

An approach to epidermotropic lymphoid infiltrates

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Lymphocyte Sub-populations in normal skin

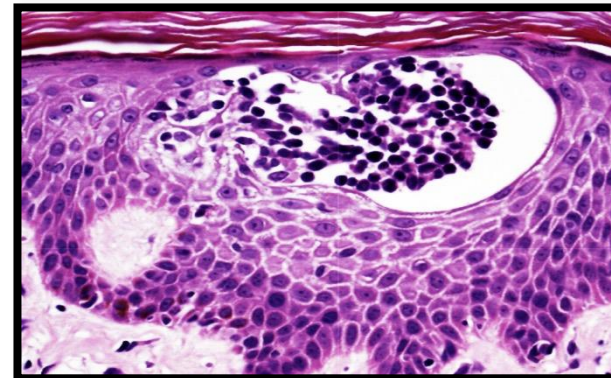
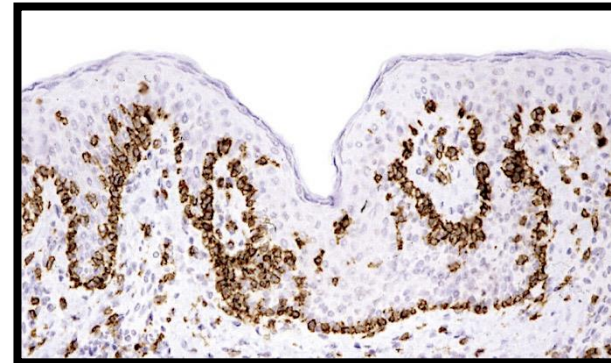
- Intraepidermal lymphocytes. Kondo 1922
- Andrews & Andrews 1949, 1-4% cells in the epidermis.
- Langerhans cells
- T cells

Epidermotropism

- Spread of cells of different origins into the epidermis from an underlying dermal/subcutaneous pathology.
- Lentiginous
- Pagetoid

Single cells

Clusters



[J Cutan Pathol](#). 2009 Oct;36(10):1037-52. doi: 10.1111/j.1600-0560.2009.01374.x. Epub 2009 Jul 22.

Epidermotropic lesions: a review.

[Abbas O¹](#), [Bhawan J](#).

- Lymphoid cells
- *Inflammatory dermatoses*
- *Lymphomas*
- Mammary Paget's disease
- Extramammary PD
- Langerhans' cell histiocytosis
- Merkel Cell carcinoma
- Sebaceous carcinoma
- Eccrine porocarcinoma
- Epidermotropic metastases

Intraepidermal conditions mimicking epidermotropic lesions

- Benign

Pagetoid Spitz
Pagetoid dyskeratosis
Clear cell papulosis
Mucinous metaplasia

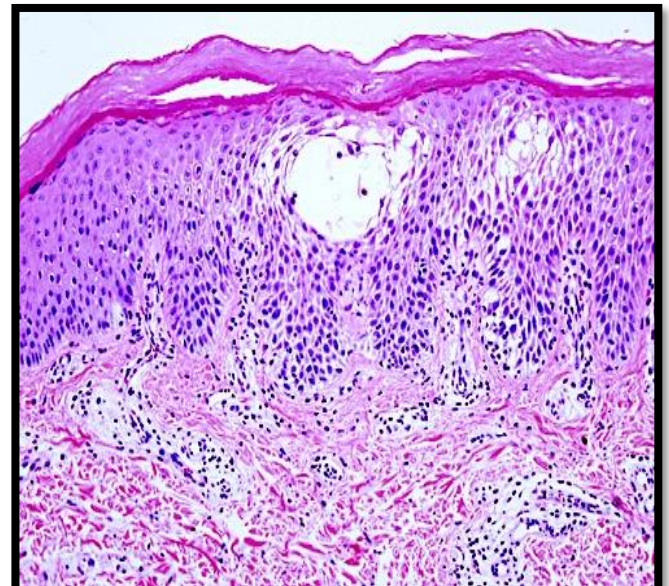
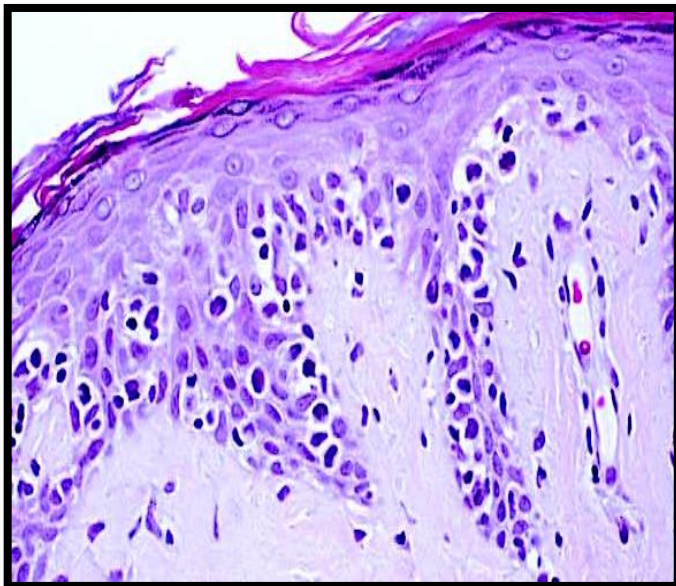
- Malignant

Melanoma
Bowen's disease

Epidermotropism vs exocytosis

Vocabulary

MF vs mimics



'Epidermotropism' vs. 'exocytosis' of lymphocytes 101: definition of terms.

Fung MA¹.

Epidermotropism

1: Atypical cells in epidermis

2: Means lymphocytes in epidermis without further implication

3: Large lymphocytes within epidermis, without spongiosis

4: Use term only to describe MF

5: Presence within epidermis disproportionate to the epidermal changes

6: Without spongiosis and interface

7: Homing of lymphocytes in a setting of lymphoma

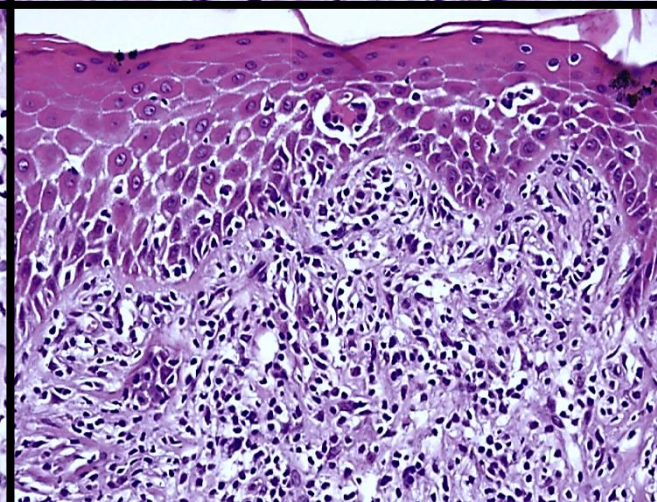
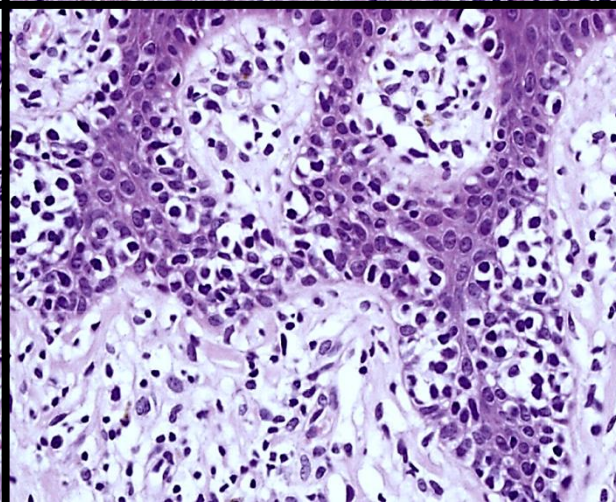
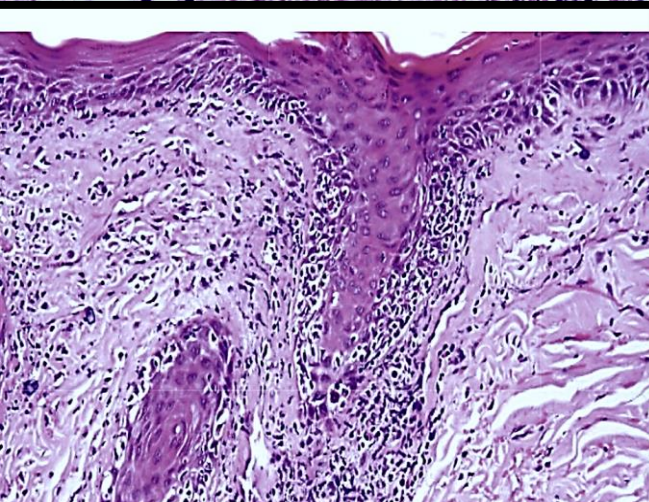
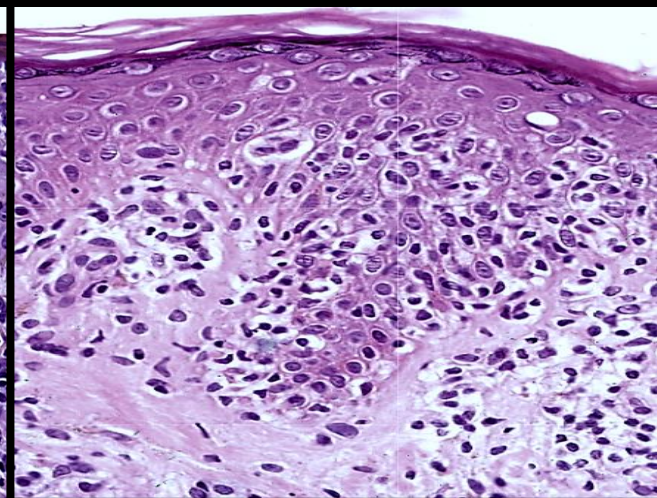
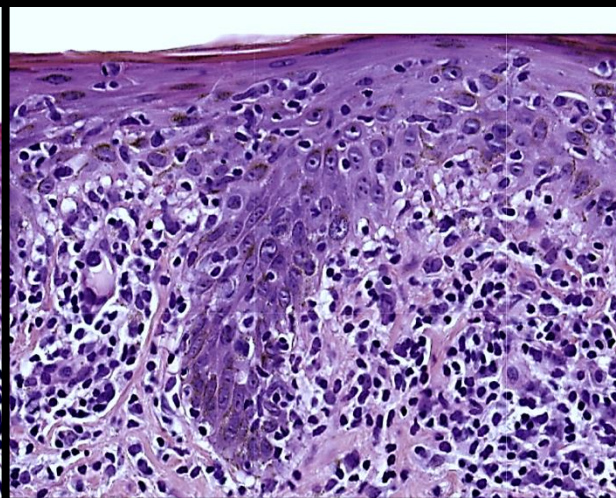
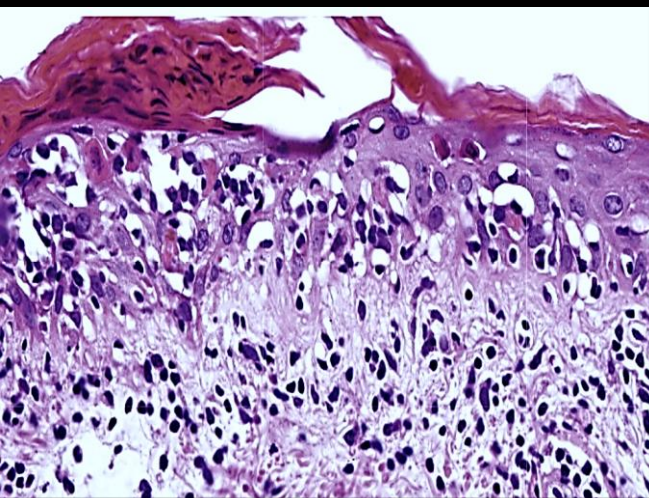
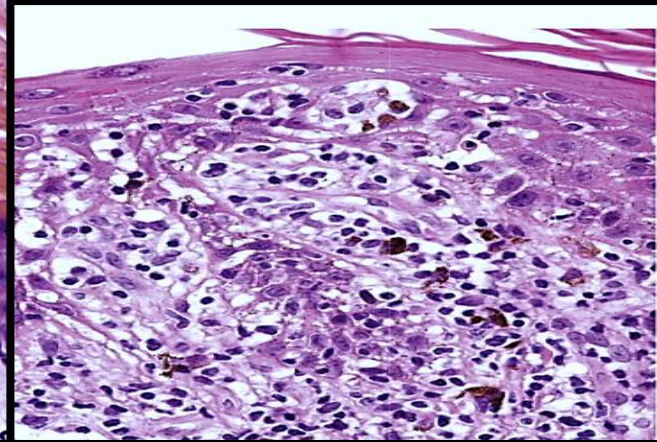
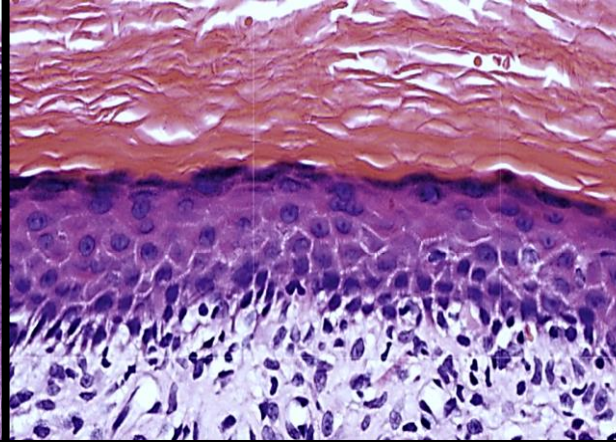
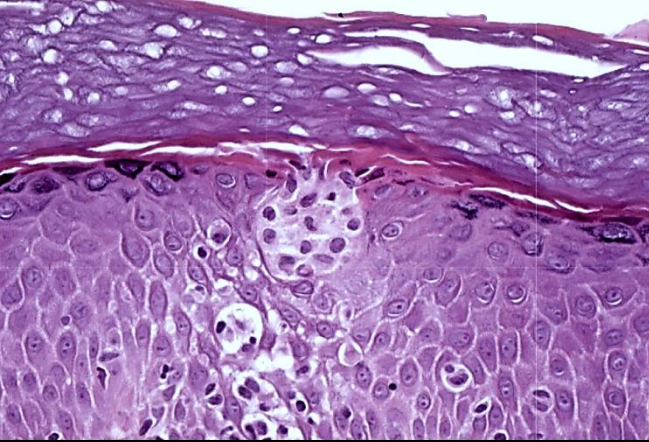
8: Single cells or clusters (3 cells); all layers of epidermis, can just be located along the basal layer

Exocytosis

- 1: Lymphocytes present at many layers of the epidermis
- 2: I never use this term. When used by others, I assume lymphocytes within the epidermis without implying more specific location.
- 3: Lymphocytes within epidermal keratinocytes, present singly, dermal infiltrate and no atypia
- 4: Randomly distributed within the epidermis and associated spongiosis
- 5: Apply to exocytosis to both benign and malignant conditions. Both can show spongiosis.
- 6: Benign lymphocytes within the epidermis. Confident of a benign diagnosis
- 7: Presence of atypical /non-atypical cells within the epidermis in context of spongiotic dermatitis, dermal hypersensitivity reaction or lymphoma
- 8: Lymphocytes within epidermis as a result of any cause, usually inflammatory dermatosis.

Table 2. Summary of selected attributes from Table 1

		Percentage
Epidermotropism	Correlates with CTCL	79 (15/19)
	Basilar/lentiginous pattern	26 (5/19)
	Cytologic atypia	26 (5/19)
Exocytosis	Correlates with reactive process	47 (9/19)
	Associated spongiosis	42 (8/19)
	Suprabasilar/pagetoid pattern	10 (2/19)



- Common to all nine pictures –epidermotropism/exocytosis!
- Extent of atypia varies.
- Number within the epidermis.
- Degree of spongiosis varies.
- Admixture with other cell types.

- Mycosis fungoides
- Large number of inflammatory mimics!

Dermatoses

- Actinic reticuloid
- Lymphomatoid contact dermatitis
- Lymphomatoid keratosis
- Lichen sclerosus
- Vitiligo (inflammatory phase)
- Lymphomatoid drug reaction
- Lichenoid/pseudolymphomatous reaction to tattoo
- Syphilis, secondary
- PLEVA
- Non-neoplastic erythroderma

Lymphomas

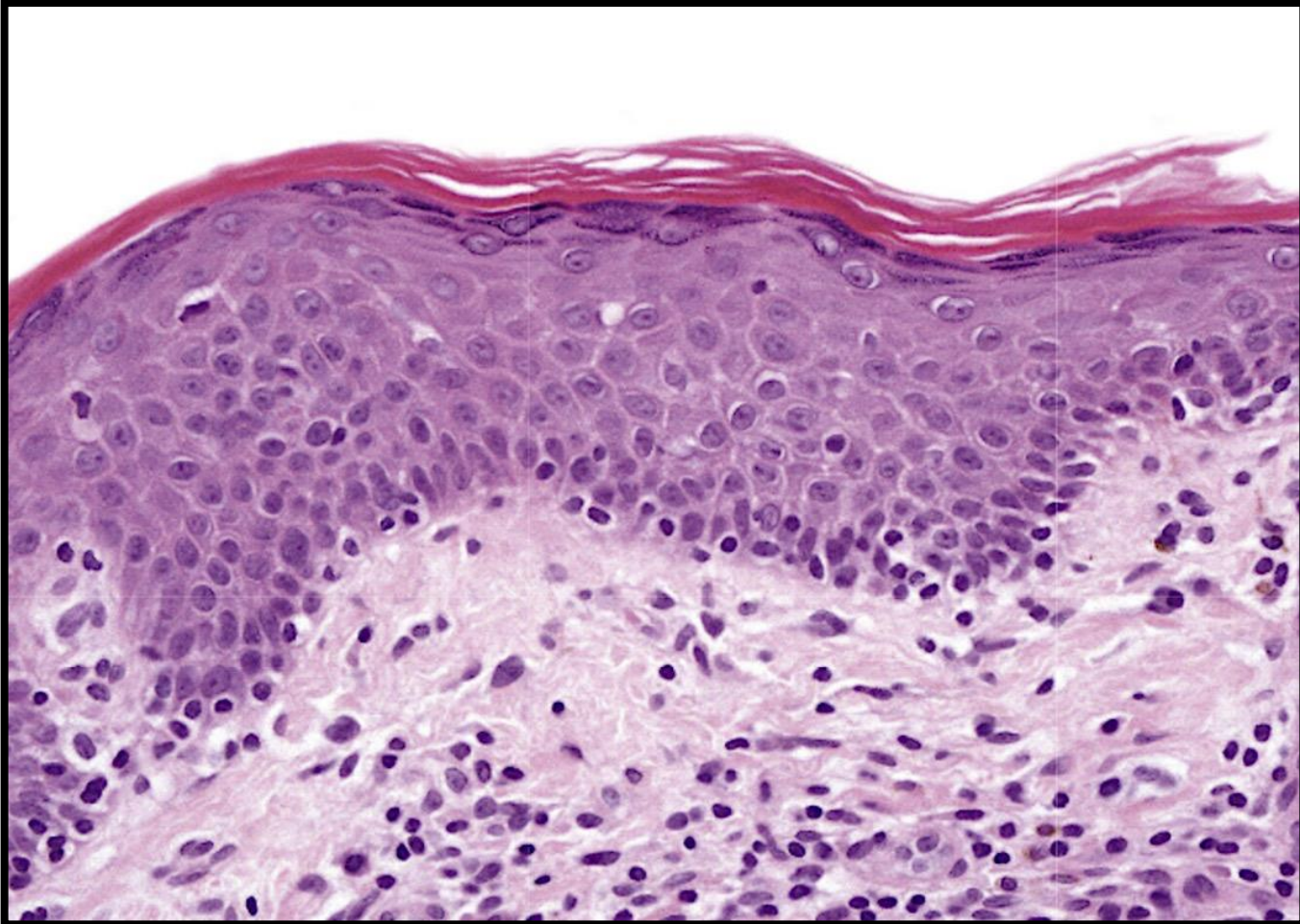
- Mycosis fungoides
- Sezary syndrome
- Lymphomatoid papulosis B and D
- CD8+ epidermotropic NHL
- Systemic T cell NHL with cutaneous involvement
- ***CD4+ small and medium T cell lymphoproliferation***
- Cutaneous gamma delta T cell NHL

Case 1

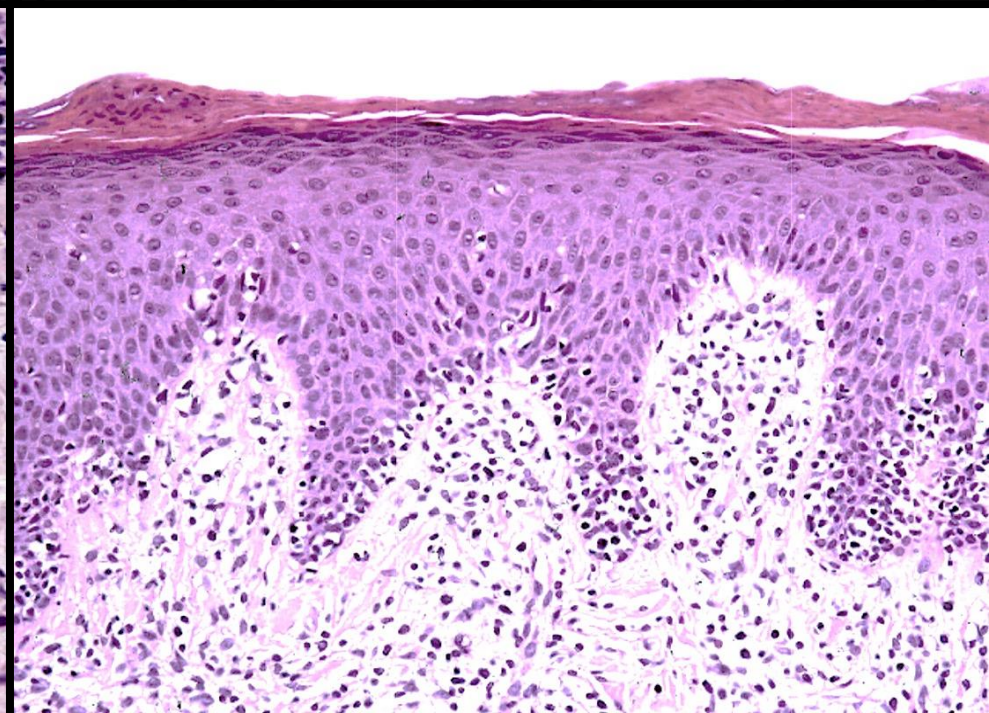
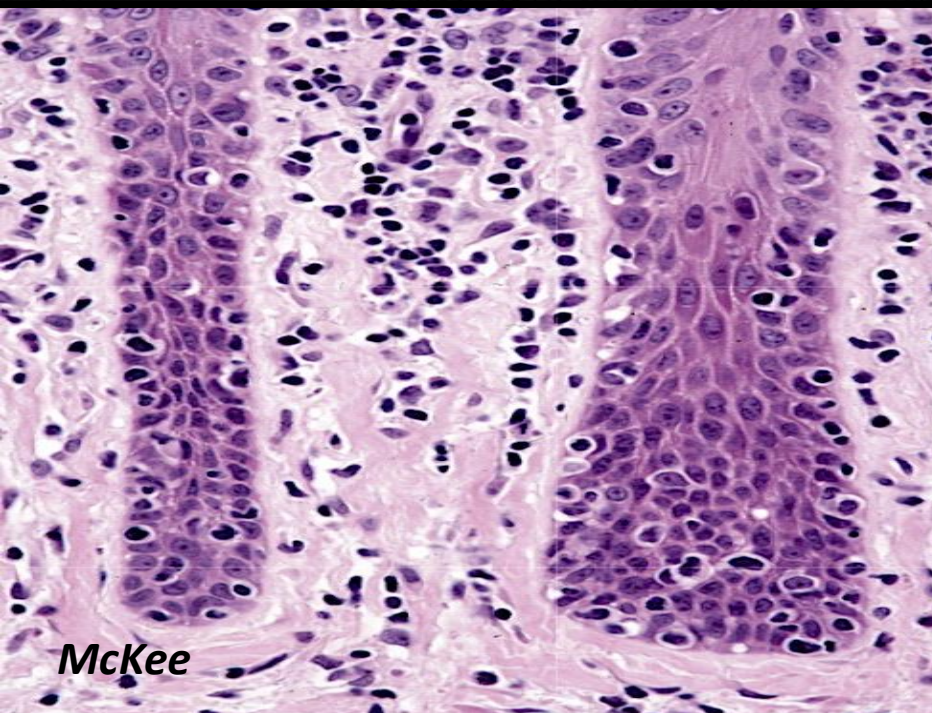
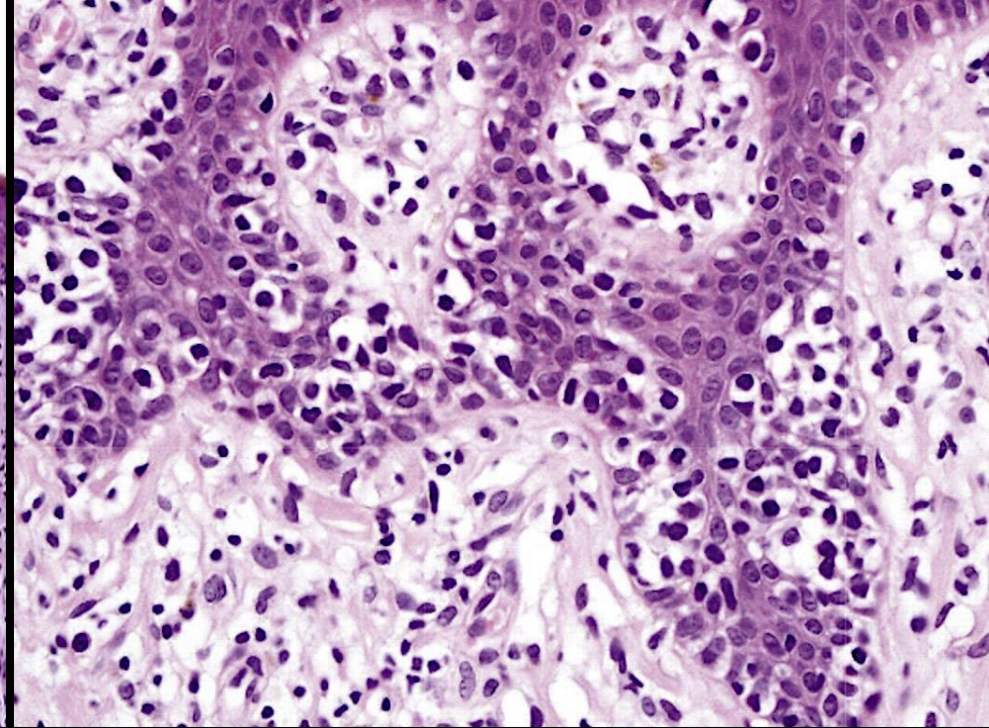
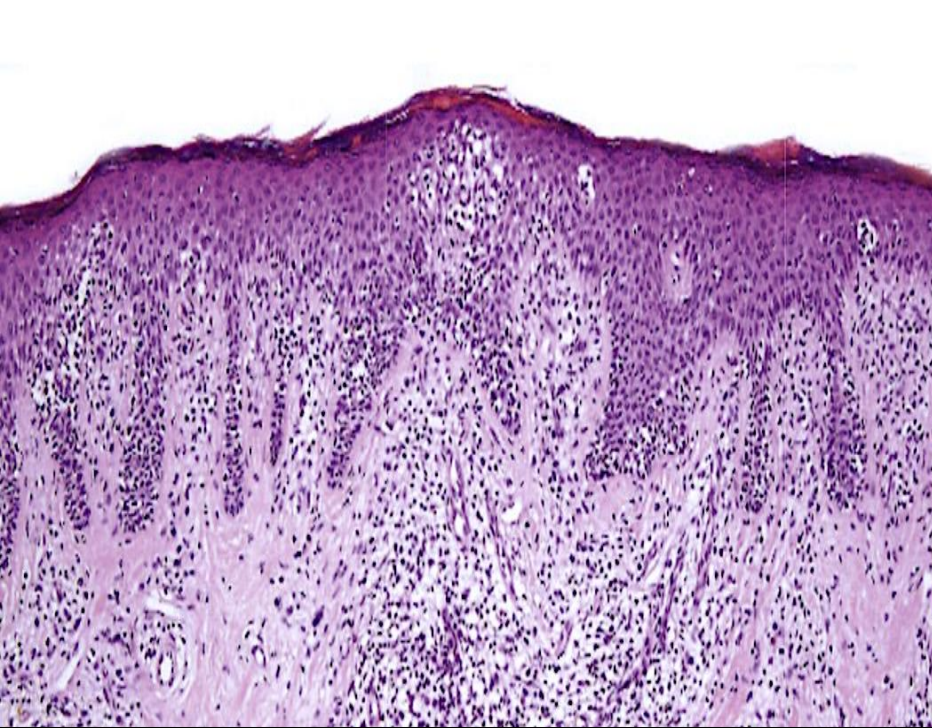
- F 80
- Incisional biopsy nodule right flank
- Previous biopsy

