Sri Lanka Journal of Medicine **SLJM**

Case Report

Citation: Gunarathna RASP, Hassan MHSM & Vigneswararjha H, et al., 2022. First reported case of hydrops fetalis following critical phase maternal dengue haemorrhagic fever. Sri Lanka Journal of Medicine, pp 112-115
DOI: http://doi.org/10.4038/sljm.v31i1.298

First reported case of hydrops foetalis following critical phase maternal dengue haemorrhagic fever

Gunarathna RASP[1], Hassan MHSM[2], Vigneswararjha H[3], Lucas MN[4]

[1,2,3,4]University Neonatal Unit, De Soysa Hospital for Women, Colombo.
[4]Department of Paediatrics, University of Colombo

Correspondence:
Gunarathna RASP
MD, University Neonatal Unit, De Soysa Hospital for Women, Colombo
E mail: sujithpriyangag@yahoo.com
: https://orcid.org/0000-0002-9825-2040

Abstract

We report a case of hydrops foetalis due to maternal dengue haemorrhagic fever (DHF). A 19-year-old mother was diagnosed to have DHF with positive NS1 Antigen (NS1) at 39 weeks of gestation. Ultrasound scan revealed fetal hypoxia. Her antenatal period was uneventful with normal antenatal scans. She delivered a 3.3kg baby at 39-weeks gestation via spontaneous vaginal delivery. Baby was diagnosed with non-immune hydrops foetalis due to pleural and peritoneal effusion at birth. Baby developed DHF on day 5 (NS1 positive) and succumbed to a massive pulmonary haemorrhage on day 9.

Keywords: *hydrops, maternal, dengue*

INTRODUCTION

Dengue infection (DI) is a major vector borne disease in Sri Lanka with 105,049 reported cases in 2019[1]. However vertical transmission of DI is infrequent[2]. We report a case of neonatal dengue haemorrhagic fever (DHF) complicated with pulmonary haemorrhage which presented as hydrops foetalis at birth following maternal DHF.

A 19-year-old mother was diagnosed to have dengue fever (DF) with positive NS1 Antigen (NS1) at 39 weeks of gestation, when she presented with fever for 3 days, arthralgia and myalgia. She was diagnosed with critical phase DHF the next day, i.e. day 04 of illness, after she was found to have thrombocytopenia, leukopenia, ultrasonic evidence of fluid in the hepato-renal pouch and bilateral pleural effusions. Fetal wellbeing assessed via obstetric ultrasound revealed fetal hypoxia. There were no maternal risk factors for sepsis, congenital infection or family history of blood disorders. Her antenatal period was uneventful with normal antenatal scans. Mother was immunized for rubella and VDRL was negative.

A baby boy was born vaginally at 39 weeks of gestation with a birth weight of 3.3 kg through moderate meconium, on day 5 of maternal illness during the critical phase of DHF. Baby cried soon after birth. APGAR score was 8, 9 and 10 at 1, 5 and 10 minutes respectively. Continuous positive airway pressure was started soon after birth due to tachypnoea and grunting, followed by intubation

Received: 2021-09-06 **Accepted revised version: 2022-04-13** **Published: 2021-07-31**

and ventilation due to desaturation. Pulmonary vasodilators (sildenafil and magnesium sulfate) and systemic vasoconstrictors (dopamine and noradrenaline) were used to treat persistent pulmonary hypertension (PPHN), that was confirmed by 2D echocardiography on day 01.

Air entry was reduced on the right side and chest X ray confirmed a right sided pleural effusion. Abdominal distension with flank dullness due to peritoneal free fluid was confirmed by ultrasound scan (USS). Presence of pleural and peritoneal effusion led to the diagnosis of hydrops foetalis at birth. Dengue NS1 Antigen, dengue IgM and IgG antibodies were negative on day 01. Peritoneal and pleural effusions spontaneously resolved by day 3 as confirmed by repeat USS. There was no evidence of congenital infection, cystic hygroma, arrhythmia, anemia, hemolysis or dysmorphism suggestive of Down or Turner syndrome. Serum albumin was within normal range and urine did not contain any albumin. Both baby and mother were B positive with a negative Coombs test.

Baby developed thrombocytopenia without other bleeding manifestations on day 4 followed by fever on day 5 when NS1 was repeated and found to be positive. Baby developed abdominal distention with worsening thrombocytopenia on day 6. USS abdomen and chest showed pericholecystic fluid, moderate free fluid in abdomen and pelvis with left side mild pleural effusion. Baby was diagnosed to have critical phase DHF with possible secondary infection and was treated at NICU with fluid resuscitation, inotropic support and broad-spectrum antibiotics in a closed and separated incubator. Both Dengue Ig M and Ig G antibodies were negative on day 6. Baby developed pulmonary haemorrhage on day 07 which persisted despite treatment with multiple blood products, increased ventilatory pressures and sedation. Baby succumbed to a massive pulmonary haemorrhage on day 9. Investigation results are shown in Table 1.

Table 1: Results of serial full blood counts, CRP, AST and ALT

Day of illness	Day 01	Day 03	Day04	Day 06	Day 07	Day 08	Day 09
White cells/µl	15.8	15.2	10.4	4.4	17.9	11.1	18.2
Neutrophils %	80	61	79	44	39	62	65
Lymphocytes %	15	25	6	42	45	23	24
Platelets/µl	231	196	95	10	29	50	40
Hemoglobin g/dl	14.3	18.9	14.7	13.5	14.4	10.2	15.4
Haematocrit %	40.8	57.7	43.6	40.8	45.4	31.8	47.8
CRP mg/dl	3.7	82.3		36.8		46.8	
AST U/L	222		356		914	345	
ALT U/L	177		238		729	545	
Blood culture	Negative	Negative					

DISCUSSION

Maternal dengue infection near term leads to viraemia in the in the unprotected neonate, due to inadequate time for conferring passive immunity via protective antibodies[2]. Dengue infection has an incubation period of 3 - 8 days but some neonates have become ill as long as 11 days after the birth[3]. This would explain why our patient presented with a negative NS1 antigen on day 1 but developed fever and had a positive NS1 antigen on day 5 of life followed by fluid leakage and bleeding manifestations from day 6.

Our patient was found to have DHF following vertical transmission. Vertical transmission usually results in primary dengue infection in the neonate whereas DHF usually follows secondary dengue infection. Mothers with 2 or more dengue infections protect their baby via the IgG antibodies at the time of birth. However, antibody dependent enhancement that occurs at the time of catabolization of these IgG antibodies increase the risk of DHF during this time.[4]

The hydrops foetalis and pulmonary hypertension at birth in our patient is possibly due to the in-utero hypoxia faced by the baby while the mother was in

the critical phase. Hydrops foetalis (HF) is a pathologic condition of excessive accumulation of fluid in at least two extravascular compartments[5]. Non-immune hydrops foetalis (NIHF) accounts for 85-90% of HF[2]. Aetiological factors for NIHF are given in table 2[6].

Table 2: Aetiology for NIHF[3]

System	Condition causing NIHF
Cardiovascular	Structural, functional, arrhythmias
Chromosomal	Trisomy, Turner syndrome
Hematologic	hemorrhage, abnormal hemoglobin production, decreased red blood cell production, increased hemolysis
Infectious	parvovirus, syphilis, cytomegalovirus, toxoplasmosis, adenovirus, varicella, coxsackie virus, herpes simplex virus, respiratory syncytial virus, rubella, trypanosomiasis
Thoracic	congenital pulmonary malformation, bronchopulmonary sequestration, congenital diaphragmatic hernia, hamartoma, teratoma, hydrothorax
Tumors	Teratoma (sacral, mediastinal, pharyngeal), hemangioma, lymphangioma, rhabdomyoma, neuroblastoma
Gastrointestinal	Midgut volvulus, malrotation, duplication, obstruction, meconium peritonitis, atresia (intestinal or biliary), hepatic cirrhosis, necrosis or fibrosis), tumor, cholestasis
Placenta, Cord	Chorioangioma, umbilical artery aneurysm, umbilical vein thrombosis
Metabolic	Lysosomal Storage Disease, Gaucher disease, gangliosidosis, sialidosis
Genitourinary	Congenital nephrosis
Skeletal	Dysplasia Thanatophoric dysplasia, osteogenesis imperfecta, achondrogenesis, short-rib polydactyly, thoracic dysplasia

Our patient did not have evidence for any of the above-mentioned causes except for dengue infection in the mother at the time of delivery. Infectious agents such as parvovirus B19, cytomegalovirus, herpes simplex virus, Toxoplasma gondii, and Treponema pallidum have been reported to affect the fetus directly by affecting the fetal bone marrow, myocardium, or vascular endothelium[7]or via the placenta[8].

The hemodynamic changes caused by dengue infection during pregnancy has been shown to affect the placenta and cause hypoxia in the fetus via the inflammatory response characterized by deciduitis, choriodeciduitis, intervillositis, focal and multifocal villitis, necrotizing villitis, proliferative villitis, and multifocal necrotizing villitis in addition to the pathological changes due to hypoxia characterized by edema of the villous stroma, pre-infarction areas, chorangiosis, and infarcted areas[5]. Some of these changes have also been described with other viruses such as rubella, cytomegalovirus and varicella zoster[8].

Decreased oncotic pressure, increased capillary permeability, obstructed venous return or lymphatic obstruction are reported as the underlying mechanisms for NIHF[6]. Our patient did not have any evidence of decreased oncotic pressure, venous or lymphatic obstruction making increased capillary permeability the most likely cause of NIHF. Hypoxia has been reported to cause endothelial dysfunction in a dose dependent manner resulting in increased capillary permeability[7]. Therefore, we postulate increased capillary permeability as the mechanism for NIHF in our patient due to the inflammatory response and fetal hypoxia (as confirmed by antenatal USS in our patient) caused by alteration of the maternal hemodynamic status by maternal dengue infection. Further studies would be needed to confirm this possibility.

Author declaration
Author contribution:
Gunarathna RASP was involved in the conception of the case report, acquisition and analysis of data and production of the initial manuscript. Hassan MHSM and Vigneswararjha H were involved in the acquisition, analysis and interpretation of the data. Lucas M N was involved in editing and revising it critically for intellectual content. All authors have read and approved the version of the manuscript being submitted for publication.
Conflict of interest:
The authors declare that they do not have conflict of interest.

Source of funding:
No funding

Consent for participation:
Parents consented to use information regarding their baby for publication.

REFERENCES

1. Epidemiology unit, Ministry of Health. Disease surveillance trend for Dengue Infection. 2021. [cited 2021. April 5]. Available from: https://www.epid.gov.lk/web/index.php?option=com_casesanddeaths&Itemid=448&lang=en
2. Yin X, Zhong X, Pan S. vertical transmission of dengue infection: the first putative case reported in China. *Rev Inst Med Trop Sao Paulo* 2016; 58: 90.
3. Sirinaveen S, Nuntnarumit P, Supapannachart S, Bwnkasidesha S , Techasaensiri C, Yokshan S. Vertical dengue infection case report and review. *Paediatric infectious disease journal* 2004; 23(11) :1042-7
4. Halstead SB, Lan NT, Myint TT, Shwe NT, Nisalak A, Kalyanarooj S et al. Dengue hemorrhagic fever in infants: research opportunities ignored. *Emerging Infectious Diseases* 2002; 8(12): 1474-1479.
5. Langlois SR, Wilson D. Fetal Hydrops, In: Pandya PP, Oepkes D, Sebire NJ, RJ Wapner, editors. Fetal Medicine (Third Edition): Elsevier; 2020. pp 427-442.
6. Snowise S, Johnson A. Nonimmmune Hydrops Fetalis. Obstetric Imaging: Fetal Diagnosis and Care (Second edition): 2018; pp 520.
7. Barron SD, Pass RF. Infectious causes of hydrops fetalis. Semin Perinatol. 1995 Dec;19(6):493-501.
8. Ribeiroa CF, Lopesb VGS, Brasilc P, Piresd ARC, Rohloffe R, RMR Nogueiraf. Dengue infection in pregnancy and its impact on the placenta. International Journal of Infectious Diseases. 2017; 55: 109–112.
9. Middleton WD, Kurtz AB, Hertzberg BS. Fetal Thorax. Middleton WD, Kurtz AB, Hertzberg BS editors. The Raditology Requisites Ultrasound (Second Edition): Mosby; 2004. pp 414-430.
10. Ogawa S, Shreeniwas R, Brett J, Clauss M, Furie M and Stern DM. The effect of hypoxia on capillary endothelial cell function: modulation of barrier and coagulant function. British Journal of Haematology. 1990; 75: 517-524.