Facing up to the challenge of HIV-related ocular complications

Dermot McGrath
in Sao Paulo

As a result of improved antiviral treatment and patient survival, ophthalmic complications are now being seen with increasing frequency in HIV/AIDS, occurring in up to 75% of patients during the course of the disease, according to leading vision scientists speaking at the World Congress of Ophthalmology.

In an overview of the manifestations of HIV/AIDS affecting the anterior segment, Thomas Liesegang MD, professor of ophthalmology, Mayo Clinic, Jacksonville, Florida, US, noted that ocular manifestations of AIDS include a wide range of opportunistic infections such as cytomegalovirus, herpes simplex virus and varicella zoster, neoplasms such as Kaposi's sarcoma and lymphoma, and inflammations, some of which may be disease or drug associated.

He also emphasised the fact that there is considerable regional variation in the ocular manifestations of AIDS.

"In industrialised countries, cytomegalovirus retinitis is a prominent problem. The same is true for Latin America, but there is also a high frequency of toxoplasmosis. And in Africa, there is a different set of diseases that define AIDS including herpes zoster, conjunctival squamous cell carcinoma and Kaposi's sarcoma.”

### Opportunistic infections

Focusing initially on opportunistic infections, Dr Liesegang said that herpes zoster ophthalmicus could occur in any patient with depressed cell immunity. In HIV-positive and AIDS patients, the incidence of herpes zoster is seven times higher than average and the recurrence rate is also seven times higher.

About five per cent to 15% of HIV-positive patients contract herpes zoster. He noted that Africans specifically have a high rate of painful corneal perforation associated with herpes zoster. Ocular complications result from inflammation, nerve damage and tissue scarring. Herpes zoster presents as vesiculobullous rash and may be associated with keratitis, scleritis, uveitis, retinitis or encephalitis.

The picture with herpes simplex is somewhat different, said Dr Liesegang. "With current evidence suggests there is no increased risk of the disease in AIDS patients, the course of the disease is longer and the rate of recurrences is also higher. It is associated with peripheral and large dendrites, and corneal ulcerations.

Another virus, molluscum contagiosum, posed few serious problems before the advent of AIDS, said Dr Liesegang. The disease, which affects the skin and mucous membranes as translucent papules, involves the eyelids in up to five per cent of HIV infected patients.

"These can be large disfiguring facial lesions and may involve the conjunctiva and the limbus. If you biopsy or remove some of these lesions, the inflammatory reaction around them is almost nil, which is very unusual. For treatment, it may respond alone to aggressive highly active antiretroviral therapy (HAART)," he explained.

He noted that extensive molluscum contagiosum is a marker for advanced HIV disease in homosexual men, correlating closely with CD4+ counts. The disease produces a profound local immunosuppression, added Dr Liesegang. Bacterial and fungal infections are generally more severe in HIV-infected patients. One of these, microsporidia, which is transmitted by contaminated water, is uncommon and occurs almost exclusively in HIV+ patients. The parasite has two clinical manifestations: stromal keratitis in immunocompetent individuals, and epithelial keratitis in AIDS patients.

#### AIDS-defining cancers

Among the group of diseases denoted as AIDS-defining cancers, Dr Liesegang cited Kaposi's sarcoma, non-Hodgkin's lymphoma and, in Africa, squamous cell carcinoma of the conjunctiva as particularly associated with HIV patients.

Kaposi's sarcoma is the only one that has declined significantly since the introduction of HAART. It is a highly vascularised, mesenchymal tumour affecting the skin and mucous membranes and occurs in up to 25% of HIV infected patients. It may present as purple papules in the eyelids, which may be either flat or slightly raised. Around 20% of these patients have asymptomatic Kaposi's sarcoma of the eyelids, conjunctiva and rarely the orbit.

Dr Liesegang noted that Kaposi's sarcoma is closely associated with human herpes virus 8. One third of individuals with both HIV and the herpes 8 virus develop Kaposi's sarcoma within 10 years. This is 20,000 times the usual rate.

