Demystifying Systemic Lupus Erythematosus: Signs and Symptoms for Early Recognition

Teaching Fellows in Lupus Project
Introduction: Why are we here?

• Lupus can take 4-6 years and 3 providers before diagnosis*

• During that time, organ damage can develop leading to 5 fold increased risk of death

• Patients go to primary care providers or emergency rooms at onset of illness, so detection of lupus by these providers is critical to early diagnosis

• These providers may have received only 90 minutes of training on lupus in medical school*

* Survey data of health professionals
How you can help: Teaching Fellows Project

- **Problem:** Education about lupus is important for all providers, but there is a shortage of peer educators

- **Solution:** Recruit fellows/junior faculty in Rheumatology to serve as lupus educators for practicing physicians

- **What you can do:** Participate in the voluntary pre and post assessment and follow up so we can evaluate the project

- **Benefits to you:** Increased self efficacy in lupus detection, access to CMEs from the ACR

- **Our goal:** To bring this project to Rheumatology Fellowship Programs nationally to expand quality education on lupus to improve detection, increase appropriate referral, and decrease diagnosis time
Pre/Post Assessment and Follow Up

Voluntary, Used solely to rate the quality of this seminar
De-identified: Linked by numeric identifier

• **Pre- assessment (before seminar)**
  – 10 multiple choice or true/false questions and 1 efficacy question
  – About 3 minutes to complete
• **Post- assessment (after seminar)**
  – Repeat pre assessment
  – Additional qualitative and demographics questions
  – About 5 minutes to complete
• **Follow up assessment (4-6 weeks after seminar)**
  – Repeat pre assessment
  – Option for comment
  – Requires an email address
• Access to CME modules available from ACR for completion
• Answers available after session
Thank you

We appreciate your time in taking our pre-seminar assessment
Presentation Goals

• To improve recognition of lupus and increase appropriate referral for diagnosis by:

• Increasing lupus knowledge in:
  – Epidemiology
  – Health Disparities
  – Genetics, Pathogenesis, ANA and other Autoantibodies
  – Disease characteristics: activity, severity, mortality

• Reviewing the classification criteria

• Discussing real case presentations of patients with lupus
Patient Voices
Systemic Lupus Erythematosus (SLE)

- An inflammatory, multisystem, autoimmune disease of unknown etiology with protean clinical and laboratory manifestations and a variable course and prognosis
- Lupus can be a mild disease, a severe and life-threatening illness, or anything in between
- The diversity of clinical symptoms in SLE is great, and all organ systems are vulnerable
- Disease is characterized by periods of flare and remission (or low level activity) and can culminate in irreversible end-organ damage
Why is diagnosis so hard?

• The Great Masquerader: can mimic viral syndromes, malignancies, allergic reactions, stress, etc.
• May be associated with depression and/or fibromyalgia.
• Initial symptoms might be non-specific: fatigue, achiness, stiffness, low grade fevers, swollen lymph nodes, rashes.
• Symptoms may develop slowly or suddenly.
• There is no gold standard diagnostic test for lupus.
• Wide variety of symptoms and organ involvement may be present.
Examples of Organs Involved, Signs, and Symptoms

- Eyes
- Skin
- Pleurisy
- Kidney disease
- Muscle
- Raynaud’s & vasculitis
- Central nervous system
- Oral & nasal ulcers
- Pericarditis
- Blood disorders
- Joints & arthritis

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Why is early referral important?

- Mortality is higher in lupus patients compared to the general population
- 5-year survival rate in 1953 was 50%, increased to 90% with better detection and treatment
- Currently 80 to 90% of lupus patients survive 10 years after diagnosis, but that drops to 60% with advanced stages of organ threatening disease
- Leading causes of mortality are preventable
- Appropriate therapeutic management, compliance with treatment and improved treatment of long-term consequences can prevent excess and premature deaths. **This starts with clinical suspicion of the diagnosis and early recognition.**
Mortality

- Cardiovascular disease is the major cause of mortality in patients with longstanding lupus
- Factors contributing to increased mortality:
  - Active lupus & infection (early stages of disease)
  - High disease severity at diagnosis
  - Younger age at diagnosis
  - Ethnicity: Black, Hispanic, Asian, and Native American populations
  - Male gender
  - Low socioeconomic status
  - Poor patient adherence
  - Inadequate patient support system
  - Limited patient education

*Indicates opportunity for improvement.

Epidemiology

- **Prevalence:** 2–140/100,000 worldwide but as high as 207/100,000
- **Incidence:** 1–10/100,000 worldwide

- **Health Disparities and At-Risk Populations:**
  - Women in their reproductive years
  - Women are 9 times more likely to develop lupus than men
  - Non-Caucasians have the highest prevalence:
    - Affects up to 1/250 Black women in US
    - 2-3 times higher risk than white women

- **Cost:** Direct costs associated with treatment (e.g., $100 billion in healthcare cost associated with autoimmune diseases) and indirect cost related to lost productivity and wages

Other Health Disparities in Lupus

- Specific racial/ethnic minorities are more likely to develop lupus at a younger age and to have more severe symptoms at onset
- Specific racial/ethnic minorities with lupus have mortality rates at least 3 times as high as White individuals
- Low income individuals less likely to receive recommended care
- Poverty associated with poor outcomes
Disease Activity and Severity

• Predictors of flare (in some but not all cases)
  – New evidence of complement consumption
  – Rising anti-dsDNA titers
  – Increased ESR
  – New lymphopenia

• Severity characterized by:
  – Abrupt onset of symptoms
  – Increased renal, neurologic, hematologic, and serosal involvement
  – Rapid accrual of damage (irreversible organ injury)
  – Associated with race, younger age, male gender, poverty
SLE
Initiation
Amplification
Perpetuation

Genetic alterations

Environmental Exposures & Behavior

Abnormally functioning
B-cells
T-cells
pDC

Autoantibodies
ICs

Proinflammatory
molecules

TISSUE INJURY

Antigen
Hormones
(estrogen)
Infections
Toxins
Medications
Sun exposure
Vitamin D deficiency
Smoking
Stress
Toxins
Pathogenesis of Lupus - Important Concepts

• Autoimmunity is an altered immune homeostasis that leads to autoreactivity, immunodeficiency, and malignancy.

• Immune dysregulation leading to autoreactivity and autoantibodies in SLE occurs in different phases and likely represents the untoward effects of environmental triggers on the genetically susceptible host.
Lupus Intangibles

Achiness, Headache

Fatigue

Memory thief “brain fog”

Depression
Lupus on the Outside

Synovitis

Malar rash

Painless oral ulcer

Raynaud’s Phenomenon

Discoid rash

Jaccoud’s arthropathy

Vasculitis

Alopecia
Lupus on the Inside

- Serositis
- Pericardial effusion
- Cerebral infarct
- Brain atrophy
- Spherocytes
- Glomerulonephritis
What Do Most Lupus Patients Have in Common—Antinuclear Antibodies (ANA)

- Autoantibodies against various components of the cell nucleus
- Present in many autoimmune disorders as well as some healthy subjects
- Sensitive (not specific for SLE)
- Because of low specificity, ANA usefulness increases if the pretest probability for lupus is high; ie, the patient has symptoms and signs that can be attributed to SLE
- Because of the high sensitivity of the ANA, a patient with negative ANA is unlikely to have lupus even when her/his clinical presentation is suggestive of lupus
Incidence of Positive ANA

- Non- lupus subjects 3%–4%
- SLE 95%–99%
- Scleroderma 95%
- Hashimoto’s thyroiditis 50%
- Idiopathic pulmonary fibrosis 50%
- Incidence increases with age, chronic infections, and other chronic conditions

- Interpret the ANA in context of clinical complaints
  ANA+ does not = SLE
<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Lupus Specificity</th>
<th>Clinical Associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>Low</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>High</td>
<td>Nephritis</td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>High</td>
<td>Nonspecific</td>
</tr>
<tr>
<td>Anti-RNP</td>
<td>Low</td>
<td>Arthritis, myositis, lung disease</td>
</tr>
<tr>
<td>Anti-SSA</td>
<td>Low</td>
<td>Dry eyes/mouth, subacute cutaneous lupus erythematous (SCLE), neonatal lupus, photosensitivity</td>
</tr>
<tr>
<td>Anti-SSB</td>
<td>Low</td>
<td>Same as above</td>
</tr>
<tr>
<td>Antiphospholipid</td>
<td>Intermediate</td>
<td>Clotting diathesis</td>
</tr>
</tbody>
</table>
When to suspect SLE:

ACR (Revised) Criteria for Classification
4/11 = 95% Specificity; 85% Sensitivity

1. Serositis
2. Oral ulcers
3. Arthritis
4. Photosensitivity
5. Blood cells
6. Renal involvement
7. Antinuclear antibodies (ANA)
8. Immunologic disorder
9. Neurologic disorder
10. Malar rash
11. Discoid rash

# Signs and Symptoms

<table>
<thead>
<tr>
<th>Symptom Occurrence (ever)</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Neurologic</td>
<td>90%*</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>95%</td>
</tr>
<tr>
<td>Fever &gt;100 F (38 Degrees C)</td>
<td>90%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>80%</td>
</tr>
<tr>
<td>Prolonged or extreme fatigue</td>
<td>81%</td>
</tr>
<tr>
<td>Skin rashes</td>
<td>74%</td>
</tr>
<tr>
<td>Anemia</td>
<td>71%</td>
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<tr>
<td>Kidney involvement</td>
<td>50%</td>
</tr>
<tr>
<td>Pleurisy and/or pericarditis</td>
<td>45%</td>
</tr>
<tr>
<td>Butterfly-shaped rash across cheeks and nose</td>
<td>42%</td>
</tr>
<tr>
<td>Sun or light sensitivity (photosensitivity)</td>
<td>30%</td>
</tr>
<tr>
<td>Hair loss</td>
<td>27%</td>
</tr>
<tr>
<td>Abnormal blood clotting problems</td>
<td>20%</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>17%</td>
</tr>
<tr>
<td>Seizures</td>
<td>15%</td>
</tr>
<tr>
<td>Mouth or nose ulcers</td>
<td>12%</td>
</tr>
</tbody>
</table>
Case Presentation A

- **History:** A 23-year-old Hispanic female with no past medical history presented to the emergency department (ED) with an 8-week history of joint pain and swelling in the hands, knees, and ankles; fever; myalgias; pleuritic chest pain; weight loss; and a facial rash that worsened with sun exposure. She had been seen initially at a local clinic and treated for “cellulitis” with oral Keflex. Two days prior, she was seen in another ED, found to have a temperature of 103 °F, proteinuria, and anemia; she was told it was a “viral syndrome” and discharged home.
Case Presentation A (cont.)

- **Exam:** T 37.9 °C, BP 130/90, painless ulceration on the palate, malar rash, diffuse lymphadenopathy, and synovitis of the MCP/PIP joints

- **Labs:** WBC 2.5x10⁹/L, total protein 9 g/dL, albumin 3 g/dL, Hgb 11g/dL, Hct 32%, BUN 11 mg/dL, Cr .06 mg/dL
  UA: 100 mg/dL protein, RBC 20–40/hpf, WBC 0–1/hpf
  ANA+, anti-dsDNA+, Sm+
Case Presentation B - What features are concerning for lupus?

• 23 year old woman from Western Africa with recently diagnosed anemia (presumed but not confirmed to be iron-deficiency anemia) presents with swelling of feet and hands and a non-specific rash on her face and arms. She reported swelling in the joints, enlarged lymph nodes, generalized body aches and sweating.

• Chart review reveals:
  – Positive ANA of 1:1280
  – 4.2 WBC with normal differential
  – Hb/Hct is 9.6/30.4 MCV 77.3
  – Plt 307
Lupus Detection—In Summary

• Early symptoms can be
  – Non-specific, easily confused with other illnesses or syndromes
  – Transient or prolonged, independent of one another

• Consider lupus if your patient presents with
  – Vague complaints from the signs and symptoms list
  – Family history of autoimmune disease

• Do an initial screening
  – CBC, BMP, LFT’s, ESR, CRP, ANA, UA

• Make a referral for assessment and diagnosis by a Rheumatologist
Final Thoughts

• **Patient engagement and trust building is critical**
  – Patients from different cultural/socioeconomic backgrounds experience illness and treatment differently
  – Physicians from different cultural/socioeconomic backgrounds perceive patients and symptoms differently

• **What you can do to reduce health disparities**
  – Discuss lupus prevalence and disparities with colleagues
  – Pursue continuing education about causes of disparities and cross-cultural communication
  – Learn about and refer patients to community resources
Resources and Information

Ongoing care of lupus patients is a team effort

For presentations, videos, interactive case studies and CE/CME courses that can help, visit the Lupus Initiative at www.tlertools.org

We appreciate your participation in the post assessment and 4-6 week follow up assessment.
Thank you!

This project is part of the American College of Rheumatology’s Lupus Initiative (www.tlitools.org) and is administered by the Lupus Research Institute (lupusresearchinstitute.org/). This project is supported by Grant Number 1 CPIMP141065-01-00 from the U.S. Department of Health and Human Services office of Minority Health.

Questions about the Project?
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