Tuberculous Pericarditis and Pericardial Disease

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Tuberculosis
• 4000 BCE: Prehistoric human skeletons show evidence of disease
History

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- 460 BCE: Hippocrates described “phthisis” - fever, hemoptysis - as most widespread disease
History

- 1800s: Cause of ¼ of all deaths in Europe
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• **1838**: John Croghan brought tuberculosis patients to Mammoth Cave to cure the disease with its constant temperature and pure air
  - They died within 1 year
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- Nobel Prize in medicine, 1905
History

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- 1906: Albert Calmette & Camille Guérin developed vaccine
  - Bacille Calmette-Guérin (BCG)
Pathophysiology

- *Mycobacterium tuberculosis*
  - Obligate aerobe
  - Bacillus
  - Does not gram stain
  - High lipid content in outer wall stains for acid fast staining
    - Ziehl-Neelsen staining

- Humans only known reservoirs
  - Spread via respiratory droplets
    - 1 to 5 microns
  - Survives in dry state for weeks
Primary Infection

• Mycobacteria deposit within peripheral airways and proliferate within macrophages
  – Unable to eradicate infection initially
  – Attract numerous other immune cells
  – 2-10 weeks after infection, effective cell-mediated immune response develops
  – Caseating necrosis within nodules
Primary Infection

- **Ghon complex**
  - Peripheral nodule plus hilar lymph nodes
  - Macrophages carry mycobacteria to lymph nodes
    - Hilar lymphadenopathy

- **Ranke complex**
  - After control of infection, fibrosis and calcification of Ghon complex occurs
  - Frequently still contain live mycobacteria
    - Latent infection
Primary Infection

• Disseminated disease
  – Hematogenous spread
    • Milliary tuberculosis
  – Local extension of Ghon complex
    • Primary caseous pneumonia
  – Risk factors
    • Immunosuppression
    • HIV
    • Malnutrition
    • Diabetes
    • ESRD
    • Major surgery
Secondary Infection

• Reactivation
  – 5-10% of healthy patients
    • Unclear what causes mycobacteria to break containment
  – Other risk factors
    • Same as disseminated disease
  – Most commonly in lung apices
Presentation

- Primary
  - Symptoms:
    - Fever (most common)
    - Chest pain
    - Fatigue
    - Cough
  - Imaging (CXR):
    - Normal
    - Hilar lymphadenopathy
    - Infiltrates rare

- Secondary
  - Symptoms:
    - Asymptomatic (1-2 yrs)
    - Cough (hemoptysis)
    - Weight loss
    - Fatigue
    - Night sweats
  - Imaging (CXR):
    - Upper lobe infiltrate
    - Cavities with air/fluid levels
Diagnosis

• Clinical scenario
  – Symptoms
  – Epidemiologic risk factors
  – Radiographic findings

• Sputum samples
  – 3 samples, >8 hours apart
  – Cough or induced
    • Inhaled aerosolized hypertonic saline
  – Acid fast staining & culture
    • 1 sample for nucleic acid amplification if available
  – 17% of cases in USA are culture negative
Diagnosis

• **Pleural effusion fluid**
  – Routine studies
  – Cultures, NAA
  – Adenosine deaminase (ADA)
    • 100% sensitive, 97% specific
  – Lysozyme, interferon-gamma

• **Tissue**
  – Histology and culture
  – Pleura
    • Caseating granulomas diagnostic for TB
  – Other affected tissue
Diagnosis

• Mantoux test (PPD)
  – Inject 5u tuberculin intradermal
  – Measure induration 48-72 hours later
    • >5mm: + in severely immunosuppressed
    • >10mm: + in patients with risk factors, BCG recipients
    • >15mm: + in healthy patients
  – Positive result → further work up
• Limitations
  • High rate of false positives, BCG can confound results
  • Reader bias, multiple visits

• Interferon-gamma release assay (Quantiferon)
  – Whole blood incubated with antigens
  – ELISA to measure interferon-gamma levels
• Advantages
  • Not affected by prior BCG
  • Results not subject to reader bias, single visit
• Disadvantages
  • Delay, errors in blood handling can confound results
Isolation

- Respiratory isolation until:
  - Other diagnosis and/or negative sputum x3
  - Good treatment response & negative sputum

- Isolation not needed for extrapulmonary disease
RIPE

- **Rifampin (RIF)**
  - Inhibits RNA polymerase
  - Stains body fluids red, hepatotoxicity

- **Isoniazid (INH)**
  - Inhibits mycolic acid synthesis (cell wall component)
  - Peripheral neuropathy, hepatotoxicity

- **Pyrazinamide (PZA)**
  - Inhibits fatty acid synthesis (cell wall components) and ribosomal activity
  - Arthralgia, hepatotoxicity

- **Ethambutol (EMB)**
  - Inhibits cell wall development, increases permeability
  - Optic neuritis, hepatotoxicity

**Treatment Schedules**

- RIF, INH, PZA, EMB x2 months
- RIF, INH x4 months
ZM

- 50 y M with 2 weeks progressive dyspnea on exertion, orthopnea, productive cough (nonbloody)
  - Last 6 months + night fevers, 10 lb weight loss
  - Denies chest pain, leg swelling

- PMH: HTN, GERD
- PSH: laparoscopic cholecystectomy

- Meds: enalapril, omeprazole
- Allergies: none

- Social: 15 pack/year tobacco, 5 beers/day
• Travel: + TB exposure in Pakistan
Physical Exam

- HR 117  BP 113/84  RR 24  Sat 100% on non-rebreather  T 99.6F
- No distress
- No JVD
- Diminished breath sounds at R base
- Diminished heart sounds
- Hepatomegaly
Labs

- CBC: 10.3> 15.0/47.9 <88
- Chem: 137/4.1, 105/23, 12/0.7 <96
- CEA: 1.1
- LFT: 7.4/2.9, 72/35, 302/1.3
Imaging

• Echocardiogram
  – Large pericardial effusion
  – Early diastolic collapse of right ventricle
Hospital Course

- HD 1: R thoracentesis
  - 2L drained, fluid exudative

- HD 2: R pigtail catheter placed
  - 1L drained

- HD 3: Pericardial window, pericardial LN biopsy
  - Pericardial Blake drain
• HD 5, POD 2: Breathing improved, afebrile, tachycardic to 100s, WBC 16k
  – 2L drained, fluid exudative

• HD 8, POD 5: Remained tachycardic, high CT output (~1L per day)
  – Pericardial LN path: “markedly enlarged lymph node with caseating granulomas and extensive necrosis.”
    • Acid fast stain: negative
  – Airborne precautions, PPD placed (negative)
  – Multi-agent anti-TB therapy (RIPE) started

• HD 9, POD 6: Increasing SOB
  – Echo: mod-large pericardial effusion with fibrinous strands
• HD 13, POD 10: To OR
  – Inability to tolerate one-lung ventilation
  – VATS aborted → anterolateral thoracotomy
  – Dark bloody fluid in pleural space
  – Thick tense pericardium
  – Dark bloody fluid in pericardial space
  – Large portion of pericardium removed
    • Path: acute and chronic inflammation
  – Level V LN biopsy
    • Path: anthracotic lymph node
  – To SICU intubated post-op
• HD 15, POD 12/2: Extubated

• HD 17, POD 14/4: Blake drain removed
  – Quantiferon results returned positive

• HD 20, POD 17/7: Downgrade to floor

• HD 22, POD 19/9: L chest tube removed

• HD 23, POD 20/10: R pigtail removed

• HD 27, POD 24/14: Discharged home
Questions?
Pericardium

- Fibrous sac enveloping heart and great vessels
  - **Fibrosa**: collagen, elastic fibers
  - **Serosa**: mesothelial cells
  - Folds onto heart & vessels
  - **Epicardium** ≈ visceral pericardium

- Borders:
  - **Lateral**: forms medial wall of pleural space
  - **Inferior**: superior surface of central tendon of diaphragm
  - **Superior**: blends with deep cervical fascia
  - **Anterior**: attached to xiphoid and manubrium
Pericardial Physiology

- 15-35 mL pericardial fluid
- Minimizes friction and energy loss from cardiac motion
- Stabilizes position and orientation of heart
- Protects heart from infection
Pericardial Effusion

- Fluid released > fluid resorbed
  - ↑ production: infection, inflammation
  - ↓ resorption: lymphatic obstruction, venous hypertension

- Chronic effusion causes distension of pericardium
  - Larger effusion volumes

- >500-750 mL requires drainage
Cardiac Tamponade

- Hemodynamically significant cardiac compression
  - >200 mL fluid

- Right ventricle first affected
  - Decreased venous return
  - Decreased stroke volume
  - Decreased cardiac output
Hemodynamic Effects

- CVP 14-30 mmHg

- Echo findings:
  - RA compression
  - RV diastolic collapse
  - IVC dilation
  - Shift of interventricular septum during inspiration

- Pulsus paradoxus
  - Fall in SBP >10 mmHg with inspiration

- Beck’s triad
  - Jugular venous distension
  - Muffled heart sounds
  - Hypotension
Pericardiocentesis

- **Echo-guided**
  - Improves safety
  - Identify location where fluid is closest to skin

- **Approach**
  - Sub-xiphoid
  - Para-sternal
  - Para-apical

- **Insert needle, aspirate fluid**
  - Confirm location with Echo

- **Over guidewire, insert pigtail catheter**
  - Remove in 24-48 hours
  - Output <100 mL per 24 hours

- **Post-procedure, watch in monitored setting**
Subxiphoid Pericardial Window

- **Advantages:**
  - Greater drainage than pericardiocentesis
  - Pericardial biopsy

- Longitudinal subxiphoid incision, ~5 cm

- Divide linea alba

- Resect xiphoid process

- Expose pericardium, resect small patch

- Fluid sent for studies, drain left in pericardial space

- Recurrence: *Up to 25%*

www.downstatesurgery.org
Trans-pleural Pericardial Window

- **Advantages:**
  - Improved drainage in chronic effusions
  - Concomitant lung biopsy possible

- **Disadvantage:**
  - Purulent effusion may contaminate pleural space

- **Left approach preferred**
  - VATS
  - Thoracotomy

- At least 4x4 cm patch of pericardium removed

- **Avoid phrenic nerve along lateral heart**

- **Recurrence:** 5%
Pericardiectomy

- For extensive pericardial adhesions, severe constrictive pericarditis

- Median sternotomy

- Incise anterior pericardium between:
  - Great vessels
  - L & R phrenic nerves
  - Diaphragm

- Free LV first
  - Avoids RV distension

- Posterior pericardial resection (optional)
  - May reduce risk of future constriction
  - Manipulation of heart may require CP bypass

- 60% achieve hemodynamic improvement
Tuberculous Pericarditis

- 1-2% of cases of pulmonary TB
- Direct extension or hematogenous spread
- Often represents reactivation disease
  - Unknown primary focus
- Manifestations
  - Effusive
  - Constrictive
Presentation and Diagnosis

• Symptoms of TB

• Cardiac signs
  – Tachycardia
  – Jugular venous distension
  – Friction rub, muffled heart sounds
  – Hepatomegaly
  – Peripheral edema

• Work Up
  – CXR
  – Sputum
  – Mantoux test or interferon-gamma release assay
  – Echocardiogram
  – CT/MRI
  – Sample fluid
  – Pericardial biopsy
Differential

- **Infectious**
  - Viral (e.g. coxsackievirus, EBV, CMV, influenza, HIV)
  - Bacterial (e.g. staph, strep)
  - Fungal (e.g. Histoplasma, Aspergillus)

- **Autoimmune**
  - Sarcoidosis

- **Malignancy**
  - Metastatic (e.g. breast, lung)
  - Primary (e.g. rhabdomyosarcoma)

- **Radiation**

- **Trauma / Hemopericardium**
Fluid vs Tissue for Diagnosis


- Positive culture results for pericardial fluid compared to pericardial tissue
  - Known TB pericarditis

- Fluid: 16/28 (57%)
- Tissue: 14/15 (93%)
  - P = 0.02
Management

• Anti-tuberculous treatment

• Corticosteroids (?)

• Drain effusion
  – Pericardiocentesis vs Surgical drainage
Corticosteroids in TB Pericarditis


- Prednisolone vs placebo x11 weeks with RIPE
  - Randomized, prospective

<table>
<thead>
<tr>
<th>Adverse events after 24 months</th>
<th>Steroids, N (%)</th>
<th>Placebo, N (%)</th>
</tr>
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<tbody>
<tr>
<td>Death from pericarditis</td>
<td>2 (3)</td>
<td>10 (14)*</td>
</tr>
<tr>
<td>Pericardiectomy</td>
<td>6 (8)</td>
<td>9 (12)</td>
</tr>
<tr>
<td>Repeat pericardiocentesis</td>
<td>7 (9)</td>
<td>17 (23)*</td>
</tr>
<tr>
<td>Subsequent open drainage</td>
<td>3 (4)</td>
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* P < 0.05
## Pericardiocentesis vs Pericardial Window


- **Pericardial window vs pericardiocentesis as needed**
  - Randomized, prospective

<table>
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<tr>
<th>Adverse events after 24 months</th>
<th>Window, N (%)</th>
<th>No window, N (%)</th>
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<tbody>
<tr>
<td></td>
<td>N = 76</td>
<td>N = 74</td>
</tr>
<tr>
<td>Death from pericarditis</td>
<td>4 (8)</td>
<td>3 (6)</td>
</tr>
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<td>Pericardiecomy</td>
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</tr>
<tr>
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<td>--</td>
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Early Pericardiectomy


- Retrospective case series, 17 patients
  - 13 with effusions
  - 10 underwent surgical drainage

- 4 patients had pericardiectomy
  - 2 with clinical evidence of constriction
  - 2 had thickened pericardium of repeat echo

- Recommendations:
  - Early window with large effusion
  - Early pericardiectomy if thick pericardium identified on window
Summary

• Tuberculosis presentation is vague – have a high index of suspicion based on history and exposure risks

• Tuberculous pericarditis rare (1-2%)

• Diagnosis aided with tissue sample
  – Role for pericardial window over pericardiocentesis

• Management
  – RIPE
  – +/- steroids
  – Effusion drainage

• Subxiphoid vs transpleural vs pericardiectomy
Additional Sources

- Sabiston and Spencer Surgery of the Chest
- www.uptodate.com
Questions?

Buy Christmas Seals
Fight Tuberculosis