

# Cytomegalovirus retinitis associated with high CD4 counts and DHEA abuse

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## Abstract

The most frequent ocular manifestation of acquired immunodeficiency syndrome (AIDS) is cytomegalovirus retinitis (CMVR). This infection is reportedly inversely proportional to the CD4 counts. Usually CMVR develops once the CD4 counts fall below 50/mm<sup>3</sup>. Our case report documents an AIDS patient who developed CMVR despite CD4 counts being persistently >200/mm<sup>3</sup>. The patient was self-administering dehydroepiandrosterone, high dose Vitamin C, testosterone and hydrocortisone. This case report describes a unique case of pharmacologically induced elevated CD4 counts, which however, did not prevent the development of CMVR in the patient.

**Key words:** Cytomegalovirus retinitis, dehydroepiandrosterone, ganciclovir

## INTRODUCTION

Individuals with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) are at increased risk for developing cytomegalovirus retinitis (CMVR). This risk is inversely proportional to the CD4 counts.

Here, we present this case report of an HIV-positive individual who obtained access to anabolic steroids and high-dose Vitamin C, leading to an elevated CD4 count. However, despite his high CD4 count, the patient developed CMVR in both eyes. This case report is being presented to highlight the possible role of supplemental medication in elevating the CD4 count and yet keep the patient susceptible to develop CMVR.

## CASE REPORT

A young homosexual male presented to our clinic with complaints of sudden onset of progressive blurring of vision in both eyes. A year earlier, he was diagnosed as HIV-positive individual, but did not seek any treatment.

However, since then, until the time of presentation, he had been injecting intravenous dehydroepiandrosterone (DHEA), testosterone, and Vitamin C on his own. He also took high-dose multivitamins and minerals orally.

On his first visit to our clinic, his best-corrected visual acuity (BCVA) was 6/60 (right eye) and 6/48 (left eye). The anterior segments in both eyes were normal. Ophthalmoscopy showed +2 vitreous cells in both eyes. There were large areas of dense white opacification, exudates, vasculitis, and scattered preretinal hemorrhages in both eyes [Figures 1 and 2]. General examination showed an alert and oriented individual. His blood pressure was 160/90 mmHg. There were generalized scabies and an intergluteal ulcer present. He also had right-sided hemiparesis, requiring him to seek assistance for ambulation.

Investigations for other systemic infections were negative. Initial CD4 counts were 267/mm<sup>3</sup> (38%), and CD8 counts

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were  $267/\text{mm}^3$  (38%). A magnetic resonance imaging of the brain showed a hematoma in the left basal ganglia.

A clinical diagnosis of bilateral CMVR was made. He was given intravitreal ganciclovir injections 2 mg/0.1 ml in each eye immediately. Subsequently, he was referred to the infectious disease department of our hospital. There, he was started on intravenous ganciclovir 350 mg twice daily for two weeks, along with tablet Bactrim (trimethoprim/sulfamethoxazole) and permethrin cream for scabies. He was also given topical miconazole cream for the intergluteal ulcer.

After 2 weeks of antibiotic therapy, he was started on highly active antiretroviral therapy (HAART) with efavirenz and tenofovir. The patient received intravitreal ganciclovir 2 mg/0.1 ml twice weekly in each eye for 5 weeks. The vitritis and retinitis progressively resolved with treatment. At the completion of therapy, the patient had BCVA of 6/12 (right eye) and 6/20 (left eye) [Figures 3 and 4].

## DISCUSSION

CMVR is the most common ocular manifestation of AIDS. With the introduction of HAART, there has been an 80% decline in the incidence of this condition.<sup>[1]</sup> Most case reports have noted CMVR occurring with CD4 counts below  $50/\text{mm}^3$ . There are only occasional case reports of patients developing CMVR with CD4 counts above  $250/\text{mm}^3$ .<sup>[2,3]</sup> In our patient, the CD4 counts were consistently  $>200/\text{mm}^3$ , and the patient developed features of CMVR before initiating HAART, thus excluding the possibility of immune-recovery uveitis.<sup>[4]</sup> CD4 counts are assumed to be surrogate markers for the level of immune dysfunction.<sup>[3]</sup> They are useful for screening patients at higher risk of CMVR. However, CD4 counts may hide subtle abnormalities in function and immune systems.<sup>[3]</sup> Apart from HIV, a number of other factors could possibly increase the susceptibility of this patient to CMVR. These include known risk factors such as unprotected homosexual behavior and self-administered intravenous injections.<sup>[5]</sup>

Clinically, CMVR can occur as indolent or fulminant forms. This ranges from mild granular opacification to large dense areas of retinitis, vasculitis, and vitritis. The diagnosis of CMVR is usually clinical, based on the characteristic posterior segment changes. Aqueous or vitreous tap can be done for polymerase chain reaction (PCR) analysis. However, PCR analysis has poor sensitivity and specificity, so clinical examination and history are more important. Most cases of CMVR respond well to ganciclovir, valganciclovir, foscarnet, or cidofovir. Untreated, the patient may become blind from extensive retinal involvement, retinal detachment, or consecutive optic atrophy. In our case, intravitreal and intravenous

ganciclovir were sufficient to produce clinical resolution of the condition.

The role of supplemental therapies abused by our patient in modifying the clinical features is conjectural. He was on intravenous, high-dose DHEA, hydrocortisone, testosterone, and Vitamin C for nearly 2 years before being seen by us. These supplements can modulate the clinical features of CMVR. DHEA is a steroid hormone synthesized in large quantities by the adrenal gland. However, its physiologic role remains unclear. In animals, DHEA was found to increase interleukin-2, which may help to guard against acute viral illness.<sup>[6]</sup> It is reported that low DHEA levels can lead to increased risk of disease progression in HIV-positive individuals. There is evidence that the DHEA levels correlate directly with the CD4 counts.<sup>[7-9]</sup> A preliminary open-labeled trial reported positive results on the effect of DHEA on mood and fatigue.<sup>[10]</sup> Studies have also demonstrated the immunomodulatory properties of DHEA. In HIV-positive patients, it inhibits the expression of HIV1 in latently infected cells.<sup>[11]</sup> However, there are no long-term clinical trials which support the use of DHEA therapy to alter the disease outcome in HIV-infected patients. Estradiol, testosterone, the steroid hormone precursor dehydroepiandrosterone-sulfate (DHEA-S), and progesterone are major immunoregulatory steroid hormones. DHEA-S is of special importance, as it is converted by the immune system to specific bioactive steroids that are required for normal immune function. HIV-positive individuals commonly have androgen deficiency. Low testosterone concentrations are associated with lower CD4 count, advanced stage of illness, medication use, and weight loss. Specific therapies recommended for HIV-associated wasting with low CD4 counts include testosterone replacement and other anabolic steroids. This also probably explains the lack of cachexia and elevated CD4 counts in our patient.<sup>[12]</sup>

In conclusion, the possibility of CMVR should not be excluded based on CD4 counts alone. The occurrence of the disease in our patient despite his high CD4 counts could probably be correlated to the self-administered supplemental hormonal therapy. Fortunately, potentially sight-threatening complications of CMVR were prevented by the prompt initiation of appropriate treatment in this case.

## WHAT IS NEW?

- CMVR in HIV-positive patients usually develops in those with CD4 counts below  $50/\text{mm}^3$ . In our patient, CMVR occurred even though CD4 counts were consistently above  $200/\text{mm}^3$ . Thus, CMVR should not be overlooked based on CD4 counts alone.
- The occurrence of CMVR in our patient, despite



Figure 1: Ophthalmoscopic picture of the right eye at first presentation



Figure 2: Ophthalmoscopic picture of the left eye at first presentation



Figure 3: Ophthalmoscopic appearance of right eye following treatment



Figure 4: Ophthalmoscopic appearance of left eye following treatment

the high CD4 counts, could be correlated to the self-administered supplemental hormonal therapy.

- This case report highlights the role of high-dose DHEA, hydrocortisone, testosterone, and Vitamin C in modulating the systemic and ocular features of HIV and secondary infections such as CMV.
- There are no long-term clinical trials supporting the use of DHEA therapy to alter disease outcome in HIV-infected patients. However, this case report points to a possible role of this agent in modulating HIV and related secondary infections.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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