



Parallels between central and peripheral neurological manifestations of HIV infection

Gérard Said

Hôpital de Bicêtre, Le Kremlin Bicêtre, Paris, France

Both the central and the peripheral nervous systems are involved in a number of ways in the course of the HIV infection. At early stages of the disease, the virus seems to penetrate the nervous system without inducing clinical manifestations in most cases. In a small proportion of patients however, early invasion of the nervous central and/or peripheral system can lead to severe, usually self limited, neurological manifestations, with a more or less complete recovery. These early manifestations are occasionally observed in association with an acute infectious mononucleosis-like illness, together with headache and myalgias, as manifestations of seroconversion to HIV. Inaugural and presenting manifestations of HIV infection may thus include acute encephalopathy with headache, photophobia, confusion, fever, myalgias, seizures, meningoencephalitis and cognitive deficit persisting during a few weeks. During this period, or later in the course of HIV infection, but usually in patients with a normal or near normal CD4 T cell count, a Guillain-Barré syndrome with mild to severe motor deficit, facial diplegia, areflexia, and distal sensory symptoms can develop within a few days. CSF analysis frequently reveals a mononuclear pleocytosis. Oligoclonal bands and intrathecal synthesis of antibodies to HIV and viral antigens have been demonstrated in such cases. Central and peripheral manifestations are associated in some patients. Early manifestations of HIV infection usually carry a good prognosis and the patient recovers spontaneously.

The pathogenesis of early manifestations is not fully understood. An immune mediated mechanism triggered by penetration of the virus and a strong response of the host is likely to play a major role, since the lesions found in the PNS of such patients are similar to those of classical Guillain-Barré syndrome, a characterised immune mediated polyneuropathy.

After the early manifestations, symptomatic involvement of the central nervous system is uncommon until the onset of immunosuppression, but peripheral neuropathy, especially multifocal inflammatory, axonal and demyelinating, occurs, often associated with different patterns of vasculitis, which may also play a role in alteration of the CNS.

In patients with a low CD4 T cell count, the pattern and prognosis of neurological manifestations is different from the early ones. Many of the

neurological manifestations are related to opportunistic infection or to development of lymphomas, and the prognosis of the neurological manifestations specifically related to the HIV is poor. Interestingly, peripheral neuropathy is virtually unknown in HIV positive children, while CNS involvement is very common.

In the CNS, the opportunistic infections are dominated by *T. gondii* infection, the prevalence of which has been decreased by prophylaxis of patients seropositive for the toxoplasmosis. Any tissue previously infected, but above all, brain, skeletal and heart muscle cells may harbor these cysts allowing reactivation in the context of an impaired cell-mediated immunity with the unwelcome release of invasive tachyzoites. This is not the case for the PNS which does not harbor cysts.

The JC Papova virus, is responsible for progressive multifocal leukoencephalopathy, a disorder of the cerebral white matter subsequent to infection of oligodendrocytes by the Papova virus. The JC virus has been identified in oligodendrocytes and in a few astrocytes, but not in neurones, macrophages or endothelial cells, which accounts for its absence from the PNS. Conversely, cytomegalovirus infection, the most common viral opportunistic infection in immunodepressed HIV patients, can affect both the central and the peripheral nervous system, because the CMV predominantly infects the endothelial cells, which are ubiquitous. The prognosis of treated CMV polyneuropathy, especially in its mononeuritis multiplex pattern, carries a much better prognosis than CMV encephalitis. Central nervous system involvement by malignant lymphomas is common at end stages of HIV infection and occasionally affect the spinal roots.

The role of the HIV itself in deterioration of patients late in the course of the disease is increasing because of the longer survival of these patients mainly due to a better control of opportunistic infections. The onset of mental deterioration is usually insidious with fluctuation of symptoms or relapsing encephalitis in some patients. Patients develop difficulty in writing and reading, with temporo-spatial disorientation, slowing of rapid movements, moderate weakness of the lower limbs and gait ataxia. Tendon reflexes are usually brisk, often with Babinski's sign. Cognitive, behavioural and motor disorders evolve gradually, but fluctuate.

tions and transient, spontaneous, improvement may occur. The HIV-ADC usually evolves as a subcortical subacute encephalitis. The clinical presentation of HIV encephalitis offers some variations, including involuntary hyperkinetic movements. Cerebral atrophy with neuronal loss is commonly found at autopsy in these patients, together with signs of opportunistic infection. Relapsing multiple sclerosis-like illness occurs. It can be paralleled to relapsing demyelinating polyneuropathy, which both predominantly affect the white matter, of the central and peripheral nervous system, respectively.

The late onset distal symmetrical predominantly sensory polyneuropathy is a common and disabling manifestation. It is characterised by a more or less rapidly progressive painful, distal, axonal neuropathy. The reason why the neurons often degenerate in patients with AIDS is not clearly related to the presence of the virus in these cells. The pathogenesis of the lesions of the CNS underlying the AIDS dementia complex, including HIV myelopathy, as well as those of the late onset distal symmetrical predominantly sensory polyneuropathy, are not well understood and deserve further studies.