Systemic Lupus Erythematosus: Diagnosis and Management

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Disclosures

• None
Objectives

1. Identify clinical features and common manifestations of SLE
2. Identify immunologic findings of SLE
3. Recognize common SLE treatments and associated side effects
4. Recognize complications that may be seen with SLE and the importance of health maintenance management

What is SLE?

• **Systemic autoimmune** disease characterized by heterogenous **multisystem** involvement and production of **autoantibodies**
  • Driven by **loss of immune tolerance** and abnormal innate and adaptive immune function
  • Immune complex mediated reactions and tissue destruction
  • Variable clinical presentation and clinical course
Risk factors for SLE

• Women of childbearing age
• More in African American, Hispanic, other ethnic minorities
• Genetics
  • Polygenic
  • Early complement deficiencies
  • Family history
• Environment
  • Infections, smoking, UV exposure, drugs, stress
• Genetics + environment $\rightarrow$ Immune dysregulation

Diagnosis vs Classification

Diagnosis
• based on clinical presentation combined with serologic findings
  • +ANA is not enough
• No diagnostic criteria
• Diagnosis made by experienced physician/rheumatologist

Several Classification criteria
• ACR/EULAR, SLICC
• For categorizing patients for research purposes
• Not intended as diagnostic criteria
  • Can be used as guide to organize thoughts

Exclude alternative diagnosis
### 1997 ACR Classification criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema over malar eminences sparing nasolabial fold</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scale and follicular plugging, often with atrophic scars</td>
</tr>
<tr>
<td>Photosensitivity rash</td>
<td>Rash from unusual reaction to sunlight</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>Oral or nasopharyngeal ulcers, usually painless, observed by physician</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Nonerosive, 2 or more peripheral joints with tenderness, swelling or effusion</td>
</tr>
<tr>
<td>Pleuritis or pericarditis</td>
<td>Convincing history or objective evidence</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>Persistent proteinuria, &gt;0.5g/24hr or &gt;3+ on dipstick, cellular casts</td>
</tr>
<tr>
<td>Neurologic disorder</td>
<td>Seizures or psychosis in the absence of offending drugs or metabolic derangements</td>
</tr>
<tr>
<td>Hematologic disorder</td>
<td>Hematolytic anemia, leukopenia, lymphopenia, or thrombocytopenia</td>
</tr>
<tr>
<td>Immunologic disorder</td>
<td>Anti-dsDNA, Sm, or antiphospholipid antibodies</td>
</tr>
<tr>
<td>Positive ANA</td>
<td>Abnormal titer at any point in time, in absence of drugs known to be associated with drug induced lupus</td>
</tr>
</tbody>
</table>

≥4 criteria, excluding other causes

**Arth Rheum 1997**

### 2012 SLICC Classification criteria

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Immunologic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute cutaneous lupus: malar rash, SCLE, others</td>
<td>ANA above lab reference range</td>
</tr>
<tr>
<td>Chronic cutaneous lupus</td>
<td>Anti-dsDNA above lab reference range, except ELISA: twice above lab reference range</td>
</tr>
<tr>
<td>• Discoid, panniculitis, lupus tumidus, chillblains</td>
<td></td>
</tr>
<tr>
<td>Oral ulcers: palate</td>
<td>Anti-Smith</td>
</tr>
<tr>
<td>Nonscarring alopecia</td>
<td></td>
</tr>
<tr>
<td>Synovitis involving 2 or more joints</td>
<td>Low complement (C3, C4, CH50)</td>
</tr>
<tr>
<td>Serositis: Pleuritis, pericarditis</td>
<td>Direct Coombs test in the absence of hemolytic anemia</td>
</tr>
<tr>
<td>Renal disorder</td>
<td></td>
</tr>
<tr>
<td>• UPCR or 24hr urine protein ≥500mg/24hr</td>
<td></td>
</tr>
<tr>
<td>• RBC casts</td>
<td></td>
</tr>
<tr>
<td>Neurologic</td>
<td>Antiphospholipid antibody: any of the following:</td>
</tr>
<tr>
<td>• Seizures, psychosis</td>
<td>• Lupus anticoagulant</td>
</tr>
<tr>
<td>• Mononeuritis multiplex</td>
<td>• False positive RPR</td>
</tr>
<tr>
<td>• Myelitis</td>
<td>• Medium or high titer anticardiolipin (IgG, IgM, or IgA)</td>
</tr>
<tr>
<td>• Peripheral or cranial neuropathy</td>
<td>• Anti-B2 glycoprotein I (IgG, IgM, or IgA)</td>
</tr>
<tr>
<td>• Acute confusional state</td>
<td></td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td></td>
</tr>
<tr>
<td>Leukopenia (&lt;4000/mm3) or lymphopenia (&lt;1000/mm3)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;100,000/mm3)</td>
<td></td>
</tr>
</tbody>
</table>

≥4 criteria:  
• 1 clinical and  
• 1 immunologic  
• exclude other causes  

Lupus nephritis can be made by biopsy and +ANA alone

**Arth Rheum 2012**
## 2019 EULAR/ACR SLE Classification Criteria

**Entry criteria:** ANA ≥1:80

**Additive criteria:** at least 1 clinical and ≥10 points
- Only the highest weighted criteria is scored within each domain
- Criteria does not need to be simultaneous

Exclude alternative causes

### Clinical domains and criteria

<table>
<thead>
<tr>
<th>Domain</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional</td>
<td>2</td>
</tr>
<tr>
<td>Hematologic</td>
<td>3</td>
</tr>
<tr>
<td>Neuropsychiatric</td>
<td>2</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>6</td>
</tr>
</tbody>
</table>

### Additive criteria:

- Leukopenia
- Thrombocytopenia
- Autoimmune hemolysis
- Delirium
- Psychosis
- Seizure
- Non-scarring alopecia
- Oral ulcers
- Subacute cutaneous
- Discoid lupus
- Acute cutaneous lupus

### Immunology domains and criteria

<table>
<thead>
<tr>
<th>Domain</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiphospholipid antibodies</td>
<td>2</td>
</tr>
<tr>
<td>Complement</td>
<td>3</td>
</tr>
<tr>
<td>SLE-specific antibodies</td>
<td>6</td>
</tr>
</tbody>
</table>

### Clinical domains and criteria

<table>
<thead>
<tr>
<th>Domain</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serosal</td>
<td>5</td>
</tr>
<tr>
<td>Renal</td>
<td>4</td>
</tr>
</tbody>
</table>

### Exclude alternative causes

**Aringer M. Arth Rheum 2019**

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## Antinuclear antibody (ANA)

- Antibodies against proteins or nucleic acids in nucleus
- Found in >95% of SLE but only 57% specific
- Detection assays
  - Indirect immunofluorescence (IIF)
    - Gold standard
    - Titer
    - Staining pattern may guide clinical thinking
    - Time consuming, labor intensive, may have false positive
  - ELISA
    - Antibodies to different nuclear antigens
    - Faster, detect specific antibodies
    - High sensitivity but less specific

### By Simon Caulton - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=20521932

ANA more likely to have clinical significance with titers ≥1:80

ANA is sensitive but not specific for SLE, higher titer more likely to be associated with autoimmune disease
ANA titer and prevalence

- ANA common in general population
  - 25-30% have 1:40 titer
  - 10-15% have 1:80 titer
  - 5% have 1:160 titer or higher

ANA Prevalence increases with age

ANA is common in healthy subjects

- ANA is common and nonspecific

- Can be triggered by
  - Infections
  - Smoking
  - Silica, other chemicals and pollutants
  - Medications:
    - Hydralazine
    - Procainamide
    - Isoniazid
    - Minocycline
    - TNF alpha inhibitors

- Can be seen in other conditions:
  - Other autoimmune disease
    - Other systemic autoimmune rheumatic disease
    - Hashimoto’s thyroiditis
    - Multiple sclerosis
    - Psoriasis
    - Autoimmune hepatitis
    - Idiopathic thrombocytopenic purpura
  - Atopic diseases
  - Infections
  - Malignancies
  - Liver disease
  - Family history of autoimmune disease

