

# Incidence and prognosis of ocular hypertension secondary to viral uveitis

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**Abstract** This retrospective study was designed to estimate the cumulative incidence of glaucoma in viral uveitis. Seventy-six consecutive patients with viral stromal keratouveitis were divided into two groups according to the etiologic agents herpes simplex virus (HSV) keratouveitis ( $n = 58$ ) and herpes zoster virus (HZV) keratouveitis ( $n = 18$ ). The groups were evaluated for the incidence and prognosis of ocular hypertension. Etiologic agents were determined with the help of clinical observation supported by the polymerase chain reaction (PCR) of aqueous humor. All patients received oral acyclovir therapy for at least six months and topical prednisolone in tapered doses. There was no significant

difference in the recurrences of HSV and varicella zoster virus (VZV) keratouveitis between groups ( $P = 0.431$ ). The total incidence of secondary glaucoma was 13.1%. Most of the patients responded to antiviral and antiglaucomatous therapy. Trabeculectomy with mitomycin C was performed in only two patients. Secondary glaucoma can be regarded as a frequent complication of viral uveitis. As it has a good prognosis, surgical intervention is rarely required.

**Keywords** Viral keratouveitis · Secondary glaucoma · Ocular hypertension · Herpes simplex virus · Herpes zoster virus

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The authors have no proprietary interest in any material or method described in this study.

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## Introduction

Herpetic anterior uveitis due to either herpes simplex virus (HSV) or varicella zoster virus (VZV) infection accounts for 5–10% of all uveitis cases seen at tertiary referral centers, and it is the most common cause of infectious anterior uveitis [1]. The accompanying characteristics of the herpetic uveitis can be dermatitis, conjunctivitis, keratitis, scleritis, or retinitis [2]. Anterior uveitis associated with sectorial iris atrophy was often attributed to VZV, even when there was no history of zoster dermatitis [3]. HSV keratouveitis (with or without focal iris atrophy), on

the other hand, is a well recognized manifestation of herpetic eye disease [3].

The acute increase in intraocular pressure (IOP) has been attributed by most authors to the inflammation of the trabecular meshwork, a notion supported by the observation that IOP typically normalizes in response to steroid therapy [2]. Such hypertensive episodes resemble, in many ways, the attacks of Posner-Schlossman syndrome, which is suggested by some authors to be due to HSV infection [3].

## Materials and methods

A retrospective study was made in 76 consecutive patients with viral stromal keratouveitis seen at the Uveitis-Behçet Service, Department of Ophthalmology, Ankara Research and Training Hospital, between January 1993 and January 2005. Seventy-six patients were divided into two groups according to the etiologic agent as HSV keratouveitis (group 1) ( $n = 58$ ) and herpes zoster virus (HZV) keratouveitis (group 2) ( $n = 18$ ). Patients were evaluated for the incidence and prognosis of ocular hypertension (OHT)—a temporary rise in IOP during an active uveitis period. Permanent IOP rise during the remission period is termed as secondary glaucoma. Etiologic agents were determined with the help of historical information, seropositivity, and clinical observation supported by polymerase chain reaction (PCR) analysis of aqueous humor for each patient. All patients fulfilled all of the following criteria: (1) anterior uveitis, (2) sectorial atrophy of the iris-associated keratitis. Data on these patients were reviewed with an emphasis on the medical history (herpes labialis, herpes dermatitis previously), onset of disease, number of recurrences during their follow-up, persistence of elevated IOP (secondary glaucoma), occurrence of peripheral anterior synechia, the status and pigmentation of the angles, biomicroscopic findings, and surgical interventions. All patients received oral acyclovir therapy for at least six months and topical prednisolone in tapered doses. Antiglaucomatous medications were used when necessary.

### Statistical analysis

Analysis performed with the SPSS for Windows, version 11.5 (SPSS, Chicago, IL) software package.

Pearson's Chi-square test, the Mann–Whitney  $U$  test, and Fisher's exact test were used to calculate the association between the variables.  $P$ -values  $< 0.05$  were considered to be statistically significant.

## Results

Among 76 patients with the diagnosis of viral keratouveitis, 58 (76.3%) had HSV and 18 (23.6%) had HZV infection. Table 1 shows the demographical features of groups. The VZV keratouveitis group (group 2) was older than the HSV keratouveitis group (group 1) ( $P = 0.001$ ). There was no significant difference between groups in terms of sex and follow-up period.

The number of recurrences of uveitis in the two groups are given in Table 2. No statistically significant difference was found between groups when the number of recurrences was considered.

Table 3 illustrates the IOP elevations in the groups. The total incidence of OHT in the 'active uveitis' period was 47.3% (36/76). There was no difference between groups for OHT incidence during the active uveitis period. Secondary glaucoma (persistent IOP elevation) incidence in the remission period was 13.1% (10/76). There was no difference between groups for glaucoma incidence during the remission period. The follow-up time in patients with OHT was  $33 \pm 14.7$  (22–71) months, and it was  $47 \pm 19.2$  (24–85) months in patients with glaucoma. There was no difference between OHT and glaucoma patients according to the follow-up time.

Table 4 demonstrates the association between the number of attacks and IOP elevation. The number of uveitis attacks associated with high IOP per patient per year was higher in patients who developed glaucoma than in the patients who had OHT during their follow-up (0.036).

The biomicroscopic findings of the groups are given in Table 5. The most common was corneal nephelion in both groups, followed by iris atrophy, corneal neovascularization, and heterochromia. The difference between groups according to the biomicroscopic findings was not significant.

Table 6 illustrates the gonioscopic findings. Of the overall cohort of patients, 32.8% had pigmentation of the angle, 91% had Grade 4 open angle, 9% had Grade 3 open angle, and 5.3% had peripheral anterior

**Table 1** Demographical features according to group

Demographical features	HSV, <i>n</i> = 58	VZV, <i>n</i> = 18	Total, <i>N</i> = 76
Mean age	41.5 ± 15.6 (18–61)	58.9 ± 15.9 (42–80)	45.6 ± 17.3 (18–80)
Male/female ratio	27/31	12/6	39/37
Follow-up period (months)	36 ± 18.2 (24–120)	38 ± 11.7 (24–70)	37.2 ± 18.1 (24–120)

HSV = herpes simplex virus; VZV = varicella zoster virus

**Table 2** Recurrence of uveitis

Number of recurrences	HSV, <i>n</i> = 58	VZV, <i>n</i> = 18	Total, <i>N</i> = 76
No recurrence	26 (45%)	11 (61%)	37 (49%)
1 recurrence	20 (34%)	5 (28%)	25 (32%)
≥2 recurrences	12 (21%)	2 (11%)	14 (19%)

**Table 3** Intraocular pressure (IOP) elevation

IOP elevation	HSV, <i>n</i> = 58	VZV, <i>n</i> = 18	Total, <i>N</i> = 76	<i>P</i> -value
OHT (during active uveitis period)	28 (48.3%)	8 (4%)	36 (47.3%)	0.79
Secondary glaucoma (during remission period)	7 (12%)	3 (2%)	10 (13.1%)	0.69

OHT = ocular hypertension

**Table 4** Association between the number of attacks and IOP elevation

IOP elevation	Median number of attacks	Number of uveitis attacks with high IOP/year	<i>P</i> -value
Ocular hypertension ( <i>n</i> = 36)	0 (0–3)	0.57 ± 0.81	0.036
Secondary glaucoma ( <i>n</i> = 10)	1 (0–6)	1.9 ± 2.07	

**Table 5** Biomicroscopic findings

Biomicroscopic findings	HSV, <i>n</i> = 58	VZV, <i>n</i> = 18	Total, <i>N</i> = 76	<i>P</i> -value
Corneal nephelion	43 (74.1%)	10 (56%)	53 (69.7%)	0.13
Iris atrophy	13 (22.4%)	5 (22.2%)	18 (23.6%)	1.00
Corneal vascularization	2 (3.4%)	1 (5.5%)	3 (3.9%)	0.3
Heterochromia	1 (1.7%)	0 (0%)	1 (1.3%)	0.5

