Pediatric Hematology Oncology Journal 1 (2016) 35–37

Contents lists available at ScienceDirect

Pediatric Hematology Oncology Journal

journal homepage: https://www.elsevier.com/journals/pediatric-hematology-oncology-journal/

Bilateral cytomegalovirus retinitis in a child with acute lymphoblastic leukemia while on maintenance chemotherapy

Vaidehi S. Dedania [a], Pawan Bhatnagar [b], Robert P. Santos [c], Vikramjit S. Kanwar [d, *]

[a] Albany Medical Center, Department of Ophthalmology, Lions Eye Institute, Albany, NY 12208, USA
[b] Retina Consultants PLLC, Albany Medical College, Department of Ophthalmology, Division of Vitreoretinal Surgery, Slingerlands, NY 12159, USA
[c] Albany Medical Center, Department of Pediatrics, Division of Pediatric Infectious Diseases, Albany, NY 12208, USA
[d] Albany Medical Center, Department of Pediatrics, Division of Pediatric Hematology-Oncology, Albany, NY 12208, USA

ARTICLE INFO

Article history:
Received 31 May 2016
Received in revised form
15 July 2016
Accepted 17 July 2016
Available online 22 July 2016

Keywords:
Acute lymphoblastic leukemia
Bilateral
Cytomegalovirus
Retinitis

ABSTRACT

We report a case of bilateral cytomegalovirus retinitis in a 12 year-old with neutropenic fever after maintenance chemotherapy for acute lymphoblastic leukemia. Ophthalmologic examination for photophobia prompted a diagnosis of cytomegalovirus retinitis. With early diagnosis and prompt treatment, this patient had a favorable visual outcome.

Cytomegalovirus (CMV) infection is a major cause of morbidity and mortality in immunocompromised patients. CMV retinitis is the most common opportunistic intraocular infection in HIV-infected adults [1] and can impact any severely immunocompromised patient, including patients who have received a solid organ or hematopoetic stem cell transplant (HSCT) [2]. In patients with acute lymphoblastic leukemia (ALL), who undergo less immunosuppressive chemotherapy, CMV retinitis has been described in only two children and one adult [3–5]. We describe a case of bilateral CMV retinitis in a pediatric patient receiving chemotherapy for the treatment of B-lineage ALL.

1. Case report

A 12 year-old male with a history of fetal alcohol syndrome and B-lineage ALL was treated on Children's Oncology Group protocol AALL0331 [6] with good response. While he did not have candidiasis or other fungal infections throughout therapy, his clinical course was complicated by seizures, transient methotrexate leukoencephalopathy and sensitivity to 6-mercaptopurine, leading to myelosuppression. Two weeks after concluding standard maintenance chemotherapy with oral mercaptopurine, methotrexate and monthly pulses of vincristine and oral steroid, he was admitted for neutropenic fever and a focal parenchymal consolidation in the lung. The patient was noted to have photophobia in both eyes of two weeks duration and a best-corrected visual acuity (BCVA) of 20/30 OD and 20/50 OS. Anterior chamber examination revealed 1+ white blood cells in both eyes, without flare, fibrin or keratic precipitates. Fundoscopic examination revealed perivascular white infiltrates along the superior arcades of both eyes and the inferior arcade of the left eye, and a small retinal hemorrhage nasal to the optic disc in the right eye (Fig. 1).

Bilateral CMV retinitis was diagnosed and intravenous (IV) ganciclovir was started. Aqueous tap of the right eye and intravitreal injection of ganciclovir 2 mg/0.1 ml into both eyes was performed. Serologic testing confirmed the presence of CMV in the serum as well as in the aqueous fluid by polymerase chain reaction (PCR). Laboratory studies revealed an absolute CD4 count of 473 cells/mm^3 and CD8 count of 1440 cells/mm^3. A total of two intravitreal injections of ganciclovir per eye were administered and the patient received three weeks of treatment with IV ganciclovir

* Corresponding author. Albany Medical Center, 43 New Scotland Avenue MC-24, Department of Pediatrics, Division of Pediatric Hematology-Oncology, Albany, NY 12208, USA. Fax: +1 518 262 5889.
E-mail address: KanwarV@mail.amc.edu (V.S. Kanwar).
Peer review under responsibility of Pediatric Hematology Oncology Chapter of Indian Academy of Pediatrics.

http://dx.doi.org/10.1016/j.phoj.2016.07.003

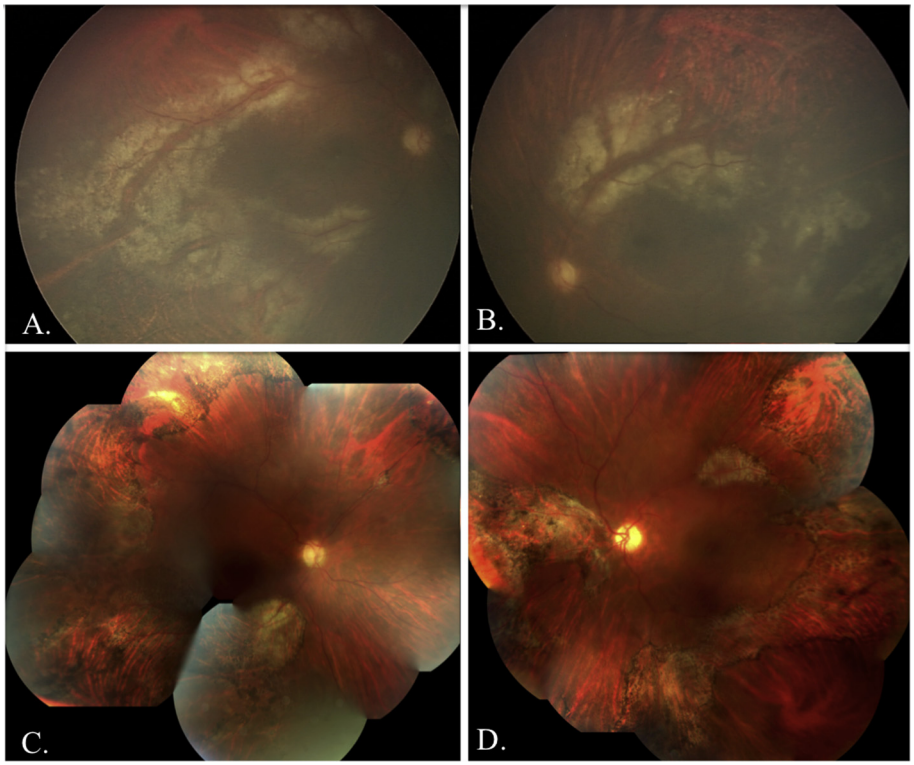

Fig. 1. Fundus photographs of the **A**. right and **B.** left eyes at diagnosis and the **C.** right and **D.** left eyes post-treatment.

175 mg twice a day before being transitioned to oral valganciclovir 900 mg daily. After one week, the oral valganciclovir was discontinued as the patient developed a maculopapular rash on his face, chest and trunk. Additionally, cystoid macular edema was visualized on optical coherence tomography, presumed secondary to immune recovery uveitis, and nepafenac was started.

At one-month follow-up, the perivascular white infiltrates had resolved and there was pallor of the optic discs and perivascular retinal pigmentation representing resolution of the retinitis. Over three years of follow-up his leukemia and retinitis both remain in remission. The patient developed posterior subcapsular cataracts that were removed surgically.

2. Discussion

Cytomegalovirus is a member of the herpes virus family of DNA viruses known to cause a sight-threatening infection of the neural retina. Although immunosuppressed patients are at risk of developing disseminated CMV disease, and can present with retinitis, gastroenteritis, encephalitis and/or pneumonitis, the mildly immunosuppressive nature of childhood ALL maintenance regimens means that CMV retinitis is typically not encountered in this population.

In the reported case the patient was brought to ophthalmologic attention due to a history of photophobia prompting the diagnosis of CMV retinitis upon dilated fundoscopic exam. In general the diagnosis of CMV retinitis is based upon clinical suspicion, and the classic features of CMV retinitis, including perivascular areas of retinal opacification with hemorrhage and retinal necrosis. PCR testing of the aqueous humor or vitreous can be utilized to establish a diagnosis, as was confirmed in our case. It is noteworthy that while ocular specimens accurately reflect the status of CMV retinitis, they do not necessarily reflect the status of systemic CMV infection, therefore, a systemic work-up is also necessary.

