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CYTOMEGALOVIRUS RETINITIS ASSOCIATED WITH OCCLUSIVE VASCULOPATHY IN AN ELDERLY, HUMAN IMMUNODEFICIENCY VIRUS–NEGATIVE MAN

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Abstract

Purpose—To present a case of cytomegalovirus (CMV) retinitis associated with occlusive vasculopathy presenting as sudden unilateral loss of vision in a human immunodeficiency virus–negative elderly man.

Methods—Clinical case report and literature review.

Results—An 84-year-old Chinese man with diabetes mellitus and primary open-angle glaucoma was seen in consultation by our uveitis service for evaluation of sudden vision loss in the right eye. Examination revealed an occlusive retinal vasculopathy. An extensive diagnostic workup was performed, including fluorescein angiography, serologic testing for infectious etiologies including syphilis and tuberculosis and a temporal artery biopsy. The patient was treated with high-dose oral prednisone, after which the biopsy returned negative for giant-cell arteritis. Three weeks after initial presentation, the patient was noted to have a new area of retinitis in the temporal periphery. An anterior chamber paracentesis was performed, and the fluid was sent for directed polymerase chain reaction testing, which returned positive for CMV. Human immunodeficiency virus testing was negative. He was treated with oral valganciclovir and intravitreal foscarnet injections and the infection subsequently resolved.

Conclusion—Cytomegalovirus infection can be associated with occlusive vasculopathy in human immunodeficiency virus–negative individuals. The diagnosis of CMV retinitis should be considered in patients with human immunodeficiency virus–negative who have other conditions

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that may compromise immune function, particularly advanced age, diabetes mellitus, malignancy, or use of immunosuppressive agents.

Keywords

herpetic eye disease; retinitis; uveitis; vascular occlusion

Cytomegalovirus (CMV) retinitis is common in patients with profound immunosuppression in the setting of human immunodeficiency virus (HIV) infection and is the most common reason for visual acuity loss in patients with AIDS.^{1,2} Studies of the ocular complications of HIV/AIDS before the advent of highly active antiretroviral therapy found that one-third or more of patients developed CMV retinitis.³

Although CMV retinitis can also occur in patients with HIV-negative, the majority of such patients have other identified causes of relative immunosuppression, such as advanced age, diabetes mellitus, malignancy, or use of corticosteroids and/or noncorticosteroid immunosuppressive agents.^{4,5} We describe here an elderly, diabetic patient who presented with occlusive retinal vasculopathy before the development of CMV retinitis.

Case Report

An 84-year-old Chinese man with a history of primary open-angle glaucoma, Type II diabetes mellitus, chronic kidney disease, congestive heart failure, coronary artery disease, systemic hypertension, and hyperlipidemia was seen in consultation by our uveitis service for evaluation of sudden loss of vision in the right eye with associated mild pain. Four months ago, his visual acuity was 20/40 in each eye, and intraocular pressure by Goldmann applanation tonometry was 16 mmHg in the right eye and 17 mmHg in the left eye. Slit-lamp examination was notable only for optic nerve cupping in both eyes (Figure 1, right eye only). On evaluation, he reported excellent vision in both eyes until three weeks ago, at which point he suddenly lost vision in the right eye and had mild right-sided aching pain. His vision deteriorated to count fingers in the right eye and remained stable at 20/40 in the left eye. Intraocular pressure was elevated to 24 mmHg in the right eye and was stable at 14 mmHg in the left eye. A right afferent pupillary defect was present. Slit-lamp examination was notable for 1+ cell in the anterior chamber, optic nerve pallor and arterial attenuation, and occlusive vasculopathy in the right eye (Figure 2A). Examination of the left eye was unchanged.

Fluorescein angiography of the right eye showed delayed arterial filling and marked absence of retinal perfusion sparing only the superonasal macula (Figure 2, B and C). Late frames showed leakage at the edges of the perfused retina (Figure 2D).

Given his age and sudden onset of vision loss with associated pain, C-reactive protein and erythrocyte sedimentation rate were ordered with concern for giant-cell arteritis. C-reactive protein was normal at 3.5 mg/mL, but the erythrocyte sedimentation rate was moderately elevated given the patient's age at 73 mm/hour. Treponemal antibody testing was negative. He was started on high-dose oral prednisone (40 mg/day) and underwent temporal artery biopsy, which returned negative for giant-cell arteritis.

The patient returned for follow-up 3 weeks later noting mild improvement in pain while on prednisone. His visual acuity remained count fingers in the right eye and 20/40 in the left eye. Intraocular pressure was 31 mmHg in the right eye and 19 mmHg in the left eye. Slit-lamp examination was notable for inferior keratic precipitates in a ring distribution and 1+ cell in the anterior chamber of the right eye (Figure 3). Posterior segment examination was notable for development of an area of retinitis inferotemporally in the right eye (Figure 4). Slit-lamp examination of the left eye was unchanged.

An anterior chamber paracentesis was performed, and an aqueous sample was sent for CMV-directed polymerase chain reaction, which returned positive (271,000 IU/mL). Serum HIV antibody and antigen were negative. He was subsequently treated with combined dorzolamide-timolol topical drops, valganciclovir, and intravitreal foscarnet injections in the right eye. Despite appropriate renal dosing, valganciclovir was discontinued after 4 months because of a rising creatinine in the setting of chronic kidney disease. He received a total of 12 foscarnet injections. On examination 6 months later, the area of retinitis had resolved. Three months later, he developed an inferior rhegmatogenous retinal detachment and underwent repair with pars plana vitrectomy, endolaser, and silicone oil. At last follow-up three months after retinal detachment repair, visual acuity remained count fingers.

Discussion

Ocular manifestations of CMV infection are typically seen in severely immunocompromised patients, such as patients with HIV/AIDS. Many previous reports have described CMV retinitis in HIV-negative individuals, the majority of whom have had one or more reasons for relative immunosuppression.^{6–8} In 2013, Schneider et al described five patients with HIV-negative who presented with CMV retinitis with an occlusive vasculopathy similar to that presented in this report.⁴ All 5 patients had some level of immune dysfunction: 4 of the 5 patients were older than 70 years, four had diabetes mellitus, and three patients were on immunosuppressive agents (one for polymyositis, one for graft-vs.-host disease after bone marrow transplantation, and one after renal transplantation). Our patient differed in that the development of retinitis followed the occurrence of diffuse, occlusive retinal vasculopathy.

In 2016, Downes et al⁵ reviewed 208 HIV-negative patients with CMV retinitis, the majority of whom had one or more factor contributing to relative immune dysfunction. Approximately 80% were either older than 60 years or had diabetes mellitus, an autoimmune disorder requiring immunosuppression, an underlying malignancy, or underwent organ transplantation and were treated with immunosuppressive agents; 10% received intraocular or periocular corticosteroids; and 5% had Good syndrome—a rare, adult-onset primary immunodeficiency associated with the presence of thymoma and hypogammaglobulinemia. Only 5% had no identifiable contributor to relative immune suppression.

Our patient has multiple factors that contributed to immune dysfunction, including advanced age, diabetes mellitus, and a number of other chronic medical conditions as mentioned above. Of note, the elevated intraocular pressure and ring-shaped keratic precipitates similar to that shown in Figure 3 have been described in patients with CMV anterior uveitis.⁹

We acknowledge that the patient's medical history contains multiple risk factors for the development of occlusive disease, and we cannot exclude the possibility that the occlusive vasculopathy on initial presentation was at least in part due to factors other than a concurrent ocular CMV infection. Furthermore, this case demonstrates that CMV retinitis and occlusive vasculopathy can occur in succession, as the area of retinitis was not clinically evident at the initial presentation when the vasculopathy was noted. In previous reports in which the retinitis and occlusive vasculopathy were concurrent, the retinal findings are similar to what is described herein.

In summary, CMV infection should be considered in patients who present with an occlusive retinal vasculopathy, particularly when retinitis is present, or in the elderly or those with diabetes mellitus or one or more other conditions that might contribute to systemic immunosuppression.

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Fig. 1.
Color fundus photograph of the right eye showing optic nerve cupping.

Fig. 2.

A. Color fundus photograph of the right eye showing optic nerve pallor, severe arterial attenuation, and occlusive vasculopathy. **B.** Fluorescein angiogram of the right eye at 32 seconds showing choroidal flush and arterial filling limited to the superonasal macula. **C.** Fluorescein angiogram of the right eye at 1 minute and 10 seconds showing occlusive vasculopathy sparing only the superonasal macula. **D.** Late-phase fluorescein angiogram of the right eye at 5 minutes and 41 seconds showing leakage at the edges of perfused retina.

Fig. 3.
Slit-lamp photograph of the right eye showing inferior keratic precipitates in a ring distribution.

Fig. 4. Color fundus photograph of the right eye showing an area of retinitis temporally and the aforementioned optic nerve pallor, severe arterial attenuation, and occlusive vasculopathy.