A Case Report of Dengue Fever in the Second Trimester of Pregnancy

H Meng, D Hoang, S Inglis

Objectives

To report the first known case of dengue fever in the second trimester of pregnancy in the United States. To remind practitioners of this diagnosis in cases of viral syndrome associated with international travel. To highlight the hematological attributes of dengue fever which can be confused with HELLP syndrome in pregnant patients.

Abstract

A 27-year-old gravida 1 at 22 weeks and 3 days gestation presented with malaise, fever, chills, and body aches for 1 week. She was found to have anemia, severe thrombocytopenia, mild leukopenia, and elevated liver function enzymes. The initial differential diagnosis was between HELLP syndrome (Haemolysis, liver damage, and low platelets), thrombotic thrombocytopenic purpura (TTP) and viral syndrome. The patient was observed in the hospital with close monitoring and serial laboratory evaluations. After 24 hours, the patient's symptoms began to improve. The laboratory findings gradually normalized after supportive therapy for 5 days. After her discharge, laboratory findings confirmed the patient actually had been suffering from dengue fever with both IgG and IgM positive. The patient subsequently delivered at term a healthy male infant weighting 8 lbs 5oz. The neonate demonstrated a positive IgG and negative IgM titers indicating passive immunity

Conclusion

Dengue fever can occur in pregnancy in this country, and always should be considered in patients who travel to endemic areas of the world. Pregnant patients should take precautions against dengue fever during travel to those areas, as this infection can be serious and even life threatening. Obstetricians should be aware of the features of this viral syndrome, and coordinate with other health professionals for prompt diagnosis and care.

Case Report

A 27-years-old presented at the delivery unit when at 22 weeks gestation in her first pregnancy, dated by her last menstrual period and consistent at her 13-week ultrasound. She presented with a complaint of fever and chills, left-sided headache, decreased appetite and muscle aches that started 6 days before. She reported that she had just come back to the US from Guyana the day before coming to the hospital. She was staying in Guyana for a 2-week vacation from 7/9/2010 to 7/23/2010. She reported no past medical, surgical, or relevant social histories. She took no medications other than prenatal vitamins and had no drug allergy. Her pregnancy was uncomplicated other than hyperemesis during the first trimester, for which she took ondansetron. She had regular prenatal care and her antepartum laboratory values were unremarkable. She had had 18 and 20 weeks ultrasounds with normal fetal anatomy except for mild left pyelectasis in the fetus.

Review of systems revealed a complaint of fatigue, muscle and joint aches, headache, and a single episode of nausea and vomiting occurring 5 days earlier, for which she took ondansetron. She denied cough, wheezing, and shortness of breath, diarrhea or sick contacts.

On admission, her temperature was 99.9F, blood pressure was 90/52 mmHg, respiratory rate was 20, and pulse was 102, with an oxygen saturation of 99% on room air. She was 5 feet, 4 inches tall and weighed 160lb, which yielded a body mass index (BMI) of 27 kg/m2. She was in no acute distress and had no jaun-dice or petechiae. Her fundal height was 23 cm and the fetal heart rate was 140 beats per minute. Bedside sonogram revealed a normal single intrauterine pregnancy with an estimated fetal weight 580g with normal amniotic fluid volume.

Her admission laboratory tests showed mild leukopenia, anemia and thrombocytopenia, as well as elevated liver function enzymes (table 1). She was admitted with the diagnoses of viral syndrome versus atypical HELLP syndrome. Other differential diagnosis included thrombotic thrombocytopenic purpura, acute fatty liver, and hepatitis. Close observation was planned and serial laboratory studies were obtained. Workup including a hepatitis panel, coagulation profile, peripheral blood film, and 24-hour urine col-lection were done. Maternal fetal medicine consultation was also requested.

Five hours after the admission, the patient continued to have the same complaints. Due to persistent thrombocytopenia and worsening liver function enzymes (table1) atypical HELLP was considered. The possibility of the need for termination of pregnancy was discussed with the patient and family should worsening of her condition occur. At the same time, a medical intensive care specialist was consulted.

Subsequently, the patient gradually improved. Her persistent thrombocytopenia had a nadir platelet count of 67 K/ul, the leukopenia had a nadir of 4.5 K/ul and liver function enzymes a maximum of AST 419 and ALT 218 then normalized (see table 1). The peripheral blood film done 9 hours after admission revealed no schistocytes. Her hepatitis panel study returned negative and abdominal ultrasound was unremarkable. The reticulocyte count was 0.8%. The
hematology department was consulted for the persistent thrombocytopenia. Following their suggestion, Dengue viral serology and an antinuclear antibody (ANA) test were sent on day 3 of hospitalization (9 days after onset of symptoms).

On the 5th day of her hospital stay, the patient was feeling much better. Her laboratory studies had nor-malized (see table 1) and the patient was discharged home. A few days later, her Dengue serology returned positive (IgG 9.17, IgM 2.90). This patient later had an uneventful ante-partum course. At term, she deliv-ered an 8lb 5oz healthy male infant whose serum dengue IgG of 8.8, and IgM of 0.1.

