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Intermediate Uveitis

Andrew Gregory, MD

Case Presentation

A 24-year-old woman presented to our clinic as a new patient with complaints of floaters and photopsia in both eyes, more pronounced in the right eye. Her past medical and surgical history was unremarkable for systemic or ocular disease. During the review of systems, she reported numbness and tingling in both her hands and feet. The best-corrected visual acuity was 20/80 in the right eye and 20/25 in the left eye. On examination, vitreous cells (snowballs) and snowbanking were detected in both eyes. Laboratory tests were negative or within normal limits except for positive HLA-DR15. Brain MRI demonstrated hyperintense foci suggestive of multiple sclerosis. The patient was diagnosed with intermediate uveitis in the setting of multiple sclerosis. The patient was treated with ocrelizumab, a humanized anti-CD20 monoclonal antibody used for the treatment of multiple sclerosis, which induced remission of her intermediate uveitis.

Definition

Intermediate uveitis is an anatomic subtype of intraocular inflammation characterized by predominant involvement of the vitreous, pars plana, and peripheral retina [1-2]. According to the Standardization of Uveitis Nomenclature (SUN) working group criteria, the term "intermediate uveitis" should be applied when the vitreous is the primary site of inflammation, regardless of whether an associated systemic disease or infection is present [3]. The diagnostic term "pars planitis" is reserved specifically for idiopathic intermediate uveitis characterized by snowball or snowbank formation in the absence of an identifiable infectious or systemic etiology [2]. This anatomic classification distinguishes intermediate uveitis from anterior uveitis (involving the iris and ciliary body), posterior uveitis (affecting the retina and choroid), and panuveitis (involving all uveal structures) [1][3]. This evolution in nomenclature has facilitated more precise epidemiologic studies, improved diagnostic accuracy, and enabled better comparison of treatment outcomes across different patient populations and geographic regions.

Epidemiology

Intermediate uveitis represents 9-15% of all uveitis cases in the United States and Europe, though the prevalence varies significantly by geographic region and ethnic background [1]. Pars planitis predominantly affects children and young to middle-aged adults, with most cases occurring between 5 and 40 years of age and demonstrating a bimodal distribution with peaks at 5–15 and 20–40 years [1]. There is no gender predilection in pars planitis.

The disease is characteristically bilateral in approximately 79% of cases, distinguishing it from anterior uveitis, which is more commonly unilateral [1]. The etiology of intermediate uveitis is idiopathic in 80% of cases (pars planitis), with the remainder associated with systemic diseases or infections [5].

Multiple sclerosis is the most frequently identified systemic association, occurring in 1-5% of intermediate uveitis cases overall and representing 20% of cases with identified systemic disease [1][4]. Sarcoidosis accounts for approximately 10% of cases with systemic associations [4-5]. In endemic regions, tuberculosis represents an important infectious cause, accounting for up to 15% of intermediate uveitis cases in some populations [6]. Other less common associations include Lyme disease, inflammatory bowel disease, and bronchial asthma [1][7].

Clinical Features

Patients with intermediate uveitis typically present with painless blurred vision and floaters, distinguishing this condition from anterior uveitis, which characteristically causes eye pain, redness, and photophobia [8]. The absence of pain reflects the lack of significant anterior segment inflammation in most cases. Visual symptoms result from vitreous opacities, cystoid macular edema, or other complications affecting the macula, posterior pole, and retinal periphery [2][4]. The hallmark clinical findings on examination include vitreous cellular infiltration, often described as "snowballs" (aggregates of inflammatory cells suspended in the vitreous), and "snowbanking" (white exudative material overlying the pars plana and peripheral retina, particularly in the inferior quadrants) [2][9]. These characteristic findings are pathognomonic for pars planitis when occurring in the absence of systemic disease [2].

Additional clinical features may include peripheral retinal vasculitis (periphlebitis), optic disc edema, and epiretinal membrane formation [5][9]. Anterior chamber inflammation is typically minimal or absent, though mild anterior chamber cells or flare may be present in some cases [1]. Cystoid macular edema represents the most common complication and primary cause of vision loss, occurring in 28-41% of patients [4][10-11]. The diagnosis is

established through comprehensive ophthalmologic examination including slit-lamp examination to assess anterior chamber inflammation, indirect ophthalmoscopy to evaluate the vitreous and peripheral retina, and optical coherence tomography to detect macular edema [1]. Fluorescein angiography is typically utilized as well to rule out any retinal vasculitis involvement as well. Patients with intermediate uveitis should undergo systemic evaluation to exclude associated conditions, particularly multiple sclerosis, sarcoidosis, tuberculosis, syphilis, and Lyme disease [1].

Prognosis

Intermediate uveitis generally demonstrates a favorable long-term visual prognosis despite its chronic nature and frequent complications [4-5][11]. In large cohort studies with extended follow-up, median best-corrected visual acuity remained stable at 20/30 at presentation, 5 years, and 10 years, indicating preservation of good vision in most patients [4]. Approximately 60% of eyes maintain visual acuity better than 20/25 after more than 10 years of follow-up, and 92.8% of pediatric patients achieve best-corrected vision of 20/40 or better with appropriate treatment [5][12]. However, the disease follows a chronic course with a low rate of spontaneous remission, estimated at 8.6 per 100 eye-years [13]. Permanent moderate visual loss (≤20/50) occurs in approximately 21% of eyes after 2 years of follow-up, with most permanent vision loss occurring during the first year of disease [11].

