

Sarcoidosis

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Definition

- Noncaseating (nonnecrotic) granulomas
- Unknown cause
- Systemic disease
- Clinical consistency
- No pathognomonic criteria
- Diagnosis of exclusion

Epidemiology

- Age range - 20 to 40 y.o.
- 2:1 Female:Male
- Presents more commonly in the winter and early spring months
- Incidence rates in the United States
 - 10.9/100,000 for whites
 - 35.5/100,000 for African-Americans
- Lifetime risk in the United States
 - 0.85% for whites
 - 2.4% for African-Americans

Pathogenesis

- Unknown
- Person-to-person transmission or shared exposure to an environmental agent
- No definitive identification of an infectious organism
- Genetic factors
 - Familial clusters of sarcoidosis
 - Associations with class I HLA-A1 and B8, and class II HLA-DR3

Immunologic Features

- Three major events
 - Exposure to antigen
 - Acquired cellular immunity directed against the antigen
 - Appearance of immune effector cells that promote a more nonspecific inflammatory response
- Mainly a CD4 T helper 1 event

Clinical Evaluation

- Thorough history with emphasis on occupational and environmental exposure
- Physical exam with emphasis on lung, skin, eye, liver, heart
- Biopsy to obtain histologic confirmation of noncaseating granulomas
- Chest radiography
- Pulmonary-function testing
- Electrocardiography
- Ophthalmologic evaluation with slit-lamp examination
- Biochemical panel to evaluate hepatic and renal function, serum Ca^{++}

Organ Involvement

- Respiratory tract
- Larynx
- Sinonasal
- Ocular
- Salivary Gland
- Cervical Lymph Node
- Skin
- Nervous System
- Cardiac
- Bone, Liver, Spleen, Kidney

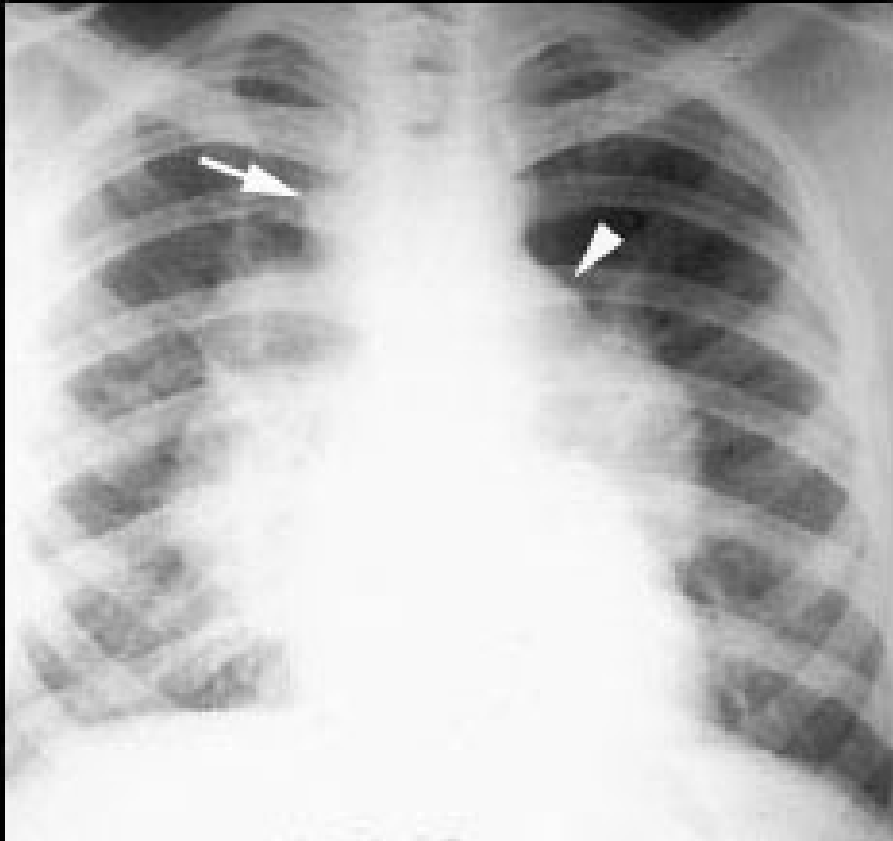
Respiratory Tract

- Occurs at sometime in all patients
 - 90% as sole manifestation of sarcoidosis
- Interstitial lung disorder involving alveoli, blood vessels, bronchioles (i.e. - “T cell alveolitis”)
- Transbronchial lung biopsy diagnostic in >80% of cases

