ASCO ASSOCIATION of SCHOOLS and COLLEGES of OPTOMETRY

Optometric Education The Journal of the Association of Schools and Colleges of Optometry

Abstract

Blebitis is an uncommon infection that can occur following trabeculectomy. Because blebitis may transition to endophthalmitis, prompt and aggressive treatment is necessary. This case report describes a patient presenting with blebitis and the treatment course to resolution. Management of blebitis does not have a standard regimen, but the use of topical antimicrobials has been shown to result in favorable outcomes.

Key Words: *blebitis, endophthalmitis, trabeculectomy, bleb leak, Pseudomonas aeruginosa, antibiotics*

Background

The following case report explores the presentation, diagnosis and treatment of a bleb-related infection. The case may benefit third- and fourth-year optometry students as well as optometry residents in managing a complex eye condition in the setting of multiple ocular and systemic comorbidities. Understanding the management of blebitis and bleb-related infections is important for optometry students and residents. This condition may appear in their future practice, and prompt treatment will benefit patients.

Case Description

An 83-year-old white male presented to the clinic with complaint of mild irritation and foreign body sensation of the right eye for two days duration. The patient recalled getting topical fluorouracil cream for his skin cancer into his right eye before the symptoms began. The eye had become red with sticky discharge the day after the onset of irritation, which was confirmed by the accompanying nurse from his assisted-living residence. The patient denied eye pain or changes in his vision. He did note a brow ache above the eye, and the eyelids of the right eye had been stuck together upon awakening for the past two mornings.

The patient's medical history was remarkable for actinic keratosis on the right facial region, hypertension, transient cerebral ischemia, peripheral neuropathy, benign prostate hyperplasia, abdominal aortic arch repair and a previous myocardial infarction. He had no known medication allergies, but he did have known adverse drug reactions to lisinopril and pseudoephedrine. Active medications for the patient included amlodipine besylate, ammonium lactate lotion, aspirin, atorvastatin, azathioprine, digoxin, duloxetine, finasteride, fluorouracil 5% cream, metoprolol, tamsulosin and warfarin. The patient's past ocular history was remarkable for primary open angle glaucoma and past trabeculectomy surgeries in both eyes of unknown date. He had severe visual impairment and glaucomatous visual field loss consistent with the Social Security Administration definition of legal blindness. The patient noted that his topical glaucoma eye drops (latanoprost at bedtime OS and dorzolamide twice a day OS) had been instilled into his left eye by his assisted-living residence staff every day, with good compliance.

The patient's entering distance visual acuity with correction was 8/180 OD on Feinbloom chart and 20/70 OS on Snellen chart. Pinhole acuity was not an improvement in either eye. Extraocular muscles demonstrated a full range of motion, without diplopia or pain in either eye. Pupils were equal, round and reactive to light OU; no afferent pupillary defect (APD) was present. Anterior segment evaluation by slit lamp biomicroscopy revealed matted eyelashes and thick mucopurulent discharge OD; clear OS. The bulbar conjunctiva had 3+ diffuse injection and a white, elevated bleb on the superior-temporal area OD. There was an elevated and quiet bleb on the superior-temporal area of the conjunctiva OS. The corneas of both eyes showed a mild amount of fine, superficial punctate staining. Anterior chamber evaluation showed 2+ cells without flare OD; no cells or flare OS. Anterior chamber angle estimation was open OU by Van Herick technique. The irides had bilateral superior-temporal peripheral iridectomies consistent with the history of prior bilateral trabeculectomies, but were otherwise unremarkable without synechiae, nodules or neovascularization OU.

Two cotton tipped applicators of a Transystem Sterile Transport Swab (Copan Diagnostics Inc.) were utilized to swab the nasal and temporal cul-de-sac debris and tears OD in order to run a culture for antimicrobial susceptibility and resistance detection. One drop of sodium fluorescein dye (Ful-Glo, Akorn Inc.) was instilled onto the superior bulbar conjunctiva of both eyes. There was no Seidel sign on the corneas nor the blebs OU. One drop of Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution USP, 0.25%/0.4% (Bausch & Lomb Inc.) was then instilled into both eyes. Intraocular pressures (IOPs) measured by Goldmann applanation tonometry were 3 mmHg OD and 9 mmHg OS, which were slightly lower than his typical reading in both eyes. The patient's right pupil was dilated with one drop of 1% tropicamide, one drop of 2.5% phenylephrine and one drop of 1% atropine. The patient deferred dilation of the left eye, which did not have signs or symptoms of inflammation. Internal eye examination of the right eye was performed utilizing a slit lamp with a 78D lens and binocular indirect ophthalmoscopy with a 20D lens. The posterior segment revealed a clear and centered posterior-

chamber intraocular lens. The vitreous cavity had a complete posterior vitreous detachment with Weiss ring. Posterior segment evaluation revealed a cup-to-disc ratio of 0.95H/0.99V with minimal nasal rim remaining, mild pigment mottling at the macula without edema, and mild attenuation and tortuosity of blood vessels. The mid-peripheral and peripheral retina was flat and intact. There were no signs of retinopathy or posterior inflammation OD.

Based on the clinical presentation, a diagnosis of blebitis was considered most likely, and the patient was prescribed moxifloxacin hydrochloride ophthalmic 0.5% solution (Vigamox, Alcon Laboratories Inc.) every hour OD. A loading dose of the medication was instilled into his right eye every 15 minutes for one hour in-office. A combination ointment of Neomycin and Polymyxin B Sulfates and Bacitracin Zinc Ophthalmic Ointment USP (Bausch & Lomb Inc.) was prescribed to be used in the right eye at bedtime. The patient was instructed to instill Vigamox into the right eye if he woke up during the night. The patient was also instructed to continue his current topical glaucoma medications (latanoprost at bedtime OS and dorzolamide twice a day OS), as previously prescribed. All instructions for medications were written for the patient and accompanying caretaker to deliver to the care team in his assisted-living residence. The patient was scheduled for a one-day follow-up appointment. He was counseled on the condition, the importance of medication compliance and the need for follow-up visits. The purpose of the prescribed medications and the purpose of long-acting iris dilatation with atropine were explained. The Transystem Sterile Transport Swab was hand-delivered to the hospital's laboratory for bacterial susceptibility and culturing.

Follow-up visit #1

The patient presented the next day to follow up on his anterior segment condition. He reported that his eye felt slightly less achy and his vision remained unchanged. He noted that the caretakers at his assisted-living residence instilled Vigamox every hour into his right eye the day before, but they stopped the eye drops the day of the follow-up appointment. The caretakers also instilled the antibiotic ointment in the right eye at bedtime the prior night. The patient's distance visual acuity with correction was 5/300 OD on Feinbloom chart and 20/100+ OS on Snellen chart. The pupil OD was pharmacologically dilated, and the pupil OS was normal and reactive to light. No APD was noted by inverse testing. Anterior segment evaluation with slit lamp biomicroscopy revealed matted eyelashes and less discharge OD than at the initial presentation. The bulbar conjunctival injection was less diffuse and mainly localized around the white, avascular, elevated bleb OD. The cornea was clear. There was no Seidel sign on the corneas nor the blebs OU. Anterior chamber evaluation still showed a moderate 2+ cells without flare OD. All anterior segment findings OS were unchanged. One drop of sodium fluorescein/benoxinate solution was instilled into both eyes. IOPs measured by Goldmann applanation tonometry were 4 mmHg OD and 12 mmHg OS. Internal eye examination by slit lamp, funduscopy and binocular indirect ophthalmoscopy revealed unchanged findings OD compared to the prior visit.

The patient was given written instructions to deliver to his caretakers regarding the importance of compliance with the eye drops as well as changes with directions to the medications. Instructions were given to the patient verbally and in writing to continue Vigamox every hour in the right eye and the neomycin combination ointment at bedtime in the right eye. Atropine 1% was added to the regimen to be used once a day OD only. The addition of a topical steroid was considered at the visit, but deferred until infection signs improved. The patient was instructed and scheduled to return one day later.

Follow-up visit #2

The patient presented the next day and reported that his right eye was less red and felt much better and he was experiencing less photosensitivity. Medications were reviewed with the patient, and all medications were being instilled as directed with good compliance. The patient's distance visual acuity with correction was 5/300 OD on Feinbloom chart and 20/80- OS on Snellen chart. The pupil OD was pharmacologically dilated, and the pupil OS was normal and reactive to light. Anterior segment evaluation by slit lamp biomicroscopy revealed mildly matted eyelashes and no discharge OD. The bulbar conjunctiva had mild injection only around the bleb OD. Anterior chamber evaluation showed a mild 1+ cell reaction OD. All anterior segment findings OS were unchanged. One drop of sodium fluorescein/benoxinate solution was instilled into both eyes. IOPs measured by Goldmann applanation tonometry were 3 mmHg OD and 14 mmHg OS.

The blebitis appeared to be resolving well. Vigamox was decreased to four times a day OD, neomycin combination ointment was increased to twice a day OD, and atropine 1% was continued once a day OD. The patient was instructed and given written instructions regarding the changes to his topical medications. The addition of a topical steroid was once again considered at this visit but deferred until the final bacteria culture report was available. The patient was instructed to call the eye clinic's 24-hour on-call service if symptoms worsened over the weekend. He was scheduled for a follow-up visit in three days.

Follow-up visit #3

The patient presented three days later, on the following Monday. He reported that his eye was much less red and no longer painful, but he felt dryness with occasional foreign body sensation OD. He reported good compliance with all medications. The patient's distance visual acuity with correction was 8/400 OD on Feinbloom chart and 20/70 OS on Snellen chart. The pupil OD was pharmacologically dilated, and the pupil OS was normal and reactive to light. Anterior segment evaluation by slit lamp biomicroscopy revealed mild dry debris along the eyelashes OD. The bulbar conjunctiva had trace injection around the white, elevated bleb OD. Anterior chamber evaluation showed trace cell reaction OD. The cornea showed mild diffuse superficial punctate staining, greatest on the inferior and nasal epithelium OD. One drop of sodium fluorescein/benoxinate solution was instilled into both eyes. IOPs measured by Goldmann applanation tonometry were 7 mmHg OD and 12 mmHg OS.

The lab culture report from the swab taken at the initial exam was positive for *Pseudomonas aeruginosa*. The anterior chamber reaction and blebitis appeared to be nearly resolved. There was mild medicamentosa at the visit. The patient was verbally instructed and given written instructions to stop both the neomycin combination ointment and the atropine. He was instructed to continue Vigamox four times a day OD for seven days, then stop. Preservative-free Refresh Plus carboxymethylcellulose artificial tears 0.5% (Allergan Inc.) were prescribed to be used four times a day or more OU. Once again, the patient was instructed to call the eye clinic's 24-hour telephone triage service if symptoms worsened. He was scheduled for a two-week follow up.

Follow-up visit #4

Two weeks later the patient presented for follow-up and reported complete resolution of his symptoms. However, he was still using Vigamox four times a day OD. The patient's distance visual acuity with correction was 8/220 OD on Feinbloom chart and 20/70 OS on Snellen chart. Pupils were equal, round and reactive to light OU; no APD was present. Anterior segment evaluation by slit lamp biomicroscopy revealed mild dry debris along the eyelashes OU. The bulbar conjunctiva had an elevated, clear, avascular bleb OD and was otherwise unremarkable. Anterior chamber evaluation showed no cells OD. The cornea showed no staining OD. One drop of sodium fluorescein/benoxinate solution was instilled into both eyes. IOPs measured by Goldmann applanation tonometry were 6 mmHg OD and 12 mmHg OS.

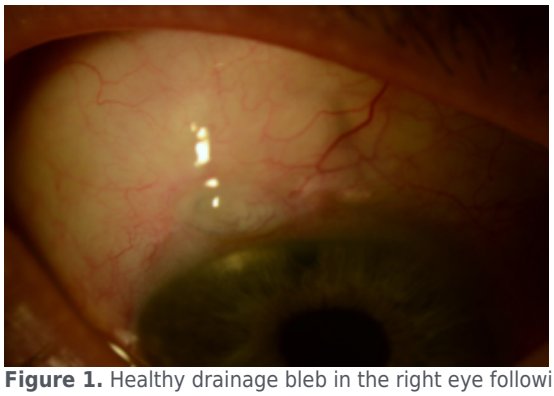

Figure 1. Healthy drainage bleb in the right eye following successful treatment of infection.
Click to enlarge

TABLE 1
Summary of Office Visits

Visit	Visual Acuity	Anterior Chamber Reaction	Intraocular Pressure	Related Symptoms	Treatment
Initial visit	OD: 8/400 OS: 20/70	OD: 2+ cells	OD: 3 mmHg OS: 9 mmHg	OD: brow ache, mucopurulent discharge, 3+ injection, trace corneal staining	Vigamox Q1H OD Neosporin QHS OD Atropine in-office OD
Follow-up #1 (1-day)	OD: 5/300 OS: 20/100+	OD: 2+ cells	OD: 4 mmHg OS: 12 mmHg	OD: mild brow ache, less discharge, 2+ injection	Vigamox Q1H OD Neosporin QHS OD Atropine Q1D OD
Follow-up #2 (1-day)	OD: 5/300 OS: 20/60-	OD: 1+ cells	OD: 3 mmHg OS: 14 mmHg	OD: no pain, 1+ injection	Vigamox QID OD Neosporin BID OD Atropine Q1D OD
Follow-up #3 (3-day)	OD: 8/400 OS: 20/70	OD: trace cells	OD: 7 mmHg OS: 12 mmHg	OD: trace injection, 1+ diffuse corneal staining	Vigamox QID OD x 7 days, Preservative-free Refresh Plus QID OD
Follow-up #4 (2 wks)	OD: 8/220 OS: 20/70	OD: no cells	OD: 6 mmHg OS: 12 mmHg	N/A	Refresh Plus as needed

Table 1. Click to enlarge

The blebitis and anterior chamber reaction were completely resolved at this visit **(Figure 1)**. The patient was counseled and given written instructions to discontinue use of Vigamox. Refresh Plus eye drops were to be continued as needed for dryness OU. Glaucoma medications were to be continued OS as directed. The patient was reminded to call the eye clinic's 24-hour telephone triage service if symptoms recurred. He was scheduled for a two-month follow-up appointment to continue glaucoma testing. **Table 1** provides a summary of the patient encounters.

