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RESLES in spectrum of dengue encephalopathy: A case report

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Abstract

Dengue encephalopathy is a spectrum of disease with mild to severe manifestations. The pathophysiology remains unknown in patients with dengue infection. We report a case of reversible splenial lesion syndrome (RESLES) due to dengue virus in hope of shedding more light to this conundrum.

Keywords

dengue infection; dengue encephalopathy; resles; splenial lesion; cytotoxic edema

Introduction

Dengue fever is one of the commonest mosquito borne diseases in the world. It is endemic in certain parts of the world, especially in tropical countries, accounting for 100-200 million infections per year in more than 100 countries [1]. In general, neurological manifestations are uncommon. These include dengue encephalopathy, ADEM, transverse myelitis and Guillain-Barre syndrome [2]. It is unclear how does dengue fever result in encephalopathy, but we postulate that it is due to direct viral infiltration of the central nervous system. We report a case of reversible splenial lesion syndrome (RESLES) due to dengue virus. This is a rare clinicoradiological disease that should be identified early by managing physicians to avoid unnecessary investigation and treatment as it is usually self-limiting.

Case Report

A thirty years old Malay lady with history of thalassemia minor, presented to us with three days history of fever, associated with sore throat and cough. On the day of admission, her husband found her to be lying on the floor unconscious.

On arrival to the emergency department, she was pyretic with temperature of 40.7°C and confused, Glasgow coma scale (GCS) was 14/15. She required intravenous sedation due to agitation. Initial assessment and physical examination did not reveal any focal neurological deficits. There was no skin rashes or petechiae noted.

She was treated presumptively for infective meningoencephalitis with intravenous aciclovir and ceftriaxone. She was also started on oral levetiracetam for concern of seizure. Her full blood count showed hemoglobin of 7.4g/dL, white cell count of $5.6X10^9$/L, platelet of $335X10^9$/L. Serum electrolytes were normal. Liver function test showed mildly raised aspartate transaminase (AST) of 70 U/L, serum bilirubin was normal. CT Brain did not reveal any intracranial abnormality. Lumbar puncture was performed for cerebral spinal fluid examination, which showed clear cerebrospinal(CSF) fluid, RBC >200/uL, WBC 1/uL, total Protein 0.39g/L. CSF analysis for meningitis (viral, bacterial and tuberculosis causes) were negative. EEG performed was normal.

On the third day of admission, she was found to be pancytopenic, hemoglobin 6.7g/dL, white cell count was $1.83X10^9$/L, platelet $96X10^9$/L. MRI brain was performed, it showed restricted diffusion involving the splenium of the corpus callosum with 'boomerang sign' (Figure 1A & 1B). Serum dengue IgM and IgG were subsequently performed, and was found to be positive. Her CSF fluid dengue PCR was also positive.

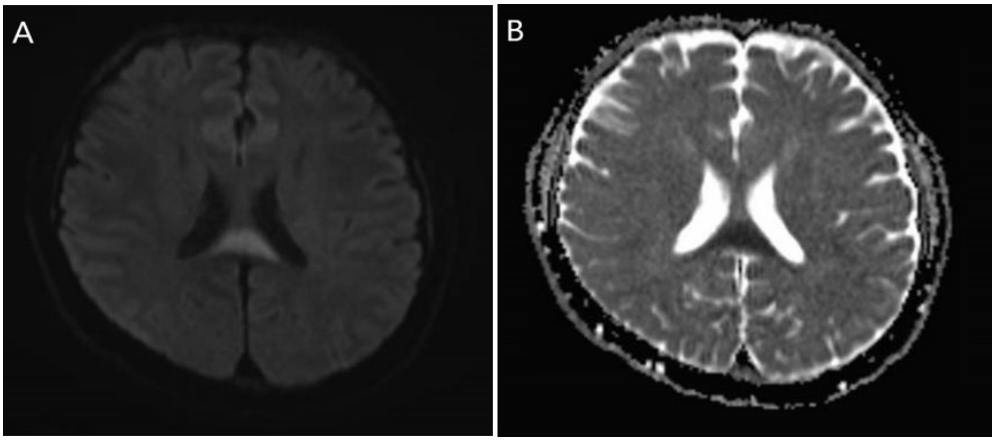

Figure 1: MRI brain A) DWI sequence and B) ADC sequence showing 'boomerang sign' over splenium of corpus callosum.

Her fever and confusion completely resolved by day five of admission and she was discharged well on day eight. We repeated MRI Brain for her two weeks later after discharge which showed complete resolution of splenial lesion (Figure 2A & 2B). She was reviewed 1 month later in clinic completely well.

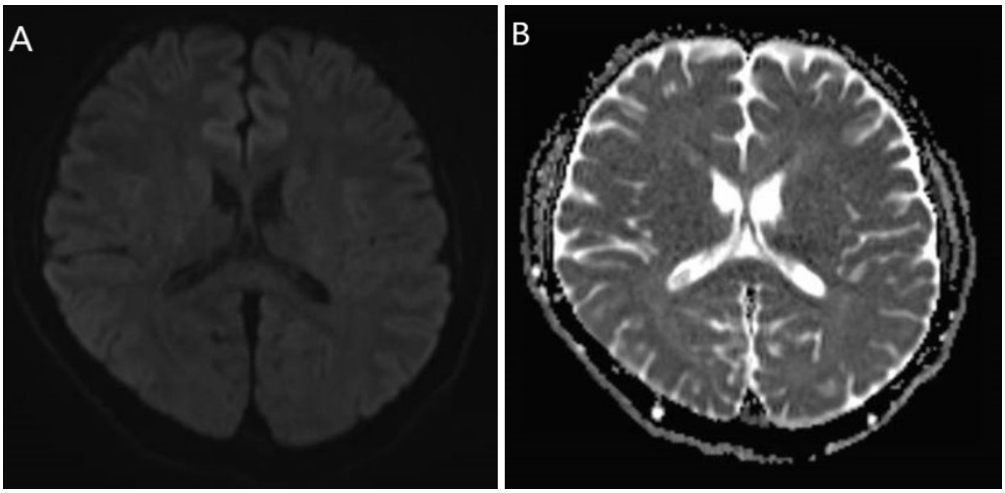

Figure 2: Repeat MRI brain A) DWI sequence and B) ADC sequence showing complete resolution of splenial lesion two weeks later.

Discussion

RESLES is a rare clinicoradiological syndrome characterised by cytotoxic edema over splenium of carpus callosum, followed by complete resolution within one to two weeks. The exact mechanism is unknown, but it is postulated that inflammation provokes a cytokine releasing cascade, with resulting cytotoxic edema in the splenium [3]. Due to it's rarity, many physicians and radiologists alike are not aware of this disease entity. RESLES is often mistaken as something more sinister such as ischemic stroke or demyelinating disease, hence resulting in unnecessary investigation and treatment, which contributes to increasing healthcare cost as well. It is important to note that RESLES rarely causes long lasting sequalae.

There have been evidence of impairment of functional interactions between both cortical hemisphere in patients with agenesis of corpus callosum, causing disconnection syndrome [4]. Splenial lesions may also cause various clinical signs and symptoms including confusion, ataxia, dysarthria and seizure [5]. Other than dengue fever, other infections which have been reported to be associated with RELSES include *E. Coli*, Salmonella, rotavirus and EBV [6]. Targeted history such as fever and travel history to endemic countries, and physical examination to look for signs of meningism are vital steps for diagnosis. Non-infective causes of RESLES include drugs, seizure, malignancy, metabolic disorder and trauma.

The typical features of RESLES on MRI are restriction diffusion on DWI sequence and hypodensity on ADC over splenium of the corpus callosum. Various shapes have been described such as 'dot sign' and 'boomerang sign' [3]. The hallmark of RESLES though is complete resolution of the lesion, hence a repeat MRI brain is essential for diagnosis. It is postulated that splenium has vulnerable cellular fluid mechanics compared to surrounding tissues, this resulted in predilection of splenial injury in RESLES [7].

Dengue encephalopathy is uncommon, incidence ranging from 0.5% to 6.2% have been reported [8,9]. It is a spectrum of disease ranging from mild to severe manifestation, these included encephalitis, cerebral edema and intracranial hemorrhage. RESLES due to dengue virus have been reported in a few case reports, however it has not been regarded as a form of dengue encephalopathy due to its rarity. This case report highlights the evidence of direct invasion of dengue virus in the central nervous system in RESLES.

Treatment for RESLES due to dengue virus is mainly supportive therapy including intravenous hydration and thrombocytopenia precaution when it develops. Antiepileptics may be considered if patient develops seizures. Otherwise, expectant management is advised to avoid unnecessary treatment that may be harmful to the patient.

To the best of our knowledge, this is the first reported case of RESLES due to dengue virus with confirmation of presence of dengue viral RNA in CSF. Positive CSF viral PCR is highly diagnostic of viral infiltration of the central nervous system [10]. This further supports the postulation of direct neural infiltration of dengue virus causing RESLES. There are no other identified causes that can explain the encephalopathy in our patient.

Conclusion

RESLES should be regarded as part of the spectrum of dengue encephalopathy in patients who present with confusion and dengue infection. It is important to recognise this radiological finding to avoid unnecessary investigation or invasive treatment.

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