Acute Dengue Encephalopathy in children: Time to look beyond JE

Dr. Swathi Chacham¹, MD, DM, Dr. Renu Yadav², MBBS, [MD], Dr. Bindhu Vechangi³ MBBS, [MD], Dr. Manideepa Maji⁴, MBBS, [MD], Dr. Nikhil Rajvanshi⁵, MBBS, [MD], Dr Nowneet Kumar Bhat⁶, MD
Department. of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.249203

Dr. Swathi Chacham: MBBS, MD Pediatrics, DM [Neonatology, PGIMER, Chandigarh], MNAMS, [PhD]
Additional professor (Former head), Provost, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

Dr Renu Yadav: MBBS, [MD] Designation: Junior Resident, Department of Pediatrics, Institute: All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

Dr Bindhu Vechangi: MBBS, [MD]Junior Resident, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhnad, India.

Dr Manideepa Maji: MBBS, [MD]Junior Resident, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhnad, India.

Dr Nikhil Rajvanshi: MBBS, [MD]Junior Resident, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhnad, India.

Dr Nowneet kumar Bhat: MBBS, MD Professor & Head, Department of Pediatrics,
Corresponding author: Name: Dr. Swathi Chacham: MBBS, MD Pediatrics, DM (Neonatology, PGIMER, Chandigarh), MNAMS,(PhD)

Abstract:
Background: Dengue encephalopathy is a rarely reported entity in children with an incidence of 0.5 to 6.2 %. Although dengue is a non-neuropathotropic virus, possibility of direct neuronal injury due to the dengue virus cannot be ruled out. We are here with two cases of dengue encephalopathy.

Case summary: An 8-year-old girl presented with acute onset fever with rash, myalgia, and arthralgia and on evaluation was found to have hemoconcentration, leucopenia and thrombocytopenia. Dengue IgM was found to be positive. On day 3 of illness the child developed altered sensorium for around 24 hours and one episode of generalized seizure. CSF Examination was suggestive of viral etioloogy and neuro imaging was normal. Similarly, another 13-year-old boy with similar history and NS1 antigen positivity developed severe incapacitating headache lasting for around two weeks, more in retroorbital region. CSF examination showed mononuclear pleocytosis with normal sugar and protein. MRI brain showed mild gyral swelling in bilateral fronto temporal region. Fundus examination was normal in both the cases. Both the cases did not have significant hepatic dysfunction or coagulopathy and had normal serum electrolytes and recovered with symptomatic management and intravenous fluid therapy.

Conclusion: Dengue is an emerging cause of encephalopathy competing with JE especially in non endemic areas. Clinicians need to be aware of this rare presentation of a common febrile illness like Dengue with encephalopathy, seizure and headache for timely identification and proper management.

Key word: Encephalopathy; Encephalitis; Dengue

Date of Submission: 27-04-2020 Date of Acceptance: 10-05-2020

I. Introduction

Dengue encephalopathy is an under reported entity with an incidence ranging from 0.5 to 6.2 %. (1) The possible pathophysiology includes hepatic encephalopathy, cerebral hypoperfusion, cerebral edema, deranged electrolytes, and intracranial bleeding. (2) Although dengue is a non-neuropathotropic virus, possibility of direct neuronal injury due to the dengue virus cannot be ruled out in few unexplained cases. (3) Hereby we are presenting two cases of dengue encephalopathy.

DOI: 10.9790/0853-1905034244 www.iosrjournals.org
II. Case summary

Case 1: An 8-year-old girl presented with acute onset fever with rash, myalgia, and arthralgia and on evaluation was found to have homocentration, leucopenia and thrombocytopenia. Dengue IgM was found to be positive. On day 3 of illness the child developed altered sensorium which lasted for around 24 hours followed by one episode of generalized seizure. Fundus examination was normal and neuro imaging revealed mild cerebral edema. CSF examination revealed lymphocytes with normal sugar and protein. In view of salient clinical features, and Dengue serology positivity the child was diagnosed and treated as dengue encephalopathy. Anti epileptics were started for seizures. Child was started on measures to reduce intra cranial pressure and supportive and symptomatic treatment.

Case 2: A 13-year-old boy with similar history of fever with myalgia, erythematous rash was admitted with the possibility of Dengue fever. Investigations revealed NS1 antigen positivity and was started on supportive and symptomatic treatment. He later developed from day 4 of illness severe incapacitating headache more in retro-orbital region which lasted for around two weeks. Fundus examination was normal. MRI brain showed mild gyral swelling in bilateral frontotemporal region. CSF examination showed mononuclear pleocytosis with normal sugar and protein. Child was treated in lines of dengue encephalopathy.

Both the cases did not have significant hepatic dysfunction or coagulopathy, serum electrolytes were normal and recovered with symptomatic management and intravenous fluid therapy.

III. Discussion

Dengue is an RNA virus which is single stranded and belongs to flavi virus genus. It comprises 4 serotypes, DEN-1 to DEN-4. Classical presentation of dengue virus includes fever, headache, retro-orbital pain with rashes. Patient can have severe arthralgia along with myalgia. It has a short incubation period of 5-8 days. (4) Dengue virus has the potential to infect any organ system. Various central nervous system [CNS] manifestations of dengue infection include Guillain-Barre syndrome, acute disseminated encephalomyelitis, transverse myelitis. (5,6) Encephalopathy with dengue infection is an emerging entity. (4) The commonest serotype which are responsible for neurological manifestations include DEN2 and DEN3. (5) However, in cases of dengue encephalopathy, classical dengue infection symptomology is seen in less than half of the affected patients. (5) In our case series, both the cases presented with classical symptoms and later on developed features of encephalopathy.

Encephalitis is a histological diagnosis, referred to the inflammation of the brain parenchyma. Clinical presentation of encephalitis consists of altered sensorium, headache, projectile vomiting, seizures and focal neurological deficits. Encephalopathy refers to the state of reduced or altered consciousness, which can be manifestation of various CNS insults like metabolic derangements, drug intoxication and less commonly by encephalitis because of neurotropic viruses.

It is still unclear whether encephalopathy in case of dengue infection is a result of direct neurotropism or indirectly via other mechanism. Hepatic encephalopathy is a predominant manifestation with dengue infection. (5) Dengue encephalitis can entirely be a different clinical entity as in a fair proportion of these children, indirect mechanism of encephalopathy is successfully ruled out. (4) Moreover, both dengue virus and anti-dengue IgM has been isolated from CSF, so the possibility of dengue virus being neurotropic cannot be ruled out. (1,7)

Previous studies have revealed predominantly secondary infections in cases of encephalitis. (8) However, dengue IgG antibodies were negative in both of our cases. Onset of encephalopathy usually occurs from 3-7 days after onset of fever as in our cases. (9)

Laboratory confirmation of the infection can be done either by RNA detection via PCR which has a specificity of 100% and sensitivity of 70% if done within the five days of fever onset. (10) Other option is detection of viral antigens by immunohistochemistry with a sensitivity of 89% which provides a cheaper and rapid method for establishing the diagnosis. (11) Similarly, antibody detection (IgM and IgG) can be done. Yield of these different modalities depends on the timing of the infection at which they are done. MRI findings in dengue encephalopathy can vary from hemorrhages to focal abnormalities and edema in hippocampus, basal ganglia and thalamic region as highlighted by our case. (12) In these two children the diagnosis of dengue encephalopathy has been made based on the definition of Varathraj, (1) which is further supported by positive anti-dengue IgM and NS1 antigen in the serum.

As no specific antiviral therapy exist, management of dengue encephalopathy is principally based on supportive care and maintaining adequate oxygenation, fluid and electrolyte balance. Seizures and features of raised intracranial pressure and mandate anti epileptic therapy when present. Also sufficient measures to tackle the raised intra cranial pressure should be taken.
IV. Conclusion

It is time to look beyond Japanese encephalitis in children presenting with acute viral encephalitis, especially in non endemic regions. Dengue with encephalopathy is a potential cause for morbidity and mortality in children with dengue infection. Clinicians need to have high index of suspicion for this rare manifestation of a common febrile illness like Dengue. Early diagnosis and timely management can curtail the sequelae to some extent.

Acknowledgements: We thank the parents of the children for their support.

Conflicts of interest: None

Funding: None

Ethical clearance: From Institute ethics committee

Consent: Obtained from parents

References: