CUTANEOUS T-CELL LYMPHOMA

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University of Iowa
Saturday, October 19, 2019
Objectives

• To adopt the “Who-What-When-Where-How-Why?” format to better understand and manage cutaneous T-cell lymphoma (CTCL)
• To highlight the critical importance of clinicopathologic correlation for accurate diagnosis and optimal management
• To appreciate the value of multidisciplinary care
• To recognize that care must be patient-centered and address quality-of-life issues in decision-making
Alphabet Soup

• WHO-EORTC
  – World Health Organization-European Research Treatment of Cancer
• USCLC
  – United States Cutaneous Lymphoma Consortium
• ISCL
  – International Society for Cutaneous Lymphoma
• CLF
  – Cutaneous Lymphoma Foundation
• NCCN
  – National Comprehensive Cancer Network
• LRF
  – Lymphoma Research Foundation
Questions for Cutaneous Lymphoma Clinic

- Who
- What
- When
- Where
- How
- Why
Overview

• **Who**
  – Inform diagnosis
  – Guide treatment

• **What**
  – Clinicopathologic presentation lead to specific diagnosis (**classification**)
  – Diagnosis portends prognosis, management

• **When**
  – Evolution updates diagnosis(-es)
  – Progression dictates treatment

• **Where**
  – Staging component
  – Nuances of therapy

• **How**
  – How can we help-> **management**

• **Why**
  – Research into etiopathogenesis
**WHO is the patient?**

**Overall story**
- HPI - esp pt concerns
- PMH
  - Implications for presentation
  - Implications for tx
- SH
  - Implications for tx
  - Pt concerns
- FH
  - Oncologic hx

**Cutaneous lymphoma story**
- How & when did it present?
- Work-up
  - Who evaluated pt?
  - Histopathology- skin bx, LN bx
  - Laboratory studies- bloodwork
  - Imaging
- Treatment
  - Skin-directed tx
  - Systemic tx
Patient #1
Patient #2
Patient #3
Is it “lymphoma”?

• Clinical differential diagnosis
  – Inflammatory
    • Erythema annulare centrifugum
  – “Pseudolymphomas”
  – T-cell dyscrasia
    • Parapsoriasis
    • Pigmented purpura
  – Drug-induced MF
  – Infectious
    • Syphilis

• Pathologic differential diagnosis
  – Langerhans cell histiocytosis
  – Other histiocytic disorders
  – Melanoma

What type?

• Primary vs Secondary
• T/NK vs B
• Specific diagnosis
Cutaneous T-Cell (and NK-Cell) Lymphomas: 

**WHO-EORTC Classification**

- **Mycosis fungoides**
- **MF-variants**
  - Pagetoid reticulosis
  - Folliculotropic, syringotropic, granulomatous variants
- **Subtype of MF**
  - Granulomatous slack skin
- **Sezary syndrome**
- **CD30-positive lymphoproliferative disorders**
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- **Subcutaneous panniculitis-like T-cell lymphoma**
- **Extranodal NK/T-cell lymphoma, nasal-type**
- **Primary cutaneous peripheral T-cell lymphoma (PTL), unspecified**
- **Subtypes of PTL**
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
  - Cutaneous gamma/delta-positive T-cell lymphoma (provisional)
  - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)
- **Adult T-cell leukemia/lymphoma**
- **Angioimmunoblastic T-cell lymphoma**
Mycosis Fungoides - Background

- **History**: Coined in 1806 by Alibert for resemblance to fungating tumors
- **Epidemiology**: Male:Female = 2:1; Black > White; Median age 55 yo
- **Incidence**: 0.29/100,000/yr
- **Etiology**: ?HTLV-1; ?ionizing radiation; ?chronic antigen stimulation (silicone breast implants)
Mycosis Fungoides: Pathology

• Epidermis
  – Epidermotropism of atypical lymphocytes
    • Pautrier’s microabscesses
    • Haloed lymphocytes along dermal-epidermal junction
  – Relative paucity of spongiosis

• Dermis
  – Papillary dermal sclerosis
  – Lymphocytic atypia
Mycosis Fungoides: Pathology
Mycosis Fungoides: Immunophenotype

- CD3
- CD20
Mycosis Fungoides: Immunophenotype

- CD4
- CD7
Mycosis Fungoides - Variants

Mckee’s Pathology of the Skin. Elsevier.
NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

DIAGNOSIS

ESSENTIAL:
• Biopsy of suspicious skin sites
• Dermatopathology review of slides

USEFUL UNDER CERTAIN CIRCUMSTANCES:
• HIC of skin biopsy (CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD25, CD56, TIA1, granzyme B, bF1)
• Molecular analysis for TCR gene rearrangements (assessment of clonality) of skin biopsy
• Assessment of peripheral blood for Sezary cells (in cases where skin is not diagnostic, especially T4) including Sezary cell prep, flow cytometry, and PCR for TCR gene rearrangement
• Biopsy of suspicious lymph nodes (in absence of definitive skin diagnosis)
• Assessment of HTLV-1 serology in at-risk populations.

WORKUP

ESSENTIAL:
• Complete physical examination
• Examination of entire skin: assessment of %BSA (palm plus digits <1% BSA) and type of skin lesion (patch/plaque, tumor, erythroderma)
• Palpation of peripheral lymph node regions
• Palpation for organomegaly/masses
• Laboratory studies:
  - CBC with Sezary screen (manual slide review: “Sezary cell prep”)
  - Sezary flow cytometric study (optional for T1; 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)

USEFUL IN SELECTED CASES:
• Bone marrow biopsy (not required for staging but used to document visceral disease in those suspected to have marrow involvement including B2 blood involvement and in patients with unexplained hematologic abnormality)
• Biopsy of suspicious lymph nodes for identical clones (recommend assessment of clonality for all but particularly NCI LN 2-3) or suspected extracutaneous sites
• Rebiopsy if suspicious of large cell transformation
• Neck CT

STAGE (MFSS-2 and MFSS-3)

Stage IA
→ TCR gene rearrangement of peripheral blood lymphocytes if blood involvement suspected
→ Comprehensive metabolic panel
→ LDH
→ Imaging studies (CT or PET/CT)
→ Pregnancy testing in women of child-bearing age

Stage IB-IIB
→ See Primary Treatment (MFSS-3)

Stage IIIB
→ See Primary Treatment (MFSS-6)

Stage III
→ See Primary Treatment (MFSS-7)

Stage IV
→ See Primary Treatment (MFSS-8)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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DIAGNOSIS

ESSENTIAL:
- Biopsy of suspicious skin sites
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USEFUL UNDER CERTAIN CIRCUMSTANCES:
- IHC of skin biopsy^a,b,c,(CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD25, CD50, TIA1, granzyme B, B^F1)
- Molecular analysis for TCR gene rearrangements (assessment of clonality) of skin biopsy^e, 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, 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
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CD30+ Lymphoproliferative Disorders: 
Lymphomatoid Papulosis

• Demographics
  – Median age: 45
  – Male-to-female: 1.5:1

• Chronic, recurrent, asymptomatic, self-healing papulonodular/papulonecrotic eruption
  – Trunk and limbs
  – Lesions and course similar to PLEVA
  – Hypopigmented scarring

• Course
  – Develops over days/weeks
  – Duration: months to >40 years
CD30+LPD: Primary Cutaneous Anaplastic Large Cell Lymphoma

- Demographics
  - Older adults
  - Generally older than systemic ALCL with skin involvement

- **Skin-colored to erythematous nodules, plaques, and tumors**

- Few to several centimeters in diameter
- Trunk, extremities, and occasionally face, affected
- Ulceration not uncommon
MF vs CD30+LPD?

Integration

MF

CD30+

LPD

Integration
Clinicopathologic Correlation
Evolution of features

• Progression assessment

• Transformation
  – MF large cell transformation

• Dual processes
  – MF & CD30+ LPD

Implications

• Prognosis

• Therapy
  – Aggressiveness
  – Tx of other malignancy
    • CLL
    • Plasma cell dyscrasia

**WHEN did this happen?**
WHERE is the disease?

Staging
- Skin
  - Morphology
  - BSA
- Reticuloendothelial system
  - Lymph nodes
  - HSM
- Blood
  - B-symptoms

Testing
- Skin Biopsy
  - H&E
  - Immunohistochemistry
  - Clonality
- RES
  - ?CXR Stage IA/IB
  - CT(PET) for >=Stage I
- Blood
  - Labs:
    - CBC
    - LDH
    - Chem-7
    - LFTs
    - Lipids
    - TSH
    - U/A
  - Flow cytometry of peripheral blood
  - Clonality studies of peripheral blood
WHERE is the disease?

