Abstract

Anterior uveitis is an ocular inflammatory condition of the uveal tract characterized by ciliary flush, keratic precipitates and an inflammatory reaction within the anterior chamber. While the condition can be idiopathic, systemic etiologies must be considered and investigated when specific signs are present. This case report discusses the appropriate laboratory workup and treatment for a severe, persistent, anterior uveitis.

Key Words: anterior uveitis, HLA-B27, sarcoidosis, syphilis, Lyme disease, Posner Schlossman syndrome, herpes simplex virus, secondary glaucoma

Background

Uveitis is, by strict definition, an inflammation of the uveal tract. The term can also be used to describe many other forms of intraocular inflammation involving not only the uvea but also the retina and its vasculature. The uveal tract is divided into anterior and posterior portions. The anterior portion of the uveal tract consists of the iris, while the posterior portion contains the ciliary body as well as the choroid. Uveitis can be classified in many different ways, all dependent on what part of the eye is affected: anterior uveitis occurs when the iris and/or the pars plicata of the ciliary body is involved; intermediate uveitis involves the pars plicata, the peripheral retina and the vitreous; posterior uveitis involves the fundus posterior to the vitreous base; panuveitis involves the entire uveal tract; endophthalmitis involves all intraocular tissues except the sclera; and panophthalmitis involves the entire globe. Anterior uveitis is the most common form of uveitis, followed by posterior, intermediate and finally panuveitis.

The diagnosis of anterior uveitis is based on inflammation limited to the anterior chamber. Diagnosis and management require a thorough case history and collection of detailed history of present illness, as well as review of systems, in order to uncover any potential systemic conditions that could contribute to the development of the uveitic episode. Standard ophthalmic treatment for anterior uveitis includes a topical steroid with slow taper once the inflammation has resolved. Cycloplegic drops are also used for pain management, the prevention of posterior synechiae formation and, in extreme cases, the formation of iris bombé. All ocular treatment strategies are focused on reducing symptoms, controlling inflammation, minimizing treatment complications and preserving vision. Observing the course of the disease and response to treatment can provide additional insights into identifying a cause for the episode. Additional laboratory tests may be indicated if the uveitis is bilateral, granulomatous or recurrent. The most common vision-threatening complications of uveitis include macular edema, cataract and glaucoma.

This teaching case report highlights the appropriate management of a patient with a severe, persistent presentation of anterior uveitis. It is intended for third- and fourth-year optometry students actively involved in clinical patient care. Because this ocular condition can be intimately related to systemic health, sound knowledge of anterior uveitis as well as the systemic conditions associated with it is essential for the practicing optometrist in a clinical environment. This case can be used as a teaching tool in a didactic setting and it can be utilized in clinical seminars focused on patient care.

Case Description

A 30-year-old Turkish male presented to the clinic as an emergency walk-in on a Friday morning complaining of a persistent red eye for the past 3 weeks. His only symptoms consisted of a constantly red right eye and occasional watering. He denied any recent illness, contact with someone else having a red eye, light sensitivity, discharge, pain or noticeable changes in vision. He denied any previous contact lens wear. He reported that he had gone to the Student Health Center a few weeks ago when he first noticed the redness and he was given a prescription for ciprofloxacin. He experienced no improvement with ciprofloxacin so he went back to the health center and was given a prescription for polymyxin B and trimethoprim ophthalmic (Polytrim). He failed to see any improvement with Polytrim so he presented to the clinic. The patient’s most recent eye exam prior to the appointment was 7 months earlier and there were no remarkable findings at that exam. His ocular history was unremarkable. His medical history was unremarkable and he was not taking any medications, prescribed or over the counter, at the time. His family ocular history was unremarkable. His family medical history was positive for diabetes mellitus, cancer and heart disease. Social history was positive for occasional alcohol consumption, and he denied use of tobacco products. He denied any allergies to medications. He was a full-time student at the time of this exam. He was oriented to time, place and person, and his mood was appropriate.

Entering uncorrected visual acuities at distance were 20/80 in the right eye (OD) and 20/25 in the left eye (OS). Pupils were equal in size, 4 mm OD and OS measured in bright room illumination, round and reactive to light, with no signs of an afferent pupillary defect in both eyes (OU). There was a slightly sluggish direct and consensual response to light observed...
OD when compared to OS. Extraocular motilities were smooth and exhibited full range of motion OU. Confrontation visual fields were full to finger counting in each eye. Best-corrected visual acuities with refraction were 20/25 OD and 20/20 OS at distance. Intraocular pressure (IOP) measured with Goldmann applanation tonometry was 36 mmHg and 19 mmHg at 11:31 a.m. in the right and left eye, respectively. IOPs from his exam 7 months ago were checked and measured (with Goldmann) 16 mmHg and 18 mmHg in the right and left eye, respectively.

Anterior segment exam with slit lamp biomicroscopy revealed normal adnexa, lids, lashes and puncta in both eyes. In the right eye, 1+ diffuse bulbar conjunctival injection as well as 2+ perilimbal injection were observed. Also noted in the right eye were diffuse corneal edema and diffuse endothelial mutton fat keratic precipitates (KPs), coalesced inferiorly (Figure 1). No mucus discharge was observed, and there was no significant papillary reaction observed within the palpebral conjunctiva. The anterior chamber of the right eye was difficult to accurately assess for cells and flare due to diffuse corneal edema, but cells and flare were determined to be present. The corneal edema also made it difficult to obtain clear views of the posterior segment during the dilated exam. Though significant vitreal haze was observed, it was not possible to document the presence of intermediate or posterior uveitis at this visit. B-scan ultrasonography would have provided further assessment of the posterior segment of the right eye; however, there was no B-scan equipment available in the clinic. Optical coherence tomography (OCT) of the posterior segment was not pursued due to the significant corneal edema and vitreal haze that would have correlated with poor image quality and poor reliability. Gonioscopy might have revealed additional information; however, due to the emergent presentation and time constraints of this case, it was not performed. The left eye presented with unremarkable findings, including a clear cornea and quiet bulbar and palpebral conjunctiva. Undilated examination of the posterior segment OS showed normal findings to the extent seen: clear crystalline lens, flat and intact macula, normal vasculature, and well-perfused optic nerve with cup-to-disc ratio of 0.35/0.35.

Differential diagnosis for the persistent red eye included bacterial conjunctivitis, viral conjunctivitis, anterior uveitis, bacterial keratitis and infectious endophthalmitis. Bacterial conjunctivitis was ruled out due to lack of mucus discharge, papillary reaction, and lack of improvement with previous topical antibiotic treatment. Viral conjunctivitis was excluded due to lack of palpebral conjunctival follicles. Bacterial keratitis was ruled out because no epithelial defect was present, no infiltrate was observed during slit lamp examination, and no evidence of epithelial staining with fluorescein was seen. Infectious endophthalmitis was excluded mostly due to the patient’s denial of any prior surgical procedure. Eye pain, hypopyon, eyelid edema and chemosis were also absent.

The diagnosis for the persistent red right eye was anterior uveitis. One drop of brimonidine tartrate/timolol maleate ophthalmic solution (Combigan) and one drop of homatropine were instilled in the office in the right eye only. Prescriptions for prednisolone acetate 1% (Pred Forte 1%) every hour while awake OD only and Combigan twice daily every 12 hours OD only were provided. The patient was instructed to get the prescriptions filled as soon as possible. He was instructed to return to the clinic the next day for IOP monitoring and compliance with medications. It would have been beneficial to check the patient’s IOP after instillation of Combigan to ensure it was effectively lowering IOP, but the patient refused to wait in office and declined the procedure despite being educated on the importance of assessment. Because the patient was scheduled to return to the clinic the following morning, it was decided not to force him to wait for an IOP check that afternoon.

The patient returned to the clinic the following day for his second examination and he reported no change in symptoms. His symptoms included a red right eye; however, he did not complain of light sensitivity, pain or changes in vision. He reported good compliance with topical medications. Uncorrected visual acuities at distance had improved slightly to 20/50 OD and 20/20 OS. Pupils were unequal in size, but the right eye was still dilated from homatropine instillation at the
motilities were smooth with full range of motion OU. IOP with Goldmann applanation tonometry was measured to be 18
pupillary defect OU. The reaction to light OD was no longer sluggish and appeared equal to that of OS. Extraocular
distance with refraction were 20/20 OD and OS. Pupils were equal, round and reactive to light with no signs of an afferent
atropine. Uncorrected visual acuities at distance were 20/25-2 OD and 20/20-2 OS. Best-corrected visual acuities at
determined not to be necessary to force the patient to wait for an IOP check after he declined. The patient received a
strong loading dose of Pred Forte 1% after the first examination, and the prescription was changed from every hour while
awake to every 2 hours OD only while awake. A prescription for atropine was also provided to maintain cycloplegia, and
the patient was initially instructed to use one drop of atropine once weekly OD only. The duration of atropine 1% is
typically 7-10 days so this original prescription was intended for once weekly use but was subject to change based on the
patient’s response and compliance. It was possible that the duration of action of atropine could be reduced due to the
severe inflammation the eye exhibited, but given the patient’s financial situation it was unknown if the drop would be
purchased at all. The original instruction for once weekly use was potentially under-prescribed, but the goal was to avoid
overuse until his reaction to the drop was determined. Atropine was prescribed rather than homatropine due to the severe
inflammatory reaction observed in the affected eye and the longer duration of action. The patient was instructed to return
to the clinic in 2 days.

Dorzolamide (Trusopt) was considered as an additional drop for treatment; however, given the patient’s financial situation,
the oral treatment available in-office was ultimately pursued. The patient’s IOP was not checked after the first tablet of
Diamox was administered because he refused to stay in the office for further assessment. It would have been beneficial to
ensure IOP was decreasing, and the patient was educated on the importance of assessment; however, because the patient
was instructed to return in 2 days and to call the emergency care line if any changes or new pain occurred, it was
determined that it was necessary to force the patient to wait for an IOP check after he declined. The patient received a
strong loading dose of Pred Forte 1% after the first examination, and the prescription was changed from every hour while
awake to every 2 hours OD only while awake. A prescription for atropine was also provided to maintain cycloplegia, and
the patient was initially instructed to use one drop of atropine once weekly OD only. The duration of atropine 1% is
typically 7-10 days so this original prescription was intended for once weekly use but was subject to change based on the
patient’s response and compliance. It was possible that the duration of action of atropine could be reduced due to the
severe inflammation the eye exhibited, but given the patient’s financial situation it was unknown if the drop would be
purchased at all. The original instruction for once weekly use was potentially under-prescribed, but the goal was to avoid
overuse until his reaction to the drop was determined. Atropine was prescribed rather than homatropine due to the severe
inflammatory reaction observed in the affected eye and the longer duration of action. The patient was instructed to return
to the clinic in 2 days.

He returned to the clinic 2 days later for his third examination and reported that the redness had resolved. The patient said
he was still using his medications as directed. At this point he was still using Pred Forte 1% every 2 hours and Combigan
twice daily OD only. The patient denied filling the atropine prescription due to financial reasons. Uncorrected visual
acuities at distance, 20/40-2 OD and 20/20-2 OS, showed signs of improvement. Extraocular motilities were still smooth
with full range of motion OU. Pupils showed minimal change with pupil size 6 mm OD and 4 mm OS in bright room
illumination. The right pupil was still slightly larger, most likely due to homatropine. Duration of action for homatropine
can be up to 72 hours. Both pupils were reactive to light with the right eye exhibiting a sluggish reaction. Best-corrected
visual acuities with refraction were 20/20 OD and 20/20 OS. IOP measurements with Goldmann applanation tonometry
revealed 11 mmHg and 14 mmHg in the right and left eye, respectively. Slit lamp exam with biomicroscopy revealed
minimal improvement; however, the anterior chamber and posterior segment of the right eye were able to be examined at
this visit due to mild reduction of the corneal haze. The cornea still exhibited signs of mild edema and the mutton fat KPs
were still diffusely scattered, coalescing inferiorly. There was 1+ cells and 2+ flare in the anterior chamber. Grading the
anterior chamber cells and flare was accomplished using the Standardization of Uveitis Nomenclature (SUN) Working
Group grading schemes. Posterior segment examination revealed no signs of intermediate or posterior uveitis. The
posterior segment exam did not reveal vitreous cells, vitreous haze, white exudative material in the peripheral retina, or
retinal or choroidal inflammatory lesions. The macula was flat and intact and the optic nerve was well perfused with
0.40/0.40 cup-to-disc ratio. One drop of homatropine was instilled in office OD only because the patient had not filled the
prescription for atropine. Diamox use was discontinued due to regulated IOP OU, but the patient was instructed to
continue using Combigan twice daily OD only. He was instructed to continue using Pred Forte 1% every 2 hours while
awake OD only. The patient was instructed to return to the clinic in 5 days.

The fourth examination 5 days later revealed significant improvements. The patient presented with no symptoms or
complaints. He denied redness, pain, light sensitivity and changes in vision. He reported good compliance with the
medications and stated that he was still using Pred Forte 1% and Combigan as directed. He did not fill his prescription
for atropine. Uncorrected visual acuities at distance were 20/25-2 OD and 20/20-2 OS. Best-corrected visual acuities at
distance with refraction were 20/20 OD and OS. Pupils were equal, round and reactive to light with no signs of an afferent
pupillary defect OU. The reaction to light OD was no longer sluggish and appeared equal to that of OS. Extraocular
motilities were smooth with full range of motion OU. IOP with Goldmann applanation tonometry was measured to be 18


Anterior Uveitis, More than a Red Eye: a Teaching Case Report | 3

| 3 |
mmHg and 17 mmHg OD and OS, respectively, at 9:18 a.m. Anterior segment exam showed significant signs of improvement with a reduced amount of mutton fat KPs distributed across the endothelium. Corneal edema had almost completely resolved. Cells in the anterior chamber had reduced from 1+ to trace and flare had decreased from 2+ to 1+. Dilated posterior segment exam, using one drop of tropicamide 1% and one drop of phenylephrine 2.5%, was unremarkable and did not show signs of inflammation that would indicate an intermediate or posterior uveitis. Dilated examination of the posterior segment OS was also unremarkable. The patient was instructed to begin taper of the topical steroid medication. He was instructed to continue use of Combigan twice daily OD only. He was also instructed to continue use of Diamox twice daily OD only. He was told to return to the clinic in 2 weeks, or sooner if any symptoms returned.

The patient returned to the clinic 2 weeks later for his fifth examination. He had no symptoms or complaints. He reported good compliance with the medications, using Pred Forte 1% 4 times daily and Combigan twice daily OD only. Uncorrected visual acuities at distance were 20/25 OD and 20/20-2 OS. Best-corrected visual acuities at distance with refraction were 20/20 OD and OS. Because the manifest refractions performed at the fourth and fifth exams were stable and nearly identical, a prescription for glasses was provided to the patient, but he reported that he was happy with his vision and would most likely not fill the prescription. Pupils were equal, round and reactive to light OU with no signs of an afferent pupillary defect. Extraocular motilities were smooth with full range of motion OU. IOP measured with Goldmann applanation tonometry was 17 mm Hg and 18 mm Hg at 10:06 a.m. OD and OS, respectively. Corneal edema was completely resolved. Mutton fat KPs were almost completely resolved with a few scattered inferiorly and their inferior placement was not visually significant. No cells or flare were present in the anterior chamber. The patient was instructed to continue taper of topical steroid. He was instructed to use Pred Forte 1% 3 times daily for 1 week, 2 times daily for 1 week, 1 time daily for 1 week, and then to discontinue use completely. He was instructed to continue using Combigan twice daily until he was finished using Pred Forte 1% and to then discontinue.

The patient’s lab results were also reviewed during the examination and each test came back within normal limits and unremarkable: CBC with differentials was within normal limits, HLA-B27 was negative, ACE was within normal limits, Lyme was negative, VDRL screening test was normal, toxoplasma gondii antibody was negative, RF was within normal limits, ANA was negative, RPR was non-reactive, and FTA-ABS was non-reactive. He was instructed to return to the clinic in 4 weeks. He returned to the clinic 4 weeks later for his sixth examination with no complaints and complete resolution of anterior uveitis.

