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Singapore Lymphoma Scientific Symposium 2025

Diagnostic Challenges in Cutaneous Lymphomas

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Agenda

1. Clinical challenges of mycosis fungoides in paediatrics
2. Clinical challenges of mycosis fungoides in adults
3. Histological challenges of mycosis fungoides
4. Clinical challenges of other cutaneous lymphomas

Cutaneous Lymphomas: Introduction

- Heterogeneous group of conditions with wide variety of clinical, histopathological, immunophenotypic features, with variable prognosis
- Overall incidence uncommon and even rarer in childhood
- Mycosis fungoides and other T-cell lymphomas are the commonest entities in children and adults
- Diagnosis often delayed due to indolent nature of disease and similarity to other more common dermatoses
- Prognosis can vary depending on type of lymphoma and stage at diagnosis, but generally good in MF
- Treatment depends on stage of disease but generally responsive to skin-directed treatment (phototherapy, topicals, systemic retinoids)

Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709
Ferenczi K et al., Clin Dermatol 2016;34:749-759

Cutaneous Lymphomas: Classification

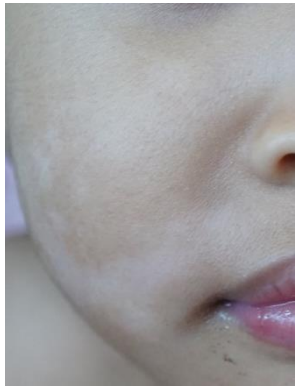
Mature T-cell and NK-cell neoplasms	
Mycosis fungoides	9700/3
Pagetoid reticulosis (localized disease)	
Follicular, syringotropic, granulomatous variants	
Granulomatous slack skin	
Sezary syndrome	9701/3
CD30+ T-cell lymphoproliferative disorders of the skin	
Lymphomatoid papulosis	9718/1
Primary cutaneous anaplastic large cell lymphoma	9718/3
Subcutaneous panniculitis-like T-cell lymphoma**	9708/3
Primary cutaneous peripheral T-cell lymphoma	
(PTL), unspecified	9709/3
Subtypes of PTL (provisional)	
Primary cutaneous aggressive epidermotropic CD8-positive cytotoxic T-cell lymphoma	
Cutaneous gamma/delta-positive T-cell lymphoma	
Primary cutaneous small/medium CD4+ T-cell lymphoma	
Extranodal NK/T-cell lymphoma, nasal type	9719/3
Hydroa vacciniformia-like lymphoma (variant)	
*Adult T-cell leukaemia/lymphoma**	
9827/3	
*Angioimmunoblastic T-cell lymphoma**	9705/3

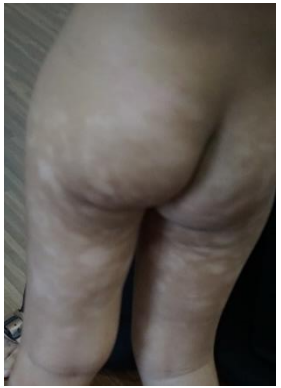
Mature B-Cell neoplasms	
Cutaneous marginal zone B-cell lymphoma (MALT-type)	9699/3
Cutaneous follicle centre lymphoma	9690/3
Cutaneous diffuse large B-cell lymphoma	9680/3
*Intravascular large B-cell lymphoma**	9680/3
*Lymphomatoid granulomatosis**	9766/1
*Chronic lymphocytic leukaemia**	9823/3
*Mantle cell lymphoma**	9673/3
*Burkitt lymphoma**	9687/3
Immature haematopoietic malignancies	
Blastic NK-cell lymphoma *** / CD4+/CD56+ haematodermic neoplasm	9727/3
Precursor lymphoblastic leukaemia/lymphoma	
*T-lymphoblasic leukaemia**	9837/3
*T-lymphoblastic lymphoma**	9729/3
*B-lymphoblastic leukaemia**	9836/3
*B-lymphoblastic lymphoma**	9728/3
*Myeloid and monocytic leukaemias**	
Hodgkin lymphoma*	

Kempf W et al., Hematological Oncology 2019;37:43-47
Willemze R et al., Blood 2019;133:1703-1714

Mycosis Fungoides in Children

- Most common cutaneous lymphoma in children
- **Clinical:**
  - May show classic presentation with erythematous patches and plaques, which is more common in adults
  - Hypopigmented form much more common in childhood / adolescents





Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709

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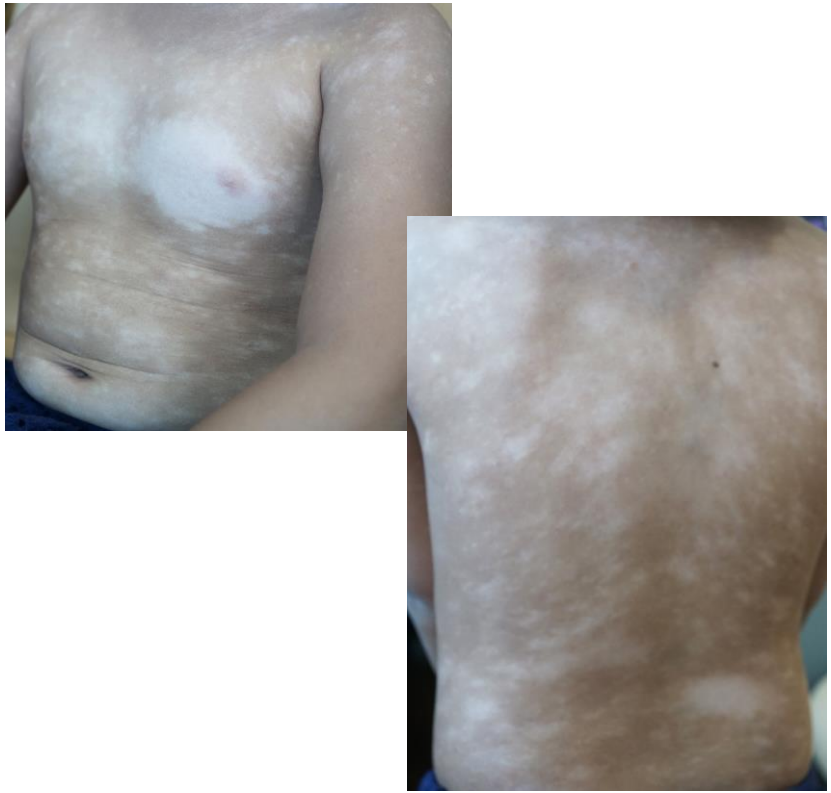
Mycosis Fungoides in Children - Mimickers



Differential:
Atopic dermatitis with post-inflammatory hypopigmentation

Mycosis Fungoides in Children - Mimickers

Differential:
Pityriasis alba

Differential:
Tinea versicolor

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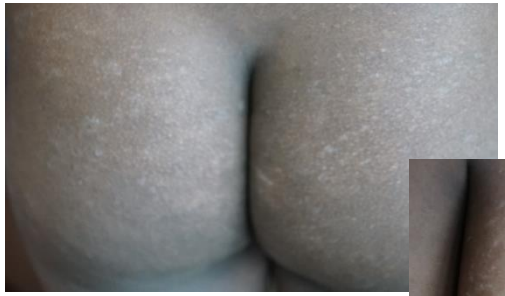
Mycosis Fungoides in Children - Mimickers



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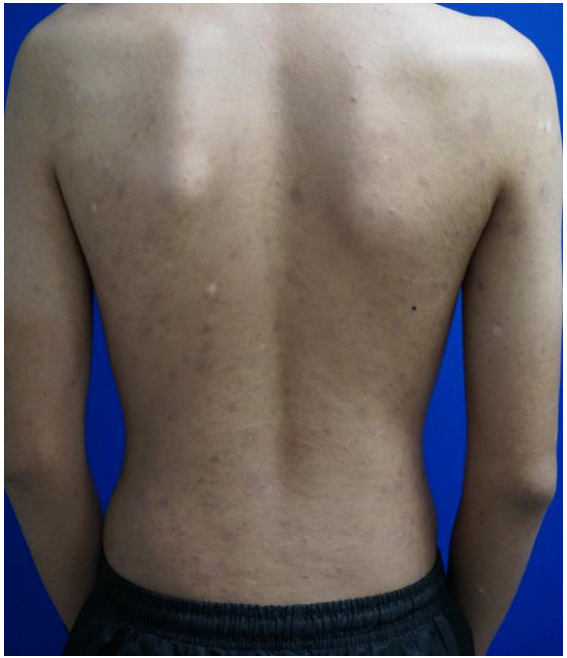
Mycosis Fungoides in Children - Mimickers

Pityriasis lichenoides-like MF

Differentials:

Psoriasis and Pityriasis lichenoides

Mycosis Fungoides – Adolescent Patients



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Mycosis Fungoides – Rarer Forms in Children

Follicular MF

Lichen spinulosus / follicular eczema

Hyperpigmented MF

Atopic dermatitis with post-inflammatory hyperpigmentation

Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709
Sidiropoulou P et al., Int J Dermatol 2020;59:314-320

