



AIDS AND ITS OPHTHALMIC MANIFESTATIONS: A REVIEW

Medicine

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ABSTRACT

Human Immunodeficiency Virus (HIV) is a retrovirus which causes Acquired Immune Deficiency Syndrome (AIDS). Since its discovery in 1981, HIV/AIDS has emerged as a global health problem. The impact of the HIV/AIDS pandemic has spurred much research into the disease and its various systemic and ocular complications. Early detection of the ocular manifestations of HIV/AIDS is critical since these ocular manifestations may be the primary presentation of the systemic infection. This has implications for the prognosis of the disease. Therefore, this review article aims to highlight the ophthalmic manifestations of AIDS and some strategies for their management.

KEYWORDS

HIV/AIDS, Ocular, Orbital, Adnexal, Anterior segment, Posterior segment and Neurological manifestations.

INTRODUCTION

HIV/AIDS is a global pandemic with cases described in almost every country in the world. AIDS was first recognized as a clinical entity in 1981¹ and the etiologic agent, the human immunodeficiency virus (HIV), a cytopathic retrovirus was first identified in 1983.² Acquired immunodeficiency syndrome (AIDS) is known to affect the body's ability to fight with the illness, caused by the Human Immunodeficiency Virus (HIV) because it attacks lymphocytes especially CD4+ T cells. HIV affects all the organs of the body which includes the eye directly by infecting the eye with various opportunistic infections affecting the anterior and posterior segments and indirectly causes neurological conditions affecting the brain, consequently leading to various vision defects and vision loss. Enough data is available about HIV, its manifestations, treatment, and prevention, however its impact on eye has not been discussed to the same extent. The purpose of this review is to emphasize on the impact of HIV/AIDS on the eye, its manifestations and management.

Ophthalmic Manifestations of AIDS/HIV

Ocular manifestations were first described in 1982.³ About 50%–75% of patients infected with HIV will develop ocular manifestations with a cumulative lifetime rate of developing at least one ocular lesion of 52%–100%.⁴ The prevalence and appearance of ocular manifestations has gradually changed, after the administration of highly active antiretroviral therapy (HAART) which restores the immune system.

Ocular Manifestations Can Be Divided As

- I. Orbital,
- II. Adnexal,
- III. Anterior segment,
- IV. Posterior segment and
- V. Neurological manifestations.

Orbital Manifestations

Orbital manifestations of HIV infection are rare. However, some cases of orbital cellulitis and orbital lymphoma have been reported in less than 1% of HIV/AIDS individuals.⁵ Both of the aforementioned conditions are associated with aspergillus infection,⁶ while Lima⁷ noted that other organisms including *Rhizopus arrhizus*, *Toxoplasma gondii*, and *Pneumocystis carinii* can also be implicated in the development of these conditions.

Adnexal Manifestations

The most common adnexal manifestations in AIDS patients are Kaposi's sarcoma, herpes zoster ophthalmicus (HZO), moluscum contagiosum and conjunctival microvasculopathy.⁸ Primary non-Hodgkin's lymphoma (NHL) of the orbit and ocular adnexa is a rare disease. Kaposi's sarcoma is a highly vascularized, painless mesenchymal tumor that affects the skin and mucous membranes. Around 20% of these patients have asymptomatic Kaposi's sarcoma of the eyelids, conjunctiva and rarely the orbit. However, there are a lower proportion of cases associated with low incidence of human herpes virus 8 in India and homosexual behaviour.⁹

Herpes Zoster Ophthalmicus

Herpes Zoster Ophthalmicus (HZO) is a painful vesiculobullous

dermatitis resulting from a reactivation of Varicella-Zoster virus (VZV) infection. Reports have suggested that HZO might be the initial clinical manifestation of HIV infection in younger individuals,¹⁰ particularly those of age 21–23. The most common predisposing factor to developing HZO is age, but, other factors include neoplasm, HIV infection, trauma, irradiation, immunosuppression, surgery or debilitating systemic disease.

Anterior Segment Manifestations

Anterior segment manifestations of HIV/AIDS have been noted in about 50% of HIV-infected individuals¹⁵ and include corneal infection (keratitis) and anterior chamber inflammation (iritidocyclitis). Common symptoms include irritation, pain, photophobia and decreased vision.

Keratoconjunctivitis Sicca

Keratoconjunctivitis sicca (KCS) is one of the most common ocular anterior segment complications and has been reported in about 20% of HIV positive individuals.^{7,11} The reported symptoms include foreign body sensation, photophobia and decreased visual acuity.⁷

Blepharitis and Blepharoconjunctivitis

Although blepharitis has not been studied in detail in HIV-infected individuals owing to the scholarly demands of understanding the more severe, blinding disorders, it has been found to be more common and more serious in HIV-infected individuals. The condition could be attributed to a reduced ability to control the normal flora that the eye is exposed to or to more complex changes that occur in the cutaneous glands of the eyelids with immunosuppression.¹²

Infectious Keratitis

Infectious keratitis in HIV-infected individuals may be caused by viral, bacterial, fungal or protozoan infections.¹³ It has been noted that the etiologic and epidemiologic pattern has most commonly been caused by VZV and Herpes Simplex Virus (HSV) in HIV positive individuals. Keratitis due to bacterial or fungal causes has not been found to be more common in HIV positive individuals. However, when found, its severity is greater. The most common fungal organisms have been found to be candida.

Varicella-Zoster Virus Keratitis

Varicella Zoster Virus (VZV) has been reported to be the second most common ocular pathogen in HIV-infected individuals.¹⁴ Varicella-Zoster Virus Keratitis present with elevated intraocular pressure. It is commonly associated with zoster ophthalmicus. As in herpes simplex keratitis, the course of the disease tends to be longer in AIDS patients. Bacterial and fungal infections are generally more severe in HIV infected patients. Following primary infection by the VZV, reactivation can occur and presents as HZO which may occur with or without dermatitis. Clinical features of HZO may be due to direct viral infection, antigen-antibody reactions, delayed cell-mediated hypersensitivity reactions or neurotrophic damage. VZV like HSV establishes a latency period after primary infection due to their morphological similarities.

Spontaneous Fungal Keratitis

Spontaneous fungal keratitis secondary to *Candida albicans* has been reported in patients with advanced HIV disease particularly common in intravenous drugs users. Although uncommon, Microsporidia is associated with a bilateral diffuse punctate epithelial keratopathy and conjunctivitis⁹ keratoconjunctivitis sicca (dry eye syndrome) results from deficiency of any of the tear film layers. It is likely caused by both the destruction of primary and secondary lacrimal glands and inflammation mediated by the HIV virus.¹⁵ Symptoms may include foreign body sensations, photophobia and decreased visual acuity.

Posterior Segment Ocular Manifestations

HIV retinopathy

HIV retinopathy is one of the most common retinal manifestations of HIV and is found in 70% of persons with HIV/AIDS.¹⁶ It has been suggested that altered blood flow may contribute to vascular damage and ocular ischaemic lesions in HIV patients.

Cotton Wool Spots

Cotton-wool spots (CWS) are ocular micro-angiopathic manifestations of HIV/AIDS, however, they are non-specific. They are seen in variety of conditions such as diabetes, hypertension, leukaemia, anaemia and systemic lupus erythematosus.^{17,18} Cotton wool spots are caused by a circulatory disturbance within tiny areas of the retina. The occlusion of pre-capillary arterioles is commonly located in the superficial retina.¹⁶ It can be mistaken, due to their colour, for the infective lesions of cytomegalovirus retinitis (CMVR). Unlike these CMVR infective lesions CWS are transient, not visually-threatening, and tend to disappear within 6-12 weeks.¹⁸ The presence of CWS suggests a microvascular alteration in AIDS that is probably related to the high levels of circulating immune complexes found in the condition.⁷

Retinal Haemorrhages

They appear as flame-shaped areas when they affect the nerve fibre layer and as dot-and-blot patterns when they affect the deeper layers of the retina.^{8,16} The histopathological findings resemble that of diabetic retinopathy, with pericyte necrosis, endothelial cell swelling and thickened basement membranes being a feature of the condition.¹⁹ It is suggested that the vascular injury includes immunoglobulin deposition, direct infection of the endothelial cells with HIV and hyperviscosity due to increased red blood cell aggregation, fibrinogen and increased polymorphonuclear leukocyte rigidity.¹⁹

Telangiectatic Vascular Changes

Retinal telangiectasias are known as a group of rare, idiopathic anomalies of the retinal vasculature characterised by irregular dilation, microaneurysms and vessel failure and may be found in HIV-infected individuals.²⁰

Neurological Ocular Manifestations

Optic neuropathies in HIV positive patients may be related to compression, infiltration, infection, vaso occlusion or inflammation. Cryptococcal meningitis and intracerebral toxoplasma cysts cause intracranial manifestations. Other neuro ophthalmic complications are visual field defects, papilledema, secondary to elevated intracranial pressure and ocular motility disorders, occurring in up to 15% of HIV-infected patients. HIV may also cause diplopia due to palsies of cranial nerves III, IV, and VI. Neurosyphilis, progressive multifocal leukoencephalopathy (PML), meningeal and parenchymal lymphoma, and intracerebral infection with herpes virus have also been related to neuro-ophthalmic manifestations. Premature atherosclerosis is also seen in HIV-infected patients due to an unknown mechanism.

