The Ochsner Journal 15:473–475, 2015

Atypical Retinal Lesion in a Heart Transplant Patient: Investigation and Management

Laurence W. Arend, MD, FACS, D. Anthony Mazzulla, MD, Jennifer A. Spiegel, MD

Department of Ophthalmology, Ochsner Clinic Foundation, New Orleans, LA

Background: A cardiac transplant patient presented to the Ochsner ophthalmology clinic with flashes of light in the left eye and a retinal lesion of unclear etiology.

Case Report: A 59-year-old male cardiac transplant patient was referred by an outside eye physician. Examination of the anterior chamber of his left eye showed inflammation, and a large hypopigmented lesion was discovered in the nasal retina of the left eye. The patient was admitted to the hospital. Empiric treatment was initiated, and all workup results were negative. During the next several days, the patient's retinal lesion extended. A tap of the eye's vitreous and aqueous fluid yielded no diagnosis. The patient underwent a chorioretinal biopsy through a pars plana vitrectomy. Fluid removed from the vitreous cavity was sent for polymerase chain reaction (PCR) testing, and intravitreal antibiotics were injected. The results of the PCR were negative for all organisms. However, the lesion stabilized, and the patient has remained stable on oral valganciclovir.

Conclusion: Cytomegalovirus PCR testing has 95% sensitivity in untreated patients but only 48% sensitivity in patients treated with systemic ganciclovir, foscarnet, or both. Cytomegalovirus retinitis was determined to be a possible diagnosis; however, the possibility exists that the patient had developed a fungal subretinal abscess.

Keywords: *Cytomegalovirus retinitis, eye infections–fungal, intravitreal injections, polymerase chain reaction, vitrectomy*

Address correspondence to Laurence W. Arend, MD, FACS, Department of Ophthalmology, Ochsner Clinic Foundation, 1514 Jefferson Hwy., New Orleans, LA 70121. Tel: (504) 842-3995. Email: larend@ochsner.org

INTRODUCTION

A cardiac transplant patient presented to the Ochsner ophthalmology clinic with flashes of light in the left eye and a retinal lesion of unclear etiology.

CASE REPORT

A 59-year-old male presented to the Ochsner Medical Center Department of Ophthalmology retina service through a referral from an outside eye physician. The patient's chief complaint was flashes of light in the left eye starting 10 days prior.

The patient's medical history included a heart transplant 3 months prior. His postoperative course included a chest wound infected by *Candida* and treated with fluconazole, with negative blood cultures. The patient also recently had had a urinary tract infection that was culture positive for *Pseudomonas aeruginosa* and treated with levofloxacin. Blood cultures were again negative. The patient's medications included tacrolimus 3 mg every 12 hours, valganciclovir 450 mg daily, fluconazole 400 mg daily, and sulfamethoxazole/trimethoprim 800 mg/160 mg three times per week.

On examination, the patient's visual acuity was 20/50 in both eyes. The examination of the anterior chamber of his left eye revealed white blood cells distributed throughout the aqueous fluid, consistent with inflammation. On dilated fundus examination, the vitreous showed minimal signs of inflammation. However, a large hypopigmented lesion was discovered in the nasal retina of the left eye (Figure 1). The lesion was somewhat thickened with overlying hemorrhage and pigment. The blood vessels overlying the lesion appeared mildly attenuated but otherwise normal. No similar lesion was found in the right eye.

The differential diagnosis focused on possible opportunistic infection related to immunosuppression secondary to organ transplantation, including cytomegalovirus (CMV) retinitis, herpetic retinitis (progressive outer retinal necrosis vs acute retinal necrosis), *Pseudomonas* abscess, *Candida* chorioretinitis, toxoplasmic chorioretinitis, and infection by less common organisms such as *Pneumocystis* and *Aspergillus*.[1] Choroidal lymphoma was also considered.

The patient was admitted to the hospital under the transplant service, and the infectious disease service was consulted to aid in the patient's workup and management. Because of the possibility of *Pseudomonas* infection, intravenous piperacillin/tazobactam was initiated at a dose of 4.5 g every 6 hours. Because of the concern for possible CMV infection, intravenous ganciclovir was started at a dose of 2.5 mg/kg every 12 hours. Because of the patient's history of *Candida* wound infection, fluconazole was

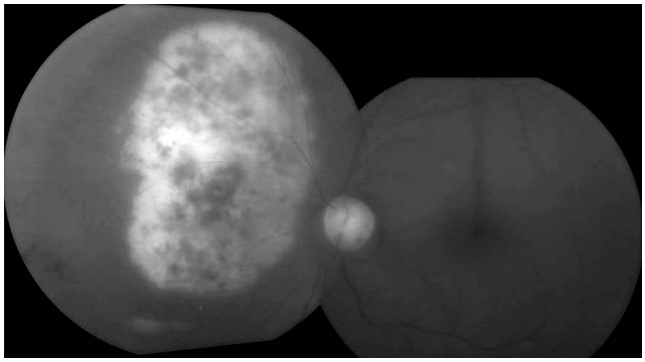

Figure 1. Chorioretinal lesion of left eye on initial presentation.

continued at a dose of 400 mg per day. Topical prednisolone 1% and atropine 1% eye drops were also started to help manage the patient's ocular inflammation.

As part of normal follow-up care, the patient's serum had been recently tested and was polymerase chain reaction (PCR) negative for CMV DNA. A previous QuantiFERON-TB Gold test was negative. Results of retests were also negative. Additional workup included PCR testing for herpes simplex virus (HSV) type 1 and 2, serum cryptococcal antigen and antibodies, *Histoplasma* antigen, *Toxoplasma* DNA, and a rapid plasma reagin test. All results were negative. The patient's blood and urine were cultured and showed no growth. The intravenous piperacillin/tazobactam was discontinued.

Three days later, the patient's retinal lesion had extended (Figure 2). He also complained of a headache. Magnetic resonance imaging was not possible because of metal hardware, but a computed tomography scan showed encephalomalacia in the occipital lobe compatible with a known prior infarct but no acute process. One day later, the retinal lesion had extended even further. Samples of the aqueous and vitreous fluids of the left eye were collected and sent for testing.[2] During the procedure, antibiotics were injected into the vitreous cavity, including voriconazole 50 mcg in 0.1 mL, vancomycin 1.0 mg in 0.1 mL, and ceftazidime 2.25 mg in 0.1 mL.[3,4] The Gram stain of the fluid samples showed no polymorphonuclear leukocytes or organisms. The oral antifungal agent administered to the patient was changed from fluconazole to voriconazole because of improved bioavailability and possible organism resistance.[3,4]

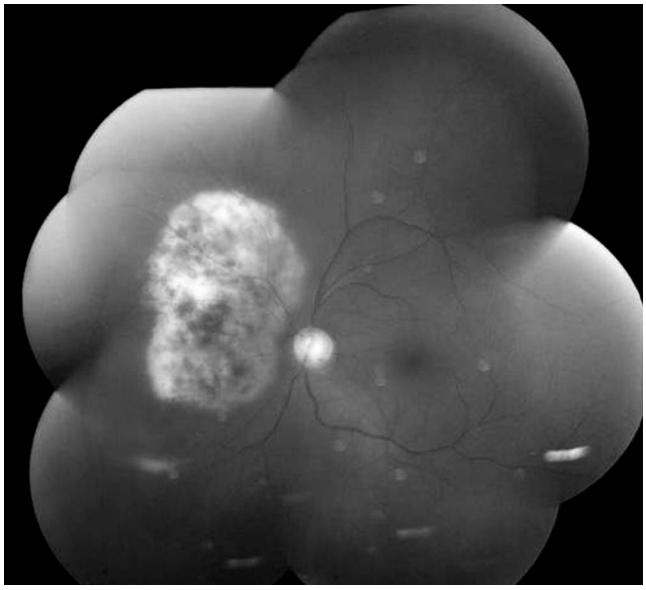

Figure 2. Extension of chorioretinal lesion 3 days after initial presentation.

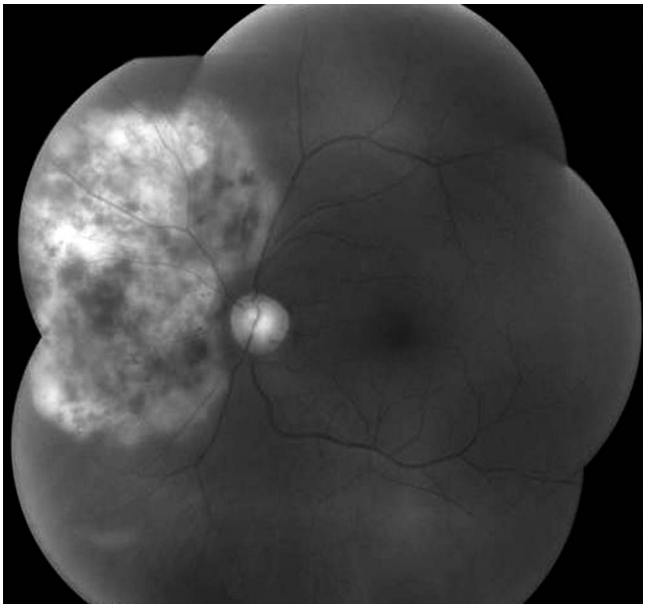

Figure 3. Continued extension of chorioretinal lesion.

The next day's bedside examination showed even further extension of the retinal lesion (Figure 3). The patient was scheduled for a chorioretinal biopsy through a pars plana vitrectomy the following day. Fluid removed from the vitreous cavity during the surgery was sent for flow cytometry and for PCR to test for CMV, HSV-1 and -2, varicella zoster virus, and *Toxoplasma gondii*.[5-8] At the end of the surgery, 2 antibiotics were injected into the vitreous cavity: voriconazole 50 mcg in 0.1 mL and ganciclovir 2 g in 0.1 mL.

The results of the PCR were negative for all organisms. The Gram stain showed rare gram-positive cocci that were determined to be a contaminant, as the sample did not grow any organisms. A potassium hydroxide preparation showed no yeast or fungal elements. A stain for acid-fast bacilli was negative. Flow cytometry was negative. The biopsy results showed choroidal tissue with a few giant cells, numerous pigmented melanocytes, and chronic inflammatory cells (lymphocytes and plasma cells) (Figure 4). We suspected that the patient had developed a fungal subretinal abscess that responded to intravitreal voriconazole.

The patient was discharged for follow-up as an outpatient. Oral valganciclovir and voriconazole were continued at home. The voriconazole was eventually discontinued when all intraocular fungal cultures were negative. The lesion stabilized, and no further progression was seen on this regimen (Figure 5). The patient has remained stable on oral valganciclovir.

DISCUSSION

This case was puzzling because of the patient's complicated medical history and a lesion appearance that was

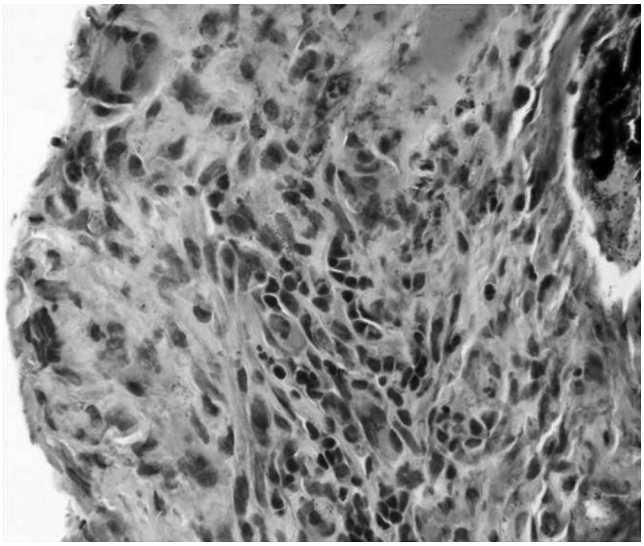

Figure 4. Chorioretinal biopsy specimen with inflammatory cells (hematoxylin and eosin stain).

atypical for the opportunistic infections in the differential diagnosis. Further investigation revealed that the sensitivity of the PCR test for CMV is drastically reduced in patients who have received systemic treatment. McCann et al published a series in which they used a PCR-based assay for detection of CMV DNA in vitreous samples.[5] They tested 19 vitreous samples from patients with acquired immunodeficiency syndrome (AIDS) who had untreated CMV retinitis and 40 vitreous samples from patients with AIDS who had been treated with systemic ganciclovir, foscarnet, or both. CMV DNA was detected in 18 of 19 samples from patients with untreated CMV retinitis. CMV DNA was detected in 19 of 40 vitreous samples from patients with previously treated CMV retinitis. CMV DNA was not detected in any of 69 patients without a clinical diagnosis of CMV retinitis. The McCann et al study reported an estimated sensitivity of 95% in detecting systemically untreated CMV retinitis and a sensitivity of 48% in detecting CMV retinitis that had been systemically treated.

McCann et al also tested for CMV DNA in 54 vitreous samples from immunocompetent patients and in 15 vitreous samples from patients with AIDS who had vitreoretinal inflammation from other causes.[5] The authors indicated that the assay did not give false-positive results in these patients.

CONCLUSION

CMV retinitis was a possible diagnosis in our immunosuppressed patient. However, the lesion's atypical appearance was not entirely convincing for a diagnosis of CMV. The possibility exists that the patient had developed a fungal subretinal abscess that finally responded to the intravitreal voriconazole injected during the vitrectomy.

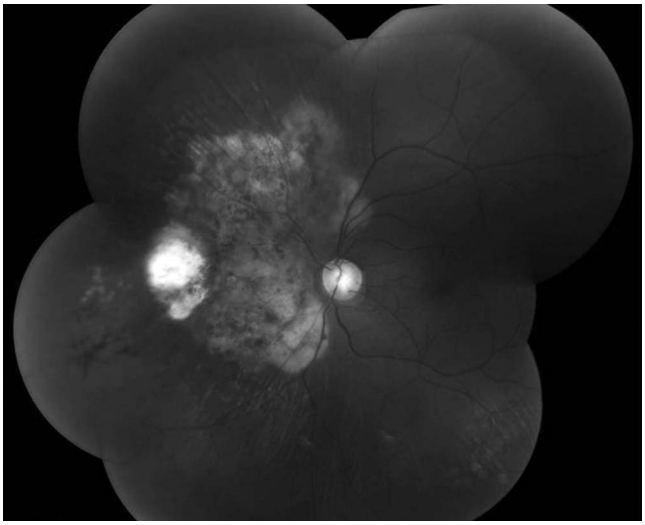

Figure 5. Postoperative day 1, leftmost white area is site of biopsy where bare sclera can be seen.

ACKNOWLEDGMENTS

The authors have no financial or proprietary interest in the subject matter of this article.

REFERENCES

1. Elkins BS, Holland GN, Opremcak EM, et al. Ocular toxoplasmosis misdiagnosed as cytomegalovirus retinopathy in immunocompromised patients. *Ophthalmology*. 1994 Mar; 101(3):499-507.
2. Rothova A, de Boer JH, Ten Dam-van Loon NH, et al. Usefulness of aqueous humor analysis for the diagnosis of posterior uveitis. *Ophthalmology*. 2008 Feb;115(2):306-311.
3. Jang GJ, Kim KS, Shin WS, Lee WK. Treatment of candida chorioretinitis with voriconazole. *Korean J Ophthalmol*. 2005 Mar; 19(1):73-76.
4. Riddell J 4th, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis*. 2011 Mar 1;52(5):648-653. doi: 10.1093/cid/ciq204.
5. McCann JD, Margolis TP, Wong MG, et al. A sensitive and specific polymerase chain reaction-based assay for the diagnosis of cytomegalovirus retinitis. *Am J Ophthalmol*. 1995 Aug;120(2): 219-226.
6. Fox GM, Crouse CA, Chuang EL, et al. Detection of herpesvirus DNA in vitreous and aqueous specimens by the polymerase chain reaction. *Arch Ophthalmol*. 1991 Feb;109(2):266-271.
7. Garweg J, Fenner T, Böhnke M, Schmitz H. An improved technique for the diagnosis of viral retinitis from samples of aqueous humor and vitreous. *Graefes Arch Clin Exp Ophthalmol*. 1993 Sep;231(9):508-513.
8. Stewart JF, Croxson MC, Powell KF, Polkinghorne PJ. Identification of cytomegalovirus in vitreous using the polymerase chain reaction. *Aust N Z J Ophthalmol*. 1993 Aug; 21(3):165-169.

This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge.