Cutaneous Lymphoma Foundation

Cutaneous Lymphoma Overview

FARAH R. ABDULLA, MD, FAAD
UNIVERSITY OF CHICAGO
JUNE 25, 2016

Overview of Cutaneous Lymphoma

- Classified as NHLs by WHO
- Rare
- 2 major groups
  - Cutaneous T-cell Lymphomas
    - Mycosis fungoides and Sézary syndrome most common types
  - Cutaneous B-cell Lymphomas

Overview of Cutaneous Lymphoma

- Cutaneous T-cell Lymphomas (CTCL)
  - Mycosis Fungoides (MF)
  - Sezary Syndrome (SS)
  - CD30+ lymphoproliferative disorders
    - Lymphomatoid papulosis (LyP)
    - Primary Cutaneous Anaplastic Large Cell Lymphoma (pcALCL)
- Cutaneous B-cell Lymphomas (CBCL)

Overview of Cutaneous Lymphoma

- CTCL: 75–80% of all cutaneous lymphomas.
  - Mycosis fungoides and Sézary syndrome the most common
  - CD30+ lymphoproliferative disorders: for 10–15%
- Cutaneous B-cell lymphomas: 20–25% of all cutaneous lymphomas
  - Primary cutaneous follicle center lymphoma is the most common form

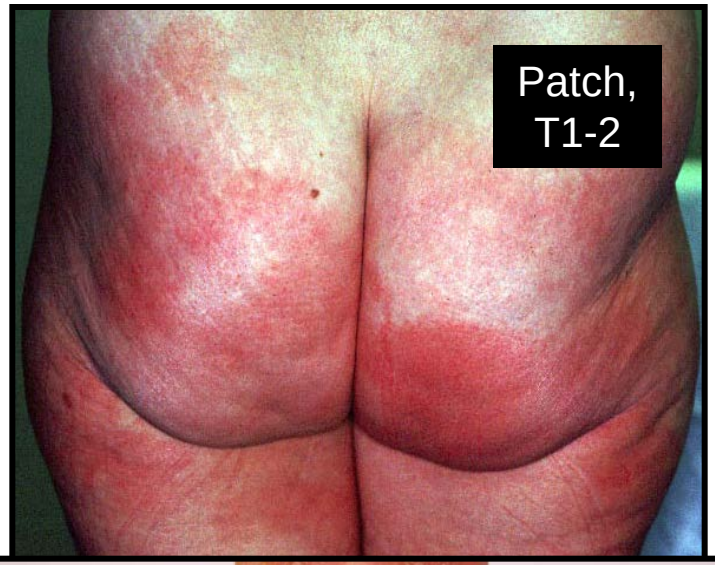
WHO-EORTC Classification of Primary Cutaneous Lymphomas

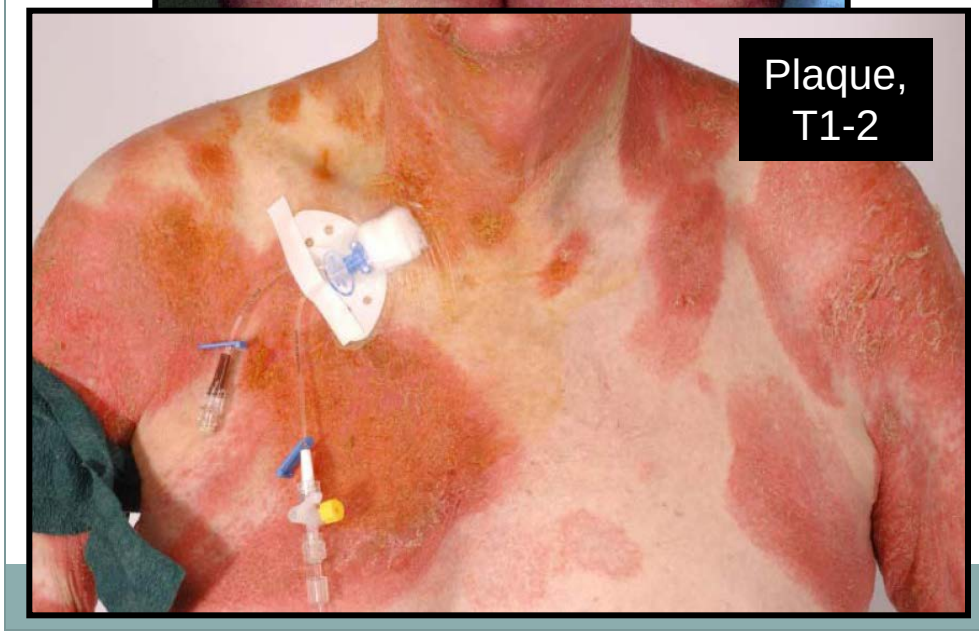
- **Cutaneous T-cell lymphomas**
  - Mycosis fungoides
  - Sézary syndrome
  - Primary cutaneous CD30+ lymphoproliferative disorders
    - Lymphomatoid papulosis
    - Primary cutaneous anaplastic large cell lymphoma
  - Subcutaneous panniculitis-like T-cell lymphoma
  - Adult T-cell leukemia/lymphoma
  - Primary cutaneous peripheral T-cell lymphoma, unspecified
    - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
    - Cutaneous γ/δ T-cell lymphoma (provisional)
    - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)

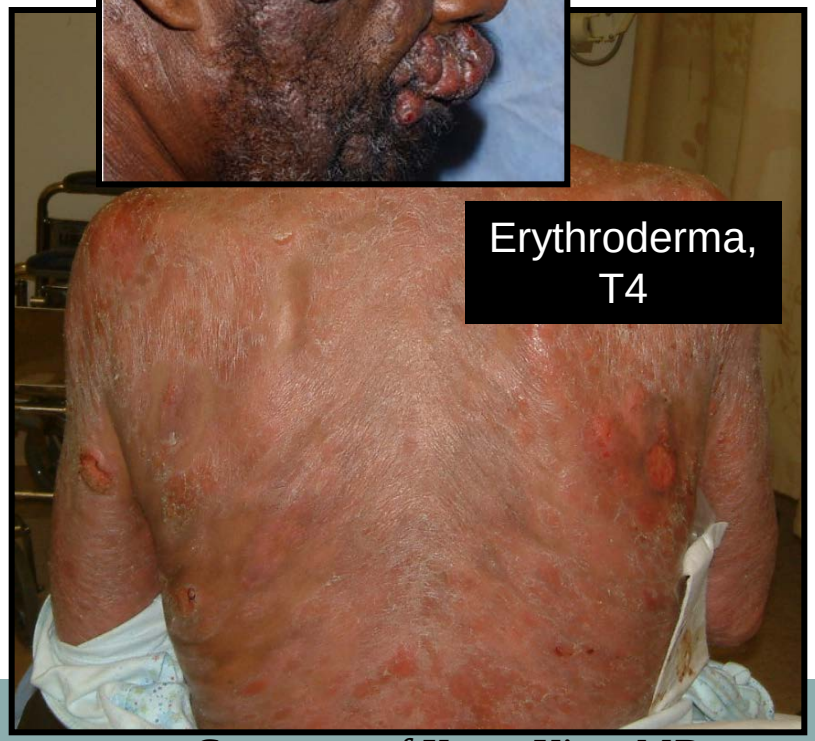
Mycosis Fungoides

- Most common cutaneous T-cell lymphoma
- Accounts for half of all cutaneous T-cell lymphomas
- Typically slow growing
- Appear as patches, plaques, or tumors

Cutaneous Manifestations, T-classification



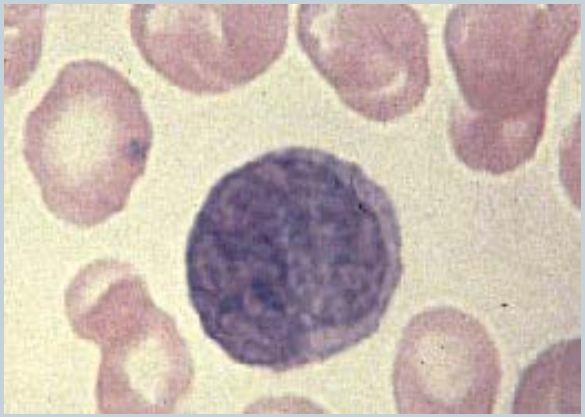




Courtesy of Youn Kim, MD

Sézary Syndrome

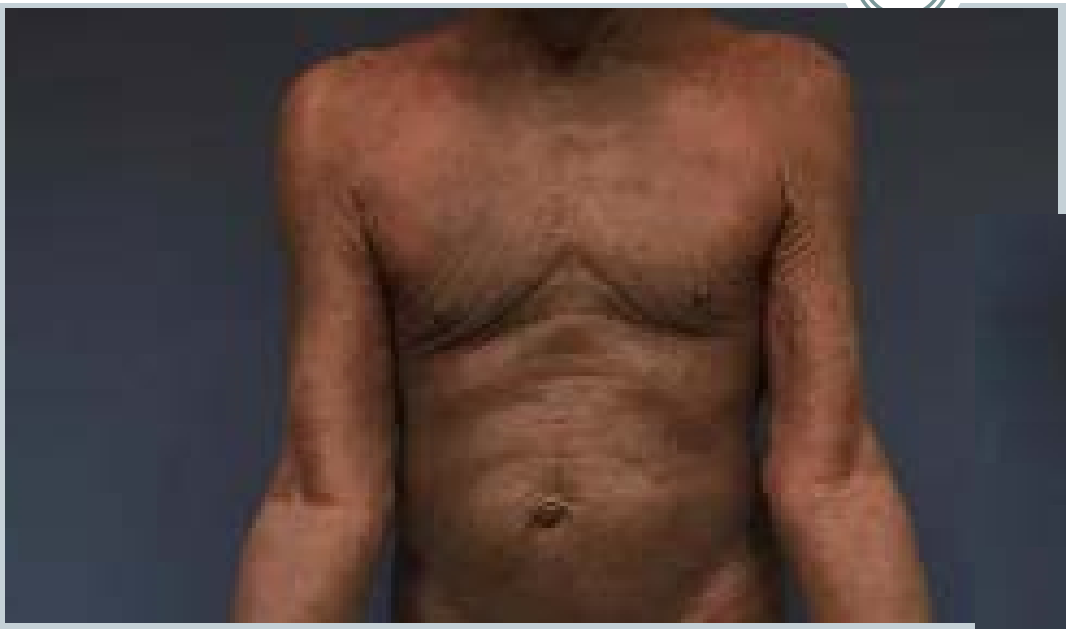
- Erythrodermic, leukemic variant of mycosis fungoides
- Extensive thin red, itchy rashes covering over 80 percent of the body known as erythroderma
- Lymphadenopathy
- Blood involvement
  - Morphology (manual slide review)
  - Flow parameters: expanded CD4 with increase in CD4+/CD7- and/or CD4+/CD26- populations

