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Visual Dysfunction System and Human deficiency Virus

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Abstract

During the first 15 years of the AIDS epidemic patients experienced a high incidence of blindness due to cytomegalovirus (CMV) retinitis and other severe ocular opportunistic infections. Highly active anti-retroviral therapy, introduced in 1996, dramatically decreased the incidence of CMV retinitis. Though CMV retinitis still causes 40% of vision loss in AIDS patients, other conditions such as immune reconstitution uveitis, cataracts, and a significant other category -which most investigators believe is directly due to HIV - comprise the majority of cases. HIV causes vascular abnormalities of the conjunctiva and retina in the majority of AIDS patients, as well as retinitis, anterior and posterior uveitis and vasculitis. HIV frequently causes an optic neuropathy and is responsible for the majority of eye movement disorders among HIV patients. Physicians need to be aware that these problems may be the initial manifestation of HIV infections or a sign of highly active anti-retroviral therapy (HAART) failure. Therefore, patients with identifiable risk factors for AIDS who present with ophthalmologic conditions of unknown etiology should be considered for HIV testing. Finally, anti-retroviral therapy has been reported to cause asymptomatic deposits as well as degenerative conditions of both the anterior and posterior segments of the eye.

Keywords: Uveitis; HIV retinopathy; Neuroretinal disorder; Neuroretinitis

Introduction

The groundbreaking reports of 5 young men afflicted with unusual opportunistic infections due to an acquired immunodeficiency disorder ushered in the AIDS era in 1981. Affected patients rapidly succumbed to the lethal complications of opportunistic infections (pneumocystis carinii pneumonia, cytomegalovirus (CMV) disease, cryptococcal meningitis, and candidiasis) and tumors. Although most investigators correctly attributed the immunodeficiency to an unidentified microbe, it took 2 years before identification of the HTLV-III (human T-lymphocyte virus), later named HIV-1 (human immunodeficiency virus). Although targeted anti-retroviral therapy began with the introduction of zidovudine, a nucleoside reverse transcription inhibitor, in 1987, life expectancy was extended by at most 1 year [1]. Unfortunately, many patients developed drug-induced neutropenia that frequently required cessation of therapy or prevented the co-administration of drugs with similar toxicity profiles that were given to control opportunistic infections. As a result, long-term survival was rare.

The introduction of highly active anti-retroviral therapy (HAART) in 1996, originally defined as two nucleoside reverse transcriptase inhibitors (NRTIs) combined with a protease inhibitor (PI), and recently (2004) expanded by the DHHS/Kaiser panel to include a PI, a non-nucleoside reverse transcriptase inhibitor, one of the NRTIs (abacavir or tenofovir), an integrase inhibitor [2], or an entry inhibitor became a watershed event in the therapy of HIV-infected patients. Successfully treated patients experienced several measurable improvements. The rate of viral replication significantly decreased and, for the first time since 1981, patients experienced reconstitution of their immune systems. As a direct consequence, the incidence rates of many opportunistic infections fell, with CMV retinitis dropping by 80%. At the same time, immune reconstitution inflammatory syndromes (IRIS) emerged, with immune reconstitution uveitis (IRU) affecting 15% to 25% of AIDS patients [3].

During the pre-HAART era, retinal necrosis or detachment due to CMV caused more than 90% of AIDS-related vision loss. Following the introduction of HAART, the incidence of vision loss decreased by more than 50%, even after excluding patients with infectious retinopathies. CMV retinitis now accounts for only 40% of vision loss cataracts are responsible for 25%, and in 10% the reason for vision loss cannot be determined [4]. Although 10% of AIDS-related vision loss has been termed idiopathic, many investigators believe that this results from HIV damage to the retina and optic nerve.

Unfortunately, HAART fails in up to 50% of AIDS patients due to non-compliance, side effects of the drugs, adverse drug interactions, or HIV resistance. As a result, up to 69% of newly diagnosed cases of CMV retinitis are due to HAART failure [5], as defined by either persistently low CD4+ T-lymphocyte counts or high HIV RNA blood levels. In addition to being at risk for developing opportunistic infections, these patients experience more HIV-related complications.

Several in-depth reviews have covered the characteristics of CMV retinitis and other ocular opportunistic infections. This manuscript, however, will discuss the characteristics and direct consequences of HIV infection and anti-retroviral treatment on the visual system.

HIV Infection

HIV infection causes both activation and destruction of the host's immune system. The initial HIV infection is confronted by the expected inflammatory response by the host against the virus. This is characterized by polyclonal activation of both T-lymphocytes and B-Lymphocytes with the release of inflammatory cytokines. Patients exhibit a 3 to 4 fold increase in the production of both CD4+ and CD8+ T-lymphocytes. T-lymphocyte turnover is promoted by the production of interleukin-6, interleukin-1, interleukin-2 and tumor necrosis factor

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(TNF)-α, all of which promote HIV replication [6]. This cascade further accelerates the destruction of the immune system. Advancing infection is accompanied by further CD4+ T-lymphocyte destruction and worsening of the immune status.

Under the influence of the thymus, lymphocytes mature from stem cells and carry on their surfaces unique receptors for various antigens. On the surface of each T-lymphocyte resides 1 receptor, which is specific to a unique antigen. Healthy individuals have a register of T-lymphocytes that allow them to respond to various foreign stimuli. Thus, CD4+ cells, which are responsible for long-term memory, are responsible for organizing the immune system's response against specific invading organisms [7].

A CD4+ T-lymphocyte that has never encountered a foreign antigen is said to be at ground state (G0) and is called a naive cell. Once exposed to an antigen, the CD4+ cell activates and replicates; these clones are now considered memory cells. As the HIV infection progresses the patient experiences a blunted response to new antigens followed by a decreased response to recall antigens. This is due to a loss of CD4+ memory cells accompanied by an inability to activate and subsequently replicate new CD4+ cells. The progressive loss of CD4+ clones puts the patient at increasing risk of opportunistic infections. Therefore, the CD4+ count is an instantaneous overall measure of the patient's susceptibility to opportunistic infections. Additionally, the HIV load is a predictor of the future likelihood of further erosion in the patient's immune status.

Most of the CD4+ cells lost due to HIV infection are the naive ones, thereby decreasing the body's ability to respond to new antigens. With reconstitution of the immune system due to successful HAART, memory CD4+ cells are the first to increase, followed later by an increase in naive CD4+ cells. Despite apparent reconstitution of the immune system, however, gaps in the immune system's register frequently remain. Since thymus involution occurs during the teenage years, infected patients are frequently unable to mount an immune response to new antigens.

HIV has been found in mononucleotide white blood cells and HIV infected macrophages which may act by releasing neurotrophic factors, enzymes, or cytokines, or by directly releasing virions, enveloping glycoproteins, or inflammatory mediators. Elevated levels of cytokines, particularly TNF-α, interleukin-1 and interleukin-2, have been reported in the serum of AIDS patients. These cells probably play an important role in promoting HIV infection of eye and central nervous system [8].

A major deficiency of HAART concerns its inability to prevent HIV-infected cells of the monocyte-macrophage line from establishing latent infections within the immunoprivileged central nervous system. Monocytes circulate within the blood stream for 3 days before migrating into tissues where they differentiate into macrophages. When they cross the blood brain barrier they differentiate into perivascular, meningeal or choroidal plexus macrophages, or microglia, after which they remain latent within the central nervous system for extended periods of time. Passage of infected macrophages into the brain, referred to as the Trojan Horse hypothesis, is one of the mechanisms by which HIV infects the CNS. These cells contain a potentially large reservoir of HIV that escapes surveillance by the immune system. When exposed to the correct stimulus, frequently an opportunistic infection and the macrophages reactivate and shed virions. Additionally, reactivated CNS macrophages can return to the peripheral circulation, thereby causing recurrent viremia.

Unlike infected CD4+ lymphocytes, CNS macrophages survive for weeks to months, retain their viability, and continue to shed low levels of virions. Activation of these macrophages is believed responsible for AIDS related dementia. Furthermore, CNS infiltration by HIV-infected monocytes leads to phosphorylation of functional proteins and activation of matrix metalloproteinases [9], thereby causing breakdown of the blood-brain barrier which further exposes the host to opportunistic infections of the CNS.

Retinopathy

HIV infection leads to micro vascular changes in several vascular beds: conjunctiva, optic disc and, most commonly, the retina. HIV retinopathy is seen in 40% to 100% of infected patients and has been found in 89% of autopsy specimens. The likelihood of a patient developing clinically apparent retinopathy depends somewhat upon the patient's lowest CD4+ count, as retinopathy occurs in 45% of patients with counts below 50 cells/mL but in only 6% of patients with counts greater than 50 cells/mL. HIV infected children have a lower incidence of ocular involvement (20%) than do adults. Also, retinopathy is seen less commonly in subSaharan Africa, perhaps due to genetic differences, environmental conditions pertaining to organisms, early mortality, and poor access to healthcare or fewer screening programs.

