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Case Report

Internal Medicine Section

Plasma Exchange as a Rescue Therapy for Acute Liver Failure

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ABSTRACT

Acute Liver Failure (ALF) is a life-threatening condition and often necessitates Liver Transplantation (LT). However, LT is not available to most patients in developing countries due to resource constraints. Here, authors presents a case of 30-year-old female with ALF and fulfilled the criteria for LT. The aetiology of ALF could not be diagnosed in her. Due to the lack of LT facilities, she was offered plasma exchange as a therapeutic option, which resulted in improvement in sensorium and Liver Function Tests (LFT) {bilirubin, International Normalised Ratio (INR), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT)} over a period of two weeks. She was discharged and was doing well during follow-up. Plasma exchange is a less studied but potential treatment option for ALF when LT is not feasible.

Keywords: Gastroenterology, Hepatitis, Liver function tests

CASE REPORT

A 30-year-old female presented to the Emergency Department with a history of jaundice for 10 days and altered sensorium for one day. There were no prodromal symptoms of fever, nausea, vomiting, loss of appetite, abdominal pain, pruritis, abdominal distension, swelling of legs, gastrointestinal or gum bleed, or skin rashes. She had received Antitubercular Therapy (ATT) for genitourinary tuberculosis (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for two months followed by Isoniazid and Rifampicin for four months) until day of presentation.

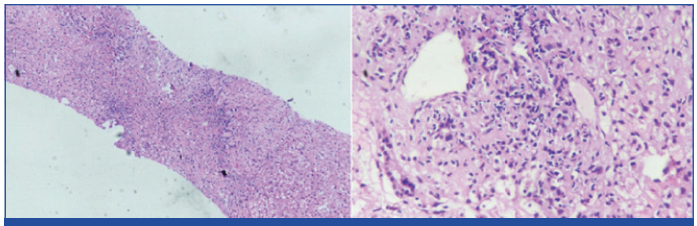
Liver Function Tests (LFT) before initiation of ATT was normal and she did not have any prior co-morbid illness or history of alcohol consumption. She was evaluated elsewhere with laboratory investigations [Table/Fig-1] and was diagnosed with probable drug induced liver injury. ATT was stopped and she underwent Transjugular Liver Biopsy (TJLB) which showed portal and lobular inflammation, confluent necrosis of hepatocytes and bile duct injury [Table/Fig-2]. She was subsequently referred to the Department on the ninth day of her illness after she developed altered sensorium.

On presentation, she had Glasgow Coma Score (GCS) of 6/15 with bilateral equal pupils reacting to light. She had bilateral extensor planters. Her blood pressure was 110/68mmHg, pulse rate was 50/minute, respiratory rate was 24/minute, oxygen saturation was 95% and capillary blood glucose was 130 mg/dL. Clinical examination revealed icterus and there were no stigmata of chronic liver disease, hepatosplenomegaly or ascites.

The blood investigations on admission are detailed in [Table/Fig-1]. Arterial blood gas analysis showed metabolic acidosis with elevated lactates. LFT were suggestive of hepatocellular injury. Ultrasound abdomen revealed hepatomegaly with patent hepatic artery, hepatic vein and portal vein. There were no features of chronic liver disease or portal hypertension. A provisional diagnosis of ALF was made in view of hepatitis and coagulopathy followed by encephalopathy and patient was admitted to the Intensive Care Unit (ICU).

LFT	Day three of illness (Evaluated elsewhere)	Day nine of illness (Admission to hospital)	Day 10 (Post 1st TPE* session)	Day 12 (Post 3rd TPE* session)	Day 14 (Post 5th TPE* session)	Day 18	Day 23	Day 26	Day 30	Day 90
Haemoglobin (g/dL)	8.1	8.8	8.6	9.2	9.5	10.1	9.3	9	9.7	-
Total leucocyte count (per microliter)	5700	6680	6904	8923	5600	4700	5600	6800	6800	-
Platelets (per microliter)	215000	100000	90000	90000	88000	211000	230000	256000	240000	-
Total bilirubin (mg/dL)	6.5	5.2	4.1	4.1	3.6	3.7	3.2	2.46	1.1	0.52
Direct bilirubin (mg/dL)	4.5	3.4	3.2	2.0	1.46	1.63	1.46	0.8	0.6	0.31
Aspartate aminotransferase (IU/L)	353	290	50	50	63	68	71	68	48	42
Alanine aminotransferase (IU/L)	343	347	101	76	97	108	99	78	63	45
Alkaline phosphatase (IU/L)	134	72	147	148	198	322	157	132	120	121
Serum protein (g/dL)	7.1	6.9	6.3	5.7	5.1	5.6	6	6.6	6.2	6.79
Serum albumin (g/dL)	4.3	2.5	3.1	3.1	3.6	3.3	3.4	3.6	4	3.52
International Normalised Ratio (INR)	4.8	4.4	2.2	2.79	2.3	2.3	2.1	1.75	1.2	1.09
Blood ammonia (mg/dL)	-	234	-	-	-	-	-	-	-	-
Urea (mg/dL)	-	33.1	32	28	21	12.2	22	14	24	-
Creatinine (mg/dL)	-	0.81	0.6	0.4	0.58	0.32	0.31	0.45	0.9	-

[Table/Fig-1]: Laboratory investigations of the patient in the course of illness.
TPE: Therapeutic plasma exchange; LFT: Liver function test; mg/dL: Milligram per decilitre; IU/L: International unit/Litre; g/dL: Gram/decilitre



[Table/Fig-2]: Liver biopsy images. (Left) Low power image showing portal and lobular inflammatory activity and confluent necrosis of hepatocytes. (Right) High power image showing portal tract with moderate inflammation and features suggestive of bile duct injury.

She underwent endotracheal intubation for airway protection and was started on standard of care including with Intravenous (i.v.) mannitol for cerebral oedema, empirical i.v. antibiotics (Piperacillin-Tazobactum) and 10% dextrose infusion. Her blood sugar, renal function tests and serum electrolytes were regularly monitored. Aetiological evaluation was negative for hepatotropic viruses Hepatitis B surface Antigen (HBsAg), Immunoglobulin M (IgM), Hepatitis B core (HBc) antibody, anti-Hepatitis C Virus (HCV) antibody, IgM-anti-Hepatitis A Virus (HAV) antibody, IgM anti-Hepatitis E Virus (HEV) antibody}, autoimmune liver disease {Anti-Nuclear Antibody (ANA), anti-Smooth Muscle Antibody (SMA), anti Liver Kidney Microsome type 1 (LKM1) antibody}, Wilson disease (normal serum ceruloplasmin level).

Although she fulfilled Kings' College criteria for emergency LT in ALF [1], it was not feasible due to logistic reasons and financial constraints. A decision to do Therapeutic Plasma Exchange (TPE) for ALF was taken. She underwent daily sessions of TPE with 1.7 times plasma volume (approximately, four litres) for five days with centrifugal TPE system. Fresh Frozen Plasma (FFP) was used as the replacement fluid. Bradycardia and sensorium improved after the second session of TPE. On the third day of her Intensive Care Unit (ICU) stay, she developed gross ascites. Diagnostic paracentesis suggested portal hypertensive ascites. The ascites was diuretic responsive. She was gradually weaned off the ventilator and extubated on sixth day of ICU.

She was shifted to the ward after seven days of ICU stay. Sensorium and appetite continued to improve. LFT improved gradually and normalised over a month [Table/Fig-1]. She was discharged after three weeks of hospital stay. There was no subsequent recurrence of ascites after discontinuation of diuretics. She was doing well until the last follow-up visit, three months post discharge.

DISCUSSION

This is a case of ALF, where timely TPE salvaged the patient, in the lack of LT facilities. This is the first reported instance of successful use of TPE for ALF from Uttarakhand, with limited availability of advanced healthcare facilities. The work-up for usual aetiologies of ALF was negative. Despite ATT exposure, causality for ALF could not be established, because of the longer ATT-Encephalopathy Interval (AEI). ATT is the most common cause of Drug-Induced Liver Injury (DILI) in India [2]. The reported median AEI is 30 (7-350) days [3], whereas in the index patient AEI was six months. In fact, a significantly longer AEI was noted in patients with ATT induced ALF and concomitant hepatitis virus co-infection [3]. Hence, the possibility of an undetected aetiology in the present patient cannot be ruled out. She had portal hypertensive ascites, which though uncommon in ALF, has been documented in previous studies and has been postulated to occur due to reticulin collapse in the liver [4,5]. The presence of confluent necrosis and absence of fibrosis on liver biopsy further supported the diagnosis of ALF.

The reported survival in ALF varies from 30-40% (with medical management alone) to 74% (with LT) [3,6]. Various criteria like the Kings' College criteria have been developed for the early identification of patients who merit LT [1]. Due to resource constraints and demand for LT in India, outnumbering the supply by a factor of ten, emergency LT is challenging [7]. In such constrained situations, an effective non surgical option may act as bridge to LT or sometimes salvage the patient in the lack of it. In a retrospective analysis of 55 patients with severe Acute on Chronic Liver Failure (ACLF) and ALF standard-volume PE (1-1.5 plasma volume) significantly improved the levels of total bilirubin, prothrombin time and liver enzymes [8].

Cainelli F et al., have proposed practical approach in resource-constrained countries to reduces mortality where LT is not available. These approaches includes measures to reduce intracranial pressure (hypertonic saline and mannitol, preventing hypoglycaemia, gastroprotective agents, use of broader antibiotics and antifungal, correcting coagulopathy, haemofiltration of indicated, temporary partial portal vein arterialisation etc., [9]. Maheshwari A et al., have conducted a retrospective study on 45 critically ill liver disease patients and found that TPE resulted in a statistically significant reduction in the bilirubin level, AST, ALT, Prothrombin Time (PT), INR, serum ferritin level [10]. In a systematic review by Tan EX et al., high-volume plasmapheresis has been shown to improve survival in non transplanted patients with ALF in terms of 30-and 90-d mortality [11]. Maiwall R and Moreau R, have emphasised the role of TPE and stem cell therapy in hepatitis B related ACLF [12].

Recently, published literature has provided encouraging results for TPE. Larsen FS et al., in a randomised controlled trial of ALF patients, reported decline in pro-inflammatory markers and monocyte activation and improved transplant free survival with TPE compared to standard medical treatment [13]. Akin to the emerging evidence describing favourable effects of TPE on laboratory parameters and clinical outcomes in liver failure patients [14], the present study patient could be salvaged by a timely TPE in the lack of LT facilities. However, the data on TPE in ALF is limited and evolving. Further studies are required to improve our understanding of this potentially lifesaving option especially in resource constrained settings of developing countries like India.

CONCLUSION(S)

Acute Liver Failure (ALF) is a potentially fatal conditions which requires early diagnosis of the condition and initiation of supportive management. LT is at present the only proven definitive therapy for ALF but is limited by availability and resource constraints. TPE in a potential treatment option for ALF and should be considered in ALF patients when LT is not available.

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