Our Dermatology Online

Case Report

Transition from follicular lymphoma with cutaneous metastasis to diffuse large B cell lymphoma in ethnic skin: A rare case of aggressive transformation and spontaneous resolution by reverse koebnerization

Raju Sahana, Rao Aishwarya, Loganathan Eswari, Kanathur Shilpa

Bangalore Medical College and Research Institute, Department of Dermatology, Venereology, Leprosy, Bangalore, India

Corresponding author: Raju Sahana, MD, E-mail: angelashlris@gmail.com

ABSTRACT

Follicular lymphoma is a slow-growing B-cell lymphoproliferative disorder, with survival calculated in years. It is thought that patients with follicular lymphoma (FL) who undergo histologic transformation (HT) will not have a good outcome. Diffuse large B-cell lymphoma (DLBCL) is the most prevalent histologic subtype of a transition from FL, making up 90% of all cases. Recognizing reverse koebnerization is clinically useful as a skin biopsy may be an unintended therapeutic option for local skin disease in follicular lymphoma. Herein, we report a case of an elderly Indian male patient with cutaneous metastasis from primary follicular lymphoma presenting as diffuse large B cell lymphoma with spontaneous resolution post-biopsy. Our case report will be a beneficial addition to the existing literature of rare cases with aggressive cutaneous metastasis yet spontaneous resolution by reverse Koebner.

Key words: Diffuse large B cell lymphoma, Follicular lymphoma, Cutaneous metastasis, Reverse koebnerization, Ethnic skin

INTRODUCTION

DLBCL is the most common type of lymphoma in India, with a median age of 57 years at presentation, whereas follicular lymphoma (FL) is the second most common indolent type of non-Hodgkin's lymphoma [1]. It typically involves the para-trabecular area of the bone marrow and is composed of centrocytes and centroblasts, which are rapidly dividing B-cells [2].

The 5th edition of the WHO classification of hematolymphoid tumors (WHO-HAEMS) classified FL into four main subtypes: classic FL, predominantly diffuse FL, FL with unusual cytological features, follicular large B-cell lymphoma [3]. 2–3% of cases of FL are said to transform to more aggressive forms per year. The most common histologic subtype of transformation is DLBCL (90%) [4].

Mortality associated with lymphoma is high in low/medium High Development Index (HDI) countries such as India for reasons like limited access to tertiary care cancer-specialized centers, lack of specially trained lymphoma histopathologists, and socio-economic reasons [1].

CASE REPORT

Herein, we present the case of a 71-year-old Indian male who reported to the dermatology department in view of multiple, gradually progressive, asymptomatic, red, raised lesions on the medial aspect of the right thigh and the shaft of the penis persistent for three months (Figs 1a and 1b).

He had been a known case of follicular lymphoma—stage 3, grade 2, GELF-positive, FLIP 3/5—since the

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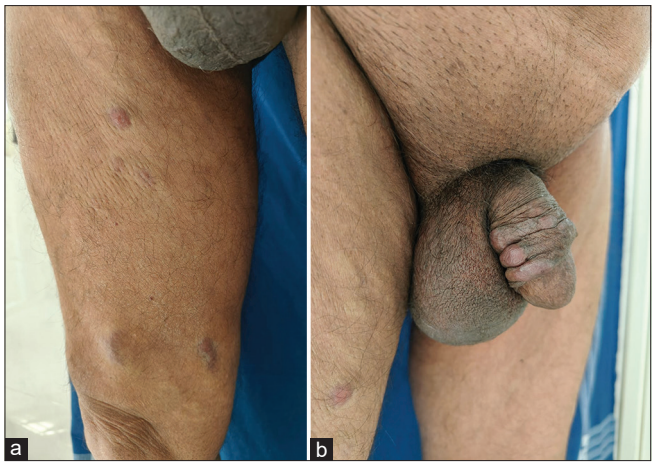

Figure 1: (a) Multiple, discrete, asymptomatic, erythematous, firm nodules and plaques over the medial aspect of the right thigh. (b) Multiple, discrete, asymptomatic, erythematous nodules over the shaft of the penis and coronal sulcus, which showed resolution.

past three years, and was actively treated in the past with one cycle of rituximab (lymphoma protocol) and five cycles of Bendamustine with rituximab; and five cycles of R-CHOP. PET-CT revealed multiple hypermetabolic enlarged lymph nodes in the neck, axilla, mediastinum, abdomen, and inguinal region. Due to the severity of the side effects of chemotherapy, treatment was stopped and a maintenance regime with lenalidomide was initiated. He was subjected to a biopsy to exclude primary cutaneous B cell lymphoma and cutaneous metastasis secondary to follicular lymphoma.

Histopathology and Immunohistochemistry

Histopathology of the dermis showed dense, diffuse sheets of monotonous, intermediate to large, atypical lymphoid infiltrates. The individual cells were medium-sized with hyperchromatic nuclei and scant cytoplasm. Also seen was a population of cells with large atypical lymphoid cells with individual cells showing vesicular chromatin and 1–3 prominent nucleoli (Fig. 2).

IHC findings were as follows (Fig. 3):

CD20- Diffuse, strong positivity seen among neoplastic lymphoid cells.

CD3- Focal positivity among T cells.

Bcl2- Diffuse strong positivity among neoplastic lymphoid cells.

Ki67-Strong nuclear positivity in neoplastic lymphoid cells 80–90%.

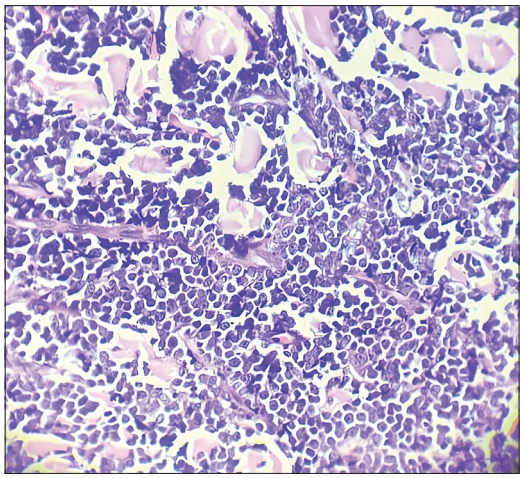

Figure 2: Histopathological features suggesting diffuse large B cell lymphoma (H&E stain; 40x, inset showing 100x).

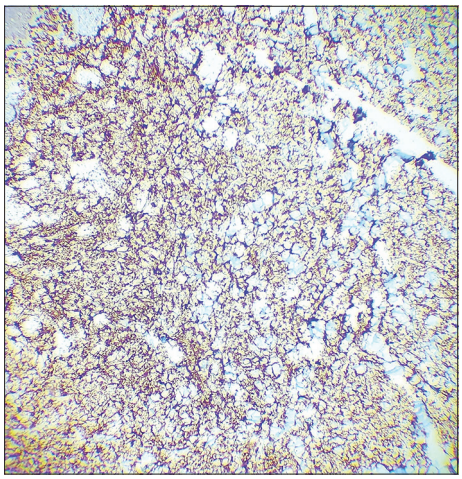

Figure 3: IHC findings showing positive CD20, BCl2, and Ki67 and negative CD3.

Histologic features were of cutaneous lymphoma morphologically suggesting high-grade diffuse large b cell lymphoma.

A histopathological examination of the axillary lymph nodes showed atypical lymphoid cells arranged in sheets with individual cells showing irregular nuclear chromatin with inconspicuous nucleus. IHC markers were positive for CD 20, BCl2, CD10 and negative for MUM1 Cyclin D1. Ki 67 was 15–20%.

Follow-up

Two weeks post-biopsy, the cutaneous lesions resolved spontaneously (Figs. 4a and 4b), and the patient was referred back to the oncology department for further management. Despite the successful outcome of the cutaneous lesions, the patient's general condition

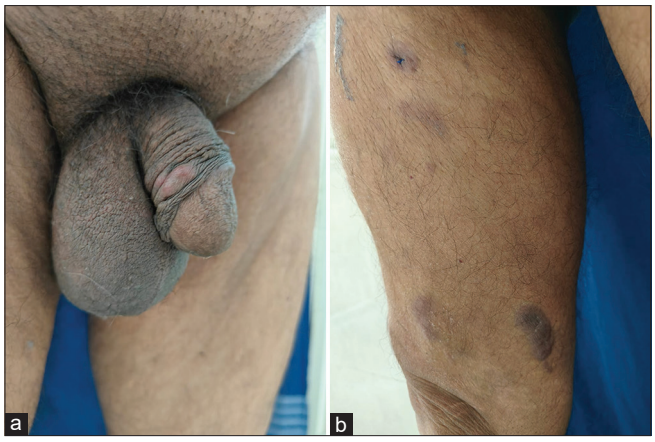

Figure 4: (a) Photographs taken two weeks apart after a punch biopsy showing partial resolution of the lesions. (b) One of the lesions on the thigh post-biopsy.

deteriorated and he succumbed to death due to sepsis and multi-organ failure.

DISCUSSION

Herein, we report a rare manifestation of primary follicular lymphoma presenting with secondary cutaneous involvement. Only two cases have been reported in the literature [5,6]. Primary cutaneous lymphomas are the second most common extranodal lymphomas, the first being gastrointestinal lymphomas. Although primary cutaneous lymphoma is fairly common, secondary involvement in the form of cutaneous metastasis is not widely reported.

The presence of cutaneous metastases may signal a transformation to aggressive lymphoma subtypes [7].

Although histopathology in our case showed changes suggestive of high-grade diffuse large B-cell lymphoma, we were unable to perform specific IHC markers for DLBCL or FISH to identify the translocation/mutation due to the deteriorating general condition of the patient and financial constraints. Treatment is only palliative for disseminated follicular lymphoma with cutaneous metastasis. Our patient had already been treated with multiple R-CHOP regimes doses, Bendamustine, and finally only maintained on lenalidomide. Lenalidomide, mainly through its mechanism of inhibition of TNF-alpha and NF-kB has shown superior outcomes in DLBCL, especially the non-germinal center B-cell DLBCL [8].

We also noticed a peculiar and rare resolution of cutaneous lesions, following the biopsy in our patient. This phenomenon of reverse koebnerization has been reported in conditions such as granuloma annulare, leukocytoclastic vasculitis, and bullous pemphigoid. It is said to occur due to alterations in the immunologic microenvironment at the site of the trauma. It has been previously reported in only one other case of follicular lymphoma [9].

CONCLUSION

This was a rare case of follicular lymphoma with cutaneous metastasis, which was resolved by reverse koebnerization following a skin biopsy. Treatment options for relapsed follicular lymphoma with isolated cutaneous metastasis or involvement of other organs are mainly palliative yet could also include anti-CD 20 antibody therapy with radiation and stem cell transplantation. Early recognition of the cutaneous disease and relapse may have a positive effect on the outcome and management. Awareness of reverse koebnerization may serve as a simple yet effective treatment of the cutaneous lesions.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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