Solomon DH et al. Arth&Rheum 2002


Soloman DH et al. Arth Care & Res 2002
Recognize common autoantibodies in SLE

**ANA subsets/Extractable nuclear antigen antibodies (ENAs)**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Frequency</th>
<th>ANA pattern</th>
<th>Clinical associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>dsDNA</td>
<td>70%</td>
<td>Homogenous</td>
<td>Can fluctuate with disease activity. Gold standard Crithidia assay is very specific, but common ELISA assay not very specific</td>
</tr>
<tr>
<td>SSA</td>
<td>30%</td>
<td>Speckled</td>
<td>Sicca, photosensitivity. Seen with Sjogren’s, SCLE, NNL, CHB</td>
</tr>
<tr>
<td>SSB</td>
<td>20%</td>
<td>Speckled</td>
<td>SCLE, Sjogren’s, NNL, CHB</td>
</tr>
<tr>
<td>U1RNP</td>
<td>25-40%</td>
<td>Speckled</td>
<td>MCTD, Raynaud, ILD, pulmonary hypertension</td>
</tr>
<tr>
<td>Histone</td>
<td>50%</td>
<td>Homogenous</td>
<td>SLE and DIL (75%)</td>
</tr>
</tbody>
</table>

NNL: neonatal lupus, CHB: congenital heart block

**Antiphospholipid antibodies (aPL)**
- Lupus anticoagulant
- B2glycoprotein I IgG, IgM
- Cardiolipin IgG, IgM

**Complements**
- C3
- C4
- CH50
- C1q

**Antibody specificity and sensitivity limited by commercial assays**

**Choosing wisely campaign:**
Avoid ordering ANA sub-serologies if ANA negative and low clinical suspicion of immune-mediated disease
Exceptions: Jo1 and SSA

**Antibodies alone are not sufficient to make diagnosis**

Consider other lupus-related diseases

**Other forms of lupus and lupus-related disorders**

- Cutaneous lupus
- Neonatal lupus
- Mixed connective tissue disease
- Antiphospholipid syndrome
- Sjogren’s syndrome
- Undifferentiated connective tissue
- Overlap syndrome

**Drug-induced lupus**

- Hydralazine
- Propytiouracil
- Sulfonamides
- Lithium
- Anticonvulsants
- Quinidine
- Diltiazem
- Beta blockers
- Interferon gamma
- TNF inhibitors
SLE Management

SLE treatment goals
- Control disease activity
  - Goal of remission or low disease activity
  - Minimize complications from disease and treatment
- Improve quality of life

Preventative measures
- **Smoking** cessation
- **Photoprotection**
  - Avoid medications that may trigger lupus if possible

Treat reversible causes of symptoms
- Physical and lifestyle measures
  - Address fatigue, sleep, exercise
  - Provide emotional and psychosocial support
- Assess and treat fibromyalgia

Treat associated comorbidities
- Other autoimmune disease: T1DM, Hashimoto’s

Health maintenance
- **Cardiovascular** health assessment
  - Assess and treat reversible risk factors given increased risk of CVD
- **Bone** health assessment
  - Increased risk of osteoporosis, avascular necrosis due to SLE, sun avoidance, steroid use
- Age-appropriate **cancer screening**
  - Increased risk of malignancy in SLE
- **Immunizations**
- **Contraception** counseling
- **Pregnancy** planning

All SLE patients require multi-disciplinary care with PCP, rheumatology and other specialists to optimize management and outcomes

Systemic corticosteroids

- For rapid control of inflammatory activity
- Usually given as taper
- **Pulse dose**
  - IVMP for severe organ threatening disease
- **High dose**
  - For severe disease such as serositis, nephritis, hemolytic anemia
  - Prednisone 20mg or higher
- **Moderate dose**
  - For moderate disease such as arthritis
  - Prednisone 7.5-20mg
- **Low dose:**
  - Usually used as slow taper or maintenance
  - Prednisone 7.5mg or lower

Steroids can be given for SLE flares but limit use as it is associated with significant side effects

Side effects:
- Osteoporosis, avascular necrosis, bone fractures
- Weight gain, Cushingoid features
- Hyperglycemia, diabetes
- Fluid retention, hypertension
- Arrhythmia
- Cataracts, glaucoma
- Gastritis, PUD
- Mood disorder, psychosis
- Muscle weakness
- Adrenal insufficiency
- Skin thinning, ecchymosis, striae
### Anti-malarials

**Hydroxychloroquine, Chloroquine, Quinacrine**
- For active, non-organ threatening SLE
  - Rash, arthritis, alopecia
- Many benefits in SLE:
  - Reduce risk of flares in SLE
  - Prevent progression of disease
  - Reduce thrombotic and cardiovascular complications
  - Improve glucose and lipid profiles
- Slow onset of action
  - Weeks to months to see effect
- Hydroxychloroquine dose
  - Up to 5mg/kg/day (max 400mg/day)
  - Dose reduce for renal insufficiency

