Histopathological Approach to Cutaneous Lymphoid Infiltrate

Uma Nahar Saikia, Manoj Gopal Madakshira
Department of Histopathology, PGIMER, Chandigarh, India

Abstract
Cutaneous lymphoid infiltration is common histology seen in the day-to-day practice of dermatopathology. The reasons for this infiltration can range from a spontaneously remitting pseudolymphoma such as Jessner’s infiltration to a sinister and aggressive cytotoxic T-cell lymphoma. Before analyzing the slide, the clinical perspective needs to be borne in mind as a diagnosis can never be made in isolation, especially in dermatopathology. In this article, we discuss in brief the various common cutaneous lymphoid infiltrative entities encountered in routine practice, discuss the differentiating features, and suggest an algorithmic approach to arrive at the possible diagnosis.

Keywords: Cutaneous, epidermotropism, lymphoma, pseudolymphoma

INTRODUCTION
Skin is not a mere barrier but plays an active role in the immune system of the body.[1] It is a rich source of antigen-presenting Langerhans cells along with the ability of epidermal cells to produce cytokines and influence T-cell maturation.[2,3] It also has skin-associated lymphoid tissue (SALT) similar to mucosa-associated lymphoid tissue (MALT) seen in the bronchial tree and gastrointestinal system.[4] However, unlike MALT which has prominent lymphoid follicles rich in B-cells, SALT is characterized by the presence of Langerhans cells and predominantly memory T-cells.[1] This makes the profile of inflammatory and lymphomatous lesion of the skin distinct with a higher predominance of T-cell-rich lesions.

Cutaneous lymphoid infiltration is always a challenge for a dermatopathologist to provide a precision diagnosis as a large consort of both nonneoplastic and neoplastic lesions can present with cutaneous lymphoid infiltration. The diagnosis can be arrived at including clinical correlation and histopathological patterns with immunophenotyping and molecular studies, whenever needed. This review provides an attempt for an algorithmic approach in cutaneous lymphoid infiltrates, briefly outlining the salient features of clinical entities with their histological patterns.

The most important aspect of histopathology remains recognition of patterns and cytomorphology by a pathologist.[5] There are two major patterns of cutaneous lymphoid infiltrations, i.e., a predominant dermal or a predominant epidermotropic infiltration (EI) pattern.[6,7] Hence, it is pertinent to remember the thumb rule of histological patterns of T-cell and B-cell lymphoid infiltrates as enumerated in Table 1.

EPIDERMOTROPIC INFILTRATION PATTERN
The EI pattern is characterized by infiltration of the epidermis by neoplastic lymphoid cells, with prototype lesion being mycosis fungoides (MF).[8] In contrast, exocytosis refers to reactive lymphoid cells infiltration into epidermis and is being synonymously used as epidermotropic pattern. Due to archetypal homing character of T-cells, all cases of epidermotropic lymphoid cells are always of T-cell type.[7] However, there are other neoplastic and nonneoplastic lesions [Table 2] which can have a predominant epidermotropic pattern. The major histological differences between neoplastic and nonneoplastic EI are enumerated in Table 3.

Immunophenotyping/immunohistochemistry (IHC) is a powerful and useful adjunct to assess lymphoid infiltrates using cluster differentiation (CD) markers.[9] To ascertain nature of lymphoid infiltrates, a T-cell marker (CD3) and a B-cell marker (CD20) are used followed by proportion of

Address for correspondence: Prof. Uma Nahar Saikia.
Department of Histopathology, PGIMER, Chandigarh - 160 012, India.
E-mail: umasaikia@gmail.com

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.

For reprints contact: reprints@medknow.com

How to cite this article: Saikia UN, Madakshira MG. Histopathological approach to cutaneous lymphoid infiltrate. Indian J Dermatopathol Diagn Dermatol 2019;6:1-13.
Table 1: Differences in B-cell and T-cell dominant lymphoid cell infiltrations

| T-cell infiltrate                  | B-cell infiltrate                  |
|-----------------------------------|-----------------------------------|
| Top heavy infiltrate              | Bottom heavy infiltrate           |
| Band like infiltrative pattern    | Nodular infiltrative pattern      |
| Epidermotropism and folliculotropism present | Epidermotropism or folliculotropism absent |
| Grenz zone absent                 | Grenz zone usually separates the dermal infiltrate |

Table 2: Cutaneous lymphoid infiltrates with predominant epidermotropic pattern

| Neoplastic                        | Nonneoplastic                        |
|-----------------------------------|---------------------------------------|
| Mycosis fungoides (plaque and patch stage) | LCD                                  |
| Pagetoid reticulosis              | LDR                                  |
| Lymphomatoid papulosis            | Actinic reticuloid                    |
| Primary cutaneous aggressive CD8+ epidermotropic T-cell lymphoma | CD8+ T-cell pseudolymphoma in immunodeficiency |
| Cutaneous γ/δ T-cell lymphoma      | PO                                   |
| Extramodal NK/T-cell lymphoma      |                                       |
| Adult T-cell leukemia/lymphoma     |                                       |

PO: Papuloerythroderma of Ofuji, LDR: Lymphomatoid drug reaction, LCD: Lymphomatoid contact dermatitis

Table 3: Salient differences between neoplastic and nonneoplastic lesions with epidermotropic infiltration by lymphoid cells

| Neoplastic EIL                     | Nonneoplastic EIL                     |
|------------------------------------|---------------------------------------|
| Predominant medium-to-large cells  | Predominant small cells               |
| Nuclear hyperchromasia with irregular contours | Nuclei show regular contours |
| Shows complete or partial loss of pan-T-cell markers | Preserved pan-T-cell markers |
| TCR rearrangement present         | TCR rearrangement absent              |
| De novo                            | History of immunosuppression, drug intake, allergy or photosensitivity |

EIL: Epidermotropic infiltration by lymphoid cells

T-cells, CD4 (helper T-cell) and CD8 (cytotoxic T-cell) IHC, i.e., CD4:CD8 ratio which is normally 2:1.[9] The skewed pattern of CD4:CD8 is an important clue to diagnosis of T-cell-rich infiltrate, e.g., CD4:CD8 ratio is seen increased in the early stages of MF whereas typically seen decreased in advanced stages.[10] An additional battery of IHC for CD2, CD5, and CD7 provides an insight into probable neoplastic nature of T-cells. Of these, CD7 is the first to be lost in the neoplastic T-cell proliferation.[11] However, many nonneoplastic T-cell proliferations may also show loss of T-cell markers, emphasizing the importance of clinical correlation.[10]

Further molecular methods including antigen receptor gene rearrangements and clonality of neoplastic process and T-cell receptor gene rearrangements using polymerase chain reaction can be done. However, they need to be interpreted carefully excluding false positives due to oligoclonality or preferential amplification.[12,13] Nevertheless, molecular methods are most suited to identify clonality and diagnose neoplastic cutaneous lymphoid infiltrates.[12]

**Nonneoplastic Lesions with Epidermotropic Pattern**

**Lymphomatoid contact dermatitis and lymphomatoid drug reaction**

Lymphomatoid contact dermatitis (LCD) is a type of chronic contact dermatitis with a consistent history of exposure to allergens.[14] Lymphomatoid drug reaction (LDR) presents as a reaction following the administration of drugs such as anticholinesterase inhibitors, antidepressants, antihistamines, beta-blockers, benzodiazepines, and lipid-lowering agents.[15] Both LCD and LDR present in adults as eczematous papules, patches, or plaques. LCD lesions, in addition, are pruritic. Histomorphology of LCD and LDR shows spongiosis of epidermis with pseudo-Pautrier collections accompanied with exocytosis of reactive lymphoid cells having uniform nuclei admixed with eosinophils. The IHC reveals admixture of both CD4+ and CD8+ T-cells with few large CD30+ immunoblasts in the epidermis and upper dermis [Figure 1].[14,15]

**Actinic reticuloid**

Actinic reticuloid (AR) is associated with severe photosensitivity seen over face and neck in the middle and elderly males. The AR lesions are persistent erythematous lichenoid papules and plaques.[16] On histology, AR is characterised by psoriasiform hyperplasia with spongiosis and epidermotrophic lymphocytic infiltrate composed of CD8+ T-cells having uniform nuclei admixed with few eosinophils. The papillary dermis, in addition, shows vertically arranged collagen fibers.[16]

**Cluster differentiation 8+ T-cell pseudolymphoma in immunodeficiency**

CD8+ T-cell pseudolymphoma (CD8+ TCPP) is seen exclusively in patients with severe immunosuppression, including advanced stage of HIV infection. It presents as a generalized hyperkeratotic pruriginous erythroderma. Histology shows epidermotropic and perivascular dermal infiltration by CD8+ lymphocytes with uniform nuclei.[17]

**Papuloerythroderma of Ofuji**

Papuloerythroderma of Ofuji is a generalized itchy erythematous papule with a characteristic “deck-chair sign” pattern of distribution, seen usually in the seventh decade.[18] Histology shows prominent epidermotropism by an equal admixture of both CD4+ and CD8+ lymphocytes with a dermal perivascular infiltration by similar T-cells. In addition, accompanying eosinophils and plasma cells are also seen.[18]

**Neoplastic Lesion with Epidermotropic Pattern**

**Mycosis fungoides (patch and plaque stage)**

MF is an indolent cutaneous T-cell lymphoma (CTCL) which is more common in the elderly and can present in three
stages – plaque, patch, and nodule. The four most important histological features to diagnose MF are (i) epidermotropism by atypical lymphocytes with minimal spongiosis, (ii) atypia of lymphocytes with nuclear hyperchromasia and nuclear convolutions, (iii) fibrosis of the papillary dermis, and (iv) dermal band of lymphocytic infiltration. The Pautrier abscess is seen in 25% of cases and if present is a useful indicator of MF. The nonneoplastic mimics can be differentiated by lack of spongiosis, lack of basal cell vascular degeneration, and presence of nuclear atypia. The immunophenotype though not specific, aids in the diagnosis when used as a panel. The MF cells are CD3+, CD4+, CD8–, CD30–, and CD56– immunophenotype with an accompanying loss of T-cell antigens such as CD2, CD5, or CD7 \[\text{Figure 2}\]. However, rare cases of MF with aberrant immunophenotype have been reported such as CD4+/CD8+, CD4+/CD8–, and CD56–; hence, clinical correlation is required for definite diagnosis in early stages. The detection of clonal T cell receptor (TCR) gene rearrangement remains a sensitive tool in differentiating MF from its reactive mimics. However, keeping the indolent nature of the disease, it is safe to not to diagnosis MF in cases with lack of definite histological and IHC phenotype. A close follow-up is advised with a repeat biopsy after a period of 3–6 months if the lesion progresses in doubtful cases.

**Pagetoid reticulosis**

Pagetoid reticulosis (PR) is a rare variant of MF and presents as erythematous solitary lesion over extremities. Histopathology shows psoriasiform hyperplasia of the epidermis with pagetoid proliferation of atypical lymphocytes having irregular hyperchromatic nuclei and moderate-to-abundant pale cytoplasm. The important point to note is that there is a lack of dermal infiltration by atypical lymphoid cells as in classic MF having similar immunophenotype. The other differential diagnosis includes primary cutaneous aggressive CD8+ epidermotropic T-cell lymphoma, which has a more aggressive presentation in contrast to indolent nature of PR and has much larger and atypical cells involving the dermis and subcutaneous fat as well.

**Lymphomatoid papulosis (Type B and D)**

Lymphomatoid papulosis (LyP) is a type of indolent lymphoma seen in the fifth decade with self-regression and is characterized by waxing and waning course of eruptive erythematous papules and plaques. Of many subtypes of LyP, B and D subtype present with a prominent epidermotropism by small-to-medium-sized lymphoid cells with pleomorphic nuclei and irregular nuclear contours. The B-type LyP in addition has a band-like dermal infiltration of lymphocytes with CD4+/TIA-1+ immunophenotype, while the D type has a CD8+/TIA-1+ immunophenotype. Nearly 70% of cases of LyP are multiple myeloma oncogene 1 (MUM1)+ which may help in differentiating it from plaque/patch stage MF and primary aggressive CD8+ epidermotropic T-cell lymphoma. However, the diagnosis is based on clinical correlation with special emphasis on waxing–waning course.
Primary cutaneous cluster differentiation 8+ aggressive epidermotropic T-cell lymphoma

