

AQUIRED IMMUNO DEFICIENCY SYNDROME AND ITS OPHTHALMIC MANIFESTATIONS. SHORT REVIEW ARTICLE.

Dr G. D. Channashetti^{1*}, Dr S. S. Kottagi².

^{1*}Department of Ophthalmology, Shri B M Patil Medical College, Bijapur, Karnataka, India.

²Department of Biochemistry, Shri B M Patil Medical College, Bijapur, Karnataka, India.

Received 20 October 2014; Accepted 03 November 2014

ABSTRACT

Rising trend of HIV seropositivity in TB patients in India and involvement of multi organ system and multiple opportunistic infections in AIDS is quite worrying¹⁻³. India is emerging globally as a country with the largest number of AIDS patients.

Non-infectious HIV retinopathy: This is the most common ocular finding in AIDS patients seen in more than ½ to ¾th of patients. Superficial and deep retinal hemorrhages

External infection of the eye: *Molluscum contagiosum* is a common skin infection caused by a large DNA pox virus. In patients with AIDS

INTRODUCTION:

Rising trend of HIV seropositivity in TB patients in India and involvement of multi organ system and multiple opportunistic infections in AIDS is quite worrying¹⁻³. India is emerging globally as a country with the largest number of AIDS patients. The lifetime cumulative risk of at least one abnormal ocular lesion developing in an HIV positive patient ranges from 52% to 100% in various studies. Ocular lesions in AIDS are varied, affecting almost all structures of the eye. During the early phase of AIDS, ophthalmic manifestations of the disease in fact helps to suspect underlying HIV infection and its associated opportunistic infections^{4,5}.

AIDS-related ocular lesions:

These can be categorised into four main groups⁴:

1. Non-infectious retinopathy
2. Opportunistic infections caused by viruses, bacteria, fungi, and protozoa.
3. Unusual neoplasms, such as Kaposi's sarcoma and Burkitt's lymphoma.
4. Neuro-ophthalmic lesions.

The posterior segment of the eye, i.e., retina and choroid is mainly affected. However, less frequently ocular adnexa, anterior segment, orbit, and neuro-ophthalmic lesions can also occur. Various ocular lesions in AIDS⁶⁻¹² are summarized in the Table I to IV.

Table I : Ocular lesions in AIDS⁶⁻¹².

A. Adnexal lesions

1. Herpes zoster ophthalmicus

2. Kaposi's sarcoma of eyelid, conjunctiva.

3. Molluscum contagiosum of the eyelid.

B. Orbital lesions

1. Burkitt's lymphoma

2. Orbital cellulitis (aspergillus).

Table II : Anterior segment lesions in AIDS.

1. Dry eye

2. Conjunctival microvasculopathy

3. Infective keratitis (*Varicella zoster*, *Herpes simplex microsporidia*)

4. Anterior uveitis.

- a) Rifabutin-induced

- b) Spill-over from cytomegalovirus retinitis.

- c) Herpes zoster ophthalmicus.

Table III : Posterior segment lesions in AIDS.

1. HIV retinopathy

2. CMV retinitis

3. Toxoplasmic retinochoroiditis

4. CMV optic neuritis

5. Pneumocystis carinii choroidopathy

6. Acute retinal necrosis

7. Herpes zoster retinopathy

8. Progressive outer retinal necrosis

9. Endogenous endophthalmitis

Table IV : Neuro-ophthalmic lesions in AIDS^{12a}.

1. Cranial nerve palsies

2. Papilloedema

Non-infectious HIV retinopathy

This is the most common ocular finding in AIDS patients seen in more than ½ to ¾th of patients.

Superficial and deep retinal hemorrhages, microaneurysms, and cotton wool spots are early signs of HIV infection. A cotton wool white fluffy spot is caused by a circulatory disturbance in a tiny area of the retina,

usually distributed along the vascular arcades, and may mimic diabetic and hypertensive retinopathy. However, hard exudates of diabetic retinopathy are absent in HIV retinopathy. Cotton wool spots from hypertensive retinopathy are accompanied by vascular changes like arteriolar narrowing.

