IDCases 6 (2016) 97–99

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

No light at the end of the tunnel . . . an unfortunate case of varicella-associated progressive outer retinal necrosis in a patient with neglected HIV infection

Robert E. Winsett, DO[a,b,*], Holly M. Day, MD[a,b], Gregory M. Anstead, MD, PhD[a,b]

[a] Medical Service, South Texas Veterans Health Care System, San Antonio, TX,United States
[b] Department of Medicine, University of Texas Health Science Center at San Antonio, United States

ARTICLE INFO

Article history:
Received 13 July 2016
Received in revised form 20 September 2016
Accepted 20 September 2016

Progressive vision loss was an ominous sign in a 41-year-old Caucasian female with untreated human immunodeficiency virus (HIV) infection that had progressed to acquired immunodeficiency syndrome (AIDS). She initially presented to a rural hospital with a four-week history of painless, progressive vision loss that was preceded by a rash above her right eye. She denied contact with animals, recent interstate travel, or sexual activity for several years. A local ophthalmologist prescribed oral acyclovir and steroid eye drops but did not perform a dilated funduscopic exam. The cutaneous symptoms improved, but the patient's vision rapidly deteriorated and she was referred to our university-affiliated facility for specialty evaluation.

The patient had been diagnosed with HIV infection seventeen years prior and had been on anti-retroviral therapy (ART) for several years. However, she lost access to continued medical care when she moved to a small rural town (population 1,700), almost 100 kilometers from tertiary care medical facilities and an HIV clinic that could have provided low-cost healthcare services and access to treatment. She lacked the knowledge and transportation to seek appropriate care for both her HIV infection and vision problems.

On presentation, the patient was resting comfortably and did not appear acutely or chronically ill; her vital signs were normal and she was afebrile. She had several crusted vesicles above her right eye and fixed, dilated pupils bilaterally that were unreactive to light; she reported no light perception in her left eye and minimal light perception in her right eye. Basic lab results in the Emergency Department were remarkable only for lymphopenia, and her CD4 count was less than 40 cells per microliter (the lowest our lab reports due to non-linearity at such low levels). A non-contrast head CT ruled out intracranial hemorrhage or large mass. Extensive bilateral peripheral retinal necrosis with areas of hemorrhage and hyperpigmentation was seen on dilated fundoscopic exam (see Fig. 1).

Immunocompromised patients present a special diagnostic challenge as they have increased risk of both common and uncommon pathogens, and even some malignancies. We were able to quickly narrow our differential to an infectious cause based on the history and patient's funduscopic exam, although the specific etiology remained unclear. The primary differential diagnosis was varicella zoster virus (VZV) retinitis versus cytomegalovirus (CMV) retinitis; herpes simplex virus (HSV), toxoplasmosis, tuberculosis, and neurosyphilis were also considered, but much lower on the differential.

Intravenous antiviral acyclovir therapy was immediately initiated to treat suspected varicella zoster virus (VZV), thought to be the most likely diagnosis given the patient's history of recurrent zoster infections and the preceding supraorbital rash that resolved with acyclovir; additionally, the ophthalmology service performed multiple intravitreal ganciclovir injections. HSV infection of the eye may present with similar dermatologic manifestations, but the cornea and anterior eye are usually involved; retinal necrosis is less common. There were no ring-enhancing lesions consistent with toxoplasmosis on the head CT (or any other masses); antibodies (IgG and IgM) to toxoplasma were also not detected. Central nervous system tuberculosis was not definitively ruled out, but our patient had no prior history, current signs and symptoms, or risk factors for tuberculosis. Neurosyphilis was less likely given the acuity of her presentation

* Corresponding author at: Department of Medicine, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900, United States.
E-mail address: winsett@uthscsa.edu (R.E. Winsett).

http://dx.doi.org/10.1016/j.idcr.2016.09.010

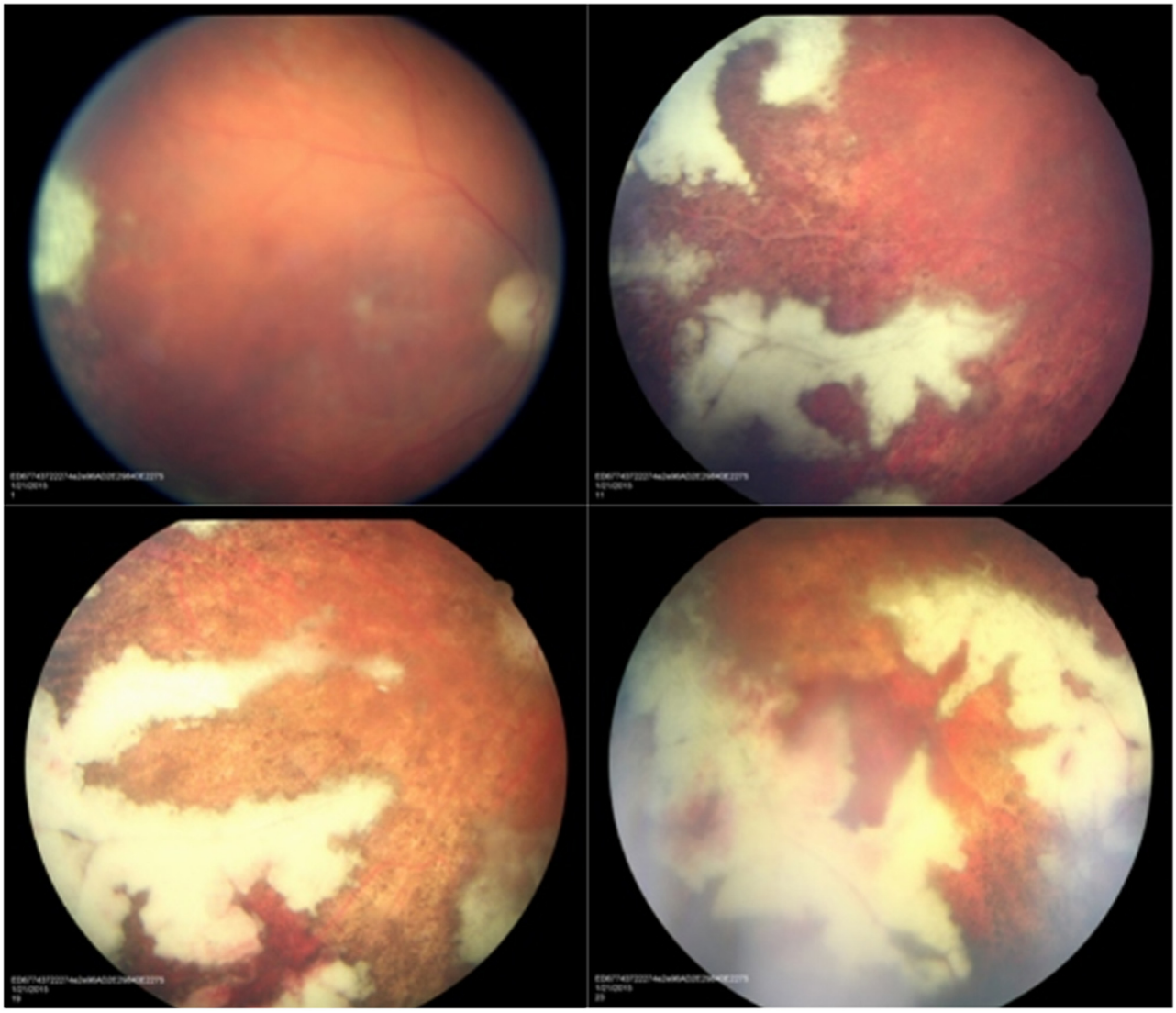

Fig. 1. Ophthalmoscopy reveals bilateral peripheral retinal necrosis with areas of hemorrhage and hyperpigmentation.

and physical findings, and a nonreactive rapid plasma reagin test suggested against this diagnosis.

Unfortunately, the patient's vision loss progressed despite intravenous and intravitreal antiviral therapy and the patient was subsequently found to have a high blood viral load of CMV (74,500 IU/mL). The antiviral regimen was changed to ganciclovir and foscarnet because acyclovir is less active than ganciclovir in vitro against CMV, and ganciclovir with or without foscarnet is more effective for VZV retinitis than either acyclovir or foscarnet [5]. Although history and physical exam, including funduscopic exam, are usually sufficient to diagnose VZV infection, our case was complicated by the detection of CMV in the blood; CMV viremia does not prove end-organ disease, but it is associated with worse overall mortality and is therefore reasonable to treat [1]. It is important to differentiate CMV retinal infection from VZV and HSV infection because the latter two viral infections may potentially be treated with less toxic acyclovir. Polymerase chain reaction (PCR) analysis on a vitreal aspirate, which was positive for the presence of VZV and negative for CMV, ultimately confirmed the final diagnosis of progressive outer retinal necrosis (PORN), a form of retinal necrosis resulting from VZV retinal infection.

Varicella zoster virus reactivation involving the ophthalmic branch of the trigeminal nerve, specifically called herpes zoster ophthalmicus (HZO), requires special consideration as it can lead to acute retinal necrosis, potentially causing blindness and therefore necessitates prompt antiviral treatment and ophthalmologic evaluation. PORN is a variant of retinal necrosis that is unique to immunocompromised patients, most commonly those with uncontrolled HIV infection. PORN can be caused by several pathogens of the herpes family of viruses, including HSV, VZV, CMV, and EBV [4,8]. Retinitis due to CMV/VZV, EBV/HSV/VZV, and CMV/HSV/VZV co-infections have also been reported [6,7]. There are also non-infectious mimics of PORN, including vitreoretinal lymphoma and retinal vasculitis [9,11].

In PORN, vision loss is rapidly progressive and usually results in complete blindness despite aggressive therapy [2,3]. One of the heralding signs of HZO (although our patient did not exhibit this finding) is vesicles on the tip of the nose, known as Hutchinson's Sign; this finding is almost always associated with ocular involvement of VZV [10]. Clinical history of zoster lesions on the face and vision loss is diagnostic and may be supported by dilated fundoscopic exam; vitreal sampling and PCR analysis may confirm infection with VZV or another herpes family virus.

Despite aggressive therapy, our patient's vision deteriorated rapidly to complete blindness. Initiation of anti-retroviral therapy was delayed due to concern about immune reconstitution

syndrome/vitritis further exacerbating vision loss if CMV retinitis (reported in up to 63% of CMV retinitis patients) [6]. When it was obvious after two weeks that her condition had progressed to complete blindness, despite aggressive therapy with anti-CMV and VZV agents, HIV therapy was initiated with elvitegravir, cobicistat, emtricitabine, and tenofovir (Stribild®).

The tragedy of this case is that blindness may have been prevented if the patient had stayed on antiretroviral therapy or even if she had been referred to a tertiary care facility in a timely manner when her visual symptoms first arose.

References

[1] Boffi El Amari E, Combescure C, Yerly S, Calmy A, Kaiser L, Hasse B, et al. Clinical relevance of cytomegalovirus viraemia. HIV Med 2011;12:394–402.
[2] Engstrom Jr. RE, Holland GN, Margolis TP, Muccioli C, Lindley JI, Belfort Jr. R, et al. The progressive outer retinal necrosis syndrome: a variant of necrotizing herpetic retinopathy in patients with AIDS. Ophthalmology 1994;101:1488–502.
[3] Gore DM, Gore SK, Visser L. Progressive outer retinal necrosis outcomes in the intravitreal era. Arch Opthal 2012;130:700–6.
[4] Guex-Crosier Y, Rochat C, Herbort CP. Necrotizing herpetic retinopathies: a spectrum of herpes virus-induced diseases determined by the immune state of the host. Ocul Immunol Inflamm 1997;5:259–65.
[5] Karavellas MP, Plummer DJ, Macdonald JC, Torriani FJ, Shufelt CL, Azen SP, Freeman WR. Incidence of immune recovery vitritis in cytomegalovirus retinitis patients following institution of successful highly active antiretroviral therapy. J Infect Dis 1999;179:697–700.
[6] Matos K, Muccioli C, Belfort Jr. R, Rizzo LV. Correlation between clinical diagnosis and PCR analysis of serum, aqueous, and vitreous samples in patients with inflammatory eye disease. Arq Bras Oftalmol 2007;70:109–14.
[7] Nakamura T, Daikoku T, Shiraki K, Hayashi A. Detection of cytomegalovirus in an immunocompetent adult presenting with acute retinal necrosis due to varicella-zoster virus: a case report. Clin Ophthalmol 2015;9:853–8.
[8] Oe C, Hiraoka M, Tanaka S, Ohguro H. Acute retinal necrosis associated with Epstein-Barr Virus in a patient undergoing immunosuppressive therapy. Case Rep Ophthalmol 2016;7:195–201.
[9] Rosenbaum JT, Sibley CH, Lin P. Retinal vasculitis. Curr Opin Rheumatol 2016;28:228–35.
[10] Zaal MJ, Volker-Dieben HJ, D'Amaro J. Prognostic value of Hutchinson's sign in acute herpes zoster ophthalmicus. Graefes Arch Clin Exp Ophthalmol 2003;241:187–91.
[11] Zloto O, Elkader AE, Fabian ID, Vishnevskia-Dai V. Primary vitreoretinal lymphoma masquerading as refractory retinitis. Case Rep Ophthalmol 2015;6:345–50.