OCULAR MANIFESTATIONS IN HIV POSITIVE PATIENTS IN THE ERA OF ANTIRETROVIRAL THERAPY

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ABSTRACT

BACKGROUND

Human Immunodeficiency Virus (HIV) infection/Acquired Immune Deficiency Syndrome (AIDS) is a multisystem disorder affecting the eye either directly or indirectly through various opportunistic infections. It is one of the most feared infectious diseases of the twentieth century posing a significant occupational hazard to the medical community.

Aim- To study the ophthalmological profile of HIV positive patients presenting with ocular symptoms to the ART clinic and to study the ocular changes induced by Anti-Retroviral Therapy (ART).

MATERIALS AND METHODS

All patients diagnosed with HIV infection with ocular symptoms including decreased vision, floaters, pain and photophobia underwent a complete ophthalmological examination including best corrected visual acuity, slit-lamp examination and indirect ophthalmoscopy. B-scan ultrasonography and automated perimetry were done wherever required. CD4 cell count estimation was done in all patients.

RESULTS

69 male and 31 female HIV positive patients between the ages of 6 to 60 years were included in the study. 33% had bilateral eye involvement. All except 17 patients were already on ART. 20 patients had purely refractive errors only. The most common anterior segment lesions were conjunctivitis, iridocyclitis and adnexal glandular swellings. Most common posterior segment lesions were CMV retinitis and vitritis due to Immune Recovery Uveitis. All cases of CMV retinitis and other posterior segment infections were seen in patients having CD4 count < 50 cells/uL and Immune Recovery Uveitis was seen when CD4 count was between 100-200 cells/uL.

CONCLUSION

Even when patients are on ART, many varied ocular manifestations are still noted, especially drug-induced changes, which can be sight threatening if not treated early. Ocular symptoms may point to falling immunity in the HIV positive patients. Vision threatening manifestations are seen in HIV patients with low CD4 counts. Early treatment can reduce the incidence of visual morbidity.

KEYWORDS

HIV Infection, Anti-Retroviral Therapy, Ocular Manifestations, CMV Retinitis, Immune Recovery Uveitis.

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BACKGROUND

The Human Immunodeficiency Virus infection, since its first detected case in India in 1986, has rapidly spread to involve about 0.36% of adult population. Of the 2.5 million people living with HIV in India in 2006, 88.7% are adults, 7.5% are aged 50 and above, while 3.8% are children.⁽¹⁾ Ocular manifestations were seen in about 70% patients in the pre antiretroviral therapy (ART) era,⁽²⁾ and were often an indication of irreversible end-stage AIDS disease. But with the advent of effective antiretroviral therapy, more patients are surviving and therefore the eye changes can be important indicators for the initiation and effectiveness of treatment, as these manifest when CD4 count drops below 100 cells / μ L.

The spectrum of ophthalmic manifestations in HIV disease is very broad and ranges from adnexal to posterior segment disorders. They can be broadly classified into five groups-

1. HIV retinopathy.
2. Opportunistic infections.
3. Neuro-ophthalmic lesions.
4. Neoplasms like Kaposi's sarcoma.
5. Adverse drug reactions.

Due to potentially devastating rapid course of opportunistic infections in the eye, all HIV positive patients should undergo routine baseline ocular examinations and should receive prompt and competent eye care without delay. In the early stage of the disease, when CD4 count is high the chances for having ocular syndromes associated with immunosuppression is very low. Routine ocular history taking and examinations can provide clues regarding falling immunity.

Because of significant improvement in antiviral therapy, infected persons are living much longer with better quality of life. Anti-Retroviral Therapy is an effective regimen used to reduce the viral load to <50 copies/mL. Eyes can also become victims to drug-related adverse reactions of ART, immune

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recovery uveitis and anaemic changes in the eye being commonly observed manifestations. Thus, ocular examination is also an integral part of followup of patients on ART.

We conducted a study at Government Medical College, Thrissur to study the ophthalmic profile of patients with HIV who presented at our outpatient department with ocular symptoms in order to understand the varying presentations of the disease, and the changes induced by treatment, during the course of National ART programme, which consists of a combination of two nucleoside reverse transcriptase inhibitors, and a non-nucleoside reverse transcriptase inhibitor.

Aims of the study were to study the ophthalmological profile of HIV positive patients presenting with ocular symptoms, to study the ocular changes induced by Anti-Retroviral Therapy and to study the relationship between CD4 count and various ocular manifestations.

MATERIALS AND METHODS

This was an observational study of 100 consecutive HIV positive patients with ocular symptoms who presented to the ART centre of Government Medical College, Thrissur between January 2008 to June 2009. Patients presenting with symptoms of visual loss, redness or pain in eye, photophobia, or floaters were referred by the primary physician to the Ophthalmology department for further evaluation.

They included both pre-ART patients as well as those already on Antiretroviral Therapy. Patients with neurological, psychiatric or other multisystem disorders who were either too sick or unwilling to give informed consent for the study were excluded from the study.

A detailed history regarding ocular symptoms was taken. All the patients underwent a complete ocular examination including best corrected visual acuity, refraction, slit-lamp examination, intraocular pressure by non-contact tonometry, fundus examination by indirect ophthalmoscopy and 90D contact lens. Automated perimetry, anterior segment and fundus photography and B-scan ultrasonography were done when indicated. The HIV status was confirmed using the guidelines by NACO (Ref). CD4 cell count estimation was done in all patients every 6 months and when clinically indicated. Treatment for ocular lesions was given wherever necessary and followup examinations were done within 1 month, at 3 months and 6 months and at the end of one year of enrolment in the study.

The study was approved by the Institutional Review Board and Institutional Ethics Committee of Government Medical College, Thrissur.

RESULTS

The age of the patients ranged from 6-60 years with mean age being 33 years. 69 were male and 31 were female. Majority were in the 30-40 years age group.

Out of 100 patients with ocular symptoms examined, 20 patients were found to have refractive errors only. 80 patients had ocular lesions other than refractive errors out of which twenty six patients (33%) had bilateral eye involvement.

Defective vision was the most common symptom (58%) followed by eye pain (12%), redness (11%), floaters (8%), watering (7%), and lid swelling (2%).

The details of anterior and posterior segment manifestations are shown in Table 1 and 2.

Sl. No.	Manifestations	Number of Eyes	(%)
1.	Conjunctivitis	15	14
2.	Lid Swelling	7	6.6
3.	Immune Recovery Iridocyclitis	3	2.8
4.	Cataract	4	3.8
5.	Episcleritis	2	1.9
6.	Lateral Rectus Palsy Following Meningitis	2	1.9
7.	Toxic Epidermal Necrolysis	2	1.9
8.	Superficial Punctate Keratitis	1	0.9
9.	Lymphomatous Lid Involvement	1	0.9
10.	Scleral Abscess	1	0.9

Table 1. Anterior Segment Manifestations

Sl. No.	Manifestations	Number of Eyes	(%)
1.	CMV Retinitis	28	27
2.	Vitritis in Immune Recovery Uveitis	18	17
3.	Optic Atrophy	9	8.5
4.	Acute Retinal Necrosis	7	6.6
5.	Retinal Microvasculopathy	4	3.8
6.	Retinal Detachment	3	2.8
7.	Toxoplasma Retinochoroiditis	2	1.9
8.	Anaemic Fundus due to Zidovudine Toxicity	2	1.9
9.	Progressive Outer Retinal Necrosis	1	0.9
10.	Branch Retinal Arterial Occlusion	1	0.9
11.	Tubercular Choroiditis	1	0.9

Table 2. Posterior Segment Manifestations

Ocular Changes with Initiation of Antiretroviral Therapy (ART)

In our study, there were seventeen pre ART patients. Eleven patients had ophthalmic lesions and six had visual complaints due to uncorrected refractive error. Four patients were initiated to ART following diagnosis of ocular lesions, three patients for CMV retinitis and one for Toxoplasma retinochoroiditis.

Eight patients expired during the followup period due to various systemic complications.

Immune Recovery Uveitis was seen in twenty one eyes with CMV retinitis. All of these had development of manifestations by the fourth month of initiation of therapy. Three eyes had initial iridocyclitis followed by vitritis and eighteen eyes presented with vitritis. All responded well to systemic and local corticosteroid treatment.

Two eyes of a patient developed haemorrhages and Roth spots following pancytopenia at the fifth month, induced by Zidovudine treatment.

Twenty one patients presented with CMV retinitis in our study. All were given ART regimen. CMV retinitis healing was noted in ten patients during the one year followup and three eyes subsequently developed rhegmatogenous retinal detachment due to holes developing in necrotic retina. All the

rest of eyes with posterior segment lesions showed marked improvement and stabilisation of ocular disease on ART.

One patient with unexplained progressive optic atrophy showed stabilisation of vision and fields after 6 months of ART.

Chart Showing the CD4 Count of Patients at Baseline

Relationship of CD4 Count and Ophthalmic Lesions

CMV retinitis and other posterior segment manifestations were seen only in patients with <50 cells/uL.

All cases of Immune Recovery Uveitis was seen in patients with CD4 between 100-200 cells/uL at the time of diagnosis of IRU.

The patient suffering from lymphoma had CD4 of 833 cells/uL.

DISCUSSION

In our study, which included patients with HIV infection and ocular symptoms, ocular lesions were seen in 80% of patients. Thus, a proper history taking by the treating physician can detect majority of vision threatening complications early.

Among anterior segment lesions, conjunctivitis both infective and allergic was the commonest diagnosis found in the anterior segment in our study. In our patients with posterior segment disease, CMV retinitis was the most common cause, similar to other studies^(2,3,4,5) and in three patients it was the indication for initiation of ART. HIV retinopathy was less commonly seen in our patients unlike other studies,^(2,3) probably because this manifestation alone is asymptomatic and we included only symptomatic patients in our study.

CD4 counts represent the immune status of the individual. In our study 38% patients had <200 cells/uL. CMV retinitis occurred exclusively in the group of patients with CD4 <50 cells/uL which is similar to the other studies.^(6,7) The lesions showed marked improvement and stabilisation with ART even without standard anti-cytomegalovirus therapy.

This favourable outcome of ART has been reported elsewhere.⁽⁸⁾

Immune Recovery Uveitis (IRU) was the most common ophthalmic complication seen due to ART initiation and it occurred around the fourth month of initiation. Most of these patients had underlying CMV retinitis. But all of these patients including the patient with papillitis who received two doses of intravitreal ganciclovir, were controlled on ART and systemic corticosteroid therapy. Though ART caused healing of CMV lesions subsequent development of holes in necrotic retina caused retinal detachment in 2.8% eyes.

CONCLUSION

Anti-retroviral therapy is an important and effective management regimen for ocular HIV manifestations. But even when patients are on ART, many varied ocular manifestations are still noted especially drug-induced changes, which can be sight threatening if not treated early. The development of IRU can be effectively controlled with corticosteroids. Development of ocular symptoms may be a warning sign of falling immunity of the HIV positive patient.

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