Case Study
Frost in the Forecast: A Case of CMV Retinitis

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Background
Ophthalmologic manifestations of HIV/AIDS were first described in 1982. During the AIDS epidemic, 30% of people infected with HIV developed CMV retinitis. It was typically a late manifestation of AIDS and patients rarely survived greater than two years following diagnosis. With the advent of highly active antiretroviral therapy (HAART), the incidence of CMV retinitis and other opportunistic infections have declined. The morbidity of CMV retinitis has also declined with the development of effective antiviral therapies. We present a case of CMV retinitis treated with systemic and intravitreal antiviral therapy in a patient with newly diagnosed HIV.

Patient Case
Our patient is a 36-year-old African American male presenting from an outside ophthalmologist with two weeks of blurred vision and headache which evolved into a wedge of temporal visual field loss. He noted associated floaters and flashes over the prior week as well.

His recent medical history was notable for cough, weight loss, diarrhea, and night sweats one month prior to onset of visual symptoms. At the time, he presented to an outside hospital emergency department where he tested positive for HIV with a CD4 count of 57 and a high viral load, as well as CMV via PCR with low DNA quantification. CT chest also demonstrated pulmonary nodules. Otherwise, cryptococcus antigen, total syphilis, toxoplasmosis, and QuantiFERON gold were negative. Shortly thereafter, he was initiated on HAART and appropriate prophylactic antimicrobial therapies (Bactrim, azithromycin, ethambutol). Ten days later, he noted headaches and visual changes for which he was sent to the emergency department due to concern for a central nervous system infection. Work-up at this time, including a lumbar puncture, CT head, and blood cultures, were unremarkable. Patient was discharged with instructions to follow-up outpatient with ophthalmology.
When patient presented, his exam was notable for 20/20 visual acuity in the right eye (OD) and 20/30 visual acuity in the left eye (OS). Pupils were without afferent pupillary defect but was notably irregular in the left. Intraocular pressures were 12 OD and 18 OS, and he had an inferotemporal visual field deficit OS. On slit lamp examination, the right eye was quiet with few scattered cotton-wool spots noted posteriorly. The left eye was significant for 2+ cell in the anterior chamber and trace cell in the anterior vitreous. In the posterior pole, the optic nerve was hyperemic, there were scattered CWS throughout the posterior pole, and most notably perivascular sheathing of largely nasal and posterior pole vessels. Peripherally, there was retinal whitening superonasally from 9 to 11 o’clock with patches of vascular sparing. (Figure 1)

Figure 1: A. Fundus photo of right eye at presentation; B. Fundus photo of left eye at presentation; C. Fundus photo of left eye at three weeks; D. Fundus photo of left eye at six weeks.
Fluorescein angiography was completed with early filling defect noted superonasally in the left eye with corresponding staining in the late phase. There was also patchy perivascular leakage of nasal vessels with some involvement of temporal arcades. The right eye appeared normal. (Figure 2)

OCT macula of the left eye showed vitritis, but was otherwise normal bilaterally; however, OCT retina of the periphery demonstrated notable inner to full thickness retinal thickening, subretinal fluid, and overlying dense vitritis. (Figure 3-5)
At this initial visit, an aqueous paracentesis was performed, and the sample was sent for CMV DNA quantification. Patient was also started on oral valganciclovir at an induction dose of 900mg two times daily for three weeks, prednisolone acetate four times daily in light of the anterior chamber reaction, and atropine two times daily. The patient was followed closely. The CMV DNA quantification came back with 1.7 million copies/mL, confirming the diagnosis of CMV. At one week on the oral valganciclovir and prednisolone, the areas of retinal whitening appeared to be consolidating. Given perivascular involvement within the posterior pole, intravitreal foscarnet (2.4mg/0.1mL) was administered at this time. At week three, exam was notable for decreased anterior chamber inflammation and further consolidation of retinal whitening. Valganciclovir was decreased to a maintenance dose of 900mg daily. By six weeks, there were rare, pigmented cell in the anterior chamber and the superonasal patch of retinal whitening now demonstrated discrete borders with pigmentary, or RPE, changes suggesting resolution of active inflammation.

Discussion
Cytomegalovirus is a double-stranded DNA virus in the Herpesviridae family. It is associated with HIV/AIDS with CD4 count less than 50, leukemia, lymphoma, and severe immunosuppression. Systemic involvement may include encephalitis, pneumonitis, and colitis. In the eye, it often causes a retinitis via hematogenous spread with infection of vascular endothelial cells and subsequent spread to perivascular retinal cells.

Typically, patients present with decreased visual acuity, floaters, flashes, and scotomas; however, up to 54% may be asymptomatic. Anterior chamber and vitreous reactions are usually minimal. Notably, in our patient there was an atypical moderate anterior chamber reaction with likely spill over into the anterior vitreous. CMV
retinitis is classified by three descriptive categories and zones of involvement. The three descriptive categories include fulminant, granular, and perivascular. Fulminant retinitis is the classic “pizza pie fundus” and includes dense well-demarcated areas of retinal hemorrhage usually along vascular arcades. Granular, or indolent, retinitis involves mild opacification of the retina starting in the periphery and progressing slowly with few retinal hemorrhages. Perivascular retinitis, or frosted branch angiitis, involves perivascular exudation surrounding the retinal vessels as seen in our patient. Zones are demarcated based on proximity to the macula and optic nerve. Zone 1 is considered vision threatening and is defined as within 1-disc diameter of the optic disc or 2-disc diameters from the fovea. Zone 2 is between zone 1 and the equator and zone 3 is anterior to the equator. A serious sequelae of a viral retinitis is progressive outer retinal necrosis, which is a rapidly progressive viral retinitis affecting the outer retinal layers with eventual full thickness involvement.\textsuperscript{6} It is most often seen with varicella zoster infections, however, may be seen with CMV and herpes simplex virus, as well.

Diagnosis is typically clinical, though an aqueous or vitreous tap sent for DNA quantification or PCR may be a helpful diagnostic tool. Serologic antibodies have not, however, shown to be helpful in diagnosis. Treatment involves systemic antiviral therapy with consideration of intravitreal antiviral therapy in typically vision threatening cases. The most commonly used systemic agent is valganciclovir as it comes in an oral formulation with comparable bioavailability to intravenous administration. It is administered as 900mg two times daily for three weeks followed by 900mg daily for maintenance. We must, however, remain mindful of the myelosuppressive effects of the agent, particularly in patients immunosuppressed due to chemotherapy or hematologic malignancy. Other systemic options include ganciclovir, foscarnet, and cidofovir. Cidofovir, however, has been associated with hypotony and anterior uveitis and has fallen out of favor accordingly. Long term, patients should be monitored for retinal detachment even after successful treatment.\textsuperscript{6}

While the incidence and associated morbidity of CMV retinitis has declined, it is still a potentially blinding infection. It is important to screen and evaluate immunosuppressed patients with changes in vision. This case illustrates a frosted angiitis form of CMV retinitis in a newly diagnosed patient with HIV. His case demonstrates the importance and efficacy of early detection and appropriate treatment in obtaining a good clinical outcome.