Three weeks following the patient’s sixth and final examination, the patient returned to the clinic with complaints of a red right eye. He reported that the redness had started 2 days prior. He denied complaints of light sensitivity, pain or changes in vision. He stated that he considered starting the previously prescribed drops again but he decided to return to the clinic before using any of the medications. Ocular and medical histories were reviewed but remained unchanged. Uncorrected visual acuities at distance were 20/40+1 OD and 20/20-1 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion OU. Best-corrected visual acuities at distance with refraction were 20/25+2 OD and 20/20 OS. Anterior segment exam with slit lamp biomicroscopy revealed 2+ perilimbal injection OD, mild diffuse corneal edema OD, and 2+ cells and 2+ flare in the anterior chamber OD. There were no KPs present OD. OS anterior segment examination was unremarkable. IOP measured with Goldmann applanation tonometry was 32 mmHg and 18 mmHg at 11:04 a.m. OD and OS, respectively. Dilated examination of the posterior segment using tropicamide 1% and phenylephrine 2.5% was unremarkable OU. The diagnosis at this time was recurrent anterior uveitis OD. One drop of Combigan and one drop of homatropine were instilled in-office OD only. The patient was instructed to begin treatment again using one drop of Pred Forte 1% every 2 hours while awake and to use one drop of Combigan twice daily OD only. A new prescription was provided for the patient to purchase additional topical medication as needed. The patient was also given four tablets of Diamox and was instructed to take one tablet twice daily for 2 days. He was told to return to the clinic in 2 days. The patient returned to the clinic 2 days later with improved symptoms. He reported that the redness had improved, and he denied any pain, photophobia and changes in vision. Uncorrected visual acuities at distance were 20/30+3 OD and 20/20-2 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion. Best-corrected visual acuities with refraction were 20/20 OD and OS. IOP measured with Goldmann applanation tonometry was 13 mmHg and 14 mmHg at 1:52 p.m. OD and OS, respectively.
Anterior segment exam revealed trace diffuse bulbar conjunctival injection, resolved corneal edema, trace cells in the anterior chamber, resolved flare in the anterior chamber, and an absence of KPs. Dilated exam using tropicamide 1% and phenylephrine 2.5% was unremarkable. Given the patient’s previous success with treatment, he was instructed to continue using Pred Forte 1% 4 times daily and CombiGAN twice daily OD only for 2 weeks. Diamox tablets were discontinued. The patient was instructed to return to the clinic in 2 weeks.

He returned to the clinic 2 weeks later with no complaints and reported good compliance with the topical medications. Uncorrected visual acuities at distance were 20/25+1 OD and 20/20-2 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion OU. Best-corrected visual acuities at distance with refraction were 20/20 OD and OS. IOP measured with Goldmann applanation tonometry was 17 mmHg and 19 mmHg at 2:06 p.m. OD and OS, respectively. Anterior segment exam was unremarkable with complete resolution of conjunctival injection, corneal edema, cells and flare OD. Given the normal and negative results of the lab workup and the relatively quick onset of the second occurrence after discontinuing topical treatment, it was determined that this episode was most likely a continuation of the previous episode and a longer steroid taper would be needed to completely resolve the chronic condition. The patient was instructed to continue using Pred Forte 1% 4 times daily for 2 weeks, then 3 times daily for 3 weeks, then 2 times daily for 2 weeks, then 1 time daily for 2 weeks, then 1 time daily every other day for 2 weeks, and then to discontinue. He was also instructed to continue use of CombiGAN twice daily every day while still using Pred Forte 1%. He was instructed to return to the clinic in 12-14 weeks, or sooner if the symptoms returned.

He returned to the clinic 12 weeks later with complete resolution. He reported that he followed the directions for the topical medications and did not have any flare-ups. Uncorrected visual acuities at distance were 20/25 OD and 20/20-2 OS. Pupils and extraocular motilities were normal OU. IOP measured with Goldmann applanation tonometry was 18 mmHg and 17 mmHg at 9:04 a.m. OD and OS, respectively. Anterior segment and posterior segment examinations were unremarkable OD and OS. Extensive education about the condition was reviewed with the patient and he was told that another round of lab tests may be necessary, as well as other potential tests, if the condition returned in the right eye or occurred in the left eye. A complete physical was recommended to the patient but he denied having a primary care provider at the time. The importance of a chest X-ray was discussed with the patient and he reported that as soon as he found a physician he would return to the clinic for a referral. There was also a discussion about possible referral to a rheumatologist should the condition return.

**Education Guidelines**

The following discussion points and literature review help facilitate discussion of the case and management of anterior uveitis. Additional information regarding systemic associations and appropriate laboratory testing is included to further educate the clinician.

**Learning objectives**

At the conclusion of this case discussion, students should be able to:

1. Recognize the signs and symptoms of anterior uveitis
2. Understand the differences between granulomatous and nongranulomatous anterior uveitis
3. Identify the systemic conditions associated with anterior uveitis and know which laboratory tests to order to investigate each systemic condition

**Key concepts**

1. Recognition of clinical signs and reported symptoms associated with anterior uveitis
2. Understand how to manage anterior uveitis
3. Knowledge of the systemic conditions and additional laboratory work associated with anterior uveitis

**Discussion points**

1. Clinical presentation of anterior uveitis
2. Describe common symptoms of acute anterior uveitis
3. Discuss the differences between acute, chronic, recurrent and resistant uveitis
4. Describe basic clinical signs of anterior uveitis
5. Additional exercise: create a list of appropriate questions to ask a patient when investigating a chief complaint of “red eye”
6. Clinical treatment and management
7. Discuss the clinical signs of anterior uveitis that warrant additional laboratory testing
8. Describe the differences in presentation and in systemic associations between granulomatous and nongranulomatous anterior uveitis
9. Discuss a treatment plan for an acute anterior uveitis patient with and without elevated IOP
10. Discuss topical and oral treatment options for lowering elevated IOP
11. Create an appropriate laboratory workup referral for a patient who presents with unilateral, granulomatous anterior uveitis
12. Discuss the clinical presentation and potential symptoms of a patient who presents with anterior uveitis and has an underlying systemic condition (perform this exercise with at least three different systemic conditions)

Assessment of knowledge

Additional methods of assessing the students’ mastery of content can include:

1. Quiz containing questions focused on discussion topics
2. Randomizing the systemic conditions, ocular signs and blood work/laboratory tests presented in Table 1 in a matching activity and requiring the students to accurately match the correct systemic condition to ocular signs and blood work/laboratory tests
3. Requiring the students to create their own laboratory referral (or complete an established laboratory referral form for a local clinical laboratory) indicating the tests that should be ordered for an anterior uveitis case that requires additional systemic tests. The students should indicate the systemic condition associated with each test

Discussion
Pathophysiology

Acute anterior uveitis is generally characterized by cells and flare in the anterior chamber, ciliary flush and KPs. The hallmark sign of an anterior uveitis is the detection of leukocytes within the aqueous humor of the anterior chamber. Symptoms associated with acute anterior uveitis include sudden onset of unilateral deep ocular pain, redness, photophobia, excessive tearing and reduced vision; some cases are relatively asymptomatic. Symptoms may be mild or absent in patients with chronic anterior uveitis. The pain arises from structures inside the globe, commonly as a consequence of inflammation of uveal structures, which is typically also associated with photophobia. Pain after inflammation of the uveal tract is due to enhanced activity in the abundant polymodal nociceptor fibers innervating the uveal structures. The mechanism for the photophobia experienced is uncertain, but reflex contraction of the ciliary and/or iris muscles triggered by light exposure or accommodation may become painful if nociceptor sensory nerve endings in these structures were also sensitized. While photophobia secondary to ciliary muscle spasm is common, it can also be induced by anterior chamber cellular infiltration, corneal epithelial edema and pupillary muscle involvement. The pain associated with anterior uveitis can vary, but it is usually a dull aching type or a throbbing sensation in the eyebrow area.

The patient in this case did not complain of pain or light sensitivity, which is potentially unusual for anterior uveitis; however, the patient also did not complain of any visual changes even though visual acuity was reduced to 20/80 in the affected eye. It is possible that the patient had a high pain tolerance and was not significantly affected by any possible painful symptom, or it is possible that the patient did not want to fully disclose his symptoms. His primary concern at all of his visits was the redness in the affected eye, and he did not admit to any other symptom. It is also possible that he may have noticed some form of pain or photophobia at onset but adapted to any discomfort before his initial visit to the clinic 3 weeks later. Additionally, patients who present with a chronic case of anterior uveitis may have mild symptoms or the symptoms may be absent. Onset of acute anterior uveitis is sudden and duration is limited to 3 months or less. In addition to acute uveitis, the condition may be described as chronic, recurrent or resistant. Chronic uveitis describes persistent inflammation characterized by prompt relapse within 3 months after discontinuation of therapy. This patient can be diagnosed with chronic anterior uveitis because he had a prompt relapse of inflammation within 3 months after he discontinued therapy. Recurrent uveitis is characterized by repeated episodes of uveitis separated by periods of inactivity without treatment lasting at least 3 months. Resistant uveitis describes the condition when there is no clinical improvement despite 2 weeks of steroid treatment at maximal dose.

Clinical features may vary on a case by case basis but, as previously mentioned, the hallmark feature is cells in the anterior chamber. Inflammatory cells do not arise in the aqueous itself, so the presence of cells or increased protein (flare) in the anterior chamber is evidence of spillover from an inflamed iris or ciliary body. Aqueous cells indicate active inflammatory disease activity and their number reflects disease severity. This inflammation can result in either increased or decreased IOP. An acute attack of anterior uveitis with severe anterior chamber inflammation can lead to increase in IOP and this most commonly occurs in viral keratouveitis or Posner-Schlossman syndrome (PSS). However, idiopathic anterior uveitis can also present with increased IOP. Chronic anterior uveitis can also lead to increased IOP due to associated trabeculitis, clogging of the trabecular meshwork by inflammatory cells, or secondary angle closure. Severe inflammation of the ciliary body may lead to decreased aqueous production and subsequent reduction in IOP. The presence of a cyclitic membrane over the ciliary body in cases with chronic or recurrent intermediate uveitis with spillover anterior uveitis can also lead to severe hypotony. Gonioscopy would allow detection of peripheral anterior synechiae, neovascularization of the angle, and the presence of an open or closed angle. It would be difficult to confirm the presence of trabeculitis or inflammatory cells within the trabecular meshwork using gonioscopy; however, a closer look at the anterior chamber angle would help determine the extent of inflammation and/or damage present. Another critical sign to be on the lookout for is the presence of KPs. KPs are the most commonly reported corneal finding in uveitis, and the presence of these deposits on the corneal endothelium can provide useful diagnostic information and can indicate the current level of inflammatory activity. True KP usually appear only after a few days and are usually nongranulomatous. The type of KP present may indicate which type of systemic disease is cause for the uveitis. Generally, the larger granulomatous KPs are associated with chronic inflammation while the smaller nongranulomatous KPs occur in acute inflammation. Fine KPs typically cover the entire corneal endothelium and are associated with herpetic disease, Fuchs heterochromic iridocyclitis and cytomegalovirus retinitis. Small nongranulomatous KPs are associated with HLA-B27, trauma, juvenile idiopathic arthritis (JIA), PSS, as well as the granulomatous conditions. Granulomatous KPs are large and greasy in appearance and have been given the term “mutton-fat” KPs. These granulomatous KPs usually coalesce on the inferior cornea and are associated with sarcoidosis, syphilis, tuberculosis (TB), lens-induced changes and Vogt-Koyanagi-Harada syndrome. The patient in this case displayed large granulomatous KPs, which prompted an initial laboratory workup. A nonspecific initial laboratory workup is indicated if the uveitis is bilateral, granulomatous or recurrent.
Systemic associations

