

# Prolonged Neonatal Cholestasis: A Rare Manifestation of Dengue Fever

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## Abstract

In the initial few months of life a dengue infection is uncommon in newborns as the maternal antibodies transferred through the placenta prevent it. As such dengue infection can manifest in varied clinical spectrum ranging from asymptomatic illness to dengue shock syndrome, as well as unusual manifestations, such as hepatitis, encephalitis, myocarditis, Reye's syndrome, hemolytic uremic syndrome and thrombocytopenia purpura. A number of etiological agents have been identified for cholestasis in newborn but the dengue infection is rare cause. Here we report a case of dengue infection with prolonged cholestasis.

## INTRODUCTION

Dengue infection is uncommon in newborns as the fact that infants from southeast Asia fail to develop clinical dengue illness until around 6 months of age because of the presence of broadly reactive dengue neutralizing antibodies in their mother's serum samples and protection afforded by passively transferred dengue antibodies<sup>1</sup> and most of the cases have been reported as congenital infection. Although liver involvement is not uncommon in dengue infection most of the deranged functions tend to recover soon<sup>2</sup>. Here we report a case of dengue infection in a 21 days old newborn with prolonged neonatal cholestasis which is a rare manifestation of dengue infection.

## CASE REPORT

A 21 day old, term neonate born to previously healthy mother was admitted with complaints of fever, refusal to feed, distension of abdomen since 2 days. No history of cyanosis, convulsion, or rapid breathing. On general examination, deep icterus and generalized lymphadenopathy was present. Prenatal, natal and postnatal history was insignificant. Pulse rate: 180/min, respiratory rate: 40/min and capillary refill time 3 sec. There was no focus of infection, rash or bleeding manifestations. Perabdominal examination revealed moderate size hepatosplenomegaly. Other systemic examination was normal. A clinical diagnosis of septicaemia was considered. Baby was put on empirical antibiotics therapy. Investigations revealed hemoglobin 11.6 g/dl, TLC: 15,700/mm<sup>3</sup>, platelet count 37000/mm<sup>3</sup>, differential leukocyte count showed P46%,

L45.3%, M7.8%. Peripheral smear and rapid diagnostic test was negative for malarial parasite. Urine bile salt and bile pigment was positive. Stool color and microscopic examination was normal. Blood and urine culture was sterile and CSF study was normal. Liver function tests showed total bilirubin 10.4 mg/dl, conjugated 5.6 mg/dl, AST: 359 IU/L, ALT: 235 IU/L, Alkaline phosphatase: 295 IU/L. PT and APTT was deranged. Abdominal Ultrasonography revealed hepatosplenomegaly with minimal fluid in abdomen and right pleural effusion. TORCH titer of both baby and mother was negative. Because of outbreak of dengue fever, rapid diagnostic test for dengue was sent and turned to be IgM positive while the mother's status was found negative. Antibiotics was stopped and managed symptomatically. Neonate was discharged after improvement in condition after 10 day. A HIDA (HepatoImino Diacetic Acid) scan revealed normal biliary flow. On subsequent follow up after 3 month, features of cholestasis was gradually decreased.

## DISCUSSION

Dengue fever can present a diverse clinical spectrum ranging from asymptomatic illness to dengue shock syndrome, as well as unusual manifestations, such as hepatitis, encephalitis, myocarditis, Reye's syndrome, hemolytic uremic syndrome and thrombocytopenia purpura<sup>3</sup>. Although liver injury due to dengue infection is not uncommon and has been described in several experimental as well as in clinical studies<sup>4</sup>, most of them tend to recover soon. With the best of our knowledge prolonged neonatal cholestasis has never been described previously as a

complication of dengue infection especially in the neonatal period. Cholestasis may be defined physiologically as a measurably decrease in bile flow, pathologically as the histologic presence of bile in liver cells and biliary system and clinically as the accumulation of normally excreted in bile (e.g. bilirubin, bile acids) in blood and extrahepatic tissues<sup>5</sup>. The causes in neonatal period are mainly structural anomalies of biliary tract, both intrahepatic and extra hepatic, infections including bacterial, viral, like congenital CMV, herpes virus, echovirus, cocksackie virus, rubella virus, hepatitis B virus, other hepatitis virus, HIV and parvovirus B19, metabolic, hemodynamic or toxic insults<sup>6</sup>. Liver involvement by dengue virus has been frequently described in Asia and pacific islands the pathogenic mechanism are not get full elucidated<sup>3</sup>. Some believe that it is related to combined interaction of virus, the host and the duration of disease<sup>7</sup>. In liver varying degree of fatty metamorphosis, focal midzonal necrosis and hyperplasia of kuffer cells are found. Nonnucleated cells with vacuolated acidophilic cytoplasm resembling councilman bodies (apoptotic hepatocytes) are seen in the sinusoids<sup>8</sup>. The increase in aminotransferases mainly AST has been associated with disease severity and it serve as an early indicator of dengue infection. Indeed, liver injury is a good positive predictive factor for the development of DHF<sup>9</sup>. The jaundice in dengue infection has been associated with fulminant liver failure and by it self is already a poor prognostic factor<sup>10</sup>. Despite the presence of jaundice and increased risk of haemorrhagic manifestations, our patient showed a benign course of disease which subsides over a

couple of weeks, it could be possible because of early detection and medical management. So the dengue infection should be included in the list of viral infections associated with the prolonged neonatal cholestasis.

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