Squamous cell carcinoma is the third most common cancer in HIV after oral cavity and rectum, said Dr Liesegang. The tumours have been related to exposure to ultraviolet light and conjunctival papillomavirus infection and usually arise in the limbus of the eye. It usually occurs at a younger age than for other patients with the disease and the risk is 13 times greater in AIDS patients. In Uganda alone, the incidence of the disease increased from six million to 35 million over a 32-year period.

Primary non-Hodgkin's lymphoma (NHL) of the orbit and ocular adnexa is a rare disease, but is 200 times more common in HIV patients. Dr Liesegang said that it is usually a high-grade lymphoma and specific types are associated with herpes virus 8 and the Epstein Barr virus.

Noting that there has been a 25% reduction in AIDS-related deaths since the introduction of HAART, Dr Liesegang said that HAART can also be used to treat ocular manifestations of the disease such as retinitis, Kaposi's sarcoma, molluscum contagiosum and microsporidial infections.

While HAART has done much to reduce morbidity associated with AIDS, it has also given rise to a new set of ophthalmic challenges, said Dr Liesegang.

### Ocular Update

"In Africa, there is a different set of diseases that define AIDS including herpes zoster, conjunctival squamous cell carcinoma and Kaposi's sarcoma”

"With HAART, we restore pathogen specific immune responses and there is regression of opportunistic diseases. Consequences of HAART therapy include inflammation of ocular tissues and appearance of sub-clinical opportunistic pathogens”

Since the introduction of HAART, herpes zoster rates have increased, with dermatomal zoster occurring in about 8% of patients with AIDS, about five times the expected rate. Herpes simplex also presents as more severe and more frequent in patients on HAART.

Substantial intraocular inflammation, known as immune recovery uveitis, has also been reported in patients with healed cytomegalovirus retinitis receiving HAART, he noted.

#### HIV and the posterior segment

In a separate presentation, Jean D Vaudaux MD, Jules Gonin Eye Hospital, Lausanne, Switzerland discussed AIDS-related diseases of the posterior segment, which include vascular disease, opportunistic infections, neoplasmia and neuro-ophthalmic manifestations.

HIV-related microvasculopathy is the most common posterior segment manifestation of AIDS and is found in approximately 50% of patients and in up to 90% of autopsy eyes, said Dr Vaudaux.

Patients presenting with disciform ischemia may have cotton-wool spots (CWS) in the retina, intraretinal haemorrhages, and retinal microaneurysms; HIV-related microvasculopathy is typically associated with low CD4+ T lymphocyte counts.

Opportunistic infections of the posterior segment are numerous, said Dr Vaudaux. The most important one is cytomegalovirus retinitis, with a prevalence of around 25% in AIDS patients at some point during the course of HIV infection. The disease, which can lead to blindness if not treated, is usually associated with severe immunosuppression and low CD4+ T lymphocyte counts and was a strong predictor of mortality in the pre-HAART era.

Other AIDS-related manifestations cited by Dr Vaudaux include immune recovery uveitis, extensive toxoplastic retinochoroiditis, progressive outer retinal necrosis, syphils, chronic multifocal retinal infiltrates, tuberculous choroiditis and intraocular lymphoma, among others.

Dr Vaudaux noted that posterior segment manifestations in people with AIDS are common and that prevalence varies depending on geographic location, immunological factors and on availability of HAART.

The picture with herpes simplex is somewhat different, said Dr Liesegang. W hile current evidence suggests there is no increased risk of the disease in AIDS patients, the course of the disease is longer and the rate of recurrences is also higher. It is associated with peripheral and large dendrites, and corneal ulcerations.

Another virus, molluscum contagiosum, posed few serious problems before the advent of AIDS, said Dr Liesegang. The disease, which affects the skin and mucous membranes as translucent papules,