OCULAR MANIFESTATIONS IN HIV POSITIVE PATIENTS ATTENDING KHYBER TEACHING HOSPITAL PESHAWAR

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ABSTRACT

Introduction: Human immunodeficiency virus (HIV) infection is a global health problem. Around 90% of infected persons live in developing countries, particularly those in sub-Saharan Africa and Southeast Asia. Ocular manifestations occur in approximately 70% of these patients. The objective of this study was to document ocular manifestations in HIV positive patients attending Khyber Teaching Hospital Peshawar, Pakistan.

Methodology: It was a descriptive case series. The study was conducted at Khyber Teaching Hospital Peshawar from January to December 2007. A total of 14 patients were examined. These patients underwent complete ocular examination including assessment of visual acuity, pupillary reaction, ocular motility, ocular adnexa, anterior segment and posterior segment. CD4 count was done in all the patients.

Results: Out of the 14 patients examined 6 (42.9%) had ocular manifestations, all of whom were male. The ocular manifestations included herpes simplex keratitis, herpes zoster ophthalmicus with neurotrophic keratitis, iridocyclitis, HIV retinopathy, retinal vasculitis and cytomegalovirus retinitis in one patient each. Amongst those with ocular manifestations, 5 patients (83.3%) had CD4 cell count of 100/mm^3 or less and 1 patient (16.7%) had CD4 count between 101 and 200/mm^3; and the mode of transmission was homosexual contact in 5 patients (83.3%) and vertical transmission in 1 patient (16.7%).

Conclusion: Ocular manifestations occur in a considerable number of HIV positive patients particularly in those with CD4 cell count less than 100/mm^3. Therefore, all HIV positive patients should be screened for ocular manifestations.

Key words: HIV, AIDS, CMV retinitis, HAART, CD4 count.

INTRODUCTION

Human immunodeficiency virus (HIV) is a retrovirus that causes a wide range of diseases,[1,2,3,] like an acute mononucleosis-like syndrome, an asymptomatic carrier state, persistent generalized lymphadenopathy, AIDS-related complex, and AIDS (acquired immune deficiency syndrome). AIDS is characterized by a gradual decrease in circulating $CD4^+$ T cell count which is responsible for the various opportunistic infections and neoplasms.[4] According to the Joint United Nations Program on HIV/AIDS (UNAIDS), there were approximately 33 million people living with HIV worldwide in 2007. In 2007, 2.7 million people contracted the virus and 2 million died from AIDS.[5] Around 90% of HIV infected persons live in developing countries, particularly

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those in sub-Saharan Africa and Southeast Asia.[6,7] According to UNAIDS, approximately 96000 people had HIV infection in Pakistan at the end of 2007 and the estimated adult prevalence was approximately 0.1%.[8]

Transmission of HIV is predominantly by sexual contact, by parenteral (intravenous drug use) or mucous membrane exposure to contaminated blood or blood products and perinatally.[4] Early diagnosis and treatment of HIV/AIDS is critical in prolonging life expectancy and reducing opportunistic infections. Highly active antiretroviral therapy (HAART) is a combination of antiretroviral drugs which make them more potent and probably reduce or postpone the occurrence of drug resistance.[9] Ocular manifestations occur in approximately 70% of HIV infected persons.[4] Ocular lesions associated with AIDS can be categorized into the following groups:[9]

- HIV retinopathy
- Opportunistic infections (caused by bacteria, viruses, fungi and protozoa)
- Neuro-ophthalmic lesions
- Unusual neoplasms like Kaposi sarcoma

CD4 count can be used to predict the onset of certain ocular manifestations of AIDS. CD4 count less than 500/mm^3 is associated with Kaposi sarcoma, lymphoma and tuberculosis; CD4 count less than 250/mm^3 is associated with pneumocystosis and toxoplasmosis; and CD4 count less than 100/mm^3 is associated with retinal or conjunvtival microvasculopathy, cytomegalovirus (CMV) retinitis, varicella zoster virus (VZV) retinitis, mycobacterium avium complex infection, cryptococcosis and microsporidiosis.[10]

To the best of our knowledge, no work has been done regarding ocular manifestation in HIV positive patients in Pakistan. The purpose of our study was to document ocular manifestations in HIV positive patients attending Khyber Teaching Hospital Peshawar. Based on the results of our study, we plan to develop a large screening program for HIV positive patients in Khyber Pukhtoon Khwa (KPK), Pakistan.

METHODOLOGY

It was a descriptive case series. The study was conducted at the Department of Ophthalmology, Eye 'B' Unit, Khyber Teaching Hospital Peshawar Pakistan, which is a tertiary care hospital. Duration of study was 1 year i.e. from January to December 2007. Our study population included HIV positive patients of Khyber Pukhtoon Khwa (KPK) Pakistan. A total of 14 HIV positive patients including 10 male and 4 female were included in the study. They were all diagnosed by the physician. Diagnosis was based on detection of anti-HIV antibodies in the serum by both enzyme-linked immunosorbent assay (ELISA) and western blot tests. These patients were referred for screening for ocular manifestations of HIV infection. Informed consent was taken from all the patients. Detailed history was taken including questions about the mode of transmission, time since the diagnosis of disease and any systemic morbidity. Complete ocular examination was done including best corrected visual acuity using Snellen visual acuity chart, pupillary reaction with torch, ocular motility, examination of the ocular adnexa with torch and slit-lamp (Takagi SM-70, Japan), examination of anterior segment and vitreous with slit-lamp and fundus examination with indirect ophthalmoscope (Neitz, Japan) and 78/90D lens (Volk, USA) after pupillary dilatation with 1.0% tropicamide and 10% phenylephrine eye drops. CD4 count was done in all the patients. All the relevant data was recorded on a proforma. The study was approved by the ethical review board of the hospital.

RESULTS

Total of 14 patients were examined including 10 males (71.4%) and 4 females (28.6%). Patient's age ranged from 2 to 50 years with a mean of 32 years. The time period between the diagnosis of disease and ocular examination was ranging from 4 months to 10 years. Mode of transmission was homosexuality in 8 (57.1%), heterosexuality in 4 (28.6%), blood-borne in 1 (7.1%) and vertical in 1 patient (7.1%). The CD4 count of the patients was ranging from 5 cells/mm^3 to 427cells/mm^3. The CD4 count was 100 or less in 6 patients (42.9%),

101-200 in 4 patients (28.6%), 201-300 in 1 patient (7.1%), 301-400 in 1 patient (7.1%) and 401-500 in 2 patients (14.3%).

Ocular manifestations were present in 6 patients (42.9%) all of whom were male. Mean age of patients with ocular manifestations (29.5 years) was slightly lower than those with no ocular manifestations (34 years). The time period between the diagnosis of disease and ocular examination in patients with ocular manifestations, was ranging from 7 months to 6 years. In patients with ocular manifestations, the CD4 count was ranging from 5cells/mm^3 to 130cells/mm^3. 5 out of those 6 patients (83.3%) had CD4 count of 100cells/mm^3 or less and 1 patient (16.7%) had CD4 count between 101 and 200cells/mm^3 and the mode of transmission was homosexuality in 5 patients (83.3%) and 1 patient (16.7%) had vertical transmission of disease from his mother.

Ocular manifestations were present in 6 out of the 10 male patients (60%); none of the female had ocular manifestations. Ocular manifestations seen in our patients included herpes simplex keratitis, herpes zoster ophthalmicus (HZO) with neurotrophic keratitis, iridocyclitis, HIV retinopathy, retinal vasculitis and cytomegalovirus (CMV) retinitis in 1 patient each (Table 1).

Table 1. Summary of clinical features of all patients

Age	Gender	Mode of transmission	Duration of disease	CD4 count	Ocular Manifestations
50 years	Male	Homosexual	07 months	34	HSV keratitis
30 years	Female	Heterosexual	11 months	436	None
35 years	Female	Heterosexual	10 months	129	None
40 years	Male	Homosexual	02 years	05	CMV retinitis
27 years	Male	Homosexual	01 year	134	
47 years	Male	Homosexual	06 years	83	HZO with neurotrophic keratitis
35 years	Male	Homosexual	02 years	210	None
32 years	Male	Blood borne	10 years	326	None
50 years	Male	Homosexual	04 years	427	None
30 years	Female	Heterosexual	07 months	125	None
20 years	Male	Homosexual	06 years	43	Retinal vasculitis
33 years	Female	Heterosexual	01 year	61	None
18 years	Male	Homosexual	04 months	130	HIV retinopathy
02 years	Male	Vertical	02 years	70	Iridocyclitis

HSV keratitis - Herpes simplex virus keratitis;
CMV retinitis - Cytomegalovirus retinitis;
HZO - Herpes zoster ophthalmicus;
HIV - Human immunodeficiency virus.

DISCUSSION

The lifetime risk of developing ocular feature in a HIV positive patient varies from 52 to 100%.[11] The frequency of ocular manifestations reported from a study done in Ethiopia was 60%.[12] In another study conducted in Japan 80% of the AIDS patients had ocular manifestations.[13] In our study 42.9% patients had ocular manifestations. All these patients were male; none of the female patients had ocular manifestation. The prevalence of ocular manifestations is higher in patients who have CD4 count of 100cells/mm^3 or less.[14] In our study 5 out of the 6 patients with ocular manifestations had CD4 count less than 100 and 1 patient had CD4 count between 101 and 200. The mode of transmission was homosexual contact in 5 out of these 6 patients who had ocular manifestations and vertical transmission in 1 patient. In literature no association has been found between the mode of transmission and the presence of ocular manifestations of HIV.

HIV retinopathy is the most common ocular feature of AIDS.[15] It affects almost 50-70% of the patients and is characterized

by cotton-wool spots, intraretinal hemorrhages and retinal microaneurysms.[16,17] It is usually asymptomatic.[18] In our study HIV retinopathy was seen in 1 patient. The patient had bilateral cotton wool spots and microaneurysms. The patient was asymptomatic and had normal visual acuity in both eyes.

In our study 1 patient had cytomegalovirus (CMV) retinitis. CMV retinitis is the most common opportunistic ocular infection in AIDS patients and can occur in approximately 40-50% of untreated patients.[15] It occurs almost exclusively in patients with CD4 count below 50cells/mm^3 and may be unilateral initially but upto 52% eventually develop bilateral disease.[19] Diagnosis of CMV retinitis was made on the basis of clinical features. The patient had CD4 count of 5cells/mm^3 and had marked systemic debility and other opportunistic infections.

Herpes zoster ophthalmicus (HZO) occurs in 5-15% of HIV positive patients, resulting from reactivation of previously established primary varicella-zoster virus (VZV) infection. It is characterized by painful, vesiculobullous skin rash over the distribution of the ophthalmic division of trigeminal nerve. VZV may also cause keratitis, iridocyclitis and retinitis (acute retinal necrosis and progressive outer retinal necrosis).[10] In our study 1 patient had HZO. He had vesicular skin rash in the distribution of ophthalmic division of trigeminal nerve and had neurotrophic keratitis due to which his visual acuity was decreased to 6/36 in the affected eye.

In our study 1 patient had dendritic corneal ulcer with decreased corneal sensation. A clinical diagnosis of herpes simplex virus (HSV) epithelial keratitis was made. The patient had CD4 count of 34cells/mm^3 and had visual acuity of 6/9 in the affected eye. In one study, the prevalence of HSV keratitis was higher in HIV positive patients as compared to the general population, and approximately 67% of HSV infected patients developed epithelial keratitis.[10] According to another author, except for the recurrent rate, the incidence and clinical course of HSV keratitis was similar among patients positive and negative for HIV.[20]

Iridocyclitis was seen in 1 patient in our study. It was unilateral and non-granulomatous. Iridocyclitis, in HIV positive patients, may be associated with retinal or choroidal infection with Cytomegalovirus, Herpes simplex virus, Varicella zoster virus, Candida, Cryptococcus, Toxoplasma gondii, Treponema pallidum and Mycobacteria;[21] and some medications, such as rifabutin[22] and cidofovir.[23] Serological investigations for most of these organisms were not available in our hospital. Only the few available investigations (Anti-toxoplasma IgG and IgM antibodies by ELISA, Venereal Disease Research Laboratory, Montoux test and Chest X-ray) were done but they were negative and therefore, no cause could be found for iridocyclitis.

In one study vasculitis involving peripheral retinal vessels was observed in 31% of the HIV positive patients.[24] In our study retinal vasculitis was seen in one patient. It was unilateral, involving the peripheral retina and the patient had visual acuity of 6/12. The patient was assessed clinically and relevant investigations were done to exclude other causes of retinal vasculitis. Chest X-ray, serum angiotensin converting enzyme (ACE), montoux test, computed tomography (CT) thorax, magnetic resonance imaging (MRI) brain, antinuclear antibody (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) were done, but all of them were normal.

There are a number of drawbacks in our study. Our sample size is very small. The reason being that we started our study in collaboration with a non-governmental organization (NGO) which was working for HIV positive patients in Khyber Pukhtoonkhwa (KPK) Pakistan, but due to the political situation and due to security concerns that NGO became completely non-functional and we could not continue our project. Our study was a cross-sectional study. Most of the patients developed marked systemic debility that's why follow up was not possible in those patients. Further studies, with larger sample size and long follow up, need to be done to know precisely about the disease pattern in our population.

Since we belong to a developing country and even in our tertiary care hospitals many modern facilities

are lacking. At the time of conducting this study, a functional fundus camera was not available in our hospital and since it is very inconvenient for the ill patients to go to other centres, we could not take fundus photographs of the patients and could not do Fundus Fluorescein Angiography (FFA).

CONCLUSION

Ocular involvement occurs in a considerable number of HIV positive patients particularly in those patients with CD4 cell count less than 100/ mm^3. All HIV positive patients should be screened by an ophthalmologist in order to identify the ocular manifestations at early stage and manage them properly.

To the best of our knowledge, no work has been done regarding ocular manifestation in HIV positive patients in Pakistan. Therefore further research needs to be done to know about the disease pattern in Pakistani population.

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