Case Report

Dengue haemorrhagic fever in late pregnancy causing maternal and intrauterine foetal death – A case report

SA Gunawardena[1], V Dias[1], O Amarajeewa[2], P Ellangage[3],
S Gunarathna[3], P Gunaratne[3], H Gunawardhana[4], S Jayasuriya[4]

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ABSTRACT

Dengue during pregnancy carries a higher risk of maternal and foetal complications, either through haemodynamic instability from disruption of the placental perfusion or through vertical transmission to the foetus.

A previously healthy 29-year-old primigravidae with a POA of 34 weeks presented with one day fever to a tertiary hospital. NS 1 antigen for dengue was positive. She entered the critical phase the following day and her platelet count dropped to 3000/ml by day 3. Intra uterine death was diagnosed on day 4. She continuously deteriorated and died on day 7. At autopsy, gross bleeding manifestations were noted in the mother, along with bilateral pleural effusions, massive sub endocardial haemorrhages and an enlarged liver with sub capsular haemorrhages. The placenta was devoid of any haemorrhages or infarcts. Sub-aponeurotic and subarachnoid haemorrhages and 50ml of blood within the thoracic and peritoneal cavities were found in a mature female foetus with minimal signs of maceration. Laboratory confirmation of foetal dengue virus infection was not possible.

This is a rare case where fatal haemorrhagic manifestations were seen in both the mother and the foetus suggesting vertical transmission. The autopsy findings highlight the unpredictable haemodynamic changes in the uterine circulation which severely hinder dengue management during pregnancy. Dengue infection, especially in late pregnancy, can lead to unpredictable fatal outcomes. The potential benefit of performing an emergency caesarean in such cases should be further explored.

[1]*Department of Forensic Medicine and Toxicology, Faculty of Medicine, University of Colombo.*
[2]*Faculty of Medicine, University of Peradeniya*
[3]*Faculty of Medicine, University of Colombo*
[4]*Faculty of Medicine, University of Sri Jayewardenepura*

Address for correspondence: Dr. SA Gunawardena, Department of Forensic Medicine and Toxicology, Faculty of Medicine, University of Colombo, Tel: +94714958897 Email: sameera@fortox.cmb.ac.lk
http://orcid.org/0000-0001-9562-0533

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Introduction

Over 100 million cases of dengue are reported worldwide each year, mainly from tropical countries.[1] By November 2017, 167,198 dengue cases including 215 deaths were reported in Sri Lanka.[2,3] Clinical symptoms ranged from asymptomatic fever or undifferentiated fever to more severe forms of Dengue Haemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS).[4] Dengue during pregnancy carries a higher risk of maternal and foetal complications, such as pre-term delivery, intra uterine death, miscarriages and prolonged bleeding during deliveries.[5] It is believed that dengue infection can disrupt the physiological changes in pregnancy causing haemodynamic instability in placental perfusion[6,7] or direct infection of the foetus through vertical transmission.[8]

Case presentation

A previously healthy 29-year-old primigravid female in her 35th week of an uneventful pregnancy presented with fever for one day to a tertiary care hospital. On admission, she had a temperature of 100.8 °F with arthralgia, myalgia and shortness of breath and a blood pressure of 130/80 mmHg. NS 1 dengue antigen test was positive. She entered the critical phase on day 2 and developed gum bleeding, haematuria and bilateral pleural effusions. Her platelet count dropped from 135,000/mL to 12,000/mL by day 3 to 3,000/mL by day 4, which coincided with settling of fever and a progressive rise in haematocrit and liver enzymes. The foetal heart sounds drastically dropped on day 4 and intra-uterine death was confirmed by ultra-sound scan. Her condition continued to deteriorate, and she died on day 7.

Autopsy revealed blood stained fluid in the right pleural and peritoneal cavities along with sub-mucosal haemorrhages in the larynx. The liver was enlarged, weighing 1300g, and had sub-capsular haemorrhages (Figure 1). There were extensive sub-endocardial haemorrhages in the left ventricle (Figure 2). The brain showed mild subdural haemorrhage along with cerebral oedema and congestion.