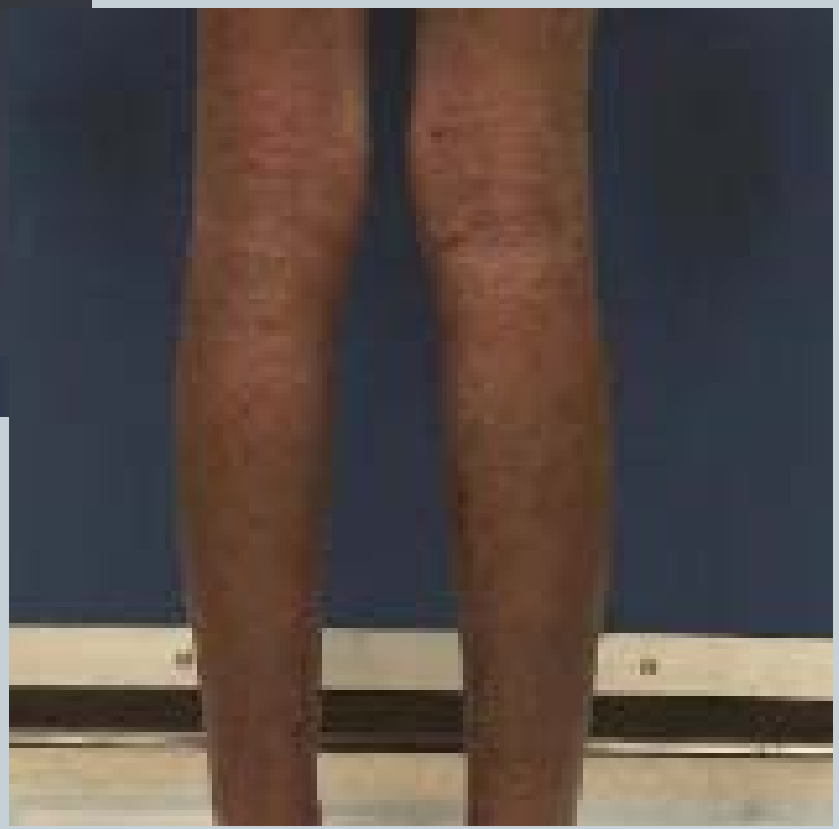


Sezary Syndrome

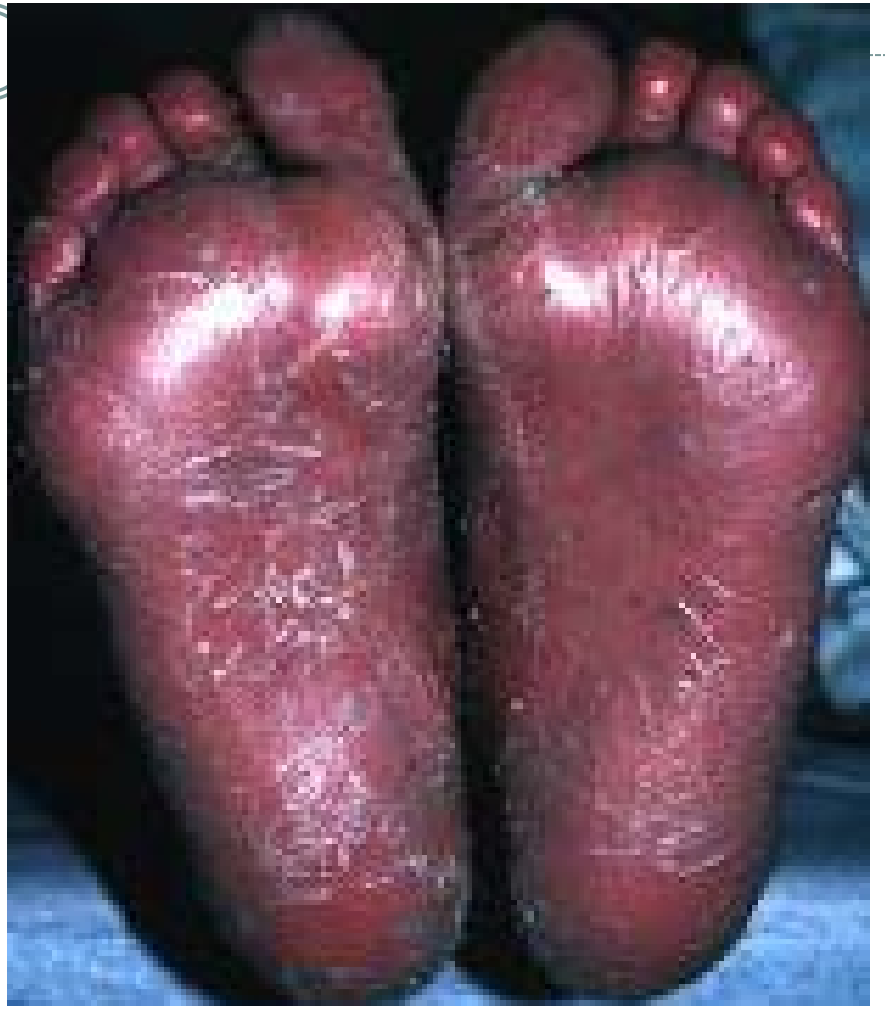
- Symptoms may be accompanied by changes in the nails, hair or eyelids
- Although this type of NHL can affect people of any age, Sézary syndrome usually occurs in adults ages 50 and over and is slightly more common in men than women.
- There are no known risk factors for this type of cutaneous T-cell lymphoma.

