Natalizumab treatment in patients with MS associated with JC virus infection

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Treatment with natalizumab in patients with multiple sclerosis (MS) appears linked with JC virus (JCV) infection, which can lead to a rare and often fatal demyelinating disease of the central nervous system called progressive multifocal leukoencephalopathy (PML) that destroys the myelin that protects nerve cells. The movement of cells with JC virus into the blood stream may provide researchers with a possible reason why patients with MS develop PML

Since natalizumab was reintroduced as a biologic therapy for MS in 2006, more than 440 cases of PML have been reported. Risk factors associated with development of PML include receiving 24 or more natalizumab infusions, receiving other immunosuppressive treatments and testing positive for JCV antibodies in a blood test.

The authors evaluated 49 patients with MS and 18 healthy volunteers by drawing blood samples and examining CD34+ cells from the bone marrow plus CD19+ and CD3+ cells. Among the 49 MS patients, 26 were beginning natalizumab therapy. For these patients, blood was drawn at baseline and again at approximately three-month intervals to 10 months.. Blood also was drawn on a single occasion from 23 patients with MS receiving natalizumab for more than two years and from the 18 healthy volunteers.

Of the 26 patients beginning natalizumab therapy, 50 percent had detectable JC virus DNA in at least one cell subtype at one or more measures. Among the 23 patients who received natalizumab treatment

for two years, 10 patients (44 percent) had detectable viral DNA in one or more cell subtype, as did three of the 18 healthy volunteers (17 percent). Of the 49 total patients with MS, 15 (31 percent) were confirmed to have JCV in CD34+ cells and 12 of the 49 (24 percent) had it in CD19+ cells.

Authors of the paper Elliot M Frohman, M.D., Ph.D., of the University of Texas Southwestern Medical Center, Dallas, and colleagues wrote: "We detected JCV DNA within the cell compartments of natalizumab-treated MS patients after treatment inception and after 24 months. The JCV DNA may harbor [live] in CD34+ cells in bone marrow that mobilize into the peripheral circulation at high concentrations. Cells with latent infection initiate differentiation to CD19+ cells that favor growth of JCV. Continued studies are needed to further investigate natalizumab treatments as the mechanism of PML."

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