Glaucoma in patients with uveitis

William C Panek, Gary N Holland, David A Lee, Robert E Christensen

Abstract

The records of 100 patients (161 eyes) with uveitis referred to and examined by one author (GHN) at the Jules Stein Eye Institute, UCLA School of Medicine, were reviewed retrospectively. Uveitis was identified by the presence of inflammation involving any intraocular structure at the time of examination or by a well documented history of intraocular inflammation. Excluded were patients with self-limited anterior chamber inflammatory reactions during a one-month period following intraocular surgery, patients with neoplastic disease mimicking uveitis ('masquerade syndromes'), and patients with cytomegalovirus (CMV) retinopathy.

Each case was examined for location of inflammation, disease chronicity, and the presence or history of increased intraocular pressure. For the purpose of this study, the patients were considered to be glaucoma suspect (primary open angle glaucoma) if the intraocular pressure was above 21 mm Hg on more than one examination at UCLA, or if the patient was receiving antiglaucoma therapy at the time of initial examination at UCLA and previously had a well documented increase in intraocular pressure concurrent with intraocular inflammation. No patients had a history of pre-existing primary open angle glaucoma.

The cases were divided into acute and chronic uveitis as defined by the International Uveitis Study Group. Cases of acute uveitis were less than three months in duration and cases of chronic uveitis were of three months or more.

Results

There were 161 eyes with uveitis among the 100 patients investigated in this study (Table 1). Twenty-four patients (34 eyes) had acute uveitis and 76 (127 eyes) had chronic uveitis. All the patients had cells and flare in the anterior chamber, indicating anterior segment inflammation, regardless of the primary site of disease. Of the patients with acute uveitis all had primary inflammation of the anterior segment except three, who had toxoplasmic retinochoroiditis with secondary iridocyclitis. Eleven patients with chronic uveitis had intermediate uveitis (pars planitis). Of the remaining 65 patients with chronic uveitis, one with Vogt-Koyanagi-Harada syndrome, one of three with sarcoidosis, and one of 33 with uveitis of unknown cause had inflammation of the posterior segment; all others had inflammation of the anterior segment alone.

Twenty-three patients (31 eyes) had secondary uveitic glaucoma by our criteria. Three patients (three eyes) had acute uveitis and 20 patients (28 eyes) had chronic uveitis. Glaucoma occurred in
12% of patients with acute uveitis and in 26% of patients with chronic uveitis. There was no statistically significant difference in the incidence of glaucoma between these two groups. All 23 glaucoma patients had at some time undergone steroid therapy — oral, topical, or periocular. Treatment regimens at the time of this review varied from prednisone 60 mg orally every day combined with prednisolone acetate 1% solution every hour to fluorometholone 1% solution every other day. Only one patient with glaucoma was off steroid therapy. No cases of glaucoma were shown to be secondary to steroid response.

Toxoplasmic retinochoroiditis was the only form of posterior uveitis in which secondary anterior segment inflammation resulted in increased intraocular pressure. Posner-Schlossman syndrome was the only acute primary anterior segment disorder that was found to be associated with increased intraocular pressure. All the other patients had chronic uveitis, either primary anterior segment inflammation alone or panuveitis. All the patients with bilateral uveitis who developed glaucoma did so in both inflamed eyes. At least five patients (eight eyes, 22% of glaucoma patients) had glaucomatous visual field defects.

Twenty-one patients (29 eyes, 91% of glaucoma patients) received antiglaucoma medications for control of intraocular pressure. Eighteen patients (26 eyes, 78% of glaucoma patients) required continuous, ongoing therapy; all had chronic uveitis. The other three patients (three eyes, 13% of glaucoma patients), all of whom had acute uveitis, required brief medical therapy only during the initial period of inflammation. The remaining two patients with glaucoma (two eyes, 9% of glaucoma patients), both of whom had chronic anterior uveitis, did not require medical therapy; they had histories of transient, self-limited increases in intraocular pressure that responded to treatment of inflammation alone. One patient (two eyes, 4% of glaucoma patients) with chronic uveitis required filtering surgery to lower the intraocular pressure.

**Discussion**

The spectrum of uveitic disorders in this series is consistent with that seen in other referral practices. Uveitis may be complicated by a variety of secondary problems including cataract formation, synchiae, macular oedema, and glaucoma. In the present series glaucoma was one of the most common complications that required therapeutic intervention.

The factors most commonly associated with problems in the management of glaucoma were disease chronicity and primary anterior segment inflammation. Toxoplasmic retinochoroiditis was the only disorder in which secondary anterior segment inflammation resulted in rises of intraocular pressure requiring medical therapy. Increased intraocular pressure associated with acute uveitis was not a significant management problem, generally responding well to brief periods of medical therapy. Glaucoma associated with chronic uveitis usually required prolonged medical therapy for control of pressure. Even with chronic uveitis, however, treatment of inflammation alone brought intraocular pressure under control in some cases. Visual field loss was a problem only in patients with chronic uveitis.

In this group of referral patients it is possible that the incidence of raised intraocular pressure among patients with acute uveitis was underestimated. A transient rise in pressure associated with the onset of intense inflammation that resolved with the initiation of anti-inflammatory therapy by referring physicians may have been missed. It is unlikely, however, that such transient increases in pressure pose a serious problem to the eye.

**Pathophysiology of Uveitic Glaucoma**

The status of the anterior chamber angle gives an important anatomical division into either closed or open angle types of glaucoma, and has important therapeutic and prognostic implications. In patients with uveitis the angle can be closed as a result of posterior synchiae producing pupillary seclusion and iris bombé. Angle closure also can occur without pupillary block. It can result from peripheral anterior synchiae (an iridotrabeal adherence-associated inflammation of iris and angle

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**TABLE I Patients with uveitis and increased intraocular pressure (IOP)**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
<th>Total eyes with inflammation</th>
<th>Patients with increased IOP</th>
<th>Total eyes with increased IOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute uveitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLA B27+</td>
<td>11</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HLA B27-</td>
<td>9</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Poster-Schlossman syndrome</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>34</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Chronic uveitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown cause</td>
<td>33</td>
<td>61</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Intermediate (pars planitis)</td>
<td>11</td>
<td>20</td>
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<td>1</td>
</tr>
<tr>
<td>Juvenile rheumatoid arthritis</td>
<td>7</td>
<td>14</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Intraocular lens-associated</td>
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<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Fuchs' heterochromic iridocyclitis</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Herpes simplex virus associated</td>
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<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>3</td>
<td>6</td>
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<td>Syphilis</td>
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<td>0</td>
<td>0</td>
</tr>
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<td>Herpes zoster virus associated</td>
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<td>0</td>
</tr>
<tr>
<td>Vogt-Koyanagi-Harada syndrome</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>127</td>
<td>20</td>
<td>28</td>
</tr>
</tbody>
</table>
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structures) and sometimes inflammatory nodules in the angle. In addition rubefacta iridis leading to fibrovascular scarring and closure of the angle can occur in patients with uveitis. In this series no cases of angle closure were seen, indicating that this mechanism may occur infrequently in patients receiving anti-inflammatory therapy.

Increased intraocular pressure associated with a clinically open angle involves microscopical changes with the trabecular meshwork. Postulated mechanisms include (1) mechanical blockage of the trabeculum by serum components that are liberated because of vascular incompetence; (2) hypersecretion associated with prostaglandin mediated vascular hyperpermeability; (3) overtaxing of outflow mechanisms by protein that interferes with active transport; (4) inflammation of the trabeculum itself with swelling that causes impaired outflow; (5) damage to trabecular endothelial cells by the inflammatory process; (6) mechanical obstruction of outflow by precipitates on the meshwork; (7) sclerosis of trabecular meshwork as a result of chronic inflammation; or (8) obstruction of the trabeculum by a hyaline membrane.