Figure 1: The liver of the deceased mother which was enlarged and bulging beyond the subcostal margin. Extensive subcapsular haemorrhages were seen throughout the parenchyma

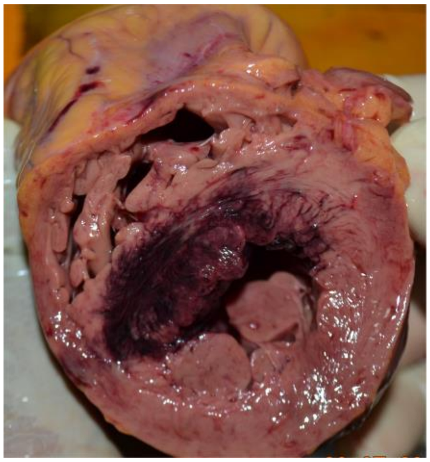

Figure 2: Massive subendocardial haemorrhage in the maternal heart

A female foetus compatible with 35 weeks of gestation was found inside the uterus. There were minimal signs of maceration. The umbilical cord was dark red and fleshy with no visible strictures or strangulations. The placenta did not show any haemorrhages or infarcts. Dissection of the foetus revealed subgaleal haemorrhage overlying the sagittal suture and a moderate amount of subarachnoid haemorrhage accumulated within the sulci (Figure 3). Both the thoracic and peritoneal cavities contained approximately 50ml of blood. There were no other visible haemorrhagic lesions. The macroscopic appearance and the distribution of the haemorrhages as well as the lack of other signs of maceration ruled out the possibility of post-mortem autolysis, hypostasis or congestion.

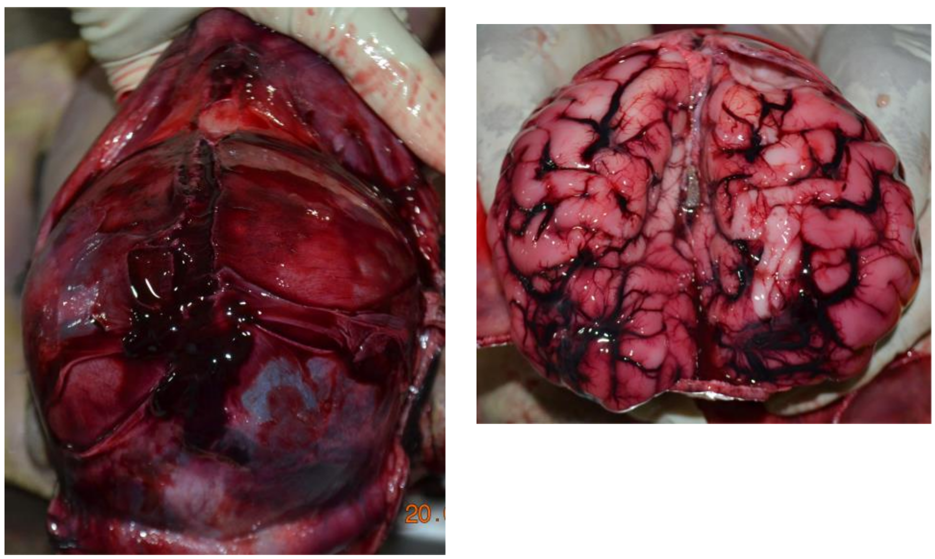

Figure 3: Subgaleal (left) and subarachnoid haemorrhage (right) were seen in the foetus

Due to practical difficulties and time constraints, the autopsy was limited to macroscopic examination. Serological and histopathological investigations were not carried out.

The cause of the maternal death was given as dengue haemorrhagic fever in pregnancy based on the antemortem clinical records and the macroscopic autopsy findings.

The timeline of the patient's clinical course is given in Figure 4.

29-year-old primigravid female in 35th week of pregnancy

Time	Clinical state		Platelets	Foetal heart sounds
Day 1	Admission with history of fever for 1 day	Fever, arthralgia, myalgia, dyspnoea, BP – 130/80 mmHg NS-1 positive	135000/mL	140-150 bpm
Day 2	Enters critical phase	Gum bleeding, haematuria pleural effusions		140-150 bpm
Day 3			12000/ml 55000/ml	˜120 bpm
Day 4	Transferred to Infectious Diseases Hospital	Fever settles haematocrit & liver enzymes rise	3000/ml	Absent (IUD confirmed by ultrasound)
Day 5 & 6		Continuous deterioration		
Day 7	Death			

Figure 4: Timeline of clinical progression

Discussion

Dengue haemorrhagic fever (DHF) is one of the more life-threatening manifestations of dengue infection, which is believed to occur from immune mediated alterations in vascular permeability, thrombocytopenia and reduced fibrogen.[9] Pregnancy increases the risk of mortality from DHF[10], especially when the infection occurs in late pregnancy.[7,11] Vertical transmission of dengue infection from mother to foetus is a well-known phenomenon[12-16] and the reported incidence ranges from 1.6%[17] to 10.5%.[18] Waduge et al believe that the endothelial damage and increased vascular permeability in DHF leads to a disruption of the placental barrier, permitting entry of the dengue virus[6] as well as a multitude of parenchymal and interstitial changes in the placenta which lead to foetal hypoxia.[19-23]

None of the reported cases of miscarriages, pre-term deliveries and still births following dengue infection during pregnancy[5,6] refer to haemorrhagic manifestations in the foetus or new born with the exception of one case where the baby died from intracerebral haemorrhage 6 days after birth.[24] The development of haemorrhage within a foetus, particularly intracranial haemorrhage, is a phenomenon that is not clearly understood and has an estimated incidence of 1 in 10000 pregnancies.[25] Established causes are mostly acquired or inherited coagulopathies or maternal trauma.[26,27] However, there is strong evidence to suggest intrauterine hypoxia as a major cause.[28,29]

In this patient, the mother was in her 35th week of gestation with a viable healthy foetus when she was admitted with dengue fever. Her deterioration was extremely rapid with bleeding manifestations and intrauterine death occurring 3-4 days after the onset of symptoms. It is not clear whether the haemorrhages detected in the foetus were a result of transplacental virus transmission triggering DHF in the foetus or due to hypoxic changes from placental insufficiency caused by haemodynamic changes within the uterine circulation. Unfortunately, the lack of serological and histopathological testing in this case restricts the possibility of deeper analysis.

This case report however clearly highlights the challenges in managing dengue during pregnancy. The pleural effusions and subendocardial haemorrhages found in the mother indicate a high degree of haemodynamic instability, possibly alternating between fluid overload and hypovolemia. Fluid management in a DHF patient is highly complicated, even without the added burden of sudden variations in placental and foetal circulation. It is perhaps worthwhile considering if this death could have been prevented if a caesarean section had been performed upon admission. This is an important consideration for future obstetric management in near-term pregnancies presenting with dengue infection, especially in tropical countries where dengue is rampant.

Conclusion

This case report presents a rare occurrence of an intrauterine and maternal death following DHF in pregnancy. This was despite the mother presenting herself to a tertiary hospital on the first day of fever and being provided the expected care. At autopsy, haemorrhagic manifestations were seen in the foetus which raises the possibility of vertical transmission of the virus, resulting in an intrauterine manifestation of fatal dengue haemorrhagic fever. Serological confirmation however was not available. Autopsy findings in the mother indicate the unpredictable nature of haemodynamic changes in the placental and foetal circulation which severely hindered successful management of her condition. Considering the high risk of maternal and foetal complications that are being reported, it is worthwhile considering if dengue fever in late pregnancies should be an indication for early termination before the onset of haemodynamic complications.

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