1st biopsy

2014

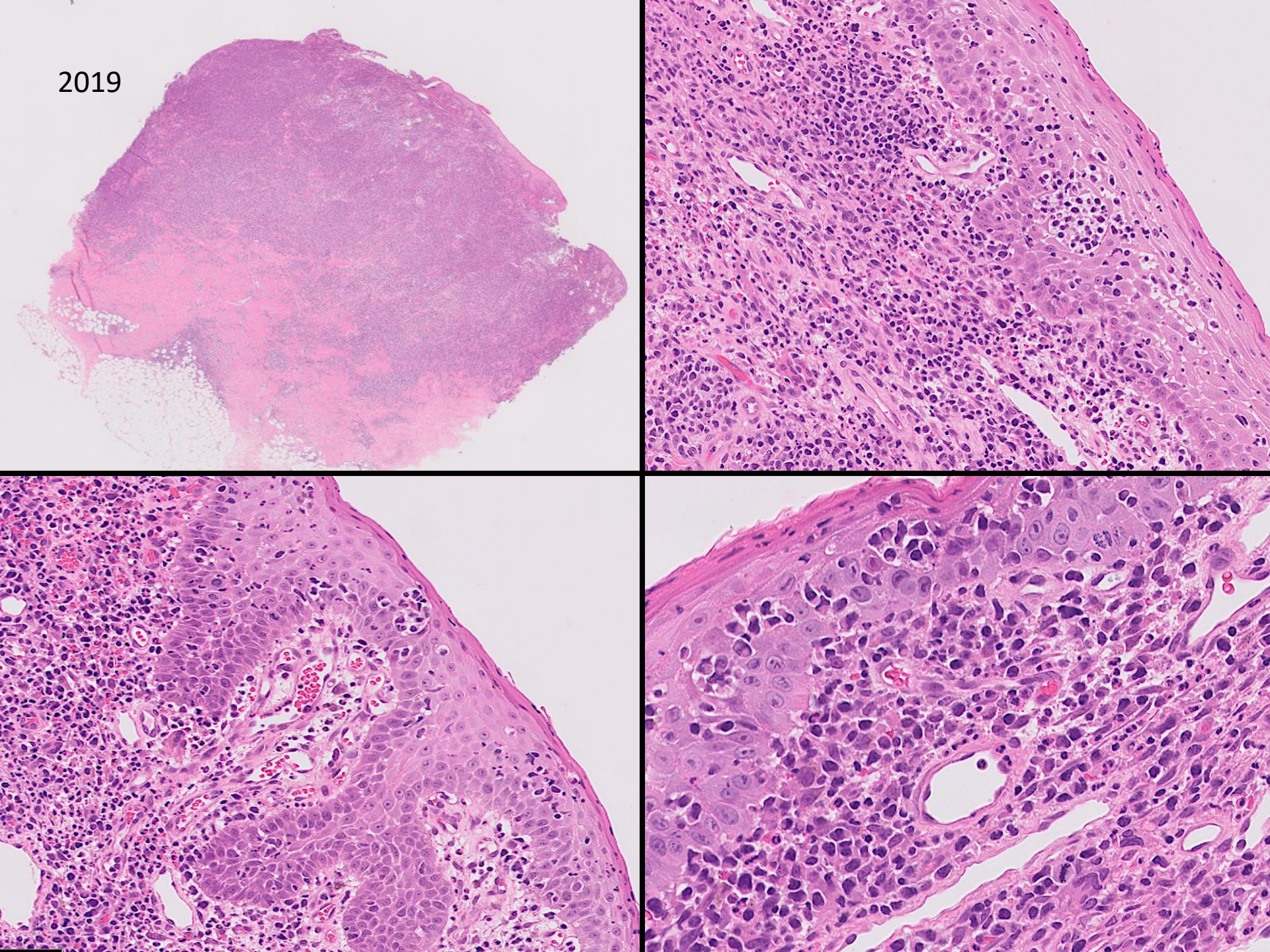


McKee

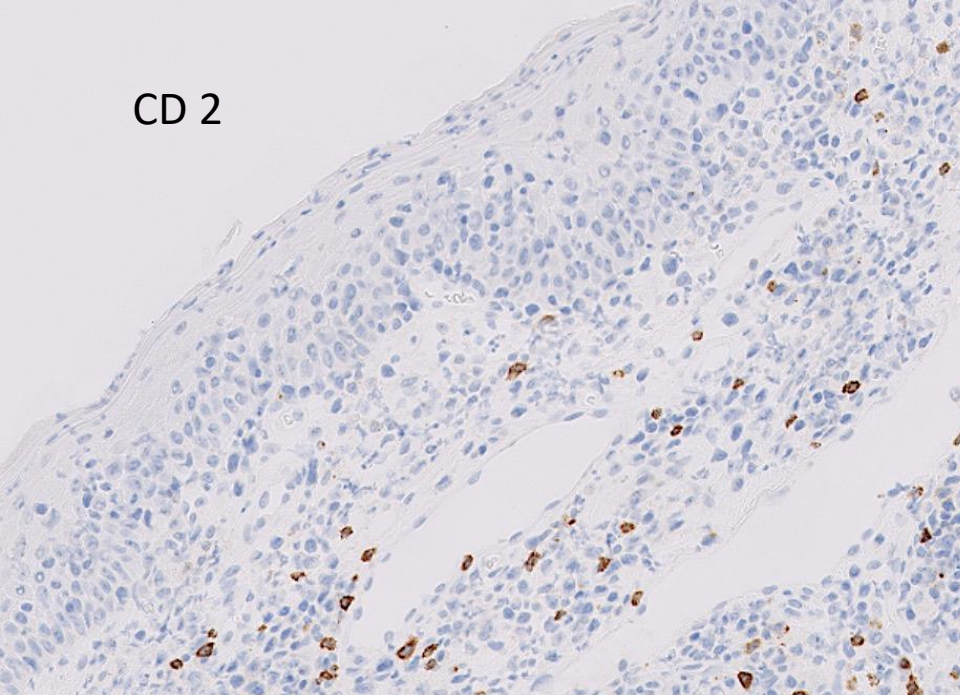


- Classical features-
- Increase in epidermal mononuclear cells
- Haloed lymphocytes along the base/string of pearls
- Relative lack of spongiosis
- Lymphoid atypia
- Papillary dermal fibrosis

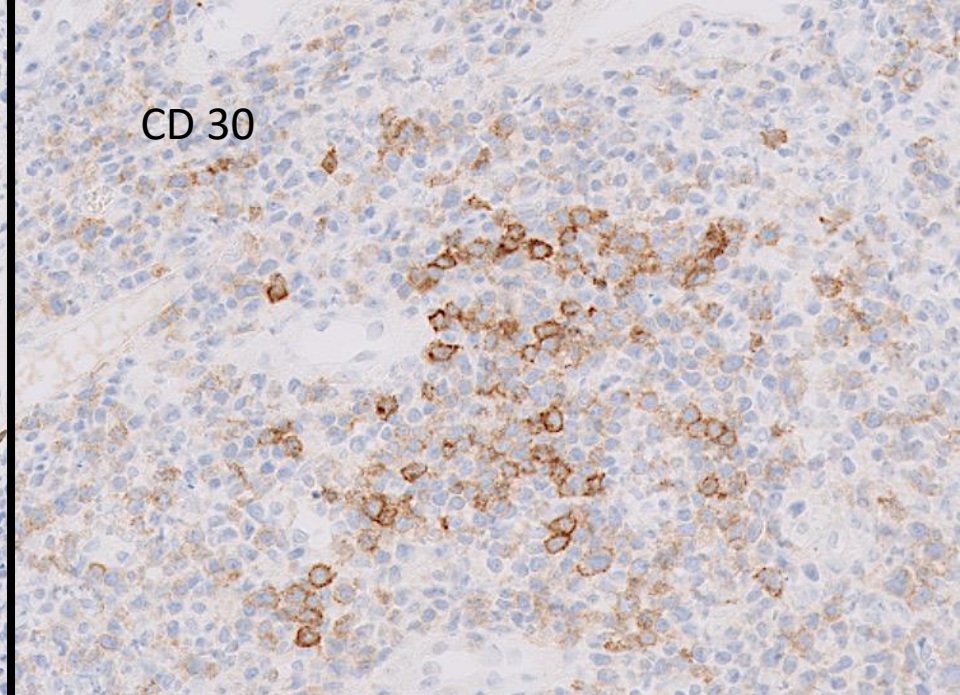
2019



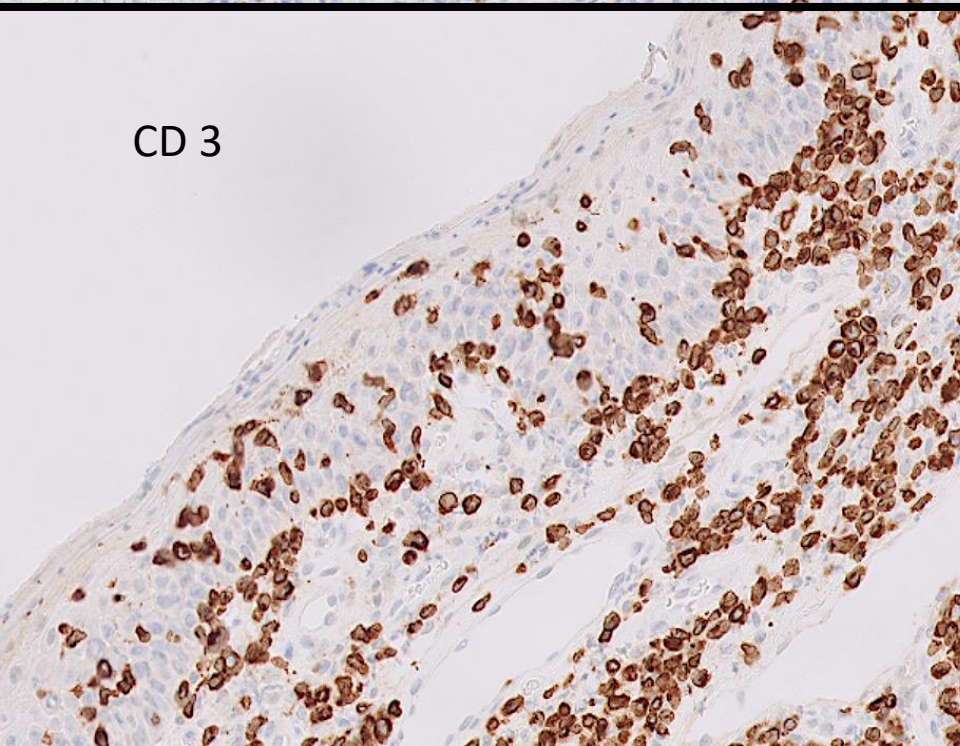
CD 2



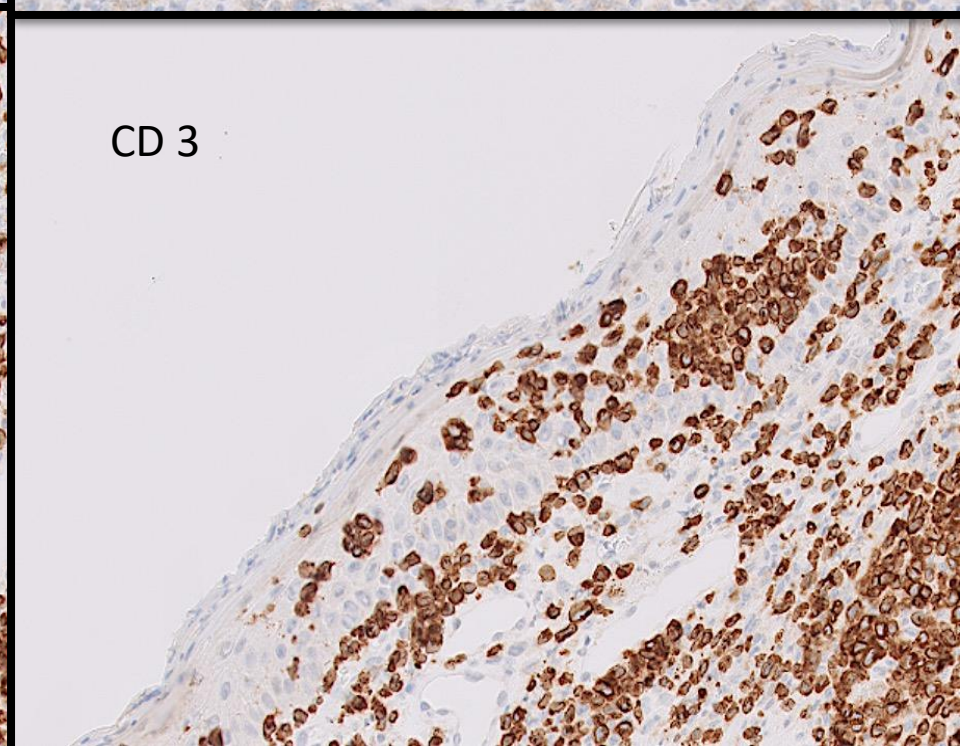
CD 30



CD 3



CD 3



CD3+

CD2 lost

CD7 lost

CD 5 partial lost

CD4 occasional cells

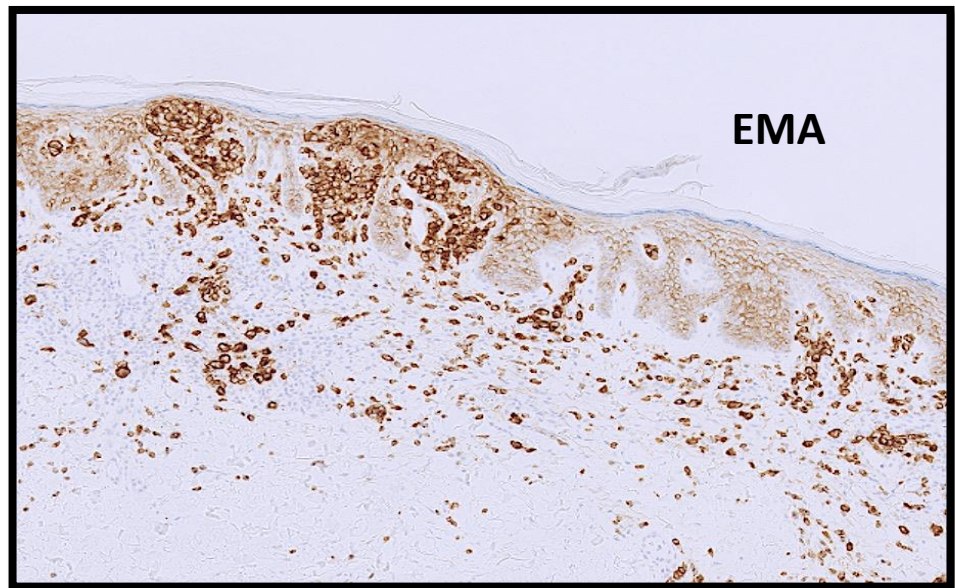
CD8 negative

CD30 15%

ALK-1 negative

EMA + Focal, strong

Mycosis fungoides (tumour stage) with large cell transformation



Patients with mycosis fungoides (MF) typically experience an indolent disease course, a minority undergo a process of large-cell transformation (LCT), which often heralds more aggressive disease and shortened survival.

LCT is diagnosed histologically; however, diagnostic biopsy is performed only if transformed lesions are suspected clinically.


- (1) LCT occurring as a new, solitary nodule within a classic MF patch or plaque,
- (2) LCT occurring as abrupt onset of multiple scattered papules and/or nodules without spontaneous resolution
- (3) LCT occurring within new or enlarging tumors.

J Am Acad Dermatol. 2012 Oct;67(4):665-72. doi: 10.1016/j.jaad.2011.12.011. Epub 2012 Jan 20.

Recognizing large-cell transformation of mycosis fungoides.

Herrmann JL¹, Hughey LC.

EMA and ALK-1 Immunostaining in Cutaneous CD30⁺ Lymphoproliferative Disorders

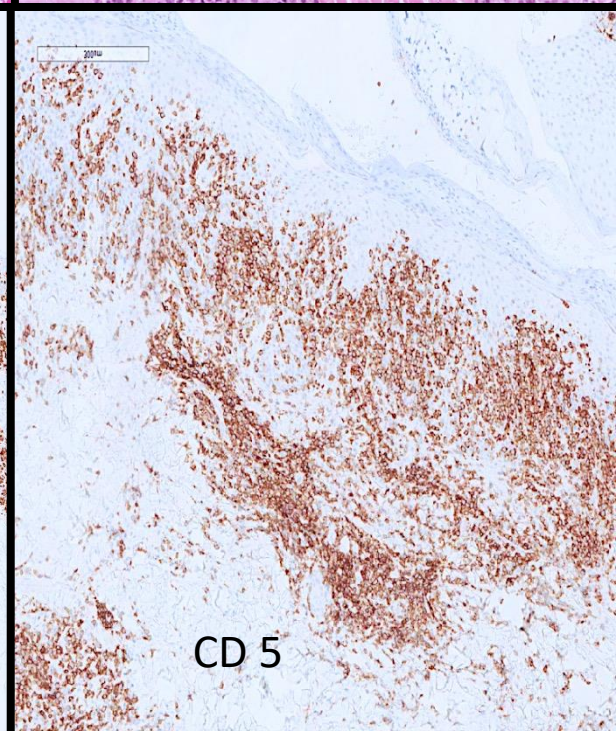
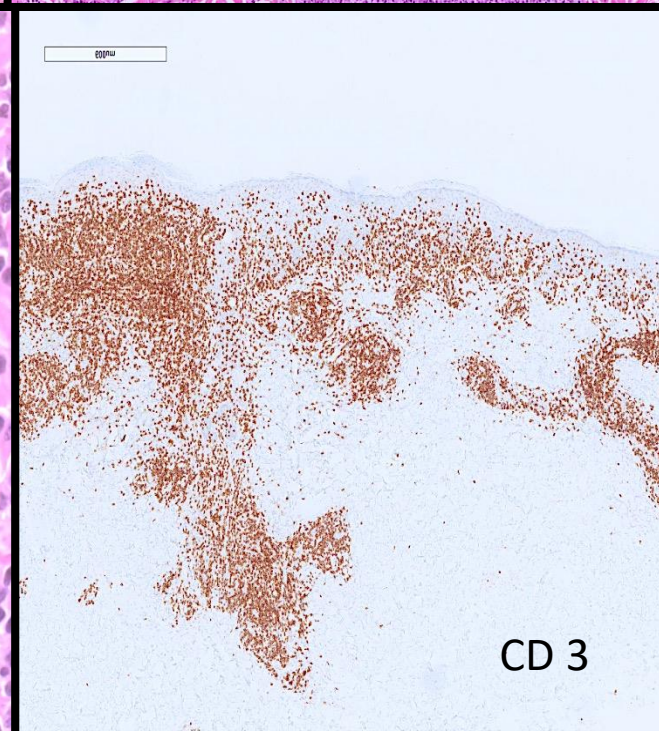
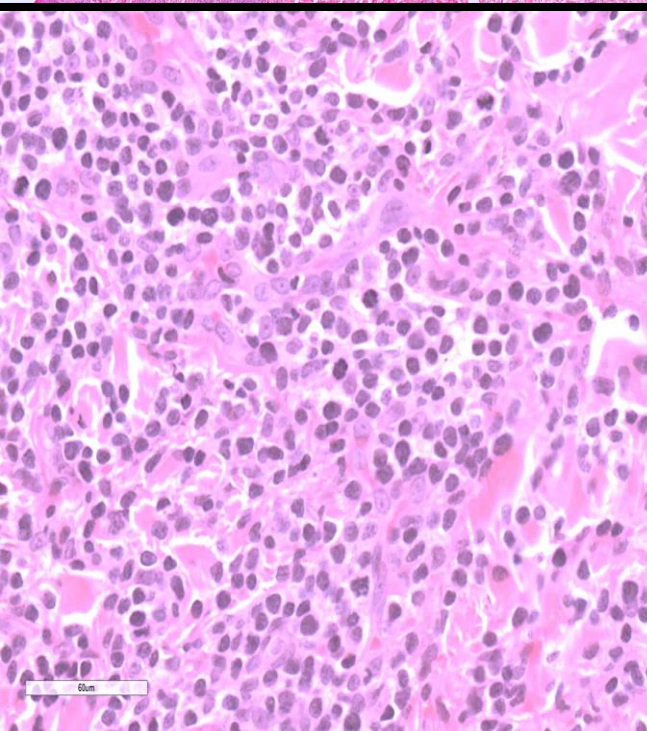
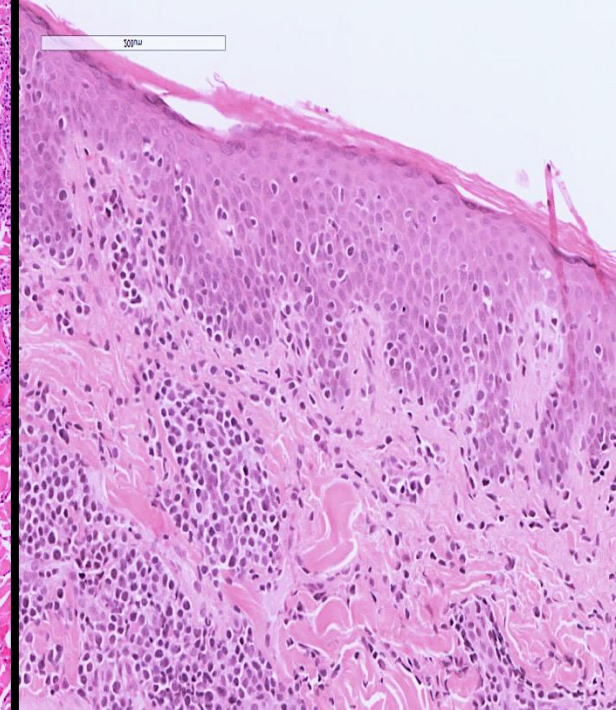
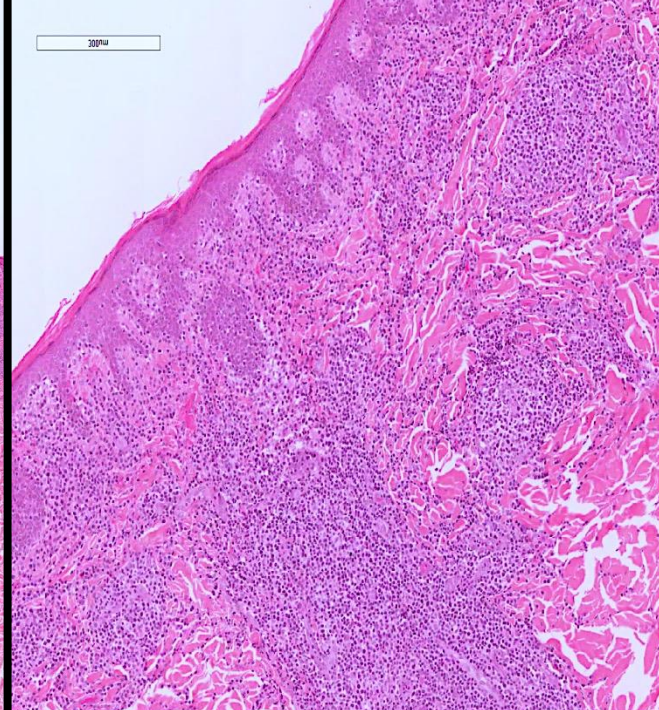
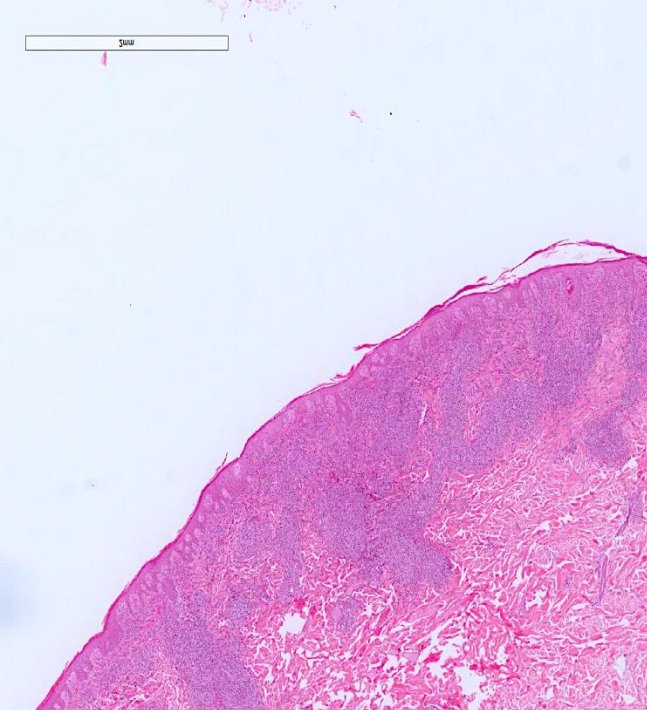
Doeden, K.S.; Sundram, U. [Author Information](#) 

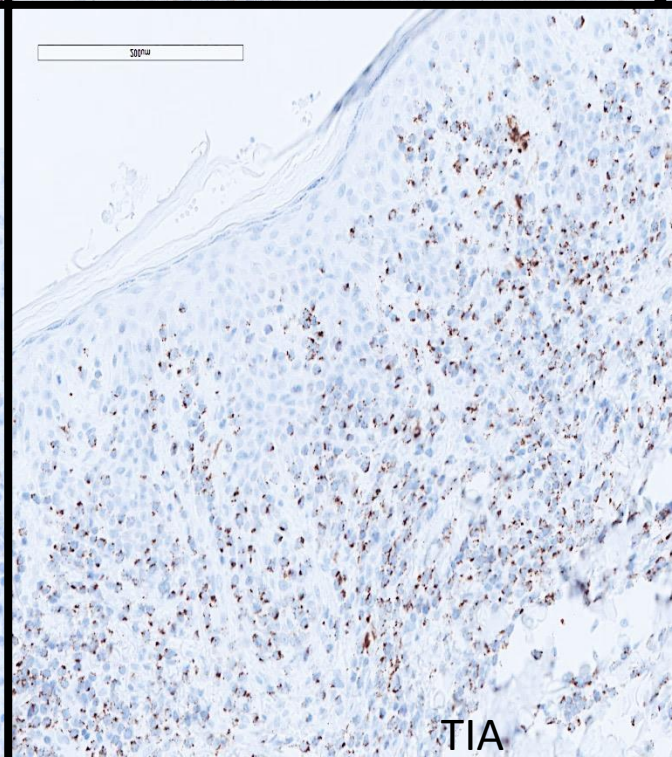
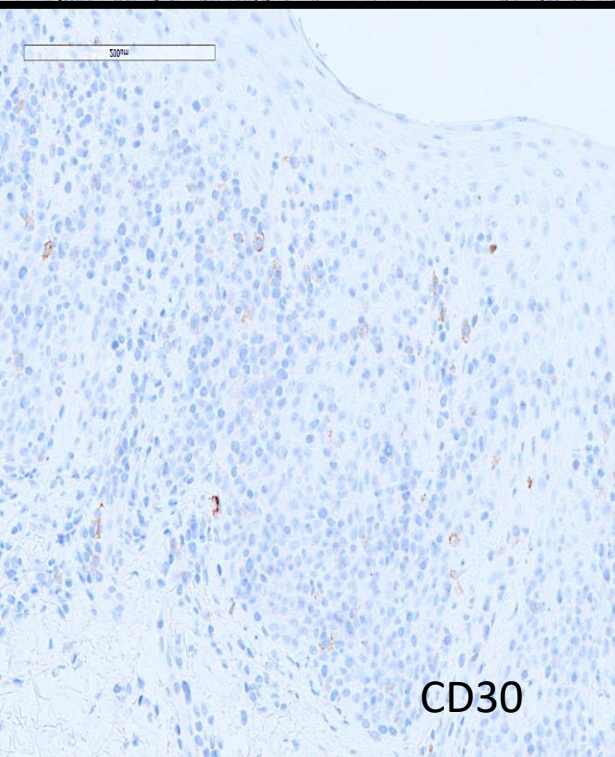
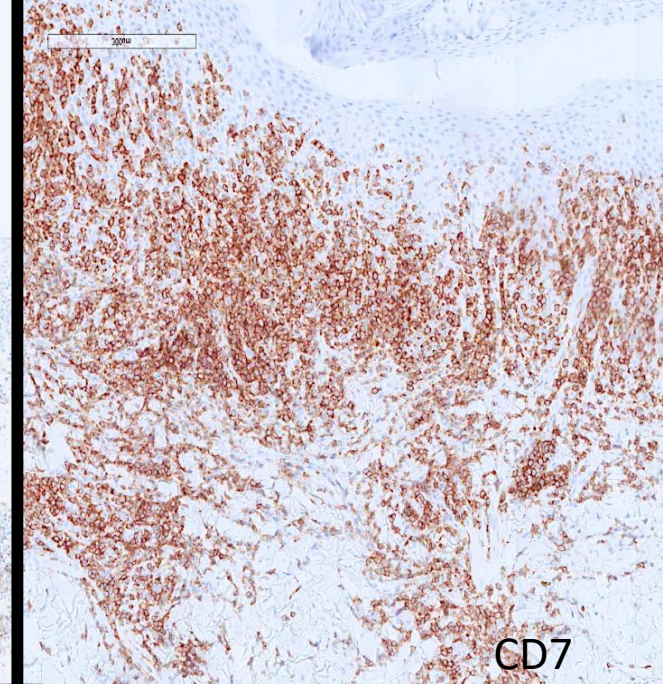
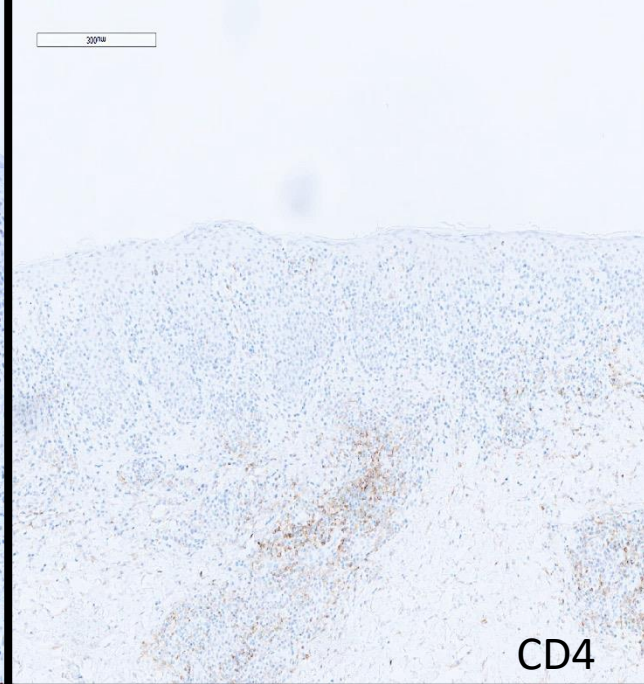
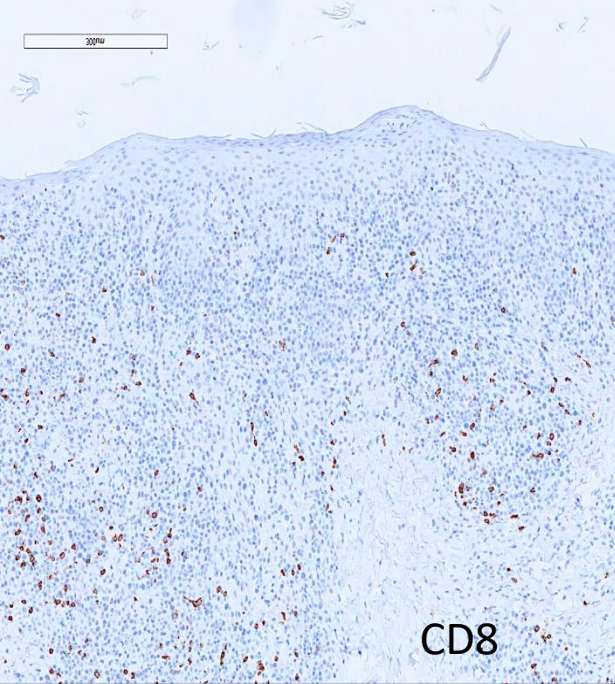
The American Journal of Dermatopathology: June 2006 - Volume 28 - Issue 3 - p 234

Cutaneous CD30⁺ lymphoproliferative disorders comprise a heterogeneous group of disorders, including primary cutaneous anaplastic large cell lymphoma (PC-ALCL), systemic ALCL with secondary cutaneous involvement (SC-ALCL), lymphomatoid papulosis (LyP), and mycosis fungoides with large cell transformation (MFLCT). The immunostaining pattern of epithelial membrane antigen (EMA) in comparison with ALK-1 staining in these disorders has not been well characterized. We studied the expression of EMA and ALK-1 by immunohistochemistry in 19 cases of PC-ALCL, 23 cases of systemic ALCL (6 were SC-ALCL), 18 cases of LyP, and 23 cases of MFLCT. ALK-1 was negative in all cases of primary cutaneous CD30⁺ lymphoproliferative disorders. EMA positivity was as follows: PC-ALCL 4/19 (21%), LyP 8/18 (44%), and MFLCT 7/23 (30%). Of the 12 cases of ALK-1-negative systemic ALCL (4 were SC-ALCL), 25% were EMA positive (1 was SC-ALCL). Ten of 11 (91%) ALK-1-positive systemic ALCL cases showed EMA expression. Both of the ALK-1-positive SC-ALCLs were EMA positive. EMA staining largely correlates with ALK-1 staining in CD30⁺ lymphoproliferative disorders but is not limited to cases of SC-ALCL.