Effect of HAART

1. Ocular IRIS:

Over the past few decades, symptomatic deterioration in patients on ART has been described, this phenomenon is known by multitude of names including, immune reconstitution inflammatory syndrome (IRIS), immune reconstitution or restoration disease (IRD), and immune reconstitution syndrome (IRS).

IRIS is most often associated with CD4+ Th1-mediated immune response; however, both CD4+ and CD8+ effector T-cells are involved. The proinflammatory Th17 cell and the regulatory T cell (Treg) play an important role. Macrophages and natural killer cells are also suspected to play a role in herpes IRIS. Among patients with CMV in the HAART era, immune recovery may be associated with complications including macular edema and epiretinal membrane

formation. Eye disease is the most common presentation of cytomegalovirus (CMV) IRIS. Three distinct ocular lesions associated with CMV-IRIS have been described: retinitis, vitreitis, and uveitis. The immune recovery uveitis secondary to HAART has become a major visually-threatening condition. AIDS patients with CMV are less likely to experience necrotizing retinitis and retinal detachment. Immune recovery vitritis is seen following treatment with protease inhibitors, which may be associated with increased cytomegalovirus-specific lymphocyte proliferation and production of inflammatory cytokines.²¹ Clinically important complications of immune-recovery uveitis may include cataract, epiretinal membrane formation, and cystoid macular edema. Drug induced uveitis was strongly correlated with prior use of cidofovir and rifabutin.⁹

2. Stevens Johnson syndrome HIV-infected individuals are frequently exposed to medications, especially nevirapine, which are capable of causing hypersensitivity or toxic reactions. Altered cell-mediated immunity and associated dry eye may also lead to increased risk of SJS as a response to infectious agents as well.⁹

3. Effect of intra-ocular viral loads HIV loads of aqueous humor declined to undetectable levels (< 400 copies/ml) after 4-8 months of HAART.²¹ HIV virus levels in the plasma of AIDS patients were significantly decreased, and the CD4 counts of these patients were significantly increased after initiation of HAART.

4. Vortex keratopathy: It can be caused by antivirals such as ganciclovir, acyclovir or atovaquone. Patients may be asymptomatic or may complain of a mild irritation, foreign body sensation or photophobia. Characteristic whorl-like pattern of gray white opacities is seen at the level of the corneal epithelium.²²

Inatrogenic/post-treatment manifestations of HIV/AIDS

Immune recovery uveitis (IRU)

Immune Recovery Uveitis is defined as “new inflammation in an eye with controlled CMV retinitis or other opportunistic infection, not attributable to an alternative cause, following substantial recovery of Immunity.”²³ This condition has emerged in patients where the increase in white blood cells brought about by immune recovery respond to pre-existing CMV infection. It is most frequent in patients with CMV retinitis who initiate HAART.^{23,24}

Stevens-Johnson syndrome (SJS)

“SJS is an immune-complex-mediated hypersensitivity disorder”. It has been associated with four aetiologic categories, which include infectious, drug-induced, malignancy related and idiopathic. In patients with HIV/AIDS, SJS has been linked with viral and drug-induced etiologies.^{25,26} The syndrome is one that affects the skin and mucous membrane. The hypersensitivity reaction results in cell death which in turn results in a separation of the epidermis from the dermis.²⁵ Vision loss accompanying the disease occurs as a result of decreased tear production and forniceal foreshortening with trichiasis.

CONCLUSION

Clinicians should be aware of changes in the clinical presentation of ocular manifestations of HIV since the introduction of HAART. As studies on HIV disease after the introduction of HAART continue to become available, more thorough descriptions of treated patients with ocular opportunistic infections will include side-effects and toxicities on therapy. As increasing number of HIV-infected individuals present with treatment failure in resource-limited settings such as India, the risk of ophthalmic complications may increase. Further research is needed to study the effects of the restored immune system following HAART on the eye and to identify the best therapeutic approach for HIV-infected patients.

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