Original article:

3 Tesla MRI evaluation of febrile and unconscious patients with CSF analysis correlation in an endemic zone for herpes and Japanese encephalitis

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Abstract:

Introduction: Encephalitis is a medical emergency and is defined as the presence of an inflammatory process in the brain parenchyma associated with clinical evidence of brain dysfunction. MRI plays an important role in patient evaluation and to know the exact etiology in febrile and unconscious patients.

Methods: A prospective study of 50 patients (adults & children) presented in the casualty with fever, altered sensorium or unconsciousness were evaluated on 3 Tesla Siemens MRI. The CSF findings were also correlated along with the MRI findings. Observations were collected in a prescribed Performa for analysis.

Results: Out of 50 patients evaluated, 44 (88%) patients reveal MRI findings s/o viral encephalitis and in remaining six patients, three cases were of SSPE (6%), 1 (2%) each of ADEM, drug induced, electrolyte imbalance and Tubercular meningitis. Out of 44 patients of suspected encephalitis, in 23 (52%) patients findings were of herpes encephalitis and in 15 (34%) patients were of Japanese encephalitis, 3 (7%) cases were diagnosed as HIV encephalitis. 3 (7%) were doubtful for both herpes / Japanese encephalitis.

Conclusions: Viral encephalitis is a neurological emergency with fatal course if remain undiagnosed. 3 Tesla MRI along with characteristic clinical manifestation & routine CSF correlation proved to be useful in detecting the etiology of unconscious and febrile patients especially for the causative agent for encephalitis and helpful in treating the patients successfully.

Key words: Herpes encephalitis, Japanese encephalitis, MRI, CSF, HIV encephalitis.

Introduction:

Encephalitis is a medical emergency and is defined as the presence of an inflammatory process in the brain parenchyma associated with clinical evidence of brain dysfunction. It can be due to various factors such as viral encephalitis which comprises of HSV – 1, VZV, EBV, JE, measles, mumps and other causes including HIV with PML. \(^1\) The diagnosis of viral encephalitis is suspected in the context of a febrile disease accompanied by headache, altered level of consciousness, and symptoms and signs of cerebral dysfunction. After the diagnosis is suspected, the
approach should consist of obtaining a meticulous history and a careful general and neurological examination. \[2\] Diagnosis is made on medical history, examination, Neuroimaging followed by analysis of cerebrospinal fluid for protein and glucose contents, cellular analysis. Magnetic resonance imaging is an essential aspect of evaluation. Lumbar puncture can follow neuroimaging when immediately available, but if this cannot be obtained at the shortest span of time it should be delayed only in the presence of strict contraindications.

MRI on one hand can confidently make the diagnosis of encephalitis and on other hand can rule out several other diseases mimicking encephalitis e.g. stroke, neoplasms, metabolic encephalopathies and other causes. MRI is more sensitive and specific than CT for evaluation of patients with encephalitis. \[3\]

The advantages of MRI include the use of non-ionizing radiation, multiplanar imaging capability, improved contrast of soft tissue, and high anatomical resolution. On the basis of previous research data it should be the imaging technique of choice in determination of encephalitis. It allows detection and treatment of inflammatory processes. MRI also provides valuable information for patient follow up.

Encephalitis should be differentiated from encephalopathy which is defined as a disruption of brain function that is not because of direct structural or inflammatory process. It is mediated via metabolic processes and can be caused by intoxications, drugs, systemic organ dysfunction (e.g liver, pancreas) or systemic infection that spares brain. \[2\]

**Aims and objectives:** Evaluation of unconscious, febrile and altered sensorium patients with 3 T MRI brain and correlation with CSF analysis.

To provide diagnostic and prognostic information on the basis of MRI for appropriate management and counseling of the patient.

**Materials and methods:**
The study was carried out in a tertiary care institute located in western UP region of India, which is also an endemic zone for herpes and Japanese encephalitis. 50 patients (adults & children) presented in the casualty with fever, altered sensorium or unconsciousness were evaluated on 3 Tesla Siemens MRI using sequences like T1, T2WI, FLAIR, Post contrast 3D gradient. New imaging technique eg SWI, DWI with ADC, magnetic transfer ratio (MTR), and MR spectroscopy. The MR findings were interpreted by experienced radiologists. Axial, sagittal and coronal plane were reviewed with basic T1, T2, FLAIR sequences. DWI with ADC mapping enables separation of cytotoxic edema from vasogenic edema and distinguishes recent from old insult which are often difficult on routine T2 and FLAIR images. These changes are earliest to demonstrate abnormality in encephalitis patients. MTR reflects myelin damage, cell destruction or changes in water content.

MR Spectroscopy identifies and quantities concentration of various brain metabolites. Spectroscopy is capable of differentiating normal from pathological brain and provides tissue specificity greater than that of imaging instances.

New MRI imaging techniques can increase sensitivity to small, yet clinically relevant lesions, these techniques may be useful for imaging protocols of patients with suspicion of encephalitis. \[2\]

These patients then underwent lumbar puncture for CSF study calculating the values of TLC (total leukocytes count) and DLC (polymorphs, lymphocytes) and amount of sugar in the
CSF. Antibodies evaluation in serum & CSF is not done due to non availability in the institute. The patients were followed up clinically and final status after completion of treatment was evaluated.

Results:
In this study we evaluated 50 patients who presented with fever, altered sensorium or unconsciousness. The symptoms were of short duration (less than a month period). Out of 50 patients evaluated, 44 (88%) patients reveal MRI findings s/o viral encephalitis and in remaining six patients, three cases were of SSPE (6%), 1 (2%) each of ADEM, drug induced electrolyte imbalance and Tubercular meningitis. Out of 44 patients of suspected encephalitis, in 23 (52%) patients findings were of herpes encephalitis and in 15 (34%) patients were of Japanese encephalitis, 3 (7%) cases were diagnosed as HIV encephalitis. 3 (7%) were doubtful for both herpes / Japanese encephalitis.

CSF correlation reveals the findings of 22 herpes encephalitis were same as that of viral encephalitis with colorless, alkaline CSF fluid, TLC were between 5 – 200 cells and they were predominantly lymphocytes, except for 1 patient in which CSF was granular, neutral PH, TLC were raised (1190) and cells were predominantly polymorphs with few choroidal cells. CSF findings in Japanese encephalitis in 13 patients were of clear alkaline CSF fluid, with TLC count between 40 to 400 and cells were predominantly lymphocytes. 2 patients present with acidic CSF with similar other findings. CSF findings in 3 cases of SSPE colorless, alkaline fluid with TLC count of 5 cells and cells were all lymphocytes. These patients were having positive history of measles.

Discussion:
“Unconscious patient presenting in casualty department always present a diagnostic dilemma. In today’s era of technology, the role of MRI especially in suspected cases of neurological cause is indispensible”

In our study we had maximum number of herpes encephalitis patients, followed by Japanese encephalitis and few cases of other encephalitis. The spectrum of brain involvement and the prognosis are dependent mainly on the specific pathogen and the immunological state of the host. Although specific therapy is limited to only few viral agents, correct immediate diagnosis and introduction of symptomatic and specific therapy has a dramatic influence upon survival and reduces the extent of permanent brain injury in survivors. In Herpes simplex encephalitis there was predominant involvement of bilateral temporal lobes with cytotoxic edema in bilateral basal ganglia, thalami, insular & medial temporal cortex and cingulate gyri. These areas appeared hypointense on T1W mages, hyperintense on long TR images with evidence of restricted diffusion (fig 1). Two patients present with edema in hippocampus, parahippocampus, and fronto temporal gyri. Post contrast images reveals minimal post contrast enhancement.

The MRI is much more sensitive in detecting early changes. [3, 4] Involvement of cingulate gyrus and contra lateral temporal lobe is highly suggestive of herpes encephalitis. Typical early findings include gyral edema on T1-weighted (T1WI) imaging and high signal intensity in the temporal lobe or cingulate gyrus on T2WI, FLAIR and later hemorrhage. High signal on DWI are additional findings as described by other authors. [5, 6] MR spectroscopy in acute lesions reveals metabolic changes in relation to neuronal
death such as a decrease of N-acetyl aspartate (NAA) signal. Resultant gliosis is reflected as an increase in inositol and creatine resonances. The reinstitution of a normal spectrum over time could then potentially be used as a marker of treatment efficacy.\[^{7, 8}\]

This zone is endemic for Japanese encephalitis as we had second highest number of cases. In most of our patients the characteristic findings were areas of altered signal intensity symmetrically involving the bilateral thalami sparing the medial temporal lobes. These areas were appearing hypointense on T1-weighted and hyperintense on T2-weighted and FLAIR images with restricted diffusion. (Fig 2, 3)

The MR imaging and CT findings of JE have been described as bilateral thalamic, substantia nigra, basal ganglia, brain stem, cerebellum, cerebral cortical, and white matter lesions. Bilateral T2 hyperintense and T1 hypointense to isointense thalamic lesions, especially hemorrhagic have been described as characteristic in an appropriate clinical setting. These lesions differentiate it from Herpes simplex encephalitis (HSE) that characteristically shows bilateral or unilateral T2 hyperintense lesions in the temporal lobes with or without haemorrhage and contrast enhancement.\[^{9}\] DWI reveals restricted diffusion appearing hyperintense in very early course of the disease process when conventional sequences may be normal.

In our study we had three patient having HIV encephalitis. All three patients had positive serological test for HIV. These patients had non specific white matter hyperintensities involving periventricular and subcortical white matter extending to subcortical U fibers as well. (Fig 4a and 4b)MRI usually shows atrophy and non-specific white matter changes. MRS detects early decreases in levels of NAA and increases in choline-containing phospholipids (Cho) levels, even before abnormalities are detected by MRI and prior to clinical symptoms. Later, with cognitive dysfunction, further reductions in NAA and increases in Cho levels may be seen.\[^{10}\] MRS can serve to monitor the efficacy of antiretroviral therapy and may even be used to predict the responsiveness to drug therapy. In the later stages of AIDS, the most common diseases affecting the brain parenchyma are secondary to opportunistic infection or malignancy and are predominantly focal. Neuroimaging is an important diagnostic tool for opportunistic infections. Toxoplasmosis (ring enhancing mass(es) in basal ganglia), cryptococcosis (gelatinous pseudocysts ), meningoencephalitis, vasculitis, infarction, cytomegalovirus (CMV)-encephalitis (diffuse white matter hyperintensities), ventriculitis (ependymal enhancement), progressive multifocal leucoencephalopathy (PML, white matter hyperintensities which usually do not enhance), lymphoma (solitary or multifocal solid or ring-enhancing lesions either in deep grey and white matter or less frequent in subcortical areas).\[^{11}\] MRS may be able to distinguish between these different space occupying lesions based on their chemical profiles.

In our study we had three patients of subacute sclerosing panencephalitis. All the three patients had positive history of measles. There were areas of altered signal intensity involving b/l gangliocapsular region, corpus callosum, and right parieto – occipital lobe appearing hyperintense on long TR images, hypointense on T1WI with restricted diffusion. On post contrast images there was no significant enhancement of the lesions. (Fig 5).

Subacute sclerosing panencephalitis is a progressive neurologic disorder that is considered to be caused by...
persistent measles virus. Previous MR imaging studies on sub acute sclerosing panencephalitis have reported typical bilateral asymmetric hyperintense lesions in the parietal and temporal lobes in the acute stage. In time, lesions become more prominent, and periventricular white matter, corpus callosum, and basal ganglia can be involved. Later, encephalomalacia and atrophy develops.\textsuperscript{[12]}

There was one patient in our study which was diagnosed as ADEM (acute disseminated encephalomyelitis). The patient had preceding history of upper respiratory tract viral illness two weeks prior to episode of altered sensorium. On MRI examination there were areas of altered signal intensity in left fronto – parietal lobe, left & right parietal lobe appearing hypointense on T1WI, hyperintense on T2WI and FLAIR images with restricted diffusion. (Fig 6) MRI is more sensitive than CT scan and an essential diagnostic tool. T2WI and FLAIR scans present multifocal, usually bilateral, but asymmetric and large hyperintense lesions, involving peripheral white and grey matter. They do not usually involve the callososseptal interface. Contrast enhanced T1-weighted images may show ring-enhancing lesions. Cranial nerves may enhance. DWI is variable. On MRS, NAA is transiently low and choline is normal.\textsuperscript{[13]}

Our study has limitation, that the serological test for diagnosing the cause of viral encephalitis were not performed due to non availability in the institution, however careful history, clinical examination associated with 3 tesla MRI findings leads us to correct diagnosis of etiological cause in majority of febrile patients with altered sensorium/ unconsciousness.

**Conclusion:**
Viral encephalitis is a neurological emergency with fatal course if remain undiagnosed. 3 Tesla MRI along with characteristic clinical manifestation & routine CSF correlation proved to be useful in detecting the etiology of unconscious and febrile patients especially for the causative agent for encephalitis and helpful in treating the patients successfully.

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**Fig 1. HERPES ENCEPHALITIS**

Herpes encephalitis:- T2W, DW, ADC, and FLAIR images – areas of altered signal intensity involving bilateral medial temporal lobes (lt>rt), appearing hyperintense on T2W, FLAIR images with restricted diffusion.
Fig 2. Japanese Encephalitis

Japanese encephalitis: T2, FLAIR, T1W, dw images – hyperintensities on long TR images, hypointense on T1, with restricted diffusion involving bilateral thalami, gangliocapsular region

Fig 3. Japanese Encephalitis

JAPANESE ENCEPHALITIS - : sequential FLAIR images revealing hyperintense signals involving bilateral thalami (lt>rt)

Fig 4a and 4b. HIV Encephalitis

Focal non enhancing areas in right periventricular deep white matter and right occipital subcortical white matter with involvement of subcortical U – fibres in right occipital region. Pt had positive h/o HIV.

Fig 5 SubacuteSclerosingPanencephalitis

SSPE : - T2W, FLAIR, T1W &DW images – areas of altered signal intensity involving b/l gangliocapsular region, corpus callosum, and right parieto – occipital lobe appearing hyperintense on long TR images, hypointense on T1WI with restricted diffusion.

Fig 6 ADEM

Areas of altered signal intensity in left fronto – parietal lobe, left & right parietal lobe appearing hypointense on T1WI, hyperintense on T2WI and FLAIR images with restricted diffusion.

References:


