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Case Report

Severe Dengue Infection in a Pediatric Case of Kidney Failure: Lesson Learned From a Management Perspective

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ABSTRACT

Background and Aim: Dengue viral infection has become a major public health concern worldwide. This situation worsens when accompanied by other comorbidities. There is a lack of published literature on dengue viral infection in pediatric patients with kidney failure undergoing maintenance hemodialysis.

Case Presentation: We report the case of a child with kidney failure who underwent maintenance hemodialysis and presented with dengue shock syndrome.

Conclusion: Prompt diagnosis, close monitoring, and individualized treatment regimens are crucial for patient survival. A significant dilemma exists in managing such cases that may guide physicians in the future.

Keywords: Severe dengue, Kidney failure, Hemodialysis, Fluid challenge, Children

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Introduction

Dengue fever is an arboviral infection caused by the dengue virus, transmitted through the bite of the Aedes-egypt mosquito. The virus belongs to the flavi-viridiae family having four serotypes-dengue viruses (DENV) 1, 2, 3 and 4. Dengue viral infection (DVI) is prevalent worldwide in many tropical and sub-tropical regions [1]. The disease has become a major public health concern in many Southeast Asian countries, and is a leading cause of morbidity and mortality in the pediatric population. The demographic changes in these countries, with the rapid population growth and urbanization, have put them at risk of dengue epidemics [2].

The clinical manifestations of DVI may vary from asymptomatic or milder forms, dengue fever (DF) to more severe and fulminant forms, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [3]. The prevalence of severe dengue (DHF/DSS) is reportedly higher in patients with kidney failure undergoing maintenance hemodialysis (HD) [4]. Careful fluid replacement and monitoring are the most crucial issues for HD maintenance in these patients compared to the general population. Their HD prescription may also need to be altered due to the increased risk of fluid overload and bleeding [5].

Currently, there are no guidelines for managing DVI in these special groups of adults and children. Here, we present a pediatric case of kidney failure presenting with maintenance HD with DSS, successfully managed with good recovery in a tertiary health care center in Bangladesh, which has experienced the worst dengue crisis in recent years.

Case Presentation

A 12-year-old boy with kidney failure due to post-surgical obstructive uropathy following blunt abdominal trauma during a motor vehicle accident in 2016 presented with high-grade, persistent fever and loose stools for 4 days and lethargy for 1 d. Fever was not associated with chills or rigor. He denied blood or mucous in stools but complained of vomiting and abdominal pain.

He was diagnosed with kidney failure in January 2023 and since then has been receiving HD via central venous HD catheter twice a week. The patient had good residual renal function (urine output 500-600 ml/day). Due to financial constraints, he had been receiving dialysis once a week for 3-4 h, against the physician's advice. He had a last HD session seven days before admission because his caregivers had been suffering from dengue fever. His maintenance medications included nifedipine, prazosin, metoprolol, folic acid, zinc supplements, calcium and sevelamer.

On examination, he was pale, lethargic, had cold extremities, pulses were not palpable, blood pressure (BP) was non-recordable, capillary refill >3 s, blood oxygen saturation (SPO_2) 90% in room air; he was in cardiovascular shock. A skin survey revealed no rashes or bleeding spots. Abdominal examination revealed tenderness and ascitic fluid. There was evidence of bilateral leg edema.

His blood sample was sent and the dengue non-structural protein 1 (NS1) rapid test was positive. He had thrombocytopenia (86,000/mm^3) with low hematocrit (HCT) (29.1%) on arrival. Figure 1 and Table 1 present the clinical course. Figure 1 shows the frequency of dialysis administered to this patient on different platelet counts. Table 1 presents the fluid management of various blood pressure measurements in this patient.

On arrival, he was in frank shock, and the volume was restored by a normal saline bolus of 20 mL/kg, followed by a gradual reduction as per guideline to 1.5 mL/kg/hr. On day two, after hypotension, fluid re-accumulation continued until day three of hospitalization, followed by several hemodialysis sessions with packed RBC and platelet transfusion due to massive hemoptysis.

The patient was discharged after 14 days of hospitalization with full recovery. All oral medications, including anti-hypertensives and HD regimes (with heparin) were prescribed accordingly.

Discussion

In recent years, dengue viral infection has emerged as a serious public health concern by World Health Organization (WHO). Bangladesh, a South Asian country, has been dengue-endemic since 2000. Dhaka, the capital city, is hyperendemic to dengue virus. Low and lower-middle-income countries like ours are vulnerable to dengue infection due to their higher population density, rapid unplanned urbanization, global warming-induced climatic changes, and poor healthcare systems [6]. Our case concerns the densely populated area of Dhaka City.

During the 2019 outbreak, a hospital-based study found that most children belonged to the 10-14 age group, as observed in other Asian countries. Younger age is associated with severe disease progression [6]. Our patient was

Table 1. Summary of fluid regime, hemodialysis regime, blood Investigations and other management of severe dengue with Kidney failure Patients

H/S	Physical Findings/ Key Events, Fluid Regime, and HD Regime (Heparin Free)	CBC Profile	Other Lab Profile
Day-1	Features of frank shock (Pulse absent, BP-non-recordable) ↓ N/S bolus - 20 ml/kg-stat ↓ Volume Restored ↓ Rate of IVF reduction 7 ml/kg/hr > 5 ml/kg/hr > 3 ml/kg/hr > 1.5 ml/kg/hr	Hb%: 9.9 TC: 5500 PC: 86 000 HCT: 28%	Renal function status S. Creatinine: 8.88 mg/dL S. Urea: 199.2 mg/dl S. Electrolyte: Na/K/Cl/TCO_2: 140/5.29/107.6/15.2
Day-2	Features of hypotension ↓ Rate of IVF increased 1.5 mL/kg/h < 3 mL/kg/h < 5 mL/kg/h	Hb%: 8.9 TC: 4000 PC: 50,000 HCT: 29.1%	
Day-3	Features of fluid overload ↓ SLEDwith Albumin ↓ Gum bleeding ↓ RCC	Hb%: 8.8 TC: 6000 PC: 25,000 HCT: 28.1	Liver function status: SGPT: 11.4 U/L SGOT: 68.7 U/L S. Albumin: 3.3 g/dl PT: 13.3 sec APTT: No coagulation INR: 1.11
Day-4	SLED with FFP (as APTT revealed no coagulation) ↓ SLED discontinued (after 2 h) as massive bleeding started (Melena, hemoptysis, bleeding from CV line) ↓ 3 units of RDP	Hb%: 7.5 TC: 6,830 PC: 19,000 HCT: 22.7	
Day-5	The bleeding stopped Fluid regime-1.5 mL/kg/h, then discontinued	Hb%: 8 gm/dL TC: 7300/mm^3 PC: 30,000/mm^3 HCT: 24.6	RFT S. Creatinine: 1.2 mg/dL S. Urea: 15 mg/dL S. Electrolyte Na/K/Cl/TCO_2: 134/2.5/93.8/24.3

Abbreviations: BP: Blood pressure; CBC: Complete blood count; Hb: Hemoglobin; TC: Total count; PC: Platelet count; HCT: Hematocrit; SGPT: Serum glutamate-pyruvate transaminase; SLED: Sustained low-efficiency dialysis; FFP: Fresh frozen plasma; APTT: Activated partial thromboplastin time; CV: Central venous; RDP: Random donor platelet; RFT: Renal function tests; Na: Sodium; K: Potassium; Cl: Chloride; TCO_2: Total carbon dioxide; IVF: In vitro fertilization; INR: International normalised ratio.

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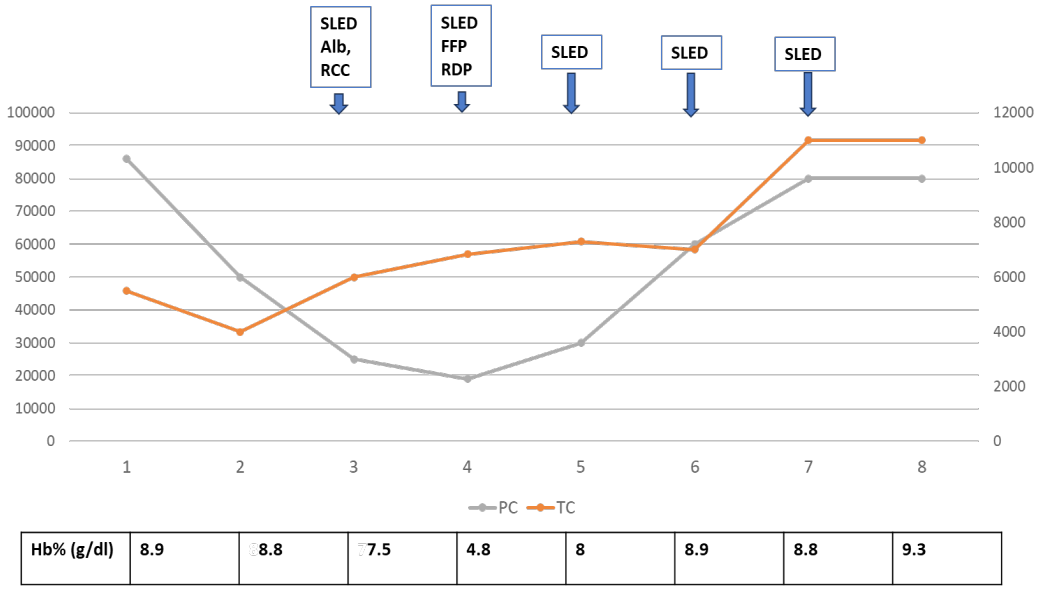

Hb% (g/dl)	8.9	8.8	7.5	4.8	8	8.9	8.8	9.3

Figure 1. Hemodialysis regimen along with albumin or blood and blood product transfusion during the hospital course

Abbreviations: PC: Platelet count; TC: Total count; SLED: Sustained low-efficiency dialysis; Alb: Albumin; RCC: Red cell concentrate; FFP: Fresh frozen plasma; RDP: Random donor platelet.

a 12-year-old boy with pre-existing comorbidity who passed a challenging clinical course.

The clinical course of DF typically starts with fever, headache, body aches, flushing, rash, nausea, and vomiting [5]. It has a wide spectrum of clinical features, ranging from simple febrile illness to severe life-threatening courses, such as plasma leakage, organ impairment, bleeding, and death in extreme cases [7]. During the 2019 outbreak, gastrointestinal (GI) symptoms were the most common presentation, along with fever and lethargy among children [6]. Our patient presented with fever, gastrointestinal symptoms and lethargy.

DHF is primarily characterized by signs/symptoms similar to those of DF. After that, plasma leakage is initiated which is the hallmark of this entity [7]. DSS is defined as DHF with features of circulatory failure, such as hypotension, narrow pulse pressure20 mm-Hg or frank shock. Warning signs include abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, hepatomegaly (size >2 cm below the edge of the rib), raised HCT, and concurrent rapid decline of platelets [8]. Pre-existing comorbidities, such as kidney failure, are crucial predictors of severe dengue. It has been previously reported that adult kidney failure patients on maintenance HD are more vulnerable to severe dengue/DHF/DSS than the general population due to the complex pathophysiology of kidney failure associated with DHF [4]. There is an extreme lack of pediatric literature in this regard. Moreover, our patient was on maintenance hemodialysis and kidney failure presented with DSS with multiple warning signs.

Diagnosis of DVI in ESRD patients is more difficult due to their immunocompromised state, constant exposure to many procedure-related infections, and dialysis-related complications [5]. There are significant similarities between uremia and dengue warning signs [4]. A high index of suspicion, detailed history taking and recent stay in the dengue hotspot are useful for prompt and accurate diagnosis of DVI in dialysis patients with kidney failure. Co-infection should always be a crucial concern for physicians dealing with them as it may worsen the situation [9]. As per our case, a high index of suspicion arose from the beginning because he resided in a hyperendemic city. Recently, his caregivers had been suffering from DVI, making early diagnosis possible.

The common diagnostic tests include the detection of NS1 antigen rapid test within 72 hours of onset of fever (high sensitivity and specificity), dengue immunoglobulin M (IgM) within 3 to 7 days (low sensitivity and immunoglobulin G (IgG) antibodies after 7 days by ELISA (high sensitivity, very low specificity), viral genome detection by reverse transcription polymerase chain reaction (RT-PCR) and virus isolation by mosquito inoculation technique and cell culture in C6/36 cell line. Despite their low specificity, serological tests are widely available and are cheaper. Detecting viral nucleic acids or antigens has higher specificity, although it is not avail-

able in all settings [10]. Our patient tested positive NS1 antigen for dengue.

Pre-existing anemia and relative thrombocytopenia in kidney failure patients on maintenance HD may also mask the hematological presentation of DVI. The HCT level correlates well with the plasma leakage features and dengue severity in the general population. The risk of misinterpretation of these data is increased among DF patients with anemia of chronic disease along with hemorrhage and fluid overload. Our patient had anemia, low HCT and thrombocytopenia [5].

