RESEARCH PAPER

Therapeutic Plasma Exchange in Complementary and Alternative Medicine–Related Drug-Induced Liver Injury: A Case Report from a Tertiary Care Hospital

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ABSTRACT

Background: Drug-induced liver injury (DILI) is an important cause of acute hepatic dysfunction and may progress to acute liver failure in severe cases. Hepatotoxicity due to complementary and alternative medicine (CAM) is increasingly recognized, particularly in regions where herbal formulations are widely used without standardized regulation. Management is primarily supportive; however, selected patients may deteriorate rapidly with coagulopathy and extrahepatic organ involvement. Therapeutic plasma exchange (TPE) has been used as an adjunctive intervention in severe liver injury by enabling removal of circulating toxins and inflammatory mediators and by providing replacement of deficient plasma components.

Case Report: A 53-year-old female presented with fever, vomiting, fatigue, and jaundice 10 days after intake of a CAM preparation. Investigations revealed severe hepatocellular injury with marked hyperbilirubinemia, deranged coagulation profile, and acute kidney injury. Viral and autoimmune etiologies were excluded, and imaging showed no biliary obstruction. Due to worsening biochemical parameters despite supportive care, TPE was initiated. Three sessions of plasma exchange were performed with exchange volumes of 3000–3500 mL per session corresponding to 1 to 1.5 plasma volumes, using fresh frozen plasma, albumin, and isotonic saline as replacement fluids. Serial laboratory monitoring demonstrated progressive improvement in bilirubin levels, transaminases, and coagulation parameters, along with recovery of renal function and patient was discharged in stable condition.

Conclusion: This case emphasizes the emerging burden of CAM-associated DILI and suggests that timely initiation of therapeutic plasma exchange may contribute to clinical stabilization and biochemical recovery in severe presentations complicated by coagulopathy and organ dysfunction, particularly where transplant facilities are limited.

Keywords: *Drug-induced liver injury, Complementary and alternative medicine, Therapeutic plasma exchange, Coagulopathy, Acute liver failure.*

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INTRODUCTION

Drug-induced liver injury (DILI) is a significant cause of acute hepatitis and acute liver failure (ALF) worldwide and continues to pose a diagnostic challenge due to its highly variable clinical presentation and absence of a definitive diagnostic marker.[1] In routine clinical practice, DILI is largely considered a diagnosis of exclusion and requires systematic evaluation to rule out competing etiologies such as viral hepatitis, autoimmune hepatitis, metabolic liver disorders, and biliary obstruction.[2] Severe forms of DILI contribute substantially to cases of acute liver failure and remain an important indication for liver transplantation in selected patients.[3,4] In recent years, hepatotoxicity related to complementary and alternative medicine (CAM), including herbal and dietary supplements, has gained increasing recognition as a major contributor to DILI.[5] The widespread use of traditional medicines in many regions, particularly across Asia, often occurs without adequate medical supervision or standardized regulation, thereby increasing the risk of adverse hepatic events.[6,7] The hepatotoxic potential of CAM products is influenced by multiple factors, including variability in preparation, undisclosed active compounds, contamination with heavy metals or toxins, and adulteration with pharmaceutical agents.[6,7] The cornerstone of management of DILI involves immediate withdrawal of the suspected offending agent and provision of supportive care with close monitoring for clinical deterioration.[2] However, in severe cases, rapid progression may occur with worsening hyperbilirubinemia,

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coagulopathy, encephalopathy, and multi-organ dysfunction, leading to acute liver failure.[4,12] Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique that facilitates removal of circulating bilirubin, inflammatory mediators, immune complexes, and protein-bound toxins, while simultaneously replacing coagulation factors and plasma proteins.[8] Evidence from clinical studies suggests that high-volume plasma exchange may improve hemodynamic stability and transplant-free survival in patients with acute liver failure.[9]

Although liver transplantation remains the definitive therapy for fulminant hepatic failure, access may be limited due to donor shortage and rapid clinical deterioration.[4,12] In such settings, TPE may serve as a bridging strategy either to transplantation or to spontaneous recovery.[9] We report a case of CAM-related DILI complicated by acute kidney injury and coagulopathy, successfully managed with three cycles of therapeutic plasma exchange, resulting in marked clinical and biochemical improvement.

CASE PRESENTATION

A 53-year-old female presented to the hepatology unit with a history of vomiting and jaundice for 4 days, accompanied by fever for one week and progressive fatigue over the preceding two months. Reduced appetite and generalized weakness was also present, along with burning epigastric pain occurring after meals. Four days prior to admission, the patient developed yellow discoloration of the sclera and dark-colored urine. There was no associated pruritus, clay-colored stools, abdominal distension, hematemesis, or melena. The patient reported intake of a complementary and alternative medicine (CAM) preparation taken for fatigue and general health and well being, following which her symptoms worsened.

