

Update on Retinal Drug Safety: Proceedings of the ASRS ReST Committee Webinar Part I

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Abstract

Purpose: To review the first Research and Safety in Therapeutics (ReST) Committee webinar and summarize the most current recommendations regarding diagnosis and management. **Methods:** The ReST Committee is comprised of members of the American Society of Retina Surgeons (ASRS). At regular internal meetings, safety issue reports from the website are reviewed. A webinar series was started in 2021 to update members on multiple relevant potential safety events. **Results:** Topics reviewed in the webinar included pentosan polysulfate sodium (Elmiron) maculopathy, intraocular pressure elevation reported with the aflibercept prefilled syringe (PFS), and brolocizumab-associated inflammation with occlusive retinal vasculitis. Retinal toxicity related to intraoperative medications was reviewed, including hemorrhagic occlusive retinal vasculitis after intraocular vancomycin, dilution errors with intravitreal aminoglycosides, inadvertent overdoses of cefuroxime after cataract surgery, and toxic posterior segment syndrome after dropless cataract surgery using compounded triamcinolone–moxifloxacin. Indocyanine green toxicity has been reported after its use as an adjuvant during macular hole surgery. **Conclusions:** The past decade has seen advances in retinal pharmaceuticals and drug-delivery devices. The ASRS ReST Committee collects data from its website reporting system to inform members about up-to-date pharmaceutical and device safety concerns. Recently, a webinar was used to inform members of pigmentary maculopathy associated with pentosan polysulfate sodium, safety regarding the aflibercept PFS, intraocular inflammation and occlusive retinal vasculitis secondary to brolocizumab, and retinal toxicity from intraoperative ocular medications.

Keywords

pentosan, pigmentary maculopathy, prefilled syringe, occlusive vasculitis, intraocular inflammation, brolocizumab, hemorrhagic occlusive retinal vasculitis, vancomycin toxicity, indocyanine green toxicity, amikacin toxicity

Introduction

The Research and Safety in Therapeutics (ReST) Committee of the American Society of Retina Specialists (ASRS) is dedicated to timely dissemination of knowledge to inform the retina community about adverse events (AEs) related to medications and surgical devices. Originally called the Therapeutic Surveillance Committee, this committee was launched in 2012 to notify ASRS members about a cluster of 14 cases of noninfectious endophthalmitis after intravitreal (IVT) aflibercept treatment of exudative age-related macular degeneration (AMD). Shortly thereafter, the ASRS devised a peer-to-peer reporting system to alert members about emerging or rare AEs that may affect patient safety. To date, the ReST Committee is the largest safety group comprised of retina physicians globally, interacting with the US Food and Drug Administration (FDA) and other retina societies. It continues to encourage ophthalmologists to report

AEs through the ASRS website (<https://www.asrs.org/clinical/adverse-events-reporting>).

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The ReST Committee Webinar Part 1 was held on May 26, 2021. It highlighted recent adverse reports relevant to the retina community. Discussion topics included pigmentary maculopathy associated with pentosan polysulfate sodium, intraocular pressure (IOP) issues with the aflibercept prefilled syringe (PFS), intraocular inflammation (IOI) secondary to aflibercept, brolocizumab-related occlusive retinal vasculitis, and retinal toxicity related to intraoperative ocular medication. This report reviews the topics presented at the webinar with up-to-date data summarizing current recommendations.