CXR Staging System

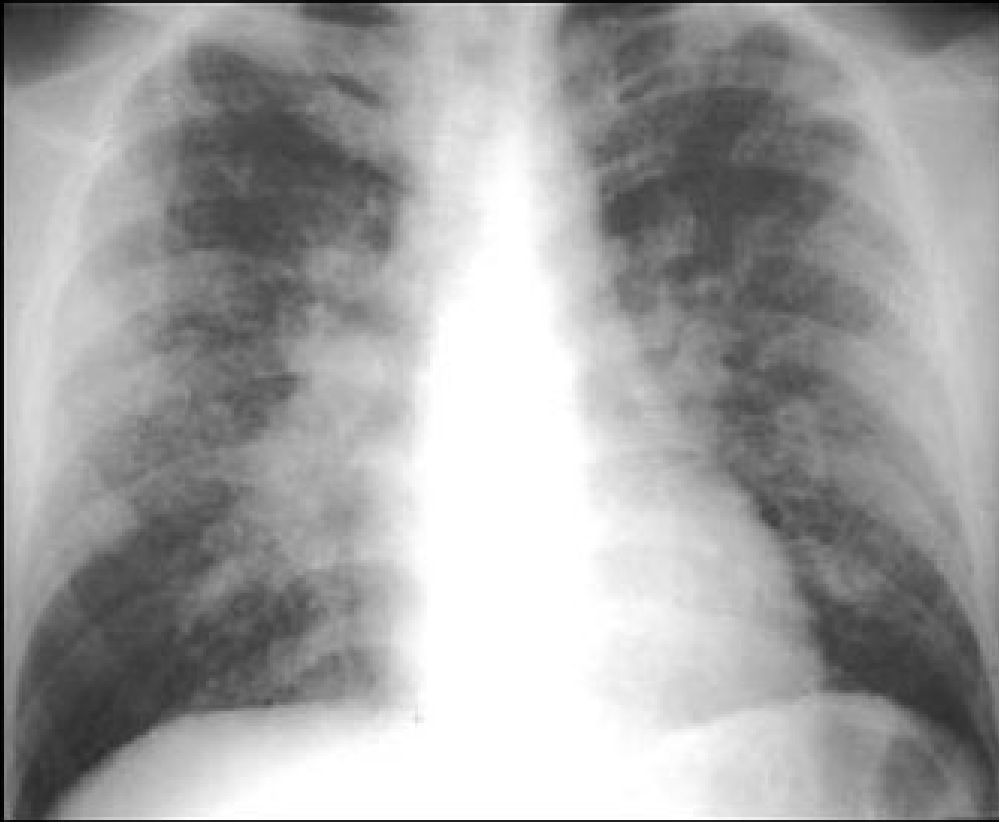
Stage	Description	Clinical Presentation	Prognosis
0	Normal	Asymptomatic Normal/mildly abnormal PFTs	Excellent
1	Bilateral hilar adenopathy	Asymptomatic Mildly abnormal PFTs	Excellent
2	Bilateral hilar adenopathy and pulmonary infiltrates	Some respiratory symptoms Mildly abnormal PFTs	Good
3	Pulmonary infiltrates only	Significant respiratory symptoms Moderately abnormal PFTs	Good to Fair
4	Pulmonary fibrosis	Severe respiratory symptoms Severely abnormal PFTs	Fair to Poor

