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Plasma exchange as a treatment for hemolytic crisis and acute liver failure in Wilson disease.

Devang Gandhi*, Suraj Patel, Hiteshee Patel

Department of Pediatrics, Veer Narmad South Gujarat University, Gujarat, India

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Abstract

Wilson Disease (WD) is a genetic disorder resulting in copper accumulation, leading to liver failure and neurological symptoms. Acute Liver Failure (ALF) in WD often necessitates urgent liver transplantation due to its poor prognosis. This report details the use of Plasma Exchange (PE) in a 7-year-old girl with WD who presented with ALF and hemolytic anemia. Despite the severe clinical condition and laboratory findings indicative of WD, the family opted for PE against immediate liver transplantation. The child was started on PE with the Spectra Optia® Apheresis System and D-penicillamine and zinc were introduced. Four PE sessions were performed on alternate day, each lasting 1.5 to 2 hours, exchanging approximately 1,100 mL of plasma per session. Post-treatment, the child showed significant improvement in hemolysis, bilirubin levels and liver function tests, providing a temporary stabilization that allowed for bridging to potential transplantation. This case underscores the role of PE as a viable option for managing WD-related ALF, highlighting its effectiveness in reducing copper levels and stabilizing the patient's condition when transplantation is not immediately feasible. This experience contributes to the growing body of evidence supporting PE as a bridging therapy in severe Wilson disease cases.

Keywords: Wilson disease, Acute liver failure, Potential transplantation, Plasma exchange.

Abbreviations

Hb: Hemoglobin; TLC: Total Leukocyte Count; Plt Platelet count; PT: Prothrombin Time; Cr Serum creatinine; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; Bil: Total serum bilirubin; Alb; Serum Albumin; Ser Cu: Serum Copper; PE; Plasma Exchange

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Introduction

Wilson Disease (WD) is a rare autosomal recessive disorder causing copper accumulation in organs like the liver and brain. Acute Liver Failure (ALF) is a severe complication requiring urgent diagnosis and treatment due to its rapid progression. This report highlights a 7-year-old girl with WD, ALF and hemolytic anemia. Her family declined liver transplantation, prompting Plasma Exchange (PE) as bridging therapy to reduce copper, control hemolysis and stabilize liver function. PE, combined with copper chelation, demonstrated potential to delay clinical deterioration. This case emphasizes personalized approaches for managing rare WD complications, considering clinical and socio-economic factors.

Case Report

A 7-year-old girl weighing 19.4 kg presented to the pediatric emergency with abdominal distension and pain for 3 days, breathlessness for 3 days, jaundice for 3 days and excessive irritability for 2 days. There was no past or family history of jaundice or blood transfusion. She had severe pallor, icterus, facial puffiness and pedal edema. She was irritable and had mild confusion. Abdominal examination revealed a firm hepatomegaly with ascites. A diagnosis of ALF with stage I hepatic encephalopathy was made and appropriate management started.

The laboratory investigations revealed: Hemoglobin-6.5 g/dL; features of hemolysis in the peripheral blood smear; direct Coombs test negative; blood urea/creatinine-17/0.7 mg/dL; total/direct bilirubin-23.4/8.4 mg/dL; Aspartate aminotransferase-117 U/L; Alanine aminotransferase-29 U/L; Alkaline phosphatase (ALP)-48 U/L; Prothrombin time-18 min, activated partial thromboplastin time-42.8, INR 3.9. On ophthalmic examination Kayser-Fleischer ring was present. The above-mentioned laboratory parameters suggested WD as the underlying cause of the ALF. Serum Ceruloplasmin was <3 mg/dL (Normal-25 mg/dL–63 mg/dL), Serum copper was 1.293 mg/dL (Normal-0.7 mg/dL–1.8 mg/dL) and 24-hour urinary copper was 263.35 µg (Normal <60 µg/d). The authors did not perform a liver biopsy in view of the clinical condition.

