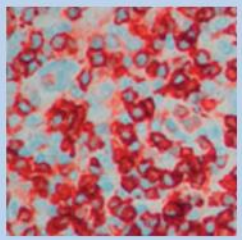
POLICLINICO DI SANT'ORSOLA

2015... 2018
T-Cell Lymphomas:
we are close to the
finalization



Bologna
ROYAL HOTEL CARLTON
May 7-9, 2018

President: **Pier Luigi Zinzani**
Co-President: **Michele Cavo**
Honorary President: **Sante Tura**

UNIVERSITÀ DEGLI STUDI FIRENZE
DCMT
DIPARTIMENTO DI CHIRURGIA E MEDICINA TRASLAZIONALE

CTCL Histology

Marco Santucci

Division of Pathological Anatomy
Department of Surgery and Translational Medicine
University of Florence School of Human Health Sciences

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Disclosures of MARCO SANTUCCI

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

NONE

World Health Organization Classification of Tumours

WHO OMS

International Agency for Research on Cancer (IARC)

WHO Classification of Skin Tumours

4th Edition, 2018

Haematolymphoid tumours	
Mycosis fungoides	9700/3
Folliculotropic mycosis fungoides	9700/3
Granulomatous slack skin	9700/3
Pagetoid reticulosis	9700/3
Sézary syndrome	9701/3
CD30+ T-cell lymphoproliferative disorders	
Lymphomatoid papulosis	9718/1
Primary cutaneous anaplastic large cell lymphoma	9718/3
Adult T-cell leukaemia/lymphoma (cutaneous)	9827/3
Subcutaneous panniculitis-like T-cell lymphoma	9708/3
Cutaneous manifestations of chronic active EBV infection	
Hydroa vacciniforme–like lymphoproliferative disorder	9725/1
Extranodal NK/T-cell lymphoma (nasal type)	9719/3
Primary cutaneous peripheral T-cell lymphomas	
Primary cutaneous gamma-delta T-cell lymphoma	9726/3
Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma	9709/3
Primary cutaneous acral CD8+ T-cell lymphoma	9709/3
Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder	9709/3
Secondary cutaneous involvement in T-cell lymphomas and leukaemias	
Systemic anaplastic large cell lymphoma, ALK-positive	9714/3
Systemic anaplastic large cell lymphoma, ALK-negative	9715/3
Angioimmunoblastic T-cell lymphoma	9705/3
T-cell prolymphocytic leukaemia	9834/3
Primary cutaneous marginal zone lymphoma	9699/3
Primary cutaneous follicle centre lymphoma	9597/3
Primary cutaneous diffuse large B-cell lymphoma (leg type)	9680/3
Intravascular large B-cell lymphoma	9712/3
Mucocutaneous ulcer (EBV-positive)	9680/1
Lymphomatoid granulomatosis	
Grade 1–2	9766/1
Grade 3	9766/3
Secondary cutaneous involvement in B-cell lymphomas and leukaemias	
Mantle cell lymphoma	9673/3
Burkitt lymphoma	9687/3
Chronic lymphocytic leukaemia/ small lymphocytic lymphoma	9823/3
Precursor T-lymphoblastic and B-lymphoblastic leukaemia/lymphoma	
Precursor T-lymphoblastic leukaemia	9837/3
Precursor T-lymphoblastic lymphoma	9729/3
Precursor B-lymphoblastic leukaemia	9836/3
Precursor B-lymphoblastic lymphoma	9728/3
Blastic plasmacytoid dendritic cell neoplasm	9727/3
Cutaneous involvement in myeloid leukaemia	9930/3
Cutaneous mastocytosis	9740/1
Mast cell sarcoma	9740/3
Indolent systemic mastocytosis	9741/1
Aggressive systemic mastocytosis	9741/3
Systemic mastocytosis with an associated haematological neoplasm	9741/3
Mast cell leukaemia	9742/3
Histiocytic and dendritic cell neoplasms	
Langerhans cell histiocytosis	9751/3
Indeterminate cell histiocytosis/ indeterminate dendritic cell tumour	9757/3
Rosai–Dorfman disease	
Juvenile xanthogranuloma	
Erdheim–Chester disease	9749/3
Reticulohistiocytosis	8831/0

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Primary Cutaneous CD30+ T-cell Lymphoproliferative Disorders

- This group includes:
  - **Lymphomatoid papulosis (LyP)**
  - **Primary cutaneous anaplastic large cell lymphoma**
- Distinction between primary cutaneous anaplastic large cell lymphoma and LyP not always possible
- The clinical appearance and course used a decisive criterion for definite diagnosis

Histological subtype (relative frequency)	Predominant phenotype	Main differential diagnoses
LyP type A (> 80%)	CD4+, CD8−	Cutaneous anaplastic large cell lymphoma, tumour-stage mycosis fungoides, and Hodgkin lymphoma
LyP type B (< 5%)	CD4+, CD8−	Early-stage (plaque-stage) mycosis fungoides
LyP type C (~10%)	CD4+, CD8−	Cutaneous anaplastic large cell lymphoma and transformed (CD30+) mycosis fungoides
LyP type D (< 5%)	CD4−, CD8+	Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma
LyP type E (< 5%)	CD4−, CD8+	Extranodal NK/T-cell lymphoma
LyP with *DUSP22-IRF4* rearrangement (< 5%)	CD4−, CD8+ or CD4−, CD8−	Transformed mycosis fungoides

W.H.O. 2018

LyP type D

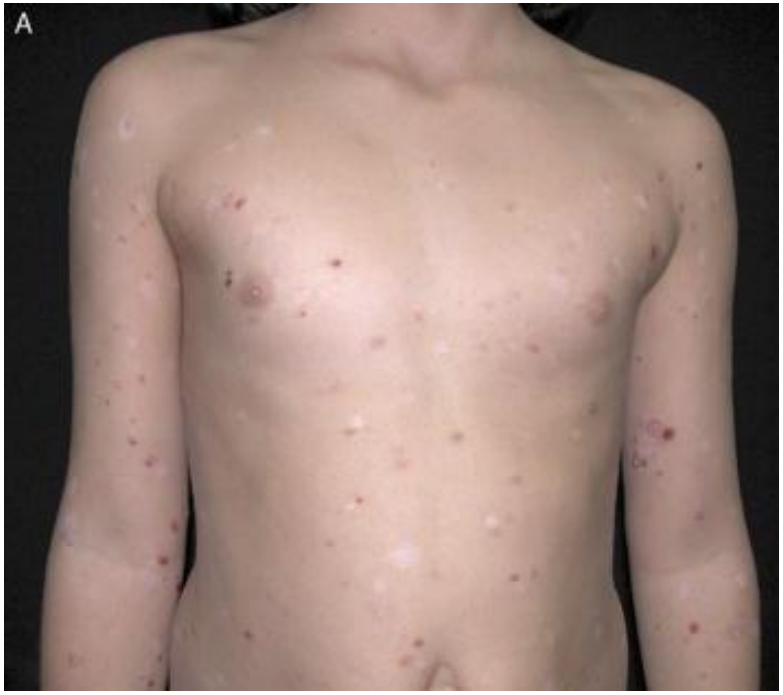
A Variant of Lymphomatoid Papulosis Simulating Primary Cutaneous Aggressive Epidermotropic CD8+ Cytotoxic T-cell Lymphoma. Description of 9 Cases

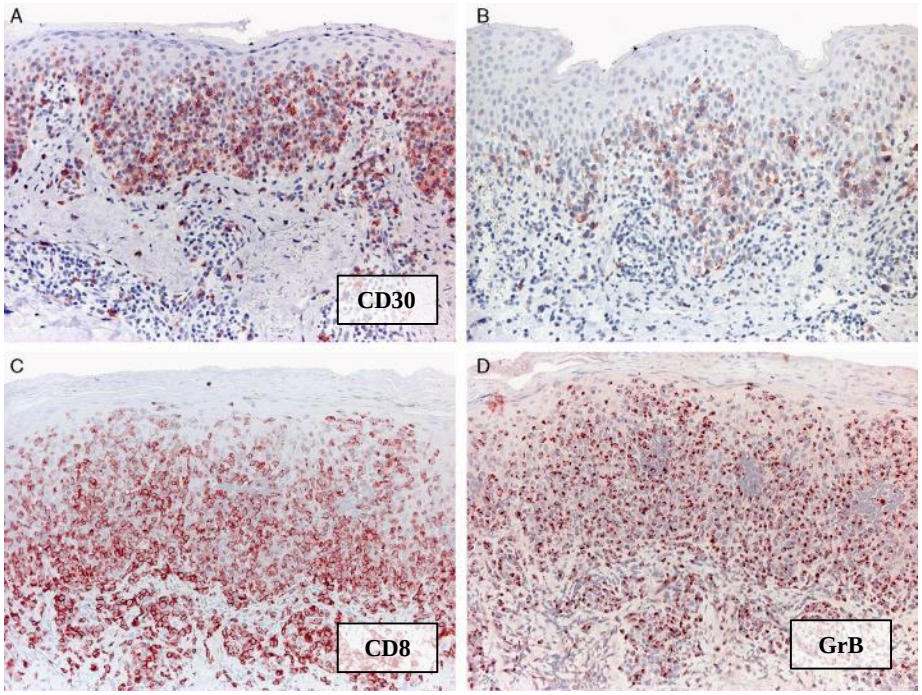
Andrea Saggini, MD,† Andrea Gulia, MD,*‡ Zsolt Argenyi, MD,§ Regina Fink-Puches,* Amelia Lissia, MD,‖ Mario Magaña, MD,¶ Luis Requena, MD,# Ingrid Simonitsch, MD,** and Lorenzo Cerroni, MD**

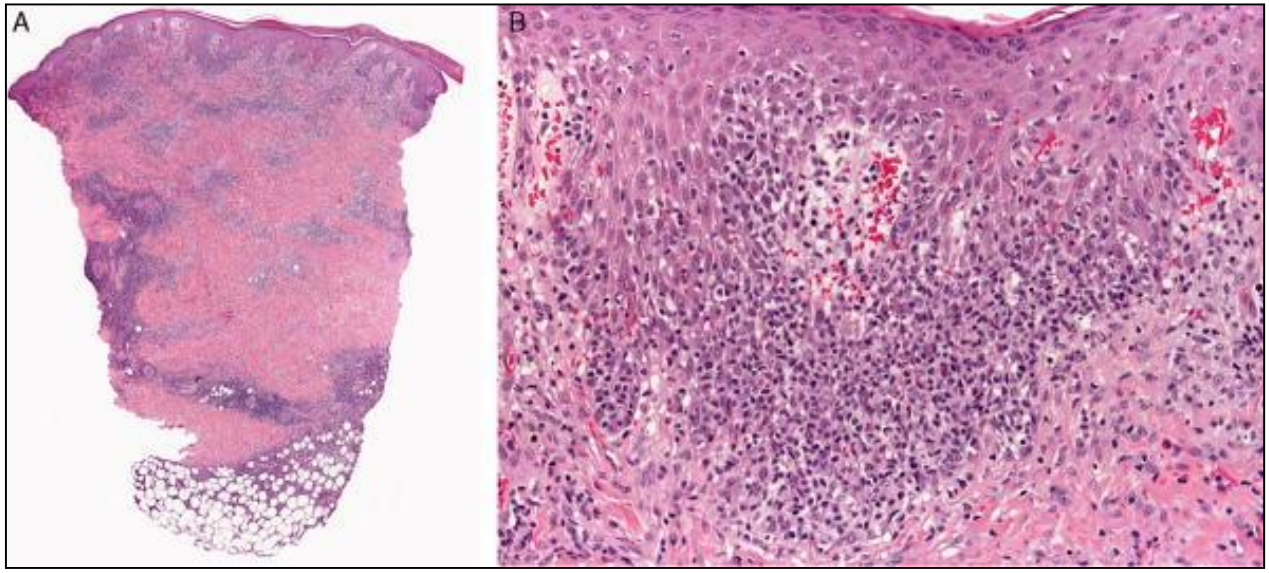
Abstract: Lymphomatoid papulosis (LyP) is a recurrent, self-healing eruption belonging to the spectrum of cutaneous CD30+lymphoproliferative disorders. Three main histologic subtypes of LyP are recognized: type A (histiocytic), type B (mycosis fungoides—(MF)-like), and type C (anaplastic large cell lymphoma–like). We reviewed 26 biopsies from 9 patients (M:F = 6:3, median age: 29; mean age 27,2; age range 10 to 38) who presented with clinical features typical of LyP but with histopathologic aspects that resembled primary cutaneous aggressive epidermotropic CD8+cytotoxic T-cell lymphoma. In all but 1 case atypical lymphoid cells showed expression of CD30, and in 8 of 9 cases a T-cell cytotoxic phenotype could be observed (βF1+, CD3+, CD4−, CD8+). Expression of at least 1 cytotoxic marker (TIA-1, granzyme B) was observed in all cases. Polymerase chain reaction analysis of the T-cell receptor genes revealed a monoclonal rearrangement in 2 of 5 cases tested. Follow-up data available for 8 patients (mean follow-up time: 84 mo, median: 32.5 mo; range: 1 to 303 mo) revealed that none of them developed systemic involvement or signs of other cutaneous lymphomas. This cytotoxic variant of LyP may be histopathologically indistinguishable from primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, and may be the source of pitfalls in the diagnosis and classification. We propose the term LyP type D for this unusual variant of the disease. Accurate clinicopathologic correlation is required in this setting, with crucial implications regarding prognosis and management of patients.

Key Words: lymphomatoid papulosis, primary cutaneous aggressive epidermotropic CD8+cytotoxic T-cell lymphoma, mycosis fungoides, cytotoxic lymphoma, cutaneous T-cell lymphoma

(*Am J Surg Pathol* 2010;34:1168–1175)







A Variant of Lymphomatoid Papulosis Simulating Primary Cutaneous Aggressive Epidermotropic CD8+ Cytotoxic T-cell Lymphoma. Description of 9 Cases.

Saggini, Andrea; Gulia, Andrea; Argenyi, Zsolt; Fink-Puches, Regina; Lissia, Amelia; Magana, Mario; Requena, Luis; Simonitsch, Ingrid; Cerroni, Lorenzo

American Journal of Surgical Pathology. 34(8):1168-1175, August 2010.
DOI: 10.1097/PAS.0b013e3181e75356

LyP type E

Angioinvasive Lymphomatoid Papulosis

A New Variant Simulating Aggressive Lymphomas

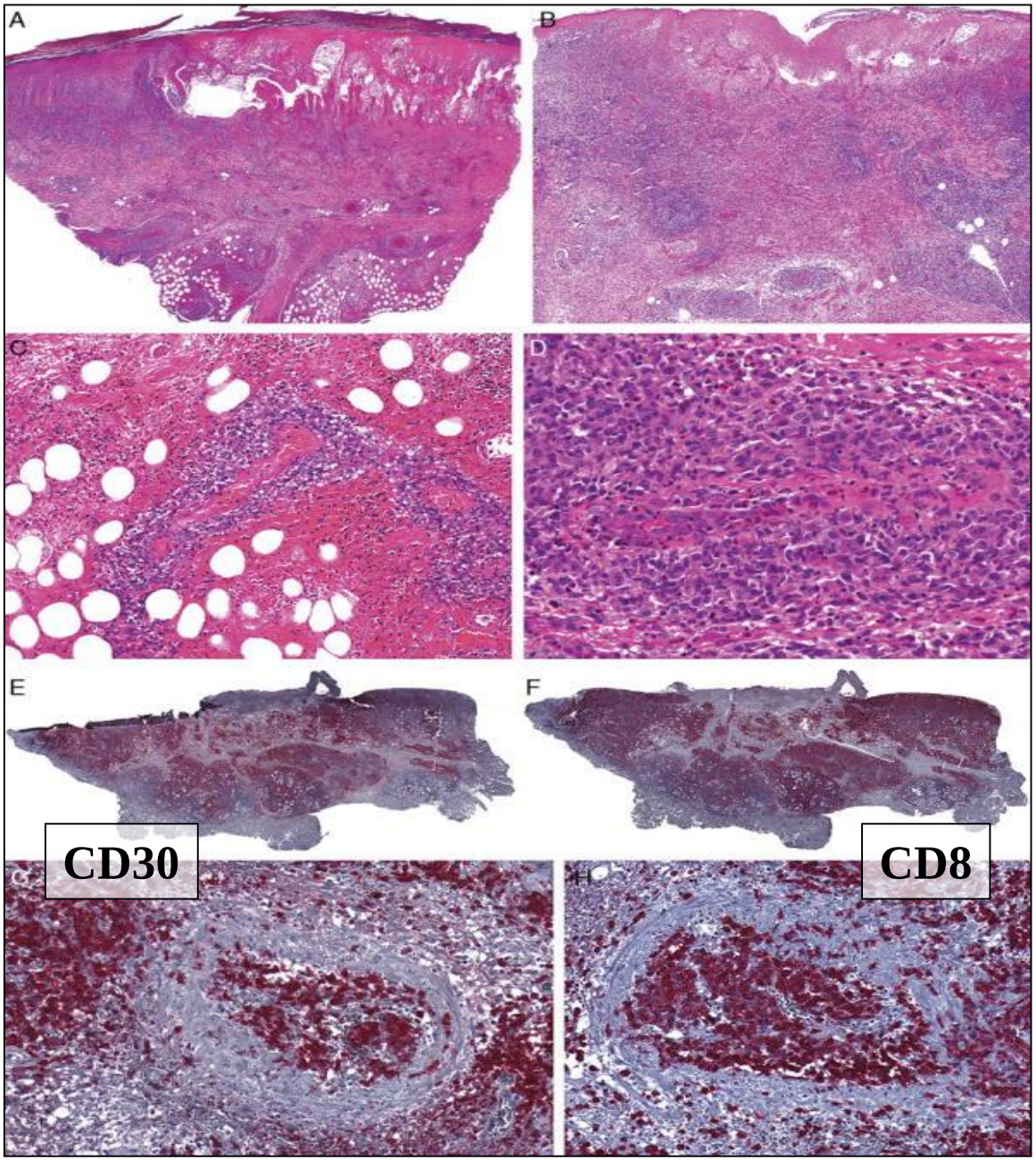
Werner Kempf, MD,† Dmitry V. Kazakov, MD, PhD,‡ Leo Schärer, MD,§ Arno Rütten, MD,§ Thomas Mentzel, MD,§ Bruno E. Paredes, MD,§ Gabriele Palmedo, PhD,§ Renato G. Panizzon, MD,‖ and Heinz Kutzner, MD§*

Abstract: Lymphomatoid papulosis (LyP) belongs to the spectrum of primary cutaneous CD30-positive lymphoproliferative disorders. Clinically, LyP is characterized by a variable number of self-healing papulo-nodular lesions, with the typical waxing and waning course. Histologically, 4 types (A, B, C, and D) have been delineated. Angioinvasive growth and large ulcers are rare findings in LyP and simulate aggressive lymphoma. We retrospectively analyzed the clinicopathologic and molecular features of angioinvasive LyP in a series of 16 patients. This new form of LyP is characterized by oligolesional papules that rapidly ulcerate and evolve into large necrotic eschar-like lesions with a diameter of 1 to 4 cm and an angiocentric and angiodestructive infiltrate of small-sized to medium-sized atypical lymphocytes expressing CD30 and frequently CD8. As in other forms of LyP, the lesions underwent spontaneous regression after a few weeks. Recurrences were common, but the prognosis was excellent with no extracutaneous spread or disease-related deaths. Complete remission occurred in 9 of 16 patients (56%). This LyP variant should be distinguished from aggressive forms of angiocentric and angiodestructive and cytotoxic T-cell lymphomas. We propose the term LyP type E for this clinically and histologically unusual variant.

Key Words: lymphoma, skin, CD8, CD30, lymphomatoid papulosis, cytotoxic lymphoma, angiotropic

(*Am J Surg Pathol* 2013;37:1–13)

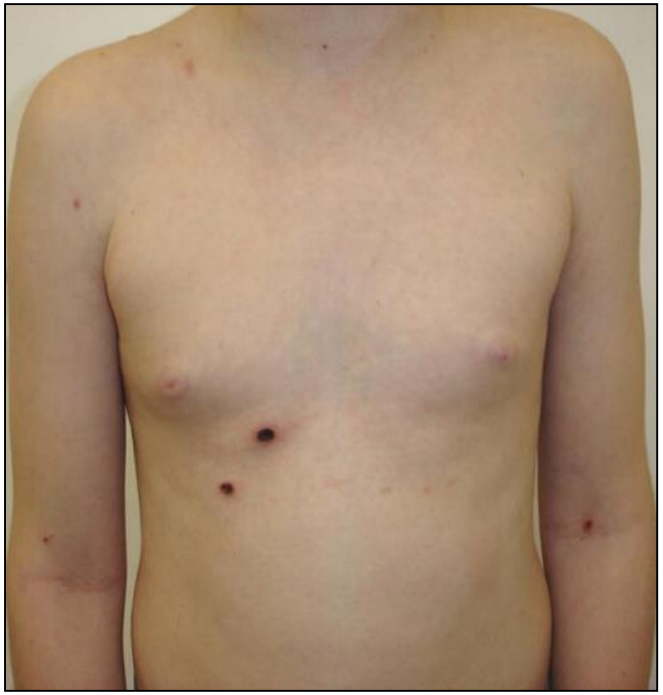
LyP types (A, B, C, and D) have been identified. Type A is characterized by the presence of large pleomorphic or anaplastic $CD30^+$ T cells scattered or in small clusters within the background of eosinophilic and neutrophilic granulocytes, histiocytes, and small lymphocytes. Type B shows epidermotropic infiltrates of small-sized to medium-sized lymphoid cells, with variable extent of CD30 expression. In type C, a nodular dense infiltrate of cohesive sheets of pleomorphic or anaplastic $CD30^+$ cells is present, and it usually contains only a few eosinophilic or neutrophilic granulocytes.[3–7] Recently, type D has been described, which displays an epidermotropic infiltrate of $CD8^+$ and $CD30^+$ small-sized to medium-sized lymphoid cells.[8] Within the same patient, different lesions may show different histologic types, either synchronously or metachronously.[9] The $CD30^+$ lymphoid cells may express CD4, CD8, or CD56, with CD4 immunoreactivity being the most common phenotype.[10,11] Independent of its histologic pattern and the immunophenotype, LyP is clinically characterized by a variable number of self-healing papulo-nodular lesions, with the typical waxing and waning course. The individual lesions undergo spontaneous regression within a few weeks, sometimes accompanied by ulceration on top of the lesions and occasionally leaving behind varioliform scars. Despite the



Angioinvasive Lymphomatoid Papulosis: A New Variant Simulating Aggressive Lymphomas.

Kempf, Werner; Kazakov, Dmitry; MD, PhD; Scharer, Leo; Rutten, Arno; Mentzel, Thomas; Paredes, Bruno; Palmedo, Gabriele; Panizzon, Renato; Kutzner, Heinz

American Journal of Surgical Pathology. 37(1):1-13, January 2013.
DOI: 10.1097/PAS.0b013e3182648596



Chromosomal Rearrangements of 6p25.3 Define a New Subtype of Lymphomatoid Papulosis

Laszlo J. Karai, MD,† Marshall E. Kadin, MD,‡ Eric D. Hsi, MD,§ Jason C. Sluzevich, MD,‖ Rhett P. Ketterling, MD,¶ Ryan A. Knudson, BS,¶ and Andrew L. Feldman, MD¶*

Abstract: Lymphomatoid papulosis (LyP) is an indolent cutaneous lymphoproliferative disorder with clinical and pathologic features overlapping those of both reactive conditions and aggressive lymphomas. Recurrent genetic abnormalities in LyP have not been previously identified. Here, we describe the clinical, immunophenotypic, and genetic characteristics of cutaneous lymphoproliferative lesions showing distinctive and previously undescribed histologic features in 11 patients. All patients were older adults (67 to 88 y) with predominantly localized lesions and clinical presentations suggesting benign inflammatory dermatoses or low-grade epithelial tumors. Histologically, lesions showed a biphasic growth pattern, with small cerebriform lymphocytes in the epidermis and larger transformed lymphocytes in the dermis. All had a T-cell immunophenotype. The pathologic features raised the possibility of an aggressive T-cell lymphoma such as transformed mycosis fungoides. However, no patient developed disseminated skin disease or extracutaneous spread. Untreated lesions regressed spontaneously. All cases harbored chromosomal rearrangements of the *DUSP22-IRF4* locus on 6p25.3. The overall findings suggest that these cases represent a newly recognized LyP subtype characterized by 6p25.3 rearrangements. The benign clinical course in all 11 patients despite pathologic features mimicking an aggressive lymphoma emphasizes the importance of clinicopathologic correlation, incorporating molecular genetic analysis when possible, during the evaluation of cutaneous lymphoproliferative disorders.

Key Words: lymphomatoid papulosis, cutaneous CD30-positive T-cell lymphoproliferative disorder, T-cell lymphoma, chromosomal translocation, fluorescence in situ hybridization, DUSP22, genetics

(*Am J Surg Pathol* 2013;37:1173–1181)

Lymphomatoid papulosis (LyP) is a chronic, recurring CD30-positive T-cell lymphoproliferative disorder (TLPD) that presents as multifocal papular lesions on the trunk, buttocks, and extremities of patients ranging in age from 4 to 88 years.[1,2] Five subtypes currently are recognized and/or have been proposed on the basis of their histologic and immunophenotypic features.[3–8] The most frequent, type A, is characterized by a dermal infiltrate of large transformed lymphocytes in a mixed inflammatory background.[9] Type B lesions have a predominantly intraepidermal lymphocytic infiltrate mimicking mycosis fungoides (MF). Type C lesions have sheets of large transformed lymphocytes in the dermis, with or without significant epidermotropism.[5] Type D LyP is a CD8-positive cytotoxic T-cell variant with epidermotropism.[6] Kempf et al[8] recently proposed another oligolesional, ulcerative, angioinvasive variant (type E).

We report 11 elderly patients with localized skin lesions clinically suggestive of inflammatory dermatoses, infections, or low-grade epithelial skin tumors. Pathologic findings raised the possibility of an aggressive lymphoid malignancy and consisted of a combination of pagetoid reticulosis–like intraepidermal lymphocytosis and a cohesive, nodular dermal infiltrate of highly proliferative CD30-positive tumor cells. However, all lesions showed

Chromosomal Rearrangements of 6p25.3 Define a New Subtype of Lymphomatoid Papulosis.
Karai, Laszlo; Kadin, Marshall; Hsi, Eric; Sluzevich, Jason; Ketterling, Rhett; Knudson, Ryan; Feldman, Andrew
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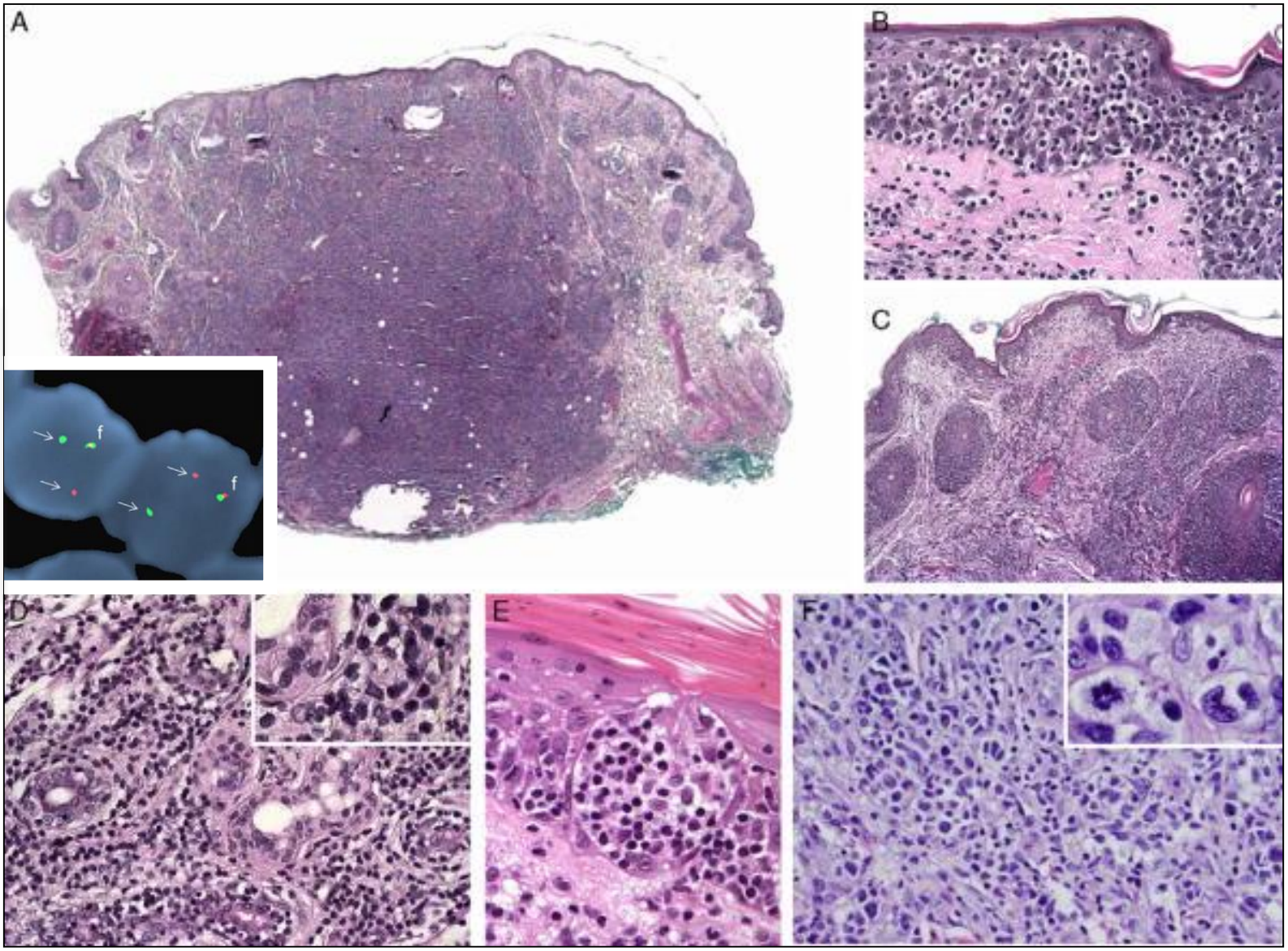


Follicular lymphomatoid papulosis revisited: A study of 11 cases, with new histopathological findings

Werner Kempf, MD,[a] Dmitry V. Kazakov, MD, PhD,[b] Hans-Peter Baumgartner, MD,[c] and Heinz Kutzner, MD[d]
Zürich and Zug, Switzerland; Pilsen and Prague, Czech Republic; and Friedrichshafen, Germany

Background: Follicular lymphomatoid papulosis (LyP) describes a variant of LyP with perifollicular infiltrates and some degree of folliculotropism of $CD30^+$ atypical lymphocytes. So far, only a few cases of follicular LyP have been described.

Objective: Our goal was to study the clinicopathologic features of follicular LyP in a series of 11 cases (9 male, 2 female; age range 7-78 years, mean age 50 years).

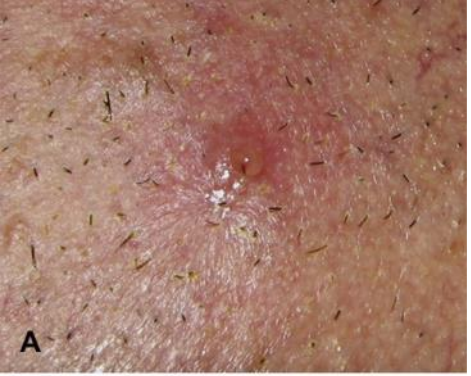
Methods: In all, 113 cases of LyP were reviewed to select cases showing follicular involvement. Histology was correlated with the clinical data to exclude cases of $CD30^+$ anaplastic large-cell lymphoma or folliculotropic mycosis fungoides.

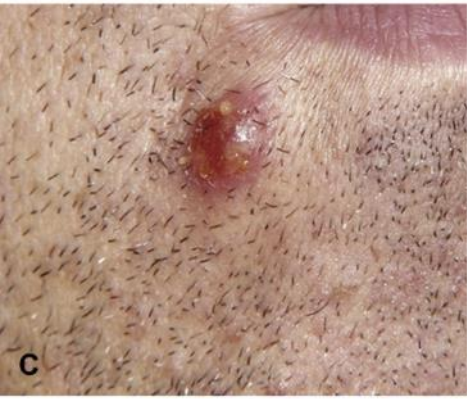
Results: Six cases were classified as type C and 4 as type A, whereas the remaining case manifested epidermotropism of small lymphocytes in a background of a typical type A lesion (overlapping type A/B). Perifollicular infiltrates of $CD30^+$ atypical lymphoid cells were seen in all 11 cases, with infiltration of the follicular epithelium in 8 cases. Hyperplasia of the follicular epithelium was observed in 4 cases; ruptured hair follicles, in 3 cases; and follicular mucinosis, in 2 cases. In addition to hair follicle infiltration, atypical cells were recognized within sebaceous glands in 2 lesions. New findings were presence of numerous intrafollicular neutrophils in 2 patients, who clinically had pustules in addition to papules. Other histopathological features encountered included perieccrine infiltration (n = 5), focal subcutaneous involvement (n = 4), granulomatous inflammation (n = 3), epidermal hyperplasia (n = 2), and 1 each of infiltration of muscle bundles, numerous eosinophils in the infiltrate, and angiocentricity.

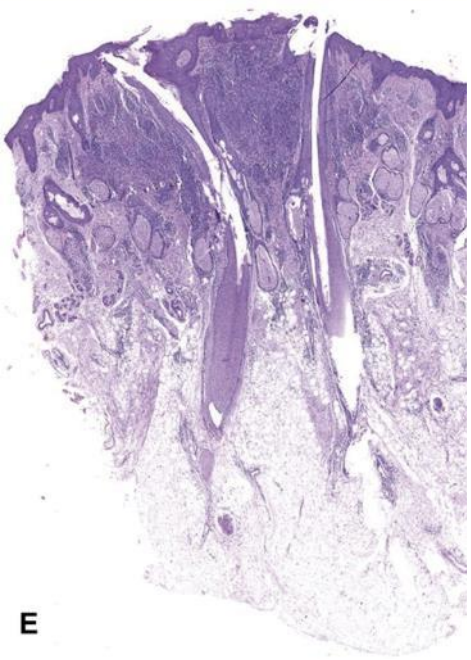
Limitations: This was a retrospective study.

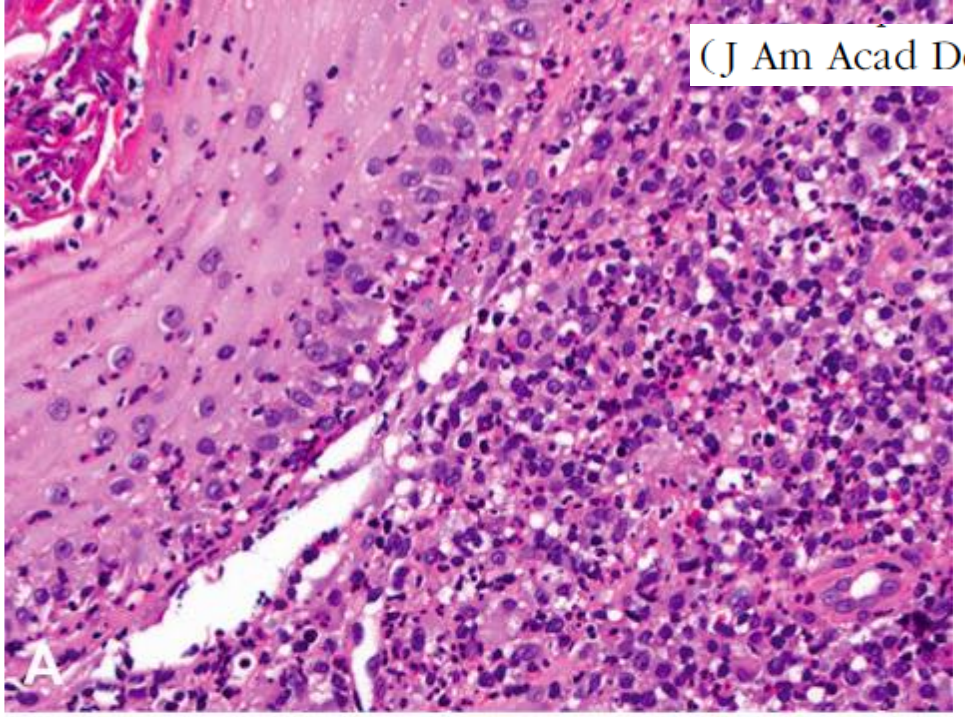
Conclusions: Follicular LyP is a variant of LyP with involvement of hair follicles, mostly in the form of perifollicular infiltrate with variable degree of folliculotropism. Other changes including hyperplasia of the follicular epithelium, rupture of hair follicle, and follicular mucinosis are less common. Rarely, intrafollicular pustules can be seen in the follicular epithelium; such lesions manifest clinically as pustules. (J Am Acad Dermatol 2013;68:809-16.)

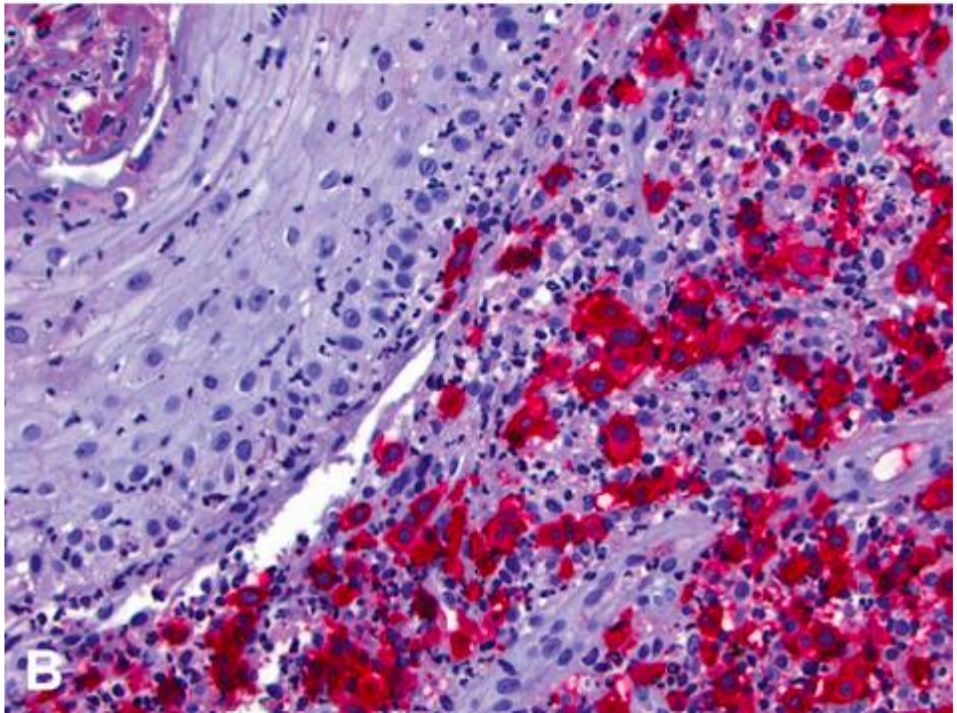
Key words: CD30; follicular mucinosis; lymphoma; lymphomatoid papulosis; skin.

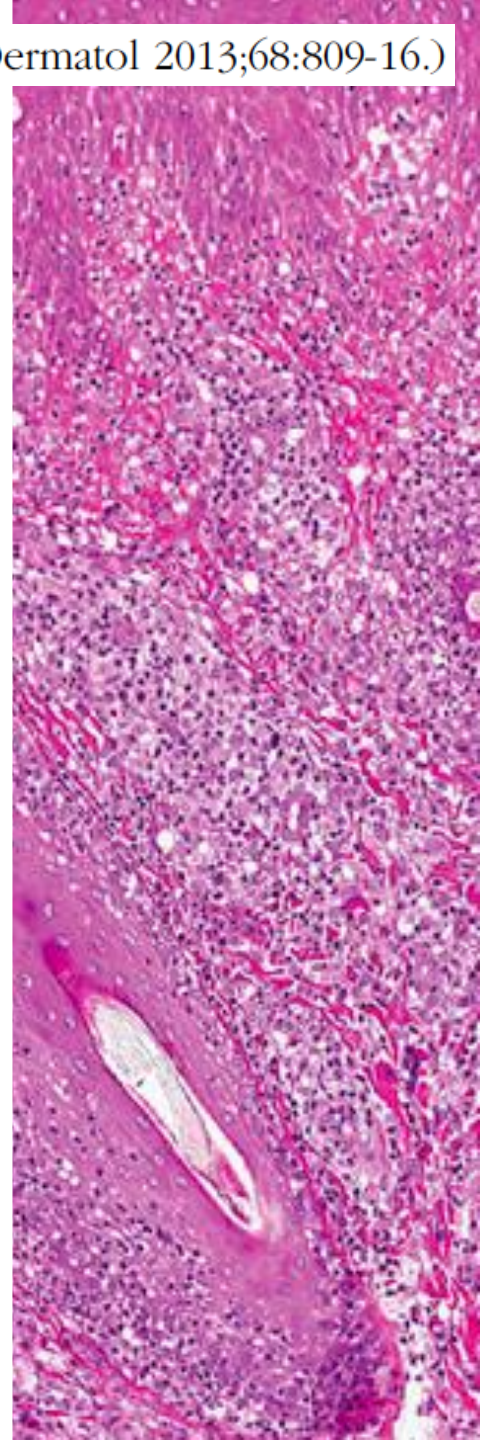












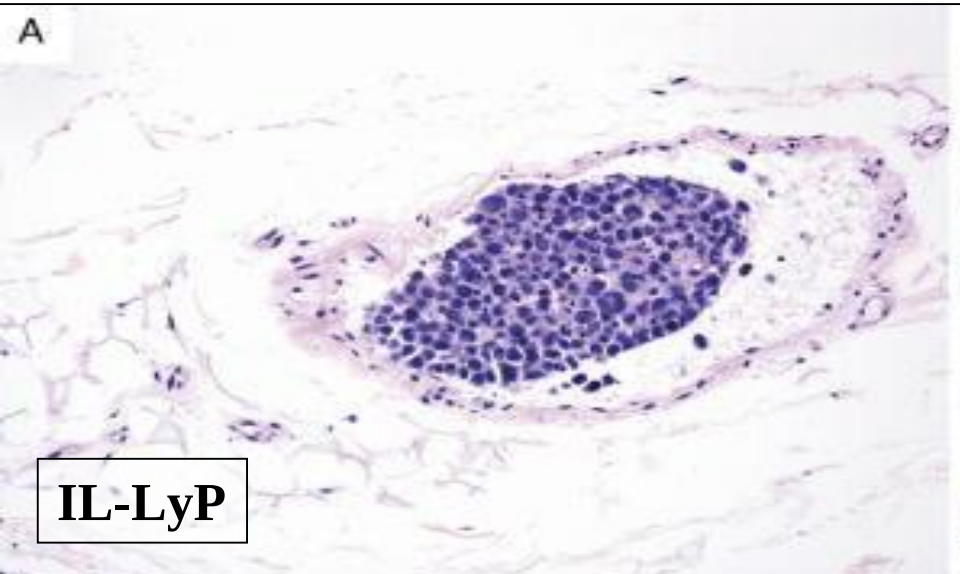
(J Am Acad Dermatol 2013;68:809-16.)

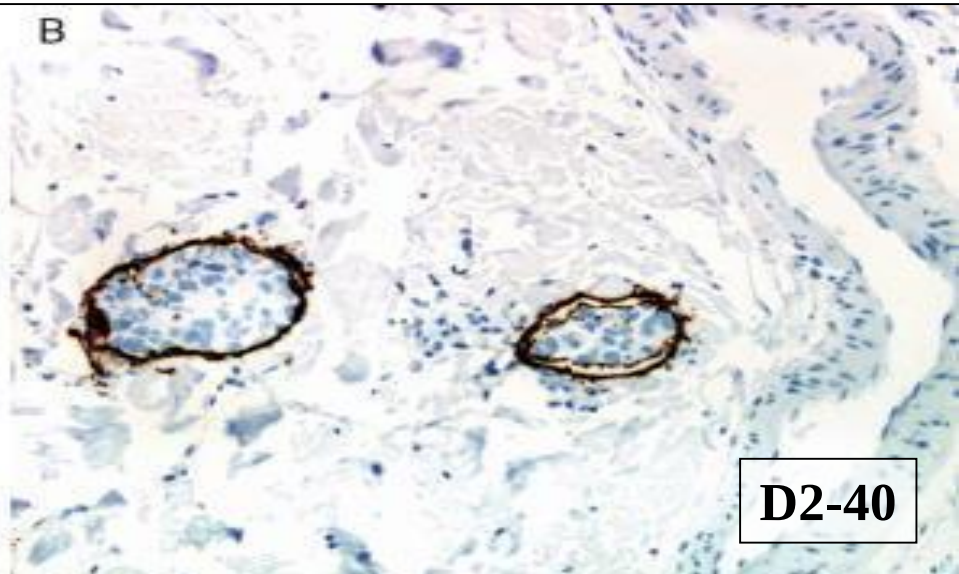
(*Am J Surg Pathol* 2014;38:1203–1211)

