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Case Report

Two cases of severe neonatal dengue fever during an outbreak in Kolkata city

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ABSTRACT

Neonates with transplacentally acquired dengue infection often present with subtle features. We report two cases of severe neonatal dengue admitted during an outbreak in Kolkata. Both the mothers tested positive for dengue. Both neonates had thrombocytopenia, elevated liver aminotransferases, progressive pallor, and third space fluid loss. One neonate required inotropic support (dopamine infusion) to manage the shock while the other neonate had to be put on continuous positive airway pressure to manage the increasing respiratory distress. Both patients were successfully managed. Neonatal dengue is an important differential diagnosis of neonatal sepsis during an outbreak. Early diagnosis and appropriate fluid resuscitation can help in avoiding complications.

Key words: *Dengue, Neonate, Shock, Vertical transmission*

Dengue fever is an acute febrile illness caused by the four serotypes (DENV 1-4) of a Flavivirus and transmitted by the bite of *Aedes aegypti* mosquito. In India, dengue causes an epidemic for every 2-5 years [1]. However, there is a lack of sufficient guidelines as well as raw literature on the effects of dengue in pregnant women and their newborns [2]. Early diagnosis and proper treatment of pregnant women with acute dengue infection, especially those in the third trimester as well as of the neonates with perinatally transmitted dengue, would be valuable in the reduction of maternal and neonatal mortality rates [3]. We report two cases of neonatal dengue admitted at the neonatal intensive care unit of our hospital during a dengue outbreak in Kolkata.

CASE REPORTS

Case 1

A 5-day-old term neonate was admitted with fever, refusal to feed, and shrill cry for the past 1 day. There was no history of rash, convulsion, or bleeding from any site. On examination, heart rate was 160/min, respiratory rate was 44/min, and axillary temperature was 38.5°C with normal perfusion. Neurological examination revealed sluggish neonatal reflexes. The neonate was treated with a presumptive diagnosis of neonatal sepsis with intravenous cefotaxime and netilmicin. Investigation revealed hemoglobin, 12.4 g%; total leukocyte count, 5600/mm^3; differential leukocyte count, N22 L72 M6; platelet count, 90,000/mm^3; and normal micro-erythrocyte sedimentation rate and serum C-reactive protein (CRP). Band cells were within normal limits, toxic granules were absent.

On day 4 of admission, heart rate was 166/min, respiratory rate was 80/min, capillary refill time was prolonged, and the child developed feed intolerance and abdominal distension. The child was passing stool normally, and peristaltic sounds were within normal range. Features of third space fluid loss were evident from increasing anasarca, respiratory distress with chest retractions, and decreasing urine output. Investigations revealed hemoglobin, 9.4 g%; platelet count, 20,000/mm^3; aspartate aminotransferase, 780 U/L; and alanine aminotransferase, 500 U/L, Stool for occult was blood positive, and ultrasonogram of abdomen revealed ascites.

As there was ongoing dengue epidemic, the case was investigated for it. Dengue NS1 and IgM came out to be positive. Mother's history was not contributory and she did not have any fever but when tested for the same also had positive IgG and IgM for dengue. The shock was managed with appropriate fluid, platelet transfusion, and dopamine infusion. Repeat hemoglobin was 10.2 g%, total leukocyte count was 6200/mm^3, platelet count was 170,000/mm^3, and CRP <1. The child improved within 72 h and was discharged after 10 days of hospital stay.

Case 2

A 4-day-old term male neonate was admitted with lethargy and refusal to suck for two days. There was no history of rash, convulsion, or bleeding from any site. The mother had low-grade fever for 2 days just prior to delivery. On examination, the neonate had normal heart rate, respiratory rate, temperature, and peripheral perfusion but was lethargic. The neonate was managed with a presumptive diagnosis of neonatal sepsis with intravenous cefotaxime and netilmicin. Initial investigations including cerebrospinal fluid study were within normal ranges.

On day 3 of admission, the child started to have respiratory distress along with passage of blood-streaked stool along with abdominal distension. Peripheral perfusion was also poor. Investigation revealed hemoglobin, 7.9 g%; platelet count, 50,000/mm^3; prothrombin time, 19 s; and normal activated partial thromboplastin time. Sepsis screen, blood culture, and urine culture were negative. Dengue NS1 came out to be positive. The mother when tested showed positive IgM and IgG. The baby's chest radiograph revealed right-side pleural effusion, and ultrasonogram of abdomen revealed ascites. Initially, feed was withheld and he was treated with appropriate fluid management, transfusion of platelet and fresh frozen plasma. The child required continuous positive airway pressure. After 2 days, the clinical condition was stabilized. Repeat tests showed hemoglobin of 9 g%, total leukocyte count of 6800/mm^3, and platelet count of 152,000/mm^3. Subsequently, he was discharged after 8 days of hospital stay.

DISCUSSION

Dengue virus infection results in a spectrum of manifestations including fever, myalgia, arthralgia, and leukopenia (dengue fever [DF]) in one hand and dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) with hemorrhage and shock on the other hand. DHF and DSS predominantly affect pediatric population with the age group of 4-6 years affected most commonly [1]. DHF/DSS shows higher incidence in two groups of pediatric patients: Children with a past history of DF and infants with progressively decreasing levels of transplacentally acquire dengue antibody. Various studies reported its rarity in early infancy and newborn age groups [4].

Neonatal dengue is different from dengue in other ages because of three reasons. First, bleeding and/or shock precipitated by dengue can severely complicate the birth injuries encountered by both the mother and the newborn during parturition [3]. Second, neonates with dengue infection often present with fever of short duration, hepatomegaly, thrombocytopenia, circulatory insufficiency, excessive bleeding from cord or venepuncture sites, and shock. Unfortunately, all these features can be seen in various other common neonatal illnesses including bacterial sepsis [5]. Hence, a high index of suspicion is needed to prevent a potential fatality. Third, if the mother had a previous dengue infection, she will have antibodies against dengue in her blood, which will be transplacentally acquired by the fetus *in utero*. Postnatally, if this newborn acquires a dengue infection with a virus of a different serotype, although it is a primary dengue infection, it may behave like a secondary dengue and precipitate a DSS [1].

The first case of vertical (transplacental) transmission of DF was reported from Tahiti [5]. In a case report of perinatal transmission of dengue virus from Puerto Rico [6], of the 33 cases reported, all developed fever and thrombocytopenia in the first two weeks after birth. Increasing number of cases of perinatal transmission of DF is being reported from Thailand, Malaysia, Puerto Rico, Sri Lanka, Port Sudan, Peru, and Brazil [5], yet no consensus has been formed against neonatal dengue till now.

Mitra et al. reported that the chance of vertical transmission is greatest (and also the risk of maternal bleeding complications) if a woman delivers at the height of viremia [7]. It should be noted that, while the dengue NS1 antigen becomes positive early, the IgM antibody, in postnatally infected newborns, requires as long as 5 days to appear [1]. Sirinavin et al. reported that the onset of fever in neonates varies from 1 to 11 days after birth (average 4 days) and lasts for 1-5 days [8]. In our case series, both the neonates presented within 1 week of birth, both had complications usually described in severe DF such as thrombocytopenia, third space fluid loss, hepatic derangement, and respiratory distress.

The exact pathophysiology of neonatal dengue is still unclear [3]. If a pregnant woman delivers at or near the peak of dengue viremia, intrauterine vertical transmission becomes likely [7]. As the maternal protective antibody in acute febrile mother is usually of IgM subtype, it cannot pass through the placenta to the child and sometimes there is insufficient transfer of protective maternal IgG, if formed. This increases the likelihood of disease in the newborn. As a newborn does not have a mature immune system, both humoral as well as cellular responses to the infection are slower than older children which probably makes them more vulnerable [7] and the disease process becomes more insidious and fulminant later than expected in comparison with older children. More research work is needed to elaborate the exact pathogenesis.

CONCLUSION

This case series may serve to enrich growing medical literature regarding the approach to neonatal dengue. During outbreaks of dengue in a community, if a neonate presents with non-specific features of sepsis, the possibility of neonatal dengue should be kept in mind.

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