Updates on CTCL in Skin of Color

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S005 Skin of Color
Disclosure of Relationships with Industry

Research/Grants: Eli Lilly, Soligenix, Helsinn, Eisai, Boehringer Ingelheim, Novartis, AbbVie, BMS, Celgene, Glenmark, Kyowa Kirin, Amgen, AnaptysBio
Advisory boards: Novartis, Boehringer Ingelheim, Helsinn, Kyowa Kirin, Regeneron
Consultant: OncoDerm LLC, Aptis Partners
Speaker: Helsinn, Kyowa Kirin
Objectives

1. Outline racial disparities in cutaneous T-cell lymphomas (CTCLs)
2. Recognize clinical appearance and diagnostic clues in skin of color patients
3. Illustrate differential diagnoses and management strategies via case presentations
Cutaneous T-cell lymphoma (CTCL)

- CTCLs are non-Hodgkin’s lymphomas presenting primarily in the skin
- Mycosis fungoides (MF), and Sézary syndrome (SS) are 2 subtypes of CTCL that comprise only 2% to 3% of all NHL cases, but ~75% of CTCLs.
- More common in men compared to women and in patients older than 50 years of age compared to younger people.

- Takes an average of 3-4 years to establish its diagnosis. Diagnosis is made based on clinical presentation, histopathologic evaluation, blood tests, molecular studies, and imaging tests.

Race, ethnicity and CTCL

- The incidence of CTCL in African-Americans in the US is higher than in Caucasians.
- Skin of color (SOC) patients present at an earlier age, with advance disease stage, and have poorer overall survival compared to Caucasian patients.
- In a survey study, SOC patients compared to non-SOC patients reported “very much” or “a lot”
  - level of itch (40% vs 20%)
  - skin-related embarrassment or self-consciousness (28% vs 10%)
  - difficulty participating in sports (20% vs 9%)
  - negative effect on social/leisure activities (20% vs 5%)
- The average hours lost from work due to CTCL among SOC patients was 2.7 compared to 0.9 in non-SOC patients
It remains controversial whether socioeconomic differences and a lack of access to medical care might play a role in racial disparities in CTCL.

Understanding the reasons for racial disparities is an urgent need.

Early diagnosis of CTCL in patients of skin of color could help improve prognosis, because appropriate management of early disease stages portends a prognosis similar to individuals without CTCL.

Race, ethnicity and CTCL

Hypopigmented MF – Diagnostic Clues

• Most common type of pediatric MF, with a mean age of diagnosis of 10-15 years, and a time to diagnosis of 2-5 years.

• Clinical presentation:
  – Isolated, multiple or confluent non-atrophic hypopigmented patches and plaques with or without fine overlaying scale or surrounding / superimposed erythema
  – +/- concomitant erythematous or hyperpigmented MF lesions
  – +/- alopecia

• Histological presentation:
  – atypical lymphocytes, epidermotropism, and Pautrier microabscesses.
  – while classic MF shows a predominance of CD4+ T-cells, hypopigmented MF is characterized by a predominance of neoplastic and reactive CD8+ T-cells.
  – Loss of CD7 is characteristic, but not specific

Hypopigmented MF - Management

- Phototherapy shifts the tumor-infiltrating lymphocytes from Th2 to Th1, eradicates malignant T-cell clones in thin lesions, and promotes a localized immune response.

- Has the highest patient satisfaction and ORR of 80-90% in early-stage MF.

- Optimal for hypopigmented lesions, as decreased efficacy is observed with increasing skin pigmentation.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Received (%)</th>
<th>Satisfaction (%)</th>
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<tr>
<td>PUVA</td>
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<td>75</td>
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<tr>
<td>Nb-UVB</td>
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<td>66</td>
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<tr>
<td>Topical steroids</td>
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<td>Nitrogen mustard</td>
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<td>Oral bexarotene</td>
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<td>TSEB</td>
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<td>ECP &amp; Interferon</td>
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<td>33</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>&lt; 10</td>
<td>25</td>
</tr>
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</table>

Not FDA approved for MF, but included in NCCN guidelines

Sézary Syndrome (SS) – Diagnostic Clues

• Clinically:
  – Erythroderma is typical but not specific. “Leonine” facies and ectropion can present.
  – Palm/sole involvement may present with hyperkeratosis and painful fissures

• Histologically:
  – Biopsies are non-diagnostic in ~ 1/2 of patients
  – ~ 23 % of SS patients show Pautrier microabcesses (they are not seen in other erythrodermic dermatoses)
  – presence of cerebriform lymphocytes, CD7 loss, decreased CD8+ lymphocytes, and increased proliferation (Ki-67(+) lymphocytes) are the strongest indicators for SS.
  – A dominant T-cell clone in the skin aids in the diagnosis of SS when it is also found in blood

• CBC:
  • Eosinophilia (~ 20%)
  • Lymphocytosis
  • Flow cytometry (+/- peripheral blood smear) and TCR rearrangement
  • Imaging studies

Extracorporeal photopheresis (ECP) for SS

• Leads to apoptosis in malignant T cells and a conversion of blood monocytes to DCs. Together these processes induce an immune response against the malignant clone.

• The ORR for ECP monotherapy ranges from 10-90% and combination therapy ranges from 20-90% in MF/SS.

• Side effects (extremely rare):
  hypotension, hematomas, CHF, arrhythmias, superficial thrombophlebitis, catheter-related sepsis, herpes infections, disseminated fungal infection, anemia.

Summary

- CTCLs present at a younger age and with more advanced disease stages in SOC individuals.
- SOC patients compared to non-SOC report worse itch, skin-related embarrassment, difficulty participating in sports, and negative effects on leisure activities.
- The most common presentation is a pruritic eczematous rash. However, consider presentations such as hypopigmented MF in SOC patients.

- Clinical presentation, histopathology, molecular studies, blood tests, and imaging studies are needed to establish a definite diagnosis.
- Treatment strategies vary according to clinical presentation, race/ethnicity, comorbidities, and disease stage.