Fluid replacement is a cornerstone of DSS management. If inadequate, it leads to refractory shock and increases mortality risk [11]. The amount of fluid recommended by the WHO may lead to hypervolemia and pulmonary edema in patients with ESRD on dialysis due to the presence of anuria. They are more prone to develop intradialytic hypotension due to plasma leakage when associated with DHF/DSS [4]. Therefore, these patients must monitor fluid status and optimal fluid replacement. In the case of kidney failure in dialysis patients, urine output cannot be a monitoring tool for fluid status, as in non-KF dengue patients. If these patients develop fluid overload, they may eventually require dialysis [12]. Our patient presented with features of frank shock and anasarca. He missed the HD schedule last week. He may have had concurrent plasma leakage and fluid overload. An IV normal saline bolus was administered as the first-line fluid regime to restore the volume status. Subsequently, fluid replacement was titrated meticulously according to his volume status, assessed by his vital signs, capillary refill time (CRT), mucosa, and skin turgor other than urine output. After that, he developed features of fluid overload that were more pronounced than plasma leakage. Slow, low-efficiency dialysis (SLED) was initiated along with colloid (albumin), and this situation was challenging for pediatric nephrologists to make appropriate decisions in this vulnerable situation.

Severe bleeding is a crucial complication of DHF due to thrombocytopenia and coagulopathy-causing mortality [13]. Platelet dysfunction and the use of heparin during HD increase bleeding tendency in dialysis patients with kidney failure [14]. This bleeding diathesis may worsen the situation. The decision to transfuse blood and blood products should be judicious, as unnecessary transfusion may result in fluid overload and hyperkalemia [15]. Our patient received fresh frozen plasma (FFP), whole blood, and RDP due to massive bleeding. We prescribed heparin-free HD until a sufficient platelet count and clinical recovery were achieved. Currently, no guidelines exist regarding the duration of heparin withdrawal during HD in this situation. The HD prescription was tailored according to the patient's clinical condition, hemodynamic status, and blood parameters. For this critically ill patient, continuous renal replacement therapy (CRRT) is the best option to exert less strain on the patient's cardiovascular system [5, 11]. Unfortunately, we considered SLED because CRRT was not available at our center.

In addition to fluid replacement, acid-base, and electrolyte balances are crucial issues. These patients have a greater chance of developing acidosis and electrolyte imbalance [8], which was addressed and managed accordingly, in our case using dialysis alone. All BP medications were adjusted accordingly along with other supportive measures.

A few similar cases have been reported, but all involved adults. To our knowledge, no pediatric literature has been published on this scenario. Among the available cases, a 77-year-old man with underlying hypertension and end-stage renal failure on regular hemodialysis was treated for dengue fever with intravenous drip, while antihypertensive, and antiplatelet, hemodialysis prescriptions were adjusted according to his fluid status [5]. Three other patients were reported, all of whom died due to diagnosis and treatment dilemmas [12]. One patient had diabetes, one had a refractory shock, and one had gout and convulsions, which differed from our patient.

Conclusion

We successfully managed a critically ill pediatric patient discharged with full recovery. More research is required on children with kidney failure undergoing dialysis who are infected with severe dengue to establish management guidelines and improve their survival outcomes.

Lesson learned

• A very small margin exists from hypovolemia to hypervolemia in kidney failure patients with severe dengue infection.

• A very high index of suspicion is required for physicians working in dengue-endemic areas.

• Fluid and bleeding management are crucial.

• SLED or CRRT is the choice of modality for these patients on maintenance hemodialysis.

• Using both crystalloid and colloid solutions is the mainstay of fluid management.

• Severe bleeding can be managed by appropriate blood product transfusion but must be judicious.

Ethical Considerations

Compliance with ethical guidelines

No ethical considerations were considered in this study.

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Authors' contributions

Conceptualization: Abdullah Al Mamun and Afroza Begum; Methodology, Software, Data curation, Formal analysis, Writing—original draft preparation, Visualization, and Resources: Rummana Tazia Tonny; Validation: Abdullah Al Mamun, Afroza Begum, Rummana Tazia Tonny, and Aditi Chowdhury; Investigation: Aditi Chowdhury; Supervision and Writing—review and editing: Abdullah Al Mamun.

Conflict of interest

The authors declared no conflict of interest.

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