Journal of Pakistan Association of Dermatologists. 2024;**34(4)**:1140-1144.

Case Report

Diffuse large B-cell lymphoma-germinal center B cell subtype presenting as cutaneous nodules

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Abstract Diffuse large B cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma worldwide, representing approximately 30-40% of all cases in different geographic regions. We report a case that highlights the atypical presentation of DLBCL-germinal centre B cell subtype as a cutaneous disease. This unique presentation emphasizes the importance of considering DLBCL in the differential diagnosis of patients presenting with infiltrated skin lesions in the absence of classic lymphadenopathy.

Key words
Cutaneous; Diffuse large B cell lymphoma; DLBCL; Germinal centre; GCB.

Introduction

Diffuse Large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma and is characterized by aggressive growth and heterogeneity. Patients most often present with a rapidly growing tumor mass in a single or multiple nodal or extranodal sites.[1,2] DLBCL is more prevalent in elderly patients with a median age in the 7th decade, although it also occurs in young adults and rarely in children. There is a slight male predominance, and 30-40% of cases present primarily in extra-nodal locations. The gastrointestinal tract is the most frequent extra-nodal site involved, and other locations may include the skin, bone, mediastinum, central nervous system, breast, and various other sites.[1] Skin involvement can be present in the form of plaques, papules, nodules, or ulcers.[3] However, lesions are often solitary, with a predilection for head and neck. DLBCL is classified according to cell-of-origin into germinal center B-cell-like (GCB) and activated B-cell-like (ABC) subtypes, with about 10-15% of cases being unclassifiable. Patients with the GCB subtype usually have a better prognosis than those with the ABC subtype. Although cell-of-origin is useful for predicting outcomes, both GCB and ABC subtypes remain heterogeneous, with better and worse prognostic subsets within each group.[3]

Case report

A 49-year-old male came to the Dermatology outpatient department with multiple asymptomatic skin lesions all over the body and two large swellings over the left side of the scalp and left arm for the past year, gradually increasing in size and number. No systemic

Manuscript: Received: September 14, 2023.
Revision: September 18, 2023
Accepted: November 08, 2023
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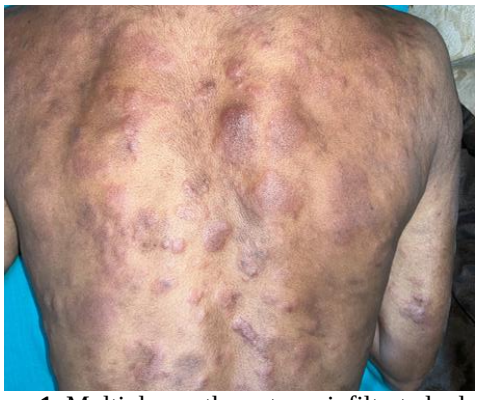

Figure 1 Multiple erythematous infiltrated plaques over trunk.

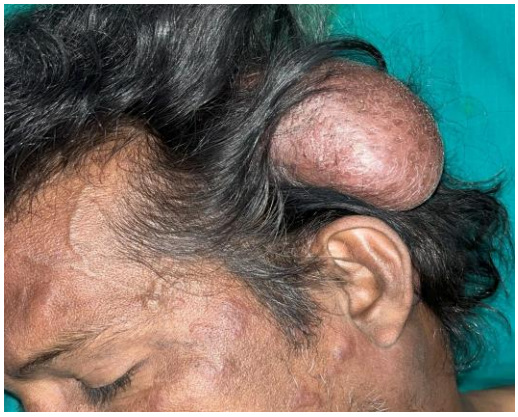

Figure 2 A large swelling over the left temporal area of scalp.

symptoms were noted. On examination, he had multiple well-defined erythematous infiltrated plaques and nodules of around 2x2 cm all over the trunk **(Figure 1)** and bilateral extremities. A large firm swelling measuring 10x10 cm was observed over the left temporal area **(Figure 2)**, and another large firm swelling measuring 10x8 cm was present over the left arm. The swelling was hard in consistency and was non-tender on palpation. There was no generalized lymphadenopathy. Differential diagnosis considered were mycosis fungoides, Sezary syndrome, lepromatous leprosy, histiocytosis, and primary cutaneous B cell lymphoma. Routine investigations such as complete blood counts, renal and liver function tests, and serology were found to be normal. Peripheral smear didn't show any atypical lymphocytes. Histopathological examination of an infiltrated plaque over the trunk showed extensive nodular perivascular collections of monomorphic, atypical lymphocytes with coarse clumped chromatin and inconspicuous nucleoli involving the dermis, suggestive of lymphoma. The epidermis was unremarkable, with no epidermotrophism or Pautrier's microabscesses. **(Figure 3,4)**.

