# *Neuroimaging Features Of Central Nervous System Diseases In HIV-Infected Patients: A Comprehensive Review*

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**Abstract**

Neurological complications remain a major cause of morbidity and mortality in HIV-infected individuals, especially those with advanced immunosuppression. Opportunistic infections such as cerebral toxoplasmosis, central nervous system tuberculosis, cryptococcal infection, and progressive multifocal leukoencephalopathy present with diverse and sometimes overlapping neuroimaging findings. Magnetic resonance imaging is the modality of choice for early detection and characterization of these conditions. In the emergency setting, neuroimaging plays a pivotal role in rapidly identifying life-threatening central nervous system complications in HIV-infected patients presenting with acute neurological symptoms. Our work aims to provide a comprehensive overview of the most common brain diseases encountered in HIV-infected patients and to highlight the crucial role of neuroimaging in facilitating accurate diagnosis and timely treatment, thereby improving clinical outcomes.

**Keywords**

HIV infection ; Brain diseases ; Magnetic resonance imaging ; Cerebral toxoplasmosis ; Central nervous system tuberculosis

## INTRODUCTION

Central nervous system (CNS) involvement remains one of the most serious and life-threatening complications in patients infected with the human immunodeficiency virus (HIV). Despite advances in antiretroviral therapy (ART), opportunistic infections and HIV-associated neurocognitive disorders continue to affect a significant proportion of immunocompromised individuals, particularly those with low $CD_4$ cell counts [1,2]. These CNS manifestations are varied, ranging from infections such as toxoplasmosis and cryptococcosis to demyelinating processes like progressive multifocal leukoencephalopathy (PML) and direct viral effects such as HIV-associated encephalitis [3].

Accurate and timely diagnosis is essential, as clinical presentations are often nonspecific and overlapping. Headache, confusion, seizures, and focal neurological deficits may be seen in several of these conditions, making clinical differentiation challenging.

In the emergency department, where time-sensitive decisions are crucial, the identification of these neurological complications can be particularly challenging. Delay in diagnosis may lead to rapid deterioration or irreversible damage. Therefore, neuroimaging, especially magnetic resonance imaging (MRI), plays a pivotal role in guiding diagnosis, differentiating pathologies, and assessing response to therapy [4–6]. Awareness of these imaging patterns is essential for emergency physicians confronted with HIV-infected patients presenting with acute neurological symptoms.

This review aims to provide a comprehensive overview of the most common brain diseases encountered in HIV-infected patients. We focus on five major entities: cerebral toxoplasmosis, CNS tuberculosis, cryptococcal infection, PML, and HIV-associated encephalopathy, highlighting the characteristic imaging findings and key differentiating features.

**1/ Cerebral toxoplasmosis (Figures 1,2):**

Toxoplasmosis is the most frequent opportunistic brain infection in HIV-infected patients. It is caused by the parasite Toxoplasma gondii and typically occurs in individuals with $CD_4$ counts below 100 cells/μL [7]. Pathologically, it results in necrotizing encephalitis.

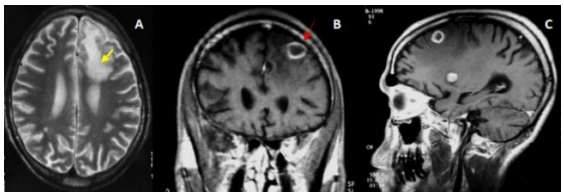


***Figure 1 : Cerebral toxoplasmosis : Axial T2 (A), coronal (B) and sagittal (C) T1 sections after injection of gadolinium: showing multiple rounded lesions including the left frontal lesion (red arrow) taking contrast in the periphery and surrounded by significant lesion oedema (yellow arrow***

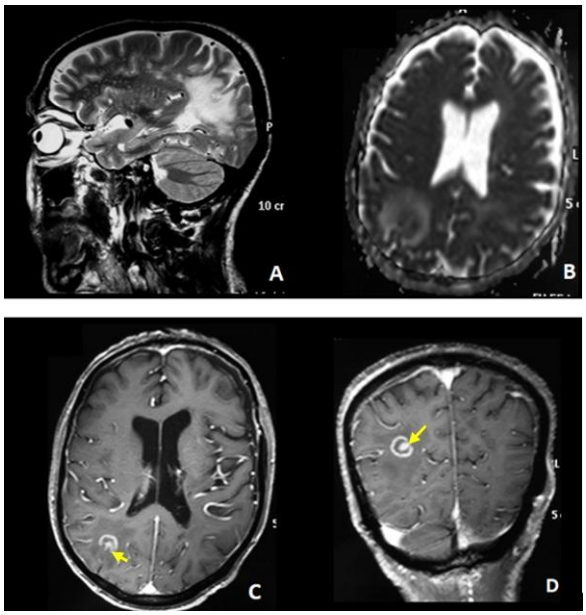


***Figure 2 : Cerebral toxoplasmosis : Sagiital T2 section (A), ADC (B), T1 after injection axial (C) and coronal (D) : The "eccentric target sign" (yellow arrow)***

MRI typically reveals multiple lesions, 1–4 cm in size, with a predilection for the basal ganglia, thalamus, and corticomedullary junction [7]. On T1-weighted images, the lesions appear hypointense, while T2-weighted images show iso- to hypointense signal, often with surrounding vasogenic edema and mass effect.

The enhancement pattern is usually ring-shaped or nodular. A distinctive but infrequent sign is the eccentric target sign, where a small enhancing nodule lies eccentrically within a ring—seen in about 30% of cases and relatively specific for toxoplasmosis [8].

Magnetic resonance spectroscopy (MRS) may show elevated lipid and lactate peaks, indicating necrosis and anaerobic metabolism [9]. Diagnosis is often clinical and radiological, confirmed by therapeutic response to anti-toxoplasmosis treatment, thereby avoiding invasive biopsy [10].

Differential diagnoses include primary CNS lymphoma and HIV encephalopathy, and may require advanced imaging techniques or brain biopsy in equivocal cases.

***SUMMARY***

Multifocal peripherally enhancing lesions involving the basal ganglia and corticomedullary junction are the hallmark of cerebral toxoplasmosis. Look for the eccentric target sign. Differentiation from lymphoma may require advanced imaging, a therapeutic trial, or biopsy.

**2. CNS Tuberculosis (Figure 3)**

The HIV epidemic has significantly increased the incidence of tuberculosis worldwide. HIV infection is the major risk factor for reactivation of latent tuberculosis, increasing the risk approximately threefold compared to HIV-negative individuals and raising the proportion of extrapulmonary tuberculosis cases fivefold [11]. CNS tuberculosis usually occurs in patients with $CD_4$ counts less than 500 cells/µL [12].

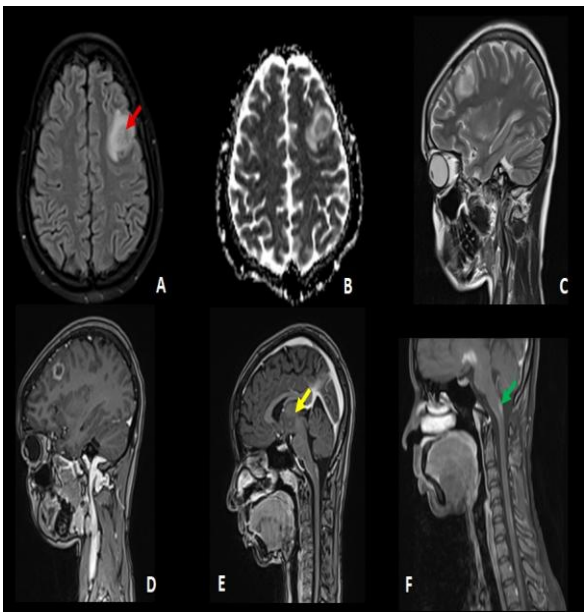


***Figure 3 :Tuberculoma with tuberculous meningitis :Axial FLAIR (A), ADC (B) and sagittal T2 (C), T1 after gadolinium injection (D, E, F): left frontal lesion (red arrow) rounded in central T2 hyposignal surrounded by a peripheral T2 hypersignal taking contrast in the periphery in an annular fashion. There is a second lesion of the same type at the base of the cerebral peduncle (yellow arrow) and meningeal contrast opposite the gracile fasciculus (green arrow).***

CNS tuberculosis presents in various forms:

- Intracranial intra-axial tuberculous granuloma (tuberculoma): These are ring-enhancing, round lesions 3–15 mm in diameter, often surrounded by extensive vasogenic edema. They are typically hypointense on T1-weighted images and hyperintense on T2-weighted images, sometimes with a hypointense rim. Tuberculomas can occur in both supra- and infratentorial regions but are more common in white matter and subcortical areas. Caseating tuberculomas with liquid centers may

resemble tuberculous abscesses, though abscesses tend to be larger and solitary [13].

-Meningeal (extra-axial) tuberculous granulomas: Appear as small (<6 mm) round foci on the brain surface, sometimes with cortical involvement, showing ring enhancement on contrast-enhanced T1-weighted images [14].

-Tuberculous leptomeningitis: Characterized by predominant basal meningeal enhancement, similar to patterns seen in immunocompetent patients [12].

*Summary*

Tuberculosis can affect multiple CNS regions with varied imaging features. CNS involvement generally occurs at $CD_4$ counts below 500 cells/µL but can present at any level of immunosuppression.

**3. Cryptococcal infection (Figures 4,5)**

Infection caused by *Cryptococcus neoformans* typically occurs with $CD_4$ counts below 100 cells/µL [15]. Pathologically, there are three main forms of cryptococcal infection: meningitis, gelatinous pseudocysts, and cryptococcomas.

MRI findings are generally nonspecific. Cryptococcal meningitis presents as focal (chronic basilar meningitis) or diffuse meningeal enhancement. Mild dilatation of the ventricular system can also be detected [16].

*Cryptococcus neoformans* pseudocysts occupy and dilate perivascular Virchow-Robin spaces, resulting in rapidly growing, non-enhancing "cysts" seen symmetrically in the basal ganglia and thalamus.

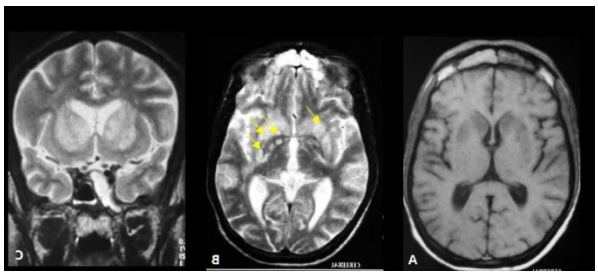

***Figure 4: Cryptoccocal infection: Cryptococcus neoformans pseudocysts and dilate perivascular Virchow-Robin spaces, non enhancing "cysts" seen symmetrically in basal ganglia (yellow arrows). These lesions are hypointense on T1W images (A) and hyperintense on T2W MR images (B,C).***

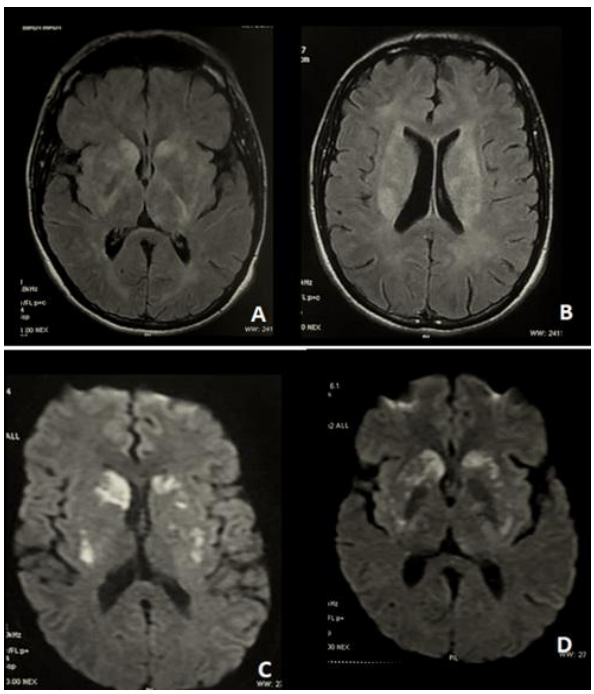

***Figure 5: Cryptococcosis with acute ischemic lesions :FLAIR (A,B) and diffusion (C,D) axial sections: multiple bilateral and asymmetric FALIR hypersignal patchy signal anomalies with diffusion restriction in the basal ganglia and external capsule in relation to ischaemic lesions***

These lesions are hypointense on T1-weighted images and hyperintense on T2-weighted MR images [17]. Cryptococcomas are rare mass-like parenchymal lesions with

nodular enhancement and have a predilection for the basal ganglia, thalamus, and cerebellum [18].

*SUMMARY*

Variable patterns of cerebral involvement occur, with the most characteristic being perivascular gelatinous pseudocyst formation.

**4. Progressive multifocal leukoencephalopathy (Figure 6)**

PML is a demyelinating disorder caused by latent reactivation of the Papovavirus (JC virus). It typically occurs in patients with $CD_4$ counts between 50 and 100 cells/µL [19].

MRI demonstrates multifocal, bilateral but asymmetric areas of T2 hyperintensity predominantly involving the periventricular and subcortical white matter, usually without mass effect or contrast enhancement. Subcortical U-fibers are commonly involved, and occasional cortical involvement is noted.

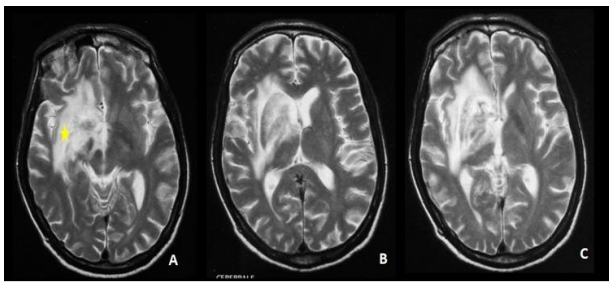


***Figure 6: Progressive multifocal leukoencephalopathy: axial T2 sections: T2 hyperintensity area (yellow star) involving predominantly periventricular and subcortical white matter, without mass effect or enhancement***

Diffusion restriction may be present at the advancing edge of acute lesions, and cystic changes may develop in late stages. Lesions have a predilection for the parieto-occipital regions, basal ganglia, and thalami [20,21].

*SUMMARY*

PML is a multifocal demyelinating disorder occurring in advanced immunosuppression. Its asymmetric distribution, absence of mass effect, and lack of enhancement help distinguish it from HIV encephalopathy, lymphoma, and toxoplasmosis.

**5. HIV Encephalitis**

HIV encephalitis results from direct neuronal injury caused by the HIV virus. The spectrum of neurocognitive symptoms is broad, with imaging correlates most evident in advanced disease, such as HIV-associated dementia [22].

Imaging findings are nonspecific and include symmetrical cerebral atrophy disproportionate to age, with confluent, bilateral, almost symmetrical and diffuse T2 hyperintensity involving deep and periventricular white matter. There is often a frontal lobe predominance. No mass effect or enhancement is seen in HIV encephalopathy [23,24].

*SUMMARY*

HIV encephalitis manifests as nonspecific, diffuse deep white matter disease due to direct viral effects. Its prevalence may paradoxically increase with longer survival of HIV-positive patients.

**CONCLUSION**

Brain infections and neurological complications remain a significant cause of morbidity and mortality in HIV-infected

patients, particularly in those with advanced immunosuppression. Neuroimaging, primarily MRI, plays a critical role in the early detection, characterization, and differentiation of opportunistic infections. Although imaging features can be similar, identifying specific patterns is key to enabling timely diagnosis and guiding appropriate treatment. In the emergency setting, prompt neuroimaging is often essential for the rapid evaluation of HIV-infected patients presenting with acute neurological symptoms, where early intervention can be lifesaving. As survival improves with ART, awareness of these varied presentations and advances in imaging techniques remain essential for optimal management and improved outcomes in this vulnerable population.

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