Sarcoidosis

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Disclosures

- Speaker for AstraZeneca
  - Symbicort
  - Bevespi
- Speaker for Merck
  - Belsomra
- Speaker for Sunovion
  - Utibron
  - Seebri

Overview

- What I feel you need to know regarding sarcoidosis
- Treatment
- Follow up
- ?Update
What is Sarcoidosis

- Inflammatory condition in which the body forms granulomas against itself
- Can occur in any organ
- Can involve one or more at a time
- Etiology is unknown
  - Genetic predisposition
  - More predominant in African Americans

Epidemiology

- 80% of patients are 20-50 years old at diagnosis
- In the US
  - Blacks have a lifetime risk of 2.4%
  - Whites have a risk of 0.85%
Organ Involvement

- Most common is the lung
  - Including mediastinal lymph nodes
- Followed by liver
- Spleen
- Kidney
- Musculoskeletal
- Peripheral lymph nodes
- Hematologic
- Skin
- Nervous system
- Cardiac
- Hypercalcemia
- Parotid glands

Lungs

- Most commonly asymptomatic
- Bilateral hilar lymphadenopathy on CXR/CT chest
- Symptoms that can be seen are cough, wheezing, shortness of breath
- Occur in one-third to one-half of all patients
- Airway hyperactivity has been reported in up to 20% of patients
- Can cause pulmonary hypertension and pulmonary fibrosis
Liver
- Also, usually asymptomatic
- Elevation of liver enzymes
- Rarely causes portal hypertension, hepatic failure, or increased mortality related to liver dysfunction

Eyes
- One of the more concerning issues as can cause blindness
- Uveitis is the most common problem
- Followed by
  ▶ Retinal vascular changes
  ▶ Conjunctival nodules
  ▶ Lacrimal gland enlargement
Uveitis

- Acute anterior uveitis usually clears spontaneously or after local therapy with corticosteroids
- Chronic uveitis may lead to adhesions between the iris and the lens (synechia)
- Glaucoma
- Cataract
- Blindness

Musculoskeletal

- Proximal muscle weakness is common
- Must be distinguished from corticosteroid-induced myopathy
- Myalgias
- Intramuscular nodules
- Evaluate with CK, muscle biopsy if necessary

Hematologic

- Anemia
- Leukopenia
- Usually requires bone marrow biopsy for diagnosis
Sarcoidosis

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Skin

- Rash
- Papules, nodules, plaques
- Erythema nodosum
- Lupus pernio

Rash

Papules, nodules, plaques

Erythema nodosum

Lupus pernio

Erythema nodosum

- Most common skin manifestation
- Usually acute, self-limiting process and rarely requires treatment
- Recurrences are uncommon
- Can occur in many other diseases
- Typically remits in 6-8 weeks

Typically remits in 6-8 weeks
Most characteristic of sarcoidosis

Typically occurs in the head and neck

Nose, cheeks, foreheads, and ears

Occurs typically in black women in their 30s and 40s

Rarely resolves spontaneously

Can be cosmetically disfiguring

Extensive involvement of the nasal cavity and the maxillary sinuses may lead to nasal obstruction
Nervous System

- Cranial nerve palsies are common
  - Tend to occur early on and respond favorably to treatment
- Optic neuritis
- Hypothalamic
- Cognitive dysfunction
- Small fiber neuropathy
- Gadolinium-enhanced MRI is the preferred test for evaluating brain parenchyma, meninges, and spinal cord.

Cardiac

- Clinical occurrence is 5%
  - Autopsy reports as high as 25%
- Conduction abnormalities
  - Heart block
  - Arrhythmias
    - Ventricular tachycardia and fibrillation
- Congestive heart failure
- Sudden death

Cardiac Diagnostics

- EKG
- Holter monitor
- Echocardiogram
- PET/CT
- Cardiac MRI
- Endomyocardial biopsy
  - May be inconclusive secondary to inhomogeneous distribution of granulomas
Hypercalcemia

- Occurs in about 2–10% of patients with sarcoidosis
- If left untreated can cause
  - Nephrocalcinosis
  - Renal stones
  - Renal failure

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Natural History of Sarcoidosis

- Spontaneous remission occurs in 65%
  - 10–30% develop chronic and progressive disease
- Blacks are more likely to have a more symptomatic, severe, and chronic disease than whites
- Lifetime mortality from sarcoidosis is less than 5%

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Presentation

- Cough
  - Shortness of breath > 50%
- Constitutional symptoms 35%
- Many are asymptomatic
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Loe gren’s Syndrome

- Acute form of sarcoidosis
  - Bilateral hilar lymphadenopathy
  - Symmetric polyarthritis or polyarthritis
  - Erythema nodosum
  - Typically self-limiting

Differential Diagnosis

- Very large and broad
- Most concerning would be lymphoma or other cancer
- Infectious
  - Fungus and mycobacterium cause caseating granulomas
- Inflammatory
  - Hypersensitivity pneumonitis
  - Many ILD
- Most common reason for biopsy

It's Lupus and Sarcoidosis
Sarcoidosis
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Work up
- Mainly based on presentation
- Labwork
  - CBC
  - Serum chemistries
  - LFT's
  - CXR
  - Pulmonary function test
  - EKG
  - Routine ophthalmologic exam

Diagnosis
- Need tissue for confirmation
  - Not always possible
- Most common method is bronchoscopy
  - EBUS (transbronchial needle aspiration)
  - Transbronchial biopsy
  - EBUS transbronchial biopsy
  - EUS
  - Mediastinoscopy
  - Skin biopsy
  - Lymph node biopsy
  - Liver and heart biopsy
Non-necrotizing (Non-caseating) Granulomas

- Hallmark of sarcoidosis biopsy
- Should be an absence of current infection
  - Mycobacterium
  - Fungus
- Especially if necrotizing granulomas are seen

Radiologic Staging

- Based on CXR
- Stage I
  - Bilateral hilar lymphadenopathy
- Stage II
  - Bilateral hilar lymphadenopathy with interstitial lung disease
- Stage III
  - Interstitial lung disease without bilateral hilar lymphadenopathy
- Stage IV
  - End-stage pulmonary fibrosis
Stage IV

- Development of pulmonary fibrosis
  - Honeycombing and irreversible damage
- Often accompanied by development of pulmonary hypertension
- Respiratory failure remains the most common cause of death in patients with active sarcoidosis

Stage IV

- Symptomatic stage II or stage III disease
  - SOB, cough, obstruction on spirometry
- Significant extrapulmonary disease
  - Cardiac, liver, uveitis, hypercalcemia
- Not indicated in stage I or asymptomatic stage II
  - Spontaneous resolution is common
  - 55 to 90% of patients with stage I
  - 40 to 70% of patients with stage II
- May not be helpful in stage IV
  - Consider lung transplant

To Treat or Not to Treat

- Symptomatic stage II or stage III disease
- Significant extrapulmonary disease
- Not indicated in stage I or asymptomatic stage II
- Spontaneous resolution is common
### Adverse Prognostic Factors

- Lupus pernio
- Nasal mucosal involvement
- Chronic uveitis
- Age at onset greater than 40 yr
- Chronic hypercalcemia
- Nephrocalcinosis
- Black race
- Cystic bone lesions
- Neurosarcoidosis
- Myocardial involvement
- Progressive pulmonary sarcoidosis
- Chronic respiratory insufficiency
- Lupus pernio
- Nasal mucosal involvement
- Chronic uveitis
- Age at onset greater than 40 yr
- Chronic hypercalcemia
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- Black race
- Cystic bone lesions
- Neurosarcoidosis
- Myocardial involvement
- Progressive pulmonary sarcoidosis
- Chronic respiratory insufficiency

### Medication

- Steroids are mainstay of treatment
  - No good data unfortunately
  - Trial of 3 months
  - If no improvement, unlikely to help
  - Usually treat for minimum of one year
  - Patients with frequent relapses or unable to wean steroids
  - Typically by an immunosuppressive

### Immunosuppressive Therapy

- Hydroxychloroquine
- Methotrexate
- Azathioprine
- Leflunomide
- Mycophenolate
- Infliximab
- Adalimumab
- Second line and require close monitoring
**Specialist’s View**

- PFT, CXR, and pulse oximetry
- Biopsy
- EBUS
- Bronchoscopy with endobronchial/transbronchial biopsy
- Fungal and AFB cultures
- Liver biopsy, skin biopsy, lymph node

- Treat based on symptoms and spirometry
- CXR mainly helpful for staging and can help with response

**My Typical Treatment**

- Prednisone 40-60 mg daily for 1-3 months
- Re-evaluate symptoms and spirometry
- If no response after 3 months
  - Stop treatment
- If response, typically continue lower dose prednisone
  - 5-10 mg/day
- Re-evaluate every 3 months
  - Symptoms and spirometry
  - If symptoms completely resolve and spirometry normalizes
  - Try to stop the prednisone early (6-12 months)

**When To Use An Immunosuppressive**

- Relapse occurs quickly
- Or frequent relapses
- Cannot tolerate longer courses of prednisone
- Typically start with methotrexate
  - 7.5 mg and titrate up to 15 mg as needed/tolerated
“Sarcoidosis”
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Monitoring

- Yearly
  - CXR
  - Spirometry
  - Ophthalmologic exam
  - LFTs
- Based on symptoms
  - EKG
  - Echocardiogram

What's Most Important Regarding Treatment

- Cardiac/neuro issues
- Initial staging
  - Stage IV disease patients do poorly
- Lung standpoint
  - Spirometry
  - Lupus pernio
  - Uveitis

What's Least Important Regarding Treatment

- Erythema nodosum
- CXR findings alone
- Stage I disease
- Mild hypercalcemia
- Lofgren’s Syndrome
Update on Sarcoidosis

- Biomarkers
  - Not sensitive or specific enough
- FDG-PET
- EBUS/EUS

FDG-PET

- Very sensitive method to assess inflammatory activity and extent of disease in sarcoidosis
- Not for screening
- Can help find a suitable area for biopsy
- Useful in detecting cardiac sarcoidosis
- May also help predict mortality
- Cardiac MRI has also been useful

Endobronchial and Endoscopic Ultrasound

- Less invasive biopsy
- EBUS
  - Bronchoscopy
  - Anterior mediastinal and hilar lymph nodes
- EUS
  - GI tract
  - Posterior mediastinal and intra-abdominal lymph nodes
- Yield is typically 80-90%
- Mediastinoscopy is rarely done
Literature Review

- Many articles
- Mostly review
- Not much from a clinical standpoint

Predictors of Mortality in Pulmonary Sarcoidosis

Gamze Kirkil, MD, Elyse E. Lower, MD, Robert P. Baughman, MD

CHEST
2017
Berylliosis

- Chronic beryllium disease (CBD)
- Formation of granulomas in the lung and other organs
  - Very similar to sarcoidosis
- Occupational exposure to beryllium
  - Aerospace, electronics, nuclear components, high-technology ceramics, dental alloy preparation, and metals extraction
- Positive beryllium lymphocyte proliferation test
  - Blood or bronchoalveolar lavage fluid
- Acute Berylliosis
  - Acute chemical pneumonitis

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