Journal of Pakistan Association of Dermatologists.2023;**33(1)**:294-297.

Case Report

Diffuse large B-cell lymphoma with secondary skin involvement

Anand Bhosale, Rajan Bindu, Praneet Awake*, Sayali Deshmukh, Pallavi Chaudhari, Vivek Dugad

Department of Pathology, Symbiosis Medical College for Women, Symbiosis International (Deemed University), Pune, Maharashtra, India.
*Department of Dermatology, Venereology and Leprosy, Symbiosis Medical College for Women, Symbiosis International (Deemed University), Pune, Maharashtra, India.

Abstract Diffuse large B cell lymphoma (DLBCL) is an aggressive subset of Non-Hodgkin's Lymphoma (NHL). It is composed of mature B-cells and can occur in both lymphoid and extra-lymphoid sites. Extra-nodal DLBCL is commonly observed in the gastrointestinal tract followed by the cutaneous involvement. DLBCL with cutaneous involvement can be further categorized into primary cutaneous diffuse large B-cell lymphoma (PCDLBCL) and DLBCL with secondary cutaneous involvement. We present a rare case of secondary cutaneous involvement in DLBCL in a 66-year woman.

Key words
Diffuse large B cell lymphoma, secondary cutaneous DLBCL, Non-Hodgkin's Lymphoma.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is an aggressive neoplasm, comprising around 30% of all the cases of non-Hodgkin's lymphomas (NHL). DLBCL is comprised of groups of several different tumors that involve both primary extra-nodal and nodal subtypes. DLBCL is more common in men and is more prevalent in the elder age group. Among the extra-nodal category, gastrointestinal, head and neck, skin and soft tissue are the primary sites in most cases.[1]

In patients with DLBCL the cutaneous involvement could either be primary or secondary. The nomenclature primary cutaneous diffuse large B-cell lymphoma (PCDLBCL) and DLBCL with secondary cutaneous involvement depends on the extra-cutaneous involvement at the time of diagnosis.[2] Depending on the primary site of involvement, DLBCL with cutaneous involvement can be sub-classified into two categories-primary cutaneous DLBCL (PCDLBCL), that is limited to the skin, and DLBCL secondarily involving skin. Differentiation amongst these two types is crucial as they differ in treatment plans and survival rates.[3]

Address for correspondence
Dr. Praneet Awake
Department of Dermatology, Venereology & Leprosy,
Symbiosis Medical College for Women, Symbiosis International (Deemed University), Pune,
Maharashtra, India. Pin: 412115
Email: p16awake@gmail.com

Case Report

A 66-year-old woman came to our dermatology outpatient with complaint of swelling over the left side of face which was present since 2 years but increasing in size rapidly over past 2 months **(Figure 1a)**. She stated that earlier she was taking oral steroids prescribed by general practitioner on and off and then her swelling used to get reduced in the past. Since past 2 months she had stopped steroids completely and

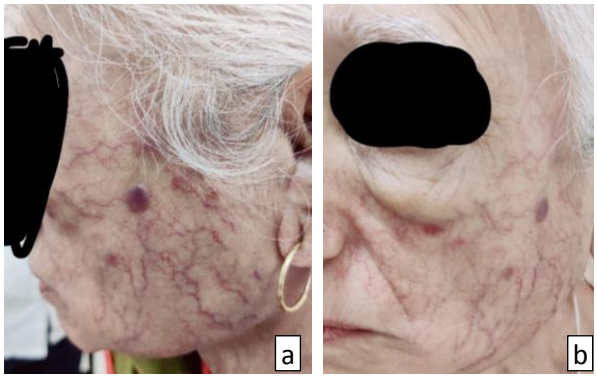

Figure 1 a) Nodular plaque over left cheek with surrounding telangiectasia b) Slight proptosis of left eye with swollen surrounding soft tissue.

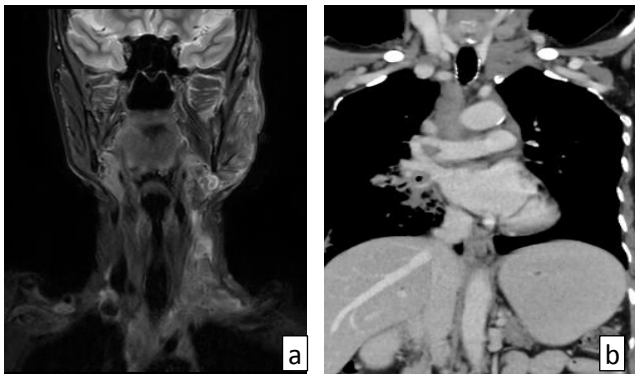

Figure 2 a) MRI left buccal pad of fat, anterior subcutaneous region of left cheek and left masticator space. b) MRI right hilar and mediastinal lymphadenopathy.

