Sezary Syndrome: The Elusive Sezary Cell

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Disclosures

- NONE
Let’s Jump In!
Chief Complaint

- Chief Complaint: Patient is a 63-year-old man who was airlifted from OSH (to tertiary center) for evaluation of diffuse rash and for higher level “bum” care.
Approximately 5 years prior, patient developed an erythrodermic rash of his lower legs that appeared to be the superficial layers of skin sloughing off. This was treated with topical medications and the rash continued to worsen. The rash continued to spread upward to his body. He was evaluated by several physicians, and treated with systemic steroids and wound care, followed by several years of chronic topical steroid application. The rash persisted and spread, progressively covering the entire surface of his body. He found temporary relief with warm baths where he could remove the dead skin.
Approximately one year prior he decided to stop all topical steroids because he “realized they weren’t helping at all.” After this, the condition worsened acutely—leading to perpetual skin sloughing over his entire body complicated infections. He also had infectious pleural effusions, pneumonia, and sepsis with numerous inpatient hospitalizations. The prior six months he had been out of the hospital for only a few weeks in total, and had suffered severe malnutrition and resulting weakness.
At the time of transfer, patient denies pain, fever, chills, chest pain, joint pain, dyspnea. He reports feeling weak and fatigued, and complains of difficulty hearing due to “crusties” in his ears.
PMH

- Psoriasis
- Coronary artery disease (stent placement in 2013)
- Hypertension
- Hyperlipidemia
- LLE arterial thrombosis
Family history is non-contributory

Former smoker for 20 years, unknown quit date, occasional alcohol use, no recreational drugs

Retired truck driver

His wife was with him at bed side
Current Medications

- Warfarin
- Clobetasol
- Vancomycin
- Zinc sulfate
- Ciprofloxacin
- Gabapentin
- Albumin
- Ceftazidime
- Hydroxyzine
- Hydromorphone
- Pipercillin/tazobactam
- Linezolid
Vital Signs

- BP: 113/48
- HR: 101
- RR: 16
- T: 36.8
- SpO2: 100% on 5L of O2 (simple mask)
Physical Exam

- **General:** Chronically ill appearing male laying in bed with **Bair Hugger head to toe, cachetic**, no acute distress
- **Psych:** Alert and oriented, pleasant, cooperative
- **Neuro:** No focal deficits, PERRL, EOM intact
- **HEENT:** **Dry mucus membranes, ectropion,** white plaques over lateral aspects of tongue, **bilateral EACs are occluded with purulent debris and exfoliated skin,** supple neck
- **Cardiac:** Normal rate and rhythm, no murmurs appreciated
- **Pulm:** Lungs are CTAB in anterior and lateral fields. Symmetric air entry, no accessory muscle use
- **Abdomen:** Soft, non-tender, normal active bowel sounds
- **Extremities:** **Atrophic,** no joint swelling or tenderness, metatarsal amputations of L foot, surgical sites are clean and dry
Erythematous desquamating rash covering greater than 90% of body, including extremities, torso, head, and face. Palms and soles are spared. Some areas including head, and groin have purulent discharge. No blood, no evidence of confluence or induration suggesting abscess.
Labs On Admission

- Na: 143
- K: 4.2
- Cl: 108
- CO2: 29
- BUN: 33
- Cr: 0.52
- Ca: 8.2
- Mg: 1.7
- Phos: 2.9
- WBC: 17.26
- Hb: 8.1
- Hct: 25
- Plt: 430
- PT: 19.3
- INR: 1.6
- PTT: 51
Differential?
Differential

- Pustular psoriasis
- Eczematous dermatitis
- Allergic contact dermatitis
- Topical steroid withdrawal
- Pityriasis rubra pilaris
- Cutaneous T cell lymphoma with Sezary syndrome
Admitting Diagnosis

Unspecified dermatitis?

Worsening psoriasis?

Complications:
- sepsis
- pleural effusions
- protein calorie malnutrition
Hospital Course: Day 1

- Consults, consults, consults
- Dermatology, ENT, Nutrition, ID, PT/OT, Nursing, Spiritual…
Day 2: More Data

- Skin Biopsies: 38.4% of T cell in the skin are abnormal
- Flow cytometry: Same immunophenotype of T cell identified in peripheral blood
- Leading diagnosis: Cutaneous T Cell Lymphoma with blood involvement
Patient continues to be very, very sick (BPs, Temps, infection, malnutrition, etc…)

Diagnosis of CTCL with blood involvement, not meeting criteria for Sezary currently

 Imaging Impression:
 1. Enlarged bilateral axillary and inguinal lymph nodes, indeterminate. However, suspicious for lymphoproliferative process.
 2. Features of volume overload including bilateral pleural effusion, moderate ascites, bilateral hydrocele, and anasarca.
 3. Multiple foci of clustered nodules in tree-in-bud pattern noted in bilateral lungs, likely representing bronchiolitis secondary to infection/inflammation
Criteria for Sezary Syndrome

- Erythroderma defined as erythema covering at least 80 percent of body surface area
- A clonal TCR rearrangement in the blood
- An absolute Sezary cell count of at least 1000 cells/μL OR one of the following two criteria:
  - Increased CD4+ or CD3+ cells with CD4 to CD8 ratio of 10 or more
  - Increased CD4+ cells with an abnormal phenotype (such as a CD4+CD7- ratio > 40% or a CD4+CD26- ratio > 30%)

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desired. Clinical and morphologic correlation is recommended. Addendum created to report the results of additional studies to evaluate for Sezary syndrome.

CLINICAL
History of psoriasis.

RESULTS

9.6% of CD4+ T Cells lack CD7. This population comprises 0.53% of the WBC’s. 42.0% of the CD4+ T cells lack CD26. This population comprises 2.3% of the WBC’s.
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A clonal TCR rearrangement in the blood

An absolute Sézary cell count of at least 1000 cells/μL OR on of the following two criteria:

- Increased CD4+ or CD3+ cells with CD4 to CD8 ratio of 10 or more
- Increased CD4+ cells* with an abnormal phenotype such as a CD4+CD7- ratio > 40% or a CD4+CD26- ratio > 30% (42%)

*Masked by cyclosporine
The Sezary Cell Morphology
The Ending

Diagnosis of Sezary Syndrome was made on hospital day 9 (T4N2M0B1)

Patient was not a candidate for medical therapy

Patient and his wife decided to transition to palliative care

He passed away on hospital day 10
What is Sezary Syndrome

- Aggressive subtype of cutaneous T cell lymphoma with leukemic involvement
- Can evolve from Mycosis Fungoides or develop de novo
- Clinical presentation
- Typical immunophenotype of abnormal T cell population is CD3+, CD4+, CD7-, CD26-, CD8-
- Cerebriform lymphocyte
- Super rare (0.8 in a million)
- Not inherited
- Clustered incidence in industrial areas
- Incurable
Sezary Syndrome is an aggressive leukemic variant of CTCL

Patients with SS present with erythroderma and lymphadenopathy developing over weeks to months, or more

Clinical manifestations that affect QoL

Evaluation with skin biopsy, blood flow cytometry and peripheral smear
This case illustrates the challenge in diagnosing SS because the disease is clinically advanced and life-threatening by the time the defining clonal cell line is detectable.

Therapeutic value of a diagnosis.


• Kirsch IR, Watanabe R, O'Malley JT, et al. TCR sequencing facilitates diagnosis and identifies mature T cells as the cell of origin in CTCL. Sci Transl Med 2015; 7:308ra158.


Questions