MR neuroimaging of HIV infected patients: A pictorial review

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Aim

The incidence of human immunodeficiency virus is low (approximately 24,000) in Australia but these patients can present with unusual infections and imaging abnormalities. We review several common CNS pathologies that affect HIV infected patients and discuss their MR imaging features.

Methods and materials

Our hospital provides a dedicated service for this small group of patients for the state.

MR imaging plays a crucial role in the diagnosis of CNS manifestation of HIV infection. The spectrum of disease can be categorised into 4 groups:

1. Direct consequence of HIV virus
   1.1 HIV encephalitis - HIV associated neurocognitive disorder (HAND) - AIDS dementia complex.
   1.2 HIV myelopathy

2. Opportunistic infections
   2.1 Cerebral toxoplasmosis
   2.2 Progressive multifocal leucoencephalopathy (PML)
   2.3 Cytomegalovirus infection
   2.4 Tuberculosis
   2.5 Cryptococcosis

3. Neoplasm predominantly due to CNS lymphoma

4. Consequence of HIV treatment: Immune resconstitution inflammatory syndrome (IRIS)
Results

1. Direct consequence of HIV virus

1.1. HIV encephalitis - HIV associated neurocognitive disorder (HAND) - AIDS dementia complex

This is the most common neurological manifestation of HIV infection. It consists of a spectrum of neurological disorders from asymptomatic to mild neurological impairment to significant impairment in activities of daily living. Patients may present with early dementia, cognitive, motor and behavioural deficits. It usually occurs prior to opportunistic infections.

Imaging features: Bilateral symmetrical periventricular and deep white matter T2 hyperintensity, which could be confluent or patchy. There may be associated cerebral atrophy but no mass effect or contrast enhancement. It may resemble chronic small vessel ischaemic changes but greater than expected for patient's age.

Fig. 1: HIV encephalitis in 36 years old patient. 1a: Axial FLAIR image demonstrates confluent periventricular white matter FLAIR hyperintensities. 1b. Axial post contrast T1 weighted image demonstrates no contrast enhancement in the periventricular white matter. Images contributed by Dr Hani Salam, Radiopedia. 1c. HIV encephalitis in 46 years old patient. Axial FLAIR image demonstrates patchy periventricular white matter FLAIR hyperintensities, more than expected for patient's age.

References: Alfred Health - SOUTH YARRA/AU

1.2. HIV myelopathy
This is the most common spinal cord manifestation of HIV infection. Patients may present with insidious onset of ataxia, urinary dysfunction and sensory loss.

Imaging features: Bilateral cord high T2 signal which spans multiple levels. The dorsal column is most commonly involved. There may be associated spinal cord atrophy but usually no contrast enhancement.

**Fig. 2:** HIV myelopathy. 1d: Sagittal T2 weighted image demonstrates a long segment T2 hyperintense cord lesion involving the dorsal column from C2 to C4 levels. 1e: Sagittal post contrast T1 weighted image demonstrates no contrast enhancement within the cord lesion. 1f: Axial T2 weighted image demonstrates high T2 signal within the dorsal columns of the cervical cord.

**References:** Alfred Health - SOUTH YARRA/AU

2. **Opportunistic infections**

Opportunistic infections occur in clinical stage 3 HIV disease (AIDS) when CD4+ < 200 cells/µL. They could be classified as:

a. Parasitic infections such as toxoplasmosis

b. Viral infections such as progressive multifocal leucoencephalopathy (PML) and cytomegalovirus infection

c. Granulomatous infections such as tuberculosis, cryptococcosis and aspergillosis.

2.1. **Cerebral toxoplasmosis**
This is the most common opportunistic infection in AIDS patients. It occurs in approximately 10% of HIV patients who have advanced untreated disease, usually with CD4+ <100 cells/µL. It is caused by toxoplasma gondii ingestion in raw meat or contact with cat feaces. Patients may present with fever, headache, malaise, confusion and seizure.

Imaging features: Multifocal ill defined, rounded T2 hypointense lesions with surrounding vasogenic oedema; commonly in the basal ganglia, corticomedullary junction or cerebellum. Peripheral nodular enhancement with central enhancing nodule "target sign" is highly suggestive of toxoplasmosis.

Fig. 3: Toxoplasmosis. 2.1a: Axial T2 weighted image demonstrates T2 hypointense lesion with surrounding oedema. 2.1b: Axial post contrast T1 weighted image demonstrates an enhancing nodule within the peripherally enhancing lesion, in keeping with target sign which is highly suggestive of toxoplasmosis. 2.1c: Axial DWI image demonstrates no restricted diffusion.

References: Alfred Health - SOUTH YARRA/AU

2.2. Progressive multifocal leucoencephalopathy (PML)

Progressive multifocal leucoencephalopathy is an opportunistic infection caused by John Cunningham (JC) polyomavirus, which infects the oligodendrocytes in immunocompromised patients. It occurs in approximately 4-7% of the HIV patients with CD4+ <100 cells/µL. However, it may occur in patients with CD4+ >200 cells/µL. Patients may presents with various neurological deficits including blindness, dysphasia, hemiplegia, dementia, headache and seizure.

Imaging features: Bilateral asymmetrical T2 hyperintensity involving subcortical U fibers extending into the deep white matter. Typically there is no mass effect or contrast enhancement. It may be solitary, multifocal or confluent, with cavitory changes in late
stage. It commonly involves the frontal lobe, parieto-occipital lobe, basal ganglia and thalamus.

**Fig. 4:** Progressive multifocal leucoencephalopathy (PML). 2.2a: Axial FLAIR image demonstrates bilateral but asymmetrical high FLAIR signal involving subcortical U fibers extending into the deep white matter. No mass effect. 2.2b: Axial DWI image demonstrates restricted diffusion at the periphery of the lesion which correlates to the areas of lesion expansion. 2.2c: Axial post contrast T1 weighted image demonstrates no contrast enhancement.

**References:** Alfred Health - SOUTH YARRA/AU

### 2.3. Cytomegalovirus infection

Cytomegalovirus, also known as Human Herpesvirus 5 (HHV-5) becomes reactivated when the patient's immune system is severely compromised, typically with CD 4's count below 50/mm$^3$. It infects the entire neuroaxis and may present with meningitis, encephalitis, ventriculitis and myelitis.

Imaging features: Enlarged ventricles with surrounding T2 hyperintensity, ependymal and periventricular enhancement, in keeping with ventriculitis. CMV encephalitis is often a ventriculo-encephalitis, located at the periventricular location. It appears as T2 hyperintense mass, typically without enhancement but necrotic lesions may have peripheral patchy enhancement.
Fig. 5: Cytomegalovirus infection (CMV). 2.3a: Axial FLAIR image demonstrates mildly enlarged ventricles with surrounding T2 hyperintensity. 2.3b: Axial post contrast image demonstrates ependymal and periventricular enhancement, in keeping with ventriculitis.

References: Alfred Health - SOUTH YARRA/AU

2.4. Tuberculosis

Tuberculosis is an infection caused by Mycobacterium tuberculosis. CNS tuberculosis is a complication of hematogenous spread from pulmonary tuberculosis. It can manifest as tuberculous meningitis (most common) or localised parenchymal infection.

Imaging findings: Tuberculous meningitis can be seen as T2 hyperintense, thick or nodular meningeal enhancement in the basal cisterns. There may be linear enhancement in the basal ganglia in keeping with vasculitis. Tuberculoma can be seen as a vividly enhancing mass, often supratentorial in location, with T2 hypointensity (unlike pyogenic abscesses) and surrounding oedema.
Fig. 6: Tuberculosis. Axial post contrast T1 weighted image demonstrates tuberculous meningitis with leptomeningeal enhancement of the basal cistern.

References: Dr Praveen Jha. Radiopedia

2.5. Cryptococcosis
Cryptococcosis is an opportunistic fungal infection caused by Cryptococcus neoformans. The infection is acquired by inhaling fungal spores causing pulmonary infections. CNS infection is a consequence of hematogenous spread and it has a tendency to spread along the perivascular spaces into the basal ganglia, thalamus, brainstem and cerebellum.

Imaging findings: Dilated perivascular spaces or basal ganglia pseudocysts in immunocompromised patients are highly suggestive of cryptococcosis. Enhancement varies from no enhancement to nodular or leptomeningeal pattern depending on the immune status of the patients. Cryptococcoma may be seen as a ring or solid enhancing mass.

**Fig. 7**: Cryptococcosis. 2.5 a,b: Axial FLAIR and post contrast T1 weighted images demonstrate nodular areas of high FLAIR signal abnormality in the perivascular spaces and basal ganglia with patchy areas of enhancement. 2.5 c,d: Axial FLAIR and post contrast T1 weighted images demonstrate high FLAIR signal abnormality in the subarachnoid spaces of both cerebral hemispheres with thickened leptomeningeal enhancement. 2.5 e: Post contrast T1 weighted image demonstrates irregular nodular leptomeningeal enhancement throughout the posterior fossa.
3. Neoplasm predominantly due to CNS lymphoma

This is the most common CNS neoplasm in HIV patients. It is much more common in HIV patients compared to the general population. It is strongly associated with EBV infection. It occurs up to 2-5% of HIV patients with advanced untreated HIV and CD4+ <50 cells/µL. Patients may present with fever, headache and confusion, similar to CNS toxoplasmosis infection.

Imaging features: Multifocal enhancing lesions, in the periventricular and basal ganglia, often involving corpus callosum. Enhancement may be solid or peripheral due to compromised immune status. Occasionally there may even be no enhancement. Typically there is mild or no surrounding oedema. Diffusion restriction and high CT density are typically seen due to the highly cellular nature of lymphoma. Susceptibility artefacts may be seen due to haemorrhage.
Fig. 8: CNS lymphoma. 3a: Axial FLAIR image demonstrates irregular rim of periventricular white matter FLAIR hyperintensity involving the corpus callosum. 3b,c: Axial pre and post contrast T1 weighted images demonstrate multifocal periventricular solidly enhancing lesions. 3d: Axial DWI image demonstrates diffusion restriction within the enhancing periventricular lesions, in keeping with highly cellular tumour.

References: Alfred Health - SOUTH YARRA/AU
Table 1: Imaging features of CNS toxoplasmosis versus CNS lymphoma.

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<thead>
<tr>
<th></th>
<th>CNS Toxoplasmosis</th>
<th>CNS lymphoma</th>
</tr>
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<tbody>
<tr>
<td><strong>Multifocal</strong></td>
<td>85%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Basal ganglia</td>
<td>Periventricular white matter</td>
</tr>
<tr>
<td></td>
<td>Corticomedullary junction</td>
<td>Subependymal spread</td>
</tr>
<tr>
<td><strong>Enhancement</strong></td>
<td>Ring or nodular</td>
<td>Solid, ring or none</td>
</tr>
<tr>
<td></td>
<td>Target sign</td>
<td></td>
</tr>
<tr>
<td><strong>CT density</strong></td>
<td>Iso to hypodense</td>
<td>Iso to hyperdense</td>
</tr>
<tr>
<td><strong>DWI</strong></td>
<td>Not elevated</td>
<td>Elevated</td>
</tr>
<tr>
<td><strong>MRS</strong></td>
<td>Decreased choline</td>
<td>Increased choline</td>
</tr>
<tr>
<td><strong>MR perfusion</strong></td>
<td>Decreased rCBV</td>
<td>Increased rCBV</td>
</tr>
<tr>
<td><strong>Thalium SPECT</strong></td>
<td>Negative</td>
<td>Positive</td>
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4. Consequence of HIV treatment: Immune reconstitution inflammatory syndrome (IRIS)

Immune reconstitution inflammatory syndrome occurs in HIV/AIDS patients following commencement of highly active antiretroviral therapy (HAART). There is paradoxical worsening of neurological symptoms due to reconstitution of immunity causing abnormal immune response to the infectious antigen. It occurs in 10-40% of patients with low CD4+ count. The main risk factors are low CD4+ count <50 cells/µL on commencement of antiretroviral therapy and high pathogen load. It can occur with any opportunistic infection but most commonly with PML and cryptococcal infection.

Imaging features: There is worsening of imaging appearance after commencement of HAART with increased cerebral oedema and increased, or development of, enhancement.
Fig. 9: PML. 4a: Axial FLAIR image demonstrates bilateral white matter high FLAIR signal abnormality in the cerebellum. 4b. Post contrast T1 weighted image demonstrates no contrast enhancement.

References: Alfred Health - SOUTH YARRA/AU

Fig. 10: IRIS after commencement of HAART. 4c: Axial FLAIR image demonstrates increased high FLAIR signal with increased cerebral oedema in both cerebellar
hemispheres. 4d: Post contrast T1 weighted image demonstrates interval development of contrast enhancement in the white matter of both cerebellar hemispheres.

References: Alfred Health - SOUTH YARRA/AU

**Fig. 11**: 2 weeks post steroid treatment 4e: Axial FLAIR image demonstrates reduced high FLAIR signal in both cerebellar hemispheres. 4f: Post contrast T1 weighted image demonstrates resolution of contrast enhancement in the white matter of both cerebellar hemispheres.

References: Alfred Health - SOUTH YARRA/AU

**Conclusion**

It is important for radiologists to recognise HIV related conditions and their imaging features to assist with prompt patient management, both in the community and in the hospital settings.

**Personal information**

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References


