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Predictors of Long-Term Visual Outcome in Intermediate Uveitis

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Purpose: To describe factors that predict visual loss and complications in intermediate uveitis.

Design: Cross-sectional study.

Participants: Subjects with intermediate uveitis were identified from a database of 1254 uveitis patients seen in the clinic of a single consultant (S.L.L.) between 2011 and 2013.

Methods: Information was gathered from the clinical notes of all subjects examined in clinic.

Main Outcome Measures: Best-corrected visual acuity (BCVA), moderate visual loss (MVL; ≤20/50), severe visual loss (SVL; ≤20/200).

Results: Three hundred and five subjects (550 eyes) were included in the study, comprising 24.3% of subjects seen in clinic. Mean (± standard deviation) age at diagnosis was 40.9±16.9 years, and 64.6% of subjects were female. Median follow-up was 8.2 years (mean, 9.7 years, 5452 eye-years). Systemic diagnosis was made in 36.1% of patients, with sarcoidosis (22.6%) and multiple sclerosis (4.6%) the most frequent systemic associations. Median BCVA was 20/30 (mean logarithm of the minimum angle of resolution [logMAR] 0.26±0.38, n = 550 eyes) at presentation, 20/30 (mean logMAR 0.22±0.42, n = 430) at 5 years, and 20/30 (mean logMAR 0.23±0.46, n = 260) at 10 years. Macular edema was observed in 224 eyes (40.7%) and was associated with idiopathic disease ($P = 0.001$) and diabetes ($P = 0.001$). Topical therapy was used in 82.7%, and 34.2% received local injections of corticosteroids. A total of 50.5% required oral steroids and 13.8% required second-line immunosuppression. Subjects with a diagnosis of sarcoidosis were less likely to require a second-line agent (4.3% vs. 16.2%, $P = 0.011$). On multivariate analysis, visual acuity at referral, retinal pigment epithelial atrophy, and macular scarring were associated with increased risk of MVL; and visual acuity at referral, local therapy, macular scarring, retinal detachment, and hypotony and phthisis were associated with increased risk of SVL.

Conclusions: Intermediate uveitis has a long disease course with frequent complications and often requires systemic treatment. Despite this, most subjects are still able to achieve good long-term visual outcomes. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology*

Intermediate uveitis (IU) has been defined by the Standardization of Uveitis Nomenclature (SUN) Working Group as the subset of uveitis in which the vitreous is the major site of inflammation.[1] IU is a relatively common occurrence among uveitis patients and is reported to constitute 2% to 31% of subjects seen in tertiary uveitis clinics.[2–4] Systemic associations are observed in 9% to 31% and vary with population studied, with sarcoidosis and multiple sclerosis reported most frequently.[5,6] Subjects with IU often have a prolonged clinical course. A study of 29 subjects with at least 10 years of follow-up observed remission of at least 1 year in only 34%, with mean time to remission 8.6 years.[7] Over this time period, complications are common. Cataract and cystoid macular edema (CME) are the most common complications, and incidence increases with duration of follow-up.[2,4,7] CME is the most frequent cause of visual loss in IU.[3–5,8]

Several medium-sized studies have been published recently examining clinical outcomes in pediatric populations compared with adult-onset IU.[2,4,9,10] These studies identified a similar clinical course and visual prognosis in childhood and adult-onset IU, and included reasonable patient numbers (26–287 subjects); however, follow-up time was short, ranging from 2.2 to 4.5 years.[2,4,9,10] Recently, a large study examining factors predictive of remission in IU was published, demonstrating greater chance of remission in subjects with prior vitrectomy, diagnosis of intermediate uveitis within the last year, older age, female gender, and Hispanic ethnicity.[11] Other studies in adult populations have examined smaller groups (29–87 subjects) and have had short follow-up periods (3.6–5.0 years),[3,5,8] with the exception of a single study that examined clinical outcomes in 29 subjects with follow-up of at least 10 years.[7] However, these studies did not address the risks of vision loss and long-term clinical outcome in these patients.

This study aimed to examine a large population of subjects with IU with a long follow-up period, to determine clinical outcome, systemic associations, treatment, complications, and risk factors for visual loss.

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Methods

Subject Selection

Subjects with a diagnosis of IU were identified from a database of 1254 subjects who attended the uveitis clinics of a single consultant (S.L.L.) at Moorfields Eye Hospital, London, United Kingdom, between 2011 and 2013 (ethical approval for data collection LIGS10201, visual loss in uveitis). All other causes of vitritis were excluded and subjects with associated occlusive retinal vasculitis were excluded. All subject notes were reviewed to confirm the diagnosis of IU under the SUN guidelines.[1]

Subjects had undergone an initial detailed ophthalmic history and review of systems, targeted toward identifying any systemic associations of IU. All subjects had screening blood tests, including full blood count, erythrocyte sedimentation rate, C-reactive protein, angiotensin converting enzyme, HLA-B27, and syphilis serology. Additional investigations such as quantiferon-TB gold, chest x-ray, and magnetic resonance imaging were performed as directed by systems enquiry, and other investigations were also undertaken where appropriate (targeted approach). Any subjects with neurological symptoms or a history of optic neuritis were referred to a neurologist. Subjects with history or investigations suggestive of a systemic disorder were referred to the relevant physician. In the absence of any identified systemic association, systems review and relevant investigations were repeated at approximately 2-yearly follow-ups or if new relevant signs or symptoms occurred.

Subjects were under the care of a single consultant and were treated according to a standardized treatment algorithm. Subjects with associated anterior chamber inflammation were treated with topical corticosteroids (dexamethasone 0.1%) titrated to degree of inflammation, with additional therapy such as mydriatics and intraocular pressure−lowering drops as required.

Treatment for IU was initiated for vitritis resulting in a drop in best-corrected visual acuity (BCVA), CME, or papillitis. Bilateral disease was treated with oral corticosteroids as first line, and unilateral disease was treated with local steroid as first line where possible. Treatment was swapped if there was inadequate response or intolerance. Children were treated with oral corticosteroids as first-line, rather than local, therapy, regardless of whether the disease was unilateral or bilateral.

Data Collection

Notes were reviewed to record demographic characteristics, systemic diagnoses, presentation, treatment, complications, and visual acuity at 1 year, 5 years, 10 years, and last follow-up appointment.

The BCVA results were converted to logarithm of the minimum angle of resolution (logMAR) units for analysis. For BCVA of counting fingers or worse, the following conversion was used: counting fingers, 2.0 logMAR; hand movements, 2.3 logMAR; light perception, 2.6 logMAR; and no light perception, 2.9 logMAR.[12,13] Visual loss was defined according to SUN guidelines: moderate visual loss (MVL), BCVA ≤20/50; severe visual loss (SVL), BCVA ≤20/200.[1]

Glaucomatous optic neuropathy was defined as typical optic disc changes believed to be secondary to glaucoma. Optic neuropathy was defined as all other optic neuropathies excluding glaucomatous. Macular pathology (CME, scarring, retinal pigment epithelial damage) was identified by review of clinical notes, fundus photography, optical coherence tomography (OCT), and fundus fluorescein angiography.

Analysis and Statistics

All data were entered into an Excel spreadsheet and analyzed using SPSS statistical software version 22 (IBM, Chicago, IL). Continuous data are presented as mean ± standard deviation for normally distributed data and median (interquartile range) for skewed data. Categorical variables are presented as n (%). Patient-related observations were compared with either independent *t* test, Mann-Whitney *U* test, or chi-square test, as appropriate. A generalized estimating equations approach to observations nested within the same individual was used to compare outcomes for eyes. The Kaplan-Meier estimator was used to examine survival from visual loss. Multivariate analysis and relative risks for causes of MVL and SVL were calculated using a Cox regression model while adjusting for correlations between both eyes of the same subject. All tests were 2-tailed, and a P value of <0.05 was considered statistically significant.

Results

There were 550 eyes of 305 subjects identified with IU (24.3% of subjects). Subject demographics are reported in Table 1. Twenty-five subjects (8.2%) were aged <16 years at diagnosis. Bilateral disease was observed in 247 subjects (81.0%). Median follow-up period was 8.2 years (interquartile range [IQR] 4.7−13.6 years, mean 9.7 years, 2959 patient-years, 5452 eye-years) and 10-year follow-up was available in 141 subjects (46.2%).

Associated systemic disease was identified in 110 subjects (36.1%) (Table 2). Sarcoidosis was reported in 69 subjects (22.6%) and was more common in black subjects (43.6%) and South Asian subjects (25.0%) compared with white subjects (12.8%) ($P = 0.014$). There was no association between a diagnosis of sarcoidosis and gender or age at diagnosis. Multiple sclerosis (MS) was reported in 14 subjects (4.6%). Mean age at diagnosis with uveitis in subjects with MS was 41.1 years, 9 subjects (64.3%) were female, and 11 subjects (78.6%) were white. There was no association between age at presentation, gender, or ethnicity and a diagnosis of MS. Diagnosis of MS was made before uveitis onset in 10 subjects (71.4%), simultaneously with the diagnosis in 1 subject (7.2%), and after the diagnosis of uveitis in 2 subjects (14.3%), and was not specified in 1 subject. MS was diagnosed between 22 years before onset of IU and 10 years after. Mean time from diagnosis of uveitis to diagnosis of MS was −7.7±9.3 years.

Visual Outcome and Complications

Median visual acuity at presentation was 20/30 (0.20 logMAR, IQR 0.00−0.50). Visual acuities at first presentation, 1 year, 5

Table 1. Demographics and Referral Source for Subjects with Intermediate Uveitis

	Result*
Female	197 (64.6%)
Age at diagnosis, years ± SD (range)	40.9±16.9 (range, 1−82)
Ethnicity	
White	134 (43.9%)
Asian	69 (22.6%)
Black	39 (12.8%)
Other	8 (2.6%)
Unknown	55 (18.0%)
Source of referral	
Accident and emergency	130 (42.6%)
Tertiary	102 (33.4%)
General practitioner and optician	43 (14.1%)
Unknown	30 (9.8%)

SD = standard deviation.
*Data are n (%), unless indicated.