Pictures of MF/SS

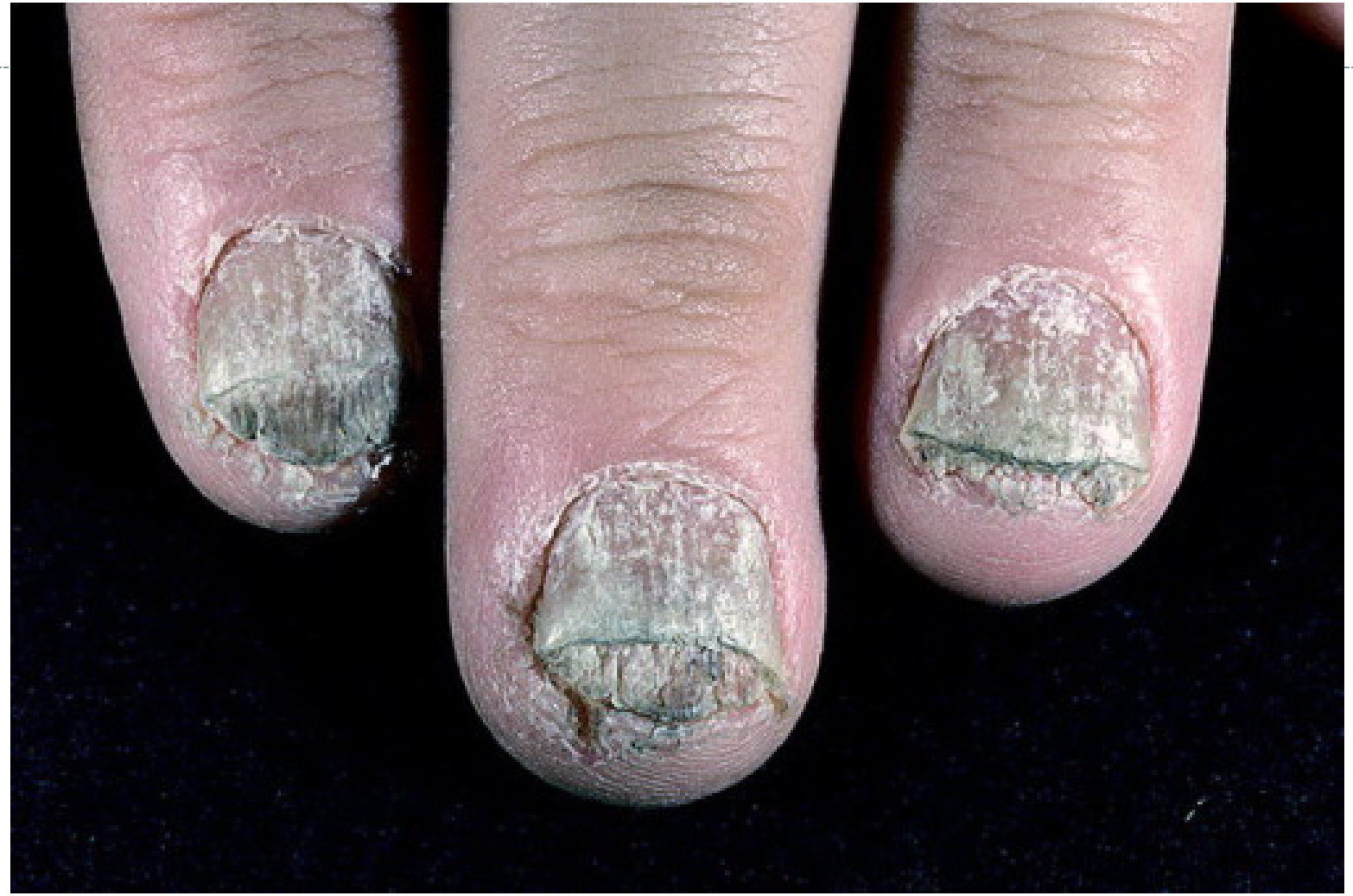




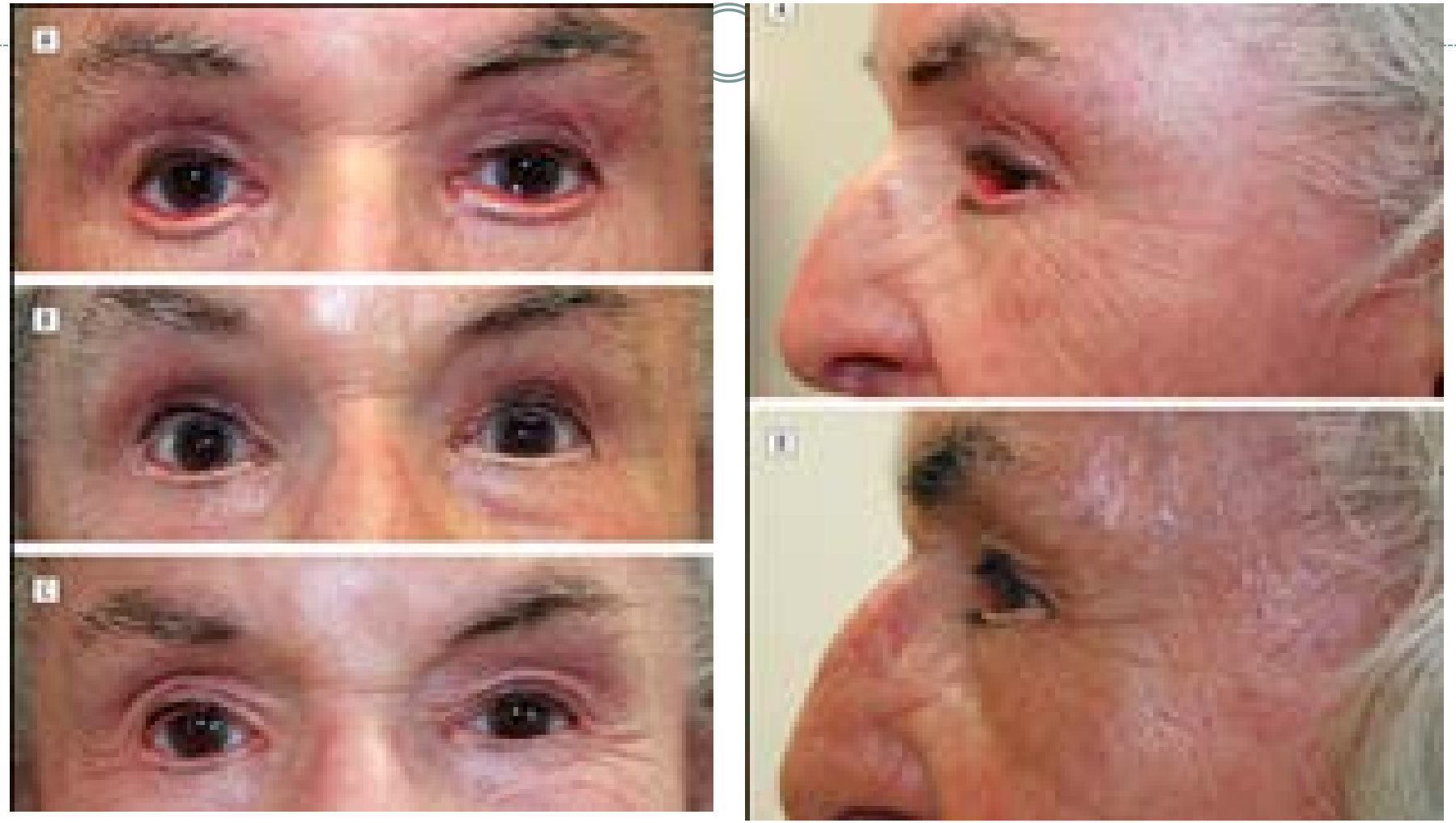
Keratoderma in Erythroderma



Nail Dystrophy in Erythroderma



Ectropion in Erythroderma



Staging of Mycosis Fungoides (MF) and Sezary Syndrome (SS)

- TNMB system (unique to CTCL)
- T: extent of skin involvement
  - T1 <10%
  - T2 >10%
  - T3 tumors
  - T4 erythroderma
- N: nodal involvement
  - Clinical or histologic
- M: visceral involvement
- B: blood involvement

NCCN Guidelines

Clinical Staging of MF and SS[h]

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
IIA	1–2	1,2	0	0,1
IIB	3	0–2	0	0,1
IIIA	4	0–2	0	0
IIIB	4	0–2	0	1
IVA_1	1–4	0–2	0	2
IVA_2	1–4	3	0	0–2
IVB	1–4	0–3	1	0–2

pc CD30+ Lymphoproliferative Disorders

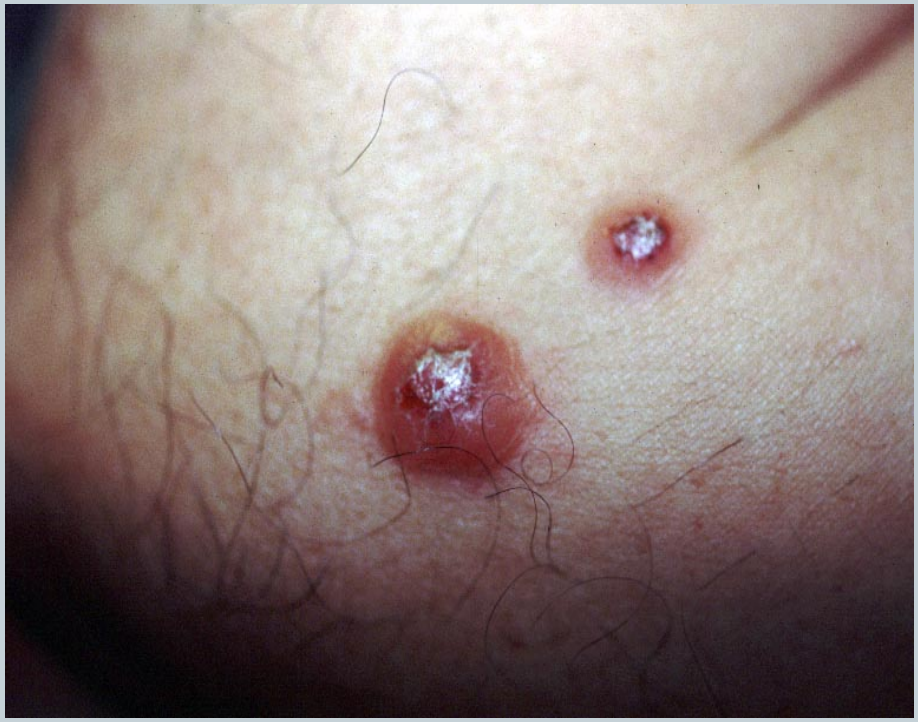
- Spectrum of lymphoproliferative disorders
  - Characterized by the size and shape of the cells under the microscope and by the uniform expression of a special marker on the lymphoma cells called CD30.
  - CD30 is transmembrane glycoprotein receptor, member of TNF-R superfamily
  - Expressed in proliferative or malignant processes (e.g. HD, ALCL, MF, subset of BCLs) and activated leukocytes (T, B, macrophages)

pc CD30+ Lymphoproliferative Disorders

- Primary cutaneous anaplastic large cell lymphoma
- Lymphomatoid papulosis (LyP)

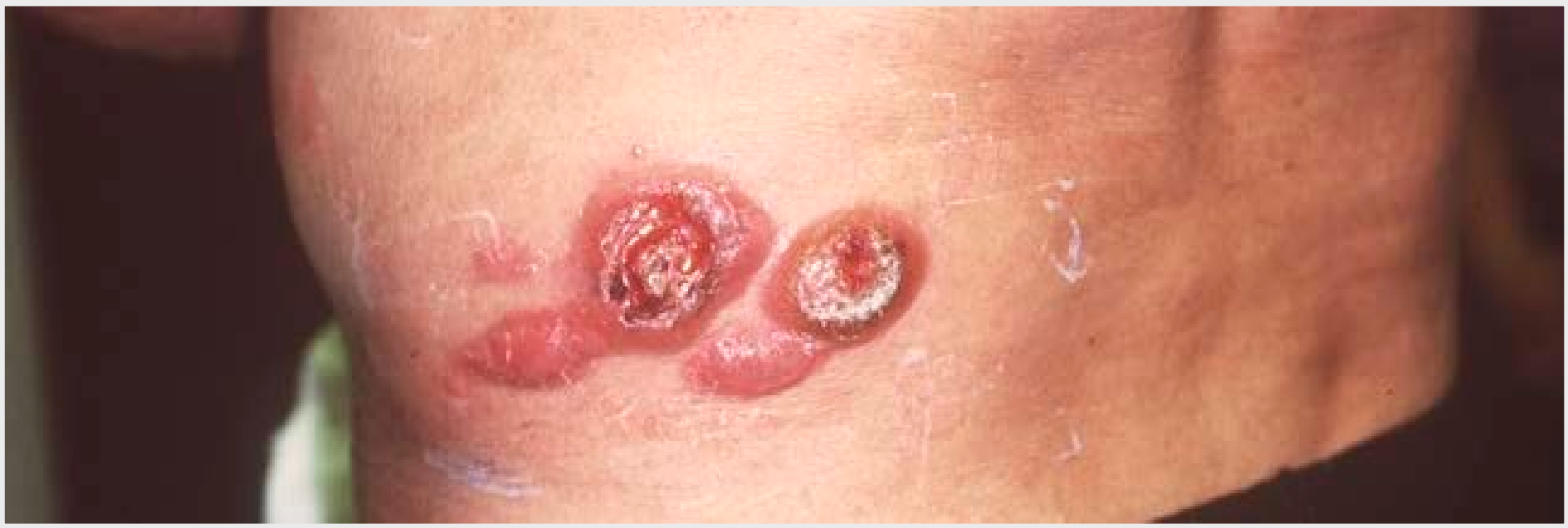
Lymphomatoid Papulosis

- Chronic, recurrent, self-regressing papulonodular skin lesions
  - red-brown bumps and spots, that may ulcerate and typically heal with scaling and crusting, and in some instances, scarring
- Most lesions <1cm
- Regression in a few weeks
- In up to 90% of cases, LyP is a persistent or self-limited disease with no associations and does not affect the overall health
- In up to 10% of LyP cases, there is an association with lymphomas, cutaneous T-cell lymphoma (mycosis fungoides (MF)), anaplastic large cell lymphoma, or Hodgkins lymphoma.



Primary Cutaneous Anaplastic Large Cell Lymphoma

- An indolent, or slow growing, lymphoma
- Solitary or multiple raised red skin lesions, nodules or tumors, which do not go away
- There are two types of anaplastic large cell lymphoma:
  - Systemic, which can affect the skin and/or lymph nodes and other internal organs
  - Primary cutaneous, which affects the skin only
- There are no known risk factors for primary cutaneous anaplastic large cell lymphoma.
- Can affect people of all ages
  - Commonly found in adults 45 to 60 years old
  - More often in men than women.



WHO-EORTC Classification

- **Cutaneous B-cell lymphomas (CBCL)**
  - **Primary cutaneous marginal zone B-cell lymphoma**
  - **Primary cutaneous follicle center lymphoma**
  - **Primary cutaneous diffuse large B-cell lymphoma**

Cutaneous B-cell Lymphomas

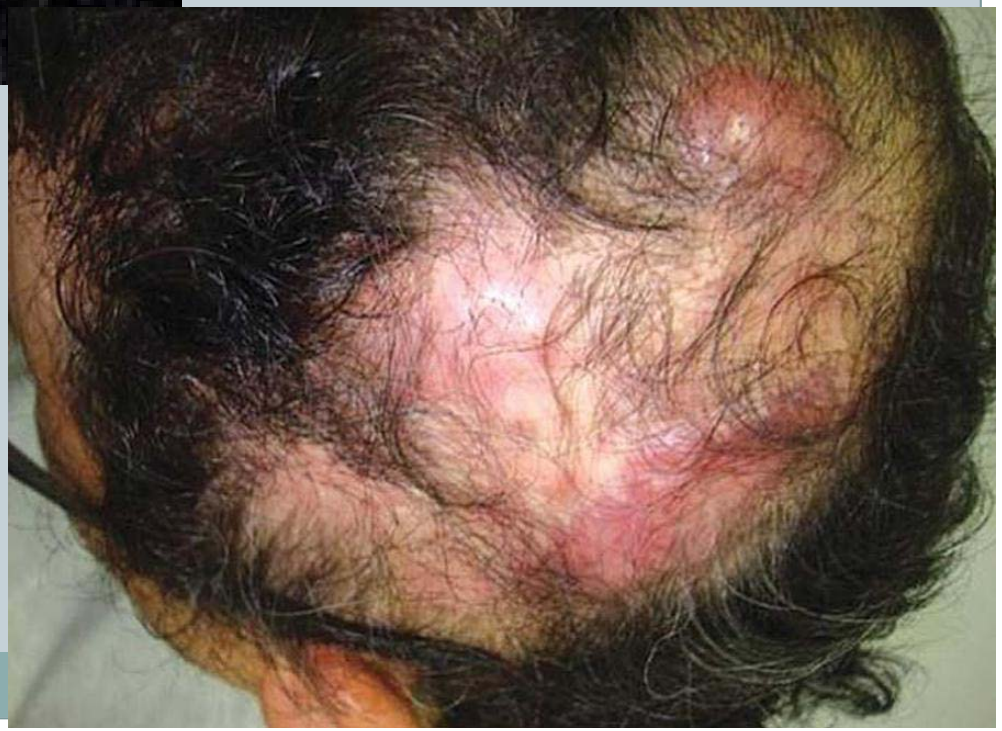
- Nearly always indolent (slow growing)
- Appear as a reddish rash, lump or nodule
- Recurs up to 50% of the time on the skin but rarely develop into metastases
- Affects men and women equally and can affect any age group.
- An acquired disease and there are no known risk factors.
  - Not inherited or contagious.

Indolent CBCL

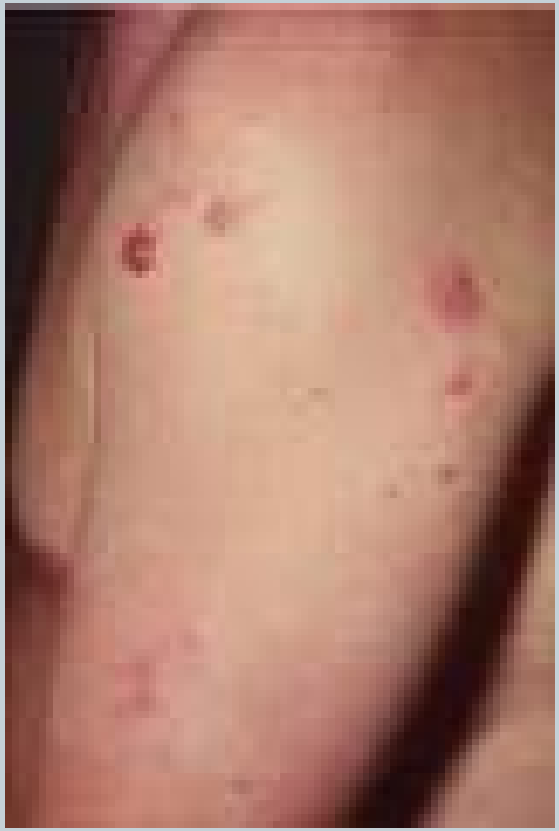
- **Primary cutaneous follicle center lymphoma (CFCL)**
  - Most common B-cell lymphoma of the skin
  - Develop slowly over months or years
  - Appears on the head, neck or trunk of the body.
- **Primary cutaneous marginal zone B-cell lymphoma (CMZL)**
  - Second most common form of CBCL.
  - Also slow growing
  - Commonly found on the extremities and trunk of the body

