Lupus & the Cardiopulmonary System
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Cardiopulmonary Disease in Lupus

Overview:
- Vocabulary
- Lupus manifestations
  - Lung effects
  - Heart effects
  - Blood vessel effects
- Accelerated atherosclerosis
  - Epidemiology
  - Risk factors
  - Management
Lupus and the Heart

Cardiac anatomy

- Pericardium
  - Thin layer of tissue around the heart and great vessels
- Myocardium
  - Muscle tissue that functions as a pump
- Coronary arteries
  - Major blood vessels that deliver oxygen and nutrients to the myocardium
- Valves
  - Separate chambers, direct blood flow
Lupus and the Heart
Lupus and the Lungs

Lung anatomy
- Pleura
  - Thin layer of tissue around the lungs
- Parenchyma
  - Tissue of the lung
    - Airways
    - Alveoli
- Pulmonary arteries
  - Major blood vessels deliver blood through the lung
- Chest wall
  - Muscles and connective tissue
  - Diaphragm
Lupus and the Heart: Medical Vocabulary

- ECG (electrocardiogram)
  - Measures heartbeat rhythm and assesses electrical movement around the heart
  - Can detect pericarditis, myocardial ischemia (low blood flow), dysrhythmia
Lupus and the Heart: Medical Vocabulary

*Echo (echocardiogram)*
- Ultrasonographic image of the heart
- Assesses:
  - Ejection fraction
    - Ability of heart to pump blood
  - Valve structure, patency, and viability
  - Pericardial fluid
Lupus and the Heart: Medical Vocabulary

- **Stress test**
  - Means of assessing risk for heart attack by detecting areas of inadequate bloodflow (low oxygen delivery)
    - Exercise
    - Persantine
    - Dobutamine
  - Measure myocardial stress via ECG leads or by perfusion
    - Thallium
    - Cardiolyte
Cardiac Catheterization
- Placement of catheters directly into either side of the heart
  - Left heart cath:
    - Measures EF
    - Visualize coronary arteries
    - Can perform interventions
      - Angioplasty
      - Stent deployment
  - Right heart cath
    - Measure right sided pressures
    - Myocardial biopsy
Arteriograms

Mesenteric arteriogram (abdomen)
Lupus and the Lung: Medical Vocabulary

- Pulmonary function tests
  - Non-invasive testing of lung function
    - Measures lung volumes
    - Measures diffusing capacity

- 6 minute walk test
  - Estimates functional status
  - Predicts morbidity in chronic lung disease

- V:Q scan
  - Overlays air movement and blood flow
  - Detects blood clots
CT scan
- Radiograph imaging of lung
- High-resolution
  - Non-contrasted
  - Images patient supine and prone
  - Detects small airway and interstitial disease (ILD)
- CTA
  - Uses contrast infusion
  - Detects blood clots
Lupus Cardiac Manifestations

- **Pericarditis**
  - Inflammation of the lining around the heart
    - May result in accumulation of inflammatory fluid
  - Clinical presentation
    - Anterior chest pain, sharp or stabbing
    - Pain worsens with inspiration and reclining
  - Complications
    - Pericardial effusion
    - Pericardial tamponade
  - Treatment
    - NSAIDs
    - Corticosteroids (with caution)
Lupus Cardiac Manifestations

Myocarditis and Cardiomyopathy

- Inflammation of the myocardium
  - Loss of ventricular contractile strength

- Clinical presentation:
  - Typically asymptomatic until heart failure develops
  - Can be associated acutely with pericarditis

- Diagnosis:
  - Echocardiogram
  - Catheterization to rule out vasculitis/ischemia
  - May require myocardial biopsy

Treatment:

- Immunomodulatory:
  - Corticosteroids
  - Intravenous immunoglobulin

- Supportive care
  - ACE inhibitors
  - Spironolactone
  - Beta blocker
Lupus Cardiac Manifestations

- Libman-Saks endocarditis
  - Bland (non-infectious) vegetations on the heart valves
  - Clinical presentation:
    - May be asymptomatic
    - May present with stroke or peripheral ischemia of vegetations are embolized
    - Rarely cause valvular injury
  - Associated with antiphospholipid antibodies
- Diagnosis:
  - Echocardiogram (transesophageal)
- Treatment:
  - Prophylactic antibiotics
  - Anticoagulation
  - Valve replacement surgery
Lupus Cardiac Manifestations
Libman-Saks Endocarditis
SLE: Vascular manifestations

- Raynaud’s phenomenon
  - White → Blue → Red
  - Incidence: 34-60%
  - Management:
    - Temperature hygiene
    - Calcium channel blockers
    - Anti-platelet therapies

- Digital vasculitis
  - Digital gangrene
  - Differentiate from APS
  - Management:
    - immunosuppression


**Lupus Vascular Manifestations**

- **Vasculitis**
  - Inflammation of the wall of a blood vessel
    - Ordinarily involves arteries
    - Results in blood vessel narrowing or occlusion
  - Clinical presentation:
    - Depends on the size, number, and location of vessels involved
    - Features reflect impaired blood flow to organs supplied by the inflamed vessels
  - Diagnosis:
    - Arteriogram, biopsy, clinical impression
  - Treatment:
    - Corticosteroids (high dose)
    - Cytotoxic agents (cyclophosphamide)
Vasculitis

- **Coronary arteritis (rare)**
  - Presents as angina or myocardial infarction

- **Mesenteric vasculitis**
  - Presents as food avoidance, abdominal pain, weight loss
  - Can cause bowel necrosis and acute abdomen

- **Cutaneous vasculitis**
  - Usually easier to treat but includes digital vasculitis (which can progress to gangrene)
Vasculitis

Nailfold infarcts

Cutaneous vasculitis at the elbow

Palpable purpura
Antiphospholipid antibody syndrome: Clinical features

- Thrombosis
  - Venous (DVT, pulmonary embolus) or arterial (stroke, mesenteric ischemia, myocardial infarction)
  - Recurrent thromboses favor same vascular bed
  - Occasional bland endocarditis (Libman-Saks)

- Pregnancy loss
  - Single miscarriage late 1st trimester or beyond
  - Three consecutive early 1st trimester miscarriages
  - Absence of other causes (hormonal, genetic, anatomic, exposure)

- Antiphospholipid antibody
  - Anti-cardiolipin antibody
    - strongest association with IgG antibodies
  - Lupus anticoagulant
    - Prolonged PTT, fails to correct with mix + confirmatory study
  - False positive syphilis test

APLS: Superior sagittal sinus thrombosis with large venous infarct

APLS: ICA thrombosis caused multiple cerebral infarcts via embolization

Shanahan JC, Ortel TL, Sem Cerebrovascular Dis Stroke, 2002
Accelerated Atherosclerosis

Mortality
- The leading cause of death in patients with SLE is complications of atherosclerotic coronary artery disease

Risk
- Myocardial infarction:
  - 5%-45% SLE patients
  - Among women with SLE <45 yrs old, risk of MI is 50 times that of age-matched healthy controls
  - Nurses Health Study: 2-fold increase risk for CAD w/ lupus diagnosis
- Independent of standard risk factors, SLE treatment
  - Risk associated with higher disease activity/severity
Atherosclerosis

- **Plaques**
  - Inflammation
    - Foamy macrophages
  - Deposits
    - Oxidized cholesterol
    - Lipids (fat)
    - Calcium
  - Fibrous caps

- **Plaque rupture**
  - Exposes tissue factor
  - Results in thrombus formation and occlusion of the vessel
Atherosclerosis in SLE

- Estimated prevalence:
  - Odds ratio for atherosclerosis in SLE:
    - 4.9 (Roman, *NEJM*) – 9.8 (Asanuma, *NEJM*)
    - Assessed by carotid ultrasound (IMT) (Roman)
    - Assessed by external beam CT (detects coronary calcium) (Asanuma)

![Figure 1. Prevalence of Atherosclerotic Plaque among Control Subjects and Patients with Systemic Lupus Erythematosus, According to Decade of Life.](chart.png)
Atherosclerosis in SLE

Traditional risk factors:
- Male gender
- Age over 50
- Hypertension
  - Higher rates of HTN in SLE
  - 11.5-75%
- Family history
  - Parent/sib w/ heart attack
- Hyperlipidemia
  - Higher rates of HL in SLE
  - 11.5-75%
- Smoking
- Diabetes mellitus
  - Metabolic syndrome
    - Overweight, HTN, HL, hyperuricemia/gout, insulin resistance
- Overweight

SLE risk factors
- Younger age at diagnosis of SLE
- Disease duration
- Anti-smith autoantibodies
- Antiphospholipid antibodies
- Dyslipidemia
- Corticosteroid use
Atherosclerosis in SLE: Management

- **Goal blood pressure:**
  - Systolic < 140
    - SBP 130-135 may be better but not at risk of side effects
    - J-shaped curve of risk suggests pressure < 126 is without much benefit
    - If type II diabetes and CAD present, consider treat to <120
  - Diastolic <90
    - DBP below 60-70 could increase stroke risk in some patients

- **Goal cholesterol**
  - Step 1: fasting lipid panel
  - Step 2: establish presence of coronary heart disease or equivalents
  - Step 3: assess CHD risk factors
  - Step 4: CHD risk calculator
  - Step 5: Treat based on risk and LDL
### Atherosclerosis in SLE: Management

#### ATP III LDL-cholesterol goals and cutpoints for therapeutic lifestyle changes and drug therapy in different risk categories

<table>
<thead>
<tr>
<th>Risk category</th>
<th>LDL-cholesterol goal</th>
<th>LDL-cholesterol level at which to initiate therapeutic lifestyle changes</th>
<th>LDL-cholesterol level at which to consider drug therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease (CHD) or CHD risk equivalent (10-year risk &gt; 20 percent)*</td>
<td>&lt;100 mg/dL (2.58 mmol/L)</td>
<td>≥100 mg/dL (2.58 mmol/L)</td>
<td>≥130 mg/dL (3.36 mmol/L); drug optional at 100 to 129 mg/dL (2.58 to 3.33 mmol/L)</td>
</tr>
<tr>
<td>2 or more risk factors (10-year risk ≤ 20 percent) Δ</td>
<td>≤130 mg/dL (3.36 mmol/L)</td>
<td>≥130 mg/dL (3.36 mmol/L)</td>
<td>10-year risk 10 to 20 percent: &gt;130 mg/dL (3.36 mmol/L) 10-year risk &lt; 10 percent: ≥160 mg/dL (4.13 mmol/L)</td>
</tr>
<tr>
<td>0 to 1 risk factor◊</td>
<td>≤160 mg/dL (4.13 mmol/L)</td>
<td>≥160 mg/dL (4.13 mmol/L)</td>
<td>≥190 mg/dL (4.91 mmol/L); LDL-cholesterol lowering drug optional at 160 to 189 mg/dL (4.13 to 4.88 mmol/L)</td>
</tr>
</tbody>
</table>
Atherosclerosis in SLE: Management

- Screening for risk factors
  - Annual: Blood pressure, fasting lipid panel, hgb a1c or fasting AM glucose

- Early, aggressive intervention for risk factors
  - Control hypertension
  - Smoking cessation
  - Treat hyperlipidemia
    - Dietary adjustment, “Statins”
    - SLE associated with “atherogenic” lipid profile
  - Weight control
    - Diet, exercise
  - Careful monitoring of blood sugar, weight, blood pressure
    - Particularly if chronic corticosteroids are necessary
Atherosclerosis in SLE: Management

Control SLE

- Hydroxychloroquine
- ACE inhibitors for chronic proteinuria
- Routine rheumatology evaluation and lab assessment
  - Quarterly appointments
  - CBC, chemistries, complement, urinalysis, anti-DNA at each visit
  - Antiphospholipid antibody screen, fasting lipid panel performed annually
Atherosclerosis in SLE: Is there something more?

- Impact of inflammation
  - Uncertain role of inflammation
  - CRP levels are independent risk for coronary artery disease

- Endothelial cell injury
  - Now four separate studies that confirm widespread endothelial dysfunction in SLE
    - Independent of atherosclerotic disease burden
Summary

- Atherosclerosis prevention and management must be aggressive.
- Multiple diagnostic techniques, including biopsy, may be necessary to understand the etiology of lupus-associated cardiovascular disease.
- Questions??
SLE: Acute Lupus Pneumonitis

- Prevalence
  - < 10%
- Presentation
  - Acute dyspnea
  - Cough
  - Fever
  - Hemoptysis
  - Chest pain/pleurisy
  - Hypoxemia
  - Preceded/ associated w/ infxn
- Prognosis:
  - Mortality 50%
- Treatment:
  - Steroids
  - PE
  - CYC/AZA
SLE: Diffuse Alveolar Hemorrhage

- Prevalence
  - 2%

- Presentation
  - Acute dyspnea
  - Cough
  - Chest pain/pleurisy
  - Hypoxemia
  - Anemia

- Prognosis:
  - Mortality 50%

- Treatment:
  - Steroids
  - PE
  - CYC/AZA
SLE: Chronic Interstitial Lung Disease

- Also called “pulmonary fibrosis”
- Prevalence:
  - Up to 3%
- Presentation:
  - Dyspnea
  - Cough
  - Decreased FVC, DLCO
- Pathology:
  - Purely inflammatory (NSIP) has best prognosis, easiest to treat
  - Mixed inflammation and scar (NSIP w/ fibrosis)

Diagnosis
- Abnormal PFDs
- Abnormal CT scan findings
- Bronchoalveolar lavage
  - Confirm inflammation
  - Rule out chronic infection
  - Rule out cancer
- Open lung biopsy

Prognosis variable

Management:
- Corticosteroids
  - For isolated NSIP
- AZA/CYC/MMF
  - For fibrosing disease
SLE: Chronic Interstitial Lung Disease

Interstitial lung disease
- Clinical symptoms & signs
  - Cough
  - Dyspnea
  - Pleural rub or dry rales
- Imaging
  - Interstitial infiltrates (early)
    - CT: “ground glass” opacities
  - Scarring (late)
    - CT: “honeycombing,” traction bronchiectasis
- Pulmonary function
  - Restrictive pattern
    - Depressed lung volumes
SLE: Pleurisy and Pleural Effusion

- **Pleurisy**
  - Chest pain, typically sharp and stabbing and localized
  - Occurs with deep inspiration
  - Caused by inflammation of the pleura (similar to and may co-occur with pericarditis and peritonitis)
  - Differential diagnosis
    - Rule out Pulmonary embolus!!
    - Pneumonia
    - Pneumothorax
    - ALP
    - Muscle strain
    - Costochondritis

- **Diagnosis**
  - Friction rub on exam
  - CXR occasionally shows fluid

- **Management:**
  - NSAIDs
  - Corticosteroids
  - Drainage if large effusion forms
SLE: Shrinking lung syndrome

- Slowly progressive dyspnea with exertion
- Rare, < 2%
- Diagnosis:
  - Decreased breath sounds
  - Reduced lung volumes on PFDs
  - Changing CXR lung aeration

Pathology:
- Probably pleural fibrosis/scar

Management
- Azathioprine
- Corticosteroids


Fig. 2: Chest radiographs showing progressive lung shrinkage over 4 months
SLE: Pulmonary arterial hypertension

- Also called PAH
- Progressive shortness of breath followed by right heart failure
- Due to inflammation, damage, dysfunction of the small pulmonary arteries
- Effectively slows blood flow through the lung, forcing the right ventricle to pump harder
- Three different causes with three different management strategies in patients with SLE
Increased Pulmonary Resistance and Pressure

Pre-Symptomatic
High flow, low resistance vessel

Symptomatic
Low flow, high resistance vessel

Severely Symptomatic
Low flow, high resistance vessel

SLE: Pulmonary arterial hypertension

Type I:
- Inflammatory vascular disease
- Reversible with aggressive immunosuppression (Cyclophosphamide and corticosteroids)
- No way presently to distinguish from chronic Scleroderma-like vascular disease except possibly presence of RNP antibodies or cutaneous manifestations of scleroderma

Type II:
- Chronic venous thromboembolic disease (CTEPH)
- Treatment includes anticoagulation along with:
  - Surgical thrombectomy
  - Adempas (riociguat) for inoperable CTEPH

Type III:
- Scleroderma-spectrum PAH
- Treatment:
  - Supplemental O2
  - Treat associated interstitial lung disease or sleep apnea
  - Meds:
    - Endothelin antagonists
    - Prostanoids
    - Adempas
    - 5’ PDE inhibitors
SLE: Pulmonary embolus

- Blood clot in the lung
  - Interferes with blood flow through part of the lung
  - If clot is large enough can cause massive vascular collapse and sudden death
  - Triggers:
    - Stasis
    - Trauma (surgery)
    - Malignancy
    - Hypercoaguable states (APLS)

- Diagnosis
  - Clinical:
    - Acute dyspnea, pleuritic chest pain, low BP
  - ECG:
    - S1, Q3, T3
  - V:Q scan or CTA
Lupus Cardiopulmonary Disease

- Numerous potential disease manifestations
- Difficult clinically to sort out causality without diagnostic testing
- Very important to get to the root of the problem as long term outcome and treatment options are variable among diagnoses

Questions
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