CASE REPORT

A Case Study of Dual Infection of Dengue and COVID-19: Presenting as Multiorgan Dysfunction in an Infant

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ABSTRACT

Dengue is a major health concern in South Asian countries transmitted by bite of day breeder mosquitoes Aedes aegypti and Aedes albopictus. Severity of plasma leak, shock, bleeding tendency and other organ dysfunction can be more pronounced in infants. The management becomes further complicated in the presence of a co-existing COVID-19 infection. Although COVID-19 infection is usually asymptomatic or has mild manifestations in children, however in presence of serious co-infection like dengue it can modify the course of the illness and lead to drastic consequences. Here, we present one such case of a 9-month-old female child who tested positive for dengue as well as COVID-19 during the ongoing corona pandemic and went on to develop shock, encephalopathy with deranged liver enzymes but managed to overcome all odds and recover from the disease by day 14 of illness.

KEYWORDS: severe dengue, COVID-19, co-infection, infant

BACKGROUND

Dengue fever is the most rapidly spreading mosquito-borne viral disease worldwide with an unpredictable clinical course and outcome [1, 2]. Most cases are usually mild which do not require hospitalization; however, few have the tendency to develop severe complications like shock, bleeding manifestations, encephalopathy with seizures, hepatic failure, renal failure, cardiac arrhythmia, myocarditis etc. Risk increases manifold in infants, young children and children with co-morbidities. The burden of severe illness lies predominantly in infants 4–9 months of age in the pediatric age group [3]. Manifestations such as convulsions and hepatic dysfunction more commonly affect infants than older children, and the fatality rate is four times higher in infants [4].
COVID-19 infection in children is usually mild or an incidental finding but recent reports from Europe and North America have described clusters of children and adolescents with SARS-Cov-2 infection presenting with acute illness accompanied by a hyperinflammatory syndrome, leading to multiorgan failure and shock with features similar to those of Kawasaki disease and toxic shock syndrome [5–7]. Thus, presence of a dengue and SARS-CoV-2 co-infection is likely to alter each other’s clinical course leading to heightened complications and worse outcomes.

CASE REPORT

A 9-month-old previously healthy and developmentally normal female child was admitted with history of fever for 4 days, diarrhea for 1 day at the onset of fever, lethargy, reduced appetite for 2 days and multiple episodes of seizures for 1 day. She was also noted to have a generalized non-pruritic erythematous skin rash and edema of limbs but no bulbar conjunctivitis, cracked lips, strawberry tongue, hepatosplenomegaly and lymphadenopathy. There was no associated history of bleeding tendencies, cough, cold, ear discharge, pain abdomen, crying during micturation or foul smell urine. On attending emergency, she was found to be in status epilepticus with Glasgow Coma Score (GCS) score of 8/15, SpO2 of 80% in room air, tachycardia (HR — 180 b/min), cold extremities, capillary refill time 4 s and hypotensive (BP 68/46, MAP 52). The child was intubated and immediately put on ventilatory support. Circulation was stabilized with 0.9% NaCl bolus followed by adrenaline infusion (0.2 μg/kg/min) and simultaneously status epilepticus controlled emergently with lorazepam bolus (0.1 mg/kg) followed by phenytoin infusion (20 mg/kg) and subsequently injection levetiracetam (60 mg/kg). As the child was throwing intermittent motor convulsion midazolam infusion was initiated and titrated upto 12 μg/kg/min for complete cessation of seizure activity.

At this juncture keeping epidemiological and clinical background in mind, we thought of possibilities of multisystem inflammatory disorder in children and adolescents (MIS-C) associated with COVID-19 infection, severe dengue, septic shock, acute encephalitis syndrome and scrub typhus with multi-organ involvement. Intravenous ceftriaxone (100 mg/kg/day), vancomycin (60 mg/kg/day), acyclovir (500 mg/m²) and doxycycline (5 mg/kg/day) was started empirically. Initial investigations revealed anemia (Hb — 7.4 g/dl), thrombocytopenia (53 000/ cmm), total leukocyte count (TLC) — 7500/cmm (57% neutrophil and 37% lymphocytes), procalcitonin (1.18 ng/ml), markedly elevated hepatic enzymes (SGPT — 1000 U/l, SGOT 4756 U/l), deranged coagulation profile with PT — 21.9 s, INR 1.57, APTT > 180 s, hyper-ferritinemia (serum ferritin — 19 226 ng/ml), very high LDH (3544 U/l), raised CRP (13.7 mg/dl), low fibrinogen (133 mg/dl). Bedside echocardiography did not reveal any myocardial dysfunction or coronary artery anomalies and follow-up scanning on days 3, 7 and 10 of hospitalization did not show any change. Lung ultrasound showed mild pleural effusion, which did not change on serial scanning. She eventually tested positive for Dengue NS1 (57.07) and Dengue IgM (30.98) by Mac Elisa. Nasopharyngeal swab for COVID-19 Real Time-Polymerase Chain Reaction (RT-PCR) was negative but bronchoalveolar fluid sample for SARS-CoV-2 qualitative Real Time PCR turned positive. Blood culture did not show any growth. Serology for Scrub typhus, Leptospira and Chikunguniya was negative.

