Brain Drain

For those with nasty neurologic infection PML, the news is hope.

February 1, 1999 By Stephen LeBlanc

My left arm would get heavy while driving, and I'd drift out of my lane," Ray Perry says, recalling his first serious complication in 17 years living with HIV. "Simple things, like holding a bowl, quickly tired my left hand and wrist. My doctor checked this and that, but found nothing. But it just got worse and then hit my left leg." That was in April '97. The former trucker had been on a protease cocktail for four months and was feeling good for the first time in a while. Now Perry was worries

So he returned to his doctor and insisted on more tests. Although a viral test of spinal fluid was inconclusive, an MRI brain scan bore bad news: lesions. "My doctor told me, 'We think it's PML, but can't be sure without a brain biopsy,'" Perry says. When his results came back, his doctor told Perry he had PML, it was untreatable, and he had one to four months to live.

But Perry had other plans. "I remember thinking, 'That's crap. I don't accept this death sentence,'" he recalls.

PML -- its appropriately intimidating full name is progressive multifocal leukoencephalopathy -- is one of the nastiest critters in the AIDS menagerie. This opportunistic infection is caused by a widespread microbe -- the JC virus (named for the first patient in whom it was found) -- that results in disease only in those chronically immunosuppressed, most commonly when CD4-cell counts fall below 50. Studies of clinical diagnoses indicate that PML occurs in 2 percent to 7 percent of all PWAs, but autopsy reviews reveal higher numbers, suggesting PML is underdiagnosed. The disease can cause a host of mental-function and movement problems, which can progress to paralysis, coma and death. For years, the threat of PML has terrified PWAs, offering the spectre of losing both one's mind and one's ability to function. But now community pressure and PWA experimentation have combined with scientific inquisitiveness to produce real hope for the possibility of several effective treatments.

PML is very tough to diagnose. Symptoms may or may not include weaknesses in one side of the body; difficulty with eyesight, including a blind spot; and a possible lack of coordination; as well as other physical or mental signs. The infection damages white matter -- nerve tissue in the brain and spinal cord -- resulting in lesions that can be read on a noninvasive MRI scan. But Dawn McGuire, MD, a San Francisco neurologist and nationally recognized PML expert, explains: "Doctors often miss PML, or call brain lesions PML when they are not. Herpes zoster, CMV and lymphoma can all imitate PML on scans and in symptoms, but they differ in treatment." Other treatable conditions

that can mimic PML symptoms -- and thus risk misdiagnosis -- include toxoplasmosis, stroke, brain tumor, mental illness, HIV brain infection, or severe vitamin B-12 deficiency (which *POZ* Science Editor Lark Lands notes may not always be reflected on often-inaccurate standard blood tests for B-12 levels). Multiple infections can also be present.

McGuire recalls two patients referred to her by experienced AIDS doctors who made PML diagnoses based on MRI scans. After running a brain biopsy on one patient, she found that his lesions were from herpes zoster, treatable with acyclovir. “We had to fight the second patient’s HMO to get them to pay for a brain biopsy,” McGuire says. “It turned out the man had treatable lymphoma, not PML. Patients have a right to get a definitive -- and quick -- diagnosis when therapies are available.” (See “How to Tell It’s PML” for a list of recommended diagnostic procedures.)

While PML can be a killer even when aggressively treated -- its most famous victim is MTV star Pedro Zamora -- some advocates charge that physicians too often simply give up when PML is diagnosed or even suspected, letting their patients die without a fight. Activist Peter Brosnan, a Hollywood-based documentary filmmaker (profiled in *POZ,* February-March 1996), has been on a mission to collect and publish case studies of successful PML treatments ever since his brother-in-law died of the disease more than 10 years ago. “I still get calls from people whose doctors say, ’There’s no treatment for PML’ and ’PML is always fatal,’” reports Brosnan. “That’s tragic -- and it’s not true.”

Just ask Ray Perry. Though Perry had never touched a computer, his diagnosis spurred him to get on the Internet at his local library. He found the names of several PML researchers and called them. After many dead ends, he learned about a clinical trial of topotecan (Hycamtim), an approved chemotherapy shown in test-tube studies to inhibit JC virus, with a study site in San Francisco. “By then my left side was paralyzed. I couldn’t walk, and I was in a wheelchair,” Perry recalls. “But I flew down and started getting infusions.”

Topotecan, marketed by SmithKline Beecham for ovarian cancer, interferes with DNA replication, the process by which both cancer cells and viruses reproduce. But blocking cell proliferation can produce dangerous neutropenia (white blood cell depletion) and anemia (red blood cell depletion), so frequent monitoring is essential and caution advisable when combining topotecan with other bone-marrow-suppressive drugs. It can also cause nausea, vomiting and diarrhea.

Perry, who began treatment in July 1997, experienced serious side effects -- but also dramatic benefits. “After one three-week infusion, there was an immediate improvement,” he says. “By the second round, the drug had suppressed my bone marrow so much that we delayed the infusions for two weeks.” Perry ultimately did three courses of topotecan, requiring 10 blood transfusions. “Last February, my MRI showed the lesions to be completely gone,” he reports. “By September, I was able to drive my stick-shift pickup truck from Oregon to San Francisco and walk through a street fair.”

While Perry and his doctor both believe the topotecan aided his recovery, the drug’s manufacturer

-- which acquiesced to the tiny PML trial in 1997 only after activist pressure -- isn't ready to claim any successes. SmithKline Beecham spokesperson Sharyn Arnold explains, "It is a difficult study because it is hard to know whether any benefit is due to topotecan or to the anti-HIV drugs" also taken by participants. The other two patients given topotecan in the San Francisco site had very advanced PML when they began treatment. Both died after their first infusions.

In fact, there are several potential treatment strategies available to people with PML. Experts widely agree that as soon as any PML-type symptoms appear, the first step is to initiate or maximize anti-HIV therapy, aiming to restore immune function and prevent PML progression. While some studies show that a standard regimen can make a key difference, another report suggests that such a combo *by itself* may not always work fast enough. This leads some neurologists to recommend considering stronger-than-standard HAART regimens. Because neurological symptoms may have multiple causes -- one of which is often HIV in the brain -- other clinicians suggest including at least one antiretroviral known to cross the blood-brain barrier. Studies have found nevirapine (Viramune) and AZT to be the most potent brain-penetrating agents (see "Nevirapine for Best Head," *POZ,* December 1998).

Another drug being studied for PML is cidofovir, a drug produced by Gilead and approved by the FDA in 1996 for cytomegalovirus (CMV) retinitis. This compound has been found to have test-tube activity against JC-like viruses. Case reports of the off-label (unapproved) use of the drug for PML, published last year, documented some improvement in 11 of 22 patients observed. But Gilead warns that cidofovir can be highly toxic to the kidneys and, to protect them, must be used with the drug probenecid and adequate IV hydration. Cidofovir can also cause toxicities to the eyes and other organs. Two PML clinical trials are under way.

Still another approach is a higher-than-usual dose of acyclovir (Zovirax), an approved antiherpes agent. Brosnan cites numerous anecdotal reports of people diagnosed with PML who noted improvement after taking 2,000 to 4,000 milligrams of acyclovir per day. However, the PML diagnosis was often not confirmed by JC viral load or biopsy, so it's possible these patients were infected or co-infected with herpes zoster.

Peptide T, a decade-old experimental AIDS drug, has had mixed results -- although virtually no toxicity -- in trials for various neurological and cognitive disorders. Test-tube studies show that it blocks JC replication, and numerous PWAs diagnosed with PML have reported dramatic improvements using the drug as either high-dose nasal spray (available through the PWA Health Group in New York City) or continuous infusions (see "PML Is for Heroes"). A multisite PML trial of infused peptide T will begin later this year.

One PML treatment option formerly in use -- the highly toxic nucleoside drug ARA-C -- was abandoned by clinicians in 1997 after a study found it did not improve survival.

While PML remains an untamed killer, Brosnan says that increasing numbers of PWAs are fighting back and winning. For now, a prudent strategy would include immediate use of all needed diagnostic procedures, maximization of anti-HIV therapy and evaluation of all possible PML

treatments. Brosnan adds, “I’ve gotten numerous reports of people who’ve benefited from immediately starting low-toxicity but unproven treatments such as peptide T or high-dose acyclovir, even while waiting for their doctors to diagnose them and decide on other treatments.”

