

CASE REPORT

PERINATAL DENGUE INFECTION : A CASE REPORT AND REVIEW OF LITERATURE

Waricha Janjindamai and Pornpimol Pruekprasert

Department of Pediatrics, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract. A case of vertical transmission of dengue infection in the perinatal period is reported. The mother, a term pregnancy, had acute dengue the day before admission. The infant was born at term and developed fever on the fifth day of life which lasted for 5 days. No bleeding or plasma leakage was detected during the course of fever in infant or mother. A liver function test showed elevated SGOT and SGPT in the infant. The infant developed a convalescent rash on day 5 of the fever. The diagnosis of secondary dengue hemorrhagic fever in the mother was confirmed by serology and primary dengue infection in the infant was confirmed by serology and serotyped as dengue type 2 by PCR. The clinical course and management of mothers and infants with perinatal dengue infection are reviewed

Dengue hemorrhagic fever (DHF) has become endemic and causes significant health problems in many countries in the Western Pacific region and Southeast Asia, including Thailand (WHO, 1998). Dengue is transmitted to humans through the bite of infected *Aedes* mosquitos, principally *Aedes aegypti*. Although DHF may affect persons of all ages in dengue endemic areas, most DHF cases occur in children less than 15 years of age. During the past three decades in Thailand the average age of patients who have DHF has increased by several years (Nimmanitya, 1987), and there has also been an increase in the incidence of the infection in pregnant women. DHF during pregnancy has not been shown to cause any congenital abnormalities (Fernandez *et al*, 1994; Carles *et al*, 1999), however transmission from mother to fetus can cause perinatal mortality and morbidity (Poli *et al*, 1994). We report a recent experience with a laboratory-confirmed case of neonatal dengue that resulted from vertical transmission. Other cases of neonatal dengue infection are reviewed.

Case report

A 21-year-old pregnant Thai woman

Correspondence: Dr Waricha Janjindamai, Department of Pediatrics, Prince of Songkla University, Hat Yai, Songkhla 90140, Thailand.

Tel: 66 (0) 74451250; Fax: 66 (0) 74212912

(gravida 1, para 0) who had no history of major medical illness was hospitalized at 39 weeks' gestation because of labor pain and bloody show. The day before admission she had developed fever, headache, and myalgia. Body temperature was 38.5°C. Laboratory findings included a hemoglobin concentration of 11.4 g/l, hematocrit 30%, white blood cell (wbc) count 7,900 cell/mm³ with neutrophils 88%, and a platelet count 145,000/mm³. She delivered a healthy term, female infant weighing 2,890 g vaginally with moderate meconium stained amniotic fluid. After delivery, the mother still had a high fever for 5 days with bleeding per gums. Dengue hemorrhagic fever was suspected due to a rising Hct from 30% to 41% with a drop in the platelet count to 36,000/mm³. She developed dengue shock syndrome on day 5 of the fever, which responded well to intravenous fluid resuscitation. A liver function study revealed SGOT 120 unit/l, SGPT 52 unit/l, alkaline phosphatase 143 unit/l, direct bilirubin 0.15 mg/dl and total bilirubin 0.22 mg/dl. She was discharged on the ninth day. Serologic studies for dengue specific IgM antibodies identified by IgM antibody capture enzyme-linked immunosorbent assay (ELISA) was 33 IU/ml and the dengue hemagglutination inhibition test (HI) titer was over 1:10,240, which is consistent with a secondary dengue infection.

The infant was transferred to the neonatal

intensive care unit (NICU) when she developed a fever of 38.6°C on the fifth day of life. She fed well using formula. Physical examination revealed a blood pressure of 70/58 mmHg, a heart rate 140/min, and a respiratory rate 50/minute. The liver was palpable 0.5 cm below right costal margin. Laboratory findings showed a Hct of 46%, wbc 14,100 cells/mm³. with PMN 45%, band 4%, eosinophil 2%, lymphocyte 43%, monocyte 5%, atypical lymphocyte 1%, and platelet count 35,000/mm³. A septic work-up was performed. Ampicillin and gentamicin were given for 2 days until the hemoculture was negative. The infant had a high fever for 5 days (from days 5-9 of life). There was no bleeding or plasma leakage detected. On the 8th day of life, liver function studies showed a direct bilirubin of 1.28 mg/dl, total bilirubin 3.68 mg/dl, SGOT 5,940 units/l, SGPT 1,510 units/l, alkaline phosphatase of 212 unit/l, total protein 5 g/dl, and albumin 3.10 g/dl. A coagulogram showed a PTT 73.5 seconds (control 28.4), PT 15.0 seconds (control 11.1), fibrinogen 116.9 mg/dl (normal 167-309), and fibrin degradation products < 5 µg/ml. Dengue specific IgM antibodies, identified by IgM antibody capture ELISA were 77 IU/ml. The first dengue (HI) titer (day 2 of fever) was < 1:20 and the second titer was 1:80, which was typical of a primary dengue infection by WHO criteria. A polymerase chain reaction test for dengue virus on day 5 was positive for dengue type 2. The infant developed a convalescent rash on day 5 of the fever, recovered uneventfully and was discharged home on day 17 of life. A cranial ultrasonographic scan obtained on day 10 was unremarkable. At 1 month of age, she had normal weight gain and normal development. A liver function study showed nearly normal results.

Reports of perinatal transmission of dengue worldwide are quite rare. Cases of neonatal dengue have been reported from Tahiti, Malaysia and Thailand (Poli *et al*, 1991; Thaithumyanon *et al*, 1994; Bunyavejchevin *et al*, 1997; Chy *et al*, 1997; Chotigeat *et al*, 2000; 2002; Kerdpanich *et al*, 2001; Petdachai *et al*, 2002). Eight reports, with a total of 14 cases of perinatal transmission of symptomatic dengue, exist in the literature. The first report from Tahiti (Poli *et al*, 1991) described 5 neonates. Two cases have been reported from

Malaysia (Chy *et al*, 1997) and 7 other cases from Thailand (Thaithumyanon *et al*, 1994; Bunyavejchevin *et al*, 1997; Chotigeat *et al*, 2001; Kerdpanich *et al*, 2001). All cases were proven to be of neonatal dengue by serologic test (HI or specific IgM), in 3 by viral isolation and 4 by polymerase chain reaction (PCR). Maternal dengue was demonstrated by serology in all cases. Asymptomatic dengue in neonates after detection in the mother during pregnancy is also possible (Bunyavejchevin *et al*, 1997; Carles *et al*, 1999). Dengue in pregnancy may induce preterm labor (Jirapinyo *et al*, 1990; Chy *et al*, 1997).

In our report, the clinical signs and symptoms of the mother and the baby were suggestive of dengue, as the mother experienced fever and non-specific symptoms such as headache and arthralgia. Thrombocytopenia was present. The infant demonstrated fever, irritability, severe thrombocytopenia and elevated liver enzymes. A diagnosis of dengue fever in both mother and the baby was confirmed by a very high titer HI and by PCR in the baby. We therefore concluded that this baby had acquired her infection from her mother during the perinatal period.

Clinical significance of women infected perinatally with dengue infection

Dengue fever in pregnant women who pass the dengue virus to their infant perinatally, develop fever from 8 days before delivery to 10 hours after delivery. The course of fever then lasts for 4-6 days as in the normal population. Other hematologic signs, such as thrombocytopenia ranging from 10,000-80,000/mm³, are found in all cases. The mode of delivery was divided equally between cesarean section and normal delivery. There were three cases that mentioned elevated liver enzymes. The SGOT level ranged 1,770-15,523 unit/l, and SGPT 689-760 unit/l. Four mothers developed dengue shock syndrome (DSS) with severe postpartum bleeding requiring platelet and red blood cell transfusion. Serology for dengue infection by HI titer and dengue specific IgM were proven to be secondary dengue infections except in two cases, one from France (Bous Semart *et al*, 2001) and the other from Malaysia (Chy *et al*, 1997). No mortality in mothers with dengue infection was reported. It

has been shown that lack of awareness of dengue infection can lead to severe and prolonged postpartum bleeding in pregnant women who have a history of peripartum fever (Thaithumyanon *et al*, 1994; Chotigeat *et al*, 2000; Petdachai *et al*, 2002). The longer the time interval between the onset of maternal fever and delivery, the sooner the appearance of fever in the infants, consistent with the incubation period of dengue infection of 5-7 days.

Clinical manifestations of neonatal dengue infection

In all of the cases of neonatal dengue caused by vertical transmission, the fever was detected from 16 hours to 11 days after birth and lasted 2-6 days. Most were low grade fevers with body temperatures between 38.0°-38.8°C. A fine maculopapular rash or convalescent rash could be found on face, neck and trunk. Petechial rash could be found on the legs and thighs (Kerdpanich *et al*, 2001; Petdachai *et al*, 2002). The liver could be palpated 0.5-2 cm. below right costal margin and the spleen could also be palpated 0.5 cm below left costal margin. In one case from Malaysia neonatal dengue developed in a preterm infant and was complicated by CNS bleeding, ultimately resulting in fatality (Chy *et al*, 1997).

Breast feeding was not given in any of the cases of neonatal dengue due to the clinical severity of the disease in the mother. Most had no sign of bleeding or plasma leakage, although in 3 cases from Tahiti dengue shock syndrome was reported (Poli *et al*, 1991).

Laboratory manifestations of neonatal dengue

Thrombocytopenia was observed in all cases, with a platelet count ranging from 15,000-50,000/mm³ that persists for 2 months (Chotigeat *et al*, 2000). Leukopenia was also observed. WBCs ranged from 5,000 to 10,500 cells/mm³. Polycythemia was never reported. One case was found to have an increased hematocrit by 40% (Bous Semart *et al*, 2001) (hematocrits ranged from 33% to 49%). Only one case from Malaysia showed an abnormal coagulopathy in preterm neonatal dengue (Chy *et al*, 1997). In our report, the partial thromboplastin time was prolonged with a mild reduction in the fibrinogen level. A

mildly elevated serum SGOT and SGPT were observed in two neonates (Chy *et al*, 1997; Bous Smart *et al*, 2001). In our report, a very high SGOT level (5,940 units/l) was found.

Laboratory tests essential for the confirmatory diagnosis of neonatal dengue infection include isolation of virus, demonstration of a rising titer of specific serum dengue antibodies and demonstration of a specific viral antigen or RNA in the tissue or serum (WHO, 1998). Isolation of virus, the most definitive approach, was proven in 2 cases (Thaithumyanon, 1994; Chy *et al*, 1997). Serological tests, which are simpler and more rapid, are performed in most cases, specifically the hemagglutination inhibition (HI) test. Some cases are proven by IgM capture enzyme linked immunosorbent assay (MAC-ELISA), which confirms the diagnosis of dengue infection (Thaithumyanon, 1994; Chy *et al*, 1997; Bous Smart *et al*, 2001; Kerdpanich *et al*, 2001). In previous studies, four cases of neonatal dengue were detected by PCR, 3 cases of dengue type 2 infection and one dengue type 1 infection (Petdachai *et al*, 2002).

Management of dengue hemorrhagic fever in pregnancy

Management of dengue hemorrhagic fever in pregnancy should be conservative, symptomatic and carry on through the shock stage. The critical period usually passes within 24 to 48 hours. If delivery is inevitable, the vaginal route is preferred. Uterine contraction after delivery will strangle the blood vessels that were torn during parturition and cause hemostasis even though coagulation defects are still ongoing. When cesarean section is unavoidable, platelet concentrate should be prepared and should be given intraoperatively or postoperatively as necessary. The route of delivery should be considered under obstetric indication with careful monitoring of the platelet count and coagulative function.

Tocolytic drugs may be considered until the patient recovers from the shock stage and the platelet count returns to a normal level; however, most tocolytic drugs can cause tachycardia which may obscure the patient's status, and magnesium sulfate might be a drug of choice in this situation from its lack of tachycardia causing properties

(Jirapinyo *et al*, 1990).

Management of neonatal dengue infection

When a pregnant or parturient woman develops signs consistent with dengue, the diagnosis in her offspring should be considered even if the newborn appears well in the first several days of life. Symptomatic and supportive treatment under close observation are the mainstay of treatment. Other infections, bacterial or viral, can cause clinical features and hematologic changes similar to those of dengue virus infection. The occurrence of subclinical infections may lend further confusion to the situation.

Conclusion

In dengue endemic areas, more cases of dengue infection in pregnancy are being found due to the increasing incidence of dengue infection in adults. Dengue infection should be suspected when a pregnant woman presents with similar pattern of symptoms and signs as a non-pregnant case. Conservative treatment should be given unless there are complications. An awareness, and hence early diagnosis and management of vertical transmission of dengue virus, is necessary to reduce the perinatal morbidity and mortality of the newborn.

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