Dengue hemorrhagic fever in pregnancy with placenta abruption and vertical transmission: a case report

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ABSTRACT

Background: Dengue Hemorrhagic Fever (DHF) is endemic in Indonesia, particularly in Bali. World Health Organization (WHO) reported Indonesia as the major contributor of DHF cases in the Southeast Asia. Moreover, Indonesia national statistical report in 2010 showed that Bali was the province with the highest incidence of DHF in Indonesia. The infection may occur in a pregnant woman.

Case presentation: A 28 years old female was admitted to our hospital with gravi2 (para 0, abortus 1) at 35 weeks and 2 days of gestational age, with threatened preterm delivery and premature rupture of the membrane. She was suspected of dengue infection accompanied by hemococoncentration and thrombocytopenia. On the following day, the dengue specific IgM and IgG were positive. Although the number of the platelet count increased, the patient developed antepartum hemorrhage due to placental abruption grade 2. Thus, she went through a Cesarean Section (C-section) code green. The preterm baby was 2500 gram, suffered from moderate asphyxia. On the first day of care, the baby's dengue NS1 antigen and the dengue-specific IgG antibodies were positive. Moreover, DENV-4 dengue was detected in the infant's serum. On the second day, the baby's serial blood counts showed a gradual rise in the hematocrit (>20% of baseline value) and a decline in platelet count. The dengue specific IgM was positive on the seventh day. The mother was discharged on the 3rd day post-C-section, while the baby was discharged on the 10th day.

Conclusion: Symptomatic dengue infection during pregnancy increases the risk of preterm labor, bleeding, and low birthweight newborn.

INTRODUCTION

Symptomatic dengue infection is a systemic and dynamic disease. Misdiagnosis or delayed diagnosis are not uncommon due to some of the overlapping clinical and or laboratory features with the better-recognized conditions of pregnancy: HELLP syndrome, pneumonia, pulmonary embolism, various obstetric cases of vaginal bleeding and other infectious diseases. A diagnosis of dengue infection is confirmed by the detection of the virus, the viral genome or NS1 Ag, or seroconversion of IgM or IgG (from negative to positive IgM/IgG or four-fold increase in the specific antibody titer) in paired sera.1,3 DHF infection during pregnancy has been associated with severe disease and higher mortality. We report a pregnant woman with DHF who developed antepartum hemorrhage due to placental abruption grade 2, thus underwent a Cesarean Section (C-Section) and the baby after the delivery.

CASE PRESENTATION

August 4, 2015

A 28-year-old woman in her second pregnancy (gravi2, para 0, abortus 1) at 35 weeks and two days of gestational age, visited Sanglah General Hospital with fever and nausea for five days. The patient also complained intermittent abdominal pain with watery vaginal discharge. No spontaneous bleeding was found. The first antenatal care was at nine weeks' gestation, with no congenital anomaly detected. The patient had a history of dengue infection ten years ago.

The patient had normal vital signs and general physical examination. From obstetric examination, the uterine contracted for 25-30 seconds every 5 minutes with a normal fetal heartbeat (FHB). At vaginal examination (VE), the cervical dilatation was 2 cm with ruptured fetal membrane and fetal head presentation at Hodge I. Neither small parts nor umbilical cord palpable. Laboratory examination showed white blood cell (WBC) 15,9/mm3, haemoglobin (Hb)16,17g/dL, haematocrit (Hct) 46,7%, and platelet (Plt) 46,7%, and platelet (Plt) 28,2x10⁹/mm³, see Table 1. IgM and IgG anti-Dengue was positive on the first day. We report a pregnant woman with DHF who developed antepartum hemorrhage due to placental abruption grade 2, thus underwent a Cesarean Section (C-section) and the baby after the delivery.

Keywords: Dengue hemorrhagic fever, pregnancy, placental abruption, vertical transmission


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showed singleton life fetus, head presentation, good fetal heartbeat, and fetal movement. The fetal biometry was gestational age appropriate. The estimated fetal weight was 2478 gram. Placenta grade II is covering the fundal to the posterior wall with single depth pocket amniotic fluid 1.5 cm. A color Doppler examination showed a normal result. Conservative management was applied to the patient by giving tocolytic for postponing the onset of delivery. The patient was monitored closely for vital and bleeding signs while a continuous fetal monitoring was done to detect fetal distress signs. A complete blood count was done every 12 hours. After a maximum dose of tocolytic, there was no sign of diminishing uterine contraction. Therefore, delivery was inevitable and expected to be spontaneous. Packed red cell (PRC) and thrombocyte concentrate (TC) were prepared to anticipate bleeding due to thrombocytopenia related to the Dengue infection.

