outline

- Introduction/Epi/Genetics
- Clinical features
  - Acute/Lofgren’s vs chronic
- Pathogenesis
- Treatment
First described 1877 by Dr Jonathan Hutchinson

Dr Caesar Boeck felt they resembles sarcoma, thus “sarcoid”

1953 Dr Sven Lofgren described the acute triad
A multisystem inflammatory disorder characterized by noncaseating granulomas that can infiltrate any organ.

Most commonly with hilar adenopathy, pulmonary infiltration, ocular and skin lesions:
- lungs, lymphatics, eyes, skin, liver, bone, nerves, heart.

Early adulthood (ages 20-40) and peak #2 in women >50.
sarcoid epi/genetics

- Does run in families
  - ACC ESS: RR = 5 among first degree relatives of patients
- Incidence: 10 - 40 per 100K (US)
  - AA 35.5/100K
  - C 10.9/100K
- Linkages and candidate genes
  - MHC locus, multiple alleles (HLA-DR3 and DQ2→Lofgren’s)
  - F allele of Factor B
  - TNFa, IL1a, IRF-4, MCP-1, ATII type I rec, ACE (DD genotype)
Acute sarcoidosis

- Abrupt onset, self-limited course
- Often associated with erythema nodosum, vesicles, or macular papular rash
- Acute iritis, conjunctivitis, nodules common
- Bell’s palsy may precede or accompany.
- Bone cysts are rare, hypercalcemia/uria in 20%
- CXR nl or with LAN but no infiltrates
- Arrhythmias if cor infiltrated
acute sarcoidosis/clinical features

- Overall good prognosis, less relapse than chronic presentation
- Synovial fluid is mildly inflammatory 3000 (80% pmn)
- Visser: 4 clinical features with high degree of diagnostic certainty for acute sarcoid...
  - Symmetric ankle arthritis
  - Symptoms < two months
  - Age less than 40
  - Erythema nodosum
Lofgren’s syndrome

- Triad of erythema nodosum, bilateral hilar adenopathy, arthritis (+/- fever, uveitis)
- Arthritis typically involving ankles and knees
- Excellent response to corticosteroids
- >90% remission rate with <30% recur
periartthritis
joint involvement

- Symmetric arthralgia or arthritis
- Commonly affects large joints
  - Ankles, knees, wrists, elbows
- Present with joint pain and stiffness
- If acute: Usually subsides without recurrence or joint deformity
  - Chronic form will destroy joints, and is usually accompanied by skin lesions
- Synovial fluid demonstrates sterile lymphocytosis and elevated protein in acute sarcoid arthritis
  - More inflammatory in chronic form
Chronic sarcoid synovial bx
chronic sarcoidosis/clinical features

- Usually insidious in onset, chronic course
- Occurs in older patients
- Skin lesions
  - Plaques
  - Keloids
  - Nodules within surgical incision lines/scars
  - Lupus pernio (a persistent, disfiguring, violet rash over the nose, cheeks, ears)
chronic sarcoidosis/clinical features

- Eye involvement
  - Chronic uveitis
  - Cataracts
  - Glaucoma
  - KCS

- Bone involvement with destructive lesions
- Pulmonary infiltrates
- Nephrocalcinosis
- Cardiac involvement with cor pulmonale
- Synovial fluid is inflammatory 25K (90% pmn)
Granulomatus involvement

- Lung (86%)
- Lymph nodes (86%)
- Liver (86%)
- Muscle (75%)
- Spleen (63%)
- Eyes (25-50%)
- Skin (30%)
- Heart (20%)
- Kidney (19%)
- Bone marrow (17%)
- Pancreas (6%)
etiology and pathogenesis

- Antigen uptake by professional APCs bearing MHC II.
- CD4+ T-helper cells recognize and proliferate and activate monos
- Endothelial cells, epithelial cells, other inflammatory cells increase tissue permeability and cell migration by producing chemokines and adhesion molecules
  - MF → IL-8,-12,-15, RANTES (regulated on activation normal T expressed secreted)
  - MCP-1 (macrophage chemoattractant protein-1)
  - MIP-1a (macrophage inflammatory protein-1a)
  - IL-8, ICAM-1 (intercellular adhesion molecule-1)
  - VCAM-1 (vascular cell adhesion molecule-1)
  - Selectins
etiology and pathogenesis

- In early alveolitis, BAL shows increased CD4/CD8 T-lymphocyte ratio
  - elevated lymphocyte count
  - Increase in macrophage number
  - CD8 V\(\alpha\) 2.3 expansions in BAL

- Granuloma morphology and histology suggests an antigen-driven process

- B-cell hyperactivity and circulation of immune complexes have been shown
therapy

Acute

- NSAIDS, steroids
  - Goal taper $\leq 15\text{mg/d}$
  - If unable add DMARD (MTX)
- Mucocutaneous
  - HCQ, minocycline

Chronic and/or internal organ involvement

- Steroids + DMARD/cytotoxic agent
  - MTX, MMF, AZA, CYC
- ?aTNF
  - Infliximab improved pulm fx in recent trial, etanercept was not helpful
references