An Unusual Presentation of Systemic B-Cell Lymphoma

Dear Editor,

Lymphomas are a diverse category of hematological malignancies that develop from cells of the lymphoid system. Non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma are two separate subtypes of lymphoma.[1] Follicular lymphoma (FL) is considered to be an indolent variant of NHL.[2] FL has been characterized as a heterogeneous malignancy that comprises of tumors originating from germinal centre B-cells, centrocytes, and rarely centroblasts.[3] Its indolent nature leads to dissemination to other sites by the time of diagnosis.[4] Here, we report a rare presentation of systemic B-cell lymphoma with cutaneous manifestations at the time of presentation.

A 41-year-old female was initially referred with a diagnosis of keloid from general surgery to the department of dermatology for evaluation of a 5-month history of painful multiple red raised lesions which started over her back, gradually progressed to involve face, neck, chest, and bilateral upper limbs. She also reported significant weight loss (5 kgs in the last 5 months). On examination pallor was present, and generalized, non-tender lymphadenopathy was noted involving bilateral superficial cervical, posterior auricular, supraclavicular, and right posterior axillary group of lymph nodes.

Cutaneous examination revealed multiple tender erythematous papules, plaques, and nodules (largest over the upper back: 5 × 4 cms) with induration of surrounding skin over face, neck, trunk, and bilateral upper limbs. Polarizing dermoscopy showed a salmon-colored background, white dots and blood vessels in a serpentine arrangement [Figure 1].

Blood investigations revealed anemia (Hb-8.7 g/dl), and other routine parameters were within normal limits. The following differentials were considered-cutaneous sarcoidosis, cutaneous lymphoma, histoid Hansen's disease, and lymphocytoma cutis. We proceeded with a skin biopsy

