

BRIEF ARTICLE

Diffuse Large B-cell Lymphoma in Bilateral Lower Extremities

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ABSTRACT

Diffuse large B-cell lymphoma, leg type, is a rare variant of primary cutaneous B-cell lymphoma. It typically presents as rapidly enlarging solitary or multiple violaceous nodules on the lower extremities. Even with adequate treatment with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, recurrence and systemic spread is common. Timely treatment is necessary as this malignancy is associated with a more aggressive course than other variants of primary cutaneous B-cell lymphoma and overall prognosis is poor.

INTRODUCTION

Primary cutaneous B-cell lymphoma (PCBCL) is a special case of B-cell lymphoma that presents on the skin with no evidence of extracutaneous manifestations. Diffuse large B-cell Lymphoma, leg type (DLBCLLT) is a rare variant that comprises only 20% of all PCBCLs and commonly presents as primary cutaneous lesions on the lower extremities.^{1,2}

There is no standard of care. Early detection and treatment is essential as DLBCLLT has a more aggressive clinical course compared to other types of PCBCL due to higher incidence of extracutaneous dissemination.² Despite the gross appearance, surgery is rarely used, instead R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) therapy with or without field radiotherapy is

the preferred treatment.³ We present a rare case of bilateral DLBCLLT in an 80-year-old male.

CASE REPORT

An 80-year-old Hispanic male was referred by his primary care physician to our dermatology clinic for 5 large bumps that first appeared on his left shin 8 months ago. The patient believed they started from a spider bite while working in the backyard. He notes the lesions are associated with pruritis, have increased in size, and expressed yellowish discharge. He was prescribed a regimen of cephalexin and sulfamethoxazole/trimethoprim by his primary doctor, without improvement. Physical examination revealed multiple crusted tumors at the left mid shin and erythematous indurated plaques at the right calf (Figure 1).



Figure 1. Erythematous indurated plaques at **A)** right medial calf and **B)** right posterior calf with **C)** and **D)** showing multiple crusted tumors at the left anterior shin

Shave biopsy, bacterial, and fungal culture was performed on the left shin. Pathology reported dense hematolymphoid infiltrates in the dermis (Figure 2). Immunohistochemistry highlighted large lymphoma cells in sheets with positive staining for CD20, PAX5, CD79a, BCL2, BCL6, MUM1, CMYC, IgM, with kappa light chain restriction and a Ki67 proliferation index of > 90% (Figure 3). The lymphocyte cells stained negative for CD10, IgD, and TdT. FISH analysis revealed a BCL6 translocation typically observed in diffuse large B-cell lymphoma (DLBCL). Bacterial culture revealed heavy growth of *Enterococcus faecalis* with sensitivity to ampicillin and vancomycin. Fungal culture was negative with no fungal growth observed at 4 weeks.

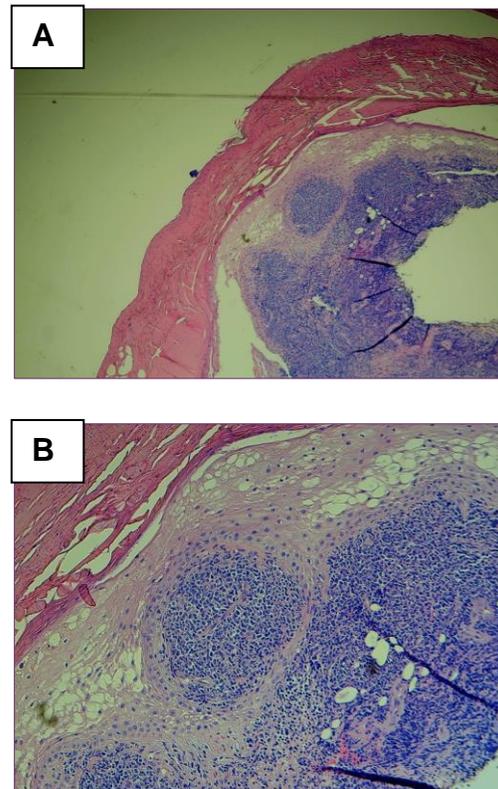


Figure 2. Hematoxylin and eosin stain showing dense hematolymphoid infiltrates in the dermis with an unaffected epidermis at **A)** 4x and **B)** 10x magnification

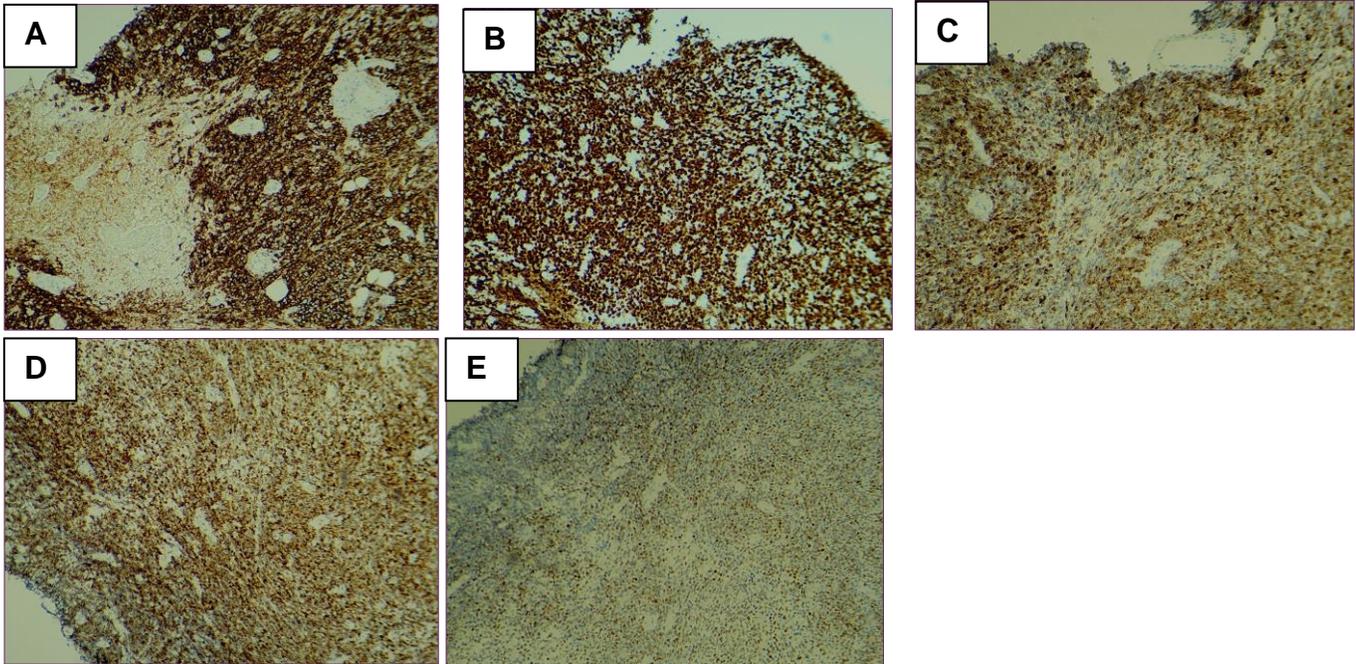


Figure 3. Positive immunohistochemical staining shown at 10x magnification for **A)** CD20 **B)** PAX5 **C)** CD79a **D)** BCL2 **E)** BCL6

Although the right leg was not biopsied, the timing and similarity in lesions strongly suggested the diagnosis of DLBCLLT of the bilateral lower extremities. The patient was started on ampicillin and referred to oncology for further work up and treatment. He was placed on the R-CHOP chemotherapy regimen with close follow up. Surgery was determined to be unnecessary at the time.

DISCUSSION

Most patients with DLBCLLT present clinically with red or violaceous large nodules on the lower extremities that enlarge rapidly, as seen in our patient. Metastasis to extracutaneous sites typically involve local lymph nodes and bone marrow; however, CNS involvement has also been reported.⁴

Differential diagnosis for DLBCLLT includes infectious etiologies, variants of squamous cell carcinoma, and other types of lymphoma. DLBCLLT is best separated from other forms of cutaneous lymphoma with histopathology and immunology. Histologically, DLBCLLT is comprised primarily of large B cells in sheets that diffusely infiltrate the dermis. A grenz zone usually separates the cancer cells from the epidermis; however, the cancer cells can occasionally extend to an ulcerated epidermis and even involve the subcutis.^{3,5} DLBCLLT stains immunopositively for B-cell markers, CD 19, CD 20, CD 22, CD79A, and PAX5.³ In contrast to other forms of PCBCL, a majority of DLBCLLT cells express Ki-67 and activated B-cell markers BCL2 and MUM1, as seen in our patient.⁵

DLBCLLT has an estimated 5 year survival rate of 41%, unlike other types of PCBCL with a more favorable prognosis.^{2,6} Negative prognostic indicators include

lesions being present on the leg, presence of multiple cutaneous tumors, and age >75 years.⁶ BCL6 translocation, is the most common aberration in DLBCL; and translocations are another poor prognostic factor that was also seen in our patient.⁷

Unfortunately, our patient has multiple negative prognostic indicators. Furthermore, distant metastasis could not be ruled out at time of visit. Thus, PET/CT will be vital in the workup to rule out metastasis. Close monitoring and treatment by oncology will be essential for our patient's long-term prognosis. Current recommendations is R-CHOP chemotherapy with or without radiation therapy; however, despite treatment, relapse and subsequent systemic spread is common.^{6,8}

CONCLUSION

DLBCLLT is a rare disease, with rapid onset and a poor prognosis. Timely treatment is essential as even with adequate treatment, relapse and systemic spread is common. Clinicians should be wary of rapidly enlarging violaceous nodules/tumors of the lower limbs and have a high suspicion for DLBCLLT.

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