Cutaneous Lymphoma Demystified

September 24, 2016

Jason Sluzevich MD
Assistant Professor of Dermatology
Mayo Clinic Florida
Main Difficulties

• Less Common

• Diagnostic Uncertainty
• Therapeutic Uncertainty

• Muddled Source Literature
Main Difficulties

• Less Common
  • Complexity ≠ Lack of Familiarity

• Diagnostic Uncertainty
• Therapeutic Uncertainty

• Muddled Source Literature
Main Difficulties

• Less Common

• Diagnostic Uncertainty
  • Non-diagnostic histopathology
  • Non-specific molecular typing

• Therapeutic Uncertainty

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Main Difficulties

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• Diagnostic Uncertainty

• Therapeutic Uncertainty
  • What To Do and When

• Muddled Source Literature
Main Difficulties

• Less Common

• Diagnostic Uncertainty

• Therapeutic Uncertainty

• Muddled Source Literature
  • Terminology: imprecise, “PARAPSORIASIS”; “TUMOUR D’EMBLEE”
  • Classification: inconsistent, divergent w/molecular techniques
  • Endpoints: variable, so hard to compare outcomes
### WHO Classification (2006)

**Primary (1°)**

**Cutaneous Lymphoma**

*Revision upcoming…*

#### List of Diseases Organized by Cell Type

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Very helpful if you are a **pathologist** but not so much as a **clinician**.
Table 1. WHO-EORTC classification of cutaneous lymphomas with primary cutaneous manifestations

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Classification System

Into Diagnostic Method
Group These Conditions Into 4 Buckets

A bucket will be defined by:

**Key History**

**Key Morphology**

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The 4 Buckets of Cutaneous Lymphoma

**Key History & Morphology**

- **Chronic Pruritic**
  - Patches
  - Later: Plaques Nodules

- **Waxing & Waning**
  - Papulonodules

- **Acute Persistent**
  - Eruptive Papulonodules

- **Progressive Pruritic**
  - Generalized Erythema
  - Usually: Erythroderma
  - Sometimes: Morbilliform
First Two Buckets of Cutaneous Lymphoma

**Chronic**
- Patches
- Later Plaques
- Nodules

**Waxing & Waning**
- Papulonodules
- Persist Sometimes
- Often Ulcerate

**Mycosis Fungoides**
- MF ≠ all CTCL

**CD30+ Lymphoproliferative Disorders**
- Lymphomatoid Papulosis
- Anaplastic Large Cell Lymphoma
Main Actors: 80% of Cutaneous Lymphoma

- **Chronic**
  - Patches
  - Later Plaques
  - Nodules

- **Waxing & Waning**
  - Papulonodules
  - Persist Sometimes
  - Often Ulcerate

**Mycosis Fungoides**
- 50%

**CD30+ Lymphoproliferative Disorders**
- 30%
Main Buckets of Cutaneous Lymphoma

**Chronic**
- Patches
- Later Plaques
- Nodules

**Waxing & Waning**
- Papulonodules
- Persist Sometimes
  - Often Ulcerate

---

**Mycosis Fungoides**
- CD30+
- Lymphoproliferative Disorders

May Proceed Or
Occur Together
Mycosis Fungoides

- Chronic
- Starts As Patches
- Progresses From Patches
- Usually Indolent
Mycosis Fungoides

• Chronic
  • If acute (<1 year) and progressive must consider diagnostic alternatives, including inflammatory disorders
• Starts As Patches
• Progresses From Patches
• Usually Indolent
Mycosis Fungoides

- Chronic
- Starts As Patches
  - Pruritic
  - *Sun Covered Areas*
  - Often Annular
  - Ddx: Dermatitis
- Progresses From Patches
- Usually Indolent
Mycosis Fungoides

- Chronic
- Starts As Patches
  - Pruritic
  - Sun Covered Areas
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  - Ddx: Dermatitis
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Mycosis Fungoides

• Chronic
• Starts As Patches
  • Pruritic
  • Sun Covered Areas
  • *Often Annular*
  • Ddx: Dermatitis
• Progresses From Patches
• Usually Indolent
Mycosis Fungoides

• Chronic
• Starts As Patches
• Progresses From Patches
  • Plaques and nodules from patches
  • If not, re-reconsider the diagnosis
• Usually Indolent
Mycosis Fungoides

- Chronic
- Starts As Patches
- Progresses From Patches
  - *Plaques* and nodules from patches
  - If not, re-reconsider the diagnosis
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Mycosis Fungoides

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Mycosis Fungoides

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- Usually Indolent
Mycosis Fungoides

• Chronic
• Starts As Patches
• Progresses From Patches
• Usually Indolent
  • 80% with skin-limited patch-plaque disease
  • Skin-directed therapy for most
Mycosis Fungoides Pitfalls

• Early Stage Disease
• Molecular False Positives
• Mimics
Mycosis Fungoides Pitfalls

• Early Stage Disease
  • *Frequent Non-Diagnostic Biopsies*
    • *Neoplastic disorder with features of inflammatory dermatosis*
  • Diagnosis Is Largely Clinical
  • No Rush to Make a Diagnosis

• Immunosuppression Accidents
• Molecular False Positives
• Mimics
Mycosis Fungoides Pitfalls

- Early Stage Disease
  - Frequent Non-Diagnostic Biopsies
  - *Diagnosis Is Largely Clinical*
  - No Rush to Make a Diagnosis
- Molecular False Positives
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**Table I. Algorithm for diagnosis of early MF**

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<th>Criteria</th>
<th>Scoring system</th>
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<tbody>
<tr>
<td>Clinical</td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>2 points for basic criteria and two additional criteria</td>
</tr>
<tr>
<td>Persistent and/or progressive patches/thin plaques</td>
<td>1 point for basic criteria and one additional criterion</td>
</tr>
<tr>
<td>Additional</td>
<td></td>
</tr>
<tr>
<td>1) Non-sun exposed location</td>
<td></td>
</tr>
<tr>
<td>2) Size/shape variation</td>
<td></td>
</tr>
<tr>
<td>3) Polikiderma</td>
<td></td>
</tr>
<tr>
<td>Histopathologic</td>
<td></td>
</tr>
<tr>
<td>Basic</td>
<td>2 points for basic criteria and two additional criteria</td>
</tr>
<tr>
<td>Superficial lymphoid infiltrate</td>
<td>1 point for basic criteria and one additional criterion</td>
</tr>
<tr>
<td>Additional</td>
<td></td>
</tr>
<tr>
<td>1) Epidermotropism without spongiosis</td>
<td></td>
</tr>
<tr>
<td>2) Lymphoid atypia†</td>
<td></td>
</tr>
<tr>
<td>Molecular biological</td>
<td></td>
</tr>
<tr>
<td>1) Clonal TCR gene rearrangement</td>
<td>1 point for clonality</td>
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<tr>
<td>Immunopathologic</td>
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<tr>
<td>1) &lt;50% CD2+, CD3+, and/or CD5+ T cells</td>
<td>1 point for one or more criteria</td>
</tr>
<tr>
<td>2) &lt;10% CD7+ T cells</td>
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<tr>
<td>3) Epidermal/dermal discordance of CD2, CD3, CD5, or CD7‡</td>
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**4 POINTS FOR MF**
Mycosis Fungoides Pitfalls

• Early Stage Disease
  • Frequent Non-Diagnostic Biopsies
  • Diagnosis Is Largely Clinical
  • No Rush to Make a Diagnosis
    • No Evidence Early Treatment Changes Outcome
    • Diagnostic Zen: “Chronic Superficial Dermatitis”
Mycosis Fungoides Pitfalls

• Molecular False Positives (and negatives....)
  • A positive T-cell gene rearrangement in isolation does not confirm a diagnosis of MF
    • Inflammatory disorders can be clonal.
  • A negative T-cell gene rearrangement in isolation does not exclude a diagnosis of MF.
    • Likelihood of positive result: patch < plaque < nodule
Mycosis Fungoides Pitfalls

• Mimics
  • Psoriasiform Dermatitis
  • Adult T-Cell Leukemia/Lymphoma
Mycosis Fungoides Pitfalls

• Mimics
  • *Psoriasiform Dermatitis*
    - Especially in the Elderly
    - Psoriasis-like eruption (without h/o of MF)
      - New onset or Flaring
    - Chronic inflammatory dermatosis → clonal T-cell expansion → MF late
      - Skeptics say ‘no’: all had MF to begin with.
  • Adult T-Cell Leukemia/Lymphoma
Psoriasiform Dermatitis

CHIEF COMPLAINT
“WORSENING PSORIASIS”

15 year history
No longer responding
to topicals.

R/O MF
Psoriasiform Dermatitis

PRIOR DX
“PSORIASIFORM DERMATITIS”

Psoriasis-like distribution

Topicals unhelpful

R/O MF
Mycosis Fungoides Pitfalls

- Mimics
  - Psoriasiform Dermatitis
  - **Adult Onset T-Cell Leukemia/Lymphoma**
    - HTLV-1 positive
    - Caribbean & South Pacific demographic
    - 50% with MF-like skin lesions
      - **Key Difference**: Lesions rapidly erupt and progress
    - Histology may be MF-like
      - **Key Difference**: Epidermotropic cells CD25+/FoxP3+
Adult Onset T-Cell Leukemia/Lymphoma

“FLOWER CELL”

Note that flow cytometry of the peripheral blood would also be abnormal.
The 2nd Bucket Of Cutaneous Lymphoma

Waxing & Waning Papulonodules

CD30+
LYMPHOPROLIFERATIVE DISORDERS
~
Two types:
Lymphomatoid Papulosis (LYP)
Anaplastic Large Cell Lymphoma (ALCL)
CD30+ Lymphoproliferative Disorders

Lymphomatoid Papulosis

A Continuing Self-Healing Eruption, Clinically Benign—Histologically Malignant

Warren L. Macaulay, MD, Fargo, ND

Original description by a community dermatologist in 1968.

Recognized a discordance between clinical behavior and an atypical histology.
Lymphomatoid Papulosis

~

Multiple Lesions
Smaller ("Papular")
Often Symmetric

100% Spontaneous Resolution
CD30+ Lymphoproliferative Disorders

Anaplastic Large Cell Lymphoma

~

Few Lesions
Larger (“Nodular”)
Localized

50% Spontaneous Resolution
CD30+ Lymphoproliferative Disorders

- Ulceration is common
- Involution is slower and may be incomplete.
CD30+ Lymphoproliferative Spectrum

Unified By A Common Histologic Feature: Variable Numbers of CD30+ Cells

A Clinical Spectrum with Two Poles

LYP
- Papular
- More Lesions
- Fully Resolve

ALCL
- Nodular
- Fewer Lesions
- May Persist
CD30+ Lymphoproliferative Spectrum

A Clinical Spectrum with Two Poles

And everything else in between...

One intuitive consequence is that more than 2 biopsy patterns may be seen.

LYP
Papular
More Lesions
Fully Resolve

ALCL
Nodular
Fewer Lesions
May Persist
CD30+ Lymphoproliferative Disorders

Lymphomatoid Papulosis

5 Biopsy Patterns

A: Classic
B: Mycosis Fungoides
C: ALCL (cutaneous or systemic)
D: Cytotoxic Lymphoma
E: Atypical Lymphocytic Vasculitis

Only with clinical correlation can the correct diagnosis be rendered.
CD30+ Lymphoproliferative Disorders
Anaplastic Large Cell Lymphoma

Histopathology identical to:
1: Systemic ALCL
2: LYP (Type C pattern)
3: Mycosis Fungoides (CD30+ transformation)

Once again clinical correlation is essential to the correct diagnosis, workup, and treatment.
# The 4 Buckets of Cutaneous Lymphoma

## Key History + Morphology

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The 3rd Bucket of Cutaneous Lymphoma
Heterogeneous in Etiology

Acute Persistent Eruptive Papulonodules

~

Leukemia Cutis
Lymphoma Cutis

~

Primary Cutaneous B Cell Lymphoma
Other Peripheral T-Cell Lymphomas
Other Extranodal Skin Lymphomas
The 3rd Bucket of Cutaneous Lymphoma
More Clinical Variability

Acute Persistent Eruptive Papulonodules

Primary Cutaneous B Cell Lymphoma
Other Peripheral T-Cell Lymphomas
Other Extranodal Skin Lymphomas

With this group especially…
The pathologist is your best friend or your foe.
The 3rd Bucket of Cutaneous Lymphoma
Three Conceptual Groups

Acute Persistent Eruptive Papulonodules
(Excluding conventional leukemia cutis and lymphoma cutis)

1° Cutaneous B-Cell Lymphoma

Other Peripheral T-Cell Lymphomas

Other Extranodal Lymphomas
The 3rd Bucket of Cutaneous Lymphoma
Three Conceptual Groups

Acute Persistent Eruptive Papulonodules
(Excluding conventional leukemia cutis and lymphoma cutis)

1° Cutaneous B-Cell Lymphoma

Other Peripheral T-Cell Lymphomas

Other Extranodal Lymphomas
Cutaneous B-Cell Lymphoma

• Constitute 10% of all primary cutaneous lymphomas
  • However…
  
  LYMPHOMA CUTIS (cutaneous involvement by systemic B-lymphoma) is far more common overall.