Case 2

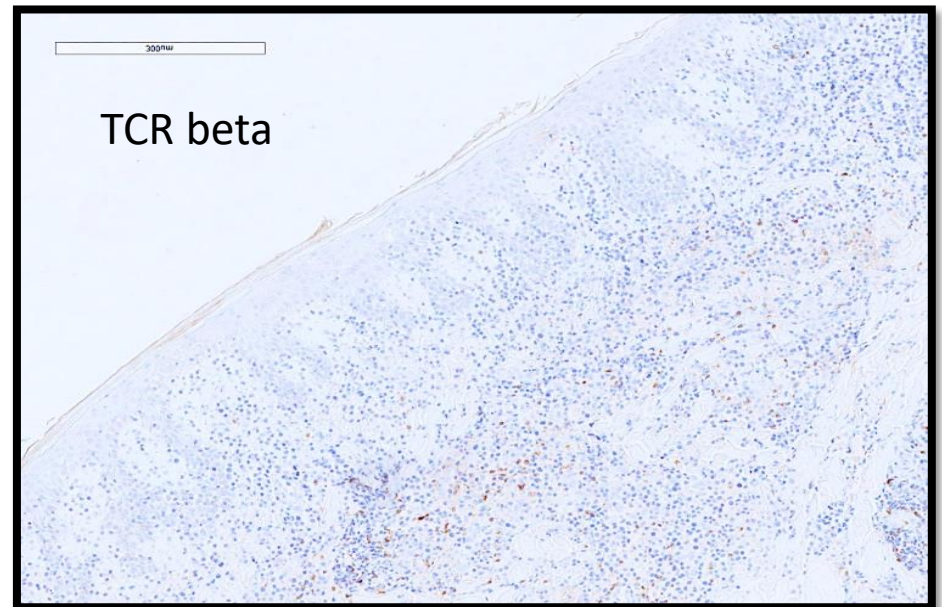
- 70M. Incisional biopsy mid-back
- ? CTCL ?lupus
- Also had biopsies from the arm and lower back





Double
negative
mycosis
fungoides

- No long standing rash. Nodules had developed over a few months.
- Type D LyP
- Aggressive epidermotropic NHL

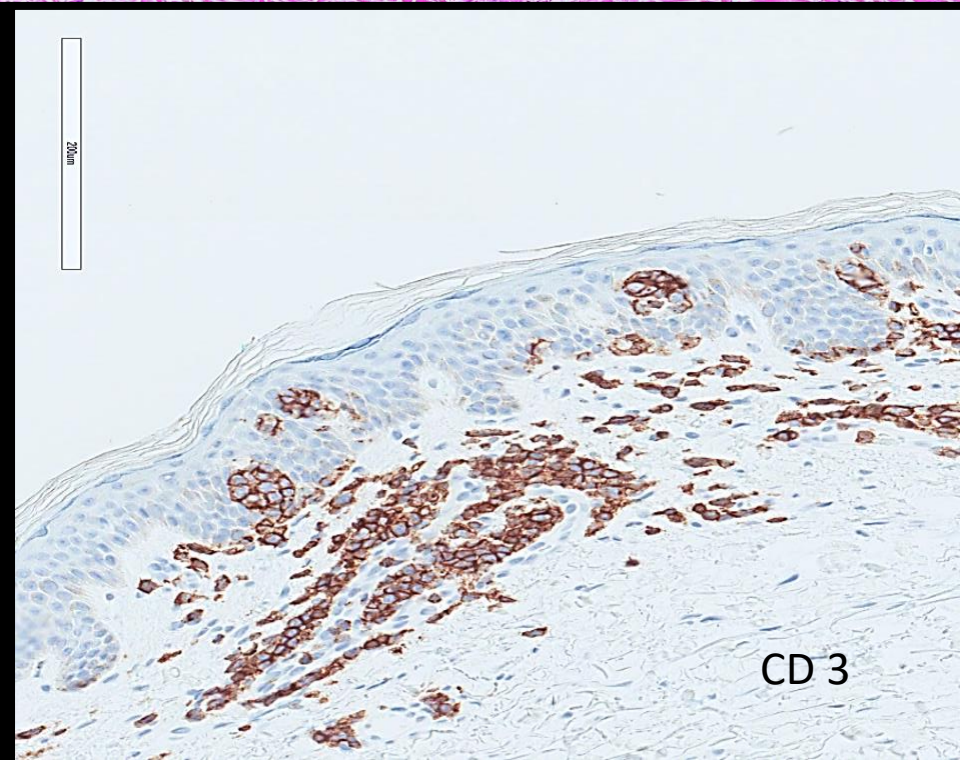
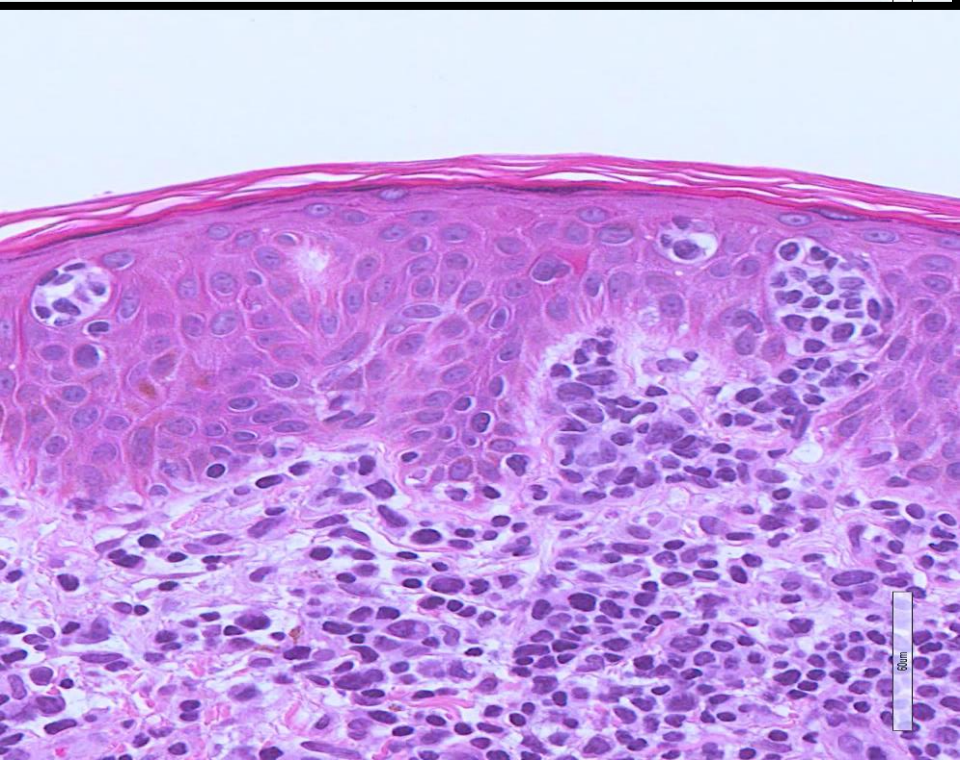
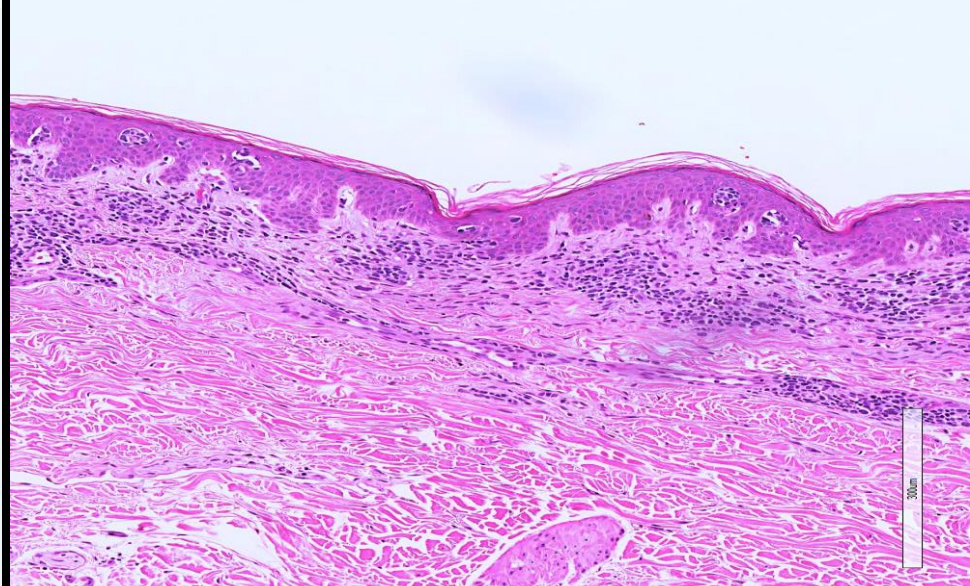
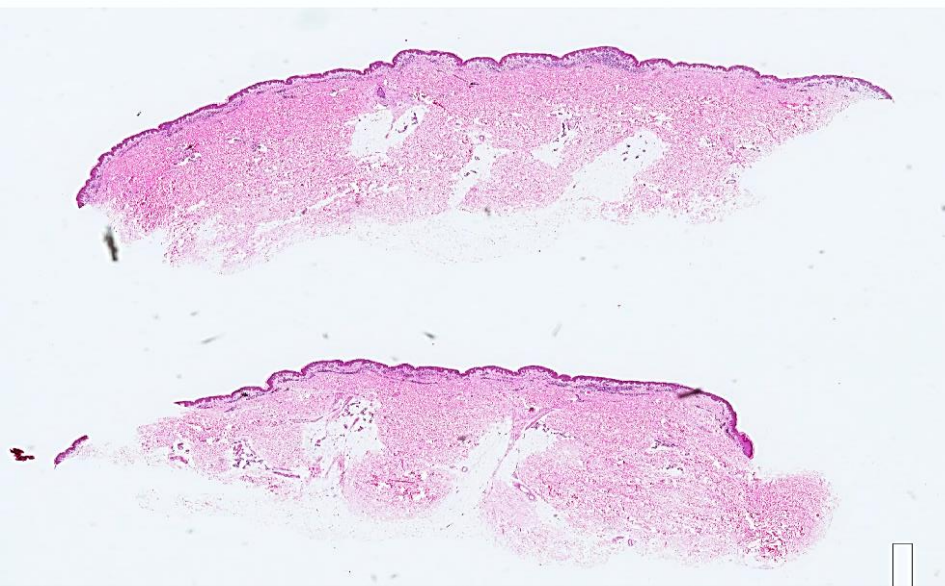


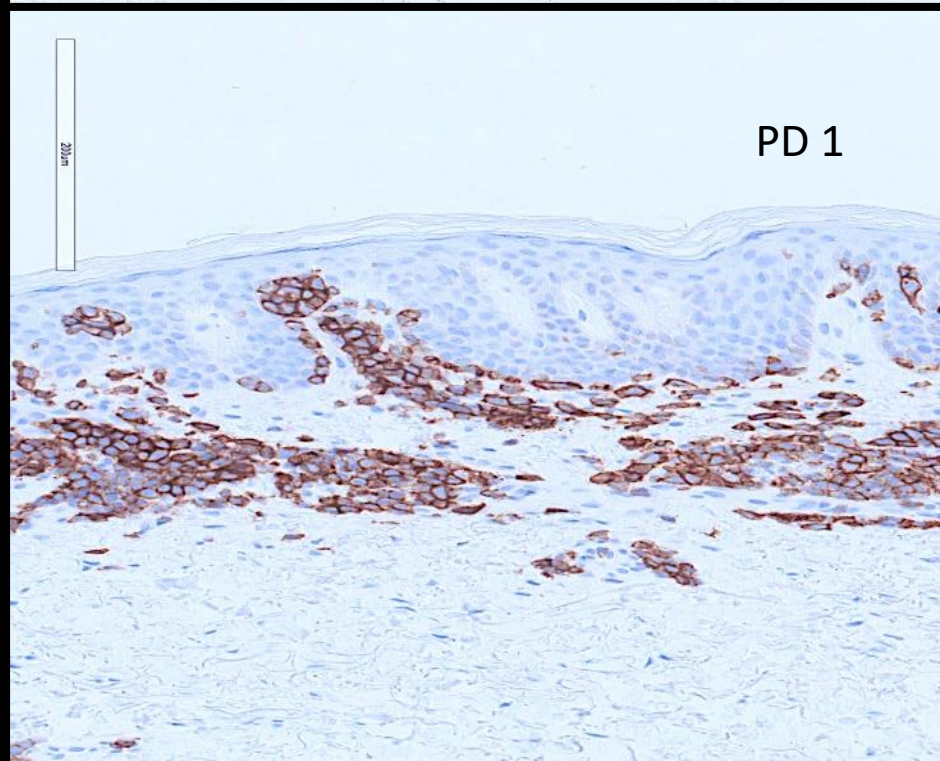
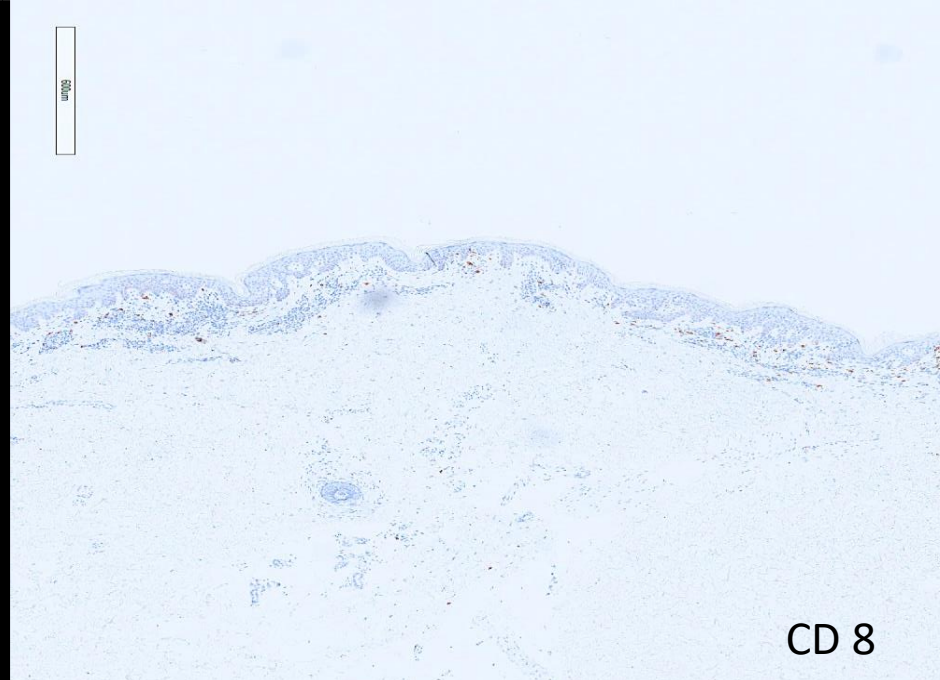
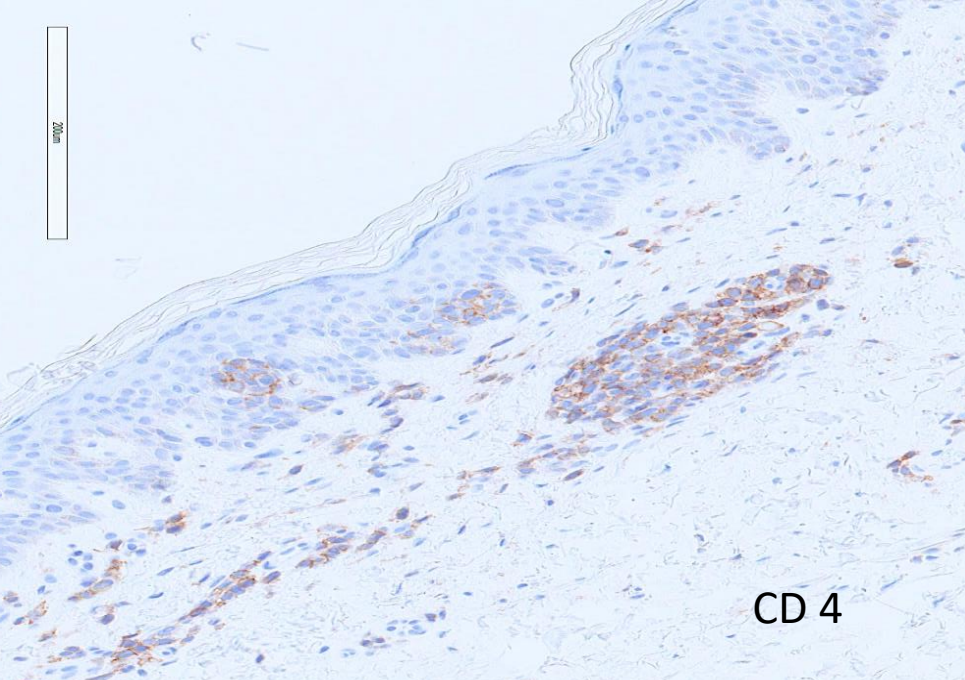
CD56
ALK 1
EBV
EBER
CD2

Widespread nodules and plaques
No long standing rash
<i>CD3+ epidermotropic TCR Beta negative lymphoid infiltrate I/K/W cutaneous gamma delta T cell NHL</i>

Case 3

- 67 F
- Incisional biopsy skin back
- Faded erythroderma
- ? Drug reaction ? Sezary





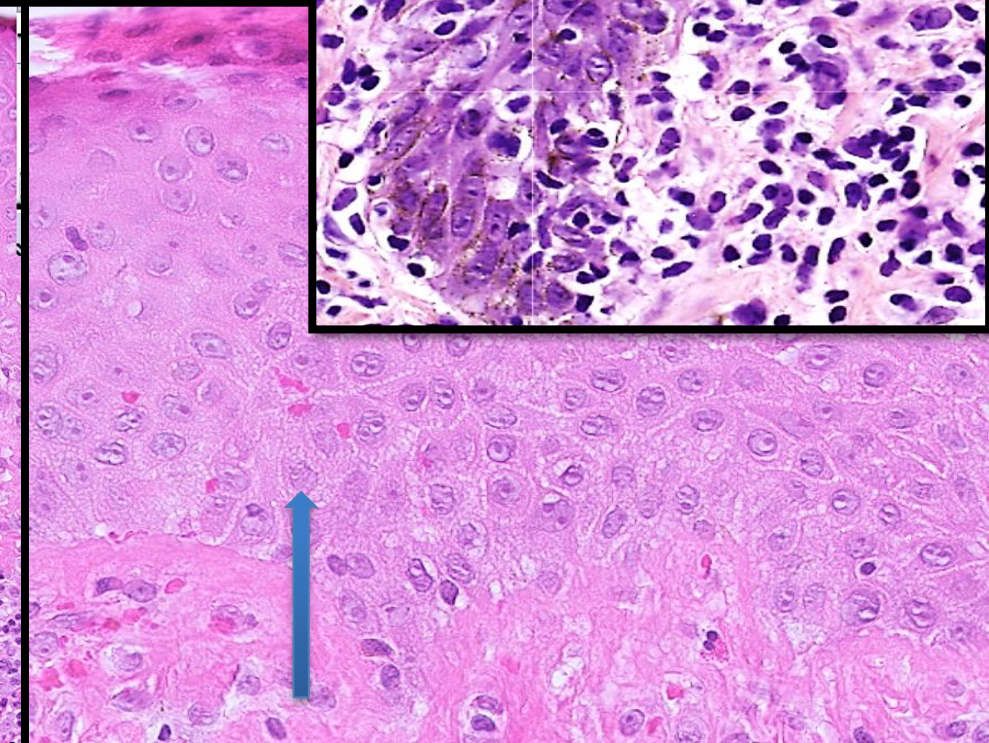
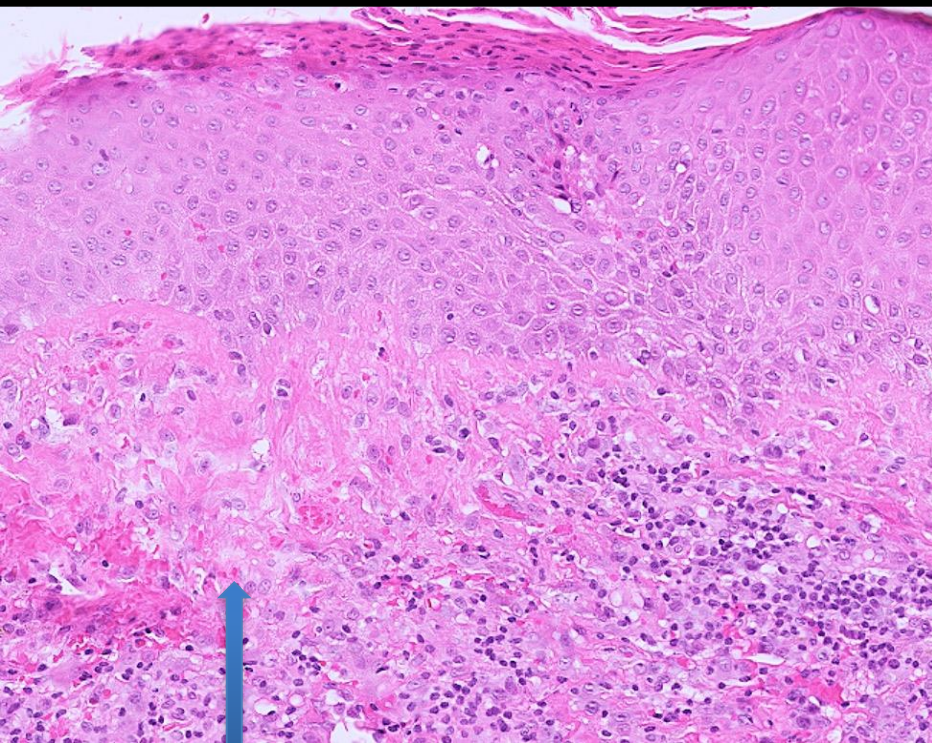
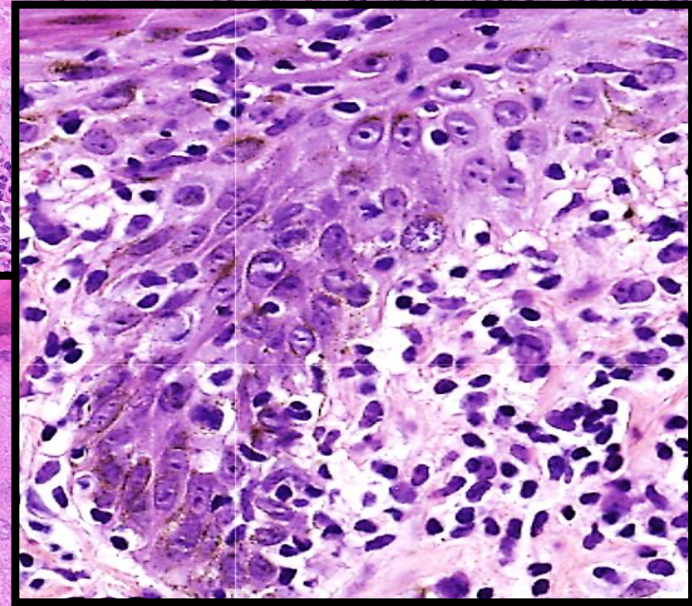
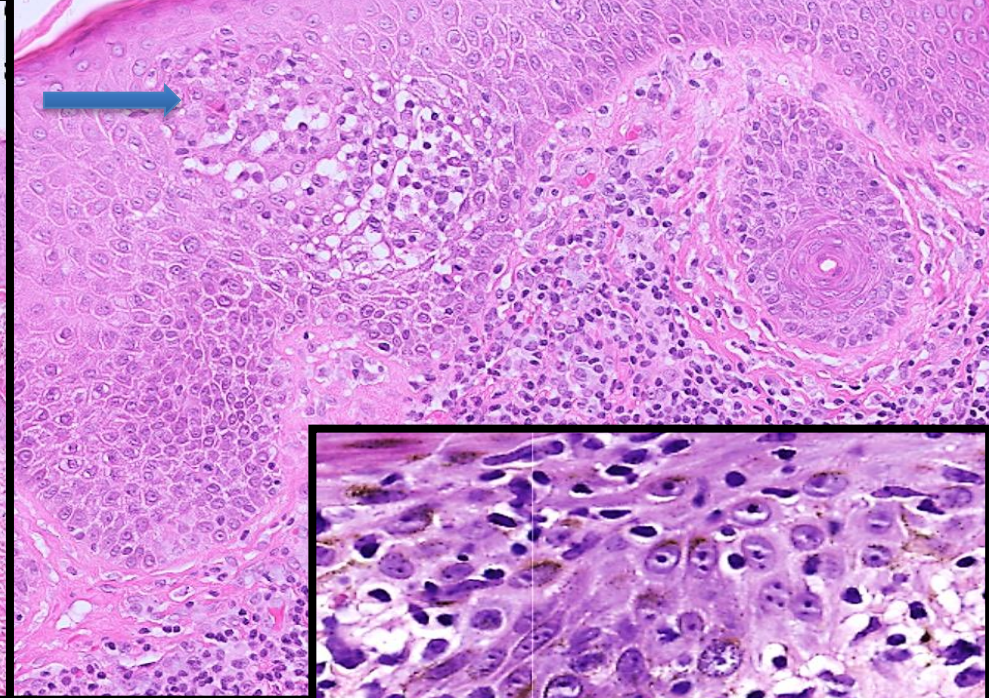
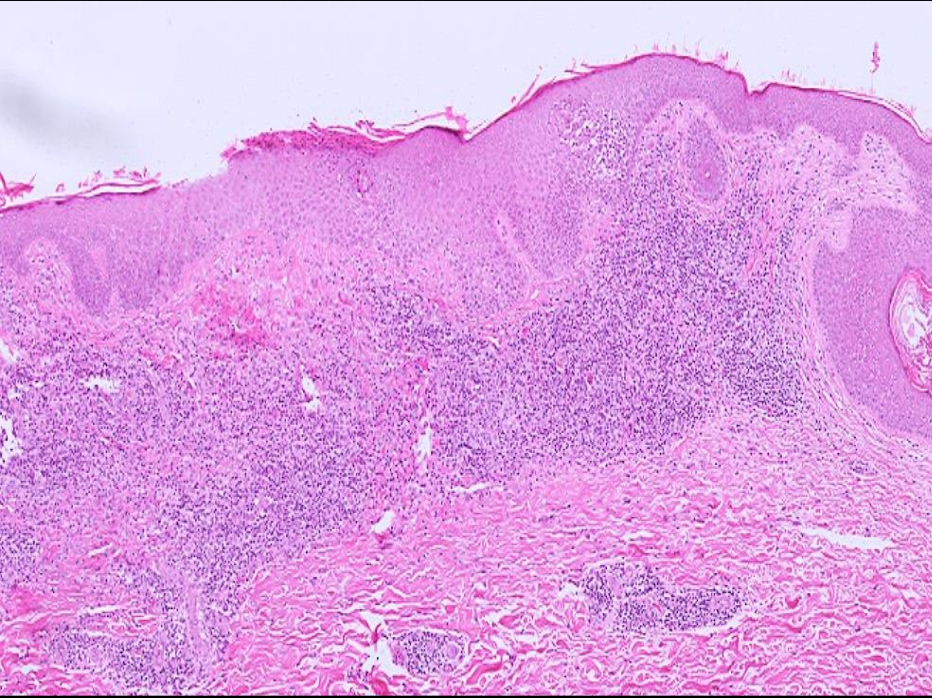
- Epidermotropic atypical infiltrate with nests of atypical cells within the epidermis.
- Darier's nests/Pautrier's microabscesses
- Atypical cells within the dermis.
- Medium to large pleomorphic cells within the epidermis and dermis, vaguely cerebriform 'Sezary cells'.

