Efficacy of Balloon-occluded Retrograde Transvenous Obliteration (B-RTO) Performed in a Patient with Primary Biliary Cirrhosis with Severe Recurrent Hepatic Encephalopathy Due to Splenorenal Shunt

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Case: A 73 year old female had been diagnosed as primary biliary cirrhosis and Sjögren's syndrome since the age of 50. With persisting hyperammonemia, the patient was admitted on several occasions for the management of hepatic encephalopathy. Computed tomography (CT) scan and magnetic resonance imaging (MRI) of the abdomen showed varices in the splenic hilar region and a splenorenal shunt. A balloon-occluded retrograde transvenous obliteration (B-RTO) using 5% ethanolamine oleate plus iopamidol (EOI) was performed for treatment of recurrent hepatic encephalopathy. Celiac and superior mesenteric angiograms prior to B-RTO demonstrated a hepatofugal portal circulation through the splenic varices, splenorenal shunt, left renal vein and inferior vena cava. Immediately following the B-RTO, the portal circulation became restored to a hepatopetal blood flow and no visualization of the splenic varices and splenorenal shunt was verified. On day 2 post-B-RTO, blood NH3 level was noted to have decreased from 134 to 61 μg/dL, indicating an improvement of hyperammonemia. The liver parenchymal blood flow using the dynamic CT time-concentration curve showed a decrease in hepatic artery blood flow and a marked increase in portal flow following the B-RTO. The patient has since been free from any signs of hepatic encephalopathy due to hyperammonemia for over 5 years following the B-RTO.
Conclusions: B-RTO may be considered useful for the treatment of severe recurrent hepatic encephalopathy due to the collateral shunt in portal hypertension.

Key words: balloon-occluded retrograde transvenous obliteration (B-RTO), hepatic encephalopathy, portal hypertension, splenorenal shunt

INTRODUCTION

Since Balloon-occluded retrograde transvenous obliteration (B-RTO) was first reported by Kanagawa et al. [1], it has become widely accepted in Japan as a less invasive radiological procedure for gastric varices with a gastrorenal shunt [2, 3]. Portal hypertension is associated with gastroesophageal varices as well as hepatic encephalopathy due to the development of collateral veins. B-RTO is now considered to be a safe and effective treatment for patients with not only gastric varices, but also hepatic encephalopathy [4]. Since severe recurrent hepatic encephalopathy is a serious disease condition that impairs the patient's quality of life, its diagnosis and treatment are crucially important. We recently encountered a patient with primary biliary cirrhosis in whom B-RTO was performed for treatment of severe recurrent hepatic encephalopathy probably caused by splenorenal shunt, and a remarkable improvement was achieved.

CASE REPORT

The patient was a woman aged 73, who had been diagnosed as suffering from primary biliary cirrhosis and Sjögren's syndrome since the age of 50. In October 2002, the patient received endoscopic injection sclerotherapy (EIS) to control rupture of esophageal varices. She was admitted to our hospital because of hepatic encephalopathy due to hyperammonemia with a blood NH3 level of 313 μg/dL around December 2002. The general condition remitted in response to treatment with Aminoleban® and lactulose. With persisting hyperammonemia, the patient was readmitted subsequently on several occasions for the management of hepatic encephalopathy. Computed tomography (CT) scans and magnetic resonance imaging (MRI) of the abdomen showed varices in the splenic hilar region and a splenorenal shunt. The patient was hospitalized in April 2003 for treatment of these lesions with B-RTO in anticipation of amelioration of hepatic encephalopathy. The patient had no history of excessive alcohol consumption.

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Physical examination on admission revealed the following findings: height, 152 cm; body weight, 47 kg; blood pressure, 112/60 mmHg; pulse rate, 70/min and regular; temperature, 36.6°C; slightly anemic and jaundiced; spider angioma (+); palmar erythema (+); facial telangiectasia (+); superficial lymph nodes not palpable; the lung fields clear; no heart murmur audible; the abdominal wall flattened, no muscle guarding, and no tenderness; the liver not palpable; the spleen not enlarged; no ascites; and no edema in the lower legs.

