

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Progressive Multifocal Leucoencephalopathy

Progressive Multifocal Leucoencephalopathy (PML) is a rare condition, most often presenting in patients with immune suppression. It is caused by activation of the polyomavirus JC (JCV). This virus infects the majority of people in childhood, but remains inactive unless severe immunosuppression occurs. When activated, the virus causes demyelination of the central nervous system.

Almost all cases of PML develop in patients who are immunocompromised, the most common associated condition being Human Immunodeficiency Virus (HIV). Only 230 cases of PML had been reported before 1984. However, at the beginning of the HIV epidemic, the number of cases of PML increased significantly, with 5% of HIV patients developing the condition. Other commonly associated conditions are haematological malignancies and solid organ tumours. PML has also occurred in transplant recipients and in patients taking immunosuppressive medications. There are few case reports of patients developing PML without any of the above conditions.

PML became more commonly recognised after the drug natalizumab was linked to new cases of PML in patients with Crohn's disease and multiple sclerosis. In Australia, patients treated with natalizumab, and prescribers of this medication, must be registered with the Australian monitoring group. For more information on natalizumab, see e-bulletin volume 33(2).

The median survival for patients with PML, who are HIV negative, is 2.6 months. Those with HIV tend to survive longer as highly active antiretroviral therapy (HAART) suppresses the activity of the JC virus.

Patients usually present with weakness, ataxia, altered mental status, and visual disturbances. Confirmation of the diagnosis is by brain biopsy or alternatively, polymerase chain reaction (PCR) detection of JCV DNA.

Treatment of PML in the HIV infected patient involves continuing and optimizing HAART therapy. It is recommended that all immunosuppressive therapies are ceased for any patient who develops PML, as case reports have shown patient recovery after their cessation.

In one study, a short course of cytarabine has been shown to stabilise the JC virus in HIV negative patients, and in vitro it has been shown to decrease JCV replication. In patients with HIV, however, studies have shown no benefit from cytarabine compared with HAART alone.

There are other agents that have been used empirically for the treatment of PML, however few studies have supported their use. Two agents that have shown some promise are topotecan and mirtazapine. In vitro studies have shown the JC virus may infect cells through 5HT_{2a} receptors and mirtazapine may improve the condition by down regulating these receptors. A few case reports have shown improvement with the use of mirtazapine, but further trials are needed to establish its benefit in patients with PML.

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FOR FURTHER INFORMATION CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@health.sa.gov.au
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