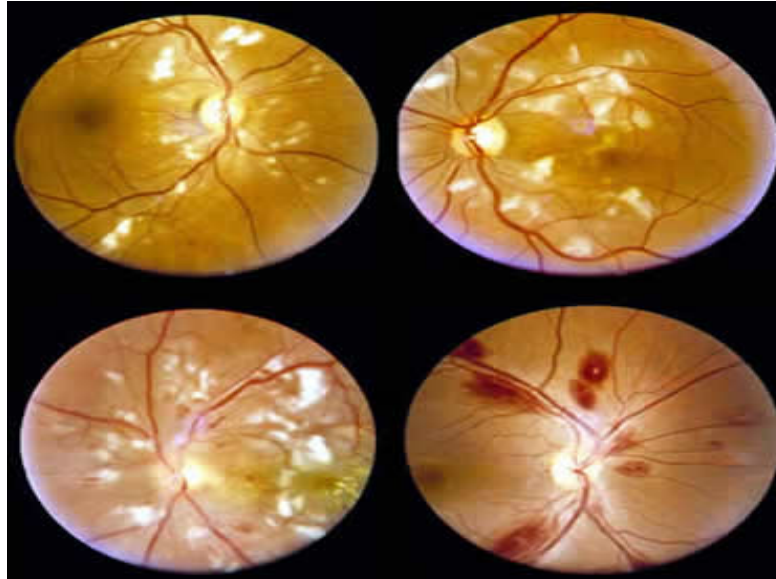


Figure 1: HIV RETINOPATHY

External infection of the eye:

Molluscum contagiosum is a common skin infection caused by a large DNA pox virus. In patients with AIDS, such lesions can occur in the eyelid and conjunctiva and are characteristically larger in number and size, often confluent and resistant to therapy. Dermal abscesses due to staphylococci, acid-fast bacilli and cytomegalovirus have been reported in molluscum lesions in patients with AIDS, indicating the tendency of such lesions to secondary infection.

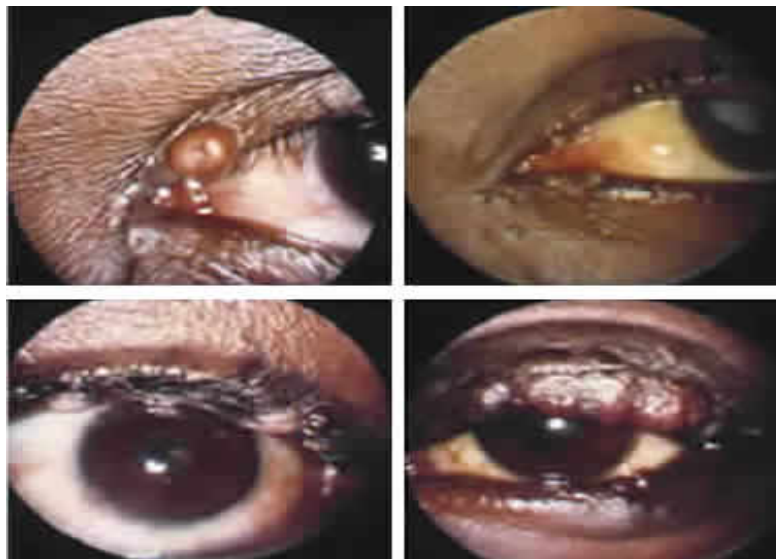


Figure 2: MOLLUSCUM CONTAGIOSUM

Herpes zoster ophthalmicus:

Ophthalmic herpes zoster may involve all three branches of the ophthalmic nerve (frontal, lacrimal, and nasociliary nerve). A rash will appear on one side of the forehead, the eyelids and the side of the nose, with a sharp demarcation in the middle (photograph on left). The rash is initially maculopapular and then becomes vesicular. These vesicles will burst

to form crusting ulcers. Ocular lesions include a mucopurulent conjunctivitis that is associated with vesicle formation on the eyelid margins. It usually resolves in one week. The picture, shows upper eyelid involvement resulting in cicatricial (scarring) ectropion. Corneal involvement is common and complex, ranging from no or mild epithelial involvement to complete opacification and even melting of the entire cornea (photograph), with perforation and loss of the eye.