Primary cutaneous CD8+ aggressive epidermotropic T-cell lymphoma (PCAETCL) is a rare lymphoma enlisted as a provisional entity in the latest WHO classification. As the name suggests, PCAETCL presents de novo as diffuse erythematous and necrotic plaques without a preceding patch stage.[23] Histopathology shows a spongiotic or necrotic epidermis with extensive pagetoid epidermotropism by medium-sized atypical lymphocytes having irregular hyperchromatic nuclei. In addition, dense band-like dermal infiltration by similar atypical lymphoid cells is also seen. The immunophenotype is of a cytotoxic T-cell, i.e., CD8+ and TIA-1+ with loss of T-cell antigens, CD2 and CD5.[23] The relentless progression, diffuse nature of plaque lesions, and cytotoxic immunophenotype separate PCAETCL from its CD8+ histological mimics, PR and MF.[19,22]

Primary cutaneous gamma/delta T-cell lymphoma

Primary cutaneous gamma/delta T-cell lymphoma (PCGDTCL) is a rare recently described lymphoma which forms 1% of all CTCL. This belligerent lymphoma has its origin from physiological γ/δ cytotoxic T-cells of innate immunity. PCGDTCL presents as generalized plaques or nodules with frequent ulceration.[23] The plaques show prominent epidermotropism while the nodules show extensive subcutaneous involvement. There is epidermotropism with dermal and subcutaneous infiltration by medium-sized atypical lymphocytes having irregular hyperchromatic nuclei. The cells show a characteristic immunophenotype of CD4−, CD8−, and TIA-1+. These cells show negativity for β-F1 chain which is a marker of α/β receptor.[25] The differential diagnosis includes NK/T-cell lymphoma (NKTCL) which is positive for CD56 and Epstein–Barr virus (EBV) by in situ hybridization (ISH).[26]

NK/T-cell lymphoma

Skin manifestation of NKTCL is second only to nasal/midline lesions. The skin lesions may vary from plaque, patch, bullae, purpuric, or ulcers. Histologically, the atypical lymphoid cells have a dominant nodular dermal infiltration, with occasional instances of epidermotropism.[26] The neoplastic infiltrate shows an angiocentric pattern with angioinvasion, resulting in prominent necrosis [Figure 3].[26] The typical immunophenotype is of CD2+, CD56+, TIA-1+ with a consistent presence of EBV by in situ expression, which distinguishes it from its histological mimickers – PCGDTCL and lymphomatoid granulomatosis (LG).[25,27]

Adult T-cell leukemia/lymphoma

Adult T-cell leukemia/lymphoma (ATLL) is a systemic disease which develops following integration of human T-cell leukocyte virus-1 DNA into the host cell DNA. Nearly 43%–72% of ATLL presents with skin lesions and is a close differential diagnosis for MF/Sezary syndrome, considering the consistent presence of a leukemic phase.[28] The cytomorphology of leukemia cells simulates clover leaf-shaped...
lobed nucleus which is a clue to diagnose ATLL.[29] The skin lesions vary from papules, plaque, to erythroderma. Epidermotropism by small-to-large atypical lymphoid cells is a constant feature. The immunophenotype resembles regulatory T-cells, i.e., CD3+, CD4+, CD25+, and FOX3P+, and negative for CD7.[28] The lack of a preceding patch stage, acute onset of symptoms, leukemic cell morphology, and immunophenotype differentiates it from Sezary syndrome.[19]

A summary of the salient differences between neoplastic epidermotropic cutaneous infiltrates is enumerated in Table 4, followed by a proposed algorithmic approach to a case with prominent epidermotropic cutaneous infiltrate as shown in Figure 4.

**DERMAL INFLITRATIVE PATTERN**

The dermal infiltrative pattern is a more common presentation in routine dermatopathological practice, encompassing a heterogeneous group of both inflammatory dermatoses and lymphoproliferative disorders (LPDs) [Table 5]. For the ease of establishing an algorithm, both pseudolymphomas and neoplastic lymphoid proliferations are approached on the basis of cell size and immunophenotype of predominant cell population infiltrating the dermis.

**NEoplastIc t‑cELL‑rICH DERMAL INFIlTRatEs**

**Mycosis fungoides: Tumor stage**

The tumor stage of MF and rare variants such as interstitial MF, follicular MF, and granulomatous MF are common neoplastic T-cell-rich dermal infiltrate without epidermotropism.[30] The tumor stage is usually preceded by patch and/or plaque stage and shows numerous large cells with brisk mitosis infiltrating dermis in vague nodules, associated with ulceration of overlying dermis. In contrast, follicular MF has atypical lymphoid cells ensheathing and infiltrating hair follicles. This rare variant is important to recognize as it needs more aggressive treatment when compared to conventional MF.[31] Granulomatous MF has atypical lymphoid cells admixed histiocytes and multinucleated giant cells and microgranulomas similar to cutaneous sarcoidosis.[32] Subtle histological clues include frequent presence of lymphophagocytosis and elastophagocytosis. Interstitial MF, as the name suggests, shows an interstitial distribution of atypical lymphoid cells and is difficult to diagnose.[31] The immunophenotype of these MF variants is similar to conventional MF.[30]

**T‑cell lymphoblastic leukemia/lymphoma**

T-cell lymphoblastic leukemia/lymphoma (TCLL) is uncommon and presents as cutaneous nodules in children. It shows dense dermal infiltration by large blastic lymphoid cells which are positive for TdT and CD99.[14]

**Primary cutaneous small-medium cluster differentiation 4+ T‑cell lymphoproliferative disorder**

Following MF, primary cutaneous small-medium CD4+ T-cell LPD is the most common cutaneous T-cell LPD presenting as a single papule or nodule. The dermis shows a diffuse infiltration by small-to-medium-sized lymphocytes having irregular noncerebriform hyperchromatic nuclei with a perivascular accentuation. These cells have a follicular helper T-cell phenotype, i.e., CD3+, CD4+, B-cell lymphoma (BCL) 6+, and PD1+. They usually show a loss of CD2 or CD7 and CD30 is negative.[35]

**Primary cutaneous acral cluster differentiation 8+ T‑cell lymphoma**

Primary cutaneous acral CD8+ T-cell lymphoma is a recently described rare entity, also known by indolent CD8+ lymphoid proliferation of ear. As the name suggests, lesions have been described to involve acral areas and ear. Histology shows
Saikia and Madakshira: An algorithmic approach to histopathological diagnosis of cutaneous lymphoid infiltrates with brief discussion on common entities

**Table 4: Salient differences of neoplastic epidermotropic cutaneous infiltration**

| Site predilection          | MF (plaque and patch stage) | Pagetoid reticulosis | LyP (Type B and D) | PCAETCL | PCGDTCL | NKTCL | ATLL |
|----------------------------|-----------------------------|----------------------|--------------------|---------|---------|-------|------|
| Temporal course            | Trunk, limb girdle          | Solitary over extremity | Trunk, limbs       | Diffuse  | Extremities | Trunk, limbs | Diffuse |
| Peculiar histology character | Halo around atypical lymphocytes, fibrosis of dermal papillae | Psoriasiform epidermal hyperplasia, moderate to abundant vacuolated atypical lymphoid cells | Fibrin thrombi in dermal capillaries and dermal edema | Waxing and waning | Acute and rapidly progressive | Acute and rapidly progressive | Indolent or acute |
| Associated systemic manifestations | Leukemic cells (Sezary syndrome) | -                      | -                  | -       | -       | -     | -    |
| Immunophenotype            | CD3+/CD4+ or CD3+/CD8+ (rare) partial or complete loss of CD2, CD5, or CD7 | CD3+/CD4+ or CD3+/CD8+ (Type B) and CD3+/CD8+ or CD3+/CD30- (Type D) MUM1+ (70%) partial or complete loss of CD2, CD5 or CD7 | CD3+/CD8+/- TIA-1+/-CD30- | Usually CD7+/CD2-/CD5- | CD2+/CD3-/- CD8-/CD30-/ MUM1-/- TIA-1/- | CD2+/CD3-/CD8-/ | CD3+/CD4+/CD8-/CD5+/TIA-1+/-EBERish+ |
| MF: Mycosis fungoides, LyP: Lymphomatoid papulosis, PCAETCL: Primary cutaneous CD8+ aggressive epidermotropic T-cell lymphoma, PCGDTCL: Primary cutaneous gamma/delta T-cell lymphoma, NKTCL: NK/T-cell lymphoma, ATLL: Adult T-cell leukemia/lymphoma, CD: Cluster differentiation, MUM1: Multiple myeloma oncogene 1, EBERish: Epstein-Barr virus-encoded RNA in situ hybridization

**Figure 4:** Algorithmic approach to epidermotropic lymphoid infiltrate

A diffuse dermal infiltration by small-to-medium-sized lymphocytes having irregular nuclear contours. The lymphoid cells have a cytotoxic T-cell phenotype with CD3+, CD8+, granzyme B+ with variable loss of CD2 and CD5 while being negative for CD30.\[^{36}\]

**Lymphomatoid papulosis (Type A, C, and rare variants)**

The LyP type A has a dominant wedge-shaped dermal infiltrate composed of large CD30+ cells admixed with polymorphous inflammatory cell background.\[^{24}\] LyP type C shows diffuse sheets of large CD30+ cells, making it a morphological mimic of
Saikia and Madakshira: An algorithmic approach to histopathological diagnosis of cutaneous lymphoid infiltrates with brief discussion on common entities

**Table 5: Lesions known to present with a predominant dermal pattern**

| T-cell-rich dermal infiltrate | Neoplastic | B-cell-rich dermal infiltrate | Nonneoplastic |
|-------------------------------|------------|-------------------------------|---------------|
| MF (nodular/tumor stage)      | Primary cutaneous marginal zone lymphoma | Primary cutaneous follicle center cell lymphoma | Cutaneous B-cell pseudolymphoma |
| Acute lymphoblastic leukemia/lymphoma | Primary cutaneous follicle center lymphoma | Lymphomatoid granulomatosis | Borrelia associated pseudo lymphoma |
| Primary cutaneous small-to-medium CD4+ lymphoproliferative disorder | Primary cutaneous diffuse large BCL -leg type | Polymorphous light eruption | CD30+ T-cell pseudolymphoma |
| Primary cutaneous CD8+ acral lymphoproliferative disorder | Primary cutaneous diffuse large BCL; NOS | Jessner’s infiltrate | |
| Lymphomatoid papulosis (Type A, C, and rare variants) | Follicular lymphoma | Tumid lupus | |
| Primary cutaneous anaplastic large cell lymphoma | Chronic lymphocytic leukemia/small lymphocytic lymphoma | Pityriasis lichenoides chronica | |
| Primary cutaneous NK/T-cell lymphoma | Lymphoplasmacytic lymphoma | | |
| Primary cutaneous gamma/delta lymphoma | Mantle cell lymphoma | | |
| Primary epidermotropic CD8+ aggressive T-cell lymphoma (nodular type) | Acute lymphoblastic leukemia/lymphoma | | |
| | Diffuse large BCL, NOS | | |
| | EBV+ diffuse large BCL | | |
| | Intravascular large BCL | | |
| | Primary effusion lymphoma | | |
| | Plasmablastic lymphoma | | |
| | Burkitt lymphoma | | |
| | Plasma cell myeloma | | |

MF: Mycosis fungoides, CD: Cluster differentiation, NOS: Not otherwise specified, BCL: B-cell lymphoma

**Figure 5:** Composite image of lymphomatoid papulosis type C: Skin biopsy showing dense dermal lymphoid infiltrate (a) composed of large cells having pleomorphic nuclei with prominent nucleoli and open chromatin (b) (H and E). These atypical lymphoid cells are positive for CD3 (c) and CD30 (e), while being negative for CD20 (d), CD4 (f), CD8 (g), and ALK (h). CD: Cluster differentiation, ALK: Anaplastic lymphoma kinase

The differentiation shall rest solely on clinical presentation. The rare variants include folliculotropic LyP, type E LyP, and LyP with DUSP22 rearrangements. The folliculotropic LyP shows wedge-shaped infiltration similar to Type A with perifollicular accentuation. Type E LyP is characterized by the presence of destructive angioinvasive infiltration by medium-sized cytotoxic CD8+ T-cells. More recently
described LyP entity shows DUSP22 rearrangement with a characteristic biphasic pattern with superficial epidermotropic weak CD30+ infiltrate and diffuse deep dermal intense CD30+ infiltrate.\(^\text{[39]}\)

**Primary cutaneous anaplastic large cell lymphoma**  
Primary cutaneous ALCCL occurs a solitary erythematous to ulcerated lesion in the seventh decade. There is a diffuse or vague nodular dermal infiltration by predominantly large CD30+ cells with pleomorphic nuclei and background showing polymorphous inflammatory cells. The dermal infiltrate extends into the subcutis. The CD30+ large cells form 75% of population and are characteristically negative for epithelial membrane antigen and anaplastic lymphoma kinase (ALK) as they do not harbor nucleophosmin-ALK fusion, unlike extranodal ALCCLs.\(^\text{[40]}\) The large cells have, in addition, a cytotoxic phenotype being positive for TIA-1 and granzyme B.\(^\text{[40]}\)

