

# THE SPECTRUM OF CD8+ CTCL

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# MF CD8+

ERYTHEMATO-SQUAMOUS  
PATCHES AND PLAQUES,  
USUALLY LOCALIZED LESIONS

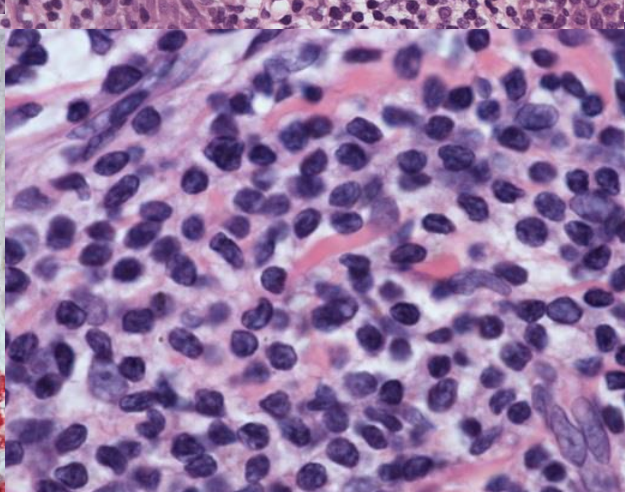
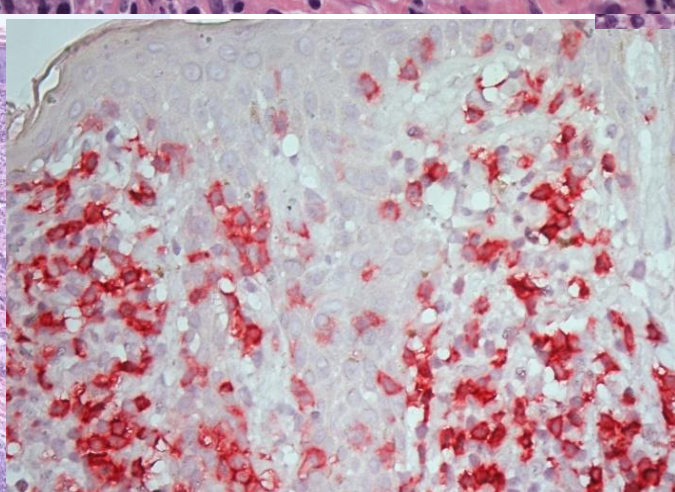
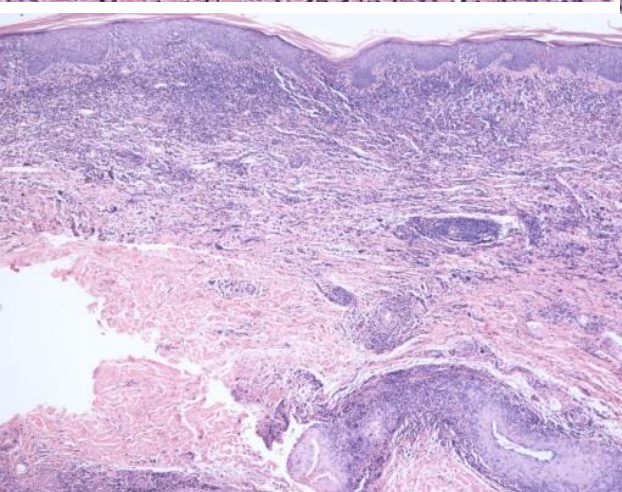
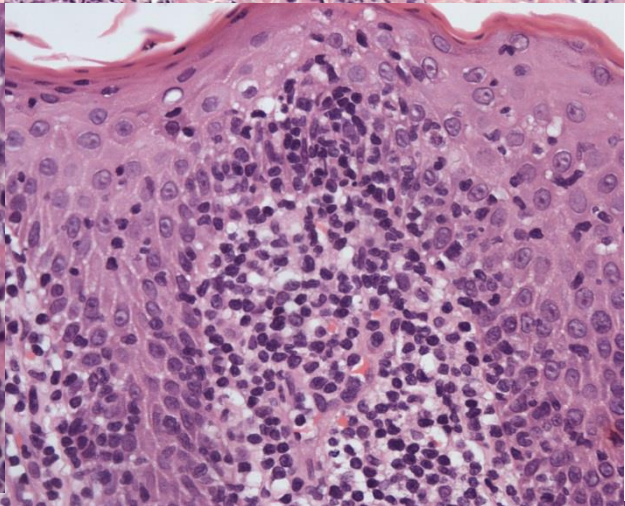
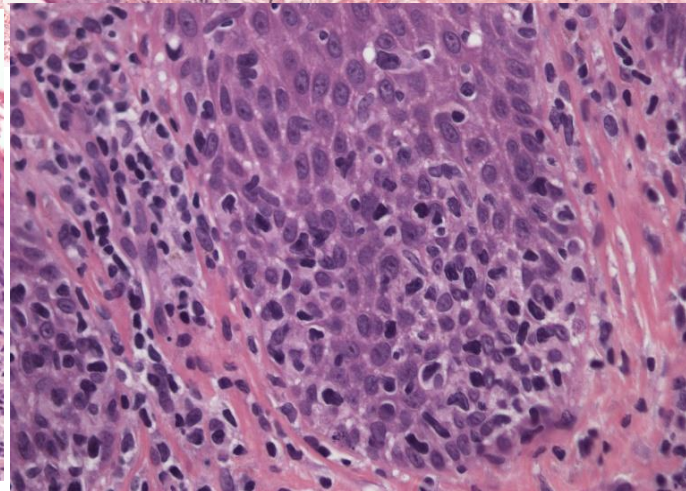
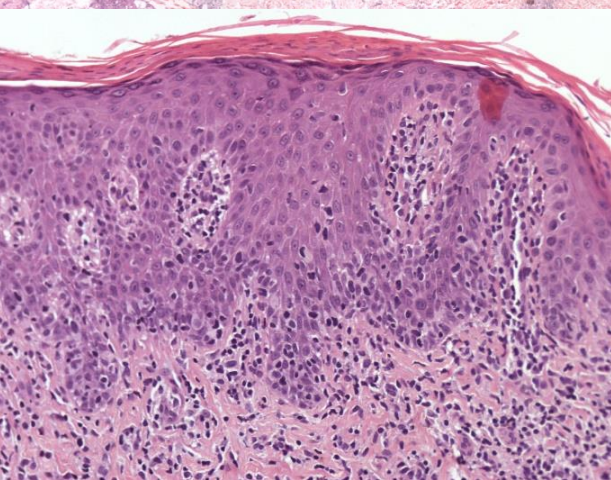
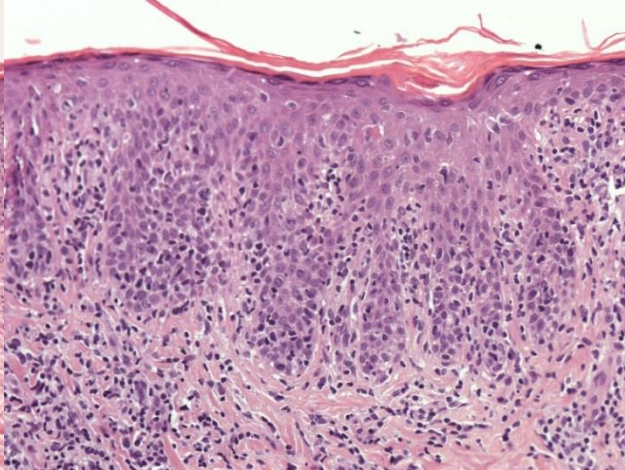
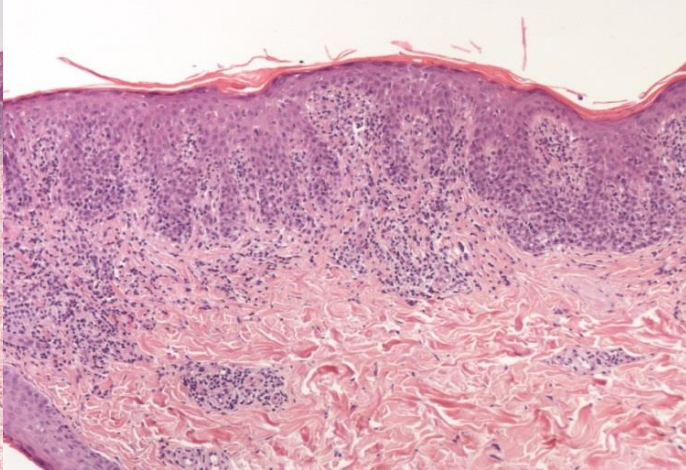
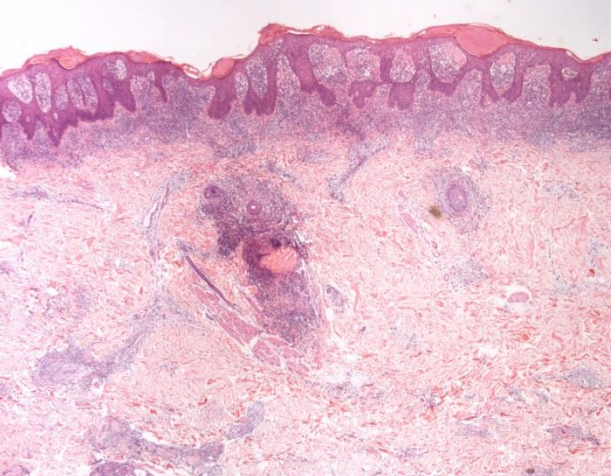
LYMPHOID INTRAEPITHELIAL  
(PAGETOID) AND/OR LICHENOID  
INFILTRATE WITH A VERTICAL  
EPIDERMOTROPISM

SPECIFIC IMMUNOPHENOTYPE:  
CD3+, **CD8+**, **CD5+/-**, CD7,  
CD103-, **CD45RA+/- (E)**,  
CD45RO+/- (D) **TIA-+**.

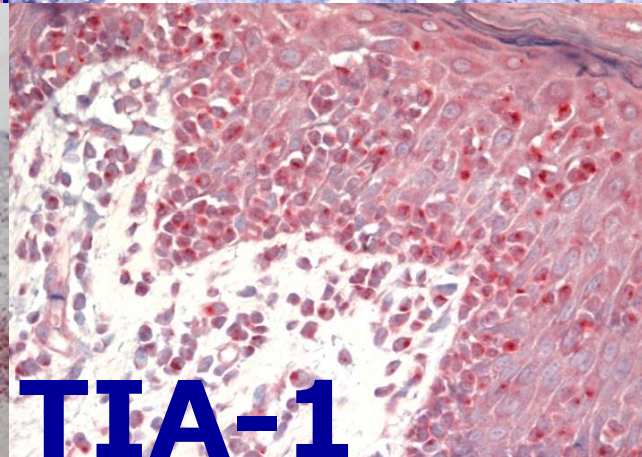
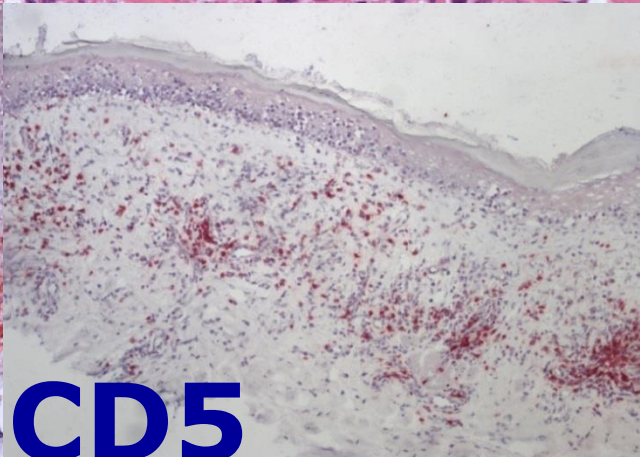
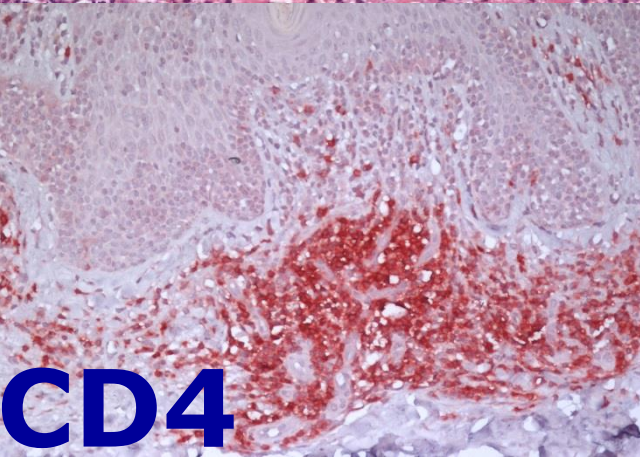
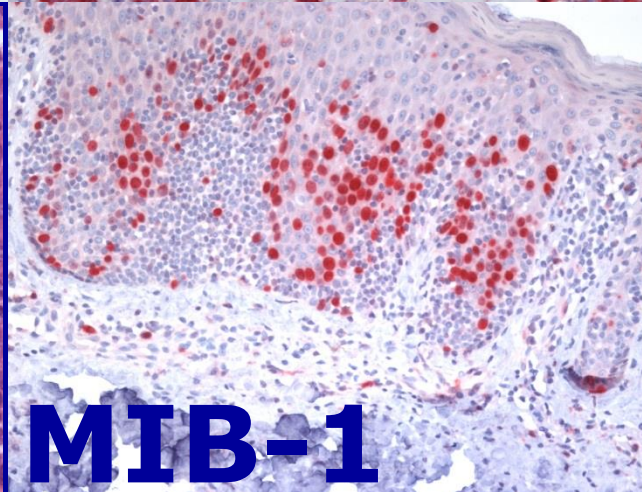
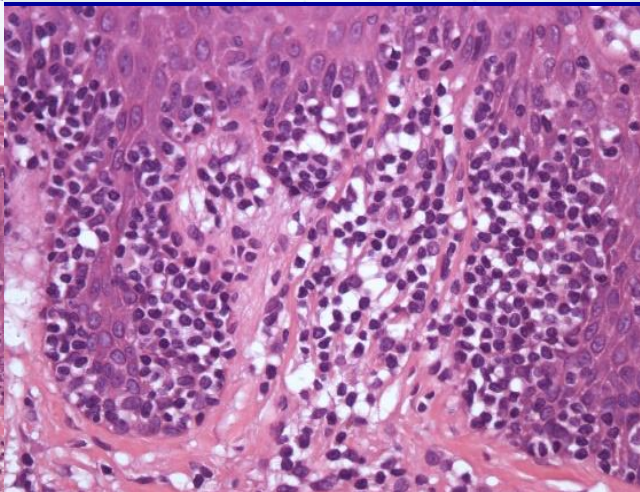
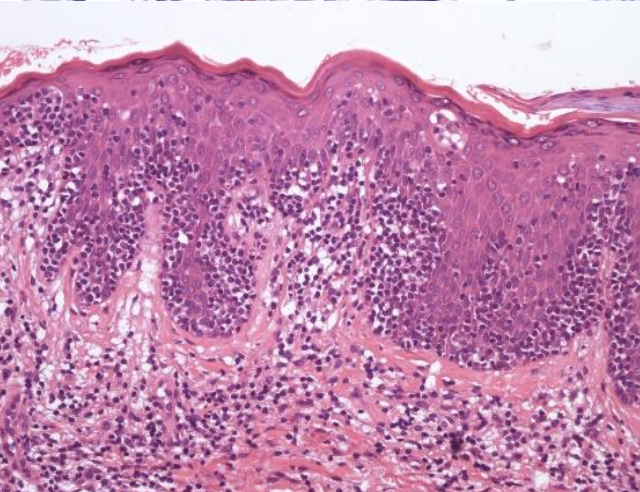
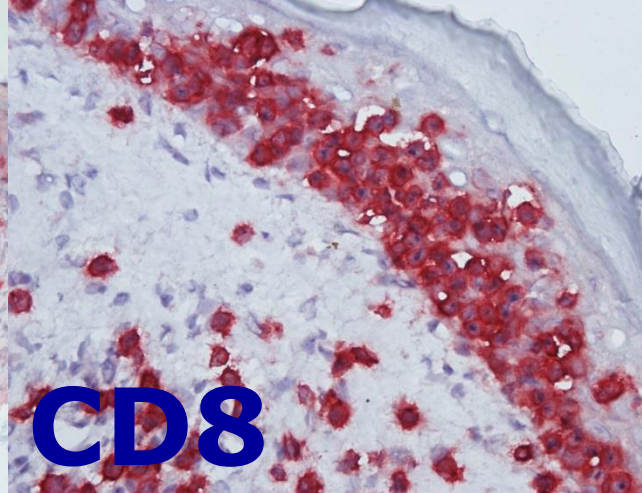
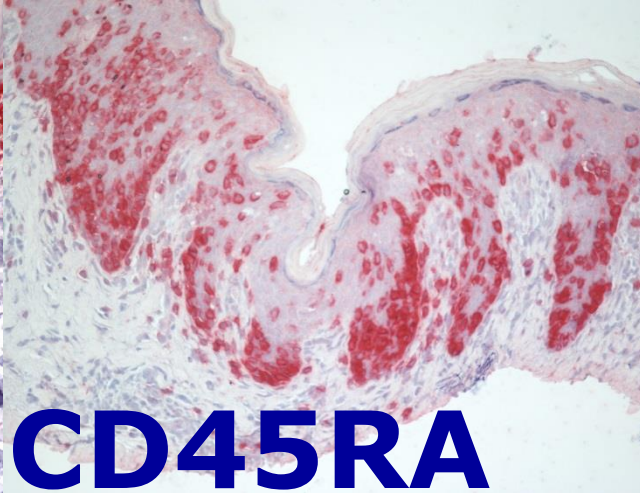
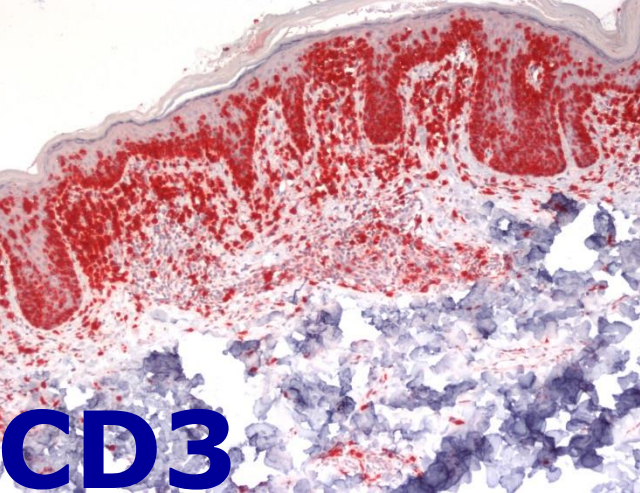
NO DIFFERENCES IN TREATMENT  
AND EVOLUTION FROM CLASSIC  
CD4+ MF



