Glaucma in patients with uveitis

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Abstract
The records of 100 patients (161 eyes) with uveitis were reviewed retrospectively to determine the prevalence of increased intraocular pressure, the forms of uveitis most commonly associated with glaucoma, and the forms that require specific glaucoma therapy. Secondary glaucoma was present in 23 patients (31 eyes): three of 24 patients with acute uveitis (three eyes, 12% of acute uveitis patients) and 20 of 76 patients with chronic uveitis (28 eyes, 26% of chronic uveitis patients). Eighteen patients (26 eyes, 78% of glaucoma patients) with chronic uveitis required long-term medical therapy to control intraocular pressure. Three patients (three eyes, 12% of glaucoma patients) with acute uveitis required short-term therapy to control intraocular pressure. The remaining two patients had transient increases in intraocular pressure that did not require treatment or that responded to treatment of intraocular inflammation alone. One patient with chronic uveitis (two eyes, 4% of glaucoma patients) required filtering surgery. At least five patients (eight eyes, 22% of glaucoma patients) had glaucomatous visual field defects. The results of this survey are consistent with the concept that secondary glaucoma is a management problem in patients with anterior segment inflammation and chronic rather than acute uveitis. An algorithm for the management of increased intraocular pressure in patients with uveitis is proposed.

Particularly complex management decisions arise when intraocular inflammation is coupled with increased intraocular pressure. The delicate tissues of the anterior segment may become swollen, scarred, and distorted, or rendered dysfunctional by the inflammatory response, leading to increase of intraocular pressure, glaucomatous damage to the optic nerve, and subsequent loss of visual field. Steroids, the mainstay of treatment for uveitis, may also cause increased intraocular pressure. The physician must evaluate carefully the effects of both disease and therapy in order to provide proper management for patients with uveitis and glaucoma.

This study was undertaken to obtain data on the prevalence of increased intraocular pressure in patients with uveitis and to identify the forms of uveitis most commonly associated with glaucoma and that require specific glaucoma therapy. With such information rational approaches to the management of uveitis-related glaucoma can be planned.

Subjects and methods
The records of 100 consecutive patients with uveitis referred to and examined by one author (GNH) 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 suspects if their 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, synechiae, 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 synechiae producing pupillary seclusion and iris bombé. Angle closure also can occur without pupillary block. It can result from peripheral anterior synechiae (an iridotrabecular adherence-associated inflammation of iris and angle.
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structures) and sometimes inflammatory nodules in the angle. In addition, ruberosis 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 hyper-permeability; (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

Management of Intraocular Pressure in Patients with Uveitis

GONIOSCOPY

CLOSED OR NARROW ANGLE WITH IRIS BOMBE

Laser iridotomy or Surgical iridectomy

Decrease in IOP to normal Persistent elevation of IOP

Increase dosage of steroids

Reduce steroids to lowest dosage that will maintain minimal inflammation

Monitor status on anti-inflammatory regimen

Glaucoma Therapy 1. Medical 2. Surgical

Figure 1: Algorithm for the management of raised intraocular pressure in patients with uveitis.
fluorescein angiography, implies a vascular cause
or the Posner-Schlossman syndrome.14
Vasculature incompetence could be associated
with a release of prostaglandins, inflammation
and a subsequent rise in intraocular pressure.15
Oral indomethacin and subconjunctival
polysporin, both prostaglandin inhibitors, have been shown to lower intraocular pressures
during attacks.12

The prognosis for control of intraocular pressure
in patients with glaucomatocyclitic
The treatment for 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.26 In one case
of the present series the control of inflammation
by chlormabucil 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 inflam-
matory process.19 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.27

The laser and surgical treatment of glaucoma
in patients with uveitis also involves special
considerations. Laser iridotomy may be difficult
to perform in inflamed eyes28 and may cause
scarring. Should 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.29 The efficacy of laser trabecu-
plasty varies in these patients30 and may lead to a
worsening of both inflammation and glaucoma.

For patients with chronic inflammatory
The pathophysiology is probably similar to that
associated with herpes simplex virus keratoconjunctivitis.31
Uveitis may complicate the use of iris
supported or anterior chamber intraocular
lenses,32 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.33 The prognosis for
the control of pressure is good if inflammation
can be controlled.
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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.

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