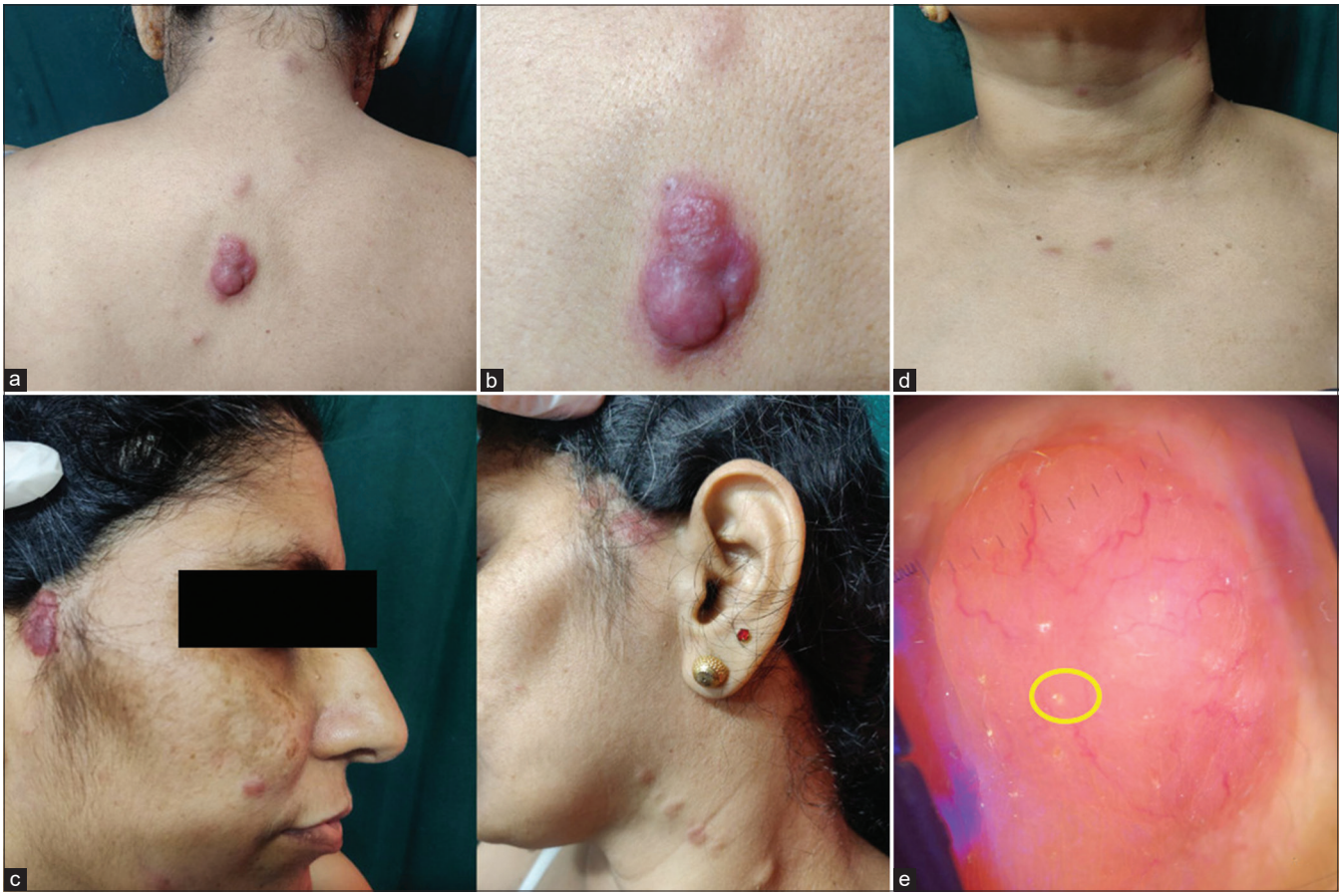

Figure 1: Multiple erythematous papules and grouped nodules noted over (a) nape of neck and upper back, (c) face, (d) anterior aspect of neck and upper chest. (b) Multiple grouped erythematous nodules noted over upper back with glossy surface and few papules overlying the same. Telangiectasia noted and surrounding skin is erythematous with induration. (e) Polarizing Dermoscopy: Salmon colored background, blood vessels (serpentine, linear, irregular vessels), white dots (marked in yellow circle)

of the largest nodule which revealed a monomorphous population of lymphoid cells arranged in sheets and occasional nodules infiltrating between collagen bundles and adnexal structures. A cell free zone (Grenz zone) was noted below the epidermis. Under high power, centroblasts, and centrocytes were visualized [Figure 2].

Immunohistochemistry confirmed the presence of lymphoid cells of B-cell lineage (CD 45+; CD20+; CD10+; Bcl-2-+; Bcl- 6-+ in 50% of lesional cells; MUM1: scattered positivity; Ki-67- 45%) [Figure 3]. A positron emission tomography (PET-CT) was done to further characterize the disease extent and for staging which revealed extensive hypermetabolic subcutaneous, retroperitoneal nodules with a standardized uptake value (SUV) max of 13.3 all over the body. Increased fluorodeoxyglucose (FDG) uptake was also noted in the left tonsillar fossa, bilateral cervical, axillary, mediastinal, abdominopelvic, inguinal lymphadenopathy with evidence of retroperitoneal, and mesenteric mass lesions. FDG avid skeletal involvement in the left posterior maxilla, marrow of medial ends of bilateral clavicles, sternum and body of the L3 vertebrae along with FDG avid hypodense lesions in segment 1 of liver, right kidney and likely involvement of spleen and suprarenal glands were also noted. In conjunction with the histopathology, immunohistochemistry and imaging studies, she was diagnosed to have B-cell non-Hodgkin lymphoma of follicular type (WHO Grade I/II) with likely dissemination to skin.

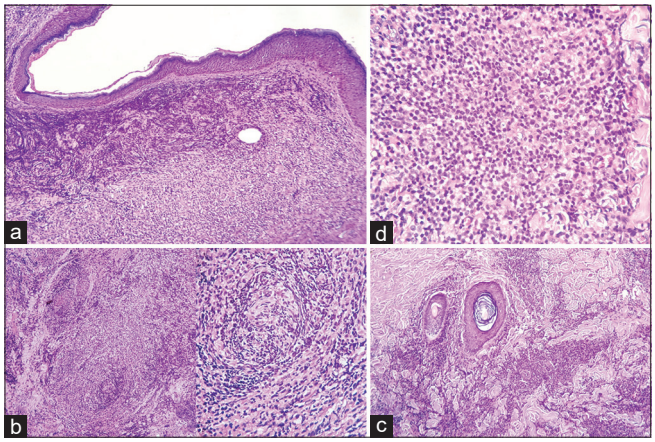

Figure 2: (a) Grenz zone noted below epidermis. Dense lymphoplasmacytic infiltrate noted in dermis, not involving the epidermis. (H and E, ×10). (b) Lymphoid cells arranged in nodules. (H and E, 10×; H and E, 40×). (c) Lymphoid cells arranged in sheets and infiltrating between collagen bundles and adnexal structures. (H and E, 10×). (d) Monomorphic lymphoid cells with centroblasts and centrocytes (H and E × 40)

Subsequently, after a multidisciplinary discussion with the medical oncology team, she received six cycles of BR (Bendamustine, Rituximab) chemotherapeutic regimen with a favorable clinical response in the form of resolution of her skin lesions and majority of the lymphadenopathy [Figure 4]. A repeat PET-CT showed localized lymph node enlargement only in the retroperitoneum (left paraaortic region, infrarenal

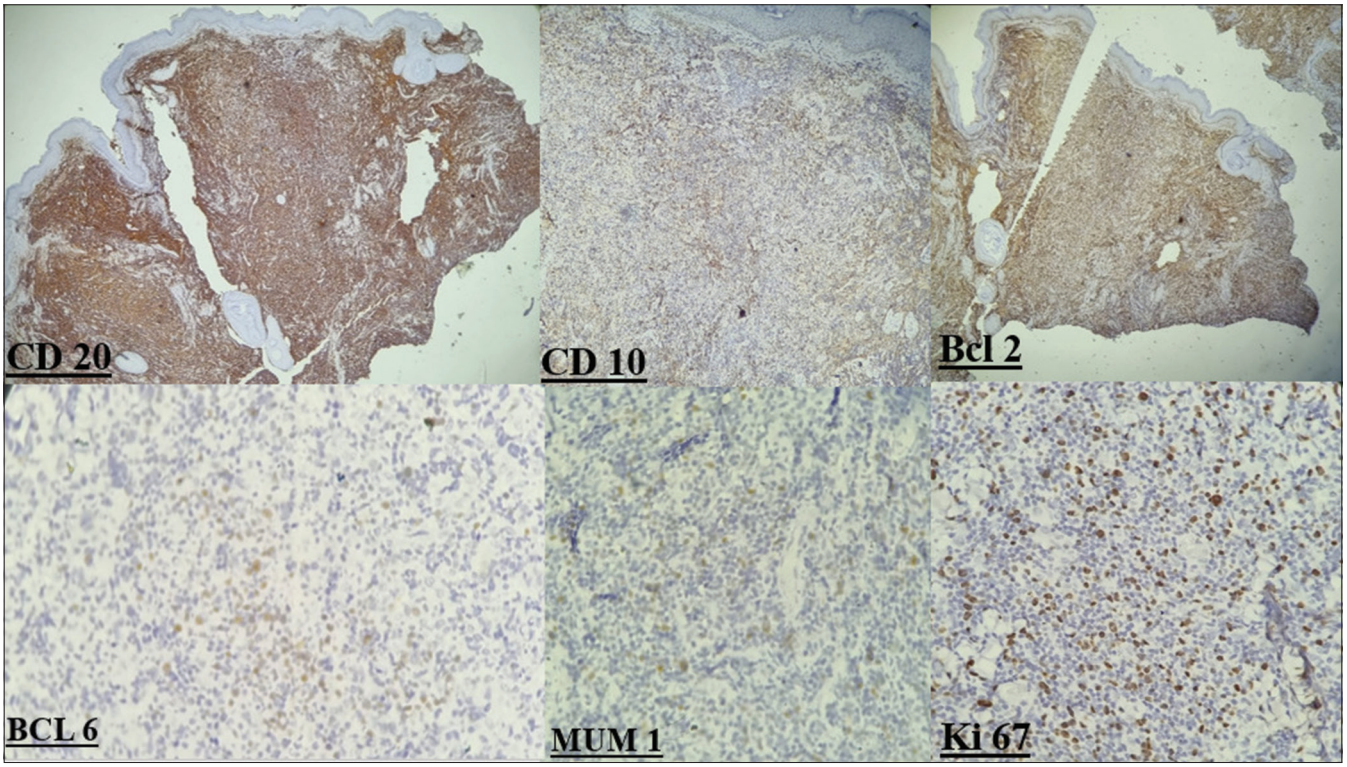

Figure 3: CD 20: diffusely positive for lesional cells, CD 10: positive in lesional cells. Bcl 2: diffusely positive in lesional cells, Bcl 6: positive in most lesional cells (50%), Mum1: scattered cells show intermediate positivity, Ki-67: 45%

Figure 4: Complete resolution of lesions after 5 sessions of BR regimen chemotherapy

abdominal aorta, left renal artery, aortic bifurcation, and left common iliac artery).

