

A Rare Presentation of Erythrodermic Mycosis Fungoides

Tarang Goyal, MD; Anupam Varshney, MD

Although rare, of all the cutaneous lymphoid malignancies, cutaneous T-cell lymphomas (CTCLs) constitute 65% of all lymphomas, of which 50% are patients with mycosis fungoides (MF). The erythrodermic variant of MF, a malignancy of mature, skin homing, clonal T lymphocytes, usually presents in mid to late adulthood. We present a man in his late 30s with intractable progressive erythroderma of 18 months' duration, patchy alopecia, palmoplantar keratoderma, mucosal thickening, hyperpigmentation, and intense itching as a case of erythrodermic MF. There was no systemic involvement. Diagnosis was confirmed by biopsies from multiple sites and immunohistochemistry. He was categorized with stage IIIA MF according to the International Society for Cutaneous Lymphomas/European Organization of Research and Treatment of Cancer (ISCL/EORTC) revised classification system. Psoralen plus UVA therapy and low-dose methotrexate resulted in clearance of lesions; regular follow-up visits were conducted to monitor progression to Sézary syndrome (SS). Progression to SS has to be monitored regularly in these patients.

Cutis. 2012;89:229-232, 236.

The skin is the second most common site of extranodal lymphomas, with the gastrointestinal tract being the most common. Mycosis fungoides (MF), a prototype of these cutaneous T-cell lymphomas (CTCLs), is defined as peripheral, epidermotropic, non-Hodgkin lymphoma of low-grade malignancy initially presenting in the skin and showing

clinical progression from patch, plaque, tumor stage, and erythrodermic stages, as well as poor survival in these progressive stages. Since MF was first described in 1806, there has been much confusion regarding this disease. Recent advances have been made in cellular and immunologic studies, and the International Society for Cutaneous Lymphomas/European Organization of Research and Treatment of Cancer (ISCL/EORTC) reclassified the disease accordingly.¹ Mycosis fungoides has many clinical variants with varied and atypical presentations, and thus has earned the title of second great mimicker after syphilis. Clinical suspicion of MF provides early diagnosis and treatment with better patient survival.

Case Report

A man in his late 30s presented in the dermatology outpatient department with concerns of hair loss in patchy areas of the scalp, thickening of skin on the palms and soles, thickening and discoloration of oral mucosa, and generalized thickening of skin with scaling. Intense itching in all of the lesions also was present. The lesions appeared 6 years prior to presentation as reddish patches with scaling and itching on covered areas of the body such as the thighs, trunk, back, and upper arms. The lesions gradually increased in both size and number, mostly in the last 18 months, to involve the whole body, scalp, oral mucosa, and palms and soles. On examination, diffuse, erythematous, lichenified, scaly lesions were present on approximately 80% of the body surface area with sparing of body folds (Figure 1). Scales were large, adherent, and polygonal in shape. The scalp showed patchy alopecia with hyperpigmentation, follicular plugging, and thickening of the skin (Figure 2A). The buccal mucosa showed lacy reticular hyperpigmentation and thickening (Figure 2B). Palmoplantar keratoderma in the form of diffuse hyperkeratosis was present. Few lymph nodes were palpable in the neck and axillary region, which were less than 1.5 cm on largest horizontal diameter, freely mobile, discrete, nontender, and rubbery in consistency.

From Muzaffarnagar Medical College, Meerut, Uttar Pradesh, India. Dr. Goyal is from the Department of Dermatology and Dr. Varshney is from the Department of Pathology.

The authors report no conflict of interest.

Correspondence: Tarang Goyal, MD, Department of Skin, VD, and Leprosy, Muzaffarnagar Medical College and Hospital, 105 Somdutt Vihar, Meerut, Uttar Pradesh, 250004 India (anupam_path@yahoo.co.in).

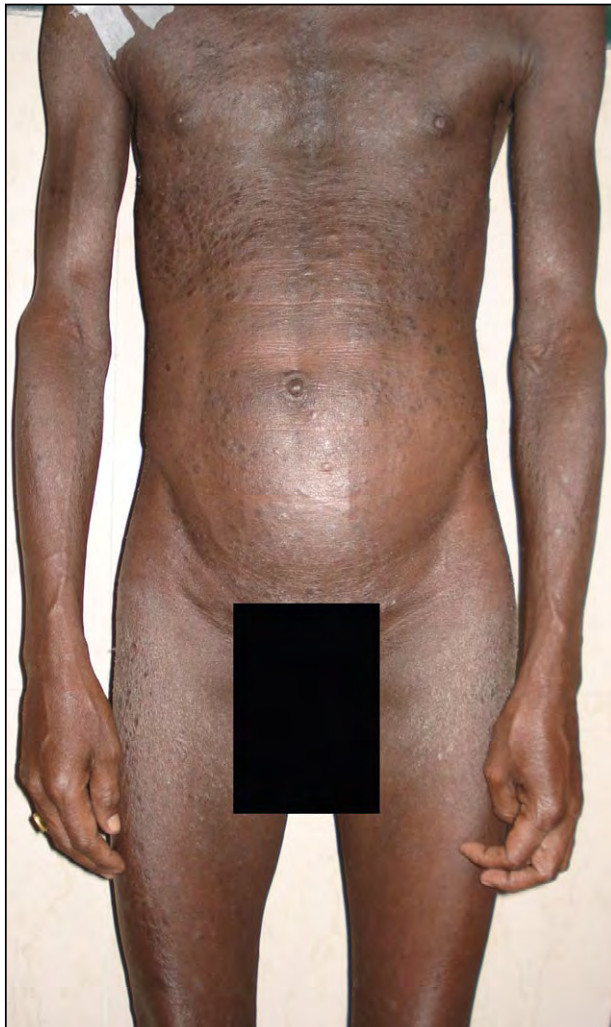


Figure 1. Erythroderma, redness, and scaling with sparing of body folds.

His complete blood cell count revealed the following levels: hemoglobin, 13.4 g/dL (reference range, 14.0–17.5 g/dL); white blood cell count, 6600 cells/ μ L (reference range 4500–11,000 cells/ μ L); differential white blood cell count (neutrophils, 73% [reference range, 66%]; lymphocytes, 25% [reference range, 34%]; monocytes, 1% [reference range, 4%]; eosinophils, 1% [reference range, 2.7%]; basophils, 0% [reference range, 0.3%]); and serum lactate dehydrogenase, 352 U/L (reference range, 100–200 U/L). Liver function and renal function tests did not reveal any abnormalities. Fine-needle aspiration cytology and histopathology of nodes showed dermatopathic lymphadenopathy. Because of the chronic nature of the lesions with itching, a presumptive diagnosis of MF was made and biopsies were performed from the scalp, skin (the most indurated area was biopsied), and buccal mucosa. The hematoxylin and eosin-stained section of the skin and mucosal biopsy showed variable acanthosis and atrophy as well as elongation of rete ridges with presence of a mononuclear cell infiltrate of variable density in the papillary dermis admixed with few eosinophils (Figure 3). There was extension of these cells in the epidermis (epidermotropism) in a lacunar space (retraction artifact) without spongiosis (Figure 4). Presence of this prominent epidermotropism distinguished it from Sézary syndrome (SS). There was prominent papillary dermal fibrosis. The atypical mononuclear cells were small to medium sized with cerebriform nuclei and formed Pautrier microabscesses at places. The scalp biopsy showed prominent folliculotropism. These atypical lymphocytes were CD3⁺ and CD5⁺ (Figure 5) and CD7⁻ (Figure 6) on immunohistochemistry. Computed tomography of the chest, abdomen, and pelvis, as well as bone marrow aspiration cytology, did not reveal any pathology.



Figure 2. Patchy alopecia with hyperpigmentation and scaling (A). The buccal mucosa showed lacy reticular hyperpigmentation (B).

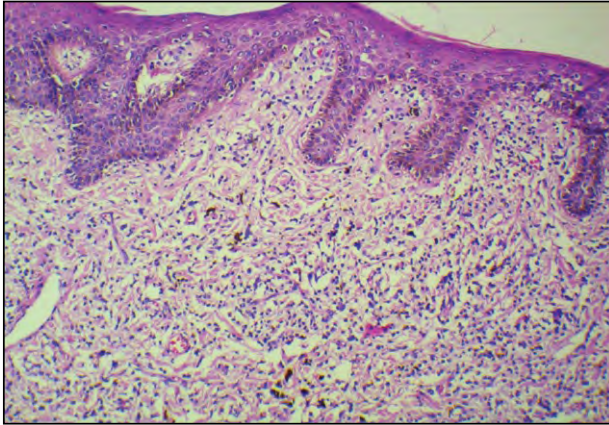


Figure 3. Epidermal thinning, elongation of rete ridges, and diffuse mononuclear cell infiltration with prominent dermal fibrosis (H&E, original magnification $\times 40$).

