Anterior Uveitis: Etiology and Treatment

A comprehensive review of systems ensures that important clues are not overlooked.

BY STEPHEN D. ANESI, MD, AND C. STEPHEN FOSTER, MD

Anterior uveitis is often perceived to be the presence of "cell and flare" in the anterior chamber, which has led to a large variability in past reports of uveitis in the literature. A group of uveitis specialists attempted in 2004 to standardize the classification and diagnostic criteria for uveitis worldwide.[1] The effort has helped to ensure better comparability in clinical data, and it has given eye care specialists a more accurate representation of different uveitic entities and their response to treatment. *Anterior uveitis* was defined as inflammation in the uvea, primarily located in the anterior chamber, including iritis, iridocyclitis, and anterior cyclitis. In addition, anterior cell and flare were each definitively quantified on a 0-to-4 scale in a 1-mm square beam (Tables 1 and 2).

Studies show that anterior uveitis is the most prevalent form of uveitis, and about half of these cases are idiopathic.[2-5] Anterior uveitis often occurs with other ocular inflammation such as scleritis, keratitis, vasculitis, or other forms of uveitis, and it is frequently associated with cataract, glaucoma, and macular edema. This article reviews several important factors in anterior uveitis.

DIAGNOSTIC CONSIDERATIONS

Etiology

Several etiologies may cause anterior uveitis. As mentioned earlier, a large number of cases are idiopathic, but infectious causes such as herpes simplex virus can produce inflammation, glaucoma, and other abnormalities. Trauma is well known to cause anterior chamber inflammation, which may easily be overlooked in the shadow of a more serious injury. Autoimmune disease can often cause or be associated with anterior uveitis, especially in

TABLE 1. THE SUN WORKING GROUP GRADING SCHEME FOR ANTERIOR CHAMBER CELLS

Grade	Cells in Field[a]
0	<1
0.5+	1-5
1+	6-15
2+	16-25
3+	26-50
4+	>50

[a]Field size is a 1-mm X 1-mm slit beam.
Abbreviation: SUN, standardization of uveitis nomenclature.
Adapted from reference 1.

TABLE 2. THE SUN WORKING GROUP GRADING SCHEME FOR ANTERIOR CHAMBER FLARE

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)

Abbreviation: SUN, standardization of uveitis nomenclature.
Adapted from reference 11.

association with specific genotypes (ie, HLA-B27[5]). Lastly, many diseases, such as pigment dispersion syndrome or leukemia,[6] can masquerade as anterior chamber inflammation when in fact they are other vision- or life-threatening problems.

A Review of Systems

Clinicians should not underestimate the importance of a thorough history and a comprehensive review of systems. It is worth taking the time to personally examine rashes, joints, sores, and any suspicious potential extraocular manifestations mentioned. A seemingly trivial symptom may be the key to the diagnosis. Refraction will generally not correct uveitis-induced blurring. A slit-lamp examination alone can reveal subtle findings that may tip the scale when weighing the evidence for a diagnosis. Knowledge of the accepted standard classification of anterior chamber inflammation[1] helps not only when comparing the findings to those in the literature, but it can assist comanaging practitioners in understanding the severity of flares when reviewing the patient's history. Cell and flare should ideally be quantified prior to pupillary dilation, as liberation of pigment can be misleading.[7] Footprints of inflammation in the form of capsular pigment dusting or synechiae can provide clues to the chronicity or laterality of cases, even when the eye is quiet. The entire eye must be checked for associated pathology (ie, scleritis, vitritis). This includes a careful dilated fundus examination, which at times can be difficult or nearly impossible in these patients.

Patient Workup and Testing

Single, isolated episodes of unilateral anterior uveitis may not warrant an extensive and costly workup. For chronic, recurrent, and bilateral cases, however, a tailored set of investigations is crucial in deciding how to approach treatment. A few tests are typically ordered to evaluate for diseases that may have a wide range of uveitic presentations (ie, RPR **and** FTA-Abs, ANA, HLA typing). Additional ocular (ie, optical coherence tomography, ultrasonography) and systemic (ie, chest radiograph, Gallium scan) imaging studies should be considered.

THERAPEUTIC STRATEGIES

Medical Management

Infectious entities should be treated with proper antimicrobial therapy. Topical corticosteroids and cycloplegics serve as the primary tools eye care specialists employ for initial and immediate control of inflammation. Severe cases of noninfectious anterior uveitis may be treated with periocular, intraocular, or systemic corticosteroids. These drugs, however, should never be administered indefinitely or relied upon to deal with chronic or recurrent disease due to inevitable complications. Clinicians can use a "stepladder" approach when choosing a systemic medication for ocular inflammation.[8]

> "Surgical management of anterior uveitis may involve a variety of procedures such as cataract extraction, implantation of a glaucoma shunt, vitrectomy, or placement of a medication-eluting implant."

