Neurological complications of HIV

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Abstract

HIV is a treatable condition and the physician should be alert to its varied neurological manifestations at all stages of the disease. Seroconversion can be associated with Guillain–Barré syndrome with characteristic cerebrospinal fluid changes. Tuberculosis can present at any CD4 count. Advanced HIV is associated with a variety of opportunistic infections, including progressive multifocal leukoencephalopathy, cerebral toxoplasmosis and cryptococcal meningitis, as well as primary central nervous system lymphoma associated with Epstein–Barr virus. HIV is neurotropic and causes a neurocognitive disorder as well as vacuolar myelopathy. Most neurological complications can respond favourably to highly active antiretroviral therapy. Treatment itself can be associated with neurological complications, particularly neuropathy, and, due to alterations in lipid metabolism, cerebrovascular disease. With increasing long-term survival, the prevalence of vascular disease and dementia may increase.

Keywords cryptococcal meningitis; dementia; highly active antiretroviral therapy; HIV; neurology; peripheral neuropathy; progressive multifocal leukoencephalopathy; toxoplasmosis

HIV is neurotropic; virus may be isolated from cerebrospinal fluid (CSF), brain, spinal cord and peripheral nerves. The introduction of highly active antiretroviral therapy (HAART) has reduced the incidence of all major AIDS-defining neurological diagnoses and markedly improved their prognosis. However, neurological complications occur commonly at all stages and may be the first presentation of HIV infection. Table 1 shows the range of neurological presentations in which HIV testing is indicated.

Seroconversion

Neurological features, particularly Guillain–Barré syndrome (GBS), may be present in addition to the more common symptoms of fever, rash, lymphadenopathy and pharyngitis (Table 1).[1] Typical GBS with an unexpected CSF pleocytosis should always trigger HIV testing.

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What's new?

- Immune reconstitution with HAART has both dramatically reduced the incidence of AIDS-defining neurological diagnoses and improved subsequent survival
- Drugs such as d4T, and DDI are now rarely used as newer, less neurotoxic alternatives are available
- The prevalence of HAND remains unchanged despite HAART
- PML can complicate monoclonal antibody therapy in a variety of non-HIV-related conditions. Research into specific anti-JCV therapies is ongoing

Neurological complications which may occur at all stages of disease

GBS may also occur during the asymptomatic phase of established infection; autoimmune demyelinating neuropathy, mononeuritis multiplex and HIV-associated headache may also present during this phase. Reactivation of latent tuberculosis is common in HIV infection with an increased risk of extra-pulmonary manifestations such as tuberculous meningitis or cerebral tuberculoma.

CSF abnormalities are found at all stages of HIV infection and include a mild lymphocytic pleocytosis, elevated protein and oligoclonal bands.

HIV-infected individuals have an increased risk of venous thrombo-embolism and stroke, and this may be further increased by protease inhibitor antiretroviral drugs.[2] Mechanisms of stroke in HIV are variable and include vasculitis, hypercoagulabilty (including acquired protein S deficiency and anticardiolipin antibodies)[3] and abnormalities in lipid metabolism in patients on therapy.

AIDS-defining neurological conditions

All AIDS-defining neurological complications tend to occur at low CD4 counts (<200/ml).

Toxoplasmosis

Reactivation of *Toxoplasma gondii* causes focal intracerebral disease in the context of advanced immunosuppression.

Clinical features include headache, seizures, focal weakness, cranial nerve palsies, dysphasia and ataxia. Confusion is followed by decreasing level of consciousness, progressing to coma if untreated.

Diagnosis is usually made on the characteristic findings on a contrast-enhanced MRI or CT scan (Figure 1), with polymerase chain reaction (PCR) for *Toxoplasma* in CSF if lumbar puncture (LP) is possible (Table 2).

Management: an empirical trial of treatment with sulfadiazine and pyrimethamine is usually instigated in patients with focal

Neurological presentations of adult HIV infection

AIDS-defining conditions	Other conditions in which HIV testing is indicated
Cerebral toxoplasmosis	Aseptic meningitis/encephalitis
Primary cerebral lymphoma	Cerebral abscess
Cryptococcal meningitis	Space-occupying lesion of unknown cause
Progressive multifocal leukoencepalopathy	Guillain–Barré syndrome
Tuberculosis*	Peripheral neuropathy
Cytomegalovirus infection	Dementia
	Myopathy*
	Myelopathy*
	Leukoencephalopathy
	Neurological symptoms associated with primary HIV infection:*
	• ataxia
	• acute disseminated encephalomyelitis
	• cranial neuropathy
	• peripheral neuropathy
	• transverse myelitis
	• polymyositis
	• brachial neuritis
	• cauda equina syndrome
	Unexplained stroke, especially in patients aged under 50 years*

Adapted from UK National Guidelines for HIV Testing 2008. British HIV Association, additions* by authors.

Table 1

cerebral lesions. Second-line combinations include clindamycin/pyrimethamine or clarithromycin/pyrimethamine. Anticonvulsants and, in severe cases, corticosteroids may be required. Response to therapy is monitored by serial brain scans until complete resolution of the lesions. Non-response should prompt consideration of alternative diagnoses, which may require brain biopsy. Treatment should be continued indefinitely or until the patient's CD4 count increases with HAART.

Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencepalopathy (PML) results from reactivation of JC virus (JCV). PML was a medical rarity before the onset of the HIV epidemic but has been recently recognized as a complication of immunologically active monoclonal antibody therapies, including natalizumab, infliximab, efalizumab and rituximab.

Clinical features: PML has an insidious onset which may include personality change, motor and visual field defects, dysphasia and ataxia.

Diagnosis is supported by the characteristic MRI appearance (Figure 2) and the demonstration of JCV by PCR in CSF.

Management: PML was invariably fatal before the availability of HAART. Immune reconstitution with HAART has improved the prognosis with survival rates of 25% at 36 months.[4] Neurological deficits usually remain stable. Currently, no other therapies are proven to be effective against JCV.[5]

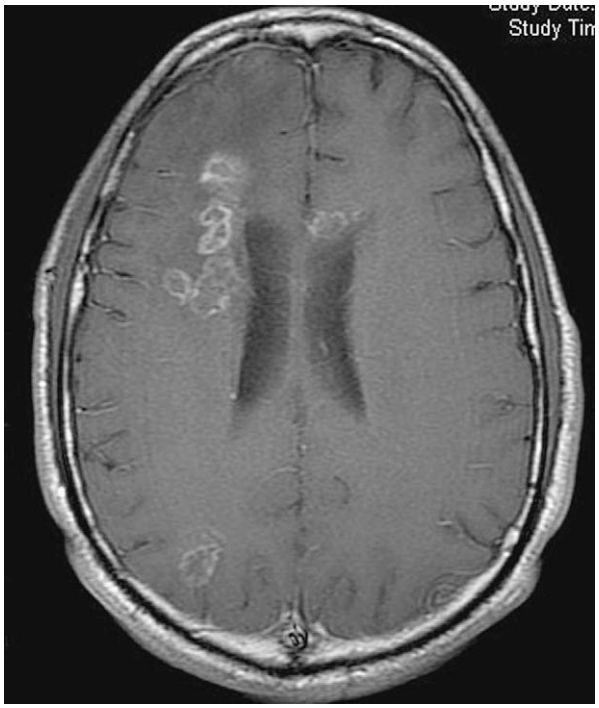

Figure 1 Toxoplasmosis. T1-weighted MRI following gadolinium-DTPA showing multiple ring-enhancing lesions.