FNAC of multiple smears studied from left temporal and left arm swelling showed a monomorphic population of atypical round lymphoid cells arranged in discohesive sheets and clusters consistent with lymphoma. PET CT was done to detect other site localizations, which showed metabolically active disease involving multiple enlarged supra- and infra-diaphragmatic lymph nodes, right palatine tonsil,

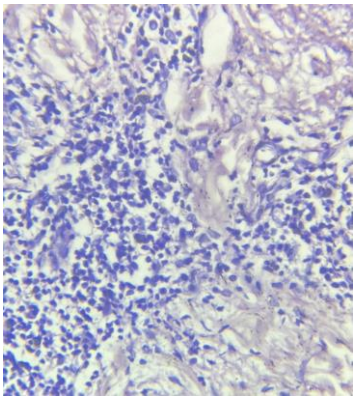

Figure 3 HPE (40x) showing atypical round lymphocytes infiltrating the dermis.

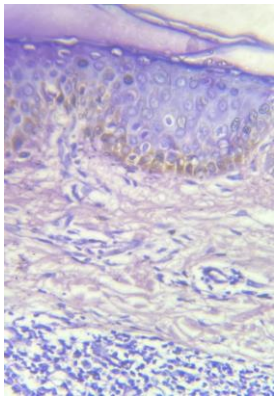

Figure 4 HPE(40x) showing normal epidermis with nodular collections of atypical lymphocytes in dermis.

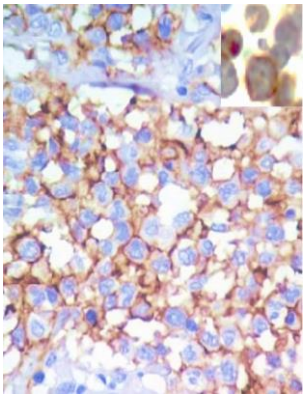

Figure 5 IHC showing CD10 membrane positivity.

Table 1 Primary cutaneous DLBCL vs. DLBCL with cutaneous involvement.

	Primary cutaneous DLBCL	*DLBCL with cutaneous involvement*
Origin	De novo in skin	Lymph nodes (most common)
Site	Legs > scalp > trunk	Legs > scalp> trunk
Dissemination	Less common, usually presents as solitary nodules	More common
B symptoms	Less common	More common
Raised LDH	Less common	More common
IHC		
MUM 1	Usually +ve	Variable
CD10	Rarely detected	More common
BCL2	Strongly positive	Strongly positive
Stage	Usually belong to stage I or II	Belong to stage III or IV
Prognosis	Better	Comparatively poor

bilateral perinephric, omental, peritoneal, and right pleural lesions, along with extensive cutaneous and sub-cutaneous soft tissue deposits. Immunohistochemistry further proved the diagnosis of diffuse large B cell lymphoma GCB subtype [CD20+, CD10+, MUM1-, BCL-2+, BCL6-, PAX 5+, 80% Ki67] **(Figure 5)**. Patient was started on chemotherapy with the R+CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen.

Discussion

Cutaneous involvement in DLBCL is relatively rare, accounting for approximately 5% of cases. The cutaneous presentation can vary and may mimic other dermatological conditions, making the diagnosis challenging. Skin involvement could be primary or secondary in patients with DLBCL. Depending on the primary site involved, DLBCL with cutaneous involvement can be divided into two groups: primary cutaneous DLBCL (PCDLBCL), limited only to the skin, and DLBCL accompanied by secondary involvement of the skin.[3] It is crucial to differentiate between these two types, as the prognosis and survival outcomes of patients vary depending on the type. Primary extra-nodal DLBCL is seen in up to 40% of cases. Skin involvement is uncommon, and in a large series of DLBCL cases, skin involvement at presentation was seen in 3.3% of cases. Non-contiguous site involvement and extensive lesions are, however, more often seen in secondary cutaneous DLBCL **(Table 1)**.

