Taiwan Journal of Ophthalmology 6 (2016) 145–149

Contents lists available at ScienceDirect

Taiwan Journal of Ophthalmology

journal homepage: www.e-tjo.com

Case report

Rapid regression of cystoid macular edema associated with cytomegalovirus retinitis in adult acute myeloid leukemia by intravitreal methotrexate combined with oral valganciclovir: A case report with comparison of binocular outcome

Evelyn Jou-Chen Huang [a, b, c, *], Chih-Ping Wang [a, b], Chien-Hsiung Lai [a, b, c], Chih-Chien Chen [d], Chien-Neng Kuo [a, b]

[a] Department of Ophthalmology, Chang Gung Memorial Hospital, Chiayi, Taiwan
[b] Chang Gung University College of Medicine, Tao-Yuan, Taiwan
[c] Department of Nursing, Chang Gung University of Science and Technology, Chiayi, Taiwan
[d] Division of Hematology & Oncology, Chang Gung Memorial Hospital, Chiayi, Taiwan

ARTICLE INFO

Article history:
Received 27 February 2015
Received in revised form
22 June 2015
Accepted 17 July 2015
Available online 1 October 2015

Keywords:
cystoid macular edema
cytomegalovirus retinitis
hematopoietic stem cell transplantation
methotrexate
valganciclovir

ABSTRACT

Cytomegalovirus (CMV) retinitis is a late complication of organ and hematopoietic stem cell transplant, the risk of which depends on the degree of immunosuppression. With the institution of preemptive ganciclovir therapy early after transplant, most patients survive episodes of life-threatening CMV infection during the early months (usually the first 3 months) after transplant and hence late onset of CMV disease, such as CMV retinitis, is being recognized more frequently. Direct involvement of the macula or optic head remains the leading cause of visual loss in patients with CMV retinitis, but there are few studies investigating the management of this condition.

Herein, we present the case of 28-year-old man who had acute myeloid leukemia and developed CMV retinitis with bilateral cystoid macular edema and optic swelling in the right eye 6 months after bone marrow transplant. He received treatment with intravitreal methotrexate in the right eye in combination with oral valganciclovir. Visual acuity improved 1 month after four weekly injections of intravitreal methotrexate 400 μg/0.1 mL. Resolved disc swelling and regression of macular edema were also observed. By comparing binocular outcome, we present our findings and discuss the possible efficacy and safety of this treatment with respect to regression of anatomical damage and improvement in visual acuity.

1. Introduction

Cytomegalovirus (CMV) is a double-stranded DNA virus belonging to the human herpesvirus family, which includes herpes simplex virus, varicella zoster virus, and Epstein–Barr virus. Clinical characteristics of systemic CMV infections were initially described in 1905.[1]

Human immunodeficiency virus (HIV) infection is the most common cause of immunosuppression leading to reactivation of CMV and symptomatic infection. Severe CMV infection has also been associated with congenital immunodeficiency syndromes, pharmacologic immunosuppression, organ transplantation, malignancy, and autoimmune disorders.[2] CMV infection is the leading viral cause of morbidity and mortality in patients receiving hematopoietic stem cell transplants (HSCTs) or solid organ transplants (SOTs).[3]

One of the major targets of CMV infection is the retina.[4] Although the virus was long known as a human pathogen, CMV infection of the retina was not described until the 1950s.[5] CMV was proven to be the causative agent in presumed CMV retinitis in 1964.[6] CMV retinitis was the AIDS-defining diagnosis in about 5% of

Conflicts of interest: The authors have no conflicts of interest and no proprietary interests related to this article.

* Corresponding author. Department of Ophthalmology, Chang Gung Memorial Hospital, Chiayi Number 6, West Section, Chiapu Road, PuTzu City, Chiayi County 613, Taiwan.
E-mail address: roro691213@gmail.com (E.J.-C. Huang).

http://dx.doi.org/10.1016/j.tjo.2015.07.004

patients with HIV infections.[7] Among SOT patients, <2% develop CMV retinitis; however, the pediatric population is at a higher risk.[8] After HSCT, the only large study published on CMV retinitis development showed an incidence of 1.4% in patients who were alive 100 days post-transplant.[9]

CMV retinitis is bilateral in approximately one third of patients.[10] It is a relentless, slowly progressive infection, which, if not treated, may result in blindness caused by total retinal necrosis, retinal detachment, optic nerve involvement, or a combination of several of these factors. Immune-mediated vascular damage may also play a role in vasculitis.

Immediate, acute loss of central vision early in the disease course rarely occurs.[11] The causes of severe central visual loss include CMV infection of the macular or optic nerve, macular serous exudation, and cystoid macular edema (CME). CMV can either infect the optic nerve directly or by extension from adjacent retinitis.[12] In the former case, optic neuritis with profound, irreversible visual loss usually develops. With CMV infection involving the disc or macular retina, an exudative neurosensory detachment develops around the optic nerve, macula, or both, often with the formation of a macular star of consisting of lipid exudation.[13]

Previous results showed that ganciclovir alone (systemic or intraocular administration) is less effective for CME in CMV retinitis probably because of the inflammatory processes associated with CME. CME tends to develop late in the clinical course, such as in the setting of resolving CMV retinitis in non-HIV patients[14] and in the case of immune-reconstitution syndrome in HIV patients.[15] Anti-inflammatory or immunomodulatory agents, in addition to ganciclovir, may be considered in such situations.

The present case is of a patient with adult acute myeloid leukemia who developed CMV retinitis with bilateral CME and associated subretinal fluid 6 months after HSCT. Optic swelling was also observed in the right eye. Hesitant to receive intravitreal ganciclovir injections twice a week in both eyes, he accepted treatment with less frequent intravitreal injection of methotrexate (MTX) once a week in his right eye (which had more severe symptoms) in combination with oral valganciclovir. With comparison of binocular outcome, we present our findings and discuss the possible efficacy and safety of this therapy for regression of macular damage and improvement in visual acuity.

2. Case Report

A 28-year-old man had acute myeloid leukemia, M2 (Chr: 46,XY {6}; MLL-PTD[−], NPM1[−], FLT3-ITD[−]) and completed chemotherapy in June 2012. He had a relapse 1 year later and received reinduction chemotherapy in June 2013 and bone marrow transplant in November, 2013. CMV disease with gastrointestinal manifestation was diagnosed 7 weeks later by the detection of CMV DNA in plasma samples using real-time polymerase chain reaction (PCR). The patient received antiviral treatment with intravenous (IV) ganciclovir 450 mg (5 mg/kg) twice daily for 2 weeks until two consecutive samples of plasma negative for CMV PCR were obtained.

In May 2014, he was referred to our clinic as he had been experiencing deteriorating vision in both eyes for 2 weeks. At the first visit, his best corrected visual acuity was counting fingers at 20 cm (2 logMAR units) in his right eye (OD) and 20/100 (0.3 logMAR units) in his left eye (OS).

Slit-lamp biomicroscopic examination of the anterior chamber in OS yielded normal results, whereas a 1+ anterior chamber cellular reaction was observed in OD. On indirect ophthalmoscopy, changes typical of CMV retinitis were observed, such as areas of yellow–white necrosis with vascular sheathing along the distribution of retinal vessels of the superior arc in OS and both the superior and inferior arcs in OD. Exudates and edema were also noted with varying degrees of hemorrhage, which presented with a brushfire pattern. Optic disc swelling was also noted in OD, which had worse visual acuity. Vitreous inflammation was mild in both eyes (Figure 1).

Optical coherence tomography showed CME with subretinal fluid in both eyes (Figure 2). Central macular thickness was 508 μm OD and 567 μm OS. On laboratory examination, CMV was identified in the aqueous humor of both eyes using PCR. The patient's hemograms revealed a relative immunocompetent status 1 month before and after he visited our clinic; however, PCR results for plasma CMV infection were positive again at that time.

CMV retinitis with right optic neuritis and bilateral macular edema was diagnosed. Since the patient was hesitant to accept frequent intravitreal injections of ganciclovir, it was decided to administer oral valganciclovir with an induction dose of 900 mg twice a day for 3 weeks and a weekly adjuvant intravitreal injection of MTX 400 μg/0.1 mL unilateral in OD, the more severely affected eye, for 1 month.

Best corrected visual acuity improved to 20/400 (1.3 logMAR units) after four MTX injections and to 20/63 (0.5 logMAR units) OS a month later. Indirect ophthalmoscopy revealed resolving disc swelling in OD (Figure 3) and follow-up optical coherence tomography revealed that macular edema had subsided in MTX-injected eyes, but persisted OS (Figure 4). A maintenance dose of valganciclovir 900 mg orally once a day was continued. No recurrence of

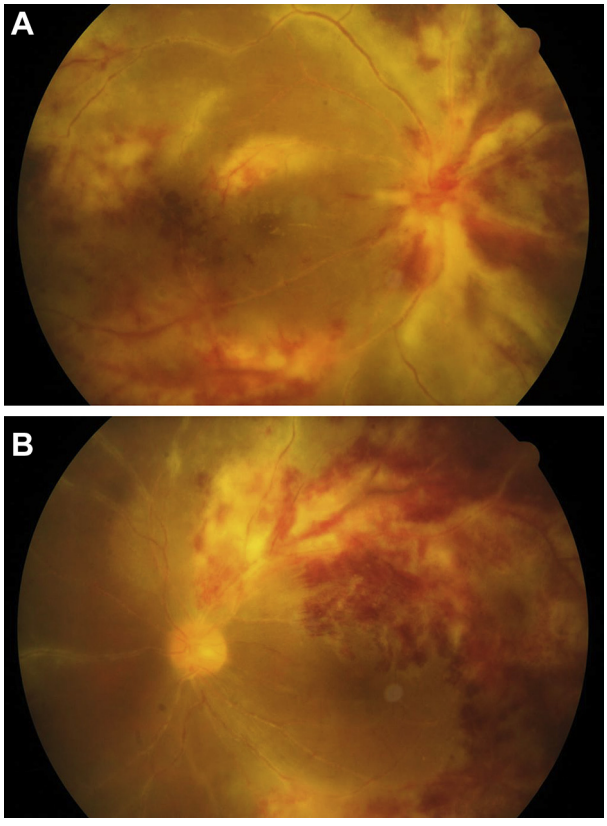

Figure 1. Classic changes of cytomegalovirus retinitis appeared as areas of yellow-white necrosis with vascular sheathing along the distribution of retinal vessel of (B) the superior arc in the left eye and (A) both superior and inferior arcs in the right eye. Exudates and edema were also noted with variable amounts of associated brushfire pattern hemorrhage. Vitreous inflammation was mild and zone 1 involvement was showed in both eyes. Optic disc swelling was also noted in the right eye, which had worse visual acuity. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)