Primary Cutaneous B-cell Lymphomas: Case Report of Two Cases

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Abstract
Primary cutaneous lymphomas are a unique, heterogeneous group of lymphoproliferative disorders which have a primary cutaneous manifestation in the absence of systemic involvement of lymph nodes, bone marrow, or visceral organs at the time of diagnosis. Among the primary cutaneous lymphomas, B-cell lymphoma is much less common and accounts for 20%–25% of cases. Primary cutaneous diffuse large B-cell lymphomas (PCDLBCLs) are aggressive neoplasms with poor prognosis. Early and accurate diagnosis is required as these patients respond well to systemic anthracycline-based chemotherapy (R-CHOP). In this article, we report two cases of PCDLBCL, other which presented with rapidly enlarging skin nodules and were diagnosed based on clinical features, histomorphology, and characteristic immunohistochemical expression. Both the patients were treated with systemic chemotherapy and responded well. During the 6 months' follow-up period, the lesions regressed. The patients are symptom free with no evidence of disease relapse or dissemination to extracutaneous sites.

Key Words: B-cell, cutaneous, lymphoma, other, primary

Introduction
Primary cutaneous lymphomas are a unique, heterogeneous group of lymphoproliferative disorders which have a primary cutaneous manifestation in the absence of systemic involvement of lymph nodes, bone marrow, or visceral organs at the time of diagnosis. The majority of primary cutaneous lymphomas are T-cell lymphomas (65%). B-cell lymphomas (25%) and natural killer-cell lymphomas (10%) are less common. The WHO-EORTC classification classifies cutaneous B-cell lymphomas (CBCLs) into four distinct types of primary cutaneous marginal zone B-cell lymphoma (PCMZL), primary cutaneous follicular center lymphoma (PCFCL), primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT), and PCDLBCL-other. These subtypes can be distinguished by histopathological features and immunohistochemical evaluation. We report two cases of PCDLBCL-other which presented as rapidly enlarging cutaneous nodules. These cases need to be diagnosed promptly due to poor prognosis and need for commencing of an early treatment.

Case Reports

Case 1
A 45-year-old female known case of HIV on antiretroviral therapy developed a small, single asymptomatic swelling on the left thigh. She consulted a local physician who suspected it to be cutaneous tuberculosis and started antitubercular therapy. However, the lesions increased in number and size over a period of 8 months. She presented to our hospital with multiple skin-colored, firm cutaneous nodules (largest 10 cm × 11 cm × 19 cm). On histopathological examination, there was a diffuse infiltration of the dermis and subcutaneous tissue by sheets of large round lymphoid cells with centroblastic morphology. There was no evidence of epidermotropism, and neoplastic cells were separated from epidermis by a clear grenz zone. On immunohistochemistry (IHC), neoplastic cells were positive for leukocyte common antigen (LCA) and were negative for CD34, CD30, and TdT. B-cell immunophenotype was established by positive staining for CD20, CD19, and CD79a. Mib-1 labeling index

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How to cite this article: Mishra S, Shelly D, Vinu Balraam KV, Bharadwaj R. Primary cutaneous B-cell lymphomas: Case report of two cases. Indian J Dermatol 2017;62:675.
was 80%–90%. To further characterize PCDLBCL into PCDLBCL-LT or PCDLBCL-other, IHC for bcl-2, MUM-1, CD10, and bcl-6 was performed. Large lymphoid cells were negative for bcl-2, MUM-1, and CD10 expression while they were positive for bcl-6 [Figure 2].

Based on a primary cutaneous presentation, the absence of systemic disease, diffuse dermal and subcutaneous infiltrate by large centroblast-like B-cells, and negative immunostaining for bcl-2 and MUM-1, a final diagnosis of PCDLBCL-other was established.

Case 2

A 66-year-old male presented with multiple, rapidly enlarging skin to plum-colored nodules involving chest and anterior abdominal wall of three months’ duration, largest 6 cm × 5 cm × 2 cm [Figure 3]. An excision biopsy performed from the lesion was diagnosed as dermatofibrosarcoma protuberans at a private hospital. Subsequently, the patient presented to our hospital due to a rapid increase in size and number of nodules which were hard in consistency and fluorodeoxyglucose avid on positron emission tomography–computed tomography. Excision biopsy revealed a diffuse infiltration of subepidermal tissue by large lymphoid cells with histomorphology as mentioned above [Figure 4].

Figure 2: (Case 1) Sections showing a high Mib-1 index of 70%. Large lymphoid cells were negative bcl-2 and MUM-1 expression

Figure 3: Photograph showing multiple, large skin to plum-colored cutaneous nodules over anterior abdominal wall and chest (Case 2). Inset shows the excised specimens of cutaneous lesions

Figure 4: (Case 2) Sections showing sheets of large lymphoid cells involving dermis and infiltrating subcutaneous fat. Epidermotropism is not seen and a clear grenz zone is noted between neoplastic cells and epidermis. On higher magnification, these cells have clumped chromatin with prominent nucleoli. These large lymphoid cells were positive for CD20
IHC [Figure 5], tumor cells were positive for LCA and CD20 and negative for CD3, CD5, CD10, bcl2, and MUM-1. Mib-1 labeling index was 80%-90%. Therefore, based on infiltration by CD20-positive large lymphoid cells, which were negative for bcl2, MUM-1, and CD10 expression, we gave a final diagnosis of PCDLBCL-other.

**Discussion**

PCBCL are lymphoproliferative neoplasms with a primary cutaneous manifestation, and no extracutaneous involvement after complete staging has been performed.[3] Conversely, secondary cutaneous lymphomas have a systemic disease with subsequent development of skin lesions at presentation. This distinction is important because primary cutaneous lymphomas are less aggressive with an overall better prognosis. Despite being second most frequent extranodal lymphomas, these are rare with an annual incidence of 0.5/100,000.[4] Unlike B-cell lymphomas of lymph node, majority of primary cutaneous lymphomas arise from T-cells. CBCLs account for only 20%-25% of all primary cutaneous lymphomas.[5]

PCDLBCL-LT classically presents as rapidly growing red-purple-colored nodules on legs in elderly females. However, in 10%-20% of patients, other areas of the body are affected.[6] Histopathologically, there is diffuse, monotonous proliferation of large cells in the dermis and subcutaneous tissue having a centroblastic and immunoblastic phenotype. Epidermotropism is not a feature and a grenz zone is seen. Immunohistochemical expression of B-cell markers, bcl-2, and MUM-1 is characteristically seen. PCDLBCL-LT also commonly expresses bcl-6 and lacks CD10 expression.[7,8]

PCFCL is the most common PCBCL and involves scalp/forehead and trunk in middle-aged patients.[2,6,7] The prognosis is excellent with >95% patients surviving after 5 years.[9] Histopathology shows dermal infiltrate of centrocytes and centroblasts in a follicular, follicular and diffuse, or diffuse growth pattern. To distinguish these cases from PCDLBCL-LT, IHC is of help as PCFCL does not express bcl-2, MUM-1, and FOX-P1, and express CD10 unlike PCDLBCL-LT. The distorted follicular dendritic cell network in PCFCL is highlighted by CD21/CD23.[7,8] The distinction is important due to better prognosis and less aggressive treatment in PCFCL.[10]

PCDLBCL-other is a very rare PCDLCL which does not meet the diagnostic criteria for either PCDLBCL-LT or PCFCL.[2] They include cases of T-cell and histioyte-rich PCDLBCL, plasmablastic lymphomas, intravascular B-cell lymphomas, or cases which are morphologically and clinically identical to PCDLBCL-LT but do not express bcl-2.[2,4] They present as solid nodules involving the leg (50%), head, trunk, and arms. They express bcl-6 (100%), MUM-1 (67%), and FOX-P1 (72%) but lack bcl-2 expression.[8] The 5-year survival rate is 50%. Due to poor prognosis, the therapeutic modalities used are similar to PCDLBCL-LT.[9]

In both of our cases, there was diffuse dermal and subcutaneous infiltrate by large noncleaved B-cells. The differentials considered were PCDLBCL-LT, PCDLBCL-other, and PCLFCL-diffuse type. Due to the absence of centrocyte-like cells with cleaved nuclei and absence of CD10 expression, a diagnosis of PCLFCL-diffuse type was ruled out. The large cells were also negative for bcl-2 and MUM-1 which are positive in the majority of PCDLBCL-LT. Thus, due to characteristic histomorphology, IHC and absence of extracutaneous involvement at the time of presentation, we finally gave a diagnosis of PCDLBCL-other in both cases.

Both the patients were treated with chemotherapy (CHOP regimen) and responded well. After 6 months' follow-up, the cutaneous lesions have regressed and there is no evidence of relapse or systemic dissemination. We have presented these cases due to rarity of PCDLBCL-other and to emphasize the need for correct diagnosis so that early chemotherapy can be given to these patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.
Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

What is new?
We present these cases so that clinicians and pathologists are sensitised to this rare disease and keep primary cutaneous lymphomas as a differential diagnosis of cutaneous nodules. An early diagnosis and prompt treatment is curative and will benefit the patients.

References
1. Bradford PT, Devesa SS, Anderson WF, Toro JR. Cutaneous lymphoma incidence patterns in the United States: A population-based study of 3884 cases. Blood 2009;113:5064-73.
2. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105:3768-85.
3. Kerl H, Fink-Puches R, Cerroni L. Diagnostic criteria of primary cutaneous B-cell lymphomas and pseudolymphomas. Keio J Med 2001;50:269-73.
4. Pandolfino TL, Siegel RS, Kuzel TM, Rosen ST, Guitart J. Primary cutaneous B-cell lymphoma: Review and current concepts. J Clin Oncol 2000;18:2152-68.
5. Zackheim HS, Vonderheide EC, Ramsay DL, LeBoit PE, Rothfleisch J, Kashani-Sabet M, et al. Relative frequency of various forms of primary cutaneous lymphomas. J Am Acad Dermatol 2000;43:793-6.
6. Kodama K, Massone C, Chott A, Metze D, Kerl H, Cerroni L, et al. Primary cutaneous large B-cell lymphomas: Clinicopathologic features, classification, and prognostic factors in a large series of patients. Blood 2005;106:2491-7.
7. Senff NJ, Hoefnagel JJ, Jansen PM, Vermeer MH, van Baarlen J, Bloks WA, et al. Reclassification of 300 primary cutaneous B-cell lymphomas according to the new WHO-EORTC classification for cutaneous lymphomas: Comparison with previous classifications and identification of prognostic markers. J Clin Oncol 2007;25:1581-7.
8. Hoefnagel JJ, Vermeer MH, Jansen PM, Fleuren GJ, Meijer CJ, Willemze R, et al. Bcl-2, Bcl-6 and CD10 expression in cutaneous B-cell lymphoma: Further support for a follicle centre cell origin and differential diagnostic significance. Br J Dermatol 2003;149:1183-91.
9. Zinzani PL, Quaglino P, Pimpinelli N, Berti E, Baliva G, Rupoli S, et al. Prognostic factors in primary cutaneous B-cell lymphoma: The Italian Study Group for Cutaneous Lymphomas. J Clin Oncol 2006;24:1376-82.
10. Senff NJ, Noordijk EM, Kim YH, Bagot M, Berti E, Cerroni L, et al. European organization for research and treatment of cancer and international society for cutaneous lymphoma consensus recommendations for the management of cutaneous B-cell lymphomas. Blood 2008;112:1600-9.