Hemodiafiltration for hepatic encephalopathy induced by Budd–Chiari syndrome in a patient with end-stage kidney disease

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Received: 17 July 2015 / Accepted: 25 November 2015 / Published online: 11 December 2015
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Abstract A 36-year-old woman who was undergoing dialysis for end-stage kidney disease (ESKD) was admitted to our hospital with consciousness disorder. She was diagnosed with Budd–Chiari syndrome due to antiphospholipid syndrome at the age of 28 years. Her kidney function and leg edema gradually deteriorated. After initiation of hemodialysis (HD), transient loss of consciousness due to hepatic encephalopathy during HD treatment occurred frequently. Her kidney replacement therapy was changed to online hemodiafiltration (HDF), which dramatically improved her hepatic coma. Compared with HD, HDF contributed to the increase in Fischer’s ratio and decrease in tryptophan level, which has a high protein-bound property. This case suggests that HDF may be beneficial for hepatic encephalopathy in ESKD patients by modulating the amino acid profile.

Keywords Budd–Chiari syndrome · Hemodiafiltration · Hepatic encephalopathy · Fischer’s ratio · Portal-systemic shunt

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Introduction

Budd–Chiari syndrome (BCS) is defined as a portal hypertension caused by obstruction of the inferior vena cava (IVC) of the liver. Polycythemia or antiphospholipid syndrome (APS) is known to be related with BCS. Severe BCS induces hepatic encephalopathy caused by perturbation of the balance of the branched chain (BCAA) and aromatic amino acid (AAA), reduction of blood flow in the portal vein, increased production of neurotoxic mediators, and so on [1]. Hepatic encephalopathy induced by liver disturbance sometimes deteriorates in patients with end-stage kidney disease (ESKD), especially during hemodialysis (HD) treatment. However, the reason has not been completely understood.

Hemodiafiltration (HDF) is an effective blood purification therapy for ESKD patients with dialysis-related complications such as dialysis-induced hypotension, restless legs syndrome, cutaneous pruritus, or dialysis-related amyloidosis [2–5]. A few reports have suggested that HDF might be better than HD in inhibiting hepatic encephalopathy possibly by the higher efficiency of removal of some encephalopathy-related molecules [6].

We present a case of ESKD complicated with severe BCS. The hepatic encephalopathy that developed and worsened during HD sessions was successfully ameliorated by HDF, possibly owing to modulation of the patient’s amino acid profile.

Case report

A 36-year-old woman was transferred to our hospital to receive detailed examination and treatment of consciousness disorder during HD. She had no history of excessive alcohol

consumption and smoking. Proteinuria was pointed out at the health examination when she was 20 years old. At the age of 21 years, she developed arthralgia, which gradually worsened. At the age of 26 years, she was diagnosed with APS because of a biological false-positive reaction to a serological test for syphilis and anti-cardiolipin antibody positivity. She was prescribed with aspirin and warfarin. At the age of 28 years, her liver function and leg edema deteriorated, and she was diagnosed with BCS according to the IVC thrombosis from the anastomotic part of the renal veins to the anastomotic part of the hepatic veins. At the age of 31 years, she received percutaneous transluminal angioplasty and right partial lobectomy of the liver for stenosis of the IVC of the liver. However, the efficacy was temporary, and both liver and kidney dysfunctions progressed gradually. At the age of 35 years, she started receiving peritoneal dialysis (PD). However, after 2 months, she developed PD-related peritonitis. Then, she switched from PD to HD. However, the occurrence of consciousness disturbance due to hepatic encephalopathy became frequent during/after HD session. Hence, she was referred to our hospital.

On admission, she was alert and oriented, with a blood pressure of 103/67 mmHg, heart rate of 96 bpm, body temperature of 36.1 °C, and oxygen saturation measured using pulse oximetry of 98 % (room air). Finger tremor, abdominal distension, overswelling of the epigastric veins, operation scar in the right hypochondrium and the abdomen, and leg edema were observed. The arteriovenous fistula for

HD was placed in the right arm. The examination results were as follows (Table 1): Briefly, she had anemia, thrombocytopenia, kidney dysfunction, metabolic acidosis, and hyperphosphatemia. She had hyperammonemia. The transaminase level was not increased, but ChE was low suggesting liver failure.

Chest radiography showed cardiac enlargement and right pleural fluid. Head plain computed tomography (CT) revealed only a small low-density area from the white matter to the cortex of the parietal lobe, suggesting chronic cerebrovascular disease. No abdominal dropsy was observed. Abdominal contrast-enhanced CT revealed diffuse swelling of the liver, rude construction of liver parenchyma, and thrombus in the IVC. A portal-systemic shunt connects from the inferior mesenteric vein to the left renal vein via the collateral circulation (Fig. 1). The HD prescription for this case was as follows: dialyzer, NV-16U (polysulfone membrane, area 1.6 m², Toray Medical Co., Ltd., Tokyo, Japan); dialysate, Kindary solution AF-2 (convection 36 L/h, Fuso Pharmaceutical Industries, Osaka, Japan); quantity of blood flow, 180 mL/min; dialysis time, 4 h; amount of drainage, 3.5–4.5 L per session; anticoagulant medicine, heparin sodium 500 IU/h; dry weight, 45.0 kg; the residual kidney function (urine volume), 200 mL/day. Around 10 min was taken for the hemostasis after needle removal.

After admission, she received intravenous infusions of BCAA and potassium during an HD session. However, flapping tremor and coma occurred during and after the HD

Table 1 Laboratory tests conducted on admission

Complete blood count		TP	7.9 g/dL	CRP	0.58 mg/dL
WBC	4350/mm ³	Alb	3.5 g/dL	NH ₃	290 µg/dL
RBC	314 × 10 ⁴ /mm ³	UN	77 mg/dL	IgG	3238 mg/dL
Hb	9.3 g/dL	Cr	3.57 mg/dL	IgA	759 mg/dL
Ht	31.6 %	UA	4.5 mg/dL	IgM	240 mg/dL
Plt	6.4 × 10 ⁴ /mm ³	Na	130 mEq/L	C3	38.7 mg/dL
Coagulation		K	3.1 mEq/L	C4	5.7 mg/dL
APTT	51.5 s	Cl	99 mEq/L	CH50	17 U/mL
Control	28.0 s	Ca	7.9 mEq/L	BNP	84.7 pg/mL
PT	46 %	iP	5.2 mEq/L	Arterial blood gas analysis (Room air)	
PT INR	1.47	AST	33 IU/L	pH	7.371
Fibrinogen	246 mg/dL	ALT	22 IU/L	PaO ₂	92.6 Torr
FDP	4.7 µg/mL	LDH	349 IU/L	PaCO ₂	33.3 Torr
D-dimer	2.1 µg/mL	ALP	679 IU/L	HCO ₃ [−]	18.8 mEq/L
Serum bio chemistry		CPK	58 IU/L	BE	5.8 mEq/L
ANA	34.6 Index	T. bil	1.8 mg/dL	STS	(+)
Anti-dsDNA	6 IU/mL	D. bil	0.8 mg/dL	TPLA	(−)
Anti-cardiolipin IgG	15 IU/mL	I. bil	1.0 mg/dL	HBsAg	(−)
		ChE	82 IU/L	Anti HCV	(−)
				HIV	(−)

Fig. 1 Abdominal contrast-enhanced computed tomographic image obtained after percutaneous transluminal angioplasty. **a, b** Plain. **c, d** Early phase. **e, f** Delayed phase. The *images* indicate a portal-systemic shunt that connects from the inferior mesenteric vein to the left renal vein via the collateral circulation. **g** Construction of a vascular image to show the portal-systemic shunt

Fig. 2 Clinical course during the hospitalization. The average grade of most severe hepatic encephalopathy in a day was expressed according to the West Haven criteria. Presented are the results of the plasma amino acid analysis and the parameters associated with the blood purification at 21, 56, and 70 days after administration.

treatment (Fig. 2). The blood test value at the time suggested no remarkable abnormality in the acid–base equilibrium, electrolyte level, blood glucose level, and ventilation. Plasma ammonia concentration was sometimes increased, although it was not accompanied with severe symptoms. Electroencephalography under the condition of consciousness disorder showed generalized and triphasic waves, and detected the exacerbated hepatic encephalopathy during the HD sessions despite supplementation with BCAA and potassium.

After 56 days of administration, we changed her kidney replacement therapy from HD to online HDF. Her systolic blood pressure was elevated to 110–120 mmHg, the frequency of the consciousness disorder decreased, and the symptoms such as finger tremor, general malaise, and fatigability became less severe. Interestingly, the ratio of BCAA to AAA during dialysis session was increased, unlike that during HD (increase in the ratio: 3.17 in HDF vs. 1.80 in HD; Fig. 2). In AAAs, tryptophan removal was dramatically increased with HDF as compared with HD (removal in the ratio: 28 % in HDF vs. –25 % in HD;

Δ %CPV percent change in Δ circulating plasma volume, PRR plasma refilling rate, Kr plasma refilling coefficient, % Δ BW/h changes in body weight per hour during HD, UFR ultrafiltration rate, spKt/V single-pool Kt/V, eKt/V equilibrate Kt/V [23–25]

Fig. 2). After 70 days of administration, she resumed undergoing HD. However, her neurological symptom deteriorated, and the ratio of BCAA to AAA during dialysis session was decreased (–1.16 in HD) again. Finally, she chose to continue online HDF. The HDF prescription in this case was as follows: online-predilutional HDF with 48 L infusate per 4 h session; dialyzer, ABH-15P (polysulfone membrane, area 1.5 m², Asahi Kasei Medical Co., Ltd., Tokyo, Japan); dialysate, Kindary solution AF-2 (convection 24 L/h and infusion 12 L/h; quantity of blood flow, 180 mL/min; dialysis time, 4 h; amount of drainage, 3.5–4.5 L per session; anticoagulant medicine, heparin sodium 500 IU/h; dry weight, 45.0 kg.

Discussion

We experienced a case of BCS complicated with ESKD. Online HDF was effective for hepatic encephalopathy exacerbated during and after dialysis sessions.

Pathophysiological mechanism of ESKD complicated by BCS due to APS

In clinical settings, kidney diseases such as renal cell carcinoma and polycystic kidney disease can sometimes induce BCS. However, little information is available about kidney injury induced by BCS. Although we have no data available for the histopathological finding in the present case, a report from a single-center study showed that 21.3 % of patients with BCS had chronic kidney disease, which is a significant predictor of liver transplantation and death [7]. A case report showed that focal proliferative glomerulonephritis was found in a patient with BCS at postmortem examination [8]. In our case, proteinuria was pointed out, and some nephritis or nephropathy related with BCS may be a concern. Meanwhile, kidney congestion induced by obstruction of the IVC may be involved with the kidney dysfunction because the patient had severe leg edema and ascites due to BCS when her kidney function deteriorated.

APS may also be involved with the development of ESKD. A previous report showed that 8.7 % of patients with primary APS had kidney dysfunction with proteinuria, which could be associated with membranous nephropathy [9]. In our case, the proteinuria from the age of 20 years may indicate the presence of APS-related glomerulopathy. Another possible pathophysiological mechanism of APS-induced kidney dysfunction is thrombotic occlusion of large vessels [10] or intrarenal small vessels [11] in the kidneys. In our case, she took aspirin and warfarin for prevention from thrombosis. CT image suggested that renal ischemia seemed to be mild although renal blood flow by ultrasound sonography was not examined.

Liver dysfunction due to BCS may also induce ESKD, as in hepatorenal syndrome. End-stage liver cirrhosis often aggravates renal dysfunction, and the severity of the liver function in this case had a Child–Pugh score of 8, or Child–Pugh class B.

Based on the above-mentioned results, the ESKD in this case may be induced by composite mechanisms, including BCS, APS, and hepatic dysfunction.

HDF for hepatic encephalopathy in patients with end-stage kidney disease

Hepatic encephalopathy can be subdivided into type A, resulting from acute liver failure; type B, resulting predominantly from portal-systemic bypass or shunt; and type C, resulting from cirrhosis [12]. Recently, type B, the so-called portal-systemic encephalopathy (PSE), has received attention in ESKD patients because it sometimes exacerbates during HD session. PSE is caused by ammonia-rich blood entry from portal circulation to systemic circulation

through collateral circulation such as the renal or splenic vein, without ammonia metabolism in the liver [13, 14]. HD treatment induces PSE possibly due to hypovolemia of the systemic circulation via decreased plasma osmolality and increased ultrafiltration [15, 16]. In this case, a shunt was observed from the inferior mesenteric vein to the left renal vein (Fig. 1) and hepatic encephalopathy was induced frequently during and after HD sessions, with rapid decrease in systemic circulating blood volume. Her hepatic encephalopathy was improved after switching her kidney replacement treatment from HD to HDF (Fig. 2), probably because HDF inhibits the decrease in plasma osmolality, unlike HD. The case tried PD at first, but switched to HD due to PD-related peritonitis. The effect of PD on PSE is controversial, but PD may improve PSE because of reduction of portal-systemic shunt (PSS) flow by removing excess blood flow induced by HD [17]. On the other hand, PD may exacerbate PSE because increase of intra-abdominal pressure causes high PSS flow [18]. In our case, the degree of hepatic encephalopathy exacerbated after switching her kidney replacement treatment from PD to HD, and PD might be effective to prevent PSE as well as HDF.

From another point of view, the improvement of consciousness might be due to the increase in Fischer's ratio [19]. In the present case, although no remarkable change was found in the clear space ratio of ammonia, Fischer's ratio was obviously increased (Fig. 2). In detail, the removal ratio of phenylalanine and tryptophan, which belong to AAAs, increased remarkably. Tryptophan is the amino acid highly bound to albumin [20], and HDF induces better removal of AAAs than HD. Tryptophan accumulation in the brain accelerates the production of 5-hydroxytryptamine (5-HT), which deteriorates hepatic encephalopathy [21]. Efficient removal of tryptophan by HDF may be more important than supplementation with BCAAs to ameliorate hepatic encephalopathy. In addition, some reports suggest that HDF is superior to HD in terms of efficiency in removing inducers of hepatic encephalopathy that have moderate molecular weights (500–3000 Da) [6, 22].

Curative approaches for BCS-induced liver and kidney dysfunctions are angioplasty or liver and kidney transplantations. However, when a patient with ESKD complicated with PSE cannot receive invasive treatment, HDF may be a better strategy to prevent PSE. Long-term use of HDF for prevention of PSE has not been reported yet, and further study is needed for confirming the beneficial effect of HDF. In conclusion, we present a case of ESKD after progression of BCS. The patient's hepatic encephalopathy associated with HD sessions was successfully ameliorated by HDF. Increased Fischer's ratio, especially reduction in tryptophan level, and prevention of rapid intravascular

volume depletion may be the mechanisms that ameliorated hepatic encephalopathy in the present case.

Compliance with ethical standards

Conflict of interest The authors declare that no conflict of interest exists.

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