MR of the CNS in Patients with AIDS

Introduction

The acquired immunodeficiency syndrome (AIDS) is a disease whose manifestations result from a breakdown in the cell mediated human immune system. Therefore, typical clinical-radiologic findings include largely uncontrolled infections and neoplastic proliferations of cells peculiar to this specific depression in the host’s defense network.

It is well recognized that magnetic resonance (MR) imaging is superior to any other imaging modality with regard to sensitivity of detection of pathologic change in the central nervous system (CNS) in patients with AIDS. The excellent diagnostic sensitivity of MR coupled with the extraordinary breadth of expression of one or multiple concomitant disease processes in individuals with AIDS reveal a profoundly striking and sometimes confounding picture of a devastating disease process.

This as yet usually (uniformly) fatal disease presents with classic as well as unique pathology on MR in isolation or in combination with one another. For the most part, the MR findings are non-specific and may be representative of infection and/or neoplasia. This review presents many of the typical as well as unusual manifestations of AIDS on enhanced MR imaging of the CNS. All cases were proved either based upon the presumptive evidence of a positive response to medical therapy (e.g. toxoplasmosis) or on the basis of direct inspection of tissue from surgical biopsy or CSF analysis (e.g. progressive multifocal leukencephalopathy, lymphoma, cytomegalovirus infection, cryptococcosis).

Primary Human Immuno-deficiency Virus (HIV) Infection

HIV is an RNA virus of the retrovirus group. It is a highly neurotropic virus which avidly infects the tissues of the CNS. The HIV particles have been found in the CNS primarily within macrophages and multinucleated giant cells. The pathologic lesion consists of microglial nodules associated with multinucleated giant cells. HIV particles have also been observed in neurons and glial cells.

Early in the course of the disease, MR imaging may be normal. The most common abnormality encountered on imaging of the brain in patients with AIDS is generalized atrophy without focal pathologic change; patchy white matter disease eventually appears that may affect the cerebral hemispheres, cerebellum, brainstem, cerebral commissures and spinal cord. This white matter disease, seen more commonly pathologically at necropsy than at imaging, is believed to be due to active HIV encephalomyelitis. This HIV involvement does not demonstrate enhancement after IV gadolinium administration which helps to differentiate this entity from other pathologic processes also found in AIDS patients that do typically enhance (e.g. toxoplasmosis, lymphoma). The cerebral imaging abnormalities are often accompanied by the AIDS dementia complex, the most common neurologic problem in patients with AIDS. (Figure 1) These patients present with decreased memory function, inability to concentrate, psychomotor retardation, and/or seizures. Approximately 50% of patients with AIDS dementia complex will also have involvement of the spinal cord manifesting clinically as varying degrees of paraparesis. The clinical...
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syndrome usually becomes manifest before MR abnormalities are detected. Thus, MR cannot be used to predict with certainty which patients with AIDS will develop the AIDS dementia complex.

Depending upon the variable severity of the findings, the differential diagnosis of this MR appearance in AIDS patients includes viral encephalomyelitis due to secondary infection e.g., cytomegalovirus, Herpes simplex virus, progressive multifocal leukoencephalopathy (PML), and ischaemic white matter disease of the type frequently seen in association with the vasculopathy common to CNS AIDS.

Secondary Viral Infection

Secondary infection by virus particles other than HIV is an important component of the clinicoradiologic picture in patients with AIDS. Cytomegalovirus (CMV) is a herpes virus that can be found in the tissues of up to 90% of AIDS patients at autopsy. Infection of the CNS occurs in approximately 33% of AIDS patients and may affect the cerebrum, cerebellum, spinal cord, spinal nerve roots and leptomeninges.\(^{25,26,27}\)

Typically, CMV involvement of the cranial nerves/spinal nerve roots demonstrate enhancement with IV gadolinium, whereas CMV infection of the parenchyma of the brain and spinal cord usually does not. This is an important observation because such active disease of nerves and nerve roots cannot be seen on T1- or T2-weighted acquisitions alone, and may be missed if enhancing agents are not used in this setting. Similarly, herpes virus may affect these same tissues, occasionally presenting with related signs and symptoms.\(^{24,25}\) Uncommonly, Herpes simplex may present in patients with AIDS as a necrotizing encephalitis preferentially involving the temporal lobes.

Parasitic Disease

By and large, the type of parasitic infection encountered in AIDS patients and its incidence will depend upon the presence of endemic infectious agents in the index population. In North America, Toxoplasma gondii predominates in AIDS.
Toxoplasmosis is one of the most common neurologic opportunistic infections in patients with AIDS. Microscopically, toxoplasmosis lesions are necrotizing abscesses consisting of three zones. The inner zone contains necrotic material with few organisms. The middle zone is hypervascular and contains many inflammatory cells and organisms. The outer zone has few vascular changes and mostly encysted organisms. The foci tend to be multiple, and may affect any area of the brain, or more rarely the spinal cord.

Bacterial Infection

Early in the clinical experience with AIDS, bacterial organisms were not thought to play a major role in regard to superinfections of the CNS in patients with AIDS. The reason for this is that in AIDS it is the cellular rather than the humoral immune response that is primarily disrupted, and it is the latter which largely accounts for the immune reaction to bacteria. Nevertheless, several bacterial organisms break these rules and are encountered with some frequency in AIDS patients.

For example, sexually transmitted bacteria such as the syphilis spirochete, may gain access to the CNS in AIDS patients and pursue a more rapid course of active disease than would be usual in the otherwise immunocompetent individual. Neurosyphilis may affect neural tissue directly as well as the vascular system serving the CNS. In meningovascular syphilis, secondary infarction and hemorrhage often accompany the vasculitis (Figure 7). In its parenchymatous form, neurosyphilis may manifest CNS gumma formation that enhances in a ring-like or solid, nodular configuration (Figure 7).

Granulomatous bacterial infections can recur from reactivation of quiescent foci of prior infection and may dominate the clinical picture in some patients with AIDS. This is dramatically illustrated in the rapidly escalating incidence of tuberculosis (TB) in world populations. Such TB may be typical or atypical, drug susceptible or drug resistant, and may affect the entire...
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Figure 7D: Axial T1-weighted (500/20) spin echo image after IV Gd-DTPA administration acquired at the same level as B.

Figure 8: Spinal tuberculous epidural empyema in 30 year-old male.

Figure 9: Cryptococcal infection in 31 year-old male.

Figure 10: Cryptococcal gelatinous pseudocysts in 35 year-old male.

Figure 18

craniospinal axis. Because of the poor immune response in AIDS patients and the nature of the tuberculous disease process, the progress of TB may be fulminant and its extent of involvement may be overwhelming. Granuloma or frank abscess formation may occur within the CNS parenchyma or epidural/subdural space in the cranium or spine. In addition, a diffuse meningitis may also be a feature of TB, often occurring concomitantly with the parenchymal deposit(s). After IV gadolinium administration, solid granulomas and phlegmonous epidural inflammatory response will enhance homogeneously, while caseating granulomas and frank TB abscess/empyema formation will show central non-enhancement (Figure 5).

Fungal Infection

Although theoretically any opportunistic fungus might affect the CNS in AIDS patients, certain fungi are characteristically observed. Cryptococcus neoformans is probably the most commonly encountered fungus in this setting.6,7,41 Cryptococcus is an opportunistic pathogen that is very neurotropic. In host tissues it has a variable yeast morphology. Its surrounding polysaccharide capsule is nearly immunologically inert and helps mask fungal surface antigens. The predilection for CNS involvement may be related to poor phagocytic response in the CNS, the presence of nutritional factors in CSF (e.g. asparagine and creatine), and perhaps to the absence of inhibitory factors in CSF that are found in serum. Cryptococcus may affect the brain and meninges focally or diffusely and can be difficult or impossible to identify on unenhanced images. The reason for this difficulty is because of the generalized, nonspecific grey and white matter disease (e.g. PML, HIV encephalitis) observed in many advanced cases of CNS AIDS. Following IV gadolinium administration, however, the foci of fungal infection are strikingly revealed as areas of parenchymal and/or leptomeningeal enhancement (Figure 9). One exception to this general rule is seen in the nonenhancing or poorly enhancing gelatinous pseudocysts typically seen involving the perivascular spaces penetrating the basal ganglia in association with cryptococcal infection (Figure 10).62

Nevertheless, virtually any fungus that gains access to the CNS in AIDS patients may progress fulminantly. Other fungi that have been reported to affect the CNS in AIDS patients include Aspergillus, Rhizopus, Coccidioides, Histoplasma and Candida species.

Neoplasia

The classic neoplastic process seen in patients with CNS AIDS is that of lymphoma. Lymphoma is second in frequency only to toxoplasmosis as a cause of cerebral masses in patients with AIDS. Typically, these lymphomas are of the large cell immunoblastic or small noncleaved cell type.63,64 Lymphoma may be primary, affecting the CNS.
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Infectious agents (e.g., bacterial, viral, parasitic, or fungal) seen in association with virtually any condition of AIDS, such as plasmacytoma, astrocytoma, and hemorrhage, may be related to a local arthritis. The major factor for cerebrovascular accidents was found to be emboli from a peripheral source (e.g., cardiac). Finally, in cases of CNS hemorrhage, an associated systemic bleeding tendency must be considered in patients with AIDS (e.g., associated with thrombocytopenia).48

Conclusion

MR has proved to be the most sensitive single imaging method for the demonstration of CNS disease in AIDS patients. The administration of IV gadolinium increases the sensitivity of the MR examination to disruptions in the blood-CNS barrier present in many pathologic processes affecting AIDS patients both in the presence and in the absence of T2-weighted MR signal changes in the cranium and spine. At the same time, the use of a paramagnetic contrast agent distinguishes enhancing from unenhancing pathology revealed on abnormal T2-weighted acquisitions.50 In some cases the judicious use of a contrast agent materially assists in focusing the differential diagnosis and thereby potentially positively affects patient management.51 Unfortunately, it must still be concluded that the patterns of contrast enhancement observed in most instances remain nonspecific with regard to a particular etiology, either inflammatory or neoplastic.

Because MR imaging of the CNS has not proven to be efficacious to survey for early, silent disease in HIV-positive patients, MR should probably be reserved for those AIDS patients who are symptomatic.31,54 As an initial diagnostic imaging examination, MR has proved to be valuable in such patients in directing further clinical diagnostic tests (e.g., CSF sampling), surgical procedures (e.g., stereotactic or open biopsy), and imaging studies (e.g., arteriography in cases of suspected arteritis).

References

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Figure 13: Metastatic subarachnoid dissemination of peripheral (non-CNS) Non-Hodgkin’s lymphoma in 37-year-old male.

A) Sagittal T1-weighted (500/10) spin echo acquisition.

B) Axial T1-weighted (500/10) spin echo image acquired at the L3 level. No abnormalities can be identified on these pre-enhancement images.

C) Axial T1-weighted (500/10) spin echo image acquired at the same level 2 weeks after DTPA administration. Enhancement is noted of virtually all structures (roots) within the spinal canal. While this is compatible with the diagnosis of subarachnoid spread of lymphoma (lymphomatous meningitis), even in the face of known peripheral lymphoma the final diagnosis must rest with cellular proof obtained from cerebrospinal fluid samples. This is necessitated by the identical appearance of lymphatic tumour dissemination and infective polyradiculitis in some AIDS patients. (Compare with Figure 2.)

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