Postoperative Hemorrhagic Occlusive Retinal Vasculitis Associated with Intravitreal Injection of Vancomycin

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Abstract

Purpose: To present a case of hemorrhagic occlusive retinal vasculitis (HORV) associated with intravitreal injection of vancomycin after pars plana vitrectomy (PPV).

Methods: Single case report.

Results: A 67-year-old woman presented with best-corrected visual acuity (BCVA) of 20/400 in the left eye. For clinical suspicion of chronic endophthalmitis, empirical treatment was initiated with vancomycin and ceftazidime without clinical improvement. The patient was submitted to pars plana vitrectomy. During surgery rhegmatogenous retinal detachment was observed and treated. At the end of surgery, intravitreal vancomycin was injected. After 18 days BCVA was counting fingers and fundus examination showed diffuse retinal vascular sheathing, intraretinal hemorrhages, and ischemic macular whitening. The clinical diagnosis was compatible with HORV secondary to retinal toxicity due to intraocular vancomycin.

Conclusions: This case illustrates the importance of including intravitreal vancomycin during PPV surgery on the list of potential causes when investigating a case of suspected hemorrhagic occlusive retinal vasculitis.

Keywords: Intravitreal injection; Pars plana vitrectomy; Vancomycin; Vasculitis; Corticosteroids

Introduction

Vancomycin is a broad-spectrum antibiotic that covers nearly all staphylococcal and streptococcal species, which are the most frequent causes of postoperative endophthalmitis after ocular surgery. This antibiotic has been recommended for widespread prophylactic use in cataract surgery in the United States. Intravitreal injection of vancomycin is a well-established treatment for bacterial endophthalmitis and has been shown to be safe for intraocular use at a dose of 1.0 mg/0.1 ml.

Vancomycin retinal toxicity has been demonstrated in rabbits receiving intravitreal injections of vancomycin in silicone-filled eyes, but human toxicity has not been suggested until recently. In 2014, Nicholson et al. reported for the first time 2 cases (4 eyes) of severe bilateral ischemic retinal vasculitis after uncomplicated cataract surgery and in 2015, Witkin et al. published another 4 cases (3 bilateral and one unilateral) with the same disorder. The authors termed the condition hemorrhagic occlusive retinal vasculitis (HORV) and postulated a delayed immune response to a surgical adjuvant, with vancomycin as the leading candidate. More recently, Witkin et al. published a retrospective case series that included thirty-six eyes of 23 patients. In this study, the authors describe the clinical characteristics of HORV and study its prevalence, cause, treatment, and outcomes.

We report, herein a case of retinal vasculitis associated with intravitreal injection of vancomycin after pars plana vitrectomy, suggesting a new spectrum of toxicity that may be under-recognized.

Case Report

A 67-year-old white woman with a past medical history of hypertension presented at the Department of Ophthalmology with complaints of progressive, painless vision loss in her left eye for the last two months. She
had undergone uncomplicated phacoemulsification five months ago with the improvement of visual acuity after surgery. In this case, no intra-cameral antibiotic was used at the end of surgery. On ophthalmology examination, the patient had best corrected visual acuity (BCVA) of 20/30 in the right eye and 20/400 in the left eye and intraocular pressure (IOP) of 12 mmHg and 10 mmHg, respectively. Slit-lamp examination of the left eye revealed mild conjunctival injection, transparent cornea, inflammatory cells in the anterior chamber (2+/4) and vitreous (2+/4) and an intraocular lens (PCIOL) in the capsular bag with mild paracentral opacification. Fundoscopy showed diffuse vitreous opacities and a retinal detachment with macula-off. The right eye was normal with no abnormal findings except mild nuclear sclerosis. For clinical suspicion of chronic endophthalmitis aqueous and vitreous samples were collected for analysis and empirical treatment was initiated with intravitreal injection of vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL). It was also prescribed moxifloxacin and dexamethasone drops every 2 hours. After one week, her vision was 20/800, IOP was 14 mmHg, and there was more inflammatory reaction in the anterior and vitreous chamber (3+/4). Retinal detachment was maintained with worsening vitreous opacities. Aqueous and vitreous samples were negative for aerobic and anaerobic microorganisms. The patient was submitted to pars plana vitrectomy (PPV) with posterior capsulotomy. Posterior capsule was sent for culture sensitivity, and aqueous and vitreous samples were collected again for analysis. During the surgery, rhegmatogenous retinal detachment with a retinal tear in the superior-nasal quadrant was observed. Endolaser, fluid-gas exchange and C3F8 gas (perfluoropropane) injection were performed. At the end of surgery, intravitreal vancomycin (1 mg/0.1 mL) and subconjunctival dexamethasone were injected. Moxifloxacin and dexamethasone eye drops every 2 hours were maintained. On postoperative day 1, her vision was hand motion; slit-lamp examination revealed moderated conjunctival injection with fibrin in the anterior chamber, and retinalexamination was impossible by severe vitreous opacities. There was no change after one week. Culture of posterior capsule was negative as well as aqueous and vitreous samples. On postoperative day 18, her vision was counting fingers at 1 m and IOP was 10 mmHg. The anterior segment showed moderate conjunctival hyperemia, transparent cornea, 2+ cells in the anterior chamber without fibrin. Posterior segment examination (Figure 1) revealed diffuse retinal vascular sheathing, intraretinal hemorrhages and ischemic macular whitening. Aqueous and vitreous culture results were negative. Optical coherence tomography (OCT) (Figure 2) showed inner retinal thinning, consistent with ischemic damage to the macula and fluorescein angiography (Figure 3) demonstrated areas of vascular occlusion coincided with regions of sectoral retinal hemorrhage on color photographs. One month after PPV her visual acuity was hand motion, IOP was 9 mmHg and there was no inflammatory reaction in the anterior segment. Retinal examination revealed multiple areas of hemorrhages with retinal atrophy and fibrosis (Figure 4).

Over the following weeks, visual acuity decreased to no light perception and fluorescein angiography continued to show complete retinal no perfusion. Neovascular glaucoma (NVG) and phthisis bulbi had developed in the left eye.
Figure 3. Retinal vascular occlusion in areas of retinal hemorrhage

Figure 3. Fluorescein angiography image demonstrating retinal vascular occlusion in areas of retinal hemorrhage.

Figure 4. Areas of hemorrhages with retinal atrophy and inferior retinal detachment with PVR

Figure 4. Dilated fundus photograph one month after PPV showing areas of hemorrhages with retinal atrophy and inferior retinal detachment with PVR.

Discussion

By the authors’ knowledge, this case presents the first report in the literature of HORV associated with intraoperative intravitreal vancomycin during PPV surgery. Although it is impossible to confirm the relationship of the disease to vancomycin exposure, we believe that it is unlikely to be related to an underlying systemic process or autoimmune disease since the patient had no history of thrombosis.

The timing of HORV is consistent with a type III hypersensitivity reaction similar to leukocytoclastic vasculitis and Henoch-Schönlein purpura, analogous reactions in the skin that have rarely been seen one to two weeks after intravenous vancomycin therapy was initiated. Both of diseases are mediated by antibody and antigen complex deposition causing small-vessel vasculitis. Since vancomycin is a small molecule and these typically are not thought to cause hypersensitivity reactions, it’s possible that vancomycin may be causing an analogous small-vessel vasculitis induced by antigen and antibody deposition in the retinal vessels.

One of the most common immune-mediated reactions to vancomycin is the red man syndrome, which is a mast cell-mediated (no allergic) skin reaction that occurs immediately upon injection of intravenous vancomycin and resolves immediately after discontinuation of medication infusion. There is no direct evidence that vancomycin caused HORV, and it is possible that the disease entity may not be related to vancomycin itself. Other potential explanations include a reaction to a surgical adjuvant other than vancomycin, a contaminant or preservative in the vancomycin mixture, or interaction between vancomycin and another compound (e.g., sodium hyaluronate) also used during surgery. In the future, if other cases of HORV are found in which vancomycin was not used, it would support further the possibility that this reaction, in fact, may not be the result of vancomycin.

For treatment of HORV, as with other hypersensitivity reactions, high-dose systemic and topical corticosteroids are likely helpful to limit the initial inflammatory response. Intravitreal corticosteroids also may be considered; they may be particularly useful because they specifically target the intraocular inflammatory response. In our case, systemic corticoids were not used in the first presentation because it was hypothesized that the patient had infectious endophthalmitis. The patient was treated only with topical corticosteroids, but there was no clinical improvement. However, the little results from patients that received intravitreal medications are very different. Witkin et al. reported in 2017, 3 eyes that received intravitreal corticosteroids with HORV. Their final visual acuities were 20/40, 20/70, and hand movements suggesting that some eyes that receive this treatment can have good visual outcomes but not always. Later in the disease course, despite the inflammatory response probably diminished; the ischemic drive toward retinal neovascularization and neovascular glaucoma ensue. Anti-vascular endothelial growth factor injections and panretinal photocoagulation are important to prevent these complications of the severe retinal ischemia found in many of the eyes with HORV.
In conclusion, hemorrhagic occlusive retinal vasculitis is a rare, potentially devastating condition that can develop after cataract surgery or intraocular injection. Disease course and findings suggest that a delayed hypersensitivity reaction to vancomycin causes HORV. This case report illustrates the importance of including intravitreal vancomycin during PPV surgery on the list of potential causes when investigating a case of suspected HORV.

References