

First description of Single Pass Albumin Dialysis (SPAD) in combination with cytokine adsorption (CytoSorb®) in a patient with fulminant liver failure and secondary hemophagocytic lymphohistiocytosis due to generalized HSV-1 infection

Silvius Frimmel¹, Jan Schipper¹, Jörg Henschel², Steffen R. Mitzner¹, Sebastian Koball¹

1. Department of Medicine, Division of Nephrology, Rostock University Medical Center, Germany

2. Department of Medicine, Intensive Care Unit, Rostock University Medical Center, Germany

Introduction

Acute liver failure (ALF) is a rare, life-threatening complication of herpes simplex virus (HSV) infection which can occur in immunocompetent patients. Liver transplantation is the ultima ratio in cases of progressive ALF despite antiviral treatment. For bridging to liver transplantation, extracorporeal liver support with the Molecular Adsorbent Recirculating System (MARS®; Gambro, Lund, Sweden) has been shown to be a therapeutic option in ALF. Only scarce data exists concerning the use of single pass albumin dialysis (SPAD) in such cases. Hemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome that can occur in many underlying conditions. Animal studies, case reports, and preliminary data from a clinical trial in septic patients demonstrated that a reduction in blood cytokine levels using an extracorporeal cytokine adsorption column (CytoSorb®; Cytosorbents GmbH, Berlin, Germany) can effectively attenuate the inflammatory response during sepsis and possibly improve outcomes.



Fig. 1: Cytosorb hemoadsorption during SPAD

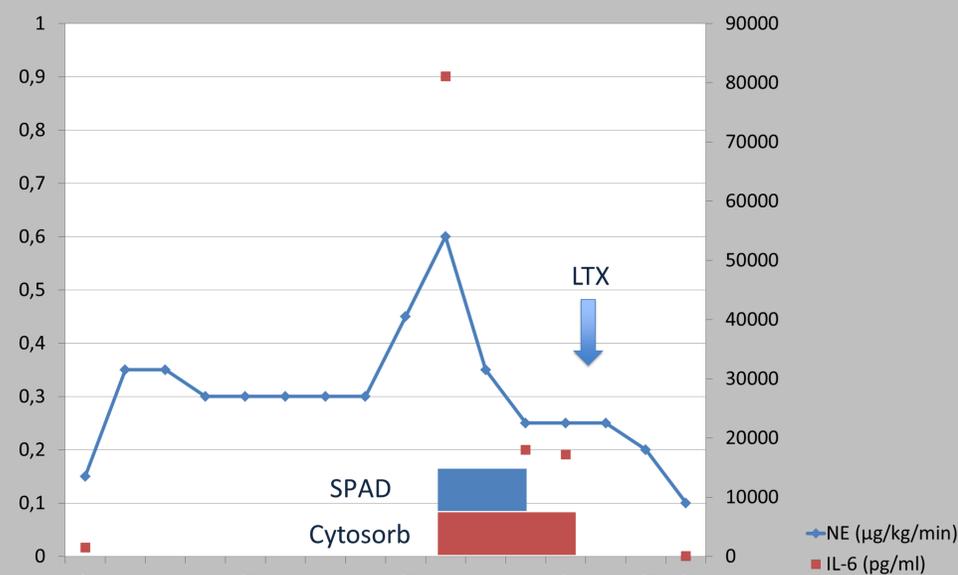


Fig 2: Dosage of Norepinephrine (NE) and plasma levels of IL-6 under therapy

Case Report

A 50-year-old immunocompetent woman was admitted to our hospital for acute hepatitis with ALF. A transjugular biopsy of the liver showed acute liver cell necrosis. Herpes simplex virus type 1 (HSV-1) was identified as the causative agent and intravenous antiviral therapy with aciclovir was initiated. As liver failure progressed, the patient was transferred to the intensive care unit. She rapidly developed multiple organ dysfunction syndrome with hepatic coma, severe coagulopathy, acute anuric renal failure, respiratory insufficiency, and arterial hypotension. The patient was listed for highly urgent liver transplantation at Eurotransplant. Hyperferritinemia up to 266,000 µg/l, (normal range 13-300) with pancytopenia and a high plasma level of the soluble interleukin-2-receptor (6815 U/ml, range 223-710) induced suspicion of secondary virus-associated HLH. A bone marrow biopsy was performed. The histological examination showed many activated macrophages with incorporation of erythrocytes and granulocytes, supporting the diagnosis of HLH secondary to HSV-1-infection.

Hemodialysis and extracorporeal liver support were initiated using MARS®-therapy for 6 hours on the first day and for 19 hours on the second day. Worsening circulatory failure with increasing need for norepinephrine (max. 0.6 µg/kg/min) and excessively elevated concentrations of inflammation markers (Interleukin-6, Ferritin) indicated ongoing severe SIRS.

Thus, the extracorporeal therapy was changed to continuous venovenous hemodialysis with SPAD (dialysate albumin concentration 2%, dialysate flow 1500 ml/h, 12 hours of treatment). A hemoadsorption column (CytoSorb®) was integrated in a predialyzer position (total treatment duration 20 hours; Fig. 1) for cytokine adsorption. Regional anticoagulation was performed using sodium citrate. Interleukin-6 (IL-6) concentration before treatment was 81,059 pg/ml (normal range <7.00 pg/ml). After 12 hours of treatment it fell to 17,177 pg/ml. Norepinephrine dosage could be reduced to 0.25 µg/kg/min (Fig. 2). Clinically, no further deterioration of the state of the patient was seen. Interestingly, a reduction of the moderately elevated bilirubin concentration was achieved during the combined treatment with SPAD and CytoSorb®, whereas during MARS® therapy there was a slight increase. Successful orthotopic liver transplantation was performed on the fourth day of ICU treatment. Two days after transplantation under immunosuppression with tacrolimus and prednisone the plasma levels of ferritin and IL-6 decreased further to 7202 µg/l and 47.2 pg/ml, respectively (Fig. 2).

Conclusions

To the best of our knowledge, this is the first report of the combined use of CytoSorb® hemoadsorption with SPAD in a patient suffering from ALF and probable HLH with severe SIRS who was listed for liver transplantation. A marked decrease of IL-6, and bilirubin, as well as a reduction of vasopressor need were the major results of this intervention. Importantly, treatment was safe and well-tolerated, without any adverse events.