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Acute Retinal Necrosis

Case presentation:

A 34 year old female with no past medical history presented with a one week history of left eye redness and blurry vision. Her visual acuity was 20/20 in the right eye and 20/30 in the left eye. Her pupils, extraocular movements, and intraocular pressures were within normal limits. Slit lamp exam was normal in the right eye but revealed 1+ conjunctival injection and 2+ anterior chamber cell in the left eye.

Dilated fundus exam was normal in the right eye. In the left eye, the exam revealed 1+ vitreous haze, disc edema, diffuse retinal hemorrhages, vascular sheathing, and peripheral retinal whitening (Figure 1). Optical coherence tomography (OCT) of the left eye showed hyperreflectivity of the inner retinal layers as well as peripapillary subretinal fluid consistent with the disc edema (Figure 2).

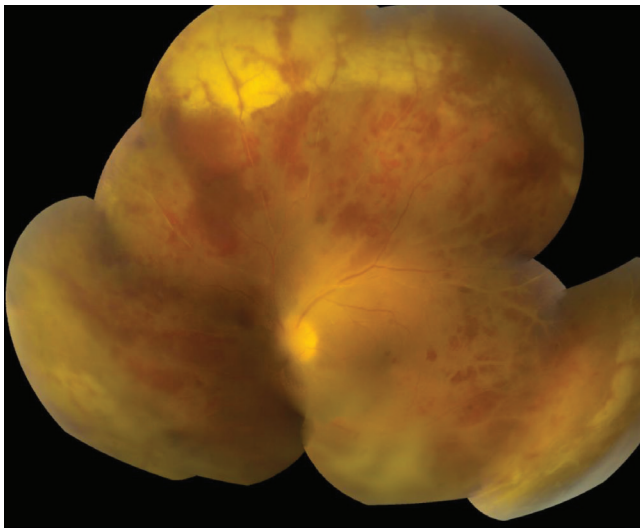

Figure 1: Color fundus photo of left eye at presentation. Exam shows vitreous haze, disc edema, vascular sheathing, retinal hemorrhages, and peripheral retinal whitening.

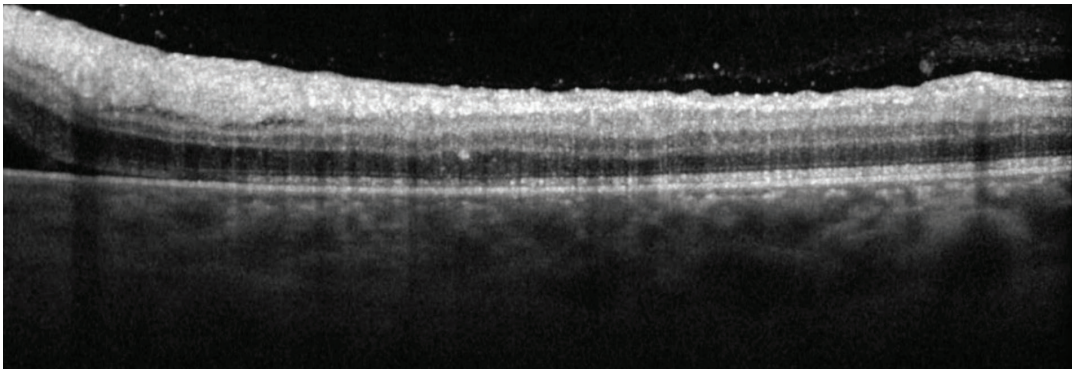

Figure 2 Optical coherence tomography image of left inferior macula at presentation. Inner retinal hyperreflectivity can be seen due to retinitis, and peripapillary subretinal fluid is present due to disc edema. Vitreous cells can be seen as well.

Due to the high suspicion for viral retinitis, the patient was sent to the hospital for further testing and management. Upon arrival, she was started on intravenous acyclovir. Anterior chamber tap of the left eye was performed, and the fluid was sent for viral polymerase chain reaction (PCR) testing. Subsequently, intravitreal injection of ganciclovir was performed. The PCR test was positive for varicella zoster virus (VZV). Despite treatment, progression of the disease caused her vision to decrease to 20/100 in the left eye. She continued to receive twice weekly intravitreal injections of ganciclovir. Her intravenous acyclovir was transitioned to oral valacyclovir 2 grams three times daily, and she was started on oral prednisone 30 milligrams to control the intraocular inflammation.

Two weeks after diagnosis, the patient unfortunately developed a rhegmatogenous retinal detachment that extended 360 degrees in the periphery. She underwent retinal detachment repair with scleral buckle, pars plana vitrectomy, endolaser, and silicone oil. As her retinitis resolved, the oral prednisone was tapered, and the valacyclovir was decreased to a prophylactic dose of 1 gram daily. The retina remained attached, and the silicone oil was successfully removed several months after the initial surgery. Her visual acuity in the left eye at her final follow-up was 20/250.

