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Presentation and etiology of intermediate uveitis in Kashmir

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Abstract
Introduction: Intermediate uveitis is a form of uveitis where the primary site of inflammation is the vitreous body. It's an important subtype of uveitis that requires specific attention due to its potential complications and association with systemic diseases. Patients with intermediate uveitis (IU) represent a heterogenous group characterized by a wide spectrum of etiologies and regional differences. Aim of the study was to analyze the characteristics of patients with IU examined in an academic center in Kashmir.
Materials and Methods: This prospective observational study was conducted to find out the clinical presentation and etiological factors of intermediate uveitis in Kashmiri population. In this study 140 eyes of 120 patients were enrolled. The diagnosis followed the Standardization of Uveitis Nomenclature criteria. Data analysis included personal data, etiology of IU, presentation, treatment, complications and visual acuity.
Results: In this study 83 (59%) patients were with chronic presentation and 57 (41%) with acute presentation. Vitritis was the most common presentation site in this study 132 (94%). 71 (59%) were tuberclosis IU, 19 (16%) with sarcoidosis, 16 (13%) with multiple sclerosis, and idiopathic IU in 14 (12%) patients. 31 (26%) patients required no systemic or parabulbar treatment. 79 (66%) received systemic steroids, 13 (11%) intravitreal steroids and 10 (8%) parabulbar steroids. Systemic immunosuppression was necessary in 20 (17%) patients. At the end of follow-up, 78% of the eyes had a best corrected visual acuity better than 20/25. Common complications seen were the development of cystoid macular edema (CME) in 49 (35%) eyes, cataract in 31 (22%), 27 (19%) from epiretinal membrane, 9 (6%) from retinal detachment, and 11 (8%) from glaucoma.
Conclusion: Intermediate Uveitis (IU) is a challenging condition requiring a comprehensive approach to diagnosis and management. Early detection and appropriate treatment are key to preserving vision and improving patient outcomes.

Keywords: Ocular inflammatory diseases, intermediate uveitis, epidemiology, etiology, Kashmiri population

Introduction

Intermediate uveitis (IU) is a chronic, relapsing disease of insidious onset. According to the standardization of Uveitis Nomenclature (SUN) working group criteria, IU ia defined as an intraocular inflammation mainly focused on vitreous, peripheral retina, and ciliary body with minimal or no anterior segment inflammation [1]. Intermediate uveitis accounts for 1.4 – 31% of all uveitis patients [2–10]. The incidence of IU varies between 1.4 – 2/100.000 [6, 11, 12]. IU can be a sight-threatening disease and usually affects young adults [6, 13]. Patients with intermediate uveitis often see floating spots or shapes, vision can become blurry or hazy and patients can feel discomfort or mild pain in the eye and sensitivity to light can occur.

The etiology of IU is not well known and is mostly believed to be associated with infectious and noninfectious diseases. It can be associated with autoimmune diseases like multiple sclerosis (MS), sarcoidosis, inflammatory-bowl disease and others [13, 14]. Less commonly it can be linked to infections like tuberculosis, leprosy, Lyme's disease, syphilis, toxocariasis, Whipple's disease, and others.

The disease is known for its prolonged course with exacerbations and hence the need for investigations to search for a specific etiology and proper management to reduce the recurrence and complications. The etiology may be variable in different parts of the world as it could be influenced by the geographic variations and ethnicity. The studies available from the developed countries [11, 15, 16] and one from North Africa [17] have mostly indicated IU to be of autoimmune in nature. In the cross-sectional epidemiologic studies done from the referral institutes in India, intermediate uveitis has been reported to be idiopathic in 77.5% in Northeast India [18], 91.4% in North India [19], and 81.6% in South India [20].

However, none of these studies describe the longitudinal course, management, and outcome of these patients labeled as intermediate uveitis. The present study was undertaken to find the etiologic spectrum, clinical manifestations, course, complications, and visual outcome in patients with IU from a single center in Kashmiri population.

Materials and Methods

This prospective observational study was carried out in the Postgraduate Department of Ophthalmology, Government Medical College, Srinagar from March 2021 and December 2022. In this study a total of 140 eyes of 120 consecutive patients with intermediate uveitis were included. The patients with a minimum of 1 year follow-up were included in this study. Patients diagnosed with any disorder other than intermediate uveitis were excluded.

A written informed consent was obtained from all patients. Intermediate uveitis was classified according to recommendations by the SUN working group [21].

The patients demographic data regards to age, sex, occupation, geographical area to which the patient belonged, race, history of recent travel, family history suggestive of tuberculosis, leprosy, syphilis, Rheumatoid arthritis, ankylosing spondylosis and focus of infection were collected and recorded. Ophthalmological history included Diminution or blurring of vision, floaters, photophobia, micropsia, macropsia, metamorphopsia, pain, lacrimation, redness, history of symptomatic attacks in chronic cases.

Laboratory studies

All patients underwent baseline investigations including complete blood counts (CBC), erythrocyte sedimentation rate (ESR) and or C-reactive protein (CRP), Angiotensin-converting enzyme (ACE), Lysozyme, Non-treponemal and treponemal testing (RPR or VDRL and FTA-ABS), IgG and IgM antibodies for toxoplasmosis, CBNAAT for tuberculosis and Tuberculin skin test.

Imaging

Chest radiography and/or chest computed tomography (CT), Brain, orbit and spinal magnetic resonance imaging (MRI) were done whenever required.

Ocular imaging

All patients underwent a complete ophthalmic examination including best corrected visual acuity, intraocular pressure, slit lamp biomicroscopy, and posterior segment examination with both slit lamp biomicroscopy and indirect ophthalmoscopy to examine pars plana area. Ancillary tests including fundus fluorescein angiography, optical coherence tomography, or ultrasound biomicroscopy.

Patients with typical pars planitis as well as those with IU with/without snow banks and posterior synechia were investigated for infectious etiologies like tuberculosis (TB), sarcoidosis, Lyme and systemic associations like MS were ruled out. In patients with preponderant vitritis, etiologies like toxocariasis, and lymphoma were ruled out. In patients with prepondrant vasculitis, MRI was done to rule out multiple sclerosis and intracranial lymphomas.

Management

Treatment was directed at the cause. Malignancy and infection was ruled out before commencing non-specific anti-inflammatory therapy. The patients received treatment if (1) the visual acuity was worse than 20/40, (2) presence of cystoid macular edema, (3) vitreous haze of 2+ or more, and (4) retinal neovascularization.

A stepwise graded approach to treatment included topical steroids + posterior subtenon triamcelone (PST) 4 mg injection, systemic corticosteroids, immunosuppressive/immunomodular therapy, and pars plana vitrectomy and repeated 3-4 injections weekly depending on the response of patient. In cases with unilateral or asymmetric involvement, the periocular steroid injections were given first, and systemic treatment was initiated only in cases with insufficient effect and/or intolerance to this treatment modality. Systemic steroids (1–1.5 mg/kg body weight) were started in cases with severe bilateral disease and/or in cases with decrease visual acuity due to vitreous opacities. Immunosuppressive agents were started as a steroid-sparing drug or when steroid failed to control the inflammation. IU patients with presumed TB in addition also received antitubercular therapy (ATT). Pars plana vitrectomy was done if the vitritis was very severe at the time of presentation to our center despite receiving initial therapy outside and the laboratory investigations were equivocal and to manage the complications like retinal detachment and vitreous hemorrhage.

Outcome

The primary outcome measure was the recurrence of inflammation occurring after a minimum of 6 months of receiving treatment. Visual improvement was defined as halving of the visual angle and visual deterioration as doubling of the visual angle. Visual acuity was said to be stabilized if the final visual acuity remained within two lines of the presenting acuity.

Results

The mean age of patients was 38.90±6.52 (range 6-67) years. In this study, there were 48 (40%) male patients and 72 (60%) females. Maximum patients were in the age group of 21-40 years. 20 (17%) patients had bilateral involvement. Maximum patients were from rural areas 73 (61%) (Table 1).

Table 1: Demographic characters of the enrolled population

Demographic characters	No. of patients	Percentage
Gender		
Male	48	40
Female	72	60
Age group		
<20 Years	11	9
21-40 years	56	47
41-60 Years	39	32
>60 Years	14	12
Geographical area		
Urban	47	39
Rural	73	61
Bilateral	20	17

In this study 83 (59%) patients were with chronic presentation and 57 (41%) with acute presentation. Vitritis was the most common presentation site in this study 132 (94%). Regarding the etiology 71 (59%) were tuberclosis IU, 19 (16%) with sarcoidosis, 16 (13%) with multiple sclerosis and tuberculosis in 14 (12%) patients (Table 2).

