



PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Summary

PML is caused by a viral infection in the brain. It may affect 2-6% of HIV-positive people, usually when their CD4+ count is below 100. Symptoms vary, depending on which part of the brain is affected, but may include speech disorders, paralysis of one side of the body, or loss of an area of vision. There is no satisfactory treatment for PML, but combination anti-HIV therapy may help.

What is progressive multifocal leukoencephalopathy?

Progressive multifocal leukoencephalopathy (PML) is a rare and usually fatal viral infection of the brain. Caused by the JC virus (the initials of the first patient from whom the virus was isolated), PML destroys the brain cells (oligodendrocytes) that produce the surrounding protective coating (myelin) of nerve cells.

The JC virus is common; by middle age approximately 80% of adults have been exposed to it. This virus doesn't cause disease in people with healthy immune systems. However, it remains dormant in the kidneys, bone marrow, or lymph nodes for many years. The virus seems to be reactivated in only about 2%-6% of people

living with AIDS, usually in those whose CD4 count is well below 100. Researchers believe that once it is reactivated, the JC virus is carried to the brain by circulating B cells. As the words "progressive" and "multifocal" indicate, PML can progress very quickly and it is not confined to only one part of the brain.

Symptoms

PML causes lesions on the white matter of the brain. The symptoms experienced are directly related to the location and size of the lesions. Lack of coordination of an arm or leg, partial paralysis of one side, partial loss of vision, impairment of thought and speech patterns, memory problems, walking or standing difficulties and dementia are reported in most cases. Not all individuals with PML will necessarily experience the same symptoms or with the same intensity.



Diagnosis

Because the symptoms of PML are similar to those caused by other HIV-related illnesses, such as toxoplasmosis, meningitis, or AIDS dementia complex, it can be difficult to diagnose.

The most accurate way to diagnose PML is by brain biopsy. This involves making an opening in the skull and removing a tiny piece of the lesion on the brain for analysis. Brain biopsies are extremely invasive and because of the risks, both doctors and patients prefer to avoid them if at all possible.

An MRI (magnetic resonance imagery) scan can detect lesions on the brain but it cannot not distinguish whether the lesions are due to PML or to other neurological conditions. Other infections may cause lesions as well, and without a biopsy, the actual infection may not be accurately diagnosed.

A computed tomographic (CT) scan may indicate abnormalities in the myelin of central nervous system (CNS), but it is not as sensitive as an MRI.

PCR technology (similar to measuring HIV viral load) may be used to identify JC virus in cerebrospinal fluid (CSF).

Treatment

At present, there is no specific, satisfactory treatment for PML. However, anti-HIV drugs seem to be useful in controlling PML. Since the introduction of triple combination therapy, there have been a few published reports of individual patients being given combination antiretroviral therapy when diagnosed with PML. Symptoms have improved, and in some patients, brain scans have shown improved results. For the treatment to be “highly active,” though, all drugs should be new to the patient.

At the 1997 ICAAC conference, Albrecht and colleagues reviewed medical charts of 29 people diagnosed with PML between 1988 and 1996. The researchers were confident in their diagnosis of PML which was made on the basis of symptoms, CT or MRI scans

(radiology), and either brain biopsies (histology) or PCR technology used to confirm the presence of JC virus in the cerebrospinal fluid.

The 29 patients (25 male, 4 female) had a median CD4 count of 40 at the time of their PML diagnosis (average CD4 count was 106 cells). The researchers reviewed the median survival times and noted that:

1. the 14 patients who had never used antiretrovirals or who had stopped their drugs when diagnosed with PML survived a median of 127 days;
2. the 10 patients who continued on double nucleoside treatment survived a median of 123 days;
3. the 5 patients who started HAART on or around the time of diagnosis survived for a median of over 500 days.

Cidofovir

In another study presented at the 1997 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), Brosgart and colleagues reported using intravenous cidofovir, a drug usually used to treat CMV retinitis, to treat 2 men with PML. Both patients had been diagnosed with PML which had progressed rapidly, leaving both of them unable to walk within a month of their diagnosis. Combination anti-HIV treatment had been started by Patient A 4 months before the PML diagnosis and 5 months before diagnosis by Patient B. After 2 months of treatment with cidofovir (5 mg/kg weekly for 2 weeks, followed by the same amount of drug every two weeks), both patients were able to walk and to live independently. Both patients' MRI scans showed improvement of the brain lesions. As well, both patients were clinically stable 7 and 9 months after their PML diagnosis.

At the 1998 World AIDS conference, Al-Shahi and colleagues reported using cidofovir to treat 6 patients with PML. All of the patients had been using HAART, and half of them had viral load measures below 500 copies/ml when PML was diagnosed. All 6 patients showed



improvement in their symptoms with zidovudine treatment. Three of the patients had MRI scans repeated after starting zidovudine with 2 showing improvement in the brain lesions.

Credits

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Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

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