Her past medical history included systemic hypertension for three years, hypothyroidism (on Thyronorm 75 mcg) for five years, and recently diagnosed type 2 diabetes mellitus. There was no history of alcohol use, smoking, or other substance abuse. No significant family history was present. On examination, the patient was conscious, oriented, and clinically stable. Vital signs showed pulse rate 84/min, respiratory rate 20/min, and blood pressure 110/80 mmHg. She was afebrile on presentation. Physical examination revealed icterus and bilateral pitting pedal edema. There was no pallor, cyanosis, clubbing, or lymphadenopathy. Cardiovascular and respiratory system examination were normal. Neurological examination revealed no focal deficits. On abdominal examination, abdomen was soft, non tender without organomegaly. Initial laboratory investigations revealed anemia with normal leukocyte count and mild thrombocytopenia. Coagulation profile showed a prolonged INR, consistent with coagulopathy. Liver parameters demonstrated severe hepatocellular injury with markedly elevated transaminases and significant hyperbilirubinemia. Serum protein analysis showed hypoalbuminemia. Serological evaluation for viral hepatitis (HAV IgM, HEV IgM, HBsAg, and anti-HBc IgM) was negative. Screening for cytomegalovirus, herpes simplex virus, and Epstein–Barr virus infection was also negative. Autoimmune markers including antinuclear antibody (ANA), antimitochondrial antibody (AMA), anti–smooth muscle antibody (ASMA), anti–liver kidney microsomal antibody (anti-LKM), and soluble liver antigen antibody (anti-SLA/LP) were negative. Urine culture was positive, and treatment was initiated using culture-sensitive antibiotics. Abdominal ultrasonography demonstrated features suggestive of acute hepatic injury with mild fluid accumulation, with no evidence of biliary obstruction. Given the history of CAM intake and exclusion of viral, autoimmune, and obstructive causes, CAM-related drug-induced liver injury was considered the most likely diagnosis.

The patient was managed with supportive measures including intravenous antibiotics, albumin infusion, diuretics, hepatoprotective medications, proton pump inhibitors, nebulization, electrolyte correction, and close monitoring. In view of worsening liver biochemical parameters, persistent coagulopathy, and development of acute kidney injury, therapeutic plasma exchange was initiated.Three cycles of TPE were performed as follows:Weight and height of the patient were 99 kg and 161 cm respectively.

Therapeutic plasma exchange was carried out in the ICU with continuous monitoring of vital parameters after obtaining informed consent. A double-lumen catheter was placed in the right internal jugular vein under aseptic precautions to ensure reliable vascular access. The patient was observed for procedure-related complications, and calcium levels were regularly monitored with calcium supplementation as needed to prevent citrate-related hypocalcemia.

Cycle 1: 3000 ml volume of plasma was exchanged (approximately 1.1 plasma volume). Replacement fluids included 800 mL human albumin, 1200 mL fresh frozen plasma (FFP), and 1000 mL 0.9% normal saline.

Cycle 2: Plasma volume exchanged was 3500 mL (approximately 1.3 plasma volume). Replacement fluids included 800 mL human albumin, 1200 mL FFP, and 1500 mL 0.9% normal saline.

Cycle 3: Plasma volume exchanged was 3500 mL (approximately 1.3 plasma volume). Replacement fluid consisted of **1200 mL of human albumin, 1600 mL of fresh frozen plasma, and 700 mL of 0.9% normal saline**.

Following the third session, the patient showed progressive symptomatic improvement and stabilization of laboratory parameters. She was discharged in stable condition. At discharge, renal parameters and liver function tests showed significant biochemical improvement along with clinical recovery.

Table 1: Serial Laboratory Parameters Before and After TPE

	PRE TPE	1st cycle	2nd cycle	3rd cycle	POST TPE
HB(g/dl)	8.0	8.2	8.7	8.8	8.0
PCV(%)	23.8	23.9	27.4	26.9	24.7
TC(cells/ul)	10780	11270	12910	12730	9130
PLT(cells/ul)	1,40,000	1,51,000	1,63,000	1,71,000	1,60,000
aPTT(sec)	45.2	42.1	37.4	34.2	31.6
PT(sec)	19.4	18.5	16.6	16.3	15.4
INR	1.71	1.63	1.45	1.40	1.33
TB(mg/dl)	22.99	22.09	18.38	15.06	14.24
DB(mg/dl)	19.17	18.07	15.81	9.14	8.53
IB(mg/dl)	3.82	4.02	2.57	5.92	5.71
SGOT(U/L)	320	269	181	138	115
SGPT(U/L)	115	95	65	48	42
UREA(mg/dl)	11	14	14	15	14
CREAT(mg/dl)	1.6	1.7	1.5	1.4	1.2
ALBUMIN	3.1	3.0	2.8	3.0	3.0
PROTEIN	5.7	5.6	4.7	4.3	4.3
CALCIUM(mg/dl)	9.2	9.0	8.9	9.0	9.1

DISCUSSION

Drug-induced liver injury represents a broad spectrum of hepatic dysfunction resulting from exposure to prescribed pharmacological agents, non-prescribed medicinal products, and herbal or dietary supplements. Clinical manifestations may range from asymptomatic elevation of liver enzymes to acute liver failure.[2] Over the past decade, CAM-related hepatotoxicity has emerged as an important global health concern, particularly in regions where herbal products are widely consumed under the perception of being inherently safe.[6,7] Reports from international registries and observational studies have shown a growing proportion of DILI cases attributed to herbal and dietary supplements.[5] The pathogenesis of DILI is multifactorial and includes direct hepatocellular injury, mitochondrial dysfunction, oxidative stress, and immune-mediated mechanisms.[11] CAM-related DILI is further complicated by poor standardization of formulations, inconsistent dosing, contamination with heavy metals, pesticide residues, or microbial toxins, and adulteration with hepatotoxic pharmaceutical compounds, resulting in unpredictable clinical patterns.[6,7] Clinically, herb-induced liver injury may present with severe jaundice and prolonged recovery periods, contributing to substantial morbidity.[6,7] In the present case, the patient developed significant hyperbilirubinemia, markedly elevated transaminases, and coagulopathy following intake of a CAM preparation. The absence of viral hepatitis markers, negative autoimmune serology, and imaging showing absence of biliary obstruction supported the diagnosis of CAM-related DILI.[1,2] The development of acute kidney injury indicated systemic involvement and severe disease, necessitating aggressive supportive therapy.[4,12] Therapeutic plasma exchange has been increasingly explored as an adjunctive intervention in acute liver failure due to its ability to remove circulating bilirubin, inflammatory cytokines, and protein-bound toxins while replenishing coagulation factors and plasma proteins.[8] The American Society for Apheresis (ASFA) recognizes acute liver failure as a clinical scenario where TPE may be considered as supportive therapy, particularly in patients with coagulopathy and systemic inflammatory response.[8] According to ASFA guidelines, TPE in acute liver failure is a Category III indication.Larsen et al. demonstrated improved transplant-free survival in patients with acute liver failure treated with high-volume plasma exchange, supporting its role as a bridging strategy.[9] Additionally, a systematic review and meta-analysis has suggested that TPE may contribute to biochemical improvement and better clinical outcomes in selected ALF patients.[10] Accurate estimation of plasma volume to be exchanged is an essential component of therapeutic plasma exchange. Plasma volume(PV) may be derived from estimated blood volume(BV) and hematocrit(Hct) using the formula **PV = BV × (1 − Hct)**. In this patient weighing **99 kg**, the estimated blood volume (70 mL/kg) was approximately **6930 mL**. With a hematocrit of **0.23**, the calculated plasma volume was approximately **5280 mL**. Accordingly, **3000–3500 mL of plasma was exchanged per cycle**. Replacement was done using a combination of **fresh frozen plasma, human albumin, and isotonic saline**, ensuring both coagulation factor replacement and maintenance of intravascular oncotic pressure. Continuous monitoring during the procedure was undertaken to promptly detect complications such as **citrate-induced hypocalcemia, transfusion reactions, hemodynamic fluctuations, and fluid overload**.

In this patient, serial laboratory monitoring demonstrated a progressive decline in bilirubin levels, improvement in INR, and reduction in liver enzyme levels following three cycles of TPE. These findings indicates that plasma exchange facilitates correction of coagulopathy and reduction of toxin burden in acute liver failure.[9,10] Improvement in renal function was also observed, which may reflect overall stabilization of systemic illness following resolution of inflammatory and metabolic derangements. A major limitation in CAM-related DILI is the difficulty in confirming the exact product formulation

and its constituents, as patients commonly do not have records or reliable information regarding the ingredient composition and dosing.[6,7] This highlights the importance of improving public awareness and strengthening regulatory oversight to minimize preventable hepatotoxic events associated with unregulated CAM use.[6,7] Although liver transplantation remains the definitive management for fulminant hepatic failure, its availability may be restricted due to donor limitations and rapid progression of disease.[4,12] In such circumstances, therapeutic plasma exchange may provide an effective supportive option either as a bridge to transplantation or as a bridge to spontaneous recovery in selected patients.[9] However, further prospective studies are needed to establish standardized protocols regarding optimal patient selection, timing, and frequency of sessions for CAM-related DILI.[8,10] This case supports the growing evidence that early initiation of therapeutic plasma exchange may improve clinical outcomes in severe CAM-related DILI complicated by coagulopathy and organ dysfunction, particularly in settings where liver transplantation is not immediately feasible. Close multidisciplinary coordination between hepatologists and transfusion medicine specialists is essential to ensure timely initiation, safe procedural conduct, and appropriate monitoring of therapeutic plasma exchange.

CONCLUSION

CAM-related drug-induced liver injury is an evolving clinical problem and may present with severe hepatic dysfunction accompanied by coagulation abnormalities and systemic organ involvement. In this patient, initiation of therapeutic plasma exchange was followed by gradual improvement in coagulation profile and liver biochemistry, along with resolution of acute kidney injury and clinical stabilization. This report supports the use of TPE as a valuable supportive modality in carefully selected cases of severe CAM-related DILI, particularly in healthcare settings where immediate liver transplantation may not be readily available. Effective outcomes depend on early recognition, prompt cessation of the suspected agent, and coordinated management involving hepatology and transfusion medicine teams.

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