Ocular Pathology in Acquired Immunodeficiency Syndrome

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ORIGINAL ARTICLE

Gross and microscopic ocular findings were prospectively studied in 38 human immunodeficiency virus (HIV)-seropositive subjects undergoing postmortem examination. Pathologic lesions were detected in 27 patients (71%), with 67% of the abnormal findings detected only microscopically.

The ophthalmic findings in the acquired immunodeficiency syndrome (AIDS) include retinal microangiopathy, opportunistic infections, neoplasms, and neuro-ophthalmic abnormalities.1-11 Several small retrospective studies have analyzed the histopathologic changes noted in eyes of seropositive subjects.8,9,12-15

We prospectively studied the ocular pathology in human deficiency virus (HIV)-seropositive subjects undergoing postmortem examination. Pathologic lesions were investigated using histologic techniques, immunohistochemistry, in situ hybridization, and correlated with clinical data and other autopsy findings.

MATERIALS & METHODS

Both globes with a long optic nerve stump were examined from 38 consecutive HIV-seropositive patients undergoing postmortem examination at the University of Texas Medical Branch Hospitals, Galveston. Thirteen patients had had an ante-mortem ophthalmologic evaluation. The globes were fixed in 10% neutral buffered formaldehyde solution. They were then sectioned in a standard fashion16 into superior and inferior calottes as well as a central 9-mm portion containing the cornea, pupil, optic nerve, and macula. Sectioned globes were examined under the dissecting microscope. Gross photographs were taken using a handheld fundus camera (Kowa Optimed Inc, Torrance, Calif). The central portion was processed for histology. The calottes were processed if gross lesions were identified. A transverse section of at least one optic nerve was examined. Paraffin-embedded sec-

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tions were stained with hematoxylin-eosin, hematoxylin-eosin with Luxol fast blue for myelin, and Masson trichrome. If infectious organisms were clinically or pathologically suspected, additional stains were obtained. These included periodic acid-Schiff, Alcian blue, Mayer mucicarmine, Gomori methenamine silver, Kinyoun acid fast stain, Brown and Hopps Gram stain, immunohistochemical stains for herpes simplex virus types 1 and 2, and in situ hybridization for cytomegalovirus (CMV). Immunohistochemical staining for glial fibrillary acidic protein was selectively performed to demonstrate reactive astrocytes in the optic nerve.

Immunohistochemistry was performed using the biotin-avidin-horseradish peroxidase technique with herpes simplex virus types 1 and 2 polyclonal antibodies (Dakopatts, Carpinteria, CA) and with a glial fibrillary acidic protein monoclonal antibody cocktail (Biomedical Technologies Inc, Stroughton, MA). In situ hybridization for cytomegalovirus was performed using a specific DNA probe (Enzo Diagnostics Inc, New York, NY) according to standard techniques.

RESULTS
Thirty-eight patients had a mean age of 35.5 years (range, 16 months to 55 years). Risk factors included homosexuality, bisexuality, or intravenous drug abuse in 36 male subjects and blood transfusion in 2 female subjects (Table 1). The average survival from HIV seroconversion to death was 23.2 months (range, 1 to 81 months). Two subjects did not have any opportunistic infections or neoplasms.

Cytomegalovirus infection was identified at autopsy in 15 patients (39%) (Table 2). Seven patients had CMV retinitis, including 2 patients without extraocular CMV infection. Gross retinal necrosis was present in only 3 patients. A fourth patient was being treated for CMV retinitis and, although no gross lesions were apparent, persistent CMV retinitis was found microscopically. Histologically, CMV retinitis appeared as full-thickness retinal necrosis, usually with a sharp demarcation between involved and uninvolved areas, and with a scant inflammatory infiltrate. Cells infected with CMV were markedly enlarged with typical intranuclear and cytoplasmic inclusions surrounded by a clear halo and a sharply demarcated nuclear membrane. Cytoplasmic inclusions were smaller, granular, and basophilic. Atypical or equivocal cases of CMV retinitis were confirmed by in situ hybridization.

Six patients with central nervous system Cryptococcus neoformans had ocular cryptococcosis. Gross ocular lesions were seen at autopsy in 2 cases. The yeasts appeared as pleomorphic budding yeasts with characteristic "soap bubble" lesions and virtually no inflammatory reaction. The yeast cell wall stained black with Gomori methenamine silver, and the mucopolysaccharide capsule stained bright red with mucicarmine.

Disseminated mycobacteriosis was present in 10 patients. These included 2 cases of Mycobacterium tuberculosis, 3 cases of Mycobacterium avium-intracellulare, and 5 cases in which acid-fast bacilli were identified histologically but were not cultured. Ocular infection with M tuberculosis was present in 1 patient with disseminated M tuberculosis diagnosed by postmortem cultures from the lung, mediastinal lymph nodes, and cerebrospinal fluid. The eyes did not have gross pathology. Microscopically, a focus of necrotizing granulomatous choroiditis in the right eye contained intracellular acid-fast bacilli.

Histoplasma capsulatum was microscopically identified in the choroid of 1 patient with disseminated histoplasmosis. The organism was cultured ante-mortem from blood and postmortem from lung tissue. The second patient with disseminated histoplasmosis also had disseminated mycobacteriosis. He had bilateral chorioretinal scars and nonspecific choroiditis. Special stains for fungi and acid-fast bacilli were negative.

In addition to the ocular and optic nerve infec-

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Sex</td>
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</tr>
<tr>
<td>Male</td>
<td>36 [94.7]</td>
</tr>
<tr>
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<td>2 [5.3]</td>
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<tr>
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<tr>
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<td>15 [39.5]</td>
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<tr>
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<td>Homosexual or bisexual</td>
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TABLE 1
Demographic Characteristics