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A study of Acute Encephalitis Syndrome – Clinical profile, aetiology, and outcome

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ABSTRACT

Aim: We aimed to study the clinical profile and etiology of Acute Encephalitis Syndrome (AES) in a tertiary care centre of western India.

Materials and Methods: All patients evaluated by the neurology department, who fulfilled the standardised case definition for encephalitis (given by International Encephalitis Consortium) over 2 year period were screened. Routine laboratory investigations, CSF, Neuroimaging and EEG were done in all patients. Short term follow-up of one month was done to see the outcome.

Results: Out of total 85 patients of AES seen over two years; viral etiology was identified in 26 (30.5%) patients; 8 (9.4%) patients had autoimmune cause and in 53 (62.4%) patients, no specific ethology could be found. Long duration of symptom onset to hospitalisation, seizures, abnormal behaviour, involuntary movements (automatism, dyskinesia, or dystonia), and autonomic dysfunction favours a diagnosis of autoimmune encephalitis. At one month, good outcome (mRS <2) was seen in 51(60%) patients and 34 (40%) patients had a poor outcome (mRS > 2), out of which 29(34.1%) patients expired.

Conclusion: Viral encephalitis was the commonest cause of AES; followed by autoimmune encephalitis. Specific cause could not be ascertained in large number of patients, even after extensive evaluation. AES patients had prolonged hospital stay and significant morbidity and mortality.

1. Introduction

Acute encephalitis syndrome (AES) is a serious form of neurologic disease which generally presents with acute onset of fever, altered mental status, new onset of focal neurologic symptoms, and generalized or focal seizures. It is an important cause of morbidity and mortality worldwide. The annual incidence of encephalitis worldwide is estimated to be 0.07 to 12.6 cases per 100,000 population.[1] Various infectious and para-infectious causes are known to produce AES. In this study, we evaluated the clinical profile, etiology, and short-term outcome of all patients with acute encephalitis in a tertiary care hospital of western India.

2. Materials and Methods

All patients with fever and altered sensorium, evaluated by the neurology department between a period of two years (2017-2019) were screened. The standardized case definition for encephalitis given by International Encephalitis Consortium[2] was used as inclusion criteria for the study. All the cases for which; hypoxic, septic, toxic, or other metabolic causes for encephalopathy were found, were excluded from the study. All patients diagnosed with acute bacterial meningitis or tubercular and fungal meningitis were also excluded from the study. A detailed history was taken with regards to the onset of symptoms, clinical features, duration, progression of illness, season of the year, geographic locale, travel history, animal contact,

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vaccination history, and immune status of the patient. The patients underwent a detailed general examination including any skin lesion, rash, eschar, myalgia, joint pain. In neurological examination, patients were assessed for level of consciousness, any signs of meningism, focal deficit, or raised intracranial pressure. Complete blood count, metabolic parameters including renal and liver function tests, electrolytes, thyroid function tests, blood smear for malarial parasite, chest X-ray, and HIV testing were done in all patients and blood culture was done if required. EEG and MRI of the brain were done in all patients and MRI of the spinal cord was done if required. CSF examination was done in all patients, if no contraindication like focal lesion with increased intracranial tension or bleeding diathesis. CSF and serological tests were done to identify a specific etiological agent. Serum NS1 antigen, and/or IgM ELISA was used to diagnose dengue. Serum IgM ELISA was used for chikungunya, JE and scrub typhus. CSF was evaluated for cells, protein, and glucose. CSF tuberculous gene expert, cryptococcal antigen, and culture for bacteria were done when indicated. Serum and/or CSF autoimmune antibodies, serum paraneoplastic antibodies were also done if required. In patients with autoimmune encephalitis, serological tumour markers and CT scan of thorax / abdomen were done and PET scan if required. Polymerase chain reaction (PCR) testing was done from the CSF sample. Patients were classified into viral, autoimmune, and unidentified groups based on etiological workup and compared with each other regarding the clinical and systemic evaluation. The functional outcome at 1 month was assessed by the modified Rankin scale (mRS) and categorised into good (mRS 0-2) and poor (mRS 3-5) prognosis.

3. Results

This was a prospective observational study of patients of acute encephalitis syndrome, carried out at a tertiary care hospital over 2 years. Out of 85 patients, 52 (61.2%) were male and 33 (38.8%) were female. The mean age of all patients was 36.29 years. 60% of patients were presented during the monsoon and post monsoon period (July-Dec). The preceding illness or event was found in a total of 22 patients. Acute gastroenteritis, herpetic skin lesions, upper respiratory tract infection, and dog bite were the most common associated findings.

The average duration of symptom onset to hospitalization was 6.2 days. Total 21 patients developed status epilepticus, out of which 4 patients had nonconvulsive status epilepticus. GCS score of < 8 on admission was present in 28 (32.9%) patients. The ventilator was required in a total of 41 (48.2%) patients. Systemic involvement was present in 28 (32.9%) patients, in the form of thrombocytopenia, hepatic involvement, renal involvement, central Diabetes insipidus, Syndrome of inappropriate antidiuretic hormone secretion, and rhabdomyolysis.

In the present study, the etiology was identified in 32 (37.6%) patients. Two patients had post HSV encephalitis NMDA encephalitis. Dengue was the most commonly identified etiology in 14 (16.4%) patients and autoimmune encephalitis in 8 (9.4%) patients as second most common etiology (NMDA encephalitis in 7 and LGI1 Encephalitis in 1 patient). Other identified etiologies were HSV1 in 3 patients, VZV in 1 patient, Rabies in 4 patients, Chikungunya in 2 patients, and JE virus in 2 patients.

Patients with autoimmune encephalitis were younger with a lower M: F ratio (1:1). All 7 patients with NMDA encephalitis were under 25 years of age. The average duration of symptom onset to hospitalization was 5.7 days in the viral group as compared to 13.3 days in the autoimmune group. The average duration of hospital stay was 15.2 days in a viral group as compared to 27.4 days in the autoimmune group. MRI brain was abnormal in 50 (59.9%) patients. The temporal lobe was involved in 12 patients, out of which, 2 patients were diagnosed as HSV1, and 2 patients with NMDA encephalitis. Out of three patients with brainstem involvement in the viral group, 2 patients had rabies and 1 patient had Japanese encephalitis. Bilateral basal ganglia involvement was identified in 2 patients of Rabies. In patients with spinal cord involvement in the viral group, 1 patient was diagnosed as Rabies and 1 patient as Chikungunya. EEG was normal in 27 (33.7%) patients, while generalized or focal slowing was there in 45 (56.2%) patients. Focal or generalized spike/sharp wave discharges were recorded in 10 patients. Four patients were diagnosed as non-convulsive status epilepticus. BIPLEDs were seen in 2 (2.5%) patients and diffuse delta slowing with superimposed fast activity (Delta brush) was recorded in 1 (1.2%) patient. Total 47 (55.3%) patients recovered completely, 9 (10.6%) patients had partial recovery on follow up and 29 (34.1%) patients expired during hospitalization or within 1 month of discharge.

Clinical profiles along with MRI, EEG, and CSF were compared among various etiology (viral, autoimmune, and unknown). (Tables 1 and 2)

MRI was abnormal in 61.5% of patients with viral as compared to 37.7% of patients in autoimmune encephalitis. All patients with autoimmune encephalitis had abnormal EEG as compared to 50% in the viral encephalitis group. Mean CSF protein and cells were 74.9 and 41.9 respectively in viral encephalitis as compared to 36.5 and 6.7 respectively in autoimmune encephalitis.

Various clinical, laboratory, and imaging parameters were evaluated for their association with prognosis. (table 3) Good outcome (mRS < 2) was noted in 51 (60%) patients and 34 (40%) patients had a poor outcome (mRS > 2).The mortality rate among viral, autoimmune and unidentified groups was 42.3%, 25%, and 30.1% respectively. Poor

Table 1: Clinical profile according to etiology

Symptoms and signs	Viral (n=26)	Autoimmune (n=8)	Unidentified (n=53)
Fever	26 (100%)	4 (50%)	51 (96.2%)
Headache	12 (46.1%)	3 (37.5%)	28 (52.8%)
Seizure	17 (65.3%)	8 (100%)	33 (66.3%)
Abnormal behavior	7 (26.9%)	7 (87.5%)	8 (15.0%)
Autonomic dysfunction	0 (0%)	2 (25%)	1 (1.8%)
Myalgia	7 (26.9%)	0 (0%)	5 (9.4%)
Joint pain	1 (3.8%)	0 (0%)	8 (15.1%)
Rash	2 (7.7%)	0 (0%)	4 (7.5%)
Dystonia	1 (3.8%)	3 (37.8%)	0 (0%)
Automatism	0 (0%)	6 (75%)	0 (0%)

Table 2: Correlation of clinical and systemic evaluation with etiology

	Viral (n=26)	Autoimmune (n=8)	Unidentified (n=53)
Mean GCS score	9.5	11.5	9.6
Symptom onset to hospitalization (mean days)	5.7	13.3	5.6
Ventilator required	14 (53.8%)	3 (37.5%)	26 (49.1%)
Thrombocytopenia	9 (34.6%)	0 (0%)	14 (26.4%)
Hepatic involvement	3 (11.5%)	0 (0%)	3 (5.6%)
Renal involvement	4 (15.3%)	1 (12.5%)	6 (11.3%)
Abnormal EEG	13 (50%)	8 (100%)	32 (60.3%)
Abnormal MRI	16 (61.5%)	3 (37.7%)	33 (62.2%)
Mean CSF findings			
Protein (mg/dl)	74.9	36.5	79.1
Sugar (mg/dl)	79.6	76.6	81.9
Cells (per mm^3)	41.9	6.7	32.9
Onset of recovery (Mean days)	4.2	7.5	3.1
Hospital stay (Mean days)	15.2	27.4	13.9
Good outcome	13 (50%)	5 (62.5%)	34 (64.1%)
Poor outcome	13 (50%)	3 (37.5%)	19 (35.8%)

Table 3: Outcome parameters

Outcome parameters		Good Outcome	Poor outcome	Total	P-value
Age	<60 years	47 (62.7%)	28 (37.3%)	75 (100%)	0.16
	>60 years	4 (40%)	6 (60%)	10 (100%)	
GCS	< 8	9 (32.1%)	19 (67.9%)	28 (100%)	0.0002
	> 8	42 (73.7%)	15 (26.3%)	57 (100%)	
Ventilator	Required	13 (31.7%)	28 (68.3%)	41 (100%)	<0.0001
	Not required	38(86.4%)	6 (13.6%)	44 (100%)	
Seizure	Present	35 (62.5%)	21 (37.5%)	56 (100%)	0.01
	Patients with SE	5 (27.8%)	13 (72.2%)	18 (100%)	
EEG	Normal	23 (85.2%)	4 (14.8%)	27 (100%)	0.002
	Abnormal	27 (50.9%)	26 (49.1%)	53 (100%)	
MRI	Normal	29 (82.8%)	6 (17.2%)	35 (100%)	0.0003
	Abnormal	22 (44%)	28 (56%)	50 (100%)	
Systemic involvement	Present	14 (50%)	14 (50%)	28 (100%)	0.18
	Absent	37 (64.9%)	20 (35.1%)	57 (100%)	

prognosis is associated with ventilatory requirement (p< 8 p=0.0002), status epilepticus (p=0.01), EEG (p=0.002) and MRI abnormality (p=0.0003).

4. Discussion

We evaluated patients with acute encephalitis syndrome, presenting to our tertiary care hospital for clinical and etiological profiles over 2 years.

In the present study, mean age is younger age (~36 years), male predominance and a seasonal (July-Dec) preference. This gender and seasonal distribution are similar to the study by Misra et al.[3] Acute encephalitis can affect patients of any age and any gender throughout the year but vector born encephalitic illnesses were presented with higher frequency during monsoon and post-monsoon period. The etiology of encephalitis was identified in 32 (37.6%) patients out of which a viral cause was identified in a total of 26 (30.5%) patients. As high as 62% had unidentified etiology after a thorough workup.

In a study by Kalita et al, etiology was identified in 61.9 % with a similar incidence of viral encephalitis (26.8%).[4] This is probably due to the endemicity of Japanese encephalitis and inclusion of bacterial etiology e.g. scrub typhus. Overall, viral etiology remains the most common identified cause of acute encephalitis. The most commonly identified viral etiology was Dengue followed by HSV1, Rabies, Chikungunya, JE, and VZV encephalitis. In a study in northern India[5] most common etiology was JE followed by dengue and then HSV, measles, and mumps and this reflects the endemicity of JE in that part.

Besides fever and altered sensorium, other common features were seizures (65.9%), headache (50.6%), and vomiting (38.9%). The mean GCS score in the present study was 9.7, while a GCS score less than 8 was found in 32.9%. These clinical features are similar to the Indian study by Misra et al while in western studies in Singh TD et al[5] study GCS score of < 8 was found in only 11.1% of patients which shows more severe disease or only patients with the more severe disease came for treatment in our study. Status epilepticus was present in 21.2 % as compared to 29.2 % in a study by Misra et al.

Systemic involvement was present in 28 patients (32.9%) of which common was thrombocytopenia (28.2%) followed by renal (11.8%) and hepatic involvement 6(7.1%). Systemic involvement especially thrombocytopenia indicates viral aetiology.

After Dengue encephalitis, the second most common identified etiology was NMDA encephalitis. All these patients were under 25 years of age and none of the patients had associated tumours.

Long duration of symptom onset to hospitalisation, seizures, abnormal behaviour, involuntary movements (automatism, dyskinesia, or dystonia), and autonomic dysfunction favours a diagnosis of autoimmune encephalitis; while systemic involvement and high CSF cell count may suggest viral aetiology.

Ventilatory requirement, GCS score < 8 on admission, status epilepticus, EEG, and MRI abnormality were associated with poor prognosis. In a study by TD Singh et al; Advanced age, immunocompromised state, coma, mechanical ventilation, and acute thrombocytopenia portend a worse prognosis in acute encephalitis.[6] In a study by Thakur et al; cerebral edema and thrombocytopenia were predictors of poor prognosis in multivariate analysis.[7]

Thus Acute Encephalitis Syndrome is a group of disorder, with substantial morbidity and diverse etiology. A large proportion of patients with acute encephalitis remain undiagnosed despite extensive workup.

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6. Conflicts of Interest

The authors declare no potential conflict of interest with respect to research, authorship, and/or publication of this article.

References

1. Granerod J, Tam CC, Crowcroft NS, Davies NW, Borchert M, Thomas SL, et al. Challenge of the unknown: a systematic review of acute encephalitis in non-outbreak situations. *Neurology*. 2010;75(10):924–32. doi:10.1212/WNL.0b013e3181f11d65.
2. Venkatesan A, Tunkel AR, Bloch KC, Sejvar J, Bitnun A, Stahl JP, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. *Clin Infect Dis*. 2013;57(8):1114–28. doi:10.1093/cid/cit458.
3. Misra UK, Kalita J, Mani VE. A Cost-Effective Approach to the Diagnosis and Management of Acute Infectious Encephalitis. *Eur*. 2017;77(1-2):66–74. doi:10.1159/000453662.
4. Kalita J, Mani VE, Bhoi SK, Misra UK. Spectrum and outcome of acute infectious encephalitis/encephalopathy in an intensive care unit from India. *An Int J Med*. 2017;110(3):141–8.
5. Jain P, Jain A, Kumar A, Prakash S, Khan DN, Singh KP, et al. Epidemiology and etiology of acute encephalitis syndrome in North India. *Jpn J Infect Dis*. 2014;67(3):197–203.
6. Singh TD, Fugate JE, Rabinstein AA. The spectrum of acute encephalitis: causes, management and predictors of outcome. *Neurology*. 2015;84(4):359–66.
7. Thakur KT, Motta M, Asemota AO. Predictors of outcome in acute encephalitis. *Neurology*. 2013;81(9):793–800. doi:10.1212/WNL.0b013e3182a2cc6d.

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