# Cutaneous Lymphoma in a Tertiary Skin Hospital and Referral Centre in Nepal

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## ABSTRACT

**Background:** Primary cutaneous lymphomas are a distinct group of rare lymphoid neoplasms with absence of extracutaneous lymphomas at the time of presentation. They are rare in Nepal and no data on cutaneous lymphoma have been published from this country till date.

**Methods:** This retrospective study included 15 cases of cutaneous lymphomas retrieved from the records of department of Dermatopathology, DI Skin Hospital and Referral Centre, Bansbari, Kathmandu, Nepal. Patients were diagnosed according to the current WHO classification for cutaneous lymphoma.

**Results:** A total of 15 cases were studied with median age of 45 years (range: 22 to 81 years) and male to female ratio of 1.5:1. Primary cutaneous lymphomas constituted 13 cases out of 15 and the most common type of cutaneous lymphoma was mycosis fungoides and variants 5 (33%), followed by CD30 positive primary cutaneous anaplastic large cell lymphoma constituting 2 (13%). T-cell cutaneous lymphoma constituted 13 (87%) and B-cell cutaneous lymphoma 2 (13%).

**Conclusions:** Cutaneous T-cell lymphomas were more frequent than cutaneous B-cell lymphomas in Nepalese patients. Mycosis fungoides and variants are commonest type of primary cutaneous lymphomas.

**Keywords:** Histopathology; mycosis fungoides; primary cutaneous t-cell lymphoma; WHO classification.

## INTRODUCTION

Cutaneous lymphomas (CL) are distinct entities and differ from nodal lymphomas. Primary cutaneous lymphomas (PCL) lack extracutaneous lymphomas at the time of presentation.[1] The skin involvement in extracutaneous lymphomas is considered metastatic disease. The 4th edition of WHO[2] classifies cutaneous lymphomas into Mycosis fungoides and variants, Primary cutaneous CD30+ T-cell lymphoproliferative disorders etc.[2]

More than 75% of PCL are mainly T-cell type[3,4] and the majority of PCL are Mycosis fungoides and CD30+ lymphoproliferative disorders.[5] Cutaneous B-cell lymphomas constitute upto 25% of all PCL.[6] The diagnosis of PCL is made based on morphology, immunohistochemistry and molecular studies.

Primary cutaneous lymphomas are rare in Nepal and no epidemiological studies on cutaneous lymphoma have been published. However, there are few case reports namely primary cutaneous CD30+ anaplastic large cell lymphoma[7], mycosis fungoides[8] and cutaneous involvement in nodal lymphoma[9,10] published.

This study is aimed to analyze case series of cutaneous lymphomas diagnosed at a tertiary Skin Hospital in Nepal.

## METHODS

The present study is a retrospective review of 15 cases of cutaneous lymphomas retrieved from the records of department of Dermatopathology, DI Skin Hospital and Referral Centre (DISHARC), Bansbari, Kathmandu, Nepal between the period January 1, 2018 and December

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31, 2022. Approval for this study was obtained from institutional review board of Institute of Medicine, Maharajgunj, Kathmandu, Nepal. All methods carried out in this study is in accordance with guidelines of institutional review committee of Institute of Medicine.

All cases with histopathological diagnosis of cutaneous lymphoma irrespective of age and gender were included in this study. Recurrent cases were excluded. Cutaneous lymphomas were classified according to WHO classification system.[2] The demographic profiles, clinical features, histopathological, immunohistochemical & molecular findings were retrieved.

Immunohistochemical studies and molecular studies were done at Kempf and Pfaltz histological diagnostics, Zurich, Switzerland. BIOMED2 PCR was performed for molecular analysis to assess monoclonality of cutaneous infiltrates.

## RESULTS

A total of 15 cases of cutaneous lymphomas were studied and the age of the patient ranged from 22 to 81 years with median age being 45 yrs. Six out of 15 patients were female with male to female ratio of 1.5:1. The demographic and clinical features of patients with cutaneous lymphomas are summarized in Table 1. One (case 12) of the patients was immunocompromised due to HIV infection.

