Primary Cutaneous Follicle Center Lymphoma Mimicking Folliculitis

Ramya Chockalingam, MD; Savina Aneja, MD; Anisha B. Patel, MD

PRACTICE **POINTS**

- Atypical or unresponsive folliculitis should be biopsied.
- Primary cutaneous follicle center lymphoma can mimic folliculitis or Grover disease.

Primary cutaneous follicle center lymphoma (PCFCL) is the most common type of cutaneous B-cell lymphoma. The cutaneous manifestations of PCFCL typically include solitary erythematous or violaceous plaques, nodules, or tumors of varying sizes. Grouped lesions also may be observed, but multifocal disease is rare. We report the case of a 54-year-old woman diagnosed with PCFCL with an unusual clinical presentation resembling folliculitis or Grover disease. Histologic studies demonstrated extensive lymphoma cells in a nodular and diffuse pattern. Immunohistochemical studies demonstrated that the neoplastic cells were positive for CD20, CD79a, BCL-2, and BCL-6; CD3, CD5, and cyclin D1 were negative. These findings were consistent with PCFCL. Further evaluation for systemic disease via positron emission tomography–computed tomography and bone marrow biopsy was unremarkable. Increased awareness of this presentation of PCFCL can facilitate earlier diagnosis and intervention, which may result in improved patient outcomes.

Cutis. 2018;101:E30-E33.

The 2008 World Health Organization and European Organization for Treatment of Cancer joint classification has distinguished 3 categories of primary cutaneous B-cell lymphomas: primary cutaneous follicle center lymphoma (PCFCL), primary cutaneous diffuse large B-cell lymphoma, and primary cutaneous marginal zone lymphoma.[1-3] Primary cutaneous follicle center lymphoma is the most common type of cutaneous B-cell lymphoma, accounting for approximately 60% of cases worldwide.[4] The median age at diagnosis is 60 years, and most lesions are located on the scalp, forehead, neck, and trunk.[5] Histologically, PCFCL is characterized by dermal proliferation of centrocytes and centroblasts derived from germinal center B cells that are arranged in either a follicular, diffuse, or mixed growth pattern.[1] The cutaneous manifestations of PCFCL include solitary erythematous or violaceous plaques, nodules, or tumors of varying sizes.[4] Grouped lesions also may be observed, but multifocal disease is rare.[1] We report a rare presentation of PCFCL mimicking folliculitis with multiple multifocal papules on the back.

Case Report

A 54-year-old woman presented with fever and leukocytosis of 4 days' duration and was admitted to the hospital for presumed sepsis. She had a history of mastectomy for treatment of ductal carcinoma in situ of the right breast 5 years prior to the current presentation and endocrine therapy with tamoxifen. Her symptoms were thought to be a complication from a surgery for implantation of a tissue expander in the right breast 5 years prior to presentation.

During her hospital admission, she developed a papular and cystic eruption on the back that was clinically suggestive of folliculitis, transient acantholytic dermatosis (Grover disease), or miliaria rubra (Figure 1). This papular and cystic eruption initially was managed conservatively with observation as she recovered from an occult infection. Due to the persistent nature of the eruption on the back, an excisional biopsy of the cystic component was performed 2 months after her discharge from the

From the Department of Dermatology, University of Texas Medical School, Houston. Dr. Patel also is from the Department of Dermatology, University of Texas MD Anderson Cancer Center, Houston.

The authors report no conflict of interest.

Correspondence: Anisha B. Patel, MD, Department of Dermatology, University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1452, Houston, TX 77030 (apatel11@mdanderson.org).

hospital. Histologic studies showed a dense infiltrate of lymphocytes, which expanded into the deep dermis in a nodular and diffuse growth pattern that was accentuated in the periadnexal areas. The B lymphocytes were small and hyperchromatic with few scattered centroblasts (Figure 2). Further immunohistochemical studies demonstrated that the neoplastic cells were positive for CD20, CD79a, BCL-2, and BCL-6; CD3, CD5, and cyclin D1 were negative. Staining for antigen Ki-67 revealed a proliferation index of 15% to 20% among the neoplastic cells (Figure 3). These findings were consistent with either PCFCL or secondary cutaneous follicle center lymphoma.

Further evaluation for systemic disease was unremarkable. Positron emission tomography–computed tomography revealed no evidence of nodal lymphoma, and a bone marrow biopsy was negative. Other laboratory studies including lactate dehydrogenase were within reference range, which conferred a diagnosis of PCFCL. The patient was treated with localized electron beam radiation therapy to the skin of the mid back for a total dose of 24 Gy in 12 fractions at 2 Gy per fraction once daily over a 12-day period. She tolerated the treatment well and has remained clinically and radiographically without evidence of disease for more than 3 years.

Comment

Because the incidence of cutaneous B-cell lymphomas has been increasing, especially among males, non-Hispanic whites, and adults older than 50 years,[1] it is important for clinicians to have a high index of suspicion for this entity.

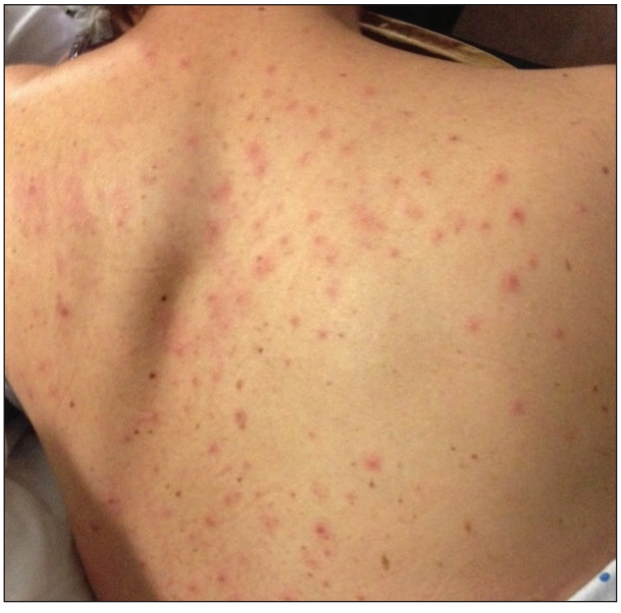

FIGURE 1. Erythematous papules scattered across the back in a follicular distribution that varied in morphology from indurated and pseudopustular to eroded and crusted, which was clinically suggestive of folliculitis.

In our patient, the clinical findings of a papular, largely asymptomatic eruption on the back with acute onset were initially thought to be consistent with folliculitis; the differential diagnosis included transient acantholytic dermatosis and miliaria rubra. Lymphoma was not in the initial clinical differential, and we only arrived at this diagnosis based on histopathologic evaluation.

The neoplastic cells typically are positive for CD20, CD79a, and BCL-6, and negative for BCL-2.[4] Most cases of PCFCL do not express the t(14;18) translocation involving the BCL-2 locus, in contrast to systemic follicular lymphoma.[1] Systemic imaging and evaluation is needed to definitively differentiate PCFCL from systemic lymphoma with cutaneous involvement. Our patient was unusual in that BCL-2 was strongly staining in the setting of a negative systemic workup.