Although the majority of lymphomas are detected in lymph nodes, bone marrow, or other viscera, the initial detection of systemic lymphomas in the skin is a rare but significant occurrence in dermatology.[5] Cutaneous manifestations of FL can be either primary (PFBCL), in which the skin lesions are localized to the skin for at least six months after initial diagnosis or secondary, wherein the lesions are an external manifestation of the disseminated illness similar to our case.[6]

In a recent study by Goyal *et al.,* systemic B-cell lymphomas presenting with cutaneous manifestations was seen in <0.3% of cases. Follicular lymphoma was the most common type (1.47%).[5]

Dabski *et al.*[7] noted that extranodal involvement affecting the skin occurs in 3.8% of patients with systemic FL. Most of the patients in this series (10/11) had onset of cutaneous lesions after a mean duration of 3.7 years from initial lymphadenopathy. Our patient presented primarily with cutaneous manifestations with the only systemic finding being weight loss. The extent of systemic involvement was later recognized after imaging studies. In the index case, the presence of lymph nodes had not been noticed by the patient before the onset of cutaneous lesions nor had it been documented elsewhere; therefore, it may be safe to presume that they had occurred concurrently. This is an extremely unusual presentation; only 1/11 cases in the cohort by Dabski reported a similar manifestation in systemic FL.[7] In contrast, primary cutaneous follicle centre lymphoma (PCFCL) is a low-grade B-cell lymphoma with no systemic or nodal involvement at diagnosis.

Our patient on IHC showed strong Bcl-2 and CD10 expression, which is another vital clue to differentiate systemic FL in our patient from PCFCL which is usually weak or negative for Bcl-2 and variable for CD10. Further studies like lymph node biopsy, bone marrow biopsy, and t(14;18) translocation would help in confirming the diagnosis of systemic lymphoma. Treatment of FL depends on the staging, radiation being an option for localized disease. In systemic FL, treatment with anti-CD20 antibody with or without chemotherapy is recommended. The majority of individuals respond well; however, recurrence is common.[8]

To conclude, we highlight the secondary cutaneous presentation of systemic FL in our case, and highlight the key clinical and immunohistochemical differences from the relatively commoner entity-PCFCL. Treatment for both the variants is different, which necessitates the need for awareness about how to differentiate between them.

Acknowledgement

The patient in this manuscript has given written informed consent to publication of their case details.

Ethics approval and consent to participate

This case report was conducted in accordance with the fundamental principles of the Declaration of Helsinki.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Sharon Joseph, Myfanwy Joanne D'Souza, Ramesha M. Bhat, Michelle Serene Fernandes

Department of Dermatology, Venereology and Leprosy, Father Muller Medical College, Mangalore, Karnataka, India

Address for correspondence:
Dr. Sharon Joseph,
Department of Dermatology, Venereology and Leprosy, Father Muller Medical College, Mangalore - 575 002, Karnataka, India.
E-mail: sharon1994joseph@yahoo.co.in

References

1. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: Evolving concepts and practical applications. Blood 2011;117:5019-32.
2. Bernstein SH, Burack WR. The incidence, natural history, biology, and treatment of transformed lymphomas. Hematology Am Soc Hematol Educ Program 2009:532-41.
3. El Behery R, Laurini JA, Weisenburger DD, Smith LM, Dave BJ, Yuan J, *et al*. Follicular large cleaved cell (centrocytic) lymphoma: An unrecognized variant of follicular lymphoma. Hum Pathol 2018;72:180-90.
4. Anderson T, DeVita VT Jr, Simon RM, Berard CW, Canellos GP, Garvin AJ, *et al*. Malignant lymphoma. II Prognostic factors and response to treatment of 473 patients at the National Cancer Institute. Cancer 1982;50:2708-21.
5. Goyal N, Rubin N, Goyal A. Differential survival of systemic B-cell lymphomas initially diagnosed in the skin: A population-based study of 883 patients. Arch Dermatol Res (published online) 2021. doi: 10.1007/s00403-021-02293-0.
6. Franco R, Fernández-Vázquez A, Mollejo M, Cruz MA, Camacho FI, García JF, *et al*. Cutaneous presentation of follicular lymphomas. Mod Pathol 2001;14:913-9.
7. Dabski K, Banks PM, Winkelmann RK. Clinicopathologic spectrum of cutaneous manifestations in systemic follicular lymphoma. A study of 11 patients. Cancer 1989;64:1480-5.
8. Freedman A. Follicular lymphoma: 2018 update on diagnosis and management. Am J Hematol 2018;93:296-305.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Website: https://journals.lww.com/idoj

Quick Response Code

DOI: 10.4103/idoj.idoj_656_22

How to cite this article: Joseph S, D'Souza MJ, Bhat RM, Fernandes MS. An unusual presentation of systemic B-cell lymphoma. Indian Dermatol Online J 2023;14:735-8.

Received: 06-Dec-2022. **Revised:** 08-Jan-2023.
Accepted: 09-Jan-2023. **Published:** 10-Jul-2023.

© 2023 Indian Dermatology Online Journal | Published by Wolters Kluwer - Medknow