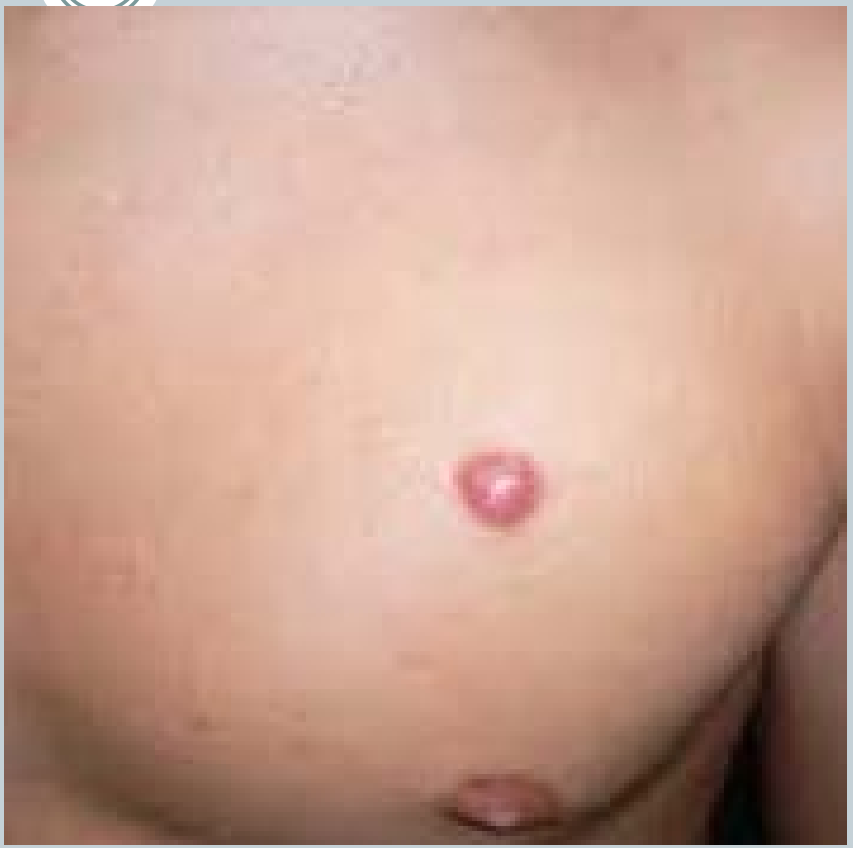
Pictures of CBCL

CFCL



Pictures of CBCL



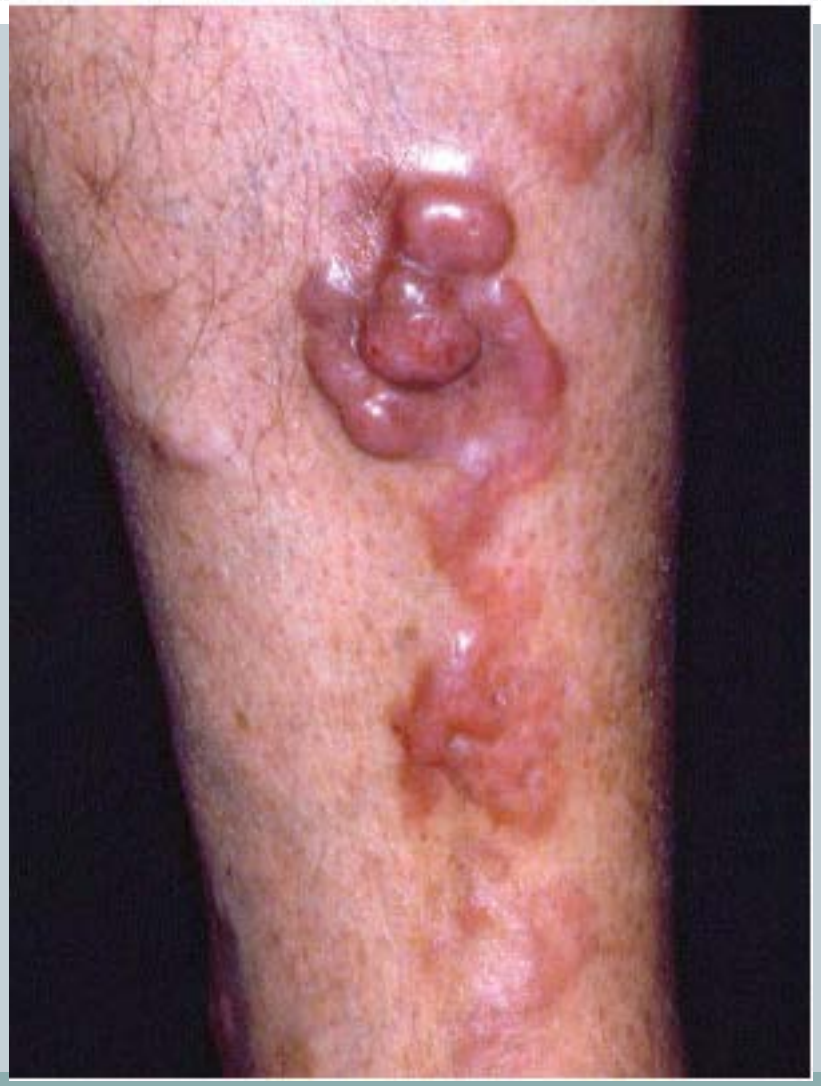


CMZL

Primary Cutaneous Diffuse Large B-cell Lymphoma

- **LBCL-L**
  - Less common than other types of CBCL and more aggressive
  - Usually appearing on the lower legs of elderly women, although lesions can occur on any part of the body.
  - Frequently grow into large tumors that become open sores
  - Develop quickly over weeks and months
  - Tend of spread outside the skin to other organs

Pictures of CBCL



How are cutaneous lymphomas diagnosed?

- History
- Physical exam
- Skin biopsy (often multiple)
- Blood tests
- Imaging (CT scans or PET/CT)
- Bone marrow, lymph node biopsy
- Additional tests
  - Special histologic stains for phenotype (surface markers)
  - Molecular tests (PCR)
  - Flow cytometry

NCCN Guidelines for Diagnosis

DIAGNOSIS

ESSENTIAL:

- Biopsy of suspicious skin sites
- Dermatopathology review of slides

USEFUL UNDER CERTAIN CIRCUMSTANCES:

- IHC panel of skin biopsy[a,b,c]
  - CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD25, CD56, TIA1, granzyme B, βF1, TCR-CγM1
- Molecular analysis of skin biopsy: TCR gene rearrangements (assessment of clonality)[a] by PCR methods[d]
- Assessment of peripheral blood for Sezary cells (in cases where skin is not diagnostic, especially T4) including:
  - Sezary cell prep
  - Flow cytometry (CD3, CD4, CD7, CD8, CD26 to assess for expanded CD4+ cells with increased CD4/CD8 ratio or with abnormal immunophenotype, including loss of CD7 or CD26) and
  - PCR for TCR gene rearrangement
- Biopsy of suspicious lymph nodes (in absence of definitive skin diagnosis)
- Assessment of HTLV-1[e] serology in at-risk populations. HTLV-1 PCR if serology is indeterminate

Why are cutaneous lymphomas so hard to diagnose?

- Rare
- Mistaken for common skin rashes
  - Can mimic other skin conditions
  - Other skin conditions can mimic cutaneous lymphomas
- Diagnosis can take years to make
  - Multiple skin biopsies may be needed
- There is no single test that decisively differentiates between cutaneous lymphomas and everything else

Why are cutaneous lymphomas so hard to diagnose?

Mycosis Fungoides can look like:

- **Psoriasis**
- **Eczema**
- **Ringworm**
- **Drug-rash**
- **Vitiligo**

Thank You

Email: fabdulla@medicine.bsd.uchicago.edu