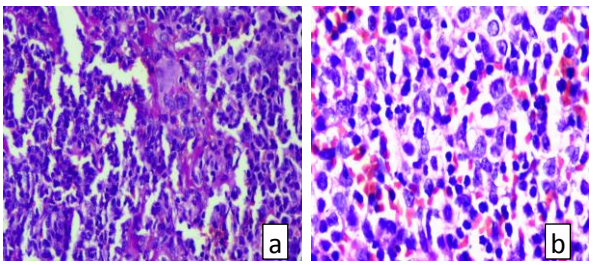

Figure 3 a) Skin biopsy from lesion on cheek showed a nodule with round cells in sheets and in small groups b) lymph node biopsy showed effaced architecture with dual cell population comprising of small lymphocytic and large round lymphoid cells.

swelling increased rapidly. Examination revealed firm mass over left side of face, involving the left submandibular region, parotid region extending upto the left eye and tragus. Slight proptosis of left eye with swollen surrounding soft tissue was noted **(Figure 1b)**. Single cutaneous nodular plaque of 1cm x1 cm was noted on left cheek. Surrounding region showed multiple telangiectasia. All the cervical group of lymph nodes were enlarged and were hard on palpation. Ultrasound was advised which revealed left generalized cervical, intra-parotid, buccal and supraclavicular lymphadenopathy. Her complete physical, otolaryngorhinological and ophthalmogical examination was done. A differential diagnosis of Burkitt's lymphoma, Kikuchi lymphadenitis, Hodgkin's lymphoma, Non-Hodgkins lymphoma, Sarcoidosis, Chronic lymphocytic leukemia was considered. For diagnostic purposes, the patient underwent a lymph node biopsy and skin biopsy of nodular plaque over left cheek. Sample was sent for histopathology examination. Full body STIR (short tau inversion recovery) sequence MRI (Magnetic resonance imaging) scan and CT (Computed Tomography) scan were performed. It revealed multiple enlarged mediastinal lymph nodes noted in the pre-tracheal, right para-tracheal, pre-vascular and sub-carinal regions and right hilum **(Figure 2a,2b)**. Visualized lower neck showed left sided enlarged lymph nodes. There was no evidence of axillary adenopathy. Skin biopsy from lesion on cheek showed a nodule with round cells in sheets and in small groups. Nuclei were large round vesicular with coarse chromatin and prominent nucleoli. Mitotic activity was evident **(Figure 3a)**. Lymph node biopsy showed effaced architecture with dual cell population comprising of small lymphocytic and large round lymphoid cells **(Figure 3b)**. On Histopathology differential diagnosis were chronic inflammation, hodgkins lymphoma and lymphoproliferative disorder. Immunohistochemistry showed neoplastic lymphoid cells positive for CD 20, BCL2 protein, BCL-6 and MUM 1 **(Figure 4a-4d)** and negative for CD-10, Cyclin D-1 AND C-Myc. MiB 1 proliferative index is 70-80%. All

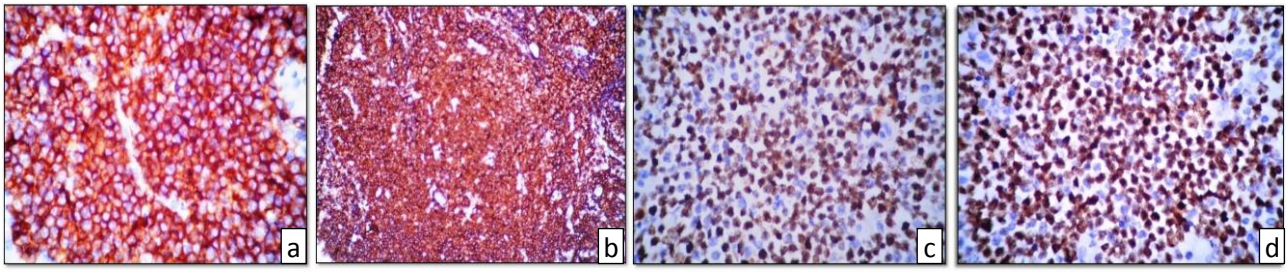

Figure 4 Immunohistochemistry (IHC) showing neoplastic lymphoid cells positive for a) CD 20, b) BCL-2 protein, c) BCL-6 and d) MUM 1.

findings were suggestive of Diffuse Large B-Cell Lymphoma.