T (Tumor): Skin

N (Node): Lymph node

M (Metastasis): Internal organs

B (Blood): Blood & Bone marrow
Body Surface Area
WHERE is the disease?
NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

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- HTLV-1 PCR if serology is indeterminate

**WORKUP**

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- Sezary flow cytometric study (optional for T1; 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

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**STAGE**

(MFSS-2 and MFSS-3)

**Stage I**

- See Primary Treatment

**Stage IA**

- See Primary Treatment

**Stage IB-IIA**

- See Primary Treatment

**Stage IIB**

- See Primary Treatment

**Stage II**

**Stage III**

- See Primary Treatment

**Stage IV**

- See Primary Treatment

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WORKUP

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  - Palpation for organomegaly/masses
- Laboratory studies:
  - CBC with Sezary screen (manual slide review, "Sezary cell prep")
  - Sezary flow cytometric study (optional for T1); 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
  - TCR gene rearrangement of peripheral blood lymphocytes if blood involvement suspected
  - Comprehensive metabolic panel
  - LDH
- Imaging studies
  - Chest/abdominal/pelvic contrast-enhanced CT or integrated whole body PET-CT (cT2, large cell transformed or folliculotropic MF, or with palpable adenopathy or abnormal laboratory studies)
- Pregnancy testing in women of child-bearing age
USEFUL IN SELECTED CASES:
- Bone marrow biopsy (not required for staging but used to document visceral disease in those suspected to have marrow involvement including B2 blood involvement and in patients with unexplained hematologic abnormality)
- Biopsy of suspicious lymph nodes for identical clones (recommend assessment of clonality for all but particularly NCI LN 2-3) or suspected extracutaneous sites
- Rebiopsy if suspicious of large cell transformation
- Neck CT
Prognosis
• Staging
• Counseling
  – Stage IA, most IB

Treatment
• Skin-directed therapy
  – Topical steroids
  – Nitrogen mustard (mechlorethamine)
• Phototherapy
  – PUVA
  – N-UVB
  – Extracorporeal photophoresis (ECP)
• Systemic therapy
  – MTX
  – Retinoids
    • Bexarotene
    • Acitretin
  – HDAC-I
    • Vorinostat
    • Romidepsin
  – IFN
  – Chemotx
  – ONTAK
  – BMT
### TNMB Classification and Staging of Mycosis Fungoides and Sezary Syndrome

<table>
<thead>
<tr>
<th>TNMB</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin</strong></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Limited patches, papules, and/or plaques covering &lt;10% of the skin surface</td>
</tr>
<tr>
<td>T2</td>
<td>Patches, papules, and/or plaques covering ≥10% of the skin surface</td>
</tr>
<tr>
<td>T3</td>
<td>One or more tumors (≥1 cm in diameter)</td>
</tr>
<tr>
<td>T4</td>
<td>Confluence of erythema ≥30% body surface area</td>
</tr>
<tr>
<td><strong>Node</strong></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>No abnormal lymph nodes; biopsy not required</td>
</tr>
<tr>
<td>N1</td>
<td>Abnormal lymph nodes; histopathology Dutch Gr 1 or NCI LN 0-2</td>
</tr>
<tr>
<td>N2</td>
<td>Abnormal lymph nodes; histopathology Dutch Gr 2 or NCI LN 3</td>
</tr>
<tr>
<td>N3</td>
<td>Abnormal lymph nodes; histopathology Dutch Gr 3-4 or NCI LN 4</td>
</tr>
<tr>
<td>NX</td>
<td>Abnormal lymph nodes; no histologic confirmation</td>
</tr>
<tr>
<td><strong>Visceral</strong></td>
<td></td>
</tr>
<tr>
<td>M0</td>
<td>No visceral organ involvement</td>
</tr>
<tr>
<td>M1</td>
<td>Visceral involvement (must have pathology confirmation and organ involved should be specified)</td>
</tr>
<tr>
<td>MX</td>
<td>Abnormal visceral site; no histologic confirmation</td>
</tr>
<tr>
<td><strong>Blood</strong></td>
<td></td>
</tr>
<tr>
<td>B0</td>
<td>Absence of significant blood involvement: ≤5% of peripheral blood lymphocytes are atypical (Sezary) cells</td>
</tr>
<tr>
<td>B1</td>
<td>Low blood tumor burden: &gt;5% of peripheral blood lymphocytes are atypical (Sezary) cells but do not meet the criteria of B2</td>
</tr>
<tr>
<td>B2</td>
<td>High blood tumor burden: ≥1000/μL Sezary cells or ≥40% CD4+/CD7- or ≥30% CD4+/CD26- cells</td>
</tr>
</tbody>
</table>

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**Plateau** Any size skin lesion that is elevated or indurated. Presence or absence of scale, crust, and/or polikiddema should be noted. Histologic features such as folliculotropism or large cell transformation (≥25% large cells), CD30+, or CD33+, and clinical features such as ulceration are important to document.

**Tumor** At least one >1 cm diameter solid or nodular lesion with evidence of depth and/or vertical growth. Note total number of lesions, total volume of lesions, largest lesion size, and region of body involved. Also note if histologic evidence of large cell transformation has occurred. Phenotyping for CD30 is encouraged.

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Clinical Staging of MF and SS

<table>
<thead>
<tr>
<th></th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>B</th>
</tr>
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<tbody>
<tr>
<td>IIA</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>IIB</td>
<td></td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>IIA</td>
<td>1-2</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IIB</td>
<td>3</td>
<td>0-2</td>
<td>0</td>
<td>0</td>
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<tr>
<td>IIIA</td>
<td>4</td>
<td>0-2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IIIB</td>
<td>4</td>
<td>0-2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IVA</td>
<td>1-4</td>
<td>0-2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>IVB</td>
<td>1-4</td>
<td>0-3</td>
<td>1</td>
<td>0-2</td>
</tr>
</tbody>
</table>

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# Current Clinical Management of CTCL

<table>
<thead>
<tr>
<th>Stage</th>
<th>IA Limited Disease</th>
<th>IB/IIA Generalized</th>
<th>IIB Tumors</th>
<th>III Erythroderma</th>
<th>IV Extracut. Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin-directed</strong></td>
<td></td>
<td></td>
<td></td>
<td>ECP (single or combination)</td>
<td></td>
</tr>
<tr>
<td><strong>Single-agent chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Alemtuzumab</td>
</tr>
<tr>
<td><strong>Phototherapy ± bexarotene or IFN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Combination chemo</td>
</tr>
<tr>
<td><strong>TSEBT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bexarotene, denileukin diftitox, IFN α, vorinostat, romidepsin (single or combination)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Allo-HSCT</td>
</tr>
</tbody>
</table>

**Clinical Trial**

* Topical steroid, retinoid gel, nitrogen mustard, phototherapy, radiation therapy.

** Methotrexate, liposomal doxorubicin, gemcitabine, pentostatin, chlorambucil, etoposide, temozolomide. ***ECP = photopheresis
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Mycosis Fungoides/Sezary Syndrome

Stage (MFSS-2 and MFSS-3)

Primary Treatment

- Skin-directed therapies (may be alone or in combination with other skin-directed therapies):
  See Suggested Treatment Regimens "Skin-Directed Therapies (Skin-Limited/Local)" (MFSS-A)

  If B1 blood involvement, consider primary treatment for Stage III, B1 MFSS-7 (category 2B)
  If histologic evidence of folliculotrophic or large-cell transformed MF

  Consider primary treatment for Stage IIB (See MFSS-6)

Response to Therapy

- CR/PR or inadequate response
  - Relapse with or persistent T1 skin disease

- Refractory disease or progression to > stage IA on skin-directed therapies
  - Systemic therapy ± skin-directed therapy
    (see Stage IIB on page MFSS-5)
    or
    Total skin electron beam therapy (TSEBT) or Clinical trial

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NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

STAGE
(MFSS-2 and MFSS-3)

PRIMARY TREATMENT

RESPONSE TO THERAPY

See Supportive Care for MF/SS (MFSS-B)

Relapse with or persistent T1-T2 disease:
• T1 (see stage IA on MFSS-4)
• T2 (see generalized skin treatment) (MFSS-A)