August 5, 2015
On the second day, we found blackish vaginal bleeding and fetal tachycardia (175 beats per minute) without further progress on cervical dilatation (2 cm). At ultrasonography examination, there was a hypoechoic space between placenta and amniotic membrane suggesting a sub-amniotic hemorrhage. Intrauterine resuscitation was done while preparing for a code green C-section. During operation, the total bleeding was 1150 ml. A bag of 250 ml PRC was transfused. The evaluation on the placenta showed blackish red blood clot and hematoma on the maternal side of the placenta. Postpartum
blood count showed moderate anemia (Hb: 6.69g/dL). Another bag of PRC was given to correct the anemia, resulting in Hb 10.8 g/dL.

The baby was born preterm at 35-36 weeks gestational age by emergency C-section due to placental-abruption-associated fetal distress with a birth weight of 2500 gram and Apgar score 5 at 1 minute, 7 at 5 minutes and 9 at 10 minutes post-delivery. After six hours observation, the baby was active and tolerant to feeding. She was alert, pink with good circulatory perfusion at the examination.

The Following Days

On the 1st day of care, she developed a low-grade fever at 37.8°C. Starting on the 1st day; the infant was fed with a standard formula milk every 3 hours because there had been no maternal

**Table 2** The baby’s serial laboratory investigations

<table>
<thead>
<tr>
<th>Date</th>
<th>At birth</th>
<th>D1 morning</th>
<th>D1 evening</th>
<th>D2 morning</th>
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<tbody>
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<td>27500</td>
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<td>29800</td>
<td>8840</td>
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<td>10700</td>
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<td>Neu %</td>
<td>21.97</td>
<td>22</td>
<td>7.57</td>
<td>12.3</td>
<td>43</td>
<td>10.7</td>
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<td>Lym %</td>
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<td>65.7</td>
<td>85.6</td>
<td>78.4</td>
<td>31.8</td>
<td>81.7</td>
<td>37.5</td>
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<tr>
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<td>19.1</td>
<td>20.9</td>
<td>18.7</td>
<td>17.9</td>
<td>17.0</td>
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<td>62</td>
<td>57.3</td>
<td>64.5</td>
<td>50.1</td>
<td>53.8</td>
<td>48.5</td>
<td>52.2</td>
<td>47.6</td>
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<tr>
<td>Platelet</td>
<td>145</td>
<td>196</td>
<td>268</td>
<td>200</td>
<td>167</td>
<td>98</td>
<td>146</td>
<td>161</td>
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**Figure 1** USG showing a hypoechoic space between placenta and amniotic membrane

**Figure 2** Blackish red blood clot and hematoma on the maternal side of the placenta

**Figure 3** The Admission test

**Figure 4** The cardiotocography leading to before code green C-cesarean Section
milk production and mother felt not yet ready to breastfeed her baby. Breastfed was started on the 3rd day. The baby vital signs were stable. There was no rash, jaundice, vomiting, diarrhea or bleeding tendency. The laboratory findings are shown in Table 2. The baby did not develop any evidence of hemorrhage or pleural effusions or ascites proved by chest x-ray and abdominal ultrasound examinations. She was discharged on 10th day old. A follow up on the baby when she was 6 months old showed that she was healthy and the growth status was normal.

**DISCUSSION**

Our patient came in a critical phase of dengue infection with a potential of developing shock and spontaneous bleeding. Obstetrically, the patient, was found with a threatened preterm delivery and risk of infection due to preterm premature rupture of membrane. Her dengue IgM and IgG was positive on the 7th day of fever.

The management of choice is conservative treatment. Nevertheless, when delivery is inevitable, the progress of labor and delivery should be anticipated and monitored closely in a hospital equipped where blood and blood products, and a team of obstetrician and neonatologist are available.

In the progress of labor, our patient developed placenta abruption. The diagnosis was confirmed with the symptoms and signs according to Wagner et al. They include blackish vaginal bleeding with sudden continuous abdominal pain, followed by fetal distress signs (tachycardia and cardiotocography category 2). The neonate had a moderate asphyxia and acidosis. The detached placenta area exceeded 25%, yet less than 50%. The maternal total blood loss was 250 to 500 ml.

Placenta abruption occurs in 0,5-1% all pregnancies and the prevalence increases when accompanied with risk factors. The structurally-weakened amniotic membrane could start the pathophysiology of placental abruption in our case due to inflammatory reaction following the dengue infection. The rupture of the amniotic membrane was subsequently expanding, breaking villi chorales on decidua basalis. Blood coagulation system may compensate the bleeding via blood clot formation which acts as a plug to stop excessive blood loss. The process happens in 1-2 minutes.

In our patient, the low thrombocyte (platelet) level caused a blood clot formation failure. Thus, more bleeding caused the blood pooled between the uterine wall and the placenta. Thus, followed by placental detachment, spiral arteries destruction. It eventually created a retroplacental hematoma.

As reported by Agrawal et al., from 25 cases of pregnancy with dengue infection, 8 cases (32%) of antepartum bleeding happened due to placenta abruption.

Our patient underwent a C-section. However, the procedure did not fully adopt the Bunyavejecoevin S. recommendation. We used a midline incision. However, we applied only a single layer of suturing and no bladder flap suturing. We did not put a subfascial drain, and the skin was sutured subcuticular. Our action was based on the observation that the bleeding during the operation was manageable and the platelet count tended to improve. Two bags of PRC was transfused during and post operation due to moderate anemia (Hb: 6,69 g/dL). It might happen due to the operation and hemoconcentration during the operation (blood clot 250 ml and bleeding 400 ml). The postoperative care was integrated with internal medicine department in a semi-intensive ward to monitor Dengue infection warning signs and bleeding. However, no hematoma was found.

The hypothesis of vertical infection, as opposed to the postnatal infection, was based on the following aspects: (1) confirmed maternal infection close to delivery time; (2) incubation period; (3) absence of *Aedes aegypti* focuses nearby the hospital and absence of other cases of dengue. The incubation period of dengue is 4-12 days. In our case, the newborn baby was infected from her mother. Because, the baby’s dengue NS1 antigen test and the dengue-specific IgG antibodies were positive on the first day of care. Moreover, PCR results showed DENV-4 positive for the newborn baby’s sera on the 1st day. A close monitoring on the newborn since delivery ensured the baby to not having any contact with Dengue vectors.

The mechanism of infection transmission in the peripartum period remains unclear. Some contended the possible route of transmissions is through oral tract, respiratory tract, or intrapartum skin defect. Our baby showed mild infection through oral tract, respiratory tract, or intrapartum skin defect. Our patient underwent a C-section. However, the surgery did not fully adopt the Bunyavejecoevin S. recommendation. We used a midline incision. However, we applied only a single layer of suturing and no bladder flap suturing. We did not put a subfascial drain, and the skin was sutured subcuticular. Our action was based on the observation that the bleeding during the operation was manageable and the platelet count tended to improve. Two bags of PRC was transfused during and post operation due to moderate anemia (Hb: 6,69 g/dL). It might happen due to the operation and hemoconcentration during the operation (blood clot 250 ml and bleeding 400 ml). The postoperative care was integrated with internal medicine department in a semi-intensive ward to monitor Dengue infection warning signs and bleeding. However, no hematoma was found.

A neonate born from a dengue–infected mother either at term, near term or at the delivery are at highly susceptible to vertical dengue transmission due to lack of time to produce maternal antibody. The peak of maternal antibody production will be on the 30th – 40th day after the onset of the fever. Moreover, the antibody may be transferred through the placenta. Maternal dengue antibody is considered to provide significant protection in severe cases of dengue infection among infants.

A neonate born from a mother infected with dengue must be carefully followed up regarding
his/her clinical evolution up to the second week of life.\(^\text{14}\) A possibility of a vertical infection must be considered. Our baby was observed for ten days. At the six-month follow-up, the baby was healthy and had a normal growth.

Breastfeeding from a mother with dengue infection is still controversial. The literature described breastfeeding would provide protection to the newborn from dengue infection due to the anti-dengue activities of the lipid component of the breast milk and the colostrums.\(^\text{15}\) In contrast, Barthel et al., in his case report on 2013, detected that the breast milk dengue viral load was in the same range as the ones found from the mother’s blood on the same day until day 10\(^\text{16}\) after fever onset.\(^\text{16}\) Several studies even described other flavivirus transmission through breastfeeding. In a yellow fever virus infection (a Flavivirus other than dengue), there were cases of transmission via breastmilk. There was also a recommendation to stop breastfeeding during the viremic phase after vaccination with a live attenuated virus. However, some studies showed the transmission of dengue virus had been described through blood and during pregnancy.\(^\text{17,18}\) Further study is required to evaluate the risk of transmission of dengue virus through breastmilk.\(^\text{16}\) Considering the benefit of breastfeeding and the unproven mechanism of dengue transmission through breastfeeding; our baby started to breastfed on the 3\(^\text{rd}\) day of delivery.

**CONCLUSION**

Symptomatic dengue infection during pregnancy may increase the incidence of preterm birth, bleeding and low birth weight newborn babies. A secondary dengue infection may develop more severe symptoms than the primary infection. A vertical transmission had been reported. However, the mechanisms of infection in the peripartum period remains unclear. A close monitoring of the mother and the fetus during the critical pregnancy phase requires notable attention from the clinicians. A further multicenter study is needed to identify the maternal and the fetus complications when a dengue infection occurs in pregnancy.

**REFERENCES**