CASE REPORT

SEVERE PERINATAL DENGUE HEMORRHAGIC FEVER IN A LOW BIRTH WEIGHT INFANT

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Abstract. A 31-year-old Hmong (Thai hilltribe) multiparous (G5P2) female with dengue hemorrhagic fever delivered a low birth weight male infant at 34 weeks estimated gestational age. The mother had fever for a total of 6 days, along with hepatomegaly, hepatic dysfunction and thrombocytopenia. Serology showed acute secondary dengue infection. She had no serious complications. The infant (birth weight 1,850 grams) developed a fever 140 hours postpartum of 37.8ºC for one day, then developed drowsiness, poor feeding and apnea. Hepatomegaly, thrombocytopenia, hepatic dysfunction and moderate coagulopathy were detected, with consequential shock and anemia due to gastrointestinal and pulmonary hemorrhage. Vigorous treatment with mechanical ventilation, packed red cells (PRC), fresh frozen plasma (FFP) and platelet concentrate transfusions were given and the child recovered successfully and commenced breast- feeding. At six months of age the child's growth and development were normal except for an impaired hearing screening test.

Keyword: perinatal DHF, low birth weight, vertical transmission

INTRODUCTION

Dengue infection is endemic in many countries of Southeast Asia, the western Pacific, the Americas (WHO, 1997) and hyperendemic in Thailand. Dengue hemorrhagic fever (DHF), a severe form of dengue infection, occurs mostly in children less than 15 years old. During the past three decades, there has been a significant increase in dengue infection/DHF cases among both the children and adults (Teeraratkul and Limpakarnjanarat, 1990). Dengue infection/DHF in pregnant women is increasingly reported from many countries. DHF in pregnancy with and without vertical transmission has been reported from Thailand (Taechakraichana and Limprapayom, 1989; Thaithumyanon *et al*, 1994). Since 1994 12 cases of vertical dengue infection/DHF have been reported from Thailand. This is the second report of parturient vertical DHF from Phetchabun Hospital, Thailand, the first one was in 2003 (Witayathawornwong, 2003).

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Table 1
Laboratory investigations of mother.

Date	Laboratory investigations
	District Hospital
June 23, 2010 Delivery day, fever day 3	CBC: Hct 37%; WBC 7,300; platelets 204,000; N 89; L 11.
June 27, 2010	Hemoculture: no growth; urine culture: no growth
June 28, 2010 Second afebrile day, convalescent rash	CBC: Hct 43%; WBC 7,500; platelets 64,000; N 16; L 72 Atyp. L 10; M 2; AST/ALT 102/75
	Phetchabun Hospital
July 2, 2010	Dengue IgM: positive (>40 units) HI Dengue 1 IgG 1: 5,120 acute secondary infection Dengue 3 IgG 1: 5,120 dengue infection
July 6, 2010 10 days after defervescence	AST/ALT = 36/47

CASE REPORT

Mother

A 31-year-old female Hmong (hill-tribe) female was admitted to Khao Kho District Hospital with labor pains and a high fever for 6 days. She was multiparous (G5P2) at 34 weeks gestation. Her antenatal care was normal; labor pains developed 16 hours before admission without premature rupture of membranes. Her vital signs before delivery were: temperature of 39ºC, a pulse rate of 100/minute, a respiratory rate of 18/minute and a blood pressure of 110/70 mmHg, a weight and height of 49 kg and 149 cm, respectively. The delivery was normal, spontaneous vertex, 6 hours after admission. She was well except for a high fever (38.5-39.5ºC) that had persisted for 6 days. She was treated as having bacterial sepsis until defervescence of fever and no growth of hemoculture. She developed an erythematous rash on both her legs on the second afebrile day in addition to developing thrombocytopenia and hepatomegaly. DHF was suspected clinically and later confirmed serologically at Phetchabun Hospital. Laboratory investigations of mother at Khao Kho District Hospital and Petchbun Hospital are presented in Table 1.

Infant

The infant born 6 hours after admission was male with a low birth weight of 1,850 g, 47 cm long; Apgars were 10 and 10 at 1 and 5 minutes. He was kept in an incubator and treated with antibiotics (ampicillin, gentamicin) until sepsis was ruled out. He became febrile during the 140th hour of life (June 28, 2010), to 37.8ºC; the fever persisted for one day only. When the fever declined the infant developed drowsiness, poor feeding (breast milk), hypoglycemia and apnea. Resuscitation and intubation were carried out and the patient was transferred to Phetchabun Hospital.

At Phetchabun Hospital the infant was continued on the ventilator. Upon presentation to the Petchabun Hospital

Table 2
Laboratory investigations of infant.

Date	Laboratory investigations							
CBC	Hct %	WBC	Platelets	N	L	Atyp.L	M	E
June 23, 2010 (at birth)	51	11,500	184,000	36	62	-	-	2
June 29, 2010 (first afebrile day)	49	3,400	60,000	44	48	-	7	1
June 30, 2010 (day of hospitalization-1)	42	3,230	12,000	62	20	13	5	-
July 1, 2010	42	5,570	15,000	16	58	19	7	-
July 4, 2010	54	10,790	42,000	63	20	2	15	-
July 5, 2010	48	10,800	152,000	41	35	15	8	1
July 9, 2010 (day of hospitalization-10)	48	6,790	362,000	52	41	1	4	2
Liver enzymes (units/l)	AST	ALT						
June 29, 2010	147	41						
July 1, 2010	91	20						
Coagulograms	PT (10-14)		PTT (21-29)		INR			
July 1, 2010	16.5		77.6		1.38			
July 2, 2010	15.6		73.7		1.30			
July 9, 2010 (day of hospitalization-10)	11.9		43.2		0.98			
CXR								
June 30,2010	Patchy infiltration of the right lower lobe, pneumonia *vs* pulmonary hemorrhage.							
July 4, 2010	Generalized fine reticulonodular infiltration of both lungs.							
	20 ml of blood from ET tube Hct after bleeding -38%.							
Serology	IgM	IgG						
July 4, 2010	Positive (> 40 units)							
July 9, 2010 (day of hospitalization-10)	83	0						
July 12, 2010 (day of hospitalization-13)	106	10						
Hemoculture and sputum culture: no growth								

he was afebrile, had a pulse rate of 130/minute, blood pressure of 59/36 mmHg, he had moderate jaundice, and a palpable liver 2 cm below the right costal margin. His spleen was not palpable. The heart and lung sounds were normal (Fig 1). Initially neonatal sepsis and hyperbilirubinemia were diagnosed. A moderate amount of coffee ground material was aspirated from the orogastric tube and the endotracheal tube (ET) a few hours after admission. The hematocrit dropped from 42% to 36% and the blood pressure was 42/31 mmHg. A chest X-ray (Fig 2) showed patchy infiltration without pleural effusion of the right lower lung field. Further investigation showed thrombocytopenia, hepatic dysfunction and coagulopathy (Table 2). The child was diagnosed with having DHF with shock, gastrointestinal hemorrhage and pneumonia or pulmonary hemorrhage. The orogastrict tube was then removed to avoid further hemorrhaging. Antibiotics, phototherapy, packed red blood cells (PRBC), fresh frozen plasma (FFP) and platelet concentrate were given. 5% D1/5NS intravenous fluid was given at 10 ml/kg/hour during the shock stage and 3 ml/kg/hour during the maintenance stage.

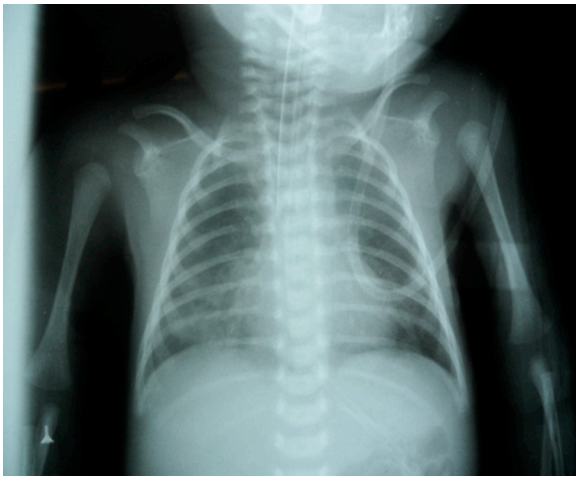

Fig 1 Patchy infiltration RLL on admission.

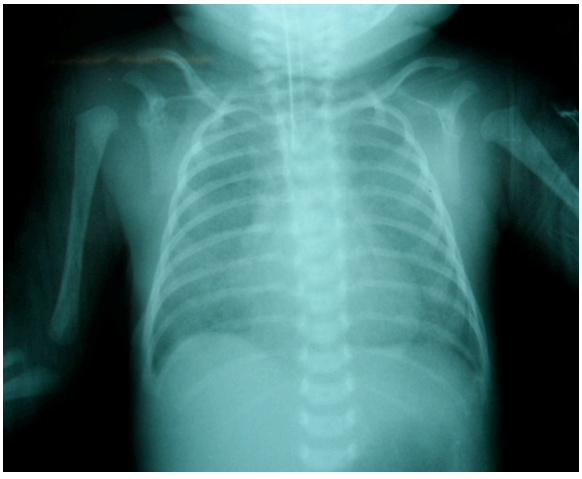

Fig 2–Generalized fine reticulonodular infiltration of both lungs (5th day of hospitalization) 20 ml of blood from ETT.

Twenty milliliters of bleeding from the ET was observed on day 5 of hospitalization. A chest X-ray showed a generalized fine reticulonodular infiltration of both lungs. The hematocrit dropped to 38% and the patient was given PRBC. The infant was kept in the incubator for 17 days, on mechanical ventilation for 7 days, and on oxygen therapy via nasal continuous positive airway pressure (CPAP) for 10 days. When the platelet count rose to normal on day 6 of hospitalization, the orogastric tube was reinserted and breast milk was given. He was moved out of the incubator to a crib when oxygen therapy was stopped, then breast feeding was initiated. He was discharged after successful breast feeding for 3 days (total length of hospitalization of 20 days).