Based on these features, the child was diagnosed as WD presenting in ALF. Liver transplantation would have been ideal treatment option for this child but as the family was not willing

for a transplant at that moment, the child was started on Plasma Exchange (PE) (Spectra Optia® Apheresis system, TERUMO BCT INC.) after obtaining a vascular access through double-lumen 8.5 French catheter placed in the femoral vein. The PE machine was primed with red cell concentrate at the start of first two PE session and normal saline for rest 3 sessions. A total of four PE sessions were done. Each session lasted 1.5 to 2 hour and about 1,100 mL plasma was exchanged in each session. Oral D-penicillamine and Zinc were also started. After starting PE, the child showed improvement in the form of reduced irritability, reduced blood transfusion requirement, fall in bilirubin and improvement in liver function tests. Table 1 and Figures 1 and 2 show the serial laboratory parameters of the child during the hospital stay.

Laboratory parameter	On admission	Day 6	Day 9	Day 11	Day 13	Day 15	Day 25 (On readmission)
Hb (g/dL)	6	9.2	11.3	11.4	11	11.7	6.3
TLC (× 10^3/µL)	26.3	4.18	7.2	10	10.4	5.29	7.8
Plt (× 10^3/µL)	159	29	29	41	52	56	122
PT (s)	>60	18	42.9	20	-	-	-
Urea (mg/dL)	57	23	37	-	38	21	15
Cr (mg/dL)	2.1	0.3	0.6	-	0.6	0.3	0.4
AST (U/L)	165	104	74	136	83	71	68
ALT (U/L)	11	26	31	38	28	27	32
ALP (U/L)	18	45	109	90	150	524	205
Bil (mg/dL)	3.8	38.2	28.2	20.4	9.8	4.8	2.4
Alb (g/L)	27	3.1	3.5	3.5	2.9	40	2.5
Ser Cu (mg/L)	-	1.293	-	-	0.9	-	-
PE session	-	1st	2nd	3rd	4th	-	-

Table 1. Laboratory parameters of the child during the hospital stay.

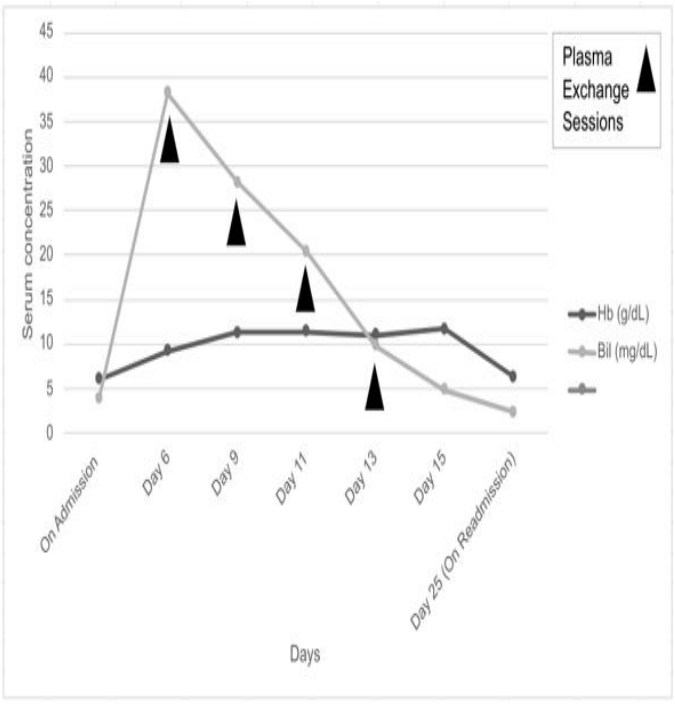

Figure 1. Serum bilirubin and hemoglobin level during the course of the hospital stay. The black arrowheads indicate Plasma Exchange (PE).

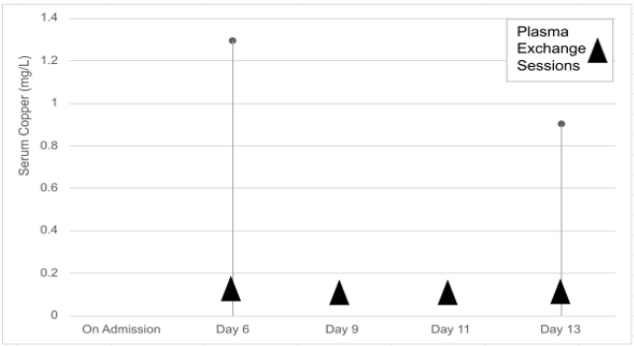

Figure 2. Serum copper levels during the course of hospital stay. The black arrowheads indicate Plasma Exchange (PE) sessions.

