



ASRS

American Society of
Retina Specialists

Clinical Alert: HORV Association with Intraocular Vancomycin

Following the first published series of hemorrhagic occlusive retinal vasculitis (HORV)^{1,2}, the American Society of Cataract and Refractive Surgery (ASCRS) and the American Society of Retina Specialists (ASRS) formed a joint task force to further analyze the prevalence, potential etiology, treatment, and outcomes of this complication associated with intraocular surgery. An HORV case registry was developed and made accessible through the ASRS website www.asrs.org and an online surveillance survey was emailed to all ASCRS members.

In addition to the first 6 cases reported^{1,2}, we have identified at least 16 additional cases of HORV for a total of 22 cases. Fourteen cases were bilateral and eight were unilateral, for a total of 36 eyes. Twelve of the cases occurred in 2015-2016, 5 cases occurred in 2013-2014, and the other 5 cases were prior to 2013. The age range was 51-84 (mean 68 years). Although reporting and data collection are ongoing, preliminary findings from these 22 cases warrant this special clinical alert because of their potential impact on patient safety.

HORV appears to be extremely rare, and can occur following any intraocular procedure (usually cataract surgery). Presentation is delayed, with a mean onset of symptoms 8 days after the procedure. Although the cause of HORV is currently unproven, there is a strong association with the use of intraocular vancomycin (including intravitreal, intracameral bolus, and irrigating solution containing vancomycin). All 36 eyes from these 22 cases received intraocular vancomycin. As of now, there has not been an association with one formulation or one manufacturer.

Visual outcomes were often poor; 22/36 eyes (61%) were 20/200 or worse, and 8/36 eyes (22%) were NLP. Notably, 7 of 36 eyes (19%) received an additional bolus of intravitreal vancomycin for treatment of presumed bacterial endophthalmitis. These patients had particularly poor outcomes and 5/7 eyes were NLP at most recent follow-up.

HORV Characteristic Findings

- Occurs after intraocular procedure with normal undilated exam on postop day 1
- Delayed onset of sudden *painless* decreased vision (Range 1-26 days postop; mean 8 days)
- Visual acuity often poor on presentation, but may be normal in mild cases
- Mild to moderate anterior chamber and vitreous inflammation, with no hypopyon

- Sectoral intraretinal hemorrhage in areas of non-perfusion (often along venules)
- Peripheral retinal involvement in all cases, with macular ischemia and whitening in advanced disease
- Sectoral retinal vasculitis and retinal vascular occlusion on FA, corresponding to areas of hemorrhage
- Rapid progression to neovascular glaucoma common (53%)

Other Associations

- Intraocular vancomycin exposure during procedure
- History of similar reaction in fellow eye
- When both eyes involved, second eye often has faster onset and more severe course
- Minimal to no corneal edema
- Retinal hemorrhages are often large and/or confluent
- Propensity for retinal venule involvement (although can affect both arteries and veins)
- No significant increase in venous dilation or tortuosity
- OCT: Hyper-reflectivity and thickening of the inner retinal layers; CME not a key feature
- Therapy with intravitreal vancomycin for presumed endophthalmitis associated with poor outcomes

HORV is different from ischemic CRVO, which is unilateral, usually presents on postop day 1 when associated with cataract surgery, and is associated with diffuse small intraretinal hemorrhages; conversely, HORV is often bilateral, has a delayed onset, and often presents with large patches of intraretinal hemorrhage only in sectors of retinal vascular occlusion. CME and severe vascular dilation and tortuosity are key features with CRVO, but not HORV, and the rates of NLP vision and of neovascular glaucoma are higher with HORV.

Consulted immunology experts hypothesize that this might represent a rare Type III hypersensitivity reaction to vancomycin, rather than direct drug toxicity. This might be similar to leukocytoclastic vasculitis and Henoch-Schonlein purpura, which are type III hypersensitivity reactions in the skin that have also been rarely associated with vancomycin. Unfortunately, there is no current method to test for such hypersensitivity either pre- or post- HORV diagnosis.

Fourteen of the 22 cases (64%) were bilateral. Because of the delayed onset, HORV did not appear in the first eye until after surgery in the second eye in the 11 cases who underwent sequential bilateral cataract surgery (3 days to 3 weeks apart). In most of these 11 sequential bilateral cases, the first eye became symptomatic first, but bilateral HORV was diagnosed simultaneously during the initial examination. Even with a long delay between eyes in the remaining 3 bilateral cases (9 months, 3 years, and 9 years) the second eye presented similarly to the first after the second eye underwent surgery.

Use of intracameral antibiotic for endophthalmitis prophylaxis is increasing. In a 2014 ASCRS member survey, 50% of respondents were using intracameral antibiotics³. Among those using intracameral antibiotic, vancomycin was used by 37% overall, and by 52% of American surgeons. Many high volume practices using intracameral vancomycin have never knowingly experienced HORV and the task force believes it to be extremely rare. Without knowing how many patients have received intracameral vancomycin, however, the actual rate is unknown.

Considerations for Intraocular Vancomycin Use

- ❖ Because HORV appears to be extremely rare, each surgeon should weigh the potential risk of HORV associated with vancomycin against the risk of endophthalmitis.
- ❖ Reconsider using vancomycin with close sequential bilateral cataract surgery.
- ❖ Surgeons using intraocular vancomycin with sequential cataract surgery should be aware that in addition to delayed onset, HORV may not cause symptoms in the first eye and a dilated retinal examination may be the only way to detect it.
- ❖ Surgeons desiring an alternative to vancomycin for intracameral prophylaxis may consider cefuroxime or moxifloxacin⁴.

Recommendations for Management of HORV

- ❖ Consider avoiding intravitreal vancomycin if both bacterial endophthalmitis and HORV are in the differential.
- ❖ Consider ocular and/or systemic work-up for other syndromes (e.g. viral retinitis).
- ❖ Aggressive systemic and topical corticosteroids; consider peri- or intra-ocular steroids
- ❖ Early anti-VEGF treatment
- ❖ Early panretinal photocoagulation
- ❖ If you identify a patient with HORV, please submit the clinical data to the HORV registry site: (links from www.asrs.org or www.ascrs.org). Patient and surgeon names will be kept confidential.

ASCRS-ASRS HORV Task Force members: David F. Chang, MD, Steve Charles, MD, Dean Elliott, MD, Richard S. Hoffman, MD, J. Michael Jumper, MD, Nick Mamalis, MD, Kevin M. Miller, MD, Andre J. Witkin, MD, Charles C. Wykoff, MD

1. Nicholson LB, Kim BT, Jardon J, et al. Severe bilateral ischemic retinal vasculitis following cataract surgery. *Ophthalmic Surg Lasers Imaging Retina* 2014;45:338-342.
2. Witkin AJ, Shah AR, Engstrom RE, Kron-Gray MM, et al. Postoperative hemorrhagic occlusive retinal vasculitis. Expanding the clinical spectrum and possible association with vancomycin. *Ophthalmology* 2015; 122:1438-1451.
3. Chang DF, Braga-Mele R, Henderson BA, Mamalis N, et al. Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: Results of the 2014 ASCRS member survey. *J Cataract Refract Surg* 2015;41:1300–1305.
4. Braga-Mele R, Chang DF, Henderson BA, Mamalis N, et al. Intracameral antibiotics: Safety, efficacy, and preparation. *J Cataract Refract Surg* 2014;40:2134–2142.

This ASCRS-ASRS Alert is provided for informational and educational purposes only. It is not intended to mandate or establish a specific standard of care or dictate the treatment of any particular patients. ASCRS and ASRS members must make independent judgments about the treatment of their patients based on all the facts and circumstances relating to each patient's condition.