Stage 1



- 50% of patients
- No respiratory symptoms
- 60 to 80% spontaneous remission

Stage 2



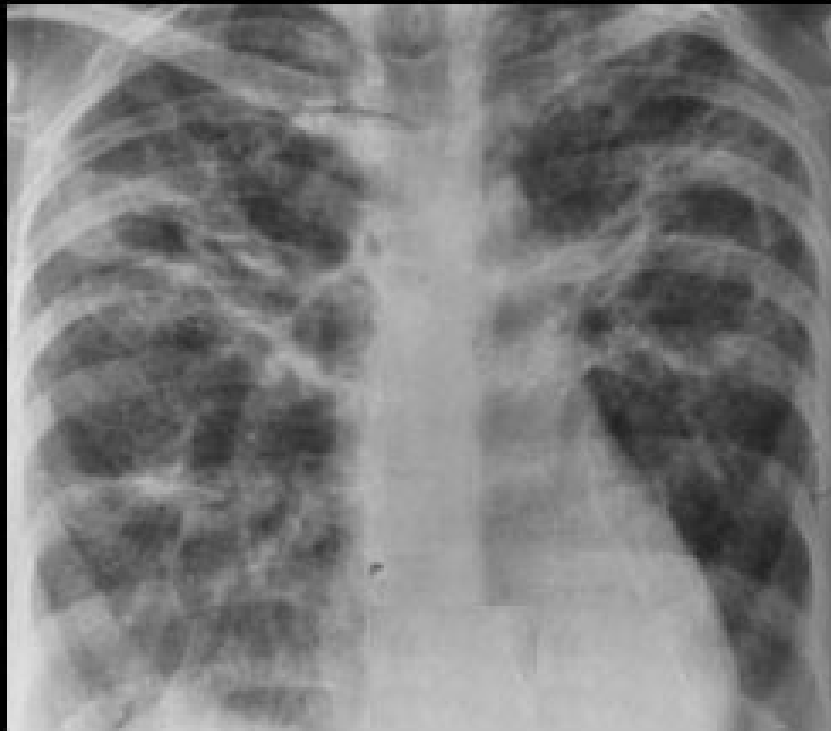
- 25% of patients
- Symptoms - fever, weight loss, shortness of breath
- 50-60% spontaneous remission

Stage 3



- 15% of patients
- Significant respiratory impairment
- <30% spontaneous remission

Stage 4



- 5% of patients
- Chronic respiratory impairment
- High mortality rate

Laryngeal Involvement

- 1 to 5% of patients
- Hoarseness, dyspnea, stridor, dysphagia, and cough
- Epiglottitis most commonly involved
- Localized erythema and edema with punctate nodules and mass lesions
- Treatment with systemic corticosteroids or intralesional steroid injections

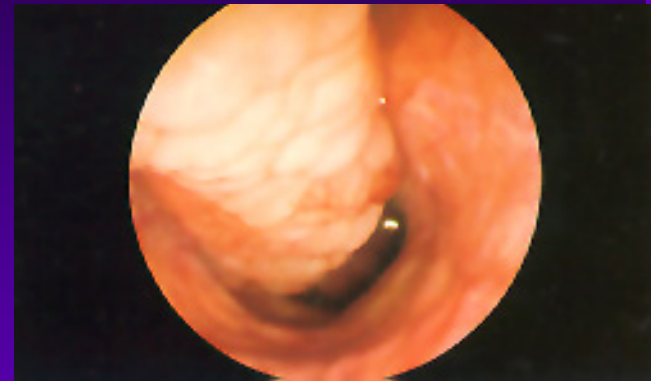


Auditory and Vestibular Involvement

- Sensorineural hearing loss
 - 1% of patients
 - sudden, asymmetrical and fluctuating
 - associated tinnitus
- Conductive hearing loss
- Vestibular dysfunction
 - Central and peripheral
 - Absent caloric responses

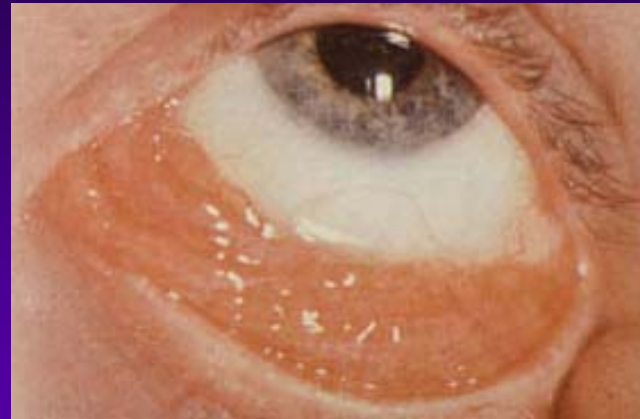
Sinonasal Involvement

- 1% of patients
- Intra- or extra-nasal involvement
- Nasal obstruction, dryness, thick discharge, crusting, epistaxis
- Predilection for septal and turbinate involvement
- Small 1 mm yellow nodules surrounded by hyperemic mucosa
- Mucosal thickening of sinuses



Ocular Involvement

- 15-25% of patients
- Chorioretinitis, retinal periphlebitis, vitreous opacities, uveitis, keratoconjunctivitis
- Lacrimal gland enlargement



Skin Involvement

- 21% of patients
- Most common presentation is erythema nodosum
- Maculopapular eruptions, skin plaques, alopecia, subcutaneous nodules, and lupus pernio
- Infiltration of old scars

Skin Involvement

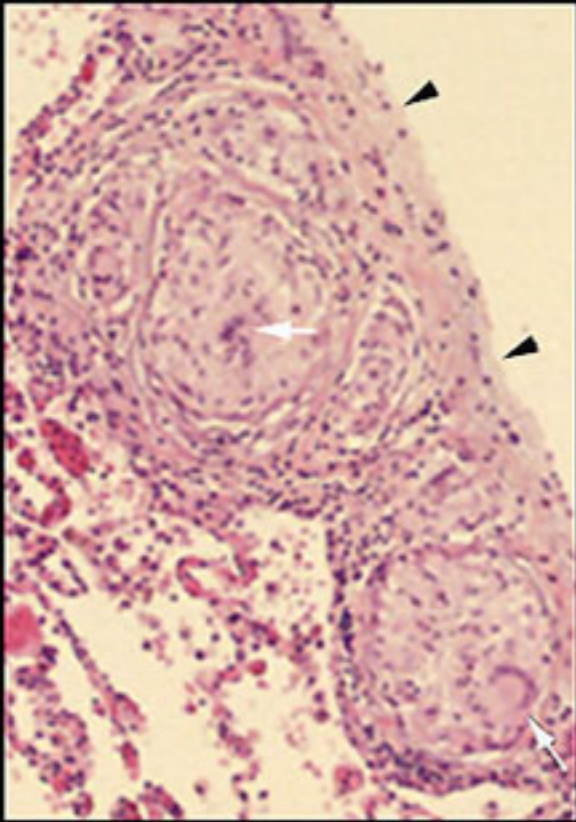


Erythema nodosum

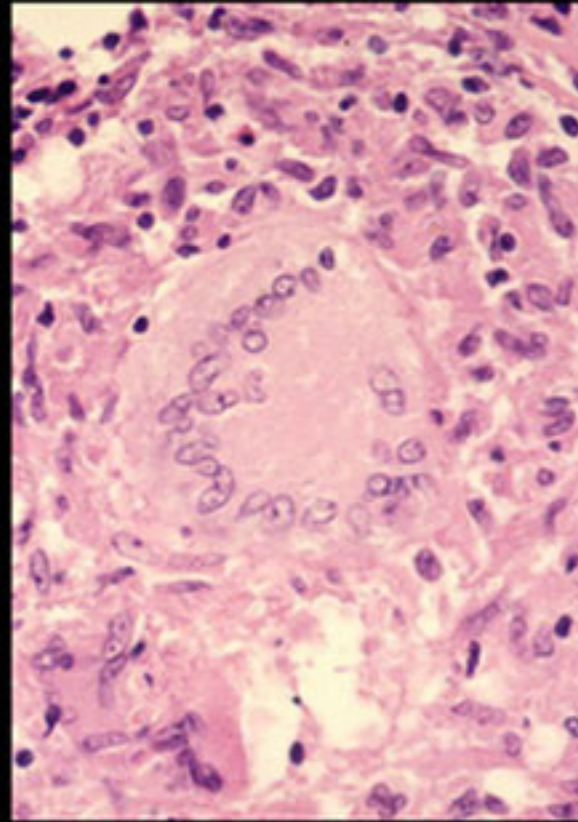


Lupus pernio

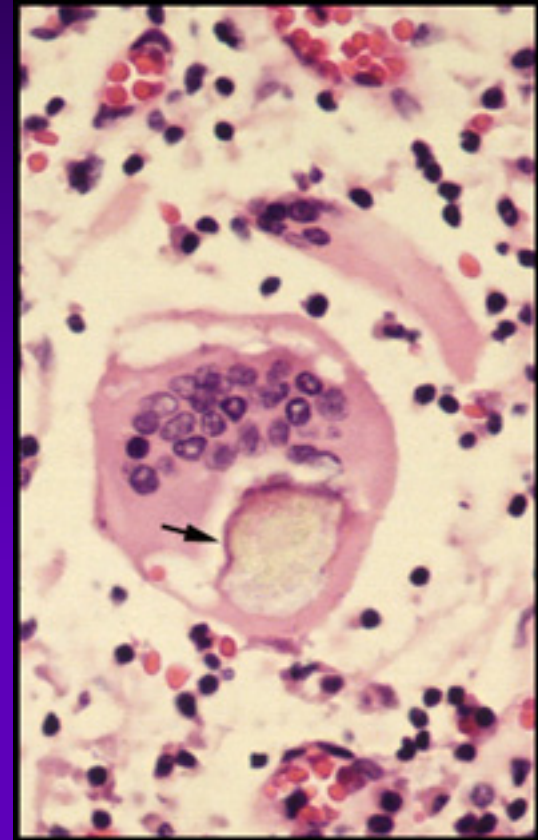
Pathology



Noncaseating granulomas



Multinucleated giant cell



Schaumann body

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Salivary Gland Involvement

- 6% of patients
- Bilateral enlarged parotid glands and dry mouth
- Self-limiting disease in 40% of patients
- 1/3 with parotid involvement experience facial nerve weakness
- Gallium-67 scanning demonstrates subclinical involvement - Panda image

Cervical Lymph Node Involvement

- 28-76% of patients
- Most common head and neck presentation
- Posterior cervical lymph nodes most frequently involved
- Usually bilateral
- FNA Biopsy can confirm diagnosis

Nervous System Involvement

- 5% of patients
- Most common presentation - unilateral facial paralysis
- Other cranial nerves involved -
CN2 > CN10 > CN8 > CN 5
- Meningitis, seizures, diabetes insipidus, or hypopituitarism

Cardiac Involvement

- 5 to 27% of patients
- 45% with ventricular dysrhythmia
- 25% may present with sudden death - usually young males
- Heart block, supraventricular dysrhythmia, and congestive heart failure

Syndromes

- Heerfordt's syndrome (Uveoparotid fever)
 - Facial paralysis
