CASE REPORT

Successful treatment of septic shock with disseminated intravascular coagulation using combined polymyxin-B direct hemoperfusion and recombinant thrombomodulin therapy

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ABSTRACT

We report successful treatment of septic shock accompanied by disseminated intravascular coagulation (DIC) resulting from infection of liver abscess in a patient using a combination of polymyxin-B direct hemoperfusion (PMX-DHP) and recombinant thrombomodulin (rTM). Although hepatic cyst had been observed over 2 years previously, drainage was not performed due to limited findings of abscess on current abdominal computed tomography and ultrasonography. Control of the focus of infection therefore took time. After initiating PMX-DHP and rTM, arterial blood pressure increased and remained high. Combination therapy with PMX-DHP and rTM provides an effective approach for septic shock with DIC.

Key words: Recombinant thrombomodulin; PMX-DHP; Septic shock; Disseminated intravascular coagulation

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[**Abbreviations used:** rTM, thrombomodulin; CHDF, continuous hemodiafiltration; PMX-DHP, polymyxin B-immobilized column direct hemoperfusion]

INTRODUCTION

High-mobility group box-1 (HMGB-1) is a DNA-binding protein found in almost all nucleated cells. Inside the nucleus, HMGB-1 maintains DNA structure and regulates transcription, and in damaged cells acts as a host-defense factor at the injury site. However, HMGB-1 is excessively released during septic shock and acts as a lethal factor.[1,2] In patients with septic shock, polymyxin-B direct hemoperfusion (PMX-DHP) improves hemodynamics by adsorbing endogenous cannabinoids and indirectly reduces cytokine concentration by adsorbing activated mononuclear cells, thereby improving regulation of HMGB-1 production and pulmonary oxygenation capacity.[3,4] However, as PMX-DHP does not directly act on HMGB-1, treatment effects are limited in cases complicated by disseminated intravascular coagulation (DIC) or multiple-organ dysfunction syndrome (MODS) in which hyper-HMGB-1-emia causes a cytokine storm. Recombinant thrombomodulin (rTM) provides an effective treatment for DIC by exerting anti-inflammatory effects in addition to anti-coagulation properties through direct anti-HMGB-1 activity.[5] Combined use of PMX-DHP and rTM may thus prevent the

cytokine storm leading to MODS in DIC.

We report herein the combined use of PMX-DHP and rTM to successfully treat septic shock with DIC in a patient in whom hepatic cyst drainage was not performed.

CASE REPORT

A 77-year-old man was admitted to our hospital with fever and weakness. He had experienced sweating, fever, weakness, and diarrhea for 2 days previously. He had a history of hypertension and rheumatoid arthritis. Physical examination on admission to the hospital revealed: temperature, 37.5 °C; blood pressure, 76/41 mmHg; heart rate, 147 beats/min; SpO_2, 91% (under O_2 at 5 L/min via face mask); and respiratory rate, 42 breaths/min. Glasgow coma scale score was 13/15.

Laboratory tests showed leucocytes and the C-reactive protein concentration was elevated (20.7×10^9/L and 19.82×10^4 μg/L, respectively). Additional results included: hemoglobin, 119 g/L; hematocrit, 0.34/L; platelets 75×10^9/L; Na, 137 mmol/L; K, 3.2 mmol/L; Cl, 107 mmol/L; urea nitrogen, 9.3 mmol/L; creatinine, 84.9 mol/L; aspartate aminotransferase, 259 IU/L; alanine aminotransferase, 46 IU/L; lactate dehydrogenase, 603 IU/L; prothrombin time-international normalized ratio, 1.23; and fibrin decomposition product, 51.1 μg/ml. Arterial gas analysis (under O_2 at 7 L/min via face mask) showed metabolic acidosis (pH - 7.46; PaO_2 - 68 Torr; $PaCO_2$ - 22 Torr; HCO_3 - 16.2 mmol/L; base excess - — 5.8 mmol/L). Urinary tract infection was initially suspected, but 2 days after admission he experienced disturbance of consciousness and shaking chills, and was transferred to the intensive care unit (ICU). A hepatic cyst had been observed on abdominal contrast enhanced computed tomography (CT) performed 2 years previously, but liver abscess findings on the current abdominal contrast-enhanced CT were limited.