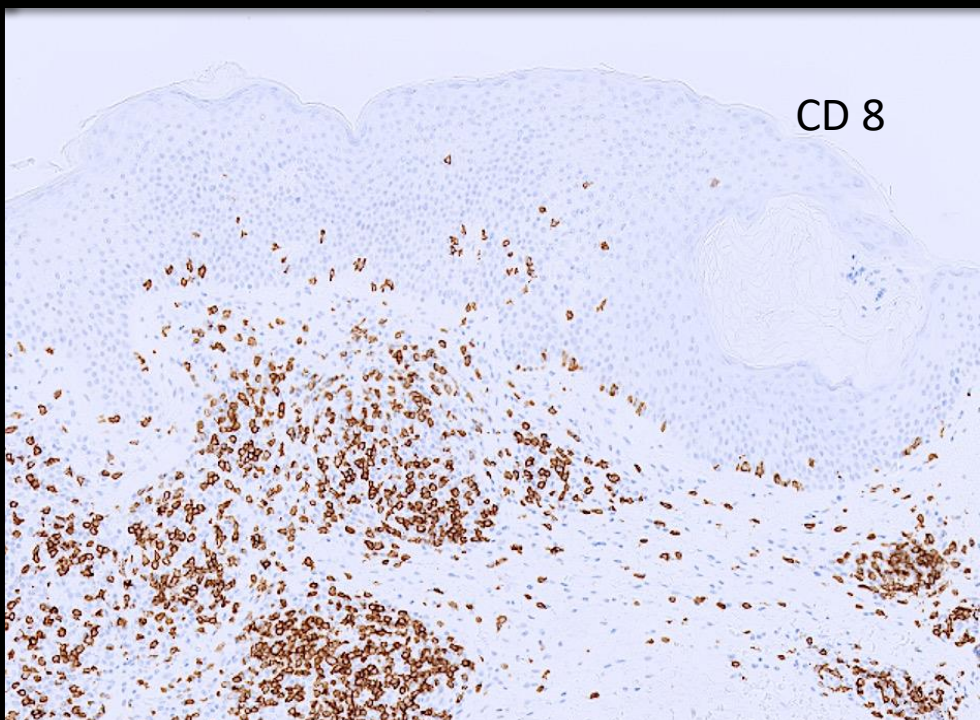
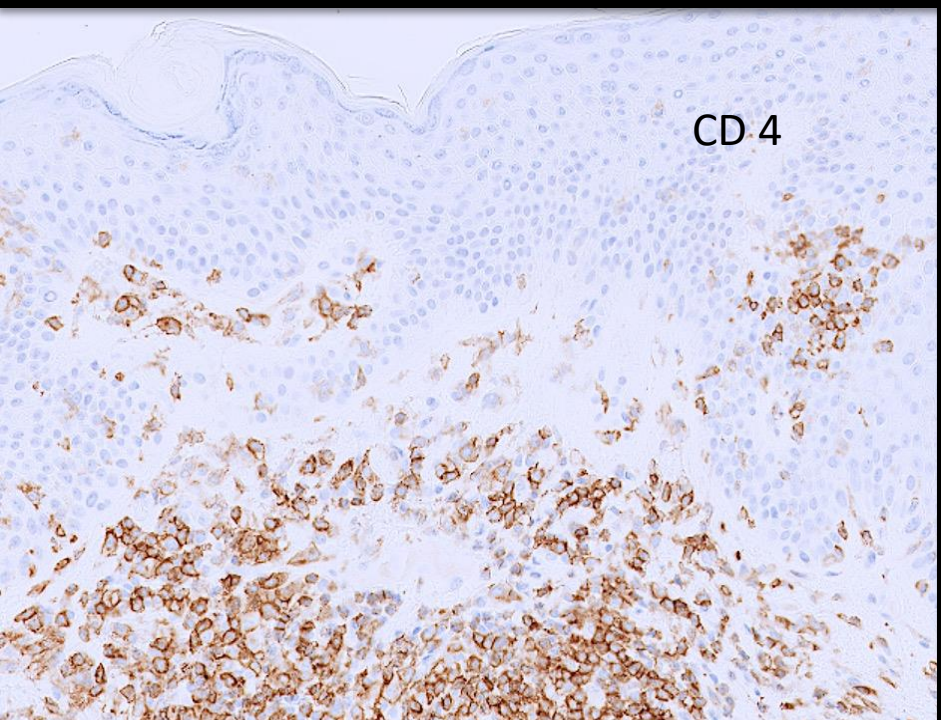
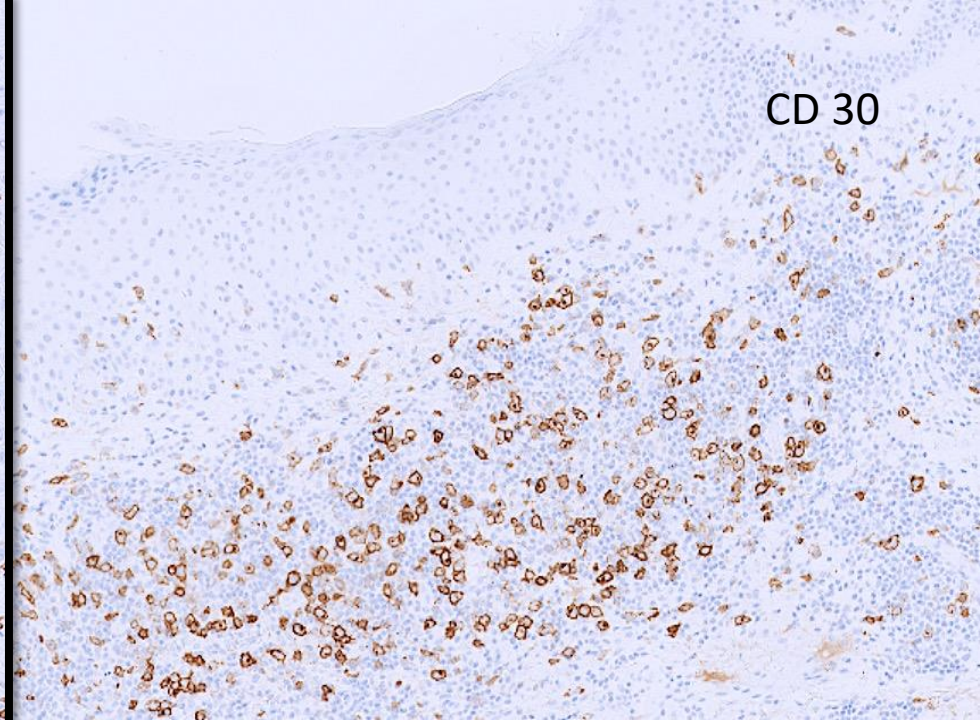
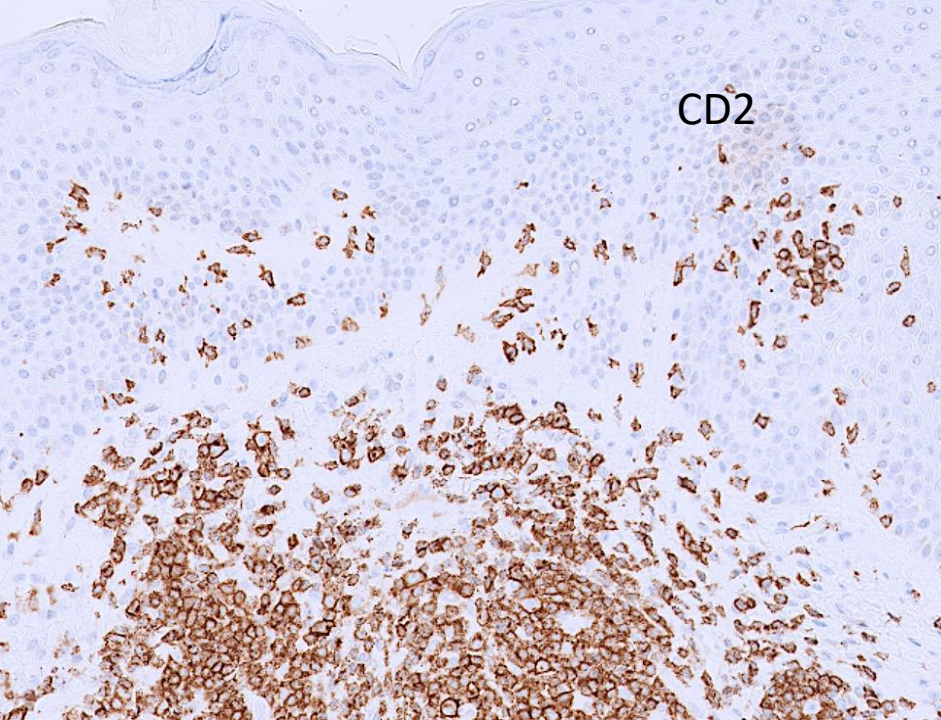
Negative
ALK 1
CD 20
CD 10
CD 56
BCL 6
CD 7
CD 8

Sezary Syndrome

Case 4


- M 56
- Incisional biopsy axilla
- Papular and itchy rash
- Wide-distribution, extensors & flexures
- No scale





Pityriasis lichenoides et varioliformis acuta (PLEVA)

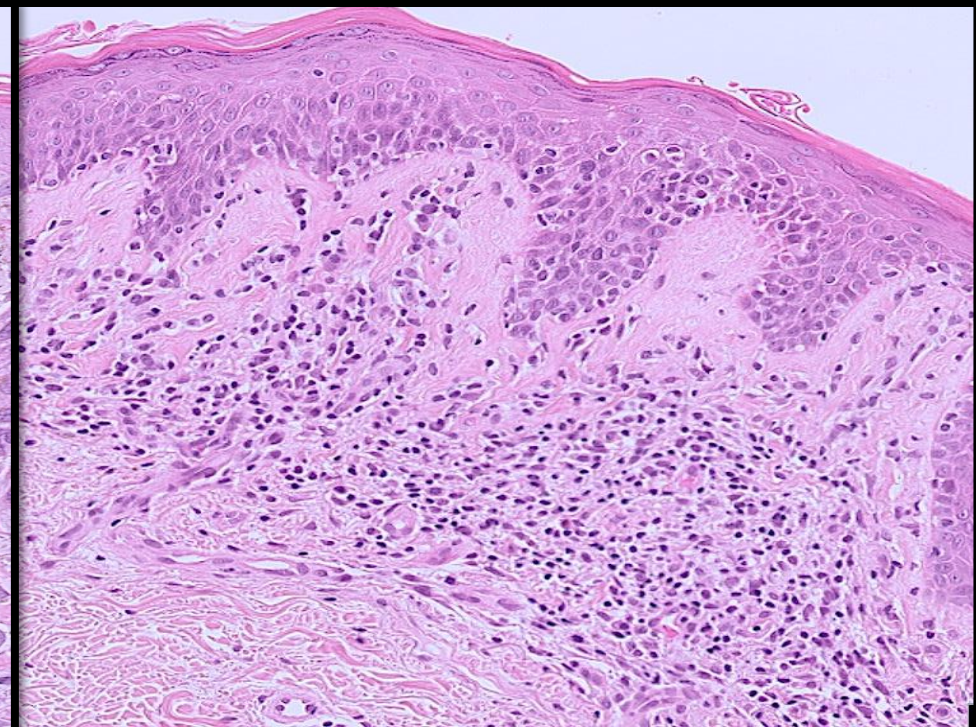
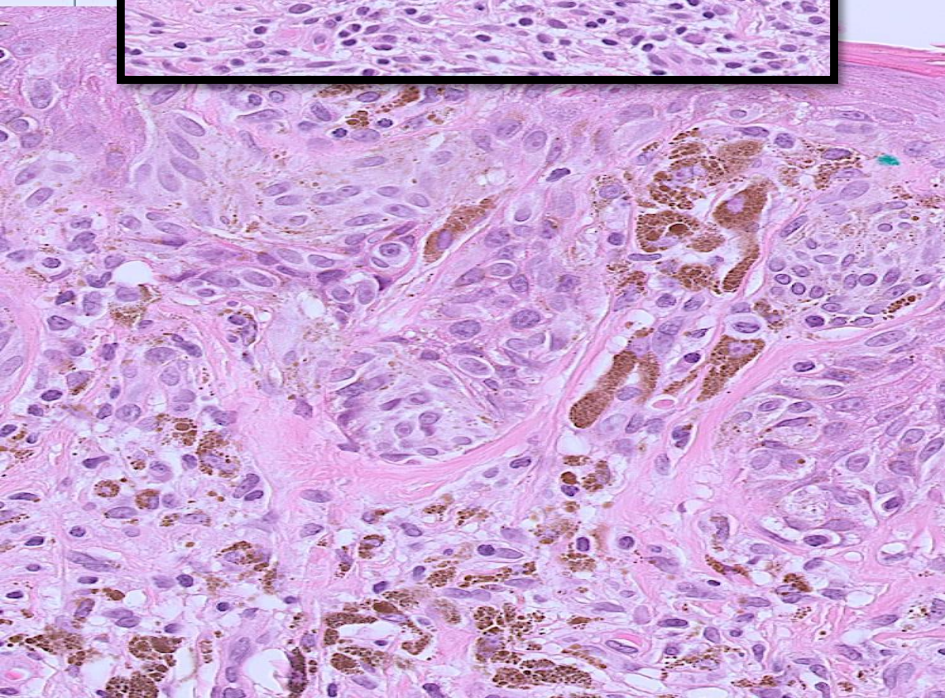
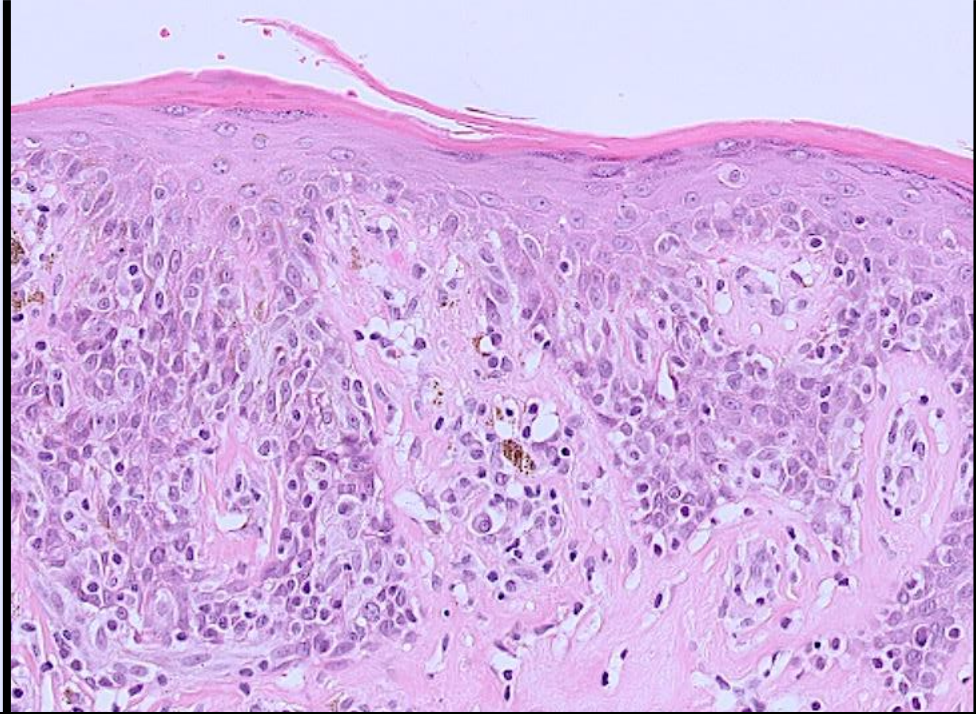
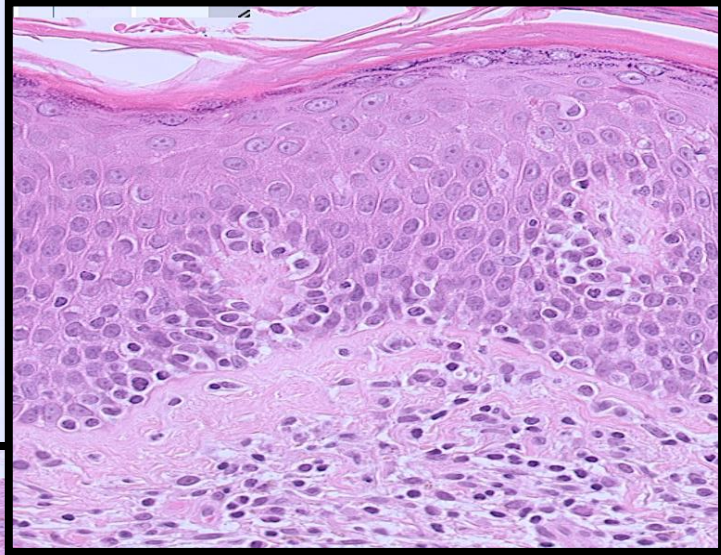
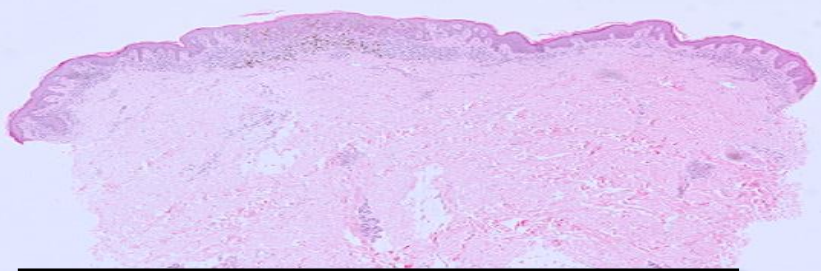
Pityriasis Lichenoides et Varioliformis Acuta With Numerous CD30⁺ Cells: A Variant Mimicking Lymphomatoid Papulosis and Other Cutaneous Lymphomas. A Clinicopathologic, Immunohistochemical, and Molecular Biological Study of 13 Cases

Kempf, Werner MD^{*,†}; Kazakov, Dmitry V. MD, PhD[‡]; Palmedo, Gabriele PhD[§]; Fraitag, Sylvie MD^{||}; Schaerer, Leo MD[§]; Kutzner, Heinz MD^{§,¶} [Author Information](#) 

The American Journal of Surgical Pathology: July 2012 - Volume 36 - Issue 7 - p 1021-1029

Case 5

- Skin punch excision naevus on back
- F 50



- Benign melanocytic naevus within a patch of mycosis fungoides



Does she have a rash, MF?



Oh, yes! She has MF for a few years now!

J Cutan Pathol. 2003 Nov;30(10):606-10.

Histologic features of melanocytic nevi seen in association with mycosis fungoides.

McNiff JM¹, Glusac EJ.

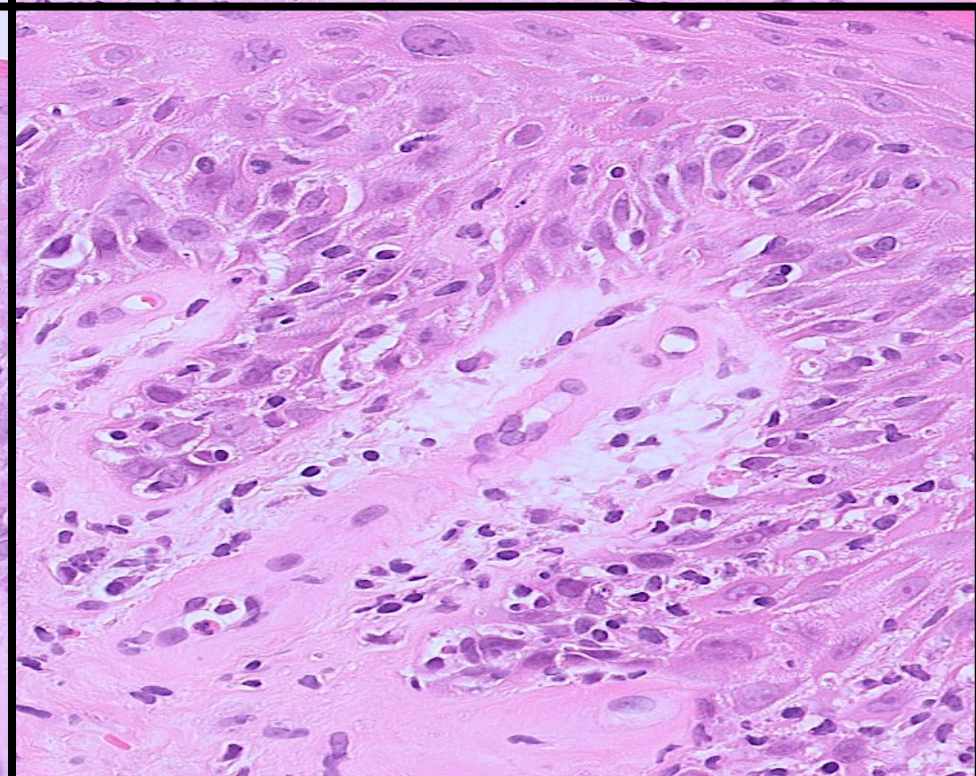
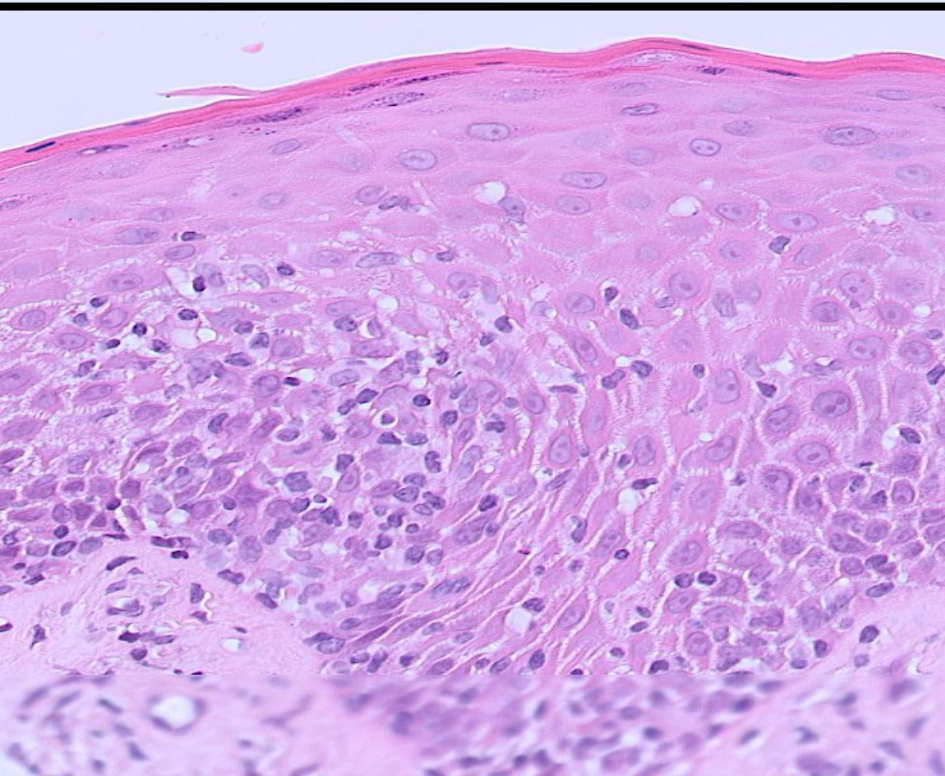
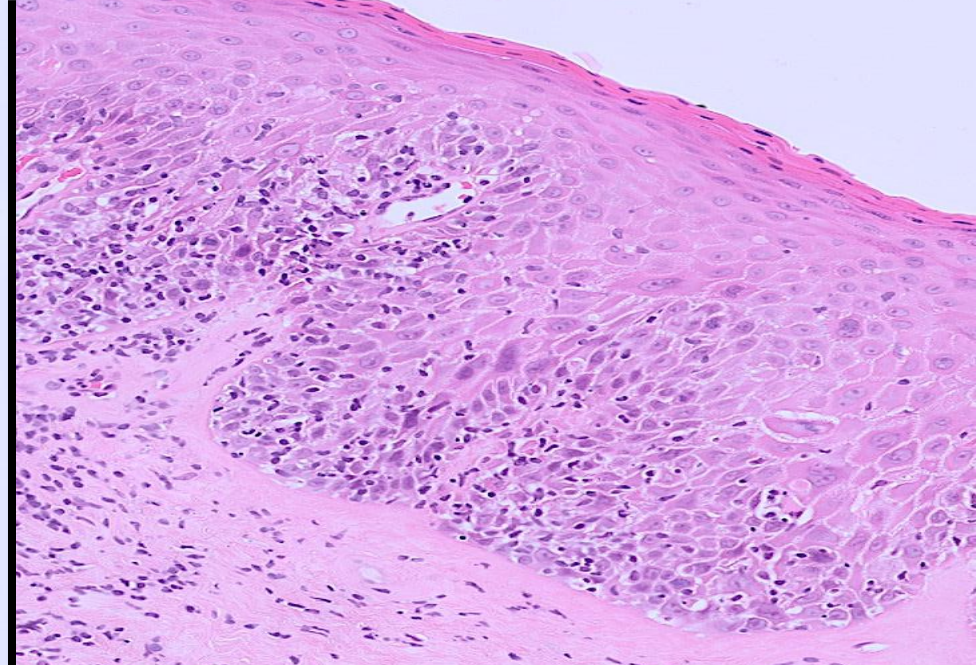
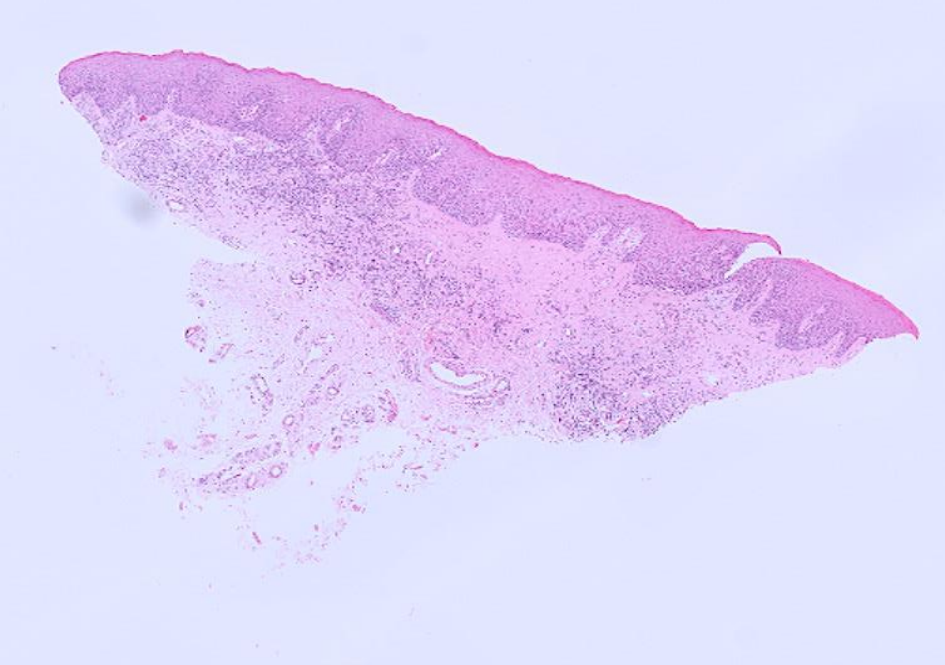
Pediatr Dermatol. 2019 Mar;36(2):232-235. doi: 10.1111/pde.13738. Epub 2019 Jan 18.

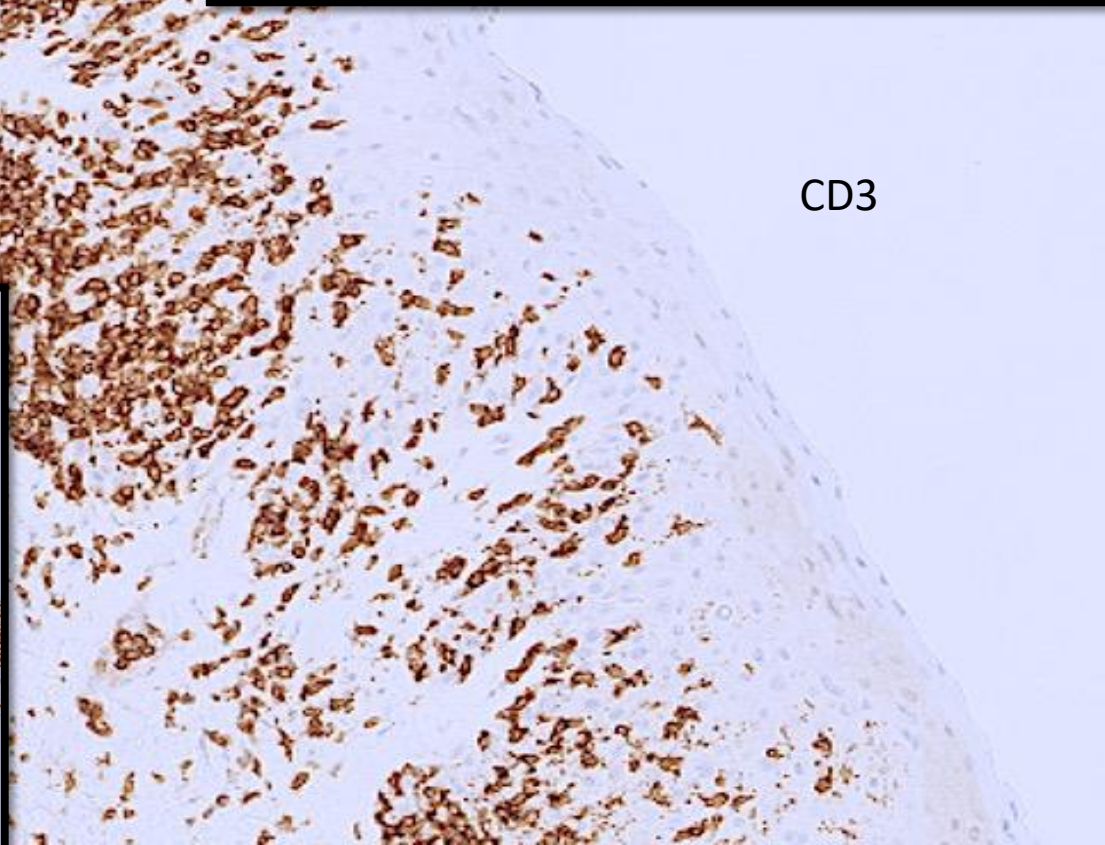
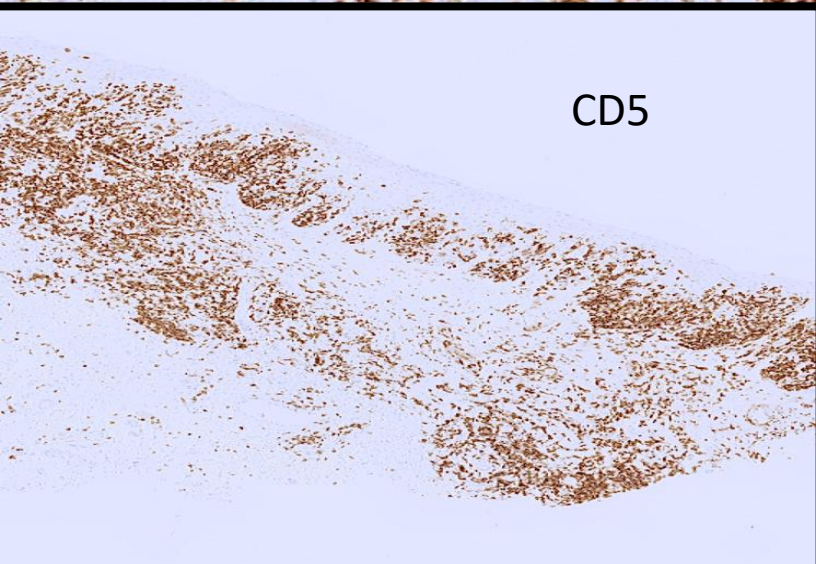
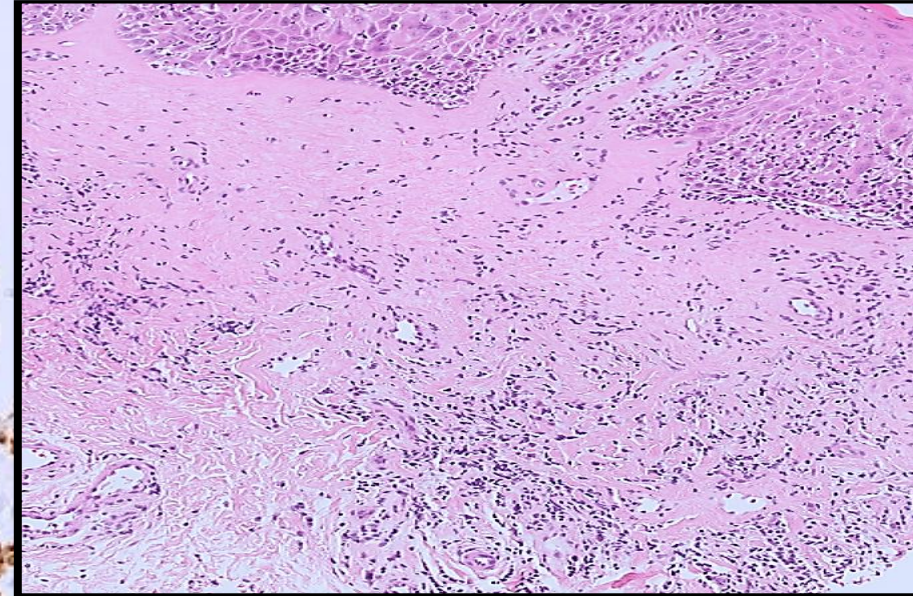
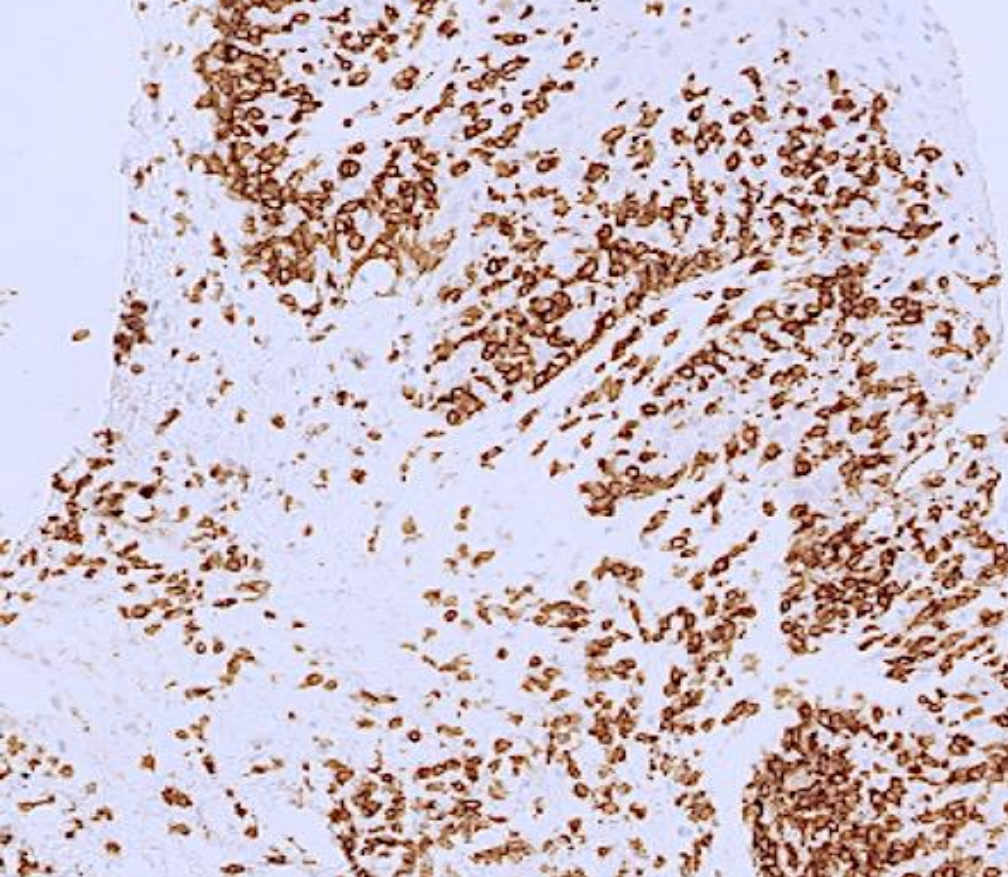
Multiple melanocytic nevi restricted to mycosis fungoides patches in pediatric and young-adult patients. The potential role of local immunosuppression.