Pigmentary Maculopathy Associated With Pentosan Polysulfate Sodium

Pentosan polysulfate sodium (Elmiron, Janssen Pharmaceuticals Inc) was approved by the FDA in 1996 as an oral treatment for interstitial cystitis. This chronic urologic condition, also referred to as bladder pain syndrome, is characterized by pelvic pain, urinary urgency, and urinary frequency.¹ Pentosan polysulfate sodium is a semisynthetic sulfated polyanion composed of beta-D-xylopyranose residues, and it appears to function by providing a protective coat to the bladder wall because of its similar structure to the glycosaminoglycan lining of the bladder.^{2,3}

Recent studies have uncovered a pigmentary maculopathy associated with chronic exposure to pentosan polysulfate sodium. Known as pentosan maculopathy, its clinical appearance may be confounded with other nonexudative maculopathies. Pearce et al⁴ initially described findings of pentosan maculopathy in 2018 in a retrospective series of 6 patients. Fundus examination found deep paracentral hyperpigmentation at the level of the retinal pigment epithelium (RPE) adjacent to vitelliform-like deposits centered around the fovea.

Subsequent larger series reported multimodal imaging findings and explored the pentosan polysulfate sodium dose-to-toxicity relationship.⁵ Symptoms reported included metamorphopsia, nyctalopia, prolonged dark adaptation, and blurred vision, all of which may be reported in the setting of relatively normal visual acuity (VA). Full-field electroretinography has shown mild attenuation of response amplitudes, and multifocal electroretinography has shown a wide range of mild to severe attenuation of response amplitudes.⁵ Retina findings are characterized by relatively symmetric hyperpigmented nodular macular spots at the level of the RPE with interspersed pale-yellow subretinal deposits (Figure 1, A–D).⁵ Spectral-domain optical coherence tomography (SD-OCT) shows foci of RPE nodular elevation and/or thickening (Figure 1, E and F) that correspond to the macular pigment clumps, hyperautofluorescence on fundus autofluorescence (FAF), and hyperreflectance on near-infrared imaging.⁵ In contrast to drusen, which appear on SD-OCT as hyperreflective deposits between the RPE and Bruch membrane, the lesions in pentosan maculopathy reside at the level of the RPE and shadow the underlying choroid. RPE atrophy and diminished hyperpigmented spots develop in late stages of the disease. Irregularity of the outer retinal bands, cystoid macular edema (CME), and

