Early central nervous system involvement in a young patient with dengue encephalitis

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SUMMARY

A previously well 13-year-old boy presented with a short history of fever and altered mental status. His mother was admitted for dengue fever and there had been a recent dengue outbreak in their neighbourhood. He was diagnosed with dengue encephalitis as both his dengue non-structural protein 1 (NS-1) antigen and cerebrospinal fluid (CSF) dengue polymerase chain reaction (PCR) were positive. He did not have haemoconcentration, thrombocytopenia or any warning signs associated with severe dengue. He recovered fully with supportive treatment. This case highlights the importance of considering the diagnosis of dengue encephalitis in patients from dengue endemic areas presenting with an acute febrile illness and neurological symptoms.

KEY WORDS:
Dengue encephalitis, altered sensorium in dengue fever

INTRODUCTION

Various neurological manifestations of dengue have been reported, including encephalopathy, encephalitis, Guillain-Barre syndrome, transverse myelitis and acute disseminated encephalomyelitis.[1] As the incidence of dengue fever continues to increase every year, uncommon complications like dengue encephalitis become more prevalent.

CASE REPORT

A 13-year-old boy with no previous medical illness was brought by his parents to the Emergency Department with high-grade fever and altered mental status for one day. His parents had found him to be more quiet than usual, confused and talking irrelevantly at times. He had complained of headache the day prior to presentation to hospital, but did not have any fits, photophobia or vomiting. He did not have any rash, bleeding or joint pains. There were no upper respiratory tract symptoms, cough, shortness of breath or chest pain. Two days earlier, the family had gone for an outing at a local beach. He did not swim in the sea or eat anything different from his family members. He was an active child who did well in school and socially. He did not smoke and had never taken any illicit substance before.

On admission, he was febrile with a temperature of 40.3°C. His blood pressure was 137/67 mmHg and pulse rate 115 beats per minute. He appeared listless and irritable. Although he was able to obey commands and answer questions appropriately, his responses appeared obtunded. He did not have neck stiffness and neurological examination was normal. His throat was injected but the tonsils were not enlarged. There was no cervical lymphadenopathy. Examination of the cardiovascular and respiratory systems were normal. There was no hepato-splenomegaly. Fundoscopy was normal.

The diagnosis on admission was acute meningoencephalitis. He was started on intravenous Ceftriaxone 2 grams twice daily and intravenous Acyclovir 500 mg thrice a day. Initial investigations revealed a haemoglobin (Hb) concentration of 11.6 g/dl, haematocrit of 36.3%, white cell count (WCC) 6.18 x 10^3uL (neutrophils 62.2%, lymphocytes 17%) and platelet count of 190 x 10^3/uL. His renal profile and liver function tests were normal apart from a slightly elevated aspartate transaminase (AST) of 52U/l.

Repeated blood films for malarial parasites were negative. His anti-streptolysin O titre (ASOT) was positive, with a titer of more than 200 IU/ml. A contrasted CT scan of the brain was normal. A lumbar puncture was performed the next day. The cerebrospinal fluid (CSF) was clear, colourless and acellular. Gram stain, Indian ink and staining for acid-fast bacilli were all negative. The CSF glucose was low at 3.1mmol/l compared to the random blood sugar of 8.3mmol/L. CSF protein was normal (0.2 g/l). Blood, CSF and urine cultures did not isolate any organisms.

In the ward, the patient was drowsy but was able to obey commands when aroused. It was also noted that his WCC was progressively reducing. Incidentally, the patient's mother was also admitted for dengue fever and we found out that there had been a recent dengue outbreak in their housing area. Both the patient and his mother were tested positive for the dengue non-structural protein 1 (NS-1) antigen. Their dengue IgM and IgG were negative. The refrigerated sample of the patient's CSF was then sent for dengue PCR which came back later as positive. The patient's diagnosis was then changed to dengue encephalitis. The frequency of Ceftriaxone was reduced from twice daily to daily dosing only, to cover for possible secondary bacterial infection while Acyclovir was discontinued. His blood counts were monitored more frequently but there was no evidence of haemoconcentration and his platelet counts never dropped below 150 x 10^3/uL. His WCC reached its nadir at 1.34 x 10^3/uL on the seventh day of illness before normalising. His aspartate transaminase (AST) also increased to 103U/L while his alanine transaminase (ALT) went up to 52U/L. The

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Table I: Summary of investigation results

Full Blood Count		
	Admission (Day 1)	**Discharge (Day 9)**
White blood cell	6.18 x 10^3 /uL	6.23 x 10^3 /uL
Hemoglobin (Hb)	11.6 g /dl	11.2 g /dl
Platelet	190 x 10^3 /uL	185 x 10^3 /uL
Liver function tests		
	Day 3	**Day 9**
Aspartate transaminase (AST)	103 U/L	36U/L
Alanine transaminase (ALT)	52 U/L	33U/L
Renal Profile		
Urea – 2.2 mmol/L		
Creatinine- 62mmol/L		
Cerebrospinal Fluid (CSF) results		
Appearance - Clear, colourless and acellular.		
Gram stain - Negative		
Indian ink staining - Negative		
Acid-fast bacilli- Negative.		
CSF glucose - 3.1 mmol/l (low)		
Random blood sugar of 8.3 mmol/L (for comparison)		
CSF protein - 0.2 g/L (normal)		
Dengue virus PCR- Positive (DEN-1)		
Culture and sensitivity results		
Blood- No growth		
Urine – No growth		
CSF - No growth		
Blood films for malarial parasites – Negative (x3)		
Dengue Serology		
Dengue non-structural protein 1 (NS-1) antigen - Positive		
Dengue IgM - Negative		
Dengue IgG- Negative.		
Imaging		
Contrasted CT Brain- Normal		

patient's fever began to settle after the fourth day of illness and he began to improve clinically. No seizures were noted throughout his stay and he was discharged after nine days. His WCC prior to discharge was 6.23 x 10^3/uL.

DISCUSSION

Symptoms of dengue encephalitis include headache, altered sensorium and seizures and can occur in the absence of intracranial haemorrhage. Recent evidence suggests that the virus is capable of central nervous system infection as the dengue virus and IgM antibodies have been isolated from the CSF of patients.[3] It has been postulated that the virus crosses the blood-brain barrier and directly invades the brain since the onset of encephalitis appears early in the course of the illness coinciding with the viremic phase.[4] As illustrated in our case, dengue encephalitis can occur as early as the first day of illness. This was confirmed by detecting dengue virus genetic material via PCR in the CSF. Among the four dengue serotypes (DEN-1, DEN-2, DEN-3 and DEN-4), DEN-2 and DEN-3 are said to have the highest propensity for neurological complications.[5] However, sero-typing for dengue virus is not readily available and not routinely done. Our case also highlights the fact that dengue encephalitis can occur in an otherwise uncomplicated dengue fever. The patient did not have haemoconcentration, thrombocytopenia or other warning signs associated with severe dengue. It is possible that the incidence of dengue encephalitis is under-reported as patients may only have subtle mental changes and dengue fever is not suspected due to the absence of significant haemoconcentration and thrombocytopenia. In fact, *Soares* CN *et al* reported that dengue fever is one of the leading causes of viral encephalitis in dengue endemic areas.[5]

To confirm the diagnosis of dengue encephalitis, it is necessary to obtain CSF samples from a patient. However, lumbar puncture may be contraindicated when the patient has thrombocytopenia. Furthermore, neurological manifestations associated with dengue encephalitis are self-limiting and the patient usually recovers without any sequelae, thus making the procedure useful only in ruling out alternative diagnoses. It is important to maintain a high index of suspicion for other causes of fever and altered sensorium, namely intracranial bleeding and bacterial meningoencephalitis. Magnetic resonance imaging (MRI) of the brain is the imaging modality of choice in dengue encephalitis although it is not able to distinguish between encephalitis caused by other viruses. Hyperintense areas can be seen in the global pallidus, temporal lobes, thalamus,

hippocampus, pons and spinal cord.[2] The management of dengue encephalitis remains supportive, including the control of seizures if present. Careful monitoring of the patient's clinical condition and haematocrit levels are important to prevent complications like dengue shock syndrome.

CONCLUSION

Dengue encephalitis is a rare but recognized manifestation of dengue fever. It can present early in the course of the illness or as an undifferentiated viral fever with normal blood counts. It is important to maintain a high index of suspicion for this condition, especially in areas where dengue fever is endemic. Dengue encephalitis can be confirmed by dengue PCR of the CSF. Treatment is supportive but careful monitoring of the patient is essential to avoid complications like dengue shock syndrome.

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