Sarcoidosis and Uveitis

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Sarcoidosis
a multisystem chronic inflammation
causing multifocal non-caseating granulomas
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a multisystem chronic inflammation
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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.granulosisum*
  – 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
Sarcoid uveitis - Demographics

- Incidence of sarcoidosis 5:100,000:yr
  - Male 1:1.5 female
  - 20-25% get uveitis
- Asian 19% (pop 6.5%)  
- Black 21% (pop 1.7%)
  - (MUC Figures)
  - (USA black 15:1 white)
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
The full package

Overall commonest description of sarcoid-associated uveitis:
Chronic panuveitis (34% MUC)
Retinal vasculature

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

• Typical - multifocal choroiditis
  – Smallish, creamy, moderately-well defined
  – Especially in inferior and nasal fundus, but may be widespread
Choroid and retina

- Multifocal choroiditis scars
  - Punctate, peripheral, inferior hemisphere
- Peripheral multifocal chorioretinitis
  - Sometimes associated with sarcoidosis
Choroid and retina

- Very uncommon – solitary nodule
Optic nerve head
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 IU/l
  - 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, overwhelming likelihood of sarcoidosis

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

- Bronchoalveolar lavage/biopsy
- Fine-needle liver biopsy – if clinically indicated
- Conjunctival biopsy – directed only
- Skin biopsy – yes!
- Kveim test - historical
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 – failure of Type IV hypersensitivity
  – Antigens: Tuberculoprotein, tetanus toxoid, Candida antigen, mumps virus
  – Possibly abnormal dendritic cell response
Diagnosing Sarcoidosis – F18,FDG-PET

- Fluorine18, fluorodeoxyglucose Positron Emission Tomography
- Preferential take-up by rapidly metabolising cells
- Extensively used for oncological tumour mapping

- Also identifies occult inflammation in sarcoidosis
  - especially extrapulmonary
  - especially where ACE normal
  - facilitates guided biopsy to confirm diagnosis
Diagnosing Sarcoidosis – F18,FDG-PET
NPJ diagnosis/referral

• “Qualifying” uveitis:
  – ACE
  – 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 if risk identified from patient history
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

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

- Hydroxychloroquine for skin involvement
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