Figure 3: HERPES ZOSTER OPHTHALMICUS.

Opportunistic infections:

Several opportunistic infections caused by organisms like viruses, bacteria, fungi, and protozoa that would not otherwise cause infection in healthy persons, may occur in AIDS patients. Cytomegalovirus (CMV) is the most common of all these infectious agents which affects retina, optic nerve, or both in AIDS patients. Less common infections include *Toxoplasma gondii*, *Varicella zoster virus*¹², and *Pneumocystis carinii*.

Cytomegalo virus retinopathy:

CMV retinopathy develops in 15% to 35% of patients with AIDS^{8,10}. Floaters are the earliest warning signs of CMV retinitis. They appear as small dark specs that move slowly throughout the visual field and are best seen against a blue or white background. They may be seen normally on many occasions, but an increase in the number of floaters is an important early warning sign. Distortions and blind spots may occur in any part of the field of vision. CMV retinitis can easily be diagnosed by examination of fundus, that appears as full thickness retinal necrosis with white granular areas accompanied by perivascular exudates and haemorrhages. The appearance is also called 'cottage cheese' with 'tomato ketchup' appearance. The vitritis is typically absent or minimal. Clinically, CMV retinitis is usually seen sometime after diagnosis, at around nine to 15 months, correlating strongly with low CD4+T-lymphocyte count. Visual loss is frequently associated with CMV retinitis, possibly due to retinal necrosis, macular oedema secondary to retinitis, optic nerve involvement, and retinal detachment. Retinal detachment is seen in 30% of cases in the healed stage of the disease. Four drugs have currently been approved, i.e., ganciclovir, foscarnet, cidofovir, and fomiverson. Ganciclovir can be given intravenously, intravitreally, and by sustained-release timed device implanted in the vitreous cavity to release ganciclovir at a slow rate over five to eight months. Currently, intravitreal cidofovir and fomiverson (ISIS 2922) are being tried for CMV retinitis and show favourable response^{13,14}. These drugs produce improved immune function, patients survive longer and opportunistic infections are few. Nevertheless, treatment of CMV retinitis has also become more and more complex¹³⁻¹⁵. Patients of CMV retinitis who are on combination antiretroviral therapy, particularly protease inhibitors, a new syndrome called "immune recovery vitritis"(IRV)¹⁶ emerges, that causes visual morbidity in patients with AIDS. Atypical ARN seems to involve primarily the outer retinal layers and has been named progressive outer retinal necrosis (PORN).

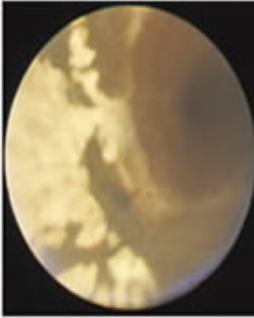
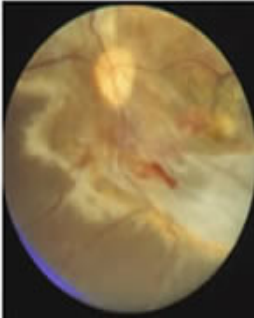
	CMV	PORN	
Lesions	1, 2 or 3	multifocal	
Necrosis	granular	confluent	
Retinal hges.	typical	uncommon	
Progress	slow	rapid	
Detachment	less common	common	
T4 cells	<50/ cu.mm	up to 100/ cu.mm	

Figure 4: PORN AND CMV RETINITIS.

