

CASE REPORT

Open Access



A rare case of dengue encephalopathy complicating a term pregnancy

Lavanya Rajagopala*, Ravindra L. Satharasinghe and Madhava Karunarathna

Abstract

Background: Dengue fever has an expanded clinical spectrum ranging from an asymptomatic infection to life threatening dengue hemorrhagic fever and refractory shock. Dengue infection in pregnancy can be a diagnostic dilemma, particularly considering the physiological changes in pregnancy and the obstetric complications encountered in clinical practice. Hence the knowledge of its diagnosis and management in its atypical presentations is of paramount importance. Here we report an unusual case of uncomplicated dengue encephalopathy in a term mother, probably the first to be reported from the Indian subcontinent.

Case Presentation: A 28 year old woman, 37 weeks of pregnancy presented with fever of four days duration. She eventually developed irritability, altered sensorium, somnolence, and unresponsiveness to commands by the 5th day of febrile illness without any circulatory compromise. Physical examination and investigations including serology confirmed dengue fever. After excluding all other possible causes, the transient neurological deterioration was finally attributed to dengue encephalopathy which is an uncommon manifestation of the disease, particularly in pregnancy. Her deteriorated neurological status which had lasted for 6 days improved spontaneously with the convalescence of dengue infection. Cautious fluid management was carried out in correlation to clinical and hematological parameters. The pregnancy was continued uncomplicated till the platelet count had risen to more than 50,000 cells/cumm. She delivered vaginally a healthy male baby.

Conclusions: Dengue fever in pregnancy is increasingly being encountered due to its rising disease burden. Dengue encephalitis/encephalopathy must be suspected in the differential diagnosis of fever and altered sensorium, even in pregnancy, in the tropical countries where the infection is rampant. Management of dengue infection in term pregnancy is a challenge for both the clinician and obstetrician. Further discussion and research are mandatory to decide on optimal management of these patients, with regard to monitoring, fluid management, and the precise timing and mode of delivery in order to prevent fatal morbidity and mortality to both mother and fetus.

Keywords: Dengue fever, Encephalopathy, Term pregnancy

Background

Dengue is an mosquito-borne infection, caused by flavivirus serotypes (I–IV). It represents a significant burden of disease in the tropics, the global incidence is rising [1]. Dengue infection is a self limiting infection which may manifest with a spectrum of disease ranging from an uncomplicated febrile illness to various hemorrhagic manifestations and refractory shock. According to the world health organization dengue haemorrhagic

fever is based on fever, thrombocytopenia and evidence of plasma leakage. Plasma leakage is confirmed in the presence of hemoconcentration (haematocrit rises 20% higher than the baseline) or any clinical evidence of bleeding.

Atypical manifestations in dengue are less recognized especially in a dengue epidemic situations [2]. Neurological involvement is one such example. Various neurological manifestations have been reported in literature [3]. These include encephalopathy, encephalitis, meningitis, myelitis, Guillain–Barre syndrome, myositis, optic neuritis to name a few. A typical neurological manifestations

*Correspondence: lavpoo@yahoo.com
Sri Jayewardanepura General Hospital, Sri Jayewardanepura, Kotte, Sri Lanka

of dengue, particularly in pregnancy lacks a distinctive clinical picture and leads to diagnostic difficulties and poses a challenge to both the clinician and obstetrician. A high index of suspicion is mandatory in such clinical scenarios. We report a rare occurrence of a reversible dengue encephalopathy in a term mother with uneventful recovery.

Case presentation

A 28 year old woman, 37 weeks of pregnancy presented with fever of four days duration to the casualty medical ward. The following day she appeared to be irritable, somnolent, aggressive and thereafter followed by unresponsiveness to commands. On examination she was febrile, anicteric and not pale. She was confused, poorly responsive and her GCS was 9 (eyeopening = 2, verbal response = 2, motor response = 5). Respiratory, cardiovascular and abdominal examinations were unremarkable. There was no neck stiffness, Kernigs and Brudzinksi signs were negative. Cranial nerves were intact. Pyramidal and extrapyramidal signs were absent. Dilated funduscopy did not reveal any papilledema. Her full blood count revealed an isolated thrombocytopenia. White cell count 9000 cells/cumm, Hemoglobin 10 g/dl, mean corpuscular volume 85 ft, Platelets 60,000 cells/mm, counts progressively dropping up until 8000 cells/cumm. Hematocrit was stable at 33%. ESR was 20 mm/h and was CRP 4 mg/dL. LDH was <200 u/L. Blood picture revealed a thrombocytopenia in keeping with a possible viral infection, there were no features of microangiopathic hemolytic anemia. Urine analysis excluded proteinuria and hematuria. Hepatic profile which was initially normal started to escalate. Aspartate aminotransferase 25 U/L up till 250 U/L (<40 U/L), alanine aminotransferase 20 U/L up till 250 U/L (<40 U/L), alkaline phosphatase 300 U/L (30–300 U/L) and serum bilirubin 0.7 mg/dL respectively, revealing an anicteric hepatitis which is a common finding in dengue infection. Renal functions and serum electrolytes were normal. Clotting profile was PT 10S, APTT 38S, INR 1.2 and FDP < 0.2 u/L, excluding the possibility of disseminated intravascular coagulation. Ultrasound scan did not reveal any pleural effusions or ascites excluding the early signs of capillary vascular leakage. Dengue non structural protein-1(NS) antigen was positive at day 4 of the illness. Dengue IgM antibodies were high in titre by day 6. Due to deterioration of clinical status she was transferred to intensive care unit for closer observation. An electroencephalography revealed bilateral rhythmic delta wave activity consistent with a diffuse cerebral dysfunction. CSF analysis was not performed due to profound thrombocytopenia, thus making it difficult for us to exclude other encephalitic pathogens as a cause for the encephalopathy. Nevertheless since serology was strongly

