Abstract

Purpose: Up to 70% of patients with acquired immunodeficiency syndrome (AIDS) have AIDS-related ocular involvements which may severely affect their quality of life caused by visual impairment. This study was designed to investigate the ocular manifestations in patients infected with human immunodeficiency virus (HIV).

Methods: In this case series study, 41 HIV positive patients were investigated through the first 6 months of 2003, in Farabi eye hospital, in Tehran, Iran. They were all under highly active antiretroviral therapy (HAART), but none was taking rifabutin, protease inhibitors or cidofovir. Complete ocular examination was carried out for each by Slit-lamp biomicroscope and indirect ophthalmoscope after pupil dilation.

Results: Thirty seven percent of patients had ocular disorders. 93% were male, 40% of all patients were 30-40 years old, 93.3% were in HIV stage (not AIDS stage). Intravenous drug (IVD) pathway had infected 86.6% of the patients, and 46.6% (n=19) had been infected throughout the previous three years. The most common ocular involvements among HIV positive patients were cotton wool spots (CWS) and vitritis (12.2%), which includes 66.6% of ophthalmic symptoms.

Conclusion: A variety of ophthalmic symptoms might affect HIV positive patients. These symptoms may cause severe disability in their lives, so ophthalmologists should pay more attention to HIV patients with ocular manifestations. Further studies are required for a better understanding of risk factors or possible human genes involved in occurrence of ocular involvement in HIV patients.

Keywords: Ocular Manifestation, Human Immunodeficiency Virus, Cotton Wool Spots, Cytomegalovirus Retinitis, Posterior Uveitis, Visual Impairment
Introduction
Up to 70% of patients with acquired immunodeficiency syndrome (AIDS) have AIDS-related ocular involvements. By 2007 an estimated 33.2 million people were infected with human immunodeficiency virus (HIV) worldwide and this means that about 23 million of them will be involved with ocular manifestations.

HIV related ophthalmic disorders occur due to several causes like opportunistic infections, vascular abnormalities, neoplasm, drug induced and neuro-ophthalmic lesions. Among them opportunistic infections are the major cause of morbidity and the most devastating ophthalmic disorder in people with AIDS. HIV-cytomegalovirus (CMV) co-infection occurs in 75-85% of patients, more than half of which develop CMV retinitis. Despite this high incidence, difficulties concerning the therapeutic approach and the result are relatively unsatisfactory even with the highly active antiretroviral therapy (HAART). There is a 63% risk of immune recovery uveitis (IRU) in patients with regressed CMV retinitis (a granular border with multiple dot-like satellite lesions in retina).

The most common ophthalmic finding in people with AIDS is cotton wool spots (CWS) as a retinal microvasculopathy. However, CWS -resulting from infarction in the nerve fiber layer- has relatively little clinical signs in healthy HIV positive patients. The incidence of CWS in patients with advanced HIV disease is related to the severity of immunodeficiency and is a negative prognostic sign. On the other hand, Chen S et al (2007) found that up to 7.2% of HIV positive patients have ophthalmic symptoms on first admission which may be neglected by ophthalmologists in the early stages. This may severely affect patients’ quality of life by visual acuity reduction. This study was designed to investigate the ocular manifestations in patients with HIV.

Methods
In this case series study 41 HIV positive patients were included. They were investigated in Farabi eye hospital, Tehran, Iran, through the first 6 months of 2003, and complete ocular examinations were carried out for each. All the patients were under HAART treatment with Lamivudine, Zidovudine and Indinavir, and their infection was proved through the Western blot test, but none were taking rifabutin, protease inhibitors or cidofovir.

None of the patients had a past history of ocular disorders, and ocular manifestations like CMV retinitis, CWS, exudation, central disk neuropathy (CDNP), reduced vision and anterior and posterior uveitis were investigated for each subject.

In the ocular examination, their vision was examined initially, followed by the anterior segment investigation by Slit-lamp biomicroscope. In the next process retinal examination was performed by indirect ophthalmoscope after pupillary dilation with Mydriacil. Each patient’s examination results were recorded.

The study protocol was approved by the Medical Ethics Committee in Tehran University of Medical Sciences. Each patient gave informed consent before enrollment in the study. All the statistical analyses were performed using SPSS software (version 13.0) for windows.

The results have been reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables.

Results
A total of 41 patients including 38 (92.6%) males and 3 (7.4%) females with the mean age of 32.1±6.4 years were enrolled. Five patients (12.2%) had CWS (4 males and 1 female), all of them were over 30 years old and were infected through his mother, and the others were above 30 years and were infected through IVD or sexual pathway.

CMV retinitis was confirmed in a 38-year-old male who was infected through intravenous injection in the past 3 years. Some red patches were seen in his posterior pole and his CD4 level was more than 200 cell/mm³ (Figure 1).

Five males (12.2%) with CD4 count more than 200/mm³ had vitritis, one of them was under 10 years of age who was infected through his mother, and the others were above 30 years and were infected through IVD or sexual pathway.
In this study 4 patients (9.7%) were seen with the visual disorder, all of them were male and were infected through IVD or sexual pathway. None of the patients had exudation, CDNP or anterior uveitis. In a patient with 10 years of HIV history, no ocular manifestations were found.

37% of the patients had ocular disorders, most of them were male (93.3%), 30-40 years old (40.0%), in HIV stage (93.3%), IVD pathway infected (86.6%) and infected in the 3 past years (46.6%). The most common ocular involvements among HIV patients were CWS and vitritis (12.2%) composing 66.6% of ophthalmic symptoms (Table 1).

**Table 1. Features of ophthalmic disorders in HIV patients**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CWS*</th>
<th>Vitritis</th>
<th>CMV** retinitis</th>
<th>Visual disorder</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>4 (9.7%)</td>
<td>5 (12.2%)</td>
<td>1 (2.4%)</td>
<td>4 (9.7%)</td>
<td>14 (34.1%)</td>
</tr>
<tr>
<td>30-40 years old</td>
<td>2 (4.9%)</td>
<td>1 (2.4%)</td>
<td>1 (2.4%)</td>
<td>2 (4.9%)</td>
<td>6 (14.1%)</td>
</tr>
<tr>
<td>HIV stage</td>
<td>4 (9.7%)</td>
<td>5 (12.2%)</td>
<td>1 (2.4%)</td>
<td>4 (9.7%)</td>
<td>14 (34.1%)</td>
</tr>
<tr>
<td>Recent 3 years</td>
<td>2 (4.9%)</td>
<td>3 (7.3%)</td>
<td>1 (2.4%)</td>
<td>1 (2.4%)</td>
<td>7 (17.1%)</td>
</tr>
<tr>
<td>IVDU infection†</td>
<td>4 (9.7%)</td>
<td>4 (9.7%)</td>
<td>1 (2.4%)</td>
<td>4 (9.7%)</td>
<td>13 (31.7%)</td>
</tr>
</tbody>
</table>

* CWS: Cotton wool spots  
** CMV: Cytomegalovirus  
† IVDU: Intravenous drug user

**Discussion**

Since 1982, there has been a profound focus on HIV in ophthalmology. Long incubation time, high incidence of ocular manifestations, difficulties in therapeutic approaches and relatively unsatisfactory results make this lentivirus a worldwide disaster.

Prevalence of ocular disorders in HIV positive patients had been reported between 7.2% and 70%. In this study more than one-third of patients had ocular disorders. Uemura A et al also confirmed ocular complications in almost one third of HIV positive patients. The most prominent ophthalmic problems were CWS and posterior uveitis.

CMV retinitis was confirmed in 12.2% of patients while some studies reported CMV retinitis as the most prevalent ocular disorder. On the other hand, numerous studies demonstrated CWS as the most common ophthalmic finding in people with AIDS.

Anterior uveitis is a rare symptom of HIV positive patients and none of the examined patients in this study had this problem;
however, Verma S et al found 6.9% of 172 HIV positive patients with anterior uveitis.\textsuperscript{17} Despite the high incidence of ocular involvements in AIDS patients, the etiology and pathogens of these manifestations are not well understood.\textsuperscript{20} In our study all the patients with CMV retinitis and vitritis had CD4 levels more than 200 cell/mm\textsuperscript{3}. The HIV-induced immunosuppression had a determining role in a way that about 90% of CMV retinitis cases occur in HIV infected individuals with CD4 T lymphocyte counts fewer than 50-100 cell/mm\textsuperscript{3}.\textsuperscript{3,4,21,26} It seems there is a non linear correlation between CD4 levels and occurrence of ocular complications\textsuperscript{22}; so HAART regimen with immune system restoring and viral load decreasing action could improve up to 80% of patients with CMV retinitis.\textsuperscript{7,8} All the ophthalmic symptoms in HIV infected patients are not established by HIV itself. Nwosu NN found 20% of HIV infected patients with non-HIV related ocular disorders.\textsuperscript{27} However, ocular problems like CMV retinitis can be the first symptom of HIV disease.\textsuperscript{28} Some other complications like CWS may be related to the severity of immunodeficiency\textsuperscript{12-15} and could demonstrate poor prognosis of the disease.\textsuperscript{4}

\section*{Conclusion}

It can be concluded HIV positive patients might suffer from different kinds of ophthalmic symptoms, which may cause severe disability in their lives, so ophthalmologists should pay more attention to HIV patients and their ocular manifestations. Further studies are required for a better understanding of risk factors or possible human genes involved in the occurrence of ocular complications in HIV positive patients.

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