

Case Report

Dengue as a cause of fever during pregnancy: a report of two cases

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Abstract

Dengue infection has not been routinely investigated among pregnant women and parturients with acute febrile syndrome in endemic settings. Here, we report two cases of dengue fever detected at the time of delivery in parturients enrolled in a cohort prospective study conducted in a hospital in Recife, Brazil. The parturients reported fever onset within seven days prior to delivery, and dengue infection was confirmed upon detection of viral ribonucleic acid (RNA) by using the reverse transcriptase-polymerase chain reaction. Dengue infection should be considered as a diagnostic possibility in cases of fever during pregnancy and labor, especially in endemic areas.

Keywords: Dengue. Pregnant women. Vertical transmission.

INTRODUCTION

Dengue fever is a growing health risk in urban areas and a major cause of hospitalizations and deaths in tropical countries⁽¹⁾. It is caused by four different serotypes [dengue virus (DENV)1-4] and is transmitted by a mosquito bite, mainly of the *Aedes aegypti*⁽¹⁾. Since the re-emergence of dengue fever in Brazil in the 1980s, the country has been affected by successive outbreaks, resulting in a high incidence of cases⁽²⁾.

Case reports of dengue fever during pregnancy document several complications such as maternal death, stillbirth, prematurity, low birth weight, fetal abnormalities, and abortion⁽³⁾⁽⁴⁾. The symptoms of dengue fever during the gestational and perinatal periods are usually similar to those found in the general population and the clinical management is similar to that in non-pregnant women⁽¹⁾.

Although fever is one of the main symptoms of dengue⁽¹⁾, tracing this infection in pregnant women with acute fever or other symptoms of the disease has not been fully incorporated into routine prenatal care in Brazil. Nevertheless, laboratory investigation of dengue fever is important since it is a potential health risk for mothers and their fetuses and requires targeted clinical management to prevent and treat the associated complications⁽⁵⁾.

We encountered two cases of dengue fever in parturients with fever onset seven days prior to labor. The blood samples were collected during labor in the maternity ward of the *Instituto de Medicina Integral Prof. Fernando Figueira* (IMIP), a teaching hospital in Recife, Pernambuco, Brazil. The diagnosis was confirmed by using real-time reverse transcription-polymerase chain reaction (RT-PCR). Both parturients were enrolled in a prospective cohort study conducted between March 2011 and May 2012 to investigate the incidence of dengue infection and the kinetics and transplacental transfer of maternal antidengue antibodies⁽⁵⁾.

CASE REPORT

Case 1

A 17-year-old, single woman in labor was admitted to our maternity ward in June 2011. She reported an episode of urinary tract infection in the second trimester of pregnancy, which was treated with antibiotics. On admission, she reported headache, chills, weakness, and fever (temperature, 38.1°C). The obstetric exam revealed a 6-cm dilated cervix, intact amniotic membranes, fetus in cephalic presentation, and fetal auscultation of 160 beats per minute. Four hours before the delivery, an amniotomy was performed and we observed a foul-smelling, moderate meconium-stained amniotic fluid. Antibiotic therapy was administered. Our patient delivered vaginally, giving birth to a healthy term, male infant weighing 3,045g with an Apgar score of 6 and 8 at the 1st and 5th min, respectively. A macroscopic examination of the placenta did not show any abnormalities. After 24h, the parturient was discharged with a

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Received 9 September 2015

Accepted 6 January 2016

prescription of oral antibiotics to be taken at home. Laboratory tests for dengue infection in the maternal blood sample showed the following results: antidengue immunoglobulin G (IgG) indirect enzyme-linked immunosorbent assay (ELISA) (PanBio, Brisbane, Australia), positive; antidengue immunoglobulin M (IgM)-capture (PanBio and Focus Diagnostics, Cypress, CA) ELISA, negative; and DENV RT-PCR positive for DENV 2.

At birth, the neonate was hypotonic with generalized cyanosis, intercostal retractions, nasal flaring, and grunting. The newborn was successfully resuscitated and intravenous antibiotic therapy was administered. He was discharged on the 7th day of life with a diagnosis of septicemia secondary to chorioamnionitis. Blood and cerebrospinal fluid cultures were negative for dengue infection; however, the cord blood sample was IgG-positive, IgM-negative, and RT-PCR-negative.

Case 2

A 20-year-old, married woman in labor was admitted to our maternity ward in October 2011. She reported asthenia, nausea, myalgia, and fever in the seven days preceding labor.

This patient had been hospitalized at 18 weeks of pregnancy due to low back pain, fever, and headache. She was diagnosed with pyelonephritis and underwent antibiotic therapy. After discharge, she was referred to prenatal care. On admission for delivery, she had a satisfactory general condition and the obstetric examination showed 5-cm dilated cervix, intact

amniotic membranes, fetus in cephalic presentation, and fetal auscultation of 140 beats per minute. The next day, she delivered vaginally and gave birth to a healthy term, male infant weighing 3,680g with an Apgar score of 9 at the 1st and 5th min. At the macroscopic examination, the placenta was whole and normal. Twenty hours after delivery, the patient experienced dizziness, presyncope, asthenia, and an episode of vaginal bleeding. Her hemoglobin level was 6.6g/dL. Complete patient recovery was achieved 46 h after delivery. Both the mother and baby were discharged 2 days later.

The DENV-specific laboratory tests carried out using the maternal blood sample showed the following results: IgG-ELISA, positive; IgM-ELISA, negative; and RT-PCR, positive for DENV 4. The cord blood sample was IgG-ELISA-positive, IgM-ELISA-negative, and RT-PCR-negative for dengue. **Table 1** presents the clinical and laboratory characteristics of both cases.

DISCUSSION

Although dengue fever predominantly affects the adult population, clinical and epidemiological data on dengue infection in pregnant women and newborns are scarce in Brazil^{(4) (5) (6)}. Worldwide, most of the medical data on dengue fever during pregnancy is available from case reports and descriptive studies conducted in Asia⁽³⁾.

TABLE 1 - Clinical and laboratory characteristics of maternal and pregnancy outcomes.

Clinical and laboratory characteristics	Case 1	Case 2
Age (years)	17	20
Gestational age (weeks)	40.6	40.5
Type of delivery	Vaginal	Vaginal
Reported infection event during pregnancy	Two urinary tract infection episodes: Early pregnancy and during labor	Urinary tract infection/pyelonephritis 18 weeks
Reported dengue fever during pregnancy	No	No
Presenting complaints	Fever, myalgia, and chills during labor	Fever, myalgia, nausea, in last week pregnancy and increased bleeding postpartum
Neonatal clinical characteristics	3,045g Apgar 6/8 Chorioamnionitis Sepsis Meconium	3,680g Apgar 9/9 Normal vitality
Dengue IgM/IgG/	IgG (+)	IgG (+)
RT-PCR/DENV maternal	IgM (-) RT-PCR (+) DENV 2	IgM (-) RT-PCR (+) DENV 4
Dengue IgG/IgM/RT-PCR umbilical cord	IgG (+) IgM (-) RT-PCR (-)	IgG (+) IgM (-) RT-PCR (-)

IgM: immunoglobulin M; **IgG:** immunoglobulin G; **RT-PCR:** reverse transcription-polymerase chain reaction; **DENV:** dengue virus.

In case 1 of the current study, abundant amniotic fluid and thick meconium with fetid odor was reported during labor and chorioamnionitis was diagnosed. These manifestations were also reported by Phongsamart et al.⁽⁷⁾ and Sinhabahu et al.⁽⁸⁾ in parturients in Thailand and Sri Lanka, respectively, and these parturients were confirmed to have virological dengue. Therefore, their findings reinforce the evidence that such clinical signs may constitute one of the manifestations of dengue fever during childbirth.

Postpartum hemorrhage and low hemoglobin level were seen in the parturient in our Case 2. Hemorrhagic manifestations of various intensities such as vaginal bleeding or surgical wounds bleeding in caesarean sections, with or without thrombocytopenia during labor or at the time of delivery have also been described by other authors in previous studies on pregnant women with dengue fever⁽³⁾⁽⁴⁾.

The concordance of our clinical findings with those of other case reports in Brazil⁽⁴⁾ and other countries⁽³⁾ provide further evidence that these symptoms are associated with dengue infection during late pregnancy. Consequently, these data warrant the need for analytical studies, preferentially in prospective longitudinal studies in pregnant women at risk of dengue infection in order to better define the prognostic factors and clinical manifestations of dengue and other arboviruses in this population.

The detection of viral ribonucleic acid (RNA) in maternal blood samples by using RT-PCR is indicative of the acute phase of dengue infection. The detection of antidengue IgG (a serological marker detected approximately 10-15 days after infection) in the maternal and cord blood samples, in both our cases, is indicative of prior exposure of the mothers to the dengue virus and transplacental transfer of the maternal antidengue IgG to the neonate. These laboratory results indicate that both mothers had secondary infections of dengue (viremic phase) at delivery. The occurrence of dengue reinfection is recognized as a risk of progression to severe dengue⁽⁹⁾.

In our study, DENV RNA or antidengue IgM (a serological marker of recent dengue) was not detected by RT-PCR or ELISA, respectively, in the umbilical cord blood samples of both cases, confirming the absence of vertical transmission. Vertical transmission of DENV seems to be a rare event in endemic areas, but several cases have been described in mothers-infants pairs in Brazil⁽⁷⁾ and other countries⁽³⁾. According to a previous study, DENV-2 serotype is most often associated with vertical transmission⁽⁷⁾. This serotype was detected in the parturient in Case 1, and her newborn showed clinical manifestations described in cases of DENV vertical transmission⁽⁷⁾⁽⁸⁾.

The serological diagnosis of dengue is confirmed by the detection of a specific IgM antibody or the increase in IgG antibody titers that occurs in consecutive samples during the acute and convalescent phases⁽¹⁾. In neonates, the detection of antidengue IgM antibodies in umbilical cord blood samples is indicative of transplacental transfer of DENV, whereas the detection of antidengue IgG in these samples is indicative of the transfer of maternal IgG antibodies⁽³⁾. On the other hand, the detection of antidengue IgG antibodies and DENV RNA during the acute phase of the disease (viremia) in mothers,

as observed in the two cases reported here, is indicative of secondary infection⁽¹⁾.

Although both parturients exhibited signs and symptoms of dengue fever⁽¹⁾ and were living in a highly endemic area⁽¹⁰⁾, the possibility of dengue fever was not considered during medical assistance. Since urinary tract infection during pregnancy is one of the most frequent causes of fever⁽¹¹⁾, the report of this symptom by the women possibly directed the clinical rationale for this diagnoses. Therefore, our report of two parturients with dengue highlights the need to include dengue fever as one of the possible causes of acute febrile syndrome or bleeding events during pregnancy or childbirth, especially in the months of the highest incidence of dengue in Brazil, i.e., January to July⁽¹²⁾. It is also important to perform laboratory tests for the rapid diagnosis of dengue fever in pregnant women in the health care units, especially during periods of peak occurrence of the disease.

Conflict of interest

The authors declare that there is no conflict of interest.

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