Case Report

CMV retinitis in an HIV patient with clinical and immunological failure on HAART

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Abstract

Cytomegalovirus (CMV) retinitis is a complication of patients infected with human immunodeficiency virus (HIV) in advance stage when CD4 count is less than 50 cells/cumm. Before the introduction of highly active antiretroviral therapy (HAART), approximately 30% of patients with AIDS developed CMV retinitis, which declined in 75% of cases after the start of HAART. We report a case of CMV retinitis in an HIV-positive patient who developed it as a WHO clinical stage 4 condition representing clinical failure along with dramatic decrease in CD4 count due to immunological failure on failing first-line HAART.

KEY WORDS: Cytomegalovirus retinitis, human immunodeficiency virus, highly active antiretroviral therapy, immunological failure, clinical failure

Introduction

Cytomegalovirus (CMV) retinitis is a rare disease that mainly affects patients with acquired immune deficiency syndrome (AIDS). It can also be found in immunosuppressed patients such as organ transplant recipients on immunosuppressive drugs, patients on chemotherapy, and patients with systemic lupus erythematosus.[1,2] CMV retinitis is the most common manifestation of end-organ CMV disease among patients with AIDS.[3,4] CMV disease mostly represents reactivation in persons with latent CMV infection.[5] The risk of developing CMV retinitis depends on the degree of immunosupression; approximately 30% of patients with AIDS developed CMV retinitis before the start of highly active antiretroviral therapy (HAART).[6] Studies have shown that CMV retinitis occurs mostly at CD4 count less than 50 cells/cumm.[5,6] With the use of potent antiretroviral therapy, the incidence of CMV retinitis has declined in 75% of cases.[7] Nowadays, CMV retinitis occurs in HIV-positive patients who despite having low CD4 count (<50 cells/cumm) are not on HAART or have repeatedly failed HAART.

The initial symptoms of CMV retinitis comprise floaters, flashes, field defects, and falling vision that is generally unilateral to start with. Typically, CMV retinal lesions appear as areas of white necrosis with edema along the distribution of retinal vessels with associated hemorrhages. CMV retinitis is managed initially for 14–21 days with induction therapy followed by maintenance therapy, which is discontinued if the patient has inactive retinitis and maintains a CD4 count more than 100–150 cells/cumm for at least 3–6 months. According to the recommendation from the Centers for Disease Control and Prevention, the National Institute of Health, and the HIV Medicine Association/Infectious Diseases Society of America, the initial therapy for CMV retinitis should be based on location and severity of lesions, underlying immunosupression, adherence factor, and other factors such as use of concomitant medication.[5] Certain HIV specialists recommend the use of oral valganciclovir with intraocular ganciclovir implant for initial therapy (especially for patients with immediate site-threatening retinitis), but some experts recommend the use of oral valganciclovir alone for initial therapy mainly because of its ease of administration and lack of requirement for ophthalmologic surgery or placement of an indwelling catheter.[5] Even with the use of intraocular ganciclovir pellet, concurrent systemic therapy is strongly recommended to prevent disease in the contralateral eye and to prevent dissemination to other organs.[8]

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A 27-year-old man was detected to be HIV positive in May 2011 with initial CD4 count of 42 cells/cumm and was started on HAART (zidovudine + 3 lamivudine + nevirapine) along with cotrimoxazole prophylaxis after unremarkable opportunistic infection screen. Two months after the start of therapy,