No organomegaly was evident. Sézary cells were less than 5%, the absolute value being 66 cells/mm³ (Sézary cells ≤ 1000 cells/mm³) in peripheral blood smears. Lymph node biopsy showed dermatopathic lymphadenopathy. According to updated ISCL/EORTC staging classification,¹ he was diagnosed with the erythrodermic variant of MF, stage IIIA (T4N1M0B0): T4, erythroderma; N1, clinically abnormal peripheral lymph nodes, histopathology Dutch grade 1; M0, no visceral organ involvement; and B0, absence of significant blood involvement, $\leq 5\%$ of peripheral blood lymphocytes are atypical (Sézary) cells.¹ Psoralen plus UVA therapy and low-dose methotrexate resulted in clearance of lesions; regular follow-up visits were conducted for monitoring of progression for SS.

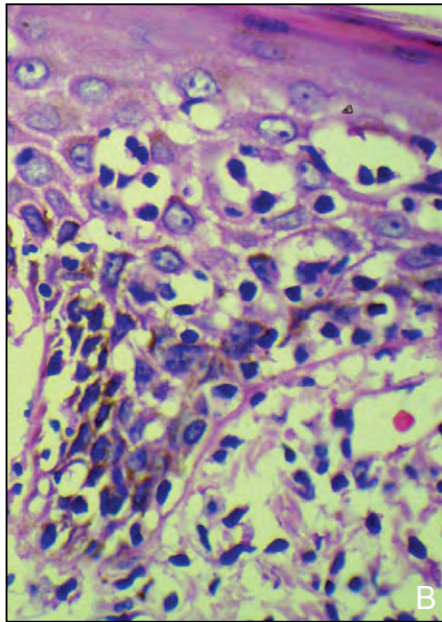
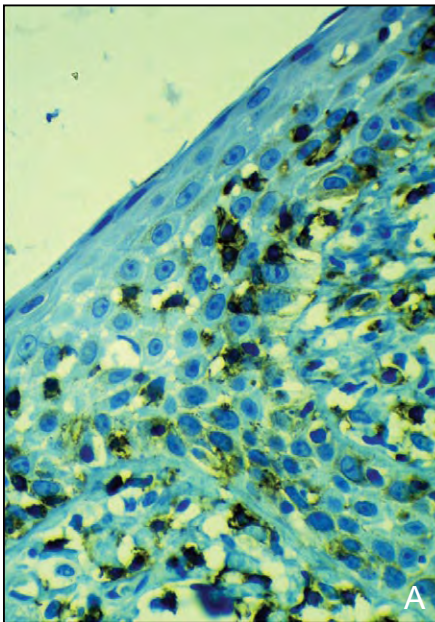


Figure 4. Prominent epidermotropism with CD5 atypical cells (A [CD5, original magnification $\times 100$] and B [H&E, original magnification $\times 100$]).

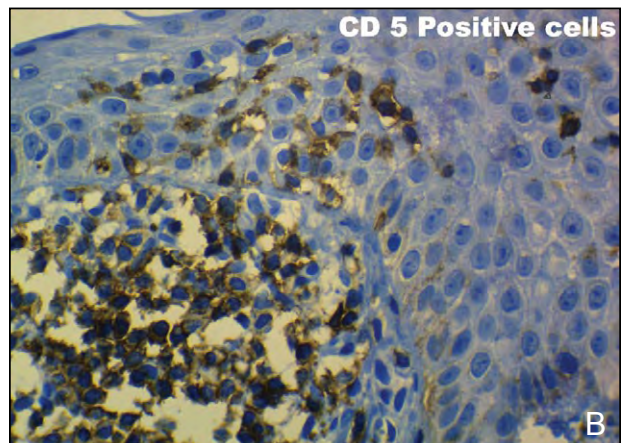
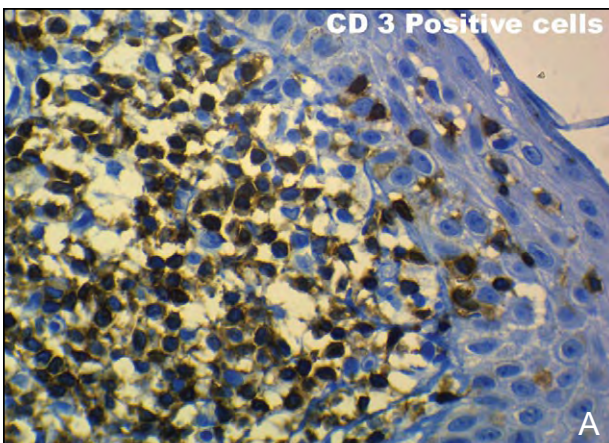


