Sarcoidosis

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Introduction

Sarcoidosis is a common multisystem granulomatous disorder of unclear aetiology characterized by focal accumulations of epithelioid cells, macrophages & lymphocytes, particularly T cells

Risk Factors

- Northern European origin
- Afro-Caribbean ethnicity
- Females > Males
- 3rd to 5th decade of life
- Family history
- Rural populations
- Non-smokers

Presentation

Incidental diagnosis (20-40%)
- Bilateral hilar lymphadenopathy (BHL) &/or pulmonary infiltration on CXR/CT

Pulmonary
- Cough, dyspnoea, chest pain

Systemic
- Fevers, weight loss, fatigue, splenomegaly, lymphadenopathy

Hepatic
- Deranged LFTs (typically mild), hepatomegaly

Ocular
- Anterior uveitis, keratoconjunctivitis sicca, conjunctivitis, glaucoma

Renal/Metabolic
- Hypercalciuria, nephrocalcinosis, renal calculi

Cutaneous (10-30%)
- Erythema nodosum, lupus pernio

Neurological (2%)
- Cognitive dysfunction, headache, cranial nerve palsies, mononeuritis multiplex, peripheral neuropathy, seizures

Cardiac (3%)
- Arrhythmia, heart block, cardiomegaly, sudden death

Musculoskeletal
- Arthralgia, terminal phalangeal bone cysts

Löfgren syndrome
- Common presentation associated with favorable prognosis of BHL, fever, arthralgia & erythema nodosum

Heerfort's syndrome
- Fever, uveitis, parotitis, cranial neuropathies (uveoparotid fever)

Differential for BHL

- Sarcoidosis
- Lymphoma
- Pulmonary TB
- Bronchial carcinoma
- Extrinsic allergic alveolitis
- Histiocytosis X

Investigations

Bloods
- Normochromic normocytic anaemia & lymphopenia (chronic disease)
- Hypercalcaemia (10-20%) & hypercalciuria (30-50%)
- Baseline creatinine & LFTs advised.
- Immunoglobulins if features of common variable immunodeficiency
- Serum ACE: Elevated in 60-75% of untreated sarcoid, nonspecific.

Chest radiograph *(see Scadding criteria)*
- BHL & /or pulmonary infiltrates

High Resolution CT Thorax (HRCT)
- Mediastinal adenopathy (fibrosing mediastinitis in severe cases)
- Pulmonary nodularity (may cause beading along airways, vessels and fissures or coalesce to form masses)
- Classic upper lobe distribution of pulmonary fibrosis

Bronchoalveolar Lavage (BAL)
- Exclude alternative aetiologies (particularly tuberculosis)
- Cell differential: Lymphocytosis is common, especially CD4 T-helper cells

Biopsy
- Not always required in typical presentations
- Guided by sarcoid distribution: Consider transbronchial biopsy or cryobiopsy if lung parenchyma involvement; endobronchial ultrasound if mediastinal/hilar adenopathy present.
- Histology: Typically well-formed, non-caseating granulomata.

Pulmonary Function Tests (PFTs)
- Restrictive defect with reduced gas transfer in pulmonary fibrosis
- Obstructive & mixed pattern also observed with endobronchial disease
- Consider sarcoid associated pulmonary hypertension (SAPH) if markedly reduced gas transfer & no/mild pulmonary fibrosis.

Kveim Test
- Now obsolete: Intradermal injection of splenic/lymph node tissue from sarcoid patient into a patient with suspected disease.

Cardiac Diagnostics
- MRI if cardiac sarcoid suspected. Right heart catheterization if SAPH suspected.

PET-CT
- Has a role in clarifying disease distribution & activity (FDG uptake)

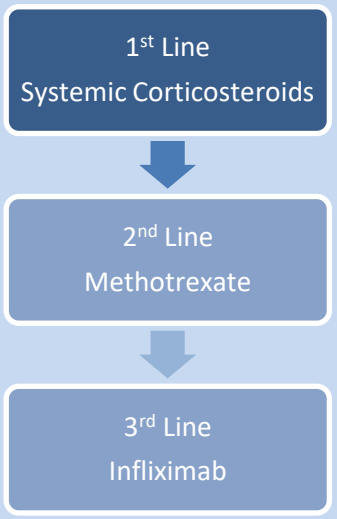
Scadding Criteria (based on chest radiograph)

Stage	Chest XR findings	Frequency at presentation	Spontaneous resolution
Stage 0	Normal	5-15%	
Stage I	Hilar or mediastinal nodal enlargement	25-65%	60-90%
Stage II	Nodal enlargement & parenchymal disease	20-40%	40-70%
Stage III	Parenchymal disease only	10-15%	10-20%
Stage IV	Pulmonary fibrosis	5%	0%

Treatment

- Individualised treatment decisions are guided by the site & severity of the disease, response to previous therapy, patient preference & overall clinical picture.
- Topical steroids may be used for cutaneous and ocular disease
- Indications for systemic therapy include worsening PFTs, pulmonary imaging, hypercalcaemia or neurological or cardiac involvement.
- Systemic corticosteroids are first line agent in pulmonary sarcoid requiring treatment (consider bone health)
- Steroid sparing agents include methotrexate, azathioprine, mycophenolate mofetil, hydroxychloroquine, ciclosporin, cyclophosphamide, leflunomide, adalimumab, infliximab, rituximab
- Lung transplantation can be considered in select cases of end-stage pulmonary disease & respiratory failure.
- All patients on active treatment should be monitored closely in a specialised service

Treatment options for Pulmonary Sarcoid



Prognosis

- Unpredictable: Spontaneous remission of pulmonary sarcoidosis may occur in 60% within 2 years of diagnosis.
- Poor outcomes associated with Afro-Caribbean or Asian ethnicity, extra-thoracic disease, chronic pulmonary involvement, lupus pernio & chronic hypercalcaemia