### Side effects
- **Retinal toxicity:**
  - Risk increases with time
  - Irreversible
  - Need retinal exam yearly
- Drug rash
- Blue-gray discoloration of skin
- GI upset
- Myopathy
- Cardiomyopathy
- Arrhythmia
- CNS disturbance (dizziness, headache, insomnia, psychosis)
- Caution in G6PD deficiency
- Safe in pregnancy

### Systemic immunosuppressive therapy

- **Cytotoxic therapy**
  - Azathioprine
  - Mycophenolate
  - (Methotrexate)
  - (Leflunomide)
  - Cyclophosphamide
- **Calcineurin inhibitors**
  - (Cyclosporin)
  - (Tacrolimus)
  - Voclosporin

- **Biologic therapy**
  - Belimumab
  - (Rituximab)
  - (Others to come)
Case #1

- 40 yo Hispanic F w/ h/o HTN, anemia
- Joint pain and swelling in hands with morning stiffness
- Facial rash and body rashes
- Alopecia, oral ulcers
- No smoking
- Fam hx: No autoimmune disease

Jaccoud’s arthropathy

Case #1: Workup and diagnosis

- +ANA 1:320 speckled
- +Sm, +SSA
- +ribosomal P, +chromatin
- +dsDNA 48
- +RF 27, -CCP
- Cq1 7 (L) → early complement deficiency increases risk of SLE
- C3 39, C4 <8 (L)
- CBC with ACD otherwise normal
- ESR, CRP normal
- UA, UPCR normal
- Skin biopsy: interface dermatitis

Diagnosis:
SLE (+ANA, +Sm, +SSA, +ribosomal P, +chromatin, +dsDNA, +RF) with hypocomplementemia, anemia, Jaccoud’s arthropathy, oral ulcers, alopecia, acute cutaneous lupus
Cutaneous lupus

**Acute cutaneous lupus**
Localized: Malar rash
- Distinguish from:
  - Rosacea
  - Seborrhea dermatitis
  - Dermatomyositis

**Generalized**

**Subacute cutaneous lupus erythematosus (SCLE)**
- Types
  - Annular
  - Papulosquamous
- Photosensitive
- 50% have SLE
- 70% with +ANA, +SSA, 30% SSB

**Chronic cutaneous lupus**
- Discoid lupus
- Lupus profundus (panniculitis)
- Chilblain
- Tumid lupus

**Other cutaneous manifestations**
- Raynaud
- Vasculitis
- Livedo reticularis
- Urticaria
- Others

Alopecia

**Non-scarring alopecia**
- Focal or diffuse
- Differential:
  - Traction alopecia
  - Female pattern hair loss
    - crown, frontal, hereditary
  - Telogen effluvium
  - Iron deficiency
  - Hypothyroidism

**Scarring alopecia**
- Inflammatory, infiltrative conditions
- More focal than diffuse
- Discoid lupus
**Case #1: Treatment**

- Topical therapy for cutaneous lupus
  - Topical corticosteroids
  - Topical calcineurin inhibitors
- Immunomodulator
  - Hydroxychloroquine
- Clinical course:
  - Inadequate control on plaquenil
  - Intolerant to azathioprine, mycophenolate
  - Started on belimumab
  - Complicated by infection

**Belimumab used as add-on therapy for SLE**

- Monoclonal ab against BLyS
- SQ and IV
- For active seropositive SLE
  - Best for +dsDNA, low complements, skin, MSK manifestations
- Adverse effects
  - Infection
  - Injection site/infusion reaction
  - Diarrhea, nausea
  - Headache
  - Psych: depression, suicidal ideation
  - Cytopenias
  - PML

**Infection evaluation, management, prevention**

<table>
<thead>
<tr>
<th></th>
<th>Infection</th>
<th>SLE flare</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>ESR</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>CRP</td>
<td>↑</td>
<td>--/↑</td>
</tr>
<tr>
<td>C3, C4, CH50</td>
<td>--/↑</td>
<td>↓</td>
</tr>
<tr>
<td>dsDNA</td>
<td>--</td>
<td>↑</td>
</tr>
</tbody>
</table>

**SLE flare can be triggered by infections**

Management during infection
- Hold immunosuppressive therapies until infection resolves
- Ok to continue:
  - Hydroxychloroquine
  - Prednisone if chronic

**Vaccinations**

- Recommended vaccines on immunsuppressive therapy:
  - Yearly influenza
  - Prevnar13
  - Pneumovax23
  - HAV and HBV
  - HPV
  - Shingrix
- Avoid live vaccines
- Vaccines may be more effective when given before starting immunosuppressive therapy
Case # 2

- 40 yo AAF with h/o cervical lymphadenopathy (biopsy negative for malignancy) who presented with SOB and leg swelling
- SOB worse with lying down
- Smoker

Exam
- BP 115/80, HR 101, RR 20, 96% RA
- periorbital edema, diffuse anasarca, ascites
- Distant heart sounds
- Rash on trunk, extremities, hands and feet

EKG: sinus tach, low voltage

Chest pain, SOB in SLE

Cardiac manifestations
- Pericarditis
- Myocarditis
- Libman-Sacks endocarditis
- Coronary arteritis
- Arrhythmia
- CAD/MI
  - Accelerated atherosclerosis
    - 2+ fold increase risk of CAD, CVA, PAD

Pulmonary manifestations
- Pleuritis
- Parenchymal lung disease
  - Pneumonitis
  - Diffuse alveolar hemorrhage
  - Interstitial lung disease
- Pulmonary vascular disease
  - Pulmonary hypertension
  - Pulmonary embolism
- Shrinking lung syndrome

Differential for cardiac and pulmonary manifestations in SLE
Sent to hospital

- WBC 3.02 (L), abs lymph 0.4 (L) → concern for SLE flare
- Hb 8.3 (L), MCV 85
- Plt 175 → less likely hemolytic
- Troponin normal → less likely MI, myocarditis
- Cr 0.84 (baseline; BMP normal)
- UA trace proteins, no casts → less likely GN
- LFT normal except Albumin <1.5 (L)
  → Protein loss leading to anasarca
- Chest XR: cardiomegaly, left pleural effusion
  → Serositis from SLE
- TTE: large, circumferential pericardial effusion with early signs of tamponade → serositis from SLE (No endocarditis)

CT a/p: bowel wall edema
→ Concern for protein-losing enteropathy

Case #2

Serologies

- ANA >1:1280 speckled
- +Sm, +RNP, +SSA, +SSB
- +dsDNA 70 (H)
- Low C3 39, C4<8
- IgG 384 (L), IgA 59 (L), IgM normal.
- ESR 91 (H), CRP normal
- UPCR 0.484
- Stool alpha1antitrypsin 310 (H)

Serologies suggestive of SLE

- Pericardiocentesis and paracentesis
  - Exclude infection, malignancy
- Colonoscopy excluded alternative causes

Diagnosis:

SLE (+ANA, +Sm, +RNP, +SSA, +SSB, +dsDNA, low complements, leukopenia, lymphopenia, anemia) with acute cutaneous lupus, pericarditis, pleuritis and protein-losing enteropathy
Case #2: Management

**Treatment:**
- **IVMP** for rapid control
  - Followed by PO taper
- **Hydroxychloroquine**
- **IVIG**
  - for hypogammaglobulinemia
- **Cyclophosphamide**
  - For induction therapy for severe organ threatening disease
  - IV vs PO

**Cyclophosphamide**
- Used as Induction therapy for severe organ damage
- Toxicity increases with cumulative dose
- Transition to alternative agent for maintenance

**Adverse effects:**
- Hemorrhagic cystitis, transitional cell carcinoma
- Cytopenia: Leukopenia/neutropenia
  - Monitored closely and adjust dose
- GI upset, mucositis, stomatitis
- Alopecia
- Gonadal failure, teratogenic
  - Fertility discussion with obgyn prior to initiation

Case #3

40 yo Caucaisan F w/ h/o Factor V Leiden and h/o DVT who presented with blurry vision, found to have retinal hemorrhages by ophthalmology and admitted to hospital for hypertensive emergency

