

CASE REPORT

Primary cutaneous B-cell lymphoma—leg type in a young adult with HIV: a case report

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Abstract

Primary cutaneous B-cell lymphoma is a very rare entity. Skin lesions mainly occur on the lower extremities. Sheets of immunoblasts and centroblasts are characteristic findings at histologic examination. This case report highlights diagnostic and therapeutic strategies for primary cutaneous B-Cell lymphoma-leg type.

INTRODUCTION

Primary cutaneous B-cell lymphomas-leg type (PCBCL-L) usually present in elderly female patients, and with a pathophysiology poorly understood its possible origin is most likely multifactorial involving genes from chronic antigen stimulation from viral or bacterial infections. Diagnosis is mainly determined by skin biopsy that shows diffuse distribution of atypical lymphoid cells showing positivity for markers of CD20+, CD79a+ and negative for CD5 and CD3. It also presents with frequent cutaneous relapses and compared to other cutaneous B-cell lymphomas, that usually have >90–95% survival rate, PCBCL-leg type has a <60% of 5-year survival rate.

This lesions can easily be mistakenly as chronic skin wound infections and many times misleads its diagnosis and treatment, which is why we present the case of young male with a history of chronic leg wound that was treated first as an infection and then finally by obtaining a skin biopsy the final diagnosis of PCBCL-L lymphoma was made. He was started on standard chemotherapy regimen with rituximab, cyclophosphamide, doxorubicin,

vincristine and prednisolone (R-CHOP). Patient presented initial excellent response but he relapsed shortly afterwards. He is currently on salvage chemotherapy with a different regimen consisting of rituximab, ifosfamide, carboplatin and etoposide (R-ICE) with close monitoring.

CASE PRESENTATION

We present the case of a 45-year-old male with past medical history of human immunodeficiency virus (HIV) for 9 years on highly active antiretroviral therapy, type 2 diabetes mellitus and essential hypertension, who presented to the emergency room (ER) with ongoing right lower extremity pain for the last 4 months. At initial work-up, his HIV viral load was undetectable, and his CD4 count was 800 cells/mm³ (600–1200 cells/mm³). Four days before hospital admission, the patient noticed new ulcerations on his right lower extremity (Fig. 1), associated with increased swelling and subjective febrile episodes. Initially, he was diagnosed with cellulitis, warranting surgical debridement

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Figure 1: Right lower extremity chronic wound, overlying scaling and raised erythematous wound was noted.

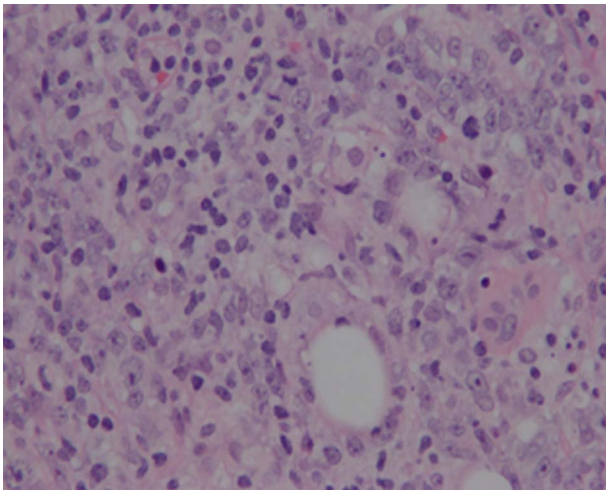


Figure 2: Large and round with centrally located nucleoli (immunoblasts) seen in skin lesion biopsy (hematoxylin-eosin).

and antibiotic therapy with doxycycline. His condition was stable on discharge, however, his symptoms worsened, and he was readmitted after 12 days.

A thorough physical examination also revealed a new scaling and raised erythematous indurated lesions on his left lower extremity. Antibiotic therapy did not provide any significant improvement in either of both extensive skin lesions. Therefore, he underwent a second wound debridement and a tissue sample for biopsy was obtained. Culture of the tissue grew *Staphylococcus aureus* and *Enterococcus faecalis*. Skin biopsy showed histological findings consistent with diffuse large B-cell lymphoma (Fig. 2). Bone marrow involvement was ruled out. He was diagnosed with PCBCL-L per pathology report, which showed atypical lymphoid cells in subcutaneous regions with appearance of immunoblasts positive for CD20 and CD79a, consistent with B-cell origin. The patient was discharged for outpatient oncologic evaluation. His right lower extremity, however, became progressively more swollen, painful and with worsening ulcerations and he was readmitted.

During his second hospital admission, computed tomography (CT) of the right lower extremity revealed images concerning for myositis. He was started on broad spectrum antibiotics with vancomycin, meropenem and clindamycin. Surgery and interventional radiology were consulted; they recommended against acute surgical intervention. Before initiation of chemotherapy by the oncology service, he underwent cancer staging with CT of the head, chest, abdomen and pelvis. Fortunately, no findings of lymphadenopathy, lymphoma or metastatic spread to adjacent or distant organs were noticed. Lumbar puncture confirmed no central nervous system (CNS) involvement, and prophylactic methotrexate was administered intrathecally due to the disease's high risk of CNS involvement. Positron emission tomography/CT scan showed extensive and diffuse subcutaneous indurations with associated hypermetabolic activity involving the right lower extremity, supporting the absence of any neoplastic extension. He started chemotherapy as inpatient with a regimen consisting of a combination of R-CHOP. He tolerated well the regimen without developing significant side effects, and within the next few months, his skin wound decreased in size along with symptomatic improvement. Approximately 3–4 weeks later, CT scans showed there was near complete interval resolution of tissue edema, decreased caliber of reactive right inguinal and pelvic sidewall lymph nodes and no new lymphadenopathy. Due to the patient's good clinical baseline performance and age, the decision by the oncology team was to pursue treatment with R-CHOP chemotherapy and intrathecal methotrexate for 5 cycles with excellent response initially, but after his fifth cycle, patient was found to have significant progression of cutaneous lesions. During his most recent hospital admission, he started a salvage treatment with R-ICE and the medical care team will continue to monitor response.

