OPHTHALMIC MANIFESTATIONS OF HIV

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INTRODUCTION

There are about 14000 new HIV infections occurring everyday globally, of which 95% in developing countries. It was first detected in India in 1986 at Chennai.

Numerous ophthalmic manifestations of HIV infection may involve the anterior or posterior segment of the eye. Anterior segment findings include a variety of external infections and tumors of the periocular tissues. Posterior segment changes include an HIV-associated retinopathy and a number of opportunistic infections of the retina and choroid. The increasing longevity of individuals with HIV disease may result in greater numbers of patients with infections of the retina. Fortunately, many of these infections are now treatable with therapeutic agents. It is important to recognize these infections early so that appropriate therapy can be instituted. Partial immune system recovery following initiation of highly active antiretroviral therapy (HAART) may modify clinical presentation of ophthalmic infections and can affect response to treatment. In addition, in one eye, several infections may occur at the same time, rendering diagnosis and therapeutic intervention more difficult.

Due to the potentially devastating and rapid course of retinal infections, all persons with HIV disease should undergo routine ophthalmologic evaluations. Any HIV-infected person who experiences ocular symptoms also should receive prompt and competent ophthalmologic care. In patients with early stage HIV disease (CD4 count >300 cells/µL), ocular syndromes associated with immunosuppression are uncommon. Nonetheless, eye infections associated with sexually transmitted diseases (STDs) such as herpes simplex virus, gonorrhea, and chlamydia may be more frequent in HIV-infected persons. Therefore, clinicians should screen for HIV in the presence of these infections.

CLASSIFICATION OF LESIONS

Extra Ocular Lesions

- Adenexal
  - Herpes Zoster Ophthalmicus.
  - Kaposi Sarcoma
  - Squamous Cell Carcinoma of Conjunctiva
  - Molluscum contagiosum
- Orbital
  - NHL (Burkitts lymphoma)
  - Orbital cellulites due to Aspergillus.
  - Pyogenic Cellulitis

Anterior Segment Lesions

- Conjunctival microvasculopathy
- Infectious Keratitis (Herpes Simplex, Varicella Zoster and Microsporidia)
- Anterior uveitis (due to HZO, CMV Retinitis, Drugs like Cidofovir and Rifabutin)

Posterior Segment Lesions

- HIV Retinopathy
- CMV Retinitis
- Toxoplasma retinochoroiditis
- Acute retinal necrosis
- Pneumocystitis carinii chorioretinopathy
- Fungal endophthalmitis
- Progressive outer retinal necrosis
- Ocular Syphilis
- Mycobacterial Chorioretinitis
- Fungal Endophthalmitis (Cryptococcus and Candida)

Neuro Ophthalmic Lesions

- CN Palsy
- Papilloedma
- Optic neuropathy

EXTRA OCULAR LESIONS

Kaposi Sarcoma

Kaposi sarcoma is a highly vascular tumor affecting 30%

HIV patients in USA .However it is rare in India. It appears as multiple purple to red nodules on the skin and mucous membranes and in approximately 20% of individuals with HIV-associated kaposi sarcoma. The tumor involves the eyelids, conjunctiva and in rare cases the orbit.[1]. The appearance of KS on the eyelids is similar to that of kaposi sarcoma lesions elsewhere on the skin. In the conjunctiva, kaposi sarcoma may appear as a persistent subconjunctival hemorrhage or as a raised, purplish-red mass(Fig 1).[2] It does not invade the eye and no treatment is necessary if it causes no symptoms and is cosmetically acceptable. However, kaposi sarcoma may cause discomfort through a mass effect and secondary corneal changes and also may be disfiguring. Under these circumstances, it may be treated by cryotherapy, surgical excision, radiation or chemotherapy.

Squamous Cell Carcinoma of Conjunctiva

Though rare this type of carcinoma have been reported. Histopathology shows spindle shaped cells with abnormal mitotic figures.

Molluscum Contagiosum

It is a common skin infection caused by large DNA Pox virus. In normal immunity the molluscum lesions are fewer and unilateral. But in HIV infected individuals the lesions are larger in size and number, sometimes confluent bilateral and even found in conjunctiva. They are resistant to treatment.

