Primary cutaneous diffuse large B-cell lymphoma, leg type mimicking cellulitis

Dear Editor,

The skin is the second most common site of primary extranodal non-Hodgkin lymphoma following the gastrointestinal tract. The 2005 World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) scheme recognizes 3 types of primary cutaneous B-cell lymphomas: primary cutaneous marginal zone B-cell lymphoma, primary cutaneous follicular center cell lymphoma, and primary cutaneous diffuse large B-cell lymphoma (DLBCL), leg type (PCLBCL-leg), with the last one carrying the worst prognosis. PCLBCL-leg most commonly arises in the leg and constitutes 4% of primary cutaneous lymphomas and 20% of primary cutaneous B-cell lymphomas. These lymphomas preferentially affect elderly women and usually present with rapidly growing red or bluish-red cutaneous nodules or tumors on one or both lower leg. The large transformed B-cells extend into the subcutaneous tissue and often disseminate to extracutaneous sites. PCLBCL-leg shows an inferior prognosis as compared to those presenting at other anatomical sites.

Cellulitis is an inflammatory disorder of the skin and subcutaneous tissue, and is most commonly caused by an infectious agent. Non-infectious causes such as malignant neoplasms may masquerade as infectious cellulitis and lead to a delayed diagnosis. To date, there are only a few single-case reports of lymphoma masquerading as cellulitis. Here we present the first case of PCLBCL-leg masquerading as cellulitis. Our case underscores the importance of physicians in recognizing those patients with a clinical diagnosis of cellulitis but not responding to antimicrobial treatment.

A 72-year-old woman presenting with reddish discoloration, swelling and pain over her left lower leg for a week had been unsuccessfully treated with antibiotics following a diagnosis of cellulitis. Physical examination revealed erythema, swelling, and local heat with focal induration (Figure 1A and B). There was no lymphadenopathy. The patient’s performance status score was 1. Her serum lactate dehydrogenase level was elevated, while her C-reactive protein and hemogram were normal including white blood cell count at 4630/μL. Blood cultures showed no growth. Sonography was compatible with cellulitis without abscess formation.

After admission, the patient continued to receive antibiotic treatment for 10 days, during which the swelling subsided but the induration and local heat persisted. Cutaneous biopsy showed a dense and diffuse lymphocytic infiltration in the dermis (Figure 1C). The lymphocytes were medium-to-large sized with frequent mitosis (Figure 1D) expressing CD20 (Figure 1D inset), bcl-2, bcl-6 and IRF4/MUM1 with a proliferation index of 90%. They were negative for CD3, CD10, CD34, terminal deoxynucleotidyl transferase or cyclin D1. The patient was diagnosed as having PCLBCL-leg with a non-germinal center phenotype according to the Hans algorithm. Staging workup including bone marrow biopsy revealed stage IE disease and an international prognostic index score of 2. She received cyclophosphamide, doxorubicin, vincristine and prednisolone plus rituximab (R-CHOP) and achieved a dramatic response, with complete remission after six courses of treatment.

Unfortunately a relapsed nodule, 5 × 5 × 2 cm in size without features of cellulitis appeared 15 months later in her left forearm. Biopsy of the recurrent tumor showed the same histological features as the initial specimen. She received salvage chemotherapy but passed away 23 months after initial diagnosis due to disease progression.

Infectious agents cause most cases of cellulitis. For cellulitis that does not respond to antimicrobial treatment, clinicians should consider several noninfectious disorders. The most common causes include thrombophlebitis, contact dermatitis, insect stings, drug reactions, eosinophilic cellulitis (Wells syndrome), gouty arthritis, carcinoma erysipelatoides, familial Mediterranean fever, and foreign-body reactions. The less common causes are urticaria, lymphedema, lupus erythematosus, sarcoidosis, lymphoma, leukemia, Paget’s disease, and panniculitis. Rare cases of lymphoma, such as primary DLBCL of the skeletal muscle, orbital plasmablastic lymphoma and DLBCL, subcutaneous panniculitis-like T-cell lymphoma, extranodal peripheral T-cell lymphoma, and extranodal natural killer/T-cell lymphoma, may masquerade as infectious cellulitis.

PCLBCL-leg is a recently-defined subtype of DLBCL and is composed exclusively of large transformed B-cells occurring most commonly (in around 70% cases), but not exclusively, on the legs. Other entities such as primary cutaneous follicle center lymphoma, primary cutaneous T-cell-rich large B-cell lymphoma and intravascular large B-cell lymphoma (IVLBCL) should be excluded. IVLBCL is a rare type of DLBCL with neoplastic cells preferentially growing within the vascular lumens and is usually widely disseminated in extranodal sites, most commonly in the central nervous system. When IVLBCL masquerades as cellulitis, the diagnosis is based on histopathology. Here we described a rare case of PCLBCL-leg mimicking cellulitis, supporting the need to consider alternative diagnoses in cases of cellulitis with atypical clinical presentation.

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nervous system and skin. Cutaneous lesions of IVLBCL have a widespread morphology and distribution, including painful indurated erythematous eruption, poorly circumscribed violaceous plaques, swelling overlying skin ‘peau d’orange’, cellulitis, large solitary plaques, painful blue-red palpable nodular discolorations, tumor, ulcerated nodules, small red palpable spots, and erythematous and desquamative plaques. Patients with disease limited to the skin were predominantly females with a better prognosis. Our case is distinct from IVLBCL by a diffuse infiltration of large neoplastic B-cells in the dermis without a preferential growth in the vascular lumens. The reason for the erythematous change of our patient’s cutaneous lesions was unclear. It might be due to vascular involvement as well, which could not be confirmed in the small biopsy.

The prognosis of patients with PCLBCL-leg is poor, with a 5-year survival of 50%. Treatment modalities include radiotherapy, single and multi-agent chemotherapy, chemoradiotherapy, and rituximab as single agent or in combination with chemotherapy agents. R-CHOP with or without radiotherapy is recommended by the European Organisation for Research and Treatment of Cancer Cutaneous Lymphoma Group and the International Society for Cutaneous Lymphomas as first-line treatment. The efficacy of this approach in patients with PCLBCL-leg is still poorly documented, however, because no systematic reviews or randomized-controlled trials are available, and these recommendations are mainly based on retrospective studies and small cohort studies. Whether radiotherapy should be considered the first choice of treatment in patients presenting with a small solitary tumor is a matter of debate. Our patient was treated with the internationally recommended regimen (R-CHOP) and obtained complete remission for 1 year; unfortunately, the disease relapsed at the other cutaneous site, reflecting the aggressive behavior of this lymphoma type.

In conclusion, we present a rare case of PCLBCL-leg with clinical features of cellulitis. Diagnosis of lymphomas masquerading as cellulitis is challenging for physicians. Our case underscores the importance of searching for possible underlying causes in patients with a clinical diagnosis of cellulitis that does not respond to antibiotics.

References


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