

INTRACRANIAL HEMORRHAGE IN PREMATURE INFANT OF LOWEST WEIGHT WITH CONGENITAL DENGUE: A CASE REPORT

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Abstract. We report a case of congenital dengue in the smallest patient with dengue vertical transmission reported in the literature to date. A premature infant was admitted to a neonatal intensive care unit at San Francis Hospital, Francisco Beltrão, Brazil (2012) with suspected dengue infection owing to thrombocytopenia, confirmed by ELISA detection of anti-dengue specific IgM. The patient received four transfusions of 15ml/kg body weight (BW) of packed red cells and 15 mm³/kg BW platelets. On Day 13 post-admission platelet counts reached a minimal level (28×10³/mm³) and gradually returned to normal (165×10³/mm³) on the 20th day of life, by which time the patient had also gained weight. Transfontanelar ultrasound performed on Day 19 showed marked hydrocephalus, brain hemorrhage grade III and ventriculitis. On Day 23, the patient presented a convulsive crisis, which required mechanical ventilation and subsequently developed pneumonia, sepsis and renal failure; and expired on Day 38. We discuss the importance of examining the clinical history of mothers of premature newborns with thrombocytopenia, especially in regions where dengue is endemic.

Keywords: dengue infection, premature baby, thrombocytopenia, vertical transmission

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INTRODUCTION

Dengue is endemic and constitutes an important public health problem in many tropical countries (Maroun *et al*,

2008). There are three mechanisms for fetal transmission of dengue, namely, hematogenous dissemination secondary to maternal transplacental infection,

viremia in mother thereby increasing risk of transmission owing to exchange of blood during childbirth and severe dengue in mother that directly compromises placental function (Manzano Núñez *et al*, 2017).

Since 1993, when the first case of vertical dengue transmission was reported in Thailand, few cases have been described (Thaithumyanon *et al*, 1994). There is evidence of a high-risk vertical transmission in pregnant women with symptomatic dengue who are close to the end of their pregnancy (Sirinavin *et al*, 2004; Paixão *et al*, 2017) and newborns of low weights have a higher risk of severe dengue (Kerdpanich *et al*, 2001). As of 2012, the smallest newborn with congenital dengue was a premature infant of 1,850 g delivered at the 34th week of gestation (Witayathawornwong *et al*, 2012). Here, we report, to the best of our knowledge, a case of the smallest newborn with congenital dengue.

CASE REPORT

The patient (female) was delivered by caesarean section due to maternal preeclampsia at the 29th week of gestation (12 April 2012), with the mother receiving two doses of antenatal corticosteroids (12 mg intramuscular dexamethasone every 12 hours). The patient weighed 850 g, receiving an Apgar score of 8 and 9 at 1st and 5th minute respectively, and was transferred to a neonatal intensive care unit and placed in an incubator equipped with a helmet-based ventilation system of 60% O₂, which was gradually decreased to 25% by Day 3 post-admission.

Prophylactic phototherapy was performed with no observable complications until on Day 7 the patient presented signs of apnea, a clinical picture compatible with neonatal sepsis, hypoactivity, bulging cranial fontanelles, scleredema in limbs but no other dermatological changes such as rash, and no significant abnormalities in pleuro-pulmonary and precordial areas during auscultation or in abdomen from a physical examination.

Blood samples were collected for bacterial screening (resulting in negative culture) and total blood counts, revealing leukopenia and thrombocytopenia, obviating the need for cerebral spinal fluid collection (Table 1). Broad-spectrum antibiotics (ie ampicillin [100mg/kg day], cefotaxime [100mg/kg day], and gentamicin [5mg/kg every 48 hours]) were prescribed, and hypovolemic shock was corrected. By Day 8, clinical conditions were stabilized. On the same day, the mother informed that 17 days prior to cesarean section she had developed a rash and a mild headache but no fever and was subsequently diagnosed as having had dengue by an IgG/IgM ELISA-based diagnostic test (PlateliaTM NS1 ELISA; BioRad, Marnes-la-Coquette, France). Serology test of the patient for dengue produced negative IgG but positive IgM results (NS1 BioeasyTM; Standard Diagnostics INC, Suwon City, Korea).

The patient received transfusions of packed red blood cells (15 ml/kg body weight (BW) on Days 11, 13, 15 and 27) and filtered platelets (15 ml/kg BW on Days 8, 11, 13 and 31). By Day 13, number of platelets reached its

Table 1
Complete blood counts of premature infant with congenital dengue, San Francis Hospital, Francisco Beltrão, Brazil

Parameter	Year 2012													
	April 12 ^a	April 18	April 22	April 23	April 25	April 27	April 28	May 1	May 5	May 17	May 19	May 20 ^b		
Hemoglobin (g/dl)	15.3	13.7	10.9	9.8	10.7	13.0	12.8	10.6	9.2	11.0	10.3	9.4		
Globular volume (%)	46	41	33	29	32	39	39	32	28	33	31	28		
White blood cells (x10 ³ /mm ³)	4.0	6.4	17.1	15	12.2	17.2	17.8	11.2	16.9	13.4	4.8	4.4		
Band cells (%)	1	3	0	3	7	2	3	5	4	7	7	2		
Segmented neutrophils (%)	22	41	65	48	59	67	73	51	31	52	52	35		
Eosinophils (%)	1	1	1	0	1	5	0	3	14	1	0	2		
Lymphocytes (%)	73	52	24	47	31	22	18	39	46	38	34	53		
Monocytes (%)	3	3	10	2	2	4	6	2	5	2	7	8		
Platelets (x10 ³ /mm ³)	116	63	60	39	28	71	96	165	172	74	52	49		

^aDate of birth; ^bDate of death

g: grams; dl: deciliter; mm³: cubic millimeter

lowest value ($28 \times 10^3/\text{mm}^3$) and gradually returned to normal number ($165 \times 10^3/\text{mm}^3$) by Day 20. During this period, the patient began to gain weight. Transfontanelar ultrasound performed on Day 19 demonstrated marked hydrocephalus, brain hemorrhage grade III and ventriculitis. Anatomopathological examination of the placenta showed a third-trimester placenta but with infarction sites typical of maternal hypertension. On Day 23, the patient began to present a convulsive crisis, which was difficult to control, requiring mechanical ventilation, and developed into pneumonia, sepsis, renal failure, and ultimately death on Day 38.

The study protocols were approved by the Research Ethics Committee, Western Paraná State University (approval no. 4.374.552).

DISCUSSION

This case had an atypical presentation from those previously reported, namely this was a case of vertical transmission of dengue occurring in a premature birth (after 29 weeks of gestation), whereas previous cases occurred in close to or full-term babies (Sirinavin *et al*, 2004; Paixão *et al*, 2017).

The mother, unlike others who transmitted dengue to her conceptus, had a mild clinical picture, without fever, one of the main symptoms of this pathology (Sondo *et al*, 2019). In previous reports, a risk factor for vertical transmission of dengue is a disease with exuberant maternal symptomatology (Sirinavin *et al*, 2004; Paixão *et al*, 2017). The time between onset of symptoms in

pregnant women and newborns ranges from one day to 13 days (Chotigeat *et al*, 2003; Sirinavin *et al*, 2004). However, in the patient of the present case report symptoms manifested 21 days after those of the mother. This extended period for symptoms onset raises the possibility of acquired neonatal infection. However, this could be ruled as the patient was, throughout life, kept in an incubator located in a neonatal intensive care unit where ventilation is controlled by a complex air filtration system preventing access to flying insects.

Neonates affected by dengue often present with short-term fever, hepatomegaly, circulatory insufficiency, bleeding at puncture sites, and shock; such findings were also observed in other pathologies in the neonatal period, such as bacterial sepsis (Chye *et al*, 1997; Ghosh *et al*, 2017). As a result of the clinical features, the patient was treated for bacterial sepsis with broad-spectrum antimicrobials, but this diagnosis was ruled out by negative blood culture results and slightly altered C-reactive protein. Dengue infection was suspected from investigation of the mother medical history, and serologically confirmed in both mother and patient. The discrepancy between IgG positivity found in the mother but not newborn is rare, but 4% of such phenomenon were observed in Brazil among mothers with dengue and transplacental transfer of anti-dengue antibodies (Leite *et al*, 2014). Harapan *et al* (2020) attribute this discrepancy between dengue antibodies in mother and newborn to immune status of the individuals.

There are few reports of severe

intracerebral hemorrhage due to congenital dengue (Thaithumyanon *et al*, 1994). However, the patient in this case study presented extreme prematurity, a concomitant risk factor for this outcome (Silveira and Procianoy, 2005) and probably for eventual death. However, three other cases of newborns who died of neonatal dengue were late preterm infants (Chye *et al*, 1997; Choudhry *et al*, 2004; Ekanayake *et al*, 2014).

In conclusion, despite the pertinent signs and symptoms presented by the premature infant, investigation of the mother clinical history led to diagnosis of maternal dengue and transmission to the newborn, highlighting the importance of anamnesis in clinical practice.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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