Dengue Encephalopathy in Hadoti Region: Clinical Presentation, Diagnostic Evaluation, Management and Outcome

Manoj Saluja1, Yogesh Kumar Swami2*, Saurabh Chittora3, Hemant Vimlani1

Abstract

Background: Dengue viral infection is common worldwide. Recent studies have shown dengue viral infection causing encephalopathy, with high morbidity and mortality. Dengue encephalopathy patients usually present with altered sensorium, elevated lab parameters and high antibody titres at the time of admission. Dengue infection was very common and virulent in Hadoti region during August to November 2017 and many patients presented with encephalopathy.

Aims: To study the clinical presentation, lab parameters and other diagnostic features, management and outcome of patients of dengue fever with encephalopathy in Hadoti region in August to November 2017.

Settings and Design: The study was done in Govt Medical college Hospital Kota and other multi-speciality hospitals of Kota. Study population comprised of 60 patients presenting with febrile illness and thrombocytopenia, serologically proved to be having Dengue fever. Among these 60 patients, 30 patients had encephalopathy who presented with altered sensorium, seizures or any other neurological symptoms and remaining 30 had no signs and symptoms of encephalopathy.

Results: Among 30 patients with encephalopathy and positive serology (NS1/IgM/ IgG), fever and altered sensorium was most common symptom, while amongst patients without encephalopathy fever with chills and generalised bodyache was more common clinical feature. Convulsions and respiratory distress were very common among encephalopathy patients. Out of 30 encephalopathy patients 16 patients (53%) had convulsions, 14 (46%) had respiratory distress, 17(56%) had shock and 3 patients (10%) had hemiplegia. 2 patients also had visual blurring and dysarthria. Mean duration between appearance of fever and altered sensorium was 4.6 (±2.1) days. Most of patients with encephalopathy had deranged hepatic (bilirubin, SGOT, SGPT), renal (urea, creatinine, decreased urine output) and coagulation parameters (PT/INR, bleeding manifestations). 9 (30%) patients died and 21(70%) patients improved with complete recovery (except 3 hemiplegic patients).

Conclusions: Increased incidence of dengue fever with encephalopathy in the recent years, in the absence of single sensitive test for detecting dengue encephalopathy, variable CSF and MRI Brain features, and associated high morbidity and mortality poses a big problem for clinician. This study may be helpful in focussing on early diagnosis and aggressive initial management which can influence final outcome.

Introduction

RNA virus of family Flaviviridae that spreads by Aedes mosquitoes is responsible for dengue fever.1 Approximately 2.5 billion people are at risk primarily in the densely populated areas of tropical and subtropical countries, with an estimated infection load of 50 million worldwide annually. According to the World Health Organization (WHO), India is considered in endemicity category A, in which dengue is a major public health problem. Presentations in symptomatic patients include undifferentiated viral fever, dengue fever, and dengue hemorrhagic fever. Expanded dengue spectrum includes unusual manifestations like neurological, hepatic, renal, and other isolated organ involvement.

Common clinical features are fever, arthralgia, headache, petechial spots, rashes and hemorrhagic manifestations. Dengue virus is considered as a non-neurotropic virus.1 However, increasing number of studies and case reports of central nervous involvement (CNS) involvement are being reported.2-4 The CNS manifestations can be attributed to three factors (a) neurotropic effect, (b) secondary to systemic manifestation, and (c) postinfectious sequelae including immune-mediated reactions.5,6 Numerous neurological manifestations are reported like encephalopathy, encephalitis, Guillaine Barre syndrome, transverse myelitis, acute disseminated encephalomyelitis, and myositis. These neurological complications are rare and its pathogenesis is controversial. Few theories states that dengue neurological manifestation is secondary to systemic manifestation (Encephalopathy), but recent evidence is in favour of dengue neurotropism, because dengue virus7 and dengue IgM antibodies has been discovered in CSF of encephalopathy patients which suggests that dengue virus is capable of central nervous system infection. Dengue fever associated with encephalitis has high morbidity and mortality and only few studies or case series has been published regarding dengue encephalitis.8 This study may be useful in early detection of dengue fever patients with encephalopathy (which might be encephalitis) using clinical features and laboratory parameters in resource limited countries which are

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1Professor, 2Resident, 3Assistant Professor, Govt. Medical College, Kota, Rajasthan; *Corresponding Author

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having maximum number of dengue cases, so that early diagnosis of dengue encephalopathy and timely supportive therapy can reduce or avoid morbidity and mortality. We present a total of 30 cases of dengue fever with encephalopathy.

**Material and Methods**

This epidemiological prospective study was done Govt Medical College Hospital Kota and other multispeciality hospitals of Kota.

This study included total of 60 patients serologically proved to be having dengue fever. Among which 30 patients had encephalopathy (or encephalitis) who presented with altered sensorium, seizures or any other neurological symptoms. Rest 30 patients of dengue fever without encephalopathy served as control.

The diagnosis of dengue fever was based on clinical features, (fever, headache or bodyache, altered sensorium, hemorrhagic manifestation, jaundice, and shock) and positive serum NS1/IgM / IgG antibodies. The diagnosis encephalopathy was based on clinical features (Low GCS, altered sensorium, headache, and seizures or any other neurological deficits), MRI brain findings (Hyperintense areas) and CSF study (Cell count, protein and sugar).

The detailed medical history, age, area of residence, and clinical features were noted. Consciousness was assessed by Glasgow coma scale (GCS), Systemic manifestations such as lymphadenopathy, hepatosplenomegaly, jaundice, Cardiac, Renal and Respiratory findings were also recorded.

The laboratory tests included complete blood examination (hemoglobin, hematocrit, WBC counts, platelet counts), blood sugar, blood urea, serum creatinine, bilirubin, SGOT, SGPT, prothrombin time, INR, and Dengue serum antibodies. Electrocardiogram, Chest X-ray (PA view) done in all patients, and CT scan and/or MRI brain, Cerebrospinal fluid analysis (analyzed for protein, sugar, cells) were carried out in as much as possible patients of encephalopathy group.

**Exclusion criteria**

Patients with previous liver or kidney failure and recent cerebral events (stroke, meningoencephalitis), malaria, and hepatitis were excluded.

**Results**

Among 30 patients of proved dengue fever with altered sensorium, seizures, or any other neurological symptoms suggestive of encephalopathy/encephalitis, 22 patients were male and 8 were female. All patients presented with fever with or without chills. Headache, vomiting, pain abdomen were also prominent features. Detailed symptomatic profile of encephalopathy group and controls is given in Table 1.

Most common clinical features in patients with encephalopathy were fever with altered sensorium. Clinical features like seizures, shock, generalised weakness and shortness of breath were significant.

All 30 patients had altered sensorium, among which 19 patients required intubation and ventilator support and 2 patients required BIPAP support, 9 patients were maintained on oxygen supply by face mask.

**Neurological examination**

All encephalopathy patients presented with altered sensorium, 11 patients had exaggerated DTR, 12 patients had extensor plantar reflex, rest all had normal DTR and normal plantar reflex.

Hepatic dysfunction was found in most of patients as deranged transaminases or bilirubin levels. 14 patients (46%) also had renal impairment as deranged urea/creatinine or decreased urine output. All patients had thrombocytopenia of varying degree. Detailed lab results are analysed in Table 2.

All 30 encephalopathy patients had severely deranged liver enzymes (SGOT, SGPT), coagulopathy (Raised PT, INR), severe thrombocytopenia and positive serology (NS1/Ig-M /Ig-G), 3 patients required CRRT for Acute Kidney Injury for short period of time. 16 patients had generalized seizures, 14 patients had respiratory distress out of which 2 patients had ARDS and 1 patient had hemoptysis.

7 patients (23%) had hyponatremia and required IV sodium. CSF study showed high protein and normal cell counts in 10 patients and normal protein and cell count in 14 patients (CSF was not done in 7 patients).

**MRI Brain study**

MRI brain was done in 23 patients, out of which-

1. 4 patients had diffuse cerebral edema
2. Hyperintensities in temporal lobes/thalamus or pons seen in 10 patients, among which 6 patients had hyperintensities in thalamus, 3 patients in temporal lobes and 1 patient’s MRI shows diffuse cerebral atrophy and multiple small infarct
surveillance shows that global incidence of children with suspected encephalitis in Thai hospital were found to have dengue infection.

The patients who died in encephalopathy group (9 out of 30 patients), all of them presented with – low GCS, seizures, headache. Hence patients with dengue fever with predominance of these clinical features and severely deranged lab parameters are probably manifesting encephalopathy which has high morbidity and mortality, so early diagnosis and aggressive management should be given to prevent anticipated complication.

In case of dengue Encephalitis diagnosis can be made either by detection of virus in CSF (viral culture/PCR) or immune response by the body (Ig-M antibodies in CSF). The gold standard method is viral culture which is difficult and time consuming. Regarding CSF IgM and IgG antibodies, together with viral antigen, however exact reason is not known.

Table 3: Comparative study between improved and died patients of dengue encephalopathy

<table>
<thead>
<tr>
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<th>Improved patients (n=20)</th>
<th>Died patients (n=9)</th>
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<tbody>
<tr>
<td>Seizures</td>
<td>9 (45%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>10 (50%)</td>
<td>4 (45%)</td>
</tr>
<tr>
<td>Mean bilirubin</td>
<td>2.6</td>
<td>2.75</td>
</tr>
<tr>
<td>Mean urea</td>
<td>61.65</td>
<td>71.2</td>
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<tr>
<td>Mean creatinine</td>
<td>1.5</td>
<td>2.13</td>
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<tr>
<td>Time between fever and altered sensorium</td>
<td>4 to 6-7 days (mean-4.85)</td>
<td>4 to 6-7 days (mean-4.11)</td>
</tr>
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3. 7 patients had normal MRI study
4. 1 patient’s MRI showed left basal ganglia bleed and 1 had only sinusitis.

Among 30 dengue patients with encephalopathy, 20 patients recovered completely at the end of 1 month (independent for activities of daily living), and 9 patients died (due to severe sepsis with MODS).

Comparative study of patients who survived and died on the basis of various parameters are given in Table 3.

Among all patients, 24 patients were given mannitol/dexamethasone, and 16 patients also received inj. acyclovir.

Inj. Acyclovir found to be beneficial in dengue encephalopathy patients, mostly due to cross reactivity with viral antigen, however exact reason is not known.

Discussion

Dengue is endemic to over 100 countries and approximately 2.5 billion people are at risk. It is estimated that 50–100 million infections and 25,000 fatalities occur worldwide every year. World health organization (WHO) surveillance shows that global incidence is increasing. The primary vector is the mosquito Aedes Aegypti. Dengue fever has varying clinical presentation ranging from asymptomatic infection to life threatening hemorrhagic fever and dengue shock syndrome. Complications of dengue fever are common and usually related to renal and hepatic dysfunction. In our study almost all patients had severely deranged liver enzymes (SGOT, SGPT), coagulopathy (Raised PT, INR), severe thrombocytopenia and positive serology (NS1, Ig-M and Ig-G). Patients were managed conservatively as per WHO guidelines. In the patients with hemorrhagic diathesis, platelet concentrate and/or fresh frozen plasma were administered as indicated. Among all patients with low GCS were intubated to protect the airway and majority of them extubated after 5-7 days. 9 patients were on prolonged ventilation who died later due to refractory septic shock and MODS due to secondary bacterial sepsis. CRRT done for 3 patients with AKI (Acute kidney injury) having oliguria/anuria, Pulmonary edema, Hyperkalemia and severe metabolic acidosis.

Neurological complications are rare and its pathogenesis is controversial, few theories states dengue neurological manifestation is secondary to systemic manifestation (Encephalopathy), but recent evidence is in favour of dengue neurotropism, because dengue virus9 and dengue IgM antibodies10 has been discovered in CSF of encephalopathy patients which suggests that dengue virus is capable of central nervous system infection.

In our study the features of encephalitis (headache, altered sensorium, and seizures) in majority of patients were seen more commonly after 4-7 days of onset of fever. Among the four dengue serotypes (DEN-1 to DEN-4) DEN-2 and DEN-3 have highest propensity to neurological complications.11,12

Cam BV et al, and Hendarto SK et al, have reported the encephalopathy incidence ranging from 0.5% to 6.2%. Kankirawatana et al., found that 18% of children with suspected Encephalitis in Thai hospital were found to have dengue infection.

In Hadoti region mortality rate was high among dengue encephalopathy patients as comparative to other studies may be due to more virulent strain of dengue virus or delayed reach to health care centre.

Conclusion

Increased incidence of dengue fever with encephalopathy in the recent years, in the absence of single sensitive test for detecting dengue encephalitis, variable CSF and MRI Brain features, and associated high morbidity and mortality, this study may be helpful in focussing on early diagnosis and aggressive initial management which can influence final outcome.
References

2. Ruikar D, Jayalakshmi S, Surath M. Neurological Manifestations of acute Dengue virus infection: A study from tropical country- India (44-SD). Neurology 2015; 84:14-SD.