positive for dengue infection and with the present dengue epidemic in our country we strongly suspected dengue encephalopathy as our first differential diagnosis. A CT scan of head was not performed due to possible risk of radiation to the fetus and the patients relatives refused consent for any imaging modalities. She was monitored closely, careful fluid management according to guidelines were carried out with regular fetal monitoring and bleeding precautions were undertaken. With the gradual rise in platelets, the patients neurological status improved spontaneously by day 10 of the illness. The encephalopathy had lasted approximately for 6 days. Fortunately, she did not have any clinical evidence of increased vascular permeability suggestive of dengue hemorrhagic fever or go into dengue shock syndrome. Once the platelet reached 70,000/mm³, she was induced for labour and delivered vaginally the baby without any peripartum or postpartum complications.

Discussion

Neurological manifestations are uncommon in dengue infection. Encephalopathy is an unusual neurological complication of dengue fever. Its incidence ranges between 0.5 and 6%. Several studies report that DEN-2 and DEN-3 have the highest predisposition to neurological complications. The possible pathogenesis being described in literature include hepatic encephalopathy, cerebral hypoperfusion in dengue shock syndrome, cerebral edema due to increased vascular permeability, deranged electrolytes, and intracranial bleeding due to thrombocytopenia or coagulopathy [3–6]. The infection causes activation of cytokines and complements which result in endothelial dysfunction, platelet dysfunction and consumptive coagulopathy.

Dengue virus was primarily thought to be a non-neurotropic virus [7]. However, recent studies reveal the direct neuronal infiltration by the virus and the possible neurotropism leading to dengue encephalopathy and encephalitis. There are reports of demonstration of dengue virus and IgM antibody in the CSF of very few patients with encephalopathy/encephalitis [8, 9]. Virus or antibody can be isolated from the serum nevertheless CSF samples may be negative. In the case of our patient, we were unable to confirm the direct neuronal invasion with a CSF study due to profound thrombocytopenia, a strong limiting factor in confirming the diagnosis. Brain imaging modalities have shown a bilateral thalamic predisposition in dengue encephalitis [10]. However MRI findings in dengue fever have not been very clearly explained due to the paucity of the condition. Interestingly, Japanese encephalitis virus which closely resemble dengue virus characteristically produces bilateral thalamic involvement, hence being an important differential

in the workup of the diagnosis [10] and can be confirmed by a CSF study. Though initially there was uncertainty about dengue encephalitis as an entity, it is established that dengue virus has neuroinvasive potential. The international encephalitis consortium has recognized this as an emerging area of encephalitis [11].

The diagnosis and management of dengue fever in pregnancy is a challenge to the clinician and the obstetrician. The physiological changes in pregnancy, pregnancy related complications and medical disorders must be kept in mind before interpreting the laboratory values. The entities in pregnancy that resemble dengue fever and need to be excluded include Idiopathic thrombocytopenic purpura (ITP) complicated with an intracranial haemorrhage, systemic lupus erythematosus (SLE) with cerebral vasculitis, antiphospholipid antibody syndrome (APLS) with CNS complications and pregnancy related complications such as pre-eclampsia, hemolysis, elevated liver enzymes and low platelets (HELLP), thrombotic thrombocytopenic purpura (TTP), sepsis and disseminated intravascular coagulation (DIC). The normal hematocrit levels in pregnancy may be as low as 33% (non pregnant female hematocrit is about 38%) [12]. As there is a physiological increase in the intravascular volume in the third trimester, the identification of plasma leakage syndrome through hemoconcentration or hypoproteinemia may be compromised which may underestimate the proportion of dengue haemorrhagic fever in pregnant women. There is increased risk of hemorrhage (maternal and fetal), pre eclampsia, miscarriages, fetal anomalies, low birth weight, premature births, increased rate of cesarean sections, increased maternal and fetal mortality and a risk of vertical transmission of dengue infection in pregnancy [13, 14].

Our patient is the first reported pregnant mother to suffer from dengue encephalopathy in the Indian sub-continent. Interestingly, the transient neurological deterioration spontaneously improved with the rise in platelet counts. This also raises the question of whether an immuno tolerant state such as pregnancy predisposes more to dengue encephalopathy/encephalitis.

