A Life Saving Exchange: A Case of Severe Direct Hyperbilirubinemia And Liver Failure in Leptospirosis Successfully Treated with Plasma Exchange

AMBD Alahakoon¹, WWLA Jayanaga²

¹Teaching Hospital Peradeniya. Sri Lanka
²National Hospital of Sri Lanka - Colombo, Sri Lanka

ABSTRACT

Leptospirosis is an infection with multiorgan involvement and a high mortality rate. Extreme hyperbilirubinemia in leptospirosis has been reported to exert multiple cellular toxic effects on kidney and liver cells. We describe a young man with leptospirosis who had extreme hyperbilirubinemia, acute liver injury, coagulopathy, hepatic encephalopathy, and pulmonary haemorrhages. Early initiation of therapeutic plasma exchange (PEX) dramatically improved patient’s clinical and biochemical parameters. We conclude that, in addition to the mortality benefit provided by PEX in severe pulmonary hemorrhage syndrome in leptospirosis, PEX is also beneficial in reducing systemic toxic insults of hyperbilirubinemia.

Keywords: Plasma exchange, Leptospirosis, hyperbilirubinemia, pulmonary haemorrhage

INTRODUCTION

Therapeutic apheresis plasma exchange is an extracorporeal blood purification technique for the removal of large molecular weight substances or cells from plasma. Indications for therapeutic plasma exchange have been described based on evidence of clinical efficacy in literature (1). Early therapeutic plasma exchange has shown to reduce mortality in leptospirosis associated severe pulmonary haemorrhage syndrome (2). Direct hyperbilirubinemia caused by different pathogenic factors can also be treated by plasmapheresis (3). However, plasma exchange for hyperbilirubinemia is not a pathogenesis-oriented therapy. Therefore, proper treatment of underlying condition is of paramount significance for a better clinical outcome.

CASE REPORT

A 29-year-old previously healthy young man presented with fever, arthralgia, and myalgia for 3 days. He noticed yellow color discoloration of the body and reduced urine output on the 3rd day of the illness which prompted him to a health care facility. On examination he had conjunctival suffusion, deep icterus, severe muscle tenderness but remainder of examination was normal. Laboratory investigations revealed neutrophil leucocytosis 18000 mic/l (4000-11000),
thrombocytopenia 9800 mic/l (150000-450000), elevated creatinine phosphokinase 890 U/l (100-400), elevated serum creatinine 2.1 mg/dl (0.4-1.2) red cells in urine, normal coagulation profile, slightly elevated transaminases AST 112 U/L (<50), ALT 139 U/L (<50) and severe direct hyperbilirubinemia 156 mmol/l (1.7-20.5). With a history of exposure to rodents in paddy fields, a presumptive diagnosis of leptospirosis complicated with acute kidney injury and hyperbilirubinemia was made and he was treated with intravenous ceftriaxone. Over next two days with proper fluid management and antibiotic therapy his urine output improved, and serum creatinine values improved from 3.2mg/dl to 0.8 mg/dl (0.4-1.2).

However, on 6th day of the illness, patient developed confusion and melena. It was noted that the icterus was becoming deep. His GCS dropped to 7. In addition, he developed shortness of breath with desaturation to SpO2 86% on air. He was transferred to Medical Intensive Care Unit for invasive mechanical ventilation. Repeat laboratory work-up was performed. AST, ALT remained below 300U/l, direct hyperbilirubinemia was worsening with a value of 1600micmol/l, INR was 3.1 with normal APTT and fibrinogen levels, USS abdomen excluded an obstructive liver pathology, NCCT brain was normal and CXR was suggestive of diffuse pulmonary haemorrhages (Figure 1). A diagnosis of severe pulmonary hemorrhage syndrome and acute liver injury associated with hepatic encephalopathy and coagulopathy was made. After correcting anemia and coagulopathy with Fresh Frozen Plasma, cryoprecipitate and whole blood, therapeutic plasma exchange (PEX) was initiated. Patient demonstrated a dramatic clinical and biochemical improvement after 3 cycles of PEX. He was extubated on day 14th of the illness. On discharge from the ICU, Lepto MAT was informed as positive in 1:160 titre with negative hantavirus/HSV/Hepatitis ABCE antibodies, confirming the diagnosis of leptospirosis.

**DISCUSSION**

Leptospirosis is a common zoonosis in Sri Lanka. Clinical spectrum of leptospirosis can range from a simple febrile illness to life threatening hepatorenal failure, diffuse alveolar hemorrhage and coagulopathy. Conjugated hyperbilirubinemia and oliguric renal failure are associated with a higher mortality (2).

The pathogenesis of direct bilirubinemia in leptospirosis is largely unknown. Destruction of bile canaliculi by direct bacterial invasion, intercellular junction disruption by bacterium subsequently leading to bile leaks from bile canaliculi are been described as pathogenic mechanisms of jaundice in leptospirosis (4). Our patient had a severe degree of leptospirosis associated direct hyperbilirubinemia which could not be attributed to any other pathology. Extreme hyperbilirubinemia has been reported to exert multiple cellular toxic effects, including effects on cellular respiration, membrane integrity, and transport functions, and excessive accumulation of bilirubin has been incriminated as causing renal tubular damage, thereby contributing to persistence of renal failure. Treatment of the hyperbilirubinemia per se may therefore be beneficial in reducing toxic insults to kidney and liver cells.

Therapeutic plasma exchange (PEX), if initiated within 48 hrs of detection, has shown to reduce mortality of patients with leptospirosis associated diffuse pulmonary hemorrhage (2). It is elucidated that the mechanism of therapeutic outcome is by removing circulating antibodies and immune complexes. However, liver failure and hyperbilirubinemia in leptospirosis are not direct indications to commence PEX, as the evidence for such is lacking.

In acute liver failure, there is significant hepatocyte necrosis that is followed by the release of cytokines and adhesion molecules. PEX reduces this proinflammatory cascade by removing plasma cytokines, adhesion molecules and toxins while replacing plasma factors, thereby reducing systemic disturbances associated with liver failure; encephalopathy, coagulopathy (5). Hyperbilirubinemias can be treated by different methods such as hemoperfusion, hemodialysis, molecular adsorbent recycling system and PEX, or by a combination of these methods (3). Studies show that three mechanisms did not differ in terms of lowering bilirubin levels, therefore recommended choosing a technique based on
costs, availability of expertise and duration of treatment. Another study demonstrated that PEX, hemoperfusion and molecular adsorbent recycling system could reduce bilirubin levels by 46.53%, 21.20%, and 37.69% (6).

However, PEX for hyperbilirubinemia is not a pathogenesis-oriented therapy. It may be used as an adjunctive therapy in patients with severe prolonged hyperbilirubinemia. Therefore, PEX, together with a proper treatment of any underlying condition, may allow sufficient time for regeneration of the liver and a better clinical outcome.

**CONCLUSION**

Although initiation of early therapeutic plasma exchange is commonly practised to reduce mortality in leptospirosis associated severe pulmonary haemorrhage syndrome, the importance of PEX in treating acute liver failure and severe direct hyperbilirubinemia in leptospirosis is largely overlooked by medical community. This case report highlights the favourable outcome of PEX in treatment of severe hyperbilirubinaemia and acute liver failure where the primary therapeutic decision to initiate PEX was made to treat coexisting pulmonary haemorrhages.

**REFERENCES**


**Author declaration**

**Authors’ contributions:**
Drafting of the manuscript: A.M.B.D.A; Study supervision: W.W.L.A.J.

**Conflicts of interest:**
The authors declare that there is no financial or non-financial conflict of interest.

**Funding statement:**
Self-funded

**Ethics statement:**
Written informed consent was obtained from the patient.

**Statement on data availability:**
All data generated during this study are included in this published article.