Toxoplasma gondii:

Toxoplasma gondii, a protozoa, affects about 10% of AIDS patients, but toxoplasmic retinochoroiditis is relatively rare and accounts for 1% of AIDS-related retinal infections only. It produces necrotising retinitis similar to CMV retinitis. Among the fungi, *Cryptococcus neoformans* can cause multifocal choroiditis, usually through haematogenous dissemination and is often associated

with cryptococcal meningitis. *Pneumocystis carinii* can also cause multifocal choroiditis. 80% of AIDS patients develop *Pneumocystis carinii* pneumonia and in 60% of these patients, it is an initial opportunistic infection¹⁷. Extra-pulmonary dissemination of this organism can cause *Pneumocystis carinii* choroiditis, in which numerous slightly elevated yellow round lesions are seen in the choroid, with minimum or little inflammation.



Figure 5: TOXOPLASMOSIS RETINOPATHY.

Tuberculosis:

Mycobacterium avium intracellulare occurs in 15% to 20% of patients with AIDS. In an autopsy series, 6% of AIDS patients had *M. avium intracellulare* in the choroid. Ocular syphilis in HIV-infected patients can lead to severe

uveitis, necrotising retinitis, papillitis, optic neuritis, and acute posterior type of chorioretinitis. The posterior segment lesions in the AIDS patients are enumerated in the Table III.

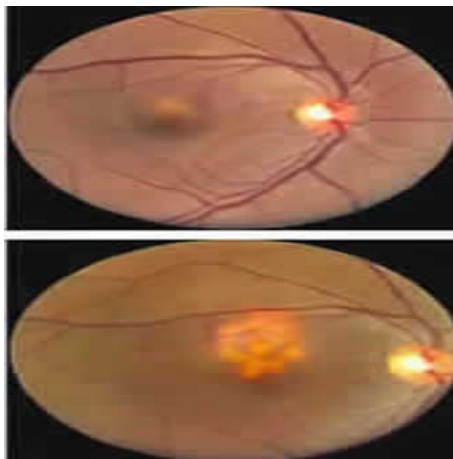


Figure 6: TUBERCULAR RETINOPATHY

Unusual neoplasms:

Kaposi's sarcoma is a rare form of cancer that appears as a non-tender purple nodule in the eyelid. It can occur in upto 25% of AIDS patients in the west¹⁸. If it affects the conjunctiva, it appears as a bright red fleshy mass and is commonly seen in the fornix. The conjunctival Kaposi's sarcoma may mimic pyogenic granuloma. Kaposi's sarcoma lesions of skin and mucous membrane tend to

grow slowly. Recent reports reveal that DNA sequences of human herpes virus-8 have been detected in Kaposi's sarcoma in patients with and without HIV infection¹⁹. The low prevalence of human herpes virus-8 in India could also be another reason for the low frequency of Kaposi's sarcoma. Localised radiotherapy is the treatment of choice for isolated lesions.

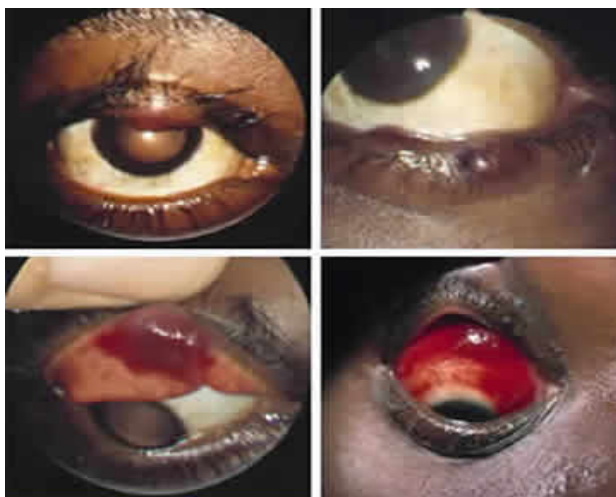


Figure 7: KAPOSIS SARCOMA

Conjunctival squamous cell dysplasia and neoplasia have been associated with HIV infection and AIDS in the sub-Saharan African population. Leucoplakia and a conjunctival mass as the initial manifestations of HIV

infection have also been reported. Histopathologic study of the excised tissue revealed conjunctival dysplasia on the nasal side and squamous cell carcinoma on the temporal bulbar conjunctiva⁹.

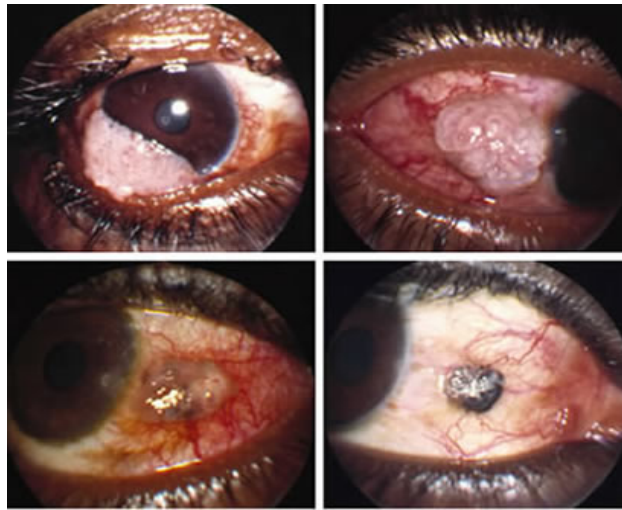


Figure 8: SQUAMOUS CELL CARCINOMA .

Neuro-ophthalmic lesions:

In the final stages of the HIV disease, the brain is frequently involved, either with direct infection by HIV or with opportunistic infections. Neuroophthalmic complications are known to occur in 10% to 15% of HIV infected patients²⁰. Because over 50% of the human brain is concerned in some ways with the act of seeing, the eyes may show signs of brain involvement, resulting

in blurred vision, problems with eye movement, or double vision. Papilloedema, the most common ocular sign in cryptococcal meningitis, is present in one third of patients . Haemorrhagic papilloedema is shown in picture. The association of headache and even mild papilloedema, with or without fever, should always raise the possibility of cryptococcal meningitis.

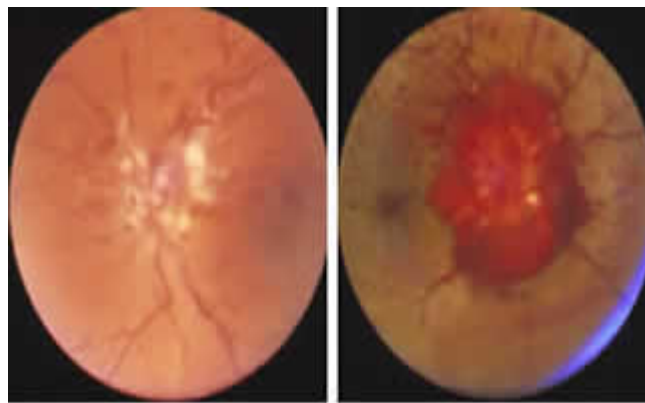


Figure 9: CRYPTOCCAL MENINGITIS WITH PAPILOEDEMA

Prevention:

Great deal of awareness among the primary care physicians and ophthalmologists are needed as ocular lesions are the earliest manifestation of AIDS¹⁸⁻²⁴. Early and proper treatment can salvage their vision and improve the quality of life. When operating on

known HIV-positive patients, surgeons need to observe additional safeguards. The 'no-touch' technique, mandates that neither the surgeons nor the scrub nurse handles any sharp instruments at the same time⁴. Double gloving to decrease the risk of percutaneous exposure may also be a useful precaution.



Figure 10: A risk of spread of HIV infection through ophthalmic procedures, either from patient to patient or from patient to eye care provider.

