Clinical Assessment of Posterior Uveitis

Philip I. Murray
Centre for Translational Inflammation Research
University of Birmingham
Birmingham and Midland Eye Centre

Introduction
- Classification of uveitis
- Common causes of posterior uveitis
- Clinical clues
  - History
  - Examination
- White dot syndromes – pattern recognition
- Activity and damage
- Quality of life
- Key points

Anatomical Classification

<table>
<thead>
<tr>
<th>Type</th>
<th>Primary site of inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior uveitis</td>
<td>Anterior chamber</td>
</tr>
<tr>
<td>Intermediate uveitis</td>
<td>Vitreous</td>
</tr>
<tr>
<td>Posterior uveitis</td>
<td>Retina or choroid</td>
</tr>
<tr>
<td>Panuveitis</td>
<td>Anterior chamber, vitreous, le retina or choroid</td>
</tr>
</tbody>
</table>

Clinical Classification

Table 3: Proposed IUSG clinical classification of uveitis.

<table>
<thead>
<tr>
<th>Infections</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Fungal</th>
<th>Parasitic</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-infectious</td>
<td>Known systemic associations</td>
<td>No-known systemic associations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masquerade</td>
<td>Neoplastic</td>
<td>Non-neoplastic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Posterior uveitis
- Isolated posterior uveitis relatively uncommon
- Frequently associated with retinal vasculitis
- Symptoms include floaters and loss of vision
- May be idiopathic or part of a systemic disease process
- Specific syndromes (e.g. white dot syndromes)
- Very important as often results in loss of vision
- Systemic therapy is usually required

Common ‘causes’ of non-infectious posterior uveitis
- Idiopathic
- Sarcoidosis
- Multiple sclerosis
- ‘White dot’ syndromes
- Multifocal choroiditis
- V-K-H syndrome
- Behcet’s disease
- Birdshot
- Masquerade (primary NHL-CNS)
Common ‘causes’ of infectious posterior uveitis

- Toxoplasmosis
- Herpes viruses
  - VZV
  - HSV 1 and 2
  - CMV
- TB
- Syphilis
- Fungi

MUST exclude infection

Don’t forget about masquerade

Ocular examination - clues

- Unilateral / bilateral
- AC / vitreous inflammation
- Granulomatous / non-granulomatous
- Retinal / choroidal
- “White dot” syndromes
- Optic nerve involvement

History - clues

- Sudden / Insidious
- Unilateral / Bilateral
- Age
- Ethnicity
- Family history
- Social history
- Systems enquiry e.g. oro-genital ulcers, CNS symptoms
- Colour vision
- Dark adaptation
- Immunocompromised

Look at the whole patient
White Dot Syndromes
- A group of disorders characterized by multiple whitish-yellow inflammatory lesions located at the level of the outer retina, retinal pigment epithelium and choroid
- Frequently includes anything that gives white ‘dots’ in the fundus
- They present important diagnostic and therapeutic challenges
- History and examination findings extremely important
- Look for the clues

Associated Features
- Ocular and non-ocular
- Ocular include:
  - Uveitis (or absence of)
  - Vitreous cells / abnormalities
  - Retinal vascular changes
  - Macular changes
  - Disc changes
- Non-ocular
  - e.g. CNS signs and symptoms

The Dots
- Unilateral / bilateral
- Single / few / multiple / confluent
- Depigmented / pigmented
- Size
- Shape
- Natural history
  - Acute vs. chronic
  - Evanescent / persistent
  - Response to treatment
- Fundal distribution
- Level

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Age</th>
<th>Sex</th>
<th>Laterality</th>
<th>Vitritis</th>
<th>Leukemia</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIC</td>
<td>20–40</td>
<td>F/M</td>
<td>Bilateral</td>
<td>–</td>
<td>+V100D</td>
<td>Guarded</td>
</tr>
<tr>
<td>POHS</td>
<td>20–30</td>
<td>M/F</td>
<td>Bilateral</td>
<td>–</td>
<td>+V100D</td>
<td>Guarded</td>
</tr>
<tr>
<td>MSYWS</td>
<td>20–40</td>
<td>M/F</td>
<td>Unilateral</td>
<td>+</td>
<td>+V100D</td>
<td>Good</td>
</tr>
<tr>
<td>A+P+PETE</td>
<td>20–40</td>
<td>M/F</td>
<td>Bilateral</td>
<td>+</td>
<td>+1 OD</td>
<td>Good</td>
</tr>
<tr>
<td>Geographic chorioidopathy</td>
<td>30–60</td>
<td>M/F</td>
<td>Bilateral</td>
<td>–</td>
<td>–</td>
<td>Poor</td>
</tr>
<tr>
<td>Retinoschisis</td>
<td>23–79</td>
<td>F/M</td>
<td>Bilateral</td>
<td>++</td>
<td>+V400D</td>
<td>Guarded</td>
</tr>
<tr>
<td>Multifocal choroiditis</td>
<td>30–60</td>
<td>F/M</td>
<td>Bilateral</td>
<td>++</td>
<td>+5/100D</td>
<td>Guarded</td>
</tr>
</tbody>
</table>
Why determine disease activity and damage?

- Uveitis is often relapsing with recurrent episodes of potentially reversible disease activity
- Effective therapy can limit the development of irreversible organ damage
- It is important to have measures of activity that allow the disease to:
  - Be monitored
  - Assess the response to therapy
  - Determine the need for further therapy

Activity and damage indices allow the clinician to account formally for each clinical feature, thus improving treatment decisions. Index-generated scores may be a component of prognostic and outcome measures. Facilitates standardization of research, allows better comparison of data between centres and facilitate multi-centre trials. Outcome measures should include the patient’s perspective of the effect of the disease and its therapy on physical and emotional function.

Rheumatology

- RA
  - ACR 20, 50, 70
  - DAS 28
  - SDAI
  - CDAI
- AS
  - BASDAI
- SLE
  - BILAG
- Systemic Vasculitis
  - BVAS

Assessing disease activity in uveitis

- Activity vs damage
- What are we treating?
  - Cystoid macular oedema, macular ischaemia, new vessels, optic disc disease, vitritis
- Is it treatable?
- If so, how do we quantify an improvement?
- What parameters should we measure?
Assessment of activity - response to therapy

- Clinical (SUN)  
  - Acuity – BCVA, Snellen, logMAR, pinhole, near  
  - Slit-lamp – AC activity, vitreous cells  
  - Hand held lenses – CMO, retinal vasculitis  
  - BIO – vitreous haze

- Imaging  
  - OCT  
  - FFA / ICG  
  - Electrodiagnostics  
  - (B-scan ultrasound)

- Quality of life

The ‘distraction’ of visual acuity

- Visual acuity is a very poor marker of the efficacy of a drug in inflammatory eye disease  
- The impact of uveitis on visual acuity will depend on both the activity of the disease and the damage caused by the disease

Subjective outcome measures

- NEI vitreous haze score is the key outcome recognized by the FDA/EMA - the gold standard  
- It has a number of limitations:  
  - Subjective  
  - Non-continuous, leading to very large steps in disease activity between categories  
  - Poorly discriminatory at lower levels of vitreous haze  
  - Limiting of recruitment and sensitivity in a clinical trial context (where a 2 point change is usually required to be counted as a significant change)
Patient Reported Outcome Measures (PROMs)

- Patient choice over treatment and care is a central feature of the NHS
- Need to assess the quality of care delivered to NHS patients from the patient perspective
- Patients’ experience of treatment and care is a major indicator of quality and there has been a huge expansion in the development and application of questionnaires, interview schedules and rating scales that measure states of health and illness from the patient’s perspective

PROMs provide a means of gaining an insight into the way patients perceive their health and the impact that treatments or adjustments to lifestyle have on quality of life
- These instruments can be completed by a patient or individual about themselves, or by others on their behalf

What impact does uveitis make on activities of daily living?

- Quality of life affected by:
  - Visual impairment
  - Any associated disease
  - Therapy - response, side-effects
- Visual function does NOT = reading a Snellen chart at 6 metres using one eye at a time
- Visual quality of life
  - VCM1 of VR-QOL (UK)
  - VFQ-25 / VF-14 (USA)
- General health quality of life
  - SF-36/EQ-5D-5L
Key Points

- Detailed history and examination
- Look for the clues
- Pattern recognition
- Activity and damage indices
- Quality of life

MUST exclude infection

Don’t forget about masquerade