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LETTER TO THE EDITORS

Lethal hepatic infarction following plasma exchange in living donor liver transplant patients

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Plasma exchange is known to improve the prognosis of postoperative progressive liver failure. However, Yamamoto *et al.* [1] reported that 16 (35%) of 46 living donor liver transplantation (LDLT) patients who received plasma exchange had poor prognosis, although the cause of death in those patients was unclear.

We report the case of two LDLT patients who died of hepatic infarction immediately after plasma exchange.

Case 1: A 70-year-old woman with primary biliary cirrhosis underwent left-lobe LDLT. Her model for end-stage liver disease (MELD) score was 23 and graft size was 56% of the standard liver volume (SLV). On postoperative day (POD) 10, she developed sepsis because of pneumonia. She recovered from sepsis after treatment with antibiotics and γ-globulin, but her liver function gradually deteriorated on POD 17: 27 mg/dl of total bilirubin (TB), 27.8% of prothrombin time (PT)%, 125 IU/l of aspartate aminotransferase (AST) and 114 IU/l of alanine aminotransferase (ALT). However, liver biopsy revealed no rejection. Plasma exchange was performed. The patient's blood was pumped out at 100 ml/min, and nafamostat mesilate (30 mg/h) was used as an anticoagulant. Approximately 3200 ml of plasma was replaced with the same volume of fresh frozen plasma (FFP) and hemodynamic stability was achieved. However, 12 h later, laboratory data revealed rapid progression of liver failure: 29.8 mg/dl of TB, 30.1% of PT%, 2335 IU/l of AST and 1162 IU/l of ALT. A computed tomography (CT) scan showed an infarct at the central area of the hepatic graft, without any thrombosis of the patent left portal vein and left hepatic artery (Fig. 1a). Although we started anticoagulant therapy and steroid administration, the hepatic infarction did not improve, and the patient died 2 days after plasma exchange.

Case 2: A 41-year-old woman with fulminant hepatitis underwent left-lobe LDLT. Her MELD score was 34 and graft size was 29% of the SLV. As a result of small-for-size graft syndrome, she developed gradual liver failure on POD 7: 11.3 mg/dl of TB, 28.9% of PT%, 162 IU/l of AST and 102 IU/l of ALT. Plasma exchange was performed without any hemodynamic disturbances. However, 12 h after plasma exchange, laboratory data revealed rapid progression of liver failure: 9.0 mg/dl of TB, 29.1% of PT%, 1720 IU/l of AST and 701 IU/l of ALT. A CT scan showed an infarct of central area with patent left portal vein and left hepatic artery (Fig. 1b). Although we started anticoagulant therapy and steroid administration, the hepatic infarction did not improve, and the patient died 2 days after plasma exchange.

Recently, researchers are focusing on a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13 (ADAMTS13), which is mainly produced in the hepatic sinusoid, because deficiency of this enzyme in LT recipients results in thrombotic microangiopathy or microcirculatory disturbances in the hepatic sinusoid [2]. Changes in the levels of ADAMTS13 and von Willebrand factor

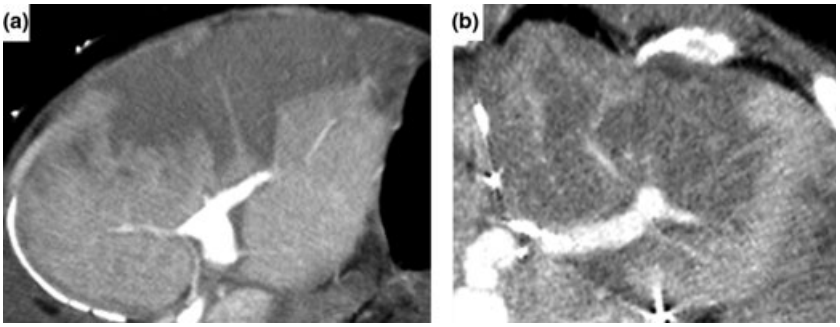

Figure 1 Computed tomography (CT) scans of case 1 (a) and case 2 (b). Both of them revealed hepatic infarction of central area of the graft liver without any visual thrombosis.

Table 1. Hepatic sinusoidal damages before plasma exchange.

	Normal range	Case 1	Case 2
ADAMTS13 (%)	80–100	57	39
Thrombomodulin (TU/ml)	<4.5	25.1	31.4
vWF propeptide (%)	100	362	621
ATIII (%)	>70	45.3	60.1
D-dimer (mg/ml)	<2	39.52	31.6
Soluble fibrinogen (mg/ml)	>130	12.6	75.3
TAT (ng/ml)	<4	25.1	80

ADAMTS13, a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13; vWF, von Willebrand factor; ATIII, antithrombin III; TAT, thrombin-antithrombin III complex.

(vWF) could be a good early indicator of adverse events in LT patients [3]. Thrombomodulin (TM) is also a marker of liver sinusoidal damage [4], and down-regulation of TM leads to immediate thrombotic microangiopathy.

Sepsis and small-for-size graft syndrome after LT are known to impair the microcirculatory environment in the hepatic sinusoid [5,6]. Retrospective analysis of our cases revealed that the patients had severe sinusoidal damage before they underwent plasma exchange (Table 1).

In our cases, severe hepatic sinusoidal damage facilitated the plasma exchange-mediated induction of hypercoagulopathy, resulting in lethal hepatic infarction that appeared as nonthrombotic hepatic infarction, which is occasionally noted in deceased donor transplantation.

Although infusion of FFP may help maintain coagulation homeostasis, excessive infusion of FFP can cause hepatic artery thrombosis in liver transplant patients [7,8]. To avoid this fatal complication, plasma exchange should not be performed in cases of severe hepatic sinusoidal damage.

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Conflicts of interest

I and co-workers of this manuscript have no funding and no conflicts of interest to disclose.

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