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Case Report

Exploring the Rare Coexistence of Expanded Dengue Syndrome and Wilson Disease in Acute Liver Failure: A Case Series

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Abstract:

Dengue fever, a viral infection transmitted by the Aedes mosquito, is common in tropical and subtropical regions. It is frequently linked to severe complications, including acute liver failure. Wilson disease is a rare hereditary illness that impacts copper metabolism, can also lead to fulminant hepatic failure, and is a well-known cause of acute liver failure in young adults. The simultaneous occurrence of both dengue and Wilson disease is extremely rare, posing significant challenges in diagnosis and treatment. This case series explores the complexities of diagnosing and managing acute liver failure in patients with expanded dengue syndrome, who were subsequently diagnosed with Wilson disease.

Keywords: *Copper Chelation, Expanded Dengue Syndrome, Wilson Disease.*

Introduction:

Dengue fever, caused by the dengue virus, is a major health concern in many tropical regions. The disease is primarily spread by the mosquito Aedes aegypti. While most cases present as mild flu-like symptoms, severe dengue can lead to serious complications, including hemorrhagic manifestations, shock, and liver involvement.[1] Severe liver dysfunction, which can progress to acute liver failure (ALF), is a rare but recognized complication of dengue infection. ALF in dengue is characterized by rapid liver cell necrosis and dysfunction, typically accompanied by elevated serum transaminases (ALT and AST), hyperbilirubinemia, and coagulopathy.[2]

Wilson disease (WD) is a rare autosomal recessive illness characterized by impaired copper metabolism due to faulty copper transport, leading to its buildup in essential organs, particularly the liver, brain, and corneas. Individuals with Wilson disease typically have hepatic or neurological manifestations, and if not addressed, the disorder may advance to acute liver failure. Wilson disease is usually diagnosed in young adults, with ALF being the most common hepatic presentation.[3,4]

The simultaneous occurrence of dengue fever and Wilson disease is exceptionally rare. Due to the overlap in liver-related complications, differentiating between the two conditions presents a significant diagnostic challenge. We present three cases of young adults diagnosed with expanded dengue syndrome complicated by acute liver failure.

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Case 1

A 19-year-old male reported to the emergency and casualty center of Combined Military Hospital (CMH) Dhaka from CMH Chittagong with complaints of fever for 5 days, vomiting for the same duration, and irrelevant talking since morning, and was levelled as a case of acute hepatitis with hepatic encephalopathy with electrolytes imbalance. On examination, the patient was unconscious, GCS 6 (E2V2M4), Pulse 96 b/min, BP 130/90 mm Hg, Temp102.8˚ F, and icteric. The patient was on 3 liters of oxygen via nasal cannula and shifted to the Intensive Care Unit (ICU) for further management. After admission to the ICU on July 07, 2025, initial laboratory investigations revealed hemoglobin level of 12.3 gm/dl, hematocrit of 36.8%, white blood cell count of 7 × 10^9/L, neutrophil percentage of 77.1%, platelet count of 58 × 10^9/L, and serum sodium, potassium, and chloride levels of 140, 3.92, and 118.3 mmol/L, respectively, with calcium at 8.96 mg/dL**;** Uric Acid: 6.91 mg/dl; Serum Urea: 41 mg/dl; Serum Creatinine: 1.10 mg/dl; Serum Bilirubin: 8.45 mg/dl; ALT: 3130 u/L; AST: 1047 u/L; ALP: 161 u/L. Albumin: 31.8 g/L; LDH: 1103 u/L; S. Amylase: 238 u/L. Lipase: 855 u/L; CPK: 6021 u/L; RBS: 8.13 mmol/L. Fibrinogen: 107 mg/dl; APTT: 53 seconds; PT: 46.3 seconds; INR: 3.93. Serum Procalcitonin was measured at 6.91 ng/ml, Troponin I at 28 pg/ml, NT-pro BNP at 89 pg/ml, and Serum Ferritin 12300 ng/mL. Ultrasound of the whole abdomen was performed, which revealed hypoechoic liver parenchyma. Echocardiography findings indicate no regional wall motion abnormalities, with a left ventricular ejection fraction of 65%.

