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 identifable 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

e groundbreaking reports of 5 young men a icted with unusual opportunistic infections due to an acquired immunode ciency disorder ushered in the AIDS era in 1981. A ected 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 immunode ciency to an unidenti ed microbe, it took 2 years before identi cation of the HTLV-III (human T-lymphocyte virus), later named HIV-1 (human immunode ciency virus). Although targeted anti-retroviral therapy began with the introduction of zidovudine, a nucleoside reverse

Virus. Optom Open Access 7: 171.

(TNF)-α, all of which promote HIV replication [6]. is 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 in uence 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 speci c to a unique antigen. Healthy individuals have a register of T-lymphocytes that allow them to respond to various foreign stimuli. us, CD4+ cells, which are responsible for long-term memory, are responsible for organizing the immune system's response against speci c 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. is is due to a loss of CD4+ memory cells accompanied by an inability to activate and subsequently replicate new CD4+ cells. e progressive loss of CD4+ clones puts the patient at increasing risk of opportunistic infections. erefore, 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 rst 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 in ammatory mediators. Elevated levels of cytokines, particularly TNF-α, interleukin-1 and interleukin-2, have been reported in the serum of AIDS patients. ese cells probably play an important role in promoting HIV infection of eye and central nervous system [8].

A major de ciency 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 di erentiate into macrophages. When they cross the blood brain barrier they di erentiate into perivascular, meningeal or choroidal plexus macrophages, or microglia, a er 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. ese 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.

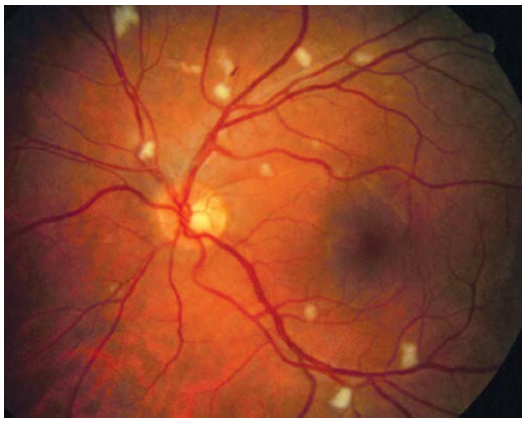
Unlike infected CD4+ lymphocytes, CNS macrophages survive for weeks to months, retain their viability, and continue to shed low levels of virions. Activation of these macrophages is believed responsible for AIDS related dementia. Furthermore, CNS in ltration by HIV-infected monocytes leads to phosphorylation 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. e 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 di erences, 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). e 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 ber 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. e presenting visual acuity in these patients may range from 20/20 to counting ngers, with nal 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 su ciently damage the nerve ber 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 ndings occur in patients with CD4+ counts greater than 120. As expected, this retinitis responds well to HAART [11]. Serous detachment of the macula and



Several cotton wool spots, typical of HIV retinopathy.