Perry urges PWAs and AIDS docs to learn about PML and address it quickly. “God forbid that anyone else should have their doctor misdiagnose them for two months, then tell them to go home and pick out a casket,” he says.

PML IS FOR HEROS

Greg Corbin lives to tell the tale

Two years ago, the doctor treating Greg Corbin for PML made him promise he would stop smoking by age 50. Corbin, who has been outsmarting people since he was a pudgy gay kid with glasses in rural Rhode Island, figured his seemingly terminal condition made it a safe bet. Now at 38, after what he calls “a health-restoring regimen of peptide T and determination,” Corbin worries that this time he’s outsmarted himself.

He couldn’t have envisioned such a predicament in late 1995, when the first, subtle signs of PML appeared. Soon he was having trouble walking. Yet it wasn’t until January 1996 that Corbin -- as sick of doctors as he was of AIDS after a decade of both -- submitted to a spinal tap. When the test for the JC virus came back positive, Corbin recalls his doctor saying, “You better put your affairs in order -- quickly.”

As the PML short-circuited his nervous system and robbed him of clear vision and mobility, Corbin waited in his Boston bed to die. It was at Corbin’s lowest point, in Spring 1996, that his brother read in *POZ* about Peter Brosnan’s comprehensive report on PML treatments. After contacting Brosnan and learning of several PWAs’ success with an experimental treatment called peptide T, he ordered a bottle from a San Francisco buyers club. Corbin took his first dose on April 7, 1996.

The date marked his “first step out of PML hell.” Three days after starting the intranasal spray, his vision was corrected. By April 20, he was able to transfer himself to a wheelchair. Then he switched to a walker, and in May 1997, a cane. The wheelchair is now locked in the closet -- “where it belongs,” he says.

Corbin has come out of the closet as a PML survivor with a webpage, “Greg’s Ascent” (www.skepsis.com/~gregc). “There can’t be more than a handful of us alive with this,” he says to explain why a confirmed homebody like Corbin is sacrificing his privacy to get his story out. “When you’re a trailblazer, it’s nice to know that others can take the path you made.”

He shares his life with his 11-year-old cat, Hug (“I didn’t name him”), and his AIDS Action buddy, Fred, 56, who provides conversation and cribbage. “There’s a large gap of gay men in their 40s and 50s who are missing, ” says Corbin. “Fred and I can talk about things.”

A few days after our talk, Corbin calls to make sure our story mentions Kate Katz, a 73-year-old

who drives him to Friday chiropractor appointments. It’s not a request, but a reminder that Corbin is now in charge. “I control my future, not some initials,” he says. Make a note of it.

BRAIN DRAIN

The devil’s in the details

If PML is suspected, other possibilities have been carefully excluded, and treatment is desired, what’s next? PML expert Sidney Houff, MD, PhD, chief of the Neurology Service at the Veterans Affairs Medical Center in Washington, DC, recommends the following diagnostic steps:

1. Immediately get an MRI brain scan -- it’s more sensitive and may reveal more lesions than would a CT scan.

2. If characteristic white-matter lesions are seen, a brain biopsy should be seriously considered to confirm the diagnosis -- but only at an institution experienced with the procedure. One of two methods for detecting the JC virus must be used:

- The virus’ genetic material can be easily identified via what’s called in situ hybridization using a JCV DNA probe, an extremely sensitive and specific test.
- JC antibodies can be applied to the brain tissue to prove the virus is present.

While less than 7 percent of biopsies result in serious complications (under 1 percent at experienced centers), discuss with the surgeon the possibilities for harm.

Although some clinicians suggest that PCR testing of cerebrospinal fluid (CSF) might substitute for brain biopsy in confirming PML, NIH researchers have found that only 80 percent of people with biopsy-confirmed PML have JC virus in the CSF, and that a small percentage with other neurological conditions do have JC virus in the CSF. So, using CSF as a primary diagnostic tool may lead to a misdiagnosis, making a brain biopsy best.

© 2026 Smart + Strong All Rights Reserved.

http://beta.docker.poz.com/article/Brain-Drain-1462-4100