What Is Your Diagnosis?

A 59-year-old white man presented with 2 large erythematous lesions on the right side of the chest wall that had gradually progressed over the last 1.5 years. The patient denied any fever, night sweats, fatigue, unintentional weight loss, or loss of appetite. Physical examination revealed 2 large, well-circumscribed, nearly contiguous, firm, erythematous tumors. One tumor measured 7.5×4.5 cm and the other measured 4×3.5 cm.
Biopsies from the right side of the chest wall (Figure 1) revealed an atypical dense and diffuse lymphocytic infiltrate throughout the dermis. There was extensive crush artifact throughout the specimen. However, the findings were consistent with cutaneous B-cell lymphoma (CBCL), and the diffuse large B-cell type was favored (Figure 2). Atypical lymphocytes stained positively for antibodies against CD20 (Figure 3), CD79a, and BCL-6, and stained negatively for antibodies against MUM-1 and BCL-2. Although flow cytometry revealed no definitive immunophenotypic lymphoma population, polymerase chain reaction analysis revealed a monoclonal immunoglobulin heavy chain gene rearrangement. Computed tomography (CT) scans of the chest, abdomen, and pelvis were unremarkable. A preliminary diagnosis of primary CBCL (PCBCL) was formulated. Diffuse large B-cell lymphoma (DLBCL) and follicle center lymphoma subtypes were each considered, which triggered further workup to rule out systemic involvement.

A bone marrow biopsy from the posterior iliac crest revealed normocellular bone marrow with normal trilineage hematopoiesis. However, whole-body staging with positron emission tomography (PET)–CT scanning revealed osseous disease in the left proximal humerus (Figure 4) as well as a slightly hypermetabolic right axillary lymph node. Magnetic resonance imaging of the brain showed no evidence of intracranial disease. Because of the apparent systemic involvement, stage IV non-Hodgkin lymphoma (DLBCL) became the new suspected diagnosis. The patient was started on the first of 6 cycles of chemotherapy with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), and the skin lesions quickly dissipated and flattened. A faint pink discoloration remained over a slightly indented area. A repeat PET-CT scan following 4 cycles of R-CHOP chemotherapy also confirmed a complete response to therapy.

In general, CBCL tends to affect adults and presents as relatively firm and plum-colored papules, nodules, tumors, or plaques, which can be either fast or slow growing. Cutaneous B-cell lymphoma may be primary or secondary to systemic involvement. Primary CBCL refers to a group of non-Hodgkin lymphomas that initially present in the skin with no evidence of extracutaneous involvement. Secondary CBCL (SCBCL) refers to cutaneous disease that occurs secondary to systemic B-cell lymphoma.

The initial staging techniques that are preferred for cutaneous lymphomas have been debated. For cutaneous lymphomas, except mycosis fungoides and Sézary syndrome, the International Society for Cutaneous Lymphomas and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer recommends obtaining a complete blood cell count with differential; complete metabolic studies including lactate dehydrogenase; and imaging studies of the chest, abdomen, and
pelvis. Bone marrow biopsies and imaging studies of the neck or whole-body PET-CT scanning also may be useful depending on the clinical scenario. Although a more limited workup may be sufficient for PCBCLs such as primary cutaneous marginal zone lymphoma, a bone marrow biopsy is recommended for cases of primary cutaneous DLBCL (leg type). Senff et al supported the use of a bone marrow biopsy in the evaluation of follicle center lymphomas first presenting in the skin, though this method is controversial. In our patient, the laboratory results; bone marrow biopsy; and CT scan of the chest, abdomen, and pelvis failed to suggest extracutaneous disease, while the PET-CT scan revealed systemic involvement.

The differential diagnosis of CBCL includes cutaneous lymphoid hyperplasia (pseudolymphoma), which may be the result of insults such as arthropod bites, stings, vaccinations, or trauma. The clinical presentation, histology, and results of molecular studies and immunohistochemistry are essential in differentiating benign versus malignant processes. Lymphomas are expected to be larger and more persistent than benign processes, demonstrating an atypical lymphocytic infiltrate and monoclonality; immunohistochemistry will aid in the distinction between B-cell and T-cell processes and can delineate the type of B-cell lymphoma. Histology for CBCL typically reveals an atypical lymphocytic infiltrate showing a CD20+ and CD79a+ immunophenotype. Staining for antibodies against BCL-2, BCL-6, CD10, and MUM-1 also plays an important role in the diagnosis of cutaneous lymphoma and determining where the lesion(s) falls within the classification schemes. For example, to differentiate between primary cutaneous lymphoma subtypes, BCL-2 negativity and BCL-6 positivity in the context of a CD20+ and CD79a+ immunophenotype supports a follicle center lymphoma or a DLBCL (non-leg type). By contrast, CD20, CD79a, BCL-2, and MUM-1 positivity would favor a DLBCL (leg type).

The natural history and therapeutic options differ greatly between subtypes of CBCL. For example, the prognosis of primary cutaneous follicle center lymphoma is generally favorable with a 5-year disease-specific survival rate of roughly 95%, and radiation therapy is recommended as a first-line therapy for localized disease. Conversely, primary cutaneous DLBCL (leg type) frequently spreads to extracutaneous sites and carries a much lower estimated 5-year disease-specific survival rate of 55%. Chemotherapy with R-CHOP is typically included in initial therapy for primary cutaneous DLBCL (leg type). The prognosis of systemic B-cell lymphomas also is highly variable and may depend on the type of B-cell lymphoma, the stage of disease at
A focus of increased radiotracer deposition is seen in the left proximal humerus on positron emission tomography–computed tomography scanning.

Although it is uncertain whether the cutaneous lesions preceded systemic disease in our patient, the cutaneous lesions could be arbitrarily classified as secondary because extracutaneous disease was discovered within 6 months of the initial diagnosis. However, classifying the CBCL as primary or secondary did not alter the course of treatment in our patient, as the presumed systemic disease necessitated treatment with systemic chemotherapy; both PCBCLs that develop systemic involvement and SCBCLs (primary extracutaneous disease) usually are treated with systemic chemotherapy. Our case highlights the importance of whole-body staging, as PET-CT scanning changed the course of care by detecting osseous involvement, necessitating systemic therapy as opposed to local radiation therapy alone. A multidisciplinary team with a focus on the diagnosis and management of cutaneous lymphomas helped streamline our patient’s laboratory testing and imaging studies, diagnostic and therapeutic decision making, and treatment implementation. Open channels and frequent opportunities for communication among dermatologists, dermatopathologists, medical oncologists, hematopathologists, radiologists, and radiation oncologists are needed to optimize and coordinate care for patients with cutaneous lymphoma who require transdisciplinary care.

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REFERENCES