




Wilson Disease-Induced Acute Liver Failure (NWI = 13) Salvaged without Liver Transplant by Plasmapheresis

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Abstract

Wilson disease (WD) is a disorder of copper metabolism resulting in accumulation of copper in vital organs of the human body, predominantly in the liver and the brain. Acute liver failure in WD has a bad prognosis, especially with a score ≥ 11 in the revised WD prognostic index; emergency liver transplantation is considered the only life-saving option in this scenario. Here, we reported a girl patient with WD-induced liver failure and poor prognostic score who was rescued by plasmapheresis. She also manifested severe Coombs negative hemolytic anemia and acute kidney injury. This case report highlights the utility of an adjunctive modality besides liver transplantation for the management of fulminant liver failure caused by WD.

Keywords

- ▶ acute liver failure
- ▶ Wilson disease
- ▶ plasmapheresis

Background

Wilson disease (WD) is a disorder of copper metabolism resulting in accumulation of copper in vital organs of the human body, predominantly in the liver and the brain. WD has a variety of clinical manifestations, the most common being hepatic and neurological disorders. Liver disease typically begins with a presymptomatic period, during which copper accumulation in the liver causes subclinical hepatitis that progresses to liver cirrhosis. However, it may rarely present as fulminant hepatic failure with an associated Coombs-negative hemolytic anemia and acute renal failure. While presenting as fulminant/acute liver failure, emergency liver transplantation is considered as the only life-saving option especially with a score ≥ 11 in the revised WD prognostic index.¹ Here, we report a girl with WD-induced liver failure and poor prognostic score who was rescued by plasmapheresis. This case highlights the utility of an adjunctive modality besides liver transplantation for the management of fulminant liver failure caused by WD.

Case Report

A 9-year-old girl patient presented with a 5-day history of progressive jaundice that was associated with low-grade fever, generalized weakness, decreased appetite, and increased sleepiness for last 2 days. Antenatal, birth, and postnatal history were unremarkable. There was no prior history of jaundice, bleeding, abdominal distension, or altered sensorium. Parents also denied any history of blood transfusion, itching, joint pain, weight loss, and any intake of over-the-counter medication/herbal drug. There was no history of similar illness in the family. On examination, she was lethargic (Grade 1 encephalopathy), afebrile with normal vital parameters. Abdomen was soft, slightly distended with mild hepatosplenomegaly (liver span –12 cm, spleen—just palpable below left costal margin). Initial laboratory investigations revealed mildly elevated aspartate transaminase, low alkaline phosphatase levels, increased serum bilirubin, hypoalbuminemia, and elevated international normalized ratio indicating hepatocellular injury with deranged liver synthetic functions (▶ **Table 1**). Also, low hemoglobin was noted with raised reticulocyte count and lactate

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Table 1 Biochemical parameter on admission

Biochemical parameter	Reference value	Day 1 Morning	Day 1 Evening	Day 3	Day 4	Day 5	Day 6	Day 7
Total bilirubin	0.3–1.2 mg/dL	25.6	27.6	11.4	9.2	7.9	4.8	4.5
Direct bilirubin	0.0–0.2 mg/dL	16.8	19.2	7.3	4.3	4.2	3.3	3.0
ALT	10–49 U/L	13	10	17	17	20	17	30
AST	<34.0 U/L	94	70	37	27	33	37	46
ALP		14	9	34	43	42	38	66
PT INR	1.0–1.3 seconds	2.1	2.5	2.0	1.9		2.1	2.0
Albumin	3.5–4.2 g/dL	2.2	2.1	3.4	3.1	3.4	3.3	3.4
Creatinine	0.7–1.1 mg/dL	1.2	1.4	0.7	0.6		0.4	
Hemoglobin	11–14 g/dL	7.4	5.1		6.1	8.7	8	
TLC	4,000–9,000/mm ³	12000	11800		5600	4100	4200	
Platelets	1.5–4 *10 ⁵ /mm ³	1.2	1.1		1.1	0.86	0.96	

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; PT-INR, international normalized ratio of prothrombin time; TLC, total leukocyte count.

dehydrogenase level and a negative direct Coombs test. She was managed in pediatric intensive care unit conservatively with intravenous fluids, *N*-acetyl cysteine infusion, packed red blood cell (RBC) transfusion, and broad-spectrum antibiotics.

On further investigations, markers for viral hepatitis (A, B, C, E) and autoimmune etiology (anti-nuclear antibody, ANA, anti-LKM1, smooth muscle antibody, SMA, anti-LC1, anti-SLA) were found to be negative. Her serum ceruloplasmin level was low at 5.45 mg/dL. Abdominal Doppler ultrasound showed findings of chronic liver disease with enlarged nodular liver, mild ascites, and splenomegaly with few portosystemic collaterals. On ophthalmologic evaluation, bilateral Kayser-Fleischer rings were seen. The characteristic clinical and biochemical findings pointed toward a diagnosis of fulminant hepatic failure due to WD. Her condition worsened over the next 24 hours with encephalopathy progressing to grade 2/3, also associated with further drop in hemoglobin. New WD prognostic index was 13, and a score of more than 11 is known to carry a very grave prognosis without liver transplantation. The family was counseled for living donor liver transplant and workup for the same was sought. Meanwhile, high volume

plasma (HVP) exchange was used as a bridge therapy to liver transplant. A total of three sessions of HVP exchange were performed on alternate days. Later, as the report of elevated 24-hour urinary copper level of 1786 µg/dL became available, the diagnosis of WD confirmed. Significant improvements in neurological status and biochemical parameters were noted soon after the first session of HVP. Further progress was documented with subsequent sessions of HVP. Penicillamine and zinc were started once she recovered from the encephalopathy. She recovered from the acute liver failure without liver transplant and was discharged on oral penicillamine and zinc. She is in regular follow-up for ~6 months and her liver function test has shown consistent improvement (► **Table 2**).

Discussion

Here, we have reported a 9-year-old girl child who presented with jaundice, encephalopathy, acute kidney injury, and hemolysis secondary to WD-induced acute hepatic failure and recovered on a treatment regimen of repeated

Table 2 Biochemical parameters on follow-up

Biochemical parameter	Reference value	At discharge	After 2 weeks	After 1 months	After 2 months	After 6 months
Total bilirubin	0.3–1.2 mg/dL	3.3	2.5	1.43	0.94	0.7
Direct bilirubin	0.0–0.2 mg/dL	2.4	1.4	0.93	0.4	0.4
ALT	10–49 U/L	30	109	62	64	54
AST	<34.0 U/L	66	129	81	52	46
ALP	<500 U/L	66	411	625	824	450
PT-INR	1.0–1.3 seconds	2.0	1.42	1.54	1.32	1.1
Albumin	3.5–4.2 g/dL	3.4	3.1	3.2	3.24	3.6

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; PT-INR, international normalized ratio of prothrombin time.

plasmapheresis that thwarted the need for a liver transplant. WD is an autosomal recessive disorder due to mutation in ATP7B gene, which encodes a metal-transporting ATPase, having functions of transmembrane transport of copper within hepatocytes. Decreased hepatocellular excretion of copper into bile occurs due to absent or reduced function of ATP7B resulting in copper accumulation in the liver that further goes through the blood and gets deposited in other organs (mainly brain, kidneys and cornea). WD presents widely as symptomatic hepatomegaly, isolated splenomegaly, persistently elevated serum aminotransferase activity, fatty liver, acute hepatitis, compensated or decompensated cirrhosis, and acute liver failure.¹ WD accounts for 6 to 12% of all patients with acute liver failure who need emergency liver transplantation and it is more common in young females (female: male ratio 4:1).² Acute liver failure due to WD often has a fulminant course resulting in almost 95% mortality if left untreated. It is associated with highly elevated circulating free copper levels. Though exact trigger for acute liver failure in WD is not known, intravascular hemolysis and renal failure result from damage to RBC membranes and renal tubular cells by deposition of excessive circulating copper.³ The New Wilson index is based on serum bilirubin, international normalized ratio, aspartate aminotransferase, and white cell count at presentation. This index identifies a grave prognosis at a score of ≥ 11 with 93% sensitivity, 98% specificity, and a positive predictive value of 88%; liver transplantation should be considered in patients with WD-induced acute liver failure if they have a prognostic score of ≥ 11 .⁴ Supportive measures for fulminant liver failure secondary to WD that may help bridge patients to transplantation include exchange transfusion, plasmapheresis, the molecular adsorbent recycling system, albumin dialysis, and continuous renal replacement therapy; these treatments aimed at lowering copper levels in circulation to decrease hemolysis and secondary organ damage. However, the results were variable with no single method proven to be effective. HVP with fresh frozen plasma replacement has shown to be efficacious in rapid reduction of serum copper levels.⁵ Plasma exchange has been mainly reported as a bridge to liver transplantation aiming at removal of ceruloplasmin-bound and albumin-bound copper resulting in decreasing hemolysis and renal injury.⁶ Significant improvement in survival in acute liver failure due to all causes has been noted with incorporation of HVP as an integral part of management.⁷ However, our patient survived without liver transplant with a prognostic index of 13 with worsening encephalopathy. Though there are features of chronic liver disease including small collaterals in periesophageal, peri-splenic and perigastric regions, the reason for survival might be absence of advanced liver disease. Although plasmapheresis as a bridge therapy to liver transplant has been widely described in

literature, only few case reports have reported survival with only plasmapheresis without requiring liver transplant.⁸⁻¹²

Conclusion

WD should be suspected in young patients presenting with liver failure. Plasmapheresis helps in stabilization of patients by removing excess copper from the circulation. It can be used as a bridge to liver transplant. This case further supports this modality of treatment where it not only helped in stabilization but also in recovery, obviating the need for liver transplantation.

Conflict of Interest

None declared.

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