---

### Table 6: Salient differences of primary cutaneous neoplastic T-cell dermal infiltrates

| Site predilection     | MF (nodule and others) | PCSMTCLPD | PCATCL | LyP (Type A, C and others) | PCALCL |
|-----------------------|------------------------|-----------|--------|---------------------------|--------|
|                       | Trunk, limb girdle     | Solitary over head and neck or upper trunk | Ear and acral regions | Diffuse | Extremities |
| Temporal course       | Indolent and progressive | Indolent and progressive | Indolent with no dissemination | Waxing and waning | Acute and rapidly progressive |
| Peculiar histology character | Diffuse dermal infiltrate, perifollicular, interstitial or giant cells with sarcoïd-like granulomas | Diffuse, perivascular or nodular infiltrate with <30% large cells | Diffuse dermal and subcutis infiltration separated from epidermis by a Grenz zone | Wedge shaped dermal infiltrate, diffuse dermal infiltrate, folliculotropic or angiocentric | Usually ulcerated, diffuse dermal and subcutis infiltration |
| Associated systemic manifestations | Leukemic cells (Sezary syndrome) | - | - | - | Lymphophagocytosis |
| Immunophenotype       | CD3+/CD4+ partial or complete loss of CD2, CD5, or CD7 | CD3+/CD4+/BCL6+/PD1+/CD30 – partial or complete loss of CD2, CD5, or CD7 | CD3+/CD8+/TIA1+/CD30– Partial or complete loss of CD2, CD5, or CD7 | CD30+ variable CD2/CD3/CD4/CD8/CD5/CD7 positivity | CD30+/EMA–/ALK– |

PCSMTCLPD: Primary cutaneous small-medium CD4+ T-cell lymphoproliferative disorder, PCATCL: Primary cutaneous acral CD8+ T-cell lymphoma, LyP: Lymphomatoid papulosis, PCALCL: Primary cutaneous anaplastic large cell lymphoma

---

**Figure 6: Algorithmic approach to dermal lymphoid infiltrate**
A summary of the salient differences between neoplastic dermal lymphoid infiltrates is enumerated in Table 6, followed by a proposed algorithmic approach to a case with prominent dermal lymphoid infiltrate as shown Figure 6.

**Lymphoproliferative disorders with dominant dermal infiltrate and frequent epidermotropism**

Primary cutaneous NKTCL, primary cutaneous gamma/delta lymphoma, and nodular type of primary epidermotropic CD8+ aggressive T-cell lymphoma are a group of LPDs which present with a dominant dermal infiltrate having frequent epidermotropism.[23,25,26]

**B-Cell-Rich Dermal Infiltrates**

B-cell-rich dermal infiltrates can be divided into two groups based on the composition of cells – B-cell dominant infiltrate and B-cell predominant infiltrate with admixed reactive T-cells.

**B-cell dominant dermal infiltration**

B-cell dominant dermal infiltration includes uncommon secondary infiltration of the dermis by nodal BCLs – chronic lymphocytic leukemia/small lymphocytic lymphoma, lymphoplasmacytic lymphoma, mantle cell lymphoma, and acute lymphoblastic leukemia/lymphoma. These infiltrates mirror the nodal cellular morphology and immunophenotype.[41-44] In view of rare presentation, a diagnosis can only be made with a high index of suspicion.

**B-cell predominant infiltrate with admixed reactive T-cells**

Presence of B-cell predominant dermal infiltration with admixed reactive T-cells is a more common presentation of primary cutaneous B-cell LPDs which include small-to-medium-sized LPDs and large cell LPDs. The small-to-medium-sized LPDs include primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicular center cell lymphoma (PCFCL), follicular lymphoma, and LG. The large-sized LPDs include primary cutaneous diffuse large BCL-leg type (PCDLBCL-LT) and rare instances of secondary involvement by nodal diffuse large BCL, EBV+ diffuse large BCL, intravascular large BCL, primary effusion lymphoma, and Burkitt lymphoma.

**Primary cutaneous marginal zone lymphoma**

PCMZL forms about 11% of all MZL. It presents as violaceous papules or nodules over trunk and peripheral extremities in the fourth decade. There is a diffuse dermal proliferation of small centrocyte-like cells with peripherally placed lymphoplasmacytoid and plasma cells. These cells show pan-B-cell markers and BCL2 positivity with light chain restriction.[45]

**Primary cutaneous follicular center cell lymphoma and follicular lymphoma**

PCFCL is the most common cutaneous B-cell neoplasm manifesting as solitary violaceous plaques and nodules over head and neck. There is follicular or diffuse proliferation...
of centrocyte-like cells admixed with scattered larger centroblasts. These lymphoid cells show pan-B-cell markers and germinal center markers, CD10 and BCL6, but show characteristic absence of BCL2 [Figure 7].\(^{46}\) In contrast to the PCFCL, the secondary cutaneous involvement of skin by follicular lymphoma (FL) presents as multiple nodules with dermal infiltrate showing BCL2 positivity.\(^{47}\)

### Lymphomatoid granulomatosis

LG is seen in patients with an underlying immunodeficiency and primarily involves lung with secondary involvement

---

**Table 7: Salient differences of primary cutaneous neoplastic B-cell dermal infiltration**

|            | PCMZL                                      | PCFCL                                      | LG            | PCDLBCL-LT        | PCDLBCL-NOS       | IVLBCL                      |
|------------|--------------------------------------------|--------------------------------------------|---------------|-------------------|-------------------|------------------------------|
| Site predilection | Nodules over trunk, peripheral extremities | Solitary nodule over head and neck       | Diffuse papules | Solitary nodule over legs | Solitary nodule over extremities | Diffuse telangiectatic, purpuric or ulcerated lesions |
| Temporal course    | Indolent and progressive                    | Indolent and progressive                  | Waxing and waning, but aggressive course | Acute and rapidly progressive | Acute and rapidly progressive | Acute and rapidly progressive |
| Peculiar histology character | Diffuse or nodular infiltration by centrocyte-like cells with peripherally placed plasma cells | Diffuse or nodular infiltration by centrocytes admixed with large centroblasts with absent mantle zones | Polymorphous angiocentric infiltration with many large cells | Nodular or diffuse infiltrate of large immunoblasts or centroblasts | Nodular or diffuse infiltrate of large immunoblasts or centroblasts | Epidermal necrosis, intravascular collections of large cells with minimum extravasation |
| Associated systemic manifestations | -                                          | -                                          | Pulmonary involvement | -                    | -                    | Central nervous involvement |
| Immunophenotype    | Pan-B-cell markers, BCL2+, light chain restriction | Pan-B-cell markers, CD10+/BCL6 + BCL2- | Pan-B-cell markers, CD30+, BCL2/ MUM1+/MUM1+/MUM1+/BCL6+ | Pan B-cell markers, BCL2+/ MUM1+/MUM1+/MUM1+/BCL6+ | Pan B-cell markers, BCL2+/ MUM1+/MUM1+/MUM1+/BCL6+ | Pan B-cell markers, BCL2+/ MUM1+/BCL6/CD10 |

