U006 Primary Cutaneous Lymphomas: Diagnosis, Staging and When to Refer
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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY
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Cutaneous lymphomas in the 2016 update of the WHO classification
1) Specific entities of mature B-cell neoplasms
   a) Primary cutaneous follicle center lymphoma
   b) Primary cutaneous diffuse large B-cell lymphoma, leg type

2) Specific or provisional entities of mature T- and NK-cell neoplasms
   a) Hydroa vacciniforme-like lymphoproliferative disease
   b) Subcutaneous panniculitis-like T-cell lymphoma
   c) Mycosis fungoides
      (1) Mycosis fungoides variants
         (i) Pilotropic mycosis fungoides
         (ii) Granulomatous slack skin
         (iii) Localized pagetoid reticulosis
   d) Sézary syndrome
   e) Primary cutaneous CD30+ T-cell lymphoproliferative disorders
      i) Lymphomatoid papulosis
      ii) Primary cutaneous anaplastic large cell lymphoma
   f) Primary cutaneous gamma-delta T-cell lymphoma
   g) Primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T-cell lymphoma
      (provisional)
   h) Primary cutaneous acral CD8+ T-cell lymphoma (provisional)
   i) Primary cutaneous CD4 positive small/medium T-cell lymphoproliferative disorder (provisional)
   j) Epstein-Barr virus (EBV) positive mucocutaneous ulcer (provisional)

3) Other lymphomas with frequent primary cutaneous involvement
   a) Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma
   b) Intravascular large B-cell lymphoma
   c) Adult T-cell leukemia/lymphoma
   d) Extranodal NK/T cell lymphoma, nasal type

T-cell: CD3
B-cell: CD20 (CD79a, PAX-5)
NK/T-cell: CD56

What are the tools?
- Hematoxylin and Eosin Biopsy
- Immunohistochemistry
- Flow cytometry
- Molecular studies
Flow cytometry: cell suspension, blood, tissue, RPMI media or Saline soaked gauze
Count and sort cells using surface and cytoplasmic antigens (e.g. CD markers)
Utility
1. B-cell lymphomas: tissue, low yield
2. Sézary syndrome: blood

Molecular studies
Polymerase chain reaction (PCR)
Technology in molecular biology used to amplify a single copy or a few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequences
Preformed on: Paraffin embedded tissue or Fresh tissue
Utility: rearrangements
1. T-cell receptor (TCR): molecule found on the surface of T lymphocytes that is responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules
2. Immunoglobulin heavy locus (IgH): region on human chromosome 14 that contains a gene for the heavy locus of human antibodies (immunoglobulins)

H+E biopsy
Formalin fixed and embedded in paraffin
Two 4mm punch biopsies: B-cell lymphoma or more than one morphology
1 long shave and one 4 mm punch: Mycosis fungoides patch or plaque

Can do molecular studies on paraffin embedded tissue but cannot do flow cytometry

Extranodal NK/T cell lymphoma nasal-type
Lethal midline granuloma, polymorphic reticulosis, midline malignant reticulohistiocytosis
Asia, Mexico, Central and South America
The skin is the second most common site of involvement after the nasal cavity/nasopharynx
skin involvement may be a primary or secondary manifestation of the disease
Most common lymphoma of the nasal cavity
Usually presents with upper aerodigestive tract symptoms
Immunology: CD2+, CD56+, cytoplasmic CD3e+, TIA-1+,CD3-, CD4-, CD5-, CD8-, CD30-
Negative for germline rearrangement of T lymphocytes
EBV positive
Epstein-Barr encoding region (EBER) by in-situ hybridization
EBV LMP-1 IHC gives inconsistent results

Cutaneous B-cell Lymphomas
Approximately 20-25% of all cutaneous lymphomas
Cutaneous lymphoid hyperplasia (CLH): Shows considerable clinical overlap so repeat skin biopsies with review by dermatopathology and/or hematopathology is important
Bloodwork
Complete blood count (CBC) with differential, Lactate dehydrogenase, Comprehensive metabolic panel, HIV, Lyme ELISA/titer
Consider: Peripheral blood flow cytometry - lymphoma panel
**Systemic evaluation**
- Recommended for every patient even if only a solitary lesion to distinguish between primary cutaneous B-cell lymphoma versus secondary involvement of skin
- Computed tomography (CT) chest/abdomen/pelvis with and without contrast OR Positron emission tomography (PET) / CT scan
- Bone marrow biopsy: No consensus for indolent cutaneous B-cell lymphomas, suspect a secondary CBCL or patient has abnormal bloodwork or systemic symptoms

Autoimmune associations: Helicobacter pylori, Hepatitis panel, Thyroid-stimulating hormone

Molecular: Monoclonal rearrangement of Immunoglobulin heavy chain gene, 50% indolent lymphomas

Treatment:
- follow clinically
- Topical / intralesional steroids
- XRT
- Rituximab infusions or IL Rituximab
- Loss of CD20 expression in cutaneous B-cell lymphoma (both primary and secondary) after treatment with rituximab

1) **Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)**
   (Primary cutaneous marginal zone lymphoma)
   Papules and nodules on extremities, trunk
   Immunology: CD20+, CD79+, Bcl2+, CD5-, CD10-, Bcl6-
   Monoclonal expression of either kappa or lambda Ig light chain (10:1)

2) **Primary cutaneous follicle center lymphoma**
   Papules coalescing into a plaque or plaques on scalp, face, back
   Immunology: CD20+, CD79a+, Bcl6+, CD10+ follicular / CD10- diffuse, Bcl2- (usually, except when secondary cutaneous), IgM negative, Ki-67 reduced proliferation of neoplastic follicles
   Follicular Lymphoma (systemic) with cutaneous involvement: CD20+, CD10+, Bcl2+, Bcl6+

3) **Primary cutaneous diffuse large B-cell lymphoma, leg type**
   Leg but can arise elsewhere, nodules that can ulcerate and can have lymphadenopathy
   Immunology: CD20+, CD79a+ BCL-2+, BCL-6 +(-), MUM-1+, FOX-P1+, IgM positive
   Monoclonal rearrangement of Ig genes in majority of cases

**Cutaneous T-cell Lymphomas**
1) Other Cutaneous T-cell Lymphomas
2) Mycosis Fungoides
   - Variants
3) Sézary Syndrome

1) **Other Cutaneous T-cell Lymphoma Variants**
- Adult T-cell leukemia/lymphoma (ATLL)
- Cutaneous gamma/delta T-Cell Lymphoma (CGD-TCL)
Primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphoma – provisional entity
Subcutaneous panniculitis like T-cell lymphoma alpha/beta (SPTL)
CD30+ Lymphoproliferative Disorder
  - Lymphomatoid Papulosis (LyP)
  - Anaplastic large cell lymphoma (ALCL)

Adult T-cell leukemia/lymphoma (ATLL)
Four clinically distinct entities: acute, chronic, smoldering and lymphomatous
Acute ATLL is characterized by the presence of leukemia, lymphadenopathy, organomegaly, hypercalcemia and skin lesions (in approximately 50%)
The lymphomatous type is characterized by lymphadenopathy without extranodal lesions, lymphomatosis or hypercalcemia, and with sporadic leukemic cells in less than 1%
The chronic type is characterized by lymphocytosis, elevated LDH, and no hypercalcemia with 5% or more of atypical lymphocytes in the blood
The smoldering variant of ATLL is characterized primarily by skin lesions, which closely resemble mycosis fungoides in presentation and bears a more favorable prognosis than the other variants
Cutaneous manifestations are generally a presentation of disseminated disease and can occur in 43-72% of cases
Endemic in south of Japan and in the Caribbean
ATLL can appear on the skin as erythroderma, infiltrated plaques, localized or generalized macules, papules, patches, nodules, or tumors.
The gold standard for the diagnosis of ATLL is a positive HTLV-1 serology
Histopathology: Features similar to mycosis fungoides
Immunology: CD3+, CD4+, CD8-, CD25+, FOX-P3+/-, PD-1+

