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Case Report

Bilateral Endophthalmitis After Immediately Sequential Bilateral Cataract Surgery (ISBCS) in an Immunodeficient Patient

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Abstract

Introduction: Bilateral simultaneous postoperative endophthalmitis (BSPOE) is a rare but potentially devastating complication following immediately sequential bilateral cataract surgery (ISBCS). We present a case of BSPOE in an immunocompromised patient to suggest actionable precautions in this patient population.

Patient and clinical findings: A 79-year-old male with specific pneumococcal antibody deficiency underwent uneventful ISBCS with prophylactic intracameral 0.1 mL undiluted moxifloxacin 0.5%. The patient returned with decreased visual acuities of light perception in the right eye (OD) at 5 days and count fingers in the left eye (OS) at 7 days postoperatively with severe anterior chamber inflammation in each eye.

Diagnosis, Intervention, and Outcomes: The patient was diagnosed with BSPOE. Tap-and-inject was performed emergently on day 5 OD and day 7 OS with intravitreal vancomycin 1 mg/0.1 mL, dexamethasone 0.4 mg/0.1 mL, and ceftazidime 2.25 mg/0.1 mL. Cultures done OD were positive for methicillin-resistant coagulase-negative *Staphylococcus epidermidis*. The patient later underwent an anterior chamber washout, pars plana vitrectomy, and intravitreal injections of vancomycin 1 mg/0.1 mL and dexamethasone 0.04 mg/0.1 mL in both eyes (OU) and recovered 20/20 visual acuity OU at 6 weeks postoperatively.

Conclusions: This case raises critical issues about the adequacy of intracameral prophylaxis methods for immunosuppressed patients.

Keywords: Vancomycin; Bilateral Simultaneous Postoperative Endophthalmitis (BSPOE); Immediately Sequential Bilateral Cataract Surgery (ISBCS)

Introduction

Immediately sequential bilateral cataract surgery (ISBCS) is an increasingly popular technique due to immediate achievement of the planned refractive state, patient convenience and reduced number of required medical visits, especially in the context of the COVID-19 pandemic. However, one dreaded risk of ISBCS is the possibility of bilateral simultaneous postoperative endophthalmitis (BSPOE). We present a case of BSPOE in an immunocompromised

patient to suggest actionable precautions for this patient population as two of the nine BSPOE cases reported over the past 50 years were immunodeficient patients [1].

Patient consent statement

Written consent was obtained from the patient to publish the details of the case.

Case Report

In 2021, a 79-year-old male Quebec farmer presented to a private ophthalmology clinic with cataracts and known chronic obstructive pulmonary disease (COPD), allergic bronchopulmonary aspergillosis (ABPA), and pneumococcal specific antibody deficiency (SAD), causing repeated episodes of pneumonia. He was on long-term corticosteroids (prednisone 10 mg daily), intravenous immunoglobulins every 4 weeks and oral trimethoprim/sulfamethoxazole for 3 months. He had preoperative uncorrected visual acuity (UCVA) of 20/40 in the right eye (OD) and 20/50 in the left eye (OS) and requested toric intraocular lenses (IOLs) to correct his astigmatism.

He underwent uneventful ISBCS with AcrySof® toric IOLs in both eyes (OU). Prophylactic IC injection of 0.1 mL undiluted 0.5% moxifloxacin (Vigamox®), was administered as the final step of surgery for both eyes. On postoperative day 1, UCVA was 20/30 OD and 20/25 OS. Intraocular pressure (IOP) was 34 mmHg OU, but the ophthalmologic exam was otherwise within normal limits. On postoperative day 5, he presented urgently with decreased visual acuity and floaters OD without pain. UCVA was decreased to light perception (LP) with 4+ cells in the anterior chamber (AC). Examination OS was within normal limits. A vitreous tap and intravitreal injection of vancomycin 1 mg/0.1 mL, dexamethasone 0.4 mg/0.1 mL, and ceftazidime 2.25 mg/0.1 mL was emergently performed. The tap was difficult and induced hyphema. The patient was prescribed topical prednisolone 1%, fortified vancomycin 31 mg/mL, and fortified tobramycin 14 mg/mL hourly, as well as atropine 1% twice daily OD. Cultures came back positive for *Staphylococcus epidermidis*, resistant to cloxacillin, amoxicillin/clavulanic acid, cefadroxil, cefazolin, trimethoprim/sulfamethoxazole, and moxifloxacin (at serum attainable levels) with a reported minimum inhibitory concentration (MIC) for moxifloxacin of >2 mg/L (as high as that lab reports). This was therefore a strain of MRCoNS, but it showed sensitivity to vancomycin 1.5 mg/L, erythromycin, clindamycin, rifampicin, and doxycycline.

