What do you need to know about posterior uveitis

Dr. Anthony Hall  MD FRANZCO
Director of Ophthalmology
Alfred Hospital,
Melbourne, Australia
Alfred Hospital
Disclosures

• Off label treatments
• Paid advisory board Bayer
• Paid research support Allergan (makers of Ozurdex)
• Paid research support B and L (makers of Retisert)
• Paid research support Novartis
My aim: to give you an easy diagnostic approach to posterior uveitis
Your aims of assessment

• Make a descriptive anatomical diagnosis
• Recognise specific named uveitis entities
• Diagnose significant underlying systemic inflammatory/infective disease
• Diagnose intra-ocular/systemic infections/masquerade syndromes
• Diagnose the cause of visual loss
Diagnostic possibilities in intermediate or posterior uveitis

• Isolated ocular disease
  • Idiopathic
  • Named
  • Infectious
• Ocular disease as part of systemic disease
  • Non-infectious
  • Infectious
  • Malignant
• Masquerade syndromes
• Attempt to make an anatomic and descriptive diagnosis
• Use recognised nomenclature
PERSPECTIVES

Standardization of Uveitis Nomenclature for Reporting Clinical Data: Results of the First International Workshop

THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP

PURPOSE: To begin a process of standardization, the methods for reporting clinical data in the field of uveitis.

METHODS: A group surveyed current diagnostic terminology, inflammation grading schemes, and outcome measures, and the results used to develop a series of proposals to better standardize the care of these patients. Small groups completed small group techniques in active conversion on several of these issues.

RESULTS: The group agreed that anatomic classification of uveitis should be the framework for the subsequent and diagnostic criteria for specific uveitic syndromes, and the classification of uveitis enables the description of the diversity of the uveitis and not on the presence of structural abnormalities. In this paper we report the use of the term "classification immune" and "immune" and "irritable" and "inflammatory" and "inflammatory" and "irritable" and "inflammatory" and "irritable" and "inflammatory" for the reporting clinical data sources.

CONCLUSIONS: A process of standardizing this approach to reporting clinical data in uveitis research has begun, and we look forward to its future standardization.

THE AMERICAN COLLEGE OF RHEUMATOLOGY has developed classification criteria for the majority of the uveitis diagnoses such as rheumatoid arthritis and systemic lupus.

©2005 by Lippincott Williams & Wilkins. All rights reserved.
Anatomical classification of uveitis

- Anterior uveitis
- Intermediate uveitis
- Posterior uveitis
- Panuveitis
Anatomical classification of uveitis

• Anterior uveitis
  • Inflammation limited mainly to the anterior segment inc
    • Iritis
    • Anterior cyclitis
    • Iridocyclitis
  • Can be acute or chronic
Anatomical classification of uveitis

• Intermediate uveitis
  • Inflammation limited mainly to the vitreous but may include anterior retina, retinal vasculitis or macular oedema inc
    • Pars planitis
Anatomical classification of uveitis

• Posterior uveitis
  • Inflammation limited mainly to the retina, choroid or optic nerve inc
    • Focal, diffuse or multifocal choroiditis
    • Chorioretinitis
    • Neuroretinitis
    • Serous detachment
Anatomical classification of uveitis

• Panuveitis
  • Inflammation involving the whole eye without preference for anterior or posterior segment
Different clinical pictures in intermediate/posterior/panuveitis

- Diffuse uveitis/vitritis
- Unifocal chorioretinitis
- Multifocal chorioretinitis
- Confluent chorioretinitis
- Retinal vasculitis
- Optic papillitis
- Serous retinal detachment
Different clinical pictures in intermediate/posterior/panuveitis

- Diffuse uveitis/vitritis
- Unifocal chorioretinitis
- Multifocal chorioretinitis
- Confluent chorioretinitis
- Retinal vasculitis
- Optic papillitis
- Serous retinal detachment

- Isolated ocular disease
  - Idiopathic
  - Named
  - Infectious

- Ocular disease as part of systemic disease
  - Non-infectious
  - Infectious
  - Malignant

