Original Article

Cytomegalovirus retinitis in acquired immunodeficiency syndrome patients: A problem worth giving attention to

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Abstract

Background: Cytomegalovirus (CMV) retinitis remains the most common ocular opportunistic infection in patients with acquired immunodeficiency syndrome even in the era of highly active antiretroviral therapy (HAART). Increased survival of patients on HAART has increased incidence of blindness, which will further increase in the future. The objective of this study was to determine the incidence of CMV retinitis and the effect of HAART on the natural history of CMV retinitis in patients referred from ART center. **Materials and Methods:** Patients with baseline/current CD4 counts <150 cells/μl were evaluated for CMV retinitis. Complete ophthalmological evaluation was carried out and records of CD4 counts, HAART regime, presence of any form of CMV retinitis and response to HAART were noted. **Results:** Out of 800 patients registered with CD4 <150 cells/μl in ART center, 100 patients reached us. Among these, CMV retinitis was observed in 15% patients, with median CD4 count at the time of examination being 56 cells/μl (range: 24-306 cells/μl). 66.67% patients were HAART non-responders and 63.6% eyes were economically blind. **Conclusion:** CMV retinitis occurs even in patients with higher CD4 counts. Timely diagnosis and intervention of this treatable condition can reduce the number of blinding years in these young patients who otherwise live longer as a result of HAART.

Key words: Acquired immunodeficiency syndrome, CD4, cytomegalovirus retinitis, highly active antiretroviral therapy

INTRODUCTION

The most common ocular opportunistic infection in patients with HIV is cytomegalovirus (CMV) retinitis. Prior to epidemic of HIV, CMV retinitis was rarely documented. In the pre- highly active antiretroviral therapy (HAART) era, there was 30% lifetime probability of developing CMV retinitis in acquired immunodeficiency syndrome (AIDS) patients.[1] Since the introduction of HAART in mid-1990's, the incidence has reduced by 80%.[1] In developing countries like ours, the scenario was different. CMV was highly under diagnosed and data available are insufficient to quantify the magnitude of blindness caused by CMV retinitis.[2,3] Increasing cases of CMV retinitis are being documented as HAART is increasing the survival of patients with AIDS. ART centers at government set-up provide a good opportunity to observe a large number of patients and determine the magnitude of CMV retinitis. This study was therefore conducted with the aim to observe patients with low CD4 counts and the effect of HAART on natural history of CMV retinitis.

Access this article online

Quick Response Code:

Website: www.ijstd.org

DOI: 10.4103/0253-7184.132411

MATERIALS AND METHODS

Ethical permission was taken from Human Research and Ethics Committee.

How to cite this article:
Gupta PK, Patel NV, Patel SD, Patel KJ. Cytomegalovirus retinitis in acquired immunodeficiency syndrome patients: A problem worth giving attention to. Indian J Sex Transm Dis 2014;35:21-4.

ART center chief medical officer and counselors were contacted and explained the importance of studying CMV retinitis in the early phase of the disease and were asked to refer patients to our outpatient department for complete ophthalmic evaluation. As per National AIDS Control Organization guidelines,[4] incidence of CMV retinitis increases when CD4 count falls below 100 cells/μl. A cut-off value of 150 cells/μl was therefore considered for the study to include variations.

During the study period, around 800 patients were registered with CD4 counts <150 cells/μ and we were able to evaluate a total of 100 patients. These patients were pre-diagnosed known cases of HIV infection attending ART center and on HAART.

Inclusion criteria

- All patients referred form ART center with baseline or current CD4 counts <150 cells/μl
- Patients aged more than 18 years
- Previously diagnosed cases of CMV retinitis.

Exclusion criteria

- Patients having baseline or current CD4 count more than 150 cells/μl
- Patients aged less than 18 years as they have different immunologic profile in them when compared to adults[5]
- Patients having retinal pathologies due to diabetes mellitus, hypertension, syphilis, tuberculosis or other systemic illnesses.

Methods of examination and recording

Visual acuity was assessed using self-illuminated Snellen's chart.

Anterior segment examination was carried out on Appasamy slit lamp (AIA-11 5S), to rule out any anterior segment inflammation.

For fundus assessment, the pupils of both eyes were dilated with tropicamide 1% or tropicamide 1% with phenylephrine 2.5% eye drops. Indirect ophthalmoscopy was performed using Heine indirect ophthalmoscope with +20D lens.

Documentation

The patient's relevant history (ocular symptoms, mode of transmission), baseline and current CD4 counts, HAART regimen and ophthalmic clinical findings were recorded on a detailed printed proforma. Patients were classified into HAART responders and non-responders. Responders were defined as patients having an increase in CD4 counts on follow-up by 50 or more cells/μl above the level at the time of CMV retinitis diagnosis to an absolute level of at least 100 cells/μl.[6] Those who had CD4 counts above 100 cells/μl, response was considered as a rise in CD4 by 50 cells/μl on follow-up. HAART non-responders were defined as those who either showed no increase or showed a decrease in CD4 counts from base line counts. Patients recently diagnosed and having baseline CD4 <150 cells/μl were classified as 1st timers. CMV retinitis was classified into active, healed or advanced disease. Active disease was further subdivided into classic hemorrhagic, granular and frosted branch angiitis patterns. History regarding any treatment for CMV retinitis previously received was also noted.

Fundus photographs were taken on Topcon fundus camera (TRC 50DX) with the patients informed consent for documentation, except for those patients who were highly moribund and unable to sit for long times. B-scan ultrasonography was carried out using Biomedix B-Scan/UBM machine in patients suspected of having retinal detachment.

Follow-up

The patients who attended our outpatient department after being referred from ART center were told about the importance of ocular examination for them and advised to follow-up 3 monthly or early if they had ocular disease. They were advised to come immediately if they developed significant ocular complaints which they were made aware about. On follow-up, their latest CD4 counts and HAART regimen were recorded; visual acuity was assessed and detailed dilated fundus examination was performed.

OBSERVATIONS

Study population

We evaluated a total of 100 patients with baseline, or current CD4 counts <150 cells/μl. 94% of the patients belonged to the age group of 21-50 years of age with the median age of 35 years (range: 18-70 years). Male to female ratio was 2.1:1 with 68% males and 32% females. The predominant mode of HIV transmission was through heterosexual route, being the mode in 92% patients. Median baseline CD4 count for the study group was 85 cells/μl (range: 12-404 cells/μl), 60% patients having counts <100 cells/μl. 40% patients were HAART responders, 35% HAART non-responders and 25% patients were 1st timers.

CMV retinitis

CMV retinitis was observed in 15% of patients with 22 eyes being affected. Median age was 35 years (range: 18-45 years) with 73% males and 27% females [Table 1].

Median CD4 count at examination was 56 cells/μl (range: 24-306 cells/μl) with 40% patients having CD4 counts <50 cells/μl and 20% having counts more than 151 cells/μl [Table 2]. Bilateral disease was present in 47% patients.

In patients with CMV retinitis, 54.5% had active disease [Table 3] of which 75% patients had classic hemorrhagic pattern [Figure 1], 8% had frosted branch angiitis [Figure 2] and17% had granular pattern [Figure 3 and Table 4]. Nearly 22.7% of patients had healed/necrotic lesions [Figure 4]. 22.7% had advanced disease with retinal detachment

In the present study, 63.6% eyes had visual acuity <6/60 on Snellen's chart (economically blind) with 27.27% eyes having only perception of light or no vision at all [Table 5].

All the patients were receiving 1st line HAART regime [Table 6], but 66.67% patients had 2nd line and substituted HAART regimen at the time of examination. Nearly 66.67% patients with CMV retinitis were HAART non-responders, 20% were responders and 13.33% were 1st timers [Table 7].

Among 15 patients, 13 patients (19 eyes) were diagnosed at our department and 2 patients (3 eyes) were diagnosed and treated for CMV retinitis elsewhere prior to the examination. Only 6 patients could be given treatment at our department as there was scarcity of drugs and funds at the ART center and anti-CMV medications are highly expensive for patients to purchase.

DISCUSSION

HAART has changed the natural history and outcome of CMV retinitis. CMV retinitis is not just limited to patients with the highest risk (CD4 counts <50 cells/μl), but also occurs in patients with higher CD4 counts. HAART has increased survival of HIV patients, so CMV retinitis continues to occur later in the course of the disease when they develop immune failure due to the development of drug resistance. Thus, ophthalmological screening is recommended even in patients on HAART and not developing immune recovery.

As per the records, 800 patients with CD4 counts <150 cells/μl were registered during

Table 1: Age and sex distribution

Age group (years)	Male	Female	Patients
<20	1	0	1
21-30	1	2	3
31-40	6	1	7
41-50	3	1	4
Total	11	4	15

Table 2: Distribution according to CD4 count at the time of examination

CD4 count	Patients (%)
<50	6 (40)
51-100	3 (20)
101-150	3 (20)
>151	3 (20)

Table 3: Type of CMV retinitis

Types	Eyes (%)
Active	12 (54.54)
Healed/necrotic	5 (22.72)
Advanced	5 (22.72)

CMV=Cytomegalovirus

Table 4: Subtypes inactive CMV retinitis

Subtypes	No. of eyes (%)
Classic hemorrhagic	9 (75)
Granular	2 (17)
Frosted branch angiitis	1 (8)

CMV=Cytomegalovirus

Table 5: Visual acuity at the time of diagnosis

Visual acuity	No. of eyes (%)
≤6/12	1 (4.54)
6/18-6/60	7 (31.81)
<6/60-1/60	8 (36.36)
<1/60-PL absent	6 (27.27)

Table 6: Duration of HAART being taken at the time of diagnosis

Duration in years	No. of patients (%)
<1	3 (20)
1-2	1 (6.66)
2-3	2 (13.33)
3-4	5 (33.33)
4-5	3 (20)
>5	1 (6.66)

HAART=Highly active antiretroviral therapy

Table 7: HAART response

HAART response	No. of patients (%)
Responders	3 (20)
Non-responders	10 (66.67)
1st timers	2 (13.33)

HAART=Highly active antiretroviral therapy

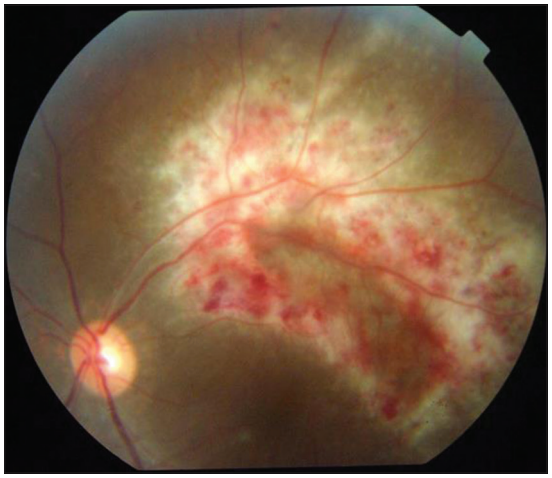

Figure 1: Active classic hemorrhagic pattern in an 18-year-old male with CD4 counts of 24 cells/μl on the second line highly active antiretroviral therapy

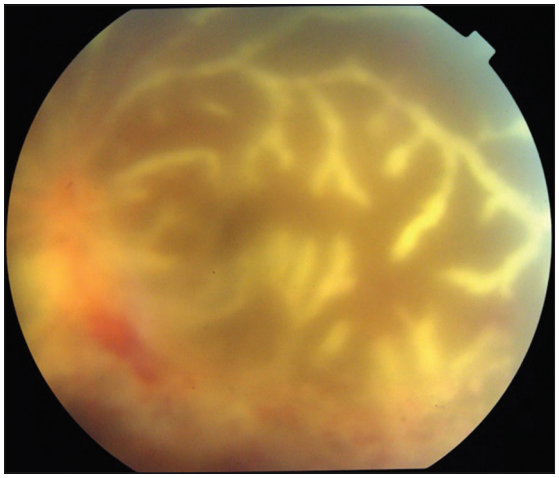

Figure 2: A 35-year-old male with frosted branch angiitis pattern in the left eye, with CD4 count of 90 cells/μl, who later on developed retinal detachment

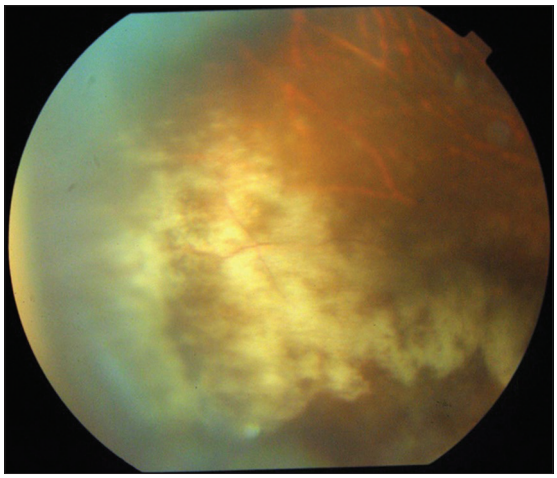

Figure 3: Granular pattern in the right eye of a 43-year-old male with CD4 count of 39 cells/μl

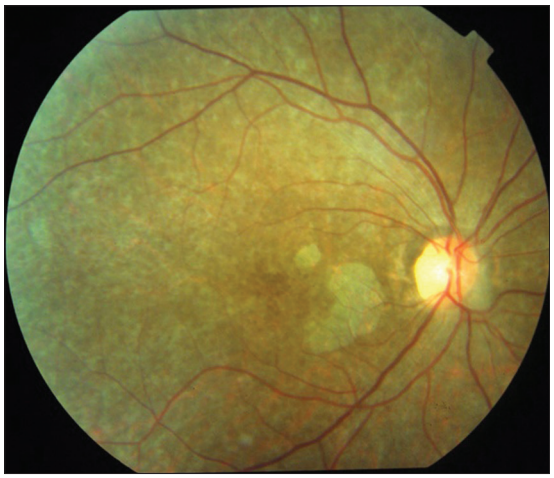

Figure 4: Healed lesions (salt and pepper appearance) in the right eye of a 43-year-old female with CD4 count of 49 cells/μl, on the second line highly active antiretroviral therapy. Visual acuity was 6/36 PH6/18 and she did not have significant visual symptoms

the study period, but we were able to evaluate only 100 patients. Many patients did not visit our out-patient department as they did not have any ocular complaints, others were not ready to volunteer for detailed eye examinations and severe systemic morbidity and poor socio-economic conditions did not allow some patients for regular follow-ups. To save valuable resources, primary AIDS care clinicians can be trained in diagnosing CMV retinitis using indirect ophthalmoscopy as it will provide benefit to the maximum number of patients and timely diagnoses of CMV retinitis will reduce the burden of blindness on the society.

Non-availability of oral valganciclovir did not allow us to treat all patients with CMV retinitis.

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Source of Support: Nil. **Conflict of Interest:** None declared.