As seen from Table 1, the results of laboratory and other examinations on admission showed pancytopenia, hypoalbuminemia, hyperbilirubinemia and hyperammonemia, as well as a highly positive anti-mitochondrial antibody titer, indicating a decompensated stage of primary biliary cirrhosis. A contrast-enhanced CT scan of the abdomen demonstrated the markedly dilated splenic vein and the presence of distended and tortuous splenic varices in the splenic hilar region. A magnetic resonance angiography (MRA) showed the narrowed portal vein and a continuously dilated vascular structure coursing tortuously from the splenic vein and draining into the left renal vein, hence indicating the presence of varices of the splenic vein and a splenorenal shunt (Fig. 1).

On April 9, abdominal angiography was performed. Celiac angiograms taken during the portal phase showed that the bloodstream from the splenic vein mostly formed varices of the splenic vein in the splenic hilar region, then entered the left renal vein via a splenorenal shunt, and drained into the inferior vena cava. The splenic vein was not visualized. Superior mesenteric angiograms demonstrated a narrowed portal trunk and that the superior mesenteric vein entered through the splenic vein hepatofugally, thereby forming splenic varices in the splenic hilar region, and

drained via the splenorenal shunt into the left renal vein, thus into the inferior vena cava (Fig. 2). Inferior mesenteric angiograms showed that the blood flow from the inferior mesenteric vein also drained through the splenorenal shunt into the inferior vena cava. Angiograms of the splenorenal shunt revealed markedly dilated splenic varices and a monileform, dilated vein descending from thence almost vertically over the anterior aspect of the vertebral body and draining into the inferior vena cava. The dilated vein was considered to represent the left inferior phrenic vein. A B-RTO was performed with 50mL of 5% ethanolamine oleate plus iopamidol (EOI) injected through a catheter advanced into the splenorenal shunt (Fig. 3). Celiac angiograms taken after the B-RTO demonstrated the hepatopetal draining through the splenic vein as it should be, while the splenorenal shunt was no longer visualized. By superior mesenteric angiography, the portal trunk was shown to have been dilated with visualization of the intrahepatic portal veins (Fig. 4). Postoperative inferior mesenteric angiograms disclosed an alteration to hepatopetal circulation in contrast to the hepatofugal draining through the splenic varices via the splenic vein observed prior to B-RTO. After 24 hours of inlying catheterization, angiograms of the splenic varices were taken and revealed that the splenorenal shunt was thrombosed and no longer visualized, except its origin.

On Day 2 post-operation the blood NH3 level was noted to have lowered from a preoperative value of 134 μg/dL to 61 μg/dL; hence indicating an obvious improvement of hyperammonemia. No clinical signs of hepatic encephalopathy were noted, and the total bilirubin level and albumin level improved from 4.3 to 2.2 mg/dL and from 2.7 to 3.4 g/dL, respectively, following the B-RTO, reflecting an improvement in liver metabolic function. A CT scan of the abdomen on Day

Table 1 Laboratory findings on admission

white blood cell	2200/mm³
hemoglobin	11.6 g/dL
platelet	9.9X10⁴/mm³
prothronbin time	71%
albumin	2.2 g/dL
aspartate aminotransferase	76 IU/L
alanine aminotransferase	38 IU/L
alkaline phosphatase	877 IU/L
Ð-glutamyl transpeptidase	32 IU/L
choline estarase	77 IU/L
total cholesterol	86 mg/dL
total bilirubin	4.3mg/dL
total bile acid	495.5 μM/L
creatinin	0.6 mg/dL
NH3	134 μg/dL
anti-M2 mitochondial antibody	135 U/mL

Fig. 1 Magnetic resonance angiogram (MRA) prior to B-RTO.
The MRA scan demonstrates splenic varices draining continuously from the splenic vein into the left renal vein and a splenorenal shunt.

5 post-operation showed no visualization of splenic varices and splenorenal shunt, both being thrombosed, after the B-RTO (Fig. 5). There was a slight degree of ascites in the perihepatic regions, which was considered due to portal pressure elevation associated with the shunt occlusion as there was no concurrent hepatic infarction.

The liver parenchymal blood flow was quantified by analyzing the dynamic CT time-concentration curve, and the results showed a decrease in hepatic artery blood flow from 0.44 to 0.22 mL/min/mL and a marked increase in portal flow from 0.35 to 0.92 mL/min/mL following B-RTO (Fig. 6). Neither hepatic encephalopathy nor recurrence of esophagogastric varices has been observed in the patient who is in her fifth postoperative year.

DISCUSSION

It seems to have achieved a practically general consensus that B-RTO represents the first-line treatment for solitary gastric varices with a gastrorenal shunt, since the procedure was reported by Kanagawa et al [1]. Laparotomic shunt closure has usually been undertaken before for the treatment of chronic recurrent portosystemic encephalopathy, and some case reports have demonstrated disappearance of hepatic encephalopathy and improvement of liver function [2, 3, 4]. In recent years, B-RTO has been selected over surgical treatment as a therapy for hepatic encephalopathy on account of its reliability and minimal invasiveness [5-9]. The goal of B-RTO is to close a huge shunt between the portal and the systemic circulation, so that, needless to say, precise delineation of the portal hemodynamics is essential to the conduct of this procedure. Closure of a huge shunt would lead to an alteration from hepatofugal to hepatopetal circulation with a consequent increase in hepatic blood flow.

In the present case, blood NH3 level markedly decreased from 134 to 61 μg/dL, the total bilirubin improved from 4.3 to 2.2 mg/dL, and the plasma

Fig. 2 Abdominal angiographic findings prior to B-RTO.
a. celiac angiogram. b. superior mesenteric angiogram.
These angiograms demonstrate narrowing of the portal vein, and they showed hepatofugal circulation via the splenic vein and a portosystemic shunt that forms splenic varices in the splenic hilar region, draining via the splenorenal shunt into the left renal vein and eventually into the inferior vena cava.
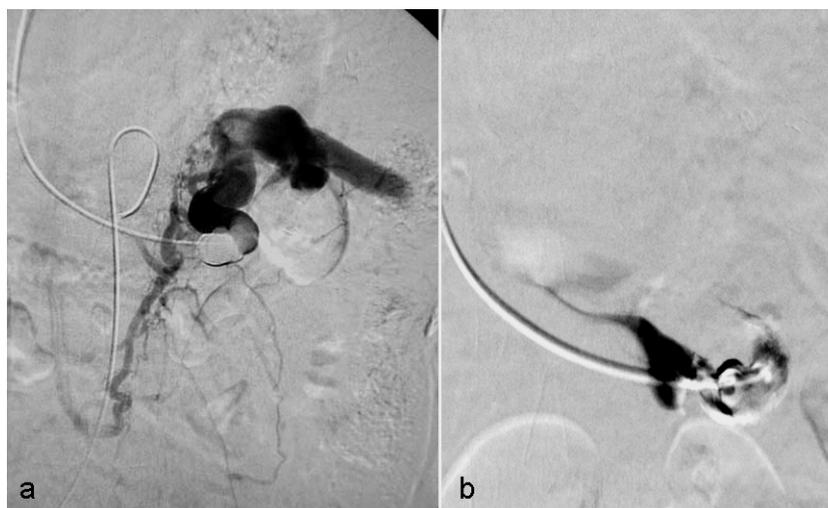
Fig. 3 Angiograms of the splenorenal shunt on B-RTO.
a.Prior to B-RTO. The angiogram of an area within the splenorenal shunt shows distended tortuous splenic varices. The occlusion pressure was 22 mmHg with the balloon inflated, as against 20 mmHg with balloon deflated.
b.Post B-RTO. The angiogram of splenic varices taken 24 hours after infusion of 50 mL of 5% EOI. Note that no splenic varices are visualized.

albumin increased from 2.7 to 3.4 g/dL following the B-RTO. Hayashi et al. demonstrated improvements in albumin and cholinesterase levels in 22 patients at 1 year post-operation, and a significant amelioration of ICGR15 value was achieved in patients with a shunt measuring more than 10 mm in length and with a partial hepatofugal circulation via the left gastric or splenic vein as viewed during the venous phase of superior mesenteric angiography [10]. This may be interpreted as implying that the shunt occlusion by B-RTO resulted in a relative increase in hepatopetal portal flow, thereby producing an improvement in liver function [11, 12, 13]. Studies have investigated indicators of pre- and post-B-RTO liver function, including measurements of the branched-chain amino acids/tyrosine ratio (BTR) [14] and amino acid load [15] besides albumin, cholinesterase and ICGR15.