ANTERIOR SEGMENT LESIONS

Conjunctival Microvasculopathy

70 to 80 % of all HIV patients have some form of conjunctival microvascular changes.These include segmental vascular dilation or narrowing, microaneurysms, comma shaped vascular fragments and sledging of blood coloumns.

Infections

Herpes Zoster Ophthalmicus

Herpes zoster ophthalmicus (HZO) is characterized by a vesiculobullous rash over the ophthalmic branch of the trigeminal nerve and may be associated with keratitis,

conjunctivitis, blepharitis and uveitis.[3] Although HZO most commonly affects individuals in the sixth and seventh decades of life, it may be an initial manifestation of HIV infection in young persons[4,5].It affects 15% of HIV patients In New York City, 61% of patients less than 45 years of age with HZO had HIV risk factors and 91% had a reduction in the T-lymphocyte helper-suppressor ratio. None of the older patients had risk factors for HIV infection or unexplained depression of the helper-suppressor ratio.[6] In Africa, 100% of a consecutive series of patients with HZO who were younger than age 47 had HIV antibodies. HIV infection appeared to correlate with more severe corneal involvement and post-herpetic neuralgia.[7]

Although acyclovir may diminish ocular sequelae of HZO in immunocompetent patients, this treatment has not been evaluated systematically in HIV-infected patients[8]. However it can be given Intravenously in doses of 10mg/kg body weight three times daily followed by oral regimen. Adults with an acute, moderate-to-severe skin rash may receive acyclovir orally and bacitracin in ointment form for skin lesions. In the presence of uveitis, topical prednisolone and a cycloplegic should be applied.

Herpes Simplex Keratitis

Herpes simplex virus (HSV) can cause painful and often recurrent corneal ulcerations with a characteristic branching or dendritic pattern on slit lamp exam. HSV keratitis is often associated with corneal scarring and iritis, require a prolonged course of treatment and recurs frequently. Treatment consists of trifluorothymidine and cycloplegic drugs with debridement of the ulcer using a cotton-tip applicator. Oral acyclovir (400 mg twice daily for 1 year) decreases the risk of recurrent HSV keratitis by 50%.[9]

Fungal Infections

Defects in cellular immunity also may play a role in susceptibility to corneal infections. Spontaneous fungal keratitis secondary to Candida parapsilosis and Candida albicans has been observed in persons with advanced HIV disease and a history of antecedent trauma.[10,11]

Uveitis

Uveitis occurs with and may be the first sign of several chronic infections seen frequently in patients with HIV disease including tuberculosis, syphilis, histoplasmosis, coccidioidomycosis, and toxoplasmosis. Unexplained uveitis in an HIV-infected patient should prompt a search for an underlying infection. Clinical signs of anterior uveitis include cells in the anterior chamber, keratic precipitates, posterior synechiae and hypopyon. Clinical signs of posterior uveitis include vitritis, chorioretinal infiltrates, vascular sheathing and retinal hemorrhages.

Conjunctivitis and uveitis have occurred in HIV-infected patients in association with reactive arthritis also known as Reiter syndrome.[12] This syndrome consisting of asymmetric oligoarthropathy, urethritis and conjunctivitis or uveitis, is of unknown etiology but may represent an abnormal host response to an infectious agent.[13] Although the association of reactive arthritis and HIV disease may be no more than a chance occurrence, derangement of the cellular immune system may play a pathogenic role.

POSTERIOR SEGMENT DISEASE

Manifestations Not Associated with Opportunistic Infections

HIV retinopathy

HIV retinopathy is a noninfectious microvascular disorder characterized by cotton-wool spots, microaneurysms, retinal hemorrhages, telangiectatic vascular changes and areas of capillary nonperfusion. These microvascular changes are the most common retinal manifestation of HIV disease and are clinically apparent in about 70% of persons with advanced HIV disease.[19] They also are seen in approximately 40% of patients with symptomatic intermediate-stage HIV disease and in approximately 1% of those with asymptomatic HIV infection.[20]

Cotton-wool spots occur in approximately 50-60% of patients with advanced HIV disease and are the earliest and most consistent finding in HIV retinopathy (Figure-2).[21-24] They represent infarcts of the nerve fiber layer and are no different from cotton-wool spots seen with other systemic disorders such as diabetes mellitus and systemic hypertension. They are not vision threatening, although we have seen several patients with advanced HIV disease who presented with small visual field defects corresponding to the cotton-wool spots. Although they can be confused with early cytomegalovirus (CMV) retinitis lesions, cotton-wool spots usually can be distinguished by their smaller size, superficial location, lack of progression and tendency to resolve over weeks to months.

