Indications of a New Virus in MS Patients

Some multiple sclerosis patients show signs of infection by a potential new relative of HTLV-I; it may—or may not—be causally related to the disease

Multiple sclerosis is an incurable and often debilitating neurological disease that afflicts some 250,000 persons in the United States alone. Over the years attempts to pin down the cause or causes of the disease have proved highly frustrating. A variety of evidence suggests that a virus may be involved and numerous candidates, among them measles, parainfluenza, and canine distemper viruses, have been proposed. However, investigators have never been able to prove definitively that any of them actually causes multiple sclerosis.

Now a group of investigators, including Hilary Koprowski of the Wistar Institute and Robert Gallo of the National Cancer Institute (NCI), has detected in some multiple sclerosis patients traces of what may be a new viral relative of the human leukemia virus called HTLV-I (human T-cell lymphotropic virus-I).* Many uncertainties still surround the meaning of this finding. First and foremost, as Gallo himself points out, the existence of the putative virus remains to be established. So far it has not been isolated.

Then, if the virus does prove to be real, much additional work will be required to determine whether it has anything to do with the etiology of multiple sclerosis. "It is important to remember that none of us now considers that this is the cause of multiple sclerosis or is diagnostic for multiple sclerosis," Koprowski stresses. Nevertheless, identification of a new HTLV in multiple sclerosis patients could at least expand the scope of that viral family and perhaps also provide clues to the origins of a disease for which such clues are badly needed. The current work might produce a new lead by linking a previously undiscovered virus to multiple sclerosis, Gallo notes. The other suspected agents have all been common, well-known viruses.

The first hint that individuals with multiple sclerosis might harbor an HTLV-I-like virus came from Elaine DeFreitas of the Koprowski group. Although viruses have been implicated as contributing to the development of multiple sclerosis, the direct cause of the nerve cell damage appears to be an abnormal immune attack, which may (or may not) have been triggered by a viral infection. The cerebrospinal fluid of the patients contains increased numbers of immune cells, including the helper T cells which are the prime targets of the HTLV's. Ordinarily T cells do not divide in culture, but DeFreitas found that those from the cerebrospinal fluid of some multiple sclerosis patients could divide indefinitely. In fact, the characteristics of the cells bore a striking resemblance to T cells infected by HTLV-I.

In collaboration with the Gallo group, the Wistar workers then found that blood and cerebrospinal fluid from multiple sclerosis patients from Sweden and Key West, both areas of high risk for the disease, often contain antibodies that react with proteins from HTLV-I, -II, or -III. A few patients with other neurological diseases also have the antibodies, but samples from normal individuals either do not have them or have them in much lower concentrations.

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The results could mean that the multiple sclerosis patients had been infected with an HTLV relative, but the evidence is not clear-cut. Only about 60 percent of the 52 patients tested had the antibodies, which were not present continuously. Consequently, the antibody test cannot be used diagnostically. Moreover, Stephen Rheingold of the National Multiple Sclerosis Society points out that high antibody concentrations in multiple sclerosis patients may simply be a reflection of their autoimmunity.

Results obtained by Mary Harper of the NCI group provide stronger evidence that multiple sclerosis patients might be infected by an HTLV-related virus. She has found indications that T cells from the patients' cerebrospinal fluid are expressing genes of a virus that shows some similarity, but is definitely not identical, to HTLV-I. Signs of the viral gene expression could be detected in cells from four of eight patients but not in cells from two healthy persons.

Harper did not detect any traces in the T cells of viral material related to HTLV-III, which causes acquired immune deficiency syndrome (AIDS). Multiple sclerosis patients thus have no reason to fear that they have an increased risk of developing that disease. The structure of the genome of HTLV-III, which is also called lymphadenopathy/AIDS virus (LAV), differs substantially from that of HTLV-I.

The investigators want to isolate the postulated HTLV-I relative as the next step toward pursuing its possible involvement in multiple sclerosis, but have so far been unsuccessful. "What I don't like is that there is no assurance of an appropriate follow-up because there is no virus in hand," Gallo says. The NCI workers are intensifying their efforts to isolate the virus, while also trying to clone and determine the nucleotide sequence of the HTLV-I-related genes. The cloning will allow them to determine whether what they have identified has the necessary characteristics of a human retrovirus. If they do not find definitive proof of a retrovirus, the work could reach a dead end.

But if the cloning or virus isolation succeeds, then the investigators will have a specific probe to use for further studies. They could determine, for example, whether the brains of multiple sclerosis victims carry the virus, although even this would not necessarily prove that it helps to cause the disease.

Nevertheless, there are precedents for suggesting that the HTLV's might produce neurological diseases. HTLV-III not only infects and destroys helper T cells, thereby causing the severe immune deficiency of AIDS, but can also be found in the brain, where its presence has been linked to dementia and other neurological problems. In addition, Guy de Thé of the Faculté de Médicine Alexis Carrel in Lyon, France, and his colleagues have linked HTLV-I itself to tropical spastic paraparesis, a paralytic disease of unknown cause. Rheingold says of the current results with multiple sclerosis, "It's a potentially interesting finding if only it can be confirmed and amplified." —**JEAN L. MARX**

*H. Koprowski *et al.*, *Nature (London)* **318**, 154 (1985).