



Case Study

A case of Dengue Haemorrhagic fever with fatal encephalopathy

Sharma Shweta^{1*}, R.K. Mahajan¹, A.Jain¹ and A.K.Gadpayle²

¹Department of Microbiology, Dr Ram Manohar Lohia Hospital & PGIMER, New Delhi, India

²Department of Medicine, Dr Ram Manohar Lohia Hospital & PGIMER, New Delhi, India

*Corresponding author

ABSTRACT

Keywords

Dengue viral infections;
Encephalopathy

Clinical spectrum of dengue infection ranges from asymptomatic infection to severe life threatening phenomenon like dengue hemorrhagic fever and dengue shock syndrome. Dengue has classically been considered a non-neurotropic virus and neurological complications in general are uncommon. But there is ever increasing evidence that some cases of severe dengue may develop an element of encephalopathy which may follow aggressive course and prove fatal.

Introduction

Dengue infection is one of the most important arboviral infections afflicting South-East Asia. This is transmitted by female *Aedes aegyptii* mosquito and caused by four antigenically distinct serotypes of dengue virus. This may present as asymptomatic infection, dengue fever to life threatening dengue hemorrhagic fever or dengue shock syndrome. Fever, headache, arthralgia, retro-bulbar pain, macular rash, petechial spots and hemorrhagic manifestations are common features. Encephalopathy associated with dengue infection is considered to be a rare condition, and is usually secondary to multisystem derangement like shock, hepatitis, coagulopathies etc (Chotmongkol, 2004). Here, we present an adult patient with

DHF who developed fatal encephalopathy after the fever had subsided.

Case Report

A previously healthy forty-five year old female patient was brought to the casualty department of hospital in unconscious state. Patient had been suffering from high grade fever with chill for the past 7 days, abdominal distension and difficult breathing since two days. At the time of admission, patient was unconscious, afebrile, pulse rate was 70/min, her blood pressure was 100/70mmHg and respiratory rate was 26/minute. Her general condition was poor & score in Glasgow coma scale was 3 (E₁V₁M₁) i.e. Patient doesn't open eye even to pain, no verbal response and

no motor response. Pupils were dilated and sluggishly reacting to light. Chest examination revealed bilateral basal crepts and on per abdomen examination, there was no organomegaly or tenderness but small amount of free fluid could be elicited. Cardio-vascular system was normal. During the very first day of admission when the respiration became effortful she had to be intubated and put on mechanical ventilation. Laboratory findings showed- white blood cell count of $19.9 \times 10^9/L$ (Polymorphs 78%, Lymphocytes 20%, Eosinophils 1%, and Basophils 1%), Haemoglobin 14.9 gm% and platelet count 40,000/cu.mm. Serology for dengue infection was reactive for IgM antibodies against dengue virus by MAC ELISA (kit supplied by NIV Pune). Also the serum sample was positive for NS1 antigen by NS1Ag ELISA. Malarial parasite was not seen in the peripheral smear and it was negative in the immunochromatographic rapid card test also. Serology for HIV, HCV and HBsAg was non-reactive. Serum VDRL and TPHA were non-reactive. Blood serology for Japanese encephalitis virus was also negative. Patient's renal function tests were deranged i.e. her blood urea nitrogen was 88mg/dl and creatinine was 6.5mg/dl. Chest X-ray revealed bilateral alveolar infiltration along with bilateral pleural effusion. Ultrasound abdomen was suggestive of bilateral pleural effusion with minimal ascites. MRI brain showed altered signal intensity in the midbrain, bilateral thalamus and medial temporal region, with the periventricular and corona radiata on both sides showing scattered areas of restriction on diffusion weighted imaging and patchy areas of enhancement in the bilateral thalamus and corona radiata - features suggestive of acute necrotising meningo-encephalitis. The blood, urine, CSF and endotracheal

aspirate cultures did not grow any organism within 48 hrs of incubation. Patient was started on Piperacillin-Tazobactam & Metronidazole along with intravenous fluids and supportive treatment. Multiple platelet transfusions done to improve platelet count to 1,00,000/cu.mm. Fifty cycles of peritoneal dialysis were given but when patient didn't respond, haemodialysis started on alternate days but her renal function status continued downward trend and despite best of efforts to improve the condition of patient, she succumbed to her illness after 10 days of admission in the hospital.

Discussion

Amongst all flaviviruses, Dengue virus infections are the most common and are emerging as a major cause of hospital admissions in the Northern Indian states. According to WHO, the incidence of dengue has grown dramatically around the world in recent decades. Over 2.5 billion people i.e. over 40% of the world's population are at risk for dengue infection. WHO estimates project dengue infection load of 50–100 million worldwide every year with fatalities of about 2.5% (WHO, 2013)

Dengue encephalopathy is a rare but well recognised clinical entity, the incidence ranging from 0.5 to 6.2% (Misra *et al*, 2006). The possible pathogenic mechanisms involved in development of encephalopathy include encephalopathy secondary to liver and renal impairment, cerebral hypoperfusion due to shock, cerebral edema because of vascular leak, deranged electrolytes and intracranial bleeding due to thrombocytopenia or coagulopathy (Angibaud *et al*, 2001). There are some cases where the cause of neurological injury remains unclear.

On admission, diagnosis of dengue infection in our patient was established on the basis of reactive IgM antibodies against dengue virus in MAC ELISA and positive NS1 Antigen in NS1 ELISA serology. Patient had clinical features suggestive of plasma leak and there was laboratory evidence of deranged renal functions. The altered sensorium initially appeared to be a sequelae to impaired renal function but MRI findings indicated not only features of encephalopathy but also the possibility of direct neuronal injury due to dengue virus.

There are some reports of nervous system involvement from various parts of the world, but neuro-virulent properties of dengue virus are not well known, though dengue serotypes DEN-2 and DEN-4 have been shown to have the highest propensity to neurological complications (Koley *et al*, 2003). The exact pathogenesis of nervous system involvement is not yet clear as to whether the neuronal injury is the result of immune phenomenon, metabolic insult or direct viral injury and hence lot of further studies are needed to understand the pathophysiology of the disease. This needs to be underscored that clinical features of dengue encephalopathy share a large similarity with conditions like cerebral malaria, Japanese encephalitis etc. and a high index of suspicion coupled with rapid relevant laboratory investigations are extremely important to arrive at correct diagnosis.

Dengue virus has not been classically characterised as a neurotropic virus although recently there is evidence of direct neuronal injury in laboratory confirmed dengue cases. Presently when serological diagnostic tools do not appear competent enough to pick up dengue virus

antigen or antibody in the CSF and culturing this virus would need specialised virology laboratories. It becomes clinically extremely prudent to include investigations like MRI in suspected cases of encephalopathy, especially during increased reporting of dengue cases so that early signals of neuronal involvement would be picked up. Also this is high time that role of antiviral agents is also investigated for intervention in cases with features indicating unfavourable outcome.

References

- Angibaud G, Luaute J, Laille M, Gaultier C. 2001. Brain Involvement in Dengue Fever. *Journal of Clinical Neuroscience*. 8: 63-5.
- Chotmongkol V and Sawanyawisuth K. 2004. Dengue hemorrhagic fever with encephalopathy in an adult. *Southeast Asian J Trop Med Public Health*. 35(1):160-1.
- Koley TK, Jain S, Sharma H, Kumar S, Mishra S, Gupta MD, *et al*. 2003. Dengue encephalitis. *J Assoc Physicians India*. 51: 422-3.
- Misra UK, Kalita J, Syam UK, Dhole TN. 2006. Neurological manifestations of dengue virus infection. *J. Neurol. Sci*. 244: 117-122.
- World health organization. 2013. Dengue hemorrhagic fever; diagnosis, treatment, prevention and control. Geneva: *WHO* Fact sheet N°117, Updated September 2013.