PML Still a Risk and Often Progressive

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Even though combination antiretroviral (ARV) therapy effectively reduces the risk and severity of many AIDS-related conditions, progressive multifocal leukoencephalopathy (PML) remains a debilitating and deadly disease for many people living with HIV, according to a study published in the September 1 issue of the *Journal of Acquired Immune Deficiency Syndromes*.

PML, caused by the JC virus (JCV), is a rare disease that causes lesions in the brain. In the years before effective ARV therapy became widely available, PML eventually developed in 3 to 7 percent of HIV-positive people and almost always led to a rapid loss of mental and physical functioning and ultimately death. Other than strengthening the immune system through ARV treatment, no therapies have been proved effective at curing PML.

Once combination therapy was introduced in the mid-1990s, the number of new PML cases among people living with HIV dropped substantially. Unlike some other brain-related diseases that are almost wholly prevented when an HIV-positive person's CD4 count is kept above 100 cells, PML can occur at CD4 counts over 100. Moreover, PML can still cause progressive disease and death, even among those using ARV treatment.

To determine the outcomes of PML diagnosis in recent years, Vicenç Falcó, MD, from the Hospital Universitario Vall d'Hebron in Barcelona, and his colleagues examined the medical records of 61 people living with HIV who were diagnosed with PML at one of seven Barcelona hospitals between 2002 and 2006. Most of the patients were men, the average age was 42, and the average CD4 count was 90. Fifteen percent of the patients were diagnosed with PML and HIV simultaneously. Of the 52 cases where the patients were aware of their HIV status before the PML diagnosis, only 40 percent were receiving ARV treatment and the majority of those had a detectable viral load. The majority of the patients were also former or active IV drug users.

During the four-year study period, 33 percent of the patients diagnosed with PML died. About 30 percent were lost to follow-up, meaning that the researchers were unable to determine what happened to them.

Nearly 20 percent of the patients experienced at least some degree of recovery from this formerly incurable disease, and 15 percent had a halt in disease progression. In those who received ARV treatment post-diagnosis with PML, 28 percent were still alive after three years.

Twenty-three percent of the patients developed PML as a result of immune reconstitution

inflammatory syndrome (IRIS). This is when the immune system becomes overly stimulated after ARV therapy is initiated in people with low CD4 counts and can cause some of the symptoms of an underlying disease, in this case PML.

The authors note that though the majority of the patients had a low CD4 count and were not on ARV therapy at PML diagnosis. Sixteen percent did have a CD4 count above 200 at diagnosis, however, and some were on ARV treatment with an undetectable viral load. Dr. Falcó's team states that these factors, combined with the fact that the incidence of new PML diagnoses has remained steady in recent years, lend weight to arguments that ARV treatment should perhaps be initiated even earlier than current guidelines recommend.

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