and bilateral lower legs with less prominent involvement of chest, abdomen, and back (Figure A). A few patches on the bilateral upper arms proximal to the triceps demonstrated subtle crinkling atrophy (Figure B).

The clinic differential diagnoses included an eczematous dermatitis and mycosis fungoides. Two punch biopsies were performed. The patient was prescribed triamcinolone (TAC) 0.1% cream to use twice daily for a four-week trial. Pathology examination revealed a superficial band-like infiltrate of lymphocytes (Figure C) and epidermotropism (Figure D). The epidermotropic lymphocytes displayed irregularity in nuclear size and shape (Figure E) with CD4 to CD8-positive T-lymphocyte ratio of approximately 3:1 and loss of CD7 staining (Figure F). A Periodic Acid Schiff (PAS) stain was negative for fungal organisms.

After clinicopathologic correlation, the patient was diagnosed with stage IA mycosis fungoides. He had already noticed marked improvement of his lesions with use of the TAC cream. He was instructed to taper his dosage of TAC cream to once every other day. He was also referred to Hematology-Oncology.

The patient later discontinued the TAC cream and switched to 3 times per week casual sun exposure to affected areas. To date, he remains in clinical remission with no symptomatic or clinically apparent lesions.

Discussion

Mycosis Fungoides (MF) is a form of cutaneous T-cell lymphoma (CTCL).¹ MF is the most common primary cutaneous lymphoma and represents about 44% of primary cutaneous lymphomas.¹ The disease is characterized by a proliferation of small- to medium-size T lymphocytes that are epidermotropic and contain cerebriform nuclei.¹

The median age of diagnosis of MF is between 55-60 years old, and the incidence in males is approximately twice that seen in females.¹ Staging of mycosis fungoides is dependent on the type of lesion seen (patch vs plaque vs tumor), as well as body surface area involvement, with an increased risk of mortality for more advanced stages of the disease. Cutaneous lesions classically affect photoprotected sites such as the breasts, buttocks, inner arms, groin, and lower trunk. Breasts, lower trunk and groin may appear at different stages of progression.^{1,2} Ulceration of cutaneous lesions is a poor prognostic factor. The risk factors for MF include male gender, African-American ancestry, and advanced age.³

MF cells usually arise from CD4⁺ CD45RO⁺ effector memory T cells, which express CCR4 receptors, CCR6, and CCR10; therefore, they fail to circulate in peripheral blood and instead remain fixed within the skin.⁴ Chronic antigenic stimulation, which leads to clonal expansion of the effector memory T cells, is implicated in the development of MF.² Although the mechanism of pathogenesis has not been fully elucidated, CTCL is resistant to apoptosis *in vivo* and extrinsic factors, such as increased number of dendritic cells in early lesions that may contribute to the early growth of MF tumors.^{2,4}

Unlike B-cell lymphomas, the T-cell receptor (TCR) gene loci are rarely involved in chromosomal translocation in T-cell lymphoproliferative disorders.⁴ Several different regulatory cell-cycle pathways are thought to contribute to the development of CTCL, and include NF- κ B (constitutive activation), diminished Fas expression (reduced sensitivity to apoptosis), cyclin upregulation, and loss of RB1.⁴

Diagnosing MF usually requires multiple biopsies and may be clinically challenging due to its often non-specific

presentation. Furthermore if initial biopsies show few reactive lymphocytes that lack cellular atypia, it can be mistaken for an inflammatory skin disease.² When present, crinkling or “cigarette paper” atrophy of cutaneous lesions is a key diagnostic clue. One retrospective study found the median time from symptom onset to diagnosis of MF was 3-4 years but can range to greater than 40 years.⁴ Even though typical early MF displays nonspecific histological findings, identifying a population of cells lacking CD2, CD5, and/or CD7 is highly specific (>90%) for MF.⁴ The International Society for Cutaneous Lymphoma (ISCL) developed a point-based diagnostic algorithm to standardize the diagnostic criteria for MF given the often non-specific histopathologic findings.

The 5-year survival rate of MF is 91%.³ Stage IA MF patients have similar life expectancies as their counterparts of the same age, sex, and race.⁵ Treatment depends on the extent of the disease, the patient’s risk factors, and the impact on the patient’s quality of life.⁵ Early MF (stages IA-IIA) treatment may include skin-directed therapies including topical corticosteroids, topical nitrogen mustard, topical retinoids, phototherapy, total skin electron beam therapy, and low-dose local radiation therapy.⁵ Advanced stage (IIB-IVB) treatment requires systemic therapy. Treatments of advanced MF can include immunomodulators (interferons and retinoids), histone deacetylase inhibitors, alemtuzumab, chemotherapy for refractory or rapidly progressive advanced MF, and allogeneic stem cell transplant for advanced disease, which is potentially curative.⁵

Figure Titles and Legends

Figure A. Clinical Image: Ovoid patch on right thigh.



Figure B. Clinical Image: Ovoid patch on left arm.



Figure C. Histopathology Image: Low-magnification of biopsied skin revealed a superficial band-like infiltrate of lymphocytes with extension upward into overlying epidermis (epidermotropism) (*hematoxylin and eosin at 100x*).

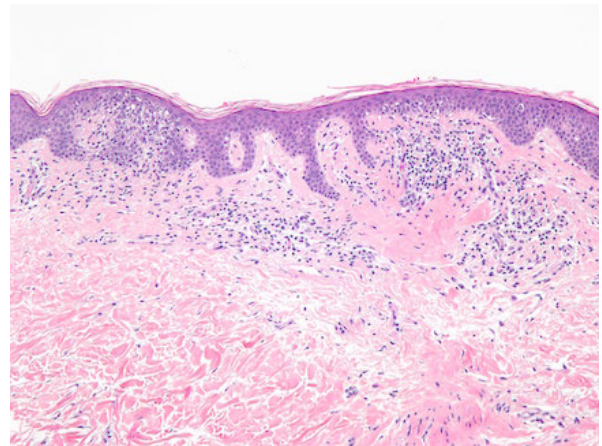


Figure D. Histopathology Image: Closer examination of epidermotropic lymphocytes revealed some “lining up” along the dermal-epidermal junction as well as focal clustering within overlying somewhat thinned epidermis (*hematoxylin and eosin at 200x*).

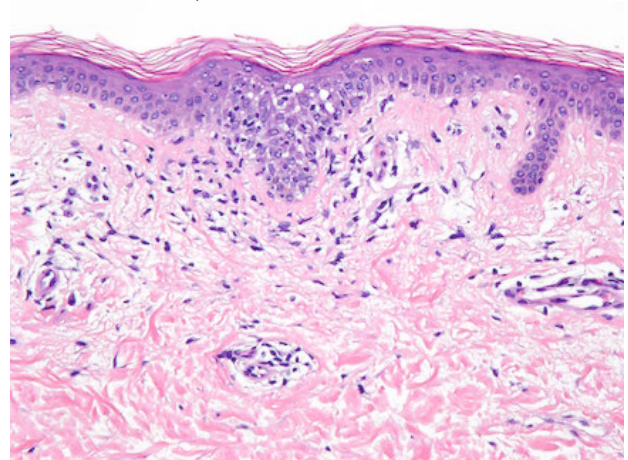


Figure E. Histopathology Image: Close examination of epidermotropic lymphocytes revealed irregularity and clefting of atypical T-lymphocytes extending up to the epidermal surface (*hematoxylin and eosin at 400x*).