Figure 5. Immunohistochemistry showed CD3⁺ (A)(original magnification $\times 100$) and CD5⁺ (B)(original magnification $\times 100$) cells.

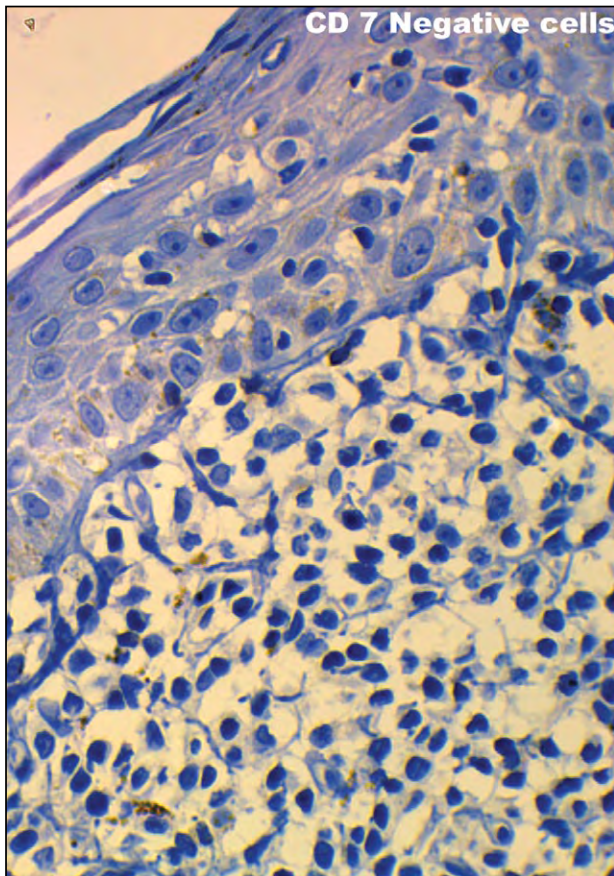


Figure 6. Immunohistochemistry showed CD7⁻ cells (original magnification $\times 100$).

Comment

Mycosis fungoides, a rare CTCL of mature, skin homing, clonal, malignant T lymphocytes, has an annual incidence of 0.36 per 100,000 person-years in the United States.² It usually presents in mid to late adulthood (5th–6th decades) with a male to female ratio of 2 to 1. It is less common in Asians and Hispanics. The erythrodermic variant was originally described in 1892. Erythroderma occurs as progression from the plaque or patch stage of MF (secondary SS) or it may arise *de novo*. It differs from SS by the lack of elevated numbers of circulating Sézary cells and often is termed *pre-Sézary erythroderma*, indicating that some of the cases eventually progress to SS.³

Sézary syndrome, an erythrodermic and leukemic variant of CTCL, is defined by a triad of erythroderma; generalized lymphadenopathy; and circulating Sézary cells in the skin, lymph nodes, and peripheral blood. There is diffuse infiltration of skin by T cells. According to the EORTC and World Health Organization classification, a case of SS must demonstrate 1 or more of the following criteria: an absolute Sézary cell count of at least 1000 cells/mm³, a CD4/CD8 ratio of 10 or higher

caused by an increase in circulating T cells and/or an aberrant loss or expansion of pan T cell markers evidenced by flow cytometry; increased lymphocyte counts with evidence of a T cell clone in the blood by Southern blot analysis or polymerase chain reaction; or chromosomally abnormal T cell clone.⁴ On histopathology of lymph nodes, paracortical areas are seen infiltrated with Sézary cells, which further acknowledges that SS is part of a broader spectrum of erythrodermic CTCL.

On the other spectrum, pre-Sézary erythroderma is defined by the same clinical presentation but without organomegaly, blood involvement of Sézary cells less than 1000 cells/mm³, and no Sézary cell infiltration seen in the lymph nodes. Clinically, it presents as refractory erythroderma with pruritus, palmoplantar keratoderma, alopecia, onychodystrophy, ectropion, and leonine facies.

The 5-year survival rate of SS is only 24%, whereas the erythrodermic CTCL form is a chronic, slow-growing CTCL with a better prognostic and survival rate. Various prognostic factors include patient age, TNMB stages, overall clinical stage groupings, and presence or absence of extracutaneous disease. According to Kim et al,⁵ patient age at presentation, the overall stage, and peripheral blood involvement were the strongest predictive factors for patient survival in SS. When extracutaneous involvement or transformation into high-grade lymphoma occurs, expected survival usually is 1 year.⁶

Our patient presented in an earlier age group and was better seen as progression from plaque stage to erythrodermic stage but without systemic involvement. Erythrodermic MF should be differentiated from SS, adult T-cell leukemia, actinic reticuloid, atopic dermatitis, drug reactions, psoriasis, and other causes of erythroderma.⁷ In patients with such refractory erythrodermas, a diagnosis of this disorder can be considered and evaluated with proper treatment, staging, and future monitoring for progression to more aggressive indolent lymphomas for better patient survival and outcome.

REFERENCES

- Olsen E, Vonderheid E, Pimpinelli N, et al. Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood*. 2007;110:1713-1722.
- Weinstock MA, Horm JW. Mycosis in the United States. increasing incidence and descriptive dermatology. *JAMA*. 1988;260:42-46.

CONTINUED ON PAGE 236

11. Hoffmann K, Laperre J, Avermaete A, et al. Defined UV protection by apparel textiles. *Arch Dermatol*. 2001;137:1089-1094.
12. Palm MD, O'Donoghue MN. Update on photoprotection. *Dermatol Ther*. 2007;20:360-376.
13. US Food and Drug Administration. Rulemaking History for OTC Sunscreen Drug Products Final Monograph. US Food and Drug Administration Web site. http://www.access.gpo.gov/nara/cfr/waisidx_06/21cfr352_06.html. Accessed April 19, 2012.
14. Lim HW, Wang SQ. The Skin Cancer Foundation's guide to sunscreens. Skin Cancer Foundation Web site. <http://www.skincancer.org/prevention/sun-protection/sunscreen/the-skin-cancer-foundations-guide-to-sunscreens>. Published 2011. Accessed April 19, 2012.

CONTINUED FROM PAGE 232

3. Beuchner SA, Winkelmann RK. Pre-Sézary erythroderma evolving to Sézary syndrome. a report of seven cases. *Arch Dermatol*. 1983;119:285-291.
4. Slater DN. The new World Health Organization-European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas: a practical marriage of two giants. *Br J Dermatol*. 2005;153:874-880.
5. Kim YH, Bishop K, Verghese A, et al. Prognostic factors in erythrodermic mycosis fungoides and the Sézary syndrome. *Arch Dermatol*. 1995;131:1003-1008.
6. Toro JR, Stoll HL Jr, Stomper PC, et al. Prognostic factors and evaluation of mycosis fungoides and Sézary syndrome. *J Am Acad Dermatol*. 2007;13:54-58.
7. Nashan D, Faulhaber D, Ständer S, et al. Mycosis fungoides: a dermatological masquerader. *Br J Dermatol*. 2007;156:1-10.



NEED MORE INFORMATION?

Access these related articles
in our online archives at
www.cutis.com

- ▾ Carbamazepine Hypersensitivity Syndrome Mimicking Mycosis Fungoides
- ▾ Hypopigmented Mycosis Fungoides: A Report of 7 Cases and Review of the Literature
- ▾ Recalcitrant Tinea Corporis as the Presenting Manifestation of Patch-Stage Mycosis Fungoides

Use our Advanced Search to find
these articles and more online!