• Main diagnostic pitfall:
  • Each primary cutaneous B-cell lymphomas has a corresponding systemic (nodal) B-cell counterpart
  • This can lead to under or over treatment without appropriate staging studies
Primary Cutaneous B-Cell Lymphoma

• Three Major 1° Cutaneous B-Cell Lymphomas:
  • Diffuse Large, Leg-Type: Aggressive (5-year survival 65%)
  • Follicular Cell: Caution (5-year survival 95%)
  • Marginal Zone: Outstanding (5-year survival 98%)

• Role of Clonality Studies in Diagnosis:
  • IgH gene arrangement by PCR
    No false positives
Marginal Zone Lymphoma

- Younger (middle-aged)
- Favors trunk and extremities
- Solitary or multi-focal involvement
- Red-purple ("Plum") plaques, papules, or nodules.
  - Ulceration rare
Marginal Zone Lymphoma

• “Barely” lymphoma: extraordinarily indolent

• Skin-directed Rx is the norm
  • Excision
  • Local radiation
  • IL Kenalog

• Immunophenotype:
  • CD79A >> CD20
  • Bcl-6 & CD10 negative
  • $\lambda$/$\kappa$ restriction often
Follicular Cell Lymphoma

- Most common $1^\circ$ PCBL
- Favors Head & Neck
  - Upper torso also common

- Solitary or Multi-focal involvement

- Very good prognosis
  - Rarely, extra-cutaneous involvement develops
Follicular Cell Lymphoma

- Red-purple ("Plum") papules, plaques, papules, or nodules.
  - Growth rate variable
  - Ulceration rare
Follicular Cell Lymphoma

- Red-purple (“Plum”) papules, plaques, papules, or nodules.
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- Sometimes arcuate plaques involving the torso.
Follicular Cell Lymphoma

• Extensive involvement of the head and neck may necessitate systemic treatment
  • Extent of multi-focal disease does not necessarily correlate with prognosis

• Rituximab is often very helpful in this setting
Follicular Cell Lymphoma

• Histopathology
  • Follicular pattern: good prognosis; vast majority of cases
  • Diffuse pattern: more aggressive disease; uncommon.
    • Why prognostic caution compared to marginal zone type

• Immunophenotype:
  • CD20+
  • Bcl-6 & CD10 positive (follicular markers)
  • Bcl-2 negative (excludes systemic follicular B-cell lymphoma)
Diffuse Large B-Cell Lymphoma, Leg Type

- Elderly (80+)
- Female predominance
- Lower legs but not exclusively so
- Aggressive
  - Always extra-cutaneous spread
  - Always systemic treatment
- Immunophenotype:
  - CD20+, CD10-
  - MUM-1+, FoxP3+ (“activated” B-cell markers)
The 3rd Bucket of Cutaneous Lymphoma
Three Conceptual Groups

Acute Persistent Eruptive Papulonodules
(Excluding conventional leukemia cutis and lymphomacutis)

1° Cutaneous B-Cell Lymphoma

Other Peripheral T-Cell Lymphomas

Other Extranodal Lymphoma
Other Peripheral T-Cell Lymphomas

• “Peripheral”
  • Means the T-cells are mature (post-thymic origin)
  • Does not refer to the clinical distribution of lesions

• Clinically, **T-Cell** lymphomas that are:
  • Not Mycosis Fungoides
  • Not CD30+ Lymphoproliferative Disorder

• May be indolent or aggressive
Other Peripheral T-Cell Lymphomas

- Acute eruptive nodule on cheek x 1 month
  - Can exclude MF by history alone:
    - No precursor patch/plaque
Other Peripheral T-Cell Lymphomas

