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Ocular Inflammation in Behçet's Disease: Incidence of Ocular Complications and of Loss of Visual Acuity

R. Oktay Kaçmaz, MD, MPH[1], **John H. Kempen, MD, PhD**[3,4,5], **Craig Newcomb, MS**[5], **Sapna Gangaputra, MBBS, DO, MPH**[6], **Ebenezer Daniel, MBBS, DO, MS, MPH**[6], **Grace A. Levy-Clarke, MD**[8], **Robert B. Nussenblatt, MD, MPH**[8], **James T. Rosenbaum, MD**[9,10], **Eric B. Suhler, MD, MPH**[9,11], **Jennifer E. Thorne, MD, PhD**[6,7], **Douglas A. Jabs, MD, MBA**[6], and **C. Stephen Foster, MD**[1,2] **for the Systemic Immunosuppressive Therapy for Eye Diseases Cohort Study Group**

[1] *Massachusetts Eye Research and Surgery Institution, Cambridge, Massachusetts* [2] *Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts* [3] *Ocular Inflammation Service, Scheie Eye Institute, The University of Pennsylvania, Philadelphia, Pennsylvania* [4] *Center for Preventive Ophthalmology and Biostatistics, Department of Ophthalmology, The University of Pennsylvania, Philadelphia, Pennsylvania* [5] *Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics and Epidemiology, The University of Pennsylvania, Philadelphia, Pennsylvania* [6] *Department of Ophthalmology, The Johns Hopkins University, Baltimore, Maryland* [7] *Department of Epidemiology, The Johns Hopkins University, Baltimore, Maryland* [8] *Laboratory of Immunology, National Eye Institute, Bethesda, Maryland* [9] *Department of Ophthalmology, and Oregon Health & Science University, Portland, Oregon* [10] *Department of Medicine, and Oregon Health & Science University, Portland, Oregon* [11] *Portland Veteran's Affairs Medical Center, Portland, Oregon*

Abstract

Purpose—To estimate the risk of structural ocular complications and loss of visual acuity in cases of Behçet's Disease (BD); to evaluate potential risk and protective factors for these events

Design—Retrospective cohort study

Setting: Five academic center ocular inflammation subspecialty practices

Study Population: A total of 168 consecutive patients with BD-associated ocular inflammation

Procedures: Clinical data on these patients were ascertained by standardized chart review

Outcome Measures: Visual acuity, structural ocular complications of inflammation, intraocular pressure (IOP)

Results—Over a median follow-up of 1.05 years, the incidence of specific structural complications and IOP disturbances were common: the incidence rate of any ocular complication was 0.45/eye-

Corresponding Author: C. Stephen Foster, M.D., Address: Massachusetts Eye Research and Surgery Institution, 5 Cambridge Center, 8th Floor, Cambridge MA 21042; Phone: 617 577 1370, email: sfoster@mersi.us.
Reprint Requests: John H. Kempen, M.D., Ph.D.; Address: Center for Preventive Ophthalmology and Biostatistics; Department of Ophthalmology; University of Pennsylvania; 3535 Market Street, Suite 700; Philadelphia, PA 19104; email: john.kempen@uphs.upenn.edu

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year (EY). Rates of loss of visual acuity to 20/50 or worse and to 20/200 or worse were 0.12/EY and 0.09/EY respectively. Risk factors for loss of visual acuity during follow-up were persistent inflammatory activity, presence of posterior synechiae, presence of hypotony, and presence of elevated IOP. In a time-dependent analysis, current activity of ocular inflammation was associated with an increased risk of loss of visual acuity to 20/50 or worse (RR = 2.45, 95% CI: 1.1–5.5, p = 0.03) and to 20/200 or worse (RR = 2.67, 95% CI: 1.2–5.8, p = 0.01).

Conclusions—Loss of visual acuity and occurrence of ocular complications were common in patients with ocular inflammation associated with Behçet's Disease, even with aggressive therapy. Ongoing inflammation during follow-up, presence/occurrence of posterior synechiae, hypotony, and elevated IOP were associated with an increased risk of loss of visual acuity.

Introduction

Behçet's Disease (BD) is a chronic, relapsing inflammatory disorder of unknown etiology. The first series of patients with BD was published in 1937[1] as a triad of symptoms consisting of oral aphthae, genital ulcers, and hypopyon iritis. Behçet's Disease is characterized by episodic inflammation which may affect every tissue and organ in the body[2]. The International Study Group for Behçet's Disease established the diagnostic criteria as recurrent oral aphthous ulcers plus two of the following: recurrent genital ulcers, ocular inflammation, skin involvement, and/or a positive pathergy test[3]. Ocular involvement occurs in approximately 70% of the patients and is associated with a high risk of blindness[4]. Ocular features of BD are anterior uveitis, retinal vasculitis (both veins and arteries), optic neuropathy, retinal infiltrates, scleritis, and vitritis. Behçet's Disease is more prevalent along the ancient Silk Road that extends from the Eastern Mediterranean to Japan. Males are affected more than women with a 2–10:1 ratio in these countries[5]. Geographic variability in the clinical course is thought to exist, with a milder course and a reversal of the male: female ratio described in at least one Western population[5].

Previous studies often have reported frequencies of complications over variable follow-up, an approach which can provide misleading results. Few true complication rates have been described. Also, little has been reported about the extent of specific structural complications causing loss of visual acuity over time in patients with BD in the United States, who may have a better prognosis than in populations along the ancient Silk Road.

The Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study is a retrospective cohort study conducted at five university-affiliated ocular inflammatory diseases subspecialty practices in the United States[6]. One of the aims of the study is to describe the outcomes of ocular inflammatory diseases.

The purpose of this paper is to assess the risk of loss of visual acuity and of structural ocular complications in this large, Western cohort of patients with BD and ocular involvement, and to evaluate potential risk factors for changes in visual acuity.

Methods

Study population

The methods of SITE Cohort study have been previously described[6]. All patients with BD-associated ocular inflammation from the SITE cohort were included. These patients had been seen between 1978 and 2007 inclusive. The centers involved in the SITE study are: the Uveitis Clinic, Casey Eye Institute, Oregon Health & Sciences University (OHSU); the Laboratory of Immunology, National Eye Institute (NEI); the Ocular Immunology Service, Wilmer Eye Institute, Johns Hopkins University (JHU); the practice of C. Stephen Foster, formerly at the Massachusetts Eye and Ear Infirmary (MEEI), and now at the Massachusetts Eye Research

and Surgery Institution (MERSI), and the Ocular Inflammation Service, Scheie Eye Institute, University of Pennsylvania (PENN). The study was performed with the approval of all the participating centers' Institutional Review Boards and conducted in accordance with the Declaration of Helsinki.

Data collection

Information on all patients evaluated and treated for BD-associated ocular inflammation was entered into a database using a computer-based standardized data entry formset, specifically prepared for the SITE Cohort study. The system includes extensive intrinsic quality control checks, requiring correction of potential errors in real time. Potential errors also were identified through post-hoc range and logic checks, investigated, and rectified when appropriate. Data collected that are relevant to this report include: demographic characteristics, ophthalmologic examination findings, and all medications that patients (or eyes) were receiving at each clinic visit, including dose and route of administration. Ophthalmologic examinations included measurement of visual acuity (VA), intraocular pressure (IOP) assessment, and details regarding the activity and complications of the ocular inflammation. Retinal vasculitis was defined as "active vascular sheathing" seen in clinical examination and/or fluorescein angiography.

Main Outcome Measures

Incidence rates for loss or improvement in visual acuity and of structural ocular complications and IOP disturbances were assessed. Loss or gain of visual acuity was evaluated across the 20/50 or worse (visual impairment) and the 20/200 or worse (legal blindness) thresholds according to the recommendations of the Standardization of Uveitis Nomenclature Working Group[7]: improvement or worsening by 3 logMAR lines was also evaluated, transforming Snellen visual acuity measurements into logMAR equivalents[8], when necessary

Ocular complications evaluated included posterior synechiae, occurrence of cataract surgery, ocular hypertension (IOP ≥21mmHg and 30mmHg), hypotony (IOP ≤5 mmHg), epiretinal membrane, macular edema, exudative retinal detachment, retinal neovascularization, and choroidal neovascularization.

Statistical analysis

Confidence intervals (CI) on proportions were calculated assuming a binomial distribution. Incidence rates were calculated as the number of events divided by the amount of person-time or eye-time at risk. P values for proportions were calculated using the χ^2 test or Fisher's Exact Test when expected cell counts were less than 5. Confidence intervals on incidence rates were generated assuming a Poisson distribution. Potential risk factors for loss or gain of visual acuity were evaluated using survival analysis, including Cox regression with adjustment for clustering between eyes of the same patient[9] (when applicable) to obtain adjusted risk ratios. Because vision loss events were exceedingly rare in the anterior uveitis only and other ocular inflammation groups, analyses for loss of visual acuity were limited to the cases of BD-associated uveitis which had involvement of the posterior segment.

Results

Study population at presentation

Demographic and clinical characteristics of the study population (168 patients and 317 affected eyes) are summarized in Table 1. The median follow-up time was 1.05 years (range 0–19.5 years). For the patients that had more than one visit, there were a total of 3082 visits with an average of 16.05 visits per person/year of follow-up. The median age at the time of diagnosis

of uveitis was 31.3 for anterior uveitis and 27.6 for uveitis involving the posterior segment. Anterior uveitis was defined for the purpose of the study as the inflammation primarily in the anterior segment. Uveitis classified as intermediate using IUSG/SUN criteria[7] was included with the posterior/panuveitis group, hereafter called the posterior involvement group. The anterior uveitis group comprised about 11% of all patients; 44% of whom were male, as opposed to 53% of the posterior/panuveitis group. The non-uveitis group consisted of five patients with scleritis and one patient each with retrobulbar neuritis, orbital inflammation, and missing diagnosis. Bilateral ocular inflammation was present in 88% of the posterior segment cases versus 78% of anterior uveitis cases (P = 0.26). The median duration of uveitis prior to presentation to the referral center was 3 years for the anterior uveitis group and 2.2 years for the posterior segment group. Posterior synechiae were present in 12.5% of anterior uveitis and in 8% of posterior segment cases at the time of presentation to the referral center. Retinal vasculitis and macular edema were the most common ocular findings present in posterior segment group eyes (22% and 14% respectively). Among patients with posterior involvement, about 10% had already had cataract surgery compared to 6% of anterior uveitis eyes (P = 0.75). Elevated IOP ≥21 mm Hg was present in 19% of the eyes with anterior uveitis, compared to 13% of posterior/panuveitis eyes (P = 0.41). Reduced visual acuity was common in both groups, but more common in the eyes with posterior segment involvement; with 25% of the anterior uveitis and 60% of the posterior uveitis eyes presenting with a visual acuity of 20/50 or worse (P = 0.0001). A similar pattern was observed for visual acuity of 20/200 or worse: 16% for the anterior uveitis cases and 34% for the posterior involved cases (P = 0.035).

