PREDOMINANT AREAS OF BRAIN INVOLVED IN CHILDREN (0 TO 15 YRS.) WITH JAPANESE ENCEPHALITIS BY MRI STUDY

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ABSTRACT

BACKGROUND

Japanese Encephalitis (JE) caused by Flavivirus is the most common cause of endemic encephalitis. It usually affects the children and is a life-threatening disease having high morbidity and mortality.

The aim of the study was to identify the pattern of involvement of brain in confirmed cases of Japanese encephalitis.

MATERIALS AND METHODS

We had done an institution based observational study in our Dept. of Radio-diagnosis, NBMC & H. 19 children suffering from Japanese encephalitis confirmed by IgM ELISA underwent MRI of Brain and frequency of involvement of different sites of brain was evaluated.

RESULTS

Based on characteristic MRI findings, different areas of brain involved were bilateral thalami, basal ganglia, cerebellum, brainstem, temporal lobe etc. of which thalamic involvement (84%) was most common.

CONCLUSION

After the data collection, we have come to a conclusion that among the different sites of brain involved in JE, thalamus is most frequently involved.

KEYWORDS

Encephalitis, Japanese Encephalitis, Basal Ganglia, Thalamus, IgM ELISA.

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BACKGROUND

Encephalitis is a life-threatening inflammatory disease of the brain which may occur at any age. There are various factors causing encephalitis, viral agents being one of the most common cause. Herpes simplex encephalitis (HSE) is the most common cause of sporadic encephalitis worldwide, while Arboviruses are the most common cause of endemic encephalitis.[1]

The most common type of Arbovirus causing encephalitis is Japanese Encephalitis Virus (JEV). Arbovirus (arthropod- borne virus) are virus of vertebrates, biologically transmitted through hematogenous route by insect vector. Arbovirus are classified according to their physical and chemical nature in to taxonomical families named, Toga, Flavi, Bunya, Reo and Rhabdo virus. Arbovirus are worldwide in distribution but are more common in the tropical rather than the temperate zones. Some arboviruses known to be prevalent in India are Group A (Alpha virus), Sindbis, Chikungunya, Group B (flavi virus), Dengue, KFD, JE, West Nile virus.

JEV is a single stranded RNA virus. Japanese encephalitis serocomplex consist of 10 genetically and antigenically related viruses which belongs to the family Flaviviridae.[2]

The first case of Japanese encephalitis (JE) was documented in 1871 in Japan. The annual incidence of clinical disease varies both across and within endemic countries, ranging from <1 to >10 per 100 000 population or higher during outbreaks. It is the most common endemic encephalitis in South East Asia.

JE is transmitted by Culex mosquitoes, (Culex tritaeniorhynchus), a rural mosquito that breeds in rice fields, shallow ditches and pools.

Among these, C. tritaeniorhynchus and vishnui have been implicated as the most important vector in south India. Pigs and wild birds are reservoir for the virus.[3,4] Basic cycle of transmission is:

Pig-Mosquito-Pig.

The Ardeid bird-Mosquito- Ardeid bird.

Man is an incidental dead-end host. There is no person to person transmission.

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JE primarily affects children.[5] Most adults in endemic countries have natural immunity after childhood infection, but individuals of any age may be affected.

Clinical features vary from mild fever and headache to severe clinical illness. Focal reflex loss behavioural abnormalities are common. Severe disease is characterized by rapid onset of high fever, headache, neck stiffness, disorientation, coma, seizures, spastic paralysis and ultimately death. Movement disorders such as parkinsonian symptoms and akinetic-rigid status are present in 26.7% of JE patients and are the most frequently recognized neurological sequelae.[6]

Early diagnosis is crucial for decreasing mortality and morbidity rates. Diagnosis is based on blood counts, serum biochemistry, CSF studies and Anti JEV antibody IgM ELISA. Detection of Japanese encephalitis virus (JEV)-specific IgM by IgM-capture ELISA is standard method for serological diagnosis. The detection of JEV-specific IgM in CSF by IgM-capture ELISA is a reliable laboratory diagnostic method for confirmation of JE throughout the disease period, while the detection of IgM in serum samples is a reliable method on day 9 or later.[7]

Prevention can be done by vaccination and control measures for mosquitos. Currently three types of vaccines are available:

(i) Mouse Brain Derived, Purified, inactivated JE vaccine which is based on either Nakayama or Beijing strains of JE virus and produced in several Asian countries.
(ii) The cell culture desired, inactivated JE vaccine based on Beijing P-3 strain.
(iii) Cell culture desired, live attenuated vaccine based on SA-14-14-2 strain of JE virus[8]

The mouse brain desired, inactivated vaccine has been used successfully to reduce the incidents of JE in a number of countries.

Treatment for JE is mainly supportive. The case-fatality rate can be as high as 30% among those with disease symptoms.[9]

However, 25-40% of survivors may left with various neurological complications.[10]

Role of imaging methods in the management of encephalitis remains limited to suggestion of diagnosis. Magnetic resonance imaging (MRI) is widely accepted as a sensitive method for detection of early changes in encephalitis.

JE frequently involve bilateral thalami. Midbrain, pons, cerebellum, basal ganglia, cerebral cortex and spinal cord. Later in the disease course haemorrhagic lesions, hydrocephalus, atrophy may be seen.

In the region of North Bengal there are high number of cases presenting with Acute encephalitis syndrome of which significant number of cases are found to be due JEV. Here also JE is more common in Children than in adults.

Aims and Objectives of Study

This observational study was carried out with the aim:

- To evaluate the role of MRI in JE.
- To identify the pattern of brain involvement in 0-15 years age group children who have suffered from Japanese encephalitis.

MATERIALS AND METHODS

Inclusion Criteria

0-15 years age group children who have suffered from Japanese encephalitis confirmed by IgM ELISA.

Exclusion Criteria

Patient having MRI features of Encephalitis but negative for IgM ELISA.

- Children who could not be sedated
- Children who have metallic implants not compatible with MRI.
- Parents did not give consent inspite of proper explanation.

This study was carried out in the Department of Radio-diagnosis, NBMC & H for a time period of two years among 19 children of 0-15 years age group who have suffered from Japanese encephalitis confirmed by IgM ELISA. It was institution based observational study, purposive sampling was done, and cross-sectional study design was applied.

These patients were referred from department of Paediatrics for MRI study.

Demographic details of patients including age, gender, and residence were noted. All the patients had undergone clinical assessment, Blood count and CSF studies. MR imaging features of patients suffered from JE confirmed by IgM ELISA were studied.

- We had used the MRI machine-1.5 tesla m/s GE make, BRIVO model
- Only non-contrast MRI scans were done

The MRI scans were performed in acute phase within two to three days of admission i.e. 2 to 7 days of onset of symptoms.

In everyday clinical practice at our center the scans are performed using shortened protocol, which in majority of cases, allow us to obtain diagnostic images free from motion artifacts associated with the child awakening.

We used Following Sequences-

- DWI (Diffusion Weighted Images)
- coronal T2-weighted images,
- axial T1-weighted images,
- axial GRE/T2*-weighted images,
- sagittal T2-weighted images,
- axial T2-weighted images,
- axial FLAIR images

Involved sites of brain is best seen in Diffusion weighted MR imaging (DWI) which appears white (Restricted diffusion). Hyperintensity is also seen in T2WI and FLAIR MR Images. These findings are due to cytotoxic oedema in involved part of brain.

ELISA test for JE was done in CSF, serum or both. ELISA plates (96 well) were used. It includes serum sampling, positive control, negative control & blank. It was then incubated for 1 hr at 37° c temperature. After completing the test procedure according to kit manual, optical density is read by automatic ELISA reader.

No follow up scan was done in our study.

RESULTS

In our study we included 19 patients with Japanese encephalitis admitted in the year 2016 and 2017 which was confirmed by anti JEV antibody ELISA. 11 patients were male and rest ware female. Brain MRI was performed in early course of illness. Thalamic involvement was present in 16 patients (84.21%), cerebellum in 5 patients (26.31%), midbrain in 4 cases (21.05%), pons 4(21.05%) Basal Ganglia involvement was in 4 patients (21.05%), temporal involvement was present in 3(15.78%), insular 2(10.52%) cortical involvement in 3 children (15.78%).

Restriction was noted in DWI images. T2/FLAIR images showed hyper intensity but less marked than DWI images. No significant changes were noted in T1WI images however some T1WI images showed faint hyperintensity denoting haemorrhage. DWI and ADC correlation was not done.

Sex	No. of Patients
Male	11
Female	8

Table 1. Distribution of Patients According to Sex

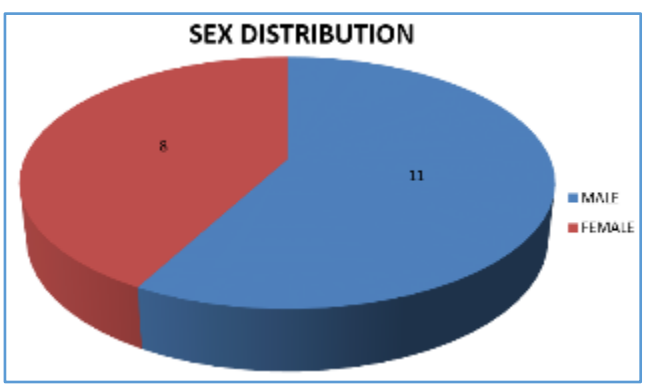

Figure 1. Showing Distribution of Patients According to Sex

Clinical features	
Clinical Variable	**Number**
Fever and altered sensorium	19
GCS score at admission	
GCS <13	5
GCS <8	3
Neck stiffness	3
Seizure	10
Status epilepticus	8
Behavioural abnormality	12
Focal deficit	13
Hemiparesis /Quadriparesis	14
Focal reflex loss	15
Movement disorder	

Table 2. Showing Different Clinical Features

MRI Features (Areas Involved)	N=50
Thalamus	16
Cerebellum	5
Basal Ganglia	4
Midbrain	4
Pons	4
Temporal lobe	3
Cerebral cortex	3
Insular cortex	2

Table 3. Showing Distribution of Lesions According to Different Sites of Brain Involved

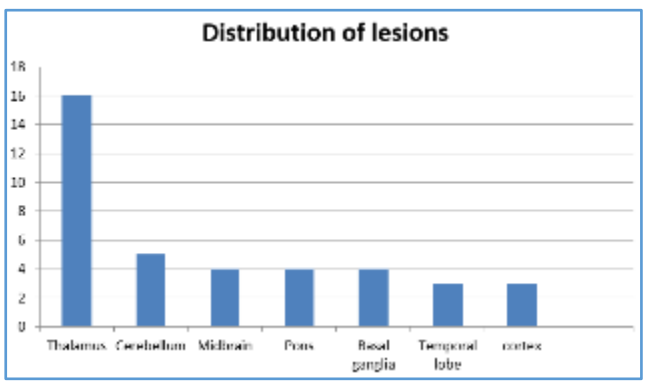

Figure 2. Showing Distribution of Lesions DWI (Diffusion Weighted Images)

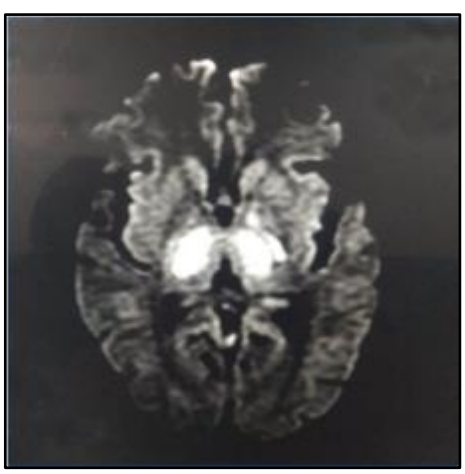

Figure 3. Restricted Diffusion in Bilateral Thalami

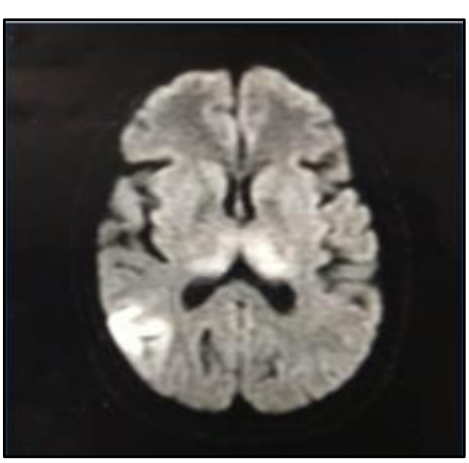

Figure 4. Restricted Diffusion Thalami and in Right Temporal Lobe

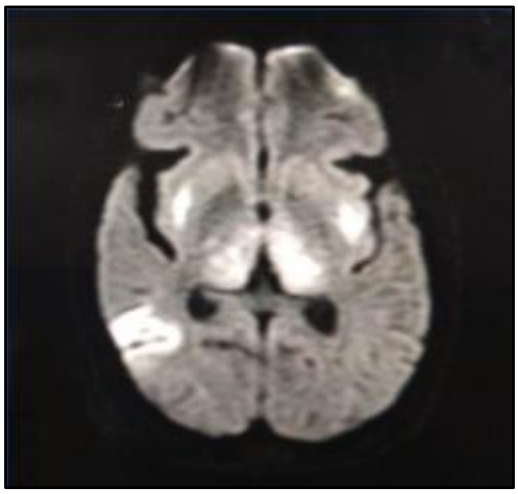

Figure 5. Restricted Diffusion in Thalami, External Capsule and Right Temporal Lobe

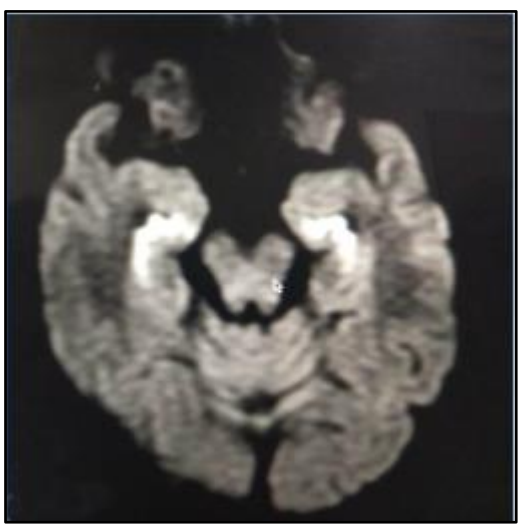

Figure 6. Bilateral Medial Temporal (Uncus) Involvement on DWI

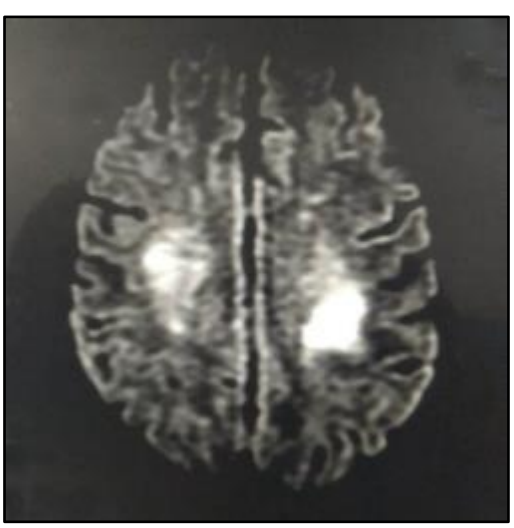

Figure 7. Bilateral Centrum Semiovale Involvement

Figure 8. Involvement in Right Temporal Lobe (DWI)

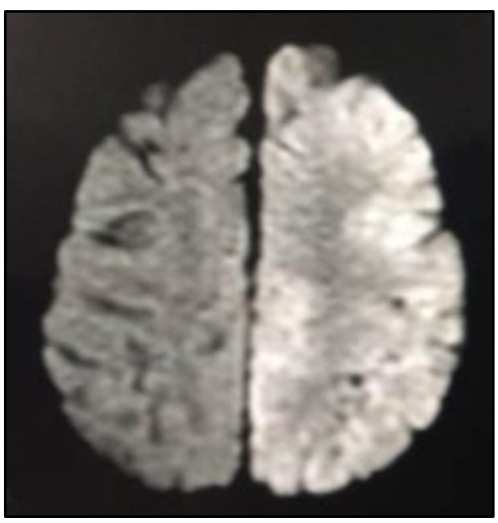

Figure 9. Predominant Involvement of Left Cerebral Hemisphere

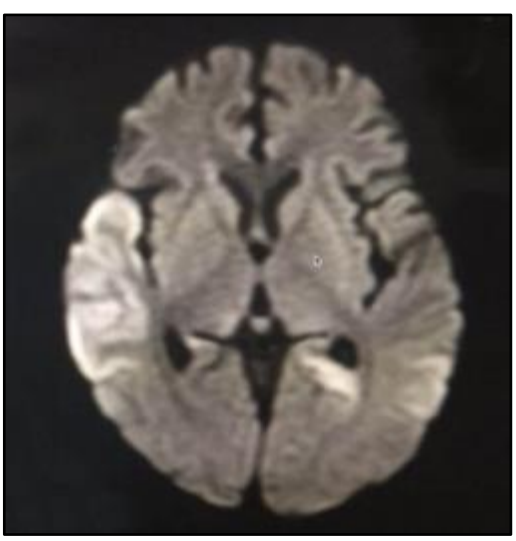

Figure 10. Right Temporal Lobe and Left Occipital LOBE Involvement on DWI

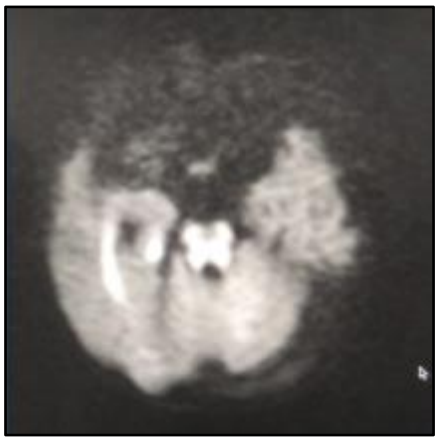

Figure 11. Restricted Diffusion in Brain Stem and Right Temporal Lobe

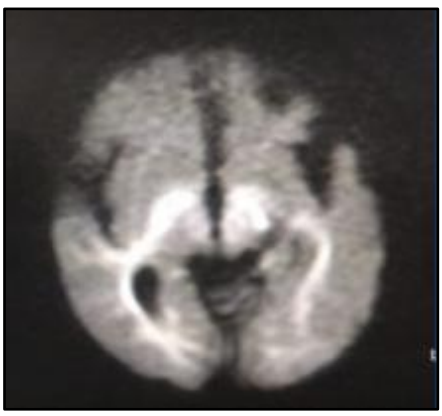

Figure 12. Bilateral Thalami and Temporo-Occipital Lobe Involvement

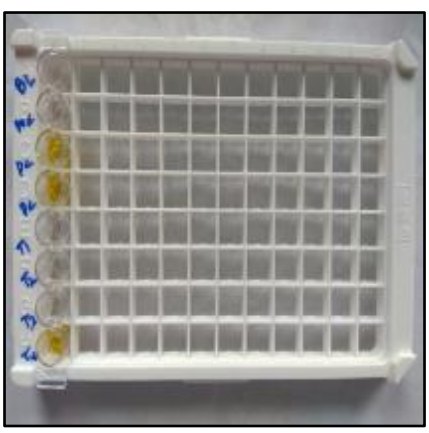

Figure 13. ELISA Test Wells

Figure 14. Automatic Optical Density ELISA Reader

DISCUSSION

Japanese encephalitis frequently involves thalamus, basal ganglia, cerebellum, and brain stem with thalamus being most commonly involved area. In our study, most of the JE patients were admitted between August and October in the post-monsoon period which may be explained by high density of mosquito vectors during this time.[11]

In our study most common presenting features were focal reflex loss, flaccid weakness, movement disorder which may be explained by anterior horn cell involvement as reported in autopsy and neurophysiological studies by some workers.[12,13]

In our observational study MRI scan was performed in 19 patients out of which 11 were male and rest female. The pattern of involvement of different sites of brain in decreasing order of frequency were as such, Thalamus (84.21%), Cerebellum (26.31%), Midbrain (21.05%), Pons (21.05%), Basal Ganglia (21.05%), Cerebral cortex (15.78%), Temporal lobe (15.78%) The most frequently involved area was Thalamus.

Study done by McCabe K et al. found high frequency of thalamic involvement in JE by DWI Weighted MRI study, which is consistent with our finding.[14]

In a study by Kalita J et al. neuroradiological findings of JE were demonstrated with computed tomography (CT), cranial MRI, and SPECT of regional cerebral blood flow showed that the most commonly involved area was thalamus, substantia-nigra, basal ganglia and cerebral cortex this approximates with our study.[15,16]

Studies done by Kumar s et al. have shown that thalamus, basal ganglia, mid brain, pons are particularly involved with thalamic involvement being the most characteristic finding. This correlates with our study.[17]

In a study done by S.K. Handique et al. temporal involvement has been shown in 19 % patients which approximates with our study.[18]

In an autopsy study by Leake CJ et al. virus was isolated in 6 patients from thalamus. In four patients it was isolated from frontal, occipital cortex, cerebellum, medulla and two from pons.[19] This is consistent with our study.

In study by Shankar et al in 34 patients who died within 15 of days of illness, high frequency of thalamic, basal ganglia, cerebral cortex, brainstem and cerebellar involvement were reported. In 2 patients, there were frank haemorrhagic lesions in thalamus, corpus striatum.[20,21] It corroborates our findings.

CONCLUSION

- Japanese encephalitis frequently involves thalamus, cerebellum, basal ganglia and brain stem with thalamus being most commonly involved area.
- MRI is a very useful non-invasive technique for detection of signal changes in JE and to exclude other aetiology.
- Most common presenting feature is movement disorder and focal reflex loss.

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