Factors associated with worse visual outcomes include lower visual acuity at presentation, longer duration of uveitis (particularly >10 years), presence of cystoid macular edema at baseline, retinal pigment epithelial atrophy, macular scarring, retinal detachment, and hypotony [4][11][14]. Conversely, resolution of active inflammation, successful treatment of macular edema, and appropriate use of immunomodulatory therapy are associated with improved visual outcomes [12][14]. Patients with sarcoid-associated intermediate uveitis appear to have a more favorable prognosis and require second-line immunosuppression less frequently than those with idiopathic disease [4]. The 5-year risk of developing any ocular complication in patients with noninfectious intermediate uveitis is approximately 66%, emphasizing the importance of long-term monitoring and appropriate therapeutic intervention [15].

Complications

Cystoid macular edema represents the most common and visually significant complication of intermediate uveitis, occurring in 28-41% of patients and serving as the primary cause of vision loss in 85% of cases with visual impairment [4][10-12]. The development of macular edema is associated with idiopathic disease, chronic

inflammation, and baseline presence of lower visual acuity [4][16]. Incidence rates for new-onset cystoid macular edema range from 5.9 per 100 eye-years, with higher rates observed in patients not receiving immunomodulatory therapy [11-12]. Structural complications affecting the vitreoretinal interface and posterior segment occur frequently during the disease course. Cataract develops in 18-49% of patients, with incidence rates of 6.6 per 100 eye-years, often related to chronic inflammation or corticosteroid therapy [1][4][11-12].

Epiretinal membrane formation occurs in approximately 19% of cases, with incidence rates of 1.2 per 100 eye-years [5][9][11]. Secondary glaucoma or ocular hypertension affects 7-56% of patients, representing a significant cause of irreversible vision loss [1][12][15]. Additional complications include retinal detachment (occurring in 11% at 5 years), vitreous hemorrhage, peripheral retinal neovascularization, optic nerve edema, and in severe cases, hypotony and phthisis bulbi [4][9][15]. The absence of immunomodulatory therapy has been identified as the strongest predictive factor for development of new macular edema (odds ratio 6.3) and glaucoma (odds ratio 6.6), underscoring the importance of appropriate systemic treatment in preventing sight-threatening complications [12]. Patients with persistent or severe disease demonstrate substantially higher complication rates, with 5-year risks of visual disturbance (29%), cataract (35%), glaucoma (20%), and retinal detachment (11%) significantly exceeding those of matched controls [15].

Treatment

The management of intermediate uveitis follows a stepwise approach tailored to disease severity, with the primary goals of controlling inflammation, preventing complications, and minimizing corticosteroid-related adverse effects [1]. Mild intermediate uveitis without vision-threatening complications may be monitored without initial treatment, as some cases remain stable or improve spontaneously [1]. In patients requiring acute intervention, regional corticosteroid therapy is generally used as the initial treatment modality, including periocular injections of triamcinolone acetonide or intravitreal corticosteroid implants. [1][4]. Approximately 34% of patients receive local corticosteroid injections, and 82.7% utilize topical therapy during their disease course [4]. Systemic corticosteroids are required in approximately 50% of patients, though long-term use at doses exceeding 7.5 mg/day prednisone equivalent is associated with unacceptable adverse effects and should be avoided [4][17-18].

For patients with moderate to severe intermediate uveitis at high risk of sight-threatening complications, systemic corticosteroids combined with immunomodulatory therapy (IMT) constitute first-line therapy [1][17]. Methotrexate and mycophenolate mofetil represent the preferred initial corticosteroid-sparing agents, with methotrexate achieving control of

inflammation in 74.9% of intermediate uveitis patients at 12 months and mycophenolate mofetil controlling inflammation in 76.7% [1][19-20].

For patients who fail to respond to or cannot tolerate conventional immunosuppression, biologic agents particularly tumor necrosis factor-alpha (TNF-α) inhibitors such as adalimumab serve as second-line therapy, with adalimumab extending time to treatment failure from 13 to 24 weeks compared with placebo [1][17][21]. It is important to note that TNF-α inhibitors may induce or exacerbate demyelinating diseases such as Multiple Sclerosis. Therefore, brain MRI and neurologic evaluation are recommended before initiating TNF-α inhibitor therapy in these patients. In such cases, alternative agents, including IL-6 inhibitors and B-cell–targeted therapies, may be considered.

Surgical interventions, including pars plana vitrectomy (diagnostic and therapeutic) with or without peripheral laser photocoagulation, are reserved for specific indications such as non-clearing vitreous opacities, tractional retinal detachment, epiretinal membrane, or refractory inflammation, with vitrectomy associated with increased probability of disease remission (hazard ratio 2.39) and improvement in visual acuity in 69% of cases [13][22-24].

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