

## CASE REPORTS

# Bilateral thalamic internal medullary lamina involvement in a case of dengue encephalitis

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### Abstract

There are 50-100 million dengue infections each year, but dengue encephalitis is relatively uncommon. The aetiology of neuronal injury is proposed to be due to direct viral neurotropism or host immune response-mediated inflammation causing neuronal damage. We report a case of severe dengue encephalitis, presenting during the acute viraemic phase of the disease. This was associated with inflammation and haemorrhage of the internal medullary lamina of both thalami which, to our knowledge, has not yet been reported in other infections of the central nervous system.

### INTRODUCTION

Dengue fever is caused by an arbovirus belonging to the *Flaviviridae* family. Neurological manifestations of dengue fever has been reported to occur up to 0.5% - 7.4% of symptomatic cases.<sup>1</sup> The etiology of neuronal injury varies and at times remain uncertain, including systemic complications and metabolic disturbances resulting in encephalopathy, viral neurotropism, or host-immune response causing neuronal damage and inflammation.<sup>1</sup> We report a case of dengue encephalitis with extensive, bilaterally symmetrical inflammation and haemorrhage of the thalamic internal medullary lamina, which has not yet been described in any central nervous system infection.

### CASE REPORT

A 30-year-old man of Bangladeshi origin was found unresponsive at home following six days of fever, vomiting and poor oral intake. He was drowsy upon arrival in the hospital, only opening eyes to voice and localizing to pain stimuli. Pupils were equal in size and reactive with no ophthalmoplegia. There was no meningism or rash. His tone was flaccid in all limbs, with brisk reflexes and extensor plantar responses

bilaterally. He was febrile (temperature of 39°C), normotensive but tachycardic (pulse rate of 107 beats per minute). His conscious level deteriorated within two hours of admission and he was subsequently intubated. He had mild renal impairment (creatinine 124  $\mu\text{mol/L}$ , urea 6.1  $\text{mmol/L}$ ), mildly raised aspartate aminotransferase (39 U/L) and hyponatraemia (122  $\text{mmol/L}$ ). Full blood count (Table 1) and coagulation profile were normal. There was no evidence of metabolic acidosis and his chest X-ray was unremarkable. Initial computed tomography (CT) of the brain on admission showed ill-defined hypodensities in the thalamus bilaterally.

He was diagnosed with encephalitis and treated with intravenous fluid, ceftriaxone and acyclovir. The correction of serum sodium was monitored closely, not exceeding more than 8  $\text{mmol/day}$  to avoid osmotic demyelination syndrome. He was haemodynamically stable throughout admission and did not require inotropic support. Repeated blood investigations showed development of thrombocytopenia and leucopenia (Table 1). Dengue non-structural protein 1 (NS1) antigen test was detected from the initial serum sample obtained on admission (remaining positive on days 7 and 11 of illness). At this time, serum dengue IgM and IgG antibodies were negative (becoming

**Table 1: Full blood count pattern showing initial worsening of thrombocytopenia and leucopenia, which started to improve on day-11 of illness**

DATES	1/10	2/10	3/10	4/10	5/10	6/10	7/10	8/10	12/10
No of days from onset of illness	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>	9 <sup>th</sup>	10 <sup>th</sup>	11 <sup>th</sup>	12 <sup>th</sup>	13 <sup>th</sup>	16 <sup>th</sup>
	Defervescence phase					Recovery phase			
Serum NS1 antigen	+	+				+			
Serum IgM	-						+		+
Serum IgG	-						+		+
CSF RT-PCR							-		
CSF IgM/IgG							-		
Hb (g/L) (13.0-17.0)	13.2	11.6	12.2	13.4	13.8	13.7	12.4	11.0	11.5
Hct (L/L) (0.40-0.50)	0.40	0.35	0.37	0.41	0.42	0.41	0.39	0.35	0.36
WCC (10 <sup>9</sup> /L) (4.0-10.0)	6.1	5.3	3.1	2.0	2.7	4.1	7.1	5.8	13.2
Plt (10 <sup>9</sup> /L) (150-400)	168	138	124	98	87	95	115	157	326
ALT (mmol/L) (10-49)	20	17	22	38	58	96	82	194	278
PT (sec) (9.6-11.8)	13.4	13.5	11.5		9.5		9.7	10.2	10
INR	1.2	1.3	1.1		0.9		0.9	0.9	0.9
APTT (sec) (25.2-35.0)	26.2	37.6	38.6		43.2		28.3	26.4	23.7
Na (mmol/L) (136-145)	133	136	138	138	138	140	143	142	141
K (mmol/L) (3.6-5.2)	3.4	3.0	3.8	3.7	3.7	4.4	4.7	4.9	3.9
Urea (mmol/L) (3.2-8.2)	6.1	6	6.4	4.6	5.1	9.1	13.8	16.4	11.0
Creatinine (mmol/L) (54-97)	124	101	74	67	59	77	76	70	52

NB: Day-1 of illness is considered as the first day of fever onset. CSF – cerebrospinal fluid, Hb – haemoglobin, Hct – haematocrit, WCC – white cell count, Plt – platelet, ALT – alanine aminotransferase, PT – prothrombin time, INR – International Normalized Ratio, APTT – partial thromboplastin time, Na – sodium, K – potassium. Serum IgM and IgG measured using rapid test and CSF IgM and IgG was measured using ELISA. “+” indicates a positive result and “-“ indicates a negative result.

positive on day 12 and remaining so on day 16) (Table 1).

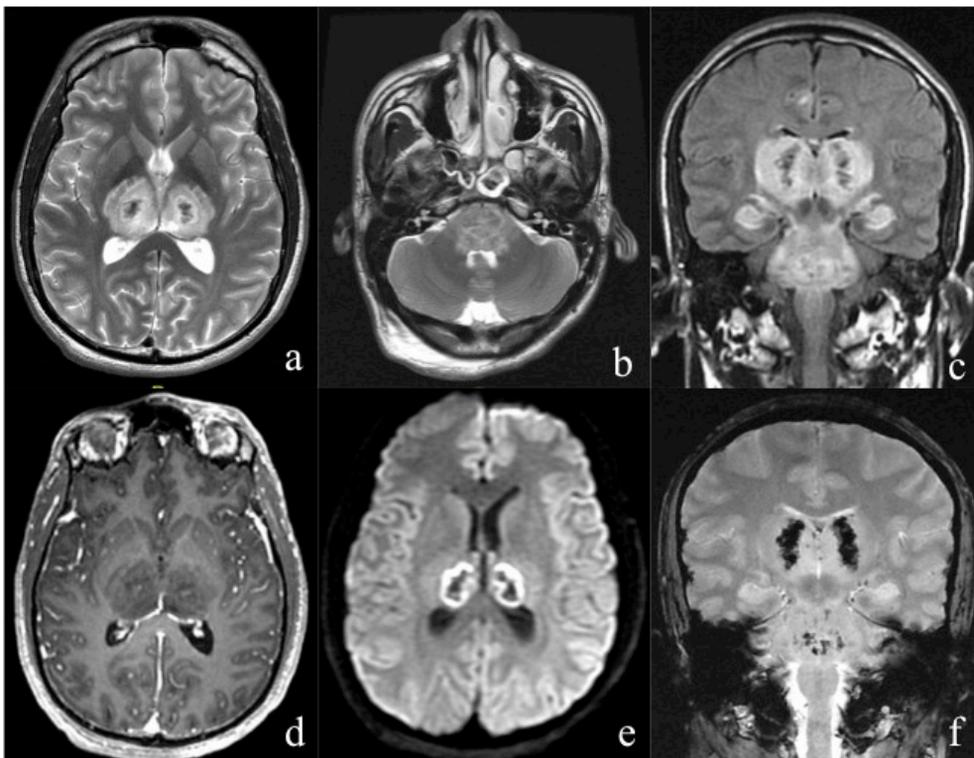
His conscious level remained poor on day 5 of admission with new neurological findings of 3mm unreactive pupils and absent vestibulo-ocular reflex. Brain MRI on the same day showed multiple high signal areas on T2-weighted (T2W) and fluid attenuation inversion recovery (FLAIR) sequences, which were symmetrically distributed in both thalami, medial temporal lobes, pons, midbrain, medulla, cerebellar peduncles, and parietal lobes (Figure 1). There was restricted diffusion in the thalami in keeping with cytotoxic oedema, as well as minimal contrast enhancement. Gradient echo (GRE) sequences showed blooming hypointensities in both thalami at the region of the internal lamina and pons, in keeping with haemorrhages (Figure 1). There was no obstructive hydrocephalus. He was diagnosed with dengue encephalitis and given

intravenous methylprednisolone 500mg/day for three days (days 10-12 of illness), followed by oral prednisolone 60mg daily for a month.

Lumbar puncture was performed on day 12 of illness, with normal opening pressure and content, apart from a mildly elevated protein level of 0.81g/L. Repeat brain MRI on day13 of illness showed findings similar to the initial MRI, but with less prominent hyperintensity and mass effect. Magnetic resonance venography (MRV) showed patent internal cerebral veins and no cerebral venous sinus thrombosis (Figure 2). Serum IgM for herpes simplex and leptospirosis were negative. Dengue reverse transcriptase polymerase chain reaction (RT-PCR) in serum and CSF, and dengue CSF serology (IgM and IgG) were negative on day12 of illness. Japanese encephalitis (JE) RT-PCR, IgM and IgG in both serum and CSF on day12 of illness were also negative.

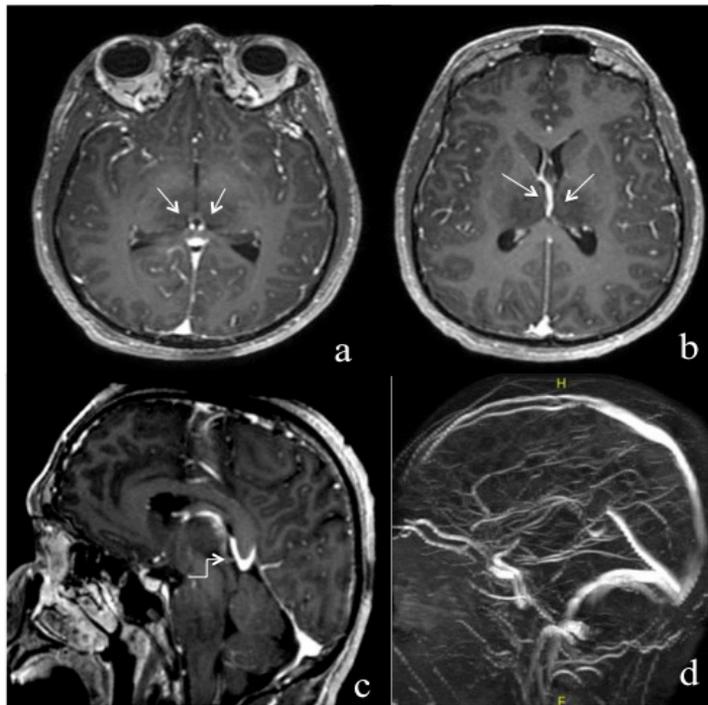
His conscious level gradually improved within

Figure 1: MRI of the brain (General Electric HDx Signa 3-T, USA) showing multiple areas of high signal intensities on T2W and FLAIR (a,b,c). Minimal contrast enhancement was seen in the thalamus (d). Concentric pattern of altered signals and restricted diffusion noted in the thalamus on the diffusion weighted (DWI/ADC) sequences (e). Blooming artifacts were noted in both thalami and pons on the gradient echo (GRE) in keeping with haemorrhagic components. Note the symmetrical haemorrhagic changes in both the thalamic internal medulla lamina (f).



(a, b) axial T2-weighted, (c) FLAIR coronal, (d) post gadolinium axial T1-weighted, (e) diffusion weighted image (DWI), (f) Gradient Echo (GRE).

Figure 2: Magnetic resonance venography (MRV) of the brain showing patent cerebral venous sinuses.



(a, b, c) Post contrast axial and sagittal FSPGR images demonstrating patent internal cerebral veins (arrows) with no filling defects seen to indicate thrombosis.

a week of steroid treatment and his overall condition improved partially over the next two months of his hospital stay. Upon discharge, he could ambulate with a walking frame and needed assistance with self-care. His coordination was poor despite having full muscle power. His cognitive function remained poor, however, detailed assessment could not be performed partly because of the language barrier.

## DISCUSSION

The diagnosis of dengue encephalitis in our patient was based on (i) clinical and MRI evidence of encephalitis; and (ii) serological and haematological evidence of dengue infection. The negative dengue PCR from the CSF and serum may be explained by low CSF viral load and low sensitivity of viral PCR, especially when performed later in the disease course.

The MRI changes in dengue encephalitis are usually non-specific, involving cortical and subcortical white matter changes.<sup>2,3</sup> Bilateral thalamic involvement is less commonly reported. In the only large series of neuroimaging changes in dengue encephalitis involving 21 cases, Bhoi *et al.* found 9/21 (43%) cases with MRI abnormalities,

one third of whom (three patients) had bilateral thalamic lesions.<sup>4</sup> Bilateral thalamic changes were also reported in three other case reports.<sup>5-7</sup> Similar changes have also been described in JE<sup>8</sup> and thrombosis of the internal cerebral vein<sup>9</sup>, both of which were excluded in our patient. The patient had no history of alcohol intake, the vomiting was minimal, there was no history to suggest nutritional deficiency; he also improved without thiamine replacement, thus making thiamine deficiency (Wernicke encephalopathy) unlikely. Abnormalities of the periaqueductal region and mammillary bodies are seen on brain MRI in the majority of cases of Wernicke encephalopathy<sup>10,11</sup>, but were not observed in our case.

Our case is the first to show such an extensive symmetrical inflammation associated with haemorrhage of both thalami, specifically in the region of the thalamic internal medullary lamina. The internal medullary lamina is a midline white matter sheath of the thalamus separating the rest of the thalamic nuclei and contains intralaminar nuclei, which is involved in arousal and cognitive function. Inflammation and haemorrhage in this specific region has not yet been reported in any other CNS infection and its pathophysiology is still unknown.

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