American Journal of Ophthalmology Case Reports 13 (2019) 127–130

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Endophthalmitis following cataract surgery and intracameral antibiotic: Moxifloxacin resistant *Staphylococcus epidermidis*

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ARTICLE INFO

Keywords:
Endophthalmitis
Post-surgical infection
Moxifloxacin
Intracameral antibiotic

ABSTRACT

Purpose: To describe an immunosuppressed patient who developed acute-onset postoperative endophthalmitis caused by a moxifloxacin-resistant strain of *Staphylococcus epidermidis* after cataract surgery despite the use of intracameral moxifloxacin.

Observations: A 76-year old woman with a history of birdshot chorioretinopathy controlled on systemic immunosuppression underwent uneventful cataract surgery in her right eye. Compounded intracameral moxifloxacin 0.2 cc of 1mg/0.1mL (Edge Pharmacy, Syracuse, NY) was injected intraoperatively as prophylaxis, and the patient was placed on a standard regimen of trimethoprim-polymyxin b (10000-0.1unit/mL) and prednisolone acetate 1% postoperatively. Four days later, the patient experienced a sudden decrease in vision in the right eye. Anterior chamber inflammation, vitritis, and vasculitis were seen in the operated eye. The patient underwent a vitreous tap and intravitreal injections of vancomycin (1mg/0.1mL), ceftazidime (2.25mg/0.1mL), and dexamethasone (0.4mg/0.1mL). Cultures grew *Staphylococcus epidermidis,* resistant to moxifloxacin (MIC ≥ 8mg/L). The inflammation resolved over two months. Eight months later, the patient underwent uncomplicated cataract surgery in the left eye. Intracameral antibiotics were not used, however her systemic immunosuppressive therapy was held for several weeks perioperatively. One year after the initial surgeries, the patient had an uncorrected visual acuity of 20/20 in each eye.

Conclusions and Importance: S. epidermidis, the most common cause of postoperative endophthalmitis, is increasingly resistant to fluoroquinolones. Adequate concentrations of intracameral antibiotics need to be achieved in order to exceed minimal inhibitory concentration values of the targeted pathogen. Although intracameral moxifloxacin has been reported to decrease the rate of endophthalmitis after cataract surgery, it does not eliminate the risk.

1. Introduction

Endophthalmitis is a rare but potentially sight-devastating complication after cataract surgery, estimated to affect between 0.012% and 0.2% of patients.[1–3] Intracameral (IC) antibiotics are used by cataract surgeons with increasing frequency in the United States (U.S.) in an attempt to decrease this rate.[4]

Herein, a case of endophthalmitis after cataract surgery with intracameral moxifloxacin in an immunocompromised patient is reported. The causative bacterium was determined later to be a fluoroquinolone-resistant strain of *Staphylococcus epidermidis*.

2. Findings

A 76- year old female with a past medical history of quiescent birdshot chorioretinitis (BSCR) and rheumatoid arthritis (RA) was referred for cataract surgery. The patient's autoimmune conditions were maintained on long-term immunosuppression with adalimumab (Humira, AbbVie, North Chicago, IL) 40mg every two weeks and mycophenolate mofetil (CellCept, Genentech, South San Francisco, CA) 1.5g daily.

The patient underwent uneventful clear corneal phacoemulsification with insertion of a posterior chamber intraocular lens (PCIOL) for the right eye. The posterior capsule remained intact, and the PCIOL was well-centered in the bag. Moxifloxacin (0.2mL of 1mg/0.1mL, Edge Pharmacy, Syracuse, NY) was injected intracamerally at the end of the case. A single 10-0 nylon suture was placed at the main incision, and the wounds were confirmed to be water-tight. Topical trimethoprim-polymyxin b (10000-0.1unit/mL) and prednisolone acetate 1% drops were prescribed four times daily in addition to nepafenac 0.3% daily.

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https://doi.org/10.1016/j.ajoc.2018.12.003
Received 11 July 2018; Received in revised form 22 November 2018; Accepted 3 December 2018
Available online 08 December 2018

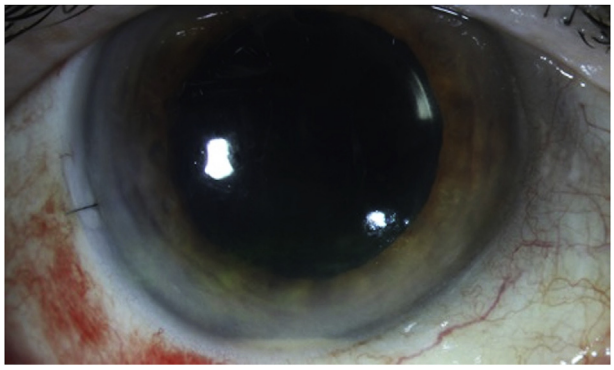

Fig. 1a. Anterior chamber reaction with hypopyon formation (arrow) with mild conjunctival injection; 10-0 nylon suture is intact at the main corneal wound (POD 5), POD 5 = postoperative day 5.

On postoperative day one, uncorrected visual acuity (UCVA) was 20/40 in the right eye. Four days later, the patient reported decreased vision and new onset floaters. She was seen urgently in clinic on the same day. UCVA was reduced to count fingers, and the intraocular pressure was 12 mmHg. On examination, there was a moderate anterior chamber reaction with no hypopyon. The PCIOL was well-centered in the capsular bag. Dilated fundus examination revealed 3 + vitreous haze and cell, extensive whitening of the retina vasculature, and diffuse intraretinal hemorrhages. Since the patient presented urgently on a Sunday evening, no ancillary testing was performed. Given the suspicion for endophthalmitis, the patient underwent an anterior chamber paracentesis, vitreous tap, and intravitreal vancomycin (1mg/0.1mL) and ceftazidime (2.25mg/0.1mL) injections. Systemic immunosuppressive therapy was suspended.

The following day, the UCVA had decreased to hand motion, a hypopyon had formed, and the vitreous cellular reaction had worsened (Fig. 1A and B). Intravitreal dexamethasone (0.4mg/0.1mL) was injected in the right eye. Cultures of the vitreous aspirate grew *Staphylococcus epidermidis,* resistant to moxifloxacin (MIC ≥8mg/L) and ceftazidime but sensitive to trimethoprim and vancomycin. Sensitivity to polymyxin B was not tested due to the very high resistance of staphylococci to this agent.

One week later, the UCVA in the right eye improved to 20/150, along with resolution of the hypopyon and improvement in the vitreous inflammation (Fig. 2). However, a spectral domain optical coherence tomography (SD-OCT) revealed cystoid macular edema (CME) and submacular fluid. The patient was switched from nepafenac to ketorolac 0.4% due to cost, and was continued on prednisolone acetate 1% 1 drop four times daily. One month postoperatively, her vision remained

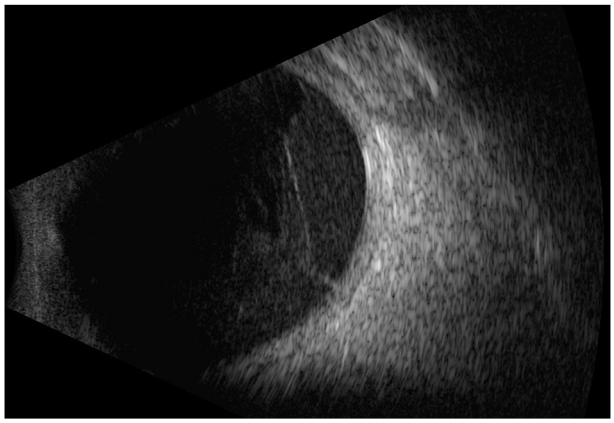

Fig. 1b. Vitreous opacification consistent with a dense inflammatory reaction seen on B-scan ultrasound (POD 5). POD 5 = postoperative day 5.

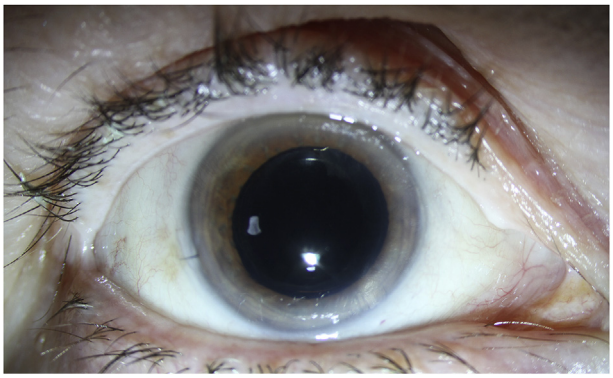

Fig. 2. Resolution of the hypopyon and conjunctival injection (POW 1). POW 1 = postoperative week 1.

at 20/150 due to persistent retina edema and residual vitreous inflammation. Mycophenolate mofetil and adalimumab were reinitiated. The patient continued on ketorolac 0.4% but was switched to difluprednate 0.05% four times daily. Two months postoperatively, the patient's UCVA improved to 20/40 with complete resolution of the posterior segment findings.

The patient subsequently underwent uncomplicated cataract surgery of the left eye ten months after her initial surgery. No intracameral antibiotics were injected intraoperatively; however, the patient's mycophenolate mofetil and adalimumab were held for one and three weeks, respectively, in the perioperative period. Eight weeks later, at her most recent visit, the UCVA was 20/20 in each eye.

3. Discussion

This immunosuppressed patient developed acute-onset postoperative endophthalmitis caused by *Staphylococcus epidermidis* despite the use of IC moxifloxacin. Cases of endophthalmitis after IC injections of licensed cefuroxime (Aprokam, Thea Pharmaceuticals, Clermont-Ferrand, France)[5] and compounded cefuroxime have been described.[6–8] In comparison, fewer cases of endophthalmitis after IC moxifloxacin have been reported. Matsuura et al. described a case of endophthalmitis after uneventful cataract surgery that resolved favorably although no microbe was identified.[9] Similar to the current patient, a case of endophthalmitis was reported in 2016 caused by a moxifloxacin-resistant strain of *S. epidermidis*.[10] However, details of the patient's postoperative course were not provided.

The patient's surgery was uncomplicated, without posterior capsular rupture or vitreous loss, risk factors that increase the incidence of endophthalmitis by up to 10-fold.[11] However, the patient was on immunosuppressive treatment, which has been associated with a 3- fold increase in the risk for endophthalmitis.[12,13]

In 2013, the European Society of Cataract and Refractive Surgery (ESCRS) reported a 5.86-fold reduction in endophthalmitis rates after cataract surgery with the use of IC cefuroxime in a multicenter prospective randomized study.[6] Critics of this study point to the high rate of endophthalmitis in the group not randomized to receive intracameral cefuroxime (0.226%), inclusion of multiple surgical techniques, and the use of topical levofloxacin 0.5% rather than a fourth-generation fluoroquinolone.[14] Ongoing debate regarding efficacy and safety of IC antibiotics remains. Both dosing errors and toxic anterior segment syndrome (TASS) have been reported as risks of compounded IC antibiotics.[15]

There are no randomized clinical trials to suggest an optimal IC antibiotic of choice, although alternatives to vancomycin have been sought due to its association with hemorrhagic occlusive retinal vasculitis.[16] Cefuroxime is supported by the ESCRS trial; however, one series reported that it was associated with only a marginal reduction in

acute endophthalmitis after cataract surgery and an increase in gram-negative infections.[17] Thus, many surgeons are employing moxifloxacin given its theoretical advantages of potency, broad spectrum bactericidal activity, and self-preserved commercial formulation (Vigamox, Alcon laboratories, Fort Worth, TX, USA).[4] The efficacy of IC moxifloxacin has been suggested by several retrospective trials.[7,8,10,18–22]

