A case of hyperbilirubinemia associated with sepsis with a good outcome after bilirubin adsorption therapy

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Introduction

Bile stasis associated with severe bacterial infections can cause acute lung injury and renal failure due to prolonged hyperbilirubinemia [1]. When patients with severe sepsis are complicated by acute hepatic or renal injury, the mortality rate is remarkably high (54.3% for hepatic injury and 38.2% for renal injury) and the prognosis is poor [2].
Sepsis-associated cholestasis and prolonged hyperbilirubinemia cause destruction of hepatocytes and bile ducts and progress to liver failure [3].

In Japan, plasma exchange is performed in more than 90% of patients with acute liver failure, and hemodiafiltration is performed in 70-80% [4].
We report a case of acute hepatic failure secondary to septic shock for whom hemodiafiltration and bilirubin adsorption therapy (Plasma Apheresis; PA) were treated to prevent further organ damage and who had a good outcome.

Case Presentation

A 9-year-old Japanese boy was diagnosed septic shock due to *Pseudomonas aeruginosa* during induction of remission after relapse of B-cell precursor acute lymphoblastic leukemia.

His Pediatric Logistic Organ Dysfunction 2 score was 24 points and his Pediatric End-stage Liver Disease score was 17 points. He was critically ill and he was predicted poor prognosis in terms of both his life and liver (Figure 1). He received ventilatory support, vasopressors, intravenous fluids, steroids, broad-spectrum antimicrobial agents, continuous hemodiafiltration for acute kidney injury, and endotoxin adsorption therapy (PMX) in an intensive care unit.

Although his blood pressure stabilized and his hepatic enzyme levels tended to improve, his biliary system enzymes increased on the fourteenth day of the disease, and he developed marked hyperbilirubinemia with a total bilirubin level of 25.0 mg/dL and direct bilirubin level of 20.0 mg/dL.

There was no improvement despite attempts at diuresis with ursodeoxycholic acid; therefore, bilirubin adsorption therapy (blood separation membrane: OP-05D, plasma adsorption membrane: Plasova BRS, blood flow rate: 50 mL/min, plasma separation rate: 30%, plasma therapeutic dose: 4,500 mL/dose, and anticoagulation: 25 mg/hour nafamostat mesylate (Table 1)) was administered on the sixteenth to eighteenth day.

Total bilirubin clearance was 64.4%, 51.8%, and 52.5% on the sixteenth, seventeenth, and eighteenth day, respectively. Total bilirubin and direct bilirubin levels improved to 5.7 and 4.2 mg/dL (Table 2).
Since then, bilirubin has normalized and no complications of organ damage have appeared (Figure 2, 3).

Vascular access	right internal jugular vein, urokinase-coated double-lumen catheter 7 Fr
Plasma separator	Plasmaflo OP-05D (Asahi Kasei Medical Co. Ltd.)
Bilirubin absorber	Plasorba BRS-350 (Asahi Kasei Medical Co. Ltd.)
Machine	TR-55X-II (Toray Medical Co. Ltd.)
Priming solution	saline
Anticoagulant	namfamostat mesylate
Blood flow rate	50 mL/min
Plasma flow rate	15 mL/min (30% of blood flow)
Processed plasma volume	4,500 mL/session

Table 1. Dialysis circuit settings

	PA①		PA②		PA③	
Total proteins	6.1→5.7	g/dL	5.1→5.2	g/dL	5.2→4.9	g/dL
albumin	3.9→3.9	g/dL	3.3→3.6	g/dL	3.6→3.5	g/dL
Direct bilirubin	25.0→8.9	mg/dL	13.7→6.6	mg/dL	12.0→5.7	mg/dL
clearance	64.4	%	51.8	%	52.5	%
Indirect bilirubin	20.2→6.7	mg/dL	10.4→4.8	mg/dL	9.0→4.2	mg/dL
clearance	66.8	%	53.8	%	53.3	%
AST	39→42	U/L	52→58	U/L	86→118	U/L
IgG	1000→919	mg/dL	869→871	mg/dL	818→780	mg/dL
Total bile acid	42.9→51.0	mmol/L	59.0→81.7	mmol/L	54.8→62.5	mmol/L

