Hypopyon in Patients with Uveitis

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Purpose: To evaluate the risk of and risk factors for hypopyon among patients with uveitis and to evaluate the risk of visual changes and complications after hypopyon.

Design: Retrospective cohort study.

Participants: Patients with uveitis at 4 academic ocular inflammation subspecialty practices.

Methods: Data were ascertained by standardized chart review.

Main Outcome Measures: Prevalence and incidence of hypopyon, risk factors for hypopyon, and incidence of visual acuity changes and ocular complications after hypopyon.

Results: Among 4911 patients with uveitis, 41 (8.3/1000) cases of hypopyon were identified at the time of cohort entry. Of these, 2885 initially free of hypopyon were followed over 9451 person-years, during which 81 patients (2.8%) developed hypopyon (8.57/1000 person-years). Risk factors for incident hypopyon included Behçet's disease (adjusted relative risk [RR]=5.30; 95% confidence interval [CI], 2.76–10.2), spondyloarthropathy (adjusted RR=2.86; 95% CI, 1.48–5.52), and human leukocyte antigen (HLA)-B27 positivity (adjusted RR=2.04; 95% CI, 1.17–3.56). Patients with both a spondyloarthropathy and HLA-B27 had a higher risk than either factor alone (crude RR=4.39; 95% CI, 2.26–8.51). Diagnosis of intermediate uveitis (± anterior uveitis) was associated with a lower risk of hypopyon (with respect to anterior uveitis only, adjusted RR=0.35; 95% CI, 0.15–0.85). Hypopyon incidence tended to be lower among patients with sarcoidosis (crude RR=0.22; 95% CI, 0.06–0.90; adjusted RR=−0.28; 95% CI, 0.07–1.15). Post-hypopyon eyes and eyes not developing hypopyon had a similar incidence of band keratopathy, posterior synechiae, ocular hypertension, hypotony, macular edema, epiretinal membrane, cataract surgery, or glaucoma surgery. Post-hypopyon eyes were more likely than eyes not developing hypopyon to gain 3 lines of vision (crude RR=1.54; 95% CI, 1.05–2.24) and were less likely to develop 20/200 or worse visual acuity (crude RR=0.41; 95% CI, 0.17–0.99); otherwise, visual outcomes were similar in these groups.

Conclusions: Hypopyon is an uncommon occurrence in patients with uveitis. Risk factors included Behçet's disease, HLA-B27 positivity, and spondyloarthropathy. Intermediate uveitis cases (± anterior uveitis) had a lower risk of hypopyon. On average, post-hypopyon eyes were no more likely than other eyes with uveitis to develop structural ocular complications or lose visual acuity.

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Hypopyon—layering of white blood cells in the anterior chamber—signifies severe anterior segment intraocular inflammation. The frequency of hypopyon has been described in 2 small to moderate-sized series of patients with various types of uveitis. D'Alessandro et al[1] retrospectively reviewed 155 cases of acute anterior uveitis and found 11 cases (7%) of hypopyon (duration of follow-up not reported), 9 of which were associated with human leukocyte antigen (HLA)-B27. BenEzra and Cohen[2] reviewed 49 patients with Behçet's disease, finding that 17 (35%) developed hypopyon over 6 to 10 years of follow-up. The incidence of hypopyon for other forms of uveitis is unclear.

Data regarding the risk factors for hypopyon and its prognostic significance are limited. Nussenblatt[3] reported that the occurrence of hypopyon did not worsen the visual prognosis of patients with Behçet's disease. However, the relationship between hypopyon and subsequent outcome in other forms of uveitis is not well understood. To better characterize the risk and importance of hypopyon, we report the incidence rate, risk factors, and risk of adverse outcomes in a large cohort of patients with uveitis.

Materials and Methods

Study Population

The design of the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study has been detailed.[4] In brief, the SITE Cohort Study is a retrospective cohort study of patients with inflammatory eye diseases seen at 5 tertiary ocular inflammation centers in the United States from the inception of these centers. One of these centers used a co-management approach, which resulted in ascertainment of clinical outcomes substantially later than they occurred. To avoid this bias, patients from this clinic

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were excluded from this report. Patients reported in this article were seen between 1978 and 2007.

Data Collection

Information on patients with inflammatory eye disease was entered into a database using a computer-based standardized data entry form set specifically prepared for the SITE Cohort Study. For this study, patients from 4 sites were included. At the largest site clinic, an approximate 40% random sample of patients was included because of logistic and funding constraints. A random sampling was performed to avoid bias in selecting the sample to be studied. The data-collection system included extensive intrinsic quality control checks, requiring correction of errors in real time. Only data from patients with noninfectious uveitis were included in the study; patients with known human immunodeficiency virus infection were excluded.