Mycosis Fungoides – Rarer Forms in Children

Unilesional MF:

Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709
Sidiropoulou P et al., Int J Dermatol 2020;59:314-320

Mycosis Fungoides in Adults

- Most common cutaneous lymphoma in adults
- **Clinical:**
  - Usually present with patches -> plaques -> tumours, progressing over months or years
  - Difficult to diagnose, require high index of suspicion, may require several biopsies over months or years

Patch stage

Plaque stage

Tumour stage

Mycosis Fungoides in Adults - Mimickers

Patch stage MF

Mycosis Fungoides in Adults - Mimickers

Patch/plaque stage MF

Differential:
Atopic dermatitis / Eczema

Mycosis Fungoides in Adults - Mimickers

Tumour stage MF

Differential:
Other skin tumours

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Mycosis Fungoides in Adults - Mimickers

Psoriasiform MF

Differential:
Psoriasis

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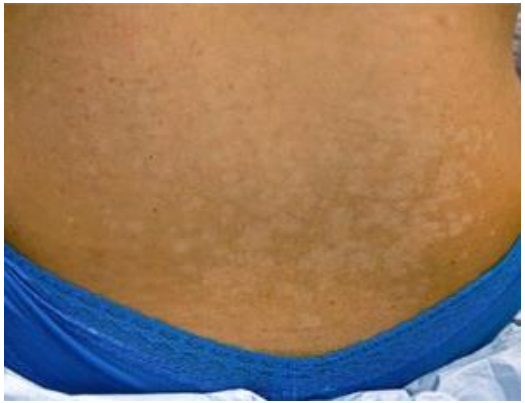
Mycosis Fungoides in Adults - Mimickers

Differential: **Parapsoriasis / digitate dermatosis**

Mycosis Fungoides in Adults - Mimickers

Hypopigmented MF

Differentials:
Post-inflammatory hypopigmentation



Progressive macular hypomelanosis

Tinea versicolor

Mycosis Fungoides in Adults - Mimickers

Hyperpigmented MF

Differential:
Post-inflammatory hyperpigmentation

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Mycosis Fungoides in Adults - Mimickers

Folliculotropic MF

Differential:

Lichen spinulosus / follicular eczema

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Mycosis Fungoides in Adults - Mimickers

Folliculotropic MF

Mycosis Fungoides in Adults - Mimickers

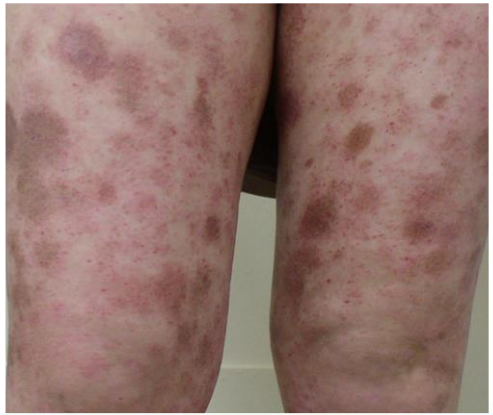
Erythrodermic MF / Sezary syndrome

Differential:
Generalised exanthematous dermatitis (GED)

Mycosis Fungoides – Rarer Forms in Adults

Granulomatous slack skin MF

Age-related “saggy” skin



Pigmented Purpuric dermatosis-like MF

Pigmented Purpuric dermatosis

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Mycosis Fungoides – Rarer Forms in Adults

Pagetoid reticulosis

Lichen simplex chronicus or tinea corporis

Palmo-plantar MF

Hand-feet eczema / psoriasis

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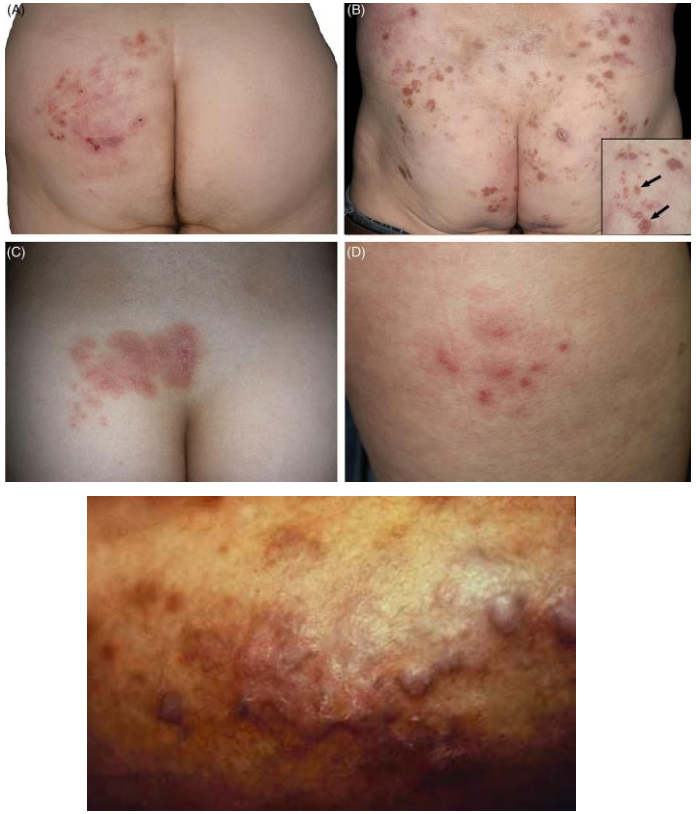
Mycosis Fungoides in Adults - Mimickers



Pseudolymphomas

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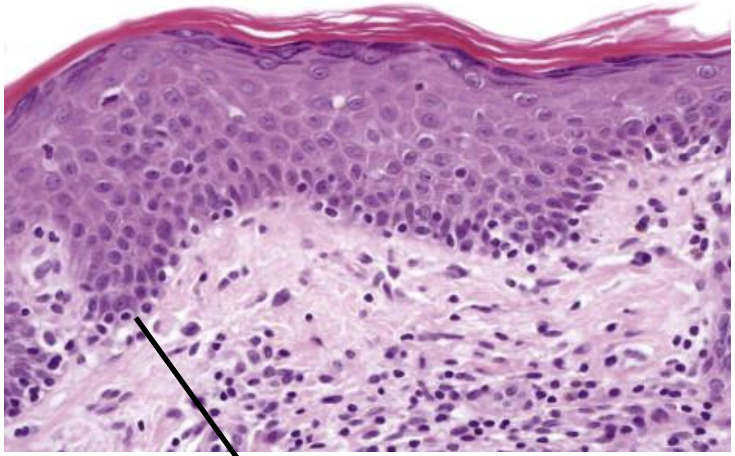
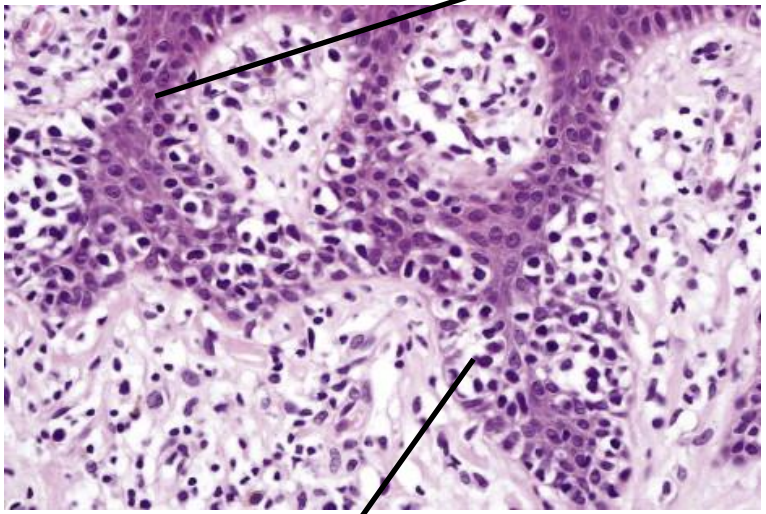
Mycosis Fungoides - Histology

Patch Stage: *** Stop treatment 2 weeks before biopsy**



Small lymphocytes
"tagging" basal epidermis

No or minimal spongiosis



Small-to-medium sized epidermotropic lymphocytes in basal layer, some lying within a clear halo

