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CASE SERIES OF ATYPICAL PRESENTATIONS OF DENGUE IN CHILDREN

Ratan Kumar[1*] and Adyasha Mishra[2]

[1]Pediatric Intensivist, Department of Pediatrics, Tata Main Hospital and Manipal Tata Medical College, Jamshedpur, India.
[2]Post Graduate Student, Department of Pediatrics, Tata Main Hospital, Jamshedpur, India.

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***Corresponding Author: Ratan Kumar**
Pediatric Intensivist, Department of Pediatrics, Tata Main Hospital and Manipal Tata Medical College, Jamshedpur, India.

ABSTRACT
Dengue infection typically manifests with a course of 3 phases. Initial **Febrile phase** is characterized by fever, body ache, bone pain, muscle pain, and generalized weakness. Next, **critical phase** starts with defervescence and is characterized by bleeding and increased capillary permeability leading to third spacing of fluid and shock. Finally, stabilization of hemodynamic parameters and diuresis is seen in **convalescent phase**. Here, we present a series of 4 cases of dengue in children presenting differently from the typical course of illness. First case is of a 12 year 8 months old male who presented with status epilepticus on day 1 of illness. Second case is of infantile dengue, who presented with acute gastroenteritis and hypovolemic shock on day 2 of fever. Third case, 14 year 4 months old male, who presented with syncope followed by shock and acute kidney injury (AKI) stage 1. Fourth case is of 14 years old male who presented with shock on Day 1 of illness and then with hyperinflammatory response. All 4 cases required intensive care and recovered completely with appropriate and timely treatment. This case series highlights that deviation from natural course of illness in dengue is frequent in children. High index of suspicion in dengue endemic region and early diagnosis helps in improving outcome.

KEYWORDS: Dengue, Atypical, Expanded Dengue Syndrome, Hyperinflammation.

INTRODUCTION

In 1997, World Health Organization (WHO) classified dengue into 3 groups: dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).[1] In 2009, WHO revised the classification as dengue without warning signs, dengue with warning signs, and severe dengue.[1] Dengue shock can lead to reduced perfusion of various organs and manifestations due to organ dysfunction. Other mechanisms like immune-mediated injury, direct viral invasion, co-infection, plasma leakage, and hypoxic injury can also lead to organ dysfunction and atypical manifestations.[2] In 2012, WHO grouped these dengue cases with atypical manifestations that cannot be classified into DHF or DSS into "Expanded Dengue Syndrome" (EDS).[3] This is a series of four dengue cases in children presenting atypically.

CASE SERIES

Case 1:

A 12-year-8-month-old male presented with repeated vomiting and status epilepticus on day 1 of fever, which was managed with anti-seizure medication (lorazepam followed by phenytoin) and anti-edema measures, along with other supportive treatment. After post-ictal state, there was no neurological deficit. No abnormality was found in fundoscopy, CT (Computed Tomography) scan Brain and CSF (Cerebrospinal fluid) examination (including viral panel). Dengue ELISA NS1 was positive, and Scrub ELISA IgM was negative. His sensorium improved following the day of presentation, and he was discharged after 9 days of hospital stay with improved clinical and laboratory parameters. On follow-up till next 2 months, he remained asymptomatic on phenytoin.

Case 2

A 5-month-old male infant presented with features of severe dehydration and hypovolemic shock following multiple episodes of loose stools and vomiting on 2nd day of fever. He received a bolus of normal saline on admission in emergency department and shifted to PICU (Pediatric Intensive Care Unit). Further fluid correction was given as per WHO guidelines, with which hydration and hemodynamic parameters improved. Initial normal anion gap metabolic acidosis improved with dehydration

correction. Dengue NS1 ELISA was positive. Blood and urine cultures were sterile. After 6 days of hospital stay, he was discharged with improvement in clinical and laboratory parameters.

Case 3

A 14-year 4-month-old male was admitted with syncope but no features of shock on day 2 of fever. He was started on maintenance IV (intravenous) fluid along with other supportive management. Three hours after hospitalization, he developed hypotensive shock [cold peripheries with prolonged capillary refill time, wide pulse pressure with rising lactate (highest being 4 mmol/L)], and reduced urine output, for which he was managed as decompensated dengue shock protocol. As he remained hypotensive despite 2 boluses of crystalloid and functional echocardiography showed distended inferior vena cava (IVC) with mild cardiac dysfunction (Left Ventricular Ejection Fraction 50%), adrenaline infusion was started. Dengue NS1 ELISA was positive. Blood and urine cultures were sterile. Other investigations showed raised C-reactive protein, indirect hyperbilirubinemia with normal liver enzymes, and acute kidney injury—stage 1. Empiric antibiotic and other supportive treatment were continued. With improvement in hemodynamic parameters, adrenaline was weaned and stopped over next 24 hours. He was discharged after 8 days of hospital stay with improved clinical and laboratory parameters.

Case 4

A 14-year-old male adolescent was admitted in decompensated shock on day 1 of fever. Fluid bolus was given, following which hemodynamic parameters improved. Further fluid management was continued as per dengue protocol, and IV fluid was weaned and stopped over 48 hours. Dengue NS1 ELISA was positive. On 3rd day of illness, IV fluid was restarted for compensated shock, and IV antibiotic was added for suspected bacterial infection. He developed respiratory distress on 4th day of illness, for which he was supported with oxygen by high flow nasal cannula. Functional two-dimensional echocardiography showed full IVC with good respiratory variation, good biventricular function, and no pericardial effusion. However, abdominal ultrasonogram revealed diffuse inflammatory changes with serositis, and right sided pleural effusion was noted in chest x-ray. Fever spikes were persistently present, even beyond febrile period of dengue. Other infectious causes for fever were negative. Inflammatory work up revealed very high serum ferritin (>15000 ng/ml) along with raised D-dimer, triglyceride, and lactate dehydrogenase, which supported a diagnosis of dengue fever with hyperinflammatory syndrome. Hence, IV dexamethasone was started. Fever spikes and respiratory distress gradually subsided; respiratory support was weaned off. With clinical improvement, the adolescent was discharged after 8 days of hospital stay.

Table 1: Brief of 4 cases.

Case no.	Age/ Sex	Presentation	Organs Involved	Hospital Stay	Outcome
1.	12 Y 8 M / M	Status epilepticus	CNS, Hematology	9 days	R (D/A)
2.	5 M/ M	AGE + hypovolemic shock	CVS, GI	6 days	R (D/A)
3.	14 Y 4 M / M	Shock	CVS, Renal, Hematology	8 days	R (D/A)
4.	14 Y/ M	Shock + Hyperinflammation	CVS, Respiratory, GI, Hematology	8 days	R (D/A)

*[**Abbreviations for Table 1:** Y = Years; M = Months; CNS = Central Nervous System; CVS = Cardiovascular System; GI = Gastrointestinal; R = Recovery; D/A = Discharged with Advice]*

Table 2: Investigation Summary of All 4 cases.

Parameter	Case 1	Case 2	Case 3	Case 4	Normal range & Unit
Highest Hemoglobin (Hb)	13.1	10.8	14.8	13.7	11.5-16.5 g/dl
Highest Haematocrit (HCT)	41.7	35.1	46.5	44.7	35-50 %
Lowest Total Leukocyte Count (TLC)	2740	7580	3290	3410	4000-11000 per cumm
Lowest Platelet Count	31,000	1,35,000	62,000	30,000	150000-450000 per cumm
Highest C-Reactive protein	0.27	0.85	9.26	1.78	0.08-0.79 mg/dl
Highest Blood Urea	30.5	115.9	31.2	24.8	18-45 mg/dl
Highest Serum Creatinine	1.04	0.83	1.09	1.78	0.5-1.5 mg/dl
Highest Serum Bilirubin	0.39	0.21	2.04	0.97	0.2-1.0 mg/dl
Highest Alanine Aminotransferase (ALT)	31.5	34.8	22.1	419.3	5-45 U/L
Highest Aspartate Aminotransferase (AST)	52.1	68.7	40.7	1088.6	0-35 U/L
Lowest pH	7.41	7.24	7.44		7.35-7.45
Lowest PCO2	31	30.1	32		35-45 mmHg
Lowest HCO3-	20.8	14	22.5		20.8 mmol/L

DISCUSSION

Dengue illness follows 3 phases: Febrile, Critical, and Convalescent. Complications like plasma leakage and shock usually present in critical phase once child becomes afebrile.[4]

Hyperinflammatory response to infection is defined as persistent fever with one of the following. marked hyperferritinemia, cytopenias, hepatomegaly and/or splenomegaly, or hemophagocytosis.[5]

Fever with seizures has been reported in children with dengue meningoencephalitis.[6] Other than direct viral invasion, immune-mediated injury, capillary hemorrhage, disseminated intravascular coagulation, metabolic imbalance (dyselectrolytemia and metabolic acidosis), and cerebral edema have been seen to cause seizures in dengue.[7]

Common neurological manifestations of dengue include encephalopathy, encephalitis, acute symptomatic seizure, syncope, optic neuritis, and Guillain‑Barre syndrome (GBS). **Dengue encephalopathy** is defined as dengue fever with reduced consciousness secondary to shock, metabolic abnormality, hypotension, hepatic failure, or renal failure with normal CSF finding. **Dengue encephalitis** is defined as dengue fever with acute signs of cerebral involvement in absence of any metabolic abnormality, or any other explanation for reduced consciousness with any one of the following: CSF pleocytosis (CSF corrected white blood cell count >5 cells/mm3), focal neurological signs, seizures other than simple febrile seizures, abnormal imaging consistent with encephalitis, presence of dengue IgM antibodies in CSF or CSF positive for dengue PCR.[8] **Acute symptomatic seizure** is defined as seizure in a patient with dengue fever with altered sensorium during post‑ictal phase lasting for a maximum duration of 48 hours. **Syncope** is defined as transient loss of consciousness with immediate post‑event recovery without tonic‑clonic movements. **Optic neuritis** is defined as impairment of visual acuity and colour vision due to inflammation of optic disc in the setting of dengue infection.[9] **Guillain‑Barre syndrome (GBS)** is defined as acute, severe polyradiculoneuropathy in the setting of dengue fever.[10] **Posterior reversible encephalopathy syndrome (PRES)** is defined as acute onset neurological deficit with characteristic bilateral symmetrical white matter hyperintensities on magnetic resonance imaging (MRI) in the setting of dengue.[11] Other neuromuscular manifestations of dengue include stroke, myoclonus, brachial plexopathy, hypokalemic paralysis, and myositis.

Gastrointestinal symptoms in infantile dengue have been reported in more than one-fourth of patients[12], but gastroenteritis in dengue leading to hypovolemic shock on day 2 of illness (febrile phase) is unusual. Other uncommon gastrointestinal complications of dengue includes acute hepatitis and hepatic failure, acalculous cholecystitis, and acute pancreatitis.

The patients were followed up till 2 months of discharge from the hospital. All of them presented with atypical and serious features of dengue, but they recovered without complications as they were diagnosed early based on epidemiological characteristics.

CONCLUSION

This case series emphasizes that dengue in children frequently presents differently from the typical course of three phases. The awareness of pediatrician and high index of suspicion in dengue endemic regions or during dengue outbreak helps in early diagnosis and streamlined management leading to improved outcome.

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