Inflammatory eye disease: An overview of clinical presentation and management

Authors: James RC Miller\textsuperscript{A} and Daren Hanumunthadu\textsuperscript{B}

Inflammatory eye diseases are responsible for a significant proportion of presentations to ophthalmic emergency facilities and knowledge of how to differentiate between broad categories of disease and refer accordingly is important for the practising physician. This review aims to provide an overview of inflammatory eye disease, with a focus on clinical presentation, diagnosis and management.

Introduction

Inflammatory eye disease encompasses a wide spectrum of conditions, ranging from the relatively benign to sight-threatening emergencies. The ocular inflammation can be infectious or non-infectious in aetiology. All parts of the eye may be variably affected, and eye inflammation can occur in isolation or as part of a systemic inflammatory disease. Here we provide an overview of inflammatory eye disease, with a focus on clinical presentation, diagnosis and management.

Uveitis

Uveitis describes ocular inflammation that affects the uveal tract (iris, choroid and ciliary body), but is often used synonymously with inflammatory eye disease and to refer to any form of intraocular inflammation. Uveitis has a vast range of underlying causes, and categorisation of these is particularly useful. The most common distinction utilises the location of ocular inflammation: anterior uveitis (iris and ciliary body), intermediate uveitis (vitreous), posterior uveitis (retina and choroid) and panuveitis (whole eye).\textsuperscript{1} Further classification may then be performed on the basis of clinical features (onset, duration and course), cause (infectious or non-infectious) and histopathology (granulomatous or non-granulomatous).\textsuperscript{2}

Anterior uveitis

Acute anterior uveitis (AAU) or ‘iritis’ is the most common sub-type, comprising approximately 80\% of cases.\textsuperscript{3} It typically presents as an acutely painful, photophobic red eye with variable change in visual acuity (VA). Conjunctival hyperaemia near the cornea (‘perilimbal’) is typical. An irregular pupil may be noted, owing to adhesions between the iris and lens called posterior synechiae. Bilateral presentations are less common, though patients often have both eyes affected at different times. The hallmark of AAU is the presence of inflammatory cells circulating in the anterior chamber (AC) on slit lamp examination. Other findings may include corneal precipitates or hypopyon (a white fluid level of inflammatory AC cells indicating severe inflammation). Idiopathic AAU accounts for most cases, and in a first presentation with no systemic symptoms it is reasonable to treat the uveitis empirically without further investigations. However, if there are repeated presentations, systemic features or bilateral disease then a thorough workup should be considered.

Key points

\begin{itemize}
  \item Uveitis is the most common form of inflammatory eye disease and may be classified into anterior, intermediate or posterior uveitis depending on the location of the inflammation.
  \item Anterior uveitis typically presents with an acutely painful, photophobic red eye, whereas intermediate and posterior uveitis more commonly present with floaters and/or blurring of vision.
  \item Anterior uveitis is typically treated with topical steroids; however, systemic steroids and other immunosuppressive agents may be required for all forms of uveitis.
  \item Scleritis causes severe pain worsened by eye movements and palpation and is treated with either oral non-steroidal antiinflammatory drugs or systemic steroids.
\end{itemize}

Both uveitis and scleritis have significant associations with systemic disease often requiring full medical workup and MDT management; where underlying conditions are present their effective treatment is vital for control of ocular inflammation.

\textbf{Keywords:} ophthalmology, uveitis, scleritis, episcleritis

\textbf{DOI:} 10.7861/clinmed.2022-0046

Authors: \textsuperscript{A}ophthalmology specialist registrar, Royal Free London NHS Foundation Trust, London, UK; \textsuperscript{B}ophthalmology consultant, Royal Free London NHS Foundation Trust, London, UK
Intermediate uveitis

Intermediate uveitis (IU) comprises inflammation in the vitreous cavity (‘vitreitis’), and in contrast to AAU often presents with painless floaters and reduced VA. While IU may be idiopathic, recognised associations include MS, sarcoidosis and lymphoma; there should therefore be a lower threshold for physician referral for systemic investigation. The decision to treat depends on the degree of symptoms or the presence of CMO, and in mild cases it is reasonable to monitor while treating any underlying systemic causes. In comparison to AAU topical steroids are usually less effective. Local steroid treatment may be given with intravitreal injections, with slow-release dexamethasone implants available to reduce their frequency. Long-term systemic treatment with corticosteroids, steroid-sparing agents and/or biological therapy may be required to suppress ocular inflammation, again under appropriate MDT supervision.

Intermediate uveitis (IU) comprises inflammation in the vitreous cavity (‘vitreitis’), and in contrast to AAU often presents with painless floaters and reduced VA. While IU may be idiopathic, recognised associations include MS, sarcoidosis and lymphoma; there should therefore be a lower threshold for physician referral for systemic investigation. The decision to treat depends on the degree of symptoms or the presence of CMO, and in mild cases it is reasonable to monitor while treating any underlying systemic causes. In comparison to AAU topical steroids are usually less effective. Local steroid treatment may be given with intravitreal injections, with slow-release dexamethasone implants available to reduce their frequency. Long-term systemic treatment with corticosteroids, steroid-sparing agents and/or biological therapy may be required to suppress ocular inflammation, again under appropriate MDT supervision.

Intermediate uveitis (IU) comprises inflammation in the vitreous cavity (‘vitreitis’), and in contrast to AAU often presents with painless floaters and reduced VA. While IU may be idiopathic, recognised associations include MS, sarcoidosis and lymphoma; there should therefore be a lower threshold for physician referral for systemic investigation. The decision to treat depends on the degree of symptoms or the presence of CMO, and in mild cases it is reasonable to monitor while treating any underlying systemic causes. In comparison to AAU topical steroids are usually less effective. Local steroid treatment may be given with intravitreal injections, with slow-release dexamethasone implants available to reduce their frequency. Long-term systemic treatment with corticosteroids, steroid-sparing agents and/or biological therapy may be required to suppress ocular inflammation, again under appropriate MDT supervision.
cause devastating necrotising retinitis in both immunocompetent and immunocompromised patients, while CMV retinitis is typically only seen with significant immunosuppression (eg from HIV or post-transplant). It is essential to treat infectious causes with the appropriate antimicrobial agent, and long-term local or systemic immunosuppression strategies are often required. Where profound immunosuppression is required, systemic biological therapy with adalimumab has shown effective control of non-infectious IU and PU. Treatment with other agents including infliximab has also yielded excellent outcomes.

One condition worthy of specific mention is TB, where ocular manifestations occur in about 1% of patients. The whole eye may be affected; however, granulomatous AAU and severe PU are of particular importance. Treatment is with systemic anti-tuberculous treatment and ocular immunosuppression; however, it is important to remember that ethambutol may itself cause a profound optic neuropathy.

Systemic fungal infections in immunocompromised patients (eg candidaemia) are also of specific ophthalmic importance to hospital physicians, as endogenous endophthalmitis may develop via haematogenous spread. Ophthalmic screening to exclude retinitis is vital in patients who are either symptomatic or unable to report symptoms (eg while ventilated), and all cases of fungal endogenous endophthalmitis require systemic treatment. Fluconazole is often the first-line treatment, but IV amphotericin may be required in some circumstances. Intravitreal anti-fungal treatment may be needed when there is vitreous involvement. Advanced cases may also benefit from surgical intervention with a vitrectomy.

| Table 1. Important distinguishing features of uveitis, scleritis and episcleritis |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Condition**                  | **Location of inflammation**    | **Key symptoms**                | **Examination findings**        | **Causes/associations**          |
| Anterior uveitis               | Anterior chamber, iris and ciliary body | Pain; photophobia; blurred vision; watering | Conjunctival hyperaemia; AC cells; posterior synechiae; hypopyon | Idiopathic; non-infectious, eg HLA-B27 arthropathies, JIA, sarcoidosis; infectious, eg syphilis, viral, TB |
| Intermediate uveitis           | Vitreous                        | Floaters; blurred vision        | Vitreous cells; vitreous haze   | Idiopathic; non-infectious, eg sarcoiosis, MS, lymphoma; infectious, eg post-operative endophthalmitis, Lyme disease |
| Posterior uveitis              | Retina and choroid               | Blurred vision; distortion; field defects; floaters | Retinal and choroidal inflammation; retinal vasculitis and haemorrhages; retinal detachment; optic disc swelling | Idiopathic; non-infectious, eg sarcoiosis, Behcet’s disease; infectious, eg TB, viral, toxoplasma, syphilis, candidiasis; neoplastic |
| Scleritis                      | Sclera                          | Severe pain, worse on eye movement and palpation; photophobia; watering; loss of vision | Diffuse or localised redness; does not blanch with phenylephrine; blue tinge if scleral thinning | Idiopathic; rheumatoid arthritis; SLE; vasculitis eg GPA; PAN |
| Episcleritis                   | Episclera                       | Discomfort; watering            | Localised injection; blanches with phenylephrine; VA usually normal | Idiopathic; rheumatoid arthritis; SLE; vasculitis eg GPA; PAN |

GPA = granulomatosis with polyangiitis; JIA = juvenile idiopathic arthritis; MS = multiple sclerosis; PAN = polyarteritis nodosa; SLE = systemic lupus erythematosus; TB = tuberculosis.

| Table 2. Investigation of uveitis, scleritis and episcleritis |
|---------------------------------|---------------------------------|
| **Condition**                  | **Investigations**              |
| Uveitis                         | Bloods, eg HLA-B27, serum ACE, ESR, autoantibodies |
|                                | Infection screening, eg chest X-ray, syphilis serology, viral titres |
|                                | Ocular imaging, eg ultrasound, OCT, FFA |
|                                | Biopsy, eg vitreous ‘tap and inject’ |
| Scleritis                      | Phenylephrine test |
|                                | Autoantibodies |
|                                | Ocular ultrasound |
| Episcleritis                   | Phenylephrine test |
|                                | Other investigations not routinely required |

ACE = angiotensin-converting enzyme; ESR = erythrocyte sedimentation rate; FFA = fundus fluorescein angiography; OCT = optical coherence tomography.
Scleritis

The sclera is the outer, protective layer of the globe that is visible anteriorly as the ‘white’ of the eye. Scleral inflammation may be divided into anterior or posterior scleritis, depending on whether the inflammation is in front of or behind the insertion of the extraocular rectus muscles. Anterior scleritis is significantly more common and presents with ocular pain and redness; key distinguishing features include pain exacerbated by ocular movement and palpation of the globe. It can also be severe enough to wake the patient at night. Blue discolouration of the sclera may be noted due to inflammatory thinning. Scleritis is differentiated from episcleritis by application of 10% phenylephrine drops; these will cause blanching of superficial blood vessels in episcleritis but not deeper vessels in scleritis. The most common associated conditions are connective tissue diseases and vasculitides, and systemic workup including autoantibodies should be performed for newly presenting patients. As with uveitis, prompt specialist referral should be made where a systemic diagnosis is suspected. Initial treatment utilises oral NSAIDs; however, systemic steroids are used where these are insufficient. A high index of suspicion should be maintained for escalating therapy as necrotizing scleritis may cause ocular perforation if inadequately controlled.

Brief mention should be made of the more common episcleritis, which affects the superficial episclera and presents as an uncomfortable, localised patch of redness that blanches with 10% phenylephrine. Oral non-steroidal anti-inflammatory drugs are the first-line treatment and visual prognosis is excellent.

