TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2017;32(1):31-34
doi: 10.5505/tjo.2017.1552

CASE REPORT

Bilateral Cytomegalovirus Retinitis in a Child with Rhabdomyosarcoma

Osman Bülent ZÜLFİKAR,[1] Halil Haldun EMİROĞLU,[2] Rejin KEBUDİ,[1] Melike EMİROĞLU,[3] Samuray TUNCER[4]

[1]Department of Pediatric Hematology and Oncology, İstanbul University Cerrahpaşa Faculty of Medicine and Institute of Oncology, İstanbul-*Turkey*
[2]Department of Pediatric Gastroenterology, Selcuk University Faculty of Medicine, Konya-*Turkey*
[3]Department of Pediatric Infectious Diseases, Selcuk University Faculty of Medicine, Konya-*Turkey*
[4]Department of Ophthalmology, İstanbul University Istanbul Faculty of Medicine, İstanbul-*Turkey*

SUMMARY

Reactivation of cytomegalovirus (CMV) leading to retinitis has been commonly reported in association with human immunodeficiency virus (HIV) infection or iatrogenic suppression of the immune system, including transplant recipients. Rhabdomyosarcoma (RMS) is the most common soft tissue malignancy in the pediatric age group, and alveolar histology is associated with unfavorable outcome. Presently described is case of RMS with alveolar histology in a 12-year-old male who developed CMV bilateral retinitis during prolonged period of neutropenic fever after 40 weeks of chemotherapy. He was diagnosed based on CMV-DNA polymerase chain reaction in blood and urine samples, and responded well to intravenous gancyclovir treatment. A high index of suspicion for reactivation of CMV leading to retinitis should be maintained and, if needed, investigated, not only in patients with HIV infection or transplant recipients, but also all patients who are iatrogenically immunosuppressed, including those who experience prolonged neutropenic fever due to lengthy courses of radiotherapy and chemotherapy.

Keywords: Chemoradiotherapy; cytomegaloviral retinitis; neutropenia; rhabdomyosarcoma.

Introduction

Cytomegalovirus (CMV) can cause life-long subclinical latent infection in healthy individuals, which can be reactivated upon immunosuppression, affecting a number of different organ systems including eyes. Reactivation of CMV leading to retinitis has been reported in patients with human immunodeficiency virus (HIV) infection and in those subjects with iatrogenic suppression of the immune system including solid organ or hematopoietic stem cell transplant recipients.[1–4]

Rhabdomyosarcoma (RMS) is the most common soft tissue malignancy in the pediatric age group. RMS with alveolar histology is more common in adolescents and is associated with a poorer prognosis than the embryonal type.[5]

Here, we describe a pediatric case of RMS with alveolar histology who had reactivation of CMV leading to retinitis without a history of solid organ or hematopoietic stem cell transplantation or HIV infection.

Received: March 05, 2017
Accepted: March 22, 2017
Online: March 23, 2017

Accessible online at:
www.onkder.org

Dr. Halil Haldun EMİROĞLU
Selçuk Üniversitesi Tıp Fakültesi,
Çocuk Gastroenterolojisi Bilim Dalı,
Konya-Turkey
E-mail: haldunemiroglu@gmail.com

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Case Report

A 12-year-old boy was admitted with a history of abdominal pain, pain on sitting, groin swelling, constipation, painful defecation, and mass around the anus. Vital signs, cardiac, pulmonary, neurological and genitourinary examinations were all normal except for pale skin, an enlarged lymph node (2x1 cm in size) in the left lateral inguinal region, and a mass involving the perianal area and gluteal muscles. Magnetic resonance imaging (MRI) showed the presence of a perianal soft tissue mass (7x7 cm in size) extending bilaterally into gluteal muscles, an enlarged lymph node (2x2 cm in size) in the left lateral inguinal region, and an enlarged lymph node (1x1 cm in size) in the right lateral inguinal region. In addition, whole body bone scintigraphy (WBBS) revealed tumor involvement in the acetabulum, left iliac bone and right femur. Histopathological and immunohistochemical examination of the perianal mass showed the characteristic "alveolar" appearance of alveolar RMS with a densely cellular small round blue cell tumor with strongly positive staining for desmin on immunostaining. According to the Intergroup Rhabdomyosarcoma Study Group (IRSG) Clinical Group Staging System,[6] the patient had group IV metastatic unfavorable alveolar type of rhabdomyosarcoma (high-risk group).

After incomplete resection of the primary tumor, the patient received combination of conventionally fractionated radiation therapy and chemotherapy with vincristine/dactinomycin/cyclophosphamide plus mesna (VAC) every 3 weeks according to IRSG protocol.[6]

During the prolonged neutropenic fever period after 40th weeks of chemotherapy, he developed sudden onset of blurred vision in the left eye. Ophtalmological examination suggested bilateral acute hemorrhagic, necrotizing CMV retinitis (Figure 1a, b). The posterior pole was spared in the right eye. Anti-HIV antibody was negative, while anti-CMV IgG was positive and anti-CMV IgM was negative. Serum and urine samples tested positive for CMV antigen and a polymerase chain reaction (PCR) for CMV DNA showed a viral load of 2750 copies/mL along with the detection of low CD4 count. Treatment for reactivation of CMV retinitis was initiated with intravenous ganciclovir at a dose of 12 mg/kg/day every 12 hours. At the second week of the treatment CMV antigen was negative in serum and urine samples. In addition, PCR for CMV DNA was negative in the serum, with no evidence of active retinitis at week 7 of the treatment. Then, ganciclovir dose was reduced to 6 mg/kg/day every 24 hours for 5 days a week. He was still alive with no relapse of RMS more than 2 months after the diagnosis of CMV retinitis, despite suspended chemotherapy during this period. Later, radiotherapy and VAC chemotherapy were re-initiated with complete remission.

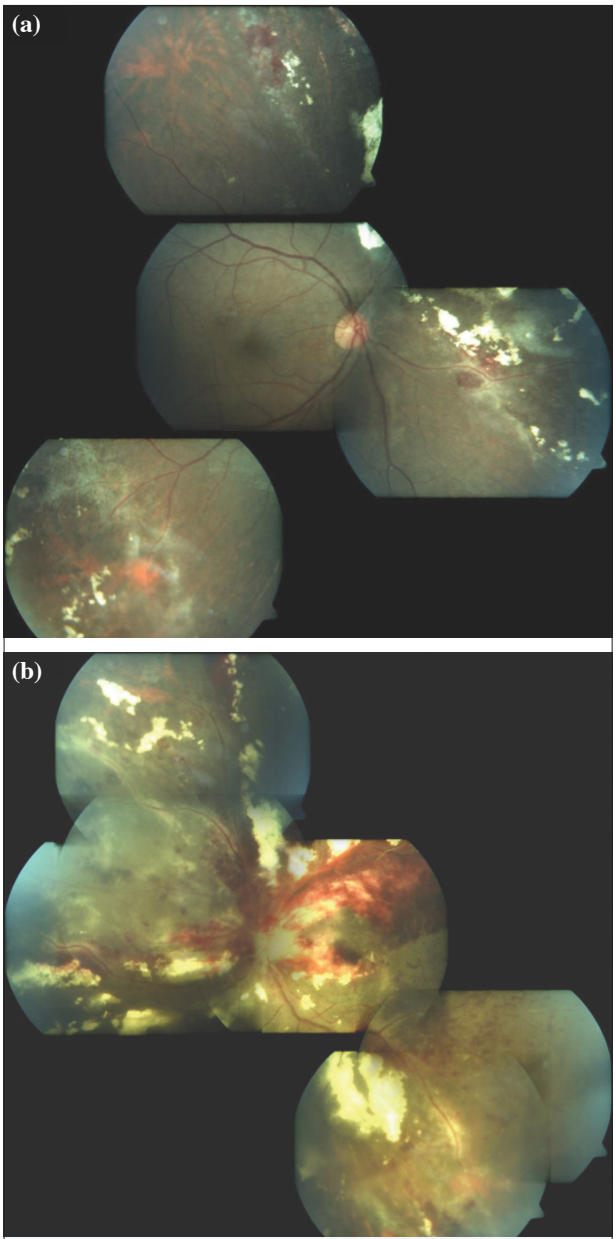

Fig. 1. **(a)** Right fundus showing active hemorrhagic necrotizing CMV retinitis in the retinal periphery. Note the sparing in the posterior pole. **(b)** Left fundus showing active necrotizing CMV retinitis with hemorrhagic areas in the posterior pole and peripheral retina.

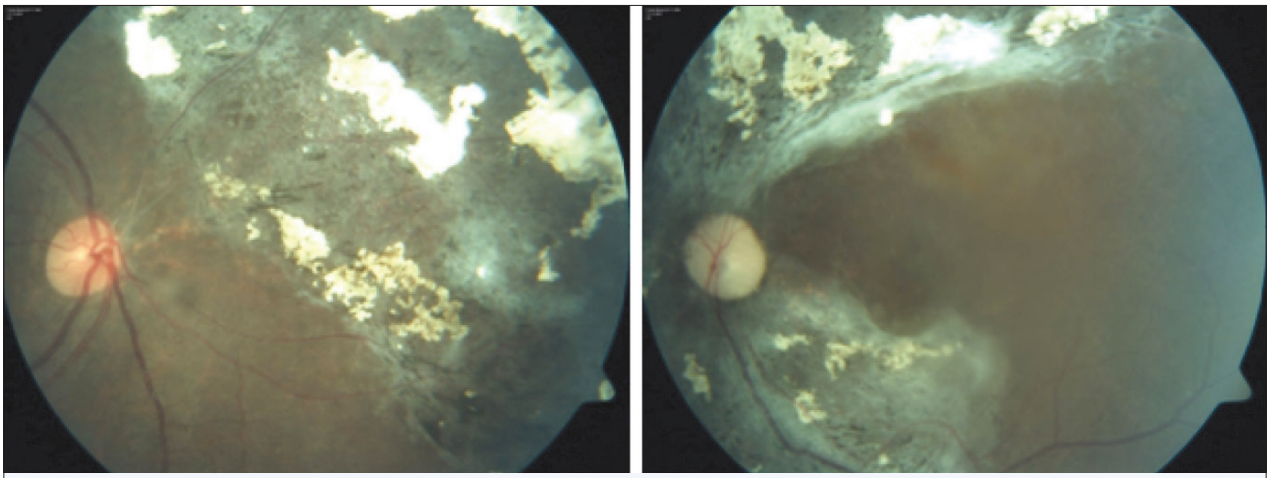

Fig. 2. Fifteen months after treatment, right and left fundus images showing total regression of the active retinal lesions with the formation of chorioretinal atrophy.

The patient was given a total of 6 months of ganciclovir treatment, which also extended 3 months beyond the completion of chemotherapy. Bi-weekly monitoring of CMV DNAemia revealed no reactivation for 3 months after cessation of ganciclovir therapy. CMV retinitis did not recur after 15 months of follow-up (Figure 2).

However, RMS consequently relapsed and the patient died at 3 years after initial diagnosis due to progressive disease despite salvage chemotherapy.

Written informed consent was obtained from the patient who participated in this study.

Discussion

CMV retinitis is the most common complication of late-stage HIV infection, occurring when CD4+ T-cell counts are ≤50 cells/mL.[7,8] In our patient without HIV infection, deficiency in humoral and cell-mediated immunity as documented by low counts of CD4 lymphocytes due to immunosuppressive effects of chemotherapeutic agents might have lead to susceptibility for CMV retinitis.

In patients without HIV infection, CMV retinitis is characterized by necrotizing retinitis, often with intraretinal hemorrhage similar to that observed in patients with HIV infection.[4] Our patient had bilateral active necrotizing CMV retinitis with intraretinal hemorrhage. Ophthalmological characteristics of CMV retinitis in children are slightly different from those observed in adults. In a study involving a total of 9 immunocompromised children with CMV retinitis under 16 years of age, Baumal et al. found bilateral disease in eight children.[9] In our patient, there was bilateral disease with posterior pole involvement only in the left eye.

Management of CMV retinitis involves a number of different medical treatment modalities such as oral (ganciclovir, valganciclovir), intravenous (ganciclovir, foscarnet, cidofovir) and intravitreal (ganciclovir, foscarnet, cidofovir, fomivirsen, and ganciclovir intravitreal implant) routes.[10,11] In our patient, the rationale of the treatment of CMV retinitis was based on improving the defective immune system by discontinuing chemotherapy, and reducing viremia and organ damage with intravenous ganciclovir.

CMV reactivation can happen that not only in transplant recipients or patients with HIV infection, but also in patients with tumor who received lengthy courses of chemotherapy and radiotherapy. A high index of suspicion for reactivation of CMV leading to retinitis should be maintained and, if needed, investigated in non-transplant tumor patients with prolonged neutropenic fever. In this regard, CMV-DNA PCR analysis for early diagnosis and follow-up is of utmost importance.

We believe that early diagnosis and prompt administration of treatment for CMV retinitis was probably the single most important factor for the prevention of progression to a more serious form of the disease because of the response to ganciclovir depends on timely administration of treatment and clinical severity of the condition.

Disclosure Statement

The authors declare no conflicts of interest.

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Financial Disclosure

The authors declared that this study received no financial support.

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