Although the majority of patients (approximately 50%) are found to have idiopathic anterior uveitis, it is essential to be aware of the systemic etiologies that could potentially be causing the ocular inflammation. HLA-B27 systemic associations include ankylosing spondylitis (AS), reactive arthritis (Reiter syndrome), psoriatic arthritis and inflammatory bowel disease. HLA-B27-associated uveitis is the most commonly diagnosed cause of acute anterior uveitis. Recurrent, severe, alternating, nongranulomatous anterior uveitis with a higher incidence of posterior synechiae is very characteristic of uveitis episodes associated with HLA-B27 conditions. Fine KP's and endothelial dusting occur, and posterior synechiae are frequently present, but the uveitis is nongranulomatous. Severe anterior chamber reaction with fibrin can occur, and a hypopyon is common as well and is associated with the severity of the systemic disease. The most common symptomatic association of AS and other forms of spondyloarthritis is with acute anterior uveitis. In fact, approximately 25-40% of patients with AS will experience a sudden onset of unilateral anterior uveitis at some point during the course of their disease. Thus, it is especially important to ask patients with anterior uveitis about any inflammatory lower back pain. The patient discussed denied any symptoms of back pain, or other bodily aches or pain, when questioned. He denied any current and previous symptoms of joint pain, as well as any current or previous history of arthritis. The lab results also revealed negative results for HLA-B27 disease association. Given this negative lab result, it was possible to rule out AS, reactive arthritis, psoriatic arthritis, inflammatory bowel disease and other conditions associated with positive HLA-B27.

Ocular manifestations of sarcoidosis include large mutton-fat KPs, iris nodules, anterior and posterior synechiae, sheathing along peripheral retinal veins (candle-wax drippings), peripheral retinal neovascularization, snow balls and vitreous body base condensates. Ocular involvement in sarcoidosis is present in up to 30-60% of patients and is frequently manifested before the systemic disease has been diagnosed. Uveitis is the most common ocular manifestation observed in patients with sarcoidosis, and it can present as anterior, intermediate or posterior. Chest radiography is the most useful test for diagnosing sarcoidosis with the radiographs being abnormal in 90% of patients with the condition. Serum ACE is elevated in 60-90% of patients with active sarcoidosis making it a useful screening test. A biopsy of the lungs can also be performed to provide the greatest accuracy for diagnosis even in asymptomatic patients with normal chest imaging results. Based on the patient’s normal ACE serum levels and on the normal CBC with differentials results, sarcoidosis was tentatively ruled out. The patient also did not show any other ocular manifestations that would indicate a posterior or intermediate uveitis reaction. Additionally, the patient did not present with any other physical complaints or signs that might indicate further investigation toward sarcoidosis. A chest X-ray or computed tomography (CT) scan would absolutely be indicated in order to confirm or rule out a definitive diagnosis of sarcoidosis should the anterior uveitis return to either eye, which is why the importance of follow-up care with a primary care doctor was stressed and discussions about additional testing and imaging took place.

Ocular conditions associated with acquired syphilis include a chancre on the eyelid or conjunctiva, uveitis, optic neuritis, active chorioretinitis, retinal vasculitis, conjunctivitis, interstitial keratitis and other variable conditions. The presentation of uveitis secondary to syphilis can be granulomatous or nongranulomatous. Ocular manifestations typically occur during the secondary stage of infection of acquired syphilis. Due to the variable presentation of syphilis, laboratory tests should be performed in all patients with uveitis who require an investigation. Diagnosis of active syphilis requires a combination of treponema-specific tests and nontreponemal tests. VDRL and RPR screening tests are nontreponemal tests that are best used to diagnose primary infection and to monitor disease activity. The results of the VDRL and RPR tests have a tendency to show negative results in early primary, latent, late stages, as well as 6-18 months after conclusion of therapy for syphilis. Treponemal antibody tests are highly sensitive and specific in all stages of syphilis and more useful for proving past infection. FTA-ABS and microhaemagglutination Treponema pallidum assay are the tests of choice in suspected ocular syphilis. When FTA-ABS results are negative, no treatment is indicated. The result of the FTA-ABS cannot be titrated and is either positive (reactive) or negative (non-reactive). The patient’s VDRL test result was normal (non-reactive), while his FTA-ABS test result was also non-reactive. Based on these two test results, syphilis was ruled out as a possible cause for his uveitis.

Lyme disease is an infection caused by Borrelia burgdorferi, and it can affect any ocular structure. Therefore, it can present with a wide variety of ocular manifestations, including uveitis. Uveitis, while uncommon, can present as anterior, intermediate, peripheral multifocal chorioiditis, retinal periphlebitis and neuroretinitis. Intraocular inflammation can occur in both early and late stages of the disease. The characteristic features of anterior Lyme-related uveitis can include granulomatous uveitis, and it is generally bilateral, although unilateral cases have been reported. The patient denied any feelings of malaise or fatigue or flu-like symptoms. He also denied any suspicious new skin lesions. However, given the granulomatous appearance of his uveitis, a Lyme disease antibody with reflex to blot (IgG, IgM) was
ordered from the laboratory. Interpreting the serology results required careful examination. The Lyme IgG/IgM Ab western blot reflex result came back negative. The Lyme Ab Igq quant result came back high at 0.99 (normal index referencing values 0.00-0.79). However, after further review it was determined that the Lyme IgM western blot result was negative. A positive result would have included two of the following IgM bands: 23, 39 or 41. The patient’s results revealed an absence of all three bands, which indicated a negative result. Lyme IgG western blot results came back as negative as well. There was one IgG antibody present, IgG P45 Ab; however, a positive result requires five Borrelia-specific bands, which was not the case with this patient’s test results.

