



PIC QUESTION OF THE WEEK: 7/14/08

Q: Please describe PML and its relationship to specific drug therapy.

A: Progressive multifocal leukoencephalopathy (PML) is a rare disease of the central nervous system caused by the typically benign *JC* virus. This virus lies dormant in up to 90% of adults worldwide; however, in immunocompromised patients, reactivation can result in severe disability and possible death. The virus was originally identified in 1971 from the brain tissue of a patient (initials JC) with Hodgkin's disease. PML was considered a very rare condition for several years; however, after initial descriptions of the human immunodeficiency virus (HIV) in the mid-1980s, PML soon became recognized as a common opportunistic infection in AIDS patients. The most frequent presenting features of PML include weakness, altered mental status, visual symptoms, and ataxia. Lesions occur in the white matter of the CNS and are typically bilateral and asymmetrical. PML is commonly observed in immunocompromised patients having hematologic malignancies or HIV/AIDS while drug-related cases are associated with administration of immunosuppressive agents in transplant patients or those with chronic inflammatory diseases. Cases of PML have been reported with fludarabine, tacrolimus, cyclosporine, saquinavir, etanercept, and other immune modifying agents. More frequently, PML has been linked to the administration of mycophenolate mofetil (CellCept) and its active metabolite, mycophenolic acid (Myfortis), as well as rituximab (Rituxan) and natalizumab (Tysabri). The mycophenolic acid derivatives are labeled for prophylaxis of rejection in patients undergoing various organ transplants. The FDA has recently notified health professionals of the increased risk of PML in patients treated with these two agents. Several cases of PML have been attributed to rituximab, a monoclonal antibody approved for use in non-Hodgkin's lymphoma and moderate to severe rheumatoid arthritis. Natalizumab, a monoclonal antibody indicated for moderate to severe Crohn's disease and relapsing forms of multiple sclerosis, was withdrawn from the market in February, 2005 due to development of PML in several patients included in clinical trials. Distribution resumed in February 2006 under restricted access. Patients must meet specific criteria and subsequently be enrolled in the manufacturer's Tysabri Outreach: Unified Commitment to Health (*TOUCH*) program. The drug is only available to registered physicians, pharmacists, and infusion centers. As the use of monoclonal antibodies and immunosuppressive agents continues to expand, health practitioners and patients should be aware of the potential risk of PML and its associated signs and symptoms.

References:

- Koralnik IJ. Progressive multifocal leukoencephalopathy revisited: has the disease outgrown its name? *Ann Neurol* 2006;60:162-73.
- Food and Drug Administration. Medwatch. Mycophenolate mofetil and mycophenolate acid (update). <http://www.fda.gov/medwatch/safety/2008/safety08.htm#mycophenolate>. Accessed July 9, 2008.

Photo by: zenmasterlauren: used under Creative Commons License; <http://www.flickr.com/search/?q=ocean&page=4> (accessed July 8, 2008)

Catherine A. Bourg and Brittney R. March, Pharm.D. Candidates

The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).