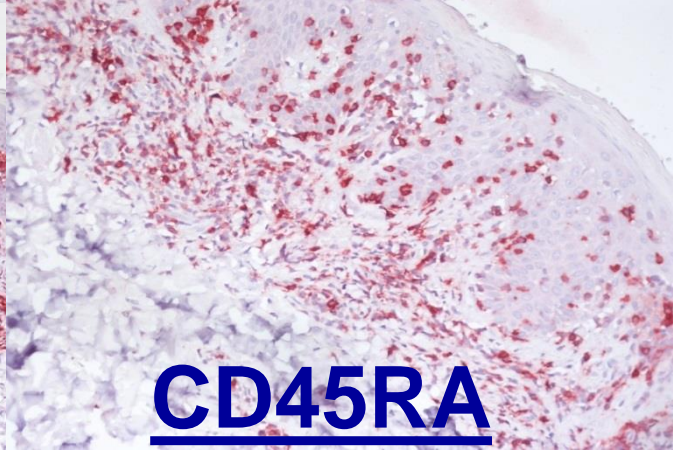
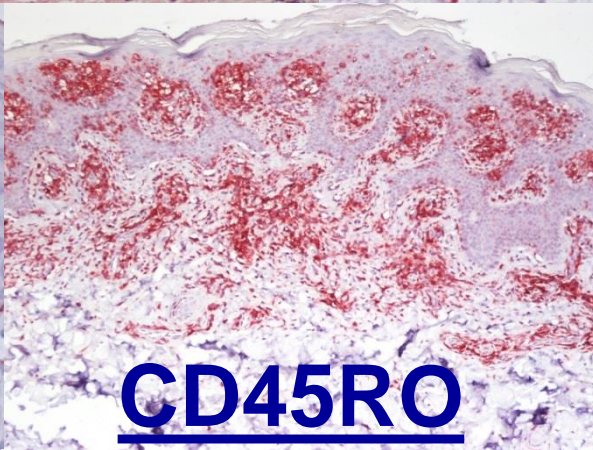
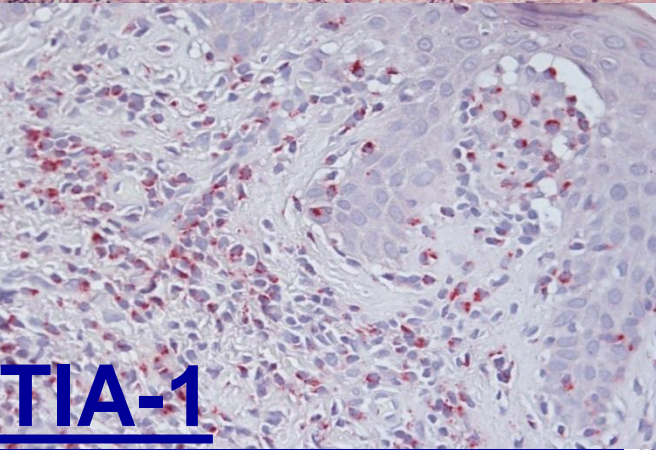
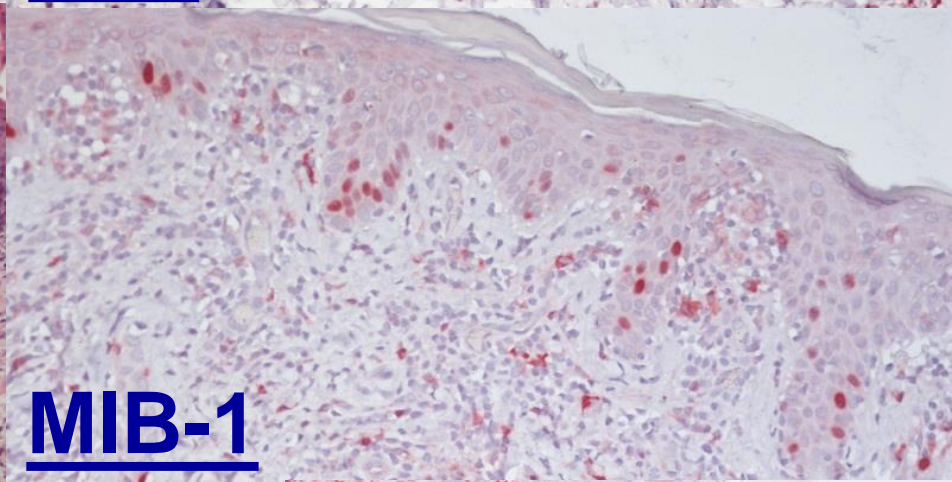
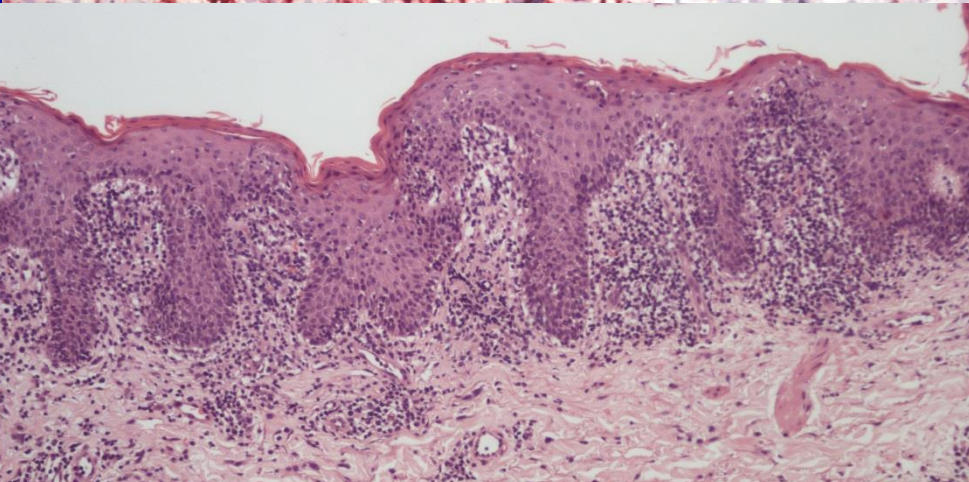
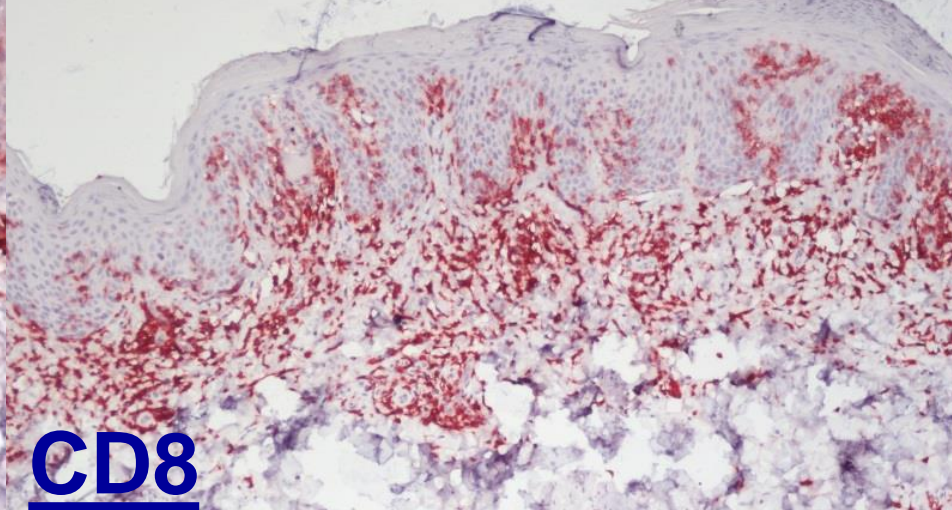
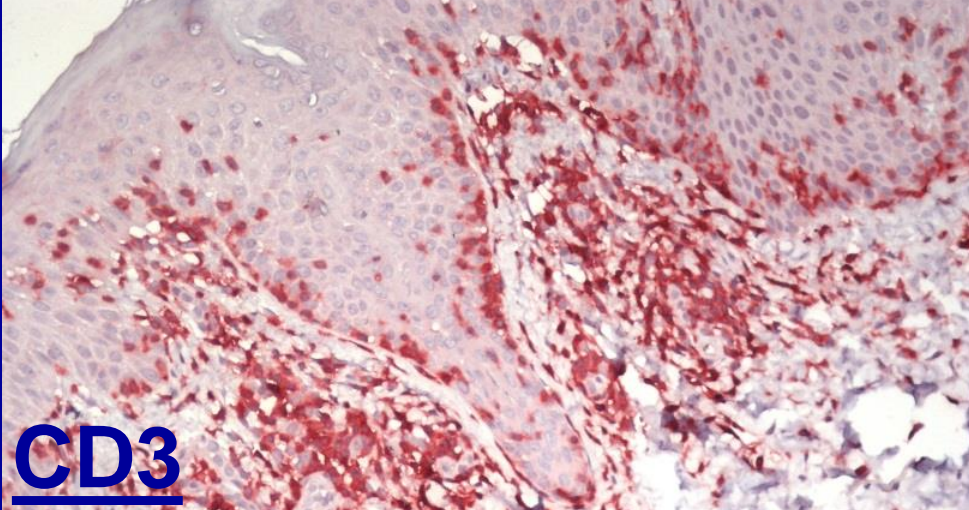






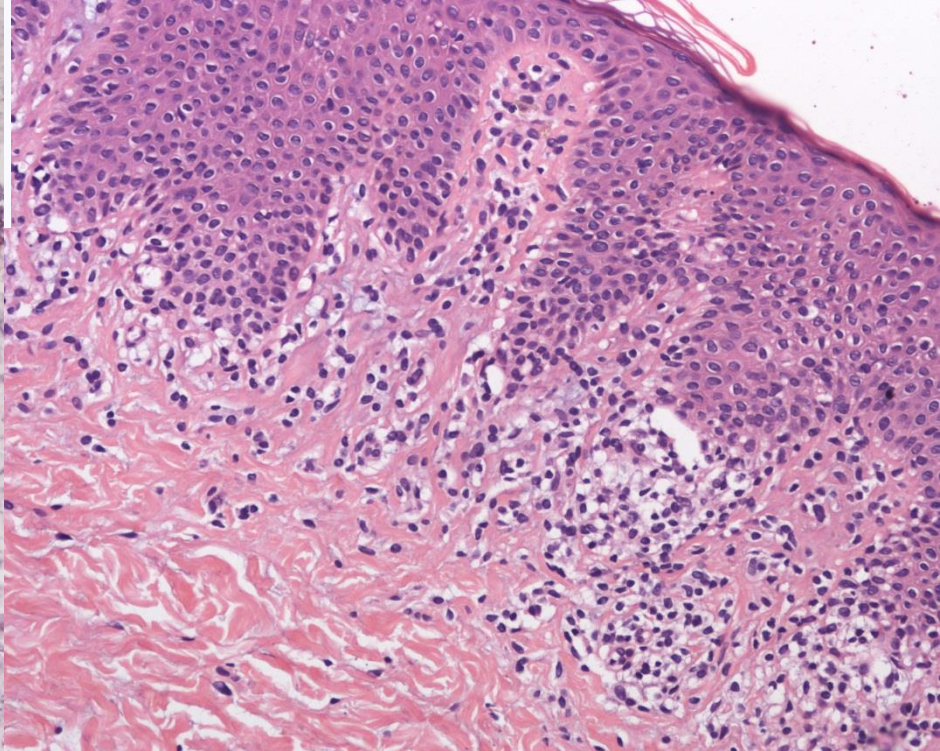
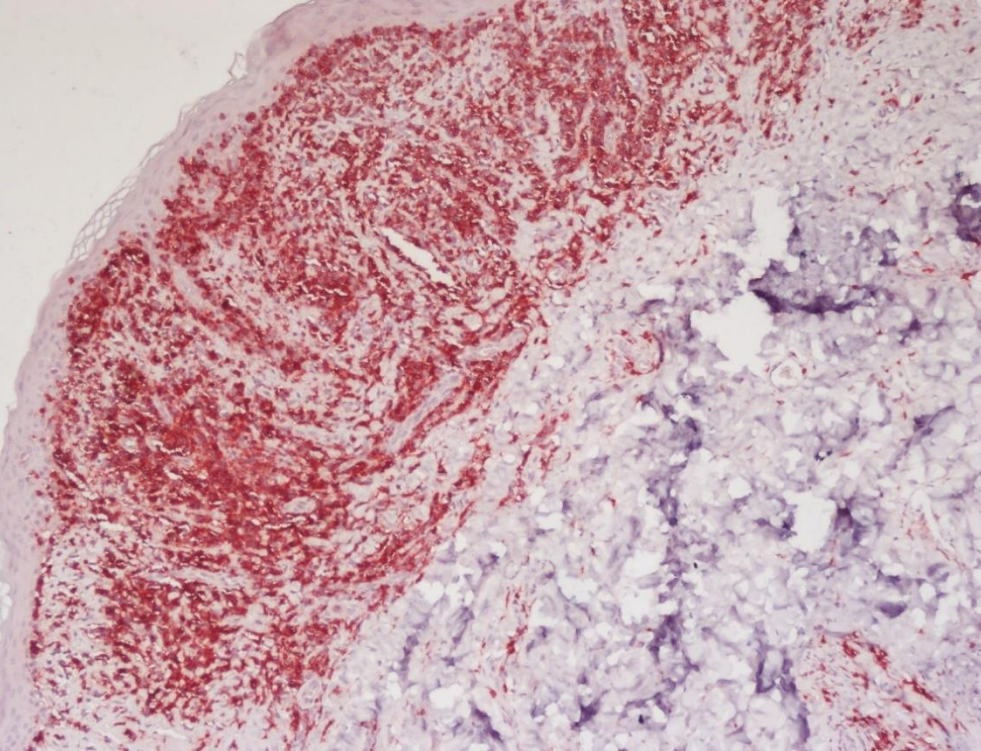
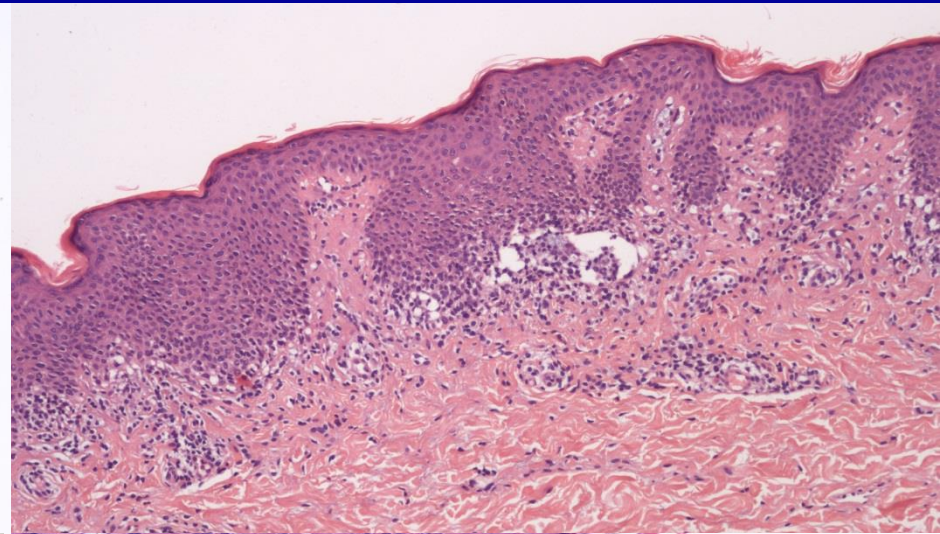
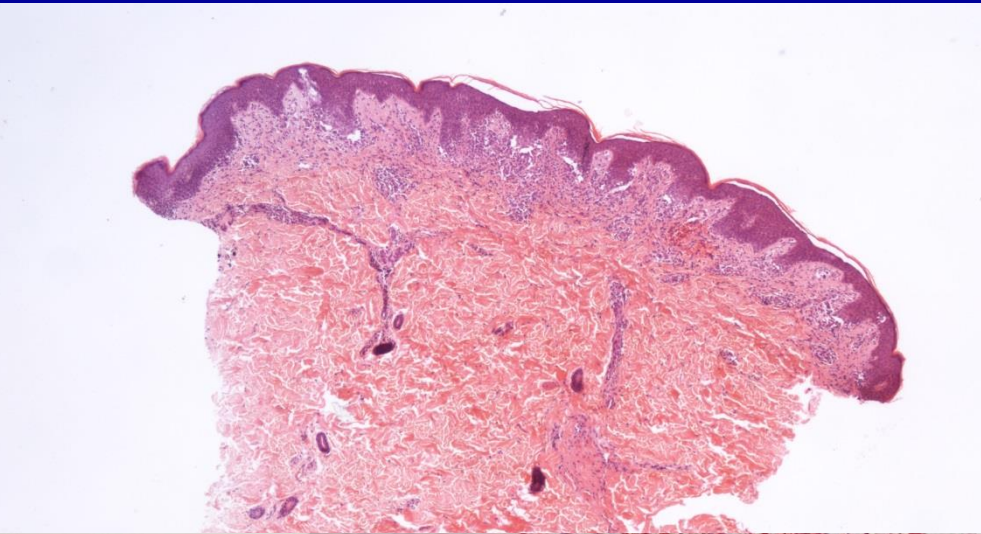




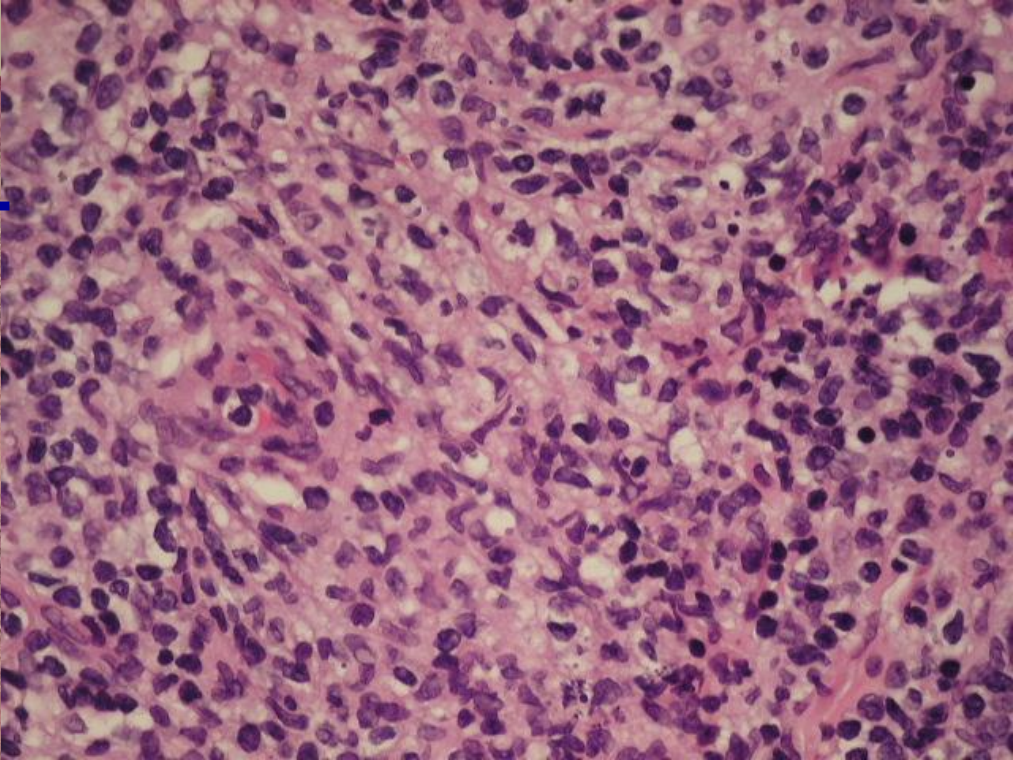
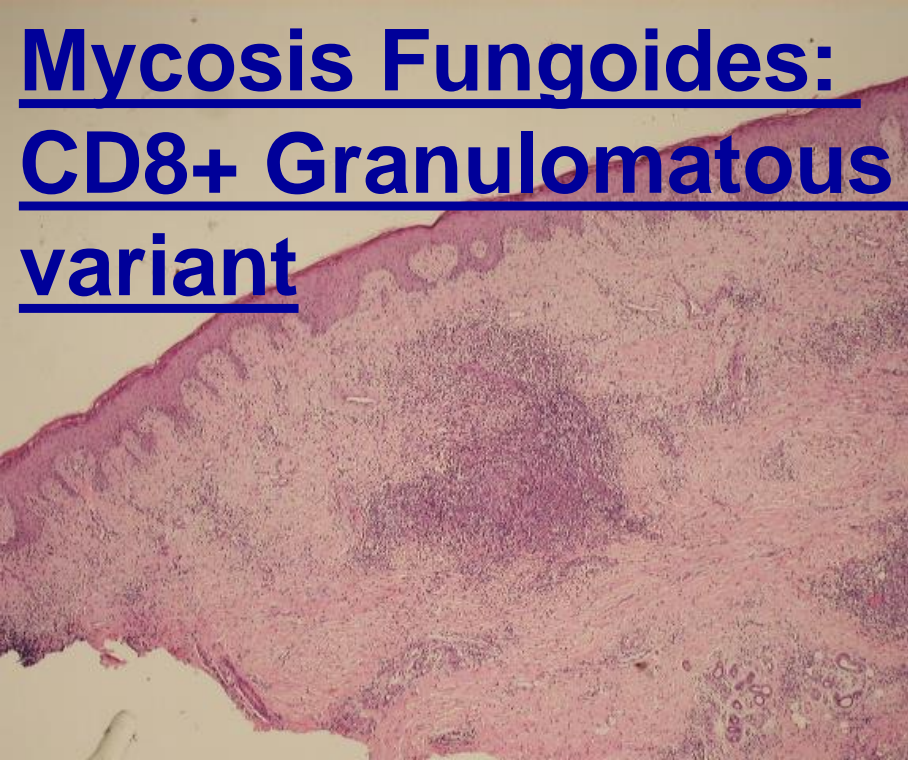
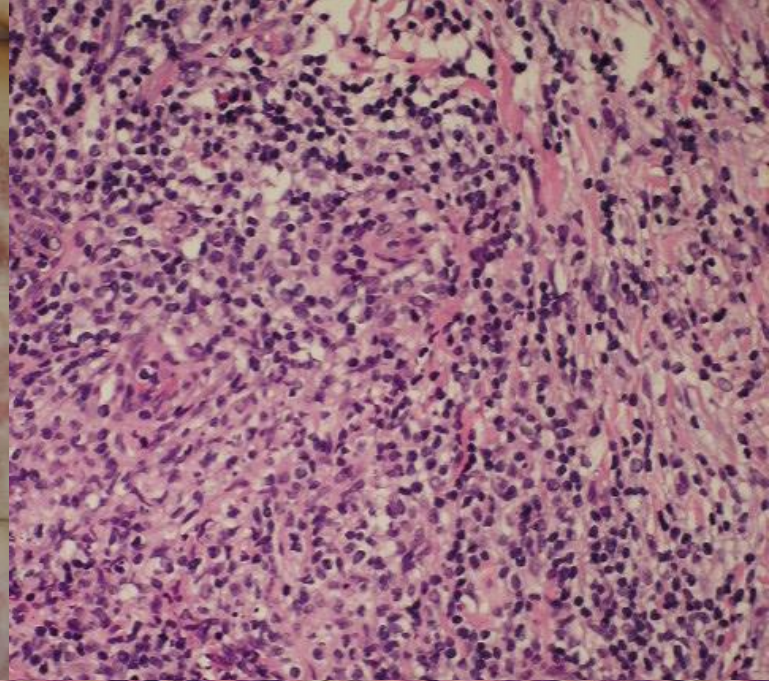




# MF/PARAPSORIASIS IN CHILDREN CD8+

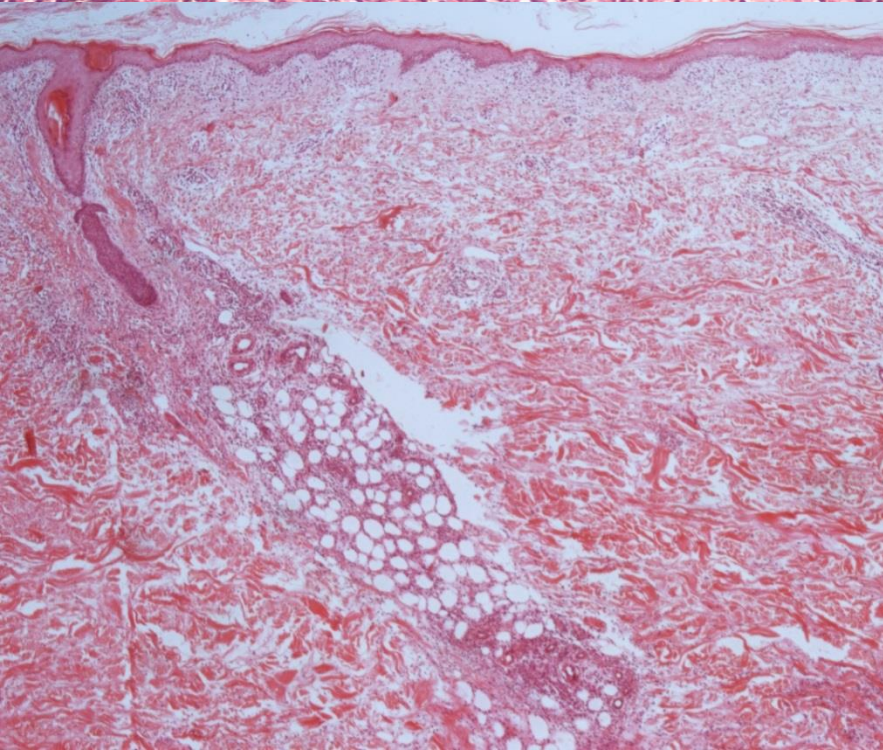
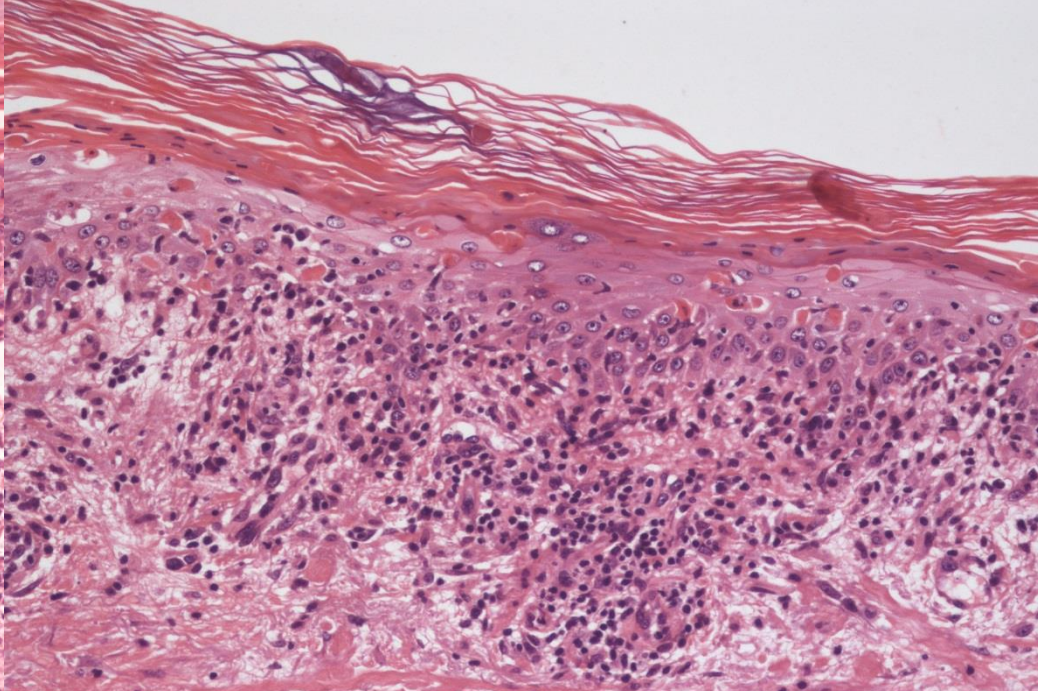
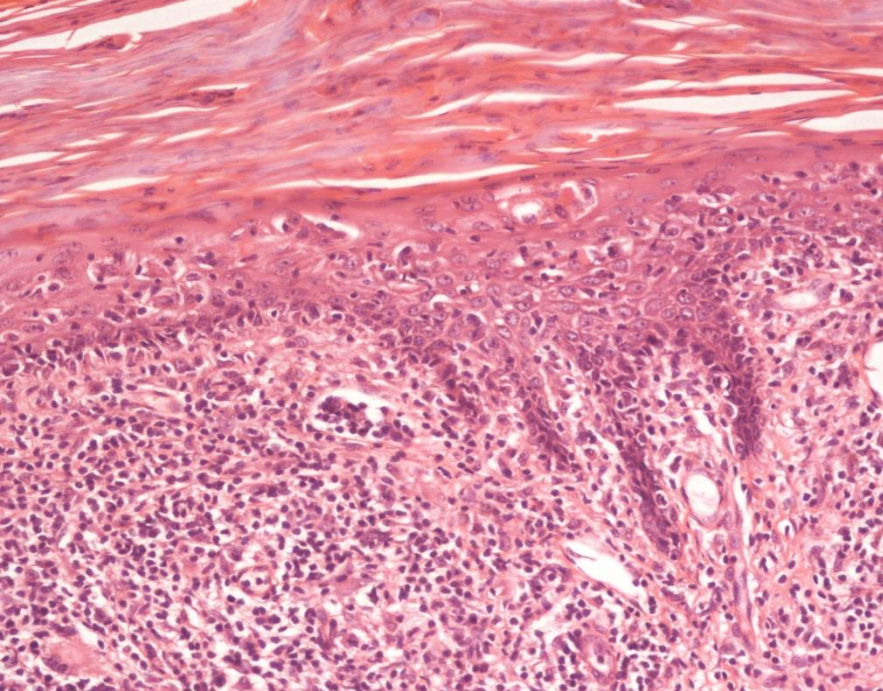






**Mycosis Fungoides:**  
**CD8+ Granulomatous**  
**variant**

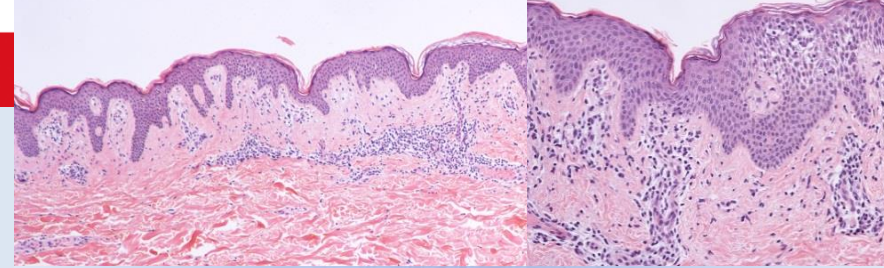




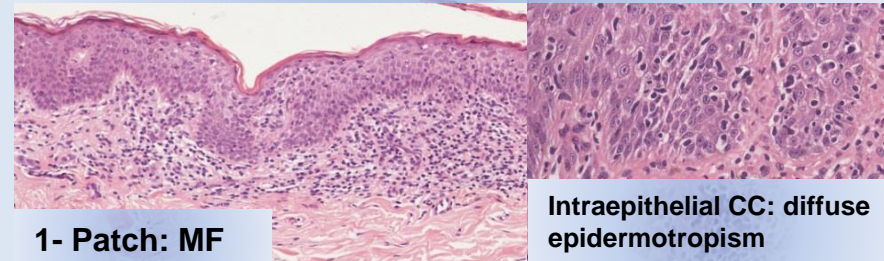


# MF - Histopathology

1. In patch stage, histopathologic findings are minimal and variable. Cerebriform cells (CC) in the dermis are less than 20-30%, while single epidemotropic CC may be observed in the epidermis in absence of spongiosis. Psoriasiform, eczematoid or pagetoid like patterns are more frequently observed.
2. With disease progression, there is a significant increases in number, proliferation and epidemotropism of CC, forming lymphoid collections (Pautrier's microabscesses), with cellular atypia, epidermal hyperplasia, fibroplasia of the superficial dermis (eosinophils and plasmocytes may be seen).
3. In tumor stage, the infiltrate shows nodular characteristics and then diffuse ones. T-cells become roundish, pleomorphic, larger, and there is loss of epidemotropism (in absence of detectable CC).
4. Large cell transformation (**WORSENING OF PROGNOSIS**)
5. MF: CD8 variant, keratinocyte's necrosis, peculiar vertical epidemotropism (see Figs. 5a, b, c).

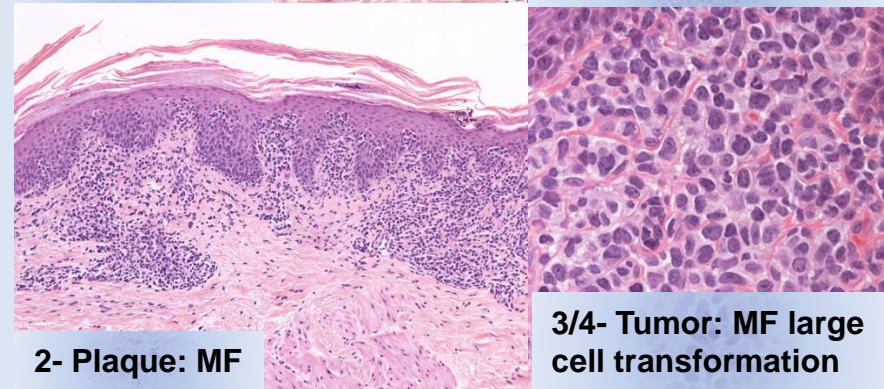


1- Patch: «parapsoriasis» the infiltrate is parallel to epidermis, focal epidemotropism and spongiosis.



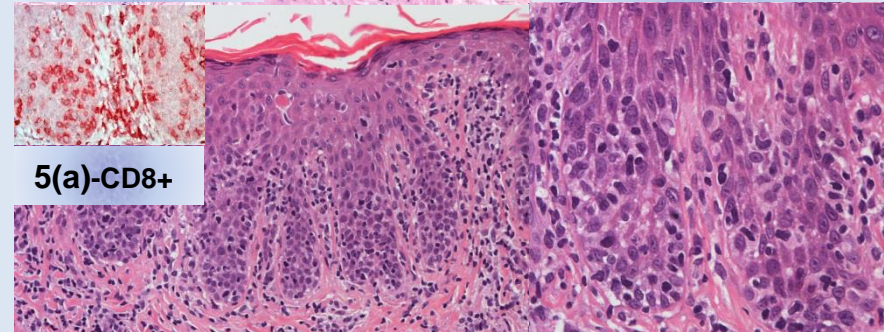
1- Patch: MF

Intraepithelial CC: diffuse epidemotropism



2- Plaque: MF

3/4- Tumor: MF large cell transformation



5(a)-CD8+

5(b)-CD8+ MF, psoriasiform-lichenoid pattern, note «vertical» epidemotropism through epithelial sheet and papillary vessels

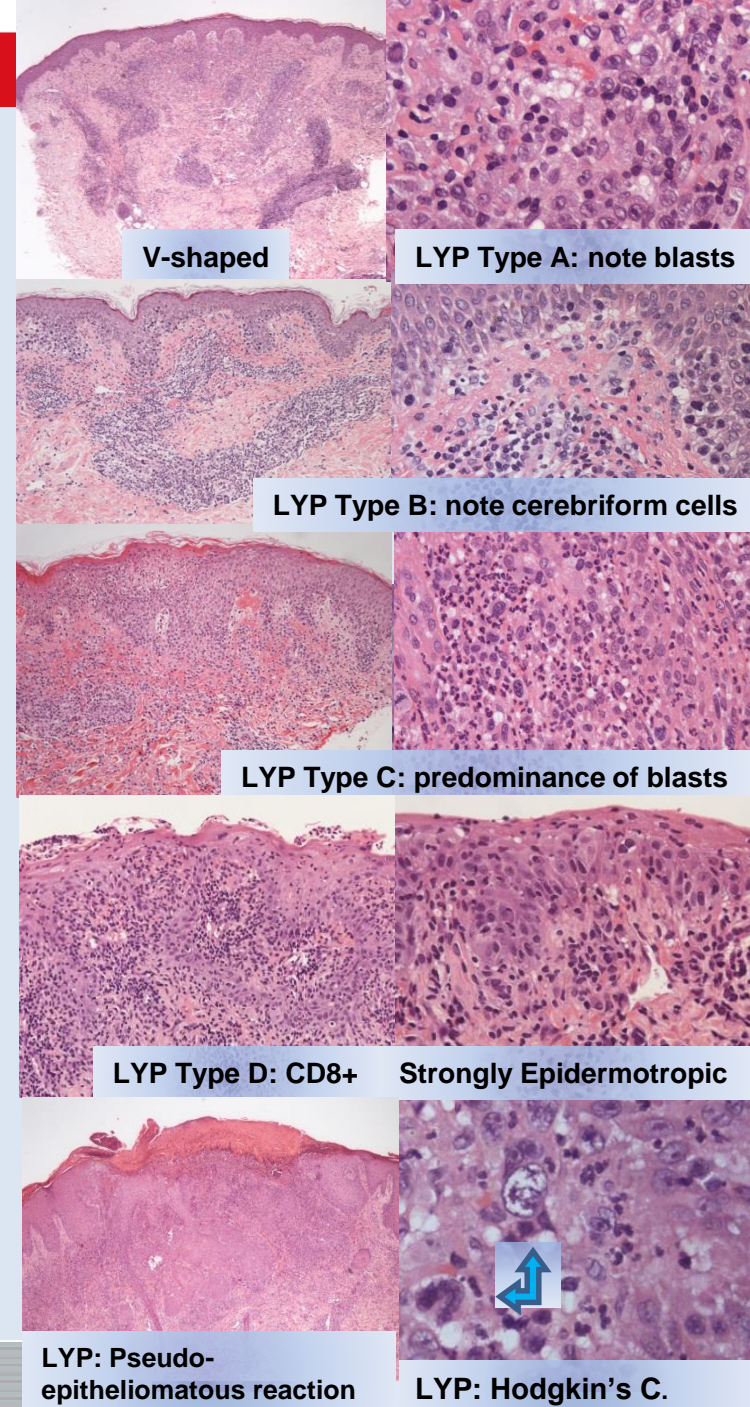


# LYP-Type:

## Histopathology.

A V-shaped lymphoid infiltrate, with scattered or groups of perivascular-interstitial CD30+ blasts, mixed with many inflammatory cells (macrophages, eosinophils, neutrophils). According to this histo-architectural pattern and immunoprofile 4 subtypes of LYP are actually recognized: type-A (classic pattern); type-B (epidermotropic, MF-like); type-C (ALCL-like); type-D (CD8+, AECL-like). This sub-classification has not prognostic relevance. Recently the chromosomal rearrangement of DUSP22-IRF4 locus was found in a series of LYP with localized lesions simulating a low grade epithelial tumour.

**Immunophenotype.** Type-A/C: CD3+/CD4+/CD5+/CD25+/CD30+/Ki-67+/MUM-1+/-/TIA1/GRB/PERF+/-/ALK-1-. Type-B: neoplastic cells may be CD4 or CD8. Type-D cells express CD8+ and other cytotoxic markers. **Molecular Biology.** Clonal rearrangement of the TCR $\gamma$  in 50% of cases; absent t(2;5)(p23;q35).



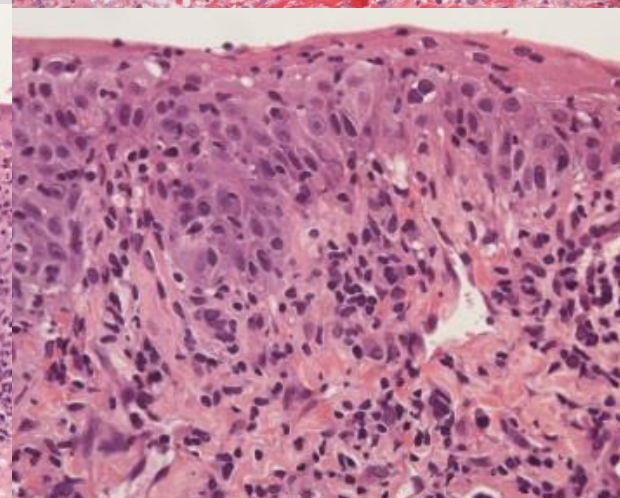
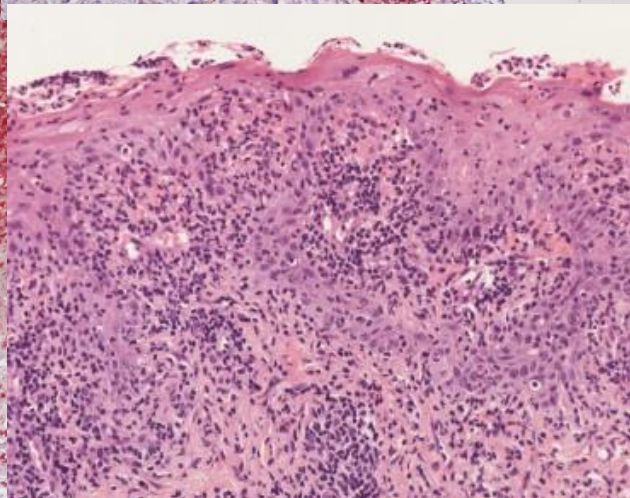
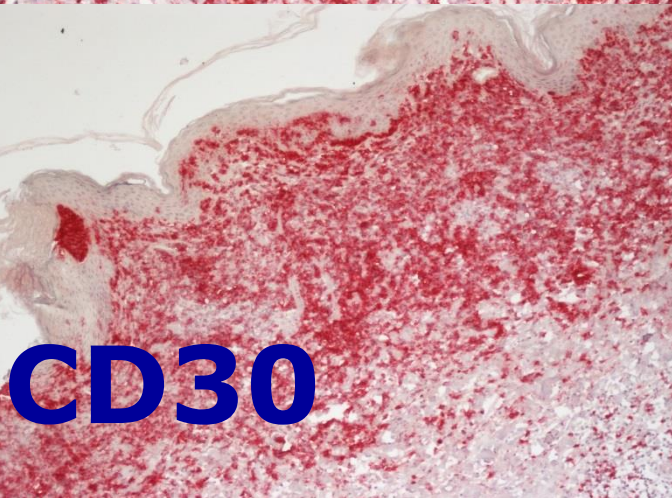
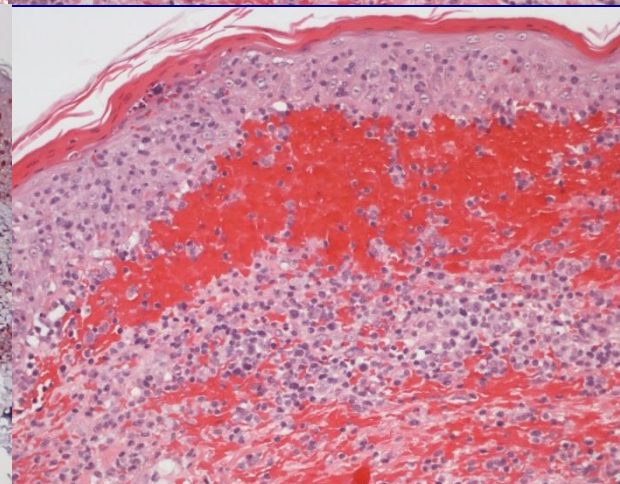
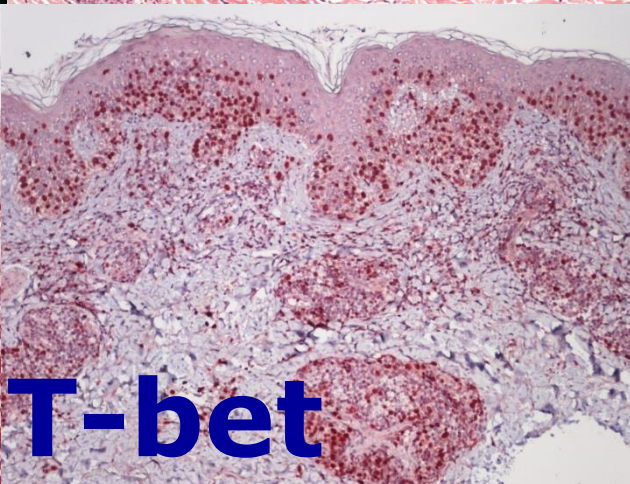
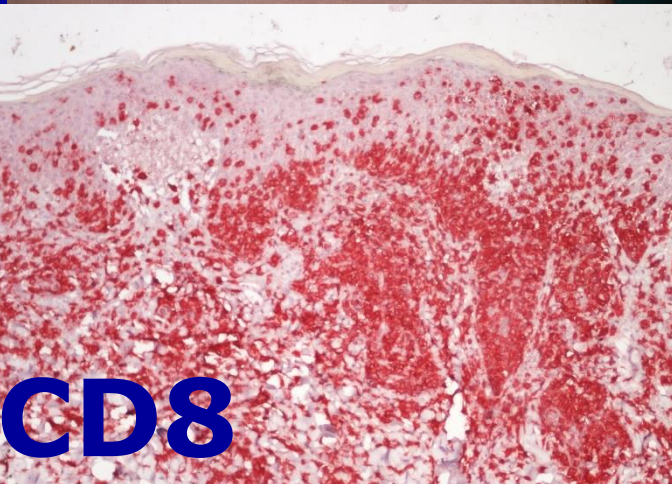
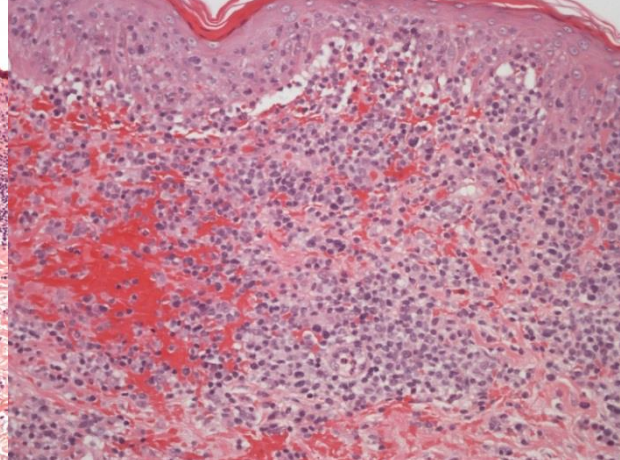
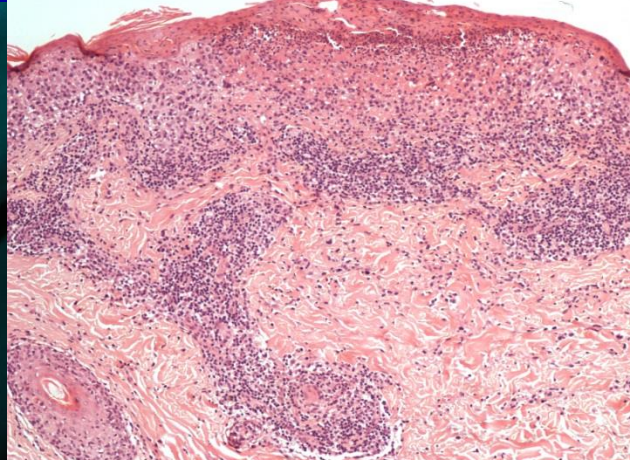




**LYMPHOM. PAPULOSIS CD8+**

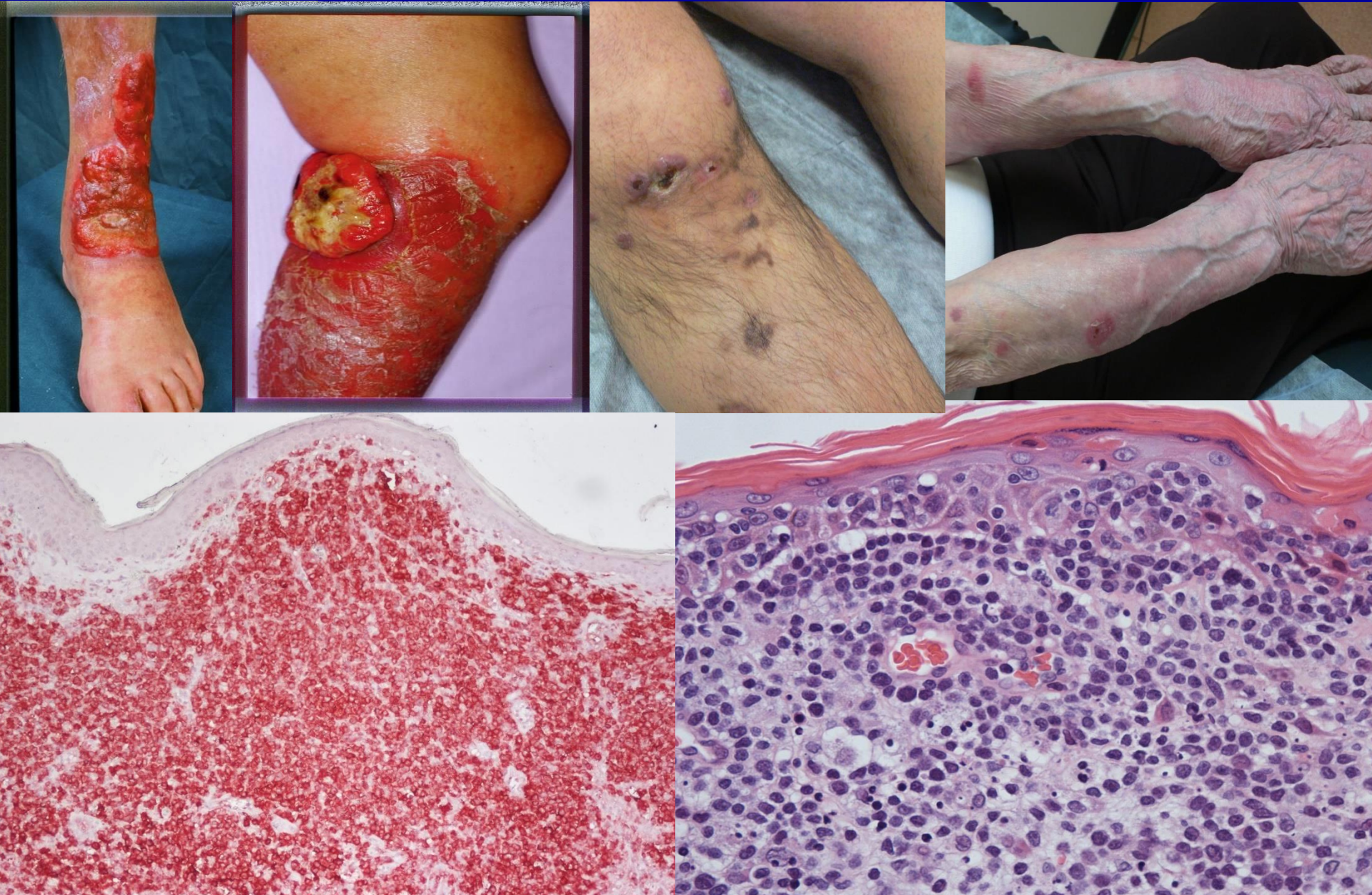








# CD30+/CD8+ C-ALC: AGGRESSIVE ? 3 CASES WITH SYSTEMIC EVOLUTION





# Subcutaneous panniculitis-like T-cell Lymphoma (Indolent)

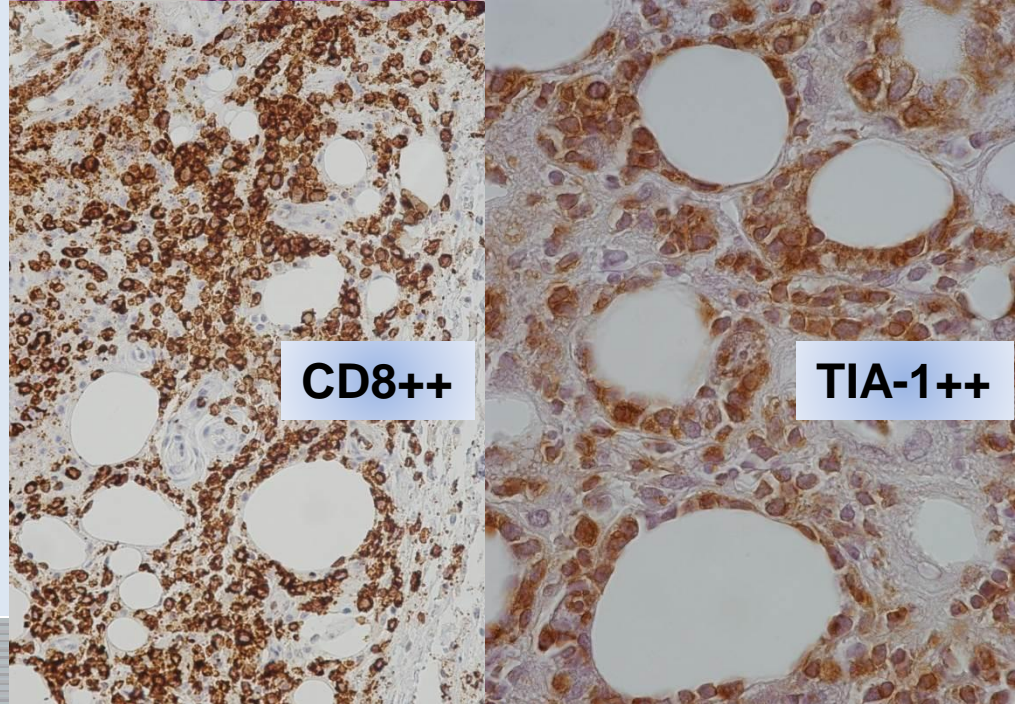
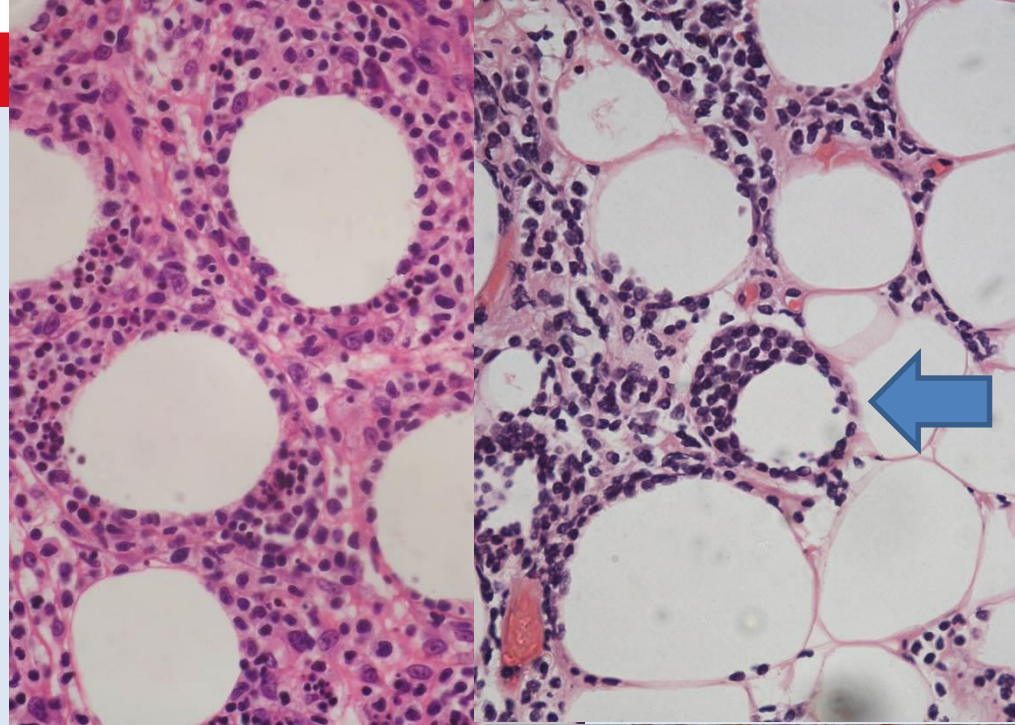
- Rare: 1% 4<sup>th</sup> decade of life male/female ratio 0,5.
- 19% of patients being 20 years or younger
- Male/female ratio 0,5
- **Subcutaneous nodules, plaques** involving the legs and the arms, more rarely diffuse.
- Initially asymptomatic, then B-symptoms **frequent cutaneous relapses**.
- 17% develop **Haemophagocytic Syndrome** (more aggressive).
- 5 years overall survival rate is about 82%. **Steroids, Cycloph. CHOEP**



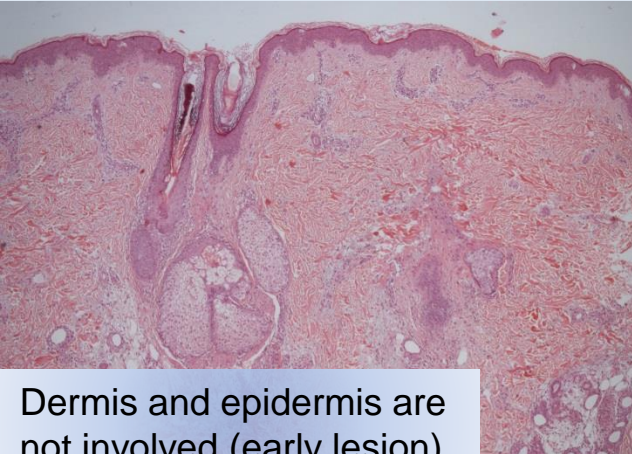


## Histology

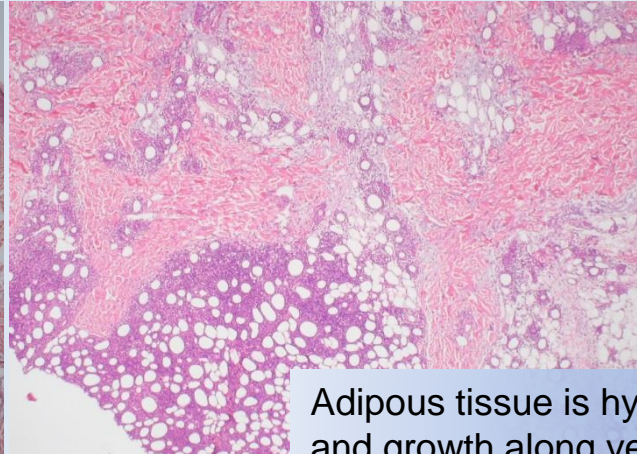
- Low magnification shows a specific “lipotropic” lymphoid infiltrate in the adipous tissue, usually sparing septa, whole dermis and epidermis. Adipous tissue may be necrotic or hypertrophic.
- Neoplastic cells (small/medium size pleomorphic T-cells) and then macrophages distribute between individual adipose lobules (arrow), proliferating and forming “rim” and “capping” images, around lymphocytes, conferring a lace-like appearance.
- **Immunoprofile** (cytotoxic) **βF1+** (TCR-αβ), **CD8+**, CD2+, CD3+, CD5+, **CD45RO+**, **TIA-1+**, Granzyme B+, **EBV-**
- **TCR** rearranged (PCR, GenScan)







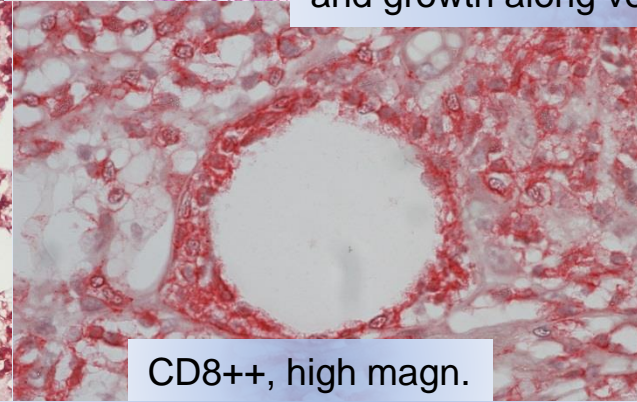
Dermis and epidermis are not involved (early lesion)



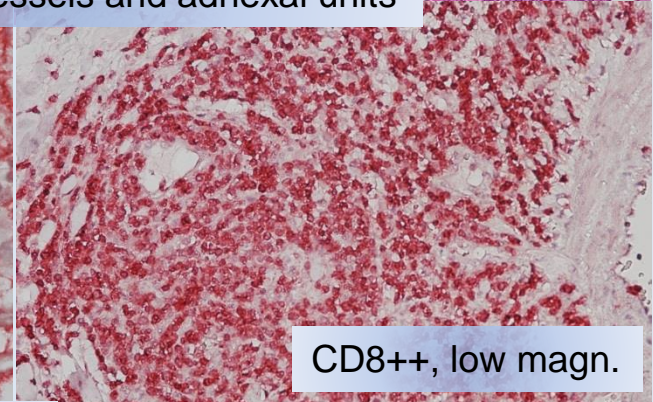
Adipous tissue is hypertrophic and growth along vessels and adnexal units



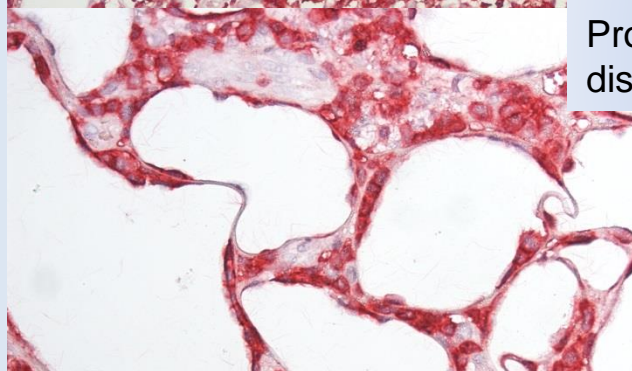
CD3++, low magn.



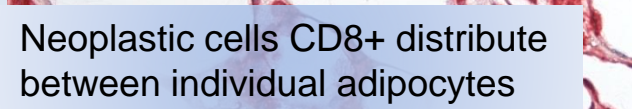
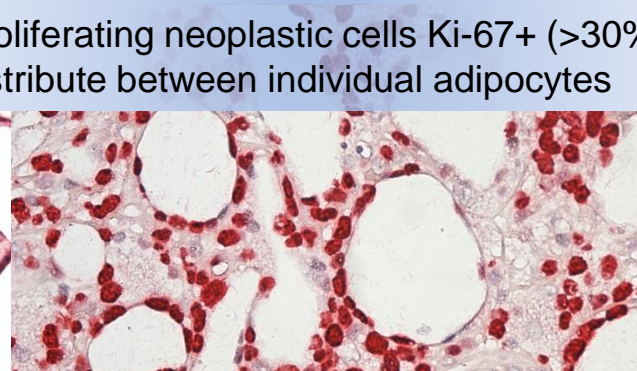
CD8++, high magn.



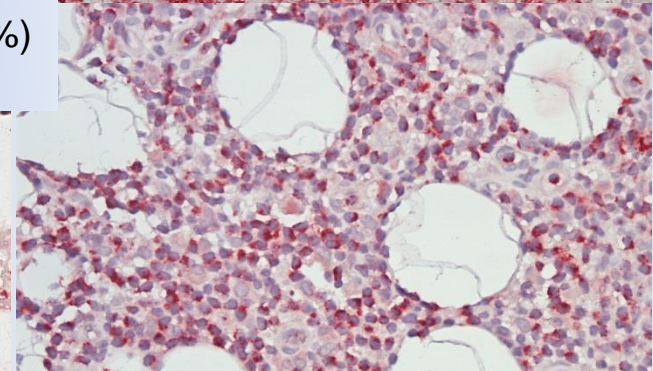
CD8++, low magn.



Proliferating neoplastic cells Ki-67+ (>30%) distribute between individual adipocytes



Neoplastic cells CD8+ distribute between individual adipocytes



Neoplastic cells are rich of cytotoxic granules (Granzyme B+)



# Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (AECTCL)

- Rare, a provisional entity.
- Nodules and plaques (Fig.4, 6), haemorrhagic-ulcerated (Fig.1-3, 5) or hyperkeratotic verrucoid lesions (Fig.2, 7).
- Rapid progression, few months-1 year, sparing superficial lymph nodes.
- Systemic involvement of CNS, testis, oral cavity, heart, spleen, liver, lung and frequent coagulopathy (Fig.8).
- Medium survival 32 months
- Histology: strongly epidermotropic and angiocentric-angiodestructive medium/large pleomorphic, immunoblastic CD8+ T-cell infiltrate.
- Partial response to multiagent chemotherapy or BMT



Fig.1: haemorrhagic plaque



Fig.2: ulcerated verrucoid nodules



Fig.3: typical papulo-nodular necrotic lesions



Fig.4: nodules-plaques, D.D. with large-B-cell lymphoma of the leg

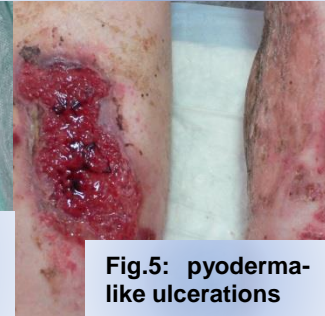


Fig.5: pyoderma-like ulcerations



Fig.6: nodular lesions



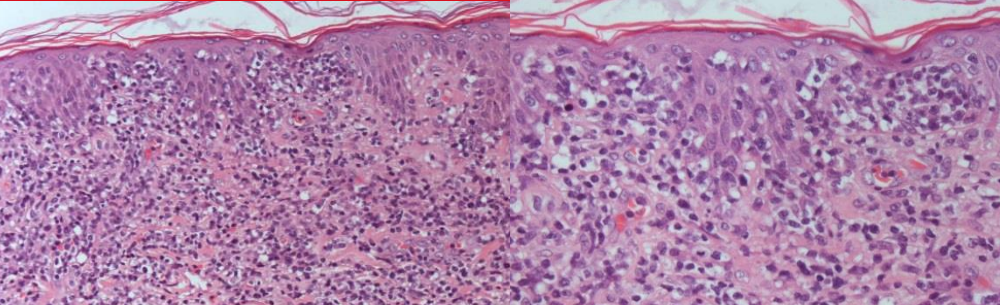
Fig.7: Verrucoid, hyperkeratotic diffuse lesions



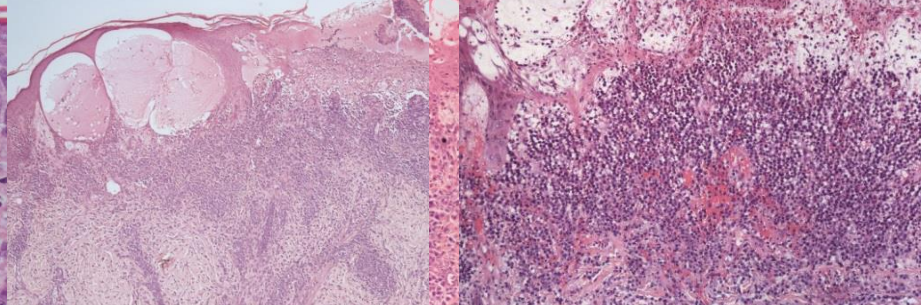
Fig.8: purpuric diffuse eruption (coagulopathy)



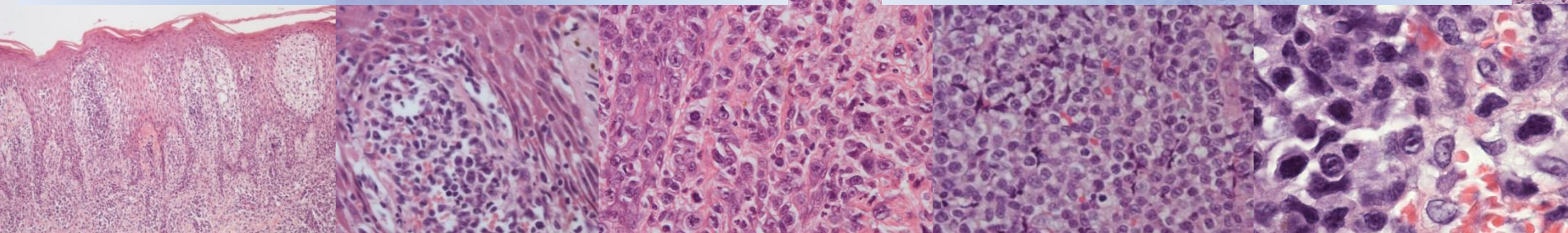




Typical Aggressive Epidermotropic pattern Patient N°2

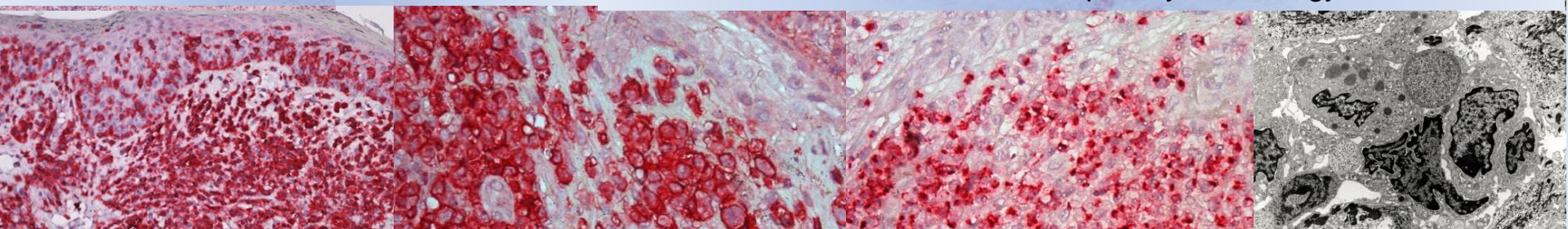


With Spongiosis and Blistering Patient N°3



Hyperkeratotic Psoriasiform pattern, Patient N°7

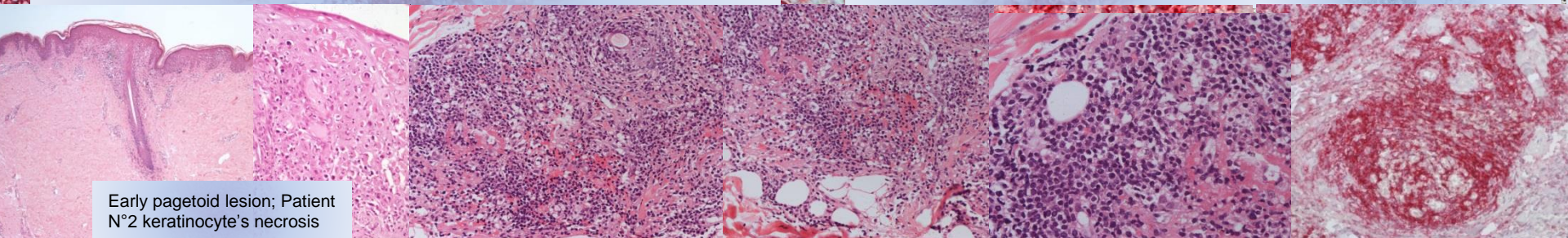
Immunoblastic/blastic and Pleomorphic cytology Patient N° 3-5



CD8+ staining: lichenoid-epidermotropic Patient N°2

Granzyme-B++ Patient N°2

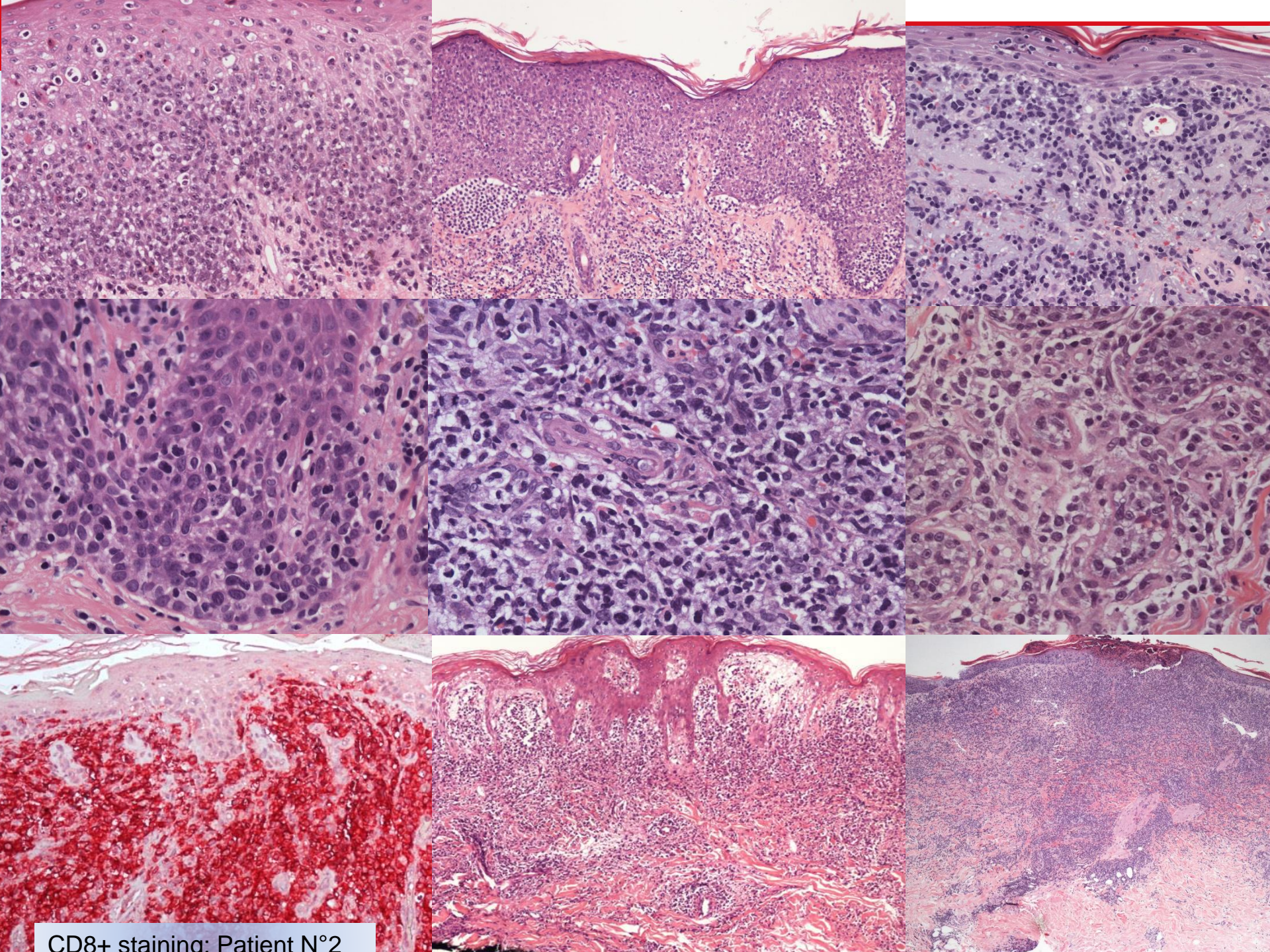
Electron microscopy



Early pagetoid lesion; Patient N°2 keratinocyte's necrosis

Typical Angiocentric pattern of neoplastic cells: histology and anti-CD8 staining. Patient N° 1, 8

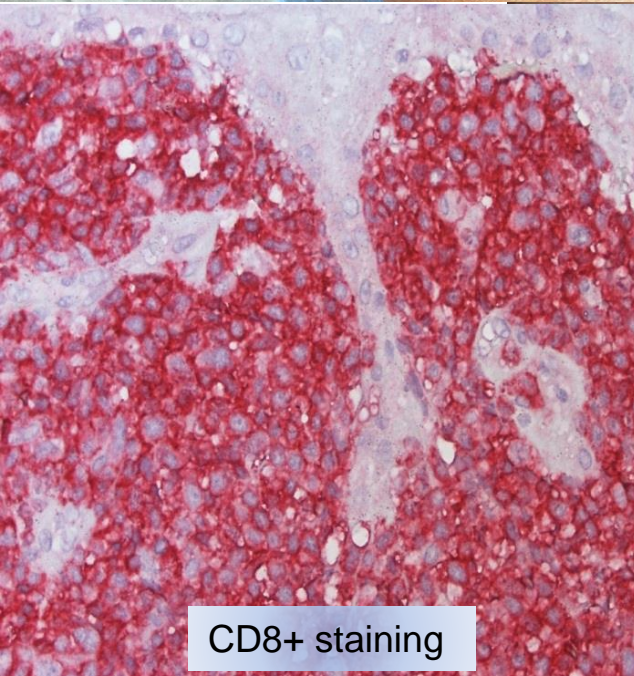
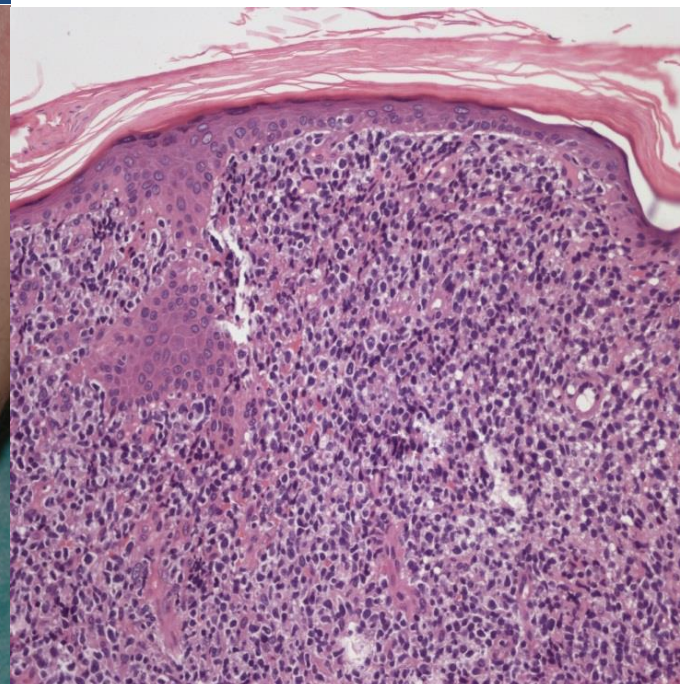




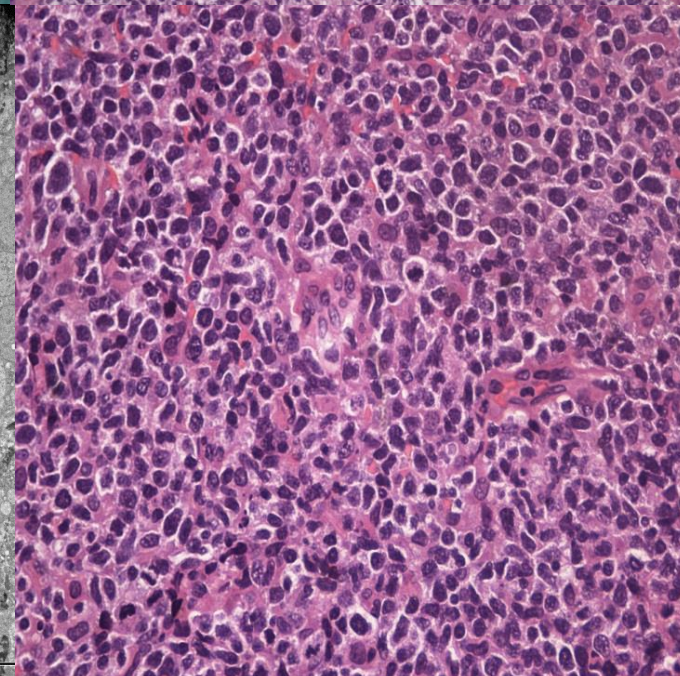
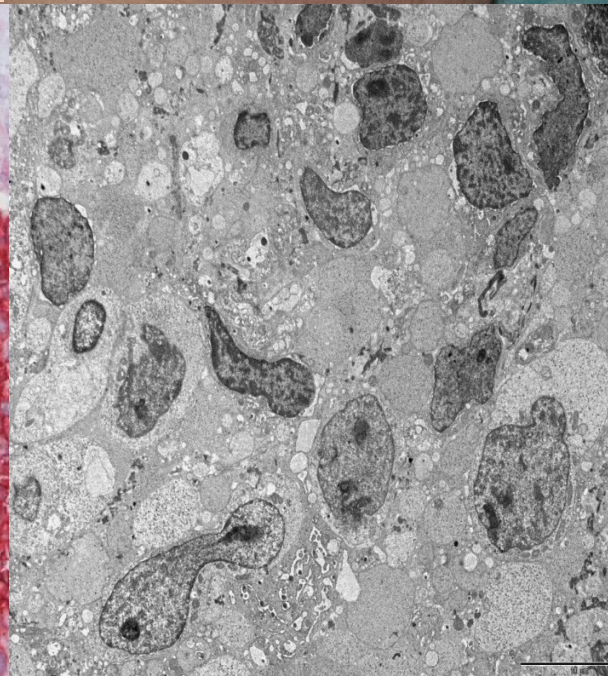
CD8+ staining: Patient N°2



CD8++/EBV++



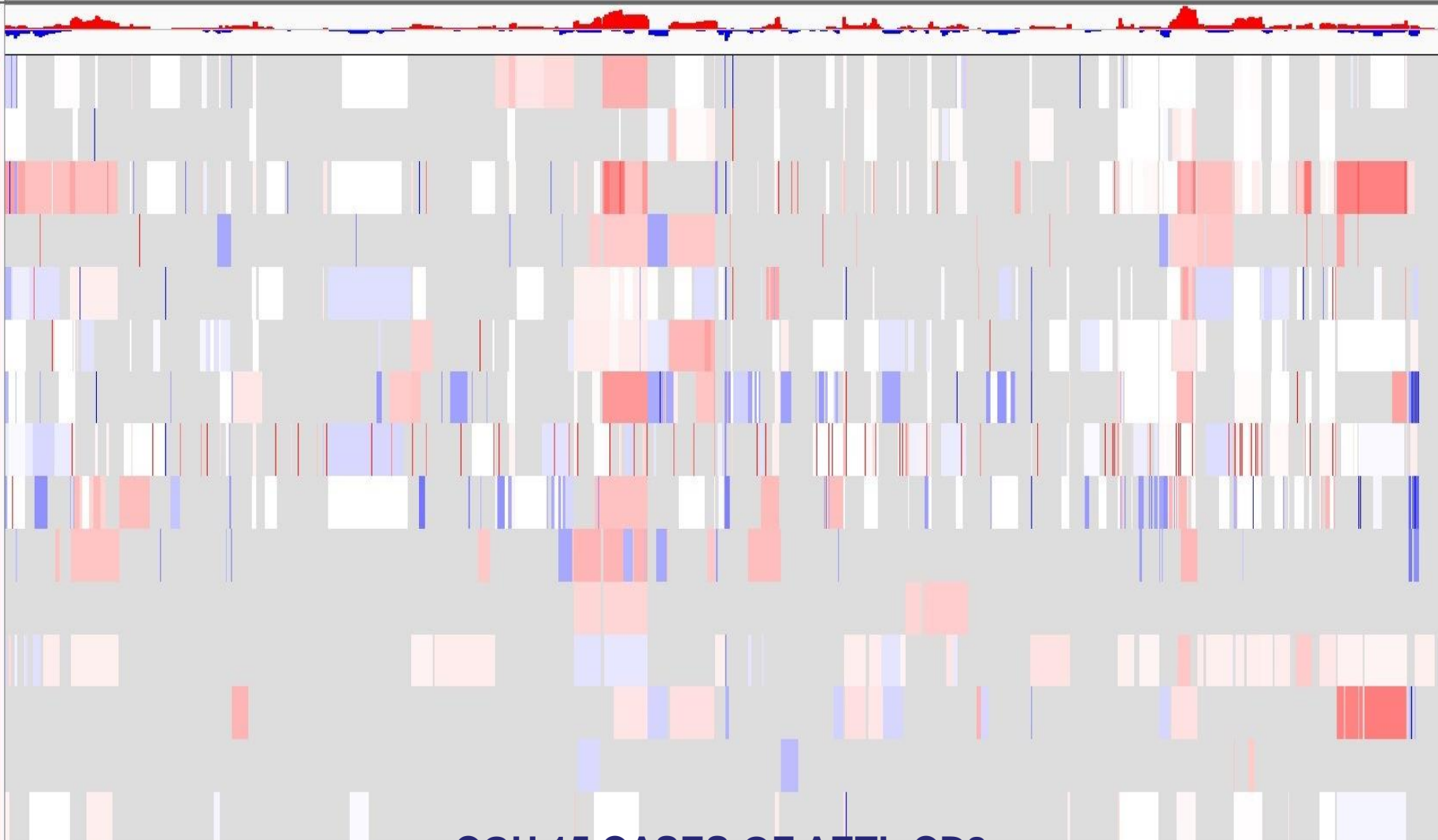
CD8+ staining





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**CGH 15 CASES OF AETL CD8+**



# CD8+ CTCL (PTL/NOS)

Clinically (aggressive)

Multiple nodular, purpuric lesions, erisipeloid plaques.

