Case Report

Primary Testicular Diffuse Large B-Cell Lymphoma Metastasizing to Skin and Mimicking a Kaposiform Lesion: A Case Report

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Primary testicular diffuse large B-cell lymphoma is a well-recognized entity known for its indolent clinical course. Rapid dissemination and extensive dermal infiltration are not commonly encountered sequelae of this malignancy. Only one case report exists about its extensive dissemination and involvement of skin and bone. Here, we report a case of primary testicular diffuse large-B cell lymphoma treated with orchiectomy and adjuvant chemotherapy and recurred with widespread dermal involvement as non-blanching violet papule and nodular lesions clinically mimicking Kaposi sarcoma. Histopathological examination confirmed the lesion to be a recurrence of the original lymphoma with similar morphology and immunophenotype. Despite the adjuvant chemotherapy and radiotherapy, the disease progressed from stage-I to stage-IV within 16 months from the date of diagnosis, making it an unusually aggressive clinical course for primary testicular lymphoma.

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INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is one of the most common mature B-cell neoplasms. The prognosis of DLBCL has improved rapidly since the inception of the treatment regimen involving rituximab and cyclophosphamide, doxorubicin (hydroxydaunomycin), vincristine (oncovin), and prednisolone (also known as R-CHOP).

Primary testicular diffuse large B-cell lymphoma (PT-DLBCL) is a well-known extra-nodal non-Hodgkin lymphoma. PT-DLBCL constitutes more than 80% of all primary testicular lymphoma and is known for its indolent clinical course.[1,2] Apart from orchiectomy, PT-DLBCL is treated with adjuvant R-CHOP and expected to have a favorable outcome. Except for the involvement of contralateral testis, aggressive behavior and distant metastasis are not usually reported. However, the use of R-CHOP is known for its immunosuppressive effect. Diseases classically related to immunosuppression such as Kaposi sarcoma has been reported in the HIV-negative patients treated with R-CHOP and other rituximab-containing treatment protocols.[3-6]

Here, we report a case of PT-DLBCL that, after surgical treatment and subsequent adjuvant chemotherapy with R-CHOP, recurred with massive skin involvement in the form of violaceous nodules clinically mimicking Kaposi sarcoma. The patient's DLBCL also subsequently involved the bone and bone marrow, resulting in pathological fracture. The patient reached from Ann arbor stage-I to stage-IV within 16 months from the original diagnosis, showing an unusually aggressive behavior for his PT-DLBCL.

CASE REPORT

A 70-year-old man with a history of depression and bipolar disorder presented in our institute with a primary complaint of painless unilateral enlargement of the left testis for the last several months. An orchiectomy was performed due to a high clinical and radiological suspicion of malignancy. On gross pathological examination, the testicular parenchyma was seen to be almost entirely replaced by a soft tan/white mass measuring 7.7 x 6.0 x 4.8 cm extending to tunica albuginea. The spermatic cord was also seen to be involved by a separate tumor focus, although the surgical margin was clear of the tumor. Microscopic examination revealed the mass to be almost entirely composed of diffused infiltrated medium to large atypical lymphoid cells with large nuclei, vesicular chromatin, prominent nucleoli, and moderate amount of cytoplasm (**Figure 1**). Immunohistochemical stains showed the atypical lymphoid cells were positive for CD20 and PAX5, and negative for pan-cytokeratin, CD117, and CD3, indicating that the primary tumor is a B-cell lymphoma (**Figure 1**). Further immunohistochemical studies showed the lymphoma cells were positive for BCL2 and MUM-1, and negative for CD10, BCL6, CD30, and Cyclin-D1 (**Figure 1**). A Ki67 stain showed the proliferative index to be approximately 90%. A

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CD21 stain did not highlight any dendritic cell meshwork. Fluorescent in-situ hybridization showed no rearrangement involving MYC, BCL2, and BCL6. In-situ hybridization was negative for Epstein-Barr virus (EBER ISH). These findings were consistent with a diagnosis of DLBCL, non-germinal center B-cell type with high-grade features. The patient was further treated with an adjuvant chemotherapy regimen of six R-CHOP cycles, and he declined adjuvant radiotherapy.