RF laboratory testing is relatively sensitive for rheumatoid arthritis, and may also be positive in patients with other rheumatic diseases including Sjogren’s syndrome and systemic lupus erythematosus (SLE). ANA is another test that can indicate underlying rheumatic diseases and connective tissue disorders including SLE. The ocular conditions associated with rheumatoid arthritis include dry eye, keratitis and scleritis; however, anterior uveitis is common among individuals with JIA. While it was unlikely that the patient in this case had an undiagnosed form of rheumatoid arthritis or JIA due to lack of systemic and physical symptoms, the laboratory workup did include RF and ANA testing to confirm or rule out these types of conditions. The patient’s lab results came back negative for ANA Direct, and the RF test revealed a normal value that did not indicate the presence of RF.

PSS, also known as recurrent glaucomatocyclitic crisis syndrome, is characterized by recurrent episodes of unilateral, acute secondary open-angle glaucoma associated with mild anterior uveitis. PSS predominantly occurs in young to middle-age patients, but it may also be diagnosed in the elderly and there is a male predilection. The condition itself is rare but it must be considered in the list of differentials in cases of unilateral uveitis associated with elevated IOP. Signs of PSS include significantly elevated IOP (usually 40-60 mmHg), open angle without posterior synechiae, minimal anterior chamber reaction, corneal epithelial edema and few fine KP's located on the central corneal endothelium. PSS was considered as a potential differential diagnosis for the patient’s condition due to his age, sex and elevated IOP; however, it was ruled out based on the patient’s clinical presentation. He presented with granulomatous KP's as well as a significant anterior chamber reaction, both of which contradict the presentation of PSS. Performing a complete glaucoma workup including pachymetry, gonioscopy, OCT and visual field testing could be indicated if the presentation changes.

Ocular involvement occurs in approximately 1-2% of patients with TB. TB can affect the anterior and posterior segments of the eye as well as the ocular adnexa and orbit. TB is most often associated with granulomatous anterior uveitis including mutton-fat KPs, iris nodules and broad posterior synechiae; however, it can also be associated with intense nongranulomatous cases of anterior uveitis. Patients with suspected TB should have a systemic evaluation to check for evidence of the disease including a chest X-ray and tuberculin skin tests. A purified protein derivative (PPD) skin test can be performed to aid in the diagnosis of TB; however, these skin tests are not 100% sensitive or specific for TB and can provide false results. TB blood tests can also be performed to confirm or rule out latent or active TB, but imaging and sputum tests provide the definitive diagnosis. Chest X-rays or CT scans will show white spots in the lungs where the immune system has walled off the TB bacteria. If the chest X-ray or CT scan shows signs of TB, samples of sputum should also be tested for TB bacteria. Unfortunately, the lab that this patient was sent to did not provide PPD skin testing for TB so it was not performed. If the patient had been able to acquire a primary care doctor, additional testing including PPD skin test, chest X-ray or CT scan could have been pursued to effectively confirm or rule out TB.

Differential diagnoses for anterior granulomatous uveitis include sarcoidosis, syphilis, TB, idiopathic and herpes simplex. Inflammation of the cornea and uveal tract from an infection with varicella zoster virus (VZV) or herpes simplex virus (HSV) is a common cause of anterior uveitis. The ocular inflammation may be due to the viral infection itself or the inflammatory response to the infection. Patients may develop redness, itching, burning and tearing and experience photophobia, moderate to severe pain and blurry vision. It is commonly associated with conjunctival injection, corneal scars, history of unilateral recurrent red eye, decreased corneal sensation, increased IOP (hypertensive uveitis) and sectoral iris atrophy. Blistered or skin vesicles may also occur on or near the eyelid. The hallmark of ocular HSV is epithelial dendritic keratitis. Herpetic keratouveitis can also exhibit an edematous cornea, fibrinous flare with heavy anterior chamber cells, medium-size granulomatous KP’s, synechiae and increased IOP arising from trabeculitis. Loss of function of the iris sphincter muscles and atrophy of the iris may also occur. Sectoral iris atrophy is considered pathognomonic for herpetic anterior uveitis. The diagnosis of herpes simplex keratouveitis is most easily made in patients with a known history of herpes simplex keratitis confirmed by dendritic epithelial defects. The patient may also present with a history of unilateral red eye episodes and scarring of the cornea. The patient in this case did not present with any signs of dendritic keratitis or epithelial herpetic disease and denied any previous ocular history that would have indicated a prior herpetic episode. He did not present with any signs of epithelial or stromal corneal scarring. Herpes simplex should also be considered in patients with a significant corneal opacity accompanied by synechiae and anterior chamber cells. The
patient did not present with synechiae despite having symptoms of redness without pain for 3 weeks prior to the exam. Herpes simplex may present with iris atrophy or reduced function of the iris sphincter muscles, which could potentially lead to a sluggish pupillary response. The patient did not present with signs of iris atrophy by slit lamp examination. The patient did present with a slightly sluggish pupil in the affected eye at the initial exam, but both pupils were equal in size. Only after he had been dilated with homatropine, which can potentially last up to 72 hours, did the size of the pupils differ and the reactions to light differ more significantly. While the patient did exhibit some clinical signs that could be attributed to a herpetic etiology, it is difficult to differentiate between signs that could indicate herpes simplex anterior uveitis and idiopathic chronic uveitis especially because the patient presented to the clinic at least 3 weeks after the initial onset of observed redness. For example, the corneal edema could have been attributed to disciform keratitis secondary to HSV infection, or the edema could have been caused by chronic elevated IOP secondary to idiopathic trabeculitis. A positive polymerase chain reaction (PCR) test for a virus can aid in the diagnosis of viral uveitis and more specifically a positive PCR for HSV1, HSV2 or VZV can be used to further support the diagnosis. A viral infection can also lower a patient’s white blood cell count. The patient’s white blood cell count was within normal limits in this case; however, this information does not conclusively confirm or rule out the presence of a viral etiology for the uveitis episode. Treatment of herpetic anterior uveitis involves topical steroids (in the absence of epithelial disease), cycloplegic agents and a topical or oral antiviral medication. The patient’s chronic condition did successfully resolve after a slow and prolonged steroid taper; however, additional investigation and medication would have been pursued if the patient had not exhibited improvements with steroid treatment alone. Elevated IOP is a frequent complication of intraocular inflammation and can affect 5 to 19% of uveitis patients. Elevated IOP can be acute or chronic and both presentations can lead to optic nerve damage and visual field defects in glaucoma secondary to hypertensive uveitis. Anterior uveitis is more likely to be associated with glaucoma than intermediate or posterior uveitis. More specifically, anterior uveitis secondary to HSV is most commonly associated with ocular hypertension and glaucoma. Glaucoma also occurs more commonly in granulomatous uveitis and in association with Fuchs heterochromic cyclitis. However, uncontrolled anterior segment inflammation can result in peripheral anterior synechiae and secondary glaucoma in any type of uveitis. Complications from chronic uveitis include cataract, cystoid macular edema, synechiae or glaucoma. Increased IOP can occur at any time during the uveitic episode, and various pathomechanisms of glaucoma can occur during early or late stages. Trabecular meshwork congestion, trabeculitis, a steroid-induced alteration of trabecular meshwork function, extracellular matrix deposition, or a pupillary block are the mechanisms that most often occur during the early stages of chronic uveitis that contribute to elevated IOP. Synechial closure, morphological changes in the trabecular meshwork due to infiltrated inflammatory cells, and altered aqueous composition are the mechanisms seen most commonly at a later stage. The patient discussed presented with anterior uveitis that had been ongoing for at least 3 weeks, and his IOP was significantly elevated so it was imperative to reduce the IOP and monitor it closely for any potential signs of secondary glaucoma. Combigan was initially prescribed so that the patient could benefit from the alpha-2-agonist qualities of brimonidine as well as the beta-blocker qualities of timolol. A prostaglandin was not considered because the desired effect of IOP-lowering takes longer to achieve and because prostaglandin analogs should be avoided while inflammation is present. Because the patient’s IOP was still significantly elevated after using Combigan, Diamox was utilized to achieve normal IOP more quickly than with topical medication alone. Additionally, oral medication was pursued because the patient could not afford additional topical medications without the help of his insurance. Once the patient’s IOP was regulated, Diamox was discontinued with hope that the lowered IOP could be maintained using only Combigan.

Treatment

Standard treatment for anterior uveitis includes a cycloplegic to assist with pain management as well as a topical steroid to control inflammation. Cycloplegic drops can also prevent the development of posterior synechiae while reducing the pain associated with ciliary body inflammation and spasm. Cyclopentolate, homatropine and atropine are the most commonly used cycloplegic agents for the treatment of uveitis. Homatropine was utilized in-office in this case because it would provide the longest duration of action when compared with tropicamide 1% and cycloplentolate. Tropicamide duration of action for cycloplegic effect is typically 6-8 hours; cycloplentolate duration of action is typically 24-36 hours; and homatropine duration of action is typically 36-72 hours. Atropine has the longest duration of action for cycloplegic effect and can last up to 7-12 days. Cyclopentolate was not considered for an initial treatment for cycloplegia because it was thought to be too weak for the severe inflammation observed in this case. Additionally, cyclopentolate has a chemotactic effect on leukocytes and may cause a sticky iris in patients with a history of uveitis. Given the patient’s severe inflammation it was deemed most appropriate to dilate the patient with the longest acting cycloplegic in-office and prescribe atropine for use at home. The patient never filled his prescription for the cycloplegic agent so he was dilated at all of his follow-ups, except for the second exam when he was still dilated from homatropine instillation the previous day, in an attempt to provide cycloglegia for the patient. While the use of cycloglecics in this case was not ideal, it was difficult to

Anterior Uveitis, More than a Red Eye: a Teaching Case Report

| 10 |
provide constant cycloplegia for the patient when he was not able to afford the topical medications for use at home. Most cases of moderate to severe acute uveitis require initial dosing of a topical steroid every 1-2 hours, but dosing may be less frequent depending on the medication being used. If there is no improvement with topical steroid use, systemic corticosteroids as well as systemic immunosuppressive agents may be utilized. Pred Forte 1% is commonly used as a topical medication but it requires frequent dosing to be effective, and such frequent dosing can lead to noncompliance among patients. Difluprednate 0.05% (Durezol) may allow less frequent dosing than Pred Forte 1% due to its higher potency. Studies reported Sheppard et al. demonstrated that dosing Durezol 4 times daily was noninferior to Pred Forte 1% dosed 8 times daily in patients with endogenous anterior uveitis. The patient in this case report was given a prescription for Pred Forte 1% despite his severe inflammatory reaction because it was more affordable than Durezol. After inflammatory signs were observed to be resolving, a slow taper was initiated. Failure to taper topical steroids may result in a rebound of the condition. Unfortunately, the patient did develop what is believed to be a rebound occurrence shortly after discontinuing all topical medications. This can also be considered a case of chronic anterior uveitis because the uveitis returned within 3 months of discontinuing the treatment. A much longer taper was utilized during the second episode, which safely resolved and has yet to recur.

Conclusion

While a systemic etiology for anterior uveitis is not always present, it is essential to be aware of the potential conditions that could cause this inflammatory reaction (Table 1). Topical treatment of anterior uveitis is usually sufficient for resolution; however, additional methods of treatment may be indicated based on the patient’s presentation and systemic conditions. Management of anterior uveitis patients should include careful case history, laboratory testing when indicated and regular supervision to monitor treatment response.

References

Anterior Uveitis, More than a Red Eye: a Teaching Case Report


Dr. Cronin is a Clinical Assistant Professor at the University of the Incarnate Word Rosenberg School of Optometry.