PCL constituted 13 cases out of 15 and remaining two cases were metastatic disease involving skin in patients with lymph nodal lymphoma. In all primary cases, any extracutaneous lymphomas were excluded by clinical examination and imaging studies.

The frequency of CL is summarized in Table 2.

The most common type of CL is mycosis fungoides and variants constituting 5 (33.32%), followed by CD30 positive primary cutaneous anaplastic large cell lymphoma constituting 2(13%). T-cell CL constituted 13 (86.68%) and B-cell cutaneous lymphoma 2 cases (13.32%).

All three cases of mycosis fungoides presented with patches and plaques (Fig.1) in sun-protected area. Tumor stage mycosis fungoides was not found in this study. Patients with folliculotropic mycosis fungoides also presented with multiple erythematous plaques and patches over the face. One case of CD30 positive primary cutaneous anaplastic large cell lymphoma developed multiple cutaneous nodules all over the body (Fig. 2), while another revealed single skin nodule. A case of primary cutaneous aggressive epidermotropic CD8 positive cytotoxic T-cell lymphoma developed necrotic plaques all over the body. Case no. 12 was HIV positive and developed small nodular lesions on both legs.

All cases of mycosis fungoides showed epidermotropic atypical lymphocytes with typical Darier's nests (Fig. 3) in two of them. The superficial dermis showed dense bandlike infiltrate of atypical lymphocytes, which were positive for CD2, CD3, CD4 and BetaF1 and negative for CD7, CD8, CD56 & TIA1. CD30 positivity was patchy with less than 30% cells positive. BIOMED2 PCR revealed a monoclonal rearrangement of T-cell receptor beta genes. Folliculotropic mycosis fungoides showed folliculotropic atypical lymphocytes which revealed immunohistochemical findings (Fig. 4) similar to cases of mycosis fungoides. In addition, follicular and perifollicular mucinosis (highlighted by Alcian blue stain) is seen in these cases. Cases of CD30 positive primary cutaneous anaplastic large cell lymphoma histopathologically revealed diffuse dermal proliferation of large atypical lymphoid cells which were positive for CD2, CD4 & CD30 and negative for CD3, CD8, CD20, EMA & ALK. CD30 positivity is seen in 100% tumor cells. Ki-67 reactivity was seen in >90% tumor cells and EBV in situ hybridization was negative. All remaining cases of cutaneous lymphoma showed morphological and immunohistochemical features compatible with the diagnoses made. Skin biopsy of case 12 (HIV positive) demonstrated diffuse proliferation of large lymphoid cells in the dermis with involvement of the panniculus. No epidermotropism is noted and there is grenz zone of collagen between the epidermis and dermal infiltrate. These lymphoid cells are positive for CD20, CD45, MUM1, BCL2 and negative for CD3, CD10, CD30, BCL6 and ALK. Ki-67 was expressed in 100% nuclei.

Follow-up information was available in four cases only. Case 1 with mycosis fungoides got chemotherapy (methotrexate) with good clinical remission. She developed classic Hodgkin lymphoma of inguinal lymph node after six months of diagnosis of mycosis fungoides. Then she was treated by medical oncologist. She didn't develop recurrence of either mycosis fungoides or Hodgkin lymphoma for three years period of follow up. Case 4 with folliculotropic mycosis fungoides is undergoing radiation therapy with significant improvement of skin lesions. Case 7 (primary cutaneous CD30-positive anaplastic large cell lymphoma) developed another skin nodule on the trunk after three months of initial diagnosis. This nodule was also excised

with similar histopathological diagnosis. She didn't get any further treatment like radiotherapy or chemotherapy. She didn't develop any new lesion in three years follow up. Case 9 with primary cutaneous aggressive epidermotropic cytotoxic CD8+ T-cell lymphoma was referred to medical oncologist for chemotherapy. He passed away after two months of chemotherapy. He survived for a total of nine months with the disease.

**Table 1. Demographic and clinical features of patients with cutaneous lymphoma.**

| Case no. | Age (Yr) | Sex | Clinical feature | Site | Diagnosis |
|---|---|---|---|---|---|
| 1 | 70 | F | Multiple erythematous plaques and patches | Leg, Arms and Trunk | Mycosis fungoides |
| 2 | 45 | M | Multiple annular erythematous plaques and patches | Legs, Arms and Trunk | Mycosis fungoides |
| 3 | 78 | M | Multiple erythematous plaques and patches | Trunk | Mycosis fungoides |
| 4 | 40 | M | Multiple papules and plaques | Face | Folliculotropic Mycosis fungoides |
| 5 | 55 | F | Multiple itchy crusted patches with exfoliation & lichenification | Face, Trunk, Upper & lower extremities | Folliculotropic Mycosis fungoides |
| 6 | 81 | M | Multiple nodules of variable size (<0.5 cm to 4 cm) | Face, Trunk, Upper & lower extremities | CD30- positive primary cutaneous anaplastic large cell lymphoma |
| 7 | 25 | F | Single nodule (1 cm) | Forehead | CD30- positive primary cutaneous anaplastic large cell lymphoma |
| 8 | 22 | F | Tender erythematous plaques & nodules | Legs | Subcutaneous panniculitis like T-cell lymphoma |
| 9 | 40 | M | Necrotic plaques | All over the body | Primary cutaneous aggressive epidermotropic cytotoxic CD8 positive T-cell lymphoma |
| 10 | 45 | F | Multiple erythematous juicy nodules | Forehead, Face and Ears | Cutaneous marginal zone lymphoma |
| 11 | 72 | M | Non-healing ulcer | Dorsum of right foot | Primary cutaneous peripheral T-cell lymphoma, NOS |
| 12 | 43 | M | HIV positive; Multiple small nodules and single ulcer | Both legs | Primary cutaneous diffuse large B-cell lymphoma, leg type |
| 13 | 59 | M | Multiple painless juicy erythematous nodules | All over the body | Extranodal NK/T-cell lymphoma, nasal type |
| 14 | 33 | M | Multiple skin non-tender nodules and plaques and cervical lymphadenopathy | Right shoulder & scapular region and chest | Cutaneous involvement of an ALK-positive anaplastic large cell lymphoma |
| 15 | 36 | F | Erythematous plaques with scales and cervical lymphadenopathy | Right earlobe | Cutaneous involvement of a diffuse large B-cell lymphoma |

**Table 2. Frequency of cutaneous lymphoma.**

| Histopathological diagnosis | Frequency (%) |
|---|---|
| Mycosis fungoides | 3 (20.00) |
| Folliculotropic mycosis fungoides | 2 (13.32) |
| CD30- positive primary cutaneous anaplastic large cell lymphoma | 2 (13.32) |
| Subcutaneous panniculitis like T-cell lymphoma | 1 (6.67) |
| Primary cutaneous aggressive epidermotropic cytotoxic CD8-positive T-cell lymphoma | 1 (6.67) |
| Cutaneous marginal zone lymphoma | 1 (6.67) |
| Primary cutaneous peripheral T-cell lymphoma, NOS | 1 (6.67) |
| Extranodal NK/T-cell lymphoma, nasal type | 1 (6.67) |
| Primary cutaneous diffuse large B-cell lymphoma, leg type | 1 (6.67) |
| Cutaneous involvement of an ALK-positive anaplastic large cell lymphoma | 1 (6.67) |
| Cutaneous involvement of a diffuse large B-cell lymphoma | 1 (6.67) |
| **Total** | **15 (100.00)** |

