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Congenital Dengue and Myocarditis

A Case Report and Systematic Review of Literature

Richa Sharma, DCH, Natwar Parwal, DCH, Nirmal Kumar, MD, and Jacob M. Puliyel, MD

Abstract: We report a newborn with congenital dengue infection and cardiomyopathy. Congenital dengue is known to occur owing to vertical transmission of the virus from an infected mother to her baby through the placenta. Dengue-related cardiomyopathy has been reported previously. This is arguably the first time cardiomyopathy is being reported in the context of congenital dengue. A systematic review of literature on congenital dengue as cited in Pubmed is also presented.

Key Words: congenital dengue, cardiomyopathy

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Dengue infection is caused by arbovirus pathogens (*Flavivirus*). Serologically, there are 4 types of dengue virus. Infection with one serotype does not confer immunity against infection with other serotypes. On the other hand, previous dengue infection (primary dengue) and the developed antibodies predispose the patient to more severe illness when infected with other serotypes subsequently (secondary dengue).¹ Congenital infection occurs when the virus is directly transmitted to the baby through the placenta, and there is insufficient time for protective antibodies developed in the mother to be transferred to the baby.² However “infection-enhancing antibodies” acquired by the mother from previous *Flavivirus* infections are passively transmitted to the baby, and this results in serious manifestations in the newborn.³ It is reported that although hemorrhagic manifestations are mainly a feature of secondary dengue infection, it also manifests in congenital dengue owing to these infection-enhancing antibodies.⁴

Cardiomyopathy has been described in adults with dengue infection.^{5–7} Cardiomyopathy, however, has not been previously reported in congenital dengue to the best of our knowledge. A systematic review of congenital dengue in PubMed is also presented.

CASE REPORT

AQ1 A term 3.2-kg male baby was delivered by cesarean birth with Apgar scores 2, 4, and 4 at 1, 5, and 10 minutes, respectively. His mother had a history of fever with thrombocytopenia for 2 days before delivery. Result of her dengue nonstructural antigen 1 (NS1) test was positive. The mother’s serological test results were negative for human immunodeficiency virus, HBsAg, and VDRL. The baby developed severe respiratory distress and bradycardia soon after birth. His peripheral pulses were feeble, and his blood oxygen saturation fluctuated between 70% and 80% on pulse oximetry. He was centrally cyanosed; had massive

hepatomegaly (liver 4 cm in the right midclavicular line), decreased air entry in right basal region of the lung, and a systolic murmur in mitral and tricuspid areas. His dengue nonstructural antigen 1 test was positive. The first blood sample taken soon after delivery showed C-reactive protein of 0.45 (positive, >0.5), and platelet count was 21,000/mL of blood; blood culture was sterile. A chest x-ray showed cardiomegaly with bilateral pulmonary infiltrations. An echocardiogram (ECG) done on the unit by a pediatrician with special interest in pediatric cardiology showed massive right atrial and ventricular dilatation with severe tricuspid regurgitation. Twenty-four hours after birth, the ECG repeated by a pediatric cardiologist showed cardiomyopathy with dilated left atrium and right ventricle, patent foramen ovale, small pericardial effusion with right systolic dysfunction, and moderate tricuspid regurgitation with a pressure gradient of 4 mm Hg. He was given ventilatory assistance, IV fluids, antibiotics, and blood transfusions. This shock was refractory to inotropes and hydrocortisone. He went on to develop multiple organ failure (MODS) and died on day 7 of life.

AQ4

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AQ6

DISCUSSION

Our child, born during the peak of the dengue season in Delhi India, probably had congenital dengue as evidenced by symptoms in the mother 2 days before delivery as well as the dengue antigen positivity in both the mother and the child. Echocardiography in the newborn with refractory shock suggested cardiomyopathy.

Dengue virus is known to cause cardiac complication in children. Salgado et al⁸ has reported 11 pediatric patients with myocarditis due to dengue. Sinus node dysfunction with sinus bradycardia or tachycardia and T-wave inversions on ECG, pericardial effusion, and diastolic dysfunctions have all been reported. Promphan et al⁹ described sinus node dysfunction leading to bradycardia and hypotension a day after recovery from DHF in a 13-year-old boy.

Obeyesekere and Hermon¹⁰ have listed the diagnostics criteria for dengue myocarditis:

1. Clinical evidence of myocarditis;
2. Presence of electrocardiographic evidence of myocarditis, ST segment and T wave changes, and disturbances in conduction and rhythm;
3. Recent history of denguelike fever;
4. Serological evidence of past dengue infection as revealed by the presence of antibody in high titer.¹⁰

Our neonate with congenital dengue had clinical and echocardiographic evidence of myocarditis.

The pathogenesis of myocarditis is not clear. It could be that the virus invades the myocardium and directly damages the muscle fibers or it may give rise to a hypersensitivity or autoimmune reaction causing myocardial damage. The altered state of myocardium may persist long after the initial viral infection and make it prone to recurrent damage from other agents.¹⁰ Salgado et al⁸ have demonstrated infection of heart tissue in vivo

From the Department of Pediatrics, St Stephen’s Hospital, Tis Hazari, New Delhi, India.

Correspondence to: Richa Sharma, St Stephen’s Hospital, Tis Hazari, Delhi 110054 India. E-mail: Richa.dr.sharma@gmail.com.

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AQ3

TABLE 1. Symptoms in Mothers and Newborns and Tests Used

	Citation	Pregnant Women's Symptoms	Newborn Symptoms	Outcome	Diagnostic Test
1	Witayathawornwong ¹¹ (Thailand) 2003	Fever, 5 days; thrombocytopenia and pleural effusion; postpartum anemia	Fever, 2 days (48 h of life); thrombocytopenia; pleural effusion; hepatomegaly	Recovered	Dengue virus type 2 by PCR
2	Fatimil et al, ⁴ (Bangladesh) 2003	Fever, intense body ache, tourniquet test +, bilateral mild pleural effusions with hepatomegaly	Fever, respiratory distress	Recovered	IgM and IgG for dengue with 4-fold rise of IgM
3	Janjindamai and Pruekprasert, ¹² (Thailand) 2003	Acute dengue	Fever, convalescent rash, elevated SGOT and SGPT	Recovered	Dengue virus type 2 by PCR
4	Bugna et al ¹³ (Poland) 2010	Fever, thrombocytopenia, rashes	Fever, thrombocytopenia, erythematous rashes, hepatomegaly, bilateral pleural infiltrates, mild pleural effusion	Recovered	Dengue IgM and IgG

and striated cells in vitro with dengue. It has been proposed that derangements of calcium storage in infected cells may directly contribute to presentations of myocarditis.

A systematic review of the literature looking for reported cases of congenital dengue in Pubmed was performed using the search criteria: (“congenital”[Subheading] OR “congenital”[All Fields]) AND (“dengue”[MeSH Terms] OR “dengue”[All Fields]) AND (Case Reports[ptyp] AND “infant, newborn”[MeSH Terms]). Four case reports were found. The papers were retrieved and reviewed. The symptoms in the mothers and the newborn and tests used for diagnosis are tabulated in Table 1.

CLINICAL MANIFESTATIONS OF NEONATAL DENGUE INFECTION

In all the cases of neonatal dengue caused by vertical transmission, fever was detected. All the neonates manifested a rash. Other manifestations include hepatomegaly,^{11,13} respiratory distress,⁴ pleural infiltrates,¹³ and pleural effusion.¹³ The laboratory manifestations consisted of thrombocytopenia and raised liver enzymes.¹² Diagnosis of 2 patients was based on PCR, and both were of serotype 2.^{11,12} The diagnosis of 2 other patients was based on 4-fold rise in antibody IgM titers.^{4,13} All 4 patients recovered from their illness. None of the cases of congenital dengue had evidence of myocarditis. In our case, there were features suggestive of myocarditis and shock, which was refractory to inotropes.

Cardiomyopathy seems to be a novel complication of congenital dengue fever. One must have a high index of suspicion and be vigilant for this potentially serious complication.

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