CR/PR or inadequate response

Stage IB-IIA

Generalized skin treatment
• See Suggested Treatment Regimens: “Skin-Directed Therapies (Skin-Generaled)” (MFSS-A)
• Adjunct local skin treatment
(see stage IA on MFSS-4)

If blood B1 involvement, consider primary treatment for Stage III B1 MFSS-7 (category 2B)

If histologic evidence of folliculotropic or large-cell transformed MF

Consider primary treatment for Stage II B (See MFSS-6)

CR/PR or inadequate response

Refractory disease or progression to > stage IB-IIA

See Suggested Treatment Regimens
• Clinical trial
• Systemic Therapies (SYST-CAT A) (MFSS-A)
• Combination Therapies ± skin-directed therapy

CR/PR or inadequate response

Refractory disease or progression

Stage II B (See MFSS-6)

Generalized skin treatment

Unlike other NHL subtypes, response criteria for MF/SS has not been demonstrated to correlate with prognosis. Often decisions to continue or switch therapy are on a clinical basis. However, a proposal for detailed response criteria has been published (Olsen E, Whittaker S, Kim YH, et al. J Clin Oncol 2011;29:2598-2607).

Suggested Treatment Regimens: “Synergistic Therapies (SYST-CAT B)” (MFSS-A)

For all other MF/SS, treatment is determined by the extent of disease, site(s) of involvement, and potential adverse effects of therapy. These guidelines recommend systemic treatment for patients with Stage II B disease. For patients with Stage III disease, systemic and local therapies are recommended. For patients with Stage IV disease, systemic therapy is recommended.

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Stage-Directed Management

CTCL Primary Treatment Map

- IA (limited patch, plaque)
  - Topical corticosteroids
  - Nitrogen mustard
  - UVB
  - PUVA

- IB, IIA (generalized patch, plaque)
  - Bexarotene gel

- IIB (tumors)
  - Oral bexarotene
  - Vorinostat (Zolinza) & HDAC inhibitors

- III (erythroderma)
  - Donileukin diftitox

- IVA, IVB (nodal/visceral involvement)
  - Electron beam
  - Chemotherapy

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Myeloid Fungi/Sezary Syndrome

STAGE
(MFSS-2 and MFSS-3)

Stage III

PRIMARY TREATMENT

If no blood involvement, consider skin-directed therapy
See Suggested Treatment Regimens
Skin-Directed Therapies
(MFSS-A)

or

If blood B1 involvement, systemic therapies
See Suggested Treatment Regimens
"Systemic Therapies (SYST-CAT I)" 
and skin-directed therapy

RESPONSE TO THERAPY

CR/PR or inadequate response → Relapse or persistent disease

CR/PR or inadequate response

Relapse or persistent disease

Combination therapies
See Suggested Treatment Regimens
Combination Therapies
(MFSS-A)

Clinical trial

Clinical trial

See Suggested Treatment Regimens
"Systemic Therapies (SYST-CAT B)"

Alemtuzumab

Consider non-ablative allogeneic transplant, as appropriate

REFRACTORY DISEASE OR PROGRESSION

Stage III

Relapse or persistent disease

Clinical trial

See Suggested Treatment Regimens
"Systemic Therapies (SYST-CAT B)"

Alemtuzumab

Consider non-ablative allogeneic transplant, as appropriate

Refractory or intolerant to multiple previous therapies

The role of allogenic HSCT is controversial. See discussion for further details.

Generalized skin-directed therapies (other than topical steroids) may not be well tolerated in stage III and should be used with caution. Phototherapy (PUVA or UVB) or TSEBT can be used successfully.

Mid-potency topical steroids should be included (± occlusive modality) with any of the primary treatment modalities to reduce skin symptoms. Erythrodermic patients are at increased risk for secondary infection with skin pathogens and systemic antibiotic therapy should be considered.

Combination therapy options can be considered earlier (primary treatment) depending on treatment availability or symptom severity.

Lower doses of alemtuzumab administered subcutaneously have shown lower incidence of infectious complications.