Short survival  
with possible  
leukemic evolution

Histology  
medium to large  
pleomorphic T-cell  
lymphoid infiltrate,  
angiocentric  
variable-absent  
epidermotropism

Immunophenotype:

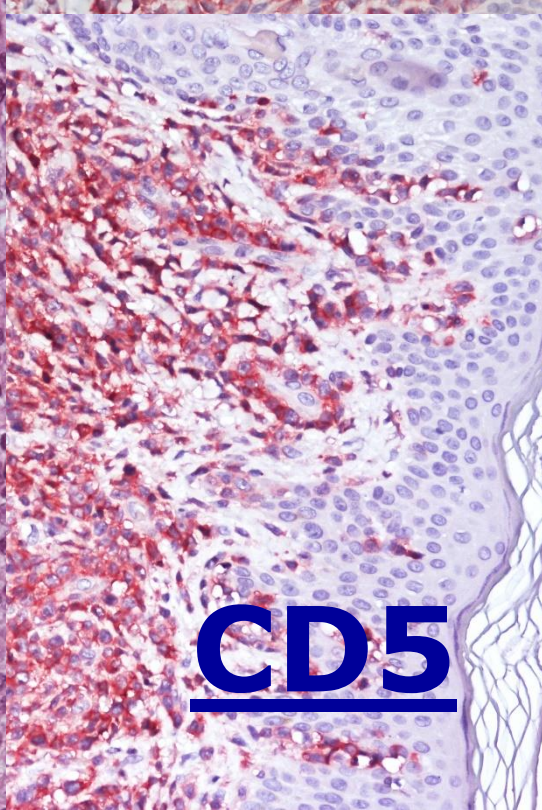
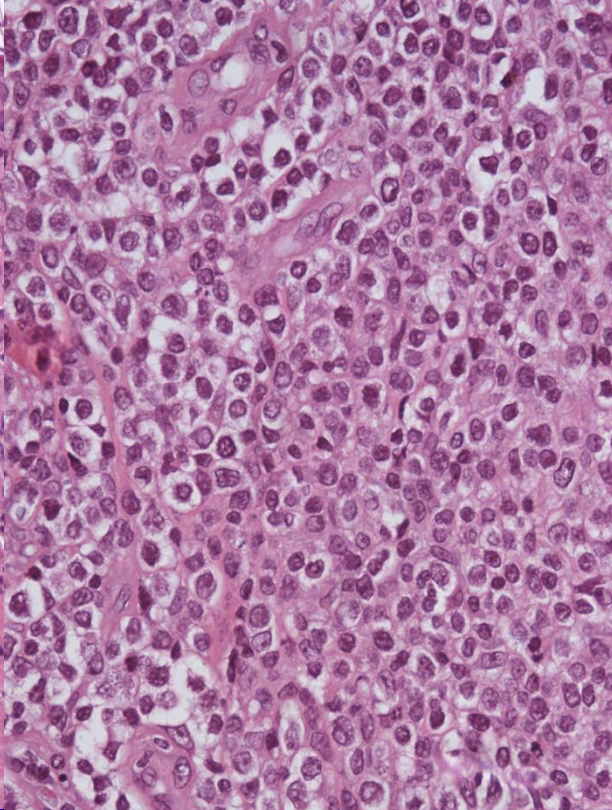
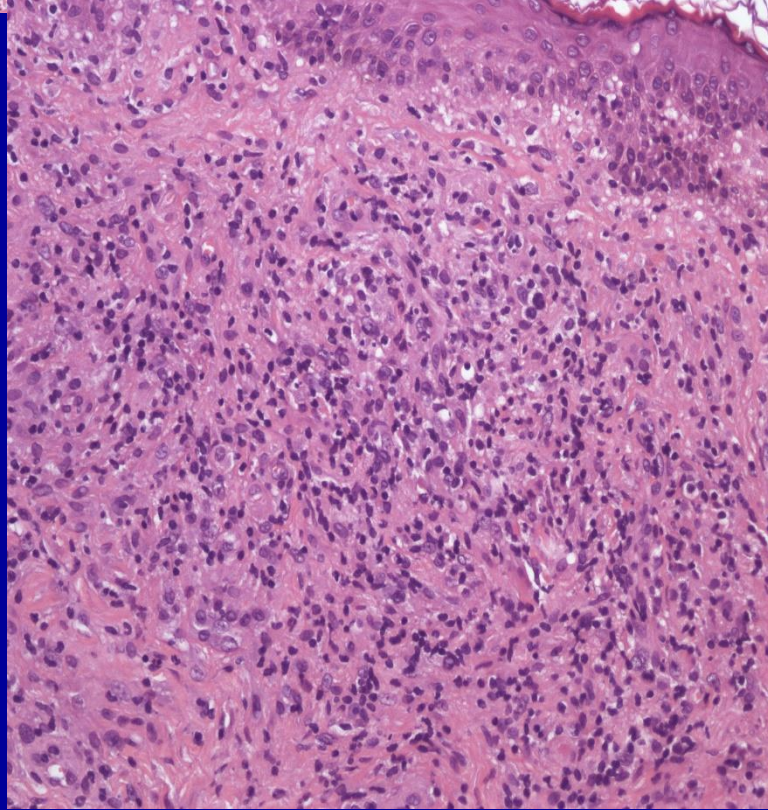
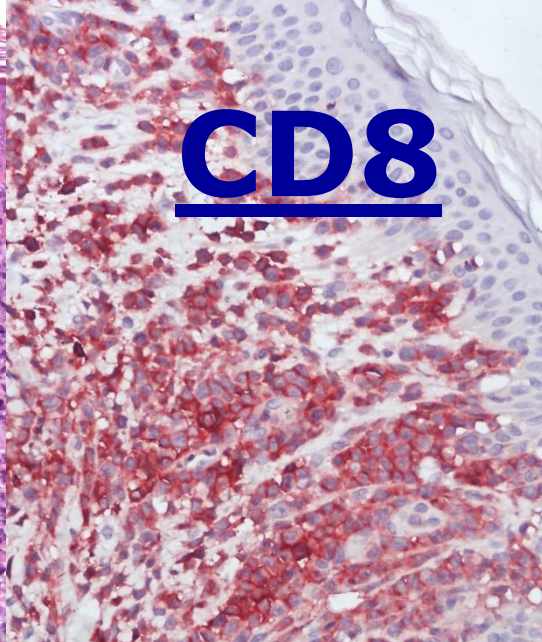
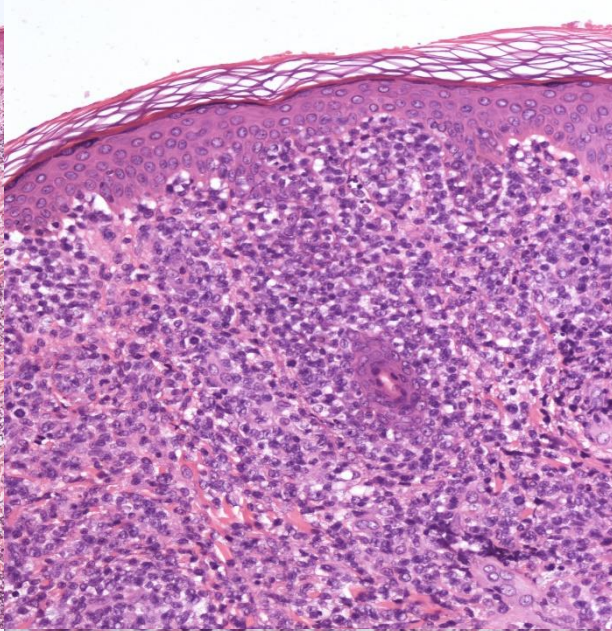
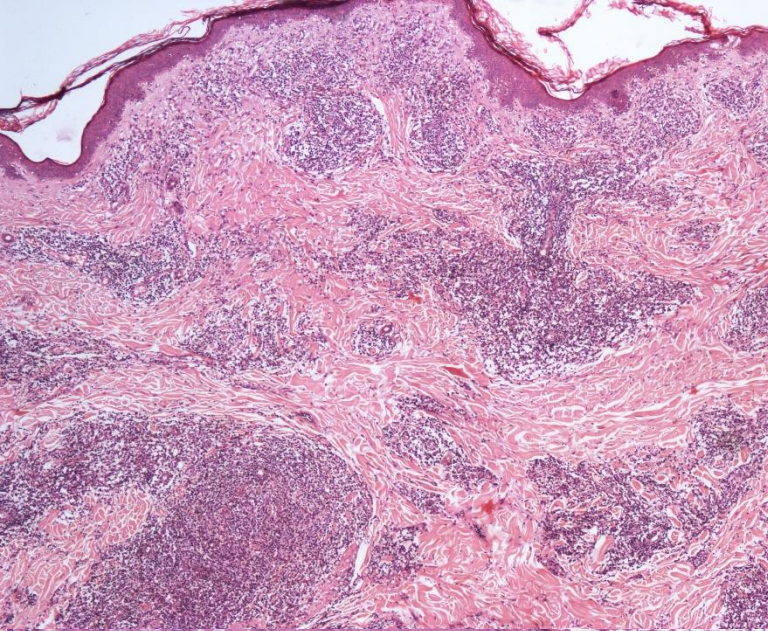
CD3+, CD4-, CD5+, CD7-,