In light of the persistent high grade fever, breakthrough seizure on reduction of midazolam infusion rate, inability to reduce inotropic support and presence of high inflammatory markers, methylprednisolone was started (10 mg/kg/day) for 3 days followed by oral prednisolone for 7 days on tapering dose. Twelve hours later her fever spikes settled and inflammatory parameters rapidly decreased (Table 1) after 24 h. Cerebrospinal fluid (CSF) study was done after stabilization on day 3 of illness showed a cell count of 5 cells/cmm, all mononuclear with normal sugar levels and slightly elevated protein levels (116 mg/dl). Dengue IgM was positive in CSF. Multiplex PCR of CSF sample was negative for other viral and bacterial panel. Antibiotics deescalated and midazolam infusion tapered gradually and inotropic support reduced to minimum and child was extubated on day 6 of illness. Rest of the hospital stay was uneventful expect two episodes of breakthrough
convulsion which was managed by adding sodium valproate. EEG revealed encephalitic changes. MRI brain (Fig. 1) was normal except mild cortical shrinkage. Child was discharged on 14th day with normal neurological status and on levetiracetam and sodium valproate. Her repeat nasopharyngeal sample for COVID-19 RT-PCR was negative. Parents were counseled and asked to return for follow-up after 14 days for assessment of neurological status and EEG.

DISCUSSION
Infants in the age group of 4–9 months are high-risk group for severe dengue due to effects of maternal antibody enhancement of dengue illness, leading to higher predisposition to plasma leak, shock and hemorrhagic tendency in comparison to older children and adolescent [8]. On the other hand though SARS COVID-19 infection thought to cause less severe disease in children, recent reports of unprecedented surge of hyperinflammatory state leading to multiorgan dysfunction (MIS-C) and intensive care admission has raised serious concern [5]. The largest cohort (186) of MIS-C patients published by Feldstein et al has shown that 73(39%) was COVID-19 RT-PCR positive [9]. Signs and symptoms of these two entities can overlap significantly and can be difficult to distinguish. Coexistence of Dengue and COVID-19 infection can modify the disease course and contribute to severity.

Our patient presented with fever, gastrointestinal symptoms, rash followed by refractory convulsion and shock. She also had anemia, thrombocytopenia, grossly deranged liver enzymes and high inflammatory markers like hyperferritinemia. Both severe dengue and MIS-C can present with similar clinical scenario. However MIS-C is more common in older children. In American cohort, out of 186 only 13 (7%) were infants and in UK cohort out of 78 only 2 (3%) were <1 year of age [9, 10]. Median CRP was 264 (192–316) in pediatric inflammatory multisystem syndrome on day 1 [10]. In contrast our patient had maximum CRP of 43.5 mg/dl. Severe thrombocytopenia is not prominent feature in COVID-associated inflammatory multisystem disorder. Median platelet was 125 × 10^9 cell/l (75–178) on day 1 in UK cohort [10]. Our patient had platelet count 53 000/cmm at presentation. Moreover in diagnostic criteria of MIS-C one important criterion is to exclude other obvious microbiological cause. Our patient was positive for dengue IgM antibody.

Co-infection of dengue and COVID-19 in children with severe multiorgan dysfunction has not been reported previously. Epelboin et al. [11] reported COVID-19 and dengue co-infection in a 40-year-old returning traveler and Verduyn et al. [12] published combination of these dual infections in an 18-year-old male adolescent. None of these two patients had severe manifestation. In areas where tropical disease like dengue fever are endemic, during the time of COVID-19 pandemics presence of dual infection can result in extra burden on healthcare. Also during the peak of COVID-19 pandemic in our country and intermittent lockdown it is difficult for regular follow-up of the patient.

CONCLUSION
In endemic areas clinicians need to consider dengue and COVID-19 in the differential diagnosis of acute
febrile illnesses. Both dengue and COVID-19 can cause severe illness that requires more aggressive therapy and prolonged monitoring.

**Ethical approval:** Ethical approval was not sought as this is a case report. Care has been taken to avoid any breach of privacy of the patient.

**Informed Consent:** Informed consent was taken from both parents prior to writing the case report.

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