After four PE sessions, there was significant improvement in general condition and in lab parameters, so PE was stopped after four sessions. The family was not willing for liver transplant at that time, so supportive care was continued. Two days later, child had fever spikes and on investigations found S. Widal positive. She was started on treatment of enteric fever and patient discharged in few days. After 10 days of discharge patient again admitted in pediatric ward for abdominal distension and breathlessness. This time the patient opted for the liver transplantation and referred to higher center for the same.

Discussion

Wilson Disease (WD) represents approximately 4% of Acute Liver Failure (ALF) cases [1]. Patients with WD presenting with ALF commonly exhibit distinctive clinical features, including coombs-negative hemolytic anemia, coagulopathy unresponsive to vitamin K and rapid progression to renal failure.

Diagnostic indicators for WD-related ALF include:

- Low serum Alkaline Phosphatase (ALP)
- An ALP to total bilirubin ratio less than 4 and
- An Aspartate Aminotransferase (ASTA) to Alanine Aminotransferase (ALT) ratio greater than 2.2 [1,2].

Our patient displayed these characteristics, confirming WD through serum ceruloplasmin, serum copper and 24-hour urinary copper tests.

Copper chelation therapy is the standard treatment for WD; however, it is less effective in acute liver failure, as substantial copper reduction typically requires 1-3 months [3]. The prognosis for WD patients with ALF remains poor with medical treatment alone, making liver transplantation the preferred option [2]. The scarcity of donor organs often delays transplantation, necessitating temporary measures to stabilize the patient. Alternative treatments include Plasma Exchange (PE) [4,5], albumin dialysis with Continuous Veno venous Hemodiafiltration (CVVHD) [6] and Molecular Adsorbent Recirculating Systems (MARS) [7].

PE, first described in 1914 [8], has demonstrated effectiveness in rapidly reducing copper levels and removing other toxins, such as aromatic amino acids, ammonia, endotoxins and phenols, which contribute to hepatic coma. Utilizing fresh frozen plasma during PE helps restore coagulation by providing essential clotting factors and eliminating activated factors.

In this case, PE effectively lowered serum copper, stabilized hemolysis and led to significant improvement in bilirubin levels and overall clinical condition. PE served as a crucial bridge to potential liver transplantation. While sustained improvement following PE alone is rare [9, 10], it often provides necessary stabilization until a liver transplant can be arranged.

Conclusion

This case report highlights the potential benefits of plasma exchange as a bridging therapy for patients with Wilson's disease presenting with acute liver failure. Despite the severe clinical condition and laboratory findings indicative of advanced Wilson's disease, the patient in this case showed significant improvement following a series of plasma exchange sessions. The procedure effectively reduced serum copper levels, stabilized hemolysis and improved liver function tests, allowing time for the introduction of copper chelation therapy.

This case demonstrates that plasma exchange can serve as a crucial temporary measure to stabilize patients and bridge them to potential transplantation when immediate liver transplantation is not feasible. The positive outcomes observed in this case contribute to the growing body of evidence supporting the use of plasma exchange as an effective management strategy for severe Wilson's disease presentations.

Conflict of Interests

Dr. Devang Gandhi, Dr. Suraj Patel and Dr. Hiteshee Patel have no conflicts of interest to disclose.

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Contributors Statement

Dr. Devang Gandhi, Dr. Suraj Patel and Dr. Hiteshee Patel conceptualized and designed the study, drafted the initial manuscript and critically reviewed and revised the manuscript.

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***Correspondence to:**

Devang Gandhi

Department of Pediatrics,

Surat Municipal Institute of Medical Education and Research,

Gujarat, India

E-mail: drdevang1981@gmail.com