Education Guidelines

Key concepts

- Recognition of the clinical manifestations of blebitis
- Treatment options and management of blebitis
- Differential diagnoses when encountering bleb-related infections

Learning objectives

At the conclusion of this case report, readers should be able to:

- Describe the signs and symptoms of blebitis
- Understand the risk factors for blebitis and bleb-related infections
- Outline a variety of differential diagnoses for blebitis
- Describe the treatment and management plan for this condition
- Appreciate different classes of antibiotic agents as well as the risk for resistance

Discussion questions

- How does blebitis differ from other red eye presentations?
- How can blebitis and endophthalmitis present similarly?
- Describe the ocular presentation of blebitis
- What are the symptoms of blebitis?
- Describe risk factors related to bleb-related infections
- Discuss treatment options for bleb-related infections
- When should intravitreal antibiotic injections be considered?
- What is the visual prognosis for blebitis?

Learning assessment

- Knowledge of the condition can be strengthened by comparing differential diagnoses in small-group environments
- Reviewing images of healthy blebs to images of bleb-related infections can improve student recognition of abnormal findings
- Case discussion in an integrative seminar can combine knowledge from the clinical and didactic points of the case in a comfortable, open environment
- Presenting interactive quizzes on PowerPoint slides can reveal concepts from the case for which students may need additional review

Discussion

Bleb-related infections are an emergent and potentially visually devastating complication of glaucoma filtering surgeries. They can occur at any time post-surgery and may not affect patients' vision during the course of infection.[1-3] IOP is typically in hypotony ranges less than 5 mmHg.[4,5] Brown et al.[6] first used the term "blebitis" in 1994 to describe an isolated bleb infection without vitreous involvement.[6] It is crucial for a clinician to develop a strong clinical acumen in diagnosing and managing this infection to control its course. Understanding risk factors for blebitis and differentials of the condition as well as employing an evidence-based management approach will help the astute clinician provide prudent care for the patient.

Presentation and symptoms

Patients usually present with a red, painful eye in both blebitis and bleb-associated endophthalmitis, but the signs and symptoms of endophthalmitis tend to progress more rapidly and the disease course is more visually devastating.[1,6-10] Blebitis may represent the initial state in a continuum of infection to early endophthalmitis.[6-9] Patients with blebitis present with a variety of symptoms including redness, irritation, photophobia, purulent discharge, intense peri-bleb conjunctival congestion, opalescent bleb, fluorescein staining defects and mild to moderate anterior segment inflammation.[1,6,8-10] Patients with bleb-associated endophthalmitis present with similar infectious signs and symptoms that rapidly worsen, including anterior chamber hypopyon and vitritis.[6,8-10] Occasionally, prodromal signs and/or symptoms, such as brow ache, headache or external eye infection or inflammation, may be present days to weeks before the diagnosis of bleb-related infection.[4]

Incidence

The cumulative incidence rate of bleb-related infections varies across different cohorts, uniformity of surgical technique and different periods of follow-up.[11] Based on the Collaborative Initial Glaucoma Treatment Study, the five-year risk of blebitis and hypotony were both 1.5%, and the risk of endophthalmitis was 1.1%.[3] A retrospective cross-sectional study utilizing a commercial health insurance claim-based database at Bascom Palmer Eye Institute found that the five-year incidence rate of blebitis in the United States was 0.55% with an average onset time of 45 months after the filtration procedure.[12] The five-year incidence rate of bleb-associated endophthalmitis was 0.45% to 1.3% with an average onset time of 33 months after procedure.[12] A large retrospective case-controlled observational study utilizing 22 years of analyzed data at St. Erik's Eye Hospital in Sweden found a 0.46% combined incidence of all bleb-related infections with a median onset time of 10 days for early infections and four years for late infections.[2] Long-term follow-up studies have shown the incidence of cumulative bleb-related infections to be less than 2% at the 10-year mark.[13]

Risk factors

Risk factors for bleb-related infections include diagnosis of juvenile glaucoma or pigmentary glaucoma, black race, presence of blepharitis, presence of punctal plugs, young age at time of surgery, inferior-placed trabeculectomy, use of perioperative antimetabolites, history of or current bleb leak, bleb manipulation and sustained low IOP or hypotony.[2,4,5,10-15] The patient in this case had a self-reported history of prior trabeculectomies, but the surgical date was unknown. Younger age at time of filtration surgery can increase the risk for blebitis, with a 1.08 conditional risk for every five years of decreasing age.[14] A retrospective chart review by Sharan et al. found that individuals with bleb-related infections had a mean age at surgery of 53.5 years compared with 64.7 years for those without infection.[15]

Antimetabolite agents

The use of antimetabolite agents mitomycin C (MMC) and 5-fluorouracil (5-FU) are known to increase filtration surgery success rates and likely lead to improved IOP reduction.[2,11-15] However, their application leads to a thin and avascular bleb, which may increase the risk for pathogens to migrate across the bleb.[2,10-14] MMC has been shown to have a higher potential to increase the risk of bleb-related infections than 5-FU.[2,10,11,13,14] A study by Wallin et al.[2] found that the incidence of late infections was 0.7% when MMC was utilized compared to 0% incidence when no antimetabolite was used.[2] This risk is higher in hypotonous eyes.[11] Risk of bleb-related infections is also increased in patients with fully functioning blebs that no longer required topical glaucoma medications for IOP control.[13]

The patient in this case report was applying fluorouracil 5% cream to the right side of his face for the management of actinic keratosis for the two weeks before eye symptoms began. The exact amount and frequency the cream was in contact with the eye was not known. The cream may have had the potential to affect the bleb, though this was less likely a risk because the patient was well outside the perioperative window where fluorouracil may have had a larger impact.

Bleb leaks

Bleb leaks can occur any time after trabeculectomy. The risk for infection is higher in late bleb leaks compared with early bleb leaks.[4,13,14] However, a leak in the bleb at any time puts patients at risk for infection.[4,10,13-15] Poulsen et al.[4] found that patients with a bleb leak were 25.8 times more likely to have a bleb-related infection than those without a bleb leak.[4] The bleb leak may also be responsible for significant hypotony at infection onset.[4] Seidel testing may be negative, even in cases where bleb trauma precedes infection, because the leak site may be plugged by mucopurulent debris.[8,9] In this case report, Seidel testing was negative on the bleb and the cornea of the patient. Discharge and/or aqueous fluid was not seen leaking from either tissue, which was an initial indication that surgical intervention was not necessary at the time. When blebs leak, surgical revision can be favorable and decrease risks of bleb-related infections.[13]

Inferior-placed trabeculectomies are a major risk factor for infection.[2,5,10,11] Inferior-located blebs are poorly covered by the lower eyelid and are more exposed to bacterial flora on the ocular surface.[5,11] The chronic mechanical abrasive movement of the lower eyelid can create a leak on the bleb and migrate bacteria into the anterior chamber.[11]

Microbial infection

The main bacterial etiologies of bleb-related infections are *Staphylococci*, *Streptococci* and *Haemophili*.[2,8,10,11] The pathogens involved in bleb-related infections are typically isolated from the ocular surface and not from within the eye.[11] The gram-positive bacteria are consistent with the normal flora typically residing on the ocular surface tissues.[7,11,16] Infections caused by virulent *Streptococci* seem to result in worse visual prognosis than infections relating to other

bacterial flora.[2,8,10,11] Broad-spectrum antibiotic coverage is therefore reasonable for empirical treatment.

Antimicrobial treatment

The patient in this case report had blebitis caused by *Pseudomonas aeruginosa*. Vigamox eyedrops and a combination antibiotic ophthalmic ointment of Neomycin and Polymyxin B Sulfates and Bacitracin Zinc USP were the medications chosen to provide broad-spectrum antibiotic coverage, before the culture report was available. The fluoroquinolone class of antibiotics provides excellent broad-spectrum antibiotic coverage.[17-19] The second-, third- and fourth-generation forms show similar antimicrobial efficacy against gram-negative bacteria, but the fourth-generation provides additional potency against gram-positive bacteria.[17,18] The newer third-generation levofloxacin ophthalmic solution 1.5% (Iquix, Vistakon Pharmaceuticals LLC) does not appear to be superior in potency to fourth-generation fluoroquinolones.[18] The reason the fourth-generation fluoroquinolones (moxifloxacin, gatifloxacin, and besifloxacin) are likely more potent and have less probability of bacterial resistance than fluoroquinolones of prior generations may be due to their unique capability of simultaneously inhibiting both deoxyribonucleic acid gyrase and topoisomerase IV enzymes in gram-positive bacteria.[17,19] Moreover, two spontaneous enzyme mutations would be necessary to generate resistance against fourth-generation antibiotics.[19,20]

Antimicrobial resistance can still develop in fourth-generation antibiotics, more frequently in gram-negative than gram-positive microbes.[19] The fourth-generation synthetic fluoroquinolone besifloxacin ophthalmic suspension 0.6% (Besivance, Bausch & Lomb Inc.) is specifically for topical application only, which theoretically reduces antimicrobial resistance.[20] Besifloxacin shows similar, if not favorable and more rapid, bactericidal activity compared with similar-generation fluoroquinolones and is a suspension formulated with the polycarbophil-based vehicle DuraSite (InSite Vision, Inc).[20-22] DuraSite is mucoadhesive and exhibits thixotropy. This formulation allows for prolonged drug exposure on the ocular surface, improved ocular pharmacokinetics and increased stability of the medication during manufacturing and storage.[20-23] Based on the strong antimicrobial efficacy and low resistance rate, these forms of fluoroquinolones seem to be an appropriate starting point for broad-spectrum antibiotic coverage.

Blebitis management

The treatment and management of blebitis is highly variable between providers. A survey conducted in the United Kingdom (UK) found that treatment regimens included topical fluoroquinolone monotherapy, dual topical antibiotic therapy, oral fluoroquinolones, subconjunctival antibiotic injections and intravitreal antibiotic injections.[7] There was not a clear consensus on the treatment protocol, but topical cycloplegic agents were widely part of the management of all infections, with greater than 90% consensus.[7] An earlier survey conducted by the American Glaucoma Society (AGS) found that the three main treatment regimens were topical fluoroquinolone monotherapy (typically initial empirical treatment), topical fluoroquinolone in combination with fortified agents, and topical fluoroquinolone in combination with unfortified aminoglycoside or trimethoprim-polymyxin combination or equivalent.[9] Oral, intravenous and subconjunctival agents were not frequently utilized.[9] In both surveys, topical corticosteroids were often prescribed but typically only after antibiotic therapy was already initiated for more than 24 hours (UK survey) or after initial antibiotic treatment was established or improvement of blebitis was noted (AGS survey).[7,9]

Topical antibiotic therapy is widely used as initial empirical treatment for blebitis.[1,7,9] Systemic, intravenous and subconjunctival agents may be considered in cases with a moderate to severe anterior chamber reaction or signs of vitreous involvement.[1] Systemic antibiotics were utilized less frequently in the past due to the minimal vitreous bioavailability, but more recent antibiotics have shown improved ability to cross the blood-eye barrier.[24] Fourth-generation fluoroquinolones should be utilized for their increased vitreous bioavailability, lower bacterial resistance and broad-spectrum activity.[24] When endophthalmitis is suspected, vitreous tap with intravitreal antibiotic injection may be warranted.[1,24] Patients with severe cases of bleb-related endophthalmitis may benefit from additional 25-gauge vitrectomy to decrease the bacterial load.[24]

Culture swab

The decision for acquiring a conjunctival culture swab varies by individual provider and extent of infection.[7,9] The bacterial flora involved in bleb infection may not necessarily equate to the colonizing flora of a positive bleb culture.[7] Interestingly, the AGS survey showed that providers who routinely acquired conjunctival culture swabs had a similar empirical antibiotic regimen to providers who did not acquire cultures.[9] Conjunctival culture swab was elected for the patient described in this report. A topical fourth-generation fluoroquinolone was chosen as the primary antibiotic regimen in the case due to its broad-spectrum activity and relatively low resistance profile. If bacterial culture and susceptibility testing revealed a

different microbe, the treatment regimen may not necessarily have changed, unless the report showed resistance to the selected fluoroquinolone.

Visual prognosis

The patient in this case report did not have a significant visual change during the course of the blebitis, though he already had low vision prior to the infection. Vision may not be affected at the onset or during the course of blebitis.[2,3,10] Visual prognosis after infection seems to be related to the degree of infection. Patients with blebitis treated promptly with intense antimicrobial agents tend to have favorable outcomes and recover visual acuity and IOP to pre-infection status.[2,4,10] Cases involving late and severe bleb-associated endophthalmitis unfortunately show poor visual prognosis (vision less than 20/200 to light perception) despite aggressive and prompt treatment.[2,4,6,10]

Differential diagnosis

- Anterior uveitis may present with a red, painful, watery eye.[25,26] Patients may experience photosensitivity, and a varying amount of cells and fibrin are seen in the anterior chamber. Vision may be reduced in some cases, depending on the turbidity of the aqueous.[25-27] The uveitis can be classified as granulomatous or non-granulomatous, depending on the nature of keratic precipitates present on the corneal endothelium.[27] IOP can be lower than the patient's normative value in the acute phase due to decreased aqueous production from ciliary body inflammation, or higher due to trabeculitis and cellular debris in the trabecular meshwork.[25]
- Herpes zoster keratouveitis may present with a unilateral red, irritated eye with tearing.[28] The patient may also experience headache, fever and malaise.[28] The cornea of the involved eye may have raised pseudodendrite lesions or mucus plaques. Depending on the time course of the condition, painful ulcerating or scabbing vesicles may be seen on the face that follow the trigeminal dermatomes.[28] IOP may also be elevated from trabeculitis.[27-29]
- HSV endotheliitis may present with a mildly red eye, photosensitivity, eye pain and variable decreased vision.[30] The corneal stroma is edematous, and a mild anterior chamber reaction may be present.[31,32] IOP may be elevated in the involved eye due to trabeculitis.[27,29,30]
- Bacterial blepharoconjunctivitis presents with an erythematous, edematous, crusty, irritated eye involving the lids and conjunctiva.[33-35] Excess bacterial flora and exotoxins may cause saponification of tears, and superficial punctate keratitis may be present on the cornea.[33,35] The condition may be unilateral or bilateral, and occasionally an oily or purulent discharge may be present.[34,35]
- Medicamentosa keratoconjunctivitis may occur due to chemical eye trauma from exposure to eye drops, cosmetics, environmental irritants, or in the case of the reported patient, topical skin creams and ointments that spread into the eye. The patient may experience vision changes, foreign body sensation, redness, lacrimation, ocular pain and blepharospasm.[36,37] The eye may show signs of superficial punctate keratitis, corneal edema, conjunctival hyperemia, erythema and blistering of the lids and adnexa.[36-38] In severe cases with alkali penetration through the cornea, an anterior chamber reaction may be present and IOP may be elevated.[36]

Conclusion

This case reviews the presentation and management of blebitis. The patient presented in the case did not experience significant visual changes during the course of the infection, though he had pre-existing poor vision at the date of diagnosis. Perioperative antimetabolite application is a known risk factor for bleb-related infections. The patient in this

case did have ocular exposure to fluorouracil cream, though the causative value is questionable. There is not an absolute guideline on the treatment of bleb-related infections, but aggressive treatment with antimicrobial agents tends to have favorable outcomes. Patients should be followed routinely during the course of treatment, and any worsening signs should indicate more aggressive treatment and further workup for endophthalmitis. With prompt and prudent treatment, blebitis typically resolves and vision has the potential to return to pre-infection status.

Disclosure

The authors do not have any financial or intellectual conflicts of interest regarding devices, medications or products mentioned in this manuscript.

References

1. Sola-Del Valle DA, Modjtahedi BS, Eliott D, Shen LQ. Treatment of blebitis and bleb-related endophthalmitis. Int Ophthalmol Clin. 2015;55(4):37-49.
2. Wallin O, Al-ahramy AM, Lundstrom M, Montan P. Endophthalmitis and severe blebitis following trabeculectomy. Epidemiology and risk factors; a single-centre retrospective study. Acta Ophthalmol. 2014;92(5):426-431.
3. Zahid S, Musch DC, Niziol LM, Lichter PR. Risk of endophthalmitis and other long-term complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). Am J Ophthalmol. 2013;155(4):674-680, 680 e671.
4. Poulsen EJ, Allingham RR. Characteristics and risk factors of infections after glaucoma filtering surgery. J Glaucoma. 2000;9(6):438-443.
5. Soltau JB, Rothman RF, Budenz DL, et al. Risk factors for glaucoma filtering bleb infections. Arch Ophthalmol. 2000;118(3):338-342.
6. Brown RH, Yang LH, Walker SD, Lynch MG, Martinez LA, Wilson LA. Treatment of bleb infection after glaucoma surgery. Arch Ophthalmol. 1994;112(1):57-61.
7. Chiam PJ, Arashvand K, Shaikh A, James B. Management of blebitis in the United Kingdom: a survey. Br J Ophthalmol. 2012;96(1):38-41.
8. Ciulla TA, Beck AD, Topping TM, Baker AS. Blebitis, early endophthalmitis, and late endophthalmitis after glaucoma-filtering surgery. Ophthalmology. 1997;104(6):986-995.
9. Reynolds AC, Skuta GL, Monlux R, Johnson J. Management of blebitis by members of the American Glaucoma Society: a survey. J Glaucoma. 2001;10(4):340-347.
10. Ayyala RS, Bellows AR, Thomas JV, Hutchinson BT. Bleb infections: clinically different courses of “blebitis” and endophthalmitis. Ophthalmic Surg Lasers. 1997;28(6):452-460.
11. Greenfield DS, Suner IJ, Miller MP, Kangas TA, Palmberg PF, Flynn HW Jr. Endophthalmitis after filtering surgery with mitomycin. Arch Ophthalmol. 1996;114(8):943-949.
12. Vaziri K, Kishor K, Schwartz SG, et al. Incidence of bleb-associated endophthalmitis in the United States. Clin Ophthalmol. 2015;9:317-322.
13. Kim EA, Law SK, Coleman AL, et al. Long-term bleb-related infections after trabeculectomy: incidence, risk factors, and influence of bleb revision. Am J Ophthalmol. 2015;159(6):1082-1091.
14. Jampel HD, Quigley HA, Kerrigan-Baumrind LA, et al. Risk factors for late-onset infection following glaucoma filtration surgery. Arch Ophthalmol. 2001;119(7):1001-1008.
15. Sharan S, Trope GE, Chipman M, Buys YM. Late-onset bleb infections: prevalence and risk factors. Can J Ophthalmol. 2009;44(3):279-283.
16. Park SH, Lim JA, Choi JS, Kim KA, Joo CK. The resistance patterns of normal ocular bacterial flora to 4 fluoroquinolone