In our patient, the suspicion of dengue encephalopathy was crucial for optimum monitoring and management to prevent adverse outcomes to both mother and fetus, although we were unable to confirm it with a CSF study. The current WHO guidelines do not elaborate on the clinical and hematological monitoring and fluid management of dengue infection in term pregnancy. More evidence based and multidisciplinary based studies are strongly and urgently indicated to decide on the diagnosis, value of CSF study, optimal fluid management with regard to dengue encephalopathy in a term pregnancy.

The guidelines to determine the precise timing and mode of delivery for term mothers suffering dengue infection are essential to facilitate management and to prevent adverse outcomes.

Conclusions

Dengue encephalopathy is a rare phenomenon complicating term pregnancy. This paper emphasizes on the hurdles of diagnosis and management of dengue fever in a term pregnancy, which definitely needs special attention. Further case reports and studies are mandatory to evaluate the exact magnitude and outcome of this clinical scenario as evidence-based data in the pathogenesis, diagnosis and the management of dengue encephalopathy in pregnancy is sparse.

Abbreviations

ESR: erythrocyte sedimentation rate; CRP: C reactive protein; CT: computed tomography; GCS: Glasgow coma scale; LDH: lactate dehydrogenase; CSF: cerebrospinal fluid analysis; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; FDP: fibrinogen degradation products; MRI: magnetic resonance imaging.

Authors' contributions

All authors have read and approved the final manuscript. LR has taken care of inward management of and monitoring the patient while in febrile phase of dengue fever and drafting the manuscript. RLS providing intellectual support in interpreting clinical and investigation results and manuscript revision. MK supervised the obstetric management of the patient including regular fetal monitoring and timing of delivery. All authors read and approved the final manuscript.

Acknowledgements

Authors would like to acknowledge the dedicated nursing staff of ward 6, ICU staff, and the obstetric team, Sri Jayawardenepura General Hospital.

Competing interests

The authors declare that they have no competing interests.

Availability of data and material

All data generated during this case report are included in this published article [and its supplementary information files].

Consent statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Standards of reporting

CARE guidelines and methodology were adhered to.

Received: 13 November 2015 Accepted: 17 January 2017

Published online: 02 February 2017

References

1. WHO. Dengue and Dengue haemorrhagic fever. Factsheet No. 117. Geneva: World health organization. 2008
2. Gulati S, Maheshwari A. A typical manifestations of dengue. *Trop Med Int Health*. 2007;12:1087–95.

3. Solomon T, Dung NM, Vaughn DW, Kneen R, Thao LT, Raengsakulrach B, et al. Neurological manifestations of dengue infection. *Lancet*. 2000;355:1053–9.
4. Cam BV, Fonsmark L, Hue NB, Phuong NT, Poulsen A, Heegaard ED. Prospective case–control study of encephalopathy in children with dengue hemorrhagic fever. *Am J Trop Med Hyg*. 2001;65:848–51.
5. Hendarto SK, Hadinegoro SR. Dengue encephalopathy. *Acta Pediatr Jpn*. 1992;34:350–7.
6. Carod-Artal FJ, Wichmann O, Farrar J, Gascón J. Neurological complications of dengue virus infection. *Lancet Neurol*. 2013;12:906–19.
7. Nathanson N, Cole GA. Immunosuppression and experimental virus infection of the nervous system. *Adv Virus Res*. 1970;16:397–428.
8. Lum LC, Lam SK, Choy YS, George R, Harun F. Dengue encephalitis: a true entity? *Am J Trop Med Hyg*. 1996;54:256–9.
9. Misra UK, Kalita J, Syam UK, Dhole TN. Neurological manifestations of dengue virus infection. *J Neurol Sci*. 2006;244:117–22.
10. Kamble R, Peruvamba JN, Kovoov J, Ravishankar S, Kolar BS. Bilateral thalamic involvement in dengue infection. *Neurol India*. 2007;55:418–9.
11. Venkatesan A, Tunkel AR, Bloch KC, et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. *Clin Infect Dis*. 2013;57(8):1114–28.
12. Cantagallo F, Perini M, Cantagallo AA. Evaluation of hemoglobin and hematocrit in pregnant women receiving folate and iron supplements. *Min Ginecol*. 1997;49:571–6.
13. Restrepo BN, Isaza DM, Salazar CL, Ramírez JL, Upegui GE, Ospina M, et al. Prenatal and postnatal effects of dengue infection during pregnancy. *Biomedica*. 2003;23:416–23.
14. Tan PC, Rajasingam G, Devi S, Omar SZ. Dengue infection in pregnancy: prevalence, vertical transmission, and pregnancy outcome. *Obstet Gynecol*. 2008;111(5):1111–7.

Submit your next manuscript to BioMed Central
and we will help you at every step:

- We accept pre-submission inquiries
- Our selector tool helps you to find the most relevant journal
- We provide round the clock customer support
- Convenient online submission
- Thorough peer review
- Inclusion in PubMed and all major indexing services
- Maximum visibility for your research

Submit your manuscript at
www.biomedcentral.com/submit