REFERENCES:

1. Bhatia RS. HIV and TB: The ominous connection. In: Manoria PC (Ed). PG Med API 1998; 12 (111): 1104-7.
2. Bhatia RS. TB and AIDS. JAPI 2000; 48: 613-6.
3. Bhatia RS. Heart and HIV/AIDS. CMJ 1997; 3 (5): 50-2.
4. Biswas J. AIDS and Eye. JAPI 2001; 49: 551-7.
5. Rao NA. Acquired immunodeficiency syndrome and its ocular complications. Ind J Ophthalmol 1994; 42:51-63.
6. Biswas J, Madhavan HN, George AE et al. Ocular lesions in the first 100 HIV positive cases in a referral eye centre in India. m J Ophthalmol 2000; 129: 1-8.
7. George AE, Biswas J, Agarwal R et al. Subretinal cysticercosis in an AIDS patient treatment with xenon arc photocoagulation. Retina 1999; 19: 467-8.
8. Battu RR, Biswas J, Agarwal R et al. Papilloedema with peripapillary retinal hemorrhage in an AIDS patients with cryptococcal meningitis. Ind J Ophthalmol 2000;48: 47-9.
9. Fogla R, Biswas J, Kumar SK et al. Squamous cell carcinoma as initial presenting sign in patient of acquired
10. Immunodeficiency syndrome due to human immunodeficiency virus type-2. Eye 2000; 14: 246-7.
11. Biswas J, Madhavan HN, Badrinath SS. Ocular lesions in AIDS: A report of first two cases in India. Ind J Ophthalmol 1995;43: 69-72.
12. Choudhury S, Biswas J, Kumar SK et al. Immune recovery vitritis presenting as panuveitis following therapy with protease inhibitors – a case report. Ind J Ophthalmol 2000; 48: 313-5.
13. Moorthy RS, Weinberg DV, Tseich SA et al. Management of varicella zoster virus retinitis in AIDS. Br J Ophthalmol 1997; 81: 189-94.
14. Wadia RS, Pujari SN, Kothari S et al. Neurological manifestations of HIV disease. JAPI 2001; 49: 343-8.
15. Jacobson MA. Treatment of cytomegalovirus retinitis patients with the acquired immunodeficiency syndrome. N Eng J Med 1997; 337: 105-14.
16. Slonim CB. AIDS and the ophthalmic practice: Refinements. Clinical education modules for today' ophthalmic team. The Foundation of the American Academy of Ophthalmology. 1990; 3 (4): Section 2.
17. Jabs DA, Bolton SF, Dunn JP, Palestine AG. Discontinuing anti-CMV therapy in patients with immune reconstitution after combination antiretroviral therapy. Am J Ophthalmol 1998; 126: 817-22.
18. Karavellas M, Lowder C, Macdonald C et al. Immune recovery vitritis associated with inactive cytomegalovirus retinitis. Arch Ophthalmol 1998; 116: 169-75.
19. Bhatia RS, Sibia SS. PCP in a patient of AIDS in India. JAPI 1994; 42: 87.
20. Tschachler E, Bergstresser PR, Stingl G. HIV-related skin diseases. Lancet 1996; 348: 659-63.
21. Moore PS, Chang Y. Detection of herpes virus-like DNA sequences in Kaposi sarcoma in patients with and without HIV infection. N Engl J Med 1995; 332: 1181-5.
22. Freeman WR, Lerner CW, Mines JA et al. A prospective study of the ophthalmologic findings in the acquired immune deficiency syndrome. Am J Ophthalmol 1995;97: 133-42.
23. Lewallen S, Courtright P. HIV and AIDS and the eye in developing countries: A review. Arch Ophthalmol 1997;115: 1291-5.
24. Singh NK. HIV infection: Mother to child transmission. In : Panja M (ed). Med Update API 2001; 11: 338-50.

25. Deshpande Alka K. Prophylaxis against opportunistic infections in HIV disease; Das AK (ed). PG Med, API, Mumbai 2001; 15: 99-103.
26. Bhatia RS, Deivanyagam CN. HIV disease – The great waster upon us. Lung India 1992; 10: 91-3.
27. R.S.Bhatia, ophthalmic manifestations in eye Journal, Indian Academy of Clinical Medicine _ 2002; 3(1): 85-8