Cytokine disruption study sheds light on increased risk for non-Hodgkin’s lymphoma in AIDS patients

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By Barbara Boughton [1]

HIV’s disruption of immune system function may cause the immune system cells themselves to become cancerous, NCI researchers have concluded. If so, this might explain why patients with AIDS are 100 times more likely to be diagnosed with non-Hodgkin’s lymphoma than the general population.

"The fact that AIDS causes cytokine disruption—that it's a condition in which cytokine signaling is recognized to be abnormal—and is also associated with high risk of NHL, made our hypothesis appealing," said lead investigator Charles Rabkin, MD.

Although previous studies have noted elevations in proinflammatory cytokines in AIDS-related NHL patients, this study is the first to analyze a wide range of cytokines. The researchers measured levels of 30 different cytokines in blood and serum samples from their subjects. Blood and serum were obtained from 66 HIV-positive cases, up to two years prior to a diagnosis of NHL. Each of these cases was compared with three HIV-positive lymphoma-free controls matched for age, race, sex, and CD4 count at diagnosis.
Dr. Rabkin’s group found that blood levels of nine different T-helper and proinflammatory cytokines were significantly higher in HIV-infected patients who later developed NHL than in similar controls. The researchers’ analysis indicated that granulocyte-monocyte-stimulating factor (GM-CSF) and interleukins (IL)-12p70 and IL-15 were most predictive of later development of NHL in the HIV-infected patients (AACR 2010 abstract 5746). “We saw a generalized pattern of increases in cytokine levels that could not be appreciated in individual studies of single cytokines,” said Dr. Rabkin, senior investigator at the NCI infections and immunepidemiology branch.

Dr. Rabkin noted that since cytokines work together to generate their effects, excessive cytokine signaling may contribute to lymphoma risk in AIDS. Their study implies that disruption of immune system function by HIV causes the immune system cells themselves to become cancerous. If the findings are confirmed, future research needs to determine whether modifying cytokine levels could prevent lymphoma in HIV-infected individuals, Dr. Rabkin said.

He noted that one of the strengths of the study was the close match investigators were able to obtain between HIV patients who developed NHL and those who did not. A newly improved measurement technique, using fluorescent beads, also made it possible to use smaller volumes of blood to analyze a wide range of cytokine levels more accurately, he added.

Dr. Rabkin acknowledged that the study sample was small, and the cases do not cover the entire spectrum of AIDS. “I think it’s a study that warrants attention and replication, but it’s not definitive,” he said.

The next step for the researchers is to study cytokine levels in a larger number of patients who develop AIDS-related NHL and match them to similar HIV patients who have not been diagnosed with the cancer. They also will look to see if cytokine signaling could be disrupted early on in the HIV infection process. They plan to revisit earlier blood and serum samples from the same patients to identify levels of cytokines.

“We’d like to see if the disruption in cytokine levels happens only close to the time of lymphoma or early on in the course of HIV infection,” Dr. Rabkin said.

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