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NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

STAGE
(MFSS-2 and MFSS-3)

Sezary syndrome →

Stage IV →

Non Sezary or Visceral disease (solid organ) →

PRIMARY TREATMENT

See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT A) (MFSS-A)

Systemic Therapies

Combination Therapies

RESPONSE TO THERAPY

CR/PR or inadequate response →

Relapse or persistent disease
• Consider allogeneic transplant, as appropriate

CR/PR or inadequate response →

Relapse or persistent disease
• See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) (MFSS-A)
  • Alemtuzumab
  • Clinical trial

Refactory disease progression →

Refractory disease progression →

See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) (MFSS-A)

See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT C) or (SYST-CAT D) or multigent chemotherapy ± RT for local control

CR/PR or inadequate response →

Relapse or persistent disease
• Consider allogeneic transplant, as appropriate

CR/PR or inadequate response →

Relapse or persistent disease
• See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) (MFSS-A)
  • Alemtuzumab
  • Clinical trial

Clinical trial

See Supportive Care for MFSS (MFSS-B)

See monocolonal antibody and viral reactivation (NHQS-R)

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

Stage (MFSS-2 and MFSS-3)

Sezary syndrome
- See Suggested Treatment Regimens
  - Systemic Therapies (SYST-CAT A) or MFSS-A
  - Combination Therapies

Non Sezary or Visceral disease (solid organ)
- See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) or (SYST-CAT C) or multigent agent chemotherapy ± RT for local control

Response to Therapy
- CR/PR or inadequate response
  - Relapse or persistent disease
    - Consider allogeneic transplant, as appropriate

- Refractory disease or progression
  - See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) or MFSS-A
  - Alemtuzumab
  - Clinical trial

- Refractory disease or progression
  - See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) or MFSS-A
  - Alemtuzumab
  - Clinical trial

See Supportive Care for MFSS (MFSS-B)
See monoclonal antibody and viral reactivation (NHOD5-B)

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NCCN Guidelines Version 1.2013
Mycosis Fungoides/Sezary Syndrome

STAGE
(MFSS-2 and MFSS-3)

Sezary syndrome

Stage IV

Non Sezary or Visceral disease (solid organ)

PRIMARY TREATMENT

SYSTEMIC THERAPIES

Relapse or persistent disease

- Consider allogeneic transplant, as appropriate

CR/PR or inadequate response

- See Suggested Treatment Regimens
- Systemic Therapies (SYST-CAT A) or MFSS-A

Refactory disease or progression

- See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) (MFSS-A)
- Alemtuzumab
- Clinical trial

See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT C) or (SYST-CAT B) or (SYST-CAT C) or multi-agent chemotherapy ± RT for local control

CR/PR or inadequate response

- See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) or (MFSS-A)

Refactory disease or progression

- See Suggested Treatment Regimens - Systemic Therapies (SYST-CAT B) or (MFSS-A)

Relapse or persistent disease

- Consider allogeneic transplant, as appropriate

See Supportive Care for MFSS (MFSS-B)

Clinical trial

See monoclonal antibody and viral reactivation (NHQDS-B)

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SUGGESTED TREATMENT REGIMENS

References

**Systemic Therapies Continued**

**Vinorelbine**


**Rituximab**


**Extracorporeal photopheresis (ECP)**


**Methotrexate**


**Liposomal doxorubicin**


**Gemcitabine**


**Pentostatin**

**Temocilomide**


**Bortezomib**

**Low-dose Palafracte**

**Palafracte**

Continued on next page
SUGGESTED TREATMENT REGIMENS

References

Allogeneic stem cell transplant

Combination Therapies
Skin-directed + Systemic:

Systemic + Systemic:

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SUPPORTIVE CARE FOR MF/SS

**Pruritus**
- Assessment
  - Pruritus should be assessed at each visit using consistent measurements
  - Generalized pruritus and localized pruritus should be distinguished
  - Correlation between sites of disease and localization of pruritus should be noted
  - Other potential causes for pruritus should be ruled out
- Treatment
  - Moisturizers, emollients, and barrier protection
  - Topical steroid (appropriate strength for body region) ± occlusion
  - Optimize skin-directed and systemic therapy
  - Topical preparations - camphor/menthol formulations, pramoxine formulations
  - Systemic agents
    - First-line
      - Antihistamines
        - Doxepin
      - Gabapentin
    - Second-line
      - Aprepitant
      - Mirtazapine
    - Selective serotonin reuptake inhibitors
    - Third-line
      - Naltrexone