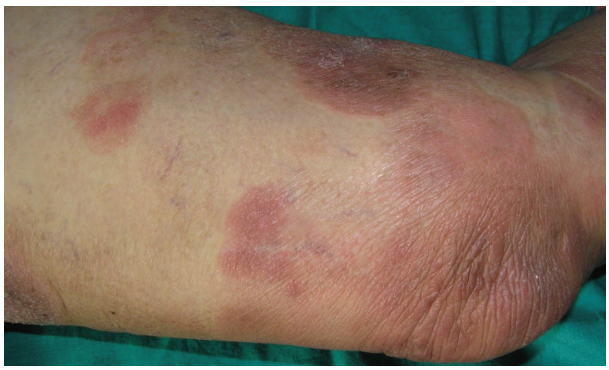

**Figure 1. Patches and plaques in thigh in a patient with Mycosis fungoides.**

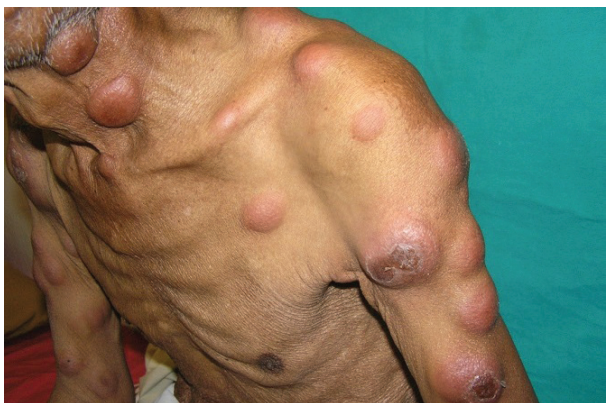

**Figure 2. Multiple skin nodules in a patient with CD30 positive primary cutaneous anaplastic large cell lymphoma.**

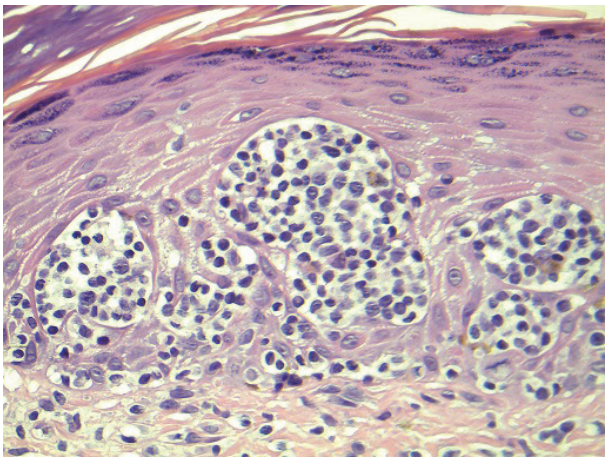

**Figure 3. Mycosis fungoides. Epidermotropic atypical lymphocytes forming Darier's nests. H&E stain, X 400 magnification.**

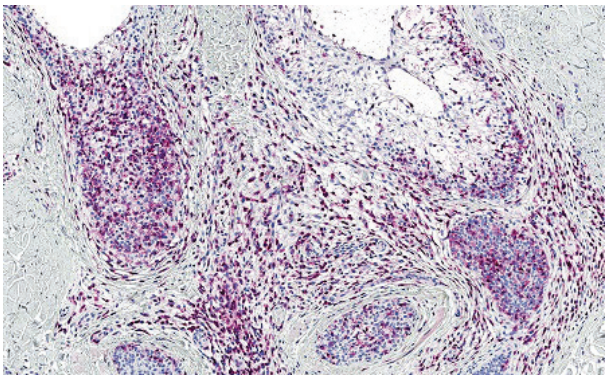

**Figure 4. Folliculotropic mycosis fungoides. CD3 positive folliculotropic atypical lymphocytes. CD3 IHC stain, X 100 magnificatio**

## DISCUSSION

Primary cutaneous lymphomas are a diverse group of extranodal non-Hodgkin lymphoma[11,12] with initial presentation in the skin. PCL constitute about 20% of all extranodal non-Hodgkin lymphoma.[4] In our centre, cutaneous lymphoma constituted 4.2% of all cutaneous malignancies.

Median age of patients with CL is 45 years in this study, but it varies with types of lymphoma. All cases of Mycosis fungoides were seen in age group 40 years or above and two of them 70 years or above. These findings correspond with other studies[11,13,14], which found that PCL affects predominantly adults or elderly people. Most of the studies[11,15-18] showed male predominance for all types of PCL and a male to female ratio in this study was 1.5:1 with clear cut male predominance.

Our study comprised of both primary and secondary cutaneous lymphomas. We didn't face any issues while distinguishing primary and secondary lymphomas due to availability of complete clinical data. Secondary cutaneous lymphomas constituted 2 cases (13.33%) only. The CTCL (86.68%) predominance over CBCL (13.32%) was found in this study and CTCL predominance is comparable with other studies.[1-3,11,14] However the percentage of CBCL is lower in Nepal than in these studies as in most studies CBCL accounts for 25-35% of all CL. I would emphasize this unique feature in our series of CL from Nepal. This perhaps represents a geographic variation in the epidemiology of CBCL. The most common type of PCL we found is mycosis fungoides (33.32%), followed by CD30 positive primary cutaneous anaplastic large cell lymphoma (13.32%) and this finding is concordant with many other studies[1-3,11-14] In addition, we found rare cases of primary cutaneous aggressive epidermotropic cytotoxic CD8 positive T-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma leg type, extranodal NK/T-cell lymphoma etc.

In this study, all three cases of mycosis fungoides presented with patches & plaques in sun-protected area. This clinical finding is typical as mentioned in the literature.[1,19] However, patients with folliculotropic mycosis fungoides presented with multiple erythematous plaques and patches in sun-exposed area (face). Most of the other types of cutaneous lymphomas presented with skin nodules, while a case of primary cutaneous aggressive epidermotropic CD8 positive cytotoxic T-cell lymphoma developed necrotic plaques. These findings are comparable with studies published.[19,20]

In our study, cases of mycosis fungoides showed epidermotropic atypical lymphocytes with typical Darier's nests (in two cases). The superficial dermis showed dense bandlike infiltrate of atypical lymphocytes, which were positive for CD2, CD3, CD4 and BetaF1 and negative for CD7, CD8, CD56 & TIA1. CD30 positivity was patchy with less than 30% cells positive. BIOMED2 PCR revealed a monoclonal rearrangement of T-cell receptor beta genes. These morphological, immunohistochemical and PCR findings are typical of mycosis fungoides as mentioned in the literature.[1,19]. In folliculotropic mycosis fungoides, follicular and perifollicular mucinosis was observed. Morphological & immunohistochemical findings of cases of CD30 positive primary cutaneous anaplastic large cell lymphoma and other remaining types of cutaneous lymphomas are compatible with findings described in the literature.[1,19,21]

Skin biopsy of case 12 (HIV positive) demonstrated diffuse proliferation of large lymphoid cells in the dermis with involvement of the panniculus and no epidermotropism. These lymphoid cells are positive for CD20, CD45, MUM1, BCL2 and negative for CD3, CD10, CD30, BCL6 and ALK and this finding is compatible with a diagnosis of primary cutaneous DLBCL, leg type.

In developing countries like Nepal, some patients do not undergo chemotherapy due to financial constraints and some do not appear after one or two cycles of chemotherapy. Because of treatment compliance, follow-up information is not available in most of the cases. We could trace 4 cases only. Case 1 got chemotherapy (methotrexate) with good clinical remission. She developed classic Hodgkin lymphoma of inguinal lymph node after 6 months of diagnosis of mycosis fungoides. Then she was treated by medical oncologist. This is the first case for us in Nepal showing association of mycosis fungoides with classic Hodgkin lymphoma, however, there are good number of articles published describing the association of these two diseases.[22,23] She didn't develop recurrence of either mycosis fungoides or Hodgkin lymphoma for 3 years period of follow up. Case 4 is currently undergoing radiation therapy with significant improvement of skin lesions. Case 7 developed another skin nodule on the trunk after 3 months of initial diagnosis and there are no any new lesions in 3 years follow up. Case 9 survived for a total of 9 months with the disease. Overall, prognosis is found to be good except for the case 9, who suffered from an aggressive type of cutaneous lymphoma and this prognosis was expected for him.

## CONCLUSIONS

This study for the first time in Nepal provides a tiny data on the distribution of cutaneous lymphomas. The data were taken from single centre and is not representative of the entire nation.

Cutaneous T-cell lymphomas were found to be markedly predominating over cutaneous B-cell lymphomas in Nepalese patients due to more frequent occurrence of mycosis fungoides & variants and CD30-positive primary cutaneous anaplastic large cell lymphoma. This study adapted WHO classification and it is recommended to follow this classification for uniform diagnosis in cutaneous lymphoma.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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