DISCUSSION

Primary cutaneous lymphomas are categorized as non-Hodgkin lymphomas involving exclusively the skin. Their incidence is 10 cases per million inhabitants per year. The vast majority of cutaneous lymphomas originate from T-cells, but 20–30% are attributed to B-cell neoplasms. Primary cutaneous lymphomas are classified based on their histological origin. It has been described that they can arise from the marginal zone, the follicle center of the B-cells, or from large B-cells [1].

Differential diagnosis can include indolent skin lymphomas that include primary cutaneous follicle center lymphoma (PCFCL) and primary cutaneous marginal zone B-cell lymphoma. The marginal zone B-cell type is considered as one of the extra nodal marginal zone lymphoma of mucosa-associated lymphoid tissue. Its median age of presentation is 50–54 years and even up to 90 years, occurring more often in men than women [2]. The follicle center lymphoma (PCFCL) is considered to be the most indolent type, due to an excellent prognosis, patient median age of presentation of 50 years and higher frequency of appearance in head or neck (60%) [3]. Both primary cutaneous marginal zone and follicle center lymphomas are considered to have minimal risk of extracutaneous spread, making them less likely to be aggressive compared to PCBCL-L.

The PCBCL can be divided by the affected zone; the most studied one is limited to the lower extremities, known as a PCBCL-leg type (PCBCL-L). This subtype is very aggressive and involves a monotonous proliferation of centroblasts. These lymphomas usually affect elderly women and present with rapidly growing tumors in one or both lower extremities [4].

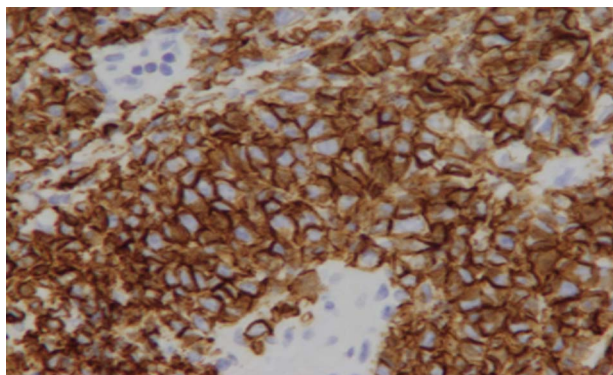


Figure 3: Neoplastic B-cells strongly express BCL-2 on immunohistochemistry.

Its pathophysiology is still not well understood. Viral or bacterial infections seem to be predisposing factors. Kaposi's sarcoma-associated herpesvirus infections, particularly in immunocompromised patients with HIV, have been associated with the development of this subtype of tumors, but proper studies that demonstrate this relationship are still lacking [5]. Our patient suffered of HIV for 9 years, raising suspicion for this to be a very likely predisposing factor.

The cutaneous pattern is usually characterized by nodular, and sharply demarcated wounds. The neoplasm is mostly allocated to the dermis, where usually neoplastic B-cells can resemble normal B-cells [6]. The PCBCL-L has a tendency to relapse, in those cases, it tends to affect other zones of the body. Location in the lower extremities and existence of multiple lesions are poor prognostic factors [7]. Markers from immunohistochemistry of the skin biopsy are CD20, CD19 antigen, BCL2 (Fig. 3) and BCL6. The PCBCL-L has an increased expression of genes involved in cell proliferation, such as mutations in p14 and p16, key genes that once mutated can result in the destabilization of the p53 protein, resulting in cell proliferation [8].

Treatment should be selected based on the type of lymphoma and its stage. These regimens are based on retrospective studies from case series or case reports. Valid randomized control trials are inexistent. Chemotherapy is indicated in PCBCL-L, and prior case reports showed good response with R-CHOP, but relapses are frequent, and treatment may not be curative [9].

CONCLUSION

Neoplasm of the skin should be suspected in HIV patients with chronic skin wounds that are not responsive to antibiotics or other interventions. Timely diagnosis can help change the management plan drastically. PCBCL-L respond rapidly to chemotherapy with R-CHOP regimen but relapses are common.

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CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

This project did not need an ethical approval due to its nature of case report.

AUTHORS' CONTRIBUTION

All authors contributed to manuscript writing and approved the final version. All authors contributed to conception and design and data analysis and interpretation. All authors contributed to the collection and assembly of data.

DATA AVAILABILITY

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

INFORMED CONSENT

The authors have no relationships relevant to the contents of this paper to disclose. Informed consent was obtained for this case.

CONSENT FOR PUBLICATION

The patient' consented and gave permission for publication of this data.

GUARANTOR

The guarantor of this paper is Pamela Contreras-Chavez, MD.

ABBREVIATIONS

CT	computed tomography
PCMZL	primary cutaneous marginal zone lymphoma
PCFCL	primary cutaneous follicle center lymphoma
PCBCL	primary cutaneous B-cell lymphoma
PCBCL-L	primary cutaneous B-cell lymphoma—leg type
PET/CT	positron emission tomography/computed tomography
R-CHOP	cyclophosphamide, doxorubicin, vincristine, prednisone and rituximab

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