Case Report

A Very Rare Case of Expanded Dengue Syndrome with Acute Liver Failure, Rhabdomyolysis, Acute Kidney Injury and ARDS: Successfully Treated with Haemoadsorption, Hemodialysis, and Plasma Exchange

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Abstract:

Expanded dengue syndrome, accompanied by liver failure, rhabdomyolysis, acute kidney injury, and severe acute respiratory distress syndrome (ARDS), represents a highly lethal condition with a significantly elevated mortality rate. Conventional treatments are ineffective in addressing all these complications concurrently. This case report discusses a young male patient who underwent haemoadsorption, hemodialysis, and subsequently plasma exchange. The patient achieved full recovery without any residual impairment. This report presents the first instance of a dengue patient undergoing simultaneous haemoadsorption and hemodialysis, followed by plasma exchange.

Keywords: *Expanded Dengue Syndrome, Haemoadsorption, Plasma Exchange.*

Introduction:

Dengue fever is a viral infection transmitted by mosquitoes, commonly characterized by symptoms including fever, headache, and myalgia. In some instances, it may result in significant complications affecting multiple organ systems, known as expanded dengue syndrome (EDS). EDS includes atypical presentations that extend beyond the conventional categories of dengue fever, dengue hemorrhagic fever, and dengue shock syndrome.[1]

Rhabdomyolysis is an example of an atypical EDS manifestation. The process entails the degradation of muscle tissue, releasing intracellular components such as myoglobin into the bloodstream. Increased myoglobin concentrations can lead to acute kidney injury (AKI) through the obstruction of renal tubules and the induction of oxidative stress.[2]

AKI represents a notable complication associated with dengue infection. Dengue-associated AKI has a multifactorial pathogenesis, which includes direct viral injury, hemodynamic instability, and rhabdomyolysis.[3]

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Liver involvement in dengue infection is common and can cause catastrophic acute liver failure. Acute dengue infection might cause asymptomatic transaminase increase or fulminant hepatic failure.[4] Acute respiratory distress syndrome (ARDS) is another severe EDS symptom. ARDS, which is rarer, causes lung fluid accumulation due to increased vascular permeability and plasma leakage. This illness requires immediate diagnosis and extensive care.[5]

Managing EDS alongside complications like rhabdomyolysis, AKI, acute liver failure, and ARDS necessitates a collaborative, multidisciplinary strategy. Timely identification and comprehensive care are essential to reduce organ damage and enhance patient outcomes. We present a case of expanded dengue syndrome featuring rhabdomyolysis, acute renal failure, and acute liver failure accompanied by ARDS, which was successfully managed through haemoadsorption with hemodialysis, followed by plasma exchange.

Case Report:

A 24-year-old male presented to the emergency room of CMH Barishal on 14 December 2024 with a five-day history of fever and a concurrent dry cough. Investigations indicated a positive Dengue IgM test, a CBC showing a low platelet count of 52,000 x 10^9/L, and a serum bilirubin level of 2.0 mg/dl. Subsequently, he was admitted and received supportive treatment, which included normal saline. On December 15, 2024, an ultrasonogram indicated early hepatic parenchymal disease. Investigations revealed a platelet count of 37,000 x 10^9/L and a white blood cell count of 8,500 x 10^9/L. Haemoglobin measured 11.3 g/dl, serum bilirubin was 6.1 mg/dl, serum creatinine was 1.2 mg/dl, S. AST was 188 U/L, ALT was 44 U/L, and alkaline phosphatase was 81 U/L. HBsAg and anti-HCV results were negative. Antibiotics, specifically Cefixime, Ursodeoxycholic acid, and Eltrombopag olamine were initiated, accompanied by additional supportive measures, and it was recommended to

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arrange for two units of FFP.

