CASE REPORT

NEONATAL DENGUE INFECTION: REPORT OF DENGUE FEVER IN A 1-DAY-OLD INFANT

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Abstract. A male infant was admitted because of fever. He was born at 37-weeks' gestation. His mother had experienced acute febrile illness with headache and myalgia. Her illness persisted with onset of active labor pain on day 5, which prompted cesarean section; postoperatively, the hematocrit decreased, requiring transfusion. The infant was well until fever developed at 16 hours after birth. There were petichiae on his face and trunk and the liver was enlarged. Fever subsided on day 5 without evidence of plasma leakage or severe hemorrhage. He made an uneventful recovery after 8 days of illness. Leukopenia and thrombocytopenia were present in the mother and infant. Both were diagnosed as dengue fever. Dengue type 1 was recovered from the infant by polymerase chain reaction. The dengue enzyme-linked immunoassay showed secondary infection in the mother and primary infection in the infant. In dengue-endemic areas, clinicians should be alert to dengue fever/dengue hemorrhagic fever in pregnant women presenting with acute febrile illness, and be prepared for proper management.

Dengue infection has become a major public health problem in tropical regions. Dengue virus is spread by mosquitos, causing variable manifestations, ranging from asymptomatic infection to flulike illness in dengue fever and sometimes severe hemorrhage resulting in shock and death in dengue hemorrhagic fever (WHO, 1997). Dengue infection is a disease of children; in recent years, the resurgence of dengue infection has been associated with an increasing incidence of dengue infection in adults with reports of dengue illness in pregnant women with transplacental transmission. Although a rare clinical occurrence, transplacental transmission imposes adverse effect on the fetus (Thaithumyanon *et al*, 1994; Chye *et al*, 1997; Carles *et al*, 2000; Chotigeat *et al*, 2000; Boussemart *et al*, 2001; Kerdpanich *et al*, 2001). We report a newborn infant with vertical transmission of dengue type 1 with early manifestation.

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A 1-day-old Thai male infant was admitted because of acute febrile illness. His mother, aged 25, gravida 2, had experienced sudden febrile illness on the day of admission. The pregnancy was at 37-weeks' gestation. Routine screening tests performed at the antenatal clinic were negative for syphilis, hepatitis B surface antigen and human immunodeficiency virus. She complained of headache, myalgia, arthralgia and frequent uterine contractions. Her temperature was 39.2ºC, pulse 120, respirations 22, and blood pressure 120/70 mmHg. The fetal heart rate was 148. A nonstress test on the fetus showed a normal reactive response. The hematocrit was 27.6%, the white-cell count was 9,710/mm^3 with 85.8% polymorphonuclear cells, 8.8% atypical lymphocytes, and the platelet count was 203,000/mm^3. Blood urea nitrogen, creatinine, and electrolytes were normal. Ampicillin, metronidazole and gentamicin were administered intravenously. Fever persisted without obvious clinical focus.

On day 5 her temperature was 39.1ºC (Table 1) with onset of active labor, the white-cell count decreased to 4,720/mm^3 with 72.4% polymorphonuclear cells, 8.0% atypical lymphocytes and the

platelet count was 52,000/mm^3. Cesarean section was performed without any complication.

Two days after the operation, the mother's hematocrit decreased to 17% without obvious bleeding from the surgical wound, the white-cell count was 1,980/mm^3 with 67.1% polymorphonuclear cells, 14.1% atypical lymphocytes and the platelet count was 120,000/mm^3. Two units of blood were transfused. Erythematous rash was observed on both legs. The complete blood count became normal on day 11. Her following clinical course was uneventful.

The infant's birthweight was 3,150 g, length 50 cm; the Apgar scores were normal. No resuscitation was required. The placenta weighed 500 g and was normal. Routine intramuscular dose of vitamin K was administered.

He appeared well until 16 hours, when fever developed. He was transferred to the neonatal care unit for close observation. The pulse was 158, the respirations were 40, and the blood pressure was 70/41 mmHg. On examination he was quiet but arousable. The liver and spleen were not enlarged. Skin perfusion was normal. Faint petechiae were observed on his face. The history was reviewed with the suspicion of dengue infection in the infant and his mother. The hematocrit was 51%, the white-cell count was 10,400/mm^3 with 81.9% polymorphonuclear cells, 3.0% atypical lymphocytes and the platelet count was 99,000/mm^3. Blood was collected for hemoculture. Intravenous fluid, ampicillin and gentamicin were started to cover sepsis-pending hemoculture result that later was reported as negative.

The body temperature continued to rise, reaching a peak of 39.8ºC at 36 hours. The infant occasionally chilled at peaks of fever although he could suck on his bottle. Petechiae increased on his face and gradually spread to the trunk and extremities (Fig 1). Respirations were 88 and shal-

Table 1
Temperature patterns of the mother and infant. Cesarean section was performed on day 5 after onset of active labor. Fever in the infant appeared at 16 hours after birth.

Day	1	2	3	4	5	6	7	8	9	10	11
Mother											
39ºC											
38ºC											
37ºC											
Hct	27.6			27.2	26.9		17.0				31.5
WBC	9,710			5,230	4,720		1,980				16,900
N	85.8			74.9	72.4		67.1				71.8
L	4.6			14.7	18.6		18.2				16.9
AL	8.8			4.9	8.0		14.1				9.2
Plt	203,000			111,000	52,000		120,000				209,000
Infant											
39ºC											
38ºC											
37ºC											
Hct						51		44		34	
WBC						10,400		8,000			
N						81.9		50.8			
L						9.2		33.6			
AL						3.0		9.3			
Plt						99,000		11,000			

Hct, hematocrit; WBC, white-blood cell; N, neutrophil; L, lymphocyte; AL, atypical lymphocyte; Plt, platelet.

low; oxygen was given via head box. On day 3, the temperature persisted at 39.1ºC. On day 4, hematocrit decreased to 44%, the white-cell count was 8,000/mm^3 with 50.8% polymorphonuclear cells, 9.3% atypical lymphocytes and the platelet count was 11,000/mm^3. The liver was palpable 3 cm below the costal margin and the spleen was just palpable. Petechiae became prominent all over the body.

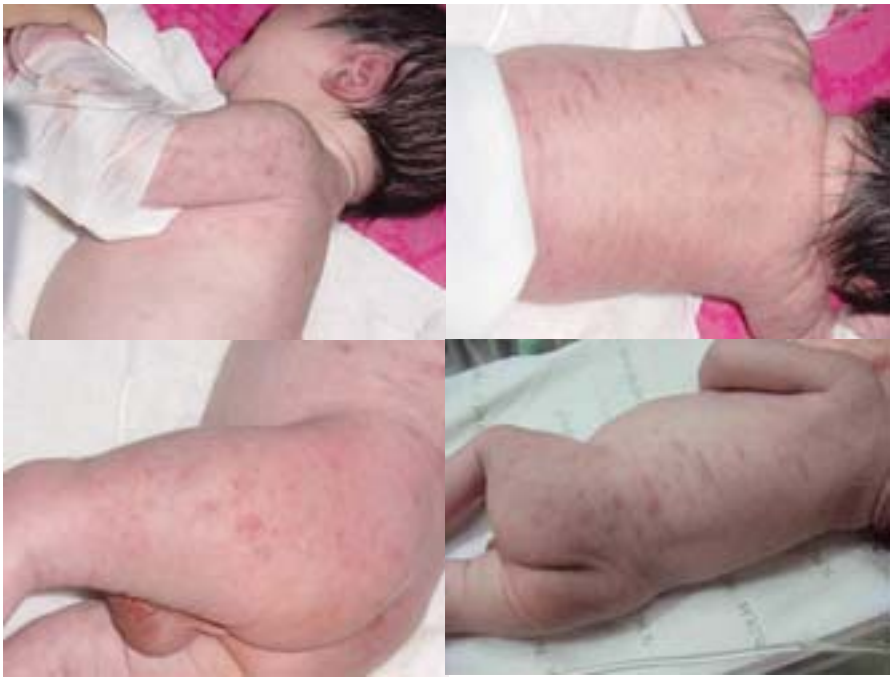

Fig 1–Petechiae began on his face and gradually spread to the trunk and extremities.

On day 5, the petechiae began to fade. Blood sugar, blood urea nitrogen, creatinine, and electrolytes were normal. Aspartate aminotransferase (AST) was elevated to 152 U/l, while alanine aminotransferase (ALT) was normal. No signs of circulatory disturbance were detected. There was no pleural effusion by chest radiograph in the right lateral decubitus position. Serial hematocrits gradually decreased to 34% on day 6 before they rose to 41% on day 8. The infant was active at defervescence on day 7. He made an uneventful recovery and was discharged after 10 days' admission.

The infant's polymerase chain reaction (PCR) result on day 5 was positive for dengue type 1, while that of the mother, obtained on day 10, was negative (Table 2). Enzyme-linked immunoassay (EIA) revealed an increase in both den-

Table 2
Reverse transcriptase polymerase chain reaction (RT-PCR) and serologic values.

Test	Variable	Mother	Infant
Polymerase chain reaction	RT-PCR	Negative	Dengue -1
Enzyme-linked immunoassay (units)	Dengue IgM	126	59
	Dengue IgG	227	11
	Japanese encephalitis IgM	27	14
	Japanese encephalitis IgG	177	6
Hemagglutination inhibition (titers)	Dengue -1	1280	10
	Dengue -2	640	10
	Dengue -3	2560	10
	Dengue -4	2560	10
	Japanese encephalitis	5120	10
	Chikungunya	80	40

gue-IgM and IgG in the mother with IgG titer higher than IgM (227 *vs* 126 EIA units), indicating secondary dengue infection. The infant's IgM increased to about 5 times higher than IgG (59 *vs* 11 EIA units), indicating primary infection. The mother's hemagglutination inhibition test (HAI) showed high titers to all 4 dengue serotypes, while in that of the infant, the titers were low.

As the incidence of dengue infection in adults has increased, it is apparent that pregnant women could be infected, although the occurrence is uncommon. Diagnosis of dengue illness in mothers began with fever leukopenia and thrombocytopenia and other symptoms associated with dengue infection. Simple and inexpensive laboratory procedures to identify acute dengue disease, include the tourniquet test and complete blood count (Halstead, 1982; Thisyakorn *et al*, 1984; Kalayanarooj *et al*, 1997; Srichaikul and Nimmannitya, 2000).

Since the symptoms occurred immediately after birth, our infant was certainly infected *in utero*. Intrauterine transmission was greatest when serum titers of viremia were high, which occurred at the time of fever. Secondary infection in mothers also caused higher titers of viremia than in primary infection (Vaughn *et al*, 1997; 2000).

The incubation period for dengue infection in infants or the duration between fever in mothers and infants, was shorter in mothers with secondary infection (3-6 days) (Chotigeat *et al*, 2000; Boussemart *et al*, 2001; Kerdpanich *et al*, 2001) than in primary infection (5-13 days) (Thaithumyanon *et al*, 1994; Chotigeat *et al*, 2000; Boussemart *et al*, 2001). The first manifestation in infants was fever, which appeared earlier postnatally in the mother with secondary infection (0.5-3 days) than in primary infection (4-11 days). All infants had primary dengue infection. Although passive maternal dengue antibodies increased the risk of developing dengue hemorrhagic fever/dengue shock syndrome in infected infants (Kliks *et al*, 1988), there were no such cases in these infants. Our infant had the shortest time before onset of manifestation; fever appeared at 16 hours after birth. The virus could have been transmitted from the mother on her first day of fever so the incubation period is 5 days.

The time of acquiring dengue virus intrauterinely could affect the fetus. Infection during the second trimester could lead to premature labor and fetal death (Carles *et al*, 1999; 2000), whereas infection near, or at, term posed little effect on the infant. Most had fever, rash, hepatomegaly and thrombocytopenia, while some infants remained asymptomatic (Bunyavejchevin *et al*, 1997).

Dengue serotypes may play a role in the severity of disease. Symptoms seemed to be more severe with secondary dengue type 2 infection (Halstead *et al*, 1970; Morens *et al*, 1991), causing severe coagulopathy and postpartum hemorrhage in mothers (Thaithumyanon *et al*, 1994; Chye *et al*, 1997; Chotigeat *et al*, 2000) and intraventricular hemorrhage and death in infants (Chye *et al*, 1997). Dengue type 1 in our case might not have such virulence, only fever and occult bleeding in the mother and fever and rash in the infant. No teratogenic effect has been reported by intrauterine dengue infection (Carles *et al*, 1999).

The mode of delivery did not change the course of disease or reduce the rate of bleeding in infants. One case of Chye *et al* (1997) was delivered vaginally with severe intracranial hemorrhage while other infants had subtle illness via this route (Boussemart *et al*, 2001;Chotigeat *et al*, 2000) as well as other infants delivered by cesarean section (Thaithumyanon *et al*, 1994; Boussemart *et al*, 2001; Kerdpanich *et al*, 2001).

There was gradual bleeding from the raw surface of the uterus, as evidenced by a drop in hematocrit in the mother 2 days postoperatively. For the infant, a drop in hematocrit was probably caused by the hemodilution effect of intravenous fluid administration. There was no sign of plasma leakage in mother or infant. The diagnosis was dengue fever for both of them.

The typical duration of viremia was 4-5 days during the febrile phase, and it persisted longer in children experiencing primary infections rather than secondary dengue infections due to more gradual antibody or cellular immune response. Therefore, PCR from the infant performed near the end of the febrile period was positive, while that from the mother performed at a later time was negative (Lanciotti *et al*, 1992; Vaughn *et al*, 2000). The EIA and HAI antibody results were useful in the diagnosis of acute dengue virus in-

fections and were able to identify infection as primary or secondary (Innis *et al*, 1989; Clarke and Cassals, 1958).

In dengue-endemic areas, there is a possibility that pregnant women may be infected with dengue virus. Therefore, obstetricians and pediatricians should be on alert to dengue disease and be prepared provide proper management for both mother and neonate.

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