Further workup of the patient revealed Dengue IgM positive. Patient was negative for ICT for Malaria, TORCH panel, HBsAg, Anti-HAV IgM, Anti-HCV, Anti-HEV IgM, Triple Antigen, and Urinary PCR for Leptospira DNA. So, the initial diagnosis of the patient was Acute liver failure with hepatic encephalopathy due to Expanded dengue syndrome.

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The patient was initiated on injectable broad-spectrum antibiotics, intravenous N-acetylcysteine, Intravenous L-ornithine L-aspartate, ursodeoxycholic acid, and rifaximin tablets. We used lactulose syrup to promote bowel movements at least twice a day. With conservative treatment patient's conscious level improved gradually, and his Serum Bilirubin reduced to 3.6 mg/dl; ALT: 173 u/L; AST: 137 u/L; ALP: 170 u/L. Albumin: 42 g/L; APTT: 40 seconds; PT: 14 seconds; INR: 1.10 on July 24, 2025.

Further workup revealed his Serum Copper was 26 µg/dl, and the concentration of ceruloplasmin was 0.11 g/L, and 24-hour urinary copper excretion was 56 ug/L. The patient was positive for Kayser-Fleischer ring on slit lamp examination. The patient also had features of hemolysis (high LDH, elevated indirect bilirubin), but both direct and indirect Coombs tests were negative. His Leipzig Score was 4. So, the final diagnosis was concluded to be Acute liver failure with hepatic encephalopathy due to Wilson disease with Expanded dengue syndrome. Copper chelation therapy was initiated upon diagnosis of Wilson's disease, which significantly contributed to the recovery of liver function. Later patient was discharged home on 21st July 2025.

Case 2

A 28-year-old male reported to the emergency and casualty center of CMH Dhaka on July 9, 2025, with complaints of fever for 3 days and body aches. He was conscious, oriented, BP130/80 mm Hg, Pulse110 bpm, Temperature 103˚F, $SpO_2$97% in room air, Dengue NS1 positive on 09/07/2025. He was labeled as a case of Dengue fever with a history of hypothyroidism. From 09.07.25 to 14.07.25, his platelet counts gradually decreased from 256 × 10^9/L to 30 × 10^9/L. On 15 July 2025, the patient was shifted to the ICU and nursed there up to 17.07.25. Then the patient was shifted to the ward again as his condition improved. Due to persistent high-grade fever, he was again shifted to the ICU on 20th July 2025 for further management and evaluation. After re admission to the ICU on July 20th, initial laboratory investigations revealed hemoglobin level of 12.8 gm/dl, hematocrit of 38.1%, white blood cell count of 10 × 10^9/L, neutrophil percentage of 30.7%, platelet count of 88 x 10^9/L, and serum sodium, potassium, and chloride levels of 131, 4.1, and 99 mmol/L, respectively, with calcium at 7.9 mg/dL; Uric Acid: 2.7 mg/dl; Serum Urea: 35 mg/dl; Serum Creatinine: 1.33 mg/dl; Serum Bilirubin: 5.36 mg/dl; ALT: 770 u/L; AST: 2330 u/L; ALP: 226 u/L. Albumin: 36 g/L; LDH: 9140 u/L; S. Amylase: 200 u/L. Lipase: 538 u/L; CPK: 1293 u/L; RBS: 6.1 mmol/L. Fibrinogen: 211 mg/dl; APTT: 38.9 seconds; PT: 14.7 seconds; INR: 1.10. Serum Procalcitonin was measured at 3.87 ng/ml, Troponin I at 19.5 pg/ml, NT-pro BNP at 1056 pg/ml, Serum Ferritin 109400 ng/mL. Ultrasound of the whole abdomen was performed, which revealed bilateral mild pleural effusion and GB wall thickening. Echocardiography findings indicate no regional wall motion abnormalities, with minimal pericardial effusion, with a left ventricular ejection fraction of 65%.

Patient was negative for QuantiFERON-TB Gold Plus, ICT for Malaria, TORCH panel, HBsAg, Anti-HAV IgM, Anti-HCV, Anti-HEV IgM, Triple Antigen, and Urinary PCR for Leptospira DNA. So, the initial diagnosis of the patient was Acute liver failure with hepatic encephalopathy due to Expanded dengue syndrome.

The patient was initiated on injectable broad-spectrum antibiotics, intravenous N-acetylcysteine, Intravenous L-ornithine L-aspartate, ursodeoxycholic acid, Levothyroxine sodium, and rifaximin tablets. Bowel movements were ensured by administering lactulose syrup. With conservative treatment patient's conscious level improved gradually, and his Serum bilirubin reduced to 3.0 mg/dl; ALT: 222 u/L; AST: 265 u/L; ALP: 130 u/L. Albumin: 44 g/L; APTT: 34 seconds; PT: 12 seconds; INR: 1.0 on August 6, 2025.

Further workup revealed his Serum Copper was 65 µg/dl, and the concentration of ceruloplasmin was 0.683 g/L, and 24-hour urinary copper excretion was 257 ug/L. The patient was positive for Kayser-Fleischer ring on slit lamp examination. The patient also had features of hemolysis (very high LDH, elevated indirect bilirubin), but both direct and indirect Coombs tests were negative. His Leipzig Score was 5. So, the final diagnosis was concluded to be Acute liver failure with hepatic encephalopathy due to Wilson disease with Expanded dengue syndrome. Copper chelation therapy was initiated upon diagnosis of Wilson's disease, which significantly contributed to the recovery of liver function. Later patient was discharged home on 6th August 2025.

Case 3

A 28-year-old female reported to the emergency and casualty center of CMH Dhaka on July 15, 2025, with complaints of fever for 10 days, progressive yellowish discoloration of skin and sclera for the same duration, and epistaxis, hematuria for the last 2 days. She was nursed in Border Guard Hospital from 11th July 2025 to 15th July 2025 and labeled there as a case of Expanded dengue syndrome, with acute liver failure with encephalopathy. The patient was intubated there as she had convulsions and was put on mechanical ventilation on 15th July 2025. On arrival at ECC, CMH Dhaka, she was on sedation, BP114/63 mmHg, Pulse 143 bpm, $SpO_2$98% on MV on FiO_2 60%, temperature was normal. The patient was shifted to the ICU for further management. After admission to the ICU on the same day, initial laboratory investigations revealed hemoglobin level of 7.3 gm/dl, hematocrit of 23.9%, white blood cell count of 6.9 × 10^9/L, neutrophil percentage of 29.9%, platelet count of 161 × 10^9/L, and serum sodium, potassium, and chloride levels of 141, 3.3, and 104 mmol/L, respectively, with calcium at 8.3 mg/dL; Uric Acid: 4.2 mg/dl; Serum Urea: 51 mg/dl; Serum Creatinine: 0.91 mg/dl; Serum Bilirubin: 27.0 mg/dl; ALT: 279 u/L; AST: 386 u/L; ALP: 456 u/L. Albumin: 35.3 g/L; LDH: 3001 u/L; S. Amylase: 127 u/L. Lipase: 154 u/L; CPK: 3472 u/L; RBS: 4.2 mmol/L. Fibrinogen: 141 mg/dl; APTT: 125.4 seconds; PT: 18.8 seconds; INR: 1.44. Serum Procalcitonin was measured at 24.30 ng/ml, Troponin I at 944.1 pg/ml, NT-pro BNP at 4872 pg/ml, and Serum Ferritin 9116 ng/mL. Ultrasound of the whole abdomen was performed, which revealed left-sided mild pleural effusion with GB wall thickening.

Echocardiography findings indicate no regional wall motion abnormalities, with mild pericardial effusion, with a left ventricular ejection fraction of 65%. CT Brain showed ill-defined hypodensity in both parieto-temporo-occipital lobes with effacement of adjacent sulci - possibility of encephalitis. MRI of the brain revealed features suggestive of hepatic encephalopathy, and the 24-hour continuous EEG was also suggestive of encephalopathy.

Patient was negative for ICT for Malaria, TORCH panel, HBsAg, Anti-HAV IgM, Anti-HCV, Anti-HEV IgM, Triple Antigen, and Urinary PCR for Leptospira DNA. So, the initial diagnosis of the patient was Acute liver failure, Pneumonia with Pleural effusion, Rhabdomyolysis, Convulsion with Expanded Dengue Syndrome.

The patient was initiated on injectable broad-spectrum antibiotics for sepsis, intravenous N-acetylcysteine, Intravenous L-ornithine L-aspartate, ursodeoxycholic acid, and rifaximin tablets. We used lactulose syrup to promote bowel movements at least twice a day.

Further workup revealed her Serum Copper Level was 80 **µ g**/dL, the concentration of ceruloplasmin was 0.8 g/L, and her 24-hour urinary copper excretion was 423 **µg**/L. The patient was positive for Kayser-Fleischer ring on slit lamp examination. The patient also had features of hemolysis (high LDH, elevated indirect bilirubin), but both direct and indirect Coombs tests were negative. Her Leipzig Score was 5. So, the final diagnosis was concluded to be Acute liver failure with hepatic encephalopathy due to Wilson disease with Expanded dengue syndrome. Copper chelation therapy was initiated upon diagnosis of Wilson's disease, which significantly contributed to the recovery of liver function.

With supportive treatment patient's conscious level improved gradually, and her Serum Bilirubin reduced from 27 to 1.91 mg/dl (27>21.64>14.97>8.44>6.32>5.38>3.93>3.80>3.18 >2.52>2.33>2.21>1.91 mg/dl) over 14 days; ALT: 218 u/L; AST: 174 u/L; ALP: 55 u/L. Albumin: 40 g/L; APTT: 31.2 seconds; PT: 13 seconds; INR: 1.1 on July 30, 2025. Her CPK rapidly rose from 24280 to 57960 u/L over 3 days, which reduced after giving the CRUSH injury protocol. On day 12 after ICU admission, it reduced to 3794 u/L. Patient was extubated on day 7, and her conscious level improved gradually over 14 days and was discharged home on 30th July 2025.

Discussion:

Globally, dengue is the primary cause of viral hemorrhagic fever. Although it is endemic in many tropical nations, non-endemic areas have reported cases more frequently in recent years.[5] According to current estimates, about 400 million cases of dengue are reported each year, putting over 5 billion individuals at risk of getting the disease worldwide.[6]

Dengue patients typically present with fever and rash, and in extreme cases, hemorrhage and shock. Liver injury is widespread, with several phases of liver dysfunction recorded as a result of dengue infection. In most cases, liver enzymes reveal a slight, transitory increase.[7] However, large elevations in transaminases higher than ten times normal levels can occur, resulting in dengue-induced severe hepatitis (DISH), which affects 4%-15% of all dengue cases.[7,8] Dengue-induced severe hepatitis (DISH) seldom progresses to acute liver failure (ALF), accounting for less than 1% of all cases.[8]

In addition to jaundice (yellowing of the eyes and skin), patients with liver involvement frequently exhibit gastrointestinal symptoms as nausea, vomiting, stomach discomfort, and anorexia. In 4% to 79% of instances, hepatomegaly has been documented.[7,9] On the other hand, complications or involvement of several organs may complicate the clinical picture in severe cases. Severe dengue patients may require multi-organ support and are frequently admitted to the intensive care unit (ICU).[10]

With an incidence of 1 in 30,000 to 1 in 50,000 instances, Wilson's disease (WD) is brought on by mutations in the ATP7B gene and is inherited autosomal recessively.[11] It was initially diagnosed as a progressive lenticular degeneration with neurological and hepatic symptoms by Kinnier Wilson in 1912.[12] The transmembrane copper-transporting ATPase, an enzyme encoded by ATP7B, is crucial for the incorporation of copper into ceruloplasmin and subsequent excretion through bile. Progressive copper buildup in a number of organs, chiefly the liver, neurological system, corneas, kidneys, and heart, is caused by defective enzyme action.[13] About 20% to 30% of WD cases begin with Acute Liver Failure (ALF), and patients who do not receive treatment usually develop cirrhosis or chronic hepatitis.[14]

WD is currently diagnosed using a scoring system that was created at the 8th International Meeting on Wilson Disease in Leipzig. It takes into account genetic analysis, metabolic testing, histological results, and clinical indicators. (Table I)[15].

The simultaneous occurrence of dengue infection and Wilson disease is extremely rare, with no case reports found in the literature. Differentiating between the two causes of acute liver failure can be highly challenging.

In the cases reported here, all three patients exhibited elevated liver enzymes, hyperbilirubinemia, and coagulopathy, leading to an initial diagnosis of acute liver failure due to expanded dengue syndrome (EDS). While liver function typically improves with supportive treatment, the delayed improvement prompted us to consider other causes of liver failure, such as viral hepatitis, leptospirosis, and Wilson disease. All three patients tested positive for Kayser-Fleischer rings on slit-lamp examination, which led us to further investigate serum copper levels, ceruloplasmin concentration, and 24-hour urinary copper levels. Despite showing signs of hemolysis (elevated LDH and indirect bilirubin), both direct and indirect Coombs tests were negative. Mutation analysis of the ATP7B gene was not available in our country. Given that the Leipzig score criteria were met, we opted not to perform a liver biopsy due to the high risk of bleeding.

Table I: Diagnostic scoring system for Wilson's disease.

Test	Parameter	Score
Kayser-Fleischer ring	Present	2
	Absent	0
Neurological symptoms	Severe	2
	Mild	1
	Absent	0
Serum ceruloplasmin	Normal (>0.2 g/L)	0
	0.1–0.2 g/L	1
	<0.1 g/L	2
Coombs-negative hemolytic anemia	Present	1
	Absent	0
Liver copper (in the absence of cholestasis)	>250 µg (>4 µmol) g^{-1} dry weight	2
	50–249 µg (0.8–4 µmol) g^{-1}	1
	Normal: <50 µg (<0.8 µmol) g^{-1}	−1
	Rhodanine-positive granules	1
Urinary copper (in the absence of acute hepatitis)	Normal	0
	1–2 × ULN	1
	>2 × ULN	2
	Normal but >5 × ULN after D-penicillamine	2
Mutation analysis of *ATP7B*	Biallelic deleterious variants	4
	One deleterious variant	1
	No mutation detected	0
Total score	Evaluation	
≥4	Diagnosis established	
3	Diagnosis possible; more tests needed	
≤2	Diagnosis very unlikely	

ULN: upper limit of normal.

The clinical and laboratory overlap between dengue-related liver failure and Wilson disease-related hepatic dysfunction makes early diagnosis particularly challenging. Both conditions were commonly present with elevated liver enzymes, hyperbilirubinemia, and coagulopathy. However, subtle differences, such as disproportionate hyperbilirubinemia, hemolysis (indicated by elevated LDH and indirect bilirubin), and low serum ceruloplasmin levels, should raise suspicion for Wilson disease, even when a viral etiology like dengue is apparent.

The management of patients with concurrent dengue and Wilson disease necessitates a multidisciplinary approach. During the acute phase, supportive care addressing dengue-related complications, including fluid management, blood pressure stabilization, and vigilant monitoring for hemorrhage and shock, is crucial. For Wilson disease, copper chelation therapy is central, aiming to reduce copper accumulation in the liver and other organs.

In this case series, initial management focused on supportive care for dengue, including intravenous N-acetylcysteine, L-ornithine L-aspartate, ursodeoxycholic acid, and rifaximin, to enhance liver function and manage encephalopathy. Once the diagnosis of Wilson disease was confirmed, copper chelation therapy was initiated, leading to significant improvements in liver function and clinical status.

The value of early copper chelation in enhancing liver function cannot be overstated. Penicillamine, Zinc, and Trientine, which are routinely used for copper chelation in Wilson disease, lower the risk of progression to cirrhosis and hepatic decompensation. Additionally, symptom control, including the use of lactulose to lower ammonia levels and encourage bowel movements, was critical in managing hepatic encephalopathy in all patients.

With timely detection and the implementation of copper chelation therapy, all three patients showed significant clinical improvement, including improved liver function tests, lower bilirubin levels, and resolution of hepatic encephalopathy. Long-term follow-up care is essential for Wilson disease patients, as ongoing treatment with copper chelators and zinc supplements is required to avoid relapse and reduce the risk of chronic sequelae.

Given the rarity of this clinical presentation, we maintained a high index of suspicion for Wilson disease in the initial cases. Subsequently, we encountered additional patients with acute liver failure, though Wilson disease was excluded in these instances. This highlights the challenge of identifying such rare comorbidities, which can easily be overlooked.

Conclusion

The co-occurrence of dengue infection and Wilson disease is rare but clinically significant. Young individuals experiencing unexplained liver failure after a dengue infection should raise the suspicion of Wilson disease in clinicians, particularly when there is disproportionate hyperbilirubinemia, hemolysis, or other unusual laboratory findings. Early diagnosis and treatment, including copper chelation, are crucial for improving outcomes in these patients.

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