The infant's thyroid stimulating hormone (TSH) screening was normal. No retinopathy of prematurity (ROP) was detected. Hearing screening was abnormal on the day of discharge; this persisted for six months, he will be sent for auditory brainstem evoked response (ABR) testing later. At sixth months his growth (weight 5.7 kg, height 60 cm) and development (stable sitting) were normal.

DISCUSSION

There were 4 forested regions in Phetchabun Province: Khao Kho, Nam Nao, Chon Daen and Nong Phai Districts. There were many previous cases of *P. falciparum* malaria reported from these endemic areas. In recent years, malarial cases have become uncommon; in 2010 only one child with PF malaria was documented in Phetchabun Hospital. However, there are still many cases of DHF reported, mainly children under 15 with complications, many were referred to Phetchabun Hospital during this time. Dengue virus had spread from crowded cities to forested communities. The infant and his mother were from one of these areas. One report from Malaysia demonstrated dengue infection among 2.5% of parturients with a vertical transmission rate of 1.6% (Tan *et al*, 2008). The exact incidence of vertical transmission of dengue infection in Phetchabun Province and other parts

of Thailand is unknown. One study of pregnant Thai women found 94.7% had antibodies to at least one strain of dengue virus but a 0% vertical transmission rate (Perret *et al,* 2005).

The women in this report was initially suspected to have a bacterial infection, a common problem. Her clinical findings and investigations suggested dengue infection which was confirmed later at Phetchabun Hospital. Her disease was mild with only a convalescent rash. The infant appeared initially well at birth. Other than a low birth weight, there were no other risk factors for bacterial infection except fever in the mother. He was treated with antibiotics until he developed apnea and then he was referred to Phetchabun Hospital.

At Phetchabun Hospital he was treated for bacterial sepsis and hyperbilirubinemia. A few hours after admission he developed shock due to gastrointestinal hemorrhage with or without pulmonary hemorrhage. An infiltration on the firsrt chest film (Fig 1) could have been pulmonary hemorrhage. Hepatomegaly, hepatic dyspfunction, thrombocytopenia, moderate coagulopathy, bleeding diathesis and shock with a history of dengue infection in the mother pointed to DHF. Dengue infection was later confirmed by serology. Vigorous treatment with mechanical ventilation, antibiotics, phototherapy, PRBC, FFP and platelet concentrate helped him to survive. A massive pulmonary hemorrhage on day 5 of hospitalization was rapidly treated with PRBC. Dengue virus type 2 appears to be more severe (Halstead *et al,* 1970; Morrens *et al,* 1991), causing coagulopathy and postpartum hemorrhage among mothers (Thaithumyanon *et al,* 1994; Chotigeat *et al,* 2000) but usually mild disease among their infants; however, severe disease among mothers and infants with intraventricular hemorrhage and death has been observed with dengue virus type 2 (Chye *et al,* 1997). Several reports have shown dengue virus type 1 causes only mild disease in mothers and infants (Witayathawornwong, 2003; Petdachai *et al,* 2004; Deesomchok, 2008). Other reports have found mild maternal and infant disease due to dengue virus type 2 (Kerdpanich *et al,* 2001; Janjindamai and Pruekprasert, 2003; Sirinavin *et al,* 2004; Phongsamart *et al,* 2008) and type 4 (Sirinavin *et al* ,2004). This infant had severe disease but his mother only had mild discase. Unfortunately, the dengue serotype in this infant could not be detected due to the short period of viremia.

The incubation period of dengue lasts 4 to 12 days (Sabin, 1952). Although it is possible the infant infected by a mosquito bite on the first or second day of life, it is unlikely, since he was treated in an incubator in the nursery since birth. He was swaddled most of time allowing little exposure to skin. Dengue infection may induce preterm labor (Jirapinyo *et al,* 1990; Chye *et al,* 1997). This infant was preterm with a birth weight of 1,850 grams. He is the smallest infant reported to have vertical DHF. A previous report was a 2,000 gram infant (Boussemart *et al,* 2001). The platelet count was normal on day 6 of hospitalization, compared to reports of 12 days (Witayathawornwong, 2003) and 2 months (Chotigeat *et al,* 2000). Platelet concentrate transfusion may play a role in this finding. An orogastric tube was reinserted when the platelet count was normal to initiate feeding with breast milk. The child successfully breast fed later. Thyroid stimulating hormone screening was normal and retinopathy of prematurity has not been detected. A hearing screen was abnormal at discharge and at sixth months. Although neonatal

hyperbilirubinemia is a cause of hearing loss (Arnold, 1996) it is usually only associated with severe hyperbilirubinemia. Hearing impairement in this infant might be due to hyperbilirunemia, DHF or other disease not diagnosed.

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