Two instructive cases of primary cutaneous diffuse large B-cell lymphoma (leg type) mimicking cellulitis and sporotrichosis

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INTRODUCTION

Primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT) accounts for 20% of all primary cutaneous B-cell lymphomas. Given its universal association with poor clinical outcome, it is imperative that the diagnosis is made soon so that treatment can be initiated as soon as possible. We present 2 interesting cases of PCDLBCL-LT clinically resembling cutaneous infections and highlight the clinical clues that can cue the physician in on the accurate diagnosis.

CASE 1

An 80-year-old Chinese man with poorly controlled type 2 diabetes mellitus, hypertension, and hyperlipidemia presented with a 1-month history of left lower limb erythema and swelling. There was no fever or pain. Investigations did not show any leukocytosis or elevated C-reactive protein. Cellulitis was diagnosed, and the patient was treated with intravenous co-amoxiclav. There was no clinical improvement over 3 days, and a dermatology consult was sought. Examination found confluent, erythematous, infiltrated plaques with a nodular surface, circumferentially affecting the entire leg from the lower thigh to the medial malleolus (Fig 1). There was no warmth or tenderness. Palpable ipsilateral, large and matted, inguinal lymphadenopathy was detected. An incisional skin biopsy found a dense, diffuse infiltrate within the dermis and subcutis (Fig 2, A). This infiltrate

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consisted of large, atypical neoplastic cells with round nuclei (centroblasts and immunoblasts) admixed with small reactive lymphocytes (Fig 2, B). The neoplastic cells expressed B-cell marker CD20 (Fig 2, C), and were strongly positive for Bcl-2 (Fig 2, D). The cells showed partial positive staining for MUM-1 (Fig 2, E). There was a high Ki-67 proliferative index of more than 90% (Fig 2, F). These findings were compatible with diffuse large B-cell lymphoma (DLBCL).

A left inguinal lymph node core biopsy found histologic features compatible with B-cell lymphoma with focal large cell morphology. Computed tomography scans of the neck, abdomen, and pelvis found a cluster of enlarged left external iliac inguinal lymph nodes. Bone marrow aspiration and trephine biopsy did not find any evidence of clonal B lymphoproliferative disorder by light chain expression analysis. A diagnosis of PCDLBCL-LT was made, and the patient started R-CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone, plus rituximab). Unfortunately, he tolerated chemotherapy poorly and died soon thereafter.
CASE 2

A 64-year-old Malay man with neuromyelitis optica (on long-term azathioprine, 75 mg once a day, with episodic courses of pulse methylprednisolone for flares) and chronic venous insufficiency, presented with progressive worsening of left lower leg swelling and erythema over 10 days. Before this, he had recurrent admissions (over a duration of 3 months) for presumed left lower leg cellulitis, which never completely resolved with courses of antibiotics. Examination by the dermatology team found a 4-cm infiltrative reddish-brown plaque with overlying hyperkeratosis at the left medial calf, with several discrete firm dermal papulonodules arranged in a sporotrichoid distribution (Fig 3). Interestingly, the patient reported that these papulonodules only appeared over the last fortnight. There was no palpable inguinal lymphadenopathy, nor history of trauma or exposure to animals or soil. There was no leucocytosis, and C-reactive protein was only mildly elevated (51 mg/L). A punch biopsy found a dense, diffuse infiltrate within the dermis and subcutis (Fig 4, A). The infiltrate consisted mainly of large neoplastic centroblasts admixed with some reactive small lymphocytes (Fig 4, B). The neoplastic cells expressed B-cell markers CD20 (Fig 4, C), Bcl-2 (Fig 4, D), and MUM-1 (Fig 4, E). There was a high Ki-67 proliferative index of more than 80% (Fig 4, F). These findings were consistent with a diagnosis of DLBCL. Initial staging scans were negative for systemic nodal involvement, hence establishing the diagnosis of PCDLBCL-LT. The patient underwent 4 cycles of chemotherapy uneventfully and remains in remission.

DISCUSSION

The classical presentation of PCDLBCL-LT is that of infiltrative plaques or nodules, which can be solitary or multifocal. Only about 10% to 15% of patients have lesions outside the lower extremities. PCDLBCL-LT often runs a rapid clinical course with extracutaneous dissemination in 10% to 20% of cases. Involvement of the central nervous system, eyes, testes, peripheral blood, bone marrow, and paranasal sinuses have been reported.
Given its often acute-to-subacute presentation coupled with asymmetrical involvement of the lower limbs, it can be misdiagnosed as cellulitis. Important clinical clues against a pyoderma include the lack of tenderness and pyrexia with a poor response to antibiotics. Absence of leukocytosis and elevated inflammatory markers can also be red flags, as these features would usually be present in typical suppurative cellulitis. Palpable nodes in the nodal basin of the affected area can be caused by ascending lymphangitis and involvement from infection. However, these lymph nodes usually remain small and mobile, rather than being large and matted, like in case 1. Interestingly, case 2 highlights how a sporotrichoid dermatosis may be the presentation of PDLBCL-LT, which has been reported rarely in the literature. This may represent lymphomatous spread aggregating at lymphatic valves. A differentiating feature between sporotrichoid spread seen in PCDLBC-LT and infections such as *Nocardia spp*, mycobacterium, and *Sporothrix spp* would be that the latter do not progress so rapidly and present as clinically fluctuant, suppurative nodules rather than infiltrated nodules.

PCDLBCL-LT is treated like systemic lymphoma and rituximab-based chemotherapy, with or without radiotherapy, is first-line therapy. The prognosis of PCDLBC-LT is poor, with a 5-year survival rate of 41% to 58%. In a study by Grange et al., of 60 patients with PCLBCL-LT, patients with leg lesions had a significantly worse prognosis with a 3-year disease-specific survival rate of 43% compared with patients without leg lesions having a survival rate of 77%. Studies also reflect that age older than 75 years and multifocal disease were poor prognostic factors.

Both our patients presented uniquely for PCLBCL-LT with features of pseudocellulitis. In such cases, we suggest that PCDLBC-LT be included as an important differential diagnosis. Diagnostic clues that should not be missed include the development of infiltrative plaques, the presence of inguinal matted lymphadenopathy, and papulonodules spreading rapidly in a sporotrichoid fashion.

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