On postoperative day 7, he presented again, this time with decreased vision OS, 2+ cells in the anterior chamber and vitreous debris. An anterior chamber tap was performed to avoid an IOP spike, followed by intravitreal injections of vancomycin, dexamethasone, and ceftazidime, as above. A vitreous tap was not performed due to fear of similar complication like the hyphema in the first eye. Culture for this eye is therefore not available.

The patient was referred to the ophthalmology clinic of the CHU de Québec – Université Laval for tertiary care on postoperative day 8. He had UCVA of LP OD and counting fingers (CF) at two feet OS. Examination revealed corneal edema OU, a 3 mm hyphema with IOP of 27 mmHg OD, and 2+ cells with IOP of 22 mmHg OS. B-scan ultrasound showed debris in the vitreous, OD greater than OS. For the right eye, an anterior chamber washout, pars plana vitrectomy with membrane peel, fluid-air exchange, endolaser, and intravitreal injection of vancomycin 1 mg/0.1 mL and dexamethasone 0.04 mg/0.1 mL was necessary. Postoperative course, thereafter, was unremarkable bilaterally.

At follow-up, six weeks after his initial ISBCS, final UCVA was 20/20 OD and 20/40 OS (correctable to 20/20 with +0.75 -1.50 x 105° OS). IOP was 20 mmHg OU on brinzolamide/brimonidine twice daily OU. Optical coherence tomography showed mild age-related macular degeneration with no detrimental residual effects attributable to the endophthalmitis bilaterally.

Discussion and Conclusion

Despite recent improvements in treatment and outcomes, postoperative endophthalmitis (POE) remains a rare but potentially devastating complication of cataract surgery [1]. Advancements in cataract surgery techniques, such as preoperative topical povidone-iodine, phacoemulsification with watertight clear corneal incisions, and others, have significantly reduced the rate of POE over the years [2]. Introduction of intracameral antibiotics has further made POE extremely rare, reported as low as 0.0059% (1:6,890) [3]. ISBCS following the International Society of Bilateral Cataract Surgeons (*i*SBCS) General Principles for Excellence in ISBCS recommendations treat each eye as a completely independent surgery, and following these appears to reduce the risk of BSPOE [1,4]. The risk of BSPOE does not appear to be higher than the risk

of delayed sequential bilateral postoperative endophthalmitis, i.e. when the surgeries are done on different days, or weeks apart, unless the specific operating room or patient carries increased infectious risks [3].

Our case highlights the risk of BSPOE in immunocompromised patients. The patient was given prophylactic 0.1 cc undiluted IC moxifloxacin. However, he had pneumococcal specific antibody deficiency (SAD, also known as selective antibody deficiency), which is a type of primary immunodeficiency disease characterized by deficient immunologic response to polysaccharide antigens but with otherwise normal immunoglobulins (Ig) A, M, total IgG, and IgG subclass levels [5]. Patients with SAD often have recurrent infections, with respiratory bacterial infections being the most common [5]. Treatments of SAD include antibiotic prophylaxis (azithromycin and trimethoprim/sulfamethoxazole) and immunoglobulin therapy, along with close follow-up and prompt management of infections [5,6]. However, continuous use of antibiotic prophylaxis can select for resistant organisms and limit future antibiotic options [7].

Although there are no established correlations between SAD and POE in the literature, possibly due to the already very low incidence of POE and the infrequency of performing cataract surgery on SAD patients, ocular involvement in primary immunodeficiency diseases does exist [8]. Thus, this patient was most likely at greater risk for POE as a result of his immunological deficit and chronic systemic corticosteroid therapy. The prophylactic use of trimethoprim-sulfamethoxazole likely contributed to his colonization by resistant bacterial strains including the methicillin-resistant coagulase-negative *Staphylococci* (MRCoNS) strain which caused the endophthalmitis.

There have been 9 reported cases of BSPOE in the past 50 years, in all which cases, the surgical protocol either had a breach to current *i*SBCS recommendations or was uncertain [1]. BSPOE cases have all presented with probable reasons and explanations for the infections, with now two cases associated with known immunodeficiency. The other reported case occurred in Sweden. In 2003, a 93-year-old woman in poor health, who resided in a chronic care home for the elderly, requested ISBCS to minimize hospital visits. Her surgeries were performed under local anesthesia, and she received 1 mg cefuroxime and 100 mg ampicillin intracamerally in each eye. The surgeon was experienced in ISBCS and the *i*SBCS General Principles for Excellence in ISBCS 2009 standards were carefully followed. She developed BSPOE 13 days postoperatively. Vitreous cultures grew MRCoNS, resistant to both IC preparations administered at surgery, but sensitive to vancomycin. The endophthalmitis was aggressively treated and at 1.5 months after surgery, her vision had improved to 20/125 OD and counting finger at 1 meter OS, but she succumbed to her medical illnesses before further ocular recovery [1,9].

We all perform cataract surgery on immunosuppressed patients, and both of these cases raise the issue of which IC antibiotic to use, and how to best administer it, to prevent infection with likely resistant bacteria. The most common bacterial cause of POE is coagulasenegative staphylococcus (CoNS). Due to possible bacterial antibiotic resistance, it is important to administer a sufficient dose of a dose-dependent antibiotic, such as moxifloxacin, for prophylaxis, because with dose-dependent agents there is no absolute bacterial resistance, especially with MRCoNS [10]. Though our patient received IC moxifloxacin at the end of surgery (500 µg in 0.1 mL), the quantity delivered and the antibiotic concentration achieved was likely insufficient to prevent POE due to a moxifloxacin-resistant strain of CoNS [10-12]. Administration of 0.1 mL is difficult and inaccurate [13]. There could have been small bubbles in the syringes used for injection, thus reducing the 0.1 ml doses of moxifloxacin delivered. To eliminate all strains of *Staphylococcus* and *Pseudomonas,* the moxifloxacin dose retained in the eye at the end of surgery should be equal to or greater than 500 µg, with no subsequent IOP adjustment [14]. The administration of a larger volumes of 0.4 mL of a diluted solution (150 µg/0.1 mL) to wash out the anterior chamber as the very last step in surgery is therefore recommended, ensuring reliable and consistent delivery of close to 600 µg of moxifloxacin, a high enough concentration in the AC for a long enough duration of over 7 hours to kill all MRCoNS strains ever reported [10-12]. Resistance to moxifloxacin is not absolute but rather dose dependent, so the amount and administration method of intracameral moxifloxacin is critical to eliminate resistant strains without inducing drug toxicity. The highest reported MIC of staphylococci to moxifloxacin is 64 mg/L (>1000 times the usual MIC) [15]. In our case, the cultured *S. epidermidis* was shown to be resistant to >2 mg/L of moxifloxacin, which is the maximum concentration tested by the local laboratory. The true MIC was likely higher considering the

patient's immunodeficiency and ongoing prophylactic antibiotic treatment for the 3 months prior to surgery [15]. The use of insufficient intracameral moxifloxacin due to a suboptimal drug delivery method and the patient's previous medical history likely contributed to the development of the BSPOE. Similarly, the Swedish patient's MRCoNS BSPOE may have also been prevented with a prophylactic injection of 0.4 mL moxifloxacin 150 µg/0.1 mL, rather than small volume injections of cefuroxime and ampicillin.

In conclusion, the analysis of infectious causes is much easier *a posteriori*. However, going forward, as the use of ISBCS is likely to be presented as a reasonable option to a progressively wider range of patients, strict anti-infection protocols should be put in place to ensure that POE is minimized. This includes impeccable sterility protocols, clean operating rooms and sufficient antibiotic prophylaxis administered in an optimal fashion, the methodology of which is only slowly becoming clearer. We must always be ready to change when a newer drug or a more effective means of antibiotic prophylaxis becomes available.

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