



not apparent on CT. Management includes initiation of empirical therapy with pyrimethamine, sulfadiazine, and folinic acid. Brain biopsy should be reserved for patients with neurologic deterioration, those with no serum antibodies to *T. gondii* who have neuroimaging findings atypical for toxoplasmosis, those with discordant results between PCR of the CSF for EBV and thallium-enhanced single-photon emission computed tomography (SPECT) scans, and those whose lesions do not respond after 10 to 14 days of antiprotozoal treatment. After the initial response, patients must remain on chronic suppressive therapy until a sustained rise in CD4 count ( $>200$  cells/mm<sup>3</sup>) is achieved with effective ART.

Primary CNS lymphoma complicates advanced HIV infection in 3% to 6% of cases and is almost invariably associated with detectable EBV DNA in the CSF. Lesions may be single or multiple and are often weakly ring enhancing. Irradiation often provides remission, which may be sustained as immune function is restored by effective ART.

PML is a demyelinating disease caused by a papovavirus (JC virus). Presenting signs and symptoms may include progressive dementia, visual impairment, seizures, and hemiparesis. MRI usually shows multiple lesions predominantly involving the white matter. These lesions are usually less visible on CT than on MRI and are not ring enhancing, helping to distinguish PML from other mass lesions of the CNS. There is no effective specific treatment for PML; the disease often, but not always, regresses in response to effective ART.

 For a deeper discussion of these topics, please see Chapter 394, "Neurologic Complications of Human Immunodeficiency Virus Infection," in Goldman-Cecil Medicine, 25th Edition.

### Central Nervous System Diseases without Prominent Focal Signs

Evaluation of the HIV-infected patient with fever and headache is difficult because of the often subtle manifestations of serious CNS lesions in immunocompromised patients. Management of bacterial meningitis is the same as for non-immunocompromised patients. Meningeal diseases in HIV-infected patients often fall into the broad categories of aseptic meningitis, chronic meningitis, and meningoencephalitis.

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#### Aseptic Meningitis

Patients with aseptic meningitis, which can be a manifestation of the acute retroviral syndrome, complain most often of headache. Their sensorium is generally intact, and findings on neurologic examination are normal. In the individual with established HIV infection, aseptic meningitis may result from several potentially treatable causes.

#### Chronic Meningitis

Patients with chronic meningitis characteristically have headache, fever, difficulty in concentrating, or changes in sensorium.

CSF examination shows low glucose concentration, elevated protein level, and mild to modest lymphocytic pleocytosis.

Cryptococcal meningitis is the most common type. The presence of cryptococcal antigen in serum or CSF or a positive CSF India ink preparation establishes the diagnosis. Treatment with amphotericin B for at least 2 weeks, followed by high-dose fluconazole, is usually effective. Serial lumbar punctures, with removal of CSF to decrease intracranial pressure, may be necessary in the early management of cryptococcal meningitis.

*M. tuberculosis* can cause subacute or chronic meningitis in the HIV-infected patient. Antituberculosis therapy should be considered in the setting of chronic meningitis if the cryptococcal antigen test is negative.

*Coccidioides immitis* or *Histoplasma capsulatum* may cause subacute or chronic meningitis in patients who reside in, or have a history of travel to, endemic regions (i.e., the U.S. southwestern deserts and the Ohio and Mississippi River drainage areas, respectively).

Neurosyphilis in patients with HIV is more common and may manifest earlier after infection. Patients may experience headaches and dizziness in the early phases, which can be followed by personality change, ischemic strokes, ataxia, seizures, and paralysis.

#### Meningoencephalitis

Patients with meningoencephalitis manifest alterations in sensorium varying from mild lethargy to coma. Patients are usually febrile, and neurologic examination often shows evidence of diffuse CNS involvement. CT or MRI may show only nonspecific abnormalities, whereas electroencephalography often is consistent with diffuse disease of the brain.

CMV encephalitis is rare and difficult to diagnose; it occurs only in the setting of CD4 counts lower than 50 cells/mm<sup>3</sup>. Patients may demonstrate confusion, cranial nerve abnormalities, or long tract signs. CSF findings may resemble those of bacterial meningitis, with a modest polymorphonuclear leukocyte pleocytosis and depressed CSF glucose levels. CT scanning or MRI may reveal periventricular abnormalities. Many patients have associated CMV retinitis. PCR detection of CMV DNA in CSF appears to be a sensitive and specific method for diagnosis of CMV encephalitis and polyradiculopathy (persistent back pain and weakness of the lower extremities).

Meningoencephalitis caused by HSV is unusual in HIV infection.

#### HIV-Associated Malignancies

The incidence of AIDS-associated malignancies has declined significantly since the advent of effective ART. Among HIV-infected MSM, the frequency of Kaposi's sarcoma fell from 40% at the outset of the epidemic to less than 15% in 1999. Human herpesvirus 8 is the causative agent. In many instances, lesions resolve after institution of effective ART. Systemic chemotherapy can cause remission in many patients with symptomatic visceral disease. Kaposi's sarcoma remains common in many parts of the developing world.

Non-Hodgkin's lymphomas (largely B cell, with small noncleaved or immunoblastic histology) occur 150 to 250 times more often in HIV-infected persons than in the general