Hemorrhages are seen less commonly than cotton-wool spots and are estimated to occur in about 20% of patients with advanced HIV disease[25-27] and in approximately 3% of patients with mildly symptomatic HIV disease.[20] They may involve both the nerve fiber layer and the deeper retina and may appear as flame-shaped, dot, or blot hemorrhages.

Telangiectatic vascular changes may be seen in patients with HIV disease and are often associated with microaneurysms.[26] Areas of capillary nonperfusion may accompany these changes. Retinal vein and artery occlusions also have been observed in patients with HIV disease.[28,29] Therefore, individuals with unexplained vascular occlusions should be considered for HIV testing.

Manifestations Due to Opportunistic Infections

A number of infections of the retina and choroid have been reported to affect individuals with advanced HIV disease.[34,35] The more commonly encountered or more debilitating infections are included in this review. Although a number of these infections also can be seen in immunocompetent individuals, HIV-infected patients may present with less accompanying inflammation, take longer to respond to therapy, and be more likely to experience recurrence after therapy. Multiple foci of infection, bilateral infection, and multiple infections in the same eye also are more likely to occur in HIV-infected patients.

Cytomegalovirus Retinitis

CMV retinitis is the most common retinal infection in patients with HIV disease, occurring in 15-40% of patients with advanced HIV disease.[20,36-39] It is bilateral in 30-50% of patients,[40] although that rate may be lower in the developed countries as the disease often presents unilaterally and the administration of anti-CMV medication

almost always prevents the onset of retinitis in the fellow eye.[36] It is uncommon to find CMV retinitis in HIV-infected patients with a CD4 count >40 cells/µL and a CD4 count >50-100 cells/µL in an individual with retinitis should prompt a reconsideration of the diagnosis of CMV retinal infection.

CMV is a DNA virus classified in the herpes group of viruses. Serologic studies indicate a past CMV infection in approximately 50% of the adult population in urban areas of the United States and Europe[41] and close to 100% in the male homosexual population. CMV disease affecting the eye, however, tends to occur only in developing fetuses and in immunocompromised patients. CMV infection of the retina leads to viral invasion of retinal cells with resultant retinal necrosis. Clinically, lesions appear within the retina as multiple granular white dots with varying amounts of hemorrhage. This is called the indolent form (Figure-3). Although they can be confused with cotton-wool spots (which may be present in the same eye), CMV lesions differ by their tendency to enlarge and coalesce over time. As areas of retinitis enlarge, they appear to follow the vascular arcades, resulting in an arcuate or triangular zone of infection This is called the Fulminant form.(Fig-4) Areas of active infection also may appear to be linear, seemingly following the retinal vessels or nerve fiber layer into the periphery. Frosted branch angiitis (Fig-5) may be seen in conjunction with CMV retinitis. After several weeks, atrophic tissue that has lost the capacity to support viral replication replaces actively infected regions of retinal tissue.[42,43] The underlying retinal pigment epithelium demonstrates pigment loss and migration, resulting in increased visualization of the underlying choroidal vasculature.Other findings associated with CMV retinitis include perivasculitis, vascular attenuation and vessel closure,[20,44] as well as vitritis, anterior uveitis and papillitis.[45-47]

Although CMV retinitis usually responds to initial therapy, the prompt recognition of recurrent CMV retinitis is of particular importance. The presentation of recurrence may be so subtle that active disease may remain undetected for extended periods of time. Early recurrences appear as subtle white or gray zones of retinitis with little, if any,

accompanying retinal hemorrhage. Recurrence usually begins at the margin of previously active infection and tends to "smolder" rather than actively progress. Nevertheless, it will continue to spread slowly but inexorably, if the treatment regimen is not altered. The reintroduction of induction doses of medication for a period of 2-3 weeks often inhibit progression of these recurrent lesions. Patients with recurrent infection that is quite "active" in appearance characterized by the presence of significant retinal whitening and hemorrhage while they are on appropriate levels of maintenance therapy, have an especially poor prognosis for preservation of sight, even with the use of increased doses of medication.