Incidence of structural ocular complications and of vision loss/gain

The incidence rates for ocular complications and loss of visual acuity among cases with posterior involvement are given as Table 2. The incidence of retinal vasculitis during follow-up was 0.17/person-year (PY) among patients without retinal vasculitis at presentation or 0.12/eye-year (EY) among eyes with inflammation but free of vasculitis at presentation. Incidence of ocular hypertension (≥21 mmHg) was 0.24/PY or 0.17/EY, and that for IOP≥30 mmHg was 0.07/PY or 0.04/EY. The rate of macular edema during follow-up was 0.23/PY or 0.14/EY. The incidence rate of loss of visual acuity to 20/50 or worse and to 20/200 or worse among affected eyes were 0.12/EY and 0.09/EY, respectively, among eyes with visual acuity better than these thresholds at presentation. The incidence of gaining 3 lines of visual acuity during follow-up was 0.38/PY or 0.21/EY.

Risk factors for visual acuity loss among eyes affected by BD

Risk factors for loss of visual acuity are summarized in Table 3. In the time-dependent multiple regression analysis, current presence of anterior chamber cell ≥ 1+, vitreous cell ≥ 2+, vitreous haze ≥ 1+, hypotony, and elevated IOP were associated with a statistically significant increased risk of visual acuity loss to 20/50 or worse. The analysis for loss of visual acuity to 20/200 or worse identified a similar set of risk factors, including the current presence of anterior chamber cell ≥ 2+, vitreous cell ≥ 1+, vitreous haze ≥ 1+, posterior synechiae, and hypotony. The relationship between measures of current (time-updated) inflammatory activity and loss of visual acuity are depicted in Figures 1 (relationship to overall activity) and 2 (relationship to vitreous haze). Overall activity of inflammation was associated with an increased risk of loss of visual acuity to 20/50 or worse (RR = 2.45, 95% CI: 1.1–5.5, p = 0.03) and to 20/200 or worse (RR = 2.67, 95% CI: 1.2–5.8, p = 0.01). Measures assessing a broader range of inflammatory activity were more strongly associated with increased risk of vision loss. The presence of anterior chamber cell ≥ 2+ was associated with a four fold increase in the incidence of 20/50 or worse visual acuity (RR = 4.1; 95% CI: 1–16.9, P = 0.05), and with an almost five fold increase in the incidence of 20/200 or worse visual acuity (RR = 4.7; 95% CI: 1.2–18.6, P = 0.03). The presence of vitreous haze ≥ 1+ was associated with a twelve fold increase in the incidence of 20/50 or worse vision (RR = 12.0; 95% CI: 2.1–68.7, P = 0.005) and more

than seven fold increase in developing 20/200 or worse vision (RR = 7.4, 95% CI: 2.5–21.8, P = 0.0003).

In general, higher risk of loss of visual acuity occurred in a dose-response pattern with increasing levels of intraocular inflammation, which was consistent across different measures of inflammatory activity. The most common causes of visual acuity loss for both outcomes were inflammatory haze, cataract, cystoid macular edema (CME), macular scar formation, and optic nerve disease (see Table 4).

Discussion

In previous reports from countries with a high incidence of BD (Turkey and Japan), the risk of blindness among patients with BD-associated uveitis is high: patients were observed to become blind in an average of 3.36 years after the onset of eye symptoms[10], and to reach a visual acuity of 20/200 or worse within 4 years in 50–90% of cases[11]. However, the prevalence of legal blindness was reported to be 25% in North America[12] and Muhaya *et al* found significant differences in the severity of ocular involvement between patients in Japan and Great Britain[13]. Our results suggest that there is a high risk of loss of visual acuity in US patients as well.

With the availability of new therapeutic approaches, this ominous outlook may be improving. Nevertheless, BD-associated uveitis still bears a guarded visual prognosis with a high risk of cataract, cystoid macular edema (CME), macular scar formation, and optic nerve disease, among others. The age of uveitis in our American cohort, ~30 years, was similar to that reported in other parts of the world: 34 years for both sexes in Japan[14, 15] and 28.5 years for males and 30 years for women in Turkey[16]. We did not observe a strong male preponderance, in contrast to what has been reported from the countries along the ancient Silk Road[15–17]. Males comprised 63% of all patients in Japan[14] and 68% in Turkey[16]. However, one report from Israel showed less male preponderance at 53% of all patients[18], and a report from Italy had a population with an even distribution (50%) in gender[19], observations similar to ours.