Steroid therapy is also a potential cause of raised pressure, though in the present series no cases of steroid induced glaucoma were recorded. Steroid induced glaucoma is very similar to primary open angle glaucoma, occurring slowly over weeks to months. Occasionally, however, an acute increase in pressure is noted. In all cases the trabeculum is clinically normal in appearance. Cessation of steroids usually leads to a return to normal of the pressure.

In many patients with anterior segment inflammation who are receiving chronic steroid therapy it is not clear whether increased intraocular pressure is due to the effect of the inflammation or steroids. There is not always a relationship between the amount of inflammation, as measured by cells and flare, and inflammation induced rise of intraocular pressure. One therefore cannot predict in which patients intraocular pressure will drop when steroid therapy is increased. The authors have seen patients with only 1+ cells in the anterior chamber who had a dramatic drop in pressure with an increased dosage of steroids.

GLAUCOMA ASSOCIATED WITH SPECIFIC UVEITIC DISORDERS

Many different types of uveitis have been associated with glaucoma, but certain disorders may have a relatively higher risk. For example, glaucoma is believed to be the major long term threat to vision in patients with Fuchs' heterochromic iridocyclitis. Though frequently intermittent and well controlled initially, glaucoma may become chronic and difficult to treat.

Glaucoma is also a major component of the Posner-Schlossman syndrome (glaucomatocyclitic crisis). Though inflammatory signs may be minimal, rises in intraocular pressure may be severe, leading to blurred vision, haloes, and ocular discomfort. Pressures of 40-50 mmHg are not uncommon. Raitta and Vannas believe that there may be a relationship between this syndrome and the eventual development of primary open angle glaucoma.

Segmental iris ischaemia, demonstrated on
fluorescein angiography, implies a vascular cause or the Posner-Schlossman syndrome. Vasculature incompetence could be associated with a release of prostaglandins, inflammation and a subsequent rise in intraocular pressure. Oral indomethacin and subconjunctival polyethylene, both prostaglandin inhibitors, have been shown to lower intraocular pressures during attacks.

The prognosis for control of intraocular pressure in patients with glaucomatomycotic crisis is good. Current treatment recommendations include both topical steroid therapy to reduce inflammation and antiglaucoma medications to control pressure during acute attacks. Future modes may include anti-prostaglandin therapy as well as treatment to modify vascular instability.

The chronic uveitis associated with systemic disease is frequently complicated by severe glaucoma. The glaucoma associated with juvenile rheumatoid arthritis commonly occurs with open angles but may be of the pupillary block, secondary angle closure type, as a result of the formation of posterior synechiae. When glaucoma occurs in patients with sarcoid uveitis, medical and surgical therapy may have only limited success.

Glaucoma may be a prominent feature of the uveitis that results from ocular infections. The prevalence of secondary glaucoma associated with toxoplasmic retinochoroiditis was reported to be 12% in one series. Although the glaucoma in that group was described as transient, a more recalcitrant form may occur with severe infections.

Herpetic uveitis may be particularly prone to the development of glaucoma. In severe cases long term antiglaucoma therapy may be indicated even after active inflammation has subsided. Herpes simplex virus keratoconjunctivitis is often associated with a raised intraocular pressure; Falcon and Williams reported glaucoma in 28% of 183 patients. Postulated mechanisms include both blockage of the trabeculum with inflammatory debris and inflammation of the trabeculum. Townsend and Kaufman found that glaucoma was also a problem in experimental herpes simplex virus keratoconjunctivitis in the rabbit. Secondary glaucoma was attributed to a mononuclear cellular infiltrate in the angle; in addition occasional peripheral anterior synechiae were seen in severe cases.

Secondary glaucoma also can be a serious problem in patients with herpes zoster virus keratoconjunctivitis; Womack and Liesegang reported uveitic glaucoma in 10 of 37 patients. The pathophysiology is probably similar to that associated with herpes simplex virus keratoconjunctivitis.