Intralymphatic Cutaneous Anaplastic Large Cell Lymphoma/Lymphomatoid Papulosis

Expanding the Spectrum of CD30-positive Lymphoproliferative Disorders

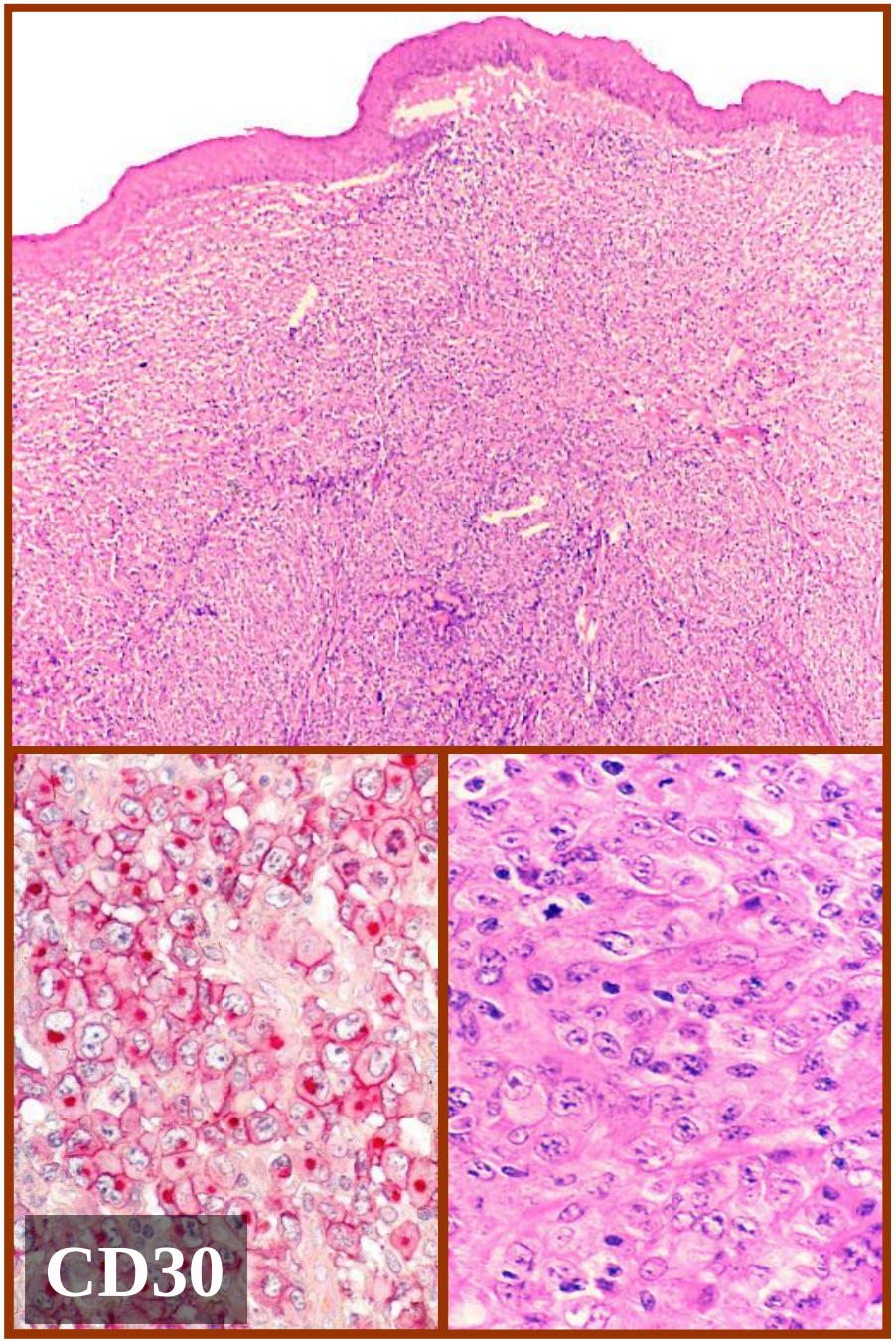
Mark A. Samols, MD, Albert Su, MD,† Seong Ra, MD,†‡ Mark A. Cappel, MD,§ Abner Louissant, Jr, MD,‖ Ryan A. Knudson, CG(ASCP)CM,¶ Rhett P. Ketterling, MD,¶ Jonathan Said, MD,† Scott Binder, MD,† Nancy Lee Harris, MD,‖ Andrew L. Feldman, MD,¶ Jinah Kim, MD, PhD,* Youn H. Kim, MD,# and Dita Gratzinger, MD, PhD**





Primary Cutaneous ALCL (CD30+)

- Diffuse non-epidermotropic infiltrates with cohesive sheets of large CD30+ tumour cells (>75%)
- Immunophenotype: CD4+, variable loss of CD2, CD5, CD7, CD3; frequent expression of granzyme B, TIA1, perforin
- Some cases CD4−/CD8+ or CD4+/CD8+
- CD15+ in ≈ 40% of cases; IRF4 (MUM1)+ in ≈ 100% of cases



Primary Cutaneous ALCL (CD30+)

Genetic Profile

- The vast majority of PC-ALCLs dos not carry translocations involving the ALK gene, however, unusual cases of ALK+ PC-ALCL, including cases showing strong nuclear and cytoplasmic staining characteristic of the t(2;5) chromosomal translocation and cases expressing cytoplasmic ALK protein (indicative of a variant translocation), have been reported in children and adults
- Rearrangements of the DUSP22-IRF4 locus at 6p25.3 are found in approximately 25% of PC-ALCL cases
- High expression of skin-homing chemokine receptor genes CCR10 and CCR8 in PC-ALCL
- A novel recurrent NPM1-TYK2 gene fusion, resulting in constitutive STAT signalling, has been described in ≈ 4% of primary cutaneous CD30+ TCLPD

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Sézary syndrome	9701/3
CD30+ T-cell lymphoproliferative disorders	
Lymphomatoid papulosis	9718/1
Primary cutaneous anaplastic large cell lymphoma	9718/3
Adult T-cell leukaemia/lymphoma (cutaneous)	9827/3
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T-cell prolymphocytic leukaemia	9834/3
Primary cutaneous marginal zone lymphoma	9699/3
Primary cutaneous follicle centre lymphoma	9597/3
Primary cutaneous diffuse large B-cell lymphoma (leg type)	9680/3
Intravascular large B-cell lymphoma	9712/3
Mucocutaneous ulcer (EBV-positive)	9680/1
Lymphomatoid granulomatosis	
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Grade 3	9766/3
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Langerhans cell histiocytosis	9751/3
Indeterminate cell histiocytosis/ indeterminate dendritic cell tumour	9757/3
Rosai–Dorfman disease	
Juvenile xanthogranuloma	
Erdheim–Chester disease	9749/3
Reticulohistiocytosis	8831/0

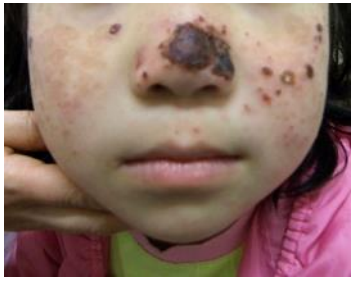
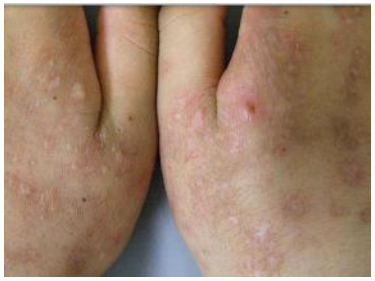
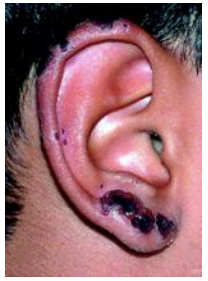
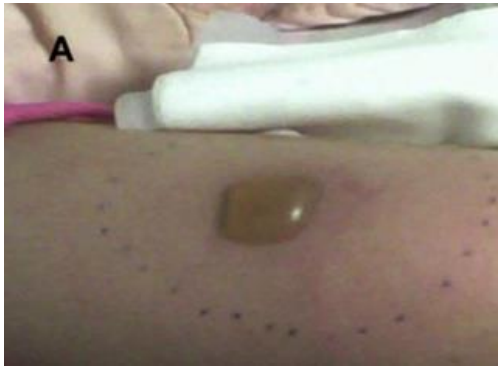
Cutaneous manifestations of chronic active EBV infection

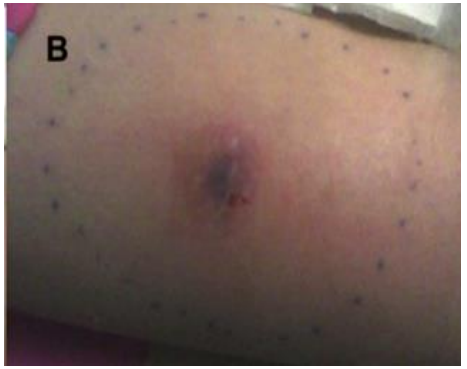
- **Definition**

  Cutaneous manifestations of chronic active EBV infection include ***hydroa vacciniforme–like lymphoproliferative disorder*** (HV-like LPD) and ***severe mosquito bite allergy***. Both conditions present primarily in children/adolescent and are associated with a risk of progression to systemic EBV-associated NK/T-cell lymphoma. HV-like LPD is derived from T cells, whereas severe mosquito bite allergy is more often of NK-cell origin.

Cutaneous manifestations of chronic active EBV infection

- **Clinical features**



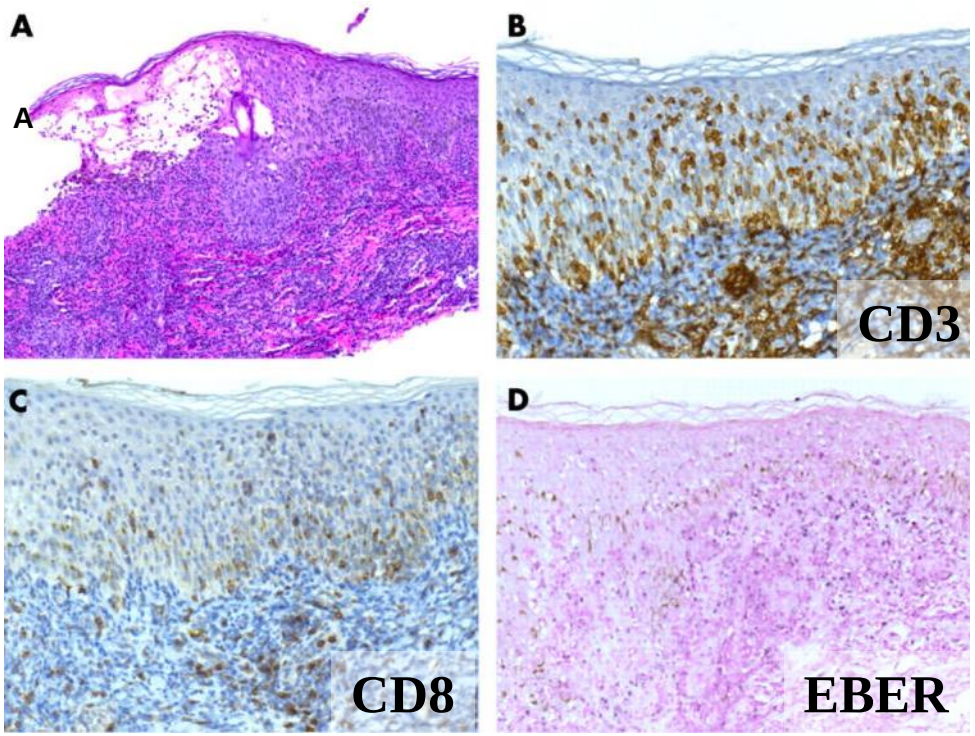
HV-like LPD affects the skin of the face, the dorsal surface of the hands, and the ear lobes. In more severe cases, systemic symptoms may be present in addition to extensive skin lesions.

In severe *mosquito bites hypersensitivity*, skin lesions at the site of the mosquito bite typically show erythema and bullae that subsequently become necrotic and ulcerated. The lesions eventually heal, with scarring. Systemic symptoms can be present

Cutaneous manifestations of chronic active EBV infection

- **Histopathology**

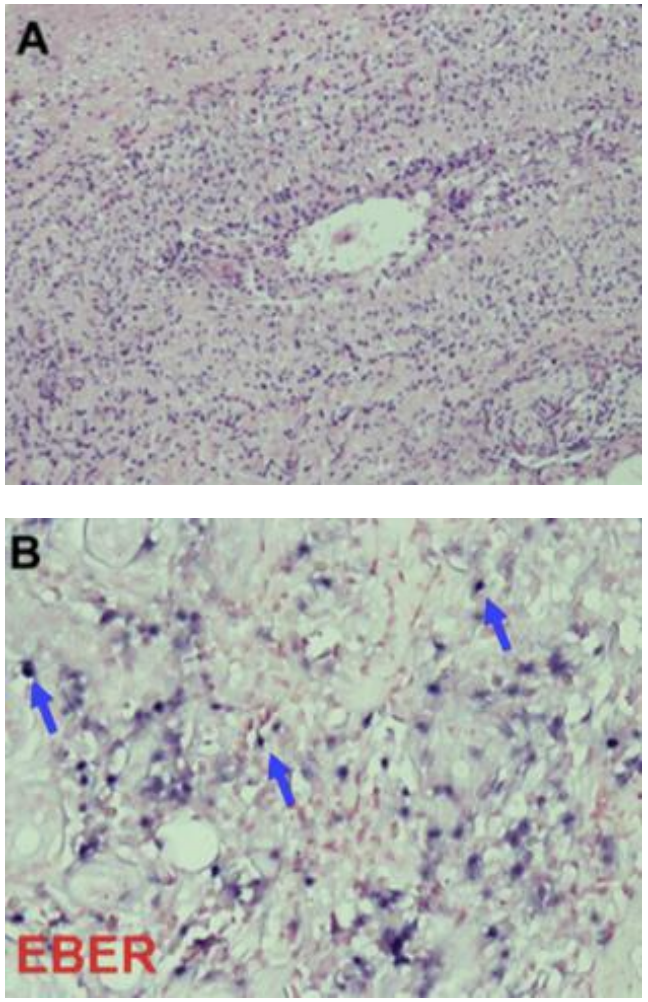
The characteristic histological feature of *HV-like LPD* is intraepidermal spongiotic vesiculation. The infiltrate is mainly located around adnexa and blood vessels, often with angiodestructive features. The neoplastic cells are generally small to medium-sized, without substantial atypia. The cells have a cytotoxic T-cell phenotype. Most cases are CD8+; a few are CD4+. Some cases show an NK-cell phenotype (CD56+). CD30 is often expressed in the infiltrating EBV+ T cells. LMP1 is usually negative



Cutaneous manifestations of chronic active EBV infection

- **Histopathology**

In *mosquito bite allergy*, the skin at the site of the bite exhibits epidermal necrosis and ulceration. The dermis shows oedema, and a polymorphic infiltrate that extends to subcutaneous tissue. Polymorphonuclear leukocytes and eosinophils with admixed nuclear debris, as well as extravasated red blood cells, are common.



Cutaneous manifestations of chronic active EBV infection

- **Genetic profile**

  Most cases of HV-like LPD have clonal rearrangements of the TCR genes and in situ hybridization for EBER is positive. LMP1 is negative immunohistochemically, but it can be detected in the peripheral blood by PCR in most cases, indicating type II EBV latency. In both HV-like LPD and severe mosquito bite allergy, EBV is clonal.

World Health Organization Classification of Tumours

WHO OMS

International Agency for Research on Cancer (IARC)

WHO Classification of Skin Tumours

4th Edition, 2018

Haematolymphoid tumours	
Mycosis fungoides	9700/3
Folliculotropic mycosis fungoides	9700/3
Granulomatous slack skin	9700/3
Pagetoid reticulosis	9700/3
Sézary syndrome	9701/3
CD30+ T-cell lymphoproliferative disorders	
Lymphomatoid papulosis	9718/1
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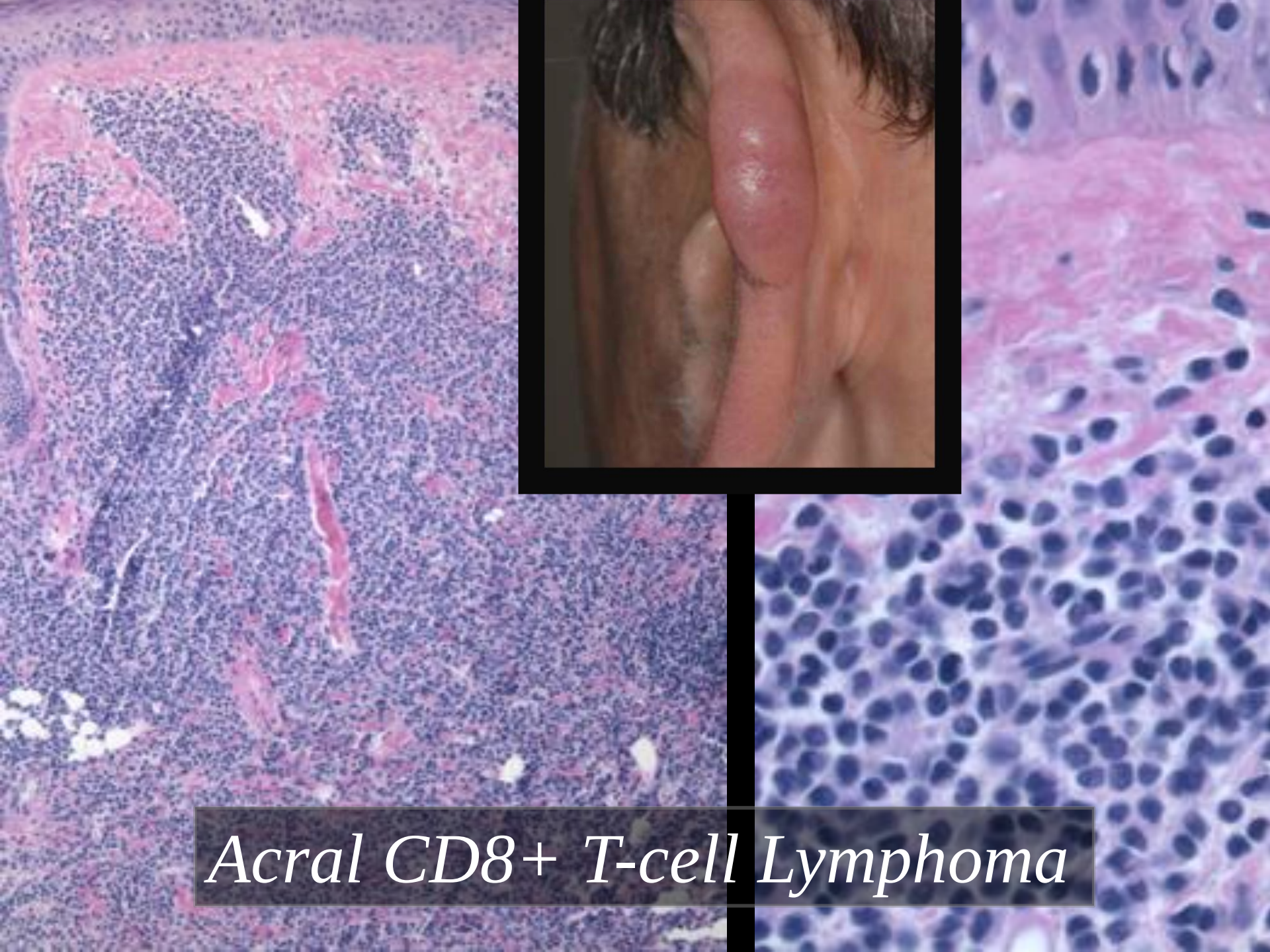
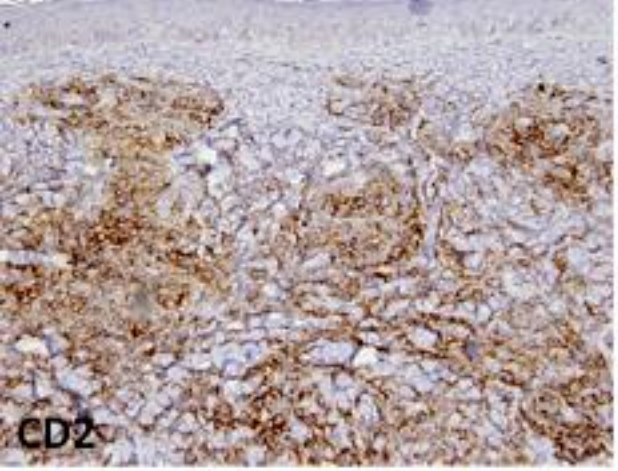
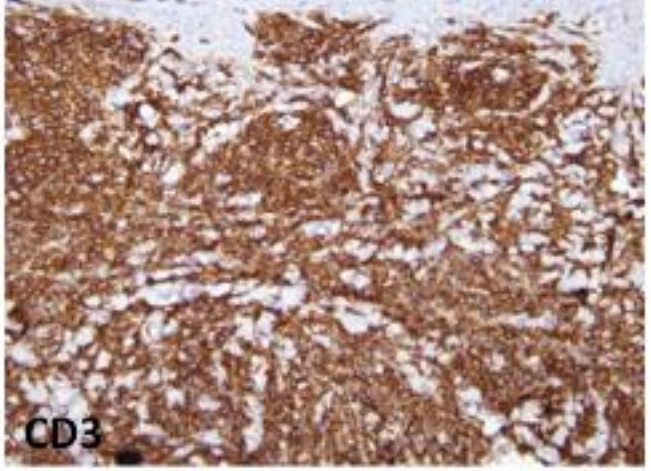
Indeterminate cell histiocytosis/ indeterminate dendritic cell tumour	9757/3
Rosai–Dorfman disease	
Juvenile xanthogranuloma	
Erdheim–Chester disease	9749/3
Reticulohistiocytosis	8831/0

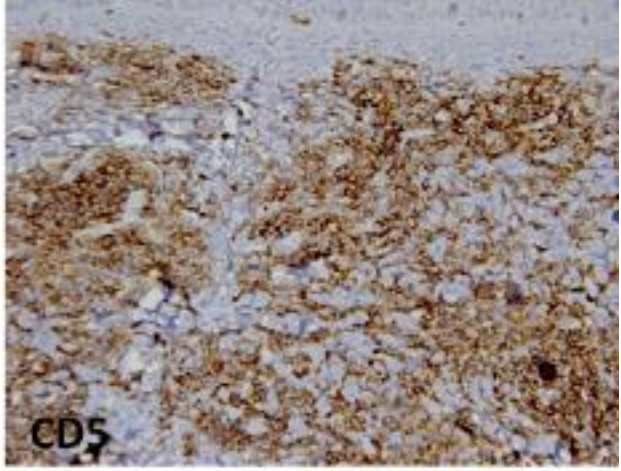
Primary Cutaneous Peripheral T-cell Lymphomas

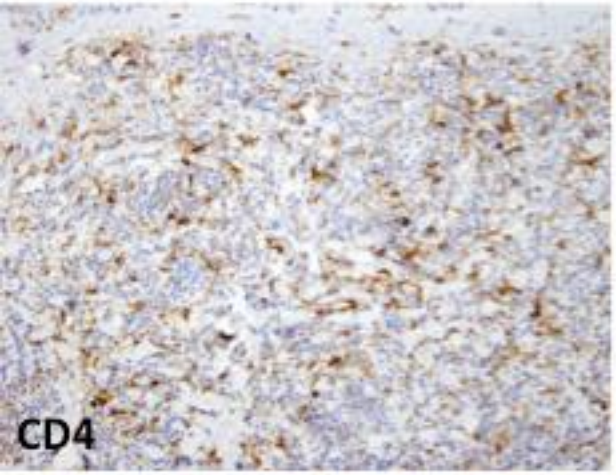
On the basis of characteristic clinicopathological and prognostic features, four subtypes of cutaneous T-cell lymphoma were defined: primary cutaneous γδ T-cell lymphoma, primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, *primary cutaneous acral CD8+ T-cell lymphoma*, and *primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder*. The last three entities are considered to be provisional.

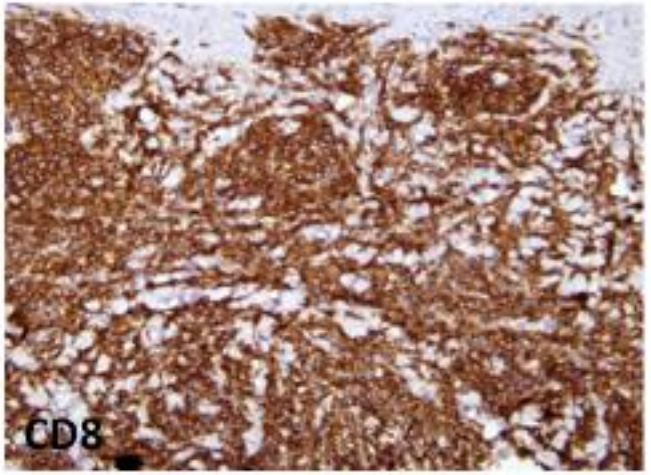

Acral CD8+ T-cell Lymphoma

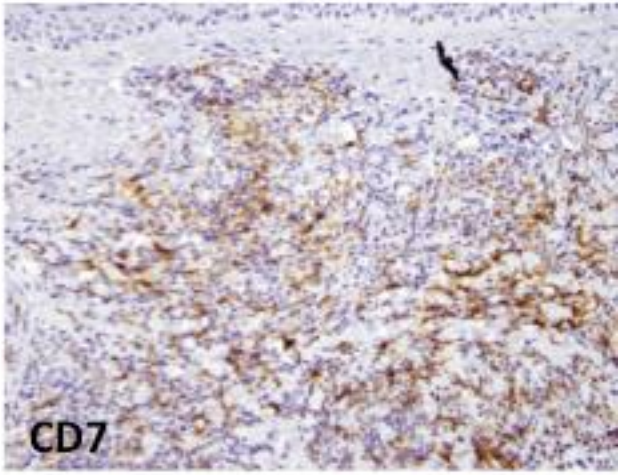

CD2

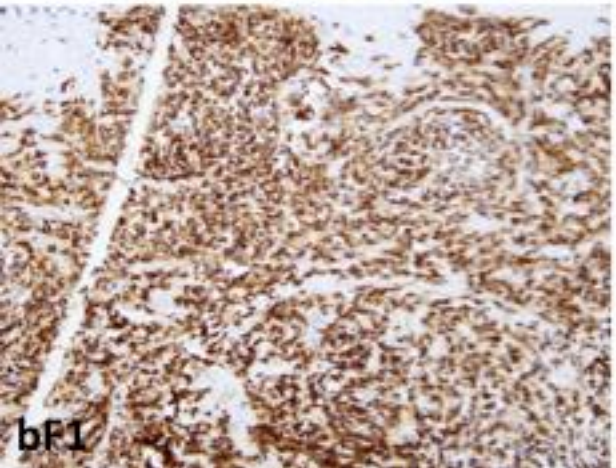

CD3

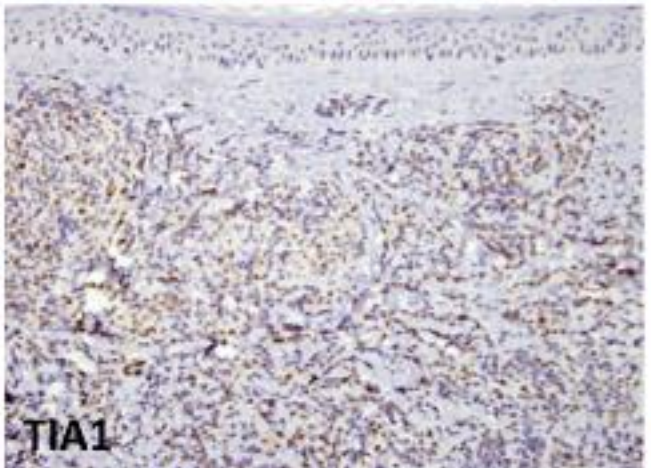

CD5

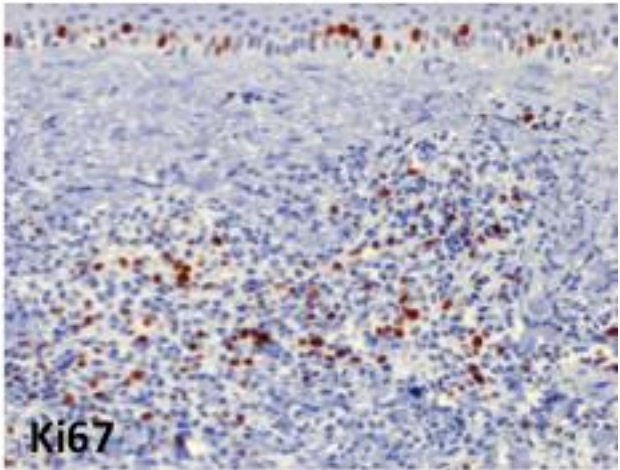

CD4


CD8


CD7


bF1


TIA1


Ki67

British Journal of Dermatology (2015) **172**, pp1573–1580

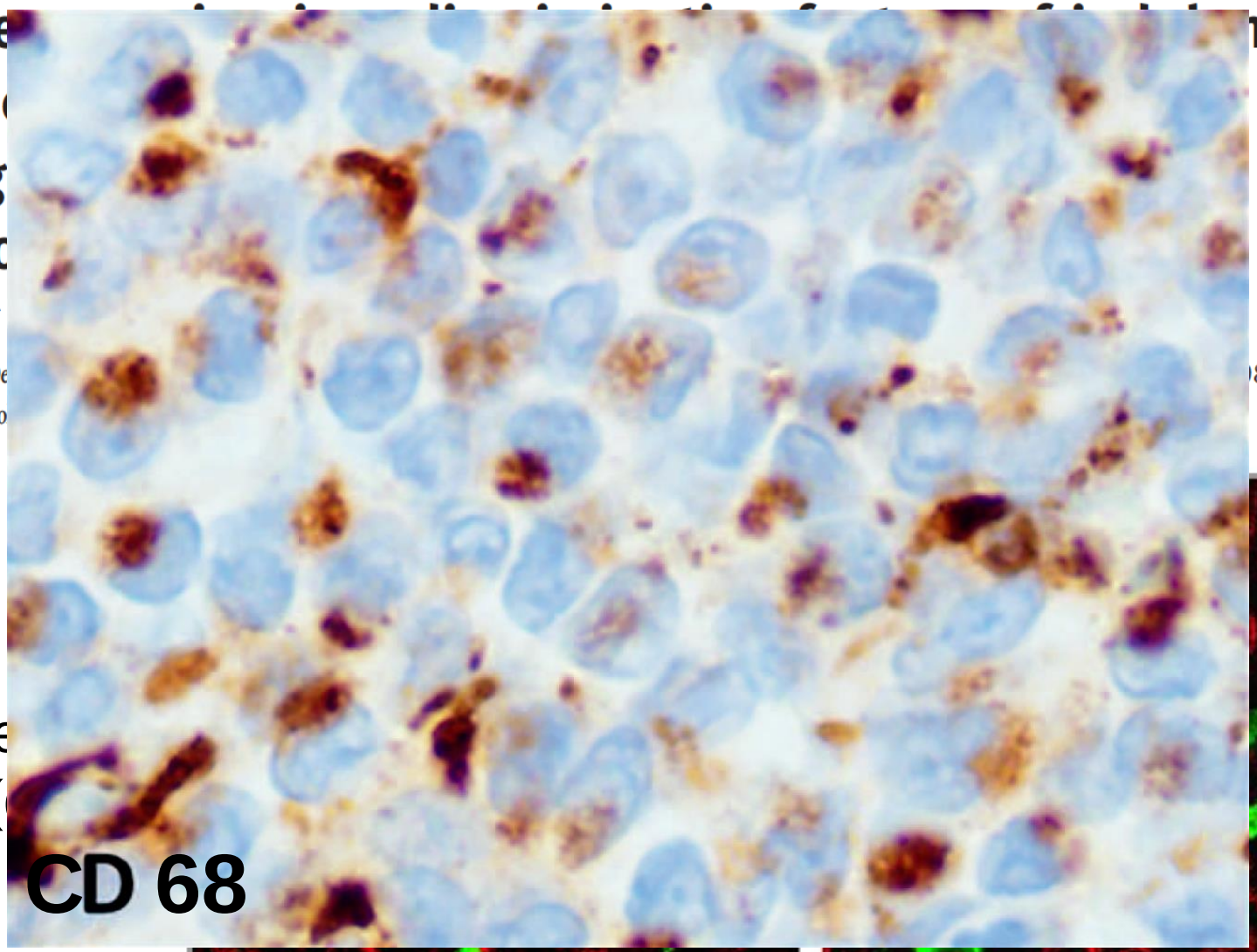
BJD
British Journal of Dermatology

CD68 e… …nt cutane… disting… CD8-po…

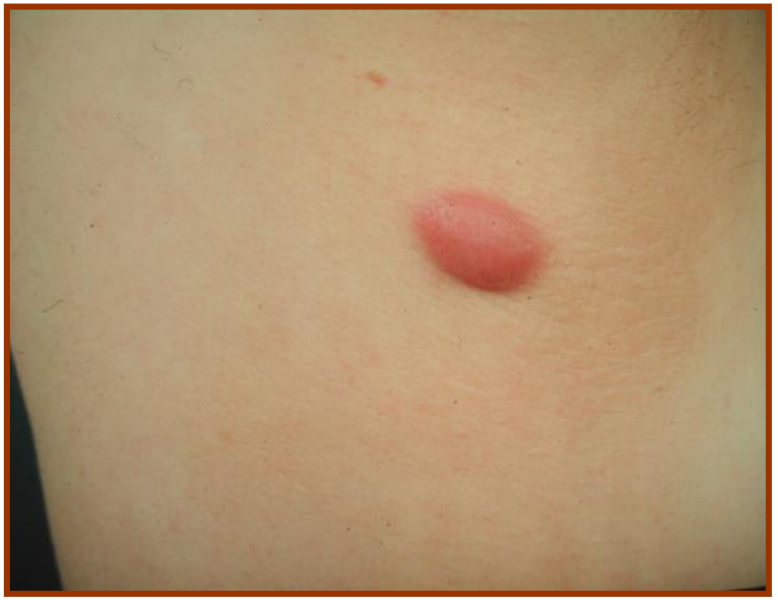
M. Wobser,[1]

[1]Department of De… …80, Germany
[2]Institute of Patho…

CD8 (re…
CD68 (…



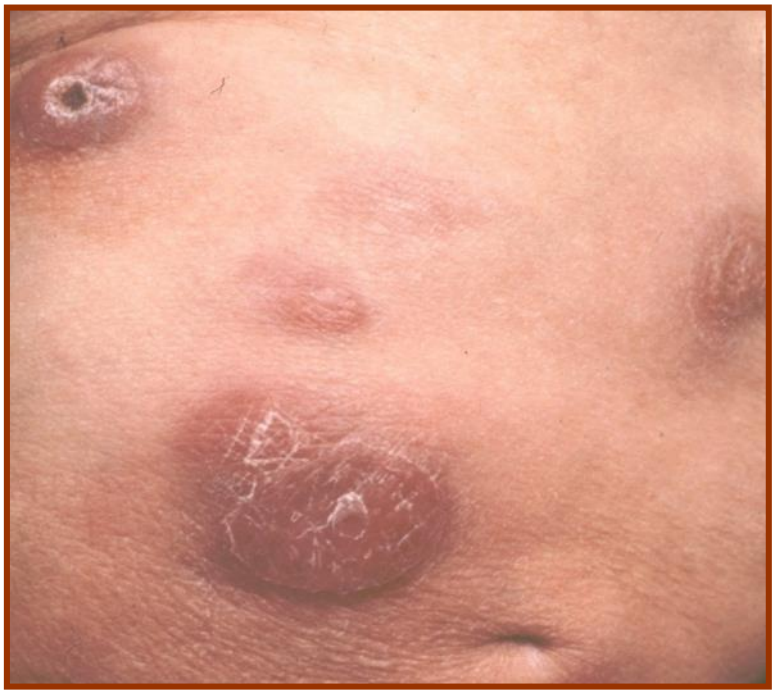
CD4+ Small/medium T-cell Lymphoproliferative Disorder



Characterized by a predominance of small to medium-sized CD4+ pleomorphic T cells, presentation with a solitary skin lesion, and no evidence of the patches or plaques that are typical of mycosis fungoides. Cases have the same clinicopathological features and benign clinical course as cutaneous pseudo-T-cell lymphomas with a nodular growth pattern(therefore,“lymphoproliferative disorder”).

Peripheral T-cell Lymphoma NOS

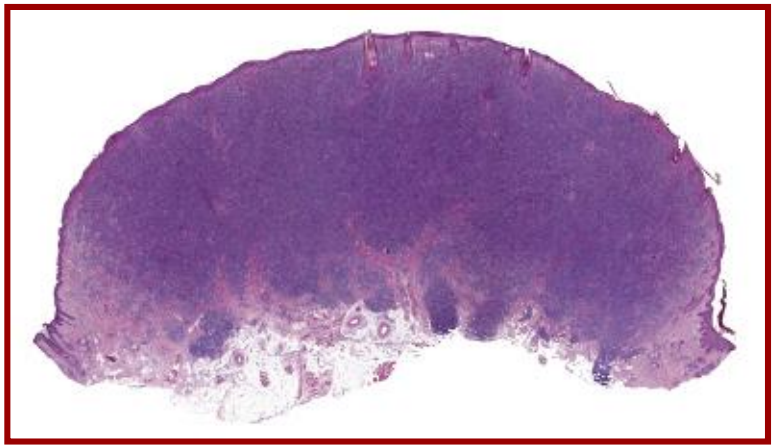
- Cases presenting with widespread skin lesions, large rapidly growing tumours, and/or a high proliferation rate do not belong to the group of CD4+ lymphoproliferative disorder

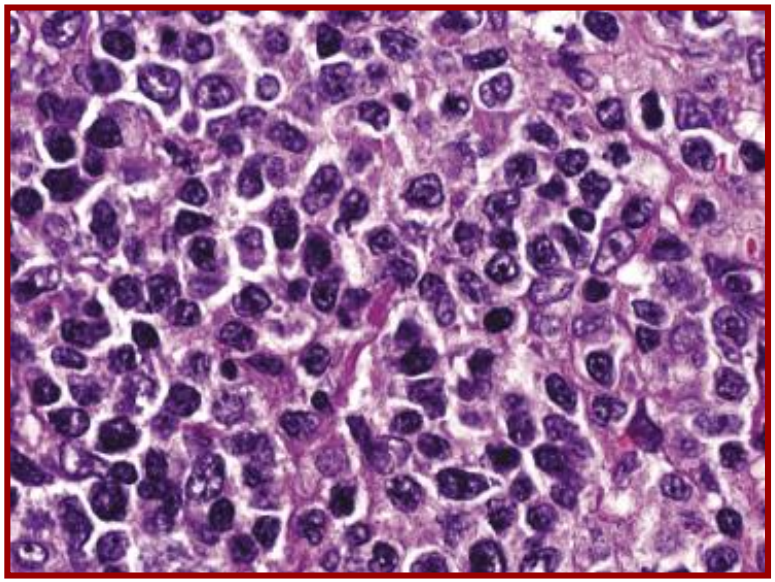


- Such cases usually have a more aggressive clinical behaviour and are better classified as peripheral T-cell lymphoma NOS

CD4+ Small/medium T-cell Lymphoproliferative Disorder

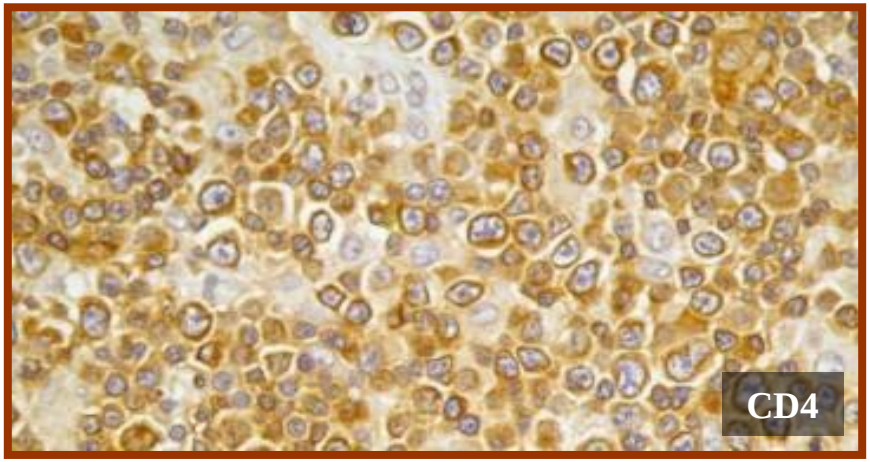
- Dense, nodular or diffuse infiltrates within the dermis with tendency to infiltrate the subcutis
- Epidermotropism may be present focally
- Predominance of small/medium-sized pleomorphic T cells (large cells <30%)
- Considerable admixture with reactive CD8+ T-cells, B-cells, plasma cells, and histiocytes

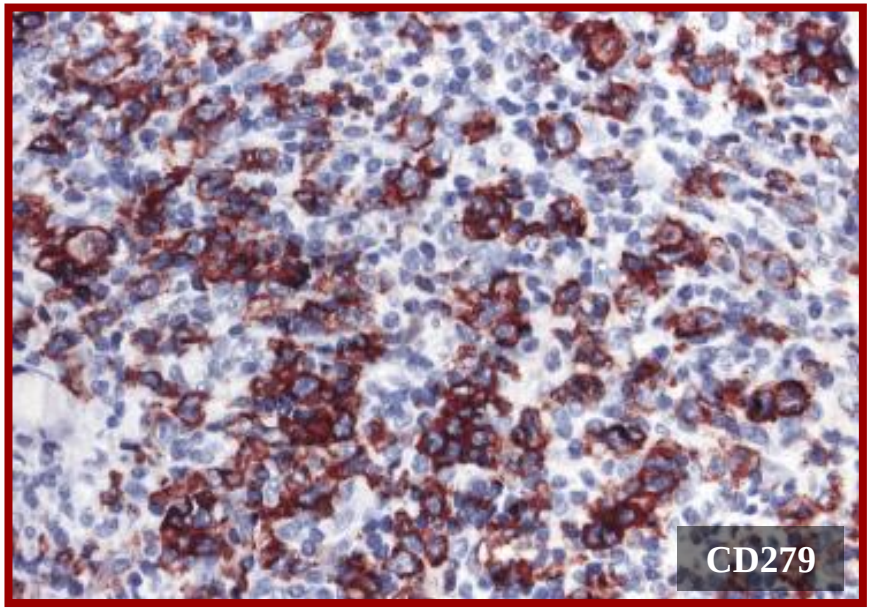




CD4+ Small/medium T-cell Lymphoproliferative Disorder

- Immunophenotype: CD3+, CD4+, CD8–, TIA1/ Perforin/ GrB–, CD30–, Ki-67+: 5-20%
- A variable proportion of atypical CD4+ T cells, grouped in small clusters and *pseudorosettes* around B-cells, express PD1 (CD279), ICOS, BCL-6, and CXCL13, suggesting derivation from T_{FH} cells





Acta Derm Venereol 2016; 96: 850–852

SHORT COMMUNICATION

Neoplastic Cells of Primary Cutaneous CD4+ Small/Medium-sized Pleomorphic T-cell Lymphoma Lack the Expression of Follicular T-helper Cell Defining Chemokine Receptor CXCR5

Dóra Krenács[1,2], Annamária Bakos[1,2], László Török[3], Lajos Kocsis[4], Enikő Bagdi[1] and László Krenács[1]*

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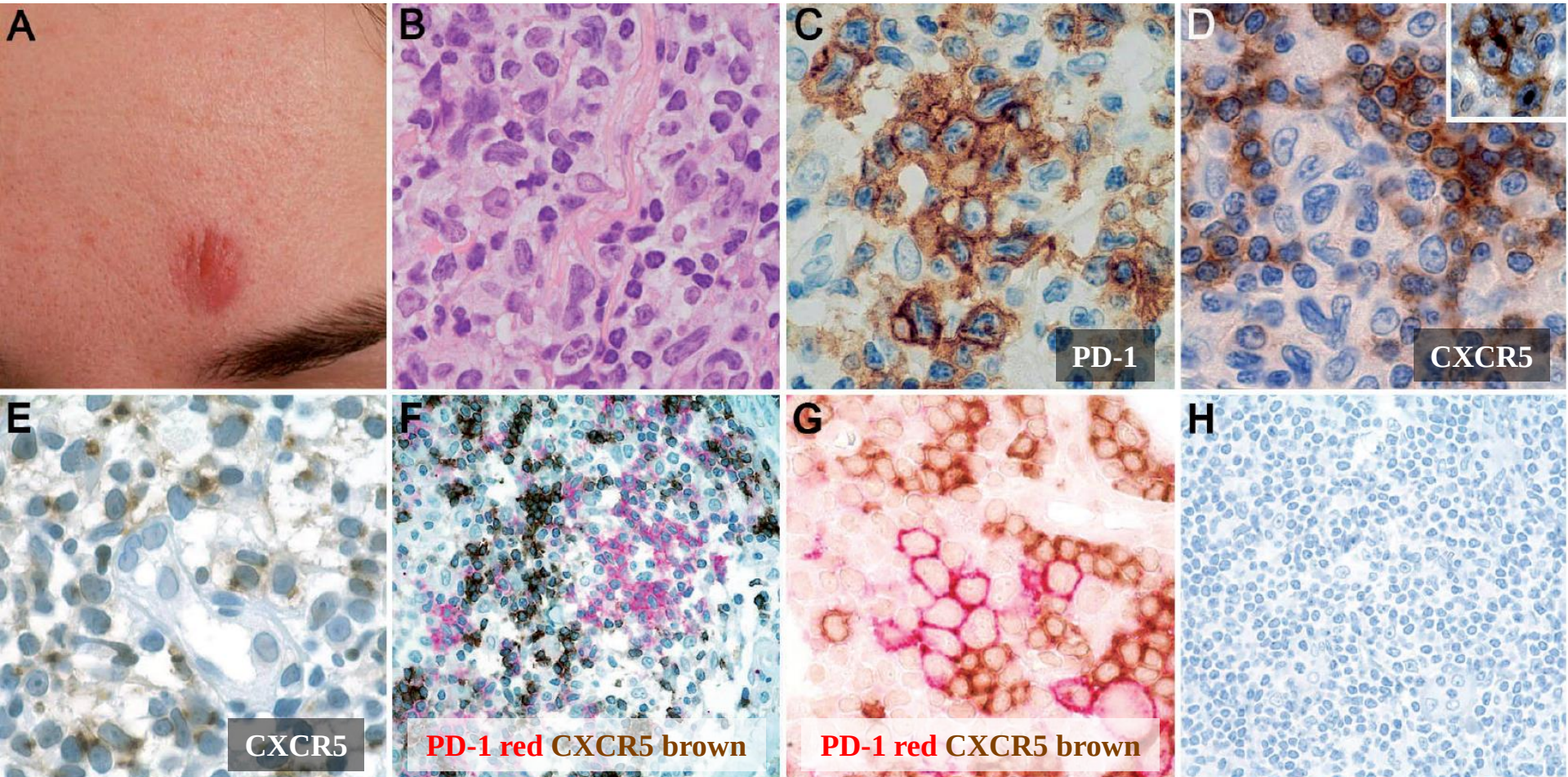
Accepted Feb 29, 2016; Epub ahead of print Mar 1, 2016



- T_{FH} cells express PD-1, BCL6, ICOS and CXCL13, together with the highest levels of CXCR5, a chemokine receptor which defines follicular homing
- Due to the expression of PD-1, BCL6, ICOS and CXCL13, *CD4+ SM-TCLD* has been suggested to be a T_{FH}-cell-derived disorder
- However, the consistent lack of CXCR5 in lesional cells argues against T_{FH} cell derivation
- *CD4+ SM-TCLD* may represent the counterpart of a unique T helper-cell population that provides help to B cells outside the follicles. Unlike T_{FH} cells, these extrafollicular PD-1+/BCL6+/ICOS+ T helper cells do not express CXCR5