Sarcoidosis and Uveitis

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Sarcoidosis
a multisystem chronic inflammation causing multifocal non-caseating granulomas

BUT – Diagnosis often made indirectly (without histology)

Clinical manifestations can be protean

Limited organ involvement well-recognised (possibly ocular only)
Aetiology?
Genetic susceptibility – environmental provocateur

• Possible associated micro-organisms:
  – Cell wall-deficient mycobacteria - \textit{MAC, M. paratuberculosis}
  – Propionibacteria - \textit{P.acnes, P.granulosum}
  – Chlamydia trachomatis
  – Human herpesvirus Type 8
  – Rickettsia helvetica

• Seasonal peaks of presentation

• Significant exposure to:
  – Titanium
  – Dust in vegetable processing
  – Sustained high humidity
  – Photocopier toner
Sarcoid uveitis – prevalence and age

- Incidence of sarcoidosis 5:100,000:yr
  - Male 1:1.5 female
  - 20-25% get uveitis

- MUC total 309
- Asian 18% (pop 6.5%)
- Black 18% (pop 1.7%)
Clinical appearance: anterior

- Characteristically a “granulomatous” uveitis:
  - Large inferior KPs
    - Greasy, mutton-fat
    - Partly confluent
    - Often glueing angle
  - Presentation subacute
  - Eye relatively white
  - Raised IOP frequent
  - PS/PAS frequent
Clinical appearance: anterior

- Iris nodules are infrequent
  - Typically irregular in distribution
  - Typically smallish, sticky
  - Rarely large:
  - If so, sometimes vascularised
The vitreous in sarcoidosis

• 15% of sarcoid uveitis presents as intermediate-type, with large-ish opacities, inferior snowballs +/- snowbanking

• 10% of intermediates diagnosed sarcoidosis
Retinal vasculature

- Intermittent periphlebitis with:
  - exudate
  - tortuosity
  - narrowing
Retinal vasculature

- Macroaneurysm
Retinal vasculature

- Vascular occlusion: uncommon
  - creeping peripheral closedown
  - acute occlusion very uncommon
  - consider TB
Choroid and retina

- Typical - multifocal choroiditis
  - Smallish, creamy, moderately-well defined
  - Especially in inferior and nasal fundus
Choroid and retina

• Very uncommon – solitary nodule
Optic nerve head
Overall commonest description of sarcoid-associated uveitis:
Chronic panuveitis (34% MUC)
Systemic involvement

- Syndromes: Löfgren’s, Heerfordt’s
- Pulmonary (<90%)
  - Hilar nodes, interstitial fibrosis
- Neurological
  - Cranial nerves, meningeal
- Skin
- Myocardial
- Arthropathy etc
Diagnosing Sarcoidosis - ACE

- Angiotensin Converting Enzyme
  - Produced by endothelial cells in lung, kidney, gonads
  - Normal adult serum levels up to 55 or more (IU/l)
    - But variable phenotypic expression in normals
  - Normal childhood/adolescent levels up to 75 IU/l

- Secreted by macrophages in sarcoid granulomas
  - Or in Gaucher’s, asbestosis, miliary TB, Hodgkin’s disease etc

- If ACE >100 IU/l, high likelihood of sarcoidosis

- Beware effect of ACE1/ACE2 inhibitors
  - ? Re-introduce lysozyme estimation
Diagnosing Sarcoidosis - Lymphopenia

• Low lymphocyte count a marker for sarcoidosis, sarcoid severity and poorer prognosis
• Holds true for uveitis as sole manifestation: 28% of sarcoid uveitis has lymphocyte count <1.0x10^9
• (5% of controls)
Diagnosing Sarcoidosis - Chest radiography

- High-resolution chest CT:
  - Better identification of hilar/subpleural nodes
  - Perivascular micronodules
  - Ground-glass parenchyma
  - Can detect nodes even if CXR reported normal
  - Absence of micronodules/ground glass on HRCT does **not** confirm absence of pulmonary granulomas
Diagnosing Sarcoid – 18FDG-PET

- 18-fludeoxyglucose specific take-up into sarcoid granulomata
Diagnosing Sarcoidosis - Biopsy

- Bronchoalveolar lavage/biopsy
- Fine-needle liver biopsy – if clinically indicated
- Conjunctival biopsy – directed only
- Skin biopsy – yes!
Diagnosing Sarcoidosis - others

• Calcium metabolism
  – Sarcoid granulomas secrete vitamin D but:
    • only 10% have hypercalcaemia
    • only 2% are symptomatic
  – Ca^{++} raised, PO_4^{-} N, Phosphatase sl raised
  – 24-hr urinary Calcium raised

• Anergy (to tuberculin or other antigens)
NPJ diagnosis/referral

• “Qualifying” uveitis:
  – ACE, lymphopenia
  – CXR: if equivocal, or if normal with raised ACE - Chest CT
  – Liver & kidney function
  – Biopsy easily-accessible skin/conj lesions
  – Abnormal CXR or systemic symptoms – physician referral for:
    • Baseline lung function
    • Bronchoscopy + lavage ? Biopsy
  – Exclude TB, especially if:
    • very asymmetric disease
    • substantial or occlusive retinal vasculitis
    • other risk factors identified
Treating sarcoidosis

• There are no aspects of ocular sarcoidosis which are disease-specific; general principles of uveitis treatment

• Almost all are steroid-responsive
  – if resistant – reconsider TB

• Depot/intraocular steroid for macular oedema

• Immunosuppression – sometimes but not often

• Anti-TNF alpha?
  – Infliximab highly effective for severe pulmonary disease (but exclude TB!)

• Cataract and glaucoma – treat as required
To conclude:

- A common cause of uveitis in Western world
- Most patients with uveitis present because of it:
  - Later development is unusual
  - Should patients be screened for ocular disease?
- Liaison with physicians - control dosage of drugs
- Only rarely a blinding disease