Treatment of CMV retinitis includes either or both systemic and intravitreal medications. Both IV ganciclovir and foscarnet have shown efficacy for the treatment of active retinitis, although as both have significant adverse effects, including myelosuppression and nephrotoxicity, respectively, a ganciclovir implant was developed [8]. Unfortunately, this implant has been discontinued for financial reasons secondary to the decreasing incidence of CMV retinitis. Recently, valganciclovir, a prodrug of ganciclovir, has become more widely used as it is more bioavailable when taken orally [8]. Intravitreal ganciclovir and foscarnet are also effective, although it is recommended that immunosuppressed patients also receive systemic therapy as studies have shown reduced mortality and involvement of the fellow eye [8]. Intravenous cidofovir can also be used for the treatment of CMV retinitis although a high percentage of patients can develop medication-related hypotony, uveitis or nephrotoxicity [9]. Finally, oral leflunomide, an anti-inflammatory agent with intrinsic activity against CMV, has shown promise in ganciclovir resistant cases [10].

Early diagnosis and prompt treatment are among the most important prognostic factors for CMV retinitis. Additionally, these patients require close, routine follow-up evaluations, as complications, such as posterior subcapsular cataracts, can develop and limit vision. Although, the incidence of CMV retinitis in moderately immunocompromised children is rare, our case re-confirms that a high index of suspicion should be maintained and prompt ophthalmologic referral should be made for any child with ALL undergoing chemotherapy who develops unexpected visual complaints. The relative lack of symptoms in pediatric patients may lead to advanced disease and in one study, three of four immunosuppressed children diagnosed with advanced CMV retinitis had bilateral disease, and none of the children (all >36 months of age) had subjective visual complaints [7]. Fortunately in our case, despite the advanced stage of the CMV retinitis our patient had a favorable outcome with aggressive therapy.

Conflicts of interest

None.

Funding statement

None.

References

[1] Holland GN, Pepose JS, Pettit TH, Gottlieb MS, Yee RD, Foos RY. Acquired immune deficiency syndrome: ocular manifestations. Ophthalmology 1983;90:859–73.
[2] Chung H, Kim KH, Kim JG, Lee SY, Yoon YH. Retinal complications in patients with solid organ or bone marrow transplantations. Transplantation 2007;83:694–9.
[3] Moritake H, Kamimura S, Kojima H, et al. Cytomegalovirus retinitis as an adverse immunological effect of pulses of vincristine and dexamethasone in maintenance therapy for childhood acute lymphoblastic leukemia. Pediatr Blood Cancer 2013;60:329–31.
[4] Singh R, Singh R, Trehan A, Jain R, Bhalekar S. Cytomegalovirus retinitis in an ALL child on exclusive chemotherapy treated successfully with intravitreal ganciclovir alone. J Pediatr Hematol/Oncol 2013;35(3):e118–9.
[5] Libby E, Movva S, Quintana D, et al. Cytomegalovirus retinitis during chemotherapy with rituximab plus hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone. J Clin Oncol 2010;28:e661–2.
[6] Sharland M, Luck S, Griffiths P, Cotton M. Antiviral therapy of CMV disease in children. Adv Exp Med Biol 2011;697:243–60.
[7] Du LT, Coats DK, Kline MW, et al. Incidence of presumed cytomegalovirus retinitis in HIV-infected pediatric patients. J AAPOS 1999;3:245–9.
[8] Pearce WA, Yeh S, Fine HF. Management of cytomegalovirus retinitis in HIV and non-HIV patients. Ophthalmic Surg Lasers Imaging Retina 2016;47:103–7 (and articles included within).
[9] Stewart MW. Optimal management of cytomegalovirus retinitis in patients with AIDS. Clin Ophthalmol 2010;4:285–99.
[10] Rifkin LM, Minkus CL, Pursell K, et al. Utility of leflunomide in the treatment of drug resistant cytomegalovirus retinitis. Ocul Immunol Inflamm 2015;11:1–4.