- Masquerade syndromes
Non specific/diffuse uveitis

- Vitritis
- +/- macular oedema
- +/- retinal vasculitis
- No focal signs
Intermediate uveitis without localizing features

- Ocular diagnoses
  - Intermediate uveitis
  - Sympathetic ophthalmia
  - Fuch’s heterochromic iridocyclitis

- Systemic diagnoses
  - Often idiopathic!
  - Sarcoidosis
  - Behcet’s
  - MS
  - Oculo-cerebral lymphoma
  - Syphilis
  - TINU
Fuch's heterochromic iridocyclitis

• Chronic unilateral uveitis
• Iris changes
  • Atrophy
  • Heterochromia
• Widespread non pig KP
• Anterior vitritis
• High incidence of cataract and glaucoma
• Poor response to topical steroids
Fuch’s

- NB
  - Characteristic KP
    - Widespread, non pigmented, stellate
  - Vitritis is common and may be severe
  - May not have heterochromia
  - 5-10% bilateral
Intermediate uveitis

- Common
- Young and middle aged
- +/- macular oedema
- +/- retinal vasculitis
- +/- inferior snow balls
- +/- snow bank

- 1/3 require topical treatment only
- 1/3 intermittent orbital or systemic therapy
- 1/3 more than steroids
Investigation of intermediate uveitis without localising features

- History
- FBE
- U&E, LFT
- Syph serology
- ACE
- If indicated
  - MR brain
  - LP
Unifocal chorioretinitis

- Uveitis
- Single focus of retinal or chorioretinal inflammation
Unifocal chorioretinitis

- **Ocular diagnoses**
  - Toxoplasmosis
  - Toxocara
  - Candida

- **Systemic diagnoses**
  - Sarcoidosis
  - Candida
  - (other fungal)
Toxoplasmosis

- Unilateral uveitis
- Active focus of chorioretinitis – usually adjacent to an old scar
  - AC activity
  - Raised pressure
- Otherwise well patient
- Clinical diagnosis!
- Can be confirmed by vitreous PCR if needed
Candida

- Unilateral uveitis
- Single (or multiple) focus of chorioretinitis with no adjacent scar
- May have vitreous puffballs or preretinal lesions
- At risk patient
  - Recent IV access
  - IVDU
  - Sick inpatients
- Diagnosed clinically and confirmed with systemic cultures or vit tap/Vx
Toxocara

- Uncommon cause of unilateral uveitis and focal chorioretinitis
- Mainly young children
  - Focal chorioretinitis
    - Peripheral
    - Posterior pole
  - Rarely endophthalmitis
Investigation of unifocal chorioretinitis

- History
- Toxoplasmosis serology
- FBE
- ACE
- If indicated
  - Toxocara serology
  - Blood/urine cultures
  - Vit tap
    - Toxoplasma pcr
    - Fungal cultures
Diffuse/confluent chorioretinitis

- Uveitis
- Widespread confluent area of chorioretinal inflammation
- Often with
  - Retinal vasculitis
  - Optic nerve swelling
Diffuse chorioretinitis

- **Ocular diagnoses**
  - Viral retinitis
  - Serpiginous choroidopathy
  - Fungal retinitis

- **Systemic diagnoses**
  - Oculo-cerebral lymphoma
  - Syphilis
  - Immuno-suppression/AIDS (and viral retinitis)
CMV retinitis

• Confluent retinitis
• Haemorrhage and progressive scarring
• Mild vitritis
• HIV positive with low CD4 count
• Treated with IV or intravitreal antivirals and with immune restoration
Acute retinal necrosis

- Rapidly progressive peripheral retinitis
- Well patients
- VZV or HSV
- High incidence of retinal detachment
- Treated with IV/intravitreal antivirals
Serpiginous choroiditis

- Relapsing remitting slowly progressive chorioretinitis with quiet vitreous
- Typical serpentine shape
- Posterior pole
- Beware TB
Serpiginous in Australia