Table 2: Different considered parameters

Parameters	No. of patients	Percentage
Presentation		
Acute	57	41
Chronic	83	59
Presentation site		
Vitritis	132	94
Snowballs	92	66
Etiology		
Tuberculosis	71	59
Sarcoidosis	19	16
Multiple sclerosis	16	13
Idiopathic IU	14	12
Visual acuity		
Initial >20/25	77	55
Final >20/25	109	78

In this study 31 (26%) patients required no systemic or parabulbar treatment. 79 (66%) received systemic steroids, 13 (11%) intravitreal steroids and 10 (8%) parabulbar steroids. Systemic immunosuppression was necessary in 20 (17%) patients.

In this study the overall prognosis was favorable. Visual acuity was stable over time in most patients. At the end of follow-up, 78% of the eyes had a best corrected visual acuity better than 20/25 (Table 2).

In this study the most common complications seen were the development of cystoid macular edema (CME) in 49 (35%) eyes, cataract in 31 (22%), 27 (19%) from epiretinal membrane, 9 (6%) from retinal detachment, and 11 (8%) from glaucoma (Figure 1).

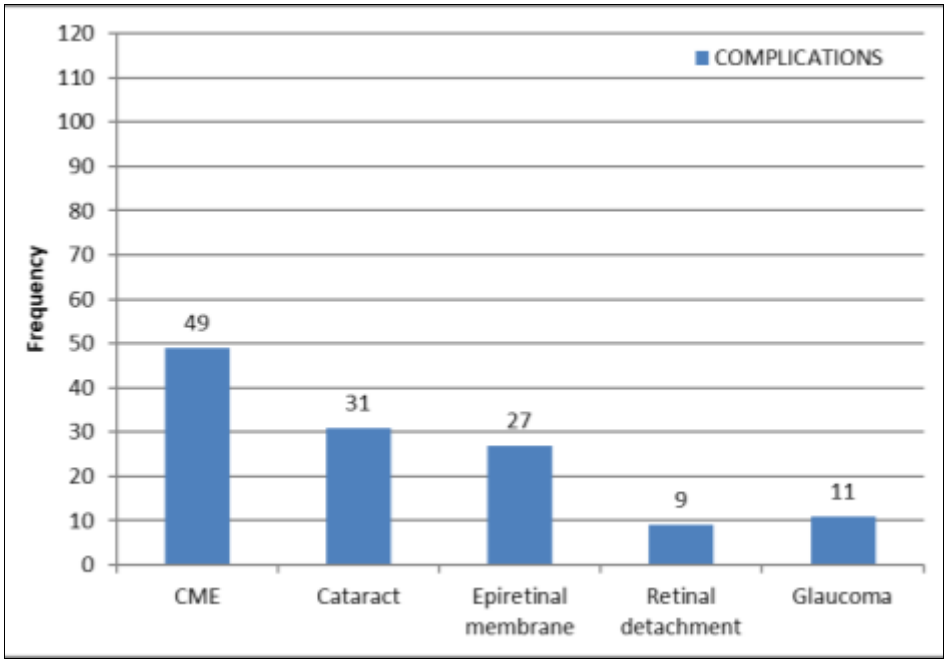

Fig 1: Complications

Discussion

Intermediate uveitis (IU) is a form of uveitis primarily involving the vitreous and peripheral retina. It can have various etiologies and presentations, and its complications can be severe if not managed properly. Globally, IU is the least common type of uveitis reported, representing about 16% of all uveitis anatomical locations [2, 22, 23]. Distribution patterns are influenced by demographic, genetic, and environmental factors.

Gender and Age

In this study the mean age of patients was 38.90±6.52 (range 6-67) years. In this study IU affects patients in all age groups, from children to adults, comparable to the studies done by Babu M. *et al*, [6] and Engelmann K. *Et al*. [24]. In this study, there were 48 (40%) male patients and 72 (60%) females and maximum patients were in the age group of 21-40 years, followed by 39 (32%) in the age group of 431-60 years. However, our study shows that intermediate uveitis commonly affects young adults, typically between the ages of 20 and 40 and a slight female predominance. These findings are consistent with the studies done by Gritz *et al*. [25], Dana *et al*. [26], Paroli *et al*. [27, 28] and Silpa-Archa *et al*. [29].

Laterality

20 (17%) patients had bilateral involvement in this study, in contrast to the literature [23, 30].

Presentation

Patients with IU typically present with floaters and blurred vision. Pain and redness are less common compared to anterior uveitis. Miserocchi *et al*. [31] noted that floaters are the most common presenting symptom, followed by decreased visual acuity. The absence of pain and redness helps differentiate IU from other forms of uveitis. Levinson *et al*. (2006) [32] found that the presentation can vary, but floaters and mild to moderate visual impairment are typical. In this study 83 (59%) patients were with chronic presentation and 57 (41%) with acute presentation. Vitritis was the most common presentation site in this study 132 (94%). Overall chronic cases dominated in our study, which was also shown by previous studies [3, 33].

Etiology

Regarding the etiology 71 (59%) were tuberclosis IU, 19 (16%) with sarcoidosis, 16 (13%) with multiple sclerosis, Lymes disease in 5 (4%) and tuberculosis in 9 (8%) patients. In our study, Tuberculosis was a frequent underlying disease in IU in our patients, in contrast to other countries where it

is rare [17, 18]. This is a significant finding as none of the previous series from other parts of the world have reported TB as an important underlying cause of IU [11, 16, 34, 35]. Sarcoidosis was the second common cause of IU. On the contrary, the study from Northeast India did report TB and sarcoidosis as important etiologies in IU [8]. Multiple sclerosis was 13%, the third common etiology in our study comparable to the literature where proportion of MS in IU patients varies from 7 to 30.4% [36, 37]. In our study, MS was very significantly associated with periphlebitis, a particular indication of IU. Others have observed the same [38]. Since IU might be the first manifestation of MS and early treatment seems to improve the overall prognosis, it is important to screen all IU patients for MS [39-41].

Treatment

In this study 31 (26%) patients required no systemic or parabulbar treatment. 79 (66%) received systemic steroids, 13 (11%) intravitreal steroids and 10 (8%) parabulbar steroids. Systemic immunosuppression was necessary in 20 (17%) patients. Main treatment indications in our series were CME. Systemic, intraocular and parabulbar corticosteroids are the predominant therapeutic options. Only 17% of our patients received immunosuppressive agents – more frequently than in literature [5, 11, 42].

Complications

Many IU patients suffer from complications. The development of cataract, glaucoma, CME, epiretinal membrane formation, retinal detachment, periphlebitis or optic neuritis is similar worldwide [6, 7]. Cataract and glaucoma might be caused by IU itself or by treatment of IU, especially with corticosteroids. There is ample evidence that CME and epiretinal membrane formation correlate with poor visual prognosis [42]. In this study the most common complications seen were the development of cystoid macular edema (CME) in 49 (35%) eyes, cataract in 31 (22%), 27 (19%) from epiretinal membrane, 9 (6%) from retinal detachment, and 11 (8%) from glaucoma.

Visual acuity

Despite the many complications, overall prognosis was encouraging in this study. Most patients have retained best corrected visual acuity of 20/25 or better. Visual acuity was stable over time in most patients. At the end of follow-up, 78% of the eyes had a best corrected visual acuity better than 20/25.

This study does have some limitations. The number of patients selected for the sample. A larger sample would provide additional accuracy. Although the sample size is small, it is in line with other studies carried out in different parts of the world. However, the results are useful for daily clinical practice.

Conclusion

In our context, IU is infrequent, does not present sex predominance, and is more prevalent in young individuals. The most common characteristics were tuberculosis etiology, insidious onset, chronic course, and persistent duration.

Intermediate Uveitis (IU) is a challenging condition requiring a comprehensive approach to diagnosis and management. Early detection and appropriate treatment are key to preserving vision and improving patient outcomes.

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Author's contribution

Dr. Aisha Ashraf: concept, study design, literature search, statistical analysis, data acquisition and manuscript preparation

Dr. Irtiqa Mohammad: literature search, manuscript preparation and statistical analysis

Dr. Rakhshanda Aziz: definition of intellectual content, data acquisition, manuscript editing, statistical analysis and manuscript review

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