With the introduction of HAART, the incidence of CMV retinitis has been noted to decrease by about 75%.[48] However, the incidence of opportunistic infections, especially new or recurrent CMV retinitis, remains high during the first few months of HAART, consistent with the delay in immune recovery following initiation of treatment.[49] Prior to the availability of HAART, the median time to progression of treated CMV was3-9 months, and the lack of CMV progression in patients on HAART is most likely due to improved CMV-specific immunity.[50] In patients with a history of CMV disease who subsequently receive HAART, immune reconstitution may result in inflammatory retinal lesions or vitritis.

Systemic Anti-CMV Therapy :

For oral and intravenous treatment of CMV infection, the drugs that are used are :

-Gancyclovir given intravenously. Induction dose is 5mg/kg every 12 hours for 14-21 days followed by maintenance dose of 5mg/kg daily or 6mg/kg 5 out of 7 days a week.

-Foscarnet given intravenously. Induction dose is 60mg/kg every 8 hours for 14-21 days followed by maintenance dose of 90 to 120mg/kg daily

-Cidofovir given intravenously. Induction dose is 5mg/kg every week for 2 weeks followed by maintenance dose of 5 mg/kg every biweekly.

Intra vitreal drugs : In the early years of the HIV epidemic, patients unable to tolerate systemic CMV therapy

sometimes benefited from intravitreal injection of ganciclovir [51,52,53-56] or foscarnet.[57]

Gancyclovir : Induction dose: 200-400 microgram 2-3times/ week followed by maintenance with same dose weekly Foscarnet -Induction dose:1.2-2.4 mg 2 times/week followed by maintenance dose of 1.2-2.4 mg weekly Cidofovir - given in 20 microgram weekly for 5-6 weeks.

Direct intraocular administration of ganciclovir has the benefit of achieving therapeutic levels by bypassing the blood-retinal barrier. Furthermore, systemic absorption is minimal. Therefore systemic complications are avoided but protection of other CMV-susceptible sites, including the contralateral eye is not achieved. Therefore, oral prophylaxis with ganciclovir or valganciclovir often is used in combination with the intraocular device.[58]

Ganciclovir Intraocular Implant

In 1996, the FDA approved intraocular implants for the treatment of CMV retinitis. The ganciclovir intraocular device (GIOD) consists of a 6 mg pellet of ganciclovir that is 2.5 mm in diameter and coated with 10% polyvinyl alcohol, which is impermeable to ganciclovir. A suturing strut is attached to one edge of the pellet and the pellet is then sealed on 3 sides by ethyl-vinyl acetate. The resultant sustained linear drug release provides 3 or 6 months (depending on pellet construction) of anti-CMV activity. The surgical technique involves a conjunctival peritomy (a 360° incision of the conjunctiva at the limbus) in the inferotemporal quadrant followed by a 5.5mm pars plana incision located 4.0 mm posterior to the limbus. A limited vitrectomy without infusion is performed through the incision and at the wound site to remove prolapsed vitreous. The suturing strut of the implant is trimmed to approximately 1 mm in length and a double armed 9-O mersilene suture is passed and locked through both edges of the strut. The implant is placed carefully into the vitreous cavity and the preplaced 9-O mersilene is sutured to the sclera and tied. The sclerotomy is then closed with a continuous 8-O nylon suture.

Toxoplasma Retinochoroiditis

Toxoplasma gondii is a protozoan parasite, the life cycle of which includes encysted and active forms. In contrast to its presentations in immunocompetent individuals, toxoplasmosis in HIV-infected patients is more likely to cause multifocal sites of retinochoroidal infection with less accompanying vitritis.[67] Bilateral eye involvement also may be seen in patients with HIV disease[68] and proliferative vitreoretinopathy may accompany later stages of the disorder. In contrast to the situation with immunocompetent individuals in whom this infection almost always represents recurrence of a congenital lesion, patients with HIV disease usually have no evidence of a pre-existing retinochoroidal scar, suggesting that these represent recently acquired infections.[69,70]

Toxoplasma retinochoroiditis may be confused with other forms of retinitis, but it usually can be differentiated by the presence of intense, almost fluffy areas of retinal whitening with accompanying vitritis (Figure-6). The degree of accompanying retinal hemorrhage is usually less than that seen in individuals with untreated CMV retinitis. Fluorescein angiography may demonstrate more leakage with active toxoplasmosis than with CMV infection. Of note is the fact that toxoplasmosis commonly involves the central nervous system in patients with advanced HIV disease and results in neurologic manifestations in 10-40% of affected individuals.[71-73]

Serologic studies have been relatively unreliable for the diagnosis of toxoplasmosis in HIV-infected patients.[67] IgG anti-Toxoplasma antibody titers in patients with toxoplasmosis are sometimes low in the presence of disease; when high, they do not distinguish old from active toxoplasmosis. However, toxoplasmosis is unlikely in a patient with a negative IgG anti-Toxoplasma antibody.

Patients with a confusing clinical presentation and a vision threatening lesion (as determined by decreased acuity and the lesion's proximity to the optic disc or macula) may warrant a therapeutic trial using antitoxoplasmosis medications. Treatment consists of pyrimethamine and either sulfadiazine or clindamycin in standard dosages.[72,73] Adjunctive steroid therapy has been reported to be unnecessary.[69,70] Maintenance therapy with pyrimethamine and either sulfadiazine or clindamycin results in fewer relapses of infection than does pyrimethamine alone,[72] and may need to be continued indefinitely while CD4 counts remain low.

Candida Endophthalmitis

Typical candidal fungal lesions appear as fluffy white "mounds," which are frequently bilateral and superficially located and often extend into the vitreous. There usually is an overlying vitritis and vitreous abscesses also may be seen.[75] Candida retinitis is not commonly seen in HIV-infected patients but may be more likely in the setting of intravenous sources of infection (including indwelling catheters).

Cryptococcus Chorioretinitis

Cryptococcus neoformans is a yeast that causes oppertunistic infection in immunosuppressed individuals.[75] CNS involvement with Cryptococcus in HIV-infected patients is relatively common and often results in meningitis with secondary ocular findings.[31] Choroiditis and chorioretinitis from cryptococcal infection also have been observed in HIV-infected patients.[26,31,77] Typical cryptococcal lesions are located in the choroid and retina and appear as multiple, discrete yellowish spots varying in size from 500 to 3,000 µm in diameter.[78,79] Papilledema may be present due to increased intracranial pressure from meningitis. Visual loss may occur and has been attributed to cryptococcal involvement of afferent tissues including the optic nerve, chiasma, and tract.[80]

Bacterial Retinitis

Several cases of endogenous bacterial retinitis have been documented in patients with advanced HIV disease including atypical mycobacteria which are seen in 15 to 20% of AIDS patients.[31,76] It may present as a vitritis or a slowly progressive retinitis with multifocal yellow-white retinal lesions, subretinal fluid and exudate.[76] Bacterial chorioretinitis, although infrequently seen, should be considered in patients with advanced HIV disease who present with posterior segment infection unresponsive to treatment for suspected viral, fungal, or protozoan causes. Tubercular infection in the eye in AIDs is not so common but it can cause Choroiditis, Chorioretinitis, Choroidal granuloma, Endophthalmitis, Subretinal abscess and even Panophthalmitis. They are associated with disseminated tuberculosis.

Syphilis

Syphilitic involvement of the posterior segment of the eye in patients with concurrent HIV infection has been well documented.[14-17] The findings are variable and include chorioretinitis, retinal perivasculitis, intraretinal hemorrhage, papillitis and panuveitis. Ocular involvement may be unilateral or bilateral and is associated with evidence of central nervous system (CNS) infection in up to 85% of patients.[14,15,17,18] In addition, one third of patients with both ocular and CNS infection manifest symptomatic neurosyphilis.[17] This high correlation between neurosyphilis and ocular involvement supports the current recommendation of lumbar puncture and cerebrospinal fluid (CSF) evaluation in patients with ocular syphilis who are seropositive for HIV.[14,17]

The most reliable laboratory studies for diagnosing ocular syphilis are the serum fluorescent treponemal antibody absorption test (FTA-ABS) and the microhemagglutination assay (MHA-TP). Both of these provide evidence of past luetic infection and remain positive for years.[14,15] CSF evaluations with determinations of protein and glucose levels, a leukocyte count and a VDRL have a high degree of accuracy in the diagnosis of neurosyphilis.[14,15]

Syphilis can run a more rapid and aggressive course in HIV-infected patients than in immunocompetent individuals.[15,17,18] One comparison of patients with ocular syphilis who were either HIV infected or immunocompetent demonstrated that the HIV-infected group had more extensive ocular disease.[15]

Antibiotic regimens recommended for ocular syphilis in immuno compromised is simillar with the antibiotic regimen for neurosyphilis (12-24 million units of aqueous penicillin G given intravenously for a minimum of 10 days).[17]
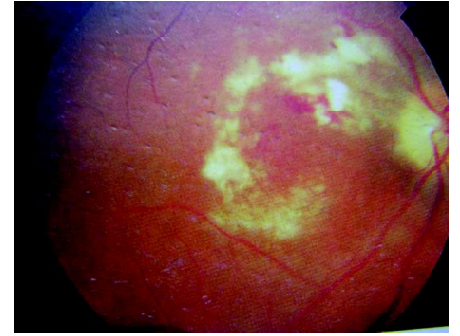
Pneumocystis Choroiditis

Pneumocystis carinii is an unusual organism that exhibits some protozoan characteristics.[5] It is the cause of P carinii pneumonia, the most common systemic infection in patients with HIV disease.[81] Pneumocystis ocular involvement in advanced HIV disease was first suspected in 1982 when a patient with advanced HIV disease and PCP had evidence of the organism in the ganglion and plexiform
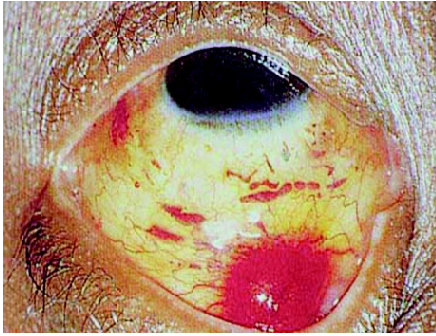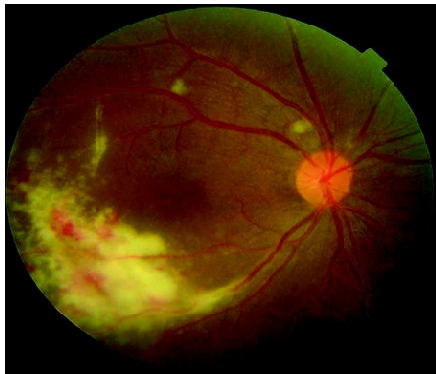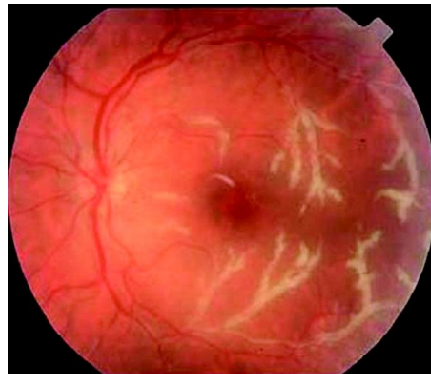
Figure-1 Kaposi Sarcoma of
Conjunctiva
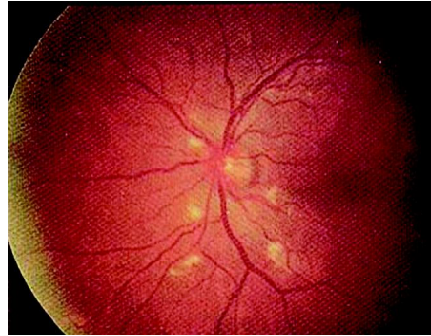
Figure-2 HIV Retinopathy

Figure-3 CMV Retinitis (Indolent form)

Figure-4 CMV Retinitis
(Fulminant form)

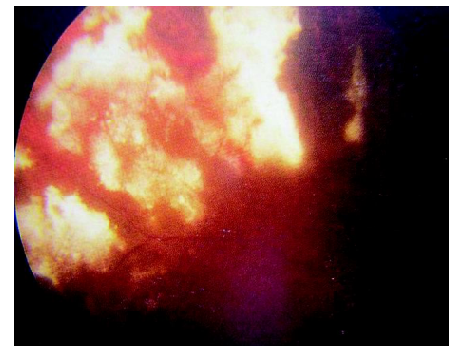**Figure-5** CMV Retinitis
(Frosted Branch Angitis)

Figure-6 Toxoplasma Chorio
Retinopathy

Figure-7 Pneumocystis Choroiditis

Figure-8 Progresive Outer Retinal
Necrosis

Figure-9 Acute Retinal Necrosis

layers of the retina on histopathologic study.[82] In 1987, postmortem histopathologic examination of eyes obtained from a patient with HIV disease and disseminated PCP revealed areas of choroidal thickening and exudate which harbored the characteristic cysts of P carinii.[83] Clinical reports of Pneumocystis choroiditis first appeared in late 1988 and early 1989.[84,85] Multiple pale yellow-white choroidal lesions, usually in both eyes, clinically characterize Pneumocystis choroiditis.[5,84,85] The lesions generally are round or ovoid and of variable size(Fig-7), and may

coalesce to form large regions of confluent involvement with resultant choroidal necrosis.[5,84] If this process involves the foveal area, loss of central vision may occur.[84] Fluorescein angiography of the choroidal lesions reveals early hypofluorescence and late staining with minimal evidence of dye leakage. Of note is the almost total lack of an associated inflammatory response in the retina, vitreous, and anterior segment. A similar choroidal lesion occurs in early cryptococcal chorioretinitis, but typically is accompanied by vitritis.[84]

Acute Retinal Necrosis

Acute retinal necrosis (ARN) is a rapidly progressive viral uveitis that was first reported as a new clinical syndrome in immunocompetent patients in 1971.[85] The first case report of this disorder in an HIV-infected patient appeared in 1985.[37] Peripheral retinal whitening that progresses to necrosis over several days characterizes ARN (fig-8). Bilateral involvement may occur, and retinal detachments with proliferative vitreoretinopathy commonly occur.[20,86] Several viral pathogens have been associated with ARN. Varicella-zoster has been the most frequently implicated virus.[31] HSV and CMV also have been associated with this disorder.[86,87-90] Whereas ARN responds to treatment with intravenous acyclovir in immunocompetent individuals, it is much more recalcitrant to treatment in HIV-infected patients. The currently recommended treatment involves standard induction dosages of ganciclovir or foscarnet, with adjunctive high-dose intravenous acyclovir (15 mg/kg of body weight every 8 hours).

Progressive Outer Retinal Necrosis

It is a rare infection due to Herpes group of viruses presenting with floater and sudden loss of vision. Characteristically it involves outer retina, progresses circumferentially sparing the retinal vessels.(Fig-9) Necrotic retina lead to large retinal breaks and detachment.

NEURO OPHTHALMIC LESIONS

Noninfectious optic nerve involvement in patients with HIV disease includes papilledema, anterior ischemic optic neuropathy, and optic atrophy.[2,27,30] Papilledema usually occurs in patients with advanced HIV disease and CNS malignancies. KS also occasionally may result in metastatic CNS involvement.[31] In addition, anterior ischemic optic neuropathy has been reported as an early manifestation of advanced HIV disease.[30] Also noteworthy is the number of patients with advanced HIV disease who present with slightly swollen, "full-appearing" discs with small or absent cups.

Evaluation of this finding did not reveal any neurologic abnormalities or evidence of other infectious processes, such as syphilis and the etiology of this condition is not clear. Among the most prevalent conditions causing increased intracranial pressure in persons with HIV disease are non-Hodgkin's lymphoma, toxoplasma encephalitis and cryptococcal meningitis.[31-33]

Extra ocular muscle palsy due to cranial nerve involvement occurs in 4% of patients of AIDS. Usually they are associated with toxoplasma infection in brainstem.(66)

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