Table 2. Results of dialysis

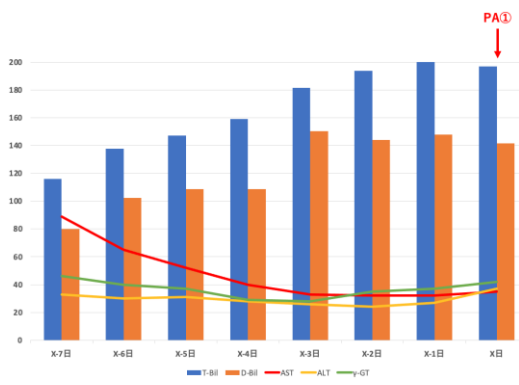

Figure 2. Changes in hepatic enzymes before PA

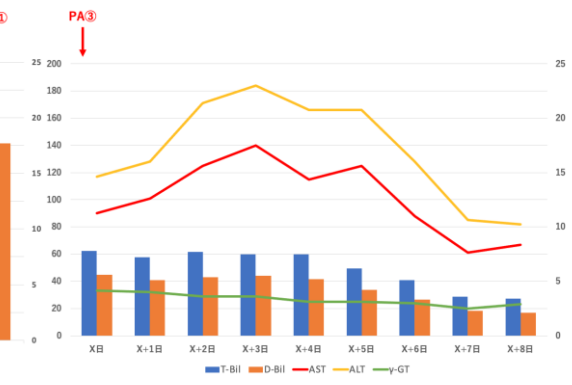

Figure 3. Changes in hepatic enzymes after PA

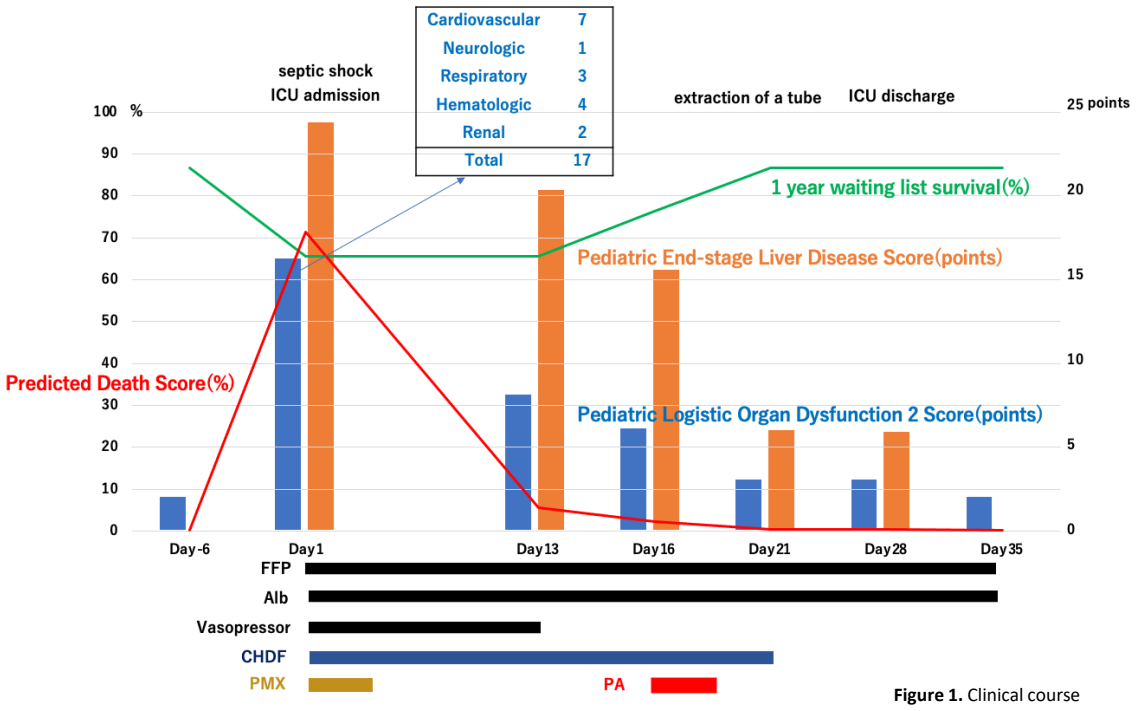

Figure 1. Clinical course

Discussion

Sepsis is often followed by organ damage. Control of the infection is important, but supportive care is also known to play a role in the prognosis.

He had marked bile congestion and acute liver failure. In general, bilirubin adsorption is used as symptomatic therapy, and FFP replacement, plasma exchange, and CHDF as liver replacement therapy. He was already on FFP replacement and CHDF, and it was difficult to decide whether to add plasma exchange or bilirubin adsorption. Plasma exchange has high removal performance, but has the disadvantage of using more blood products and a higher risk of side effects and infections. Bilirubin adsorption has a lower throughput and removes a limited number of substances, but does not require blood products and has less osmotic alteration [5].

We chose bilirubin adsorption therapy because we hoped to prevent further organ damage. Other reasons are that he had already used a large amount of blood products due to intensive chemotherapy and he had just come out of shock. We successfully achieve a good outcome due to bilirubin adsorption therapy.

Conclusions

Plasma exchange therapy has been used to treat liver failure in children. However, there are concerns about the large amount of active protein components that are discarded, post-transfusion infections due to the large amount of fresh frozen plasma administered, and huge medical costs.
We successfully treated with bilirubin adsorption therapy without large amount of fresh frozen plasma and could prevent further organ damage.

References

1. Van Slambrouck CM et al. Kidney Int 84 ; 2013;192-197
2. Shigeru Kanesaka et al. J Abdom Emerg Med, 2005; 25(5);697-700
3. Richard H. Moseley et al. Gastroenterology , January 1997; 112(1);302-306
4. Kenichi Matsuda et al. Japanese Journal of Apheresis, 2010; 200-208
5. Hanahusa N et al. Ther Apher Dial , 2011; 15 ; 421-430