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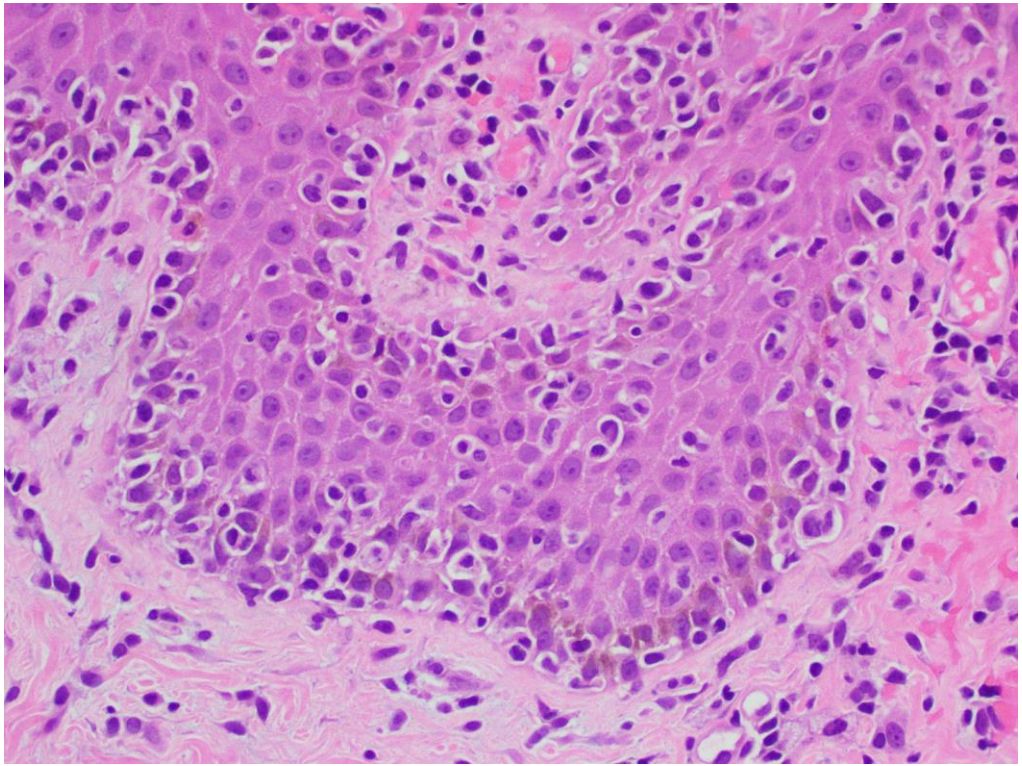
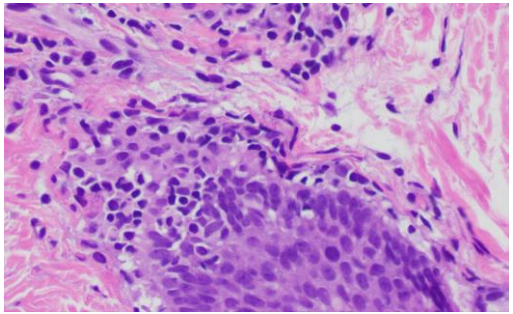
Mycosis Fungoides - Histology

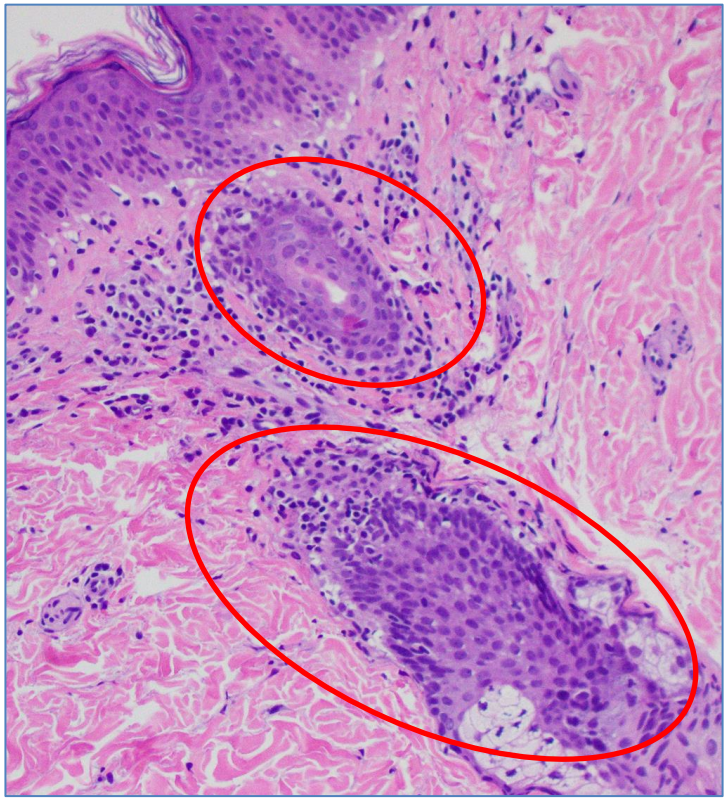
Patch Stage:

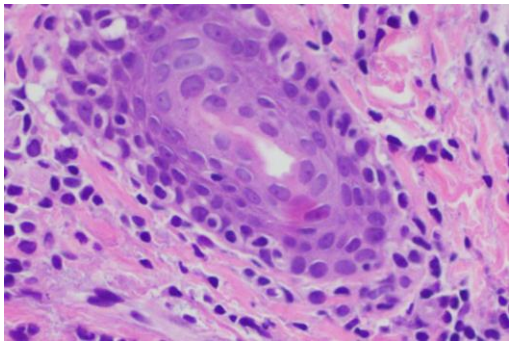


Mycosis Fungoides - Histology



Folliculotropism

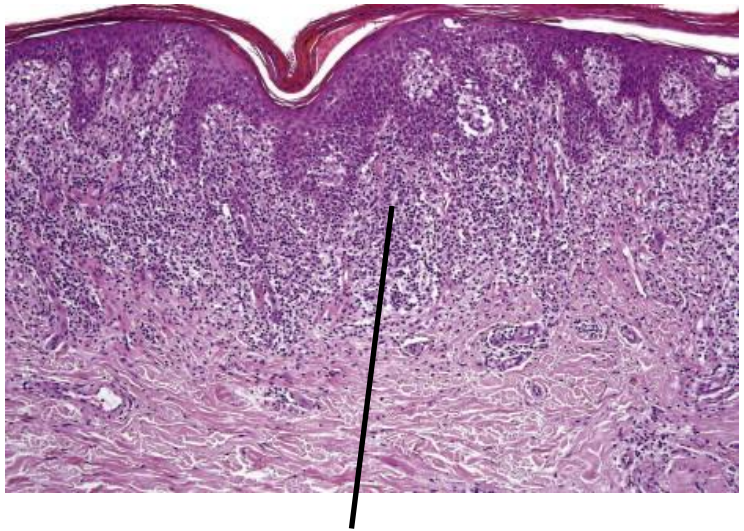




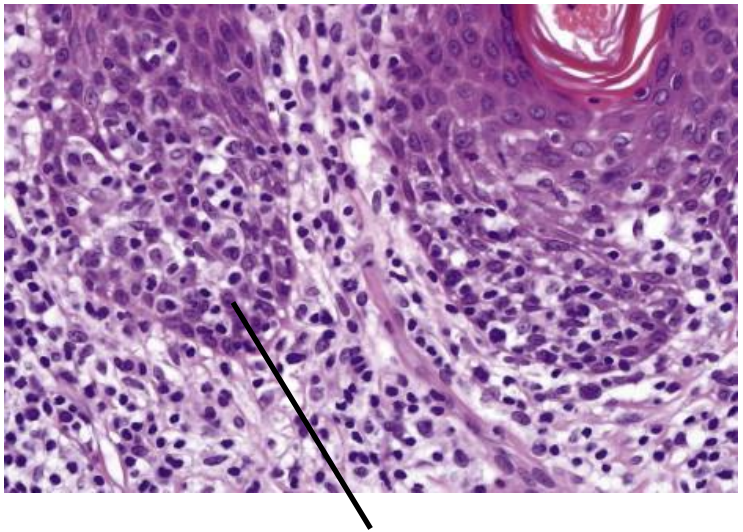
Syringotropism

Mycosis Fungoides - Histology

Plaque Stage:



Band-like infiltrate in upper dermis

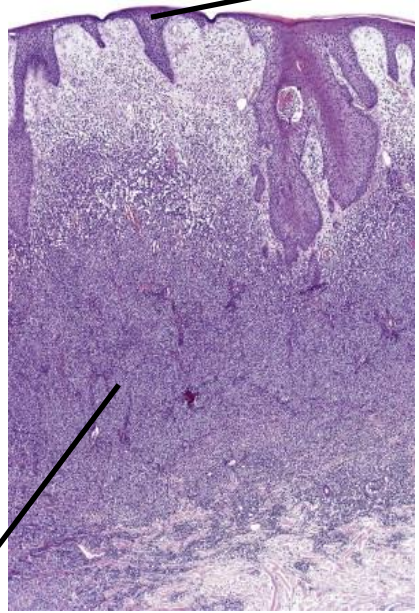


Much more epidermotropic atypical lymphocytes

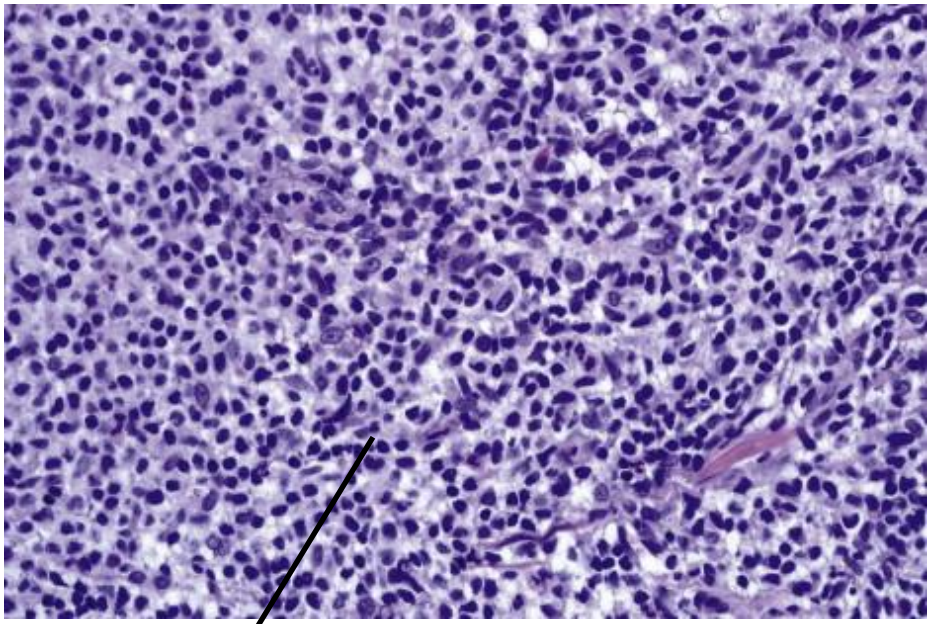
Mycosis Fungoides - Histology

Tumour Stage:

Epidermotropism may be absent or minimal



Dense infiltrate in upper to deep dermis



Dense infiltrate of atypical, medium-to-large lymphocytes

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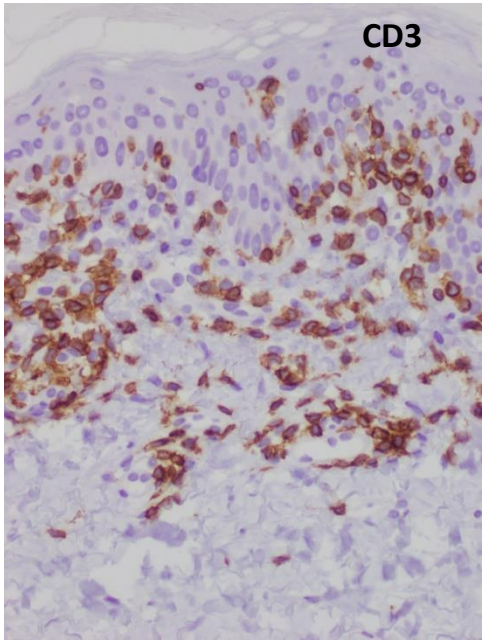
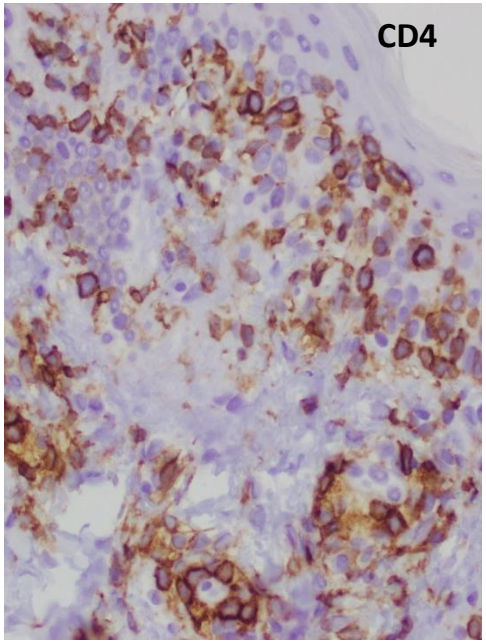
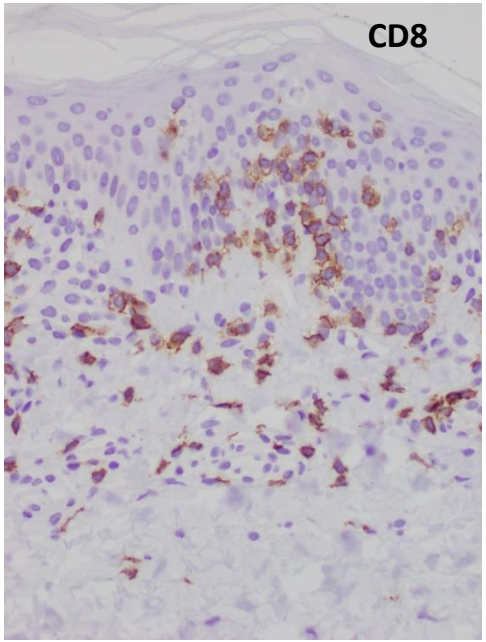
Mycosis Fungoides - Immunohistochemistry

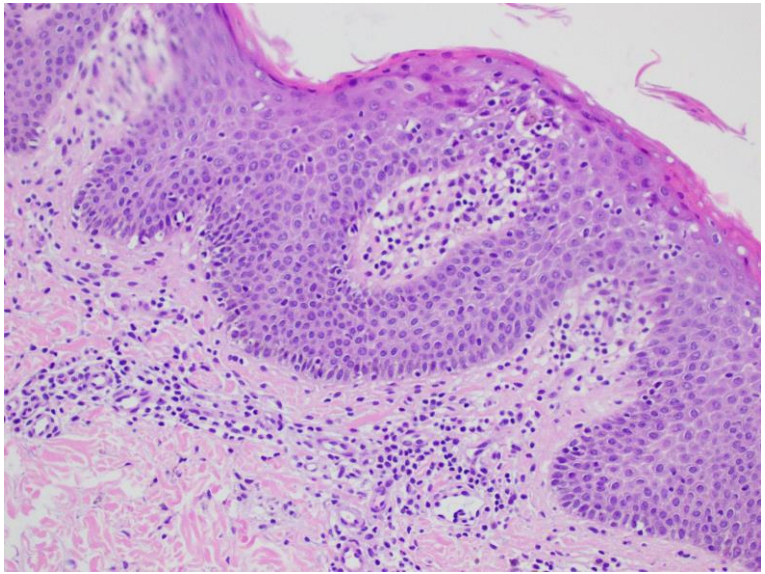


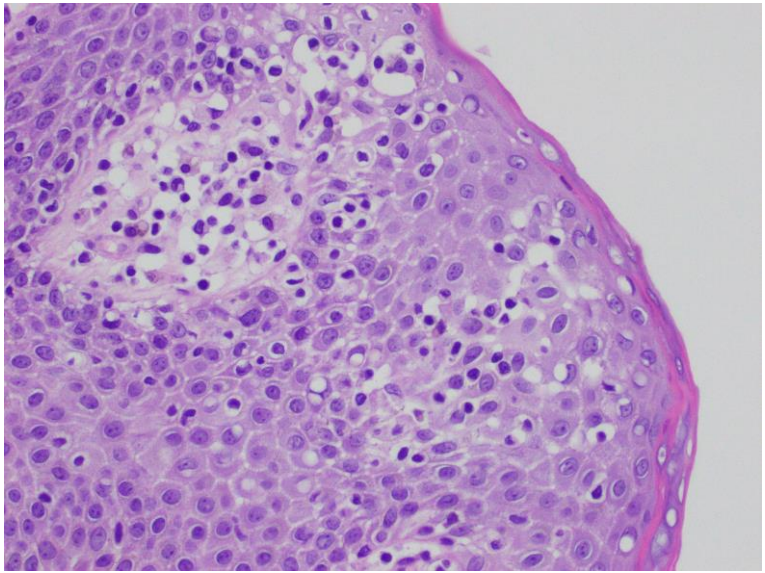




- **Most commonly predominantly CD4+ or CD8+ or CD4+/CD8+ or CD4-/CD8-**
- **Rarely, may have reduced staining to T-cell markers CD7 > CD5 > CD2**