- 1 month later: persists, increasing in size
  - By history less likely, ALCL
    - Pathology confirms CD30 negative
Other Peripheral T-Cell Lymphomas

- Staging workup unremarkable
- Treated with radiotherapy:
  - 6 years of follow up with no recurrence or systemic involvement.
CD4+ Small/Medium-sized Pleomorphic T-cell Lymphoma

- Solitary lesion
- Head and Neck typically
  - But also the trunk
- Immunophenotype:
  - CD4+, CXCL13+
- Indolent
- Skin-directed treatment

CD4 + primary cutaneous small/medium-sized pleomorphic T-cell lymphoma: a retrospective case series and review of literature

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1Department of Medical Oncology, 2Department of Medicine, 3Department of Pathology, 4Department of Dermatology and 5Department of Therapeutic Radiology, Yale University School of Medicine, New Haven, CT, USA

Abstract
CD4 + primary cutaneous small/medium-sized pleomorphic T-cell lymphoma (CD4 + PSM-TCL) is a rare T-cell lymphoma associated with a favorable prognosis. A retrospective study of 23 patients with CD4 + PSM-TCL as defined by World Health Organization–European Organization for Research and Treatment of Cancer (WHO–EORTC) and WHO classifications was conducted. Median age was 63 years. The head and neck were the most commonly affected locations, followed by the trunk. Two patients had evidence of systemic involvement at relapse. All tumors were CD3+ and CD4+. CD5 and CD7 loss occurred in 52% and 84%, respectively. The median follow-up was 33.6 months. Eleven patients had excisional biopsy only, six had localized radiotherapy and two received excision and localized radiation. Cytotoxic chemotherapy and localized radiation were used in one patient with aggressive and invasive features. All patients had a complete remission but one developed systemic involvement. Our case series demonstrates that CD4 + PSM-TCL is an indolent T-cell lymphoma that can be treated with local modalities and raises the question of its current classification as a lymphoma.

Keywords: Cutaneous lymphoma, primary cutaneous lymphoma, CD4, pleomorphic, small/medium, T-cell lymphoma

cutaneous γ/δ T-cell lymphoma and CD4 + primary cutaneous small/medium-sized pleomorphic T-cell lymphoma (CD4 + PSM-TCL) [3].

In the 2008 WHO classification, CD4 + PSM-TCL remains a provisional entity for cases involving a predominance of small- to medium-sized pleomorphic T-cells in the absence of prior MF [4]. Clinically, this disease is generally characterized by a solitary papule, nodule, plaque or tumor that predominantly involves the head and neck, with a 5-year survival of 62–82%, suggesting a favorable prognosis [5]. Histopathologically, CD4 + PSM-TCL usually presents as dense, diffuse or nodular infiltrates centered in the dermis [1], and is characterized by a predominance of CD4 + small/medium-sized pleomorphic T-cells with infrequent large lymphoid forms [6]. B-cells, histiocytes, plasma cells and eosinophils can also be found in differing proportions [3]. Immunophenotyping generally reveals CD3+, CD4+, CD8– and CD30 – neoplastic cells, although similar cases with CD8 + phenotype have been described in the literature [7]. Rodriguez-Pinilla et al. recently found that the atypical T cells in CD4 + PSM-TCL express PD-1, BCL6 and CXCL13, suggesting that these cells originate from T-follicular helper cells. By definition, the T-cell receptor (TCR) genes are clonally rearranged [1]. It is imperative to distinguish CD4 + PSM-TCL, which is gen-
Other Peripheral T-Cell Lymphomas

- Ill-defined deep erythematous nodular-plaques with minimal surface change
- Chronic and recurrent over months
- R/O MF: no patches
- R/O CD30+ disorder: possible given recurrence but morphology atypical
Subcutaneous Panniculitis-Like T-Cell Lymphoma

- Clinically resembles panniculitis
  - Recurrent often
  - Confused with lupus panniculitis
- Immunophenotype:
  - CD8+, TIA-1+, granzyme-B+
  - CD56-, EBV negative
- Outcome:
  - T-cells α/β: indolent, easy to treat, low risk of systemic involvement
  - T-cells γ/Δ: aggressive, systemic spread inevitable, poor prognosis
Other Peripheral T-Cell Lymphomas

- Sometimes see presentations with:
  - Multi-focal lesions
  - Rapid enlargement
  - Rapid extra-cutaneous spread
- Phenotypically are often:
  - Cytotoxic (CD8+) T-cells
  - Gamma-delta (γ/δ) T-cells
- Poor prognosis: mean survival 15-20 months
Other Peripheral T-Cell Lymphomas

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• Poor prognosis: mean survival 15-20 months
  • Incompletely characterized to date
The 3rd Bucket of Cutaneous Lymphoma
Three Conceptual Groups

**Acute Persistent Eruptive Papulonodules**

(Excluding conventional leukemia cutis and lymphoma cutis)

1° Cutaneous B-Cell Lymphoma

Other Peripheral T-Cell Lymphomas

Other Extranodal Lymphoma
Other Extranodal Lymphomas

• Extranodal
  • The lymphoma originates outside a lymph node

• Hybrid morphologic or phenotypic properties:
  • *NK/T Cell*
    • Hybrid of natural killer (NK) cell and a T-cell
  • *Plasmacytoid Dendritic Cell*; conceptually, it is:
    • Hybrid of a plasma cell and a macrophage
    • Presents antigen instead of making antibodies
    • Not present in non-inflamed skin
Extranodal NK/T Cell Lymphoma, nasal type

“lethal midline granuloma,” “destructive midline lymphoma,” “angiocentric lymphoma,” “malignant granuloma,” “polymorphic reticulosis”

• 60-90% present in nose and nasopharynx
• Poor prognosis: 5-year survival rate 38-62%
Extranodal NK/T Cell Lymphoma, nasal type

- Most common in Asians and Hispanics
- Ulceration ("infarctive") is a prominent clinical feature
Extranodal NK/T Cell Lymphoma, nasal type

• 40% of cases have extra-nasal skin involvement
  • May occur before or after primary nasal involvement

• Some presentations are purely cutaneous without nasal involvement
Extranodal NK/T Cell Lymphoma, nasal type

• 40% of cases have extra-nasal skin involvement
  • May occur before or after primary nasal involvement

• Some presentations are purely cutaneous without nasal involvement
Extranodal NK/T Cell Lymphoma, nasal type

**CD56**(+/−), cytoplasmic CD3-ε(+), cytotoxic markers(+), βF1(−). **NO TCR CLONE.**
Blastic Plasmacytoid Dendritic Cell Neoplasm

- Aggressive **leukemia** that presents as a primary cutaneous skin **lymphoma**

- In most cases (80%) the disease manifestations are seen **exclusively** in the skin, and then the later leukemic phase develops.
Blastic Plasmacytoid Dendritic Cell Neoplasm

- Elderly (60–70 years)
- Male predominance
- Solitary or multiple purpuric nodules and plaques.

Plasmacytoid Dendritic Cell Immunophenotype:
  - CD4+, CD56+
  - \textbf{CD123+}
  - Negative for all other B, T, and myeloid markers
# The 4 Buckets of Cutaneous Lymphoma

**Key History + Morphology**

- **Chronic Pruritic Patches**
  - Mycosis Fungoides

- **Waxing & Waning Papulonodules**
  - LYP
  - ALCL

- **Acute Persistent Eruptive Papulonodules**
  - 1° Cutaneous B-Cell Lymphoma
  - Other Peripheral T-Cell Lymphomas
  - Other Extranodal Lymphomas

**Progressive Pruritic Generalized Erythema**

- Usually: Erythroderma
- Sometimes: Morbilliform
4th Bucket of Cutaneous Lymphoma
More Inflammatory Appearance

• Eruptions resemble an inflammatory dermatosis rather than conventional lymphoma

• Two morphologic patterns of generalized erythema
  • Erythroderma:
    • Sézary Syndrome
    • Erythrodermic MF
  • Morbilliform:
    • Angioimmunoblastic T-cell Lymphoma
Erythrodermic Cutaneous Lymphoma

- Pruritic
- Whole-body erythema with fine scale
Erythrodermic Cutaneous Lymphoma

- Pruritic
- Whole-body erythema with fine scale
- *Keratoderma common*
Erythrodermic Cutaneous Lymphoma

- Pruritic
- Whole-body erythema with fine scale
- Keratoderma common
- *Prednisone responsive early*
Erythrodermic Cutaneous Lymphoma

- Pruritic
- Erythema with fine scale
- Keratoderma common
- Prednisone responsive early

Leukemic Cutaneous Lymphoma: Variable numbers of atypical T-cells in skin and blood.

SÉZARY CELL
Size > 12 µM
CEREBRIFORM NUCLEUS
CD4+, CD7-, CD26-
Erythrodermic Cutaneous Lymphoma

- Erythrodermic MF
  - Progression of MF
    - (TNM) → B
  - Low blood burden (<20%)

- Sézary Syndrome (SS)
  - Abrupt and de Novo
  - No MF, but often non-specific dermatitis and/or pruritus
  - High blood burden (>20%)

While often viewed synonymously, Sézary Syndrome and Erythrodermic MF have clinical and etiologic distinctions that may be important for therapy.
Erythrodermic Cutaneous Lymphoma

• Erythrodermic MF
  • Progression of MF
    • (TNM) → B
  • Low blood burden (<20%)

• Sézary Syndrome (SS)
  • Abrupt and de Novo
  • No MF, but often non-specific dermatitis and/or pruritus
  • High blood burden (>20%)

While often viewed synonymously, Sézary Syndrome and Erythrodermic MF have clinical and etiologic distinctions that may be important for therapy.
Erythrodermic Cutaneous Lymphoma

- 6 year history of limited patch-plaque MF (<15% BSA)
  - Well controlled with PUVA

- Over 3 months developed
  - Generalized pruritus
  - Rapid onset erythroderma

<table>
<thead>
<tr>
<th>T-B Quantification Flow Cytometry</th>
<th>CD3 (T-Cells)</th>
<th>H/S Ratio</th>
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</thead>
<tbody>
<tr>
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<td>28.30</td>
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<td>16-Jul-2008 15:05 EDT</td>
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<tr>
<td>04-Jun-2008 11:15 EDT</td>
<td>398.0 (L)</td>
<td>1.12</td>
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</tbody>
</table>

“Sézary Preceded by MF”
Rarely patients with MF develop a degree blood involvement which meets the pathologic criteria for Sézary Syndrome

**Helper : Suppressor T-Cell ratio > 10**
Morbilliform Cutaneous Lymphoma

• Rare
• Morbilliform (“macular-papular”)
  • May not persistent initially
• Pruritic
  • Secondary dermatitis possible

• Often low index of suspicion versus:
  • Drug Eruption
  • Viral Exanthem
Morbilliform Cutaneous Lymphoma

- Seen once in the ED, 3 times by PMD, 4 times by dermatology, and twice by rheumatology…
  - Diagnosed with “dermatitis” and “lupus”
  - Prior biopsies “superficial perivascular lymphocytic dermatitis”
  - No change with topical steroids
  - IM Kenalog decreased itch but otherwise no change
Angioimmunoblastic T-Cell Lymphoma

- Middle-aged elderly
- Early: Malaise, weakness, pruritus, morbilliform +/- dermatitic
- Later: B-symptoms, diffuse adenopathy
- Labs: ANA+, eosinophilia, MGUS
- Poor prognosis
  - Mean survival 15-36 months

T-Cell Lymphoma “Triggered” By Aberrant B-Cells

Activated Nodal B (EBV+) Cell = Exaggerated Follicular Helper T-Cell Recruitment = “Chronic Inflammation with Auto-Amplification” = Clonal Follicular Helper T-Cell ($T_{FH}$) Emerges $\rightarrow$ $T$-Cell Lymphoma $\rightarrow$ skin & other sites
Angioimmunoblastic T-Cell Lymphoma

- Lymph node biopsy is diagnostic
- Skin biopsies can be a pitfall as atypia can be mild
  - May resemble inflammatory disorder
  - Immunophenotype is quite characteristic

Peripheral T-Cell Lymphoma with Follicular Helper T Cell ($T_{FH}$) Phenotype

CD4+, CD279+ (PD1), CXCR5+, CXCL13+, bcl-6+
### The 4 Buckets of Cutaneous Lymphoma

**In Summary...**

<table>
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<td>~ LYP ALCL</td>
<td>~ 1° CUTANEOUS B-CELL LYMPHOMA</td>
<td>~ SÉZARY SYNDROME ERYTHRODERMIC MF AITL</td>
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<td>OTHER EXTRANODAL LYMPHOMAS</td>
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</table>

**Other**

- Other Peripheral T-Cell Lymphomas
- Other Extranodal Lymphomas
Thank You

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