- BP 215/126
- WBC 2.42 (ALC 0.6), Hb 6.8, plt 112
- Retic 2.79%, haptoglobin <30, LDH 265
- Peripheral smear +schistocytes
  → hemolytic anemia
- ADAMTS13 activity 51% (normal >68%)
- UA: RBC, proteins. No casts.
- Cr 2.4 (baseline 1)
  → TTP/HUS, TMA, GN
- LFT normal except albumin 2

Pancytopenia, serositis, hemolytic anemia, AKI, multisystem organ involvement suspicious for SLE

- ANA 1:320 speckled
- +SSA, +SSB, +dsDNA 380
- APS negative, negative DAT
- C3 38, C4 <8 (L)
- Normal ESR, CRP
- UPCR 4.2g/24hr  → nephrotic syndrome, LN
Hematologic manifestations in SLE

- Leukopenia/lymphopenia
- Anemia
  - Hemolytic anemia
  - Anemia of chronic disease
- Thrombocytopenia
  - ITP, TTP
- Thrombotic microangiopathy
- Lymphadenopathy
- Splenomegaly
- Thromboembolism → check for APS

Cytopenias:
- disease vs medications vs alternative causes

Hemolytic anemia
- Autoimmune
- TTP/HUS
- DIC
- APS
- Other: valves, malignant hypertension, PNH

Lupus nephritis

- Suspect in SLE with AKI, proteinuria, hematuria, active urinary sediment, hypertension
- 50% of SLE, high morbidity and mortality
- More common and more severe in Black and Hispanic

Role of kidney biopsy
- Establish diagnosis
- Evaluate for other causes
- Results determine treatment

Indication for biopsy
- Increase Cr without clear cause
- Proteinuria >0.5g/24hr with active urinary sediment

<table>
<thead>
<tr>
<th>Class</th>
<th>Histologic classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Minimal mesangial LN</td>
</tr>
<tr>
<td>Class II</td>
<td>Mesangial proliferative LN</td>
</tr>
<tr>
<td>Class III</td>
<td>Focal LN (&lt;50% of glomeruli)</td>
</tr>
<tr>
<td>Class IV</td>
<td>Diffuse (&gt;50% glomeruli) Diffuse segmental or global</td>
</tr>
<tr>
<td>Class V</td>
<td>Membranous LN</td>
</tr>
<tr>
<td>Class VI</td>
<td>Advanced sclerosing LN (&gt;90% sclerosed glomeruli globally)</td>
</tr>
</tbody>
</table>

Proliferative lupus nephritis (class III and IV)

Induction
- High dose steroids
- Cyclophosphamide
- Mycophenolate*
* African Americans respond better to MMF than CYC induction for lupus nephritis

Maintenance
- Mycophenolate
- Azathioprine
- Calcineurin inhibitors

Hahn BH. Arthr Care Res 2013
Case #3: Diagnosis and management

Renal biopsy:
- Diffuse proliferative lupus nephritis (Class IV)
- Active thrombotic microangiopathy
- Moderate interstitial fibrosis and tubular atrophy

Treatment:
- IVMP 1gx3 days, followed by PO prednisone
  - For rapid control of LN and hemolysis
  - Prophylaxis: Bactrim, PPI, calcium/vit D
  - Screen for hepatitis B/C, TB
- Hydroxychloroquine
- Mycophenolate
  - For LN after cell counts recover
- Anticoagulation with heparin transition to coumadin
  - For TMA
- Eculizumab for aHUS

Diagnosis:
- SLE (+SSA, +SSB, +dsDNA, low complements), with pancytopenia, serositis
- Class IV nephritis
- Thrombotic microangiopathy (aHUS)

Antimetabolites

For inflammatory lung disease, lupus nephritis, other deep organ involvement
- First line therapy

Mycophenolate *
- Inhibits purine synthesis
- PO 2-3g/day in BID dosing
- Common adverse effects
  - Infection
  - GI upset
  - Cytopenias
  - Elevated LFTs
  - PPI may reduce absorption
  - Teratogenic
  - OCP may be less effective

Azathioprine *
- Purine analog
- PO 2-2.5mg/kg/day
- Common adverse effects
  - Infection
  - GI upset
  - Cytopenia
  - Elevated LFTs
  - Headaches
  - Avoid in poor TPMT metabolizers
  - Safe in pregnancy

*Increase risk of malignancy

Recommend:
- Age-appropriate cancer screening
- High vigilance
- HPV vaccine

Mycophenolate and azathioprine are commonly used in SLE as first line therapy for deep organ involvement but may carry an increased risk of malignancy.
Case 4

- 31 yo Asian F w/ h/o SLE diagnosed in 2008 (+ANA >1:2560 speckled, +dsDNA, +Sm, +RNP, +RF, low C3/C4) with Raynaud, cutaneous ulcers and vasculitis with digital gangrene s/p amputation
- h/o non-adherence to medications and lost to follow up
- Presented with confusion and worsening cutaneous vasculitis

Exam: cushingoid, malar rash, distal vasculitic purpura, livedo reticularis, Raynaud, flat affect, hyper-reflexia in the lower extremities, up going toes bilaterally

Case #4: Workup

- Admitted and found to have bilateral basal ganglia strokes
- WBC 2.5 (ALC 0.8) Hb 10.9, plt 209
- ESR 40, CRP 10.3 (H)
- dsDNA 35 (H)
- C3 59, C4 10 (L)
- Lupus anticoagulant positive
- B2GPI IgG 196, IgM 24
- Cardiolipin IgG 48, IgM normal
- UA, UPCR normal
- CSF with mildly elevated proteins and WBC, oligoclonal bands
- Ruled out infectious etiologies
Neuropsychiatric lupus

Depression, anxiety  Neuropsychiatric evaluation
Psychosis
Cognitive dysfunction
Aseptic meningitis
Cerebritis/cerebral vasculitis
CVA/TIA
Seizures
Demyelinating syndromes
Transverse myelitis
Neuromyelitis optica
Peripheral neuropathy
Cranial nerve palsy
Autonomic disorder
Headache

MRI of brain or spine
CSF studies
EEG
Autoantibodies:
• dsDNA, NMDA, NMO, ribosomal P, APS
EMG/NCV
NCV
Autonomic testing

Case #4: diagnosis and management

**Diagnosis**

SLE with cutaneous vasculitis and encephalopathy, ischemic CVA associated with **neuropsychiatric lupus** and secondary **antiphospholipid syndrome (APS)**

**Treatment**

- IVMP followed by PO prednisone
- Cyclophosphamide
- Hydroxychloroquine
- Aspirin and anticoagulation
- Neurocognitive rehab
- Wound care
- Physical therapy
- **Close follow up to ensure adherence**

**Thromboembolic risk increased in SLE**

- 2x risk of ischemic CVA in SLE
- +aPL increases risk of thrombosis
- 40% SLE patients have aPL
- Evaluate and treat modifiable risk factors
  - Lifestyle changes
  - Hypertension
  - Hyperlipidemia
  - Smoking cessation
  - Avoid estrogen-containing contraceptives
- Treatment
  - Low dose aspirin
  - Warfarin preferred over DOACs
  - Hydroxychloroquine

SLE and aPL/APS increases risk of thromboembolism
Summary

• Clinical manifestations of SLE
  • Cutaneous lupus
  • Cardiopulmonary manifestations
  • Lupus nephritis
  • Hematologic abnormalities
  • Neuropsychiatric lupus
  • Thromboembolism
    • Increased risk of CAD, CVA, PAD
    • +aPL/APS increases risk
• Immunologic findings
  • ANA and ENAs
  • Complements
  • Inflammatory markers

• Treatments
  • Antimalarials
  • Glucocorticoids
  • Mycophenolate, azathioprine, cyclophosphamide, belimumab

• Complications
  • Infections
  • Cardiovascular disease
  • Osteoporosis
  • Malignancy

Take home points

• SLE can present with a wide range of clinical manifestations and diagnosis should be made by an experienced physician based on clinical presentation excluding alternative diagnosis and supported by serologic findings
  • Positive ANA is common and not sufficient to establish a diagnosis
• Treatment of SLE depends on areas being affected, disease activity and severity. Treatments may be associated with various toxicities that need to be monitored closely.
  • Hydroxychloroquine improves outcomes in SLE
• SLE patients have increased risk of infections (if on immunosuppressive therapy), cardiovascular disease, thromboembolism, renal disease, osteoporosis, and malignancy
  • Patient should be counseled on immunizations and infectious management, evaluated and treated for cardiovascular and thromboembolic risk factors, screened for lupus nephritis, evaluated for bone health, counseled on contraception with the use of teratogenic medications, and follow appropriate cancer screenings.
References


ANA references


Neuropsychiatric references

