

The importance of lymph node examination: Simultaneous diagnosis of hypopigmented mycosis fungoides and follicular B-cell lymphoma



Mathew X. Joseph, BS, Ashley D. Brown, MD, and Loretta S. Davis, MD
Augusta, Georgia

Key words: cutaneous T-cell lymphoma; follicular B-cell lymphoma; mycosis fungoides; simultaneous diagnosis.

INTRODUCTION

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL). Its typical course is characterized by a progression of patches, plaques, and tumors. Follicular B-cell lymphoma, the second most common non-Hodgkin lymphoma (NHL), presents with lymphadenopathy and is characterized by a translocation between chromosomes 14 and 18, resulting in overexpression of the B-cell lymphoma (*bcl*)-2 gene. In most patients, the course of each of these lymphomas is indolent with slow progression. Here we describe a case of MF and follicular lymphoma diagnosed simultaneously, a rare occurrence with only 2 previously reported cases. These contemporaneous diagnoses highlight the complexity of lymphoproliferative disorders and the importance of lymph node biopsy in the diagnostic workup of lymphoma.

REPORT OF A CASE

A woman in her late 50s complained of recurrent boils of 8 months' duration. Physical examination found erythematous perifollicular papules in the inguinal folds. Mupirocin ointment and chlorhexidine washes were recommended. Chart review documented both bilateral inguinal and axillary lymphadenopathy on physical examination by another provider 1 month prior.

At the same visit and incidentally, the patient reported a 7-year history of lighter patches of skin slowly increasing in size and number without any precedent rash. Examination found scattered irregularly shaped hypopigmented patches on bilateral thighs, left arm, and abdomen (Fig 1).

Abbreviations used:

bcl:	B-cell lymphoma gene
CTCL:	cutaneous T-cell lymphoma
MF:	mycosis fungoides
NHL:	non-Hodgkin lymphoma

Histopathology found interface dermatitis with exocytosis of lymphocytes into the epidermis (Fig 2). Immunohistochemistry found positive CD4 staining of lymphocytes, isolated weak CD8 staining, and some loss of CD7. T-cell receptor- β gene rearrangement was positive, confirming the diagnosis of hypopigmented MF, stage 1A. Narrow-band ultraviolet B therapy was initiated.

At follow-up, despite improvement of the folliculitis and no further furuncle formation, bilateral lymphadenopathy persisted. Two months after her diagnosis of MF, inguinal lymph node biopsy was performed. Histopathology found follicular and interfollicular hyperplasia with lack of polarity (Fig 3). Immunohistochemical staining was significant for aberrant upregulation of *bcl*-2 in follicular B cells and *bcl*-6 positivity within nodules. Fluorescence in situ hybridization studies found t(14;18) translocation with upregulation of *bcl*-2, and flow cytometry found B cells comprising more than 50% of lymphocytes, consistent with follicular B-cell lymphoma grade 2. Based on positive lymphadenopathy above and below the diaphragm confirmed on computed tomography and the symptom of recurring night sweats, stage IIIB disease was diagnosed. No immediate treatment was warranted given the indolent nature of follicular lymphoma. At

From the Division of Dermatology, Medical College of Georgia at Augusta University.

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Ashley D. Brown, MD, 1004 Chafee Avenue, Augusta, GA 30904. E-mail: abrown33@augusta.edu.

JAAD Case Reports 2018;4:590-2.

2352-5126

© 2018 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2018.05.017>



Fig 1. Hypopigmented patches are scattered over the bilateral thighs.

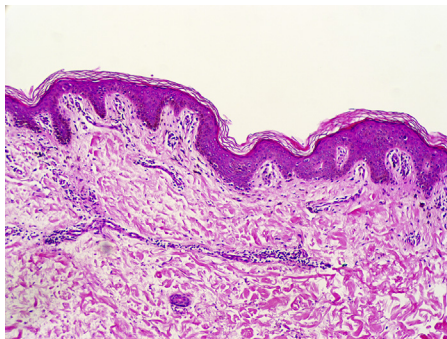


Fig 2. Histopathology found a sparse interface dermatitis, exocytosis of lymphocytes into the epidermis, and melanophages in the superficial dermis. (Hematoxylin-eosin stain; original magnification, ×10.)

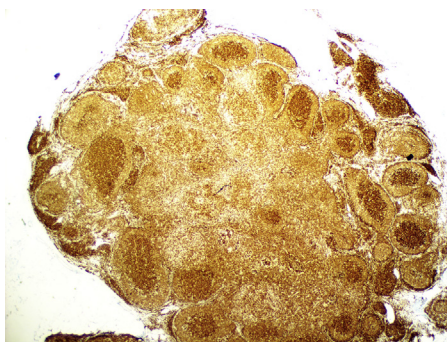


Fig 3. Follicular and interfollicular hyperplasia is seen within this enlarged lymph node. Immunohistochemical staining of follicular B-cells shows aberrant upregulation of *bcl-2*. (Original magnification, ×4.)

1-year follow-up, the patient's follicular lymphoma was stable, and her hypopigmented MF had clinically resolved with narrow-band ultraviolet B therapy.

DISCUSSION

Hypopigmented MF, typically a patch stage diagnosis without lymphadenopathy, rarely progresses past stage IB.¹ The differential diagnosis for lymphadenopathy in this particular case includes

coincident infection, dermatopathic lymphadenopathy, lymph node involvement by MF, and second malignancy. Progressing through this differential, lymphadenopathy caused by furunculosis is highly atypical.² Dermatopathic lymphadenopathy may be present in MF but typically in inflammatory varieties such as the erythrodermic form.³ As mentioned, lymph node enlargement caused by malignant T cells would be unexpected in purely patch stage MF, particularly in hypopigmented MF. Thus, second malignancy would need to be strongly considered in this case. A 2016 Surveillance, Epidemiology, and End Results (SEER) database population-based study found the standardized incidence ratio of a second malignancy developing, most commonly NHL, is greatest within the first year after diagnosis of CTCL and remains increased for years afterward.⁴ Independent of risk associated with CTCL treatments and likely owing to dysfunctional immune surveillance, a diagnosis of CTCL increases future risk of NHL; yet, simultaneous diagnosis is rare.⁴ Our literature search returned only 12 simultaneous diagnoses of CTCL and B-cell lymphoma, all from 1979 to 2009, 2 of which were MF and follicular B-cell lymphoma as in our patient.⁵ Other concurrent B-cell lymphomas included nodular sclerosing Hodgkin lymphoma, lymphoplasmacytic lymphoma, Waldenstrom macroglobulinemia, small lymphocytic lymphoma, diffuse large B-cell lymphoma, and multiple myeloma. Of the 12 CTCL diagnoses, all were MF or Sézary syndrome; none were reported as a hypopigmented variant. Based on our review of the literature, our patient would appear to be the first reported case, to our knowledge, of hypopigmented MF in conjunction with any secondary B-cell lymphoma. Given the recent acknowledgement of the increased risk of NHL in the first year after CTCL diagnosis, we posit that if there is high clinical suspicion for CTCL on initial visit, any unusual or longstanding lymphadenopathy warrants biopsy. Clinicians should have a low threshold of suspicion for simultaneous secondary malignancy when patients with low-grade MF such as this patient with hypopigmented MF present with lymphadenopathy. It follows that no matter the stage, complete lymph node examination should be performed at each visit in all patients with CTCL.

REFERENCES

1. Furlan FC, Sanches JA. Hypopigmented mycosis fungoides: a review of its clinical features and pathophysiology. *An Bras Dermatol.* 2013;88:954-960.
2. Ibler KS, Kromann CB. Recurrent furunculosis-challenges and management: a review. *Clin Cosmet Investig Dermatol.* 2014;7:59-64.

3. Vonderheid EC, Diamond LW, Lai S, et al. Lymph node histopathologic findings in cutaneous T-cell lymphoma: a prognostic classification system based on morphologic assessment. *Am J Clin Pathol.* 1992;97:121-129.
4. Amber KT, Bloom R, Nouri K. Second primary malignancies in CTCL patients from 1992 to 2011: A SEER-based, population-based study evaluating time from CTCL diagnosis, age, sex, stage, and CD30+ subtype. *Am J Clin Dermatol.* 2015; 17:71-77.
5. Herro E, DiCaudo DJ, Davis MD, et al. Review of contemporaneous mycosis fungoides and B-cell malignancy at Mayo Clinic. *J Am Acad Dermatol.* 2009;61:271-275.