Discussion:

Acute retinal necrosis (ARN) is a potentially blinding necrotizing retinopathy caused by members of the Herpes virus family, and most commonly varicella zoster virus[1-7]. ARN is rare, with an estimated incidence of one case per 2 million people per year [8-9]. ARN often affects otherwise healthy adults with no racial or sex-based predilection. However, there is evidence that suggests an underlying genetic component, in particular with certain human leukocyteantigen (HLA) expressions such as HLA-DQw7 and DR4 in Caucasian patients and HLA-Aw33, B44, and DRw6 antigens in Japanese patients[10-11].

Most cases of ARN are unilateral, but up to 30% of cases can result in bilateral ARN [12]. Therefore, when ARN is suspected, it is important to examine the fellow eye carefully for any involvement. Examination findings can include anterior chamber and vitreous inflammation, retinal vasculitis, retinal hemorrhages, and multifocal, peripheral, and confluent areas of retinal whitening consistent with retinitis. Optic disc edema can be seen in cases of optic nerve involvement. The peripheral lesions can rapidly progress to the posterior pole [13]. In later stages of the disease, vitreous traction and retinal atrophy can commonly lead to retinal detachment, with prior studies reporting rates from 47% to 66% [14-17]. Other complications of ARN include hypotony, phthisis, proliferative vitreoretinpathy, epiretinal membrane, macular edema, and optic nerve atrophy[13].

Diagnosis of ARN is made clinically as defined by the American Uveitis Society criteria: 1) at least one focus of peripheral retinal necrosis with well-defined borders, 2) rapid circumferential progression when antiviral therapy is not instituted, 3) occlusive vasculopathy (with arteritis), and 4) prominent vitreous and anterior chamber inflammation[18]. Differential diagnosis includes progressive outer retinal necrosis, cytomegalovirus (CMV) retinitis, syphilis, toxoplasmosis, tuberculosis, endophthalmitis, Behcet syndrome, and intraocular lymphoma.
Testing for HIV/AIDS is also important to assess for immunocompromised status. More recently, PCR testing has become a useful tool to establish a diagnosis. The testing can be performed using small samples of either aqueous and vitreous humor, although aqeous is usually preferable because it is safer to obtain[13].

Treatment of ARN should be initiated shortly after suspected diagnosis due to the rapid progression of untreated disease. Systemic antivirals are important in treating the retinitis and reducing the risk of fellow eye involvement. For active retinitis, treatment can be initiated with intravenous acyclovir 10 mg/kg three times per day or oral valacyclovir 2 grams three or four times per day. Both drugs have similar bioavailability, and either medication can be used to manage ARN. After induction therapy, standard practice is to maintain patients on a prophylactic dose (usually valacyclovir 1 gram daily) for at least six months[19].

Intravitreal agents are commonly used in combination with systemic antivirals. Intravitreal injection of foscarnet or ganciclovir can be used to achieve immediate therapeutic levels of intraocular antiviral drug [19]. Topical and oral steroids are also commonly used in conjunction with antivirals in order to decrease inflammation[13]. Oral steroids are typically started at least 24-48 hours after initiation of antiviral therapy.

Laser retinopexy has been used as a possible method to prevent retinal detachment. Early pars plana vitrectomy has also been proposed to remove intraocular inflammation and reduce risk of retinal detachment by releasing areas of traction. Some small case series have been performed, but there currently no clear evidence that either treatment is effective in the prophlyaxis of retinal detachment.

When rhegmatogenous retinal detachment occurs, surgical techniques for repair include pars plana vitrectomy, scleral buckle, endolaser, long-acting gas, and/or silicone oil tamponade. Unfortunately, even in some cases of anatomic success, visual outcome can be poor especially when the infection involves the macula or optic nerve[20].

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At the forefront of clinical research

The Retina Care Center continuously conducts clinical trials at our Baltimore, MD office. Our clinical research coordinators will be happy to discuss the inclusion/exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

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Enrolling Studies:

Dry AMD

Parasol: A Phase 2b, Randomized, Double-masked, Multicenter, Dose ranging, Sham-controlled Clinical Trial to Evaluate Intravitreal JNJ-81201887 (AAVCAGsCD59) Compared to Sham Procedure for the Treatment of Geographic Atrophy (GA) Secondary to Age-related Macular Degeneration (AMD)

Wet AMD

ShORe: A Phase 3, Multi-centre, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Atmosphere: A Phase 2b/3, Randomized, Partially Masked, Controlled Clinical Study to Evaluate the Efficacy and Safety of RGX-314 Gene Therapy in Participants with nAMD

NPDR

Spectra: A Phase 2 study to evaluate the safety and efficacy of OPL-0401 in patients with Non-proliferative Diabetic Retinopathy

Retinal Vein Occlusion

Quasar: A Phase 3, Randomized, Double-Masked, Active-Controlled Study of the Efficacy and Safety of Aflibercept 8 mg in Macular Edema Secondary to Retinal Vein Occlusion

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