Quinupristin/Dalfopristin in Vancomycin-Resistant Staphylococcus aureus Endophthalmitis

Postoperative bacterial endophthalmitis is the most dreaded complication of any eye surgery. Once infection is suspected, prompt treatment by vitreous tap and biopsy or by vitrectomy and injection of intravitreal antibiotics is instituted prior to identifying the specific bacteria and its antibiotic sensitivities. Of the 70% of cases that were culture positive in the Endophthalmitis Vitrectomy Study (EVS), 94% were gram-positive organisms that were all sensitive to vancomycin.1 The recent Antibiotic Resistance Monitoring in Ocular micRorganisms 2009 study reported that 39% of Staphylococcus aureus isolates were resistant to methicillin, but all were still sensitive to vancomycin.2 Several recent cases of endophthalmitis due to vancomycin-resistant S aureus and Enterococcus have also been reported.3,4 Of the few antibiotics effective against vancomycin-resistant bacteria, only intravitreal quinupristin/dalfopristin has been reported previously in a single human eye.5 In the current series, 2 additional cases are reported with successful treatment of vancomycin-resistant S aureus endophthalmitis with intravitreal quinupristin/dalfopristin.

Report of Cases. Case 1. An 83-year-old man with a history of hypertension, cardiac arrhythmia, prostate cancer, multiple hospitalizations for infections, and previous anaphylactic reaction to vancomycin had cataract surgery in his left eye 2 weeks prior to the diagnosis of endophthalmitis. Surgery was performed via scleral tunnel and was complicated by rupture of the posterior lens capsule. At the conclusion of surgery, the patient received subconjunctival cefazolin sodium, 100 mg, and dexamethasone sodium phosphate, 2 mg. Postoperatively, the patient received topical besifloxacin, 0.6%, prednisolone acetate, 1%, and bromfenac sodium, 0.09%.

At 2 weeks postoperatively, the patient had pain, decreased visual acuity to hand motions, a Seidel-positive cataract incision, plasmoid anterior chamber (AC) reaction, posterior synechia, keratic precipitates, and intraocular pressure of 8 mm Hg OS. There was no retained lens material or plaque present. After review of the literature and informed consent for off-label medication use with the patient, allergist, infectious disease specialist, and pharmacist, the patient was treated with intravitreal quinupristin/dalfopristin (0.4 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL). He received linezolid, 600 mg. Gram staining showed gram-positive cocci in clusters, and the bacteria were coagulase positive. Thirty-six hours later, he had recurrent pain, decreased vision, and reaccumulation of vitreous opacities and hypopyon. S aureus was isolated from the vitreous and AC but sensitivities were pending. Following EVS guidelines for reinjection ([1] visual acuity <1.5/60 but >light perception, [2] red reflex absent or increased media opacification compared with the initial manifestation, [3] at least an equivocal growth seen in the initial culture, and [4] ≥1 of the following: [A] a 1-mm increase in the height of the hypopyon, [B] a corneal ring infiltrate, and [C] worsening pain), vitrectomy with intravitreal quinupristin/dalfopristin (0.4 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL) was performed. The next day, the initial vitreous and AC cultures identified S aureus resistant to methicillin, vancomycin, moxifloxacin, clindamycin, imipenem, and tetracycline but sensitive to chloramphenicol, quinupristin/dalfopristin, and linezolid (determined by Vitek 2 system; BioMérieux, Inc).

The second set of cultures showed similar growth. Oral linezolid, 600 mg, and minocycline hydrochloride, 100 mg, were given for 21 days followed by rifampin and minocycline for a total of 3 months. Visual acuity improved to 20/80 at 1 week. Complete resolution of vitreous and AC inflammation as well as return to visual acuity of 20/50 occurred over 3 months.

Case 2. A 78-year-old man with a history of hypertension, cardiac disease, adult-onset diabetes, chronic obstructive lung disease, multiple hospitalizations, and previously treated methicillin-resistant S aureus skin abscess had cataract surgery of the right eye through clear corneal incision. The surgery was complicated by rupture of the posterior lens capsule. Because of a 30-year history of central retinal vein occlusion in the right eye, his preoperative visual acuity was counting fingers. At the conclusion of surgery, the patient received subconjunctival cefazolin sodium, 100 mg, and dexamethasone sodium phosphate, 2 mg. Postoperatively, the patient received topical gatifloxacin, 0.5%, prednisolone acetate, 1%, and ketorolac tromethamine.

Three days postoperatively, the patient had pain, decreased visual acuity to light perception, Seidel-positive test results, superior corneal infiltrate, keratic precipitates, 30% hypopyon, and intraocular pressure of 32 mm Hg. The patient was treated with pars plana vitrectomy, AC washout, and suture placement in the clear corneal incision. Cultures were obtained from the AC and vitreous. The patient received intravitreal vancomycin hydrochloride (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL) as well as subconjunctival vancomycin and ceftazidime. Every 2 hours beginning on the day after surgery, topical vancomycin and ceftazidime were administered every 2 hours. Gram staining showed gram-positive cocci in clus-
ters, and the bacteria were partially identified as coagulase positive the next day.

Thirty-six hours later, he had recurrent pain, decreased vision, reaccumulation of vitreous opacities, and 30% hypopyon. Following the EVS guidelines for re-injection, pars plana vitrectomy was performed and intravitreal antibiotics were administered. The next day, the initial vitreous and AC cultures identified S aureus resistant to mexitilin, vancomycin, ciprofloxacin, levofloxacin, and tetracycline but sensitive to chloramphenicol, quinupristin/dalfopristin, and linezolid (determined by Vitek 2 system; BioMerieux, Inc). He had persistent pain, worse vision, and recurrent 20% hypopyon. After informed consent for off-label use, intravitreal quinupristin/dalfopristin (0.4 mg/0.1 mL) and amikacin sulfate (0.4 mg/0.1 mL) were administered. Oral linezolid, 600 mg, and minocycline hydrochloride, 100 mg, were given for 21 days followed by rifampin and minocycline for a total of 3 months. Within 2 days there was significant clearing of vitreous debris and view of secondary vessels. During the next 3 months there was complete resolution of vitreous, AC, and corneal inflammation and return of visual acuity to his baseline of counting fingers.

Comment. Antibiotic treatment for bacterial endophthalmitis must be started promptly for optimal success, and the empirical antibiotic chosen should be active against the suspected bacteria even though sensitivities may not be available for up to 72 hours later. Clinicians need to be knowledgeable of the likely causes and sensitivity patterns of the suspected bacteria because delay in treatment can lead to poor outcomes. While all of the gram-positive bacteria in the EVS were sensitive to vancomycin, recent resistant organisms have been reported with increased frequency and are a concern.

Synercid is a streptogramin antimicrobial resulting from the combination of semisynthetic pristinamycin derivatives, quinupristin and dalfopristin, in a 3:7 ratio. The combination targets both early and late stages of protein synthesis, resulting in synergistic activity, and is bactericidal. Linezolid is an oxazolidinone antibiotic that inhibits protein synthesis by binding to the 50S ribosomal subunit. It is bacteriostatic and has potential adverse effects of irreversible optic neuropathy from systemic use, which could potentially be even greater with intravitreal use, although to our knowledge this has not been studied.

Antibiotic resistance is evolutionary and the genes responsible can be transferred between bacteria, leading to increased resistance. If resistance to established antibiotics becomes more common, newer treatment regimens need to be considered for continued successful treatment or there will be poor outcomes in those resistant cases. The EVS showed that intravitreal antibiotic effects are effective with or without use of systemic antibiotics for bacterial endophthalmitis. Clinicians should be aware of alternative intravitreal antibiotics when vancomycin-resistant bacteria are present or highly suspected. Although prolonged oral antibiotics have not been necessary in endophthalmitis, a 3-month course of systemic therapy was recommended in these cases of vancomycin-resistant organisms to eradicate any nonocular reservoir of remaining bacteria. The timing of ocular improvement in these patients demonstrates that the effectiveness of intravitreal treatments is more rapid than the reported cases treated by oral linezolid alone. In conclusion, 2 cases of vancomycin-resistant endophthalmitis were successfully treated with intravitreal quinupristin/dalfopristin and oral antibiotics. Clinicians should consider intravitreal quinupristin/dalfopristin for vancomycin-resistant bacterial endophthalmitis.

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Spectral-Domain Optical Coherence Tomographic Characteristics of Autosomal Recessive Isolated Foveal Hypoplasia

Foveal hypoplasia, also referred to as foveal planum, is a congenital condition that can be associated with other ocular abnormalities such as aniridia, albinism, microphthalmos, and achromatopsia. Isolated foveal hypoplasia (IFH) is an even rarer disorder, with similar clinical findings in the fovea. The characteristic findings of patients with IFH are nystagmus, poor visual acuity, absent or abnormal maculofoveal reflexes on ophthalmoscopy, and variable and incomplete filtering of the choroidal fluorescence in the macular area on fluorescein angiography. No single hereditary pattern has been established for patients with IFH. Reported cases include patients with autosomal dominant and autosomal recessive inheritance patterns as well as sporadic cases. Only recently has a grading system for the