

Spectrum of CT/MR Imaging Findings in Dengue Encephalitis.

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ABSTRACT

AIM: To describe spectrum of various CNS imaging findings using CT/MRI in serologically confirmed dengue fever patients who presented with neurological symptoms and to predict clinical outcome depending on the imaging findings.

METHODOLOGY: This is a prospective study done in Coimbatore Medical College hospital in 20 serologically proven dengue patients who presented with neurological manifestations. The study was done during the period of August 2017 to December 2017 using 4slice CT scanner and 1.5Tesla MRI . CT and MRI both were done in 4 patients , only CT was done in 7 patients and only MRI was done in 9 patients. CT and MRI images were evaluated to look for imaging findings and anatomical distribution of lesions.

RESULTS: Out of total 20 patients , 16 patients had positive imaging findings in CT/MRI. 4patients had normal study. Patients evaluated with MRI had increased T2, FLAIR signal intensity and reduced T1 signal intensity involving basal ganglia,thalamus, cerebral hemispheres, brainstem and cerebellar hemispheres. Focal areas of diffusion restriction and blooming in GRE representing hemorrhage was seen in 8 patients. Basal ganglia –thalamic complex was affected in 12 patients, cerebral hemispheres in 11 patients followed by brainstem and cerebellar hemispheres in 5 patients respectively.

CONCLUSION: Dengue fever has higher predilection to involve basal ganglia-thalamic complex ,cerebral cortex and white matter followed by brainstem and cerebellum. CNS imaging in dengue fever patients who presenting with neurological manifestations will help to confirm the diagnosis of dengue encephalitis.

Key Words: Dengue, basal ganglia -thalamus, MRI T2/FLAIR Hyperintensity/Diffusion restriction, Hemorrhage.

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I. Introduction

Dengue virus is a RNA virus of flaviviridae family and it is transmitted by aedes aegypti mosquito^{1,5}. Dengue fever is an acute febrile illness which is endemic in tropical ,subtropical countries with epidemic spread often occurring during rainy season due to increased breeding of vector mosquito. The disease manifests as acute febrile illness , headache, myalgia, retro orbital pain,bleeding manifestations which may progress into dengue shock syndrome. Dengue virus has 4 serotypes., Serotypes 2,3 are associated with severe disease and neurological manifestations.

Neurological manifestations of dengue fever include headache ,giddiness, vomiting, seizures,paraparesis and altered sensorium. CNS manifestations are attributed to three factors. 1. Neurotropic effect 2.Secondary to systemic manifestations. 3. Post infectious sequele due to immune mediated reactions^{1,4}. The mechanism of entry into CNS is either through vascular leak due to damaged endothelium or through infected macrophages and histamine release.

In this study we have evaluated spectrum of CT/MRI brain imaging findings of 20 dengue fever patients who presented with neurological symptoms.

II. Materials And Methods

The study was done using 4 slice CT scanner and 1.5 TESLA MRI scanner . Totally 20 patients were evaluated during the study period with serologically proven dengue presenting with neurological manifestations including headache,seizures ,ataxia, altered sensorium. The sample comprised of 12 females,8 males including 6 children.

The cases were diagnosed based on clinical findings ,laboratory results, serology. The serum samples were tested for Non Structural Protein {NS} 1 antigen in fever less than five days or ELISA-Ig M antibodies in case of fever for more than 5 days.

All of the patients had undergone either CT or MRI during the acute phase of illness. The MRI examination were done in dedicated 1.5 Tesla Siemens Magnetom scanner. The MRI images were included T1Weighted ,T2Weighted images and Fluid Attenuation Inversion Recovery sequences. Diffusion weighted images were acquired using single shot fast spinecho sequences {SSFSE} with b factors of 0, 500, 1000 sec/mm², With corresponding ADC maps were also generated to identify the diffusion restriction, MR Angiography and venography are also done as a routine. All the images were taken in 5mm thickness with interslice gap was 0.5mm.

III. Results

All the patients presented with fever and any one of the neurological manifestations of dengue. Altered sensorium was present in 9 patients, seizures were noted in 3 patients, Bleeding manifestations were noted in 5 patients. Clinical findings and platelet count were summarized in table1.

Table no.1

Number	Age/sex	Clinical findings	Duration of illness	Platelet count	NSI/Igm Ag
1	14/F	c/o fever, altered sensorium from 4 th day.	5 days	1,40,000	Positive
2	19/F	C/o fever, bleeding PR, altered sensorium	7 days	36,000	Positive
3	23/M	Fever, diplopia , dysarthria, altered sensorium.	5 days	48,000	Positive
4	31/M	Fever, altered sensorium,bleeding manifestations	3days	21,000	Positive
5	5/F	Fever ,altered sensorium	3 days	17,000	Positive
6	24/F	Fever ,bleeding symptoms,headachegiddiness	4days	80,000	Positive
7	23/F	Fevr,rigor, giddiness	3days	1,10,000	Positive
8	15/M	Fever , chills with rigor, seizures, loose stools	2days	22,000	Positive
9		Fever , seizures, rigor	7 days	30,000	Positive
10	10Y/F	Fever,altered sensorium,bleeding manifestations	4 days	1,38,000	Positive
11	43/M	Fever,seizures,irritability, altered sensorium, ventilatory support	4 days	32,000	Positive
12	32/M	Fever,seizures, bleeding PR	3DAYS	33,000	Positive
13	39/F	Fever,vomiting,headache,loose stools,altered sensorium	3days	1,57,000	Positive
14	19/F	Fever,giddiness,bleeding PR,altered sensorium	7 days	93,000	Positive
15	5/F	Fever,tremors, dysdidokokinesia	8days	1,10,000	Positive
16	14/F	Fever ,headache	4days	47,000	Positive
17	8/M	Fever,headache	5days	95,000	Positive
18	7/M	Fever,headache,vomiting	4days	53,000	Positive
19	13/F	Fever,headache	4days	75,000	Positive
20	24/F	Fever ,headache,seizures,bleeding PR	3days	43,000	Positive

IV. Imaging Findings

Out of 20 patients, 16 patients had positive findings in CT/MRI. 4 patients had normal study. MRI,CT both were done in 4patients, Only MRI was done in 9 patients, Only CT was done in 7 patients.

Summary of imaging findings are shown in table 2.

Table No.2

Number	Age /sex	Investigation undergone	AREAS OF BRAIN AFFECTED					CLINICAL OUTCOME
			Cerebral WM	BG,THA LAMUS	BRAINSTEM	CEREBELL UM	HGE/DR	
1	14/F	CT+MRI	+	+	+	+	+	DIED
2	19/F	CT+MRI	+	+	-	-	+	Residual paralysis
3	23/M	CT+MRI	-	+	-	+	+	DIED
4	31/M	MRI	+	+	+	+	+	DIED
5	5/F	CT	+	+	-	-	-	DIED
6	24/F	MRI	-	+	+	+	+	Recovered with neurological deficit.
7	23/F	MRI	-	+	-	-	-	Recovered
8	15/M	MRI	+	-	-	-	-	Recovered
9	10/M	MRI	+	+	+	-	+	Recovered
10	10/F	CT+MRI	+	+	-	-	+	DIED
11	43/M	CT	+	+	-	-	-	DIED

12	32/M	MRI(N)	-	-	-	-	-	Recovered
13	39/F	MRI	+	-	-	-	+	Recovered
14	20/F	CT	+	-	-	-	-	Recovered
15	5/F	MRI	+	+	+	+	+	DIED
16	14/F	CT(N)	-	-	-	-	-	Recovered
17	8/M	MRI(N)	-	-	-	-	-	Recovered
18	17/M	CT	-	+	-	-	-	Recovered
19	13/F	CT(N)	-	-	-	-	-	Recovered
20	24/F	CT	-	-	-	-	+ SDH	Recovered

BG-Basal ganglia, HGE-Hemorrhage, DR-diffusion restriction.N-Normal.

MRI showed T1- hypointensity, T2,FLAIR hyperintensity with diffusion restriction and hemorrhagic foci in affected areas of brain. CT showed hypodensity in affected regions of brain. Basal ganglia-thalamic complex (12 patients) is most commonly involved, followed by cerebral whitematter (11 patients),brainstem(5 patients) and cerebellar whitematter (5 patients).

V. Representative Cases

CASE 1:

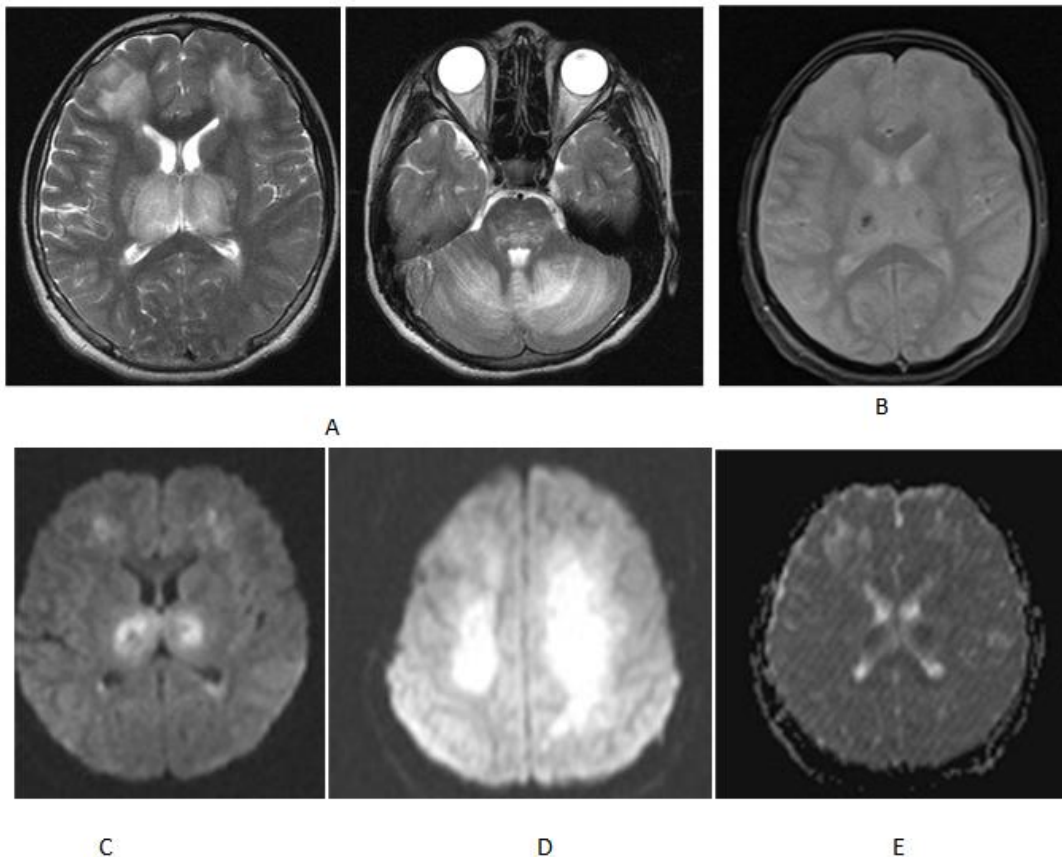
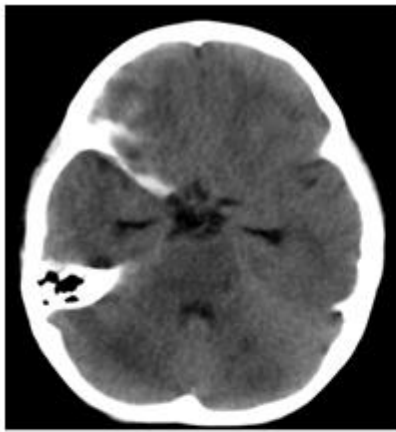
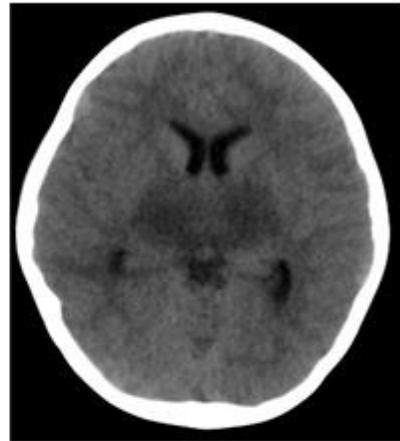


Figure 1: 14 year old female with dengue encephalitis. T2 Axial images (A) showing hyperintense lesions involving bilateral thalamus, cerebellar and cerebral whitematter. The lesion shows diffusion restriction in DWI (C,D) and hypointensity in corresponding ADC map (E). Tiny areas of blooming in GRE images (B) representing hemorrhages noted in bilateral thalamus.

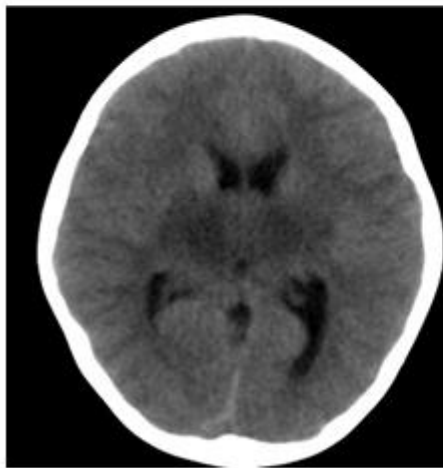
CASE 2:



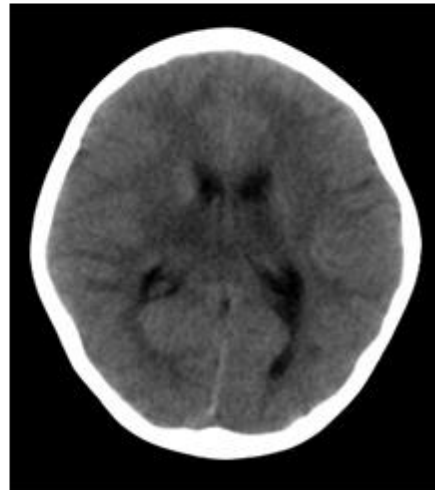
A



B



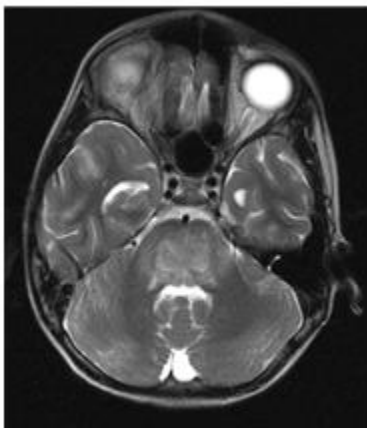
C



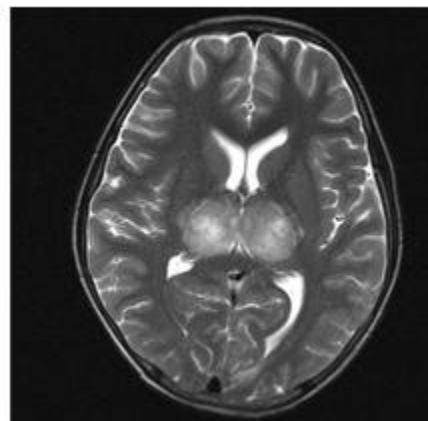
D

Figure 2: 5year female child with dengue encephalitis. CT brain axial sections show severe hypodensity involving bilateral thalamus, part of lentiform nucleus, brainstem. There is also diffuse cerebral edema with obliteration of cerebral sulci and gyri with mild dilatation of bilateral lateral ventricle.

CASE 3:



A



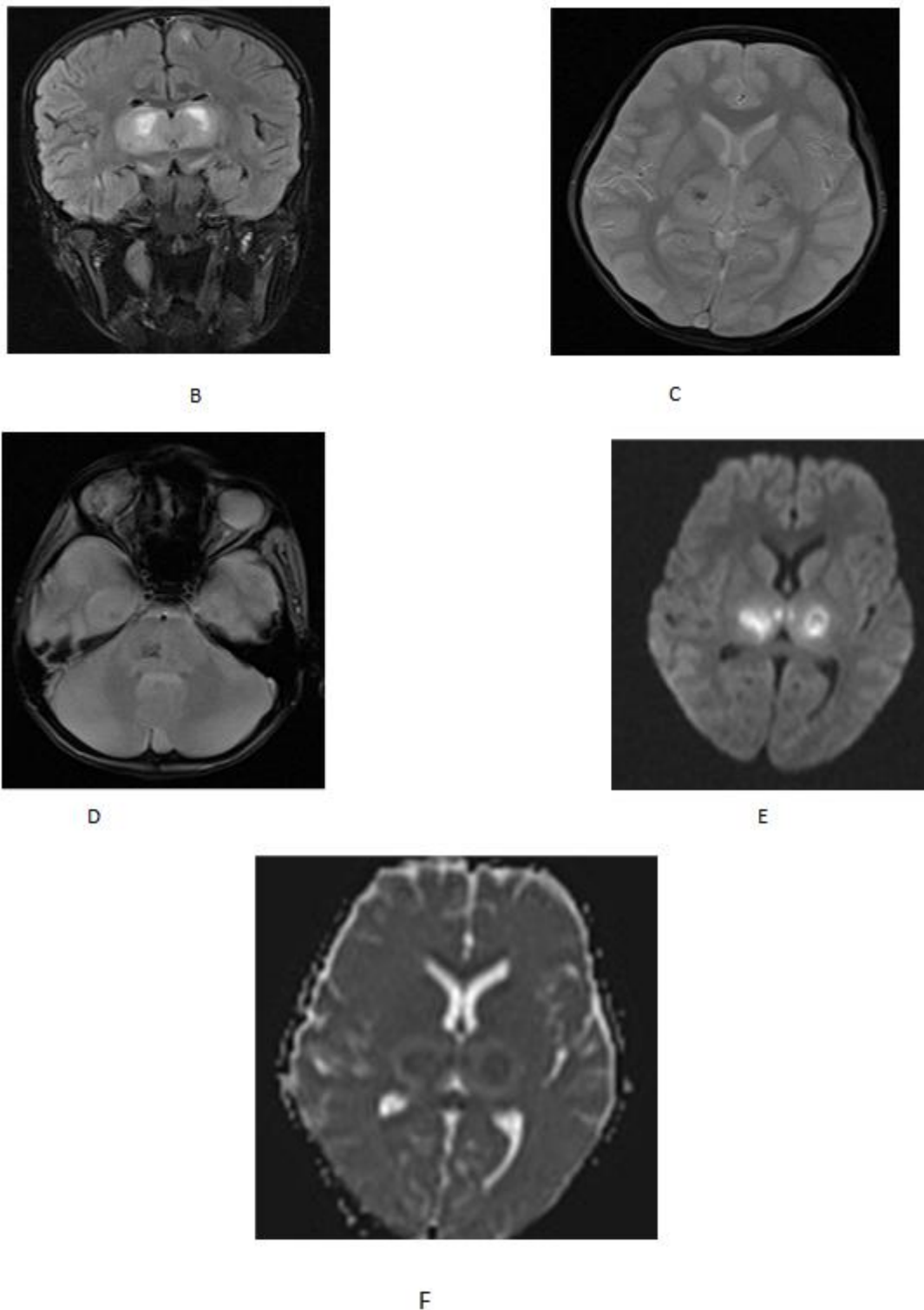


Figure 3: 10 Year old male with dengue encephalitis. T2 Axial(A) and FLAIR coronal (B) images showing hyperintense lesion involving pons, bilateral thalamus. There is diffusion restriction (E) in bilateral thalamus with low ADC value(F). There is also areas of blooming in GRE sequences (C,D) representing hemorrhages.

CASE 4:

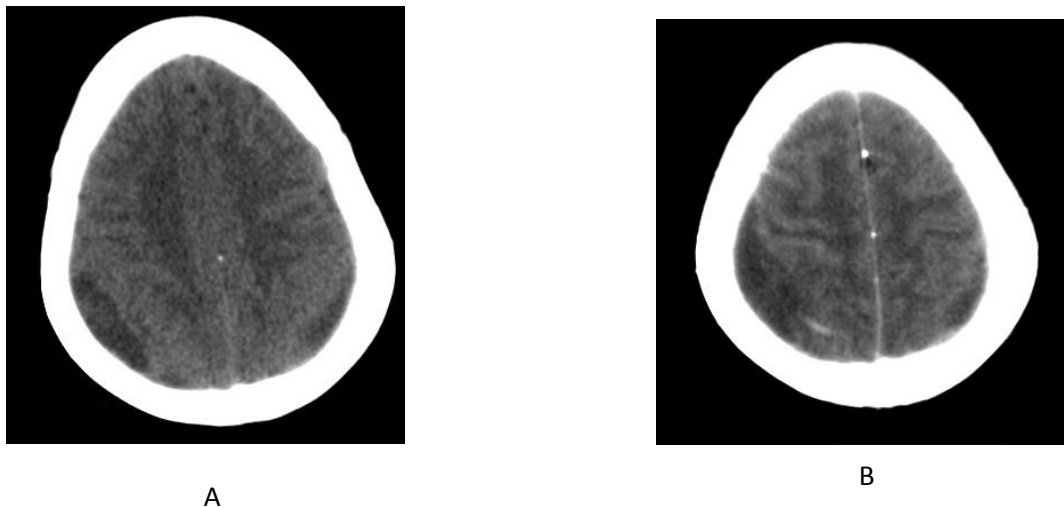


Figure 4: 24 Year old female with dengue presented with bleeding manifestations. CT brain axial images showing Right parietal convexity semilunar shaped extra axial hemorrhage suggestive of Subdural hematoma.

VI. Discussion

Dengue fever usually presents with fever, headache, rashes, retro orbital pain, myalgia and hemorrhagic manifestations^{2,3}. Dengue virus has 4 serotypes. DENV2, DENV3 serotypes are most frequently implicated in neurological manifestations^{1,2,5}. The main symptoms of dengue encephalitis are headache, seizure, altered sensorium.

The neurological manifestations of dengue fever are classified into 3 categories^{2,3}. 1. Direct viral neurotropism causing meningitis, encephalitis, myelitis. 2. Systemic complications causing encephalopathy of ischemic or hemorrhagic stroke. 3. Post infectious complications-ADEM, Myelitis.

LABORATORY DIAGNOSIS:

The gold standard method for viral detection is viral culture but it is difficult and time consuming. Newer methods are PCR and detection of viral NS1 antigen which is 89% sensitive, rapid, reliable and cheaper than PCR.

Detection of host immune response by MAC ELISA which measures dengue specific IGM Antibody. It confirms acute infection by showing rising antibody titres in 2 serum samples. Sensitivity of MAC-ELISA is 69-90%, Specificity is 80%. So it is sensible to use PCR or immunoassay in patients with fever for less than 5 days and ELISA in patients with fever more than 5 days.

BRAIN IMAGING:

Brain imaging adds definite information to the patients presenting with symptoms of encephalitis. MRI is the modality of choice compared to the CT and provides greater definition of brain anatomy and superior visualization of posterior fossa. It is not uncommon to have normal MRI in early stages. The MRI changes are brain edema, intracerebral hemorrhage, basal ganglia and thalamic involvement, cortical, subcortical whitematter changes. Thrombocytopenia and coagulopathy are although common, intracranial hemorrhage in dengue is less common than cutaneous and systemic hemorrhagic complications. The four most commonly affected regions of brain include 1. basal ganglia- thalamic complex, 2. cerebral hemispheres, 3. brainstem and 4. cerebellum^{2,1,5}. This is similar to what we have encountered in our study in which most common sites of involvement are basal ganglia-thalamus (12 patients), followed by cerebrum (11 patients), brainstem (5 patients) and cerebellum (5 patients). Involvement of internal capsule, cervical, thoracic spinal cord is also reported in the literature.

In the literature, focal lesions caused by dengue appear hyperintense on T2, hypointense on T1 weighted imaging^{1,2}. The diffusion weighted images show restriction of diffusion in some cases and diffusion facilitation in other cases. In our case study all of the lesions appeared hypointense on T1 weighted images, hyperintense on T2 weighted images, areas of diffusion restriction was noted in 8 cases. We also encountered foci of blooming representing areas of hemorrhage within the lesion in 8 cases. Transient signal alteration in the splenium of corpus callosum on MRI Brain manifesting as "dot sign" has been described in literature. In our study dot sign was not seen in any of the cases.

When all the four areas are involved prognosis is worst. Patients with all the four areas of involvement are either died or survived with severe residual neurological deficit. In our study there were 3 patients with all the four areas of involved ,all of them died.

The 3 most common differential diagnosis of similar MRI findings are Japanese encephalitis, herpes simplex encephalitis and ADEM^{2,1,5}. The sites of involvement are bilateral basal ganglia,thalamus in Japanese encephalitis but hemorrhages are uncommon. Bilateral temporal lobes, insula, basifrontal lobes are most commonly involved in herpes encephalitis , hemorrhagic areas are common in herpes encephalitis. So it is difficult to differentiate between these encephalitis based on the imaging findings alone. Clinical history ,CSF analysis along with Imaging findings will help to confirm the specific diagnosis. However in the region of dengue endemic, the possibility of dengue encephalitis should be borne in mind especially during dengue outbreaks.

ADEM has involvement of cerebral whitematter and deep gray matter nuclei. It usually develops during convalescent phase of viral infection or after vaccination. The time duration between the occurrence of lesions and the acute febrile illness along with positive serology for dengue , make the diagnosis of post dengue ADEM most plausible.

VII. Conclusion

High degree of suspicion of dengue encephalitis should be kept in mind in patients of dengue fever presenting with any neurological symptoms.MRI is more sensitive than CT in the evaluation of dengue encephalitis. Imaging can help to confirm the diagnosis of dengue encephalitis and determine the severity with high accuracy. Although it is only conservative management for dengue fever , early identification of neurological manifestations by MRI can help for timely institution of supportive management in affected patients.

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