THE RETINA PARTNERS

Encino Santa Monica Valencia Thousand Oaks Century City

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Case of the Month – March 2019

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A 59 year old man undergoing chemotherapy for Hodgkin's Lymphoma presented with a 2 week history of progressively worsening vision in the right eye. His visual acuity was 20/400 and 20/20 in the right and left eyes respectively. Intraocular pressures were normal. Examination of the anterior segment was significant for fine keratic precipitates, and trace cells in the anterior chamber of the right eye, without other stigmata of inflammation, in either eye. There was no vitritis. Imaging of the right eye is shown below. Examination of the posterior segment of the left eye was unremarkable.

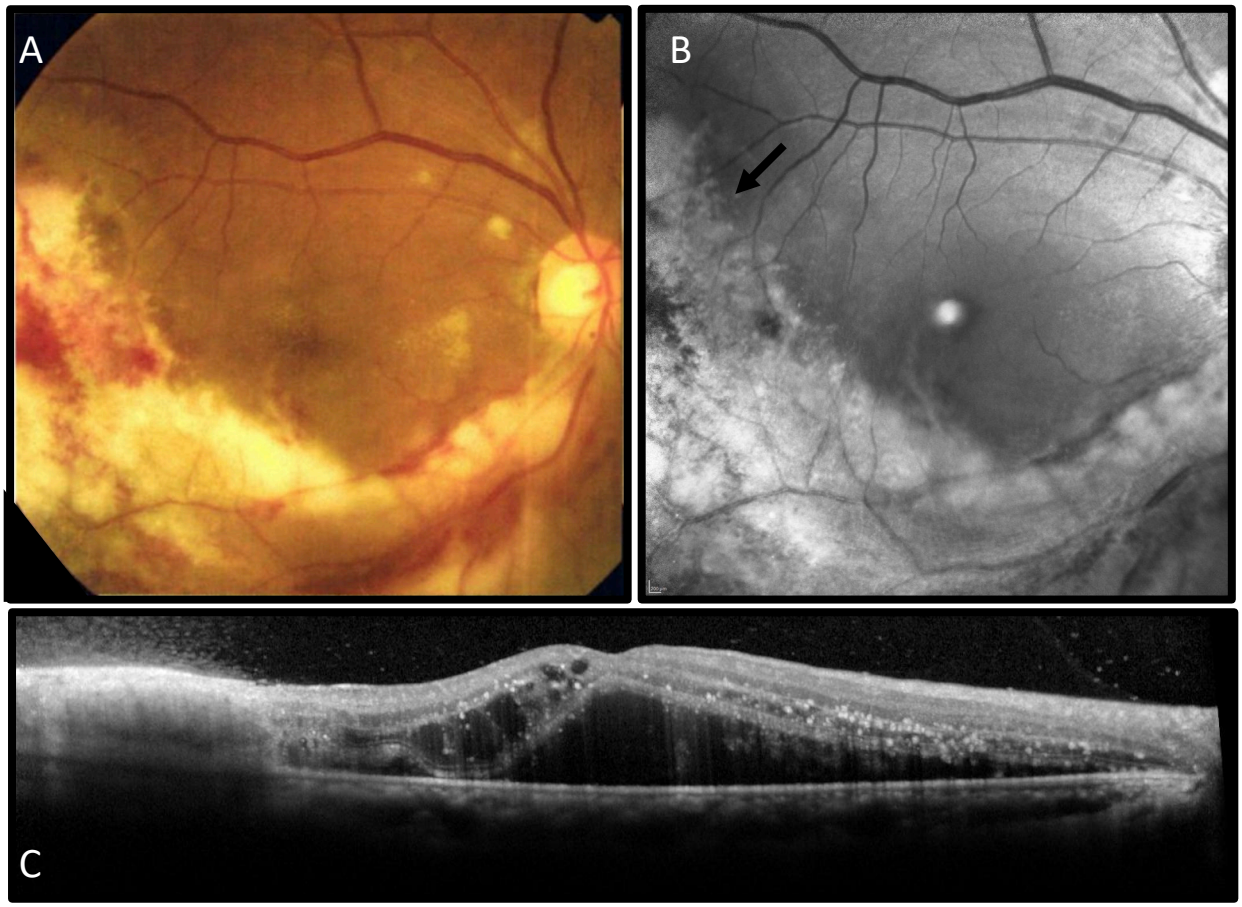

Figure 1: A. Color fundus photograph of the right eye showing intraretinal hemorrhages, and retinal whitening along the inferior major arcade and inferior macula. The inferior major arcades are narrowed and irregular indicating vascular involvement. Note the blunted foveal reflex and fine exudates indicating macular edema. **B.** Near infrared image better delineating the areas of involved retina. Fortunately, the fovea is spared. Note the granular edges (arrow) characteristic of CMV retinitis. **C.** OCT of the macula shows full thickness hyper-reflectance with complete loss of definition between the retinal layers. There is subfoveal fluid, intraretinal fluid and intraretinal hyper-reflective foci.

Differential Diagnosis: Acute retinal necrosis, progressive outer retinal necrosis, CMV retinitis, branch retinal vein occlusion.

Clinical Course:

The patient was diagnosed with cytomegalovirus associated retinitis in the right eye. Because of the proximity to the fovea, and severe immune compromise, he was referred immediately to an inpatient setting where immediate induction therapy was begun with intravenous and intravitreal ganciclovir. An anterior chamber paracentesis confirmed CMV retinitis by PCR testing. CMV viremia with a very high viral was confirmed by blood testing. He was discharged home one week later on oral valganciclovir which was supplemented with intravitreal ganciclovir as an outpatient. Scheduled doses of chemotherapy were held during this period to allow the immune system to reconstitute. At 1 month follow up, the patient's vision had improved to 20/60 with consolidation of the retinitis lesions and resolution of the macular edema and subfoveal fluid. A follow up color image, near infrared image and OCT are shown below.

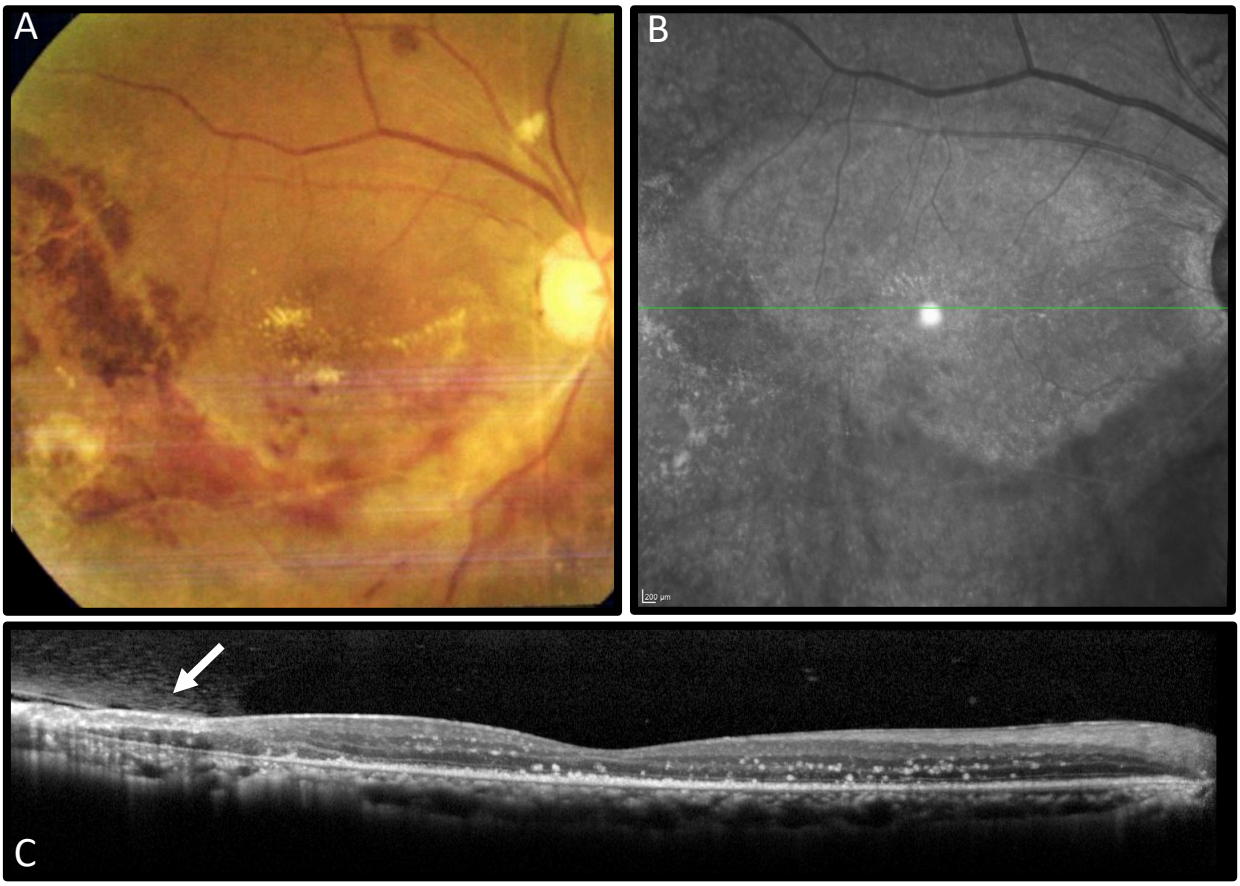

Figure 2: A. Color fundus photo showing resolving and consolidated retinal whitening, attenuation of the inferior vascular system, persistent intraretinal hemorrhages and intraretinal exudates. There is increased optic nerve pallor. **B.** Near infrared imaging clearly shows the areas of previously involved retina which have become atrophic and appear darker than the adjacent uninvolved retina. **C.** OCT of the macula shows preservation of the foveal contour with an attenuated ellipsoid band, intraretinal hyper-reflective foci and evolving atrophy of the previously seen retinitis lesion (Arrow).

Discussion:

Cytomegalovirus retinitis was first described in 1964, and became increasingly common during the HIV/AIDS epidemic of the 1980's. Prior to the advent of HAART therapy, 25-42% of AIDS patients developed CMV retinitis before death. Untreated, this infection almost universally leads to bilateral blindness in this patient population. Fortunately, with the introduction of HAART therapy and targeted anti-viral drugs like ganciclovir and foscarnet, the disease is now much less common than it previously was, and is treatable when it occurs. While initially diagnosed almost exclusively in AIDS patients, CMV retinitis has become increasingly recognized as a complication of other immunocompromising conditions. This most commonly includes patients on immunosuppression for inflammatory diseases, or those, like our patient, who are immunosuppressed from chemotherapy. Unilateral CMV retinitis has even been reported in patients who are locally immunosuppressed from intravitreal or periocular steroid injections.

It is therefore important to recognize CMV retinitis presenting in patients who do not have HIV/AIDS. Classically, CMV infection presents as a slowly progressing retinitis and retinal vasculitis. The anterior segment and vitreous are typically quiet with the exception of fine stellate keratic precipitates. The posterior segment shows regional granular whitening of the retina with associated vasculitis, intraretinal hemorrhages and optic nerve hyperemia. The posterior pole, peripheral retina or both may be affected. The disease may be unilateral or bilateral on presentation, but if left untreated, progression to bilateral disease is common. In HIV negative patients, the clinical manifestations may differ from the classic presentation described, with more anterior segment inflammation, more vitritis and more widespread vasculitis in areas free of retinitis. In some cases, the clinical picture may mimic that of acute retinal necrosis associated with HSV or VZV infection.

The diagnosis of CMV retinitis is typically based on the clinical examination and history. However, it can be confirmed by polymerase chain reaction testing for CMV DNA obtained from aqueous or vitreous fluid. It is essential that evaluation includes systemic testing for CMV viremia, a search for the underlying cause of immune compromise if not known, and treatment of that underlying problem when possible. Therefore, a coordinated approach involving the patient's internist, in consultation with an infectious disease specialist should be employed whenever possible. The bedrock of treatment is systemic therapy with oral or intravenous ganciclovir. Systemic therapy is necessary to treat underlying viremia and prevent involvement of the contralateral eye if not yet involved. Adjunctive therapy with intravitreal injections of ganciclovir, foscarnet, or a combination should be considered in cases with extensive retinal involvement, or when the macula is threatened by the infection, as it was in our case. Intravitreal delivery of medication allows for a more rapid and higher concentration delivered to the infected tissue than systemic therapy alone. Once the retinitis becomes inactive, the patient should be maintained on a lower dose of oral valganciclovir until their immune status is normalized. Late complications of the infection include reactivation of the virus should immune function wane, and rhegmatogenous retinal detachment secondary to necrotic retinal breaks. Because of poor outcomes in patients who develop a secondary rhegmatogenous detachment, some surgeons advocate for prophylactic laser barricade around the necrotic regions of the retina once the infection is controlled.

Fortunately, our patient was diagnosed prior to involvement of his fovea. He was promptly and aggressively treated which preserved his central vision. This was made possible by excellent coordination of care with his infectious disease specialist, and his oncologist.

Acknowledgements: We would like to acknowledge the excellent UCLA residents and fellows who helped in the care of this patient while he was hospitalized.

Take Home Points

- CMV retinitis is an uncommon, but potentially blinding infection of the retina.
- While classically presenting in the setting of HIV/AIDS, CMV retinitis can occur in the setting of immune compromise in HIV negative patients.
- A multi-disciplinary approach to the diagnosis and treatment of CMV retinitis should be employed with attention paid to the patient's systemic disease burden and correction of the underlying immunocompromising condition when possible.
- Treatment of CMV retinitis should include systemic therapy with adjunctive intravitreal therapies.

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