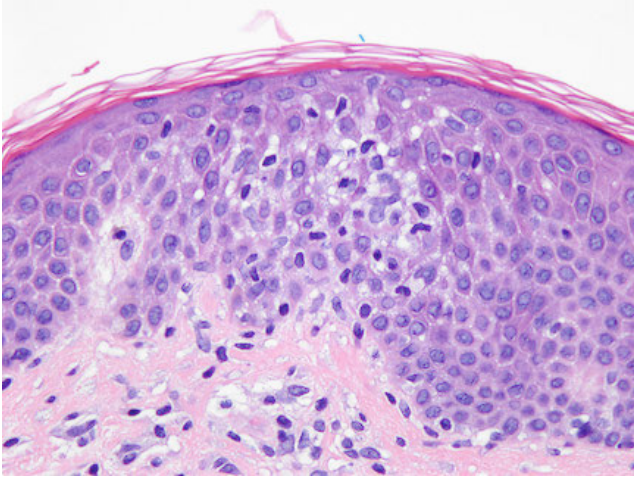
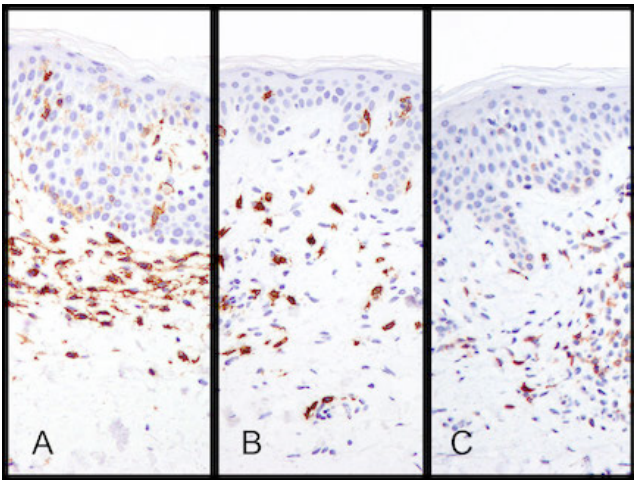


Figure F. Histopathology Image: Pertinent immunohistochemical staining revealed the following: A) Associated superficial dermal and epidermotropic lymphocytes are predominantly CD4-positive T-helper lymphocytes; B) A subset of associated lymphocytes - to include rare epidermotropic lymphocytes - are CD8-positive cytotoxic T-lymphocytes, observed in an approximate ratio of CD4:CD8 = 3:1; C) Epidermotropic lymphocytes show near total loss of CD7 (*CD4, CD8, CD7 immunohistochemistry, respectively at 400x*).



REFERENCES

1. **Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, Ralfkiaer E, Chimenti S, Diaz-Perez JL, Duncan LM, Grange F, Harris NL, Kempf W, Kerl H, Kurrer M, Knobler R, Pimpinelli N, Sander C, Santucci M, Sterry W, Vermeer MH, Wechsler J, Whittaker S, Meijer CJ.** WHO-EORTC classification for cutaneous lymphomas. *Blood.* 2005 May 15;105(10):3768-85. Epub 2005 Feb 3. Review. PubMed PMID: 15692063.

2. **Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C.** Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): part I. Diagnosis: clinical and histopathologic features and new molecular and biologic markers. *J Am Acad Dermatol.* 2014 Feb;70(2):205.e1-16; quiz 221-2. doi: 10.1016/j.jaad.2013.07.049. Review. PubMed PMID: 24438969.
3. **Bradford PT, Devesa SS, Anderson WF, Toro JR.** Cutaneous lymphoma incidence patterns in the United States: a population-based study of 3884 cases. *Blood.* 2009 May 21;113(21):5064-73. doi: 10.1182/blood-2008-10-184168. Epub 2009 Mar 11. PubMed PMID: 19279331; PubMed Central PMCID: PMC2686177.
4. **Wilcox RA.** Cutaneous T-cell lymphoma: 2014 update on diagnosis, risk-stratification, and management. *Am J Hematol.* 2014 Aug;89(8):837-51. doi: 10.1002/ajh.23756. Review. PubMed PMID: 25042790.
5. **Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C.** Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): part II. Prognosis, management, and future directions. *J Am Acad Dermatol.* 2014 Feb;70(2):223.e1-17; quiz 240-2. doi: 10.1016/j.jaad.2013.08.033. Review. PubMed PMID: 24438970.

Submitted April 22, 2015