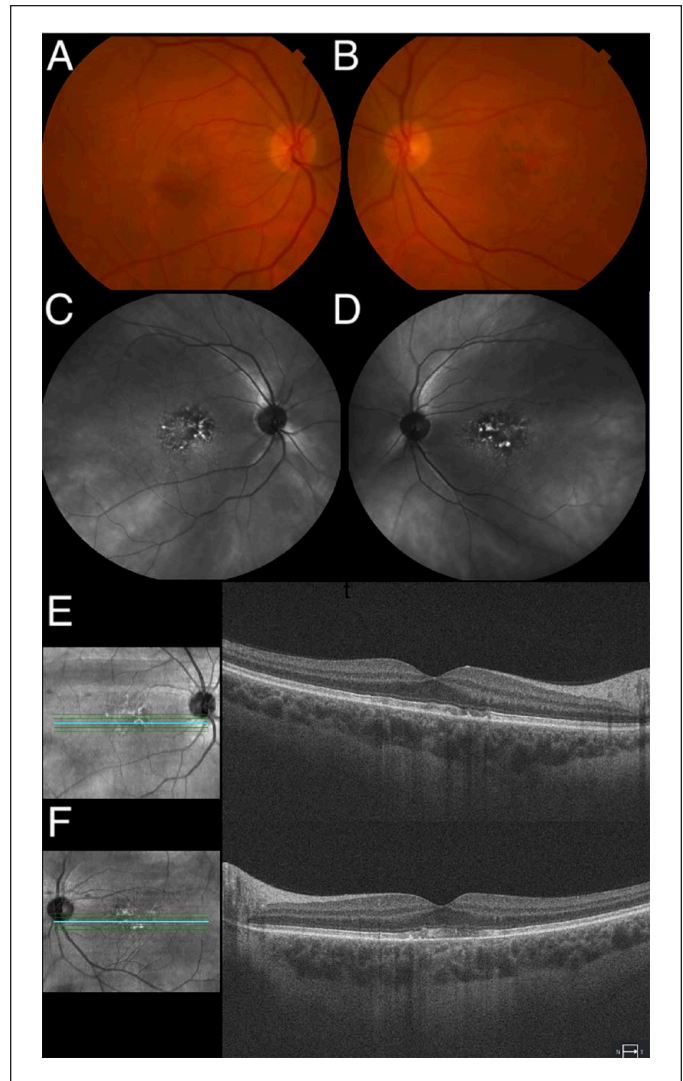


Figure 1. Multimodal imaging of pigmentary maculopathy associated with pentosan polysulfate sodium. Color fundus photographs of the right eye (A) and left eye (B) show nodular, deep, hyperpigmented spots centered around the fovea. Fundus autofluorescence of the right eye (C) and left eye (D) shows a symmetric pattern of hyperautofluorescent and hypoautofluorescent spots in the fovea. (E and F) Spectral-domain optical coherence tomography shows foci of retinal pigment epithelium elevation that shadow the underlying choroid. (Images provided by Andre J. Witkin, MD.)

choroidal neovascularization have also been described, further confounding the distinction between pentosan maculopathy and AMD.^{6,1} Pentosan maculopathy may masquerade as pattern dystrophy or intermediate AMD; however, a finding unique to pentosan maculopathy is a peripapillary hypoautofluorescent halo.⁵

Recent studies have explored the relationship between the cumulative dose of pentosan polysulfate sodium and its associated maculopathy. Vora et al.⁷ reported an overall prevalence of

maculopathy of 23.1% among pentosan polysulfate sodium users, with pentosan maculopathy in 12.7% of patients with 500 to 999 g of pentosan polysulfate sodium exposure (equivalent to 4.6 to 9.1 years of adherence), 30% of patients with 1000 to 1500 g of exposure, and 41.7% of patients with less than 1500 g of exposure. Wang et al⁸ examined a large prospective cohort (741 patients) with any pentosan polysulfate sodium consumption and found that the prevalence of pentosan maculopathy was 16%. The affected cohort had a greater mean ($\pm$ SD) pentosan polysulfate sodium therapy duration, mean daily dosage, and mean cumulative dosage (19.5 ± 5.5 years, 433.9 ± 137.6 mg, and 3103.1 ± 1402.2 g, respectively) than the unaffected cohort (7.1 ± 6.6 years, 291.6 ± 177.6 mg, and 768.4 ± 754.8 g, respectively). In a multicenter retrospective study, the median age at diagnosis of pentosan maculopathy was 62 years with a median duration of pentosan polysulfate sodium exposure of 14 years (range, 10.2–18.9) and a median cumulative exposure of 1.5 kg (range, 0.9–2.4).⁹

It has been recommended that clinicians perform a baseline pretreatment ophthalmic examination followed by yearly dilated fundus examinations for patients taking pentosan polysulfate sodium.⁶ Given that the spectrum of disease presentation is variable, retinal imaging may include SD-OCT, color and near-infrared imaging fundus photography, and FAF. In particular, FAF and near-infrared imaging may help diagnose subtle early macular changes. Pentosan polysulfate sodium should be immediately discontinued if new macular pigmentary changes consistent with pentosan polysulfate sodium use develop.

When pentosan polysulfate sodium treatment is initiated, patients should be placed on the lowest dose needed and treatment should be discontinued if it is no longer necessary because the risk for pentosan maculopathy increases with a cumulative dose greater than 500 g.^{6,7–9} It is the consensus of this panel that prescribers should be cautious using pentosan polysulfate sodium in a patient with unrelated maculopathy because there are no data on whether the medication could exacerbate pre-existing macular disease. Ophthalmologists may consider communicating with prescribers of pentosan polysulfate sodium to inform them of the pigmentary maculopathy associated with its long-term use. Clinicians should also be aware that although symptoms such as nyctalopia, blurry vision, metamorphopsia, and dyschromatopsia have been described, patients may be completely asymptomatic. Pentosan maculopathy can masquerade as AMD, pattern dystrophy, or RPE mottling, and clinicians should have a high index of suspicion when eyes have symmetric clinical findings and characteristic multimodal imaging.

Aflibercept Prefilled Syringe

Aflibercept is a recombinant fusion protein composed of human vascular endothelial growth factor (VEGF) receptors 1 and 2 extracellular domains fused to the Fc portion of immunoglobulin G1.^{10,11} It operates as a soluble decoy receptor by preventing the binding and activation of VEGF receptors.^{10,11}

Aflibercept was approved by the FDA for the treatment of neovascular AMD (nAMD) in November 2011 followed by European Medicines Agency (EMA) approval in November 2012. Shortly after FDA approval, there was a limited cluster of presumed sterile IOI after IVT injection of aflibercept.^{12,13} Another cluster was reported to the ASRS in 2017–2018, and the clinical features and outcomes of 68 eyes of 66 patients with IOI after IVT aflibercept injection were detailed.¹⁴ The mean time to presentation was 2.6 days, and the majority of patients (93%) reported blurred vision.¹⁴ Floaters (60%), mild to severe pain (50%), and photophobia (19%) were described. All patients had IOI affecting the anterior chamber, vitreous cavity, or both. Additional reported findings included keratic precipitates (22%), corneal edema (13%), conjunctival injection (10%), chemosis (4%), hypopyon (4%), and fibrin (3%). Treatment included local or systemic steroids, and 15% of eyes lost 2 or more lines of VA. Some of the clinical features of sterile IOI may overlap with infectious endophthalmitis. Increased levels of pain, rapid loss of vision, and severe ocular inflammatory features are more consistent with an infectious etiology. It may be difficult to distinguish sterile IOI from an infectious etiology, especially early in its course; thus, standard-of-care treatment with antibiotics should be considered in cases in which there is a high index of suspicion for an infectious etiology.¹⁴

Various hypotheses have been explored to account for the IOI cluster after IVT aflibercept, including medication-related factors (production, storage, molecular characteristics, immunogenicity, contamination), vehicle-related factors (silicone droplets, impurities), syringe issues, handling of medication, and patient-specific factors. In February 2018, Regeneron released a statement noting an association with certain batches of syringes that were included in specific lots of aflibercept boxes and stopped distributing these kits.¹⁵ However, Greenberg et al¹⁴ noted in their series that in some of the eyes that developed aflibercept-related IOI, the prepackaged syringes from the aflibercept kit were not used. These potential areas for IOI support the need for an aflibercept prefilled, direct-to-injection syringe, thereby eliminating the necessity of using a syringe from an outside manufacturer for transfer from the vial.

The aflibercept PFS was approved by the FDA in August 2019 followed by the EMA in April 2020. These 1 mL glass syringes prefilled with aflibercept were designed for stable transport and storage to facilitate direct IVT delivery. Since the introduction of the PFS for IVT anti-VEGF injection of aflibercept as well as ranibizumab there has been a decrease in the number of reports of IOI to the ASRS ReST Committee. There were 10 reports in 2019, 4 reports in 2020, and 6 reports in 2021. However, there may be an underreporting bias for a complication that is already known.

After the introduction of the aflibercept PFS, there have been reports of elevated IOP occurring immediately after IVT injection using the PFS, leading to transient loss of vision and, on occasion, transient occlusion of the central retinal artery.^{16,17} The etiology is thought to be the result of the design of the aflibercept

PFS, which has a wider internal diameter than the ranibizumab PFS. The wider diameter of the aflibercept PFS results in a shorter excursion of the plunger to deliver the expected dose, resulting in a greater variability in dosing depending on the distance of plunger alignment to the tip of the syringe needle. Also, the aflibercept PFS plunger has a dome shape, and the dose mark is wider (0.75 mm) than that on the ranibizumab PFS (0.25 mm). The base of the plunger dome, not the apex, should be aligned with the preexisting mark on the syringe, as illustrated in the aflibercept PFS package insert. Variability in plunger alignment with the correct mark on the syringe may result in an inaccurate volume being released.¹⁸

Guest et al¹⁸ measured the IVT injection volume from 12 physicians using the aflibercept PFS and compared it with the volume of aflibercept drawn into a Becton Dickinson (BD) Luer-Lok syringe from a vial. The average injected volume was 74.22 μm with the PFS and 53.42 μm with the BD Luer-Lok syringe. The authors found that the IVT injection volumes varied more with the aflibercept PFS than with the BD Luer-Lok syringe. The average deviation in volume injected was 11.36 μm with the PFS and 3.35 μm with the BD Luer-Lok syringe. These differences in volume may account for the elevated IOP reported with the aflibercept PFS; thus, providers should take care to properly align the plunger position. Based on reports of elevated IOP, the US label was updated with images and information regarding the location of the dosing line.

Intraocular Inflammation and Occlusive Retinal Vasculitis Secondary to Brolucizumab

Brolucizumab is an IVT anti-VEGF agent approved for nAMD by the FDA in October 2019 after the pivotal phase 3 HAWK and HARRIER trials showed visual efficacy and noninferior visual results compared with aflibercept and also a potential for increased durability and superior resolution of fluid.¹⁹ The EMA followed with approval in February 2020. Brolucizumab is a single-chain antibody fragment inhibitor of VEGF-A isoforms with a molecular mass of 26 kDa, allowing for a higher dosing per volume with the potential for some improved durability compared with other anti-VEGF agents.^{20,21}

Shortly after FDA approval, the ASRS began receiving reports of IOI after IVT brolucizumab. In addition to IOI, there were cases associated with retinal vasculitis, retinal vein occlusion (RVO), and vision loss, and these had not previously been reported as potential complications of this medication. The ASRS ReST Committee was immediately concerned by these reports, and it was instrumental in alerting retina physicians of the association between brolucizumab and retinal vasculitis and RVO. Member alerts were sent on January 23, 2020, February 23, 2020, March 23, 2020, and June 4, 2020. In the report dated March 30, 2020, a detailed analysis of 26 eyes of 25 patients with retinal vasculitis was included. Most of these cases (92%) were associated with IOI and presented a mean of 26 days (range, 3-63) after a brolucizumab injection.²² Symptoms at

AE onset included blurred vision (62%), floaters (46%), pain (31%), redness (19%), and scotomas (12%). Two eyes (8%) were asymptomatic and were found to have only retinal vasculitis on routine follow-up examination.

To address the mounting concern of retinal vasculopathy associated with brolucizumab, Novartis commissioned a safety review committee to review the cases of IOI and RVO from the HAWK/HARRIER data and found that the incidence of definite IOI was 4.6%, of IOI with vasculitis was 3.3%, and of IOI with vasculitis and RVO was 2.1%.^{19,23} Of note, the safety review committee did not review data from patients who had not had a reported AE; thus, it is possible that some cases of asymptomatic IOI from the HAWK/HARRIER trial were missed. On June 4, 2020, the ASRS and Novartis simultaneously released results from the safety review committee review. This was followed by a label update with additional safety information regarding IOI, retinal vasculitis, and RVO after brolucizumab, which was approved by the FDA on June 11, 2020.

A variety of retinal features have been reported in patients with brolucizumab-associated retinal vasculitis. Vasculopathy initially affects the large and/or small retinal arteries followed by involvement of the retinal veins, which is often associated with perivenular hemorrhages.²²⁻³⁰ Other features include anterior chamber cells, corneal edema, keratic precipitates, vitreous cells and/or dark vitreous opacities, optic nerve swelling, arterial plaques, and other signs of retinal and choroidal ischemia (cotton-wool spots, intraretinal hemorrhages, retinal whitening, choroidal whitening, paracentral acute middle maculopathy).²²⁻³³

Multimodal imaging plays a role in highlighting the features when IOI and/or occlusive retinal vasculitis secondary to brolucizumab is suspected. An expert opinion publication recommended multimodal imaging, including fluorescein angiography (FA) with widefield or peripheral sweeps and OCT, to aid clinical examination because the vitreous inflammation may obscure clinical viewing of small-vessel vasculitis.²⁴ FA may show the extent of vasculopathy, including marked delayed flow, peripheral nonperfusion, vascular discontinuity, and irregular arterial flow.²⁴ Indocyanine green angiography (ICGA) may also be helpful given that choroidal ischemia was evident in nearly one half of the eyes in one series.²²

A history of recent brolucizumab injections, delayed onset of symptoms and findings, as well as occlusive retinal vasculitis or multifocal vascular occlusions help differentiate this entity from infectious or systemic etiologies.²⁴ A retrospective review of 20 000 eyes from the IRIS Registry concluded that patients with a history of IOI or RVO within 1 year before the initiation of brolucizumab had an increased risk for secondary IOI and/or occlusive retinal vasculitis after brolucizumab treatment.³³ Women may have an increased risk, and it has been hypothesized this is related to an increased propensity for autoimmune disorders and noninfectious uveitis in women.²⁴ Enriquez et al²⁷ analyzed a consecutive series of eyes treated with brolucizumab and added bilateral same-day brolucizumab injection as another potential risk factor.

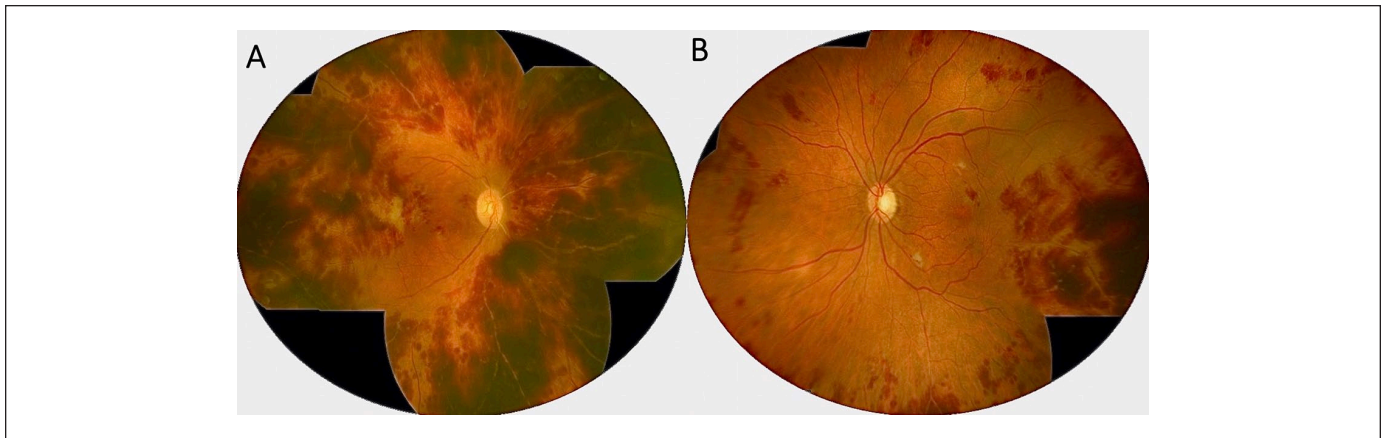


Figure 2. Imaging of hemorrhagic occlusive retinal vasculitis. The color fundus photograph shows an extensive intraretinal hemorrhage, foci of macular whitening, vascular sheathing, and an attenuated appearance of the vasculature that are more notable in the right eye (A) than in the left eye (B). (Images provided by Andre J. Witkin, MD.)

