

SARCOIDOSIS

- I. Definition: a systemic disorder of unknown etiology characterized by the formation of noncaseating granuloma; primarily affects the lung and lymphatic systems
- II. Epidemiology: occurs worldwide including all races, both sexes, and all ages; however higher incidence in adults under the age of 40 (peaking in 20-29) and in certain ethnicity including US blacks, Irish, and Scandinavians; prevalence is estimated to be anywhere from <1 to 40 cases per 100,000 population; age-adjusted annual incidence rate in US is 10.9 per 100,000 for whites and 35.5 per 100,000 for blacks; lifetime risk for US blacks is 2.4% vs. 0.85% for US whites
- III. Etiology/Pathogenesis: unclear but speculations about infectious and/or environmental agents including mycobacteria, metal dusts & organic antigens have been suggested; noncaseating granulomas are formed when mononuclear inflammatory cells accumulate in the target organs and differentiate into epithelioid and multinucleated giant cells which are surrounded by T (CD4 & 8) lymphocytes and B lymphocytes
- IV. Clinical presentation: ranges from asymptomatic to multiorgan failure; can be self-limited or chronic; typically present with acute or insidious respiratory problems including dyspnea on exertion, retrosternal chest pain, and cough; other systemic symptoms include fatigue, anorexia, weight loss, and fever; *Lofgren's syndrome* includes erythema nodosum, bilateral hilar lymphadenopathy, and polyarthralgias
- V. Organ Involvement:
 - A. Respiratory: typically an interstitial lung disorder involving alveoli, blood vessels, and bronchioles producing dry rales, restricted lung volumes and abnormal gas exchange; airways can also be affected resulting in limitations of air flow
 - B. Lymphatics: up to 90% have hilar node enlargement; peripheral nodes are typically non-tender
 - C. Heart: 5-10% have serious cardiac dysfunctions including abnormal rhythm, conduction, repolarization, papillary muscle dysfunction, infiltrative cardiomyopathy, pericarditis (Thallium 201 scan is useful but not specific)
 - D. Skin: approximately 25% present with raised, tender, red nodules of erythema nodosum, macules, papules, or plaques; granulomas are frequently absent in these biopsies
 - E. Eyes: approximately 25% develop ophthalmic lesions resulting in anterior uveitis, blurred vision, photophobia, excessive lacrimation & sometimes leading to blindness

- F. Nervous System: (5%); any part may be affected, but most commonly unilateral facial nerve palsy
 - G. Endocrine: overproduction of 1,25-dihydroxyvitamin D leads to increased intestinal absorption of Ca⁺⁺, enhanced bone resorption, and resultant hypercalciuria with or without hypercalcemia
 - H. Renal: nephrocalcinosis; nephrolithiasis; and renal insufficiency/failure
 - I. Gastrointestinal: clinically recognizable GI involvement occurs in 0.1-0.9% of sarcoidosis; 40-70% have liver involvement although clinically significant hepatic dysfunction is rare; manifestations include peptic ulcerations, nodules, pyloric obstruction, gastritis, impaired peristalsis, thickened mucosal w/ nondistensibility, chyloperitoneum
- VI. Diagnosis: diagnosis of exclusion; must rule out other potential causes of granulomatous diseases such as chronic beryllium disease (serum or BAL beryllium lymphocyte proliferation test), Wegener's (ANCA), PBC (antimitochondrial ab) fungal diseases including Histoplasmosis, and mycobacteria; suspected cases should be confirmed with a biopsy to exclude infection or malignant conditions especially if treatment is considered; other supporting tests include serum ACE activity, gallium-67 scan, CD4:CD8 ratio from BAL, Kveim-Siltzbach skin test
- VII. Stages:
- A. Stage 0: normal CXR
 - B. Stage I: bilateral hilar lymphadenopathy (remits in 60-80%)
 - C. Stage II: hilar lymphadenopathy with pulmonary infiltrates (remits in 50-60%)
 - D. Stage III: pulmonary infiltrates without hilar LAD (remits in <30%)
 - E. Stage IV: pulmonary fibrosis
- VIII. Treatment: Initially pt should be observed without therapy because of potential spontaneous remission (40%). First line therapy is corticosteroids usually indicated in severe ocular, neurologic, or cardiac sarcoidosis, malignant hypercalcemia, symptomatic stage II or higher. Current recommendations suggest prednisone 30-40 mg daily for 8-12 wks then gradually tapered to 10-20 mg every other day over a period of 6-12 months to establish the minimal effective dose. Alternative therapy includes methotrexate 10 mg per wk, cyclosporine, hydroxychloroquine, other immunosuppressants.