

Original article:

Spectrum of MRI findings in acute encephalitic syndrome in western U.P region – can imaging predict prognosis?

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ABSTRACT:

Introduction: Management of Acute encephalitic syndrome is a clinical challenge because of the associated high mortality & morbidity. Imaging, though not needed in all cases, is life-saving tool for patients in whom an etiologic diagnosis is delayed as abnormal MRI findings are commonly seen in these patients. Severe patterns of involvement on imaging portend a poor prognosis. The present study was aimed to characterize the imaging findings in acute viral encephalitis, develop a pattern-recognition approach for early imaging diagnosis of possible etiologic agent and to assess the impact of imaging in improving the prognosis of patients

Materials & methods: The study was conducted in the Department of Radiology, Rohilkhand Medical College Hospital, Bareilly over a period of 1 year from March 2017 to February 2018. A total of 60 patients with suspected acute encephalitic syndrome were included. MRI Brain was done for these patients and imaging findings were correlated with clinical & laboratory investigations.

Results & conclusions: MRI brain can reliably diagnose infectious encephalitis in the light of clinical findings. It is of prognostic importance also as specific antiviral therapy can be introduced early.

Keywords: encephalitis, MRI, enhancement, diffusion, Japanese encephalitis, dengue

Introduction:

Acute encephalitic syndrome is defined as acute onset of fever and a change in mental status and/or new onset of seizures (excluding simple febrile seizures) in a person of any age at any time of the year³. The clinical definition of AES was introduced for the surveillance of Japanese encephalitis⁴. Western U.P region has been one of the favoured regions for the epidemic outbreaks of viral encephalitis. Infectious causes, mostly viruses are responsible for most cases of AES, typically in the endemic seasons (June-September). A small fraction of cases is attributable to other infectious agents, metabolic/toxic encephalopathies and demyelinating diseases. The commonest causes of viral encephalitis in India are enterovirus 71, measles, Japanese B, varicella zoster virus and herpes simplex virus. Recently dengue has also been increasingly been implicated as one of the etiological agents particularly in the endemic seasons.

The prodromal phase of viral encephalitis is often non specific making a diagnosis clinically difficult in early stages. The disease carries a high mortality particularly in cases where diagnosis is delayed. Although the diagnosis is made on the basis of clinical and pathological examination, radiological studies particularly MRI can help in early diagnosis based on the particular pattern of involvement. At times, a viral encephalitis is difficult to distinguish from other infectious causes (bacterial, leptospiral , rickettsial etc), metabolic encephalopathy and post-infectious encephalomyelitis. However, a thorough clinical history and examination may help to narrow the differentials. Specific patterns of involvement of particular areas of brain have been described in imaging literature being associated with particular viral etiological agents. Also the morphology of the lesions on MRI , e.g presence of hemorrhage, involvement/sparing of certain areas in brain may also suggest the etiological agent.

Materials and Methods:

This was a prospective study done in the Rohilkhand medical college and hospital over a 1 year period from March 2017 to February 2018. All the patient's presenting with acute encephalitic syndrome presenting to the department of Medicine, Pediatrics, OBS & Gynae and Casualty in whom MRI was done, were included in the study irrespective of the age.

Patients who had history of any CNS infection in past 6 months or who were on some treatment for CNS infections were excluded.

- A detailed clinical history was obtained and a thorough systemic examination was performed.
- The laboratory investigations done were complete blood picture, peripheral smear for malaria parasite, and blood culture and sensitivity. Cerebrospinal fluid (CSF) examinations were carried out for viral serology & cytology.
- Diagnostic tests done were conventional PCR, RT-PCR and elisa for detection of IgM antibodies. Wherever possible, the microbiologic tests were done in other laboratories if the same was not available in the hospital. NS1 antigen test was done for dengue.
- An MRI scan of the brain was done on a HITACHI APERTA scanner installed in radiology department of Rohilkhand Medical College.

Sequences done were-

Axial – T1,T2,FLAIR, GRE, DWI (DIFFUSION)

Sagittal- T2

Coronal- FLAIR

Gadolinium contrast (gadodiamide, OMNISCAN) was administered in patients with normal serum creatinine wherever required in dose of 0.1 mmol/kg body weight.

- Any sequelae and residual neurological disability were evaluated at 2-3 months wherever possible.

Results:

- Abnormal MRI findings were seen in 70% (n=42) of the patients presenting with acute encephalitic syndrome. 30%(n=18) of the patients had normal MRI and most of them(83.3%) was excellent prognosis (**Table- 1**). The prognosis was worse in patients having multifocal lesions (>4), involvement of more than 4 locations and in patients in whom diagnosis was delayed. Incidence of residual neurological deficit was high in such patients at follow-up. An overall 10% mortality rate was seen. Mortality rate was significantly higher in patients with dengue and Japanese B.
- **LOCATION OF LESIONS (Table-2)** : Most of patients had multiple/ multifocal lesions(n=30). Basal ganglia was overall the most favoured site (n=31, 73.7%). Isolated basal ganglia involvement was seen in 10 cases. Other commonly involved sites in

decreasing order of incidence were thalami (n=30, 71.7%), subcortical white matter (n=21), cerebral cortex (n=19), corpus callosum and deep periventricular white matter(n=15). Parietal cortex was more commonly involved than frontal or temporal cortex and occipital cortex the least involved.

- Brainstem was involved in 42.9 % (n=18) of cases and cerebellum in 19%(n=8).
- Bilateral symmetric thalamic & basal ganglia involvement was seen in 90% (n=18) of patients in JE and 45.5% cases of dengue(n=5). Brain stem involvement was seen in 60% of JE cases(**Fig- 1 to 3, 5-6**).
- Sparing of basal ganglia along with temporal lobe involvement was seen in the single case of HSV encephalitis.
- **MORPHOLOGY OF LESIONS(Table-1)** : All the lesions showed T2 prolongation and were hyperintense on T2/FLAIR. T1 hyperintensity along with blooming on gradient was seen in 4 cases of JE and 1 case of dengue which suggested haemorrhage.
- Diffusion restriction was seen uncommonly (n=4, 9.5%). 1 was a case of VZV encephalitis ,2 other patients were diagnosed with tubercular meningo-encephalitis and another 1 was a suspected case of toxic encephalopathy.
- Post contrast enhancement was seen in 10 patients (23.8%). No specific enhancement pattern was seen. Parenchymal enhancement was more common than meningeal.
- 3 of the patients were finally diagnosed with tubercular meningo-encephalitis(**Fig-8**) who had acute decompensation because of complications (infarcts, hydrocephalus), one was diagnosed as ADEM on follow up and one each patient had multiple sclerosis and metabolic encephalopathy.
- Cases of dengue and JE were clustered in the endemic season from June- October (**TABLE-4**) occurring as an outbreak. Other agents were responsible for sporadic cases all the year round.
- Amount of brain damage as evidenced by multiple/multifocal lesions correlated well with prognosis. 66.6% (n=8)of patients with single lesions/ involvement of single location showed improvement in neurological status. 50% (n=15)of those having multiple lesions(>4) showed deterioration in GCS during course of hospital stay (**TABLE-3**).

TABLE – 1: MRI FINDINGS IN VARIOUS ETIOLOGICAL AGENTS

IMAGING FINDING	No. OF TOTAL (n= 60)	ENTEROVIRUS	JAPANESE ENCEPHALITIS	DENGUE	MEASLES	VARICELLA	OTHER VIRAL /UNKNOWN	BACTERIAL/ MIMICS
1.NORMAL MRI BRAIN	18	6	5	3	1	0	2	1
2.SINGLE T2 HYPERINTENSE LESION	12	4	3	2	0	0	3	0
3. MULTIPLE T2 HYPERINTENSE LESIONS	30	5	12	6	1	1	1	4
4. PARENCHYMAL ENHANCEMENT	10	1	3	2	0	0	1	3
5. DIFFUSION RESTRICTION IN LESIONS	4	0	0		0	1	1	2
6. HEMORRHAGIC LESIONS	3	0	2	1	0	0	0	0
7.HYDROCEPHALUS/ OTHER COMPLICATIONS	3	0	0	0	0	0	1	2

TABLE -2 : MRI FINDINGS(CONTD.)- LESION LOCATION

T2-HYPERINTENSE LESION LOCATION	No. OF TOTAL (N=42)	% OF TOTAL	ENTEROVIRUS	JAPANESE ENCEPHALITIS	DENGUE	MEASLES	VARICELLA	OTHER VIRAL	BACTERIAL / MIMICS
FRONTAL CORTEX	4	9.5	1	1	1	0	0	0	1
PARIETAL CORTEX	9	21.4	1	3	2	1	0	0	2
TEMPORAL CORTEX	4	9.5	0	0	1	0	1	1	0
OCCIPITAL CORTEX	2	4.8	0	1	1	0	0	0	0
SUBCORTICAL WHITE MATTER	21	50	3	6	6	1	1	1	3
DEEP WHITE MATTER	15	35.7	2	5	4	1	0	2	1
CORPUS CALLOSUM	15	35.7	2	5	4	1	1	2	0
BASAL GANGLIA	31	73.7	4	18	5	2	0	1	1
THALAMI	30	71.4	3	20	5	0	0	2	0
CEREBELLUM	8	19	1	3	2	0	0	2	0
BRAINSTEM	18	42.9	3	8	5	0	0	1	1

TABLE- 3 : PROGNOSIS OF PATIENTS

MRI FINDINGS	CLINICAL IMPROVEMENT	WORSENE SCORE/ DIED	GCS	UNKNOWN/ LAMA
NORMAL MRI EXAMINATION (n= 18)	15	1		2
SINGLE LESION/ INVOLVEMENT OF SINGLE LOCATION (n=12)	8	2		2
MULTIPLE LESIONS / MULTIFOCAL INVOLVEMENT (n= 30)	11	15		4

TABLE- 4 : SEASONAL DISTRIBUTION OF CASES

ETIOLOGIC AGENT (n= 60)		MARCH- (TOTAL- 8 , 19%)	MAY	JUNE- (TOTAL- 42 , 70%)	OCTOBER	NOVEMBER- FEBRUARY (TOTAL- 10 , 11%)
ENTEROVIRUS	n=14	4		7		3
JAPANESE ENCEPHALITIS	n=20	0		20		0
DENGUE	n=14	0		13		1
MEASLES	n=2	0		1		1
VARICELLA	n=2	1		0		1
OTHER VIRAL/ UNKNOWN	n= 5	2		1		2
MIMICS/ BACTERIAL	n= 3	1		0		2

Discussion:

The incidence of acute encephalitic syndrome parallels acute viral infectious encephalitis in India. Acute encephalitis is a life-threatening condition and timely recognition saves many precious lives. Diagnosis relies on neurological symptoms and infectious signs, but atypical presentations and mimics are not uncommon. Final diagnosis is made on the basis of serological tests from CSF & blood and after identification of the pathogen from cell cultures. Culture methods are however time-consuming and availability is also not universal. Brain imaging is crucial for the diagnosis of acute encephalitis. An MRI brain is the investigation of choice and should be done urgently.

Brain MRI detects structural lesions, assesses the extent of damage and can lead to an etiologic diagnosis based on identification of patterns. It is equally helpful in ruling out the mimickers, e.g, demyelinating diseases, brain tumors & PRES.

AES carries a high mortality rate, and in a considerable percentage of patients, there is residual neurological damage.

The imaging differentials of acute encephalitis include metabolic encephalopathy, ADEM, cerebral venous thrombosis, stroke, posterior reversible encephalopathy syndrome and low-grade tumors.

Summary:

1. Abnormality on **MRI** is frequently seen in patients with AES, even if no causative agent is identified.
2. Basal ganglia & thalamus are most commonly involved areas. Diffusion restriction and contrast enhancement do not add significantly to imaging diagnosis.
3. Bilateral symmetric thalamic & basal ganglia involvement were seen in patients of Japanese encephalitis and dengue. Sparing of basal ganglia along with involvement of temporal lobes is typical for HSV encephalitis.
4. Hemorrhagic lesions are more frequently seen in JE and dengue.
5. A vasculitic pattern along with infarcts are seen in varicella zoster encephalitis. Infarcts due to end-arteritis are frequently seen in complicated tubercular meningitis.
6. The mortality rate observed was 10%, and all of these had dengue or Japanese encephalitis.

Conclusion:

Abnormal MRI findings are frequent in patients with acute encephalitic syndrome, and MRI is often helpful in providing a possible etiologic diagnosis in appropriate clinical context. Further more severe involvement of brain as evidenced by involvement of more than 4 locations, multifocal lesions and hemorrhagic lesions portend a poor prognosis with high mortality. MRI brain therefore may play an important role in management of patients in whom the microbiologic diagnosis is delayed.

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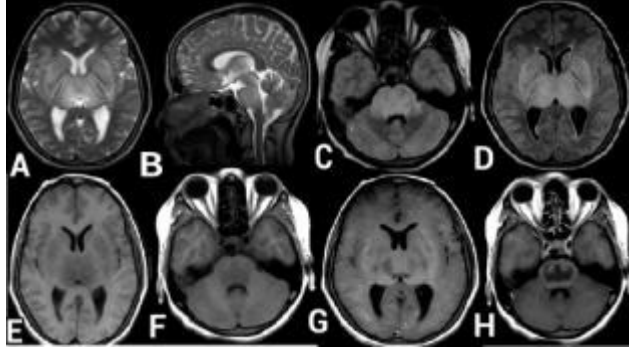


Figure no 1: MRI findings in a patient of severe Japanese encephalitis. Axial (A) & coronal T2(B) , axial FLAIR (C,D) images show hyperintense lesions in bilateral basal ganglia, thalamus & brainstem. Axial T1 pre (E,F) & post contrast(G,H)show variable heterogeneous enhancement in the lesions. The patient died in the hospital the next day of admission.

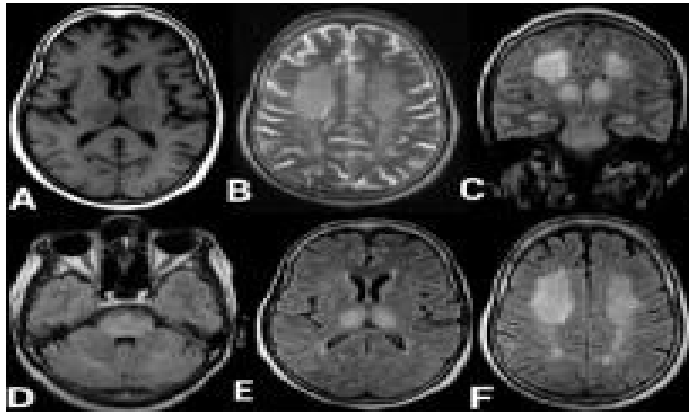


Figure no 2: Another case of JE. Axial T1 (A), Axial T2 (B), coronal (C)and axial FLAIR (D,E,F). Bilateral symmetric lesions are seen in the thalami and centrum semiovale. Involvement of the pons is also seen.

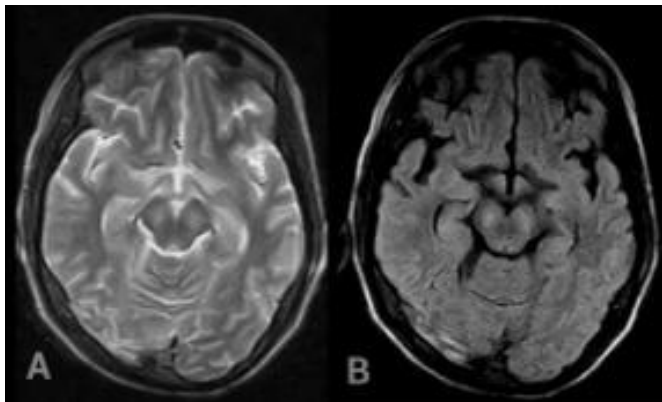


Figure no 3: Flaviviral encephalitis. Axial T2 (A) and Axial FLAIR (B) images showing symmetric T2 hyperintense lesions in the substantia nigra.

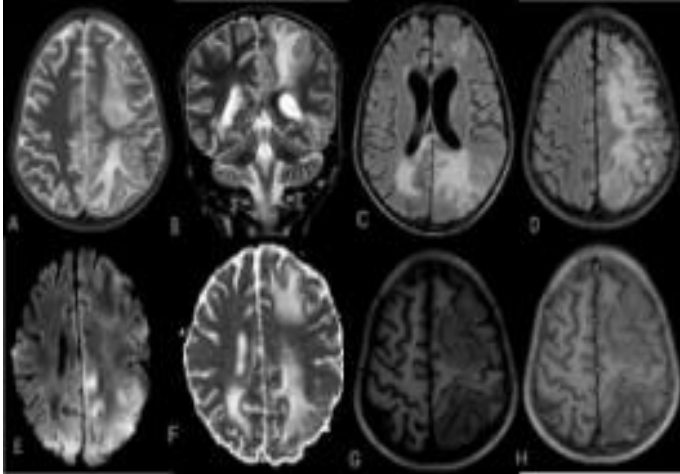


Figure no 4: Encephalitis due to unknown etiology. Axial and coronal T2 (A & B), Axial FLAIR (C,D) MR images show hyperintense lesions in the bilateral parieto-occipital cortex, left frontal cortex and underline subcortical and deep white matter without any diffusion restriction (E-DWI image &F- ADC map) or post contrast enhancement (G,H).

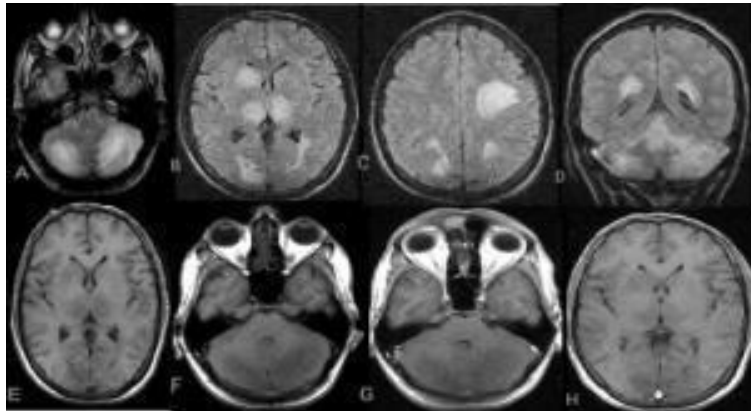


Figure no 5: Severe dengue encephalitis. Axial FLAIR (A to D) and axial T1 precontrast (E,F) and post contrast (G,H) MR images showing symmetric hyperintense lesions in the cerebellum, thalamus and deep and subcortical parietal white matter. Right caudate nucleus is also involved. No post contrast enhancement is seen in the lesions. The patient died during hospital stay

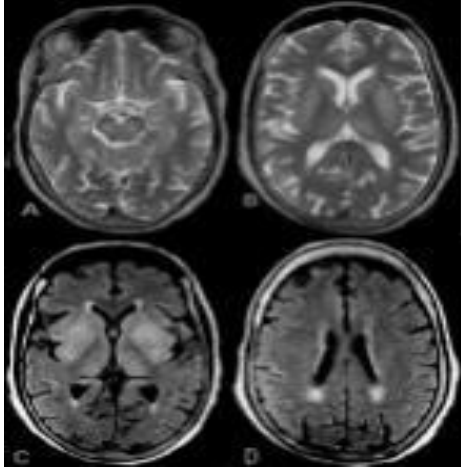


Figure no 6: Dengue encephalitis. Axial T2 (A,B) and flair (C,D) MR images showing hyperintense bilaterally symmetric lesions in the basal ganglia, ventro-medial thalamus, substantia nigra and deep posterior periventricular white matter.

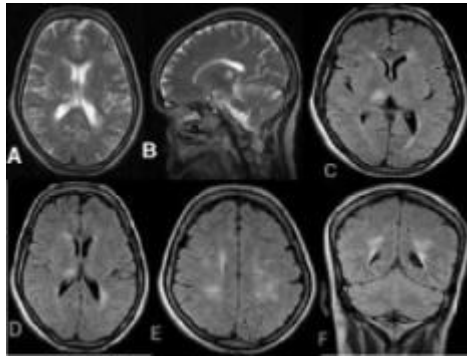


Figure no 7: MR images in a patient of suspected multiple sclerosis. Axial T2 (A) sagittal T2 (B) Axial FLAIR (C,D,E) and coronal FLAIR (F). Multiple patchy hyperintense lesions are seen in the right thalamus, periventricular white matter and centrum semiovale. Periventricular demyelination is seen along the corpus callosum.

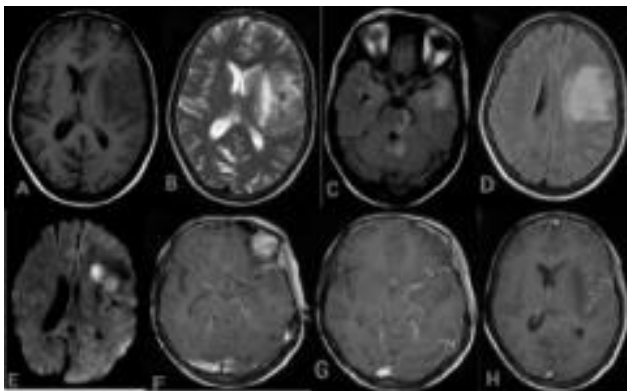


Figure no 8: Proven case of complicated tubercular meningitis. Axial T1(A), T2(B), FLAIR(C&D) MR images showing involvement of the left fronto-temporal lobe, lesions in the brainstem and cerebellum. Axial DWI (E) and T1 post contrast images show infarcts in the deep left periventricular white matter and frontal lobe. Marked meningeal enhancement is seen along the basal cisterns, left frontal sulci and sylvian fissure

REFERENCES:

1. Johnston RT. Viral infections of the nervous system, 2nd ed. Philadelphia: Lippincott-Raven, 1998.
2. Whitley RJ, Gnann JW. Viral encephalitis: familiar infections and emerging pathogens. *Lancet* 2002;359:507–14.
3. Johnson RT. Emerging viral infections of the nervous system. *J Neurovirol* 2003;9:140–7.
4. Jmor F, Emsley HC, Fischer M, Solomon T, Lewthwaite P. The incidence of acute encephalitis syndrome in Western industrialised and tropical countries. *Virology* 2008;5:134
5. Solomon T, Thao TT, Lewthwaite P, Ooi MH, Kneen R, Dung NM, et al. A cohort study to assess the new WHO Japanese encephalitis surveillance standards. *Bull World Health Organ* 2008;86:178–86.
6. F K Beig *et al* : Etiology and clinico-epidemiological profile of acute viral encephalitis in children of western Uttar Pradesh, India. *International Journal of Infectious Diseases* (2010) 14, e141—e146
7. Joshi R, Kalantri SP, Reingold A, Colford JM Jr: Changing landscape of acute encephalitis syndrome in India: a systematic review. *Natl Med J India* 2012; 25: 212–220.
8. Joshi R *et al* : Clinical presentation, etiology, and survival in adult acute encephalitis syndrome in rural Central India. *Clin Neurol Neurosurg.* 2013 September ; 115(9): 1753–1761. doi:10.1016/j.clineuro.2013.04.008
9. Sen P K *et al* : Epidemiology of Acute Encephalitis Syndrome in India: Changing Paradigm and Implication for Control *J. Commun. Dis.* 2014; 46(1): 4- 11.
10. Bykowski J , *et al* : Acute Pediatric Encephalitis Neuroimaging: Single-Institution Series as Part of the California Encephalitis Project. *Pediatric Neurology* 2015;52 : 606-614.
11. Nadarajah J, Madhusudhan KS, Yadav AK, Gupta AK, Vikram NK. Acute hemorrhagic encephalitis: An unusual presentation of dengue viral infection. *Indian J Radiol Imaging* 2015;25:52-5.
12. Granerod J *et al* : Neuroimaging in encephalitis: analysis of imaging findings and interobserver agreement. *Clinical Radiology* 71 (2016) 1050-1058.
13. Kumar R, Basu A, Sinha S, Das M, Tripathi P, Jain A, et al: Role of oral Minocycline in acute encephalitis syndrome in India – a randomized controlled trial. *BMC Infect Dis* 2016; 16: 67.
14. Soares B P, Provenzale J M: Imaging of Herpesvirus Infections of the CNS. *AJR* 2016; 206:39–48
15. Anne Bertrand, Delphine Leclercq, Laurent Martinez-Almoyna, Nadine Girard, J-P Stahl, et al.. MR imaging of adult acute infectious encephalitis. *Médecine et Maladies Infectieuses*, Elsevier Masson, 2017