On 16/12/2024, the patient was conscious and oriented and complained of persistent fever, but there was no history of respiratory distress and chest pain. Investigations revealed a platelet count of 21,000 x 10^9/L, a WBC count of 10,800 x 10^9/L, a hemoglobin level of 9.0 mg/dl, serum bilirubin of 8.3 mg/dl, ALT of 64 U/L, serum urea of 70 mg/dl, and serum creatinine of 3.5 mg/dl. In the afternoon, the patient experienced two episodes of hemoptysis and increasing shortness of breath, accompanied by a rising oxygen demand (SpO_2 60% with 10L of oxygen), leading to restlessness. He was intubated at 1600hrs due to his deteriorating condition refractory to diuretics. Later, he was Heli-evacuated to the emergency of CMH Dhaka, in a state of mechanical ventilation support, with severe hypoxia. His blood pressure was stable without any inotrope and vasopressor support. Then, the patient was shifted to the intensive care unit for further evaluation and management. After proper evaluation through clinical examinations and available laboratory investigations, he was diagnosed with a case of Expanded Dengue Syndrome with Rhabdomyolysis with Acute Kidney Injury with Acute Liver failure. He was on mechanical ventilation with sedation, maintaining saturation 94% with FiO_2 1, PEEP 18 cm H_2O, and pressure support of 10 cm H_2O on PCV mode. Upon admission to the ICU on December 16, 2024, initial laboratory findings indicated a hemoglobin level of 7.1 gm/dl, hematocrit of 21.7%, white blood cell count of 11 x 10^9/L, neutrophil percentage of 85%, platelet count of 41 x 10^9/L, and serum sodium, potassium, and chloride levels of 129, 4.71, and 92.08 mmol/L, respectively, with calcium at 8.4 mmol/L. Uric Acid: 3.5 mg/dl; Serum Urea: 86 mg/dl; Serum Creatinine: 4.17 mg/dl; Serum Bilirubin: 21.26 mg/dl; ALT: 65 u/L; AST: 112 u/L; ALP: 50 u/L. Albumin: 29 g/L; LDH: 975 u/L; S. Amylase: 1470 u/L. Lipase: 88 u/L; CPK: 8240 u/L; RBS: 6.2 mmol/L. Fibrinogen: 685 mg/dl; APTT: 26.3 seconds; PT: 16.4 seconds; INR: 1.24. Serum Procalcitonin was measured at 9.60 ng/ml, Troponin I at 1939.9 pg/ml, NT-pro BNP at 18987 pg/ml, and CRP at 24.9 mg/dl. Ultrasound of the whole abdomen was performed, which revealed reduced hepatic echogenicity, which may indicate hepatitis, accompanied by a thickened gallbladder wall, bilateral renal parenchymal changes, mild ascites, and minimal pleural effusion. Echocardiography findings indicate no regional wall motion abnormalities, with a left ventricular ejection fraction of 70%. The patient was initiated on renal dose-adjusted therapy. Injectable broad-spectrum antibiotics, antifungal agents, intravenous N-acetylcysteine, injection of L-ornithine L-aspartate, tablet form of ursodeoxycholic acid, and rifaximin tablets. We facilitated bowel movements a minimum of twice daily by administering lactulose syrup.

On December 18, 2024, the patient underwent hemodialysis utilizing a Biosky MG350 hemoperfusion cartridge due to elevated serum bilirubin levels (43.03 mg/dl), serum creatinine levels (5.7 mg/dl), serum urea levels (173 mg/dl), and worsening chest X-ray findings. The patient underwent three hemoperfusion sessions combined with hemodialysis from December 18, 2024, to December 22, 2024. On December 19, 2024, the patient developed a left-sided pneumothorax, necessitating a tube thoracostomy on the same date. Post-hemoperfusion, there was a significant reduction in CPK levels, accompanied by decreased oxygen requirements and improved lung function.

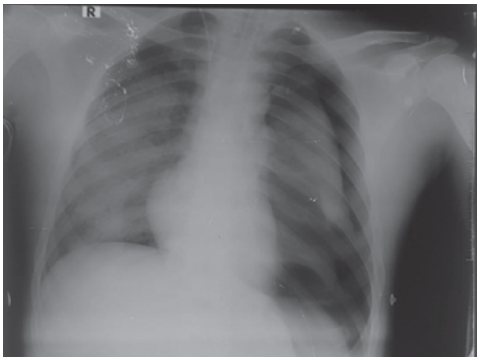


Fig 1: X-ray chest showing left-sided pneumothorax

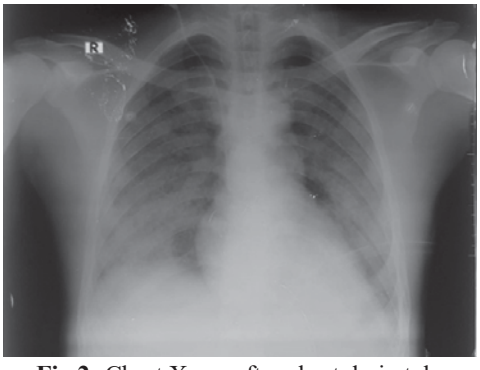
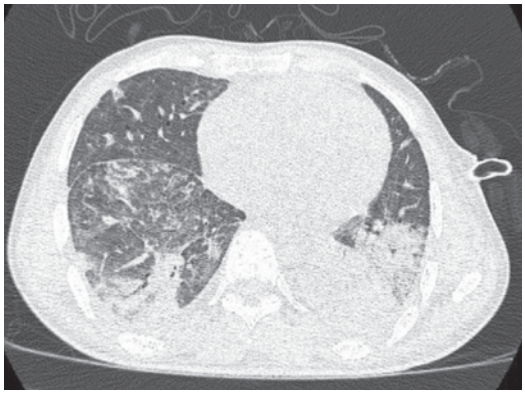


Fig 2: Chest X-ray after chest drain tube



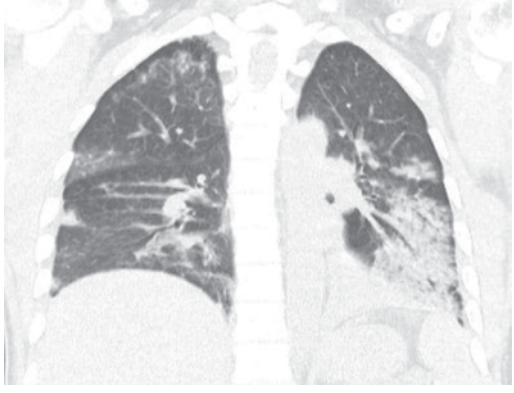


Fig 3 & 4: CT scan of chest showing bilateral pulmonary oedema & consolidation

Despite the administration of hemoperfusion and hemodialysis, the patient's condition did not improve, and serum bilirubin levels remained elevated. Between December 24 and December 26, 2024, the patient underwent three plasmapheresis sessions and received hemodialysis on December 25, 27, and 29, 2024. Serum bilirubin levels in the patient significantly decreased following plasmapheresis. The patient underwent extubation on December 27, 2024. Post-extubation, the patient's Glasgow Coma Scale (GCS) score was 15/15, and oxygen saturation (SpO_2) was maintained with 4 liters of oxygen via nasal cannula. The laboratory findings following each plasmapheresis procedure are presented in table I.

Table I: Blood biochemistry on different dates

	ICU admission	Before Haemo -adsorbtion	After Haemo -adsorbtion	Before TPE	After first TPE	After second TPE	After third TPE	Before ICU Discharge	Before Hospital Discharge
Date	16/12/24	18/12/24	22/12/24	24/12/24	24/12/24	25/12/24	26/12/24	18/01/25	29/01/25
ALT	65	75	72	75	40	29	36	295	88
AST	112	156	148	129	62	53	58	104	51
Total Bilirubin	21.26	43.03	40.2	36.13	21.85	18.66	13.33	4.36	2.2
INR	1.24	1.48	1.3	1.22	1.23	1.41	1.38	1.02	1.0
MELD Score	35	39	37	36	34	35	33	25	9
Haemoglobin	7.1	10.1	9	9.3	8.9	8.1	10	9.3	9
Platelet	41	186	113	231	239	317	384	315	290
S. CPK	8240	7220	1473	811	351	672	220	21	20
S. Creatinine	4.17	5.7	3.95	3.97	4.88	5.51	5.03	3.9	1.0

Before ICU discharge, the patient was conscious, oriented, and hemodynamically stable. The patient sustained a urine output of 60-70ml/hr without diuretics since December 30, 2024. On December 31, 2024, the left-sided chest drain tube was removed, and from January 1, 2025, the patient maintained a SpO_2 level in room air. The patient was transferred to the ward on January 18, 2025. In the ward, his renal and hepatic functions normalized to baseline levels. He was discharged home on January 29, 2025.

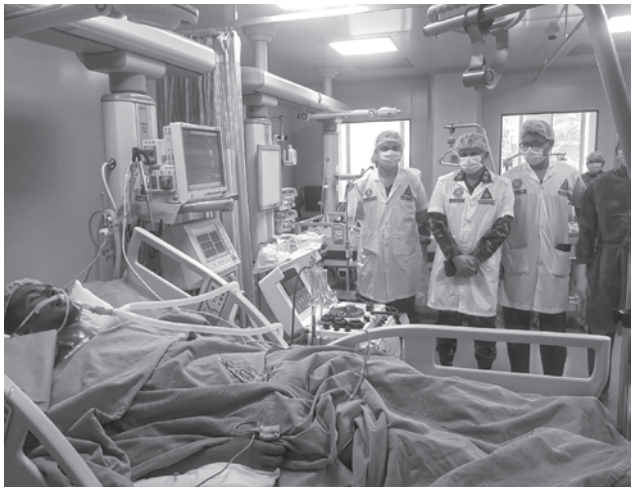


Fig 5: During the first session of plasmapheresis in the ICU of CMH Dhaka

Discussion:

Dengue infection represents the most widespread viral hemorrhagic disease in the subtropical and tropical areas of Southeast Asia, Africa, the West Pacific, and the Americas.[6-8] Dengue affects extensive areas globally, especially in Southeast Asia and the Indian subcontinent, where the initial outbreak was recorded in 1779 in Jakarta, Indonesia.[9-10] Annually, dengue is associated with roughly 400 million cases and 22,000 fatalities worldwide.[9] Clinical presentations range from mild transient fever to severe conditions with potentially life-threatening consequences, including dengue hemorrhagic shock syndrome.[11]

There have been few reports of rhabdomyolysis in dengue, and it is still unclear what pathophysiological process causes dengue rhabdomyolysis.[12] Myositis is thought to be caused by myotoxic cytokines, such as interferon-alpha (IFNα) and tumor necrosis factor α (TNFα), produced during dengue infection.[13] The CPK value in case reports that were published varied from 5000 to 325,000 U/L.

While acute liver injury is frequently seen in dengue infections, acute liver failure (ALF) is still uncommon.[6,7] Dengue infection can induce acute liver failure primarily by directly infecting hepatocytes, resulting in impaired liver function and subsequent cell death. The immune response exacerbates liver damage via cytokine release and inflammation, leading to hepatocellular injury.[14] Additionally, vascular leakage and coagulation disorders associated with severe dengue may impair microcirculation in the liver, leading to hypoxia and necrosis. These mechanisms markedly elevate the risk of acute liver failure in severe dengue cases.[15]

Hemoadsorption therapy has been investigated as an adjunctive treatment for severe dengue cases that exhibit

complications, including rhabdomyolysis, acute liver failure, and acute respiratory distress syndrome (ARDS). This extracorporeal method eliminates inflammatory cytokines and other harmful substances from the blood, which may reduce the systemic inflammatory response and avert additional organ damage.[2] Plasma exchange (PLEX), employing fresh frozen plasma (FFP), is advised as a treatment for acute liver failure (ALF) in conjunction with liver transplantation (LT), the definitive treatment.[16]

Therapeutic plasma exchange (TPE) is a medical procedure separating plasma from the cellular components of blood, replacing it with either an albumin solution or FFP.[17] PLEX was employed to manage dengue-associated acute liver failure by eliminating circulating toxins and pathological substances, including cytokines and viral particles. Plasma was substituted with FFP or albumin. PLEX stabilizes the biochemical environment, diminishes systemic inflammation, and facilitates liver recovery.[18] The procedure improves hemodynamics and addresses coagulopathies by restoring essential coagulation factors, potentially diminishing complications linked to severe dengue infection.[19] Supportive treatment is essential when liver function is significantly compromised, serving as a critical pathway to recovery or liver transplantation.[20]

The patient presented with rhabdomyolysis, acute kidney injury, severe acute respiratory distress syndrome (ARDS), and acute liver failure. Early haemoadsorption was considered due to the patient's elevated CPK levels and acute renal failure. The case report by Samarasingha et al. describes a 21-year-old patient with dengue fever who experienced severe rhabdomyolysis and acute kidney injury (AKI). Initial standard treatments proved ineffective, such as hydration and continuous renal replacement therapy (CRRT). Incorporating CytoSorb® hemoadsorption into CRRT resulted in a significant decrease in creatine phosphokinase and myoglobin levels within 12 hours, with the patient attaining full renal recovery over the following five weeks.[2] In our case, adequate hydration was ineffective to clear CPK. The patient exhibited severe ARDS, accompanied by a markedly elevated NT-pro BNP level of 18987 pg/ml. Haemoadsorption and hemodialysis were initiated to mitigate fluid overload and enhance renal function. The Biosky MG350 adsorber (Biosun Medical Technology Co. Ltd, China) was utilized in each hemodialysis session; it is a disposable hemoperfusion cartridge composed of microporous adsorptive resin. It has received approval for application in cases of sepsis and hyperinflammation. After the treatment, his CPK level reduced drastically, as shown in the chart. His lung function also improved significantly.

The ongoing advancement of liver failure necessitated the implementation of plasma exchange, a novel approach in this context. The patient improved liver function and coagulation profile following plasma exchange, resulting in a decreased MELD score. This case report indicates that plasma exchange may enhance liver function and prolong the duration of hepatocyte regeneration. Our findings align with Freeman JG et al. and Larsen FS et al., indicating that the survival group was associated with liver function recovery and improvements in MELD score following plasma exchange.[21,22] The bilirubin level decreased significantly and continued to decline following three sessions of therapeutic plasma exchange. Both fresh frozen plasma and albumin were utilized during plasmapheresis in our patient's case.

No significant adverse events were noted in our patient during the plasma exchange procedure. The primary notable finding was hypocalcemia accompanied by metabolic alkalosis. It was identified and rectified without additional complications.

Following plasma exchange, the patient was extubated without complications. Liver and kidney function gradually recovered thereafter. The case, which initially appeared impossible to overcome, progressively improved with the implementation of supportive care, haemoadsorption, hemodialysis, and plasma exchange. Now, the patient is back home and living an everyday life.

Conclusion:

This report presents the first documented case of successful treatment utilizing haemoadsorption, hemodialysis, and plasma exchange in a patient diagnosed with expanded dengue syndrome. We propose that haemoadsorption and plasma exchange are both safe and effective treatments for dengue-associated rhabdomyolysis, acute kidney injury, ARDS, and acute liver failure, particularly in settings where MARS and liver transplantation are not accessible, as is the case at our center.

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