The classification of DLBCL **(Figure 6)** by Hans *et al.*[4] into germinal centre B cell (GCB) and non-germinal centre B cell like subtypes carries a significant effect on survival outcomes, with non-GCB patients having poorer survival.

In the present case, the skin lesions appeared to mimic lepromatous leprosy, cutaneous T cell lymphoma, and primary cutaneous B cell lymphoma. However, we were able to clinically exclude Hansen's disease as a potential diagnosis. Histopathological examination in our case showed the absence of Pautrier's microabscess and epidermotropism and the absence of T cell markers in immunohistochemistry, which ruled out the possibility of cutaneous T-cell lymphoma. The presence of extensive monomorphic atypical

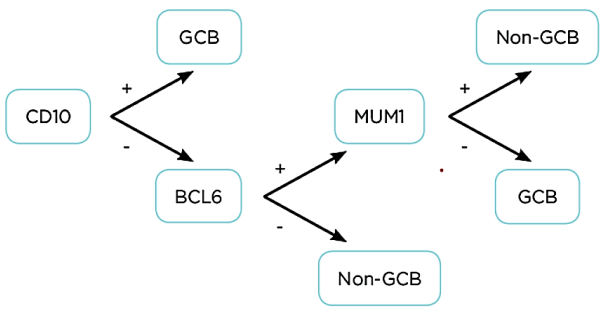

Figure 6 Hans criteria for classification of DLBCL subtypes.

lymphoid cell infiltrates in both biopsy and FNAC specimens was consistent with DLBCL. PETCT showed extracutaneous disease involving multiple enlarged supra- and infra-diaphragmatic lymph nodes, right palatine tonsil, bilateral perinephric, omental, peritoneal, and right pleural lesions. The absence of evident extracutaneous disease is a necessary condition for differentiating PDCBCL from nodal non-Hodgkin's lymphoma (NHL) with secondary cutaneous involvement.[5] Majority of primary DLBCL with skin involvement shows an activated B cell phenotype and expresses MUM1 and is negative for CD10 and Bcl-6, although other combinations can exist. However, IHC alone cannot differentiate between primary cutaneous versus systemic DLBCL.[6] Thus, the presence of extracutaneous involvement and absence of specific immunohistochemistry markers for DCBCL, like MUM1 and BCL6, eliminated the possibility of primary DLBCL being the diagnosis in our case. Finally, according to Han's criteria, the diagnosis of DLBCL with GCB subtype was established.

As reported in the literature, primary cutaneous DCBCL has a better prognosis and outcome compared to cutaneous involvement in systemic DLBCL, which is variable.[7-9] Primary cutaneous lymphomas tend to have an indolent course, whereas cutaneous involvement in systemic DLBCL classifies the patient into an advanced stage (Ann Arbor IV – **Table 2**) leading to an unfavorable prognosis.

However, cases expressing CD10 were more likely to have an advanced stage (Ann Arbor stage IV) disease compared with those who were CD 10 negative.[4] According to Takahashi *et al;*[10] skin involvement in DLBCL significantly decreases the overall survival rate. Involvement of >1 extranodal site in non-Hodgkin lymphoma is considered a poor prognostic factor according to the International Prognostic Index (IPI). In the study by Lee *et al.*[11] patients with systemic DLBCL with skin involvement had advanced disease, higher IPI scores, and poorer outcomes compared to PCDLBCL. Thus, identifying the clinical phenotypes with skin involvement is important for classification, prognostic value, and management of patients.

Conclusion

This case report highlights the atypical presentation of the DLBCL-GCB subtype as a cutaneous disease. This unique presentation emphasizes the importance of considering DLBCL in the differential diagnosis of patients presenting with infiltrated skin lesions in the absence of classic lymphadenopathy**.**

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship None.

Conflict of interest Authors declared no conflict of interest.

Author's contribution

MLPR, NM: Idetification and management of the case, manuscript writing, critical review the manuscript, has given final approval of the version to be published.

SGV, KG: Diagnose and management of the case, crtically review, contributions to acquisition of data, has given final approval of the version to be published.

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