CASE REPORT

Cytomegalovirus Retinitis After Initiation of Antiretroviral Therapy

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Abstract- Patients with human immunodeficiency virus (HIV) infection receiving antiretroviral therapy (ART), despite a reduced viral load and improved immune responses, may experience clinical deterioration. This so called "immune reconstitution inflammatory syndrome (IRIS)" is caused by inflammatory response to both intact subclinical pathogens and residual antigens. Cytomegalovirus retinitis is common in HIV-infected patients on ART with a cluster differentiation 4 ($CD4^+$) counts less than 50 cells/mm^3. We reported a patient with blurred vision while receiving ART. She had an unmasking classic CMV retinitis after ART.

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Introduction

Cytomegalovirus (CMV) retinitis is a serious eye-threatening complication associated with acquired immuno-deficiency syndrome (AIDS) and was common before introducing antiretroviral drugs (1). Jacobson *et al.* (2) reported five patients developed CMV retinitis 4-7 weeks after initiation of antiretroviral therapy (ART). They suggested the role of antiviral drugs in activation of a subclinical infection by an inflammatory response termed immune reconstitution inflammatory syndrome (IRIS).

Case Report

We present a 34-year-old HIV- infected woman diagnosed with CMV retinitis referred to our centre, Imam Khomeini hospital, Tehran, Iran.

Two months prior to admission in our centre, she was treated with a combination of zidovudine, lamivudine and efavirenz due to a low cluster differentiation 4 ($CD4^+$) cell count (<10 cell/mm^3) .She was asymptomatic without any complaints including blurred vision.

Four weeks after commencement of ART, patient was examined by an ophthalmologist for floaters and blurred vision in her left eye. Funduscopy examination has revealed vitritis, vascular sheathing and superficial retinitis associated with necrosis and haemorrhages in the lower part of the retina in the left eye, indicating development of a CMV infection (Figure 1). No other significant changes were found during eye examination.

She had anemia, leukopenia and a positive CMV IgG. Her CD4 had risen to 147 cell/mm^3 (Table 1).

Table 1. Laboratory findings of the patient during her recent admission in the hospital.

Test	Value	Normal range
White blood cell	3340 cells/mm^3	4000-10000
Hemoglubin	11.4 mg/dl	13-16
CMV[1] IgG	5.7	<0.1
CMV IgM	0.7	<0.1
CD4[2] before the introduction of ART[3]	<10 cells/mm^3	500-1500
CD4 a month later the introduction of ART	147 cells/mm^3	500-1500

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1 Cytomegalovirus 2 cluster differentiation 4 3 Antiretroviral Therapy

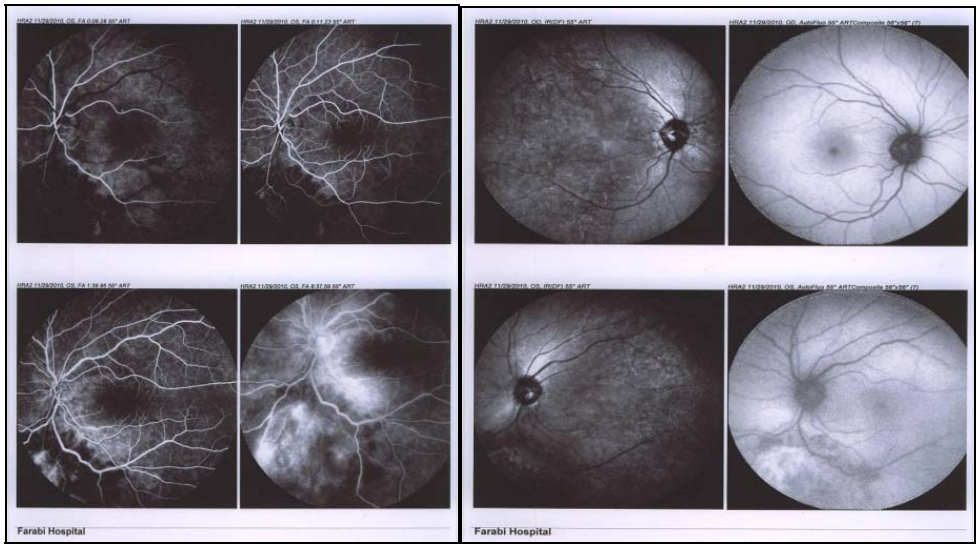

Figure 1. Funduscopy of left eye in the patient showed vitritis, vascular sheathing and superficial retinitis with necrosis and haemorrhage in the inferior part of retina.

Following diagnosis of CMV infection, patient was treated with 5 mg/kg intravenous injection of ganciclovir twice per day.

Previous anti-retroviral therapy with three drugs continued. Eye symptoms relatively improved one week after receiving the ganciclovir. Intravenous injection of ganciclovir continued for 3 weeks and the patient was discharged on maintenance therapy with ganciclovir 300 mg daily.

White blood cell count was checked every two weeks. Following reduction of white blood cell (WBC) count on week ten after commencing the outpatient therapy, the ganciclovir dosage decreased to half and three doses of granulocytes macrophage colony-stimulating factor (GMCSF) were administered. Two weeks later, the WBC count increased to its normal range and ganciclovir continued with a daily dose of 5 mg/kg.

Two months post treatment, the eye symptoms showed a significant improvement with no active lesion on ophthalmology examination. Five months later and on her last outpatient visit, no sign of retinitis was observed. The maintenance therapy with ganciclovir was discontinued after 6 month, because the CD4 count was >100 cells/mm^3 during the treatment course.

Discussion

Confirmation of CMV- related IRIS in our patient was based on the criteria of the International Network for the Study of HIV-associated IRIS (INSHI) (3). Determining the viral load is considered as a gold standard test to confirm the IRIS, but it is not cost effective in source limited countries and CD4 cell count can be used as a minor criterion (3). The CD4 cell count significantly increased after commencement of ART therapy when our patient developed blurred vision. HIV-associated IRIS in patients receiving ART can unmask the dormant infections or may lead to paradoxical clinical deterioration in patients with active infection (4, 5). IRIS-associated uveitis is characterised by a generalised inflammation of all eye compartments (6-9). Since our patient had no eye symptoms before initiation of ART, it is considered as an unmasking subclinical CMV infection due to an ART –induced inflammatory response.

Optimal treatment includes ART and systemic antiviral therapy at induction therapy for two weeks followed by a maintenance therapy until immune reconstitution occurs (10). After six months, the maintenance treatment was terminated because the patient had a normal eye sight and no active lesion was observed following consecutive eye examinations. Several studies have been shown that in patients receiving long-term medication (at least 6 months), the maintenance therapy can be discontinued with no chance of recurrence, if the CD4 cells are 100 -150 cells /mm^3 or above (11). To early diagnosis of the recurrent retinitis, it is recommended to examine the patient at a regular basis.

We present this patient because of her unusual, but important eye presentation which can be easily missed during a routine examination in patients with HIV infection. The failure in early detection of IRIS-associated retinitis may lead to complications with a significant impact.

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