**Table 6** Gonioscopic findings

Gonioscopy	HSV, <i>N</i> = 58			VZV, <i>N</i> = 18			Total, <i>N</i> = 76	<i>P</i> *
	OHT, <i>n</i> = 21	SG, <i>n</i> = 7	Normal IOP, <i>n</i> = 30	OHT, <i>n</i> = 5	SG, <i>n</i> = 3	Normal IOP, <i>n</i> = 10		
Angle pigmentation	5 (23.8%)	2 (28.5%)	11 (36.6%)	2 (40%)	1 (33.3%)	4 (40%)	25 (32.8%)	0.7
Grade 4 open angle	20 (95%)	7 (100%)	27 (90%)	5 (100%)	3 (100%)	7 (70%)	69 (91%)	1.0
Grade 3 open angle	1 (5%)	0 (0.0%)	3 (10%)	0 (0.0%)	0 (0.0%)	3 (30%)	7 (9%)	0.9
PAS	1 (4.8%)	0 (0.0%)	2 (6.6%)	0 (0.0%)	0 (0.0%)	1 (10%)	4 (5.3%)	1.1

PAS = peripheral anterior synechia, OHT = ocular hypertension; SG = secondary glaucoma; IOP = intraocular pressure

*P*\* = statistical difference between HSV (*n* = 58) and VZV (*n* = 18)

synechia (PAS). No statistical difference was present between groups (HSV and VZV) for gonioscopic findings.

Patients received oral acyclovir ( $5 \times 400$  mg/day for the first month and  $2 \times 400$  mg for the following 5 months) and topical prednisolone acetate (4 drops/day, tapering to one drop once a week, and ending at the end of 1 month), and, if needed, antiglaucomatous drugs. Most of the patients responded well to medical therapy. Trabeculectomy with mitomycin C was performed in only two (2.6%) patients. Both of the patients were in group 2 and there was not a significant difference among the two groups in terms of surgical intervention. No complication was observed after the operations.

## Discussion

HSV-associated ocular diseases comprise a number of clinical entities: blepharitis, keratoconjunctivitis, dendritic epithelial keratitis, geographic or trophic herpetic corneal ulcerations, stromal keratitis, endothelitis-trabeculitis, keratouveitis, and acute retinal necrosis syndrome [3, 4]. Anterior uveitis caused by HSV seemed to be almost always associated with active epithelial keratitis or interstitial keratitis [5].

The recurrence rates of keratouveitis in HSV were reported to be 20% in the first 2 years, 50% in the first 5 years and 67% in the first 7 years [6]. Long-term medical treatment against the recurrences resulted in a better prognosis and surgical intervention for glaucoma is seldom required.[7]. Although recurrences may continue with long-term treatment, severity of the recurrences and the rates of complications are smaller [8].

The most common complication in viral anterior uveitis is secondary glaucoma [9, 10]. The association of increased IOP and HSV inflammation was documented in the literature previously [8, 9]. In a previously published study, about 90% of the patients had an elevated IOP during an attack of active viral iritis [3]. As only a few cells in the anterior chamber was detected, trabeculitis had been considered as the cause of OHT.

In this study, the incidence of OHT was 47.3%. The response to medical treatment in increased IOP secondary to herpetic viral keratouveitis was good

and was easily managed with a combination of antiglaucomatous and antiviral agents in the first 3–4 weeks. Secondary glaucoma has occurred in 13.1% of patients. Additionally, there was no significant difference in terms of OHT among HSV and HZV uveitis. The number of uveitis attacks and the number of uveitis attacks with high IOP per patient per year were higher in patients who developed glaucoma than in patients who had OHT during their follow-up. As patients with glaucoma had a higher number of recurrences of keratouveitis, they might have received a cumulative longer duration of steroid therapy. Although the topical steroids were used in low doses, this may be a steroid-induced glaucoma.

In conclusion, secondary glaucoma can be regarded as a frequent complication of viral uveitis. It has a good prognosis and surgical intervention for glaucoma is seldom required.

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