With regard to treatment of PCFCL, electron beam radiation therapy is highly effective and safe in patients

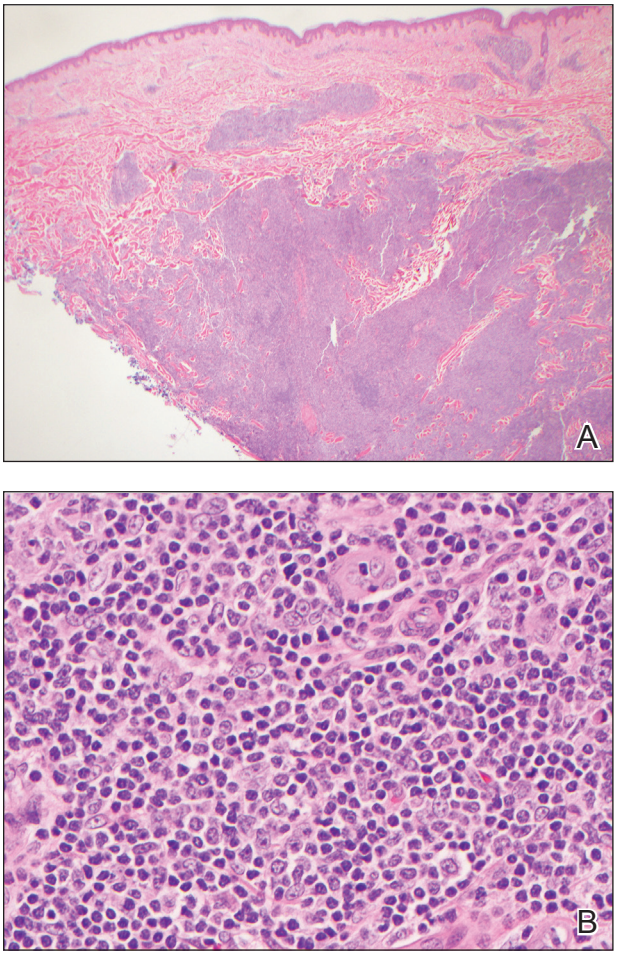

FIGURE 2. A nodular to diffuse infiltrate of lymphocytes was present in the mid and deep dermis with sparing of the papillary dermis (A)(H&E, original magnification ×40). Small hyperchromatic lymphocytes infiltrate was seen between the larger pale centroblasts (B)(H&E, original magnification ×400).