HIV vasculopathy is characterized by microaneurysms, telangiectasia, retinal hemorrhages, and cotton wool spots (CWSs) (Figure 1). The CWSs may be transient, remaining visible for only a few weeks [10]. Although most patients with retinal vasculopathy have no visual complaints, large cotton wool spots may cause either focal scotomas by preventing light penetration to the photoreceptors, or arcuate scotomas due to retinal nerve fiber layer damage.

Vision loss due to microvasculopathy is usually mild and insidious but ischemic maculopathy, characterized by multiple cotton wool spots and blots hemorrhages near the fovea, may cause sudden loss of vision in 3% of patients. The presenting visual acuity in these patients may range from 20/20 to counting fingers, with final visual acuities worse than 20/200 in 5 of 7 cases. Two cases of extensive bilateral retinal ischemia due to HIV have been described. Ischemic maculopathy has also been described in a patient with zidovudine induced anemia. Numerous large cotton wool spots may sufficiently damage the nerve fiber layer to result in optic disc atrophy. HIV can cause a non-progressive, non-hemorrhagic white-gray or yellow, multifocal peripheral retinitis with vitritis and retinal vasculitis that resembles syphilitic retinitis. Unlike HIV retinopathy and CMV retinitis, these findings occur in patients with CD4+ counts greater than 120. As expected, this retinitis responds well to HAART [11]. Serous detachment of the macula and

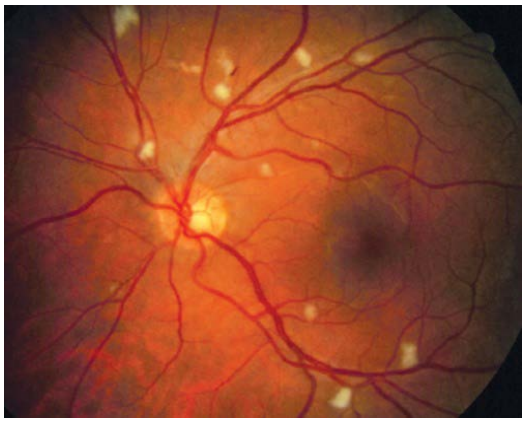

Figure 1: Several cotton wool spots, typical of HIV retinopathy.

macular edema can be seen with IRU. Though laser photocoagulation treatment of macular edema has been attempted, treatment is probably ineffective. Ciliochoroidal effusions have been seen, though the reason for their formation is unclear.

Drug Toxicity

A small number of patients have been described with retinal pigment epithelial and optic nerve abnormalities attributed to drug toxicity. Affected patients had advanced HIV disease (CD4+ lymphocyte counts) but no history of either HIV related eye disease or ocular opportunistic infection. Toxicity was attributed to a reverse transcriptase inhibitor or protease inhibitor, usually as part of HAART. Toxicity was first observed between 19 weeks and 5 years after initiation of the offending drug. This delayed response suggests that toxicity may be related to the cumulative dose of the drug, perhaps due to abnormal metabolism or excretion, rather than an idiosyncratic reaction.

Didanosine can cause progressive well-circumscribed loss of mid-peripheral retina, retinal pigment epithelium and choroid. Transmission electron microscopy of the retina shows lamellar inclusion bodies within the cytoplasm. Deposits in the mid-peripheral retina were noted in 4 children receiving didanosine, one of whom had a depressed electro-oculogram. Annular visual field defects, corresponding to the areas of retinal atrophy, were seen. Discontinuing didanosine stabilizes the degeneration and normalizes the electro-oculogram. Didanosine has also been associated with optic neuropathy.

Three patients receiving ritonavir developed retinal pigment epitheliopathy, macular parafoveal telangiectasia and intraretinal crystalline deposits with moderate loss of visual acuity. Since ritonavir is metabolized by the cytochrome p450 system, it is believed that prolonged serum drug levels due to hepatic insufficiency may cause the retinopathy. A single case of retinal whitening was described in a patient receiving efavirenz.