CD8+ or CD8-/++,

CD45RO+, TIA-1+, MIB-1++









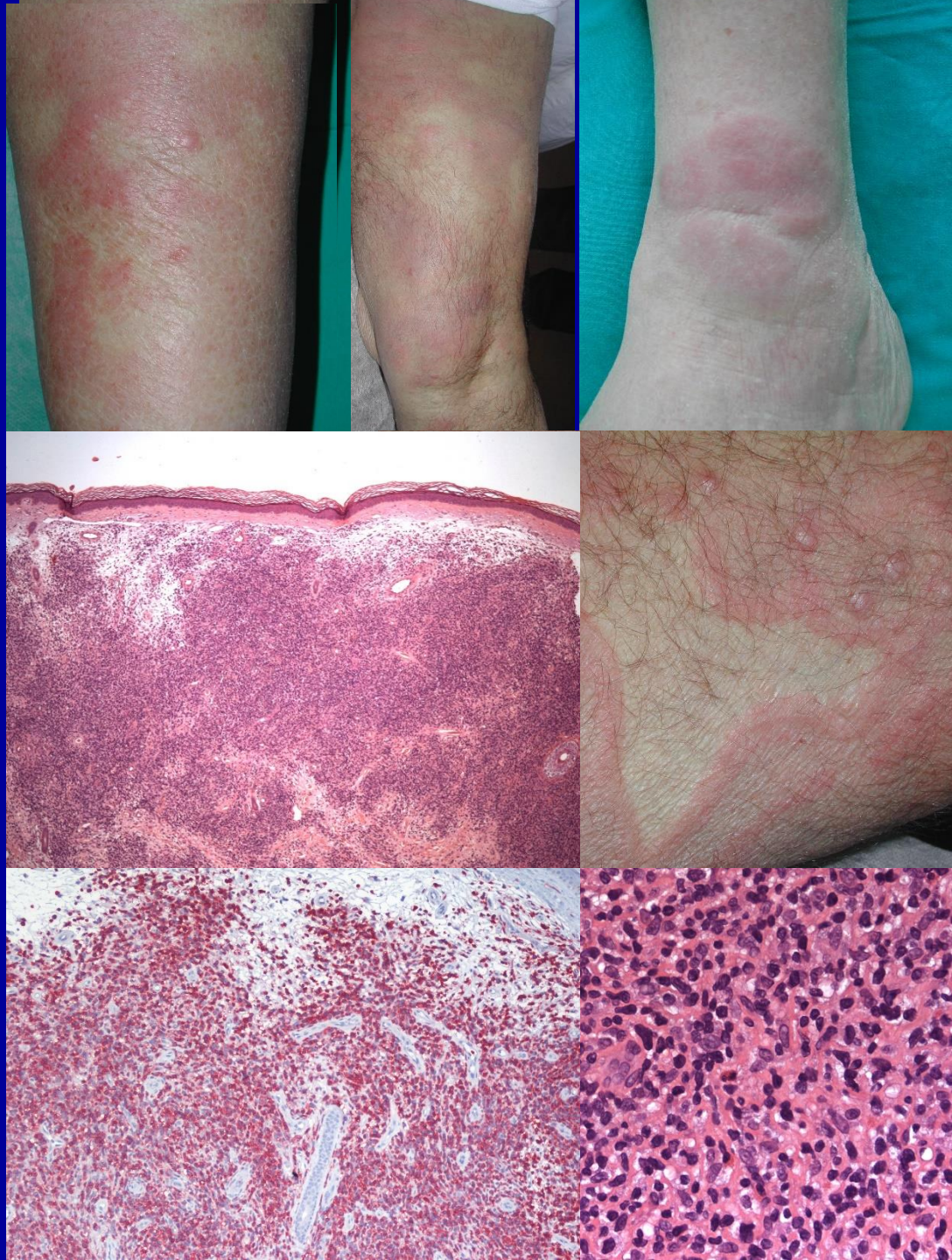
# CD8 CTCL S/M PLEOMORPHIC,

Papules/Plaques/  
Nodules

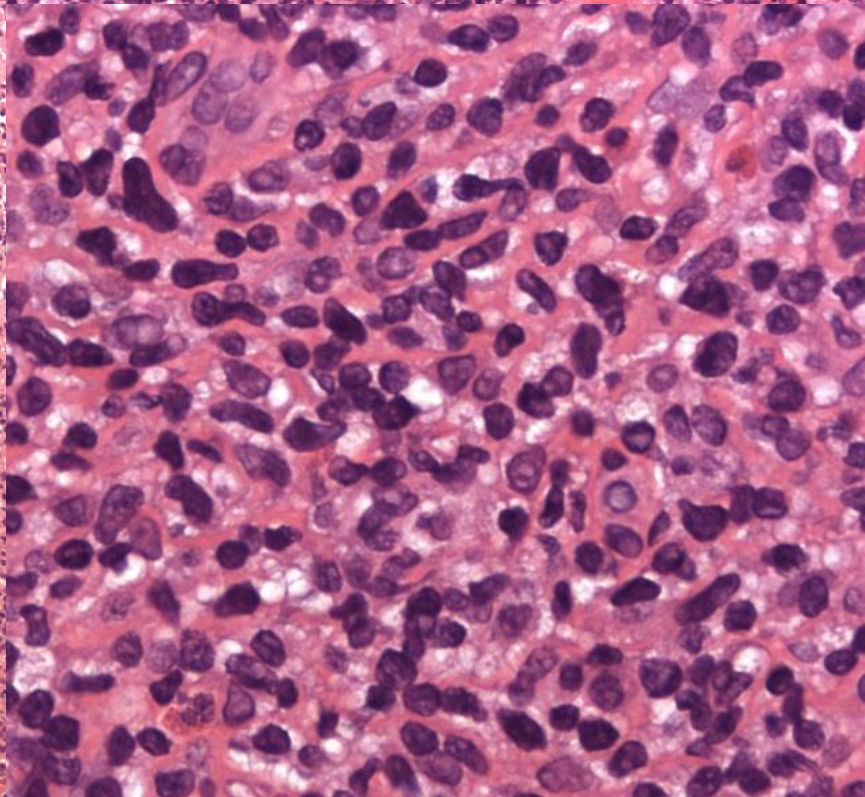
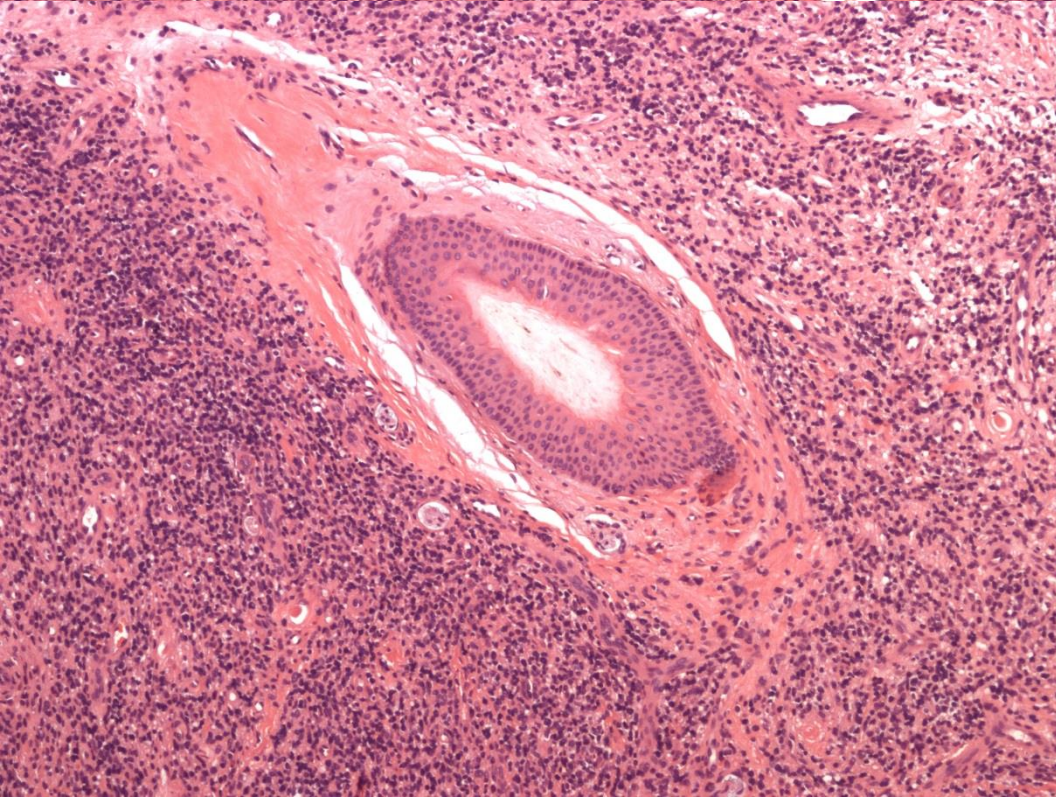
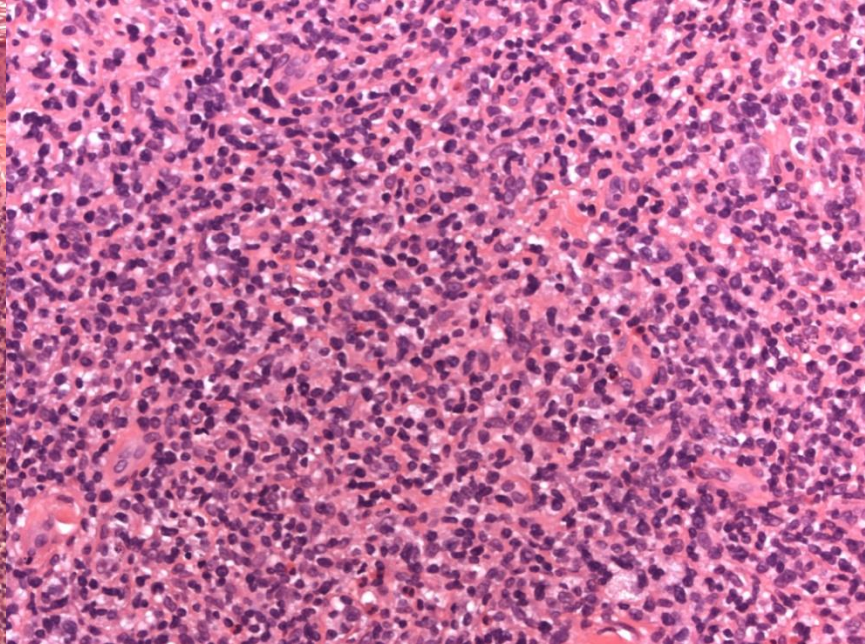
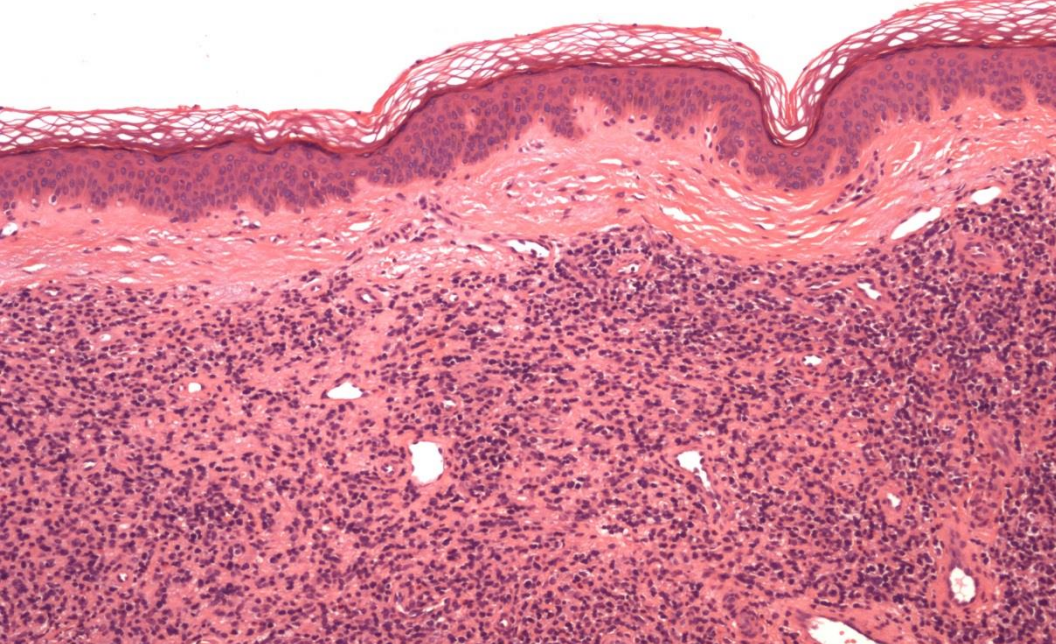
Indolent Course  
(similar to CD4+  
s/m PTL)

T-cell infiltrate,  
nonepidermotropic  
rich in eosinophils  
and macrophages

CD3+, CD8+, PD1-  
CD5+, CD45RO+,  
TIA-1+/- MIB1+/-

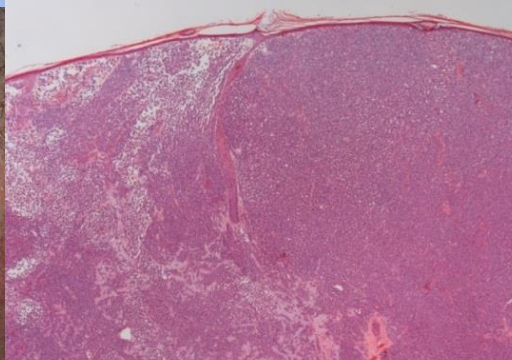




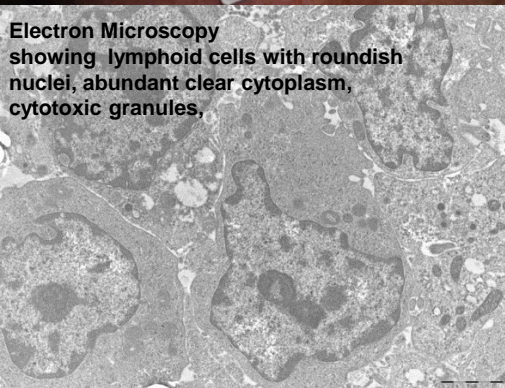
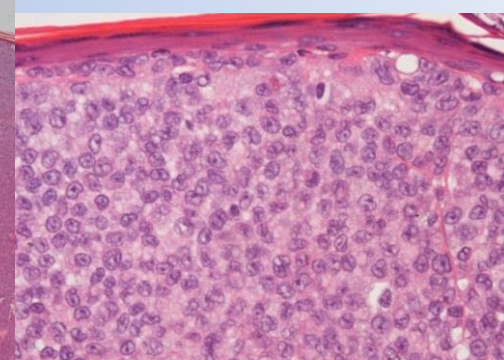




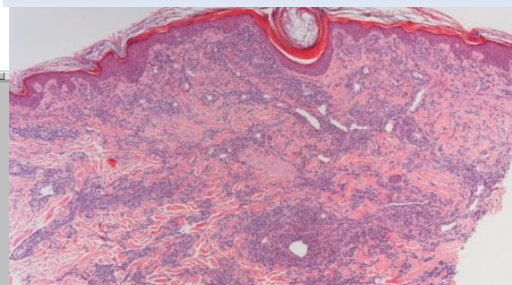
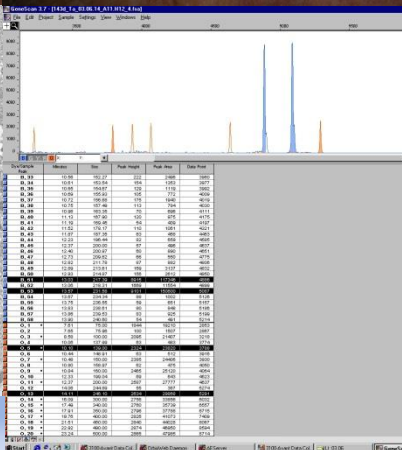
# «Pleomorphic T-cell Lymphoma of the Ear» (Indolent, s/m PTL): New Entity? Phenotype: **CD3+, CD5+, CD8+,CD45RO+, TIA-1+, GR-B-**



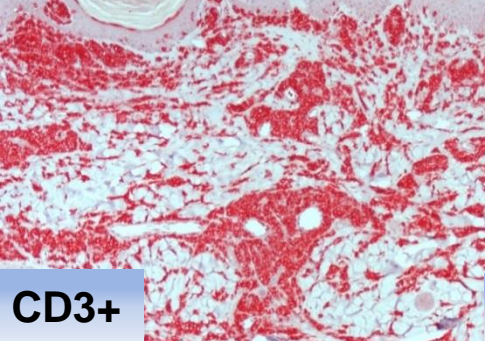
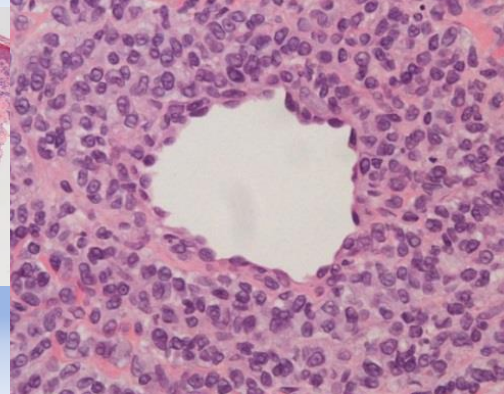
**Nodule:** proliferation of blasts-like cells with central nucleoli and abundant clear cytoplasm



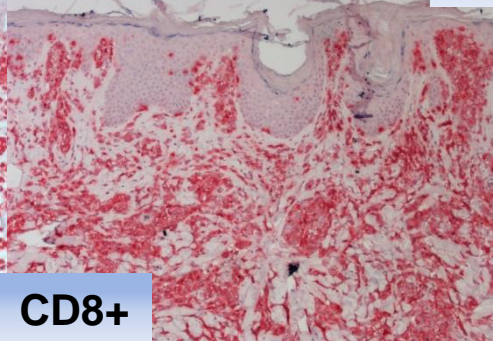
**PTL of the Ear:** central nucleoli and villous plasma membrane



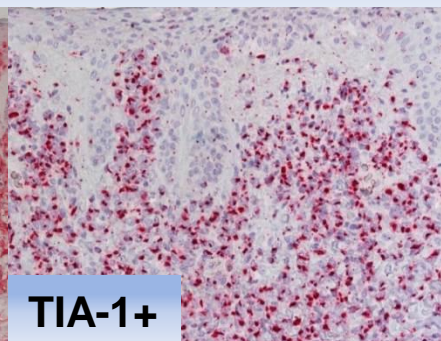
**Early lesion:** monotonous proliferation of small-medium size lymphocytes: angiocentric pattern



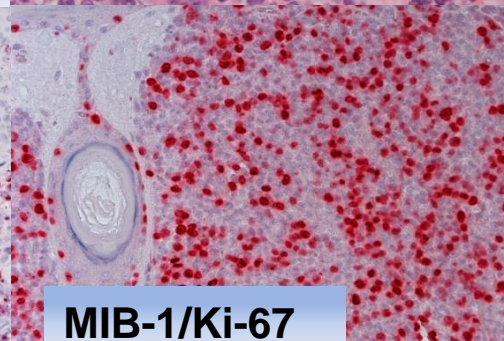
**CD3+**



**CD8+**

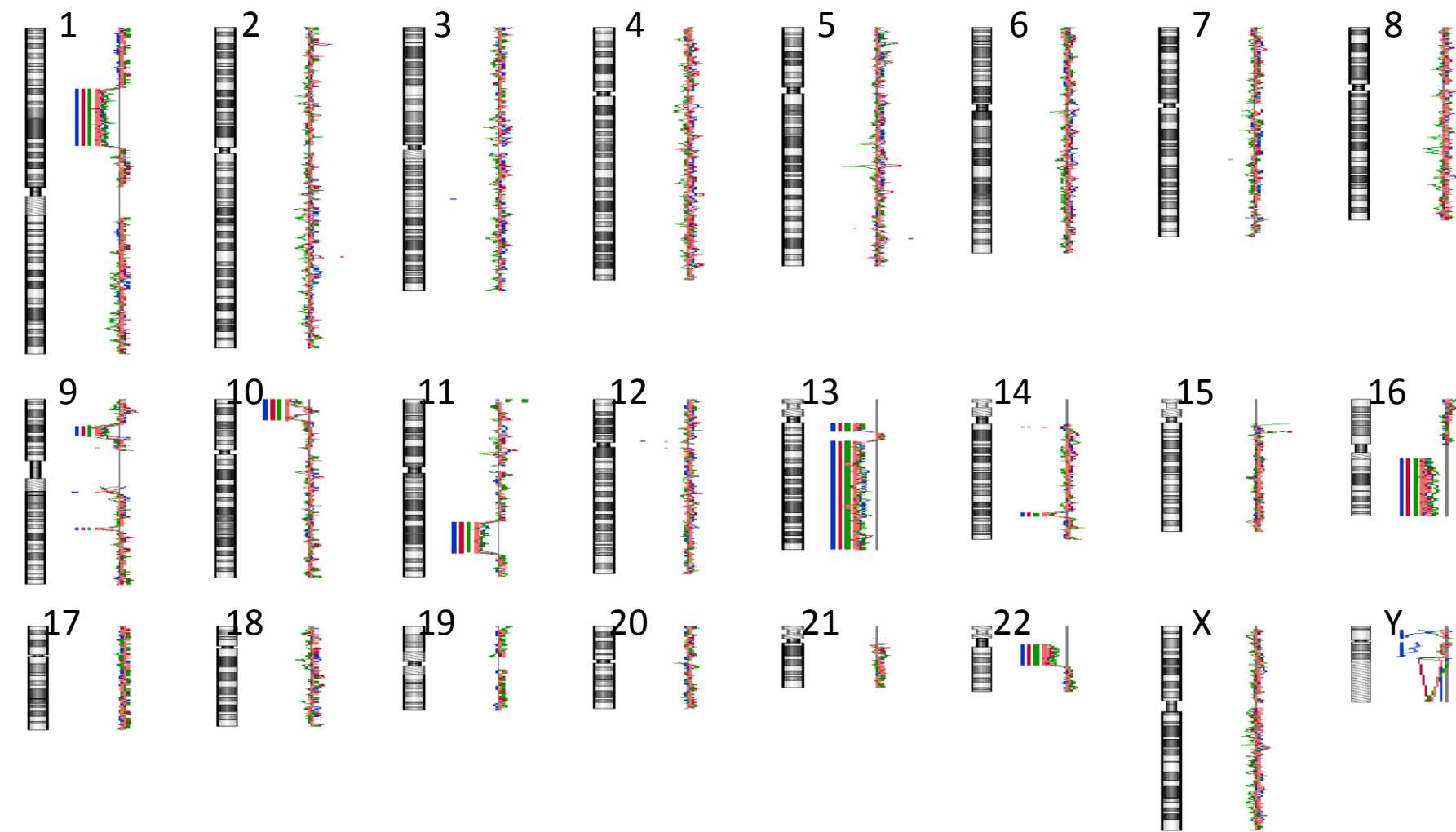
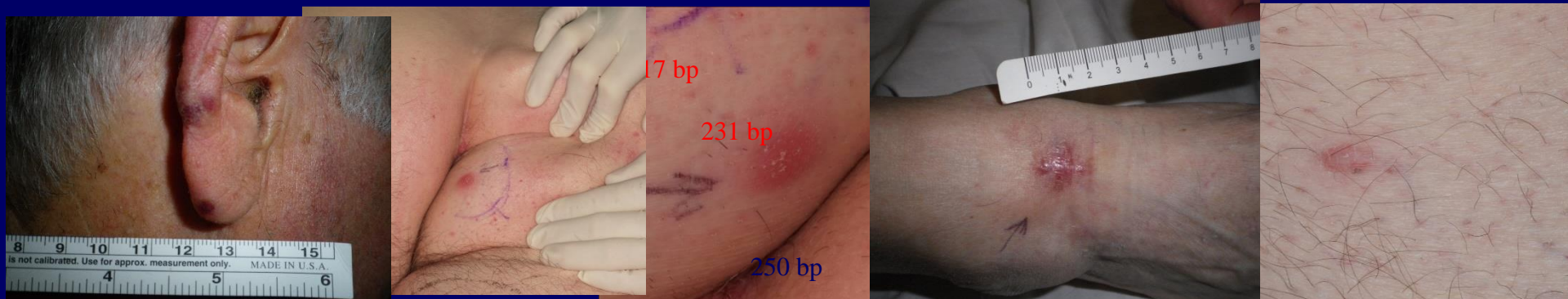


**TIA-1+**



**MIB-1/Ki-67**









FONDAZIONE IRCCS CA' GRANDA  
OSPEDALE MAGGIORE POLICLINICO



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