antibiotics. Cornea. 2009;28(1):68-72.
17. Oliveira AD, D'Azevedo PA, Francisco W. In vitro activity of fluoroquinolones against ocular bacterial isolates in Sao Paulo, Brazil. Cornea. 2007;26(2):194-198.
18. Scoper SV. Review of third-and fourth-generation fluoroquinolones in ophthalmology: in-vitro and in-vivo efficacy. Adv Ther. 2008;25(10):979-994.
19. Wong CA, Galvis V, Tello A, Villareal D, Rey JJ. In vitro antibiotic susceptibility to fluoroquinolones. Arch Soc Esp Oftalmol. 2012;87(3):72-78.
20. Khimdas S, Visscher KL, Hutnik CML. Besifloxacin ophthalmic suspension: emerging evidence of its therapeutic value in bacterial conjunctivitis. Ophthalmol Eye Dis. 2011;3:7-12.
21. Bowman LM, Si E, Pang J, Archibald R, Friedlaender M. Development of a topical polymeric mucoadhesive ocular delivery system for azithromycin. J Ocul Pharmacol Ther. 2009;25(2):133-139.
22. Bucci FA Jr, Evans RE, Amico LM, et al. Antibacterial efficacy of prophylactic besifloxacin 0.6% and moxifloxacin 0.5% in patients undergoing cataract surgery. Clin Ophthalmol. 2015;9:843-852.
23. Shafiee A, Bowman LM, Hou E, Hosseini K. Aqueous humor penetration of ketorolac formulated in DuraSite or DuraSite 2 delivery systems compared to Acular LS in rabbits. J Ocul Pharmacol Ther. 2013;29(9):812-816.
24. Busbee BG. Update on treatment strategies for bleb-associated endophthalmitis. Curr Opin Ophthalmol. 2005;16(3):170-174.
25. Pathanapitoon K, Dodds EM, Cunningham ET Jr, Rothova A. Clinical spectrum of HLA-B27-associated ocular inflammation. Ocul Immunol Inflamm. 2017 Aug;25(4):569-576.
26. Tomkins-Netzer O, Talat L, Bar A, et al. Long-term clinical outcome and causes of vision loss in patients with uveitis. Ophthalmology. 2014;121(12):2387-2392.
27. Agrawal RV, Murthy S, Sangwan V, Biswas J. Current approach in diagnosis and management of anterior uveitis. Indian J Ophthalmol. 2010 Jan-Feb;58(1):11-19.
28. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008 Feb;115(2 Suppl):S3-12.
29. Sungur GK, Hazirolan D, Yalvac IS, Ozer PA, Aslan BS, Duman S. Incidence and prognosis of ocular hypertension secondary to viral uveitis. Int Ophthalmol. 2010;30(2):191-194.
30. Garcia LM, Velez Fernandez M. Bilateral lineal endotheliitis: case report. Arq Bras Oftalmol. 2013;76(2):121-123.
31. Inoue Y. Review of clinical and basic approaches to corneal endotheliitis. Cornea. 2014 Nov;33 Suppl 11:S3-8.
32. Suzuki T, Ohashi Y. Corneal endotheliitis. Semin Ophthalmol. 2008;23(4):235-240.
33. Hammersmith KM. Blepharokeratoconjunctivitis in children. Curr Opin Ophthalmol. 2015;26(4):301-305.
34. Hosseini K, Hutcheson J, Lindstrom RL. A phase III clinical study to evaluate the efficacy of combined azithromycin and dexamethasone in the treatment of blepharoconjunctivitis. Clin Ophthalmol. 2013;7:2225-2234.
35. McCulley JP. Blepharoconjunctivitis. Int Ophthalmol Clin. 1984;24(2):65-77.
36. Morgan SJ. Chemical burns of the eye: causes and management. Br J Ophthalmol. 1987;71(11):854-857.
37. Spector SL, Raizman MB. Conjunctivitis medicamentosa. J Allergy Clin Immunol. 1994;94(1):134-136.
38. Wagoner MD. Chemical injuries of the eye: current concepts in pathophysiology and therapy. Surv Ophthalmol. 1997;41(4):275-313.

ASSOCIATION of SCHOOLS and COLLEGES of OPTOMETRY
Optometric Education The Journal of the Association of Schools and Colleges of Optometry

Dr. Ho [HoJ@neco.edu] is an Attending Optometrist in the clinical system of New England College of Optometry. He is a former optometry resident at the White River Junction Department of Veterans Affairs Medical Center in Vermont.

Dr. Gallagher is an Attending Optometrist at the White River Junction Department of Veterans Affairs Medical Center in Vermont.