- ¼ had TB

Original Article

Retrospective analysis of the natural history and management of serpiginous choroiditis in Australia and New Zealand

Jason Torrealdo MBBS, Anthony J Hall FRANZCO, Joe Sers FRANZCO,
Samantha Frazer Bell FRANZCO, Jane Ilhan FRANZCO, Christine Younan FRANZCO,
Ilhan Kent Smith FRANZCO, Stephanie Young FRANZCO, Liebo Paul MBCh
Lyndell Illman FRANZCO FRCO
Investigation of diffuse chorioretinitis

• History

• FBE, U&E, LFT
• HIV viral load, CD4 count
• CMV viral load

• Consider
  • Quantiferon
  • Vit tap
    • Herpes pcr
    • Fungal cultures
  • MRI
Multifocal choroiditis

- Multifocal choroiditis is common in many forms of uveitis and often does not carry diagnostic significance.
Multifocal choroiditis

- Ocular diagnoses
  - No inflammation
  - Mild inflammation
  - Significant inflammation

- Systemic diagnoses
  - Sarcoidosis
  - Behcet's
  - Oculo-cerebral lymphoma
  - Infection
    - TB
    - Cryptococcus
    - PCP
    - syphillis
An approach to multiple white retinal lesions

- **No inflammation**
  - Flavimaculatus
  - Punctata albescens
  - PIC
  - POHS

- **Min inflammation**
  - AMPPE
  - MEWDS

- **Lots of inflammation**
  - Multifocal choroiditis
  - Sympathetic
  - Birdshot
  - Sarcoidosis
  - Infections
Punctate inner choroidopathy (PIC)

- Myopic women
- Small pale atrophic lesions around the posterior pole
- Minimal or no vitritis
- CNVM common
POHS

- Atrophic peripheral scars and streaks
- Peripapillary atrophy
- Macular CNVM very common
- More common in the USA
AMPPE

• Young adults
• acute decrease in central visual acuity in association with subretinal yellow-white placoid lesions of the posterior pole
• Mild AC and vitreous activity
• spontaneous recovery
MEWDS

- Young women
- Sudden onset unilateral visual loss with photopsia
- Small pale evanescent white outer retinal dots
- Mild AC and vitreous activity
- Spontaneous recovery
Sympathetic ophthalmia

• Bilateral uveitis following penetrating trauma
  • Surgery
  • Accidental trauma
• Uveitis with
  • multifocal choroiditis
• Diagnosis of exclusion
Incidence of sympathetic ophthalmia after penetrating trauma (cases/1,000 injuries)
Aetiology of sympathetic ophthalmia

![Graph showing the aetiology of sympathetic ophthalmia with data from Haddassah (1970-83), NEI (1982-92), and Bascom (1976-97). The graph compares traumatic and surgical causes.](image-url)
Birdshot chorioretinopathy

- Middle aged women > men
- HLA A 29 +ve
- Bilateral widespread pale retinal lesions with minimal pigmentation
- +/- retinal vasculitis
- +/- macular oedema
Non infectious multifocal choroiditis

• Is still generally idiopathic
• Think of
  • Sarcoid
  • Behcet’s
  • SO
Infectious multifocal choroiditis

• Aetiology
  • Mycobacterial
    • Tuberculous
    • Non-tuberculous
  • Cryptococcus and other fungus
  • Pneumocystis carinii
• Pneumocystis choroiditis
  • Exclusively in AIDS patients on inhaled prophylaxis for Pneumocystis pneumonia
• Cryptococcal choroiditis
  • occurs in patients with cryptococcal meningitis
• Multifocal mycobacterial choroiditis
  • Uncommon
  • Very sick patients with disseminated TB
  • Non TB mycobacterium
Syphilitic retinitis

- Punctate inner retinitis
- Secondary syphilis
Sarcoidosis

- Focal granulomatous inflammation
- Non necrotising granulomas
- Generalised immunosuppression
“Caseating” granulomas

- Usually infectious
  - TB
  - Cat scratch
Sarcoidosis

- Focal granulomatous inflammation
- Generalised immunosuppression

- Lung
- Skin
- Nodes
- Eyes
- Liver
- Heart
- CNS
- Kidneys
Investigations for sarcoidosis

- FBE
  - Lymphopenia
- U and E, LFT, Ca
- ACE
  - Beware ACE inhibitors
- Lysozyme
- CT chest
  - Adults with pulmonary symptoms
Investigation of multifocal chorioretinitis

- History
- FBE, U&E, LFT
- ACE
- If indicated
  - HLA A 29
  - Quantiferon
  - Blood/urine cultures
  - FA
  - Syph serology
Retinal vasculitis

• Uveitis
• Inflammation localised around blood vessels (esp veins)
Retinal vasculitis - aetiology

• Aetiology in 103 patients in an Australian uveitis clinic
Development of MS in intermediate uveitis (with or without vasculitis)

- At 10 yrs the chance of MS is 28%
Uveitis in MS treatment trials

- All patients with MS on treatment were followed regularly
- 4735 unique patients in 6 different trials
- All with regular ophthalmic follow-up
- 34/4735 (0.7%) developed uveitis
Retinal vasculitis as part of systemic vasculitis

- 1286 patients with systemic vasculitis
  - PAN (393)
  - GPA (343)
  - MPA (280)
  - EGPA/CSS (270)

Investigation of “typical” retinal vasculitis

- History
- Examination

- Tests
  - ACE (CXR CT chest)
  - Quantiferon
  - T P IgG
  - Consider MRI
Investigation of “Atypical” retinal vasculitis – acute retinal microangiopathy

- History
- Examination

- Tests
  - FBE
  - U&E, LFT,
  - ANA
    - Lupus anticoagulant
    - Anti-cardiolipin antibodies
  - Se Igs and cryoglobulins
  - Se viscosity
Retinal vasculitis - aetiology

• Ocular diagnoses
  • Intermediate uveitis
  • Secondary to other uveitis
    • Especially retinal infections
    • Toxo
    • Viral retinitis
  • Eale’s disease

• Systemic diagnoses
  • Often idiopathic
  • Sarcoidosis
  • Behcet’s
  • MS
  • Rarely systemic vasculitis
Eale's disease

- Occlusive retinal vasculitis
- Veins > arteries
- Secondary neovascularisation and vitreous haemorrhage
- Most common in patients from south Asia
- Diagnosis of exclusion
Retinal vasculitis secondary to retinal infections

• Often seen with
  • Toxo
  • Viral retinitis
Optic papillitis

- Uveitis
- Inflammation centred on the optic nerve
- Note: mild disc swelling commonly accompanies many forms of uveitis and is not necessarily of diagnostic significance
Optic papillitis

- Ocular diagnoses
  - Associated with other uveitis
  - Leber’s stellate neuroretinitis
  - Bartonella

- Systemic diagnoses
  - MS
  - Sarcoidosis
  - VKH
  - Bartonella
  - Lyme disease
  - Syphilis
Bartonella

- Systemic illness following cat scratch with lymphadenopathy
- Disc swelling
- Stellate maculopathy
Papillitis and adjacent retinitis

- Immunocompetent
  - Toxo
- Immunosuppressed
  - CMV
Investigation of optic papillitis

- History
- Syph serology
- Bartonella serology
- ACE
- MRI
- If indicated
  - Lyme serology
  - Toxo serology
  - Quantiferon
  - Lebers mitochondrial gene testing
Uveitis and serous retinal detachment

- Serous detachment is uncommon in uveitis
- Usually carries diagnostic significance
Uveitis and serous retinal detachment

- Ocular diagnoses
  - Posterior scleritis
  - Sympathetic ophthalmia
- Beware
  - Steroid induced CSR
  - CNVM
  - Uveal effusion syndrome
- Systemic diagnoses
  - VKH
Posterior scleritis

