

Managing Uveitic Glaucoma

JR Smith

Casey Eye Institute, Oregon Health Sciences University, Oregon, USA

Glaucoma is a common and potentially blinding complication of uveitis. The pathogenic processes responsible for an underlying elevation in intraocular pressure are often multiple and may include both open angle and closed angle mechanisms. Successful management of uveitic glaucoma depends on recognition of the uveitis syndrome and clarification of the mechanism(s) contributing to the glaucoma. Both the inflammation and the raised intraocular pressure will require treatment. An anti-inflammatory regimen including corticosteroids, cytotoxic agents and/or specific immunosuppressive agents is chosen according to the type of uveitis, as well as various patient characteristics. When the angle is open, intraocular pressure reduction may be achieved medically using β -adrenergic antagonists, α_2 -adrenergic agonists and/or carbonic anhydrase inhibitors. When medical treatment fails, surgical intervention, in the form of a trabeculectomy with wound modulation therapy or drainage implantation, is generally indicated. Laser iridotomy or surgical iridectomy may rapidly normalise intraocular pressure in patients with a closed angle.

Introduction

Uveitic glaucoma is diagnosed when uveitis is associated with an elevated intraocular pressure (IOP), causing glaucomatous field loss and/or glaucomatous field damage. If unrecognised and untreated, this condition may lead rapidly to blindness. Glaucoma may occur in up to 20% of all individuals with uveitis, and it may affect patients of any age group. Although the complication has been observed in every type of uveitis, certain uveitides are more commonly associated with glaucoma.

In Asian populations, common causes include Fuchs' heterochromic uveitis, herpetic eye disease, and the glaucomatocyclitic crisis. Other types of uveitis which may be associated with glaucoma include Behçet's disease, Vogt-Koyanagi-Harada syndrome, and ocular toxoplasmosis. As

leprosy, tuberculosis, and syphilis are common in certain parts of Asia, these infectious diseases must also be considered. There are many possible clinical presentations of the uveitis, and consequently, systemic features and investigations may be needed to diagnose these infectious diseases. Interestingly, it is rare for HLA B27-associated uveitis to lead to glaucoma. Lens-induced glaucoma, in patients with hypermature cataract or following lens extraction or trauma, may masquerade as uveitic glaucoma.

Although uveitic glaucoma presents a management challenge for even the specialist ophthalmologist, a thorough clinical examination to identify the specific type of uveitis and the mechanism(s) of the glaucoma will allow the formulation of a rational treatment plan. Furthermore, with the recent introduction of new anti-inflammatory agents and anti-glaucoma medications, as well as

advances in glaucoma microsurgery, this condition can often be managed successfully, leaving the patient with useful vision.

Diagnosing Uveitis

A correct diagnosis of uveitis is essential, as this will directly influence anti-inflammatory treatments. Slit-lamp examination findings which may suggest Fuchs' heterochromic uveitis include a white eye with diffusely distributed white round or stellate keratic precipitates. The iris atrophy which produces a very obvious heterochromia in a Caucasian eye may be difficult to appreciate in the Asian eye. It is often visible as a subtle moth-eaten appearance. There are no posterior synechiae, but fragile angle new vessels may be present. Cataract is a common complication, and debris may accumulate in the vitreous.

In herpetic eye disease, corneal sensation may be impaired. There may be iris atrophy, characteristically as small areas with scalloped borders in herpes simplex infection, but as large sectors in herpes zoster ophthalmicus. Active or inactive corneal disease is present in some cases, and old skin scars may suggest herpes zoster infection.

During the glaucomatocyclitic crisis or Posner-Schlossman syndrome, patients complain of halos around lights. The conjunctiva is mildly injected, and there is little anterior chamber reaction with few keratic precipitates and no posterior synechiae. However, IOP elevation may be severe, resulting in corneal oedema.

Behçet's disease, an idiopathic vasculitic condition, causes recurrent anterior and/or posterior uveitis with oral and genital ulceration and a variety of skin lesions. Classically, a transient hypopyon is observed, and retinal vasculitis and the accompanying vitritis are florid.



Vogt-Koyanagi-Harada syndrome is another idiopathic multi-system disorder involving cutaneous and neurological features associated with a panuveitis and characteristic exudative retinal detachments.

Toxoplasmosis presents as a focal necrotising retinitis with vitritis. A whitish lesion with fluffy edges may be associated with a pigmented chorioretinal scar.

Identifying Mechanisms Underlying the Glaucoma

Clearly, in some patients with uveitis, there may be a concurrent primary chronic open angle glaucoma which may be recognised by factors such as history preceding the uveitis or clinical evidence of long-standing optic nerve damage, advanced age, and family history of glaucoma. However, secondary glaucoma is the more common scenario, and both closed angle and open angle types may occur. Often multiple mechanisms may be involved. Gonioscopy is essential to determine underlying mechanisms. As well as identifying an open or closed angle, other structural changes such as peripheral synechiae, a dark muddy appearance of the trabeculum suggesting trabeculitis or neovascularisation may also be noted by such examination.

Angle closure may be reversible if it results from pupillary block due to either 360° posterior synechiae formation or a pupillary membrane, or from forward rotation of a swollen ciliary body. However, peripheral anterior synechiae are frequently permanent. In uveitis, a whole variety of factors including leucocytes, protein, eicosanoids, proteolytic enzymes, cytokines, and oxygen free radicals are released into the aqueous and may therefore act on the open

angle to raise IOP either mechanically or by influencing aqueous humour dynamics. In some instances, trabeculitis co-exists with uveitis. Inflammatory mediators may also induce structural changes in the outflow channels which may not be appreciated clinically.

A variety of mechanisms have been reported for glaucoma in Fuchs' heterochromic uveitis, most being open angle in type. Trabeculitis appears to play an important role in herpetic uveitic glaucoma. High IOPs measured during the glaucomatocyclitic crisis result from temporary reduction in outflow facility and increase in aqueous humour production, presumably related to local release of inflammatory mediators. Interestingly, a recent study from Singapore demonstrated a high incidence of subsequent primary chronic open angle glaucoma in patients with Posner-Schlossman syndrome, indicating a need for formal follow-up of these individuals.

A major concern in the management of uveitic glaucoma is the propensity for corticosteroids, the mainstay of uveitis treatment, to elevate IOP to high levels in a significant percentage of patients. Both topical and systemic corticosteroids may have this effect, and although the response normally does not develop until 2 weeks after beginning therapy, it has been reported to occur at any time. The exact mechanism of steroid-induced glaucoma is not known, but hypotheses include an accumulation of glycosaminoglycans in the trabeculum, effects on prostaglandin synthesis which reduce outflow facility, and inhibition of phagocytosis by the trabecular endothelium.

Managing Uveitis

Elevated IOP in uveitis may be reduced simply by controlling the associated

intraocular inflammation. Topical corticosteroids are useful for anterior segment inflammations such as herpetic uveitis and Posner-Schlossman syndrome. Fuchs' heterochromic uveitis often requires no anti-inflammatory treatment. For posterior segment disease, systemic immunosuppression may be required, and most commonly this is with oral prednisolone. However, for so-called steroid responders, the choice of anti-inflammatory may be difficult. Often, corticosteroids will be continued in conjunction with anti-glaucoma measures. Controversy surrounds a series of new topical corticosteroids which are reported to be less likely to elevate IOP, whilst still alleviating uveitis, as a result of selective tissue partitioning.

Cyclosporine, a specific immunosuppressive agent, and the cytotoxics such as methotrexate and azathioprine are systemic steroid-sparing drugs. Such treatment is introduced in consultation with a general physician who can monitor for potentially serious systemic side effects.

Some ophthalmologists advocate the use of non-steroidal anti-inflammatory agents. A mydriatic is an important adjunctive measure to prevent permanent posterior synechiae formation. The place of anti-viral drugs in the management of herpetic uveitis is unclear.

Certainly, an early oral course of aciclovir will reduce the risk of uveitis occurring as a complication of herpes zoster ophthalmicus. In herpes simplex uveitis, topical aciclovir is frequently given to treat or avoid concurrent corneal disease.

Managing Glaucoma

When secondary glaucoma is apparent, despite efforts to control the intraocular inflammation, medical and/or surgical



anti-glaucoma therapy will be required. However, an elevated IOP below 30 mm Hg can often be observed, particularly in a young patient with no signs of an associated glaucoma.

Medical Therapies

Usually uveitis with secondary open angle glaucoma is managed medically in the first instance. Sometimes, a combination of several anti-glaucoma drugs from different families may be required to control glaucomatous damage, and this is generally preferable to surgery which carries relatively high risks for this group of patients.

The anti-glaucoma medication of choice is often a topical β -adrenergic antagonist such as timolol or betaxolol. Newer topical options include the carbonic anhydrase inhibitor, dorzolamide, and the α_2 -adrenergic agonist, brimonidine. These agents are significantly more expensive than the β -blockers, and are best reserved for patients requiring more than one agent.

Apraclonidine, another topical α_2 -adrenergic agonist, is commonly associated with development of tachyphylaxis, but may be a useful temporising agent. In treatment-resistant cases, systemic carbonic anhydrase inhibitors or even hyperosmotic agents may become necessary, although clearly these do not constitute a long-term option.

It is important to avoid medications which may aggravate the inflammation. These include both the cholinergic and the parasympathomimetic miotics. Non-selective adrenergic agonists may contribute to conjunctival hyperaemia and may cause cystoid macular oedema. The recently introduced prostaglandin analogue, latanoprost, may precipitate uveitis in otherwise healthy individuals.

Surgical Interventions

When closed angle glaucoma results from pupillary seclusion, laser iridotomy may be sufficient to adequately re-establish the flow of aqueous out of the eye. In the Asian eye, with its relatively thick, pigmented iris, it is advisable to perform a sequential procedure. An initial treatment with the argon laser is undertaken to cut a tunnel through the iris, and this is followed by a treatment using the Nd-YAG laser to enlarge the tunnel. Unfortunately a laser iridotomy is prone to closure in an eye with active inflammation, and at least 2 iridotomies should be performed in the first instance. If both iridotomies close, a surgical iridectomy will be required.

In some cases, corneal oedema or iridocorneal touch may be indications for a primary surgical procedure. The eye should be as quiet as possible prior to either intervention as aggravation of the inflammation is to be expected following iris manipulation. Clearly, prolonged angle closure will result in formation of peripheral anterior synechiae, and if 75% or more of the angle is closed, neither iridotomy nor iridectomy is likely to be successful.

When medical therapy fails to control pressure-induced optic neuropathy and/or visual field loss, be the angle open or permanently closed, a filtering or shunting surgical procedure may be required. Laser trabeculoplasty generally has no role in the management of uveitic glaucoma. There are few published studies which indicate the outcome of glaucoma surgery specifically in uveitis patients. However, it is generally accepted that an anti-metabolite, either 5-fluorouracil or mitomycin C, will improve the success of trabeculectomy in high-risk individuals. In one of the larger series of

21 uveitic eyes followed for a mean of almost 3 years postoperatively, 70% of cases had controlled IOP after trabeculectomy and 5-fluorouracil. However, a patient with uveitis is at greater risk of subsequent complications such as marked inflammatory reaction, ciliary body oedema causing malignant glaucoma and choroidal effusion.

Various shunting devices are available, such as Molteno, Baerveldt and Krupin. Complications reported in association with these implants include tube failure, ocular hypotony and various complications related to the tube position within the eye, including corneal decompensation, uveitis and cataract.

The Ahmed pump contains an intrinsic valve mechanism which may reduce the risk of hypotony. In one study of 15 eyes, followed for almost 2 years following Ahmed pump implantation, IOP was controlled in 14 eyes, with significant complications in 3 eyes. Cyclodestructive procedures such as cyclophotocoagulation and cyclocryotherapy may greatly exacerbate intraocular inflammation, and they are used only when other treatments have failed.

Although the success of filtering or drainage surgery is reduced in the presence of active inflammation, this is often just the situation in which surgery is required. Ideally, an eye should be quiet for 3 months prior to surgery. Intensive immunosuppressive therapy is indicated for both emergency and planned procedures. Frequently, a course of oral corticosteroid is prescribed, although for certain relatively low grade anterior segment inflammations such as Fuchs' heterochromic uveitis and Posner-Schlossman syndrome pre-operative topical corticosteroids may suffice. The immunosuppressive regimen



is gradually tapered during the post-operative period, depending on the clinical course.

Summary

Although glaucoma is a serious complication of uveitis, with accurate diagnosis of the uveitis and delineation of the mechanism(s) of the glaucoma, successful treatment is often possible. Recent pharmacological developments have provided a variety of effective anti-glaucoma treatments and, with appropriate immunosuppression, surgery may often succeed. Ultimately, prevention of this condition, the complication of uncontrolled intraocular inflammation, and/or treatment with non-selective corticosteroid, will require the development of highly selective immunosuppressive agents.

Further Reading

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Address for Correspondence

Dr JR Smith, MB,BS, BA, PhD, FRACO, FRACS
 Post-doctoral Fellow (Uveitis)
 Casey Eye Institute, Oregon Health Sciences University
 3375 SW Terwilliger Blvd, Portland
 Oregon 97201-4197
 United States of America
 E-mail: smithjus@ohsu.edu



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