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Case Report

Neonatal dengue: a case report and literature review

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ABSTRACT

Dengue fever is a viral infectious disease that remains a health problem worldwide. Neonates mortality and morbidity have been linked to vertical transmission of the dengue virus. Infants born to mothers with dengue infection before the days of delivery require suspicion and tracing of dengue infection, particularly in dengue-endemic areas. This case report describes the possibility of vertical transmission of dengue in an infant with a dengue-infected mother near delivery. The baby had clinical improvement during treatment and was discharged at 11 days of life. Prompt diagnosis, appropriate treatment, and close monitoring are needed to improve neonatal dengue outcomes.

Keywords: Dengue, Neonatal dengue, Vertical transmission

INTRODUCTION

Dengue infection is widely transmitted in tropical and subtropical countries around the world with an increasing incidence, reaching more than 5 million cases and causing more than 5000 dengue-related deaths by 2023.[1] Dengue fever is a disease caused by dengue virus infection (DENV 1, 2, 3, 4) that is widely transmitted through Aedes genus mosquitoes (Aedes aegypti and Aedes albopictus). In addition, other modes of DENV transmission that have been reported are through blood transfusion, organ transplantation, and vertical transmission from maternal to fetal through the placenta or breast milk.

Depending on the stage of pregnancy, the overall incidence of vertical transmission DENV ranges from 2.4% to 90.0%.[2,3] Meanwhile, during the peripartum period, the rate of mother-to-newborn transmission of DENV is very high, reaching 90.0%.[2] Variable newborn dengue outcomes have been reported in several studies. These outcomes range from an asymptomatic infection to severe disease such as Dengue Haemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS), which is marked by hypovolemia, thrombocytopenia, systemic capillary leakage, and multi-organ failure that can ultimately lead to death.[4,5] The severity of the clinical presentation of the disease in the mother was observed to be correlated with the severity of the neonatal dengue case.[6] Early diagnosis and treatments are important to reduce morbidity and mortality in neonatal dengue. We hereby report a case of neonatal dengue referred to the neonate intensive care unit (NICU) of Sanjiwani Hospital in Indonesia that may have been caused by a vertical transmission during the peripartum period.

CASE REPORT

A five-day-old female baby was referred to Sanjiwani Hospital with fever one day before admission and yellowish skin since morning. The baby was born as a singleton with a birth weight of 2820 grams by emergency caesarean section (SC) due to fetal distress with a gestational age of 38 weeks and 5 days. She appeared well at birth, and there was no evidence of mosquito bites on the baby after birth or before admission to our hospital. The baby was born to multigravida mother with a history of fever since, one day before delivery and antigen dengue NS-1 positive high results on the second day of fever. After delivery, the mother was admitted to intensive care with DHF and discharged after 8 days of treatment with

improved condition. On physical examination at admission (day 2 of fever), the infant's temperature was 39°C, heart rate 156 beats per minute, respiration rate 48 breaths per minute, capillary refilling time < 2 second, and oxygen saturation of 99% on room air. On general examination, the sclera was icteric, and the skin appeared yellowish from head to toe with the Kramer score of 4. There was no hepatomegaly, rash, spontaneous petechia, and the sign of shock in our patients. The blood test results showed thrombocytopenia, high bilirubin, and slightly elevated SGPT, meanwhile, SGOT was normal (Table 1). As the mother had dengue fever before delivery, the possibility of perinatal DENV transmission was suspected. The infant's antigen dengue NS-1 test was highly positive on day 2 of fever, however, dengue IgM and IgG were negative on the second and third days of fever. Thus, the patient was diagnosed with neonatal dengue and neonatal jaundice.

Table 1: Haematological and biochemical investigations results of the infant.

Date	D2 (31/07) (13.43)	D3 (01/08)	D4 (02/08) (9:22) (Morning)	D4 (02/08) (21:16) (Evening)	D5 (03/08) (9:18) (Morning)	D5 (03/08) (20:38) (Evening)	D6 (04/08) (07:45) (Morning)	D6 (04/08) (20:35) (Evening)	D7 (05/08) (08.30)	D7 (06/08) (09:11)	UNIT
WBC	5.7	6.61	7.65	8.18	10.32	12.36	13.88	14.6	12.91	15.88	10^3/ul
Platelets	130	54	25	31	28	41	27	33	34	79	10^3/ul
Hb	14.9	16.1	15.7	15.8	14.7	15.3	15.3	15.2	15.7	15.1	g/dl
PCV	46.9	47.4	47.1	46.8	45.9	44.6	46.5	44.7	47.3	44.0	%
Neu%	53.1	42.9	41.2	34.0	36.0	33.3	33.5	32.9	35.3	36.2	%
Lym %	10.9	34.1	43.9	49.8	48.2	54.5	50.9	49.2	45.6	47.7	%
RBC	4.7	4.53	4.50	4.49	4.36	4.30	4.45	4.32	4.58	4.32	10^6/ul
MCV	99.8	104.6	104.8	104.2	105.4	103.7	104.5	103.5	103.5	104.1	fl
MCH	31.6	35.4	34.8	35.3	33.7	35.6	34.4	35.2	34.3	35.7	pg
MCHC	31.7	33.9	33.2	33.9	32.0	34.3	32.9	34.0	33.2	34.3	g/dl
MPV	9.7	9.1	9.4	10.4	10.1	9.3	10.7	9.9	10.9	10.3	fl
Total bilirubin	38.29				4.34						mg/dl
Direct bilirubin	0.67				0.18						mg/dl
Indirect bilirubin	37.62				4.16						mg/dl
Albumin	3.88										g/l
SGOT	63	75									U/l
SGPT	13	14									U/l
NS1 antigen	Positive H										
IgM dengue	Negative	Negative									
IgG dengue	Negative	Negative									

The management of neonatal dengue and neonatal jaundice in this case was supportive therapy by giving intravenous fluids, antipyretics, phototherapy, nutrition, and antibiotics because we could not rule out the probability of sepsis. Intravenous fluids were given with D10% at a rate of 170 ml/day, then on day 4 of febrile switch with intravenous fluids Tridex100 at a rate of 170 ml/day. Formula on demand was given due to the mother's condition that does not allow breastfeeding. The baby's pulse rates, capillary refilling time, warmth of peripheries, and urine output were closely monitored to detect any hemodynamic instability. During the period of hospitalization, there was no shock developed, spontaneous bleeding, or signs of intracranial haemorrhage in the patient. Fever was gone after 3 days of hospitalization with administration of intravenous paracetamol 30 mg every 6 hours. The decrease in bilirubin level was found after 3 days of double light phototherapy. In addition, this patient was also given ursodeoxycholic acid 3×30 mg per oral and phenobarbital 2×5 mg per oral due to the risk of neurotoxicity and seizure. Intravenous antibiotic, cefotaxim 2×150 mg was stopped after 7 days of administration. During the treatments, the baby continued to have thrombocytopenia with the lowest platelet level of 25.000/mm3 on the 4th day of illness, but the baby did not have spontaneous bleeding, sign of intracranial bleeding, pleural effusion, or ascites. The clinical conditions of the baby were improved and she was discharged in good clinical condition with platelets of 79.000/mm3 and Hb of 15.1 g/dl on day 11 of life (Table 1).

DISCUSSION

Dengue fever transmission during the perinatal period is uncommon, however, it has been documented.[6,7] DENV can enter the fetal circulation through the placenta.[8] Dengue RNA has been reported to be detected in maternal serum collected 24-72 hours before delivery, in the placenta and umbilical cord serum.[3] There is a chance that

the baby will contract dengue from the infected mother's blood or through the birth canal if the mother has viremia during labor and delivery. The mother's level of viremia has a substantial correlation with the risk of vertical transmission. The chance of transmission to the fetus is increased by higher levels of maternal viremia.[9] Haryanto et al, have reported a case of vertical transmission confirmed by whole genome sequence from serum examination of both mothers and neonates revealed identical DENV-2.[10] Another study by Vats et al, reported that the peak titer of DENV infection in the placenta was found on day 7.[11]

In our case, the baby had a fever on the fourth day of life with the history of mother having a fever since, one day before and during labor. The mother was in the febrile phase with viremia confirmed by high positive dengue antigen NS-1 examination; therefore, it can cause DENV vertical transmission. On examination, thrombocytopenia and high positive NS-1 dengue antigen were found on the fifth day of life or the second day of fever. Since our patient had dengue infection four days after delivery, it is most likely that she had been infected perinatally.

In this case, since the newborn was isolated from her mother for intensive care, breast milk was not used, so transmission through breast milk could be ruled out. Although there is a possibility of horizontal transmission with a very short incubation period, there was no evidence of mosquito bites on the baby after birth or before the baby was referred to our hospital. Our case is similar to vertical dengue infection that has been reported previously.[10-13] Therefore, neonatal dengue infection should be considered for neonates born to mothers with dengue infection before delivery, especially in dengue-endemic or hyperendemic areas.

Although confirmation of vertical transmission of DENV by virus identification in umbilical cord blood or placenta was not performed in this case, there is indirect evidence supporting vertical transmission in our case. In our case, the mother was infected with dengue in the third trimester at 38-39 weeks of gestation, during labor the mother experienced a febrile phase or viremia, so the risk of vertical transmission was very high. Assuming that vertical transmission occurs during the perinatal period, with an incubation period of at least 3 days, our patient developed fever on the 4th day of life followed by thrombocytopenia and positive NS-1 on the 5th day of life.

This is by the dengue incubation period as documented in published studies and literature. The dengue incubation time is estimated by the World Health Organization (WHO) to be 5-7 days (with a range of 3–10 days). Viraemia in humans starts from two days before the onset of fever and lasts for 5 to 7 days after the onset of fever.[14] The onset of fever in newborns who had vertical transmission from mothers with DHF near delivery ranged from 16 hours to 11 days after birth and lasted for 2 to 6 days.[10,12] Duration between the onset of the mother's fever and the neonate in cases of intrauterine transmission of DENV was found to be 5–13 days (median, 7 days).[13]

The onset of clinical manifestations of neonatal dengue with vertical transmission is influenced by the interval between the onset of maternal fever and the time of delivery. Fever in infant start to develop faster the longer the time elapses between the first day of fever in the mother and delivery. Phongsamart et al have reported vertical transmission of neonatal dengue, one case of a mother with a history of fever one day before delivery with neonate had fever on the 6th day of life, and the DENV-1 serotype was detected on fever day two.

The other patient, a pregnant mother went into labor after 12 days of DHF with the baby had a fever at 9 hours of life with DENV serotype 2 detected on day one of life.[15] The case of vertical transmission of dengue also has been reported by Bopeththa et al an infant born to a mother with DHF on day 3 fever who developed fever and jaundice and a positive NS 1 test on day 5 of life.[12] Clinical symptoms in neonatal dengue with vertical transmission ranged from the day of birth to 7 days of life (mean 4 days of life) with onset between maternal and infant symptoms ranging from 0 to 8 days (mean±4.6 days).[2]

Clinical manifestations of dengue in newborns range from asymptomatic to severe dengue infection. Clinical manifestations found in neonates with dengue infection such as fever, erythematous rash, petechiae, hepatomegaly, thrombocytopenia, and transiently elevated liver enzymes.[2,13] Liver damage, respiratory distress, sepsis, gastrointestinal bleeding, and massive intracerebral hemorrhage were the complications reported to be caused by neonatal dengue.[2,9,15] In our case, the baby had a fever and severe thrombocytopenia, but no signs of spontaneous bleeding were observed.

Signs of plasma leakage, such as increased hematocrit≥ 20%, pleural effusion, and ascites, were not found in our case. The signs of shock, intracranial haemorrhage, and gastrointestinal bleeding were also not found in this patient. Our patient was also diagnosed with neonatal jaundice with a total bilirubin level reaching 38.29 mg/dl. Close monitoring of the symptoms of kern icterus (seizures, decreased consciousness). In our patient, no neurotoxicity sign was observed. Neonatal jaundice that also occurred in neonatal dengue was also reported previously.[4]

NS-1 dengue antigen can be used for early diagnosis of dengue infection. It can be detected after one day onset of fever and then decrease to undetectable after 5-6 days.[14] In our reported case, clinical symptoms of fever with thrombocytopenia were found on the second day of fever and the diagnosis of neonatal dengue infection was confirmed with dengue antigen NS-1 positive high. The results of IgM and IgG dengue antibodies on the second and third days of fever were negative. These conditions can be caused by the late appearance of IgM antibody

which usually can be detected on days 3-5 after the onset of illness and undetectable after 2-3 months. The absence of IgG antibody showed primary infection and no maternal antibodies were transferred to the patients.[14] Treatment of neonates with dengue is conservative with administration of fluids, nutrition, and supportive care.[6,14] In our case, therapy was given according to clinical symptoms, there was no clinical bleeding and did not require blood transfusion.

A decrease in bilirubin levels occurred after three days of double light phototherapy and administration of oral ursodeoxycholic acid, with total bilirubin levels from 38.29 mg/dl to 4.34 mg/dl. Empirical antibiotics was given because the sepsis condition can't be ruled out in early conditions and stopped after 7 days of administration. Our patient was discharged in good condition on day 11 of life, which no life-threatening conditions were found. Early diagnosis and appropriate supportive care are essential for enhancing the patient's outcome. During dengue outbreaks, infants born to mothers with DHF in the prenatal or peripartum period preferably should be examined for dengue infection.

CONCLUSION

Although perinatal dengue fever is a rare occurrence, it should be suspected in neonates whose mothers have febrile illness during or shortly before labor with dengue infection. The onset of clinical manifestations of dengue infection in neonates with vertical transmission is influenced by the interval between the onset of maternal fever and the time of delivery. Prompt diagnosis, appropriate management, and close clinical monitoring can prevent mortality and morbidity of neonatal dengue.

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REFERENCES

1. World Health Organization (21 December 2023). Disease Outbreak News; Dengue – Global situation. World Health Organization. Available at: https://www.who.int/emergencies/disease. Accessed on 18 August 2024.
2. Arragain L, Dupont-rouzeyrol M, Connor OO, Sigur N, Grangeon J, Huguon E, et al. Vertical transmission of dengue virus in the peripartum period and viral kinetics in newborns and breast milk: New Data. J Pediatric Infect Dis Soc. 2017;6:324–31.
3. Basurko C, Matheus S, Hilderal H, Everhard S, Restrepo M, Cuadro-alvarez E, et al. Estimating the risk of vertical transmission of dengue: a prospective study. Am Soc Trop Med Hyg. 2018;98(6):1826–32.
4. Yin X, Zhong X, Pan S. Vertical transmission of dengue infection: The Forst Putative Case Reported in China. Rev Inst Med Trop Sao Paulo. 2016;58(90):14–7.
5. Jain A, Chaturvedi UC. Dengue in infants: anoverview. FEMS Immunol Med Microbiol. 2010;59:119–30.
6. Yadav B, Gupta N, Gadepalli R, Nag VL. Neonatal dengue : an under-diagnosed entity. BMJ. 2021;14:2417-27.
7. Jain J, Lakshmi V, Shanmughsundaram R. Perinatal transmission of dengue infection in a preterm neonate: a case report. Trop Doct. 2019;49(3):239–40.
8. Ribeiro CF, Lopes S, Coelho J, Muniz AG, Maria R, Nogueira R. Perinatal transmission of dengue: a report of 7 cases. J Pediatr. 2013;163:1514–6.
9. Ahuja S, Gharde PM. A narrative review of maternal and perinatal outcomes of dengue in pregnancy. Cureus. 2023;15(11):1–10.
10. Haryanto S, Yohan B, Santoso MS, Hayati RF, Denis D, Udjung IVWG, et al. Clinical features and virological confirmation of perinatal dengue infection in Jambi, Indonesia: a case report. Int J Infect Dis. 2019;86:197–200.
11. Vats A, Ho T Chuan, Puc I, Chen Y Ju, Chang C Hsin, Chien Y wen, et al. Evidence that hematopoietic stem cells in human umbilical cord blood is infectable by dengue virus: proposing a vertical transmission candidate. Heliyon. 2021;7:6785.
12. Bopeththa BVKM, Hemapriya S, Niranga KKG, Kotigala DSK. A case report of dengue haemorrhagic fever during the peripartum period: challenges in management and a case of vertical dengue transmission. BMC Infect Dis. 2018;18(427):4–7.
13. Sirinavin S, Nuntnarumit P, Supapannachart S, Boonkasidecha S, Techasaensiri C, Yoksarn S. Vertical dengue infection. Pediatr Infect Dis J. 2004;23(11):1042–7.
14. World Health Organization. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. Revised. World Health Organization (WHO), editor. New Delhi: World Health Organization; 2011; 10–46.
15. Phongsamart W, Yoksan S, Vanaprapa N, Chokephaibulkit K. Dengue virus infection in late pregnancy and transmission to the infants. Pediatr Infect Dis J. 2008;27(6):500–4.

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