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 → 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

4 or more criteria, excluding other causes

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

Arth Rheum 1997

2012 SLICC Classification criteria

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

≥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	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Musculoskeletal	
Joint involvement	6

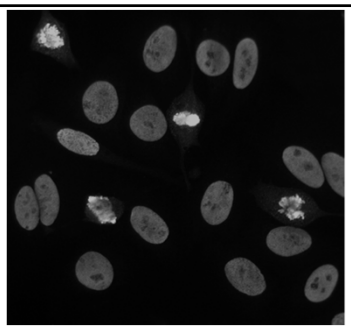
Clinical domains and criteria	Weight
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Renal	
Proteinuria >0.5g/24hr	4
Renal biopsy class II or V LN	8
Renal biopsy Class III or IV LN	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR Anti-B2GPI antibodies OR Lupus anticoagulant	2
Complement	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA or Smith antibody	6

Aringer M. Arth Rheum 2019

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



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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

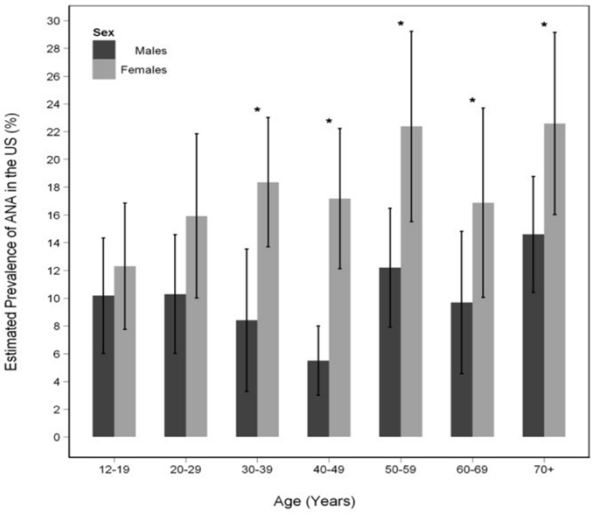
ANA titer and prevalence

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

Solomon DH et al. Arth&Rheum 2002

ANA is common in healthy subjects

ANA Prevalence increases with age



Satoh M, Chan EK, Ho LA, et al. Prevalence and sociodemographic correlates of antinuclear antibodies in the United States. *Arthritis Rheum*. 2012;64(7):2319-2327. Copyright obtained from publisher.

ANA is common and nonspecific

ANA is seen in various conditions

- 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

Soloman DH et al. Arth Care & Res 2002

Recognize common autoantibodies in SLE

ANA subsets/Extractable nuclear antigen antibodies (ENAs)

Antibody	Frequency	ANA pattern	Clinical associations
Smith	30%	Speckled	High specificity, low sensitivity. More in African Americans. More organ damage.
dsDNA	70%	Homogenous	Can fluctuate with disease activity. Gold standard Crithidia assay is very specific, but common ELISA assay not very specific
SSA	30%	Speckled	Sicca, photosensitivity. Seen with Sjogren's, SCLE, NNL, CHB
SSB	20%	Speckled	SCLE, Sjogren's, NNL, CHB
U1RNP	25-40%	Speckled	MCTD, Raynaud, ILD, pulmonary hypertension
Histone	50%	Homogenous	SLE and DIL (75%)

NNL: neonatal lupus, CHB: congenital heart block

<u>Antiphospholipid antibodies (aPL)</u>
- Lupus anticoagulant
- B2glycoprotein I IgG, IgM
- Cardiolipin IgG, IgM

<u>Complements</u>
C3
C4
CH50
C1q

Antibody specificity and sensitivity limited by commercial assays

<u>Choosing wisely campaign</u>:
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

<u>Drug-induced lupus</u>
- Hydralazine
- Propythiouracil
- 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

Antimalarials reduce flares and improves outcomes in SLE

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

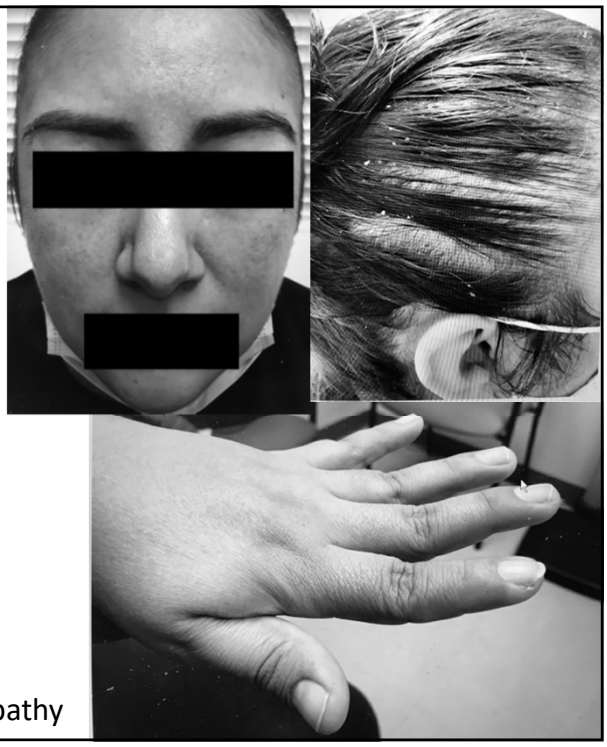
- **Retinal toxicity:**
  - Risk increases with time
  - Irreversible
  - Need retinal exam yearly
- Drug rash
- Blue-gray discoloration of skin
- GI upset
- Myopathy
- Cardiomyopathy
- Arrhythmia
- CNS disturbance (dizziness, headache, insomnia, psychosis)
- Caution in G6PD deficiency
- Safe in pregnancy

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

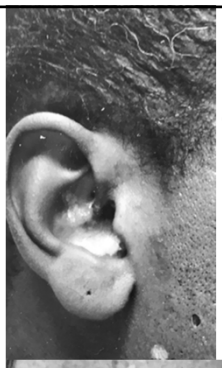
Localized: Malar rash

- 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



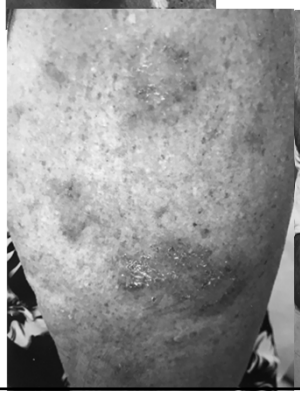
Different forms of cutaneous LE

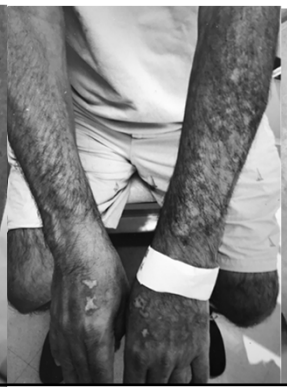
Chronic cutaneous lupus

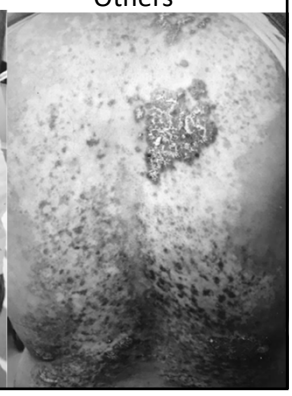
Discoid lupus
Lupus profundus (panniculitis)
Chilblain
Tumid lupus

Other cutaneous manifestations

- Raynaud
- Vasculitis
- Livedo reticularis
- Urticaria
- Others







Alopecia

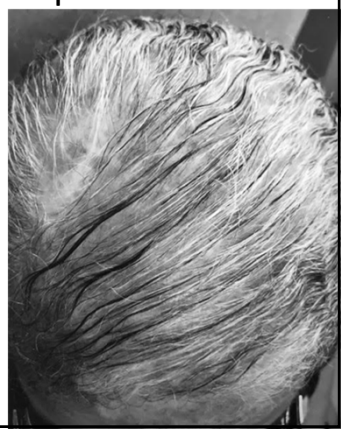
Non-scarring alopecia

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

Recognize alopecia in SLE

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

Belimumab
- 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

	Infection	SLE flare
WBC	↑	↓
ESR	↑	↑
CRP	↑	--/↑
C3, C4, CH50	--/↑	↓
dsDNA	--	↑

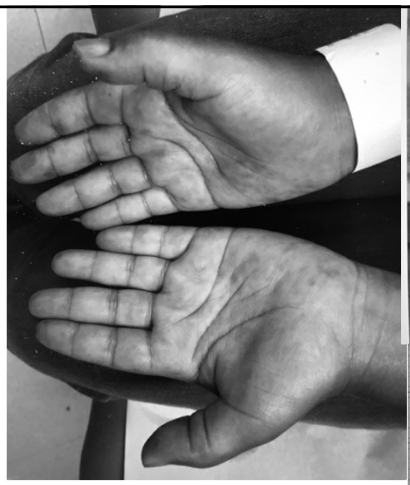
SLE flare can be triggered by infections

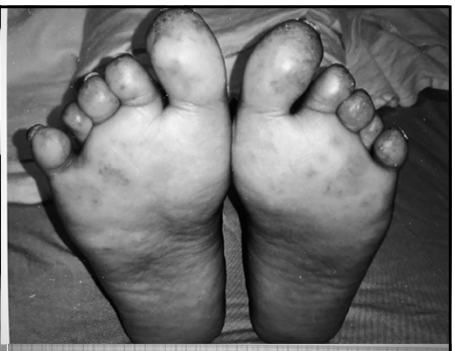
Management during infection
- Hold immunosuppressive therapies until infection resolves
- Ok to continue:
  Hydroxychloroquine
  Prednisone if chronic

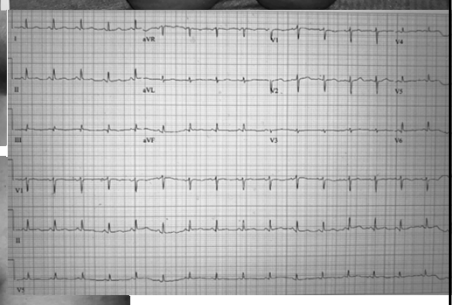
Vaccinations
- Recommended vaccines on immunosuppressive therapy:
  - Yearly influenza
  - Prevnar13
  - Pneumovax23
  - HAV and HBV
  - HPV
  - Shingrix
- Avoid live vaccines
- Vaccines may be more effective when given before starting immunosuppressive therapy

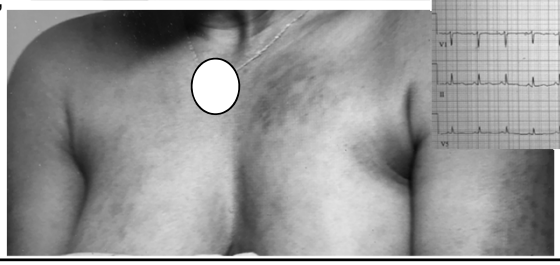
Case # 2

- 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

Differential for cardiac and pulmonary manifestations in SLE

Cardiac manifestations

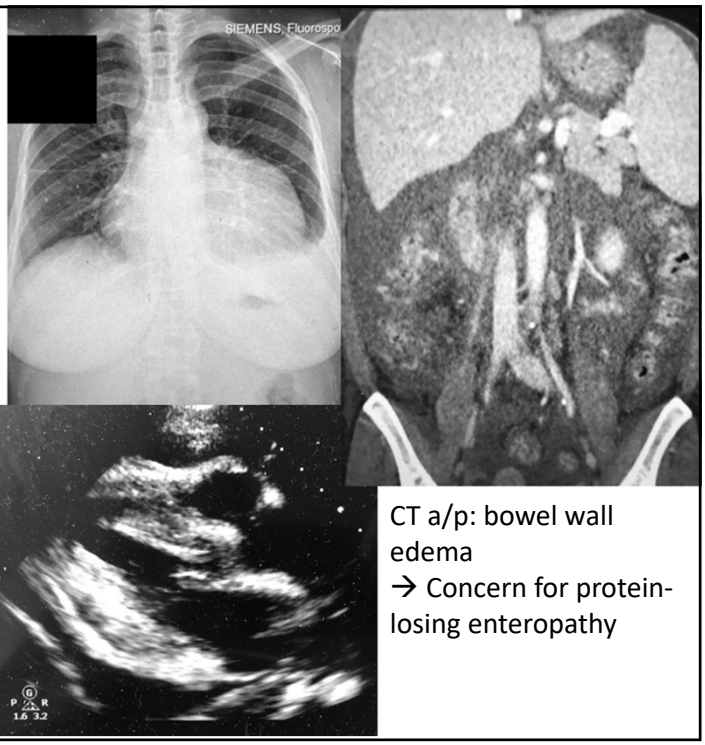
- Pericarditis
- Myocarditis
- Libman-Sacks endocarditis
- Coronary arteritis
- Arrythmia
- CAD/MI
  - Accelerated atherosclerosis
    - 2+ fold increase risk of CAD, CVA, PAD

Pulmonary manifestations

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

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

Cyclophosphamide effective induction therapy for severe SLE but has significant toxicities

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

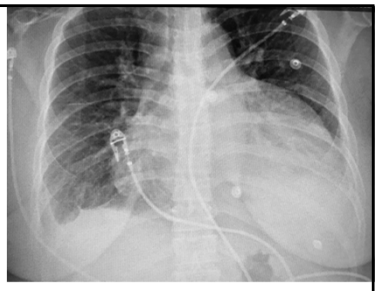
- Used as Induction therapy for severe organ damage
- Toxicity increases with cumulative dose
- Transition to alternative agent for maintenance
- Adverse effects:
  - Hemorrhagic cystitis, transitional cell carcinoma
  - Cytopenia: Leukopenia/neutropenia
    - Monitored closely and adjust dose
  - GI 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

Chest XR: Small bilateral pleural effusions, mild bibasilar airspace disease, marked cardiomegaly



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

Hahn BH. Arthr Care Res 2013

ISN/RPS 2003 Classification of LN

Class	Histologic classification
Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN (<50% of glomeruli)
Class IV	Diffuse (>50% glomeruli) Diffuse segmental or global
Class V	Membranous LN
Class VI	Advanced sclerosing LN (>90% sclerosed glomeruli globally)

Proliferative lupus nephritis (class III and IV)

Induction

- High dose steroids
- Cyclophosphamide
- Mycophenolate*

Maintenance

- Mycophenolate
- Azathioprine
- Calcineurin inhibitors

* African Americans respond better to MMF than CYC induction for lupus nephritis

Case #3: Diagnosis and management

Renal biopsy:

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

Diagnosis:

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

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

Antimetabolites

For <u>inflammatory lung disease, lupus nephritis, other deep organ involvement</u>

- First line therapy

For <u>cutaneous lupus, joints</u>

- Used after topical and anti-malarials

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

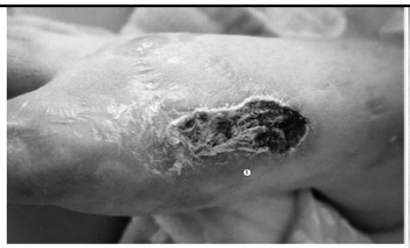
*Increase risk of malignancy

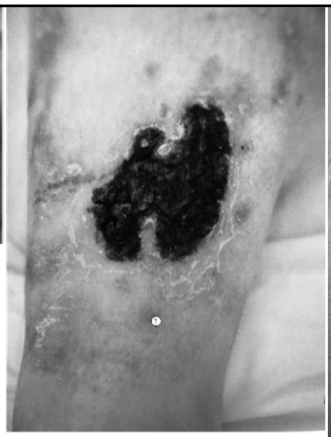
Recommend:

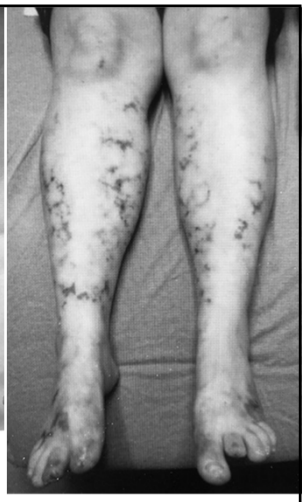
- Age-appropriate cancer screening
- High vigilance
- HPV vaccine

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





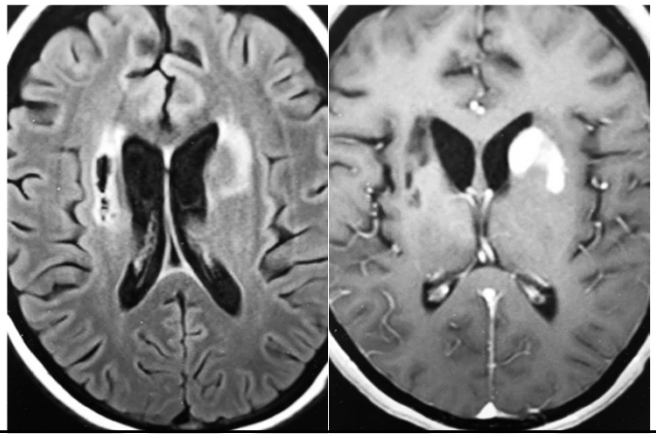


- 31 yo Asian F w/ h/o SLE diagnosed in 2008 (+ANA >1:2560 speckled, +dsDNA, +Sm, +RNP, +RF, low C3/C4) with Raynaud, cutaneous ulcers and vasculitis with digital gangrene s/p amputation
- h/o non-adherence to medications and lost to follow up
- Presented with confusion and worsening cutaneous vasculitis

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 Psychosis Cognitive dysfunction	Neuropsychiatric evaluation
Aseptic meningitis Cerebritis/cerebral vasculitis CVA/TIA Seizures Demyelinating syndromes Transverse myelitis Neuromyelitis optica	MRI of brain or spine CSF studies EEG Autoantibodies: • dsDNA, NMDA, NMO, ribosomal P, APS EMG/NCV
Peripheral neuropathy Cranial nerve palsy	NCV
Autonomic disorder	Autonomic testing
Headache	

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 manifetsations
  - 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 manifestation 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.

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