Primary cutaneous B-cell lymphomas

Part I. Clinical features, diagnosis, and classification

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Learning Objectives
After completing this learning activity, participants should be able to recognize the clinical presentations of the different types of primary cutaneous B cell lymphomas and perform appropriate skin biopsies and ancillary tests to make the correct diagnosis.

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Primary cutaneous B-cell lymphomas (PCBCLs) are defined as lymphomas with a B-cell phenotype that present in the skin without evidence of systemic or extracutaneous disease at initial presentation, after adequate staging. In non-Hodgkin lymphomas, the skin is the second most common site of extranodal involvement after the gastrointestinal tract. PCBCLs are histologically very similar to their nodal counterparts, and these histologic similarities can lead to confusion about both therapy and prognosis. This article will summarize the clinical, pathologic, and diagnostic features of the 3 main types of PCBCL: primary cutaneous follicle center lymphoma, primary cutaneous marginal zone lymphoma, and primary cutaneous diffuse large B-cell lymphoma, leg-type, and the appropriate evaluation and staging procedures for each of these entities. (J Am Acad Dermatol 2013;69:329.e1-13.)

Key words: histopathology; primary cutaneous B-cell lymphoma; primary cutaneous diffuse large B-cell lymphoma; primary cutaneous follicle center lymphoma; primary cutaneous marginal zone lymphoma; staging.

PRIMARY CUTANEOUS B-CELL LYMPHOMAS

Primary cutaneous B-cell lymphomas (PCBCLs) are B-cell lymphomas that originate in the skin and present at the time of diagnosis without evidence of extracutaneous disease.[1] PCBCLs constitute approximately 25% to 29% of all primary cutaneous lymphomas in the United States, more commonly affecting men than women, with incidence increasing with age.[2-4] In contrast to mycosis fungoides, with an incidence rate statistically higher in blacks, PCBCL is almost exclusively a disease of non-Hispanic whites.[3]

CAPSULE SUMMARY

- Primary cutaneous B-cell lymphoma is defined as B cell lymphoma of the skin without evidence of internal or nodal involvement at the time of diagnosis.
- The 3 most common types are primary cutaneous follicle center lymphoma, primary cutaneous marginal zone lymphoma, and primary cutaneous diffuse large B-cell lymphoma, leg-type.
- Management includes a high index of suspicion for the diagnosis, an adequate full-thickness biopsy specimen, and appropriate extent of disease work-up.

It is critical to distinguish PCBCL from systemic B-cell lymphomas with secondary skin involvement because the clinical behaviors, prognosis, and management differ considerably. Historically, these differences in clinical behavior were not well recognized, and previous classification systems grouped PCBCL with systemic B-cell lymphomas of similar histology.[1,5,6] While older classification systems reflected the understanding of PCBCL at the time, a better understanding of the clinical differences evolved from larger European series. These improvements in clinical insight, coupled with advances in understanding the biology of PCBCL, have led to a more uniform agreement regarding the distinct PCBCL entities.

In 2005, the World Health Organization (WHO) and European Organisation for the Research and Treatment of Cancer (EORTC) cutaneous lymphoma task force reached a consensus, reconciling these differences and eliminating older definitions that required an absence of extracutaneous disease for 6 months after diagnosis.[7] These guidelines were incorporated into the revised 4th World Health Organization classification of tumors of hematopoietic and lymphoid tissues in 2008 using the framework for nodal lymphomas. This consensus classification system distinguishes the following 3 main types of PCBCL: primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL), and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT). PCMZL and PCFCL are recognized as indolent lymphomas, while PCDLBCL-LT has a more intermediate behavior.

The new WHO-EORTC classification offers improved definitions of PCBCL types and more reliable diagnoses and therapeutic decision-making. Immunologic and molecular genetic studies have refined our understanding of the distinct

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