**Infections**
- Active or Suspected Infections
  - Erythroderma
    - Skin swab and nares cultures for Staphylococcus aureus (S. aureus) infection or colonization
    - Intranasal mupirocin
    - Oral dicloxacillin or cephalaxin
    - Sulfamethoxazole/trimethoprim, doxycycline if suspect MRSA
    - Vancomycin if no improvement or bacteremia
    - Bleach baths or soaks (if limited area)
- Ulcerated and necrotic tumors:
  - Gram-negative rods (GNR) common in necrotic tumors may lead to bacteremia and sepsis
  - If high suspicion for infection, obtain blood cultures, start antibiotics even if fever absent
  - Role of wound cultures not clear due to colonization
  - Empirical therapy for both GNR and gram-positive coagulase-negative staphylococcal infections is necessary initially
- Prophylaxis
  - Optimize skin barrier protection
  - Mupirocin for S. aureus colonization
  - Bleach baths or soaks (if limited area)
  - Avoid central lines (especially in erythrodermic patients)
  - For patients receiving alemtuzumab, see **NHODG-B**.

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Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Health-related quality of life in patients with cutaneous T-cell lymphoma?

Heather M. Holahan, MD; Ronda S. Farah, MD; Sara Fitz, MD; Sarah L. Mott, MD; Nkanyezi N. Ferguson, MD; Julie McNeill, RN; Brian Link, MD; and Vincent Liu, MD

Abstract

Background: Little is currently known about health-related quality of life (HRQOL) of patients with cutaneous T-cell lymphoma (CTCL), a condition characterized by chronic, pruritic, violaceous lesions, features which may be uniquely influential.

Objective: The aim of this study was to establish baseline HRQOL data for patients with CTCL and identify its influencing factors.

Methods: Prospective, reimbursed survey design utilizing questionnaires including parent of QoL indices obtained from 100 patients with biopsy-confirmed, Sézary syndrome, and CD30+ lymphohistiocytosis disorder. Chart review correlated QoL with years of disease, stage, diagnostic, histology of disease, current/past therapies, and medical/psychiatric diagnoses.

Results: Psychiatric condition was significantly associated with symptoms (P < 0.01), emotions (P = 0.01), and functioning (P = 0.03) subclasses along with overall composite measures (P = 0.01). High-grade systemic therapy (OR = 1.56) showed greater increased odds of a lower health status than low grade (OR = 1.04). The number of medical morbidities was significantly related to itching (P = 0.01). Increased age was a protective factor with respect to the emotions (P = 0.01), functioning (P = 0.01), and overall composite (P = 0.01) but not predictive of symptoms. Lower income was associated with higher bother on the symptoms subscale.

Conclusions: HRQOL in CTCL appears related to a number of factors, including presence of a psychiatric condition, use of systemic (particularly high-grade) therapy, number of medical morbidities, and income.
Patient-Centered, Multidisciplinary Care

- Dermatologist
- Pathologist
- Oncologist
- Radiologist
- Radiation Oncologist

Quality-of-Life
1) **MYCOSIS FUNGOIDES**

**Stage:**

**History:**

**Work-up:**
- Consultations:
- Bloodwork:
- Histopathology:
- Radiographic Imaging:
-  

**Treatment:**
- **Topical/Intralesional Therapy:**
-  
- **Phototherapy/Radiation therapy:**
-  
- **Systemic therapy:**
  - Antihistamines:
  - Systemic steroids
  - Methotrexate
  - Retinoids
  - Interferon
  - Vorinostat
  - Doxil
  - Gemcitabine
  - Pentostatin
  - Mogamulizumab
**WHY did this happen?**

**Case observations**
- Presentation
  - Unusual hx?
  - PE?
  - Work-up?
- Therapy

**Research questions**
- Clinical
- Pathologic
- Therapy
Research Into What Lies Beneath?

HOW HELP?

Lymphoma therapy | Personal, Social, Family Well-being

WHY?

Research into Diagnosis, Classification | Research into Therapy

HOW HELP OTHERS?

Improved diagnostic criteria, classification, prognosis, etc. | Improved management
Conclusions

• Clinicopathologic correlation is key to accurate diagnosis and optimal management
• Multidisciplinary care coordination is critical
• Optimal care is patient-centered and addresses quality-of-life issues in decision-making