We used rates of a specific outcome such as visual acuity calculated per “person-year” or “eye-year”, instead of “final visit” statistics, to limit the bias of variable follow-up time and to facilitate subsequent comparisons across different studies as recommended by the Standardization of Uveitis Nomenclature Guidelines[7]. Even though the median follow-up time of 1.05 years may seem to be short, the person-year and eye-year numbers are quite large: ranging from 86.3 to 549.3 person years and 284.3 to 1401.5 eye years. Because most of the older reports did not use this approach, it is difficult to precisely compare our results to these reports. In some of our analyses, the number of events was small, which limited the precision of RR estimates for certain risk factors. Nonetheless, the study suggests that the development of loss of visual acuity and structural ocular complications are very frequent in BD-associated uveitis involving the posterior segment, but not highly frequent when disease is limited to anterior uveitis or scleritis. Some form of ocular complication occurred in nearly half of the eyes with posterior segment involvement during each year of follow-up.

Visual acuity loss during BD flare-ups may be reversible following treatment. We observed an incidence rate of 0.21/EY and 0.38/PY of gaining 3 lines in the Snellen chart in this cohort, which supported this fact. To deal with the problem of reversibility, an event for VA loss was defined as VA ≤ 20/200 at two or more visits spanning 30 days in order to approximate irreversible vision loss.

One of our most striking observations was a consistent, dose-response relationship between the current (time-updated) inflammatory activity and risk of loss of visual acuity. This result confirms a principle that is widely understood in the field of uveitis even though it has been

objectively confirmed only occasionally[16, 20, 21]: that control of active inflammation is critically important to avoid vision loss in patients with BD-associated uveitis. Current (time-updated) presence of posterior synechiae, also, was associated with an increased risk of loss of visual acuity, probably representing to some extent the cumulative damage an eye had suffered from inflammation up to that point. Disturbances of intraocular pressure—particularly hypotony, but also ocular hypertension—were associated with substantially increased risk of vision loss, suggesting that both preventive and corrective therapy for these problems are an important aspect of the management of patients with BD-associated uveitis.

In this non-randomized study, we were unable to directly assess the merits of alternative forms of therapy for BD-associated uveitis, as disease severity appeared to be strongly related to the choice to use more aggressive forms of therapy. However, the benefit of treatment sufficiently aggressive to control ocular inflammation can be inferred by the strong, dose-response relationship between the current level of inflammation and risk of loss of visual acuity, as well as from the observation that a substantial group of patients/eyes developed visual improvement while under management. Yoshida *et al* reported significant improvements in visual prognosis with the use of immunosuppressive therapy[15], an approach we believe to be well justified for a disease with as poor a visual prognosis as BD-associated uveitis involving the posterior segment. This approach also is supported by other randomized clinical trials[22, 23]. However, more randomized studies would be needed to clearly identify the best specific approach to management of these cases, which may be a combination therapy of various agents[24]. Among the currently popular approaches to management are the uses of infliximab[25, 26] and of interferon-alpha[27].

Additional limitations of the study are that a referral bias may exist, because all five institutions are tertiary care centers, and it is likely that relatively severe cases of BD-associated ocular inflammation tended to be referred to these centers as suggested by high frequencies of ocular complications and poor visual acuity at presentation. The frequency of reduced visual acuity at presentation (VA of 20/200 or worse in 34% of posterior/panuveitis and in 16% of anterior uveitis patients) was similar to that reported from other tertiary care centers along the ancient Silk Road. Yoshida *et al* reported that 37% of the patients seen in the 1980s had poor visual acuity (20/200 or worse) at the first visit[15]. Tugal-Tutkun *et al* reported that 41% of the patients had an initial visual acuity of 20/200 or worse[16]. Also, it has been suggested that the first two years after the diagnosis are the most critical for the visual prognosis of patients with BD-associated uveitis[28], in which case our results may not fully reflect the potential benefits of therapy, as most patients were referred more than two years following diagnosis. Based on these considerations, the prognosis of BD-associated ocular inflammation in the total population of persons with this condition is probably better than we observed, but our observations are probably generalizable to other tertiary uveitis centers.

In summary, moderate and severe visual impairment as well as structural ocular complications occurred commonly in this cohort of patients with BD-associated ocular inflammation, despite typically aggressive management often including immunosuppressive therapy. The presence of posterior synechiae, persistence of higher grades of intraocular inflammation, elevated IOP, and hypotony were statistically significant factors for the development of vision loss after controlling for other potentially confounding variables. The most common causes of incident loss of visual acuity during follow-up were inflammatory haze, cataract, and macular disorders, all of which are potentially treatable or preventable causes of poor vision. Increased activity of inflammation is associated with increased risk of loss of visual acuity in a dose-dependent fashion, providing reinforcement to the message that treatment adequate to control inflammation is of pre-eminent importance in patients with BD-associated ocular inflammation.

