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CASE REPORT

Cytokine hemoadsorption therapy - An adjuvant in the management of septic shock with multi-organ dysfunction: A case report

Vishnu Manohar[1], Shilpa Raj[2], Sreekrishnan T P[1], Gireesh Kumar K P[1]

[1]Department of Emergency Medicine, Amrita Institute of Medical Sciences, Kochi, Kerala, India, [2]Department of Pharmacy Practice, Amrita School of Pharmacy, Kochi, Kerala, India

Correspondence to: Gireesh Kumar K P, E-mail: gireeshkumarkp@aims.amrita.edu

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ABSTRACT

Sepsis is "a life-threatening organ dysfunction caused by a dysregulated host response to infection." Cytokine hemoadsorption is found to be effective in the management of septic shock, by reducing cytokines and other inflammatory mediators, thereby improving hemodynamics and preventing multiple organ dysfunction syndrome. Here, we report a case of 22-year-old male patient, presented with fever, vomiting, loose stools, and altered mental status since 2 weeks, was provisionally diagnosed with severe sepsis/septic shock - salmonella-induced, hepatitis B-induced acute liver failure, hemophagocytic lymphohistiocytosis, and disseminated intravascular coagulopathy. The patient was admitted in intensive care unit and started on cytokine hemoperfusion therapy for 12 h. Before cytokine hemoadsorption, he was on three inotropic supports, IV antibiotics, and other supportive measures. The patient improved symptomatically and hemodynamically within 8 h of cytokine therapy, and inotropic supports were weaned off. Here, we report a successful outcome in a case of septic shock with organ damage treated with cytokine hemoadsorbant as an adjuvant along with routine conservative management.

KEY WORDS: Severe Sepsis; Septic Shock; Cytokine Hemoadsorption; Multi-organ Dysfunction; Hemophagocytic Lymphohistiocytosis

INTRODUCTION

Sepsis is defined as "a life-threatening organ dysfunction caused by a dysregulated host response to infection."[1] Septic shock may lead to multiple organ dysfunction syndrome (MODS), which is a medical emergency and should be treated early and aggressively for favorable outcome.[2]

Cytokine hemoadsorption is found to be a safe and effective adjuvant in the management of sepsis.[3] Excessive cytokine production can lead to massive inflammation, organ damage, and even death in life-threatening illnesses such as sepsis, burn injury, or trauma. Physicians have enthusiastically adopted cytokine hemoadsorption for the management of severe sepsis with MODS.[4]

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CASE REPORT

A 22-year-old male patient with no known comorbidities presented at a nearby local hospital with complaints of fever, vomiting, and loose stools since 2 weeks. He had developed all these symptoms after a long vacation of 10 days. He had chronic history of substance abuse and was habituated to ethanol, cigarette smoking (two packs/day), and cannabis use. During the examination, he was found to have leukocytosis, thrombocytopenia, jaundice, hepatitis B-positive, and deranged liver enzymes [aspartate transferase (AST) and alanine transferase (ALT) >1000 IU/L]. Since these

symptoms were not subsiding with conventional management and due to altered sensorium since 2 days, he was brought to our hospital for further evaluation. On examination, he was febrile (100 F), tachycardic (120 b/min), and hypotensive (80/40 mmHg), and hence, managed with ultrasonography-guided fluid resuscitation. With this line of management, there was a transient improvement in blood pressure. Later, he was shifted to intensive care unit (ICU) for further monitoring and management. He was empirically started on IV antibiotics (Meropenem) and continued intravenous fluid resuscitation. Due to continued altered mental status, he was catheterized and fed through Ryle's tube. Sepsis panel report was positive for hepatitis and salmonella. Laboratory investigations (refer Table 1) revealed leukocytosis, thrombocytopenia (25.4 K/uL), elevated markers of infection (procalcitonin: 12.61 ng/ml and C-reactive protein: 176.15 mg/L), elevated liver enzymes (AST: 1427.0IU/L and ALT: 521.0IU/L), elevated ferritin (45.712 ng/ml), reduced plasma fibrinogen (91.9v mg/dl), elevated D-dimer (2.3 mg/L), and elevated triglycerides (326.9 mg/dl). Ultrasound of the abdomen showed normal liver with splenomegaly. Thereby, he was provisionally diagnosed with severe sepsis/septic shock - Salmonella-induced, probably hepatitis B-induced acute liver failure (ALF), hemophagocytic lymphohistiocytosis (HLH) (score five out of eight according to 2004 HLH guidelines), and severe coagulopathy.

On the day one of ICU stay, without any delay, he was started on extracorporeal cytokine hemoperfusion therapy for 12 h. Before cytokine hemoadsorption, he was on three inotropic supports such as noradrenaline, vasopressin, and dopamine, IV antibiotics, and other supportive measures. With the cytokine hemoadsorption therapy, the patient improved symptomatically and hemodynamically within 8 h and was able to remove two inotropic supports (vasopressin and dopamine); eventually, the other inotropic support (noradrenaline) was also weaned out after 12 h (Table 2). For HLH, he was concomitantly treated with 2 g of IVIG, administered over 5 days according to the hospital protocol along with a high dose of intravenous steroids. Blood transfusions were done to meet the standard cutoff points. Within 4 days, he became completely stable and was shifted out to ward and later on discharged with antiviral therapy for hepatitis B.

DISCUSSION

Here, we report a case treated with cytokine hemoadsorption device as an adjuvant therapy in patient with septic shock and organ damage. The treatment was very effective, well-tolerated, and the patient hemodynamically improved within 8 h of therapy. The cornerstone of resuscitation in septic shock is rapid restoration of perfusion by aggressive administration of intravenous fluids, inotropic supports, and empiric therapy of antibiotics. Hemoadsorption is found to be beneficial in patients with severe sepsis or septic shock based on the clinical and experimental evidence. Pre-clinical experimental study conducted in animal models with septic shock also suggests its effectiveness in reducing infection and improving the overall survival rate.[1]

Peng et al. conducted an *in vitro* study in rat subjects with inflammation and found that the concentration of tumor necrosis, interleukins (IL) such as IL-1beta, IL-6, and IL-10, and MAP was significantly lower after hemoadsorption with Cytosorb which further resulted in significantly longer mean survival time (720 vs. 381 min; $P < 0.05$, Mann-Whitney test), better overall survival rate (11/17 vs. 2/16; $P < 0.01$), and decreased mortality rate (hazard ratio, 0.11; $P = 0.005$).[5]

A study conducted by Kogelmann et al. in 26 critically ill patients with septic shock evaluated the impact of the Cytosorb hemoadsorption device and found that treatment with cytokine hemoadsorption in these patients was associated with hemodynamic stabilization and blood lactate reduction. From their study, they came to a conclusion that hemoadsorption using Cytosorb resulted in rapid hemodynamic stabilization and increased survival rate (62.5%) without any noticeable side effects, mainly in patients whom Cytosorb therapy was early initiated which will also support our conclusion.[6]

Frimmel et al. performed Cytosorb hemoadsorption in combination with subcutaneous peritoneal access device in

Table 1: Laboratory parameters before and after cytokine hemoadsorption therapy

Parameters	On admission	Day 1 in ICU	Day 2 in ICU	On discharge
Platelet (K/uL)	25.4	50	102	130
Procalcitonin (ng/ml)	12.61	-	-	0.535
CRP (mg/L)	176.15	152.9	74.97	18.1
SGOT (AST) IU/L	1427	992.5	540.1	188.3
SGPT (ALT) IU/L	521	378.5	226.9	124.6
Ferritin (ng/ml)	45.712	26.708	7532.3	2706.5
Triglycerides (mg/dl)	326.9	-	-	178.6
Plasma fibrinogen (mg/dl)	91.9	136	153	201

AST: Aspartate transferase, ALT: Alanine transferase, CRP: C-reactive protein, SGPT: Serum glutamic pyruvic transaminase, SGOT: Serum glutamic oxaloacetic transaminase, ICU: Intensive care unit

Table 2: Inotropic support before and after cytokine hemoadsorption therapy

Inotropic supports	Dose before cytokine hemoadsorption therapy	Dose after cytokine hemoadsorption therapy	
		Day 1	Day 2
Noradrenaline (μg/kg/min)	0.1	0.1	0.02
Dopamine (μg/kg/min)	20	5	Nil
Vasopressin (IU/min)	0.06	0.02	Nil

a patient suffering from ALF and probable HLH with severe systemic inflammatory response syndrome, observed a marked decrease in IL-6 and bilirubin. This safe and well-tolerated treatment also helped to reduce the need for vasopressor use. By reducing pro-inflammatory cytokines to correct the immune response and by detoxification, cytokine adsorption is a useful tool in the management of ALF and several hyperinflammatory syndromes such as HLH.[7]

CONCLUSION

In our case, we reported a successful outcome in a high-risk mortality case of septic shock with organ damage treated with 12 h of cytokine hemoadsorbent as an adjuvant along with IV antibiotics and IV fluids. Cytokine hemoadsorption therapy in patients with severe sepsis or septic shock along with organ damage is a successful option as rescue therapy. However, further multicentered prospective studies are needed to establish the benefit of this cytokine adsorbent therapy in the treatment of septic shock.

REFERENCES

1. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. Crit Care Med. 2017;45(3):486-552.
2. Basu R, Pathak S, Goyal J, Chaudhry R, Goel RB, Barwal A. Use of a novel hemoadsorption device for cytokine removal as adjuvant therapy in a patient with septic shock with multi-organ dysfunction: A case study. Indian J Crit Care Med. 2014;18(12):822-4.
3. Shaw KM, Bamzai R, Chan P, Cramer C. Biocon Partners With CytoSorbents to Market CytoSorb® - A First-in-Class Therapy for Sepsis Management; 2013.
4. Girardot T, Venet F, Rimmele T. Immunomodulation: The future for sepsis? Annual Update in Intensive Care and Emergency Medicine. Switzerland: Springer; 2016. p. 49-57.
5. Peng ZY, Carter MJ, Kellum JA. Effects of hemoadsorption on cytokine removal and short-term survival in septic rats. Crit Care Med. 2008;36(5):1573-7.
6. Kogelmann K, Jarczak D, Scheller M, Drüner M. Hemoadsorption by CytoSorb in septic patients: A case series. Crit Care. 2017;21(1):74.
7. Frimmel S, Schipper J, Henschel J, Yu TT, Mitzner SR, Koball S. First description of single-pass albumin dialysis combined with cytokine adsorption in fulminant liver failure and hemophagocytic syndrome resulting from generalised herpes simplex virus infection. Liver Transpl. 2014;20(12):1523-4.

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