Data collected that are relevant to this study include demographic characteristics, ocular inflammatory diagnoses, diagnosis of systemic inflammatory disease(s), ophthalmologic examination findings, and ocular surgeries. Human leukocyte antigen-B27 testing was performed when clinically indicated on the basis of symptoms and clinical findings. The possibility of systemic inflammatory disease diagnoses coexisting with ocular inflammation was aggressively pursued by routine questioning; laboratory testing and consultations were obtained when indicated. Systemic inflammatory diagnoses evaluated included Behçet's disease, Cogan's syndrome, Crohn's disease, dermatomyositis, erythema nodosum, familial systemic granulomatosis, juvenile rheumatoid arthritis, pemphigus, polyarteritis nodosum, polymyositis, rheumatoid arthritis, relapsing polychondritis, sarcoidosis, systemic lupus erythematosus, scleroderma, Sjögren's syndrome, spondyloarthropathies (ankylosing spondylitis, reactive arthritis, psoriatic arthritis, enteropathic arthritis associated with inflammatory bowel disease, undifferentiated spondyloarthropathy), temporal arteritis, Takayasu's disease, ulcerative colitis, and Wegener's granulomatosis. Ophthalmologic examinations documented visual acuity, intraocular pressure (IOP), inflammatory disease activity, and the presence of inflammatory disease sequelae.

Main Outcome Measures

Both the prevalence of hypopyon at cohort entry and the incidence of hypopyon were assessed. To calculate the incidence of hypopyon, patients who were free of hypopyon at the time of cohort entry and had follow-up visits were followed until the first occurrence of hypopyon, until the patient ceased attending the clinic, or until completion of the study. Variables including age, sex, race (black, white, or other), type of uveitis (anterior only, intermediate ± anterior, and posterior or panuveitis), primary ocular diagnoses, HLA-B27 status, and the presence of systemic inflammatory disease were assessed as potential risk factors for incident hypopyon.

The incidence rates for worsening or improvement in visual acuity were assessed by the number of eyes per eye-year that worsened to 20/50 or worse (visual impairment) and 20/200 or worse (legal blindness), the number of eyes that lost or gained 3 lines of visual acuity, and the number of eyes that improved to 20/40 or better or to 20/200 or better from a worse level of visual acuity at the time of presentation.

The incidence of band keratopathy, posterior synechiae, ocular hypertension (IOP≥21 mmHg and ≥30 mmHg), hypotony (IOP≤5 mmHg), cataract surgery, glaucoma surgery, macular edema, and epiretinal membrane among eyes initially free of each of these was noted (the latter 2 based on clinical examination supplemented by fluorescein angiography or optical coherence tomography when clinically indicated).

Statistical Analysis

The prevalence of hypopyon was calculated as the number of patients with a hypopyon at cohort entry, and a 95% confidence interval (CI) was calculated assuming a binomial distribution. The incidence of hypopyon per person-year among patients initially free of hypopyon who were followed over time was calculated, and a 95% CI was generated assuming a Poisson distribution. Potential risk factors for incidence of hypopyon were evaluated on the basis of hazard ratios (relative risks [RRs]), and their 95% CIs were calculated using Cox regression.[5]

The incidence rates of adverse or favorable events in post-hypopyon eyes with respect to eyes that never were observed to have hypopyon were calculated as the number of events per eye-year assuming a Poisson distribution. Their incidence rates were compared using Poisson regression, adjusting for inter-eye correlation using generalized estimating equations-based methods.[6] The data analyses were performed using SAS v9.1 (SAS Inc., Cary, NC).

Results

Characteristics of the Study Population

A total of 4911 patients with uveitis were included in this analysis (Table 1). The median age was 39 years, with ages ranging from 4 months to 97 years. Patients were predominantly female (63%) and Caucasian (71%). By anatomic classification of the site of inflammation,[7,8] 54% of patients had anterior uveitis only, 17% of patients had intermediate (± anterior) uveitis, and 29% of patients had posterior or panuveitis. There were 41 cases of hypopyon at the time of cohort entry, a prevalence of 8.4 per 1000 (95% CI, 6.0–11 per 1000). Among patients presenting with hypopyon, 15 (37%) were HLA-B27 positive, 7 (17%) had a spondyloarthropathy (6 of whom also were HLA-B27 positive), 8 (20%) had Behçet's disease, 1 (2%) had systemic lupus erythematosus, 1 (2%) had inflammatory bowel disease, and 1 (2%) had juvenile idiopathic arthritis. The remaining 15 cases (37%) of hypopyon at the time of presentation occurred in patients not known to have systemic inflammatory conditions or HLA-B27 associated with uveitis.

Risk of Hypopyon

Of the total patients included in the study, 2885 were free of hypopyon at the time of presentation and were followed for incidence of hypopyon over 9451 person-years (Table 2). Eighty-one patients (2.8%) developed hypopyon during follow-up, an incidence of 8.57 per 1000 person-years (95% CI, 6.81–10.7 per 1000 person-years). Of these, 19 (23%) were HLA-B27 positive, 12 (15%) had a spondyloarthropathy (HLA-B27 positive or negative), 13 (16%) had Behçet's disease, 6 (7%) had juvenile idiopathic arthritis, 2 (2%) had rheumatoid arthritis, 2 (2%) had sarcoidosis, and 2 (2%) had inflammatory bowel disease. The remaining 25 incident cases (31%) were not known to have systemic inflammatory conditions or HLA-B27 associated with uveitis.

Risk Factors for Hypopyon

Crude results regarding risk factors for hypopyon are shown in Table 2; results adjusted for potential confounding are shown in Table 3. Age, gender, and race were not statistically significant risk factors for incident hypopyon. Patients with intermediate (± anterior) uveitis had a lower hypopyon incidence than patients with only anterior uveitis (adjusted RR=0.35; 95% CI, 0.15–0.85).