Uveitis may complicate the use of iris supported or anterior chamber intraocular lenses, more likely as a result of mechanical factors such as chafing of the lens against ocular tissues. The smouldering low-grade uveitis may lead to secondary glaucoma; Ellingson described a distinct syndrome of uveitis, glaucoma, and hyphaema in such patients. The prognosis for the control of pressure is good if inflammation can be controlled.

EVALUATION AND TREATMENT OF UVEITIC GLAUCOMA

The treatment of intraocular inflammation itself is an important component of glaucoma management, because it prevents damage to angle structures and blockage of outflow channels by inflammatory material and thereby maintains normal aqueous outflow. In one case of the present series the control of inflammation by chlorambucil in a patient having a 20-year history of uveitis associated with juvenile rheumatoid arthritis also resulted in lowering of intraocular pressure that could not be controlled by antiglaucoma medications alone.

There may be special considerations in the medical management of glaucoma in patients with uveitis. Miotics such as pilocarpine should be used with caution in inflamed eyes, because they may exacerbate the underlying inflammatory process. The ocular hypotensive effect of epinephrine is inhibited by cyclo-oxygenase inhibitors such as indomethacin. Patients using epinephrine should be monitored for this pressure-raising effect in those rare cases in which non-steroidal anti-inflammatory agents are used in the management of uveitis.

The laser and surgical treatment of glaucoma in patients with uveitis also involves special considerations. Laser iridotomy may be difficult to perform in inflamed eyes and may cause chafing of the lens; it is therefore contraindicated. Surgical peripheral iridectomy be required in cases of uveitis for the treatment of pupillary block glaucoma, surgical section or large peripheral iridectomies should be considered. The efficacy of laser trabeculoplasty varies in these patients and may lead to a worsening of both inflammation and glaucoma.

For patients with chronic inflammatory glaucoma some authors recommend trabeculodilation as the procedure of choice. Success rates as high as 63% with this technique have been reported, in contrast to rates of 18% with standard filtration surgery.

Adjunctive methods of treatment are under investigation to decrease postoperative inflammation and fibrosis after glaucoma filtering surgery. They include the use of locally administered agents such as 5-fluorouracil and triamcinolone in the preoperative and postoperative periods. In future these regimens may be shown to improve filter survival in patients with uveitic glaucoma.

On the basis of these concepts the authors propose a stepwise approach to the evaluation and treatment of increased intraocular pressure in patients with uveitis (Fig 1). Because steroid associated glaucoma is apparently uncommon, and because the effect of prolonged or increased inflammation is potentially worse than a transient steroid induced rise in intraocular pressure, one should first increase steroid dosage and observe both intraocular pressure and inflammation. In cases where severe glaucomatous nerve damage previously exists, antiglaucoma therapy may be included while steroids are increased and then withdrawn if pressure decreases.

If intraocular pressure remains unchanged or rises with increased steroids, and inflammation is stable or improved, steroid therapy should be
reduced to the least amount that will maintain the lowest achievable level of inflammation. If intraocular pressure remains raised as steroid therapy is reduced, glaucoma therapy is initiated. While the modes of therapy may be dictated by the presence of inflammation, the intensity of treatment – as with all forms of glaucoma – is based on the level of intraocular pressure, visual field changes, and status of the optic nerve.

Dr Panek was an Abe Meyer Fellow in Glaucoma, UCLA Department of Ophthalmology. Dr Holland is recipient of the Research to Prevent Blindness – James S Adams Scholar Award. The work was supported in part by a Research Manpower Award from Research to Prevent Blindness, Inc., New York, NY (Dr Holland), and Karl Kirchgeesner Foundation, an unrestricted grant from Research to Prevent Blindness, Inc., National Institutes of Health Grant EY07701, and the Lucile Ellis Simon Glaucoma Research Fund (Dr Lee), and the Elisie B Ballanyne Fund (Dr Christensen).

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Br J Ophthalmol 1990 74: 223-227
doi: 10.1136/bjo.74.4.223

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