BCL: B-cell lymphoma, PCMZL: Primary cutaneous marginal zonal lymphoma, PCFCL: Primary cutaneous follicular center cell lymphoma, LG: Lymphomatoid granulomatosis, PCDLBCL-LT: Primary cutaneous diffuse large BCL -leg type, IVLBCL: Intravascular large BCL, PCDLBCL: Primary cutaneous diffuse large BCL, NOS: Not otherwise specified
of skin with disseminated papules and nodules. There is polymorphous angiocentric infiltration by large CD30+ B-cells in a background of reactive T-cells. These large cells are EBV driven and show consistent nuclear positivity with EBV-encoded RNA ISH.\[^{27}\]

**Primary cutaneous diffuse large B-cell lymphoma (leg type and not otherwise specified)**

PCDLBCL-LT constitutes 20% of all primary cutaneous BCL. PCLBCL-LT presents as solitary or multiple papulonodular lesions over extremities in the seventh decade. There is diffuse infiltration by large immunoblastic and centroblast-like cells causing effacement of adnexal structures. These cells show pan-B-cell markers with positivity for BCL2, MUM1, and BCL6 [Figure 8].\[^{48}\] PCDLBC, not otherwise specified is a rare variant, has a similar histomorphology, but shows the absence of BCL2 staining.\[^{47}\]

**Intravascular large B-cell lymphoma**

This rare lymphoma manifests in the elderly with skin being one of the most common sites of infiltration following central nervous system. The skin lesion varies from telangiectatic to purpuric to ulcerated lesions over extremities. The neoplastic B-cells, due to a defect in homing receptors, are confined to intravascular location. The neoplastic lymphoid cells are seen to clog dermal capillaries, venules, and arterioles with minimal extravasation. These cells show pan-B-cell markers and are also positive for BCL2 with variable positivity for BCL6, MUM1, and CD10.\[^{49}\]

**Secondary cutaneous involvement by nodal B-cell lymphomas**

Secondary cutaneous involvement by nodal BCLs is rare. However, there have been documented reports of involvement by diffuse large BCL-activated B-cell and germinal center B-cell subtypes, EBV+ diffuse large BCL, plasmablastic lymphoma, primary effusion lymphoma, Burkitt lymphoma, and plasma cell myeloma. These entities, due to their rarity, require a high index of suspicion and correlation with immunophenotype and clinical presentation including concurrent nodal or bone marrow involvement for arriving at a definite diagnosis.\[^{47}\]

A summary of the salient differences between neoplastic dermal lymphoid infiltrates is enumerated in Table 7, followed by a proposed algorithmic approach to a case with prominent dermal lymphoid infiltrate as shown in Figure 2.

**Nonneoplastic Dermal Lymphoid Infiltrates**

**Cutaneous B-cell pseudolymphoma**

Cutaneous B-cell pseudolymphoma presents in the middle age as a solitary nodule. The biopsy shows nodular dermal infiltrates of lymphoid cells with prominent germinal centers and tingible body macrophages. These follicles show predominant small-to-medium-sized B-cells with a high Ki67 proliferative index, negative BCL2 expression, and well-formed CD23 follicular dendritic cell network. These B-cell pseudolymphomas can be as a result of arthropod bites, infections by virus/parasites/spirochetes, postvaccination, tattoos, and drugs.\[^{50}\]

**Borrelia-associated pseudolymphoma**

Borrelia has been associated with violaceous papules or nodules usually involving the tick bite areas – ear lobe, nipple, and scrotum. The dermal infiltration is in the form of nodules with the absence of mantle zone but prominent tingible body macrophages. The infiltrate shows a prominent admixture of reactive T-cells and plasma cells.\[^{51}\]

**Cluster differentiation 30+ T-cell pseudolymphoma**

These are characterized by a polymorphous lymphoid infiltrate with many scattered CD30+ large T-cells. These reactive
infiltrates can have varied etiologies, including drug reaction, scabies, hidradenitis, and viral infections such as molluscum and herpes. In comparison to their neoplastic counterparts, the CD30+ large cells are singly scattered, stain less intensely with CD30, and have variable admixture of B-cells and plasma cells.[52]

**Polymorphous light eruptions**

Polymorphous light eruption (PMLE) is a photodermatosis seen in sun-exposed areas of the face, chest, and upper extremities. PMLE is characterized by the presence of grouped erythematous papules. Histologically prominent papillary dermal edema with moderate-to-marked upper dermal perivascular lymphoid infiltrate rich in CD4+ T-cells admixed with an increased number of dermal Langerhans cells.[53]

**Jessner’s infiltrate**

Jessner’s infiltrate is an uncommon lesion characterized by self-remitting erythematous papules or plaques over cheeks, neck, and upper back. Histology shows an absence of epidermal changes or interface change. The upper and mid-dermis show a moderate perivascular lymphoid infiltrate rich in CD4+ T-lymphoid cells [Figure 9].[54]

**Tumid lupus**

Tumid lupus is a distinctive skin lesion seen on sun-exposed areas of face, chest, and neck characterized by raised erythematous plaques. Unlike other forms of cutaneous lupus, epidermis does not show features of follicular plugging or basal cell vacular degeneration. The dermis shows a marked increase in mucin with a perivasculard and perifollicular lymphocyte infiltration having an admixture of both CD4 and CD8 lymphocytes.[55]

**Pityriasis lichenoides chronica**

Pityriasis lichenoides chronica is an uncommon dermatosis involving arms, legs, trunks, and buttocks as pink crops of papules progressing to lichenoid scaly lesions. The epidermis shows parakeratosis, acanthosis spongiosis, occasional necrotic keratinocytes, and focal basal vascular degeneration. The upper dermis shows moderate perivascular lymphocytic cell infiltrate rich in CD8+ lymphocytes.[56]

**Conclusion**

The above-discussed algorithmic approach to cutaneous lymphoid infiltrates needs to be applied in consort with essential clinical inputs, histopathological pattern on low power, cytomorphology of cells in terms of size and nuclear character, and interpretation of the appropriate IHC panel.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Egawa G, Kabashima K. Skin as a peripheral lymphoid organ: Revisiting the concept of skin-associated lymphoid tissues. J Invest Dermatol 2011;131:2178-85.
2. Rubenfeld MR, Silverstone AE, Knowles DM, Halper JP, De Sostoa A, Fenoglio CM, et al. Induction of lymphocyte differentiation by epidermal cultures. J Invest Dermatol 1981;77:221-4.
3. Stirling G, Katz SI, Clement L, Green I, Shevach EM. Immunologic functions of ia-bearing epidermal Langerhans cells. J Immunol 1978;121:2005-13.
4. Streilein JW. Skin-associated lymphoid tissues (SALT): Origins and functions. J Invest Dermatol 1983;80 Suppl 1:12s-6s.
5. Subtil A. A general approach to the diagnosis of cutaneous lymphomas and pseudolymphomas. Surg Pathol Clin 2014;7:135-42.
6. Charli-Joseph Y, Toussaint-Claire S, Lome-Maldonado C, Montante-Montes de Oca D, Ortiz-Hidalgo C. Approach to dermal-based lymphoid infiltrates and proliferations. Semin Cutan Med Surg 2018;37:61-74.
7. Raghavan SS, Kim J. Histopathologic approach to epidermotropic lymphocytic infiltrates. Semin Cutan Med Surg 2018;37:56-60.
8. Olerud JE, Kulín PA, Chew DE, Carlsson RA, Hammar SP, Weir TW, et al. Cutaneous T-cell lymphoma. Evaluation of pretreatment skin biopsy specimens by a panel of pathologists. Arch Dermatol 1992;128:901-7.
9. Zola H, Swart B, Nicholson I, Aasted B, Bensussan A, Boumsell L, et al. CD molecules 2005: Human cell differentiation molecules. Blood 2005;106:3123-6.
10. Campbell SM, Peters SB, Zirwas MJ, Wong HK. Immunophenotypic diagnosis of primary cutaneous lymphomas: A review for the practicing dermatologist. J Clin Aesthet Dermatol 2010;3:21-5.
11. Vanderheiden EC, Bernengo MG, Burg G, Duvic M, Heald P, Laroche L, et al. Update on erythrodermic cutaneous T-cell lymphoma: Report of the international society for cutaneous lymphomas. J Am Acad Dermatol 2002;46:95-106.
12. Raess PW, Bagg A. The role of molecular pathology in the diagnosis of cutaneous lymphomas. Patholog Res Int 2012;2012:913523.
13. Holm N, Flajig MJ, Yazdi AS, Sander CA. The value of molecular analysis by PCR in the diagnosis of cutaneous lymphocytic infiltrates. J Cutan Pathol 2002;29:447-52.
14. Knackstedt TJ, Zug KA. T cell lymphomatomatoid contact dermatitis: A challenging case and review of the literature. Contact Dermatitis 2015;72:65-74.
15. Kardaun SH, Scheffer E, Vermeer BJ. Drug-induced pseudolymphomatous skin reactions. Br J Dermatol 1988;118:545-52.
16. Toonstra J, Henquet CJ, van Weelden H, van der Putte SC, van Vloten WA. Actinic reticuloid, A clinical photobiologic, histopathologic, and follow-u study of 16 patients. J Am Acad Dermatol. 1989;21(2 Pt 1):205-14.
17. Burns MK, Cooper KD. Cutaneous T-cell lymphoma associated with HIV infection. J Am Acad Dermatol 1993;29:394-9.
18. Maher AM, Ward CE, Glassman S, Litvinov IV. The importance of excluding cutaneous T-cell lymphomas in patients with a working diagnosis of papulocrythroderma of Oftuji: A case series. Case Rep Dermatol 2018;10:46-54.
19. Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C. Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): Part I. Diagnosis: Clinical and histopathologic features and new molecular and biologic markers. J Am Acad Dermatol 2014;70:205.e1-16.
20. Glusac EJ. Criterion by criterion, mycosis fungoides. Am J Dermatopathol 2003;25:264-9.
21. Bergman R, Faceliu D, Sahar D, Sander CA, Kerner H, Ben-Aryeh Y, et al. Immunophenotyping and T-cell receptor gamma gene rearrangement analysis as an adjunct to the histopathologic diagnosis of mycosis fungoides. J Am Acad Dermatol 1998;39:554-9.
22. Haghhigh B, Smoller BR, LeBoit PE, Warnke RA, Sander CA, Kohler S, et al. Pagetoid reticulosis (Woringer-Kolopp disease): An immunophenotypic, molecular, and clinicopathologic study. Mod Pathol 2000;13:502-10.
23. Nofal A, Abdel-Mawla MY, Assaf M, Salah E. Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma: Proposed diagnostic criteria and therapeutic evaluation. J Am Acad Dermatol 2012;67:748-59.
24. El Shabrawi-Caelen L, Kerl H, Cerroni L. Lymphomatoid papulosis:
Reappraisal of clinicopathological presentation and classification into subtypes A, B, and C. Arch Dermatol 2004;140:441-7.

25. Tripathi C, Iannitto E, Floreana AM, Pucillo CE, Piccaluga PP, Franco V, et al. Gamma-delta T-cell lymphomas. Nat Rev Clin Oncol 2009;6:707-17.

26. Rodríguez-Pinilla SM, Barrionuevo C, García J, Martínez MT, Pajares R, Montes-Moreno S, et al. EBV-associated cutaneous NK/T-cell lymphoma: Review of a series of 14 cases from peru in children and young adults. Am J Surg Pathol 2010;34:1773-82.

27. Katzenstein AL, Doxtader E, Narendra S. Lymphomatoid granulomatosis: Insights gained over 4 decades. Am J Surg Pathol 2010;34:e35-48.

28. Setoyama M, Tashiro Y, Kanzaki T. Clinicopathologic analysis of 124 cases of adult T-cell leukemia/lymphoma with cutaneous manifestations: The smouldering type with skin manifestations has a poorer prognosis than previously thought. J Dermatol 1999;26:785-90.