Cutaneous gamma/delta T-cell lymphoma
Previously described as: SPTL with a gamma/delta phenotype, Mycosis fungoides “a tumeur d’emblee,” Generalized pagetoid reticulosis (Ketron-Goodman type)
Adults affecting both sexes equally, rapidly growing disseminated plaques and/or ulceronecrotic nodules or tumors that occur mostly, but are not limited to, the extremities
A fourth of patients have an associated autoimmune disorder
Patients can present with systemic symptoms including lymphadenopathy, hepatosplenomegaly, cytopenias, and/or elevated liver function tests
Constitutional symptoms of fever, night sweats and fatigue are common
Hemophagocytic syndrome
There are three histologic patterns of involvement: epidermotropic, dermal and subcutaneous
Bone marrow examination may show histiocytic hyperplasia, hemophagocytosis or decreased cellularity
The comprehensive criteria for diagnosis of CGD-TCL: prominent involvement of the dermis and epidermotropism, CD4-/CD8- phenotype, aberrant expression of CD56, TCR gamma gene rearrangement, unresponsiveness to chemotherapy with an extremely poor prognosis
Immunology: CD3+, CD5+, TCR-γ+, TIA-1+, CD56+, CD4-, CD8-, CD30-, CD57-, BF1-
Monoclonal rearrangement of TCR genes

Primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphoma – provisional entity WHO 2016
Chronic prodrome of patch plaque lesions
Misdiagnosed as eczema, psoriasis or MF
Mucosal involvement
Poor prognosis
Subcutaneous panniculitis like T-cell lymphoma
Previously described as: Malignant histiocytosis or histiocytic cytophagic panniculitis, Cutaneous gamma/delta T-cell lymphomas
Autoimmune disorders, especially lupus erythematosus, are present in a distinct number of patients (20%)
Patients can be misdiagnosed as having lupus erythematosus panniculitis (lupus profundus)
Clinical features overlap
positive ANA, hematologic changes (anemia, neutropenia), renal changes, and positive DIF on lesional skin
Plaques or subcutaneous nodules on extremities (lower) without ulceration
Immunology: CD3+, CD8+, BF1+, cytotoxic markers expressed (TIA-1, granzyme B, perforin)
CD4-, CD30-, Ki-67 highlights ‘rimming’
Monoclonal rearrangement in majority of cases
If associated hemophagocytic syndrome worse prognosis
May be treated with oral steroids
Diagnosis of lupus panniculitis should be carefully made: clinically difficult to distinguish and histology more overlapping features than not
Patients with lupus erythematous are at increased risk of hematologic malignancies but mostly B-cell lineage

CD30+ T-cell Lymphoproliferative Disorder
30% of all CTCL
Subtypes:
1. Lymphomatoid papulosis (LyP) : WHO “clinical perspective not considered a malignant disorder”
2. Cutaneous anaplastic large cell lymphoma (C-ALCL)
3. Borderline cases
The diagnosis of primary cutaneous ALCL versus LyP is based on clinical presentation and disease course
CD30 antigen is a cytokine receptor of the TNF receptor superfamily
Interpretation of CD30 staining should be put into context of clinical information and full immunophenotype as it can be seen in arthropod bite, scabies infestations, drug reactions, present in other cutaneous and systemic lymphomas, mycosis fungoides with CD30+ large cell transformation
Therapeutic relevance: Brentuximab vedotin selectively targets tumor cells expressing the CD30

Lymphomatoid Papulosis
Occurs mostly in young adults as violaceous to reddish-brown papular, papulonecrotic, and/or nodular skin lesions at different stages of development
Mostly on the trunk and proximal extremities
Usually less than 1cm in size, self healing with ulceration and disappear within 3-12 weeks leaving behind superficial scars
Few, many, regional or generalized
Can be larger in size
Time interval between eruptions is variable, ranging from weeks to several years
Histopathology is divided into three (main) different subtypes
Type A (conventional) : wedge-shaped and have evidence of scattered or small clusters of large CD30+ cells mixed with histiocytes, small lymphocytes, neutrophils, and/or eosinophils
Type B (mycosis fungoides-like): uncommon (less than 10%) and are characterized by a wedge-shaped or sometimes band-like infiltrate of epidermotropic small atypical cells with cerebriform nuclei, similar to the histopathology observed in MF. Unlike the other types, these cells may not express the CD30 antigen except in small collections of epidermal cells and rare dermal cells.

Type C (anaplastic large cell lymphoma-like): nodular infiltrate with sheets of large CD30+ T-cells. Can not distinguish from ALCL histologically!

Other subtypes:
- Type D (cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma like)
- Type E (angiocentric/angiodestructive)
- Type F (follicular lymphomatoid papulosis)

Other histologic variants:

**Immunology:** CD3+, CD5+, CD30+, CD4+(-), MUM-1+,CD8-(+), TIA-(+),CD56-

Monoclonal rearrangement of TCR genes

At risk for a second cutaneous or nodal lymphoid malignancies: mycosis fungoides, cutaneous or nodal anaplastic large-cell lymphoma, and Hodgkin lymphoma (4%-25% of affected patients) and can occur before, concurrent with, or after the onset of LYP.

Before a diagnosis of LYP is made in setting of MF it is crucial to rule out large cell transformation.

**Staging:**
- Complete history, including previous lymphoid neoplasms (in particular Hodgkin lymphoma and MF)
- B-symptoms
- Physical examination (lymph node)
- Laboratory studies: CBC, CMP, LDH

**Treatment:**
- None of the therapies for LYP has been proven to alter course of disease or to prevent LYP-associated secondary lymphomas
- Few lesions: clinically follow or topical steroids
- Numerous, disseminated: Methotrexate, Phototherapy especially PUVA

*Primary Cutaneous Anaplastic Large Cell Lymphoma*

Occurs mainly in adults with a higher prevalence in men than women

Solitary or localized violaceous to reddish-brown nodules or tumors with ulceration
- Multifocal 20%
- Can regress, but more often result in a partial rather than complete resolution and leaves scarring

**Immunology:** CD3+, CD4+(-), CD30+, MUM-1+, TIA-1+(-), CD8-(+), CD15-,EMA-(+),CD56-

Most lesions demonstrate monoclonal rearrangement of TCR genes

Distinction of primary C-ALCL from systemic ALCL is imperative given that skin is the most common extranodal site of disease, interchromosomal (2;5) translocation and related ALK-1 positivity typically absent in C-ALCL but can be negative in S-ALCL

Should be made in exclusion of the diagnosis of mycosis fungoides

FISH analysis of IRF4 translocation is negative in MF with CD30+ large cell transformation and positive in C-ALCL

**Treatment:** XRT or Excision if skin only, Brentuximab vedotin

2) **Mycosis Fungoides**

Most common type of cutaneous T-cell lymphoma, Classic Alibert-Bazin

- Patch, plaque, tumor
- Double covered areas
Higher risk of secondary malignancy: Hodgkin lymphoma > non-Hodgkin lymphoma, Non hematologic malignancy (Melanoma)
Associated with LYP

Histopathology:
Small cerebriform cells, epidermotropism is common, Darier’s nests (Pautrier’s microabscesses)
Basilar or disproportionate epidermotropism
Papillary dermis with fibrosis
Langerhans cells are usually increased
Band-like infiltrate
Nodular to diffuse infiltrate

Immunology:
a/b T-helper memory lymphocytes
CD3+, CD4+, CD5+, CD8-, CD7- (limited relevance)
Large cell transformation: Large cells >25% infiltrate or forming nodules, CD30+/-

Clonality of T-cells can be established by polymerase chain reaction of T-cell receptor gene rearrangements (TCRs):
- Until recently, fresh tissue was of higher yield for TCRs; however, these studies can now be performed on formalin-fixed paraffin-embedded tissue
- A broad shave biopsy is also preferred for molecular studies as more DNA can be extracted by maximizing the malignant epidermotropic infiltrate
- Clonality may be stage dependent and is seen in only 20-40% of patch stage mycosis fungoides as there are admixed inflammatory T-cells
- Several benign dermatoses such as pityriasis lichenoides, have shown monoclonal populations of T-cell lymphocytes

***Diagnosis clinicopathologic correlation
Biopsies: 1 punch and 1 H+E, if patches/plaques and tumors sample all morphologies
Multiple sequential biopsies often needed
Sun protected, double covered areas, untreated for 2-3 weeks

Staging:
Physical exam for estimation of tumor burden
Computed tomography (CT) chest/abdomen/pelvis with and without contrast OR Positron emission tomography (PET) / CT scan
Laboratory studies: CMP/CBC/LDH
Blood for flow cytometry / Sézary cell count

Long-term Outcome of 525 Patients With Mycosis Fungoides and Sézary Syndrome
T1: 2% die of their disease
T2: 15% die of their disease
T3 or T4: 24% disease die of their disease
Common cause of death during the tumor phase is sepsis from Pseudomonas aeruginosa or Staphylococcus aureus caused by chronic skin infection and subsequent systemic infections

Long-term Outcome of 525 Patients With Mycosis Fungoides and Sézary Syndrome
Risk of progression cutaneous disease @ 5, 10, and 20 years
T1: 10%, 13%, and 16%
T2: 22%, 32%, and 40%
T3: 56%, 72%, and 81%
T4: 48%, 57%, and 78%

Risk of progression for extracutaneous disease @ 5, 10, and 20 years
T1: 1%, 2%, and 2%
T2: 8%, 9%, and 9%

Risk for disease progression worsened with more advanced T classification

Treatment:
Stage dependent
Early: nbuvb/PUVA, topical steroids, topical chemotherapy, imiquimod, topical retinoids
Later: bexarotene, renbuvb/repUVA, HDAC inhibitors, photophoresis, xrt, Allogenic stem cell transplantation, Total body electron beam irradiation (Limited availability)

Topical Corticosteroids for Mycosis Fungoides Experience in 79 patients
T1: 94%
T2: 82%
Patch/ plaque
Side effects:
Reversible depression of serum cortisol levels occurred in 10 patients (13%)
Minor skin irritation occurred in 2 patients and localized, reversible skin atrophy in 1
Potency: temperature, hydration, occlusion
Arch Dermatol. 1998;134(8):949-954

Mechlorethamine
Alkylating agent: cytotoxic to T-cells, immune effect?
Aqueous 0.02% ACD 67% CR 63%
Compounded ointments 0.02% - 0.04% ACD 8% CR 50%
Gel 0.016% (VALCHLOR®)
Chemotherapy in Cutaneous T-cell Lymphoma Positive Results of a Randomized, Controlled, Multicenter Trial Testing the Efficacy and Safety of a Novel Mechlorethamine, 0.02%, Gel in Mycosis Fungoides JAMA Dermatol. 2013;149(1):25-32.

Bexarotene (Targretin®) 1% Gel
CTCL (1A and 1B) refractory or failing other therapies
Second generation retinoid RXR
Inhibits cell growth and induces apoptosis
Minimal systemic absorption unless >40% BSA
Open label ORR 54-63%
QD escalating to 3-4x day
20 weeks
nbUVB 311nm
Used since 1999
DNA damage, apoptosis of cells in epidermis, immunomodulation
Induction/Clearing, Consolidation 1-3 months, Maintenance
3x/wk (2x/wk longer to clear)
1.5 to 14 months
20-52 treatments
CR 54-91%  77%
Patch vs plaque some difference
Maintenance therapy:
Maintenance therapy does decrease relapse <12 months
Short term vs long term maintenance: no difference
Side effects: >10% erythema/pruritus, Idiopathic guttate hypomelanosis, Photo-aging, conjunctivitis
Photo carcinogenicity: no significant association between nbUVB treatment and BCC, SCC or melanoma,
small increase in BCCs amongst those also treated with PUVA

PUVA
8-MOP interacts with pyrimidines to form stable DNA monoadducts -> crosslinks -> transcription inhibited
Efficacy: 1A median 90% / 1B median 77%
Side effects
Short term: Erythema, pigmentation, blistering, nausea
Long term: Actinic damage, NMSCA, melanoma

Mycosis Fungoides subtypes/variants
1. Folliculotropic (Pilotropic) / Syringotropic mycosis fungoides
2. Pagetoid reticulosis (Woringer-Kolopp)
3. Granulomatous MF ‘histology’ / Granulomatous slack skin

3) Sézary syndrome
Abrupt onset of erythroderma and lymphadenopathy, skin folds are spared, intense pruritus
Hyperkeratosis of palms and soles, alopecia, onychodystrophy
Lymph nodes: involved or dermatopathic
Bone marrow: rarely involved
Erythroderma: Sézary syndrome, erythrodermic mycosis fungoides, atopic dermatitis, psoriasis, drug reaction, pityriasis rubra pilaris, Graft-versus-host disease, Norwegian scabies, generalized contact dermatitis, paraneoplastic, and idiopathic
Sézary syndrome:
- Same monoclonal population of T lymphocytes in peripheral blood and skin
- At least 1000 circulating Sézary cells/mm3
- Increased CD4+:CD8+ ratio (>10)
- Increase population of CD4+/CD7- or CD4+/CD26-
- Loss of T-cell antigens (CD2, CD3, CD4, CD5)
Histopathology: similar to mycosis fungoides but typically less epidermotropism OR psoriasiform dermatitis
Immunophenotype: CD3+, CD4+, CD7-, CD8-
Whole genome and exome sequencing has revealed somatic copy number variations as predominant mutations in Sézary cells, affecting apoptosis, NFκB signaling, DNA integrity, and T-cell activation.

Specific type of T-cell lymphoma
Separated from mycosis fungoides
Blood for flow cytometry

Hydrochlorothiazide and Cutaneous T Cell Lymphoma
HCTZ is commonly prescribed and may be a putative antigen in a small subset of early MF patients. Careful drug histories and a trial off medication are warranted.

Psoriasis and Mycosis Fungoides?
Association between psoriasis and MF
Possibly related to the chronic lymphocyte stimulation that occurs during psoriasis that eventually leads to a dominant clone and the evolution to CTCL
Coexist or progress
Cases of early MF which are being misdiagnosed
Immunological surveillance is crucial in MF, especially at its early stages
Early stages of MF Th1 cytokines -> later stages shift to Th2 cytokines
Suppression of immune responses is induced by TNF-a inhibition / cyclosporine accelerating the disease evolution

Cutaneous lymphoma in children
Hypopigmented mycosis fungoides is over represented: CD8+, Distinction from vitiligo
Alopecia mucinosa versus folliculotropic mycosis fungoides
Lymphomatoid papulosis
Diagnosis of mycosis fungoides in children requires clinicopathologic correlation and time

Highlights of changes in 2016 WHO classification of lymphoid, histiocytic, and dendritic neoplasms - that apply to the dermatologist
1. EBV+ mucocutaneous ulcer: Newly recognized entity associated with iatrogenic immunosuppression or age-related immunosenescence.
2. Hydroa vacciniforme–like lymphoproliferative disorder: Name changed from lymphoma to lymphoproliferative disorder due to its relationship with chronic active EBV infection and a spectrum in terms of its clinical course.
3. Erdheim-Chester disease: Should be distinguished from other members of the juvenile xanthogranuloma family; often associated with BRAF mutations.
4. Lymphomatoid papulosis: New subtypes described with similar clinical behavior but atypical histologic/immunophenotypic features.
5. Primary cutaneous γ δ T-cell lymphoma: Important to exclude other cutaneous T-cell lymphomas/lymphoproliferative disorders that may also be derived from γ δ T cells such as mycosis fungoides or lymphomatoid papulosis.
6. Primary cutaneous acral CD8+ T-cell lymphoma: New indolent provisional entity, originally described as originating in the ear.
7. Primary cutaneous CD4+small/medium T-cell lymphoproliferative disorder: No longer to be diagnosed as an overt lymphoma due to limited clinical risk, localized disease, and similarity to clonal drug reactions. Remains a provisional entity.
8. Peripheral T-cell lymphoma (PTCL), NOS: Subsets based on phenotype and molecular abnormalities being recognized that may have clinical implications but are mostly not a part of routine practice at this time.

**SUMMARY**

**NK/T cell**
Extranodal NK/T cell lymphoma nasal-type: EBV positive

**B-cell**
Primary cutaneous marginal B-cell lymphoma: indolent NOW other lymphomas with frequent primary cutaneous involvement: Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
Primary cutaneous follicle center lymphoma: indolent, rule out systemic follicular lymphoma
Primary cutaneous diffuse large B-cell lymphoma, leg type: intermediate clinical behavior

**T-cell**
Mycosis Fungoides and variants
T1 <10% patches and plaques: 2% die of their disease
Sézary syndrome: Flow cytometry, Photophoresis
CD30+ Lymphoproliferative Disorder: clinicopathologic correlation
Lymphomatoid Papulosis: risk of secondary lymphoid malignancy - MF
Cutaneous anaplastic large cell lymphoma
Subcutaneous panniculitic like T-cell lymphoma alpha/beta: autoimmune association
Cutaneous gamma/delta T-Cell Lymphoma: aggressive
Primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphoma – provisional: prodrome chronic plaques with poor prognosis
Adult T-cell leukemia/lymphoma: positive HTLV-1 serology

Additional References: