Imaging Spectrum of Viral and Autoimmune Encephalitis: A Case Series.

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Abstract:
Encephalitis refers to an acute, diffuse inflammatory process affecting the brain. Viral encephalitis being the most important cause. Imaging of patients with viral encephalitis reveals edema in the affected brain parenchyma with possible diffusion restriction in the acute phase probably due to cytotoxic edema. Depending on the virus grey and white matter of the brain may be involved or a distinct site may be involved such as temporal lobes in HSV encephalitis. Viral encephalitis has a predilection for young and elderly. HSV encephalitis is the most commonly diagnosed viral encephalitis in developing countries. ADEM is an important differential diagnosis to be considered which tends to involve the white matter and the distribution is usually asymmetric. In the present case series we have presented HIV, Herpes, Rota virus, Japanese encephalitis virus manifestations of viral and autoimmune encephalitis. Both herpes and Japanese encephalitis are haemorrhagic encephalitis with a fulminant clinical course. Autoimmune-mediated encephalitis can be distinguished by its association with autoantibodies and by certain recognizable features on MR imaging, which include cerebellar degeneration, striatal encephalitis, brain stem encephalitis, and leukoencephalopathy. The purpose of this montage is to ensure that the clinician includes the specific virus and autoimmune etiology in the differential diagnosis.

Key Words: Encephalitis, HIV, Herpes, Rota Virus, Dengue, Japanese, Imaging.

Introduction:
Most common clinical manifestations of viral and autoimmune encephalitis include disorientation, speech disturbances and behavioural changes with one third of the patients developing seizures [1]. With the advent of CSF PCR, more subtle manifestations of viral encephalitis can be recognized. Although most viral encephalitis present acutely, subacute and chronic presentations can be caused by CMV, VZV, HSV, Japanese encephalitis virus especially in patients immunocompromised as a result of HIV or immunosuppressive drugs [2]. It is important to distinguish ADEM from acute infectious encephalitis, acute non-infectious encephalitis, and an acute metabolic or toxic encephalopathy [3]. Acute encephalitis constitutes a medical emergency. Early diagnosis is important for appropriate management. MRI imaging of brain is the investigation of choice and the diagnosis has to be confirmed by PCR for the virus in the CSF. CT scan is usually warranted before attempting lumbar puncture to look for signs of raised intracranial tension.

Encephalitis is a severe inflammatory disorder of the brain with many possible causes. The most common initial findings in autoimmune encephalitis with seizures are T2 hyperintensity and swelling of the limbic structures, though extra temporal involvement does not preclude a diagnosis of this condition. Recognition of these imaging findings and inclusion of autoimmune encephalitis in the differential diagnosis with other forms of limbic encephalitis.
Case 1: 41 year old gentleman who was detected to be HRV positive 3 months back with complaints of tiredness since 1 month, personality changes, confusion, memory loss, weakness of bilateral upper and lower extremities and choreoathetoid movements of left hand with fine tremors. Imaging features were suggestive of HIV encephalitis.

Figure 1: Axial T2 FLAIR image showing hyperintensities in bilateral basal ganglia, periventricular white matter & subcortical regions.
Figure 2: Coronal T2W- Fast spin echo (FSE) image showing hyperintensity in the deep white matter of left temporal lobe with cortical thickening suggestive of Herpes encephalitis.
Figure 3a: Axial DWI image showing diffusion restriction in deep white matter of bilateral fronto-temporo-parieto-occipital lobes and corpus callosum with sparing of subcortical U fibres.
Figure 3b: Axial T2W image showing hyperintensities in deep white matter of bilateral fronto-temporo-parieto-occipital lobes and corpus callosum.

Case 2: 56 year old lady with lethargy and 15 Kg weight loss over the past year was admitted to the hospital with fever, altered mental status, altered mental status and left hemiparesis. CSF revealed lymphocytic pleocytosis, elevated protein and glucose and positivity for IgM antibodies against HSV. EEG showed focal slowing and sharp waves. Imaging showed T2 hyperintensity in left temporo-parieto-occipital lobes with cortical thickening. Features were suggestive of Herpes encephalitis.

Case 3: 5 month old previously healthy male child was admitted to the hospital with a 2 day history of nonbloody diarrhea and vomiting. On the day of admission he developed fever and had a generalized tonic-clonic seizure lasting 2 min. On arrival to the hospital, he was dehydrated and drowsy. CSF analysis showed lymphocyte count of 2.4 x 10^9 /liter and bacterial cultures of blood and CSF were negative. Imaging features were suggestive of Rotavirus encephalitis. Clinically the child improved over the first 24 hours and subsequently made full recovery.

Case 4: A 22-year-old pregnant woman at 34 weeks of gestation with viral fever, erythema multiforme and myocarditis who presented with complaints of acute onset weakness in right lower limb and hyper-reflexia. Lab investigations showed thrombocytopenia and dengue positive serology. Imaging suggested hyperintensity in bilateral thalami, pons and bilateral perirolandic post central gyri. DWI images showed diffusion restriction in bilateral thalami and pons. Blooming was noted on GRE in bilateral perirolandic post central gyri. Features were suggestive of Dengue encephalitis. The diagnosis of dengue was confirmed by positive serology for IgM antibodies and NS-1 antigen positive.

Case 5: A 9-year-old boy presented with a 5-dayhistory of fever, cough, running nose, and sore throat. At clinical examination, he was lethargic with a Glasgow Coma Scale (GCS) score of 12/15. The provisional diagnosis was central nervous system infection was made. Lumbar puncture was performed. Cerebrospinal fluid (CSF) showed an elevated white cell count with lymphocytes and elevated protein content. Culture was negative for bacteria and...
The brain showed T2 FLAIR hyperintensities in bilateral thalami. A diagnosis of Japanese encephalitis was made. CSF polymerase chain reaction was performed on the fifth day and viral antibodies were detected.

**Case 6:** A previously healthy 14 year-old female patient was referred for evaluation and treatment of daily seizures and psychiatric disturbances. Symptoms began with daily holocranial headaches, neck pain, dysthymia, and hypersomnia for one week. She then had a generalized tonic-clonic seizure at school. She was brought to a local hospital, where initial evaluation included head computed tomography (CT) that was normal and lumbar puncture (LP) revealed a mild pleocytosis (18 wbc/dl) and mildly elevated protein (67 g/dl). HSV-1 PCR was negative. She developed marked personality change, with periods of catatonia, and bradykinesia. Serial brain MRI over a three week interval revealed T2 / T2 FLAIR hyperintensities involving bilateral external capsule, bilateral insular lobes & bilateral medial temporal lobes. Prior to identification of anti-NMDAR antibodies in the CSF, the patient was started on empiric high-dose intravenous methyl prednisolone.

**Discussion:**
HIV causes a type of subacute encephalitis, it is important in so far as its associated immune suppression predisposes the individual to viral encephalitis caused by, for example, HSV-1, HSV-2, VZV, and cytomegalovirus (CMV). HIV crosses the intact blood-brain barrier, and the virus has been cultured from the brain, nerve, and cerebrospinal fluid of patients at all stages of disease [4,5]. The imaging findings of AIDS dementia complex are frequently referred to as HIV encephalitis. On magnetic resonance (MR) images, a diffuse cerebral atrophy with symmetric, patchy or confluent areas of T1 and T2 prolongation are seen within the periventricular and deep white matter of patients with AIDS dementia complex. Often, there is a frontal predominance that may include involvement of the genu of the corpus callosum.

HSE can be the result of a primary infection, a reactivation of latent HSV, or a re-infection by a second HSV [6]. About 90% of cases of cases of HSE are caused by HSV-1, with 10% due to HSV-2, the latter usually being the cause of HSE in immunocompromised individuals. Herpes encephalitis is the most common cause of sporadic viral encephalitis with a predilection for temporal lobes. HSV encephalitis is associated with high mortality and in adults typically causes asymmetric bilateral FLAIR / T2WI hyperintensity in the medial temporal lobes, insular cortex and posterior-inferior frontal lobes with relative sparing of basal ganglia and neocortices of which it causes a disseminated infection.

Rotavirus is the primary cause of severe gastroenteritis in children in the winter and spring. The incidence of CNS involvement at rotavirus gastroenteritis is 25.3%. Concomination of CNS involvement to rotavirus infection can represent by different clinical findings. Meningitis, encephalitis, encephalopathy, febrile and afebrile convulsions, hemorrhagic shock, Guillian Barre syndrome and Reye syndrome are the reported neurological entites until now [7]. Ushijima et al [8] established rotavirus both at intestinal and CSF observation, so by this knowledge rotavirus seem to make CNS invasion after a primary intestinal infection. Electrolyte imbalances, destruction of blood brain barrier by fever or encephalopathy and encephalitis are the causes for occurrence of convulsions [7].

Dengue viral infections are very common in Southeast Asia and all 4 serotypes are found. It is known to cause dengue fever and dengue...
haemorrhagic fever. Encephalitis has been well reported and is thought to occur with severe dengue infection leading to liver failure, shock, coagulopathy and leading to cerebral insult. Dengue encephalitis patients usually present with fever, altered sensorium, thrombocytopenia and high antibody titres at the time of admission. Encephalitis is a very common neurological complication with dengue fever and is due to direct neuronal infiltration by the virus. Dengue encephalitis is a well-recognized and common entity with incidence ranging from 0.5 to 6.2% [9]. It may be due to intracranial bleeding due to thrombocytopenia, cerebral hypoperfusion or cerebral edema [10]. Dengue virus and IgM antibody in the CSF has been reported in patients with dengue encephalitis. Japanese encephalitis is the commonest endemic encephalitis in south-east Asia, including India. The diagnosis is commonly based on demonstrating a rising titre of antibodies against JE virus in acute and convalescent sera. Our findings were consistent with the reported distribution of pathological changes. The CNS involvement in JE is in the form of bilateral, often haemorrhagic, predominantly thalamic, putaminal, pontine, as well as cerebellar lesions. The mid-brain, hippocampus, and cerebral cortex too may be involved. Radiologic imaging is crucial in early diagnosis of JE and its differentiation from Herpes encephalitis. The deep grey matter involvement detected on MR is characteristic and diagnostic of JE, though white matter involvement has also been reported.

Autoimmune encephalitis occurs more frequently in immune competent than immunocompromised patients. Most patients with antibody-associated encephalitis and HSE have seizures. In contrast, patients with encephalitis associated to varicella zoster virus (VZV) or Mycobacterium tuberculosis infrequently develop seizures. Psychosis, language dysfunction, autonomic instability and abnormal movements are a hallmark of anti-NMDAR encephalitis. Most patients with infectious encephalitis have fever, but approximately 50% of cases with autoimmune encephalitis present or develop fever during the course of the disease.

**Conclusion:**

In acute viral encephalitis, findings include white matter signal intensity changes, cerebral edema which may progress in later stages to infarction, haemorrhage and brain atrophy. MRI features of viral and autoimmune encephalitis are highly variable according to the offending virus and patient age. Imaging changes must always be evaluated in conjunction with the clinical symptoms, signs and laboratory abnormalities, particularly the presence of a CSF pleocytosis. Unlike bacterial and fungal meningitis in which imaging abnormalities are not specific for a particular agent, many virus infections of the CNS produce MRI abnormalities not seen by any other infection. Autoimmune encephalitis occurs more frequently in immunocompetent than immunocompromised patients.

**References:**


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