

# A Rare Manifestation of Congenital Dengue Infection

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**Abstract** Congenital dengue is caused by trans-placental transfer of virus from the infected mother to the fetus. We are reporting a case of stillbirth in a mother suffering from severe dengue infection. The stillborn was found to have myocarditis and pulmonary haemorrhage on autopsy. The report illustrates myocardial tropism of the dengue virus and its propensity to cause catastrophic complications during late gestation.

**Key words** Congenital; Dengue; Haemorrhage; Myocarditis; Oedema

## Introduction

Dengue infection is caused by arbovirus (genotype flavivirus) which has four serotypes. Infection with one serotype does not confer immunity against infection with other serotypes. Congenital dengue infection is caused by direct transfer of virus across the placenta, when there is insufficient time for protective antibody formation and subsequent fetal transfer. This happens when the mother acquires infection in the latter part of third trimester, near her expected date of delivery.<sup>1</sup>

Dengue virus is known to cause cardiac and pulmonary complications in the paediatric population. However, myocarditis associated with pulmonary haemorrhage as a manifestation of congenital dengue, has not been previously reported to the best of our knowledge.

## Case Report

A term stillborn 2.8 kg male was delivered by caesarean section to a 28 year old primigravida suffering from severe

dengue infection. She was admitted at 39 weeks gestation with complaints of fever followed by development of respiratory distress. The fever was moderate to high grade and continuous without touching the baseline. It was also associated with chills and rigors. On day 5 of her illness she developed respiratory distress for which she was hospitalised. Her chest X-ray revealed features of pulmonary oedema with evolving acute respiratory distress syndrome. Ventilation had to be initiated in view of increased work of breathing and worsening arterial blood gas reports. A few hours later she went into shock (Dengue Shock syndrome) and was managed with aggressive fluid replacement followed by inotropic support. Investigations revealed haemoconcentration (haematocrit of 51%) and thrombocytopenia (platelet count of 65,000/mm<sup>3</sup>). Results of her dengue non-structural antigen 1 (NS1) test (qualitative enzyme linked immunosorbent assay) and IgM antibodies (enzyme linked immunosorbent assay) against dengue virus were positive. Blood and urine cultures were sterile. Serologies for human immunodeficiency virus, hepatitis B, TORCH (Toxoplasma, others, Rubella, Cytomegalovirus and Herpes simplex) and syphilis were negative.

Obstetric opinion for fetal well being revealed no cardiac activity; so an emergency caesarean section was performed. Upon delivery, the baby was limp, showing no signs of life in the form of heart or umbilical cord pulsation. There was no spontaneous breathing and it could not be resuscitated despite maximal effort. A post mortem intracardiac blood sample from the stillborn revealed sterile blood culture and

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positivity for NS1 antigen. It also revealed presence of IgM antibodies against dengue virus, which could have been a result of transplacental transfer.

The mother gradually recovered from the infection over a period of 10 days. Her inotropic requirement reduced by fourth day of intensive care and her ventilatory requirement diminished by day 7. She was discharged on day 13.

An autopsy of the stillborn was performed after taking parental consent. The autopsy did not reveal any congenital malformation incompatible with life (microcephaly or anencephaly/meningomyelocele). The stillborn did not show any sign of hydrops-fetalis. Histopathological examination of the viscera revealed interstitial inflammatory cell infiltrate comprising mainly lymphocytes in the myocardium (Figure 1) with normal external cardiac morphology. Lungs showed diffuse alveolar oedema with haemorrhagic foci. There were no signs of haemorrhage in any other viscera.

A diagnosis of lymphocytic myocarditis with focal pulmonary haemorrhage, secondary to dengue infection was made after corroborating the clinical presentation, positive antigen assay in both the mother and stillborn and autopsy findings. However, the isolation and culture of dengue virus from the organs and tissues of the stillborn couldn't be done due to non availability of tests.

## Discussion

Dengue is a global public health problem. Dengue fever is endemic in India and although exact prevalence is difficult to calculate, several epidemics have been described. The gestational age of the fetus at presentation of maternal dengue fever is an important predictor of fetal outcome. An early or late onset in pregnancy has a poor prognosis. Maternal infection early in pregnancy has been shown to increase the risk of abortion whereas infection beyond 31 weeks of gestation has been associated with premature delivery. There is also a risk of haemorrhage for both the mother and the baby if infection occurs near term gestation.<sup>1</sup> However, robust data analysing the effect of dengue fever on pregnancy and neonatal outcome is scarce.

Congenital dengue is known to occur when there is insufficient time for transfer of maternal protective antibodies to the fetus. Tan et al. in a study of prospective cohort, described the vertical transmission incidence rate as 1.6%.<sup>2</sup>

Few case reports have described a mild presentation in which the newborn presented with fever, rash, thrombocytopenia, respiratory distress and hepatitis in early neonatal period which was followed by spontaneous recovery.<sup>3-6</sup>

Cardiac complications with dengue fever are described in paediatric literature.

Salgado et al has reported 11 paediatric patients with myocarditis due to dengue presenting with sinus node dysfunction (sinus bradycardia or tachycardia) and T-wave inversions on ECG, pericardial effusion, and diastolic dysfunction.<sup>7</sup> Promphan et al described sinus node dysfunction leading to bradycardia and hypotension in a child suffering from dengue.<sup>8</sup>

However, myocarditis in congenital dengue infection leading to neonatal mortality has not been previously recognised as a complication of vertically transmitted dengue infection. Our case developed myocarditis and cardiac failure in utero, consequent to dengue infection in the third trimester. The pulmonary haemorrhage could have been secondary to acute left ventricular failure leading to acute pulmonary oedema.

There are several gaps in our knowledge regarding the pathogenesis of this rare presentation of congenital dengue. Results of studies in adult human cadavers have shown that dengue virus has tropism for replicating in type II pneumocytes and cardiac fibers.<sup>9</sup> Myocarditis could be caused by direct invasion of the myocardium leading to damage to the muscle fibres or it may give rise to a hypersensitivity or autoimmune reaction causing myocardial damage. Some studies have also proposed derangements of calcium storage in infected cells contributing to presentations of myocarditis.<sup>10</sup>

In conclusion, cardiac failure secondary to myocarditis is rare complication of congenital dengue infection which may contribute to significant morbidity and mortality. The etiopathogenesis is still not very clear due to unexplained and unexplored aspects of this rare presentation.

An elective caesarean section can be considered in expectant mothers presenting with dengue fever in late gestation to save the newborn from potentially life threatening complications. However this should be meticulously planned in view of risk of bleeding diathesis in mother. A careful pre-operative, intra-operative and post-operative planning along with adequate provision of blood products if required is essential for the safety of both mother and the baby.

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