Immunomodulatory Therapy

For noninfectious anterior uveitis, systemic nonsteroidal anti-inflammatory drugs (ie, diflunisal, celecoxib) can be used as first-line maintenance therapy.[9] Should these not be effective or tolerated, immunomodulatory therapy typically begins with the use of antimetabolites such as methotrexate or mycophenolate mofetil, possibly combined with a calcineurin inhibitor (ie, modified cyclosporine). Biologic response modifiers such as infliximab and adalimumab may also be used to supplement or replace these agents. Potent alkylating agents like cyclophosphamide are infrequently used to treat anterior uveitis alone but may be the last resort for otherwise stubborn and vision-threatening disease.

The goal of immunomodulatory therapy for anterior uveitis and all ocular inflammatory disease should be steroid-sparing durable remission of inflammation for no less than 2 years. Tapering any regimen prior to 2 years often leads to the recurrence of inflammation. Many patients may even experience eventual "cure" after this period. Eye care specialists must remember two important directives when faced with stubborn uveitis. First, should the current treatment not be effective or if significant activity remains (≥ 1+ cell) or should the side effects of the medication prove unacceptable, practitioners should quickly move on to more aggressive therapy. Second, clinicians unfamiliar with immunomodulatory therapy should promptly refer the patient to or comanage the case with a specialist (ie, ocular immunologist, rheumatologist, hematologist).

Surgical Management

The surgical management of anterior uveitis may involve a variety of procedures such as cataract extraction, implantation of a glaucoma shunt, vitrectomy, or placement of a medication-eluting implant, and many

patients need multiple surgeries. Surgical intervention is more challenging in the presence of chronic inflammatory changes like synechiae or pupillary membranes. IOLs may not be compatible in patients with stubborn uveitis, and these lenses may incite further postoperative inflammation. Greater care must be taken not only during surgery but in the pre- and postoperative periods as well.

The rate of postoperative complications in uveitic patients has been shown to be as high as 59%,[10] but with proper care and vigilance and/or with the expertise of a fellowship-trained uveitis specialist, the incidence should be much lower. Elective surgery should be postponed until the patient's eye has been quiet for at least 3 months without corticosteroid therapy; pushing forward too soon may end up provoking devastating postoperative inflammation. The perioperative administration of topical and systemic corticosteroids and nonsteroidal anti-inflammatory drugs for 1 week before and after surgery may allow procedures in higher-risk patients. Longer postoperative taperings of anti-inflammatory medications may also be required.

CONCLUSION

Proper evaluation of anterior uveitis involves careful consideration of its presenting signs and symptoms along with a well-planned tailored diagnostic approach. Management should be focused on alleviating inflammation as aggressively as necessary while both ensuring the patient is comfortable and avoiding chronic corticosteroid therapy. ■

Stephen Anesi, MD, is a clinical fellow in ocular immunology and uveitis at the Massachusetts Eye Research and Surgery Institution in Cambridge. Dr. Anesi may be reached at (617) 621-6377; sanesi@mersi.com.

C. Stephen Foster, MD, is founder, director, and president of the Ocular Immunology and Uveitis Foundation and the Massachusetts Eye Research Surgery Institution in Cambridge. Dr. Foster may be reached at (617) 742-6377; sfoster@mersi.com.

1. Jabs DA, Nussenblatt RB, Rosenbaum JT, et al for: The Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol.* 2005;140:509-516.
2. Gritz DC, Wong IG. Incidence and prevalence of uveitis in Northern California. Ophthalmology. 2004;111:491-500.
3. McCannel CA, Holland GN, Helm CJ, et al. Causes of uveitis in the general practice of ophthalmology. UCLA Community-Based Study Group. *Am J Ophthalmol.* 1996;121:732-733.
4. Weiner A, BenEzra D. Clinical patterns and associated conditions in chronic uveitis. *Am J Ophthalmol.* 1991;112(2):151-158.
5. Chang JH, McCluskey PJ, Wakefield D. Acute anterior uveitis and HLA-B27. *Surv Ophthalmol.* 2005;50(4):364-388.
6. Choi JY, Kafkala C, Foster CS. Primary intraocular lymphoma: a review. *Semin Ophthalmol.* 2006;21(3):125-133.
7. Aggarwal JL, Beveridge B. Liberation of iris pigment in the anterior chamber after instillation of 10 percent phenylephrine hydrochloride solution. *Br J Ophthalmol.* 1971;55:544-549.
8. Lee FF, Foster CS. Pharmacotherapy of uveitis. *Expert Opin Pharmacother.* 2010;11(7):1135-1146.
9. Fiorelli VM, Bhat P, Foster CS. Nonsteroidal anti-inflammatory therapy and recurrent acute anterior uveitis. *Ocul Immunol Inflamm.* 2010;18(2):116-120.
10. Yoeruek E, Deuter C, Gieselmann S, et al. Long-term visual acuity and its predictors after cataract surgery in patients with uveitis. *Eur J Ophthalmol.* 2010;20(4):694-701.
11. Hogan MJ, Kimura SJ, Thygeson P. Signs and symptoms of uveitis: I. Anterior uveitis. *Am J Ophthalmol.* 1964;47:155-170.