HIV and the brain—then and now

In the late 1970s doctors in North America and Western Europe began to see cases of young adults (mostly men) who sought care because of a recent history of at least the following persistent symptoms:

- swollen lymph nodes
- prolonged fatigue
- night sweats
- swollen liver and/or spleen

What puzzled doctors is that these young adults had been previously healthy and there was no obvious reason for the onset of their symptoms.

Subsequently, over the course of months or several years, the doctors found that their patients would develop more symptoms, including the following:

- unintentional and persistent weight loss
- diarrhea
- recurring herpes infections

By 1981 doctors began to see more serious symptoms in these patients, such as life-threatening infections and cancers—and so the AIDS epidemic was first recognized.

These life-threatening infections and cancers arose because of extraordinarily weakened immune systems. Trying to diagnose, treat and save infected patients became the focus of doctors who were immersed in the epidemic.

The brain

As early as 1982, neurologists reported strange symptoms in some patients that underscored the involvement of the brain with this emerging syndrome. These symptoms were not caused by any of the typical life-threatening infections that signified AIDS and could include the development of one or more of the following:

- forgetfulness
- difficulty concentrating
- slowness of thought
- changes in personality
- difficulty maintaining balance
- poor control of and weakened leg muscles
- loss of interest in everyday activities

The role of HIV

The underlying reasons for these problems involving the brain was later pinned on HIV. This virus does not infect key brain cells called neurons. However, HIV does infect cells of the immune system that travel to and sometimes reside in the brain, including T-cells, monocytes and macrophages.

Inside the brain, these infected cells of the immune system release HIV-associated proteins and chemical signals that incite inflammation. The result is that brain cells become dysfunctional and in some cases die.

HIV also infects accessory cells in the brain called astrocytes, which play a role supporting the health of neurons.
HIV-related brain issues today

In high-income countries, the widespread availability of potent combination anti-HIV therapy (commonly called ART or HAART) has made cases of severe HIV-related brain injury—commonly called dementia—uncommon among people who are engaged in their care and treatment. Indeed researchers estimate that today only about 2% of HIV-positive people will develop dementia.

Instead of dementia, researchers are now finding milder forms of HIV-related brain injury. These milder cases, particularly if they are initially symptom free, are often subtle and discovered only through complex and time-consuming neuropsychological assessments.

Today, scientists who study the brain have divided HIV-related brain injury into three categories, as follows:

- **asymptomatic neurocognitive impairment** (symptom-free neurocognitive impairment) – In such cases, testing detects subtle or mild degradation or decline in memory and thinking processes not seen in people of the same age and who have similar levels of education. This decline is not sufficiently serious to affect a person’s ability to engage in everyday activities.
- **mild neurocognitive disorder** (MND) – Testing detects at least a modest decline in memory and thinking processes. This decline is below what would be seen in healthy people of the same age and educational level. In cases of MND, the ability to carry out everyday activities is affected.
- **HIV-related dementia** – Testing reveals a severe decline in clear thinking and memory and a moderate-to-severe decrease in the ability to carry out activities of everyday living.

All three categories now make up what researchers call HAND—HIV-associated neurological disorder. Overall, neuroscientists estimate that between 50% and 60% of HIV-positive people have some degree of HAND.

An important note

Readers should note that everyone, regardless of HIV status, can have episodes of forgetfulness from time to time. However, cases of persistent problems with memory and thinking clearly need to be reported to doctors so that they can be investigated and their underlying causes can be revealed.

In this *Treatment Update*, we review several key studies of emerging issues associated with HIV and the brain.

—Sean R. Hosein

REFERENCES:

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