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Vancomycin-Associated Hemorrhagic Occlusive Retinal Vasculitis

Clinical Characteristics of 36 Eyes

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Purpose: To expand understanding of presentation, diagnosis, and outcomes of hemorrhagic occlusive retinal vasculitis (HORV).

Design: Retrospective case series.

Participants: Thirty-six eyes of 23 patients.

Methods: The American Society of Cataract and Refractive Surgery (ASCRS) and the American Society of Retina Specialists (ASRS) formed a joint task force to define clinical characteristics of HORV and to study its prevalence, cause, treatment, and outcomes. An online registry was established on both societies' web sites. Surveys were e-mailed to members of both societies soliciting cases of suspected HORV. A literature search was performed to uncover additional cases.

Main Outcome Measures: Historical data including intraoperative characteristics, images, treatment regimens, and visual and anatomic outcomes.

Results: Characteristic findings of HORV included unremarkable postoperative day 1 undilated examination, delayed-onset painless vision loss, mild anterior chamber and vitreous inflammation, sectoral retinal hemorrhages in areas of ischemia, and predilection for venules and peripheral involvement. Based on predetermined diagnostic criteria, 36 eyes of 23 patients were diagnosed with HORV. All eyes received intraocular vancomycin via intracameral bolus (33/36), via intravitreal injection (1/36), or through the irrigation bottle (2/36). Patients sought treatment with HORV 1 to 21 days after surgery or intravitreal injection. Visual results usually were poor: 22 of 36 eyes (61%) had 20/200 or worse visual acuity and 8 of 36 eyes (22%) had no light perception (NLP). Neovascular glaucoma developed in 20 of 36 eyes (56%). Seven eyes received additional intravitreal vancomycin after surgery; 5 of these 7 eyes had NLP visual acuity at the most recent examination. Three eyes received intravitreal corticosteroids and had final visual acuities of 20/40, 20/70, and hand movements.

Conclusions: Hemorrhagic occlusive retinal vasculitis is a rare, potentially devastating condition that can develop after cataract surgery or intraocular injection. All cases in this series were associated with intraocular vancomycin. Disease course and findings suggest that HORV is caused by a delayed hypersensitivity reaction to vancomycin. Early treatment with corticosteroids likely is beneficial. Subsequently, anti–vascular endothelial growth factor injections and panretinal photocoagulation are important to prevent neovascular glaucoma, a common complication. Avoidance of additional intravitreal vancomycin is recommended if HORV is suspected. *Ophthalmology 2016;■:1–13 Published by Elsevier on behalf of the American Academy of Ophthalmology*

In 2007, the European Society of Cataract and Refractive Surgeons published results from a large prospective, randomized, multicenter study demonstrating that prophylactic intracameral cefuroxime injection given at the end of cataract surgery reduced the rate of postoperative endophthalmitis by 5-fold.[1] Since that report, many ophthalmologists have advocated and adopted routine use of intracameral antibiotics during cataract surgery.[2–4] In 2 American Society of Cataract and Refractive Surgery (ASCRS) member surveys, the percentage of cataract surgeons using prophylactic intracameral antibiotics routinely during cataract surgery increased from 30% in 2007 to 50% in 2014.[2,5] Although approved throughout Europe, no commercial formulation of intraocular cefuroxime is available in the United States.[2] Therefore, the most common antibiotic used for endophthalmitis prophylaxis in 2014 in the United States was vancomycin (administered by 52% of those in the United States who use intracameral antibiotics), usually mixed by the operating room staff on the day of surgery. The popularity

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of intraocular vancomycin prophylaxis likely is based on several factors, including safety, availability, coverage, and efficacy against drug-resistant pathogens.[6]

In 2014, 2 cases of severe bilateral ischemic retinal vasculitis after cataract surgery were described for the first time.[7] An additional 4 cases (3 bilateral and 1 unilateral) were reported in 2015.[8] All 11 of the reported eyes in those 6 patients had undergone otherwise uncomplicated cataract surgery with prophylactic injection of intracameral vancomycin, and there was a delay of 1 to 14 days before the onset of the severe ischemic hemorrhagic retinal vasculitis. Visual outcomes were poor: 8 of 11 eyes had less than 20/100 visual acuity and 4 of 11 eyes had no light perception (NLP) vision. 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.[8]

Because of the popularity of intracameral vancomycin for endophthalmitis prophylaxis, the ASCRS and the American Society of Retina Specialists (ASRS) formed the joint HORV Task Force to analyze further the prevalence, potential cause, treatment, and outcomes of this newly described complication associated with intraocular surgery. The task force includes ASRS members Steve Charles, Dean Eliott, J. Michael Jumper, Andre J. Witkin, and Charles C. Wykoff, and ASCRS Cataract Clinical Committee members David F. Chang, Richard S. Hoffman, Nick Mamalis, and Kevin M. Miller. Presented here are the characteristics of all HORV cases known to the task force to date, as well as recommendations for prevention and management.

Methods

This was a retrospective case series. All data were collected by the physicians directly involved in the care of these patients at the individual institutions and were de-identified before submission to the HORV Task Force. The manuscript adheres to the guidelines and principles put forth by the Declaration of Helsinki. Institutional review board approval for collection of data was obtained through the Houston Methodist Hospital in Houston, Texas.

Cases were collected by 3 approaches. First, the HORV Task Force designed an online case registry on the ASRS web site for members to report new cases. Information about all surgical medications and adjuvants was requested with a particular goal of uncovering other associations in addition to (or besides) vancomycin. Retinal images, including optical coherence tomography images, fluorescein angiography images, and color fundus photographs, were reviewed for each case by retina specialist members of the task force. Second, to understand better the prevalence of this complication, online surveillance surveys were e-mailed to all ASCRS and ASRS members soliciting any cases of suspected HORV. Of note, surveys were worded carefully to attempt to avoid implication of vancomycin in relationship to HORV, because one of the goals of the surveys was to collect any potential cases of HORV that were not associated with vancomycin. Respondents who answered positively were sent additional queries for information that were followed up by task force retina specialists. Finally, a literature search was performed to uncover any additional cases of possible HORV reported since the initial articles were published in 2014 and 2015.[7,8] For a list of physicians who contributed data for this project, please see the Acknowledgments.

Data collected are listed in Table 1. Data for this article were gathered until September 1, 2016, and all cases were reviewed by the HORV Task Force. The task force established specific diagnostic criteria for HORV that are listed in Table 2. Suspected cases that did not meet these criteria, or that lacked sufficient data, were not included in the analysis.

Results

Identification of Cases

The HORV Task Force was notified about 35 patients with a possible diagnosis of HORV. Of these, 36 eyes of 23 patients had a complete data set, and the task force agreed that they had characteristic findings that met the diagnostic criteria of HORV. The demographics of these patients are listed in Table 3. Eleven eyes of 6 patients were presented in a previous report[8]; 3 eyes of 3 additional patients were described in recent case reports.[9–11] Examples of typical cases are shown in Figures 1, 2 and 3, and examples of more unique cases are shown in Figures 4 and 5.

Of the 12 patients who were excluded, 5 had no data provided to the task force, 2 had incomplete data without imaging or follow-up provided (vancomycin was used in both of these cases), and 2 had nearly complete data sets, but images, follow-up data, or both were not provided (vancomycin was used in both of these cases). The other 3 excluded cases had complete data sets and did not receive vancomycin during surgery, but the task force agreed that these cases did not represent HORV. Rather, these were thought likely to represent cases of cefuroxime toxicity, central retinal vein occlusion (CRVO), and gentamicin toxicity, respectively.

Table 1. Data Collected

Patient-Specific Data	Eye-Specific Data
Age	Operative
Gender	Procedure performed
Ethnicity	Laterality
Location	Surgery site
Medical history	Surgery date
Ocular history	Intraocular adjuvants used
Allergies	Route of administration
Systemic testing results	Antibiotic dose
Skin testing results	Manufacturer
	Preparation
	Surgical complications
	Postoperative
	Day 1 visual acuity
	Time until HORV presentation
	Presenting symptoms
	Treatment regimen
	Length of follow-up
	Most recent visual acuity
	Presence of neovascular glaucoma
	Use of additional antibiotics
	Pathology reports
	OCT images
	FA images
	Fundus images

FA = fluorescein angiography; HORV = hemorrhagic occlusive retinal vasculitis; OCT = optical coherence tomography.