It is still unclear why the rate of IOI is higher with brolucizumab (>4%) than with other anti-VEGF drugs (<1%). The delayed presentation of IOI in most eyes suggests a delayed immune reaction to the drug or some component of the delivery system. It is possible that an immune response is triggered by the drug itself, which is suggested by the high rates of anti-brolucizumab antibodies at baseline and even higher rates of anti-brolucizumab antibodies after treatment initiation. Inflammatory noninfectious retinal vasculitis with RVO has only been noted after brolucizumab, and it has not been associated with the other FDA-approved anti-VEGF agents (ranibizumab, aflibercept, faricimab). Thus, it does not appear to be a class effect related to the anti-VEGF mechanism of action. The presence of IOI or vitreous opacity in many eyes in patients with brolucizumab-associated retinal vasculitis suggests an inflammatory or combined immune mechanism.

MERLIN was a phase 3a study funded by Novartis to assess the efficacy and safety of brolucizumab administered every 4 weeks compared with aflibercept 2 mg dosed every 4 weeks for eyes with treatment experience, nAMD, and persistent retinal fluid.³⁴ After the first year, the study was extended to 2 years. The incidence of IOI, including retinal vasculitis and RVO, was 9.3% for brolucizumab vs 4.5% for aflibercept. Of the participants, 4.8% in the brolucizumab group and 1.7% in the aflibercept group had a loss of 15 or more letters of best-corrected VA from baseline at week 52. These findings led Novartis to terminate the second year of the MERLIN study early as well as other ongoing studies that mandated continuous 4-week dosing intervals beyond the initial 3 monthly loading doses, including the RAPTOR study (ClinicalTrials.gov identifier, NCT03802630) and RAVEN study (ClinicalTrials.gov identifier, NCT03810313), which assessed the efficacy and safety of brolucizumab in RVO.

In patients with brolucizumab-associated IOI and/or retinal vasculitis, it is advised that brolucizumab be stopped and corticosteroids given topically, via IVT injection, or systemically. In very mild cases of IOI, topical steroid eyedrops may

be sufficient. Potent corticosteroid treatment (sub-Tenon, intraocular, and/or systemic) is recommended in moderate to severe cases, especially in cases in which RVO and retinal vasculitis are present given that there have been some reports of resolution after this therapy.

Retinal Toxicity From Intraoperative Ocular Medications

Hemorrhagic occlusive retinal vasculitis is a rare, sight-threatening complication described after intraocular injection of vancomycin, typically given as endophthalmitis prophylaxis during cataract surgery. The initial report of this association was suggested by Nicholson et al,³⁵ who reported 2 cases of hemorrhagic occlusive retinal vasculitis that occurred bilaterally after otherwise uneventful cataract surgeries performed 1 week apart. These cases had IOI and profound vision loss.

Vancomycin-associated hemorrhagic occlusive retinal vasculitis is characterized by delayed-onset, painless, and often permanent decreased vision. Features include large regions of intraretinal hemorrhage, macular whitening, peripheral ischemia, anterior chamber and vitreous inflammation, vascular nonperfusion, and venous sheathing (Figure 2, A and B).³⁵ The presentation and course suggest that hemorrhagic occlusive retinal vasculitis is a delayed hypersensitivity reaction to vancomycin. When hemorrhagic occlusive retinal vasculitis occurs, treatment includes avoiding further intraocular vancomycin, using aggressive systemic and topical corticosteroids, initiating early anti-VEGF treatment for retinal neovascularization resulting from ischemia and, in select cases, performing panretinal photocoagulation to prevent neovascular glaucoma, a common complication.³⁵

Retinal toxicity attributable to IVT use of aminoglycosides has been known for many years, and this has led to the replacement of this class of medication (eg, amikacin) with IVT ceftazidime for gram-negative coverage in the treatment of endophthalmitis. Because of the low therapeutic index of

aminoglycosides, small dilution errors may produce an overdose and, subsequently, retinal toxicity.³⁶