Martinez-Escala ME¹, Amin SM¹, Sable KA¹, Gerami P¹, Guitart J¹.

Case 6

- Punch biopsy tip of penis
- M 30
- H/O Psoriasis





CD3

CD5

CD4
CD8
CD5
CD30
CD20

Genital Mycosis fungoides

Drug eruption

Lichen sclerosis

Typical clinical features of BXO/LS


Solitary plaque mycosis fungoides on the penis responding to topical imiquimod therapy

L.Y.T Chiam, Y.C. Chan

First published: 10 November 2006 | <https://doi.org/10.1111/j.1365-2133.2006.07599.x> | Citations: 18

ORIGINAL ARTICLES

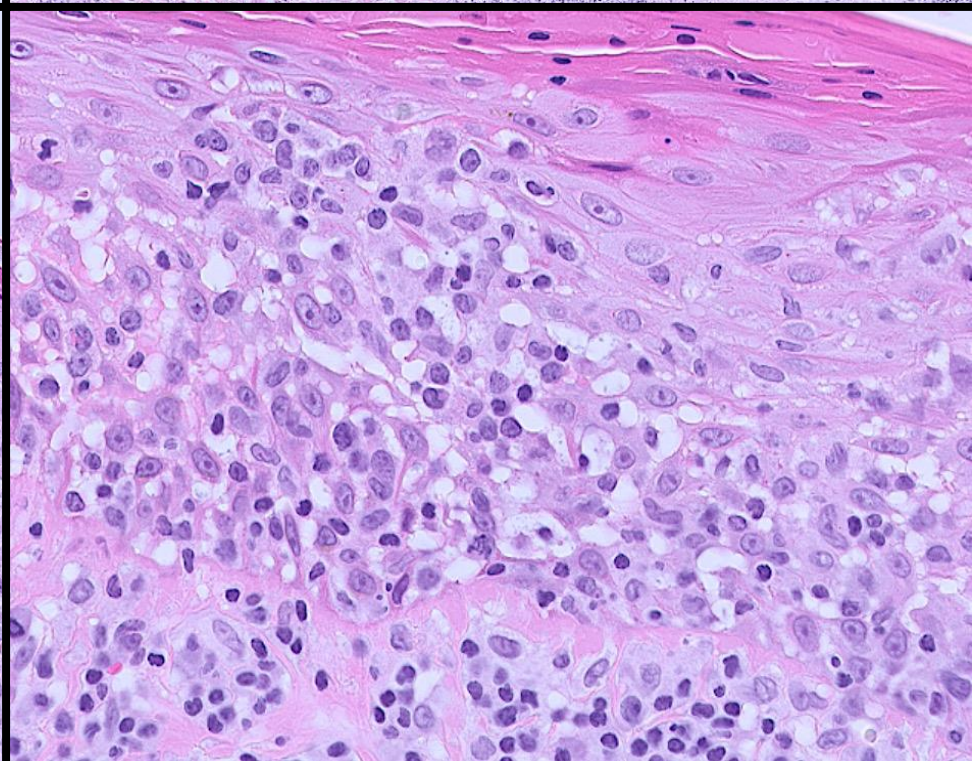
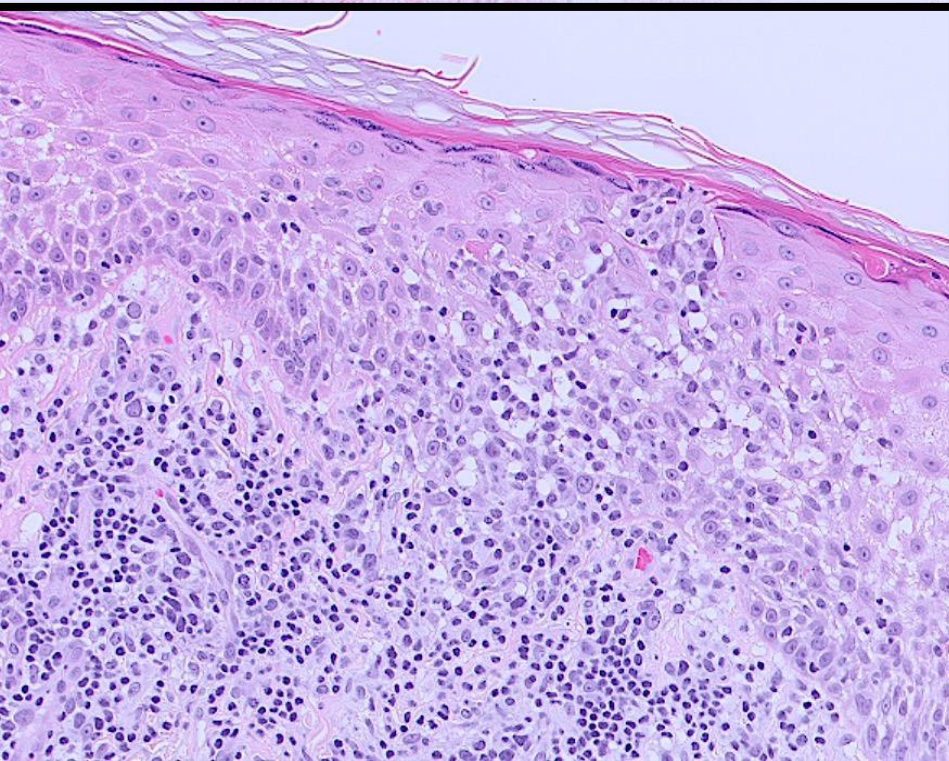
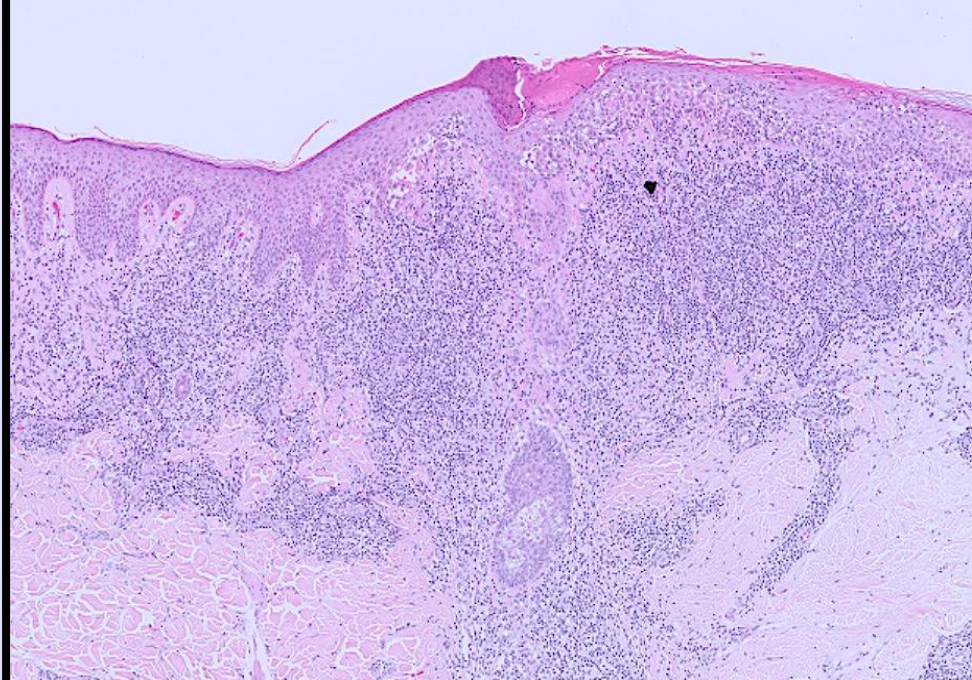
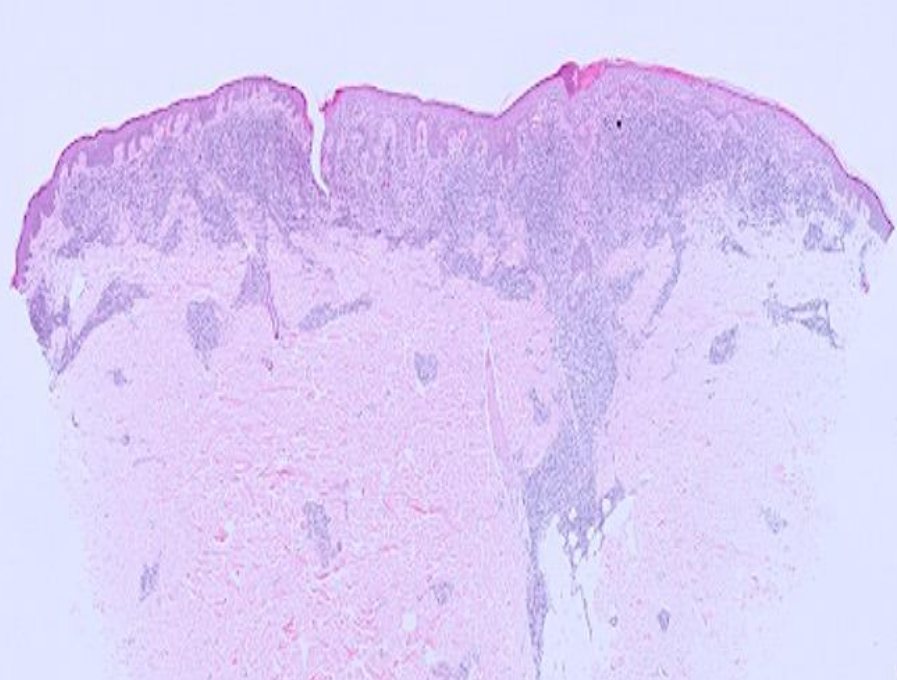
Lichen Sclerosus with Histopathologic Features Simulating Early Mycosis Fungoides

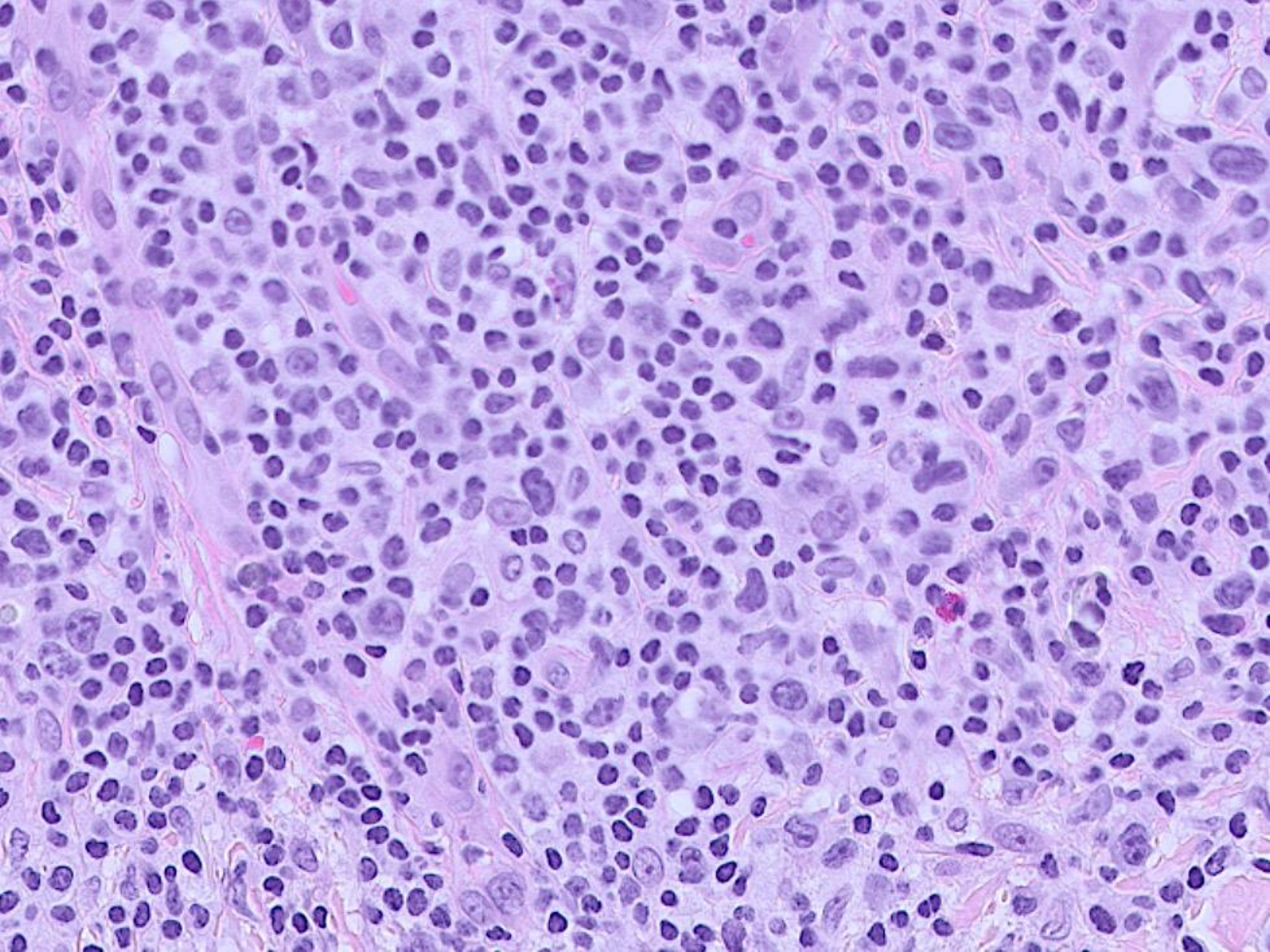
Citarella, Luigi MD; Massone, Cesare MD; Kerl, Helmut MD; Cerroni, Lorenzo MD [Author Information](#) 

The American Journal of Dermatopathology: December 2003 - Volume 25 - Issue 6 - p 463-465

Case 7

- ? BCC back, excision biopsy
- M 65





CD3

CD5 No loss

CD4 >> CD8

CD 30 10%

CD 20 small
numbers

TCR PCR
negative

Unilesional mycosis

Lymphomatoid papulosis

**CD4 + small and medium cutaneous
T cell lymphoproliferation**

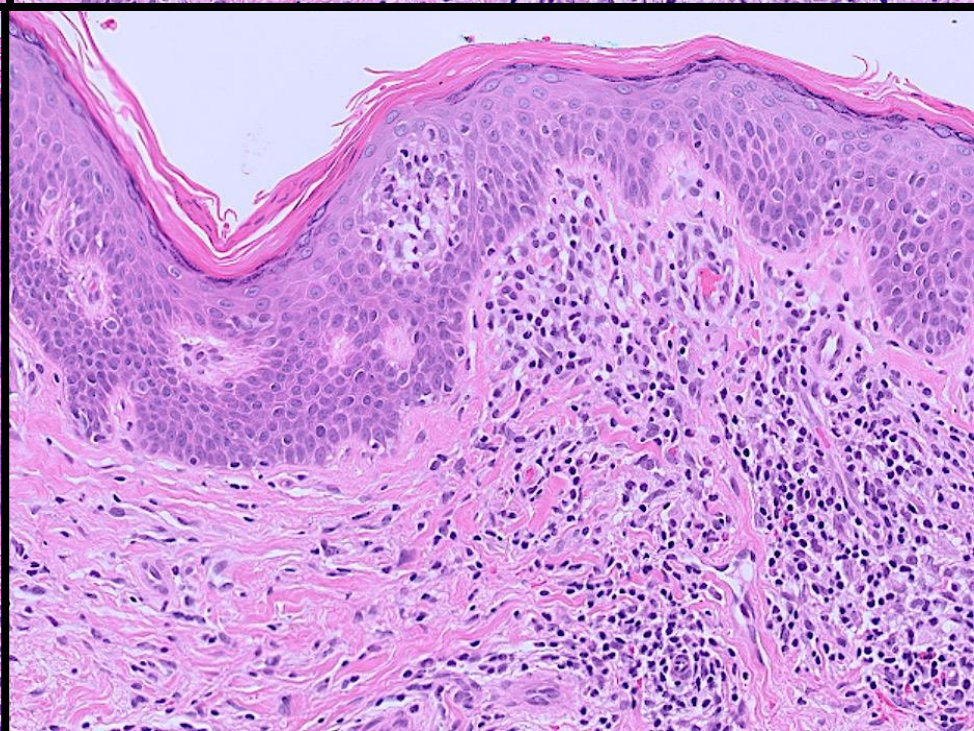
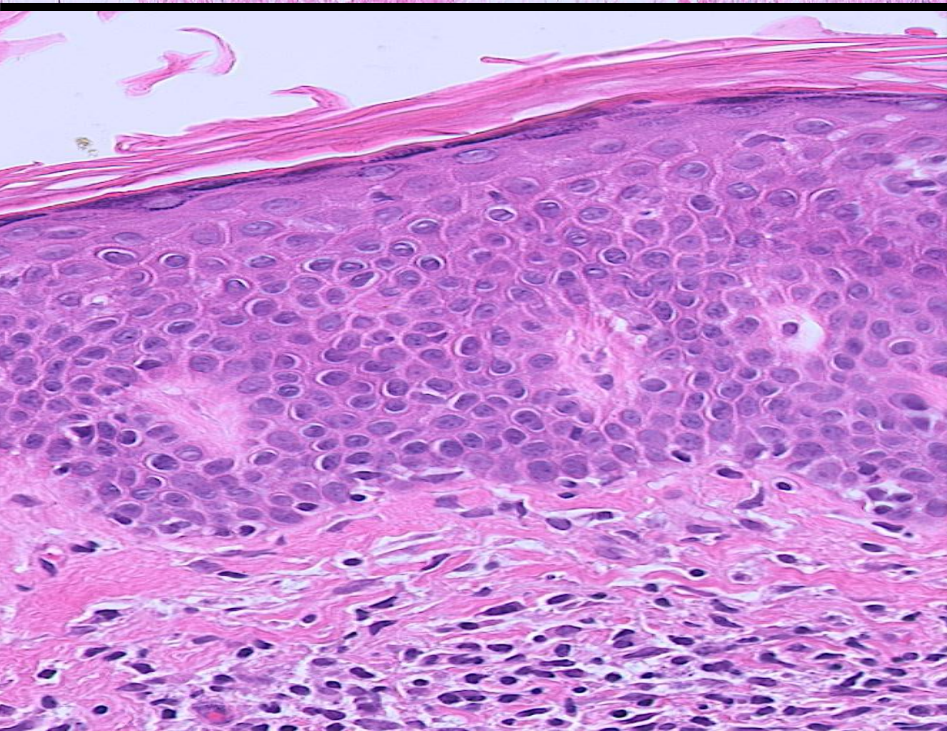
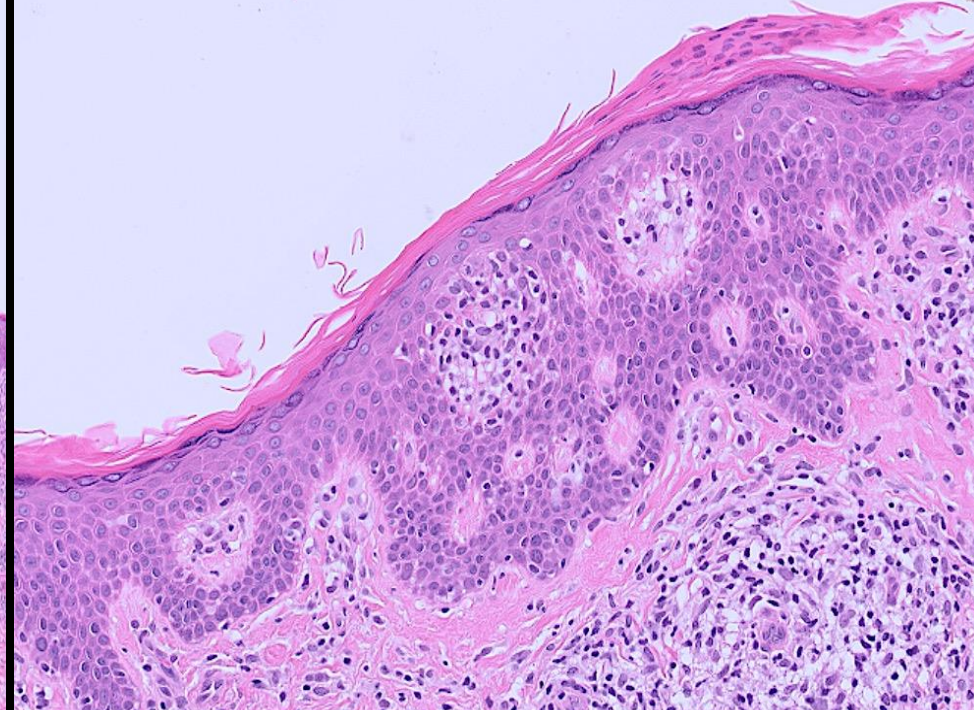
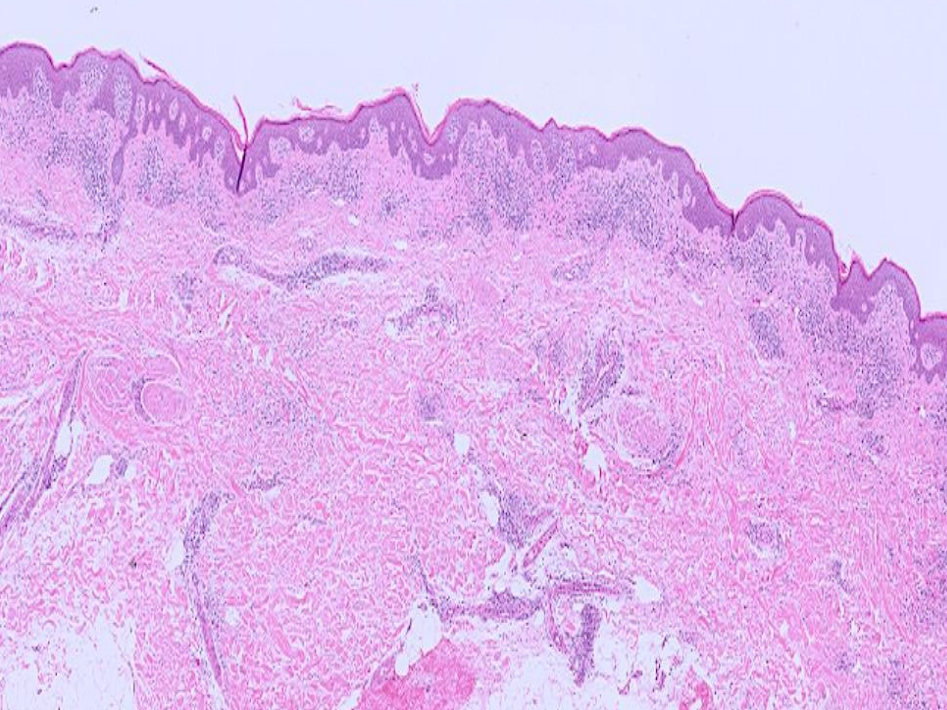
[Blood](#), 2019 Apr 18;133(16):1703-1714. doi: 10.1182/blood-2018-11-881268. Epub 2019 Jan 11.

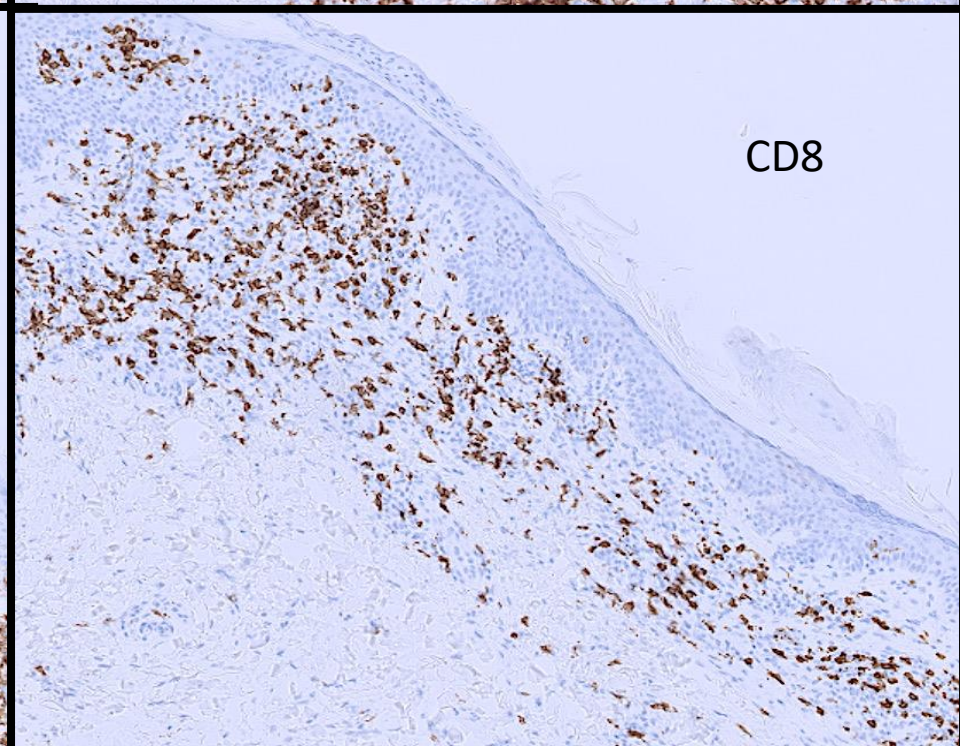
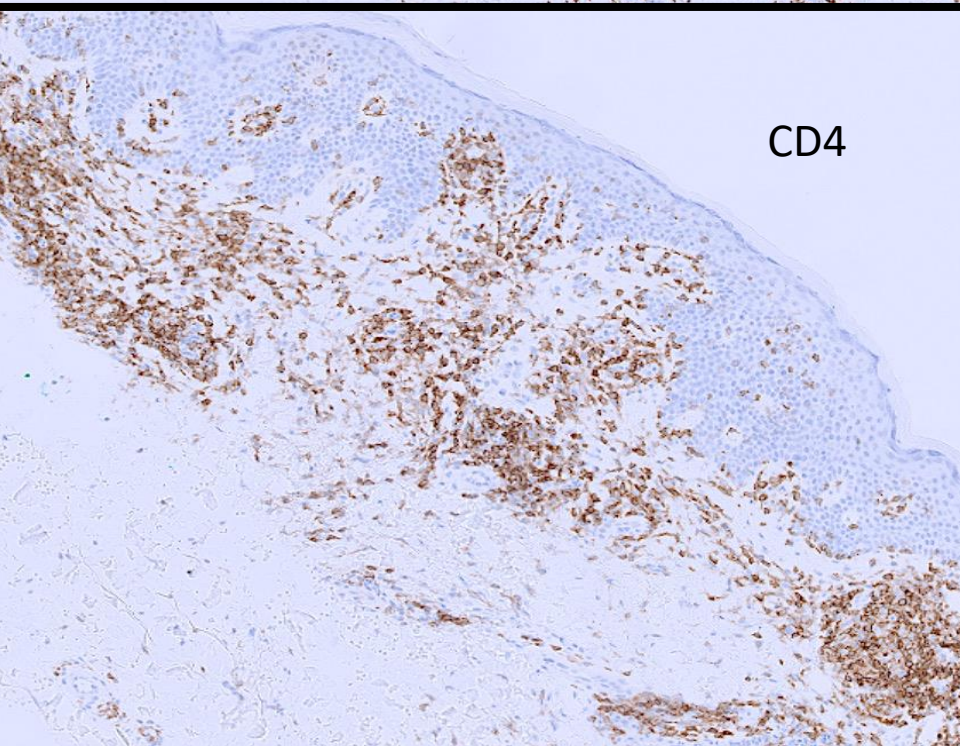
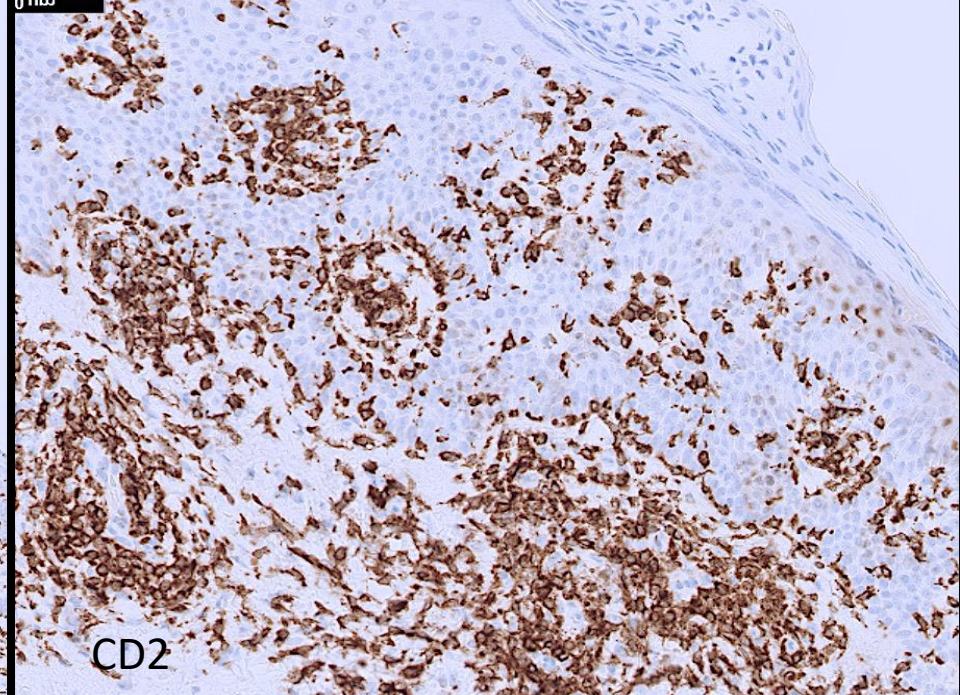
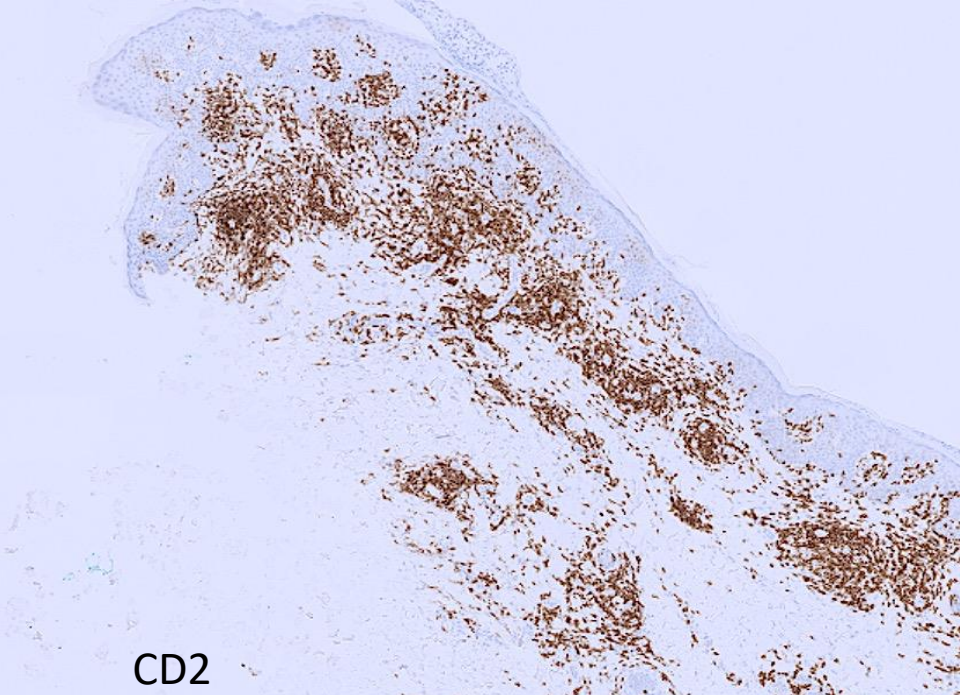
The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas.