Anterior Segment Findings

Though the retina is the most commonly affected ocular tissue, HIV patients commonly develop abnormalities of the cornea and anterior segment (50%), and ocular adnexae (25%).Commonly seen in the general population, blepharitis is both more common and more severe in HIV infected patients. Patients with B-cell deficiency are more commonly affected than those with T-cell deficiency, which may be due to either their reduced ability to clear flora or the more complex immunodeficiency-induced changes found in the tear glands. Jeng et al. reported chronic relapsing blepharitis in 3 patients a few months after starting indinavir. The patients experienced a drug-induced retinoid effect - desquamative or erosive chelitis, mucocutaneous xerosis, alopecia, asteatotic eczema, paronychia, ingrown nails. Discontinuing the indinavir was followed by resolution of the blepharitis in 2 patients [12].Acquired tricomegaly (hypertrichosis of the eyelashes) in AIDS patients may be due to the use of several drugs. Some authors suggest that an HIV protein may stimulate keratocytes and pilosebaceous structures. Some even suggest that cessation of eyelash growth may indicate effective anti-retroviral therapy. Conjunctival vasculopathy is seen in 75% of AIDS patients (Figure 2). These generally benign abnormalities include microaneurysms, segmental venous dilation, and adjacent narrowing of arterioles, similar to changes seen in patients with sickle cell disease, leukemia and ataxia-telangiectasia. Radio assays of the vascular endothelium suggest the presence of endothelin-1.97.

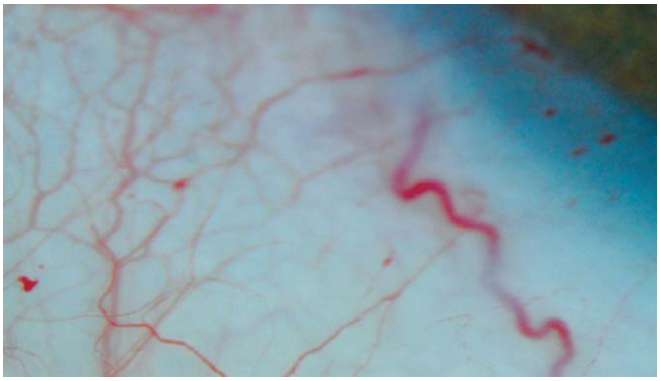

Figure 2: Micro vascular abnormalities of the conjunctiva, such as these aneurysms, occur frequently.

Conclusion

The introduction of HAART significantly decreased the incidence of opportunistic infections, especially those affecting the visual system. Although the overall prevalence of vision loss among AIDS patients has decreased, the proportion of patients suffering loss of vision due to HIV has increased. HIV-related ophthalmologic disorders should, therefore, be considered in patients with new ocular complaints or findings, or in at-risk patients with unusual ocular diseases.

References

1. Gottlieb MS, Schroff R, Schanker HM (1981) Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Engl J Med 305: 1425-1431.
2. Masur H, Michelis MA, Greene JB (1981) An outbreak of community-acquired Pneumocystis carinii pneumonia: Initial manifestation of cellular immune dysfunction. N Engl J Med 305: 1431-1438.
3. Kempen JH, Min YI, Freeman WR (2006) Risk of immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis. Ophthalmology 113: 684-694.
4. Thorne JE, Holbrook JT, Jabs DA (2007) Effect of cytomegalovirus retinitis on the risk of visual acuity loss among patients with AIDS. Ophthalmology 114: 591-598.
5. Cunningham ET, Levinson RD, Jampol LM (2001) Ischemic maculopathy in patients with acquired immunodeficiency syndrome. Am J Ophthalmol 132: 727-733.
6. Holland GN, Vaudaux JD, Shiramizu KM (2008) Characteristics of untreated AIDS related cytomegalovirus retinitis II. Findings in the era of highly active antiretroviral therapy (1997 to 2000). Am J Ophthalmol 145: 12-22.
7. Stewart MW (2010) Optimal management of cytomegalovirus retinitis in patients with AIDS. Clin Ophthalmol 4: 285-299.
8. Kempen JH, Min YI, Freeman WR (2006) Risk of immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis. Ophthalmology 113: 684-694.
9. Hughes MD, Johnson VA, Hirsch MS (1997) Monitoring plasma HIV-1 RNA levels in addition to CD4+ lymphocyte count improves assessment of antiretroviral therapeutic response. ACTG 241 Protocol Virology Sub study Team. Ann Intern Med 126: 929-938.
10. Connors M, Kovacs JA, Krevat S (1997) HIV infection induces changes in CD4+ T-cell phenotype and depletions within the CD4+ T-cell repertoire that are not immediately restored by antiviral or immune based therapies. Nat Med 3: 533-540.
11. Goldberg DE, Smithen LM, Angelilli A, Freeman WR (2005) HIV-associated retinopathy in the HAART era. Retina 25: 633-649.
12. Cantrill HL, Henry K, Jackson B (1988) Recovery of human immunodeficiency virus from ocular tissues in patients with acquired immune deficiency syndrome. Ophthalmology 95: 1458-1462.