Viral Infections

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Viruses that infect the central nervous system (CNS) include herpesviruses, arboviruses, coxsackieviruses, echoviruses, and enteroviruses. Some of these infections affect primarily the meninges, while others affect primarily the brain and result in encephalitis. The clinical manifestations are usually nonspecific and diagnosis is usually based on the laboratory investigations, especially cerebrospinal fluid (CSF) analysis.

Herpes simplex encephalitis (HSE) is a life-threatening disease caused by herpes simplex virus (HSV) infection of the CNS. In adults, HSE is caused by herpes simplex virus type 1 (HSV-1), whereas in neonates, brain involvement is more often diffuse, and the usual cause is herpes simplex virus type 2 (HSV-2), which is acquired at the time of delivery. HSV-1 has a predilection for the temporal lobes, bilateral and asymmetric temporal lobe involvement is usually detected on MRI. However, extra-temporal involvement has also been reported. HSE will be recognized by T2- and FLAIR-high signal intensity in the affected temporal lobe. Diffusion weighted imaging (DWI) is superior in the detection of the acute phase of HSE.

Key imaging features in HSVE-1:
- T2- and FLAIR-high signal intensity abnormalities in the temporal lobe
- Hypointense on T1WI
- In acute phase not enhancing, later gyriform enhancement
- Restricted diffusion in acute stage

Between 40 and 100% of individuals in the general population are seropositive for Cytomegalovirus (CMV). In the pre-HAART era CMV infection was associated with significant morbidity and mortality. With the advent of HAART, the rate of CMV disease declined in most countries where HAART is available. Five distinct neurological syndromes due to the CMV infection have been described: retinitis,
myelitis/polyradiculopathy, diffuse micronodular encephalitis, ventriculoencephalitis, and mononeuritis multiplex.

CNS infection with Varicella-zoster-virus (VZV) is seen in only 1% of patients and causes: aseptic meningitis, cerebellar ataxia, transverse myelitis, encephalitis, Guillain-Barré syndrome, arterial ischemic strokes, and optic neuritis. VZV should be considered as a possible infection in HIV-infected patients, especially in patients with a history of or concomitant herpes zoster or acute retinal necrosis.

Progressive multifocal leukoencephalopathy is a subacute opportunistic infection caused by the JC Polyomavirus (JCV). The highest incidence of PML has been recorded in AIDS patients, ranging in different studies from 0.7-11%. Furthermore, PML was also reported in a patient with multiple sclerosis (MS) treated with natalizumab.

Key imaging features in PML:
- Multifocal “scalloped” T2- and FLAIR-high signal intensity abnormalities of the white matter
- Hypointense on T1WI
- Involvement of the U-fibres
- May have peripheral faint enhancement
- On DWI centrally low signal (elevated diffusion) with peripheral high signal (restricted diffusion)

In the presence of progressive uni- or multifocal neurological disease and typical MRI lesions:
1. Histology-confirmed PML: brain biopsy (or post-mortem examination) showing typical pathologic features with JCV
2. Laboratory-confirmed PML: demonstration of JCV DNA in CSF
3. Possible PML: absence of both histological confirmation and JCV demonstration in CSF

Although at present there is no specific therapy for PML, recent studies have shown clinical and radiological improvement in patients with PML who underwent highly active antiretroviral therapy (HAART). In some patients with PML treated with antiretroviral therapy immune reconstitution inflammatory syndrome (IRIS) will occur. IRIS is a new, yet not fully understood phenomenon seen in immunocompromised patients with rapid changes of the immune status. It presents more or less
severely in different patient populations. On imaging studies IRIS should be suspected in cases where intense vasculitis-like enhancement occurs.

The introduction of highly active antiretroviral therapy (HAART) has changed *Human immunodeficiency virus (HIV)* infection from a devastating and fatal disease to a chronic illness. The neurological manifestations directly related to HIV are acute viral meningitis, chronic meningitis, HIV associated dementia, vacuolar myelopathy (VM) and involvement of the peripheral nervous system. Despite treatment HIV-related CNS complications have remained common. HIV-associated dementia (HAD) is considered as the most severe form of HIV-related injury. Mild neurocognitive disorder (MND) represents a milder form of impairment. An asymptomatic neurocognitive impairment (ANI) was introduced to recognize individuals with impairment on neuropsychological testing who report functional limitations. Ongoing milder brain injury occurs in HIV patients despite well controlled plasma viral load.

**Key imaging features in HIV-encephalitis:**
- Bilateral, symmetrical, non-enhancing high signal intensity abnormalities of the white matter (focal or diffuse)
- Iso- or slightly hypointense on T1WI
- Diffuse atrophy
- Sparing of subcortical white matter
- decreased NAA, increased MI, low glutamate

Neuroimaging plays an important role in detection of virus-related changes in the brain. Advanced imaging modalities (DWI, DTI, MRS, perfusion MR) are increasingly used to measure brain injury within white matter tracts and regional changes in brain metabolites caused by infectious processes.