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Ophthalmic Manifestations in HIV Positive patients and the Indian Perspective

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Abstract

The Eye is a vital sense organ and much like any other organ in the body can be afflicted by HIV. An ophthalmic referral at the time of presentation must be ensured by the treating physician. The ophthalmologist must take utmost care while examining and treating such patients to avoid patient to patient and patient to healthcare provider spread of HIV. A detailed ophthalmic examination for the various manifestations must be done and timely intervention for the same must be carried out which is critical to prevent ocular morbidity. Highly Active Anti Retroviral Therapy (HAART) is safe and has been instrumental in lowering sight threatening complications of HIV such as CMV retinitis.

Keywords: HIV; India; Ophthalmology; CMV Retinitis

HIV - India and the World

Human Immunodeficiency Virus (HIV) currently infects 35.3 million people across the world [1]. Overwhelming size of the Indian population makes it the country with the largest number of people living with HIV /AIDS (PLWHA). There are 2.09 million PLWHA in India and out of this number, approximately 145,000 are children [2]. Children (<15 yrs) account for 3.5% of all infections, while 83% are the in age group 15-49 years. Of all HIV infections, 39% (930,000) are among women [2].

With the advent of Antiretroviral Therapy (ART), the scenario is changing for the better. The number of people dying of AIDS-related causes fell to 1.8 million [1.6 million –1.9 million] in 2010, down from a peak of 2.2 million [2.1 million–2.5 million] in the mid-2000s [3]. A total of 2.5 million deaths have been averted in low- and middle-income countries since 1995 due to antiretroviral therapy being introduced, according to calculations by UNAIDS. [3] Much of that success has come in the past two years when rapid scale-up of access to treatment occurred; in 2010 alone, 700 000 AIDS related deaths were averted [3]. The proportion of women living with HIV has remained stable at 50% globally, although women are more affected in sub-Saharan Africa (59% of all people living with HIV) and the Caribbean (53%) [3].

There were 2.7 million [2.4 million–2.9 million] new HIV infections in 2010, including an estimated 390 000 [340 000–450 000] among children [3]. This was 15% less than in 2001, and 21% below the number of new infections at the peak of the epidemic in 1997 [3]. Thus we see that the number of people becoming infected with HIV is continuing to fall, in some countries more rapidly than others. HIV incidence has fallen in 33 countries, 22 of them in sub-Saharan Africa, the region most affected by the AIDS epidemic [3]. In India, the country with the largest number of people living with HIV, new HIV infections has fallen by 56% [3].

HIV and Eye

Ophthalmic manifestations of HIV infection are diverse. Both anterior and posterior segments of the eye can be involved and it may even lead to blindness [4]. The earliest studies on this subject stated the prevalence of ophthalmic manifestations of HIV infection ranging from 10 to 20% [4,5]. There is a lesser prevalence of ophthalmic manifestations of HIV infection in children as compared to adults as described in various studies [6-9]. Moreover the pattern of ophthalmic manifestations of HIV in paediatric patients has been found to be different from that found in adults [6-9]. Thus, it becomes challenging to screen carefully and thoroughly every HIV positive patient in order to pick up subtle, unconventional and unexpected manifestations.

Patients with visual disturbances or unremitting ophthalmic symptoms, regardless of CD4 cell count should be evaluated by an ophthalmologist. All areas of the visual system can potentially be affected in patients with HIV infection and thus a detailed ophthalmological examination is important [10] (Table 1).

Numerous ophthalmic manifestations of HIV infection may involve the anterior or posterior segment of the eye. Anterior segment findings include tumours of the periocular tissues such as Kaposi Sarcoma and a variety of infections such as uveitis, Herpes Zoster Ophthalmicus (Figure 1) and Molluscum contagiosa. Posterior segment changes include cytomegalovirus (CMV) retinopathy (Figure 2), outer retinal necrosis (Figure 3) and a number of opportunistic infections of the retina and choroid. (Table 2) The immune status of the patient is expected to influence the frequency and nature of manifestations in the eye. (Table 3) Partial immune system recovery following initiation of effective antiretroviral therapy may modify clinical presentation. In addition, in one eye, several infections may occur at the same time, rendering diagnosis and therapeutic intervention more difficult.

With the advent of drugs to control HIV infection, the incidence of complications has reduced but has not been eliminated [11]. For this reason, many individuals in training or recently in practice may have only a small experience with diseases such as CMV retinitis, progressive outer retinal necrosis, acute retinal necrosis, cryptococcal, syphilitic

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	Type	Manifestations
1	Allergic	Allergic conjunctivitis
2	Autoimmune	Reiter's syndrome, uveitis and vasculitis
3	Opportunistic infections	Bacterial, mycobacterial, viral and fungal infection of the eye and adnexa
4	Neoplasia	Ocular Lymphoma
5.	HIV related	HIV retinopathy, Cotton wool Spots
6.	Neuro-ophthalmic	Optic neuropathy, papilloedema, cranial nerve palsy, cortical blindness
7	Treatment/ drug related toxicities	Didanosine retinopathy ,Rifabutin/ cidofovir related uveitis

Table 1: Various ophthalmological manifestations in HIV positive patients.

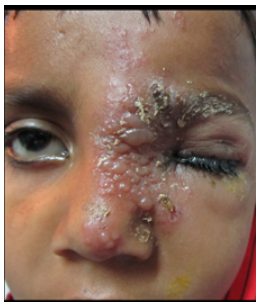

Figure 1: Herpes Zoster Ophthalmicus

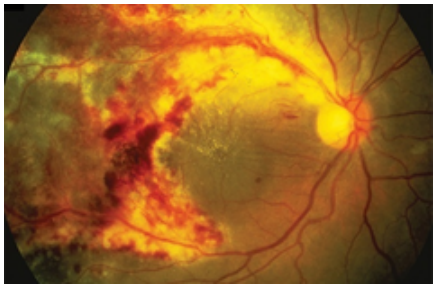

Figure 2: CMV Retinitis.

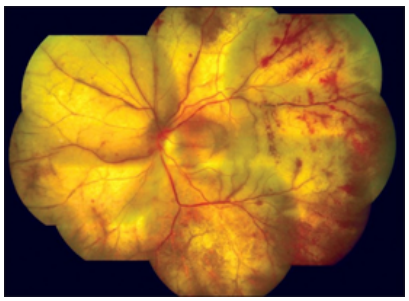

Figure 3: Progressive Outer Retinal Necrosis.

and toxoplasmal infections (Figure 4). In addition, the many types of HIV related non-infectious retinopathy may make matters confusing or lead to misdiagnosis.

In India the first cases of HIV were diagnosed among sex workers in Chennai, Tamil Nadu by Simoes et al., in 1986 [12]. Biswas et al. reported the first two cases of ocular lesions in AIDS in India. The first case was a sub retinal yellow mass and the second case had CMV retinitis and cotton-wool spots [13]. Biswas et al. further did an elaborate study and documented the ocular disorders seen in the first 100 individuals known to be HIV-positive at a referral eye clinic in India between 1993 and 1998. Most of the patients (76%) in their study were in the 20-40 years age group. CMV retinitis (17%) and HIV retinopathy (15%) were the most common ophthalmic lesions in their study [14]. Another important study conducted at the apex eye institute in India in the post HAART era was by Gharai et al where 199 eyes of HIV positive patients were examined for ophthalmic manifestations. The median age of patients in their study was 34 years and 68% of the patients were on HAART. 45% patients in this study had ophthalmic manifestations, the most common being cytomegalovirus (CMV) retinitis (20%). Retinal detachment was seen in 70% (14/20) of CMV retinitis patients. HIV vasculopathy was seen in 11% (11/100) of patients. Other lesions observed in their study included immune recovery uveitis (IRU) (5%), acute retinal necrosis (ARN) (3%), choroiditis (2%), neuro-ophthalmic manifestations (12%), complicated cataract (6%), keratouveitis (1%) and corneal ulcer . Amongst those who had ophthalmic involvement in their study, about 50% patients had CD4 count below 100 cells/micro liter and 70% of the patients had CD4 count below 200 cells/micro liter [15].

Disease	Fundus	Vitritis	Progression	CD4 cells/ mm^3	Treatment
CMV	Diffuse/ unifocal/ multifocal retinitis with haem + granular border	Minimal	Slow	<100	Systemic anti CMV therapy, ART
Toxoplasmosis	Focal dense retinitis	Yes	Slow	<200	As for cerebral toxoplasmosis
HIV micro-vasculopathy	Multiple well defined cotton wool spots with small haemorrhages	No	Regresses	<250	Nil
ARN	Widespread dense peripheral retinitis	Yes	Rapid early detachment		High dose acyclovir
PORN	Multifocal outer retinitis	No	Rapid early detachment	<50	Combination antivirals
Syphilis	Papillitis, retinitis, choroiditis or uveitis	Yes		Any	As for neurosyphilis
Fungal retinitis (candida)	Focal or multifocal vitritis, papillitis or retinitis	Yes		Any	Systemic and local antifungals
Intraocular lymphoma	Diffuse or multifocal choroiditis	Yes	Slow	<50	Radiotherapy plus chemotherapy
Cryptococcal choroiditis	Multifocal discrete pale choroidal lesions	No	Slow	<200	As for cryptococcal meningitis
Pneumocystis choroiditis	Multifocal discrete pale flat choroidal lesions	No	Slow	<250	Systemic PCP therapy
Histoplasmosis	Multifocal choroiditis	No	Slow		Systemic antifungals
Tuberculous choroiditis	Multifocal yellow/white choroiditis	Yes			As for TB

Table 2: HIV and Retina.

Stage of HIV	CD4 count cells/ mm^3	Immunity/Eye disease
Seroconversion	1000	Normal immune function, normal eyes
Early	500-1000	Sporadic autoimmune disease, allergic eye disease and uveitis.
Intermediate	200-500	Sporadic autoimmune disease, Milder opportunistic infection:blepharitis , follicular conjunctivitis,bacterial conjunctivitis,molluscum contagiosum, Kaposi sarcoma, Herpes, Tuberculous uveitis, Optic neuropathy,lymphoma, HIV retinopathy
Late	0-200	CMV retinitis, Severe opportunistic infections, aggressive neoplasms

Table 3: Ocular manifestations of HIV infection correlated with Immune status.

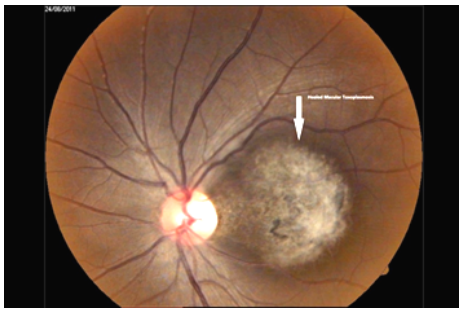

Figure 4: Macular Toxoplasmosis.

Among Indian pediatric patients, Biswas et al. in their study reported that the spectrum of ocular lesions in children with HIV infection is different from that seen in adults. Vertical transmission was found to be the most common mode of infection (58.33%). Ocular lesions were found in 50% of patients, the most common ocular lesions being anterior uveitis and CMV retinits (33% each) followed by retinal detachment (16.66%) and vitreous hemorrhage (16.66%) [16].

In the post HAART era , more elaborate studies need to be undertaken to compare our results from the pre HAART era which will enable us to know how the natural history of various manifestations have altered with increased survival of patients on ART. We also need to evaluate the newer challenges with ART. Some of these newer challenges being prolonged follow-up and close monitoring with increased lifespan of such patients on ART, regular follow up eye examinations, assessment of findings in relation to fluctuations in CD4 counts and monitoring of incidence of adverse ophthalmic side effects of ART.

In a country like India, other challenges which cannot be ignored are delayed presentation of patients to health care facilities, delayed diagnosis, increased frequency of malnutrition and susceptibility to infection which complicate disease presentation and the several social and economic factors which inhibit proper treatment compliance in our patients [17].

Ophthalmic Practice and Spread of HIV

HIV is present in very low quantities in tears and ocular tissues but the ophthalmologist is nonetheless cautious about any probable risk of transmission in the health care setting either from patient to patient or from patient to care provider [18]. Contact tonometry , Applanation tonometers, Perkins' handheld applanation tonometer and Contact lens trial sets are possible modes of spread. Corneal transplantation is a possible route of viral transmission. HIV has been isolated from corneal cells and aqueous humour [19,20]. Donor corneas are often used within hours after enucleation, not allowing enough time for routine testing of the donor serum.

During clinic procedures the risk of getting HIV from seropositive patients is probably very small but it may be wise to wear a face mask when examining patients especially with pulmonary disease and HIV and if one is to perform procedures which involve more exposure to blood such as exenteration or dacryocystorhinostomy, universal precautions must be taken without fail.

Conclusion

Ophthalmic findings in HIV patients are manifold and some findings such as CMV Retinitis can even lead to blindness. Moreover, infections which are otherwise simple and inconsequential in a seronegative patient, can be tenacious in HIV positive patients. The challenges while treating HIV positive patients are immense and immune status of the patient plays a key role in determining outcomes. Early diagnosis, local and systemic methods of treatment such intravitreal Ganciclovir implants in cases of CMV retinitis have shown promising results in reducing ocular morbidities.

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