he developed pulmonary tuberculosis and was on antituberculosis treatment for 6 months along with continuation of HAART. His CD4 count increased to 266 cells/cumm in November 2011 and to 344 cells/cumm in August 2012. Thereafter, in March 2013 his CD4 count fell to 202 cells/cumm due to less than 95% adherence to HAART. He was counseled and was continued with the same regime. In October 2013, he presented with painless, progressive diminution of vision of the right eye for 3 months. On ocular examination, his vision in the right eye was 1/60 and that in the left eye was 6/6. Slit lamp biomicroscopic examination showed normal anterior segment of both eyes. Fundus examination of the right eye showed white necrosis with edema located along the distribution of retinal vessels associated with hemorrhage in zones 1 and 2 [Figure 1], whereas fundus examination of the left eye was within normal limits. Optical coherence tomography of the right eye showed extensive necrosis of the fovea, resulting in significant destruction of the retinal nerve fiber layer. Based on the nature of lesion, the following differential diagnosis was thought of as HIV-associated retinopathy, toxoplasmosis, varicella-zoster retinitis, and CMV retinitis. Laboratory diagnosis of CMV retinitis was confirmed with positive results of serologic testing for CMV (IgM and IgG) along with CD4 count of 68 cells/cumm. CMV retinitis being a stage 4 condition according to the WHO staging for HIV, clinical failure in the patient was thought of along with immunological failure. He was started on second-line HAART, which comprised tab tenofovir 300 mg once daily (OD), tab lamivudine 150 mg BD, tab lopinavir/ritonavir (200/50 mg) 2 tab BD along with cotrimoxazole prophylaxis, and tab azithromycin 1200 mg weekly. Induction phase of CMV retinitis was started with tab valganciclovir 900 mg BD for 21 days along with twice weekly monitoring of complete blood count, serum electrolytes, and renal function test. Eye examination at the end of induction therapy showed no improvement of the visual status in the right eye, but showed dramatic improvement in the retinal whitening on fundus examination. Maintenance therapy with tablet valganciclovir 900 mg OD was continued for 4 months till April 2014 when his CD4 count was found to be 314 cells/cumm, and fundus examination showed scarring at the site of the previous retinitis in the right eye but no improvement in the visual status. His follow-up CD4 count in August 2014 was 412 cells/cumm, and no recurrence of CMV retinitis lesions or evidence of any disseminated CMV disease was observed.

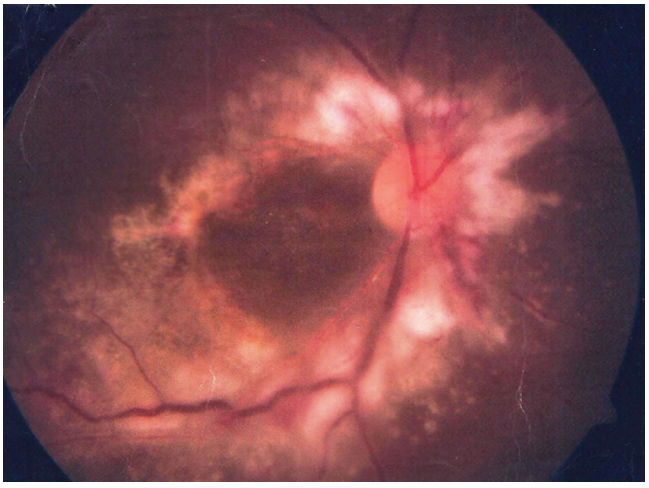

Figure 1: Fundus examination of the right eye showed white necrosis with edema located along the distribution of retinal vessels associated with hemorrhage in zones 1 and 2

Discussion

CMV retinitis is typically found in immunocompromised patients, mainly in patients with HIV.[8] Visser[7] while studying HIV-positive patients observed that approximately 30% of patients with AIDS developed CMV retinitis before the start of HAART. The rate declined in 75% of cases after the start of HAART.[7] Our case shows an immunosuppressed patient who developed his first episode of CMV retinitis as a condition indicating clinical failure along with immunological failure due to HIV infection on first-line HAART with more than 95% adherence.

Zone 1 (central lesion) is sight threatening but retinitis in zones 2 and 3 has no major symptom except for a peripheral field defect, as seen in our case where the patient reported late with vision loss on involvement of zone 1 (central lesion) because the symptoms prevailed for the last 3 months.

At the time of initial presentation with active CMV retinitis, approximately 30% of patients presented with visual acuity of 20/50 or worse and 17% had 20/200 or worse.[9] Thus, it is important for patients with low CD4 count to be educated about the symptoms of CMV retinitis and should be instructed to seek urgent eye evaluation by ophthalmologist so as to prevent CMV retinitis–induced blindness. In the modern era of potent antiretroviral therapy, the incidence of CMV retinitis has declined dramatically[6] with most cases occurring in patients with HIV not on HAART despite low CD4 count or who have repeatedly failed antiretroviral therapy.[10] As seen in our case, the individual had witnessed decrease in CD4 count to 202 cells/cumm in March 2013 from 344 cells/cumm in August 2012 because of poor adherence to recommended HAART with repeated dramatic decrease in CD4 count again to 68 cells/cumm in October 2013 when presented with CMV retinitis in right eye due to immunological failure probably because of drug resistance despite good adherence to HAART this time.

In our case, initial ophthalmological evaluation showed that there was extensive damage to the macula and the individual had already lost his substantial vision, so we used oral valganciclovir alone for the induction phase therapy followed by maintenance therapy till his CD4 count sustained more than 200 cells/cumm for 4 months. Oral valganciclovir therapy, in our case, has shown resolution of CMV retinitis lesions in the affected eye and has prevented CMV disease

dissemination to the other eye and systemic organs when followed up for 9 months posttreatment.

Conclusion

CMV retinitis can occur as AIDS-defining illness in patients due to repeated failed antiretroviral therapy. Patients with HIV infection need to be educated about symptoms of CMV retinitis such as floaters, flashes, field defects, and fall in vision so that they can be seen by the ophthalmologist at early stage of disease condition and prevent CMV-induced blindness. Oral valganciclovir alone during induction and maintenance therapy is effective in prevention of systemic dissemination of CMV disease and resolution of CMV lesions in affected eye when the vision has been substantially lost on presentation.

References

1. Coskuncan JM, Jabs DA, Dunn JP, Haller JA, Green WR, Vogelsang GB, et al. The eye in bone marrow transplantation. VI. Retinal complications. Arch Ophthalmol 1994;112(3):372–9.
2. Egbert PR, Polland RB, Gallagher JG, Merigan TC. Cytomegalovirus retinitis in immunosuppressed hosts: ocular manifestations. Ann Intern Med 1980;93:664–70.
3. Whitley RJ, Jacobson MA, Friedberg DN, Holland GN, Jabs DA, Dieterich DT, et al. Guidelines for the treatment of cytomegalovirus diseases in patients with AIDS in the era of potent antiretroviral therapy: recommendations of an international panel. International AIDS Society-USA. Arch Intern Med 1998;158 (9):957–69.
4. Gallant JE, Moore RD, Richman DD, Keruly J, Chaisson RE. Incidence and natural history of cytomegalovirus disease in patients with advanced human immunodeficiency virus disease treated with zidovudine. The Zidovudine Epidemiology Study Group. J Infect Dis 1992;166(6):1223–7.
5. Benson CA, Kaplan JE, Masur H, Pau A, Holmes KK. Treating opportunistic infections among HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America. MMWR Recomm Rep 2004;53(RR15): 1–112.
6. Kuppermann BD, Petty JG, Richman DD, Mathews WC, Fullerton SC, Rickman LS, et al. Correlation between CD4 + counts and prevalence of cytomegalovirus retinitis and human immunodeficiency virus-related noninfectious retinal vasculopathy in patients with acquired immunodeficiency syndrome. Am J Ophthalmol 1993;115(5):575–82.
7. Visser L 2003. Visser L. Managing CMV retinitis in the developing world. Community Eye Health 2003;16(47):38–9.
8. Kuppermann BD, Quiceno JI, Flores-Aguilar M, Connor JD, Capparelli EV, Sherwood CH, et al. Intravitreal ganciclovir concentration after intravenous administration in AIDS patients with cytomegalovirus retinitis: implications for therapy. J Infect Dis 1993;168(6):1506–9.
9. Kempen JH, Jabs DA, Wilson LA, Dunn JP, West SK, Tonascia JA. Risk of vision loss in patients with cytomegalovirus retinitis and the acquired immunodeficiency syndrome. Arch Ophthalmol 2003;121(4):466–76.
10. Deayton JR, Wilson P, Sabin CA, Davey CC, Johnson MA, Emery VC, et al. Changes in the natural history of cytomegalovirus retinitis following the introduction of highly active antiretroviral therapy. AIDS 2000;14(9):1163–70.

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