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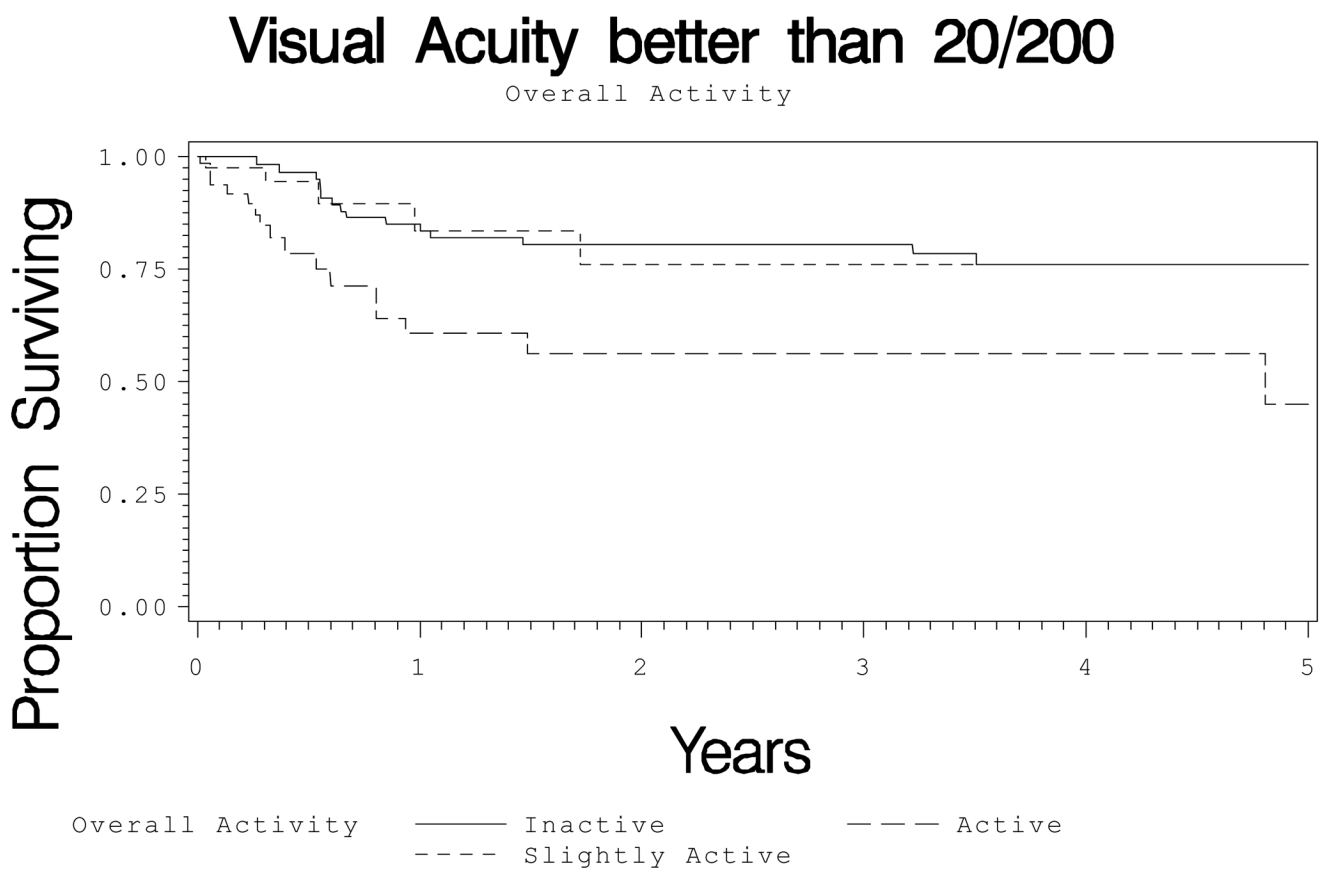

Figure 1.
Kaplan-Meier survival curve for loss of visual acuity to the 20/200 or worse level over time, in relationship to current (time-updated) overall activity of uveitis. Slightly active refers to minimal signs of activity, which cannot be properly graded as the absence of active inflammation according to SUN criteria[7]. Follow-up is truncated at 5 years; events were rare after the first five years.

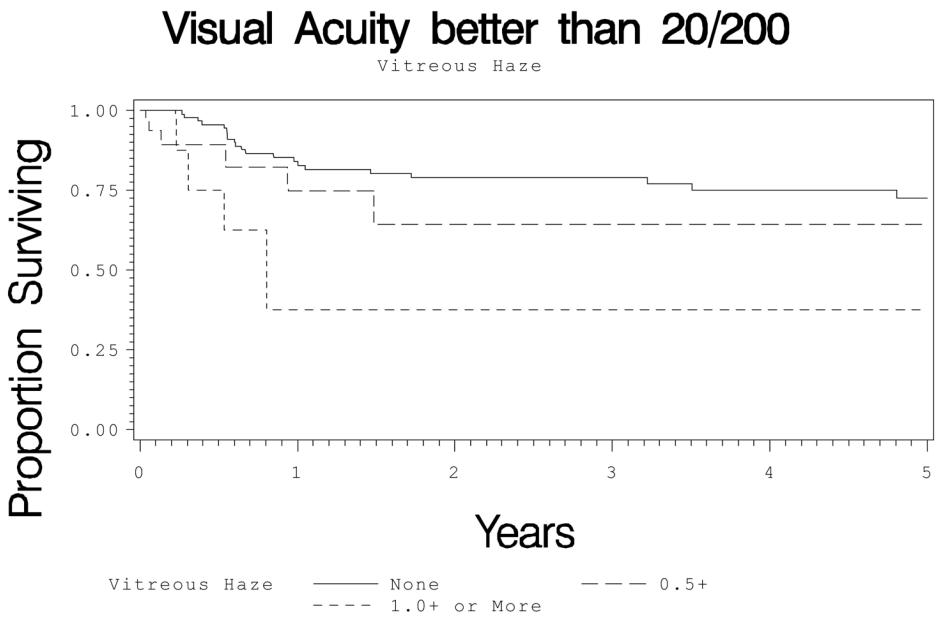

Figure 2.
Kaplan-Meier survival curve for loss of visual acuity to the 20/200 or worse level over time, in relationship to current (time-updated) level of vitreous haze. Follow-up is truncated at 5 years; events were rare after the first five years

TABLE 1

Characteristics of Patients with Behçet's Disease at Presentation*

Characteristic	Anterior Uveitis Only	Uveitis Involving Posterior Segment	Other
Person Specific Characteristics			
Patient Number	18	142	8
Median age at diagnosis of uveitis, years (range)	31.3 (13.9 – 52.9)	27.6 (4.8 – 64.3)	30.4 (22.0 54.7)
Median age at diagnosis of Behçet's Disease, years (range)	37.9 (13.9 – 55.8)	28.3 (10.4 – 65.0)	26.7 (9.6 – 59.2)
Gender, % men	10 (55.6%)	67 (47.2%)	5 (62.5%)
Race, % Caucasian	13 (72.2%)	87 (61.3%)	6 (75%)
Race, % Black	1 (5.6%)	16 (11.3%)	1 (12.5%)
Race, % Other	4 (22.2%)	39 (27.5%)	1 (12.5%)
Median duration of uveitis prior to presentation, years (range)	3.0 (0.0 – 23.6)	2.2 (0.0 – 30.5)	0.6 (0.0 – 12.2)
Bilateral uveitis, %	14 (77.8%)	125 (88.0%)	7 (87.5%)
Eye Specific Characteristics			
Number of affected eyes	32	270	15
Ocular Findings, affected eyes, %			
Any Ocular Complication	13 (40.6%)	164 (60.7%)	3 (20%)
Posterior Synechiae	4 (12.5%)	22 (8.2%)	0 (0.0%)
Retinal Vasculitis	0 (0.0%)	59 (21.8%)	0 (0.0%)
Cataract Surgery	2 (6.2%)	26 (9.6%)	0 (0.0%)
Ocular Hypertension (>21 mm HG)	6 (18.7%)	35 (13%)	2 (13.3%)
Ocular Hypertension (>30 mm HG)	1 (3.1%)	8 (3%)	0 (0.0%)
Hypotony	1 (3.1%)	2 (0.7%)	1 (6.7%)
Glaucoma Surgery	0 (0.0%)	2 (0.7%)	0 (0.0%)
Epiretinal Membrane Formation	3 (9.4%)	31 (11.5%)	0 (0.0%)
Macular Edema	2 (6.2%)	39 (14.4%)	0 (0.0%)
Exudative Retinal Detachment	0 (0.0%)	2 (0.7%)	0 (0.0%)
Retinal Neovascularization	0 (0.0%)	6 (2.2%)	0 (0.0%)
Choroidal Neovascularization	0 (0.0%)	0 (0.0%)	0 (0.0%)
Inflammatory activity, affected eyes, %			
Overall Activity - Inactive	22 (68.8%)	58 (21.5%)	7 (46.7%)
Overall Activity - Slightly Active	0 (0.0%)	61 (22.6%)	4 (26.7%)
Overall Activity - Active	10 (31.3%)	151 (55.9%)	4 (26.7%)
Anterior chamber cell - Data are missing	0 (0.0%)	5 (1.9%)	0 (0.0%)
Anterior chamber cell - No Cells	22 (68.8%)	151 (55.9%)	12 (80.0%)
Anterior chamber cell - 0.5+	2 (6.3%)	61 (22.6%)	2 (13.3%)
Anterior chamber cell - 1.0+	4 (12.5%)	23 (8.5%)	0 (0.0%)
Anterior chamber cell - 2.0+	4 (12.5%)	30 (11.1%)	1 (6.7%)
Vitreous Cell - Data are missing	2 (6.3%)	29 (10.7%)	0 (0.0%)
Vitreous Cell - No Cells	27 (84.4%)	59 (21.9%)	14 (93.3%)
Vitreous Cell - 0.5+	2 (6.3%)	53 (19.6%)	0 (0.0%)
Vitreous Cell - 1.0+	0 (0.0%)	62 (23.0%)	0 (0.0%)
Vitreous Cell - 2.0+ or Worse	1 (3.1%)	67 (24.8%)	1 (6.7%)
Vitreous Haze – Data are missing	2 (6.3%)	66 (24.4%)	1 (6.7%)
Vitreous Haze - None	27 (84.4%)	118 (43.7%)	13 (86.7%)
Vitreous Haze - 0.5+	2 (6.3%)	59 (21.9%)	0 (0.0%)
Vitreous Haze - 1.0+ or Worse	1 (3.1%)	27 (10.0%)	1 (6.7%)
Visual acuity, affected eyes, %			
20/50 or Worse	8 (25.0%)	163 (60.4%)	5 (33.3%)
20/200 or Worse	5 (15.6%)	92 (34.1%)	0 (0.0%)

* "Other" cases included 5 cases with scleritis, and 1 case each with retrobulbar neuritis, orbital inflammation, and missing types of ocular inflammation. Fourteen subjects' date of Behçet's Disease diagnosis is missing, so an age at diagnosis could not be calculated.

TABLE 2

Incidence of Structural Ocular Complications and of Visual Acuity Loss in Eyes with Behçet's Disease

Event	Person (n/N)*	Person Years	Rate/PY (95% CI)	Eye (n/N)†	Eye Years	Rate/EY (95% CI)
Ocular Findings						
Any Ocular Complication	41/45	8.44	4.86 (3.49 – 6.59)	70/90	156.03	0.45 (0.35 – 0.57)
Posterior Synechiae	25/98	359.67	0.07 (0.05 – 0.10)	38/201	791.29	0.05 (0.03 – 0.07)
Retinal Vasculitis	40/83	235.61	0.17 (0.12 – 0.23)	67/172	545.55	0.12 (0.09 – 0.16)
Cataract Surgery	32/113	376.68	0.09 (0.06 – 0.12)	31/205	878.52	0.04 (0.02 – 0.05)
Ocular Hypertension (≥21 mm Hg)	52/93	216.17	0.24 (0.18 – 0.32)	89/192	528.27	0.17 (0.14 – 0.21)
Ocular Hypertension (≥30 mm Hg)	30/110	438.77	0.07 (0.04 – 0.1)	37/214	898.63	0.04 (0.03 – 0.06)
Ocular Hypertension (Rise of 10 mm Hg)	46/123	362.1	0.13 (0.09 – 0.17)	78/376	1401.51	0.06 (0.04 – 0.07)
Hypotony	8/111	517.83	0.02 (0.01 – 0.03)	8/216	1008.59	0.01 (0.003 – 0.02)
Glaucoma Surgery	3/115	524.09	0.006 (0.001 – 0.02)	4/219	1001.57	0.004 (0.001– 0.01)
Epiretinal Membrane Formation	44/97	300.47	0.15 (0.11 – 0.20)	75/198	665.69	0.11 (0.09 – 0.14)
Macular Edema	49/93	217.12	0.23 (0.17 – 0.3)	71/188	527.41	0.14 (0.11 – 0.17)
Exudative Retinal Detachment	6/115	525.47	0.01 (0.004 – 0.03)	6/220	1016.22	0.006 (0.002– 0.01)
Retinal Neovascularization	7/111	491.81	0.01 (0.006 – 0.03)	6/214	971.96	0.006 (0.002– 0.01)
Choroidal Neovascularization	2/115	549.27	0.004 (0.000 – 0.01)	2/220	1040.02	0.002 (0.0 – 0.007)
Visual Acuity Change						
To 20/50 or Worse	18/33	86.27	0.21 (0.12 – 0.33)	35/94	284.31	0.12 (0.09 – 0.17)
To 20/200 or Worse	24/59	162.49	0.15 (0.1 – 0.22)	43/147	471.11	0.09 (0.07 – 0.12)
Loss of 3 lines	93/114	141.22	0.66 (0.53 – 0.81)	71/138	341.38	0.21 (0.16 – 0.26)
Gain of 3 lines	71/114	185.41	0.38 (0.3 – 0.48)	95/203	450.64	0.21 (0.17 – 0.26)

*Number of events/number of persons at risk

†Number of events/number of affected eyes at risk

TABLE 3

Risk Factors for Loss of Visual Acuity in Eyes with Behçet's Disease[a]

Characteristic Name		Crude RR 20/50 or worse (95% Confidence Interval (CI), P value)	Adjusted RR 20/50 or worse (95% CI, P value)	Crude RR 20/200 or worse (95% CI, P value)	Adjusted RR 20/200 or worse (95% CI, P value)
Age at Uveitis Diagnosis (10 years)		1.1 (0.8– 1.5, 0.47)	1.1 (0.8 – 1.45, 0.60)	1.1 (0.8 – 1.4, 0.63)	1.1 (0.8 – 1.55, 0.55)
Gender	Male	1.3 (0.7 – 2.7, 0.43)	1.2 (0.6 – 2.4, 0.65)	1.2 (0.6 – 2.3, 0.65)	1.2 (0.6 – 2.7, 0.61)
Race	White	1.00	1.00	1.00	1.00
Race	Black	0.7 (0.2 – 2.8, 0.62)	0.8 (0.2 – 2.9, 0.70)	0.4 (0.1 – 1.3, 0.12)	0.4 (0.1 – 1.1, 0.06)
Race	Other	2.0 (1.0 – 4.2, 0.06)	1.9 (0.9 – 4.1, 0.09)	1.1 (0.5 – 2.4, 0.80)	0.9 (0.4 – 2.1, 0.84)
Uveitis Time To Presentation		1.0 (0.9 – 1.1, 0.84)	1.0 (0.9 – 1.1, 0.75)	1.0 (0.9 – 1.04, 0.44)	1.0 (0.9 – 1.03, 0.38)
Time-dependent Characteristics					
Bilateral	Yes	0.4 (0.1 – 1.9, 0.22)	0.2 (0.04 – 1.1, 0.07)	0.4 (0.1 – 0.9, 0.03)	0.3 (0.1 – 0.8, 0.02)*
Overall Activity[b]	Inactive	1.00	1.00	1.00	1.00
Overall Activity	Slightly Active	0.8 (0.2 – 2.6, 0.69)	0.8 (0.2 – 2.6, 0.65)	1.2 (0.5 – 3.2, 0.72)	0.9 (0.3 – 2.8, 0.87)
Overall Activity	Active	2.5 (1.2 – 5.2, 0.02)	2.5 (1.1 – 5.5, 0.03)*	3.0 (1.5 – 6.0, 0.002)	2.7 (1.2 – 5.8, 0.01)*
Anterior chamber cell	No Cells	1.00	1.00	1.00	1.00
Anterior chamber cell	0.5+	2.0 (0.8 – 4.9, 0.12)	1.9 (0.7 – 4.7, 0.19)	1.9 (0.9 – 3.8, 0.08)	1.7 (0.9 – 3.5, 0.13)
Anterior chamber cell	1.0+	3.2 (0.9 – 12.0, 0.08)	3.7 (1.0 – 13.1, 0.04)*	2.2 (0.3 – 14.2, 0.43)	2.2 (0.3 – 15.0, 0.41)
Anterior chamber cell	2.0+ or Worse	3.3 (0.8 – 13.0, 0.09)	4.1 (1.0 – 16.9, 0.05)*	3.3 (1.1 – 10.4, 0.04)	4.7 (1.2 – 18.6, 0.03)*
Vitreous Cell	No Cells	1.00	1.00	1.00	1.00
Vitreous Cell	0.5+	2.2 (0.8 – 6.4, 0.15)	1.9 (0.6 – 6.3, 0.31)	0.3 (0.06 – 1.2, 0.08)	0.2 (0.04 – 1.1, 0.06)
Vitreous Cell	1.0+	3.3 (1.1 – 9.7, 0.03)	3.1 (0.9 – 10.5, 0.06)	3.5 (1.6 – 7.8, 0.002)	3.1 (1.4 – 7.0, 0.006)*
Vitreous Cell	2.0+ or Worse	3.7 (1.1 – 12.4, 0.04)	4.6 (1.3 – 15.7, 0.02)*	3.2 (1.2 – 8.7, 0.02)	2.8 (1.0 – 8.3, 0.06)
Vitreous Haze	None	1.00	1.00	1.00	1.00
Vitreous Haze	0.5+	2.2 (0.9 – 5.5, 0.09)	2.3 (0.9 – 6.1, 0.09)	2.0 (0.8 – 5.2, 0.16)	1.5 (0.5 – 4.7, 0.50)
Vitreous Haze	1.0+ or Worse	6.2 (3.2–12.2,<.0001)	12.0 (2.1 – 68.7, 0.005)*	5.3 (1.7 – 16.6, 0.005)	7.4 (2.5 – 21.8, 0.0003)*
Posterior Synechiae	Yes	Insufficient data	Insufficient data	3.73 (1.4–10.23, 0.01)	3.04 (1.07 – 8.61, 0.04)*
Retinal Vasculitis	Yes	0.8 (0.4 – 1.6, 0.45)	0.7 (0.3 – 1.6, 0.45)	1.2 (0.6 – 2.2, 0.65)	1.2 (0.6 – 2.2, 0.70)
Hypotony	Yes	6.8 (0.9 – 52.5, 0.07)	19.9 (3.2 – 124.1, 0.001)*	9.2 (1.8 – 47.6, 0.009)	24.6 (9.6 – 63.2, <.0001)*
Elevated IOP	Yes	3.5 (1.6 – 8.0, 0.003)	5.3 (1.2 – 23.6, 0.03)*	1.4 (0.6 – 2.9, 0.44)	1.8 (0.7 – 4.5, 0.24)
Prior Cataract Surgery	Yes	2.2 (0.8 – 6.4, 0.14)	2.4 (0.7 – 8.8, 0.17)	1.4 (0.6 – 3.7, 0.45)	2.6 (0.7 – 10.0, 0.18)
Prior Glaucoma Surgery	Yes	0.7 (0.1 – 6.7, 0.74)	0.6 (0.04 – 9.6, 0.74)	0.7 (0.1 – 5.5, 0.71)	1.0 (0.1 – 7.5, 0.96)

*Denotes Statistically Significant Data

[a]Adjusted for Age, Gender, Race, Duration of Uveitis before presentation, and overall activity to worse than 20/200, also includes Bilateral Uveitis. Location of inflammation is omitted because no cases of vision loss occurred in the anterior uveitis group

[b]Overall Activity – (active) vs. (slightly or Inactive) significant in adjusted models 20/50- (2.62, 0.1) 20/200 – (2.74, 0.007)

Other inflammatory activity variables were excluded from models providing adjusted estimates of relative risk for the indicators of inflammatory activity (Activity, anterior chamber cells, vitreous cells, and vitreous haze)

TABLE 4

Primary Cause of Visual Acuity Loss in Eyes Affected by Behçet's Disease

Cause	20|50 or Worse N= 211	20|200 or Worse N= 140
Inflammatory haze	73 (34.6%)	48 (34.3%)
Cataract	26 (12.3%)	18 (12.9%)
Cystoid Macular edema	14 (6.6%)	9 (6.4%)
Macular scar	7 (3.3%)	7 (5.0%)
Optic nerve disease	10 (4.7%)	6 (4.3%)
Epiretinal membrane	11 (5.2%)	4 (2.9%)
Glaucoma	2 (0.9%)	2 (1.4%)
Posterior capsular opacification	0 (0.0%)	2 (1.4%)
Non-inflammatory disease	3 (1.4%)	0 (0.0%)
Retinal neovascularization	1 (0.5%)	1 (0.7%)
Corneal sequalae of inflammation	1 (0.5%)	1 (0.7%)
Choroidal neovascularization	0 (0.0%)	0 (0.0%)
Phthisis	0 (0.0%)	0 (0.0%)
Other	32 (15.2%)	23 (16.4%)
Missing	28 (13.3%)	19 (13.6%)
No cause could be identified	3 (1.4%)	0 (0.0%)