The patient's infection was caused by a moxifloxacin-resistant strain of *S. epidermidis* with minimum inhibitory concentration (MIC) greater than 8mg/L (at least 150 times the usual MIC).[23] In 2017, Bascom Palmer Eye Institute reported increasing resistance of coagulase-negative staphylococci (CoNS) endophthalmitis-causing isolates to fluoroquinolones spanning two decades, with up to 60% of CoNS isolates resistant to moxifloxacin.[24] This is especially concerning as moxifloxacin is gaining popularity as an IC antibiotic of choice, especially outside of Europe.[4] Additionally, fluoroquinolone resistance in CoNs has been associated with a worse visual prognosis in post-cataract endophthalmitis.[25] In our patient, the administered dose of IC moxifloxacin was 200 mcg in 0.2mL resulting in an immediate anterior chamber concentration of approximately 400mg/L (assuming an estimated pseudophakic anterior chamber volume of 0.5mL according to experimental data).[10] If the half-life of moxifloxacin in the anterior chamber is one hour, *in vivo* studies[26] suggest a concentration of 150mg/L is sufficient immediately after administration to reach 90% MIC (32 mcg/mL) for *S. epidermidis*.[9,23]

It is possible that a higher concentration of moxifloxacin achieved intracamerally would have exceeded the MIC of the resistant strain isolated in our patient. Using a pharmacokinetic model, Libre et al. proposed that the highest accepted clinical level of moxifloxacin (0.5mg or 1.5mg/mL) was preferred, and lower concentrations provided inadequate coverage of staphylococci.[27] Arshinoff proposed that if a concentration of 600–1000mg/L is achieved at the time of injection, the MIC_{90} of the most resistant strain of *S. epidermidis* ever reported (320mg/L) would be surpassed by ten times for up to two hours, dependent on the pharmacokinetic model used.[10] Thus, Arshinoff increased his preferred dose of IC moxifloxacin to 450 to 600 mcg/0.3–0.4mL.[10] Unlike cefuroxime, moxifloxacin displays an initial dose-dependent elimination assuming a very high concentration is attained even for a short period of time, but does require approximately two hours to be considered effective.[28] IC moxifloxacin at concentration up to 500mg/L is reported to be safe; however, evidence is lacking regarding its safety above this concentration.[18]

This patient subsequently underwent cataract surgery of the second eye without the use of IC antibiotics. In consultation with her physicians, her systemic immunosuppressive therapy was withheld for several weeks perioperatively. There is a relative paucity of evidence regarding optimal perioperative management in uveitic patients; however, good control of ocular inflammation is known to minimize post-operative complications.[29] The contribution of the patient's systemic IMT to the infection that occurred in her right eye is not known. The patient insisted that her IMT be suspended perioperatively prior to undergoing surgery for her second eye, and this was tolerated since her uveitis was well-controlled at the time and unlikely to result in vision-limiting uveitic complications. Her postoperative course was complicated by a mild flare-up of birdshot chorioretinopathy, that improved once her systemic immunosuppressive therapy was reinitiated.

4. Conclusions

The use of IC moxifloxacin has been reported to reduce the rate of acute-onset postoperative endophthalmitis in many series. However, endophthalmitis may still occur with its use. Adequate concentrations of IC antibiotics need to be achieved in order to exceed MIC values of the targeted pathogen. Other preventive methods (such as strict aseptic measures) remain important in reducing the incidence of this devasting complication.

Patient consent

Consent to publish was obtained. This report does not contain any personal information that may result in identification of the patient.

Acknowledgments and disclosures

Funding

This study was supported by the NIH Center Core Grant P30EY014801 and an unrestricted grant from Research to Prevent Blindness, New York, New York, USA.

Conflict of interest

Dr. Schwartz discloses, within the past 3 years, personal fees from Alimera and Welch Allyn outside the submitted work. All other authors have no financial disclosures.

Authorship

All authors attest that they meet the current ICJME criteria for Authorship.

Acknowledgement

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2018.12.003.

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