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CLINICO BIOCHEMICAL CORRELATION WITH MRI FINDINGS OF SUSPECTED CASES OF MENINGO-ENCEPHALITIS

Radiodiagnosis

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ABSTRACT

BACKGROUND: Encephalitis is a fatal disease syndrome, where patient usually presents with pyrexia and neurological derangement. This is acute emergency which requires prompt investigations and urgent vigorous management to prevent irreversible neurological damage, particularly when there is rapid deterioration.

AIMS AND OBJECTIVES: To study the spectrum of MRI findings, sensitivity of MR imaging and CSF evaluation and correlation between CSF findings and MRI findings in suspected cases of meningoencephalitis.

MATERIAL AND METHODS: A prospective randomised hospital based study was conducted on 43 patients between 6 months to 80 years of age, irrespective of sex, undergone MR examination in Geetanjali Medical College and Hospital, Udaipur, Rajasthan and CSF examination during January 2016 to June 2017. Meningoencephalitis was typically identified as hyperintensities on T2 and FLAIR sequences, showing restriction on DWI which may show contrast enhancement.

RESULTS: The mean age of the study population was 37.02 ± 15.25 SD. 28 (65%) showed abnormal CSF findings. Findings suggestive of viral meningitis were most common (37%), followed by normal (35%), tubercular (21%) and pyogenic (7%). T1 MR sequences showed isointense signals in (86%) cases, T2 and FLAIR sequences showed hyperintense signals in (63%) and (72%), respectively. Most common clinical symptom was pyrexia with alt senorium (23%) and generalized weakness (23%) patients. Most common site of involvement was temporal lobe (33%) and diffuse bilateral cerebral hemisphere (32%). Edema was present in 70% and haemorrhage in 9% cases.

CONCLUSION: Apart from routine tests, brain imaging and CSF evaluation are most relevant and mandatory tests to diagnose encephalitis. Accurate and early diagnosis of meningoencephalitis is crucial for effective treatment. MRI is highly sensitive and specific in identifying the underlying etiopathogenesis in meningoencephalitis, because of its high spatial resolution, excellent soft tissue contrast multipanar imaging capability with lack of ionizing radiation as an additional benefit.

KEYWORDS

Encephalitis, Etiopathogenesis, Meningoencephalitis, MRI

INTRODUCTION

Encephalitis is a fatal disease syndrome, where patient usually presents with pyrexia and neurological derangement. This is acute emergency which requires prompt investigations and urgent vigorous management to prevent irreversible neurological damage, particularly when there is rapid deterioration. Apart from routine tests, brain imaging and CSF evaluation are most relevant and mandatory tests to diagnose encephalitis.

Encephalitis is defined by the presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction1. Findings in patients with encephalitis include acute cognitive dysfunction, behavioral changes, focal neurologic signs and seizures. In most cases, there is some concomitant meningeal inflammation, in addition to the encephalitic component (a condition commonly referred to as "meningoencephalitis"). It is important to try to distinguish between infectious encephalitis and postinfectious or postimmunization encephalitis or encephalomyelitis.

Acute Encephalitis Syndrome (AES) is a growing problem in India, incidence being 0.42/ lac population/year. The first major outbreak was in West Bengal in 1973 involving 700 cases and over 300 deaths. Subsequent serological studies identified the Japanese Encephalitis (JE) virus as the cause[2]. Between 1978 and 2007 over 100,000 cases of AES with a case fatality rate (CFR) of almost 33% were reported from 13 different states. It was widely presumed that JE was the predominant aetiological agent in these outbreaks[3].

While HIV has not been listed as it usually causes a type of subacute encephalitis it is important in so far as its associated immunosu ppression predisposes the individual to viral encephalitis caused by various viruses like HSV-1, HSV-2, VZV and cytomegalovirus (CMV). The frequency and distribution of these viruses clearly varies according to the geographical region, with large differences seen between Europe, Asia, and the USA[6].

Acute encephalitis is a medical emergency which is relatively uncommon but potentially devastating disease syndrome. Clinical involvement of central nervous system (CNS) is an unusual manifestation of human viral infection. It has an abrupt onset, with rapid progression over a few days. Without definite treatment neurological status may worsen which can lead to permanent damage or even may lead to death. To prevent this prompt and early diagnosis is necessary[5].

Magnetic resonance imaging (MRI) is more sensitive and specific than CT for the evaluation of viral encephalitis[9]. The advantages of MRI include the use of non-ionizing radiation, multiplanar imaging capability, improved contrast of soft tissue, and high anatomical resolution. It allows early detection and treatment of inflammatory processes. MRI also provides valuable information, for patient follow-up. However, in practical terms many patients with suspicion of encephalitis often undergo CT scanning before neurological consultation.

A typical MRI protocol consists of routine T1 and T2 spin-echo sequences and a fluid-attenuation inversion recovery (FLAIR) sequence which is considered extremely sensitive in detecting subtle changes in the early stages of an acute condition. Gradient echo imaging, with its superior magnetic susceptibility is also useful in detecting small areas of haemorrhage. New MR imaging techniques are being applied to the study of various brain diseases. These technologies include procedures that can increase sensitivity to small, yet clinically relevant lesions, these techniques may be useful for imaging protocols of patients with suspicion of encephalitis.

Diffusion-weighted MRI (DWI) enables separation of cytotoxic from vasogenic oedema and distinguishes recent from old insult which can often be difficult on routine T2 and FLAIR imaging. Low magnetization transfer ratio (MTR) reflects myelin damage cell destruction or changes in water content. Magnetic resonance spectroscopy (MRS) 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. Functional MRI (FMRI) uses very rapid scanning techniques that in theory can demonstrate alterations in blood oxygenation.

PET gold standard in acquiring functional imaging data, remains a complex, costly and not readily available technique. In summary,

structural information is provided by CT scan and MRI while functional and metabolic data are provided by MRS, FMRI, SPECT and PET.

Herpes simplex encephalitis: CT obtained early is often normal or subtly abnormal. Low attenuation, mild mass effect in temporal lobes and insula, haemorrhage and enhancement are late features. Follow-up scans 1-2 weeks after disease onset demonstrate progressively more widespread abnormalities with the involvement of contra lateral temporal lobe, insula and cingulate gyri. Contrast enhancement and changes of subacute haemorrhage may become readily apparent. Involvement of cingulate gyrus and contra lateral temporal lobe is highly suggestive of herpes encephalitis. Typical early findings include gyral oedema on T1-weighted (T1WI) imaging and high signal intensity in the temporal lobe or cingulate gyrus on T2WI, FLAIR and DWI and later haemorrhage. Hypointense on T1, hyperintense on T2WI, FLAIR, high signal on DWI are additional findings[7].

In paraneoplastic limbic encephalitis MRI FLAIR and DWI depict bilateral involvement of the medial temporal lobes and multifocal involvement of the brain. T2-weighted turbo spin-echo images fail to show changes[8].

In patients with neurological derangement, imaging and CSF evaluation are most commonly asked investigations. Evaluation of CSF samples is essential for all patients with encephalitis unless contraindicated. In instances in which CSF specimens are not available, the likely etiology of the encephalitis should be based on epidemiology, clinical features, and results of other diagnostic studies. In patients with viral encephalitis.CSF analysis typically reveals a mild mononuclear pleocytosis, although polymorphonuclear cell predominance may initially be seen if the sample is obtained early in the course of illness persistent neutrophilic pleocytosis has been observed in patients with West Nile virus encephalitis. CSF protein concentration is generally mildly or moderately elevated. Patients may have significant numbers of RBCs in the CSF, as a result of the development of hemorrhagic encephalitis.

A decreased CSF glucose concentration is unusual in viral encephalitis and suggests disease caused by bacteria (e.g., L. monocytogenes and M. tuberculosis), fungi, or protozoae (e.g., Naegleria species). Up to 10% of patients with viral encephalitis can have completely normal CSF findings.

The CSF findings in patients with ADEM are generally similar to those seen in patients with viral encephalitis (that is lymphocytic pleocytosis, elevated protein concentration, and normal glucose concentration). Pleocytosis in ADEM tends to be less marked than in acute infectious encephalitis, and it may be absent differentiating it from encephalitis.

AIMS AND OBJECTIVES

- To study the spectrum of MRI findings in cases of meningoencephalitis.
- To evaluate the sensitivity of MR imaging and CSF evaluation in suspected cases of meningoencephalitis.

MATERIAL AND METHODS

A prospective randomised hospital based observational / correlational study was conducted on 43 patients between 6 months-80 years of age, irrespective of sex, undergone MR examination in Geetanjali Medical College and Hospital, Udaipur, Rajasthan and CSF examination during January 2016 to June 2017. Proper consent for the study was taken.

Subjects were excluded on following criteria. Who had contraindications to MR evaluation-patients with claustrophobia, metallic implants etc. Patients who had history of hypersensitivity to intravenous contrast agents or deranged renal function test (serum creatinine <1.5 mg/dl). Patients who were unable to restrain movement during the course of examination even after appropriate sedation and patients in whom CSF collection was contraindicated, like raised ICT.
In patients undergoing MR examination, history of chief complaints with duration was recorded. Different MR sequence findings were recorded. CSF examination details like TLC, lymphocytes, neutrophils, sugar and protein were noted.

Technique of MRI Examination:

MRI was conducted on 1.5 Tesla MAGNATOM AVANTO (SIEMENS), at Geetanjali Medical College and Hospital, Udaipur. Patient was placed in supine position within a head coil (Quadrature coil) Localiser taken centering at nasion.

43 patients undergoing MR examination, showing imaging findings suggestive of meningoencephalitis were evaluated. Various MRI sequences like T1WI (T1 weighted imaging), T2WI (T2 weighted imaging), FLAIR (Fluid attenuated inversion recovery sequence), DWI (Diffusion weighted imaging), and Contrast study- AxT1, SagT1, CorT1 were studied. Meningoencephalitis was typically identified as hyperintensities on T2 and FLAIR sequences, showing restriction on DWI which may show contrast enhancement. The pattern of anatomical distribution was noted; as different viral infections have typical anatomical location.

RESULTS:

Majority of the patients i.e., 21 (49%) belonged to 21-50 age group followed by 18 (42%) in 6 months-20 yrs and 4 (9%) in >50 age group. The mean age of the study population was 37.02 ± 15.25 yrs. The most common chief complaint encountered was pyrexia with altered sensorium (22%) followed by pyrexia with seizures (21%), followed by generalized weakness (21%), fever with chills(11%), fever with headache (9%), loss of consciousness (8%), and others (8%) which includes abnormal body movement, slurring of speech, facial deviation and pyrexia only. Out of 43 patients, 28(65%) showed abnormal CSF findings. Findings suggestive of viral meningitis were most common (37%), followed by normal (35%), tubercular (21%) and pyogenic (7%). (Table 1).

Table 1: Diagnosis based on CSF findings

Diagnosis based on CSF findings		
Diagnosis	Frequency	Percentage
Normal	15	35.0
Viral	16	37.0
Tubercular	9	21.0
Pyogenic	3	7.0
Total	43	100.0

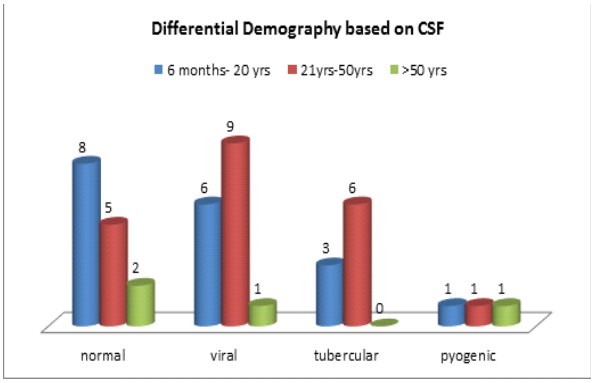
T1 MR sequences showed isointense signals in (86%) cases, T2 and FLAIR sequences showed hyperintense signals in (63%) and (72%), respectively. (Table 2).

Table 2: Different MR sequences

	T1			T2			Flair		
	Iso	Hypo	Hyper	Iso	Hypo	Hyper	Iso	Hypo	Hyper
Number	37	5	1	15	1	27	11	1	31
%	86	12	2	35	2	63	26	2	72

In our study on the basis of CSF findings 16 out of 43 patients were suggestive of viral meningitis (meningoencephalitis), in which mean age was 32.76 ± 12.90 yrs. (Graph 1).

Graph 1: Differential Demography



16 patients of viral meningitis (meningoencephalitis) were evaluated Out of 16 patients (53%) were males and (47%) were females. The most common clinical symptom was pyrexia with alt senorium (23%) and generalized weakness (23%) patients. (Table 3).

Table 3: Differential Chief Complaints

Chief complaint	Normal	Viral	Tubercular	Pyogenic
Pyrexia with Alt sensorium	33.5%	23%	6%	50%
Pyrexia with seizures	11%	3%	53%	0%
LOC	0%	7%	12%	25%
Fever with headache	0%	17%	0%	25%
Generalized weakness	33.5%	23%	18%	0%
Fever with chills	22%	10%	12%	0%
Others	0%	17%	0%	0%
Male	47%	53%	56%	67%
Female	53%	47%	44%	33%

16 patients of viral meningitis (meningoencephalitis) were evaluated. The most common site of involvement was temporal lobe (33%) followed by diffuse bilateral cerebral hemisphere (32%). Edema was present in 70% and haemorrhage was present in 9% cases. (Table 4).

Table 4: Differential MRI findings.

Anatomical location	Normal	Viral	Tubercular	Pyogenic
Diffuse bilateral	19%	32%	55%	100%
Temporal lobe	16%	33%	15%	0%
Frontal lobe	9%	10%	25%	0%
Basal ganglia and thalamus	20%	5%	0%	0%
Corpus callosum	0%	8%	0%	0%
Hippocampus	28%	7%	0%	0%
Others	8%	5%	0%	0%
Edema	56%	81%	60%	33%
Haemorrhage	0%	8%	20%	50%

DISCUSSION

Most common symptom is pyrexia with altered sensorium (23%), followed by generalized weakness (23%), pyrexia with seizures (21%) fever with chills (11%), fever with headache (9%), loss of consciousness (8%), and others (8%) which includes abnormal body movement, slurring of speech, facial deviation and pyrexia only. Most of the patients i.e., 33 (77%) had presented within 1 to 5 days of duration of illness which suggests acute presentation of disease. Among the chief complaints pyrexia with altered sensorium showed significant high positive correlation with the diagnosis of AME ($p < 0.001$).

Kennedy PGE[12], in his article on Herpes Simplex Encephalitis stated that the index of suspicion of HSE should always be high for a patient presenting with the typical features of encephalitis such as fever, headache, confusion, and clouding of consciousness. More specifically, HSE is typically associated with a constellation of fronto temporal features with aphasia or mutism, personality change, and focal or generalised seizures, and in some cases coma. Meningism, focal motor weakness, and occasionally brainstem encephalitis, which may be recurrent, have also been described[4].

Similar study was done by I. Steinera[14] on viral encephalitis: they stated that 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. These may consist of abnormalities that can be categorized into four: cognitive dysfunction (acute memory disturbances), behavioural changes (disorientation, hallucinations, psychosis, personality changes, agitation), focal neurological abnormalities (such as anosmia, dysphasia, hemiparesis, hemianopia etc.) and seizures.[14]

MR revealed diffuse bilateral cerebral hemispheric involvement as most common presentation (39%), followed by temporal lobe (23%), hippocampus (7%), followed by basal ganglia and thalamus, corpus callosum and others (7% each), and frontal lobe (5%). DWI showed restriction in (47%) cases, out of which (26%) were patchy restriction, and homogenous restriction in (21%) cases. T1 MR sequences showed isointense signals in (86%) cases, T2 and FLAIR sequences showed hyperintense signals in (63%) and (72%), respectively. Post contrast (gadolinium) T1 sequences showed no enhancement in (67%) cases. Edema was seen in (44%) cases. Hemorrhage was seen only in (9%) cases. Ventricles were dilated in (60%) cases, however age related ventriculomegaly was confounding factor; predominantly in >50 yrs age group. Above observations suggest, among all MR sequences; T2, FLAIR and DWI sequences are more sensitive and specific to diagnose AME.

Kennedy PGE[12], in their article on Herpes Simplex Encephalitis suggested that the diagnosis of HSE is usually established from the combination of the clinical and investigative features. Magnetic resonance imaging (MRI) provides the most sensitive method of detecting early lesions and is the imaging of choice in HSE[12]; if MRI is available it should be the first diagnostic step after clinical assessment. Cranial MRI may show evidence of focal oedema in the medial region of the temporal and orbital surface of the frontal lobes, insular cortex, and angular gyrus[9]. Meningeal and gyral enhancement after contrast (DTPA) administration has also been reported[11]. However, the MRI may occasionally be normal in HSE. Computed tomography may be normal for the first few days after the onset of symptoms[10]. When computed tomography is abnormal it usually shows reduced attenuation in one or both frontal or temporal lobes and sometimes areas of hyperintensity representing small haemorrhages[9] and with midline shift in about 50% of cases in one retrospective study[12].

Allan R. Tunkel[13] in another study showed CT and MRI are most frequently used to evaluate patients with encephalitis, with MRI being more sensitive and specific. These studies may also be useful in excluding other conditions with a clinical presentation similar to that of encephalitis. CT (with and without intravenous contrast administration) should only be used if MRI is unavailable, impractical, or cannot be performed.

In patients with herpes simplex encephalitis, there may be significant edema and hemorrhage in the temporal lobes, as well as hypodense areas on T1-weighted images and non homogeneous contrast enhancement; bilateral temporal lobe involvement is nearly pathognomonic for herpes simplex encephalitis, but this is a late development. More than 90% of patients with herpes simplex encephalitis documented by CSF study will have abnormalities seen on MRI[16].

In cases of suspected ADEM, MRI is the diagnostic neuroimaging procedure of choice, generally revealing multiple focal or confluent areas of signal abnormality in the subcortical white matter and, sometimes, subcortical gray matter on T2 and FLAIR sequences[15].

In our study out of 43 patients, 28 (65%) showed abnormal CSF findings. Findings suggestive of viral meningitis were most common (37%), followed by normal (35%), tubercular (21%) and pyogenic (7%). The most common clinical symptom was pyrexia with altered sensorium (23%) patients. Diffuse bilateral cerebral hemispheric involvement as most common presentation (39%), followed by temporal lobe (23%). Edema was present in 44% and haemorrhage was present in 9% cases. CSF pleocytosis was present in (68%) and raised CSF protein was demonstrated in 64% patients, while low sugar was seen in 20% cases. Kennedy PGE12 reported similar findings.

CONCLUSION

In patients of pyrexia with neurological derangement MR imaging plays a pivotal role in the diagnosis of meningoencephalitis. Accurate and early diagnosis of meningoencephalitis is crucial for effective treatment. MRI has been shown to be highly sensitive and specific in identifying the underlying etiopathogenesis in meningoencephalitis, because of its high spatial resolution, excellent inherent soft tissue contrast multipanar imaging capability with lack of ionizing radiation as an additional benefit. Conventional CSF study has significant positive correlation in diagnosis of meningoencephalitis. MRI evaluation plays a significant role in the diagnosis of meningoencephalitis along with CSF study and relevant clinical history.

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