Mycosis Fungoides – Histological Mimickers





Spongiotic Dermatitis - Eczemas

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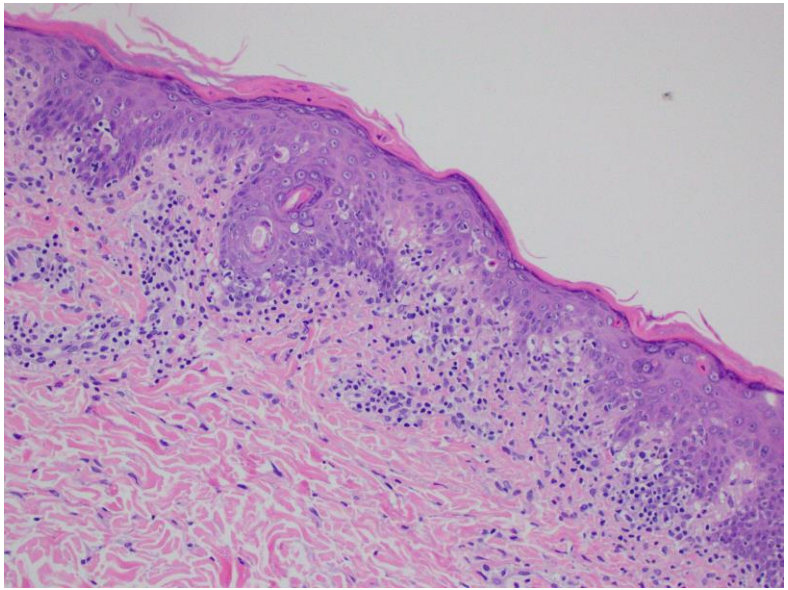
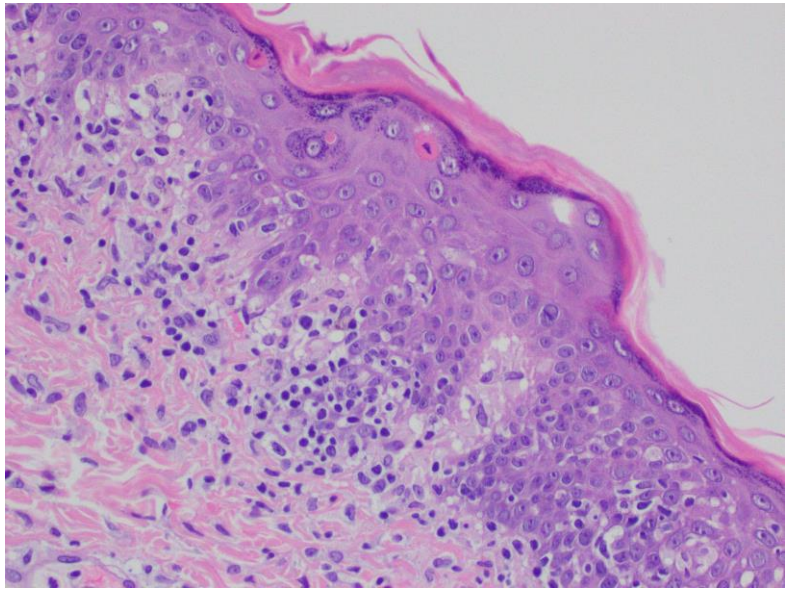
Mycosis Fungoides – Histological Mimickers





Interface / Lichenoid Dermatitis – Pityriasis Lichenoides

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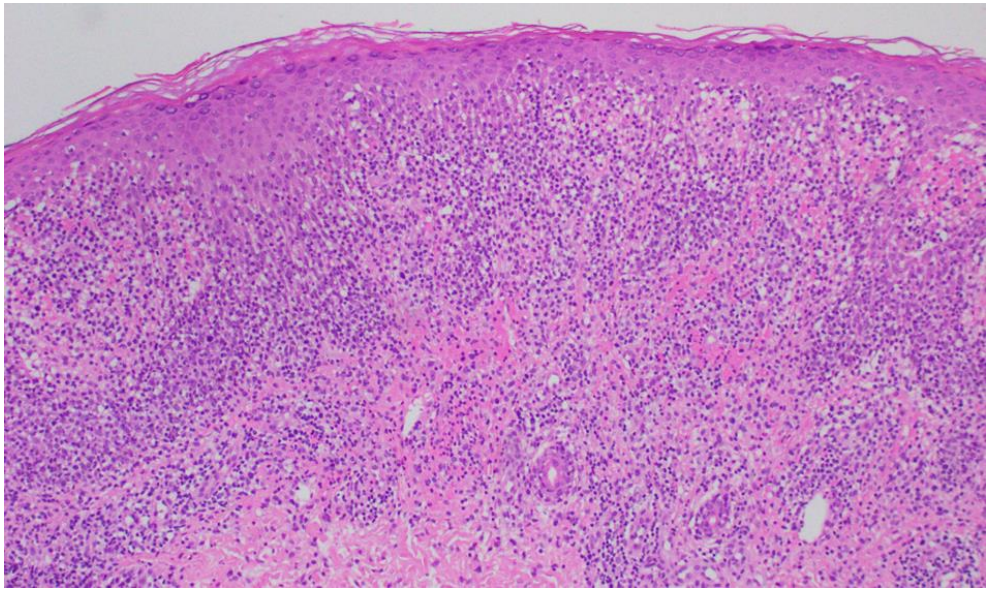
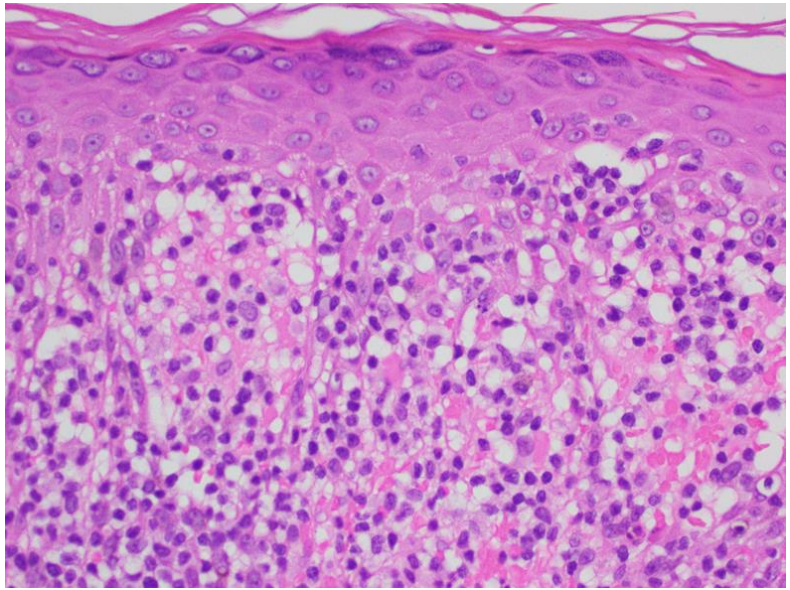
Mycosis Fungoides – Histological Mimickers





Interface / Lichenoid Dermatitis – Pityriasis Lichenoides

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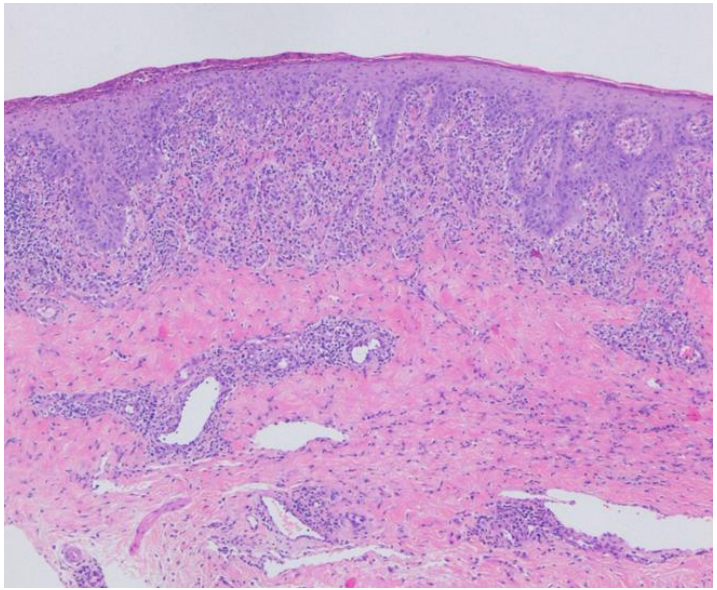
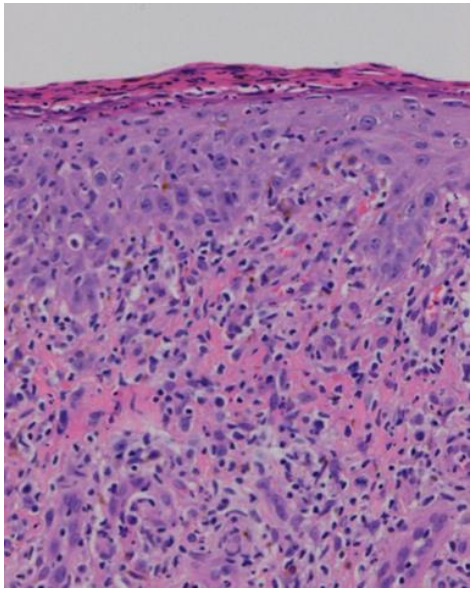
Mycosis Fungoides – Histological Mimickers





Interface / Lichenoid Dermatitis – Secondary Syphilis

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Primary Cutaneous CD30+ Lymphoproliferative Disorders

- 2nd most common form of cutaneous T-cell lymphomas
- Comprise 3 main types:
  - Primary cutaneous CD30+ anaplastic large cell lymphoma (PC-ALCL)
  - Lymphomatoid papulosis (LyP)
  - Borderline lesions

Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709

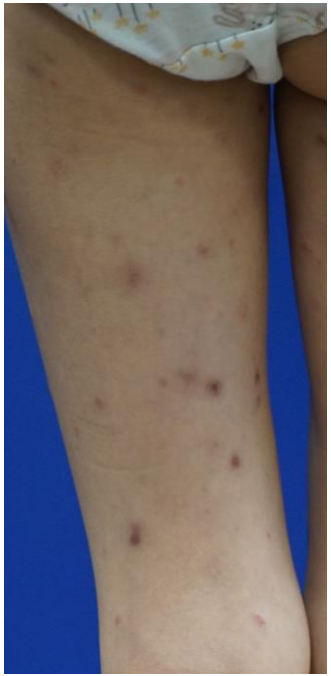
Lymphomatoid Papulosis

- **Chronic**, **recurrent** eruption with **self-healing** papules and nodules, with residual **scarring**
- Manifests clinically and histologically like LyP in adults
- May run **protracted course** over years
- May occur in association with other lymphomas, especially MF, ALCL

Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709

Lymphomatoid Papulosis

Lymphomatoid Papulosis



Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709

Lymphomatoid Papulosis - Mimickers

Pityriasis lichenoides (PLEVA)

Prurigo nodularis

Arthropod bite reactions

Dermatitis artefacta

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Primary Cutaneous Anaplastic Large Cell Lymphoma (PC-ALCL)

- Presents with solitary, large, ulcerated nodule or tumours
- Nodular infiltrates of large pleomorphic, anaplastic tumour cells
- More than 75% express CD30




Kempf W et al., J Euro Acad Dermatol Venereol 2015;29:1696-1709

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PC-ALCL - Mimickers

Squamous cell carcinoma

Cutaneous B-cell lymphomas

Basal cell carcinoma

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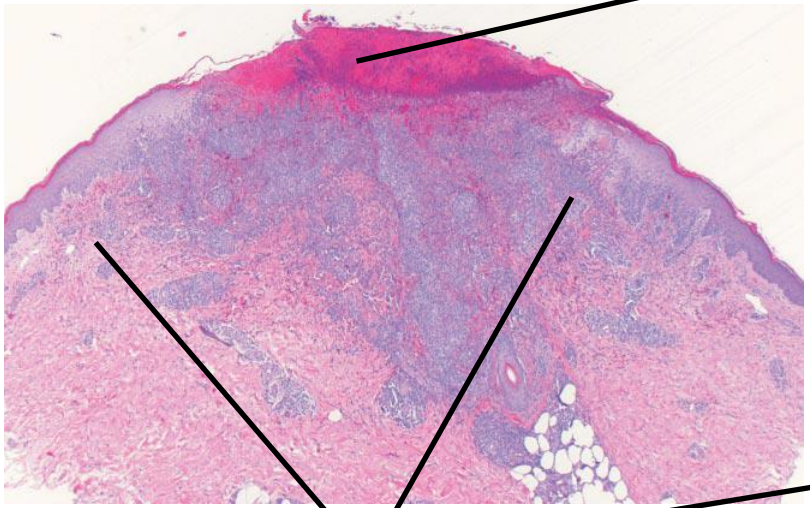
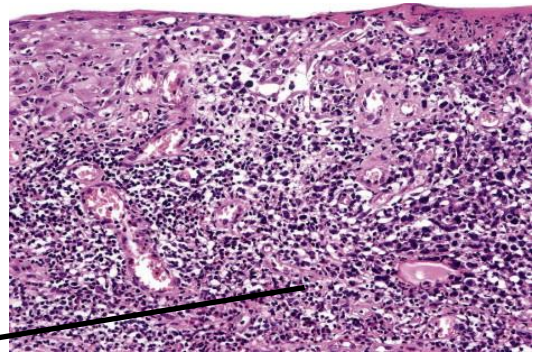
Lymphomatoid Papulosis - Histology



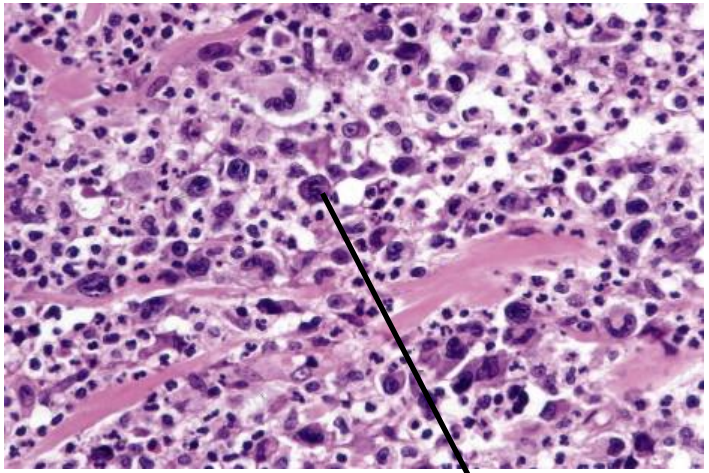
Epidermis may be ulcerated

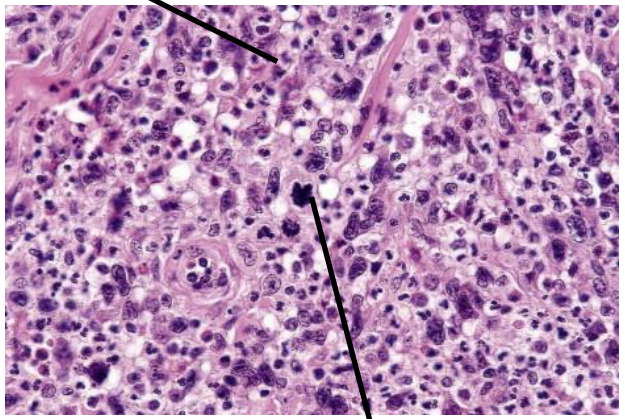


Dense wedge-shaped inflammatory infiltrate in dermis

Lymphomatoid Papulosis - Histology

Admixture of small lymphocytes, neutrophils, eosinophils and histiocytes

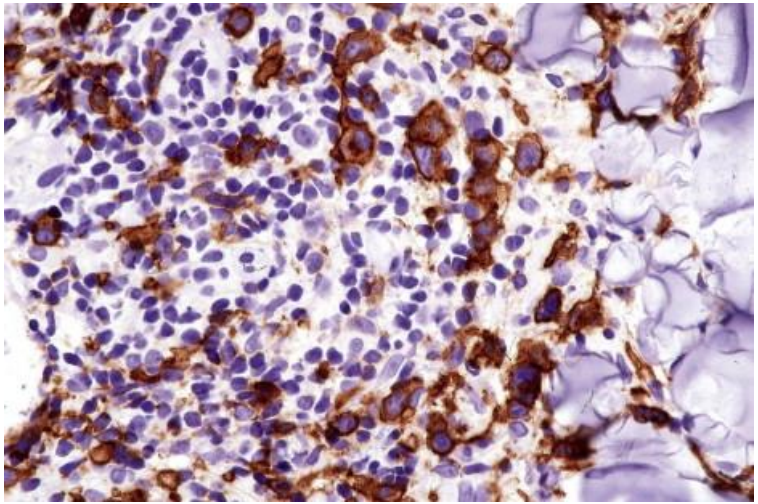




Mitoses

Large pleomorphic cells with irrgular nuclei, sparse chromatin

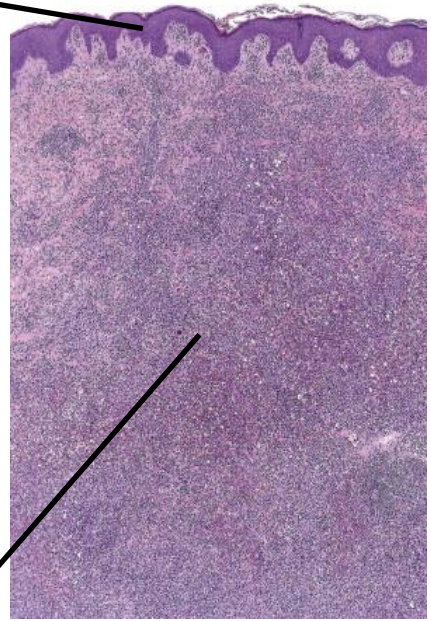
Lymphomatoid Papulosis - Immunohistochemistry

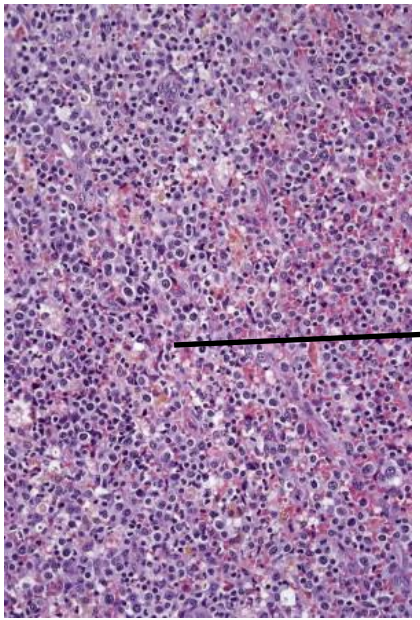


CD3+, CD4+, CD30 +
large cells

PC-ALCL - Histology

Surface may be ulcerated; Epidermotropism may be seen

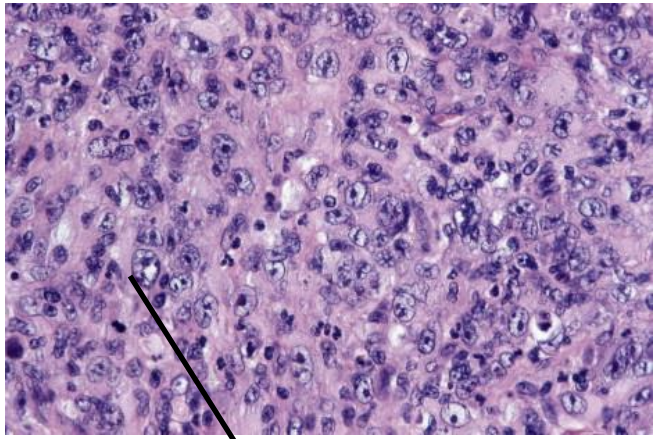




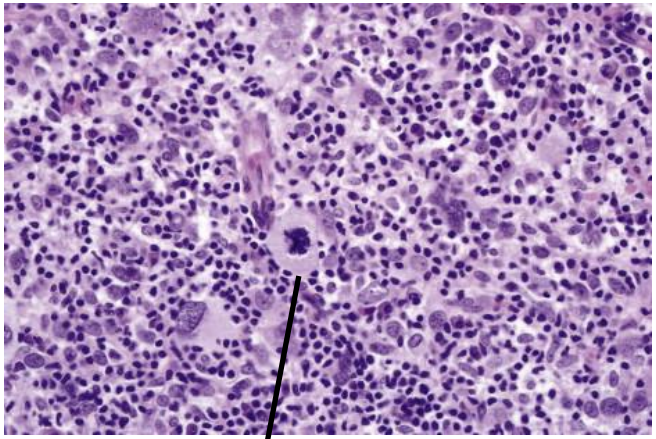
Sheets of large, atypical cells with irregular nuclei and abundant cytoplasm

Dense nodular infiltrate on dermis +/- subcutis

PC-ALCL - Histology

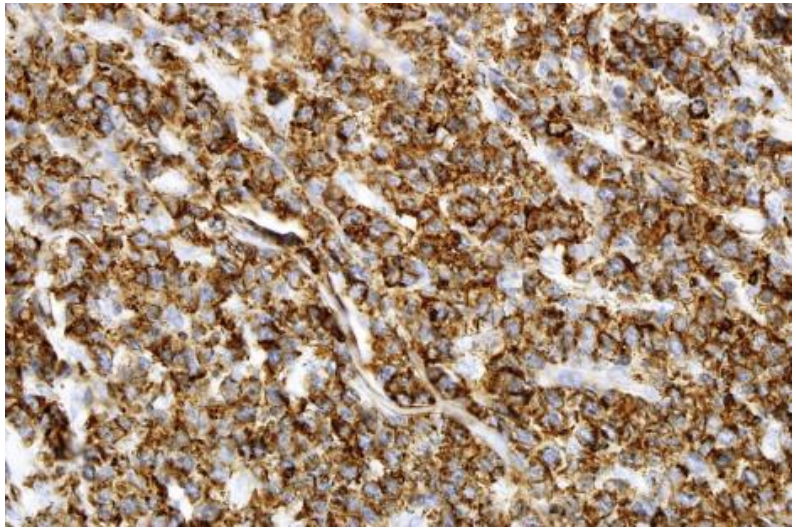


Atypical cells with large nucleus and single/multiple prominent nucleoli



Mitoses may be atypical

PC-ALCL - Immunohistochemistry



CD30+ in > 75% of large cells

CD30+ LPD – Histological Mimickers

Lymphoproliferative diseases with CD30+
CD30+ LPD (LyP and PC-ALCL)
MF and Sezary in transformation
Pagetoid reticulosis
Adult T-cell lymphoma / leukemia
Hydroa-vacciniforme like T-cell lymphoma

Dermatoses with CD30+ expression
PLEVA
Atopic dermatitis
Viral infections e.g. herpesvirus, molluscum
Parasitic infections e.g. scabies
Mycobacterial infections

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Subcutaneous Panniculitis-Like T-cell Lymphoma (SPTCL)

- Uncommon in adults, even rarer in children
- Manifests as subcutaneous nodules
- Concomitant systemic symptoms (fever, lethargy, anorexia)

Koh MJA et al., J Am Acad Dermatol 2009;61:875-881

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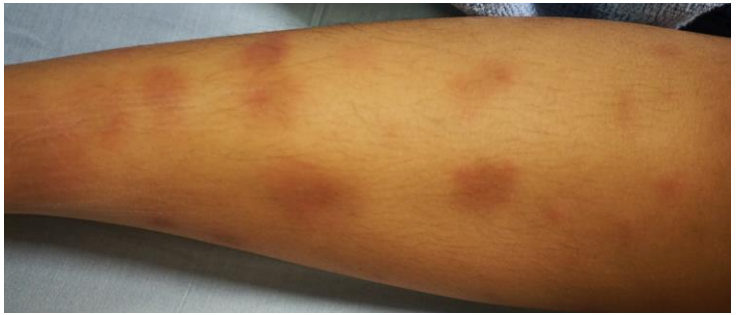
SPTCL - Mimickers



Erythema nodosum

Erythema induratum

Lupus panniculitis

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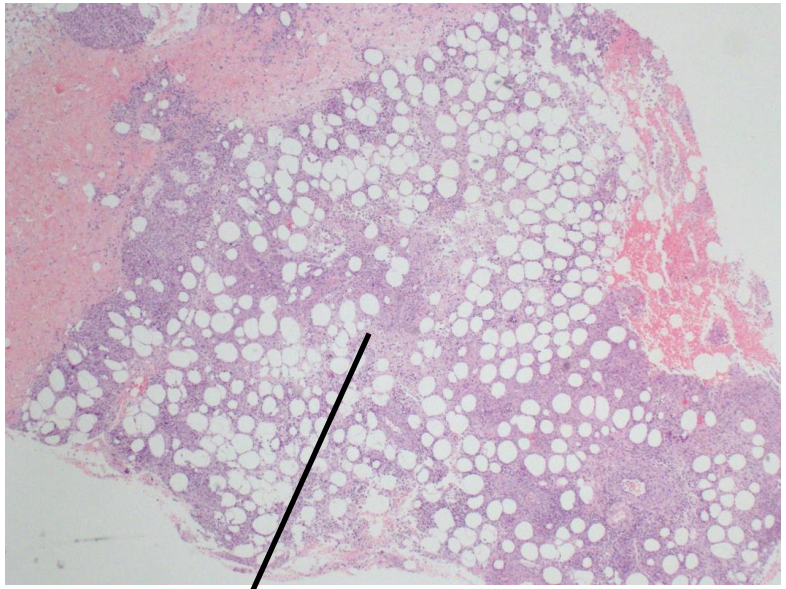
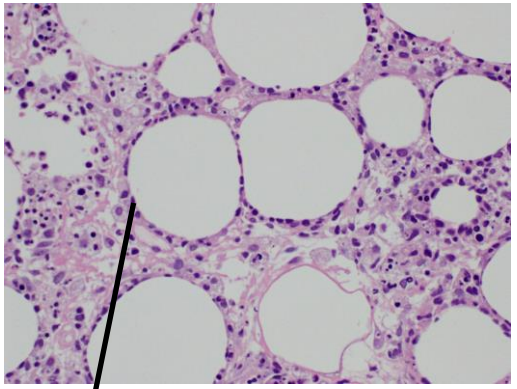
SPTCL - Histology

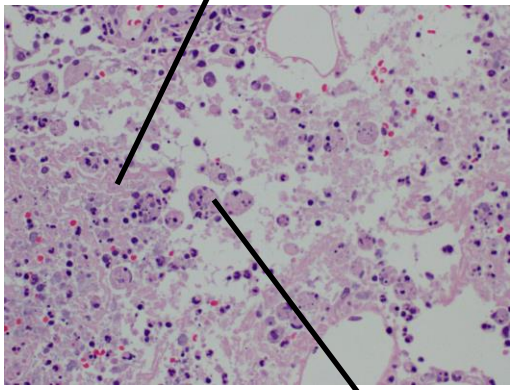


Lobular panniculitis

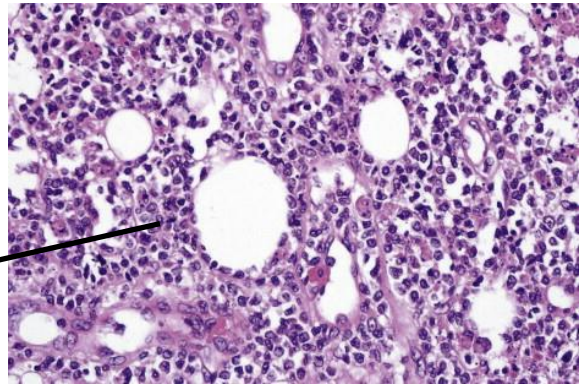


Fat rimming

Fat necrosis can be extensive



"Beanbag" cells



Atypical lymphocytes

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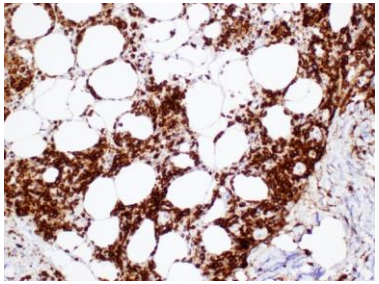
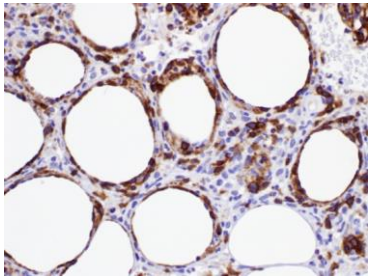
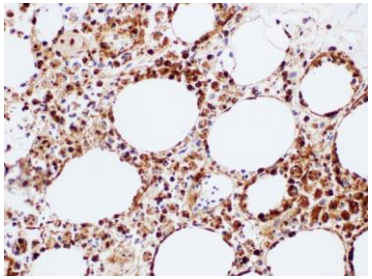
SPTCL - Immunohistochemistry



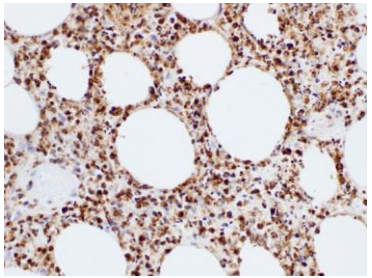
CD3+



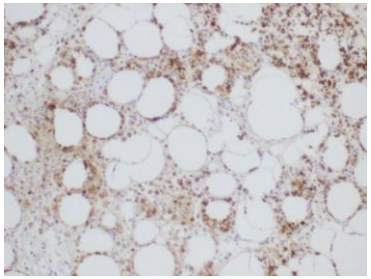
CD8+



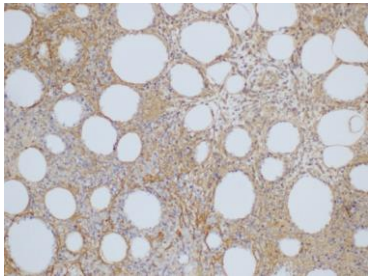
Granzyme B +



TIA 1 +



TCR beta +



TCR gamma -

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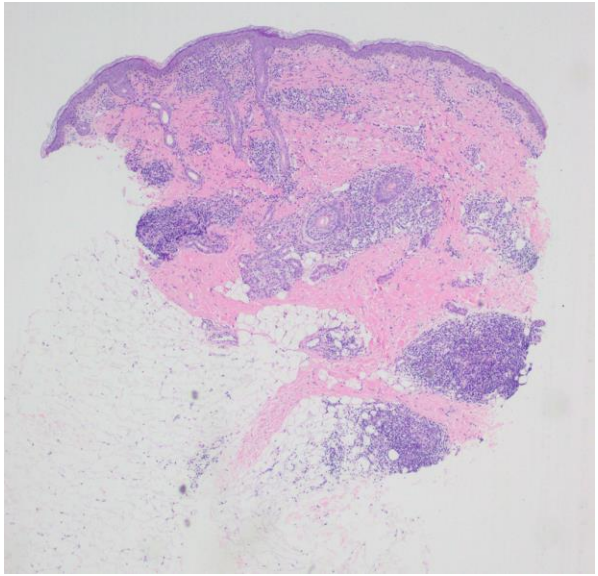
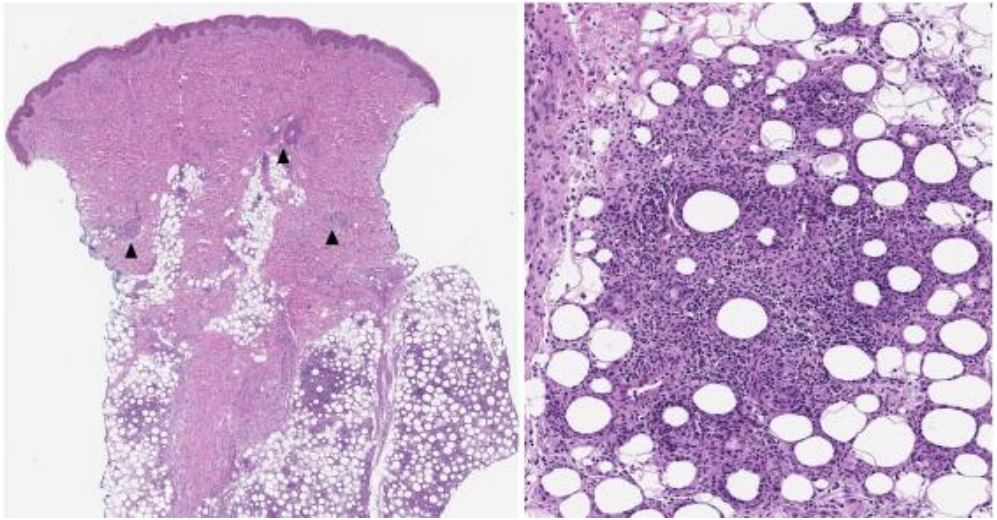
SPTCL – Histological Mimickers



Lupus Panniculitis



Cytophagic Histiocytic Panniculitis

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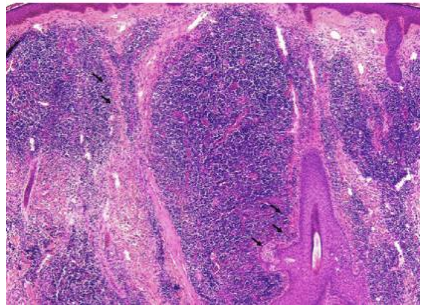
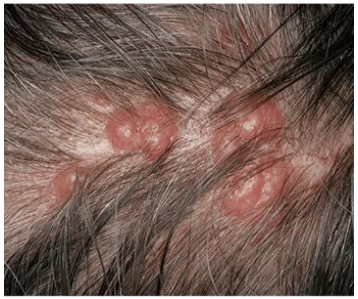
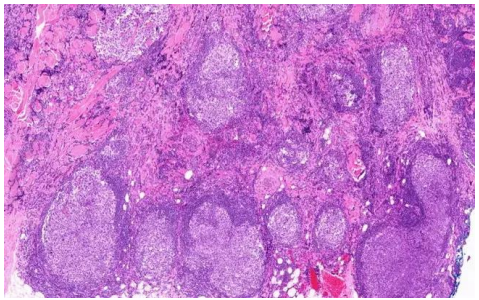
Cutaneous B-Cell Lymphomas

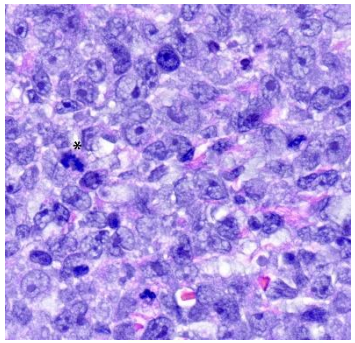


Cutaneous Marginal Zone Lymphoma

Cutaneous Follicle Center Lymphoma







Primary Cutaneous Diffuse Large B-cell Lymphoma, Leg-type

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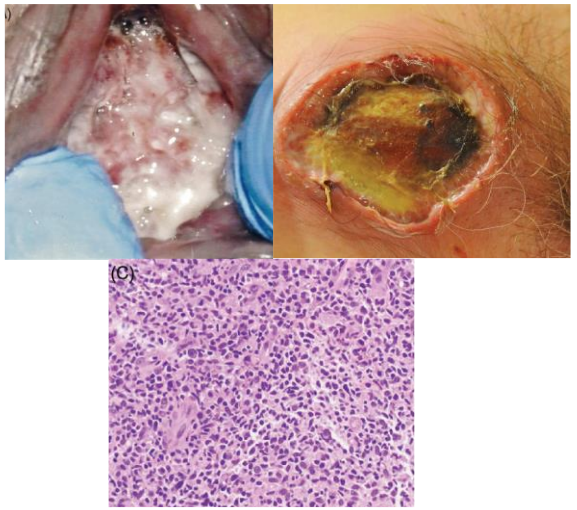
Other Rarer Cutaneous Lymphomas

Hydroa vacciniforme-like EBV lymphoproliferative disorder

Primary cutaneous CD8+ cytotoxic T-cell lymphoma:

EBV+ diffuse large B-cell lymphoma



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Conclusion

- Mycosis fungoides is the most common cutaneous lymphoma in adults and children – many clinical and histological mimickers
- Other cutaneous lymphomas are even rarer
- Requires high index of suspicion for diagnosis
- Biopsies essential to clinch diagnosis – importance of clinical-pathological correlation and may require several sequential biopsies

SGH-NCC Cutaneous Lymphoma Clinic

- Twice / month (2nd Wed AM, 4th Tue PM)
- SGH (kiv move to NCC)

Dermatology:

Medical Oncology:

Radiation Oncology:

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