The clinical course is shown in Figure 1. When the patient entered the ICU, blood pressure was low (46/25 mmHg) even after administration of noradrenaline for 0.3 μg/kg/min. He was intubated and ventilated, and treated with infusion of Ringer's solution and antibiotics. For

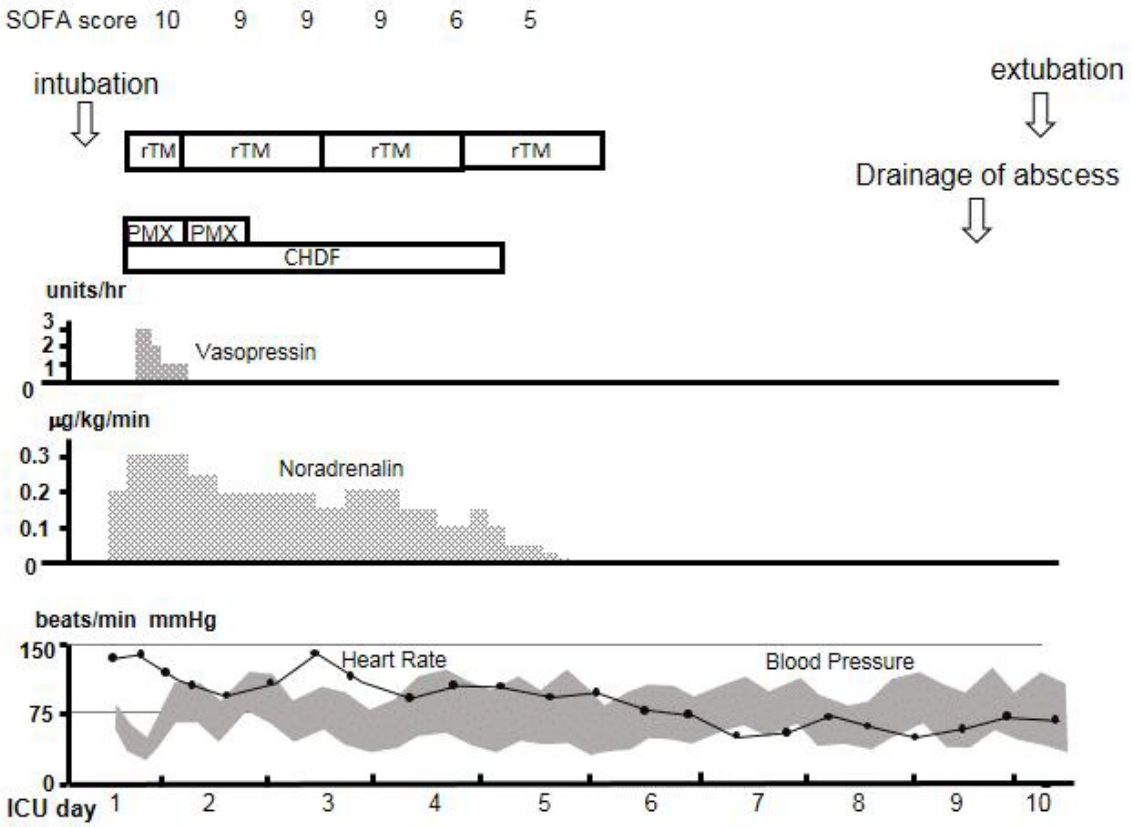

Figure 1: Clinical course of treatment and hemodynamics

all this, blood pressure continued to be low. DIC developed and rTM was administered. Moreover, continuous hemodiafiltration (CHDF) was started and polymyxin B-immobilized fibre column direct hemoperfusion (PMX-DHP) was performed for 4 h on each of days 1 and 2. After initiating PMX-DHP and rTM, arterial blood pressure and urine volume gradually increased. And the Sequential Organ Failure Assessment score (SOFA score) was decreased. The patient recovered from shock and underwent drainage of the abscess on ICU day 9 and extubated on ICU day 10.

DISCUSSION

Despite suspicion of biliary tract infection, the necessity of infection drainage was difficult to determine due to limited liver abscess findings on abdominal contrast-enhanced CT despite observation of the hepatic cyst on CT performed 2 years previously. Controlling the focus of infection took time. Antimicrobial pharmacotherapy was administered, but translocation of these agents into the infected cyst may have been inadequate. The patient developed septic shock requiring a continuous dose of vasopressin and high-dose noradrenaline, but improved hemodynamics were achieved using PMX-DHP and CHDF. Treatment using rTM for DIC improved SOFA score. Combined use of PMX-DHP and rTM may prevent cytokine storm leading to MODS in DIC. This approach proved effective in the present patient.

CONCLUSION

The findings in this case indicate that combination therapy with polymyxin-B direct hemoperfusion (PMX-DHP) and recombinant thrombomodulin (rTM) provides an effective approach for septic shock with DIC.

Conflict of interest: Nil

Authors' Contribution:

YM; treated this patient and written this manuscript

YM;treated this patient

KS; conceived of the case study, and participated in its design and coordination and helped to draft the manuscript.

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