Gentamicin toxicity is associated with sudden, severe, and irreversible retinal ischemia. McDonald et al³⁷ described the first 5 cases of severe retinal ischemia associated with gentamicin injections in 1986. Three cases were the result of an overdose; in 2 cases, it was presumed that gentamicin toxicity occurred. Findings included intraretinal hemorrhages, retinal whitening and edema, cotton-wool spots, arteriolar narrowing, and venous beading. FA showed severe retinal vascular nonperfusion. Chronic findings may include rubeosis iridis, optic atrophy, neovascular glaucoma, and retinal pigmentary changes.³⁸ Amikacin overdose can produce similar findings of toxicity after IVT injection.^{36,38} Prevention is the best way to avoid aminoglycoside toxicity, with careful ordering of medication, preparation by a pharmacy or experienced individuals, and the use of labeled injectable solutions that are double-checked by the injector and another individual.³⁷

Hemorrhagic retinal infarction has been reported to occur secondary to inadvertent overdoses of cefuroxime after cataract surgery. Çiftçi et al³⁹ described 4 patients who developed hemorrhagic retinal infarction after being administered a higher-than-intended concentration of cefuroxime, which resulted in severe toxicity. On examination, hemorrhages in the peripapillary and macular regions were detected. Unfortunately, the patients had significant, permanent vision loss. However, an overdose is not always necessary for cefuroxime toxicity to develop. Zuo et al⁴⁰ showed that despite administering a correct cefuroxime dilution, toxic retinopathy still developed after phacoemulsification. Patients developed CME with serous neurosensory retinal detachment. The toxicity was hypothesized to be related to transient RPE sodium–potassium pump dysfunction resulting from a large injection volume of a standard dose concentration.

ICG toxicity has been reported after its use as an adjuvant for macular hole (MH) surgery. Engelbrecht et al⁴¹ described 22 eyes after MH repair in which ICG was used to facilitate internal limiting membrane visualization. Ten eyes had unusual RPE atrophic changes at the site of the previous MH or in the area where the ICG solution contacted the RPE cells. Narayanan et al⁴² further evaluated human RPE cells and rat neurosensory that were treated with ICG and light exposure and discovered that treatment resulted in reduced mitochondrial dehydrogenase activity and increased DNA synthesis in retinal cells. For this reason, it may be prudent to minimize light exposure with the use of IVT ICG dye, although it appears to be rare given the large number of cases performed using ICG over the years.

Toxic posterior segment syndrome has been described after dropless cataract surgery using compounded triamcinolone–moxifloxacin. Patel et al⁴³ retrospectively reviewed 7 patients who developed toxic posterior segment syndrome secondary to intracameral compounded triamcinolone–moxifloxacin. The toxicity was attributed to abnormally high levels of the binding agent poloxamer 407 in the compounded medication.

Conclusions

The past decade has seen accelerated advances in retinal pharmaceuticals and drug-delivery devices. The mission of the ASRS ReST Committee is to collect data and inform members about up-to-date pharmaceutical or device safety concerns using national presentations, electronic communications, publications, and recently virtual webinars to notify its members about potential retinal events related to pharmacology or surgery. The ASRS ReST Webinar included up-to-date findings on pentosan polysulfate sodium (Elmiron), the aflibercept PFS, brolucizumab-associated retinal vasculopathy, and retinal toxicity from intraoperative medications. Ultimately the ReST Committee depends on ASRS members to report any potential concerns on the website (<https://www.asrs.org/clinical/adverse-events-reporting>) to best serve patients and the community.

Ethical Approval

This paper was prepared in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a US Health Insurance Portability and Accountability Act–compliant manner.

Statement of Informed Consent

Informed consent, including permission for publication of all photographs and images included herein, was obtained.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

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