29. Manoj MG, Kotwal J, Dutta V. A rare case of adult T cell leukemia/lymphoma: Clinicopathological correlation with autopsy confirmation. Indian J Hematol Blood Transfus 2014;30:77-80.

30. Olsen E, Vonderheid E, Pimpinelli N, Willemze R, Kim Y, Knobler R, et al. Revisions to the staging and classification of mycosis fungoides and sezary syndrome: A proposal of the international society for cutaneous lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). Blood 2007;110:1713-22.

31. Gerami P, Rosen S, Kuzel T, Boone SL, Guitart J. Folliculotropism of mycosis fungoides: An aggressive variant of cutaneous T-cell lymphoma. Arch Dermatol 2008;144:738-46.

32. Kempf W, Ostheeren-Michaelis S, Pauli M, Lucioni M, Wechsler J, Audring H, et al. Granulomatous mycosis fungoides and granulomatous slack skin: A multicenter study of the cutaneous lymphoma histopathology task force group of the European Organization for Research and Treatment of Cancer (EORTC). Arch Dermatol 2008;144:1609-17.

33. Ferrara G, Crisman G, Zalaudek I, Argenziano G, Stefanato CM. Free-floating collagen fibers in interstitial mycosis fungoides. Am J Dermatopathol 2010;32:352-6.

34. Chimenti S, Fink-Puches R, Peris K, Pescarmona E, Pütz B, Kerl H, et al. Cutaneous involvement in lymphoblastic lymphoma. J Cutan Pathol 1999;26:379-85.

35. Grogg KL, Jung S, Erickson LA, McClure RF, Dogan A. Primary cutaneous CD4-positive small/medium-sized pleomorphic T-cell lymphoma: A clonal T-cell lymphoproliferative disorder with indolent behavior. Mod Pathol 2008;21:708-15.

36. Beltraminelli H, Müllegger R, Cerroni L. Indolent CD8+ lymphoid proliferation of the ear: A phenotypic variant of the small-medium pleomorphic cutaneous T-cell lymphoma? J Cutan Pathol 2010;37:81-4.

37. Kempf W, Kazakov DV, Baumgartner HP, Kutzner H. Follicular lymphomatoid papulosis revisited: A study of 11 cases, with new histopathological findings. J Am Acad Dermatol 2013;68:809-16.

38. Kempf W, Kazakov DV, Schärer L, Rüttner A, Mentzel T, Paredes BE, et al. Angioinvasive lymphomatoid papulosis: A new variant simulating aggressive lymphomas. Am J Surg Pathol 2013;37:1-13.

39. Karai LJ, Kadin ME, Hsi ED, Sluzevich JC, Ketterling RP, Kudrason RA, et al. Chromosomal rearrangements of 6p25.3 define a new subtype of lymphomatomatoid papulosis. Am J Surg Pathol 2013;37:1173-81.

40. Stein H, Foss HD, Dürkop H, Marafioti T, Delsol G, Palford K, et al. CD30(+) anaplastic large cell lymphoma: A review of its histopathologic, genetic, and clinical features. Blood 2000;96:3681-95.

41. Chan I, Calonje E, Whittaker SJ. Cutaneous Waldenström’s macroglobulinaemia. Clin Exp Dermatol 2003;28:491-2.

42. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. Am J Clin Pathol 2008;129:130-42.

43. Kahwash SB, Qualman SJ. Cutaneous lymphoblastic lymphoma in children: Report of six cases with precursor B-cell lineage. Pediatr Dev Pathol 2002;5:45-53.

44. Sen F, Medeiros LJ, Lu D, Jones D, Lai R, Katz R, et al. Mantle cell lymphoma involving skin: Cutaneous lesions may be the first manifestation of disease and tumors often have blastoid cytologic features. Am J Surg Pathol 2002;26:1312-8.

45. Servitje O, Gallardo F, Estrach T, Pujol RM, Blanco A, Fernández-Sevilla A, et al. Primary cutaneous marginal zone B-cell lymphoma: A clinical, histopathological, immunophenotypic and molecular genetic study of 22 cases. Br J Dermatol 2002;147:547-58.

46. Cerroni L, Arzberger E, Pütz B, Höfler G, Metze D, Sander CA, et al. Primary cutaneous follicle center cell lymphoma with follicular growth pattern. Blood 2000;95:3922-8.

47. Kempf W, Kazakov DV, Mitteldorf C. Cutaneous lymphomas: An update. Part 2: B-cell lymphomas and related conditions. Am J Dermatopathol 2014;36:197-208.

48. Gopal MM, Malik A. Primary cutaneous diffuse large B-cell lymphoma of the upper limb: A fascinating entity. Indian J Dermatol 2013;58:366-8.

49. Asada N, Odawara J, Kinura S, Aoki T, Yamakura M, Takeuchi M, et al. Use of random skin biopsy for diagnosis of intravascular large B-cell lymphoma. Mayo Clin Proc 2007;82:1525-7.

50. Cerroni L, Borroni RG, Massone C, Chott A, Kerl H. Cutaneous B-cell pseudolymphoma at the site of vaccination. Am J Dermatopathol 2007;29:538-42.

51. Colli C, Leinweber B, Müllegger R, Chott A, Kerl H, Cerroni L, et al. Borrelia burgdorferi-associated lymphohytoma cutis: Clinicopathologic, immunophenotypic, and molecular study of 106 cases. J Cutan Pathol 2004;31:232-40.

52. Werner B, Massone C, Kerl H, Cerroni L. Large CD30-positive cells in benign, atypical lymphoid infiltrates of the skin. J Cutan Pathol 2008;35:1100-7.

53. Norris PG, Morris J, McGibbon DM, Chu AC, Hawk JL. Polymorphic light eruption: An immunopathological study of evolving lesions. Br J Dermatol 1989;120:173-83.

54. Willemze R, Dijkstra A, Chu AC, Hawk JL. Polymorphic light eruption: An immunopathological study of evolving lesions. Br J Dermatol 1989;120:173-83.

55. Fernández-Sevilla A, et al. Gamma-delta T-cell lymphomas. Nat Rev Clin Oncol 2007;4:287-98.

56. Völker S, Tichy K, Röhrig C, Kaluza M, Lehnert K, et al. Primary cutaneous CD30+ anaplastic large cell lymphoma: A review of its histopathologic, genetic, and clinical features. Blood 2000;96:3681-95.