CASE REPORT

VERTICAL TRANSMISSION OF DENGUE: FIRST CASE REPORT FROM BANGLADESH

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Abstract. We report a case of vertical transmission of dengue infection in a new born from Bangladesh. The mother was primigravida with an uneventful antenatal period except the fever she developed at 37 weeks of gestation. She underwent cesarean section for decreased fetal movement. The fever lasted for 7 days and was associated with intense bodyache, and a positive tourniquet test. She did not experience any hemorrhages including from the surgical wound. Her platelet count fell at its lowest to 100,000/mm^3. She had bilateral mild pleural effusions and positive anti-dengue antibodies (both IgG and IgM). She received symptomatic treatment. The baby was deeply meconium stained and was resuscitated by a pediatrician. His postnatal period went well until day-3 of life when he developed fever and respiratory distress. There were no signs of meconiun aspiration syndrome (MAS) and the septic work up was negative. The platelets count fell to its lowest of 40,000/mm^3 on day-3 and day-5 of his illness. Anti-dengue antibodies (both IgG and IgM) were positive with a nearly four-fold rise of IgM antibodies in the convalescent sera. The boy was treated with platelet transfusions and was discharged on day-6 after becoming ill. This report emphasizes that in a dengue epidemic or when dengue is endemic (which Bangladesh has experienced recently), a pregnant woman with fever, myalgia and/or bleeding manifestations should raise a high suspicion that the baby may develop the disease, and both the mother and baby should be closely followed-up. Viral isolation could not be done due to the unavailability of the test.

Dengue fever (DF) and dengue haemorrhagic fever (DHF) is the most important human viral disease transmitted by arthropod vectors (Rigau-Perez *et al*, 1998). Large-scale yearly outbreaks during the rainy season have been occurring in Bangladesh since the year 2000 (Ahmad, 2000; Rahman *et al*, 2002; Rasul *et al*, 2002). Dengue infection was previously uncommon in this country. An outbreak of dengue occurred in 1964, and was labeled as 'Dacca Fever', later confirmed to be due to Den-3 (Russel *et al*, 1966; Aziz *et al* 1967). Though the disease predominantly affects children under 15 years of age (Teeraratkul *et al*, 1990), scanty reports exist on the vertical transmission of dengue from pregnant mother to her fetus or offspring (Boussemart *et al*, 2001). We recently cared for a newborn baby with dengue infection, born of a mother suffering from DHF during the period of labor. We believe that the case was due to vertical transmission and is the first case report from Bangladesh.

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Mother

A 28 year old woman (para 0, gravida 1) married for one year with no past history of major disease, resident of Metropolitan Dhaka City, was admitted to a private clinic at 37 weeks (36 weeks and 4 days) gestation with a history of high fever (39.1ºC) for two days. The fever was associated with intense bodyache, but no hemorrhage in the form of petechia, purpura, epistaxis, or gum bleeding was seen. Her BP was 115/75 mm of Hg, and the tourniquet test was positive. On day-3 of her illness she noticed decreased fetal movement and underwent emergency lower uterine cesarean section (LUCS) at 20.30 hr and gave birth to a male child weighing 2.5 kg.

A complete blood count done on day-2 of her illness showed a hematocrit of 35%, Hb-11.7g%, WBC-11,500/mm^3, PMN-80%, lymphocyte 16%, monocyte 2%, eosinophil 2%, platelets count

280,000/mm^3 and the ESR was 35 mm at the end of the 1st hour. A septic screen of urine, high vaginal swab and blood clture and sensitivity were negative. In her post-operative days, high fever continued with gum bleeding on day-5, but no hemorrhage was observed from the surgical wound. On day-5 of her illness platelets count fell to 100,000/mm^3, Hct-34%; and on day-7 the platelet count was 120,000/mm^3 and the Hct-35% (Table 1). Ultrasonography on day-7 of illness showed mild bilateral pleural effusions with hepatomegaly. Her hemodynamic status was normal during the period of her illness and convalescence. The fever subsided on day-7 of her illness. Anti-dengue antibodies were positive (both IgG and IgM) on day-7 of her illness. Anti-dengue antibodies done on day-14 were IgM (antibody index: AI=1.405) and IgG (AI=3.602). AI >1 is considered as positive. Virus detection was not done by culture or PCR. At discharge on day 13 her platelet count was 442,000/mm^3 and the Hct-38.6%.

Baby

This male child of 2.5kg was born with an APGAR score of 6/10 and 8/10 at 1 and 5 minutes respectively. Immediately after birth he was resuscitated by a pediatrician by oropharyngeal suction and suction of the trachea under direct visualization, as the liquor was deeply meconium stained. The baby was closely followed -up in the neonatal intensive care unit (NICU) and had an uneventful post-natal course until day-3 of life when he developed fever (39.1ºC), grunting, respiratory distress and a reluctance to feed. His chest was not hyperinflated and air entry into both lungs was adequate. He received antibiotics after a septic workup. His initial complete blood count on day-2 of his illness showed TC-12,000/mm^3, PMN-68%, lymphocyte-27%, eosinophil-3% and monocyte-2, platelets-160,000/mm^3 and Hct-50%. On day-3 of his illness the platelet count was 60,000/mm^3 and 40,000/mm^3 in the morning and evening samples respectively (Table 2). The baby was transfused with platelet concentrate (10ml/kg). After transfusion the platelet count increased to 60,000/mm^3 and the Hct fell by 16% (from 50% to 42%). Antibiotics were stopped after the cultures were found to be negative. On day-5 he received another platelet transfusion as the count again fell to 40,000/mm^3 and the Hct was 43%. The child was stable clinically (no hemorrhage) throughout this period. On day-6 the IgG for anti-dengue was positive (antibody index-AI= 1.350) but the IgM was negative (AI= 0.900). Anti-dengue antibodies on convalescent sera (day-12 of illness) were positive for both the IgG (AI= 1.438) and IgM (AI= 3.340). Ultrasonography of the brain and abdomen, serum albumin, urine analysis and X-ray of the chest were normal. On discharge at day 6 the Hct was 37% and the platelet count was 190,000/mm^3. Isolation of the dengue virus could not be done, as facilities were not available.

Table 1
Platelets and hematocrit of mother at different days of illness.

Mother		
Day of illness	Hct (%)	Platelet count/mm^3
Day-2	34	280,000
Day-4	35	160,000
Day-5	34	100,000
Day-7	35	120,000
Day-8	35	150,000
Day-11	38	442,000

Table 2
Platelets and hematocrit of baby at different days of illness.

Baby		
Day of illness	Hct (%)	Platelet count/mm^3
Day-2	50	160,000
Day-3 (morning)	49	60,000
Day-3 (evening)	42	40,000
Day-4	41	60,000
Day-5	43	40,000
Day-6	37	190,000

With the exception of a few reports data regarding the signs and symptoms and consequences of vertical transmission of dengue from mother to offspring is scanty. In this case report, the mother had two days of fever, gum bleeding and a positive tourniquet test, a low platelet count and bilateral pleural effusions with positive anti-dengue antibodies in both acute and convalescent sera confirming the case as secondary dengue infection (DHF) (Kalayanarooj *et al*, 2002).

Bangladesh is now experiencing yearly outbreaks of dengue infection beginning in the year 2000 until the present (September 2002). Government sources reported the more than four thousand cases of DF and DHF occurred this year in the past 2.5 months, with 41 deaths; 5,500 cases with 54 deaths in the year 2000, and 4,784 cases with 43 deaths in the year 2001 (Directorate General on Health Services, Government of Bangladesh, personal communication).

The mother had high fever and severe myalgia 2 days prior to a LUCS**.** Bunyavejchevin *et al* (1997) reported 3 cases of vertical transmission; fever and myalgia was present in one mother and petechiae in the other two. Other reported clinical manifestations among mothers were gum bleeding, chills, headache and easy bruising; all of them had uneventful post-natal days. So did the mother of the case we have presented here. In this case, the mother did not experience abnormal hemorrhage from her surgical wound but had gum bleeding and a positive tourniquet test. Thaithumyaun *et al* (1994) and Chotigeat *et al* (2000) reported severe postpartum bleeding occurred in two cases from the surgical wound, into the peritoneal cavity and also into the thigh necessitating multiple transfusions of blood, platelets and fresh frozen plasma in one case (Thaithumyanon *et al*, 1994; Chotigeat *et al*, 2000). Kerdapanich *et al* (2000**)** reported one case in whom no bleeding manifestations occurred antenatally. So in areas where dengue is endemic, or an epidemic is going on, a mother with fever, myalgia and/or bleeding manifestations should raise a high suspicion of dengue infection and should be closely followed up in both clinical as well as hematological aspects. In cases where surgical procedures are performed on patients with dengue, dengue-induced hemoststic defects may result in unexpected hemorrhage. Pre-operative fevers must be investigated and hematologic signs consistent with dengue must be identified (thrombocytopenia and atypical lymphocytes). If dengue infection is suspected, the operation must be deferred; however in case of the onset of labor an exception should be made (Kerdpanich *et al*, 2001). In this case, emergency LUCS was performed due to fetal distress. The baby was found to be deeply meconium stained but did not develop clinical or radiological features of meconium aspiration syndrome. Reports of acute fetal distress in 4 cases of dengue infected mothers have been described in French Guiana. In this report, Carles *et al* (2000) described 38 women with dengue infection during the three trimesters of pregnancy. The consequences for the mothers were premature delivery in 55% of cases; one case had severe hemorrhage following cesarean section and one had abruptio placenta. The consequences for the fetuses were as follows: IUD (intrauterine death) in 5 cases, acute fetal distress in 4 cases and 2 cases of mother to fetal transmission (Carles *et al*, 2000). The infant in our report was born prematurely at 36 weeks and 4 days of gestation. During the postnatal days he had no complications until day-3 (60 hours of age) when he developed fever (39ºC), grunting, respiratory distress and a reluctance to feed, but with no bleeding manifestations. The septic work-up was negative. Anti-dengue antibody IgG (AI=1.305) was positive on day-6 and the IgM was negative (AI=0.900). The IgM specific to dengue became positive (AI raised from 0.900 to 3.340) on the convalescent sera on day-14, confirming the diagnosis of primary dengue infection in this neonate (Gibbons and Vaughn, 2002).

The source of infection could be mother or an infected mosquito. The incubation period of dengue is 3-14 days (generally 5-7 days) (Rigau-Perez *et al*, 1998), hence the theoretical possibility of being bitten by an infected mosquito exists. As the fever started at 60 hours of age, the mosquito bite had to have occured during the first day (within hours of birth). This possibility is remote as he was closely wrapped and transferred to the NICU immediately after birth, keeping little skin exposed, and the NICU is a well-netted area. The possibility of direct contact from maternal viremic blood (by ingestion, respiratory route or through breach in the skin) has been mentioned (Thaithumyanon *et al*, 1994), and we could not rule out this route of virus transmission during the LUCS. Though no hemorrhaegic manifestations were noted in this newborn, bleeding from different sites (GIT, CNS, skin) has been reported in 3 reports of vertical transmission, where one patient died from massive left intra-cerebral hemorrhage with midline shift (Poli *et al*, 1991; Chye *et al*, 1997; Kerdpanich *et al*, 2001). Hemorrhagic manifestations are mainly a feature of secondary dengue infection but can also manifest in infants

with primary infection who transplcentally acquired 'infection enhancing antibody' from the mother (Kilkis *et al*, 1988). This occurs predominantly after 6 months of age (peak- 7-8 months) when the maternal neutralizing antibodies decrease below the protective level and the infection enhancing antibodies remain in the circulation; which are assumed to be a specific risk factor for converting benign primary infection into DSS/DHF. The DHF/DSS like features in vertical transmission have not been explained. We assume that this could be due to the fact that the mother could not get adequate time to mount an immune response against the particular sero-type which has infected her during the time of parturition; and the antibodies of the other sero-type, which was already present, passed transplacentally. It is known that the antibody of one serotype is protective to that serotype but immune enhancing to the other serotypes and cause bleeding in the infant (Kilkis *et al*, 1988). Regarding the long-term consequences of perinatal dengue infection, among the 4 cases reported, there were no significant problems at 5 years (Fernandez *et al*, 1994), though throbocytopenia for two months has been reported (Carles *et al*, 2000) .

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