- Posterior scleritis
  - Pain
  - Disc swelling
  - Choroidal folds
  - Serous detachment
  - Minimal uveitis
VKH

• Headaches
  • CSF lymphocytosis

• Hearing changes

• Uveitis
  • Serous detachment
  • Disc swelling
  • Multifocal leak and disc swelling on FA
• 3 out of
• Bilateral anterior uveitis
• Bilateral posterior uveitis with
  • Serous ret det
  • Disc swelling
  • RPE changes
• CNS involvement
  • Pleocytosis
  • HA
  • Tinnitus/CN involvement
• Skin involvement
VKH

• 3 phases
• Meningo-encephalitic phase
• Uveitis/auditory phase
• Skin/hair phase
<table>
<thead>
<tr>
<th>Type of posterior uveitis</th>
<th>Ocular diagnoses</th>
<th>Systemic diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitritis/diffuse uveitis</td>
<td>Fuch’s heterochromic iridocyclitis Intermediate uveitis/pars planitis</td>
<td>Idiopathic MS, Behçet’s, sarcoidosis, lymphoma, syphilis, TINU</td>
</tr>
<tr>
<td>Unifocal chorio-retinitis</td>
<td>Toxoplasmosis, candida, toxocara</td>
<td>Sarcoidosis, candida</td>
</tr>
<tr>
<td>Multifocal chorio-retinitis</td>
<td>No inflammation: PIC POHS Min inflammation: AMPPE, MEWDS Inflammation: Sympathetic, birdshot, infections</td>
<td>Idiopathic, sarcoidosis, Behçet’s, lymphoma, syphilis, infections</td>
</tr>
<tr>
<td>Confluent chorio-retinitis</td>
<td>Viral retinitis (CMV,HSV, VZV) Serpiginous, fungal retinitis</td>
<td>Immunosupression/AIDS (+ viral retinitis), sarcoidosis, lymphoma</td>
</tr>
<tr>
<td>Retinal vasculitis</td>
<td>Associated with other uveitis (especially infection), Eale’s disease</td>
<td>Sarcoidosis, Behçet’s, MS, TB, rarely other systemic vasculitis</td>
</tr>
<tr>
<td>Optic neuritis/papillitis</td>
<td>Isolated (non MS related) optic neuritis, Leber's stellate neuroretinitis, toxo, CMV</td>
<td>MS, syphilis, cat scratch, VKH, Lyme disease</td>
</tr>
<tr>
<td>Serous retinal detachment</td>
<td>Posterior scleritis Steroid induced CSR</td>
<td>VKH, sympathetic ophthalmia</td>
</tr>
</tbody>
</table>
Important concepts in making a diagnosis in posterior uveitis

• Limited number of diagnostic possibilities for each type of posterior uveitis and a limited number of systemic diseases seen commonly in posterior uveitis
• Most posterior uveitis is not associated with systemic disease
• A good history is more important than untargeted investigation
• Many more mistakes are made in the treatment of uveitis than in its diagnosis
• The underlying diagnosis rarely guides treatment
• Handful of important systemic diagnoses
  • Sarcoidosis
  • Behcets
  • MS
  • Syphilis
  • Oculo-cerebral lymphoma
Behcet’s

- Recurrent oral ulceration plus
- Two of
  - Genital ulceration
  - Uveitis
  - Skin lesions
  - Pathergy
## Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Chancre</td>
</tr>
</tbody>
</table>
| Secondary | Skin  
|          | Liver  
|          | Joints  
|          | Eyes (2.5-5%)              |
| Latent  |                             |
| Tertiary | Neuro-syphilis  
|          | Cardiac                     |
Ocular syphilis

<table>
<thead>
<tr>
<th></th>
<th>Anterior uveitis</th>
<th>Posterior Uveitis</th>
<th>Panuveitis</th>
<th>Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV positive</td>
<td>27 (96.4%)</td>
<td>48 (60.8%)</td>
<td>18 (50%)</td>
<td>93 (65%)</td>
</tr>
<tr>
<td>HIV negative</td>
<td>1 (3.6%)</td>
<td>31 (39.2%)</td>
<td>18 (50%)</td>
<td>50 (35%)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (20%)</td>
<td>79 (55%)</td>
<td>36 (25%)</td>
<td>143</td>
</tr>
</tbody>
</table>
Infectious syphilis, 2007 – 2011, by State/Territory and year

Source: National Notifiable Diseases Surveillance System
Primary ocular lymphoma

- Elderly patients (>50 yo)
- Persistent and progressive and treatment resistant uveitis with:
  - Prominent vitritis
  - +/- multifocal choroiditis, retinitis, retinal vasculitis
Diagnosis

- Systemic
  - MRI
  - LP
  - Brain biopsy

- Ocular
  - Vit biopsy
  - +/- retinal biopsy

Ocular history taking in uveitis

- Trauma/surgery
  - Infection/SO
- Persistent unilaterality
  - infection
## Systemic history taking in uveitis

<table>
<thead>
<tr>
<th>System</th>
<th>Possible diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joints</td>
<td>B27, Sarcoid, RA, Lupus...</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Sarcoid, GPA, TB, ...</td>
</tr>
<tr>
<td>GIT</td>
<td>IBD, Behcet’s, Whipples...</td>
</tr>
<tr>
<td>GUT</td>
<td>Behcet's, Reactive arthritis, GPA, syphilis, TINU...</td>
</tr>
<tr>
<td>Skin</td>
<td>Ps arthritis, syphilis, Sarcoid, SLE...</td>
</tr>
<tr>
<td>Mouth</td>
<td>Behcet’s, HSV...</td>
</tr>
<tr>
<td>CNS</td>
<td>Lymphoma, MS, neuro-Behcets, infections, VKH...</td>
</tr>
<tr>
<td>Drugs</td>
<td>Bisphosphonates, Rifabutin, vaccines, tattoos.</td>
</tr>
</tbody>
</table>
Investigation in uveitis

- **Limited** untargeted investigations for when there are no specific features to suggest a diagnosis
  - FBE, U&E, LFT, RBG, ACE, CXR, VDRL

- More intensive/expensive/invasive investigations **only** when clinically indicated
<table>
<thead>
<tr>
<th>Underlying disease</th>
<th>Useful investigations</th>
</tr>
</thead>
</table>
| Sarcoidosis        | Most useful: ACE, CR, HRCT chest, targeted biopsy, BAL  
|                    | Less useful: Gallium scan, blind biopsy |
| Systemic vasculitis| ANA, ENA, ANCA, Rh Factor, MSU, HLA A29, Hep serology |
| Birdshot           | HLA A29 |
| VKH                | LP |
| MS                 | MRI and LP |
| Primary oculo-cerebral lymphoma | MRI brain, LP, brain biopsy, vitrectomy +/- retinal biopsy |
| Ocular syphilis (usually 2ry) | RPR, TP IgG |
| Toxocara           | Toxocara serology |
| Lyme disease       | Borelia serology |
| Cat scratch disease| Bartonella serology |
| Brucellosis        | Brucella serology |
| Viral retinitis    | Most useful: AC or vitreous PCR, systemic viral load  
|                    | Consider HIV serology/CD4 count  
|                    | Less useful: viral serology (may be useful if negative) |
| TB                 | Most useful: IFN gamma release assay (Quantiferon), CXR  
|                    | Less useful: mantoux |
| West Nile          | West Nile virus serology |
| Metastatic endophthalmitis | Blood cultures, culture site of suspected primary infection eg catheter tips, central lines, chest, urine, etc. Vitreous tap |
Summary

• Make a descriptive diagnosis of the inflammation
• Determine clinically if possible the cause of the patients visual loss
• Take a targeted history
Summary

• Investigate aggressively any features identified on history

• If no clues on history then a limited number of investigations targeting the likely causes and possible side effects of treatment
Thank you