 - Fever
 - Uveitis
 - Bilateral parotid swelling
- Lofgren syndrome
 - Erythema nodosum
 - Bilateral hilar lymphadenopathy
 - Fever
 - Acute polyarthritis

Treatment

- Initially, observation as up to 85% will have spontaneous improvement (6 mo. - 1 yr.)
- Oral corticosteroids indicated in patients with:
 - severe ocular, neurologic, or cardiac presentations
 - malignant hypercalcemia
 - symptomatic or progressive stage II pulmonary disease
 - Stage III pulmonary disease
- Suggested regimen
 - Prednisone - 30 to 40 mg qd for 3 months, with taper to 10 to 20 mg qod for 12 months

Treatment

- Methotrexate - for patients refractory to steroids or cannot tolerate side effects
 - monitor liver function, neutropenia
- Antimalarial agents - hydroxychloriquine
- Quinolones - for hypercalcemia
- Experimental drugs - azathioprine, chlorambucil, cyclophosphamide, cyclosporine A

Laboratory Evaluation

- Erythrocyte sedimentation rate (ESR)
- Hypercalcemia and hypercalcuria - 10 to 15% of patients
- Hypergammaglobulinemia - 20 to 25% of patients
- Liver function tests - 10% of patients
- Serum Angiotensin Converting Enzyme (SACE) - not predictive of disease severity or prognosis
- Suggested markers - Neopterin, IL-2R, sCD27, ADA, adhesion molecules
- Kveim-Siltzbach test

Radiologic Evaluation

- Chest Radiograph
- Chest Computed Tomography
- Gallium-67 Citrate Scanning
 - Panda image in face
 - Lambda pattern in chest

Biopsy Sites

- Transbronchial lung biopsy
- Tonsils
- Conjunctiva
- Cervical lymph nodes
- Lower lip/minor salivary gland
- Nasal mucosa (inferior turbinates)
- Skin

Note: Need to do special stains and cultures to rule out an infectious cause.