The patient returned after 14 months with complaints of rash and plaques on the bilateral lower extremities. On examination, multiple violaceous well-defined, firm, non-tender, non-blanchable pink plaques and papules measuring 0.5 - 1.5 cm are observed on the left medial posterior leg (**Figure 2**). The pathological examination of the shave biopsy of a representative lesion revealed medium to large, atypical lymphocytes positive for CD45, PAX5, BCL2, MUM-1 and negative for Pan-cytokeratin, Bcl6, Cyclin-D1, and CD30, with a Ki67 proliferation index more than 90% (**Figure 1**). FISH study again revealed no gene rearrangement for BCL2, BCL6, AND MYC. The morphology and phenotype of the lymphoma cells were similar to that of the PT-DLBCL, therefore consistent with the involvement of skin by PT-DLBCL. The patient received adjuvant radiotherapy on his lower extremity lesions.

The patient returned after two more months (16 months since the original diagnosis) with a pathological fracture of the left distal humerus. He was managed with open reduction and internal fixation. The microscopic examination of the fracture site tissue and bone confirmed bone involvement by PT-DLBCL (**Figure 1**).

DISCUSSION

PT-DLBCL is a well-recognized variant of DLBCL. Similar to its nodal counterpart, PT-DLBCL is subcategorized into germinal center B-cell (GCB) type and non-germinal center (non-GCB) type. Most PT-DLBCL shows to be of non-GCB subtype;[7] however, the GCB phenotype has also been reported.[8] PT-DLBCL also shares certain overlapping features with primary DLBCL of the central nervous system as both of them are primary DLBCL of immune-privileged sites.

Despite its usual indolent clinical course and favorable outcome, metastasis to other organs has been reported. Goel and colleagues reported a case of PT-DLBCL having an aggressive course and metastasizing to skin and bone.[9] To our knowledge, no other case has been reported with this rapid progression of PT-DLBCL and with such extensive dermal involvement simulating a Kaposiform lesion.

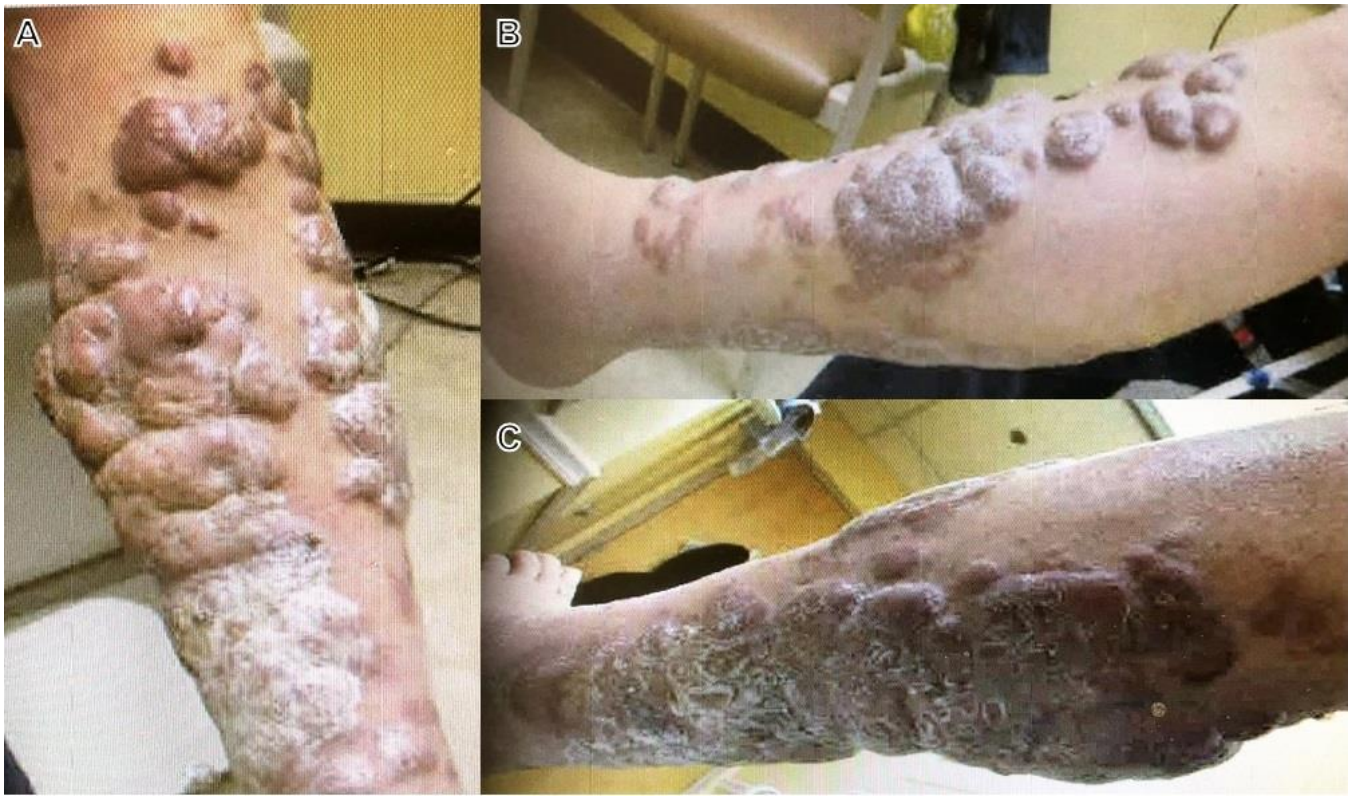

Figure 1. Clinical photographs of upper and lower extremities showing dark violet non-blanchable papules and nodules **(A-C)**.

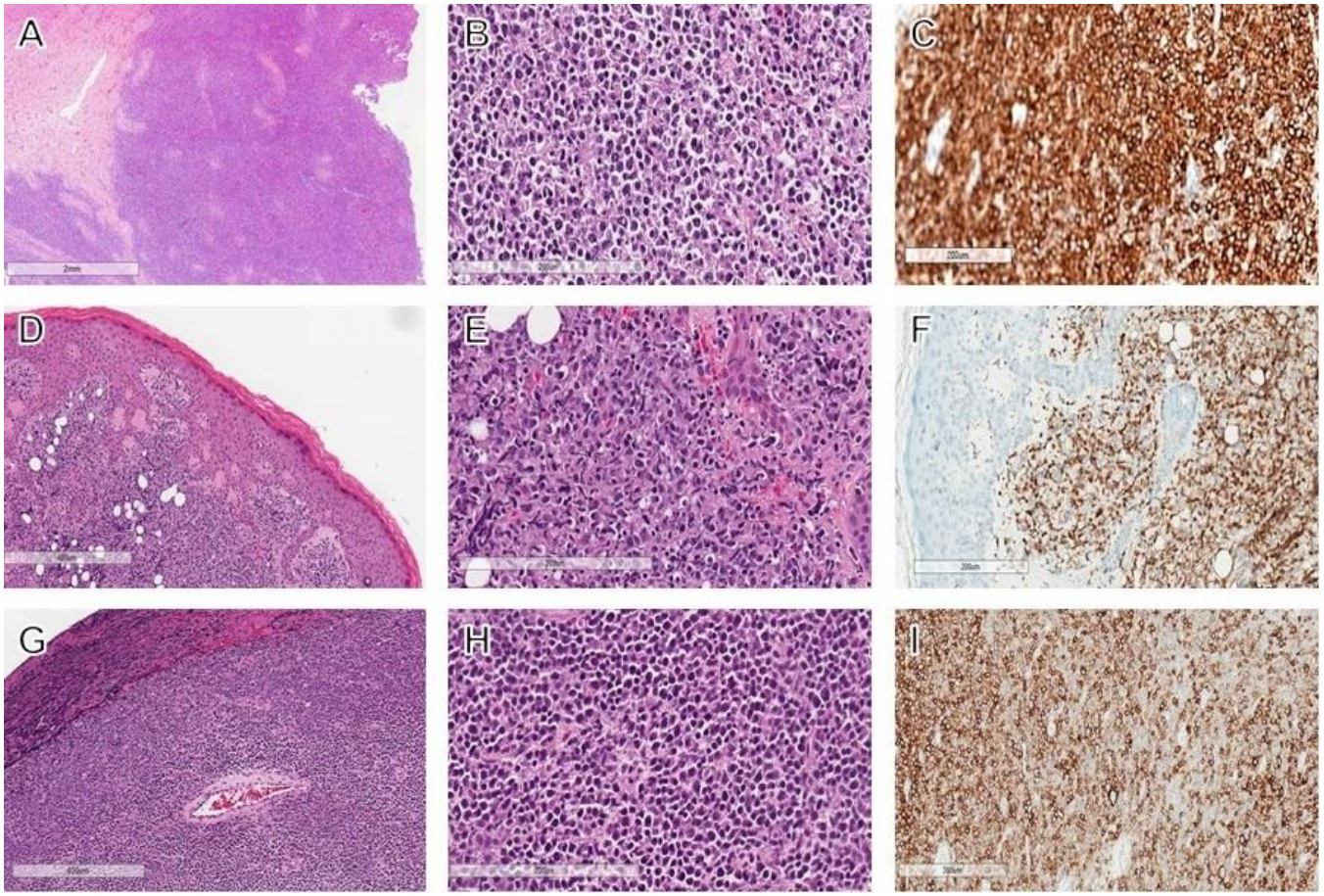

Figure 2: Photomicrographs showing the testicular, skin, and bone lesions. **A, B, C.** Photomicrograph of testicular lesion with **(A)** diffusely infiltrated lymphoma cells (H&E, 50X), **(B)** the lymphoma cells are of medium to large in size, with vesicular chromatin and prominent nucleoli (H&E, 200X), **(C)** Immunohistochemical stain for CD20 showing the malignant cells to be immunoreactive (200X). **D, E.** Photomicrograph of the skin lesion showing **(D)** monotonous dermal infiltration of lymphoma cells with epidermal sparing (H&E, 50X), **(E)** the lymphoma cells are similar to that in the testis shown in panel B (H&E, 200X), **(F)** Immunohistochemical stain for Pax-5 showing the malignant cells to be immunoreactive (200X). **G, H.** Photomicrograph of the bone lesion showing **(G)** monotonous infiltrate by the malignant cells (H&E, 50X), **(H)** neoplastic cells similar to that in the testis shown in panel B (H&E, 200X), **(F)** Immunohistochemical stain for CD20 showing the malignant cells to be immunoreactive (200X).

Kaposi sarcoma is a well-known aggressive vascular malignancy that usually presents in HIV-positive or other immunodeficient patients in the form of violaceous nodules in the skin. Other vascular malignancies such as Kaposiform hemangioendothelioma, angiosarcoma, spindle-cell hemangioma, and hobnail hemangioma are also in the differentials in a case presenting as dark violet non-blanching nodules. The distinction between Kaposi sarcoma and DLBCL requires histopathological examination of the lesion. Hence, it is crucial to be aware of cutaneous dissemination of DLBCL capable of mimicking Kaposi sarcoma.

Primary cutaneous diffuse large-B cell lymphoma, leg type is another variant of DLBCL that presents as primary cutaneous lymphoma with more aggressive clinical behavior.[10,11] It usually presents as unilateral or bilateral, rapidly growing bluish-red nodules on lower extremities.[12] Like PT-DLBCL, primary cutaneous DLBCL usually belongs to the non-GCB phenotype. However, it often involves MYC or BCL6 translocation.[13] Since PT-DLBCL is not known for cutaneous dissemination, its secondary spread to the skin has the potential pitfall of a diagnosis of primary cutaneous DLBCL. Hence, due diligence should be made to rule out primary DLBCL in other sites, including testis, before diagnosing primary cutaneous DLBCL.

CONCLUSION

Here we have summarized a case of PT-DLBCL and discussed two potential diagnostic pitfalls of its unusual aggressive sequelae. Even though most PT-DLBCL patients will show indolent clinical course and favorable outcome, we should be aware of these clinical features of an aggressive course.

CONFLICT OF INTEREST AND FINANCIAL DISCLOSURES
None.

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