Discussion

Diffuse large B-cell lymphoma (DLBCL) is a subset of non-Hodgkin's lymphomas (NHL). It is the commonest lymphoid neoplasm observed in adults. The median age of presentation of DLBCL ranges from the sixth to seventh decade and is more commonly seen in males.[4] It is also the most common type of lymphoma observed in human immunodeficiency virus infected patients. DLBCL usually presents as a rapidly growing non-tender mass which is usually a lymph node in the cervical region, groin or abdomen. It is rare for subcutaneous nodule to be the presenting sign of DLBCL.[3,5]

At times, DLBCL is diagnosed prior to other indolent lymphomas, owing to its tendency to proliferate rapidly. All DLBCLs express B-cell markers immunophenotypically and other markers are expressed in a variable proportion of tumors like Bcl-6 in 60%-90%, Bcl-2 in 50% and MUM-1 in 35-65%.[5]

Primary cutaneous lymphomas are generally inert, whereas skin involvement in systemic DLBCL, grades the patient into a higher stage (Ann Arbor IV), thus resulting in a poor outcome. Therefore, nomenclature of the cases with cutaneous involvement is important, for classification as well as treatment of patients, since skin involvement is generally affiliated with an aggressive course and poor prognosis.[2,5]

Disseminated extra-nodal disease is uncommon, and one-third of patients have systemic symptoms. Although DLBCLs are rapidly proliferating, they are potentially treatable malignancies. Secondary skin involvement is rare in DLBCL, but it has been reported in about 20% cases in literature. The skin lesions, primary and secondary, have similar features, but extensive skin lesions are more commonly seen in secondary cutaneous DLBCL compared with DLBCL, leg type.[6,7]

Conclusions

Skin involvement at presentation in DLBCL can be either primary or secondary. Differentiating them could pose a diagnostic challenge. We present a case of secondary cutaneous involvement in DLBCL for its rarity.

References

1. Awad M, Holzwanger E, Jubbal S. A Unique Presentation of Cutaneous Diffuse Large B-Cell Lymphoma. *Case Rep Dermatol Med*. 2020;**2020**:8310602.
2. Kilaru S, Panda SS, Mishra S, Mohapatra D, Baisakh M, Kolluri S, Devaraj S, Moharana L, Biswas G. Cutaneous involvement in diffuse large B cell lymphoma at presentation: report of two rare cases and literature review. *J Egypt Natl Canc Inst*. 2021;**33(1)**:25.
3. Lee WJ, Won KH, Won CH, Chang SE, Choi JH, Moon KC, Park CS, Huh J, Suh C,

Lee MW. Secondary Cutaneous Diffuse Large B-cell Lymphoma has a Higher International Prognostic Index Score and Worse Prognosis Than Diffuse Large B-cell Lymphoma, Leg Type. *Acta Derm Venereol*. 2016;**96(2)**:245-50.

4. Lloret-Ruiz C, Molés-Poveda P, Barrado-Solís N, Gimeno-Carpio E. Linfoma B difuso de células grandes sistémico con afectación cutánea secundaria. *Actas Dermosifiliogr*. 2015;**106**:685-7.
5. Magro CM, Wang X, Subramaniyam S, Darras N, Mathew S. Cutaneous double-hit B-cell lymphoma: An aggressive form of B-cell lymphoma with a propensity for cutaneous dissemination. *Am J Dermatopathol*. 2014;**36**:303-10.
6. Ferrão JB, Barreira JV, Marote S, Parmanande A. Diffuse large B cell lymphoma: cutaneous presentation. *BMJ Case Rep*. 2018;**11(1)**:e226839.
7. Takahashi H, Tomita N, Yokoyama M, Tsunoda S, Yano T, Murayama K, *et al*. Prognostic impact of extranodal involvement in diffuse large B-cell lymphoma in the rituximab era. *Cancer*. 2012;**118(17)**:4166-72.