The Many Faces of Thoracic Sarcoidosis

Jeffrey B. Alpert, MD

Department of Radiology, Cardiothoracic Section
SUNY Downstate Medical Center/Kings County Hospital Center

Objectives:

- Brief review of clinical history and pathophysiology of sarcoidosis
- Common thoracic imaging findings associated with sarcoidosis
  - Lymphatics; mediastinum
  - Lung parenchyma
  - Airways
  - Pleura

Sarcoidosis:

- Originally described in 1899: skin lesions which looked like sarcoma.
- Systemic disease of unknown etiology; thought to be disorder of immune regulation.
- Ranging from self-limited, subclinical disease to debilitation and death.
- Typically presents in 3rd-4th decades. Range: teens to 60s.

Epidemiology:

- Worldwide, highest annual incidence is in northern Europe: 5-40 per 100,000.
- Adjusted annual incidence in United States: Three times higher among blacks versus whites (35.5 vs 10.3 per 100,000).
- Black Americans more likely to have extrathoracic disease and chronic disease.
- Rare in African and South American black populations.

Mortality:

- 1988-2007: Mortality increased 3% per year.
- Highest absolute increased death rate among non-Hispanic black females.
- Mortality rate rose most sharply among patients 55 years or older (regardless of race or sex).
- Younger patients with pulmonary fibrosis: blacks > whites.
- Cause of death in the U.S. among those with sarcoidosis:
  - Sarcoidosis 16.8%
  - Cancer 16.8%
  - Lung cancer 1.6%
  - Pneumonia 1.1%

Imaging:

- Chest x-ray: bilateral hilar adenopathy is most common finding.
  - Regarding LAD:
    - Bilateral hilar adenopathy: >50%
    - Bilateral hilar, right paratracheal
    - Anterior mediastinal: <10%
    - Unilateral hilar: 1-3%
  - Older at presentation: more likely to have atypical lymph nodes.
Chest radiographs:
- Stage 0: normal 5–10%
- Stage 1: LAD 50%
- Stage 2: LAD & parenchyma 25–30%
- Stage 3: Parenchyma only 15%
- Stage 4: Lung fibrosis 10–20%

Stage does not correlate with PFTs.
Advent of computed tomography (CT) has negated the classic radiographic staging system.

CT Technique:
- Routine non-contrast chest CT:
  - Parenchymal disease, nodules
- Routine contrast-enhanced chest CT:
  - Improved evaluation of mediastinum, hila, pleura
- High-resolution chest CT:
  - Routine non-con study PLUS:
    - Thin-section high-resolution images
    - Expiratory images
    - Prone images as needed

Airway involvement:
- Respiratory system involvement >90% pts.
- Airway involvement in nearly 2/3rd pts.
  - Often overlooked; unexplained symptoms.
- Frequency of airway involvement increases as parenchymal disease progresses.
- Associated with increased morbidity and mortality.

Airway involvement:
- Range from nasal/oral passages to terminal bronchioles.
- Many forms:
  - Extrinsic compression
  - Intrinsic disease:
    - Mucosal involvement (early)
    - Luminal stenosis
    - Airway distortion (late)

Extrinsic compression:
- Enlarged mediastinal and hilar lymph nodes.
- Significant luminal stenosis from adenopathy is uncommon.
Large central airways:
Trachea, mainstem bronchi affected less frequently than lobar and distal airways.
Granuloma formation: wall thickening.
Extrinsic compression is rare.

Medium-sized airways:
- Early stages:
  - Mucosal edema and inflammation
  - Associated with endobronchial granuloma formation
  - Producing mucosal nodularity (waxy yellow nodules)
  - Most profound within lobar/segmental bronchi.
  - Develop within airways and along bronchovascular bundles, near airways.

Medium-sized airways:
- Early stages:
  - Nodules may result in luminal stenosis or postobstructive atelectasis
  - Stenosis in up to 14% patients; typically minor, asymptomatic.

Medium-sized airways:
- Late stages:
  - Fibrotic mucosal changes:
    - Airway narrowing, distortion.
  - Fibrotic parenchymal changes:
    - Traction bronchiectasis, distortion.

Sarcoid-related pulmonary fibrosis:
- Study of 80 patients; CT imaging findings:
  - Bronchial distortion, central: 47% (38/80)
  - Honeycombing: 29% (23/80)
  - Linear (reticulation, septal thickening): 14% (24/80)
  - Nodular opacities significantly associated with linear opacities (87%) but not with honeycombing (35%).

Small-airway disease:

- Involvement of bronchioles: air-trapping.
- Can occur in early stages of disease, with/without parenchymal involvement.
- Typically assessed with expiratory images (High-resolution chest CT protocol).

Davies et al:
- HRCT with expiratory imaging showed air-trapping, suggesting small airway disease in 20/22 sarcoidosis patients (95%).


Hemoptysis:

- Typically result from complication such as Aspergilloma.
- Rarely caused by traction bronchiectasis (only handful of reported cases).

Sarcoidosis and Aspergillus:

- Pena et al studied incidence of aspergillus-related lung disease in sarcoidosis:
  - Approximately 3% (10 of 427 patients)
  - Incidence higher than compared to other chronic lung diseases.
  - All affected patients had fibrotic lung disease.
  - 4 had bilateral disease (aspergillus).
  - 3 died: 2 from hemoptysis, 1 from surgery complications.

Smoking effects:

ACCESS study:
- The odds risk of sarcoidosis in patients who have ever smoked is significantly lower than lifelong non-smokers. (OR 0.65, CI 0.51-0.82, \(P < .001\))


Smoking effects:

Gerke AK, van Beek E, Hunninghake GW. Smoking inhibits the frequency of bronchovascular bundle thickening in sarcoidosis. Am J Respir Crit Care Med 2011;183:832-839.
- Evaluate effects of smoking on clinical parameters of sarcoidosis.
- In patients with sarcoidosis:
  - Smokers had decreased frequency of bronchovascular bundle thickening (BVBT) than non-smokers: 45/138 (33%) vs 63/166 (38%), \(P<.001\).
  - BVBT less likely among ever-smokers (18/61 (29%) vs 27/63 (43%), \(P=.003\)) and current smokers (4/61 (7%) vs 15/63 (24%), \(P=.008\)).
  - BVBT strongly associated with airway obstruction (25/37 (68%) vs 36/87 (41%), \(P=.008\)).

Smoking effects:

- Air trapping on expiration seen among 98% (45/46).
- No significant differences between smokers and nonsmokers:
  - Air trapping, consolidation, small nodules, reticulation.

Smoking effects:

- Smoking decreases TNF-alpha production by alveolar macrophages.
- Smoking inhibits immune response responsible for granuloma formation.

Parenchymal disease:

- Alveolitis; interstitial pneumonitis of alveolar walls.
- T-lymphocytes recruit macrophages.
- Macrophages release cytokines which change into epithelioid cells.
- Nodular collections of these cells become interstitial granulomas.
- Congregate within lymph nodes and tissues with rich lymphatic supply.
- Granulomas commonly:
  - Subpleural
  - Septal
  - Perivascular
  - Peribronchial

\(\Rightarrow\) Lung nodules
Parenchymal disease:
- Granulomas commonly:
  - Subpleural
  - Septal
  - Perivascular
  - Peribronchial
→ Perilymphatic
- Perilymphatic nodules
  - Nodular thickening of fissures, pleural surfaces
  - Nodular septal thickening
  - Thickened bronchovascular bundles

CT Imaging:
- Fine nodular pattern
- Meticulonodular pattern
- Acinar: poorly marginalized, small-large nodules, coalescent opacities.
- Alveolar: coalescent acinar opacities, with or without air bronchograms.
- Focal: rare, nodule or mass.
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4 years later

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Fibrotic parenchymal disease:

- Upper lobe predominant
- Bronchiectasis
- Architectural distortion; hilar displacement
- Conglomerate masses: overlapping with silicosis or TB
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Lymph nodes:

- Calcified lymph nodes: related to disease duration.
  - 3% at 5 years.
  - 20% at 10 years.
- Amorphous, punctate, popcorn, eggshell.
Pleural involvement:

- Small-moderate effusions, clearing within 2-3 months. Pleural thickening (chronic).

Don’t forget:

- Nuclear medicine:
  - Gallium
- Extrathoracic disease
- Active disease
- Response to treatment

References: