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Perinatal transmission of dengue virus in Puerto Rico: a case report

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Abstract

We report a laboratory confirmed case of vertical transmission of dengue in a mother-child pair in the eastern part of Puerto Rico. The clinical course of the pregnant female suggested a GBS infection, but laboratory tests confirmed it was dengue infection, one week after delivery. The male infant was healthy at birth, but one week after birth developed clinical complications related to vertical transmission of dengue. This report targets physicians in dengue endemic countries like Puerto Rico to be aware of the possibility of vertical transmission of dengue in symptomatic pregnant patients, especially around the time of delivery.

Keywords

Dengue; Perinatal Transmission; Bloodborne

1. INTRODUCTION

Dengue is caused by four related dengue viruses (DENV) −1, −2, −3, and −4, and infection with one DENV is thought to provide lifelong immunity to that virus-type and partial short term protection to other DENVs. Most DENV infections are asymptomatic especially first infections. The clinical spectrum of disease ranges from a mild, non-specific acute febrile illness, to classic dengue fever (DF) to severe, life-threatening disease including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [1]. Second and subsequent DENV (secondary) infections have been associated with more severe disease.[2]

DENV transmission is primarily between humans through infected *Aedes* mosquitoes. The incubation period in the human host is typically one week (range 3 to 14 days) with viremia occurring 1 to 2 days before symptom onset and lasting approximately one week. During this period of viremia, DENV can also be transmitted as a bloodborne infection which has been observed from receipt of donor organs or tissue, blood transfusion [3–6], after occupational accidents in healthcare settings, and perinatal transmission [7,8].

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Historically, dengue was thought to be primarily a childhood disease; however, an increasing proportion of cases are now being reported among adults [2,9,10]. In Puerto Rico, half of all reported dengue cases are adults ≥20 years of age while adolescents 15 to 19 years old have the highest incidence of laboratory-confirmed den- gue; a group whose infants make up nearly one-fifth of the birth cohort [11]. Because of this, women of childbearing age are now increasingly at risk of acquiring DENV infection while pregnant and may be more likely to develop severe disease as second infections occur later in life. Here we describe a unique case of perinatal DENV transmission involving a teenage mother and her infant.

2. CASE SUMMARY

2.1. Mother

A 17 year old woman, Grava: 1 Para: 1 Abortions: 0 Stillbirth: 0, who regularly attended prenatal care clinic since 17 weeks gestation, presented to the Emergency Department (ED) on 16 June 2010. She was 38 4/7 weeks gestation with a chief complaint of fever for one day, headache, and nausea. The patient had recently moved to Puerto Rico from Pennsylvania. She had one previous hospitalization for appendectomy at age 7 and no chronic medical conditions. The patient denied tobacco, alcohol or illicit drug use, and she was HIV, HBV and RPR non-reactive and Group B Streptococcus (GBS) positive at 34 weeks gestation. At initial presentation, she had a temperature of 38.3°C, a heart rate of 140 bpm, respiratory rate of 18 bpm, and blood pressure of 109/46 mm Hg. She was alert, active and in moderate distress with complaints of pelvic pain. On physical examination, her cervix was two centimeters dilated and she was thought to be in early labor. Laboratory studies included a complete blood count (CBC) with leukocyte count of 9500 mm^3 and a normal differential, hematocrit of 31.7%, and a platelet count of 105,000 mm^3. She was mildly hyponatremic with serum sodium of 134.0 meq/L. Blood and urine cultures were taken and the patient was admitted for intravenous hydration and empiric treatment with ampicillin and gentamicin for GBS. After intravenous hydration, the decision was made to transfer the patient to the delivery room were an amniotomy was performed to promote active labor. After $5\frac{1}{2}$ hours of active labor, the patient delivered a male infant at 16:13 on 17 June 2010 by spontaneous vaginal delivery. She did not have any abnormal bleeding during labor or delivery, and did not require any blood products.

The patient continued to have fever and headache for 5 more days, and admission blood and urine cultures, and placental cultures were all negative. Her platelet count declined further to a low of 59,000 mm^3 on the day of fever defervescence. That day a serum sample was sent to the Centers for Disease Control and Prevention (CDC) Dengue Branch Laboratory in San Juan, Puerto Rico for dengue diagnostic testing. The patient did not develop any evidence of plasma leakage as indicated by hemoconcentration, ascites, pleural effusions, or hypoalbuminemia. She did not develop any hemorrhagic manifestations other than moderate post partum vaginal bleeding that lasted about two weeks. The patient did not have any other signs or symptoms associated with dengue. However, her aspartate aminotransferase (AST) and alanine aminotranferase (ALT) were slightly elevated at 95 and 46 IU/L, respectively on 22 June 2010, while her total bilirubin (0.6 mg/dl) remained normal during the hospital stay. The patient was discharged home on 23 June 2010 with a platelet count of 118,000 mm^3, an

AST of 53 IU/L, ALT of 31 IU/L, and a hematocrit of 32.5%. When evaluated 2 weeks later, she had fully recovered without any complications.

2.2. Infant

The infant weighted 2,892 grams, and had a length of 20 inches and a head circumference of 13 inches. APGAR scores were 8 and 9 at one and five minutes after birth, respectively. The infant was transferred immediately to the Neonatal Intensive Care Unit (NICU) to be evaluated for GBS sepsis. Upon admission, the infant had a temperature of 36.5°C, a heart rate of 141 bpm, a respiratory rate of 35 bpm, and a blood pressure of 60/43 mm Hg. Blood and urine cultures were taken and the infant was given ampicillin and gentamycin empirically. Physical examination was unremarkable. Laboratory studies showed a leukocyte count of 11,000 mm^3 and a normal differential, a platelet count of 260,000 mm^3, and a hematocrit of 43.5%. Blood and urine cultures taken at birth were negative.

The infant remained stable with no changes observed in his physical examination, vital signs or behavior until the evening of June 23, when he became hypoactive and unable to suck and feed. On physical examination, the infant had a temperature of 36.5°C and a heart rate of 130 bpm, respiratory rate of 46 bpm and BP 64/39 mm Hg. He was pale and had a fine reticular rash. The remainder of his examination was unremarkable. The patient had no lymphadenopathy, petechiae, ecchymosis, purpura, or hepatomegaly. Laboratory studies showed a leukocyte count of 4900 mm^3, a platelet count of 116,000 mm^3 and a hematocrit of 36.6%; he was hyponatremic with a sodium of 130 meq/L. Blood and urine cultures were taken, and the possibility of a fungal infection was entertained as there had been recent cases in the hospital. Antibiotics were changed to vancomycin and imipenem, and amphotericin was added.

The next day on 24 June, the infant remained hypoactive, pale, and unable to suck. He had a leukocyte count of 4600 mm^3, a platelet count of 84,000 mm^3, and a hematocrit of 35.6%. No bleeding was observed, and there was no change in his physical examination or vital signs. At this point, the mother's serum was reported as positive for DENV-1 by reverse transcriptase-polymerase chain reaction (RT-PCR). The possibility of vertical transmission was entertained, and a serum sample was sent to CDC for diagnostic testing. The infant's platelet count decreased to a low of 36,000 mm^3 on June 26, and he was given a platelet transfusion. No bleeding was observed, a head ultrasound was normal, and stool and urine analyses were negative for red blood cells. On June 27, laboratory studies showed a prothrombin time (PT) of 11.4 seconds; partial thromboplastin time (PTT) of 63.3 seconds, and international normalized ratio (INR) of 1.05, and the infant was given fresh frozen plasma and evaluated for disseminated intravascular coagulation (DIC). His coagulation profile normalized on June 28. An abdominal ultrasound found prehepatic and perisplenic free fluid, suggesting ascites.

Dengue diagnostic results were received on June 29, which were positive for DENV-1 by RT-PCR. The next day, the infant was more active and his sucking improved. A CBC showed a leukocyte count of 7100 mm^3, a platelet count of 98,000 mm^3, and a hematocrit of 28.7%. He was given a packed red blood cell transfusion for symptomatic anemia with hypoxia (O_2 saturation 93%). On July 7, his platelet count reached normal values for age

(168,000 mm^3). The patient had no other complications and he was discharged home on 18 July 2010.

3. DISCUSSION

This case illustrates the importance of considering dengue as a cause of acute febrile illness in pregnant women residing in, or traveling to endemic countries, and suggests that perinatal DENV transmission is likely to be under-recognized. Unlike other cases reported in the literature [12–31] the infant we described never developed fever. Newborn infants often do not mount a febrile response to an infection, and consequently cases of perinatal DENV transmission may be missed if the mother is not identified as having dengue. This infant had non-specific findings consistent with congenital dengue including hyponatremia, leucopenia, and thrombocytopenia, an elevated PTT, and ascites. However, he was diagnosed as having dengue because DENV-1 was detected by RT-PCR in his mother's serum. Perinatal transmission of DENV was supported by the fact that the mother was acutely febrile at the time of delivery, the infant never left the hospital after an uneventful delivery and was unlikely to have had mosquito-borne DENV transmission and all cultures were negative for GBS.

Perinatal dengue, as this case illustrates, may result in severe dengue and prolonged hospital stays [22]. Of the 33 cases of perinatal DENV transmission reported with clinical data, all developed fever and thrombocytopenia in the first two weeks after birth, and 39% had a hemorrhagic manifestations, 24% developed hypotension, and 33% had hepatomegaly.

Our case and all of the perinatal transmission cases described in the literature involved a woman who was acutely ill with dengue at or near the time of delivery. It has been hypothesized that when this happens, there is an insufficient level of protective maternal anti-DENV IgG to transfer to the fetus as the women is at or near the peak of DENV viremia. In dengue endemic areas, women with intrapartum or post partum fever and a negative evaluation for bacterial or other causes should be tested for dengue and informed of the risk of perinatal dengue. Special attention should be paid to their infants who if infected, might become ill in the first two weeks of life. As with other diseases, this may mean that the infant presents with a change in their level of activity, responsiveness, muscle tone, or ability to suck and swallow, and they may not develop classic signs of dengue such as fever and rash.

For nearly four decades, the Puerto Rico Department of Health and CDC have monitored dengue incidence in Puerto Rico via a passive surveillance system. Even though dengue has been endemic since the late 1960s and it is a reportable condition by law, cases are thought to be under-recognized and under-reported. Pregnancy-associated dengue cases may not always be reported as such. Pregnant women with dengue may be diagnosed with other febrile illnesses or HELLP syndrome, especially if they present with elevated liver enzymes and a low platelet count. Since there is no rapid diagnostic test for dengue, physicians need to have a high index of suspicion and test for dengue while ruling out these other etiologies.

Future studies should aim to determine the incidence of perinatal DENV transmission, risk factors for dengue in the neonate, and poor outcomes among infants born to women with dengue during pregnancy. Increased awareness of the possibility of maternal dengue and perinatal transmission is important to prevent complications in both the mother and the newborn.

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