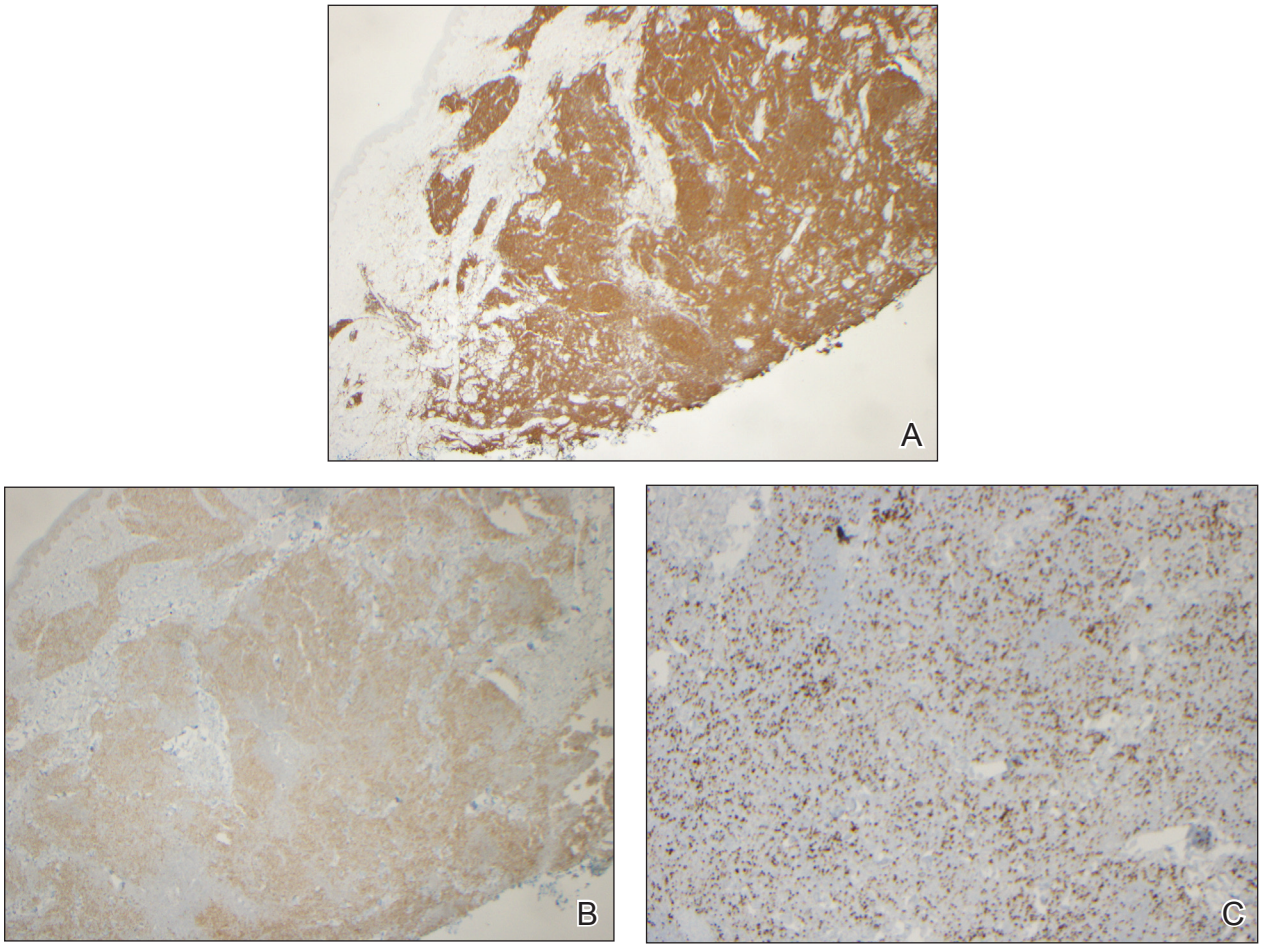

FIGURE 3. Immunohistochemistry showed diffuse staining of CD20 (A)(original magnification ×40) and BCL-6 (B)(original magnification ×40); antigen Ki-67 staining showed an increased proliferation index (C)(original magnification ×100).

with solitary lesions, as the remission rate is close to 100%.[1] For patients with multiple lesions confined to one area, electron beam radiation therapy also can be helpful, as in our patient. In patients with more extensive skin involvement, rituximab therapy may be preferable. Relapse following treatment with either radiation or rituximab occurs in approximately one-third of patients, but these relapses generally are limited to the skin.[1] The International Extranodal Lymphoma Study Group has noted that elevated lactate dehydrogenase, presence of more than 2 skin lesions, and presence of nodular lesions are negative prognostic factors in patients with PCFCL[6]; however, PCFCL has an excellent prognosis overall with a 5-year survival rate of 95%.[1]

Other rare heterogeneous presentations of PCFCL have been reported in the literature. A large multinodular mass on the scalp with multifocal facial lesions has been described in a patient with essential thrombocytopenia.[7] Another report identified a variant of PCFCL characterized by multiple erythematous firm papules that were distributed in a miliary pattern, predominantly on the forehead and cheeks.[8] Barzilai et al[9] described 4 patients with PCFCL who developed lesions that were clinically similar to rosacea or rhinophyma, including papulonodular eruptions on the cheeks; infiltrated erythematous nasal plaques; and small flesh-colored to erythematous papules on the cheeks, nose, helices, and upper back. Hodak et al[10] identified 2 cases of PCFCL that manifested as anetoderma, a condition characterized by the focal loss of elastic tissue. In the setting of chronic lymphocytic leukemia, PCFCL has been observed as a red or violaceous nodule with a centrally depressed scar on the legs.[11] In one case, PCFCL manifested as recurrent episodes of extraorbital swelling and a multifocal red-blue macular lesion that extended from the inferior orbital rim to the nasojugal fold.[12] An interesting presentation of PCFCL was noted as a small, recurring, blood-filled blister on the cheek with perineural spread of the tumor along cranial nerves V2, V3, VII, and VIII.[13] In the pediatric literature, PCFCL has been reported to present as an erythematous

nodule with a smooth surface and a hard elastic consistency that appeared on the nose and nasolabial fold and spread to the ipsilateral cheek, maxillary sinus, and soft palate.[14] In many of these unusual cases, the diagnosis of PCFCL was made after treatment with topical or systemic anti-inflammatory therapies failed.

Increased recognition of anomalous presentations of PCFCL among dermatologists can lead to more timely diagnoses and treatment. Based on our experience with this patient, we recommend considering biopsy for histopathologic evaluation when treating patients with presumed folliculitis or transient acantholytic dermatosis that does not improve with routine treatment or is accompanied by systemic symptoms.

REFERENCES

1. Wilcox RA. Cutaneous B-cell lymphomas: 2015 update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2015;90:73-76.
2. Kim YH, Willemze R, Pimpinelli N, et al. TNM classification system for primary cutaneous lymphomas other than 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;110:479-484.
3. World Health Organization. *WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues.* Lyon, France: World Health Organization; 2008: 227.
4. Dilly M, Ben-Rejeb H, Vergier B, et al. Primary cutaneous follicle center lymphoma with Hodgkin and Reed-Sternberg-like cells: a new histopathologic variant. *J Cutan Pathol*. 2014;41:797-801.
5. Suárez AL, Pulitzer M, Horwitz S, et al. Primary cutaneous B-cell lymphomas: part I. clinical features, diagnosis, and classification. *J Am Acad Dermatol*. 2013;69:329.e1-13; quiz 341-342.
6. Mian M, Marcheselli L, Luminari S, et al. CLIPI: a new prognostic index for indolent cutaneous B cell lymphoma proposed by the International Extranodal Lymphoma Study Group (IELSG 11) [published online September 25, 2010]. *Ann Hematol.* 2011;90:401-408.
7. Tirefort Y, Pham XC, Ibrahim YL, et al. A rare case of primary cutaneous follicle centre lymphoma presenting as a giant tumour of the scalp and combined with JAK2V617F positive essential thrombocythaemia. *Biomark Res*. 2014;2:7.
8. Massone C, Fink-Puches R, Laimer M, et al. Miliary and agminated-type primary cutaneous follicle center lymphoma: report of 18 cases. *J Am Acad Dermatol*. 2011;65:749-755.
9. Barzilai A, Feuerman H, Quaglino P, et al. Cutaneous B-cell neoplasms mimicking granulomatous rosacea or rhinophyma. *Arch Dermatol*. 2012;148:824-831.
10. Hodak E, Feuerman H, Barzilai A, et al. Anetodermic primary cutaneous B-cell lymphoma: a unique clinicopathological presentation of lymphoma possibly associated with antiphospholipid antibodies. *Arch Dermatol*. 2010;146:175-182.
11. Konda S, Beckford A, Demierre MF, et al. Primary cutaneous follicle center lymphoma in the setting of chronic lymphocytic leukemia. *Indian J Dermatol Venereol Leprol*. 2011;77:314-317.
12. Pandya VB, Conway RM, Taylor SF. Primary cutaneous B cell lymphoma presenting as recurrent eyelid swelling. *Clin Exp Ophthalmol*. 2008;36:672-674.
13. Buda-Okreglak EM, Walden MJ, Brissette MD. Perineural CNS invasion in primary cutaneous follicular center lymphoma. *J Clin Oncol*. 2007;25:4684-4686.
14. Ghislanzoni M, Gambini D, Perrone T, et al. Primary cutaneous follicular center cell lymphoma of the nose with maxillary sinus involvement in a pediatric patient. *J Am Acad Dermatol*. 2005;52(5 suppl 1):S73-S75.