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Inflammatory eye disease: An overview of clinical presentation and management

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ABSTRACT

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).[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).[2]

Anterior uveitis

Acute anterior uveitis (AAU) or 'iritis' is the most common sub-type, comprising approximately 80% of cases.[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

- 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.
- 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.
- Anterior uveitis is typically treated with topical steroids; however, systemic steroids and other immunosuppressive agents may be required for all forms of uveitis.
- Scleritis causes severe pain worsened by eye movements and palpation and is treated with either oral non-steroidal antiinflammatory drugs or systemic steroids.
- 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.

KEYWORDS: ophthalmology, uveitis, scleritis, episcleritis

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Infectious AAU may be caused by viruses including HSV and VZV (after ophthalmic shingles), syphilis and tuberculosis (TB). Non-infectious AAU has numerous systemic associations, and it is crucial to enquire about past medical history and recent symptom onset. The most common genetic association is HLA-B27, with up to 50% of AAU patients being HLA-B27-positive.[3] HLA-B27 is strongly associated with the seronegative arthropathies, specifically ankylosing spondylitis, reactive arthritis and psoriatic arthritis, and up to 75% of HLA-B27-positive uveitis cases have an associated systemic diagnosis.[4] These patients tend to have more recurrent disease activity than idiopathic AAU. Recent trauma or intraocular surgery should also be excluded, as delayed onset AAU following ocular insult is common.

In paediatric patients the most important association is juvenile idiopathic arthritis (JIA). In contrast to other forms of AAU, JIA patients are often asymptomatic even with significant disease; this can lead to under-treatment until significant visual impairment develops.[5] Patients with newly diagnosed JIA should be referred for prompt ophthalmic screening and are followed up every few months.[6]

Treatment of AAU follows an escalating approach, with most patients adequately controlled on topical treatment. A potent steroid drop (eg dexamethasone 0.1% or prednisolone 1%) is given at a gradually reducing frequency, with follow up to exclude rebound inflammation at lower doses. If topical treatment is insufficient then periocular steroid injections may be given (eg sub-conjunctival). In rare cases oral steroids or steroid-sparing immunosuppressive agents are required, and there has been recent interest in biologic therapies including anti-TNF monoclonals. Where systemic treatment is indicated, this is done as part of an multidisciplinary team (MDT) with close physician input, and specialist referral (eg to rheumatology) for further management is often appropriate.

Common complications of AAU include cataract formation and raised intraocular pressure; these can occur from both the initial inflammation and subsequent steroid treatment. Raised pressure can either be chronic 'open-angle' or acute 'closed-angle' if 360° posterior synechiae are allowed to block aqueous humour passage through the pupil; a history of uveitis should therefore be excluded in any patient with suspected acute angle-closure glaucoma. AAU may also result in cystoid macula oedema (CMO), whereby fluid accumulates in the retina with distortion of central vision.[7]

Intermediate uveitis

Intermediate uveitis (IU) comprises inflammation in the vitreous cavity ('vitritis'), 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,[8,9] with slow-release dexamethasone implants available to reduce their frequency.[10] 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.

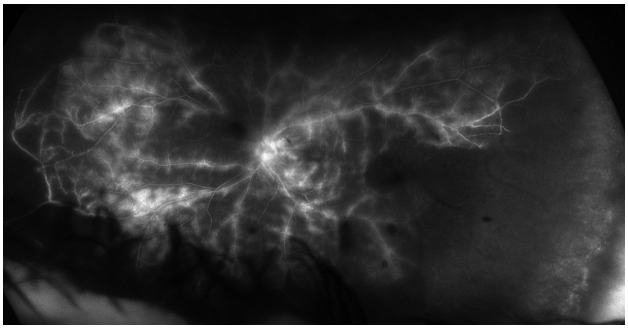

Fig 1. Fundus fluorescein angiography of a patient with tuberculosis-associated panuveitis. The image shows small and medium vessel vasculitis. Vessel occlusion and vitreous haze (causing image blurring) are also present.

Crucially, the presence of severe intraocular inflammation, particularly with vitritis, in a patient with recent intraocular surgery is highly suggestive of post-operative endophthalmitis. This potentially blinding condition can present to the emergency department as a painful red eye with visible hypopyon. It requires immediate ophthalmology referral for combined vitreous biopsy and intravitreal antibiotic injection ('tap and inject') to prevent profound permanent visual loss.[11]

Posterior uveitis

Inflammation in the retina or supporting choroid is referred to as posterior uveitis (PU) (Fig 1). PU has a vast range of causes, a full review of which is beyond this article's scope. The presenting symptoms vary depending on the location of the inflammation. Peripheral retinal inflammation may be relatively asymptomatic until severe, while disease at the macula may produce early profound central vision loss. PU also has sight-threatening complications, with retinal vein occlusion, vitreous haemorrhage and retinal detachment all being potential sequelae. All cases of PU should be managed in specialist clinics with regular physician input for associated systemic diagnoses.

Important non-infectious causes of PU include Behcet's disease and sarcoidosis, which has ocular manifestations in up to 25% of patients.[12] Infectious PU may present insidiously (eg toxoplasma, Fig 2) or with rapid visual loss and even blindness; HSV and VZV can

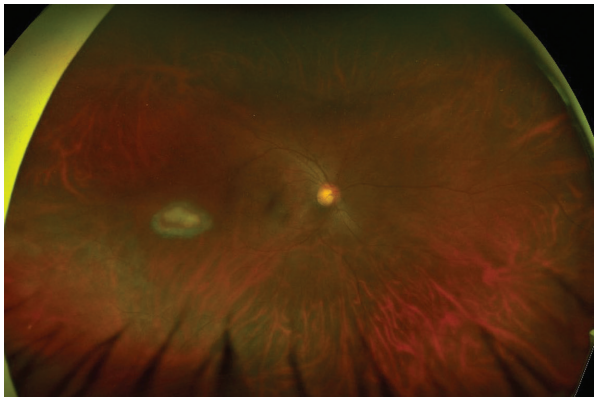

Fig 2. Pseudocolour image of a patient with toxoplasma chorioretinitis with associated vitritis. A typical toxoplasma scar may be seen temporal to the macula.

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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 sarcoidosis, 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 sarcoidosis, 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.

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.[13] 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.[3] 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;[14] however, it is important to remember that ethambutol may itself cause a profound optic neuropathy.[15]

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.[16] Advanced cases may also benefit from surgical intervention with a vitrectomy.

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.

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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 underlying conditions and providing holistic patient care. This is especially important for those individuals who require systemic immunosuppression. ■

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