Neurologic Changes Persist Despite HIV Therapy

BY DIANA MAHONEY

MONTREAL — Evidence of significant brain inflammation and neuronal damage in patients with clinically stable HIV infection suggests that central nervous system injury persists despite successful viral control, Dr. Bradford Navia reported at the Conference on Retroviruses and Opportunistic Illnesses.

He and his colleagues in the multicenter HIV Neuroimaging Consortium used a combined imaging approach to prospectively examine the effects of HIV on brain function and identify biomarkers of risk and progression of cognitive impairment in 240 HIV-positive subjects, which they then compared with findings from 28 HIV-negative control subjects. To be included in the study, HIV patients had to have been on highly active antiretroviral therapy (HAART) for at least 1 year and their nadir CD4 count had to be less than 200 cells/mm^3. Individuals with confounding neurologic, psychiatric, or medical conditions, and those with active illicit drug use were excluded, said Dr. Navia of Tufts University in Boston.

The HIV-positive subjects were classified into three groups: 124 were neurologically asymptomatic, 66 had AIDS dementia complex (ADC) stage 0.5, and 50 had ADC stage 1-3. The median age of the HIV group was 47 years, and the average duration of HIV infection was about 12 years. The median CD4 count was 309 cells/mm^3, the median nadir CD4 count was 34 cells/mm^3, and the median plasma and cerebrospinal fluid (CSF) viral loads were 177 copies/mm^3 and 68 copies/mm^3, respectively.

Neurologic, neuropsychological, and medical assessments were performed at baseline and every 6-8 months, along with plasma and CSF viral load measurement and ADC staging. Also, magnetic resonance imaging and magnetic resonance spectroscopy were used to determine a neuronal biomarker—*N*-acetyl aspartate/creatinine ratio (NAA/Cr)—and two inflammatory markers—the choline/creatinine ratio (Cho/Cr) and the myoinositol/creatinine ratio (MI/Cr)—in the basal ganglia, frontal white matter, and midfrontal cortex.

At baseline, the brains of the HIV-positive patients had increased levels of inflammatory proteins, independent of cognitive status. Compared with subjects in the control group, the HIV-positive patients had increased MI/Cr in all three brain regions and increased Cho/Cr in the midfrontal cortex. Over time, MI/Cr increased significantly in the frontal white matter and the midfrontal cortex, and Cho/CR increased significantly in the midfrontal cortex.

The results suggest that diffuse inflammatory changes can occur in the brains of HAART-treated HIV-infected patients in the absence of neurologic symptoms.

Among HIV-positive patients who had cognitive impairment, NAA/Cr was decreased in the frontal white matter, compared with the controls and the asymptomatic HIV patients. NAA/Cr decreased significantly over time in the frontal white matter and basal ganglia of these symptomatic patients, Dr. Navia reported.

A predictive model incorporating patient demographics and disease-specific variables identified four metabolic patterns of brain injury and ADC stage. Following logistic regression analysis, one of these patterns—basal ganglia with decreased NAA/Cr and increased Cho/Cr—emerged as a significant predictor of ADC stage 1-3. This suggests that the brain injury process in HIV infection may have two stages, with preliminary, diffuse inflammation followed by basal ganglia disease as ADC develops, he said.

The findings suggest that diffuse inflammatory changes can occur in the brains of HAART-treated HIV-infected patients in the absence of neurologic symptoms. Also, decreasing NAA/Cr in the basal ganglia is a critical event in patients with ADC and may provide a biomarker of the extent of changes in the brain, said Dr. Navia who reported no conflicts of interest. ■