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 - MAC, M. paratuberculosis
  – Propionibacteria - P.acnes, P.granulosis
  – 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 315
- Asian 18% (pop 6.5%) = x3 risk
- Black 18% (pop 1.7%) = x10 risk
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, very 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
UVEITIS
SECOND EDITION
Nicholas Jones FRC Ophth

All the files listed below have been made available by the author in fully editable format for adaptation and use in clinical practice.

Management protocols
- Acute Anterior Uveitis
  - Unilateral
- Aqueous Sampling
- Azathioprine
- Bevacizumab
  - Intraocular
- Cardiovascular Disease in the Uveitis Clinic
- Cataract Surgery
- Ciclosporin
- Ganciclovir - Intraocular
- Health Review Form
  - Instructions
- Health Review Form

Patient information pamphlets
- Methotrexate
- Methylprednisolone
  - Intravenous
- Mycophenolate Mofetil
- Prednisolone
- Sarcoidosis
  - Diagnosis
- Tacrolimus
- Toxoplasmosis
- Triamcinolone
  - Intraocular
- Varicella-Zoster Virus
- Viral Retinitis
- Anti TNF alpha
- Azathioprine
- Behçet’s Disease
- Birdshot Retinopathy
- Cataract
- Ciclosporin
- Fuchs’ Heterochromic Uveitis
- Glaucoma
- HLA-B27
- Immunosuppression, Vaccination and Travel Abroad
- Intermediate Uveitis
- Juvenile Idiopathic Arthritis Screening
- Macular Oedema
- Methotrexate
- Mycophenolate Mofetil
- New Patient Questionnaire
- Prednisolone
- Sarcoidosis
- Tacrolimus
- Toxoplasmosis
- Triamcinolone
  - Intraocular
- Uveitis
- Viral Retinitis
- Vitrectomy