Conclusion

Inflammatory eye disease causes significant morbidity and is an important differential in patients presenting with an acute red eye. While most cases are managed in specialist ophthalmic clinics, the extensive range of systemic associations means that a thorough medical workup is vital in identifying underlyng conditions and providing holistic patient care. This is especially important for those individuals who require systemic immunosuppression.

References

1. Jabs DA, Nussenblatt RB, Rosenbaum JT et al. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005;140:509–16.
2. Deschenes J, Murray PI, Rao NA et al. International Uveitis Study Group (IUSG): clinical classification of uveitis. Ocul Immunol Inflamm 2008;16:1–2.
3. Denniston A, Murray P. Oxford handbook of ophthalmology. 4th ed. Oxford: Oxford University Press; 2018.
4. Monnet D, Breban M, Hudry C, Dougados M, Brézin AP. Phthalimic findings and frequency of extraocular manifestations in patients with HLA-B27 uveitis: a study of 175 cases. Ophthalmology 2004;111:802–9.
5. Ben Ezra D, Cohen E, Behar-Cohen F. Uveitis and juvenile idiopathic arthritis: A cohort study. Clin Ophthalmol 2007;1:513–8.
6. Angeles-Han ST, Ringold S, Beukelman T et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the screening, monitoring, and treatment of juvenile idiopathic arthritis-associated uveitis. Arthritis Care Res 2019;71:703–16.
7. Tomkins-Netzer O, Lightman SL, Burke AE et al. Seven-year outcomes of uveitic macular edema: the multicenter uveitis steroid treatment trial and follow-up study results. Ophthalmology 2021;128:719–28.
8. Kempen JH, Altaweel MM, Hallbrook JT et al. Association between long-lasting intravitreal fluocinolone acetonide implant vs systemic anti-inflammatory therapy and visual acuity at 7 years among patients with intermediate, posterior, or panuveitis. JAMA 2017;317:1993–2005.
9. Jaffe GJ, Foster CS, Pavesio CE, Paggiarino DA, Riedel GE. Effect of an injectable fluocinolone acetonide insert on recurrence rates in chronic noninfectious uveitis affecting the posterior segment: twelve-month results. Ophthalmology 2019;126:601–10.
10. Lowder C, Belfort R, Lightman S et al. Dexamethasone intravitreal implant for noninfectious intermediate or posterior uveitis. Arch Ophthalmol 2011;129:545–53.
11. Lemley CA, Han DP. Endophthalmitis: a review of current evaluation and management. Retina 2007;27:662–80.
12. Mochizuki M, Smith JR, Takase H et al. Revised criteria of International Workshop on Ocular Sarcoidosis (IWOS) for the diagnosis of ocular sarcoidosis. Br J Ophthalmol 2019;103:1418–22.
13. Jaffe GJ, Dick AD, Brézin AP et al. Adalimumab in patients with active noninfectious uveitis. N Engl J Med. 2016;375:932–43.
14. Agrawal R, Testi I, Badgki B et al. Collaborative Ocular Tuberculosis Study consensus guidelines on the management of tubercular uveitis-report 2: guidelines for initiating antitubercular therapy in anterior uveitis, intermediate uveitis, panuveitis, and retinal vasculitis. Ophthalmology 2021;128:277–87.
15. Chamberlain PD, Sadaka A, Berry S, Lee AG. Ethambutol optic neuropathy. Curr Opin Ophthalmol 2017;28:545–51.
16. Lightman S, Montgomery H. Eye care in the intensive care unit. Royal College of Ophthalmologists, 2017. www.rcophth.ac.uk/wp-content/uploads/2021/01/Intensive-Care-Unit.pdf [Accessed 31 January 2022].

Address for correspondence: Mr Daren Hanumunthadu, Department of Ophthalmology, Royal Free Hospital, Pond Street, London, NW3 2QG, UK.

Email: daren.hanumunthadu@nhs.net