Discussion

Dengue is the most common arboviral infection, with an estimated 100 million infections worldwide per year.[1,2] Among those, 250-500,000 persons manifest severe disease.[2] Dengue fever is caused by Dengue virus (DENV), a mosquito-borne flavivirus. It is trans-mitted to humans by the Aedes (Stegomyia) aegypti or Aedes albopictus mosquito. This disease can manifest in many different forms.[3] Dengue is classi-fied as dengue fever, dengue hemorrhagic fever, or dengue shock syndrome, depending on its severity and presenting features.[3] In some cases, patients with a dengue viral infection clinically may be symptom-free.

Diagnosis of dengue fever is considered probable in the case of an acute febrile illness with 2 or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, leucopenia and positive serology (a reciprocal hemagglutination-inhibition antibody titer ? 1280, a comparable IgG enzyme-linked immunosorbant assay (ELISA) titer, or a positive IgM antibody test on a late acute or convalescent-phase serum specimen).[4] Dengue hemorrhagic fever (DHF) has the following additional characteristics, hemorrhagic tendencies and evidence of plasma leakage; while dengue shock syndrome presents as DHF plus evidence of circulatory failure.

Dengue in pregnancy is very rare in the USA and has not yet been reported after the first trimester. Little systematic research has been done in the area of dengue infection during pregnancy. Based on the lim-ited data available, pregnancy does not appear to increase the incidence or severity of dengue.[5] Vertical transmission, defined as detection of Dengue IgM in the cord serum, appears to be rare6. Increased risk for vertical transmission may occur in mothers who develop fever within a week of delivery.[7,8] Dengue infection in early gestation does not appear to affect the fetus and does not lead to vertical transmission.[9] Studies on pregnancy outcome in cases of dengue infection have yielded inconsistent results. Some have reported no change in the rates of preterm birth, mode of delivery, postpartum hemorrhage, low birth weight, and neonatal outcome6. Conversely, others show an increased risk of premature birth and even fetal death.[11,12,15] Multiple cases documenting dengue infection near term with hemorrhagic fever leading to postpartum hemorrhage and even maternal death have been reported. Such cases were frequently fol-lowed by neonatal hemorrhagic fever.[11,15] In cases of proven vertical transmission (positive IgM in cord serum) in late pregnancy, there were no long-term sequelae reported for the infants.[10] Breast feeding was not discussed in any of the case reports or review articles and this remains controversial. We assume the infant would benefit from passive immunity, but this remains unsubstantiated.

Leukopenia is the most common hematological finding in dengue infection.[13,14] Leukopenia is defined as white blood cell counts < 5000/mm3 in pregnancy, or <4000/mm3 in non-pregnant patients. Leukopenia in dengue fever may be caused by virus-induced destruction of leukocytes or inhibition of myeloid progenitor cells.[13] At any rate, mild leukopenia is often an early indicator of dengue infection.

Conclusion

Pregnant patients should take precautions against dengue fever, and be aware of the signs and symp-toms whenever travelling to endemic areas. Warning to avoid mosquito bites by using bed nets, long trousers and long sleeve shirts

should be given to travellers to endemic areas. Pregnant women developing viral syndrome, especially when travelling to endemic areas, must consider dengue fever. In these cases, careful observation and medical attention are warranted because severe hemorrhagic shock may develop. While dengue fever is rare in the United States, it should still be considered among the differential diagnoses whenever viral syndrome is associated with a history of travel to endemic area or in presence of leucopenia. Obstetricians should be aware of the features of various viral syndromes and understand that leucopenia favours this diagnosis and that it may be confused with atypical HELLP syndrome. Multidisciplinary care with other health professionals may be necessary for prompt diagnosis and optimal therapy.

Hongmei Meng, M.D., Dung Hoang, M.D., Steven Inglis, M.D. Department of OB-GYN Jamaica Hospital Medical Center, New York, USA.

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Table 1
Hematologic Parameters

	WBC (k/µL)	Hb (g/dL)	Hct (%)	Plt (k/µL)	Creatinine (mg/dL)	AST/ALT (u/L)	LDH (u/dL)
13 wk GA	9.9	11	33	228			
Arrival (22wk3d GA)	4.7	9	29	85	0.6	419/218	799
5 hr	4.5	9.3	27	76	0.6	409/222	538
9 hr	4.8	9	27	75	0.5	284/161	537
14 hr	4.6	9	27	67	0.5	262/155	
18 hr	5.8	9	28	78	0.5	247/152	
27 hr	5.3	9	27	73	0.5	201/127	
39 hr	5.2	9	28	85	0.4	165/115	
51 hr	5.5	9	28	111	0.5	154/99	602
74 hr	5.7	8	26	144	0.5	66/61	512
86 hr	8.3	9	27	171	0.5	49/67	