Sarcoidosis in the Hospital Setting

Definition and Epidemiology

Sarcoidosis is a multisystem inflammatory disease characterized by the formation of non-caseating granulomas, primarily affecting the lungs, lymph nodes, skin, and eyes. Acute exacerbations or severe manifestations often require hospitalization for diagnostic workup or management.

- Prevalence
  - Affects ~10-40 per 100,000 globally; higher in African Americans (35-80/100,000) and Northern Europeans. Peak incidence at 20-40 years, with a second peak in women >50.
- Risk Factors
  - African ancestry, female sex (2:1 ratio), family history (5-10% familial clustering).
- Rare Demographics
  - Pediatric sarcoidosis (Blau syndrome), elderly onset (>65 years), occupational exposures (e.g., beryllium).

Pathophysiology

- Mechanisms
  - Sarcoidosis results from an exaggerated T-helper 1 (Th1) immune response to an unknown antigen, leading to granuloma formation. Activated CD4+ T-cells release IL-2, IFN-γ, and TNF-α, recruiting macrophages that form non-caseating granulomas.
- Effects
  - Granulomas disrupt organ architecture, causing fibrosis (lungs), conduction abnormalities (heart), or hypercalcemia (dysregulated vitamin D metabolism). Pulmonary involvement leads to restrictive lung disease.
- Molecular Pathways
  - Upregulation of mTOR signaling drives granuloma formation. HLA-DRB1*03 and BTNL2 gene variants increase susceptibility. Macrophage-derived 1,25-dihydroxyvitamin D causes hypercalcemia.
- Key Pathway
  - Antigen presentation → Th1 activation → Cytokine storm (TNF-α, IL-12) → Granuloma formation → Organ dysfunction.

Causes

Category	Common Triggers	Rare Triggers	Notes
Infectious	Mycobacteria, Propionibacterium	Histoplasmosis, Tropheryma whipplei	Infectious mimics (TB, fungi) must be ruled out
Environmental	Dust, mold, silica	Beryllium (chronic beryllium disease)	Beryllium mimics sarcoid; requires exposure history
Autoimmune	Unknown antigens	Overlap with Sjögren's, RA	Autoimmune sarcoid may have ANA positivity
Genetic	HLA-DRB1*03, BTNL2 mutations	CARD15/NOD2 (Blau syndrome)	Familial cases linked to chromosome 6
Drug-Induced	None well-established	Interferon-α, immune checkpoint inhibitors	Drugs may unmask latent sarcoid
Neoplastic	None	Lymphoma (sarcoid-like reaction)	Sarcoid-like granulomas in cancer mimic true sarcoid

Clinical Presentation

- Symptoms
  - **Dyspnea**, dry cough (pulmonary, 90% of cases)
  - **Fatigue**, weight loss, fever (systemic)
  - **Erythema nodosum**, lupus pernio (skin, 25%)
  - **Rare Uveitis** (vision loss), cranial nerve palsy (neurosarcoidosis), arrhythmias (cardiac)
- Exam
  - **Bilateral hilar lymphadenopathy** (CXR finding)
  - **Skin** Maculopapular rash, subcutaneous nodules
  - **Ocular** Anterior uveitis (red eye, photophobia)
  - **Rare Hepatomegaly**, parotid enlargement, hypercalcemic crisis
- Red Flags
  - **Syncope** (cardiac sarcoid), vision loss, seizures (neurosarcoidosis), Ca >12 mg/dL

Labs and Studies

- Labs
  - **Serum ACE** Elevated in 60-80% (non-specific, granuloma activity)
  - **Calcium** Hypercalcemia (10-20%), hypercalciuria due to 1,25-OH vitamin D
  - **CBC** Lymphopenia (20%), eosinophilia (rare)
  - **CMP** Elevated LFTs (liver involvement), Cr (renal sarcoid)

    - **Advanced** Soluble IL-2 receptor (sIL-2R), chitotriosidase (granuloma markers)
- Imaging
    - **CXR** Stages 0 (normal), I (hilar nodes), II (nodes + infiltrates), III (infiltrates), IV (fibrosis)
    - **HRCT Chest** Reticular opacities, ground-glass, peribronchovascular nodules
    - **PET-CT** Detects active granulomas, cardiac involvement
    - **Advanced** Cardiac MRI Late gadolinium enhancement (LGE) for cardiac sarcoid
- Other
    - **Bronchoscopy** Endobronchial ultrasound (EBUS)-guided biopsy; bronchoalveolar lavage (BAL) shows CD4:CD8 ratio >3.5
    - **Pulmonary Function Tests (PFTs)** Restrictive pattern (↓FVC, ↓TLC), reduced DLCO
    - **ECG** Arrhythmias (AV block, VT in cardiac sarcoid)
    - **Advanced** Gallium-67 scan (lambda/panda sign), CSF analysis (neurosarcoidosis)

Diagnosis

- Criteria
    - Clinical/radiographic evidence (e.g., hilar lymphadenopathy) + biopsy showing non-caseating granulomas + exclusion of mimics (TB, lymphoma).
- Differential
    - Tuberculosis, lymphoma, hypersensitivity pneumonitis, chronic beryllium disease, fungal infection.
- Flowsheet
    - **Step 1 History/Exam** Dyspnea, skin lesions, or systemic symptoms; check for Löfgren syndrome (erythema nodosum, hilar nodes, arthritis)
    - **Step 2 Labs** ACE, Ca, LFTs; rule out infection (Quantiferon-TB, fungal serologies)
    - **Step 3 Imaging** CXR (hilar nodes), HRCT (nodules, fibrosis), PET-CT (if systemic)
    - **Step 4 Biopsy** EBUS, skin, or lymph node; confirm non-caseating granulomas
    - **Step 5 Exclude Mimics** AFB culture, lymphoma workup (flow cytometry), beryllium lymphocyte proliferation test

Treatment

- General Principles
  - Control inflammation, prevent organ damage, and manage symptoms; many cases (e.g., Löfgren syndrome) resolve spontaneously.
- Supportive Care
  - **Oxygen** 2-6 L/min for hypoxemia (SpO2 <92%)
  - **Pain Management** Ibuprofen 600 mg q6h for arthritis, erythema nodosum
  - **Monitoring** PFTs q3-6 months, ECG q6 months (cardiac risk)
- Specific Therapies
  - **Corticosteroids** Prednisone 20-40 mg/day (pulmonary stage II-IV, cardiac, neuro); taper over 6-12 months
  - **Immunosuppressants** Methotrexate 10-20 mg/week, azathioprine 2 mg/kg/day for steroid-sparing
  - **Anti-TNF Agents** Infliximab 5 mg/kg IV q6-8 weeks (refractory pulmonary, skin)
  - **Advanced** Anti-IL-6 (tocilizumab, research), JAK inhibitors (tofacitinib) for multi-organ disease
- Organ-Specific
  - **Uveitis** Topical steroids, adalimumab; Cardiac ICD for VT, ablation
- Rare Causes
  - Beryllium cessation, lymphoma treatment (R-CHOP)
- Surgical
  - Lung transplant (end-stage fibrosis), thymectomy (if thymic involvement)
- Monitoring
  - **Serum Ca**, Cr q1-2 weeks on steroids
  - **CXR/HRCT** q6-12 months to assess progression
  - **Annual ophthalmology** exam (uveitis risk)

Complications

- Acute
  - **Hypercalcemic Crisis** Renal failure, AMS (Ca >14 mg/dL)
  - **Cardiac Sarcoidosis** VT, heart block (5-10% mortality)
  - **Neurosarcoidosis** Seizures, hydrocephalus
- Long-Term
  - **Pulmonary Fibrosis** End-stage lung disease (5-10% of cases)
  - **Chronic Uveitis** Blindness, glaucoma

- Rare
  - **Aspergilloma** (fibrotic cavities), amyloidosis (proteinuria)

Clinical Scenarios

Case 1 Pulmonary Sarcoidosis

Presentation 35 y/o F with 3 months of dyspnea, dry cough, and fatigue. Vitals BP 120/80, HR 85, SpO2 94%, RR 18. Exam Bilateral hilar adenopathy, no skin lesions.

Labs/Studies ACE 80 U/L, Ca 10.5 mg/dL, HRCT Peribronchovascular nodules. EBUS Non-caseating granulomas.

Interpretation Stage II pulmonary sarcoidosis, moderate symptoms.

Management Prednisone 20 mg/day, taper over 6 months. PFTs q3 months. Monitor Ca, Cr biweekly. Symptoms resolve by month 4.

Case 2 Cardiac Sarcoidosis (Rare)

Presentation 50 y/o M presents with syncope and palpitations. Vitals BP 130/70, HR 100, SpO2 96%, RR 16. Exam Normal lung, irregular heart rhythm.

Labs/Studies ECG 2nd-degree AV block, Cardiac MRI LGE in septum. PET-CT Myocardial uptake.

Interpretation Cardiac sarcoidosis with conduction abnormality.

Management Prednisone 40 mg/day, methotrexate 15 mg/week, ICD placement. Cardiology follow-up. PET-CT q6 months to assess activity.

Case 3 Löfgren Syndrome

Presentation 30 y/o F with fever, ankle arthritis, and painful leg rash. Vitals BP 125/75, HR 90, SpO2 98%, RR 14. Exam Erythema nodosum, swollen ankles.

Labs/Studies CXR Bilateral hilar nodes, ACE 60 U/L, ESR 50 mm/h. Biopsy Non-caseating granulomas.

Interpretation Löfgren syndrome, self-limiting sarcoidosis.

Management Ibuprofen 600 mg q6h, colchicine 0.6 mg BID. Monitor CXR q3 months. Spontaneous resolution by month 3.

Expert Tips

Suspect Löfgren syndrome in acute onset with erythema nodosum; it often resolves without steroids

Use cardiac MRI over PET-CT for initial cardiac sarcoid diagnosis; PET better for treatment response

Monitor for hypercalcemia early (within 2 weeks of onset); pamidronate for Ca >12 mg/dL

Consider neurosarcoidosis in cranial nerve VII palsy or seizures; LP shows lymphocytic pleocytosis

Avoid anti-TNF in cardiac sarcoid with EF <35% (worsens CHF); use tocilizumab instead

Pitfall Missing lymphoma; flow cytometry on biopsy rules out clonal B-cells

Advanced Trial JAK inhibitors in refractory cases; mTOR inhibitors (sirolimus) under investigation

Key Pearls

Hilar lymphadenopathy on CXR is classic; HRCT confirms granulomatous pattern

Biopsy with non-caseating granulomas is diagnostic; exclude TB, lymphoma

Prednisone is first-line for symptomatic pulmonary, cardiac, or neuro sarcoid

Cardiac sarcoid requires ECG/MRI screening; VT or heart block needs ICD

Rare presentations (neurosarcoid, Blau syndrome) need multidisciplinary care

References

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