

CASE REPORT OF DENGUE ENCEPHALOPATHY IN PREGNANCY MIMICKING ATYPICAL ECLAMPSIA – AN INSIGHT OF NEUROLOGICAL MANIFESTATIONS OF DENGUE IN PREGNANCY

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ABSTRACT

Dengue is a global public health problem. Dengue in pregnancy carries a high maternal and perinatal morbidity and even mortality especially when the diagnosis is delayed. Often dengue with hemorrhagic shock syndrome is misinterpreted as HELLP syndrome and unnecessary obstetric interventions have to be avoided in such situations. There are case reports and guidelines on dengue hemorrhagic syndrome in pregnancy. However, rare atypical forms like neurological manifestations of dengue in pregnancy are rarely studied. Neurological events of dengue are increasingly observed nowadays. We are presenting a case report of atypical dengue (dengue encephalopathy) in pregnancy with a review of the literature. It was initially thought as meningitis then atypical eclampsia and HELLP syndrome. Whenever dengue infection presents in atypical form, strong clinical suspicion and early intervention improve the outcome.

KEYWORDS Dengue, dengue encephalopathy, atypical HELLP

Introduction

Dengue fever is a significant global health problem worldwide, and 2/5th of world's population is at risk[1]. Dengue fever, an *Aedes aegypti* mosquito-borne infection has an expanded clinical spectrum of asymptomatic infection to fatal dengue hemorrhagic fever and shock syndrome.

The impact of dengue on pregnancy needs to be better understood primarily regarding the maternal and perinatal outcome. The complications of dengue in pregnancy have been scarcely studied. There are increased risks of maternal haemorrhage, preterm labour and stillbirths.

Apart from that, Dengue infection as such in pregnancy can be a significant diagnostic challenge. This is very true in atypical presentations like dengue encephalitis /encephalopathy. Pregnancy-specific conditions like preeclampsia, HELLP syndrome can mimic such atypical presentations which can delay or misguide the clinician which often leads to poor maternal and perinatal outcome.

However, atypical forms such as neurological manifestations are not uncommon even in pregnancy. It was first reported in 1976, and worldwide literature search shows the various incidence of dengue encephalopathy from 0.5% to 6.2% with a mortality rate up to 40% [2]. Neurological manifestations of dengue are poorly studied especially in pregnancy.

Case Report

Twenty-six years Mrs A, G2P1L1 monoamniotic twin pregnancy presented at 36+2 weeks to the emergency department with history of leaking P/V.

It was spontaneous conception; she was booked at a private hospital. Her antenatal period was uneventful. There was no history of preeclampsia or anaemia. She was taken up for emer-

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DOI: 10.5455/IJMRCR.dengue-encephalopathy-in-pregnancy-mimicking-atypical-eclampsia

First Received: May 20, 2017

Accepted: August 31, 2017

Manuscript Associate Editor: George Baytchev (BG)

Editor-in Chief: Cvetanka Hristova (BG)

Reviewers: Ivan Inkov (BG)

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gency LSCS given monoamniotic twin. Her previous Obstetric history was routine. There was no significant past and family history.

Emergency LSCS was done under SA. She one recording of 150/100 intraoperative, settled on its own. There were no other intraoperative complications. Both female babies weighed 2.2 & 2.1kg, and they were by M/S. She did not receive any antihypertensive drugs.

Within 6 hours of surgery, her dressing was soaked which required exploration of subcutaneous bleed under anaesthesia. There was a brisk bleeder from the subcutaneous plane, and the same was ligated. She had one high spiking fever on a postoperative day 1. No clinical signs of puerperal sepsis. Her breasts were soft. Fundamental investigations were sent, and urine culture was sterile. Two days later she developed diffuse abdominal pain associated with vomiting which was non-bilious and non-projectile. There was no diarrhoea. Her Vitals were stable except for minimal dehydration.

The abdominal examination did not reveal any abnormality. It was soft, and there was minimal gaseous distension. On a postoperative day four, she started having signs of cerebral irritation with up drawing plantar. Her pupils were equal and reactive. Initial neuroimaging (CT) did not reveal any abnormality. She was transferred to ICU and received supportive measures. Her Bp was 110/60mmHg. The fluid imbalance was corrected. With the correction of intra volume depletion, she developed altered mental status with signs of decerebrate rigidity. Hence further imaging was undertaken to rule out any cerebrovascular accidents but showed only diffuse cerebral oedema; received fluid therapy under close monitoring. Platelets and packed cell transfusion were given. Cerebral symptoms showed improvement with anti-cerebral oedema measures. Two days later her dengue serology report came and showed a positive result for NSN1 antigen and IgM Ab. Recovered well, had secondary suturing for wound infection. The patient was discharged from the hospital on Post op day 14 without any sequelae.

Discussion

Dengue fever, which is caused by four similar but antigenically different serotypes of flavivirus has 50% mortality rate, especially if untreated [3]. There are 50-100 million new cases added every year. Even though India is an endemic area for recent dengue statistics have shown a case fatality ratio of <0.5% especially after the implication of national guidelines on clinical management of dengue fever. Even in India some areas has a case fatality rates between 3-5%.

Dengue fever in pregnancy can be confused with HELLP syndrome, SLE, thrombotic thrombocytopenic purpura (TTP), sepsis and DIC especially when it presents in atypical form [4].

Following viral infection, there is lifelong protection against similar subtype. However, subsequent infection with different subtype can be dangerous because it increases the chance of dengue hemorrhagic fever. The heterotypic antibodies form complexes, which attacks mononuclear phagocytes with enhanced efficiency. This antibody-dependent enhancement results in enhanced viral load replication which results in the severe form of dengue fever like dengue hemorrhagic fever and dengue shock syndrome. Similarly, it may also contribute to the development of atypical forms of dengue called dengue encephalopathy.

These neurological manifestations are associated explicitly with DENV-2 & 3. These serotypes were found in encephalitis, meningitis and myelitis. Even Den-4 was also detected in

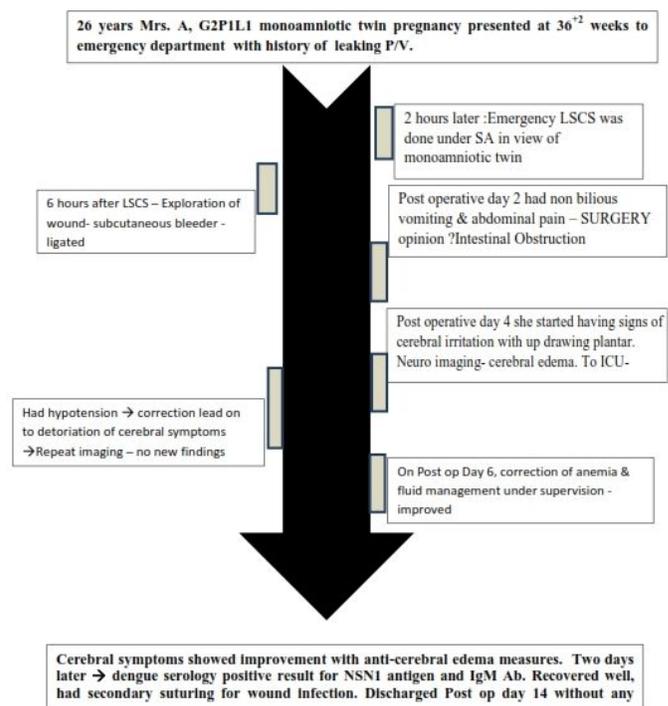


Figure 1: Timeline for case report.

brain cells by IHC in CSF of a patient with encephalitis. It could be due to direct viral infection of CNS or autoimmune reaction following dengue infection or due to metabolic/underlying hemorrhagic complication.

Atypical manifestations of dengue fever are associated with more severe grades of disease. Various case series have shown the importance of early and prompt proactive management observed nowadays and carried a high mortality. Few case series have been reported which shows different presentations like encephalopathy, encephalitis, neuropathy, and optic neuritis and Guillain Barre syndrome [5].

Even though rare, they have been increasingly reported in dengue epidemic regions. Classically it can occur in patients with few or no signs of previous dengue infection like this patient. Moreover, it can occur within 2-30 days after the onset of fever. There can be myelitis, myositis, radiculoneuritis and neuropathy. A headache, seizures and altered consciousness are the usual manifestations of dengue encephalitis [6]. However, these typical symptoms are seen in only less than 50% of patients with dengue encephalitis. Whenever patient presents with encephalitis, it should be one of the differential diagnosis in patients from dengue-endemic areas

Diagnostic criteria for dengue encephalitis:

- Fever
- Acute signs of cerebral involvement
- Presence of anti-dengue IgM/ dengue genomic material in serum/CSF MRI/CT findings may vary from cerebral oedema, haemorrhages to focal abnormalities in basal ganglia, hippocampus and thalamus.

It takes time to make an exact diagnosis of atypical manifestations of dengue fever like in our patient. It was initially thought of postoperative ileus, warranted surgery opinion later meningitis (complication following spinal anaesthesia) and then HELLP

syndrome. The most crucial presentation was encephalopathy like features which include a headache, seizure, altered sensorium and behavioural disturbances. Various pathogenesis has been described. It could be due to cerebral oedema or cerebral haemorrhage. Even microcapillary haemorrhage and cerebral hypoxia play a role. Electrolyte disturbances like hyponatremia, hepatic failure or release of toxic products might be one of the reasons for neurological manifestations.

There is no convincing evidence for a demonstration of direct invasion to the central nervous system (CNS) however recent evidence shows dengue virus is capable of direct invasion onto CNS. The entry of the virus into brain seems to occur through infiltrates of infected macrophages⁷. Few animal studies have shown the cytokines which are released in dengue plays a role in creating a breach in BBB which result in CNS invasion. The neurological manifestations can vary from altered consciousness (most common), seizure, mental confusion; limb spasticity to focal neurological deficits (least familiar). The IgM antibody was even isolated from CSF. Usually, it is self-resolving. Supportive treatment is important. There is no specific treatment as such. Fluid support and intense monitoring play a significant role in the outcome. Involvement of other systems such as hepatic failure, respiratory distress, hyperkalemia, acute kidney injury and metabolic acidosis may occur if untreated which increases the morbidity rate. Secondary infections like ventilator-associated pneumonia (VAP) may complicate the situation.

Even though misdiagnosis happened in our case, early intensive monitoring and fluid therapy along with ante cerebral oedema measures improved the outcome.

Conclusion

Dengue in pregnancy is a real threat to both obstetrician and patient. The classical presentation of dengue is unlikely to be missed. However, it is a significant diagnostic challenge when it presents in atypical form, especially during pregnancy. It can be easily misinterpreted with many other clinical conditions of pregnancy. Dengue should be the differential diagnosis even a pregnant women presents with fever and altered sensorium especially in endemic areas like India. A high index of clinical suspicion and prompt intervention in such situations improves the maternal and fetal outcome. Further studies are needed to evaluate dengue neurotropism in pregnancy.

Disclosure Statement

There were no financial support or relationships between the authors and any organization or professional bodies that could pose any conflict of interests.

Competing Interests

Written informed consent obtained from the patient for publication of this case report and any accompanying images.

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