[Willemze R](#)¹, [Cerroni L](#)², [Kempf W](#)³, [Berti E](#)⁴, [Facchetti F](#)⁵, [Swerdlow SH](#)⁶, [Jaffe ES](#)⁷.

Case 8

- F 60
- Incisional biopsy right thigh
- Erythroderma





CD2+ CD3+

CD5

CD7 lost

CD4 > CD8

CD 30
occasional

TCR PCR
negative

Erythrodermic eczema

Erythrodermic mycosis

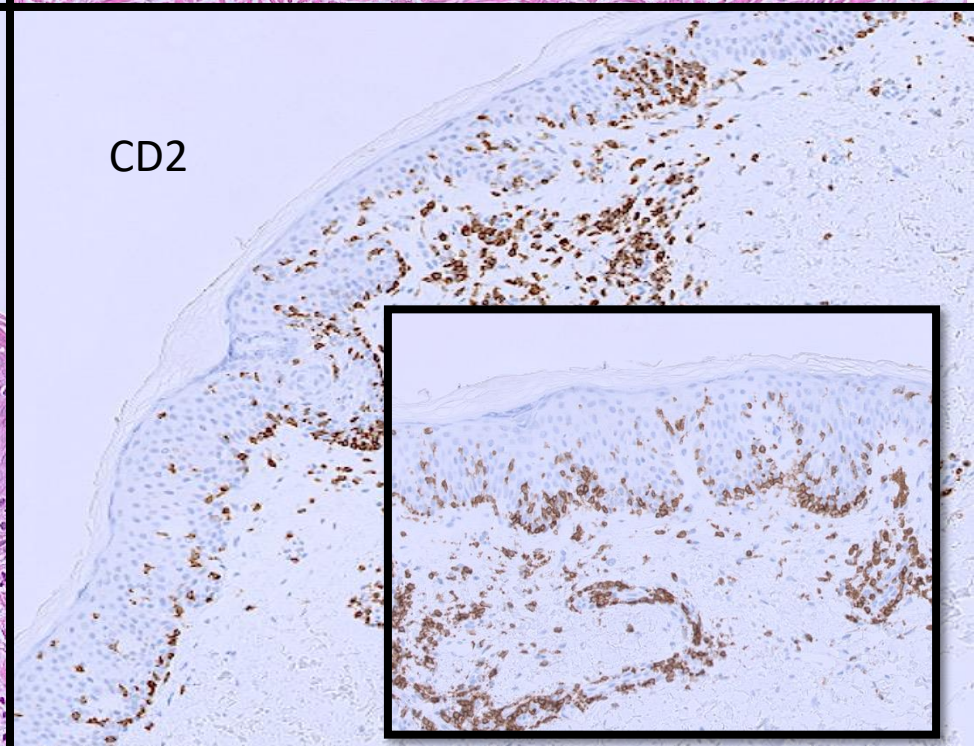
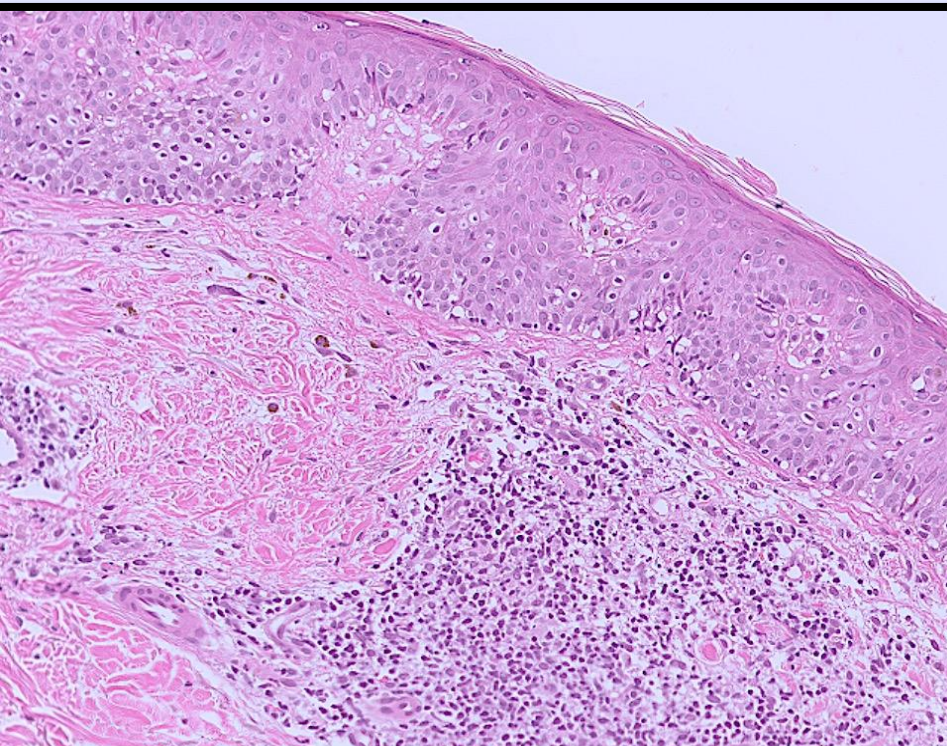
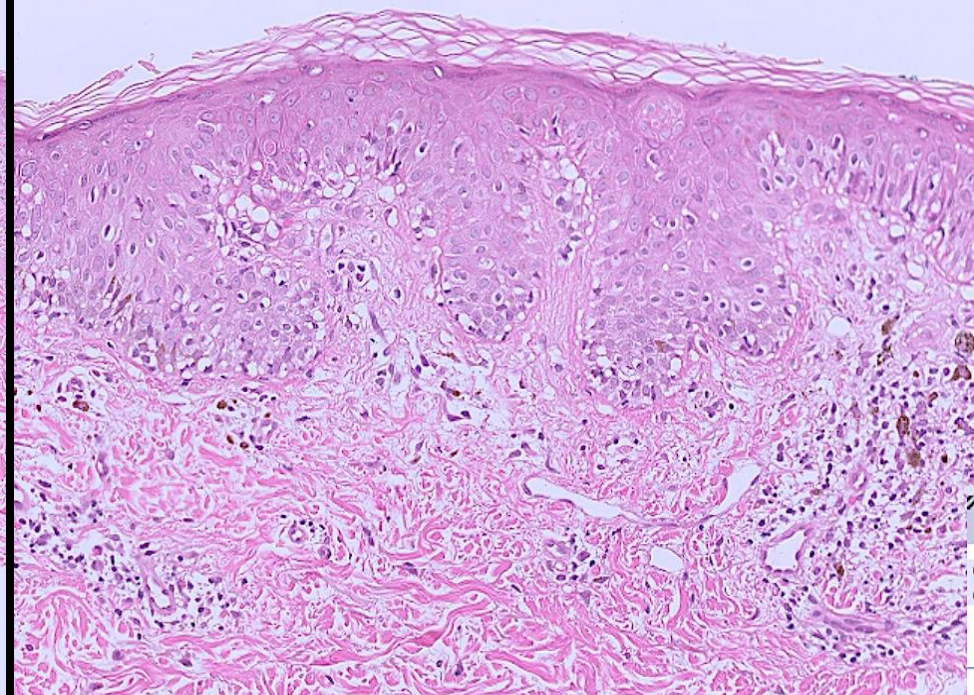
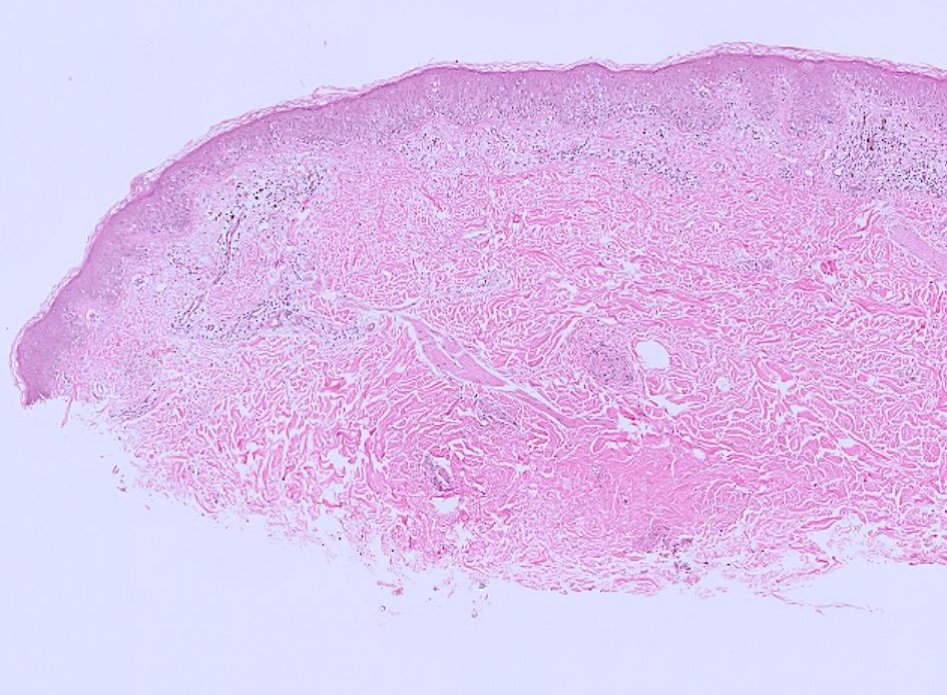
Sezary syndrome

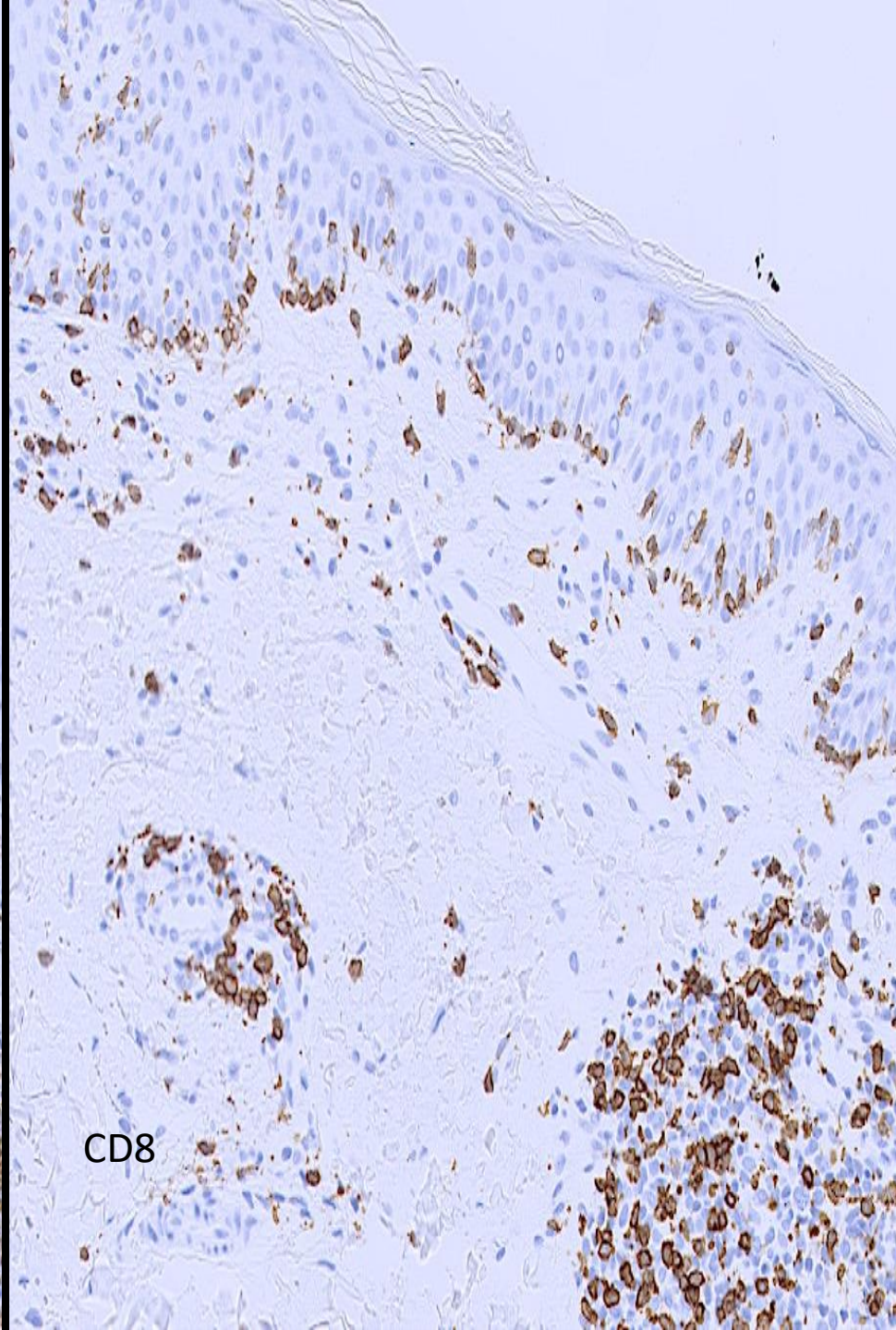
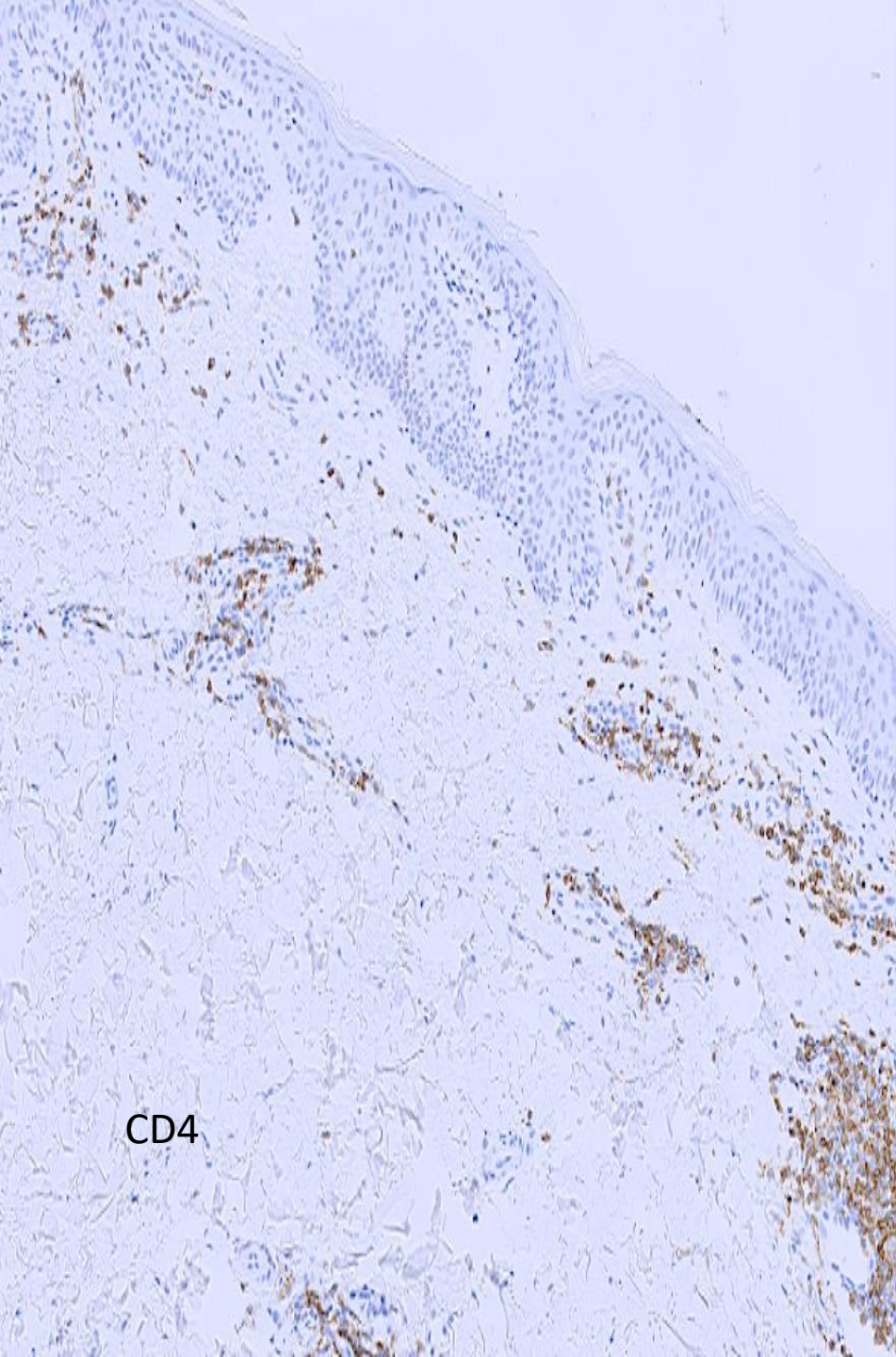
Inguinal lymph node-clone and
dermatopathic changes.

No matter how good a clinician,& no matter how good a dermatopathologist, some cases of erythroderma will evolve into a direction that both had neither predicted nor expected.

Case 9

- F 55
- Flat brown lesion left scapula





CD2+ CD3+

CD5	no loss
CD20	minor component
CD4:CD8	dermis normal
CD8	epidermal component
CD30	negative

Lichenoid keratosis with a mycosis fungoides like pattern AKA lymphomatoid keratosis

Unilesional mycosis
Thorough clinical examination



Review

A review of the solitary cutaneous T-cell lymphomas

Cutaneous T-cell lymphomas (CTCL) account for almost 65–92% of all cutaneous lymphomas, many of which usually present with multiple lesions. However, a number of well-recognized and rare types of CTCL, including mycosis fungoides, can present in isolated fashion. These solitary lesions often run a relatively indolent clinical course but often pose diagnostic difficulties. We review histopathologically challenging solitary cutaneous T-cell lymphomas, including criteria for diagnosis, clinical course and

Mina S. Ally¹ and Alistair Robson²

¹Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA, and

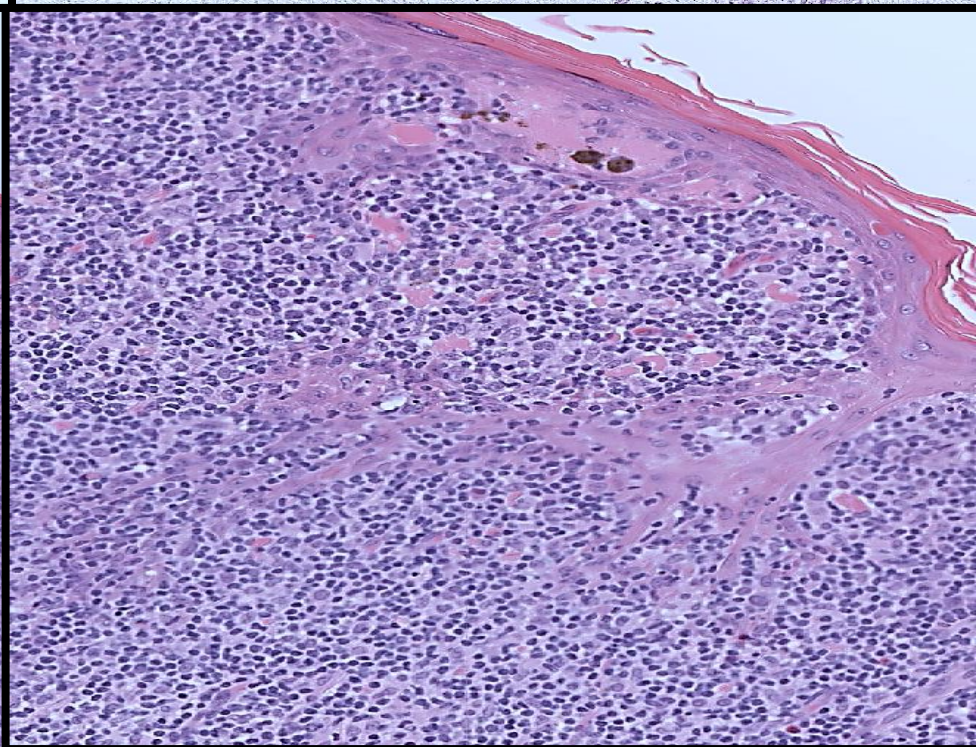
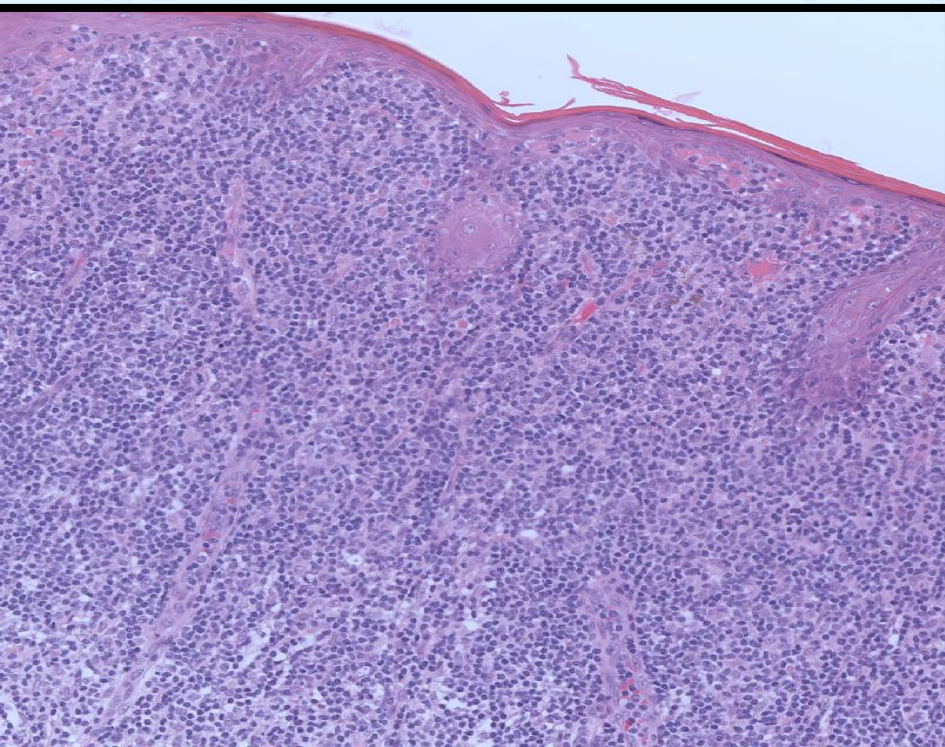
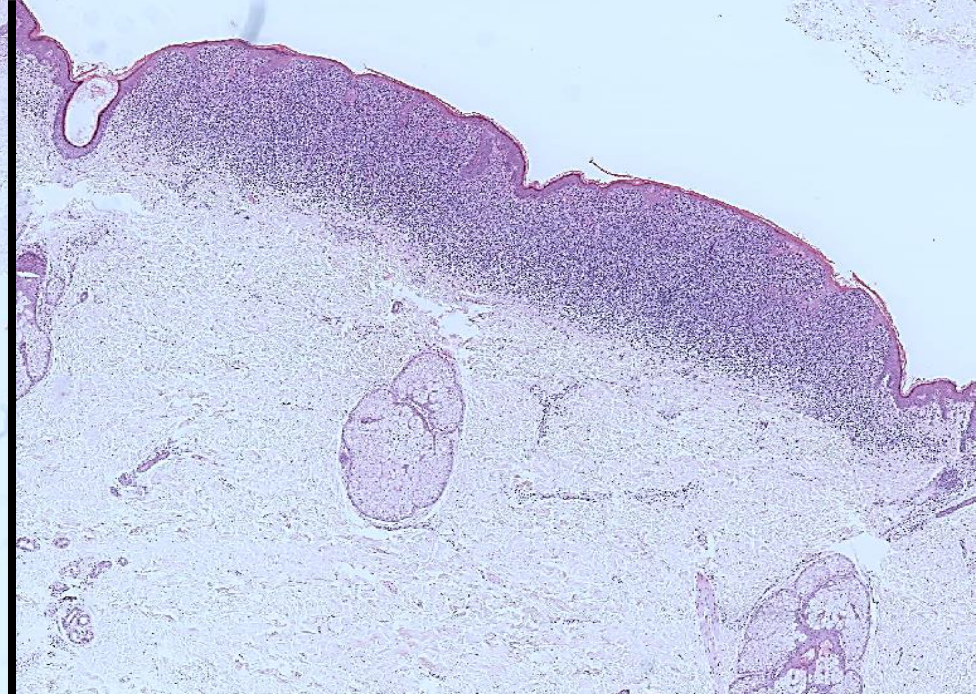
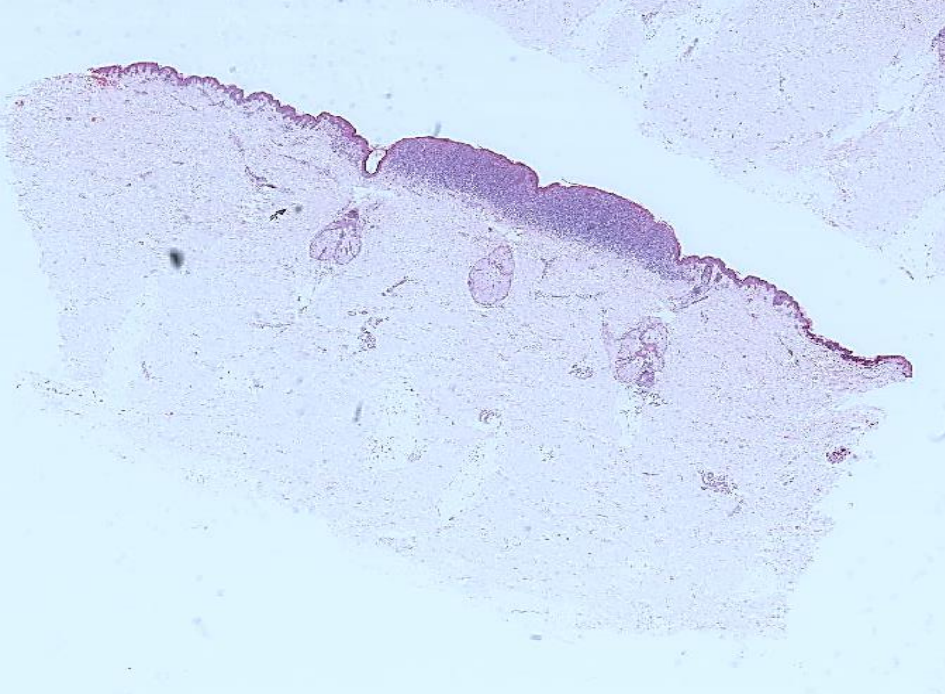
²St. John's Institute of Dermatology, St. Thomas' Hospital, London, UK

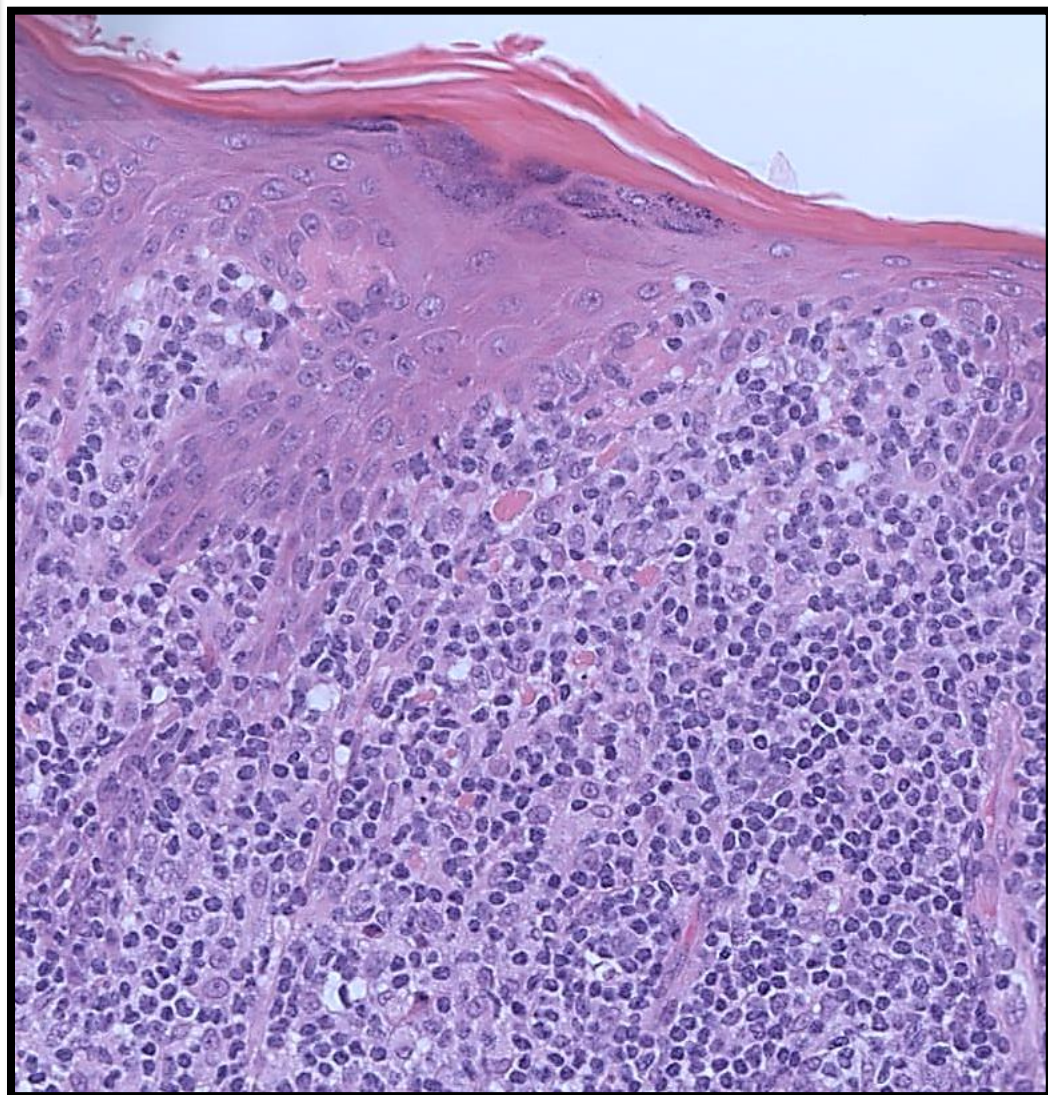
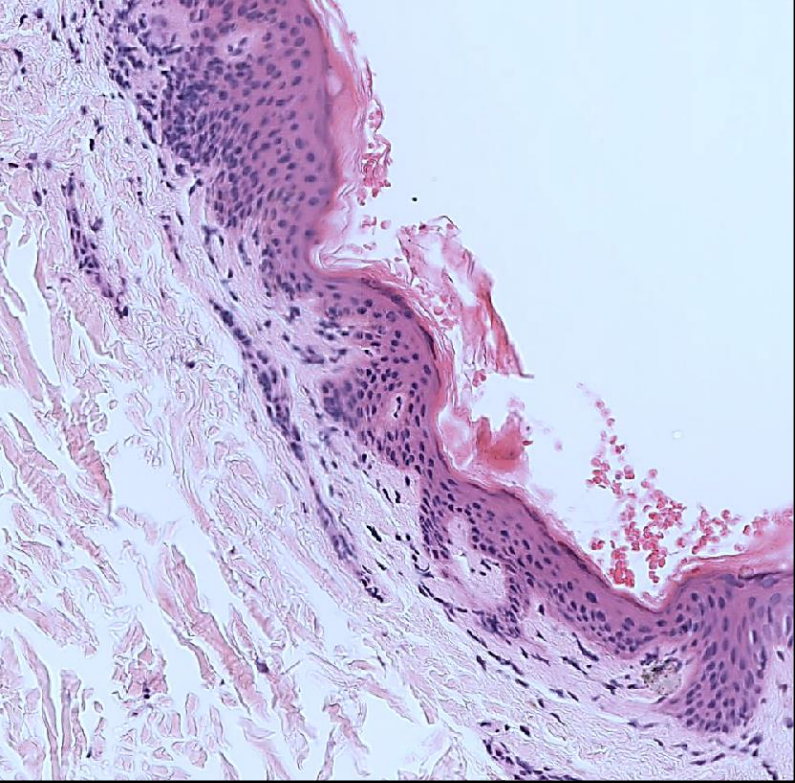
Table 1. Number of reports of each solitary cutaneous T-cell lymphoma and reported instances of recurrence or disease progression

Cutaneous lymphoma type	Total cases	Cases with cutaneous/systemic progression	Cases with lesion recurrence post-treatment*
Solitary MF	166	4 (Cutaneous spread, 3 × large cell transformation)	15 (six distant from original site)
Pagetoid reticulosis (Woringer-Kolopp)	62	1 (Cutaneous spread)	8 (1 distant from original site)
SMPTCL	231	5 (Extracutaneous spread, one died of lymphoma)	12
Indolent CD8+ lymphoid proliferation of acral sites	22	0	4 (one distant from original site)

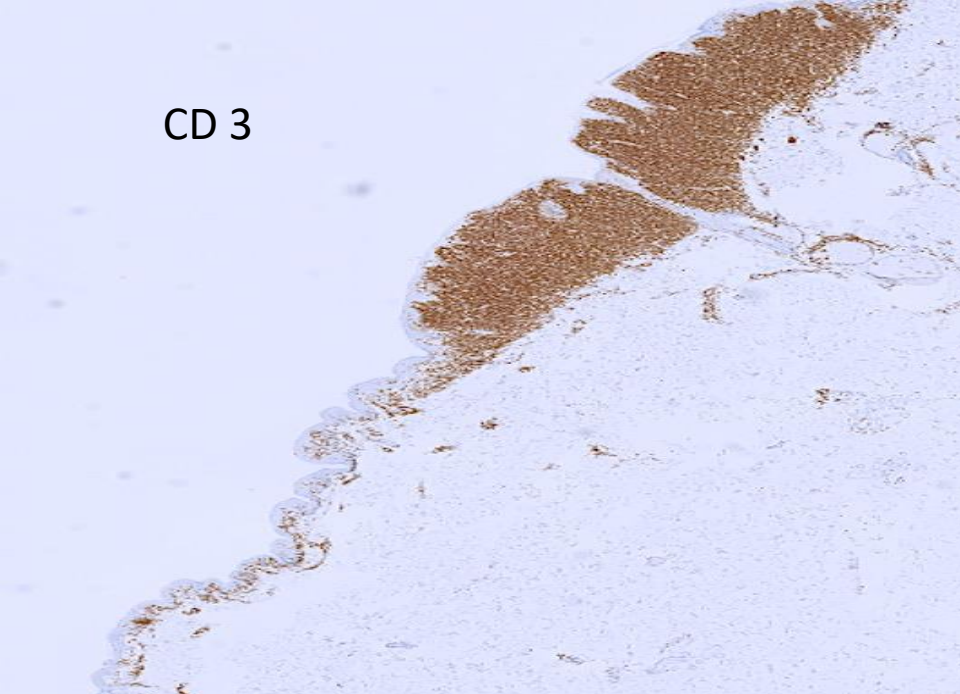
Case 10

- M 14
- Skin lesion from upper back - clinically thought to be dysplastic naevus

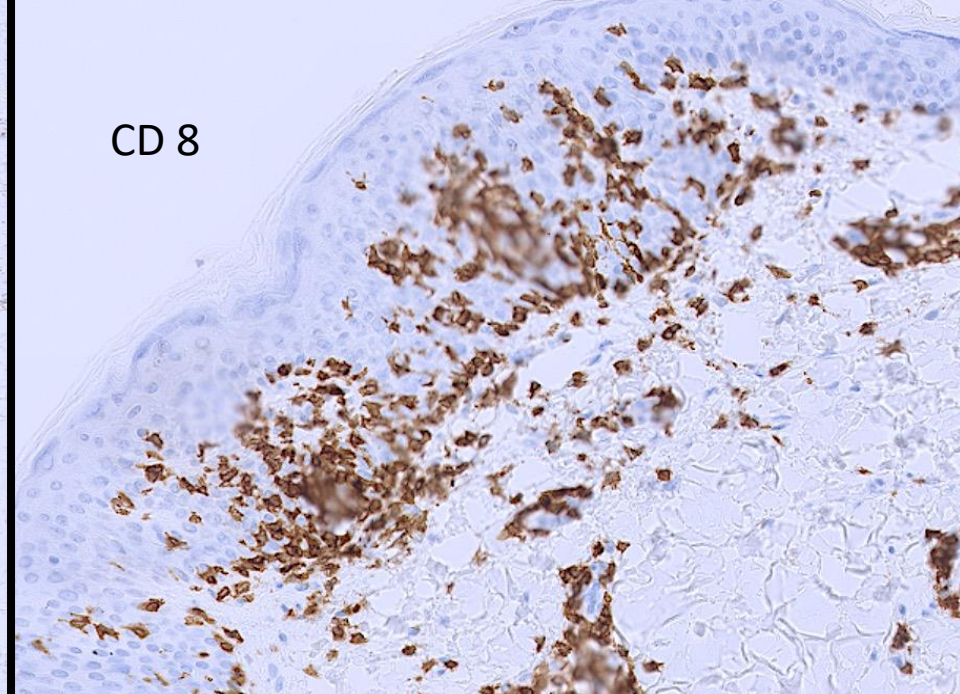




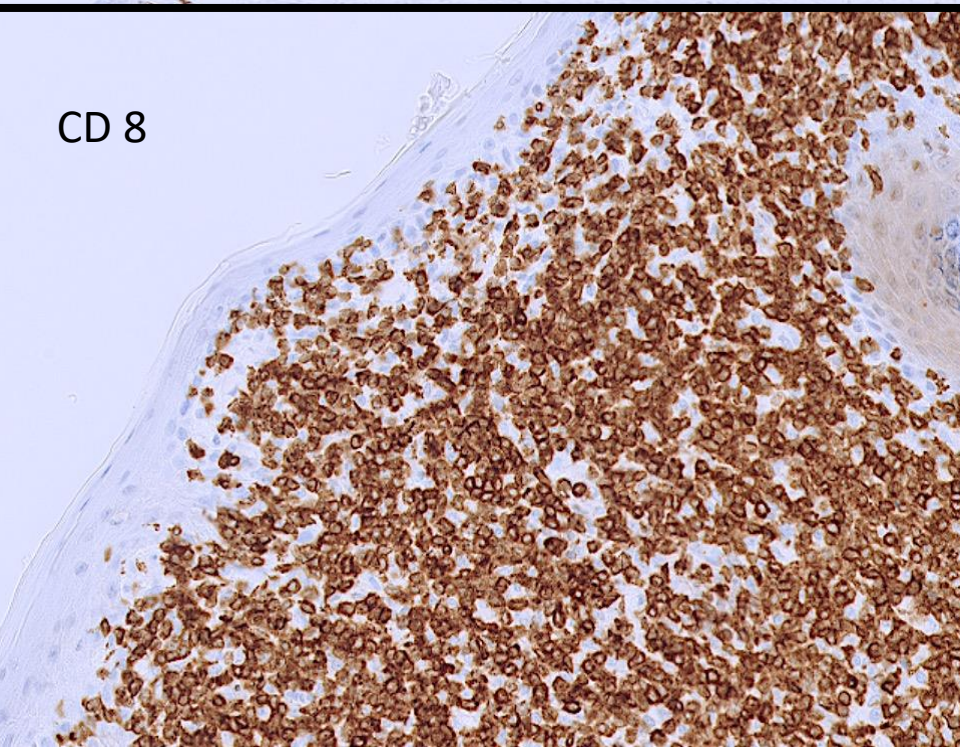
CD 3



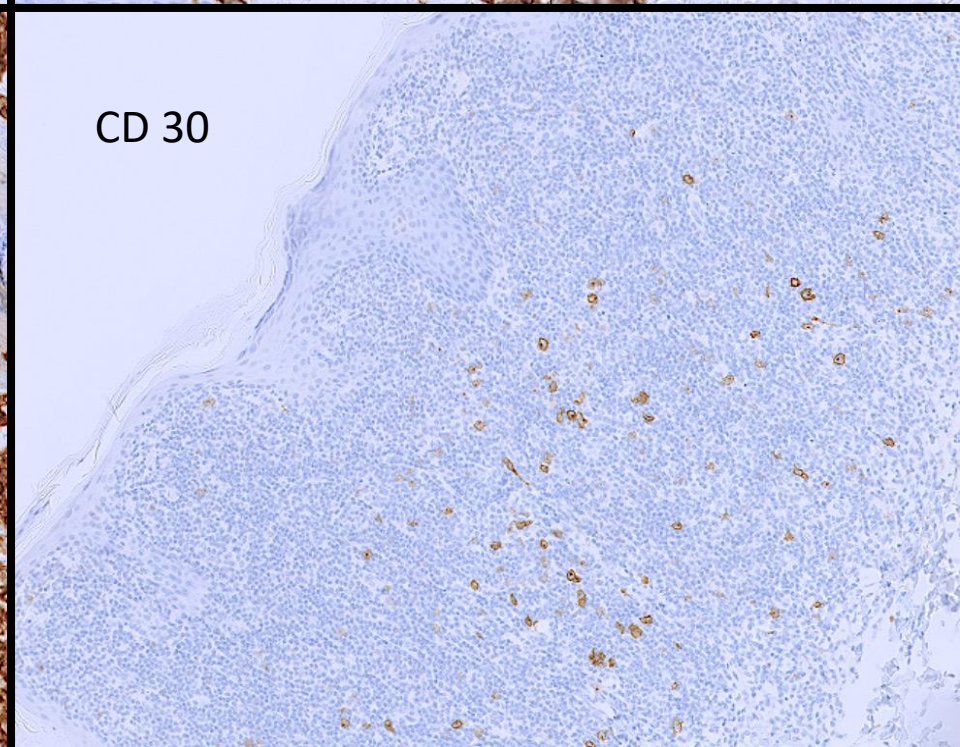
CD 8



CD 8



CD 30



CD2 and 3+

CD5

CD7 Partial loss

CD8>>CD4 10:1

CD20 fair number

CD30 occasional

TCR PCR +

Lymphomatoid keratosis

Unilesional mycosis fungoides

Hypertrophic lichen planus

Lymphomatoid Keratosis

An Epidermotropic Type of Cutaneous Lymphoid Hyperplasia: Clinicopathological, Immunohistochemical, and Molecular Biological Study of 6 Cases

Eiichi Arai, MD; Michio Shimizu, MD; Tetsuya Tsuchida, MD; [et al](#)

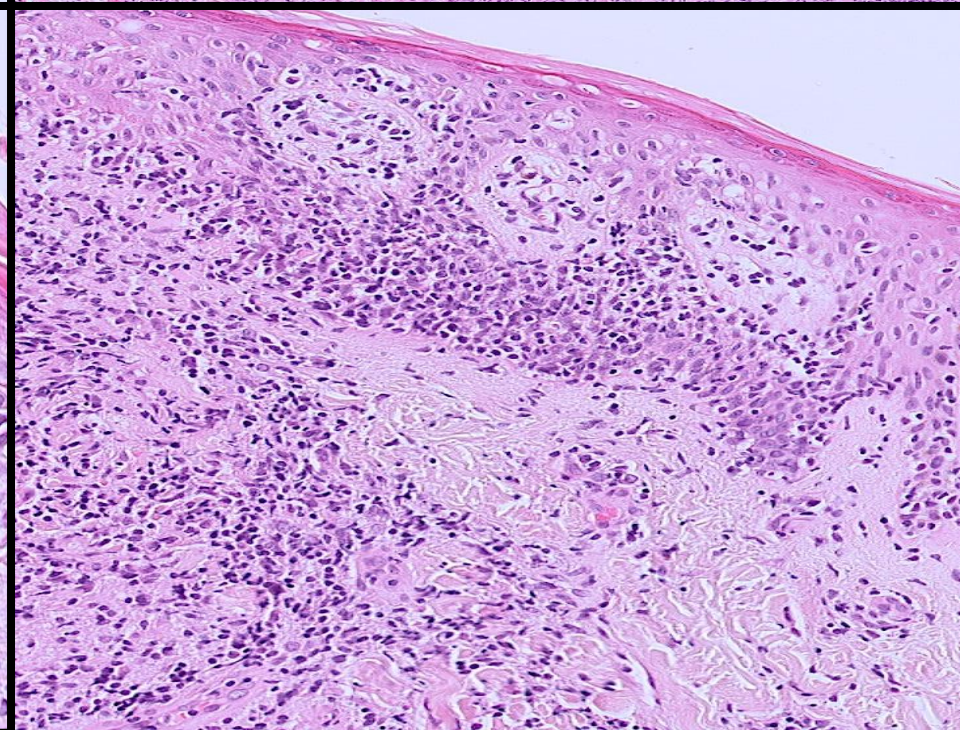
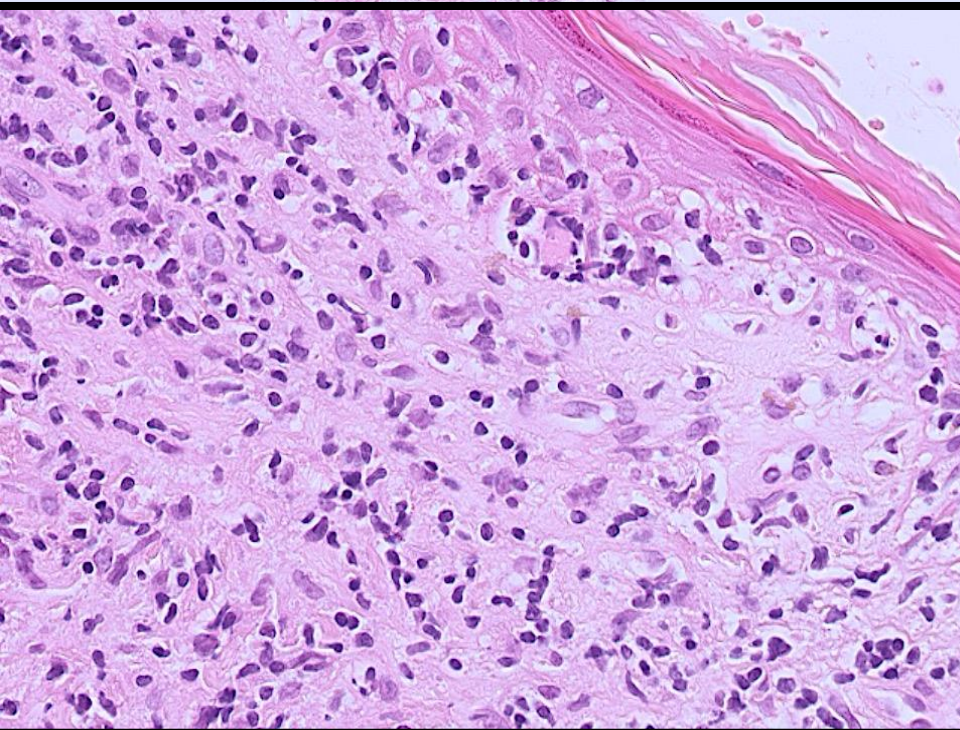
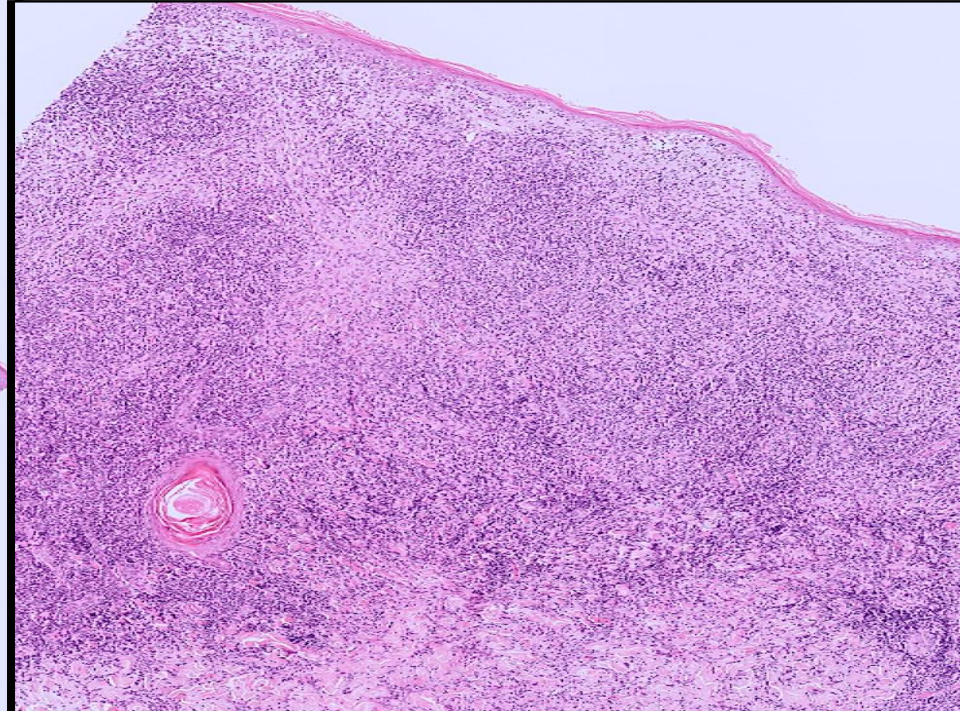
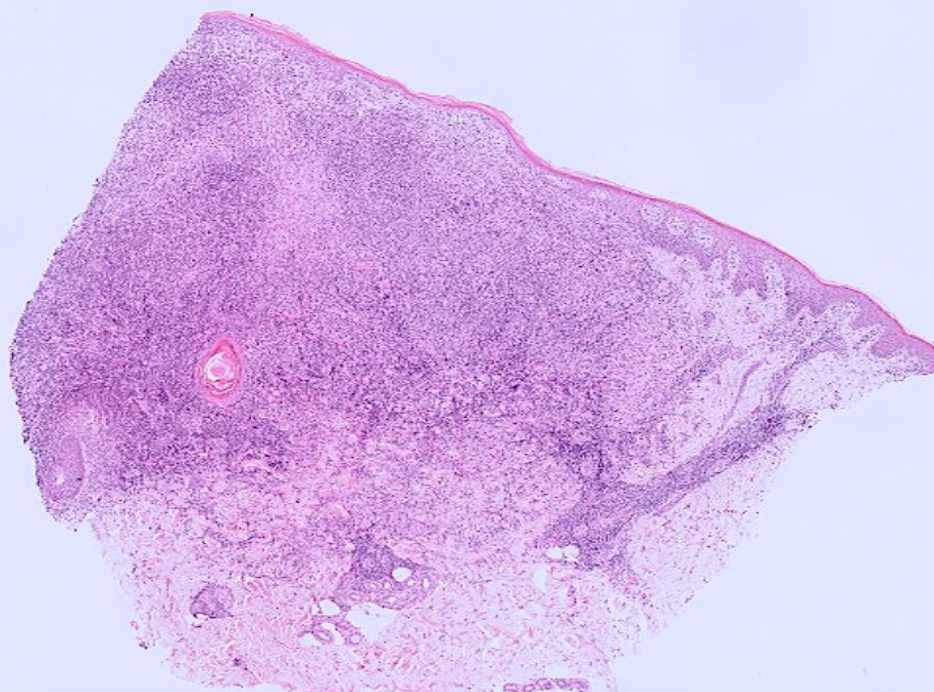
» [Author Affiliations](#) | [Article Information](#)

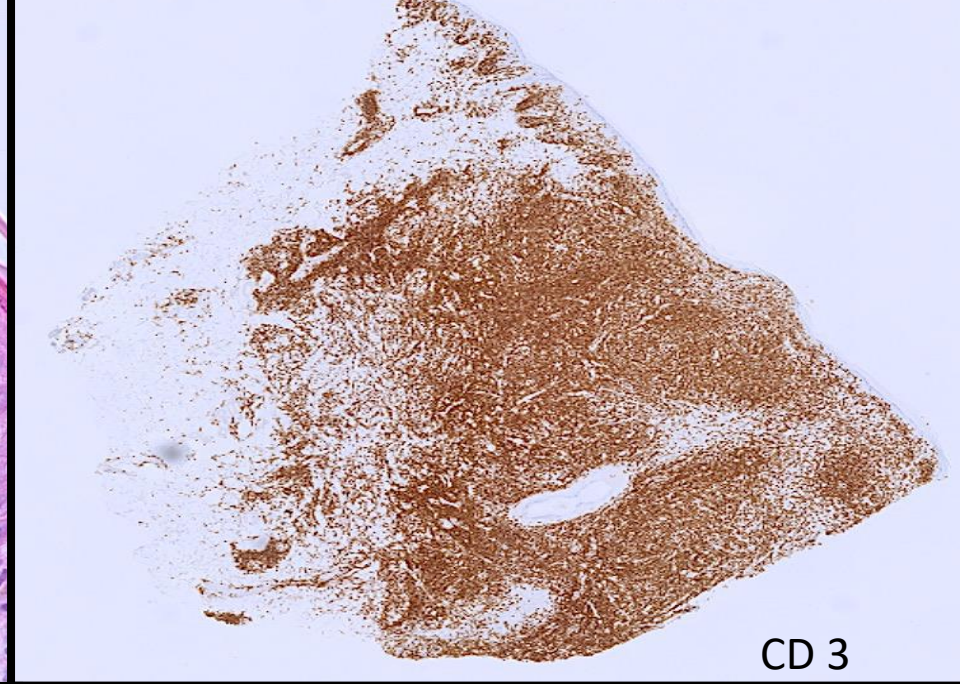
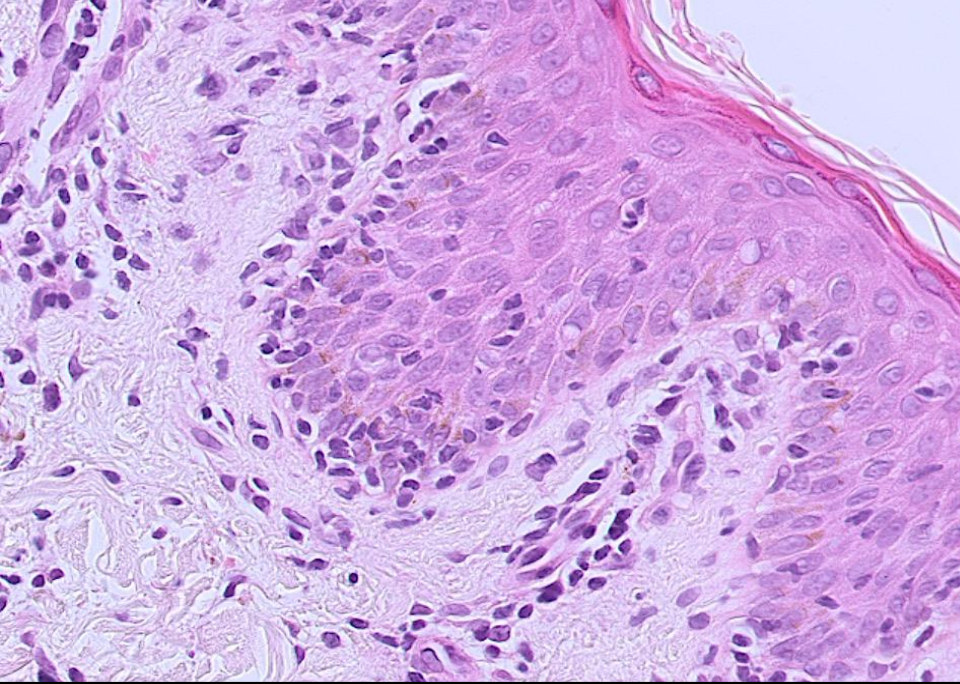
Arch Dermatol. 2007;143(1):53-59. doi:10.1001/archderm.143.1.53

The term *Lymphomatoid keratosis* was originally proposed by Kossard¹ and was thought to be a possible variant of benign lichenoid keratosis showing lymphomatoid features. He considered that the case reported by Evans et al² as a unilesional mycosis fungoides (MF) should be termed *lymphomatoid keratosis*. Clinically, the case reported by Evans et al² was characterized by an asymptomatic scaly plaque, but the histological features were those seen in MF. Therefore, the most important pathological feature of lymphomatoid keratosis is epidermotropism resembling that seen in MF.³ Namely, the term *lymphomatoid* in lymphomatoid keratosis indicates histological simulation of MF. It is noteworthy that the term *pseudolymphoma* was originally adopted to indicate a lesion clinically or histologically simulating malignant lymphoma. Therefore, the term *lymphomatoid* is considered to be equivalent to so-called pseudolymphoma.

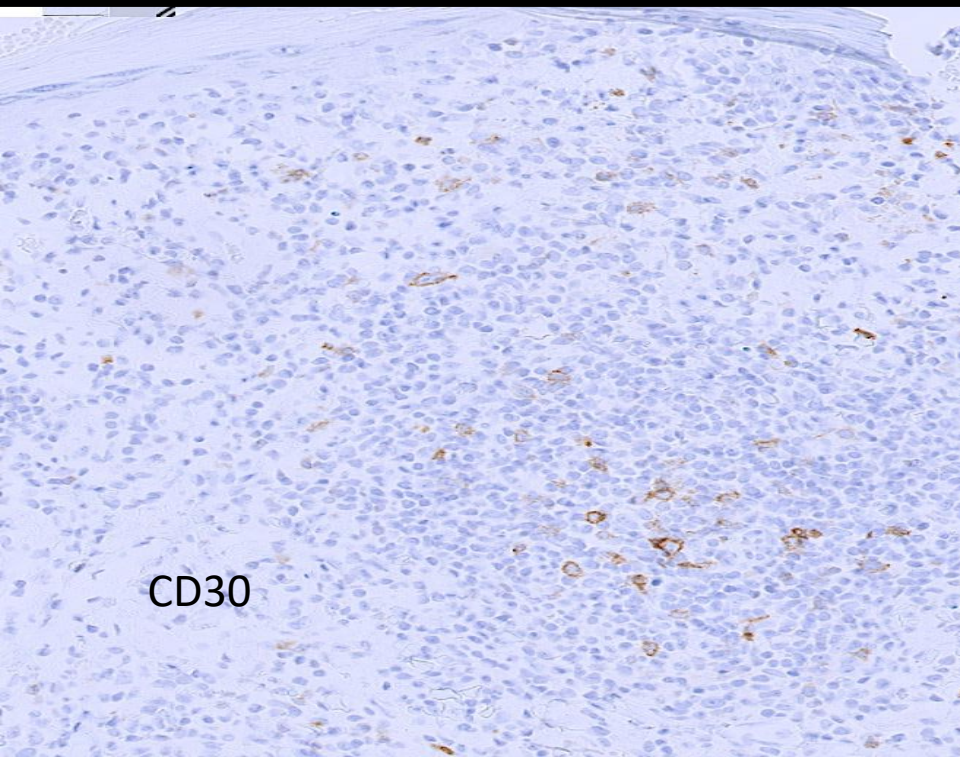
Case 11

- F 30
- Punch biopsy left wrist volar aspect
- ? diagnosis

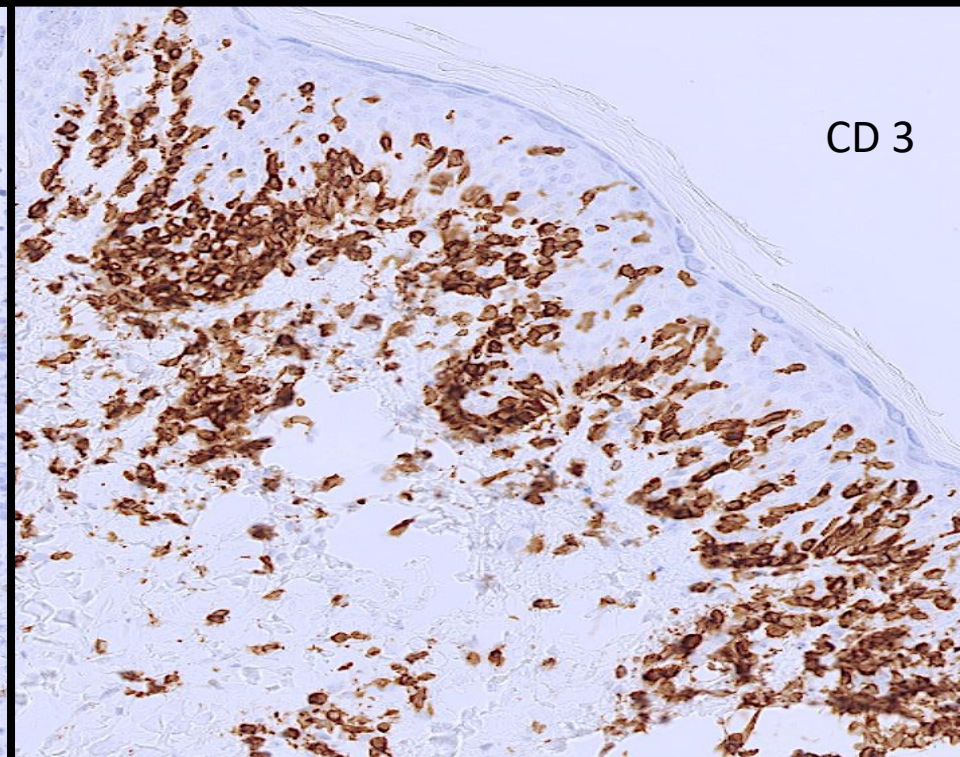




CD 3



CD30



CD 3

CD3+

CD20 occasional

CD30 occasional

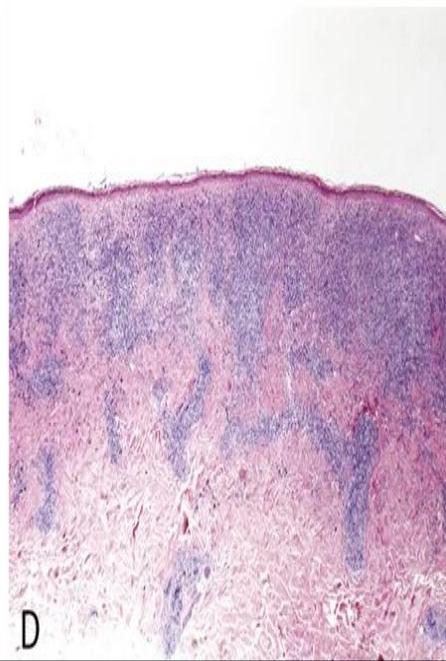
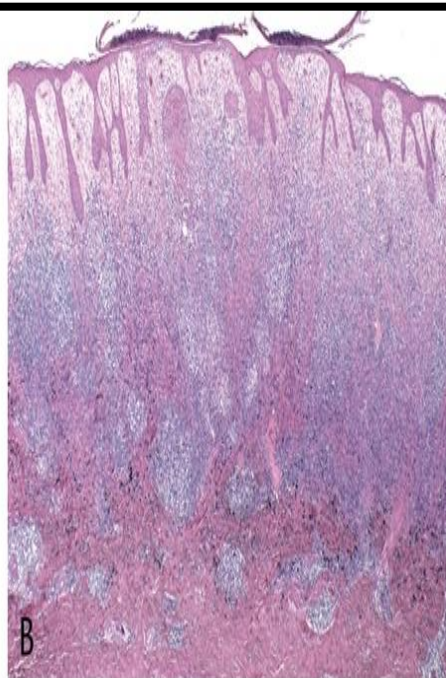
CD 8>CD4

CD5 no loss

CD7 partial loss

*Nodular pseudolymphomatoid reaction
to a tattoo*

Oedematous plaque within a tattoo.
Tattoo raised along entire red and black areas



CRITICAL REVIEW

Inflammatory Complications Related to Tattooing A Histopathological Approach Based on Pattern Analysis

Thum, Chee K. MBChB, MRCSEd, MRCOphth; Biswas, Asok MD, FRCPath, DipRCPath

[Author Information](#) ☺

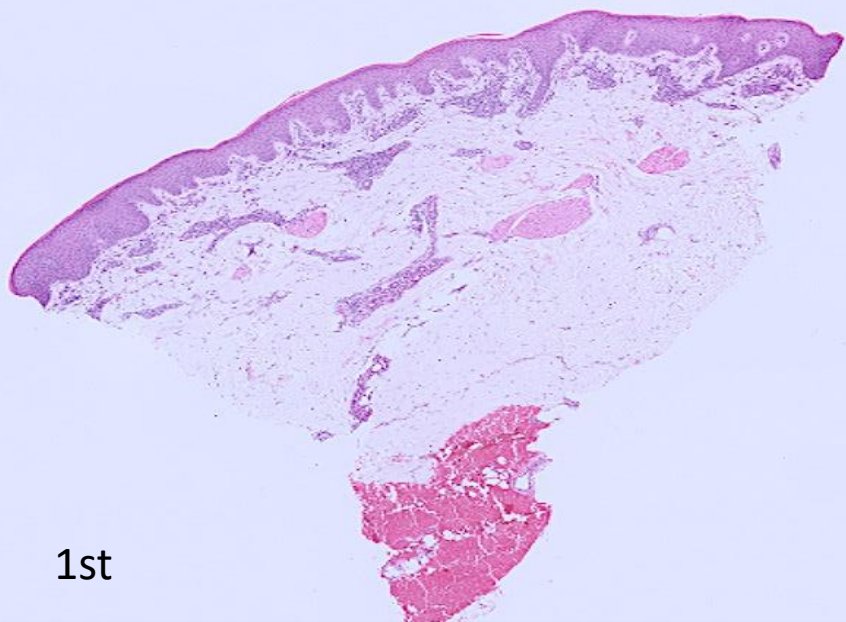
The American Journal of Dermatopathology; January 2015 - Volume 37 - Issue 1 - p 54-66

doi: 10.1097/DAD.0b013e3182974558

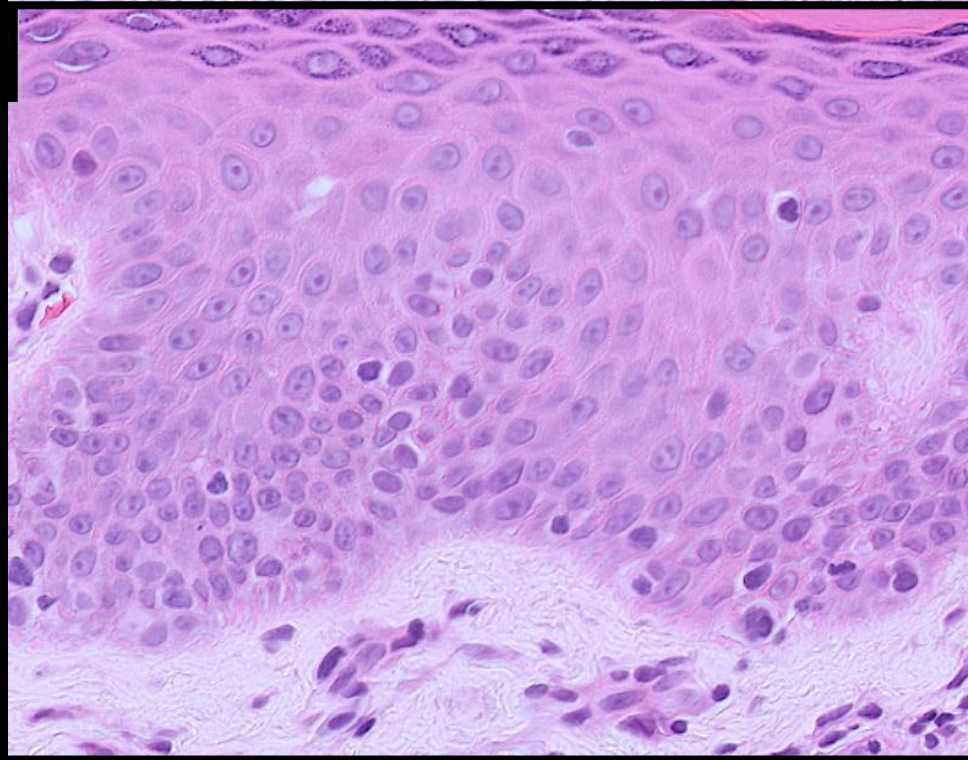
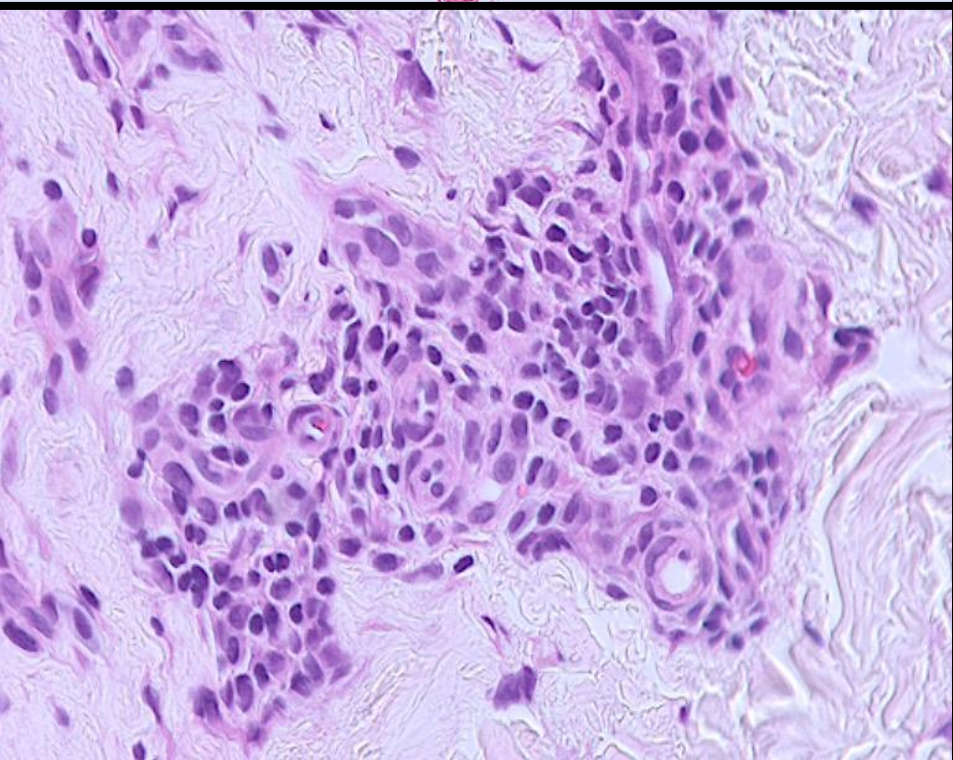
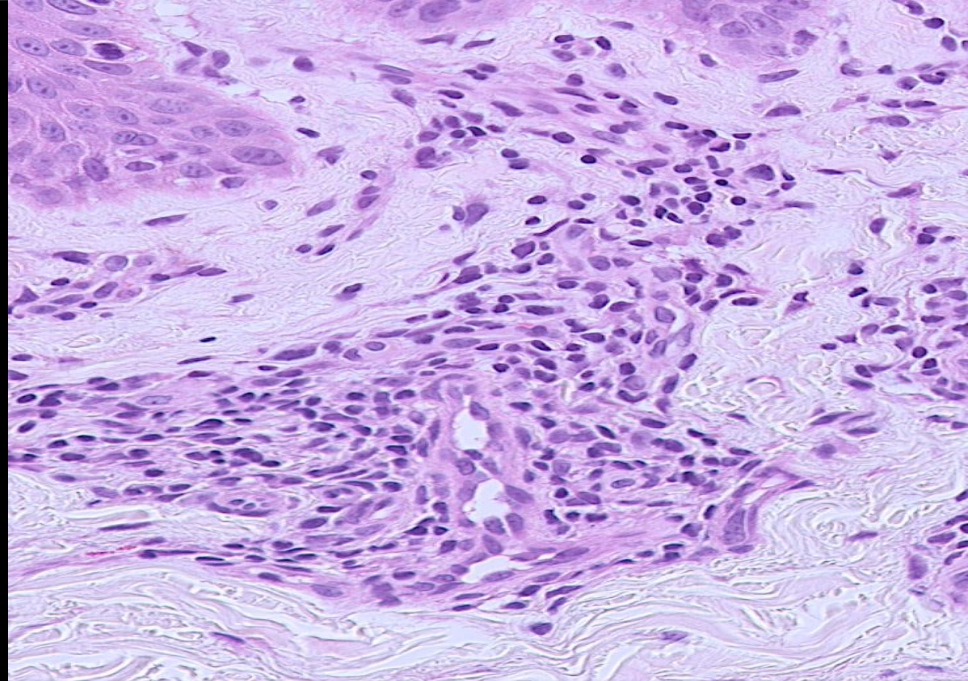
King, Brian & Lehman, Julia & Macon, William & Sciallis, Gabriel. (2017). Red Tattoo Related Mycosis Fungoides-like CD8 + Pseudolymphoma: Tattoo Related MF-like Pseudolymphoma. Journal of Cutaneous Pathology. 45. 10.1111/cup.13089.

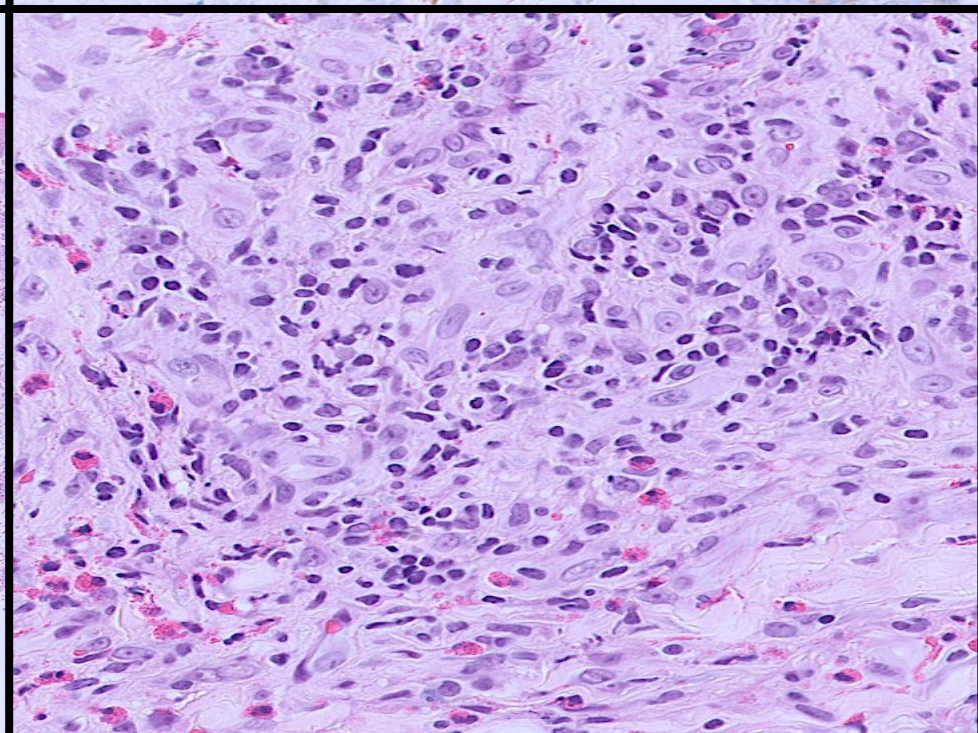
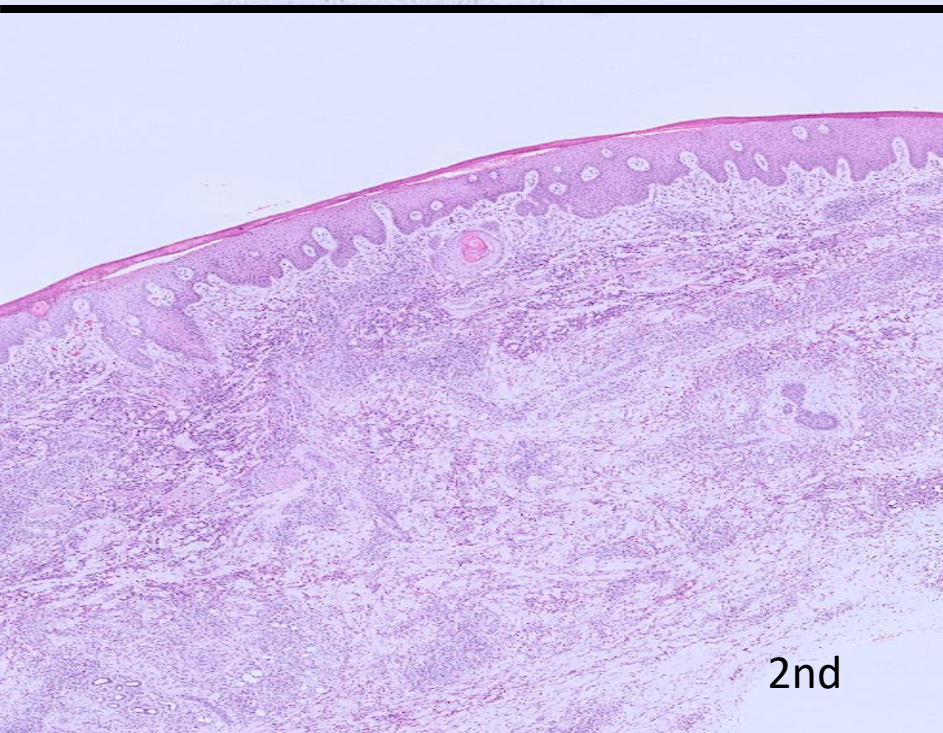
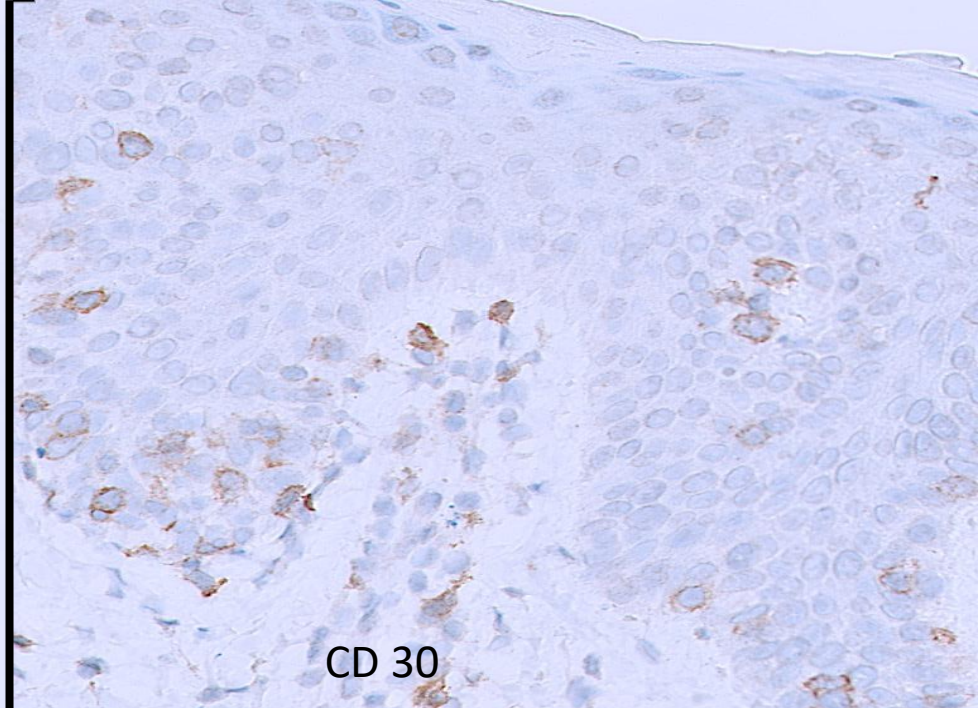
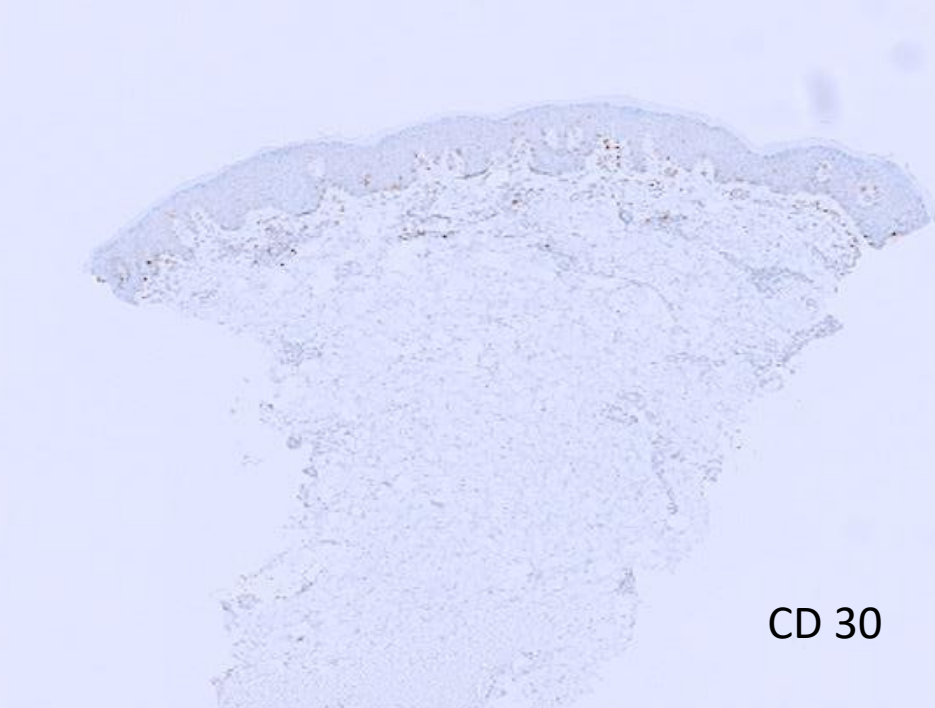
Case 12

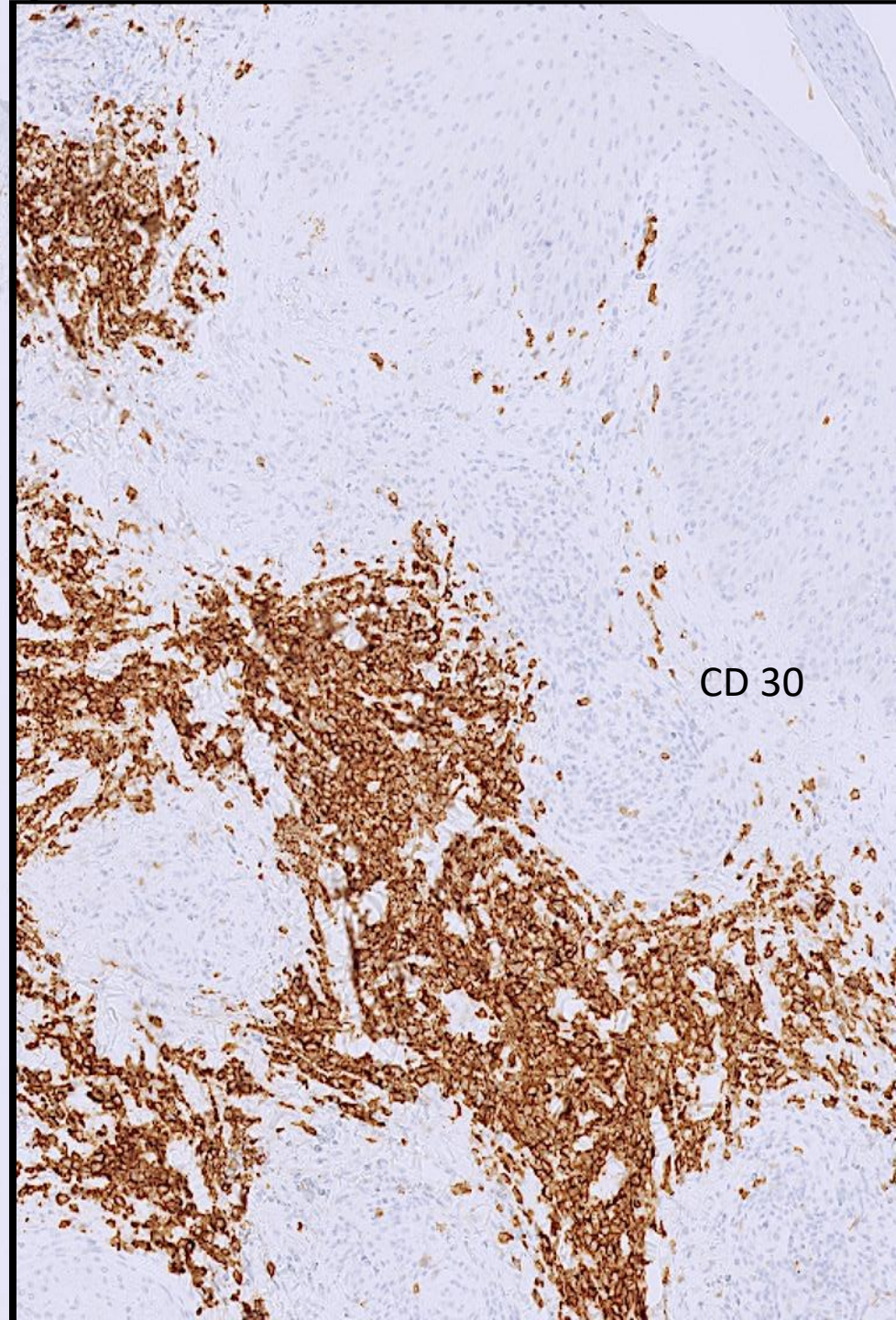
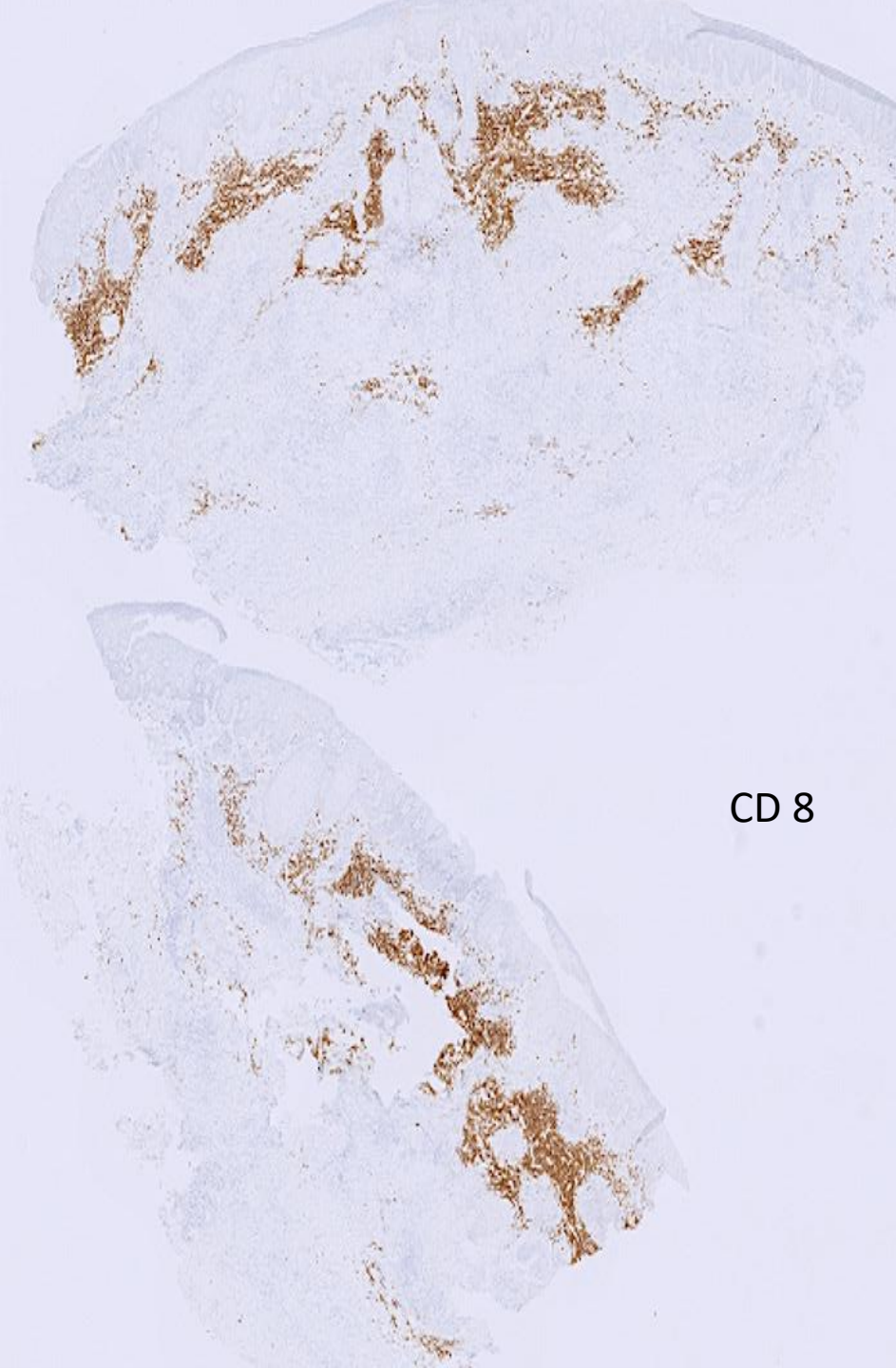
- M 45
- H/O Hodgkin's lymphoma
- Developed a plaque on the central forehead, nodules elsewhere and a maculo-papular rash.



1st







CD 30+

Loss of CD2, 3, 5 and 7

CD 8+

CD 4 negative

CD 20 negative

ALK-1 negative

TCR-PCR negative

- Atypical T cell lymphoid infiltrate
- *Mycosis fungoides and a nodule in transformation.*
- Unusual for MF to present as a maculo-papular rash.
- *Systemic lymphoma involving the skin.*
- More history!
- Several lesions have resolved. Unusual for transformed MF.
- **Nodular lesions-lymphomatoid papulosis and rash mycosis fungoides.**
- **Type D LyP**

Cutaneous Lymphomas: An Update. Part 1 T-Cell and Natural Killer/T-Cell Lymphomas and Related Conditions

Kempf, Werner MD^{*,†}; Kazakov, Dmitry V. MD, PhD[‡]; Kerl, Katrin MD[§]

[Author Information](#) 

The American Journal of Dermatopathology: February 2014 - Volume 36 - Issue 2 - p 105-123
doi: 10.1097/DAD.0b013e318289b1db

Lymphomatoid Papulosis Type D: A Newly Described Variant Easily Confused With Cutaneous Aggressive CD8-Positive Cytotoxic T-Cell Lymphoma

Cardoso, Jose MD^{*}; Duhra, Parmjit MD[†]; Thway, Yi MD[‡]; Calonje, Eduardo MD^{*}

[Author Information](#) 

The American Journal of Dermatopathology: October 2012 - Volume 34 - Issue 7 - p 762-765
doi: 10.1097/DAD.0b013e31825ba953

Take home message

- Epidermotropism can be seen in a variety of benign and neoplastic proliferations
- Clinical information paramount importance!
- Extensive CPC.
- Careful evaluation of histology, levels.
- Immunohistochemistry.
- TCRPCR.
- No rush to make diagnosis of MF
- In the evaluation of a new patient without a pre-existing diagnosis of MF, a multidisciplinary approach.
- A second biopsy!

An electron micrograph showing cellular ultrastructure. A large, dark, oval nucleus is prominent on the left. To its right, there are several smaller, oval mitochondria with visible internal cristae. The surrounding cytoplasm is filled with various organelles and a network of membranes.

Arti Bakshi
Regional Cutaneous Lymphoma Team @LUH

THANK YOU