The hepatic parenchymal blood flow per unit organ volume was quantified in the present case by analyzing the dynamic CT time-concentration curve, i.e., perfusion CT, to detect any increase in portal blood flow. In the quantification, the hepatic artery blood flow can be calculated according to the maximum slope method [16, 17] by dividing the maximum slope of the hepatic parenchymal time-concentration curve at an early arterial phase by the maximum increased aortic CT value. Likewise, the portal blood flow can be cal-culated by dividing the maximum slope of the curve at the portal phase by the maximum increased portal CT value. Normal values vary slightly from report to report and are approximately 0.1 to 0.2 mL/min/mL for hepatic artery blood flow and 1.0 mL/min/mL for portal blood flow [18]. In our case, the hepatic artery blood flow decreased from 0.44 to 0.22 mL/min/mL and the portal blood flow increased from 0.35 to 0.92 mL/min/mL following B-RTO; hence indicating a noticeable improvement in hepatic blood flow. Therefore, the perfusion CT may be a useful method for evaluation of the pre- and post-B-RTO hepatic parenchymal blood flow. A decrease in total bilirubin as well as improvements in albumin and cholinesterase values reflecting the hepatic synthetic function were attained following B-RTO in this case, and these responses are inferred to be attributable at least in part to the increase in hepatic blood flow brought about by B-RTO. Thus, the present case is considered illustrative of the improvements attained not only in hepatic encephalopathy but also in hepatic function as a result of splenorenal shunt occlusion by B-RTO.

CONCLUSION

A B-RTO was performed for the treatment of severe recurrent hepatic encephalopathy due to splenorenal shunt in a patient with primary biliary cirrhosis. The
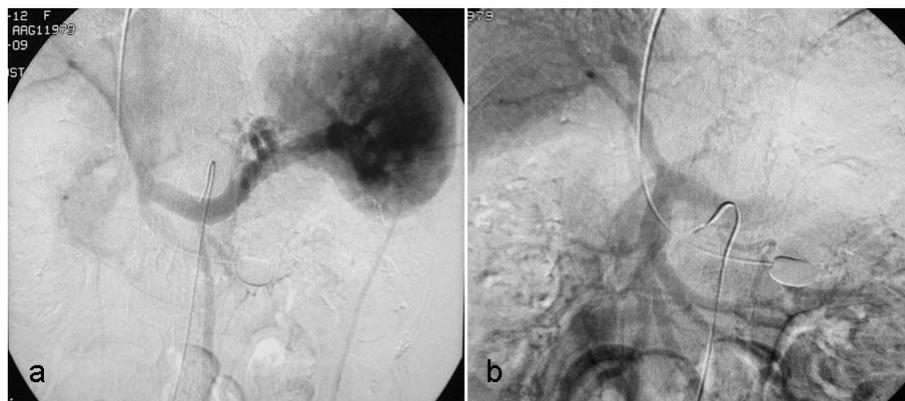
Fig. 4 Abdominal angiographic findings after B-RTO.
 a. celiac angiogram. **b**. superior mesenteric angiogram.
 The splenic vein blood flow has been restored to an original hepatopetal circulation while no splenorenal shunt is visualized.
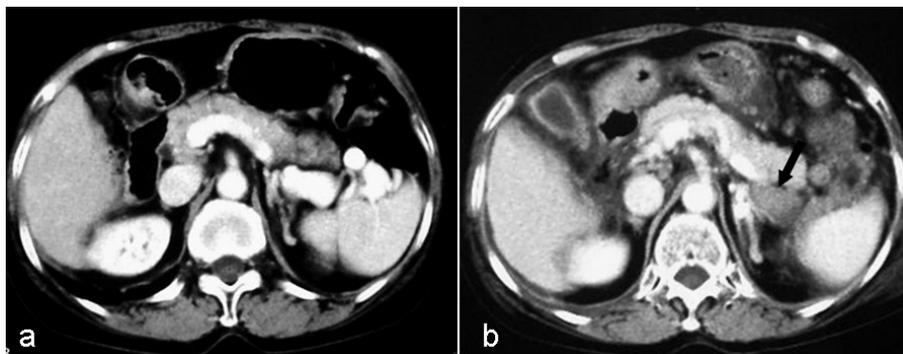
Fig. 5 Abdominal CT scans before and after B-RTO.
 The abdomen CT scans taken before (**a**) and on day 5 (**b**) after B-RTO.
 Note that there is no visualization of splenic varices and splenorenal shunt (an arrow) after B-RTO. On plain CT scan, the splenic varices are shown as a high-density area probably representing a relatively new thrombosed lesion. There was perihepatic ascites but no hepatic infarction was noted.
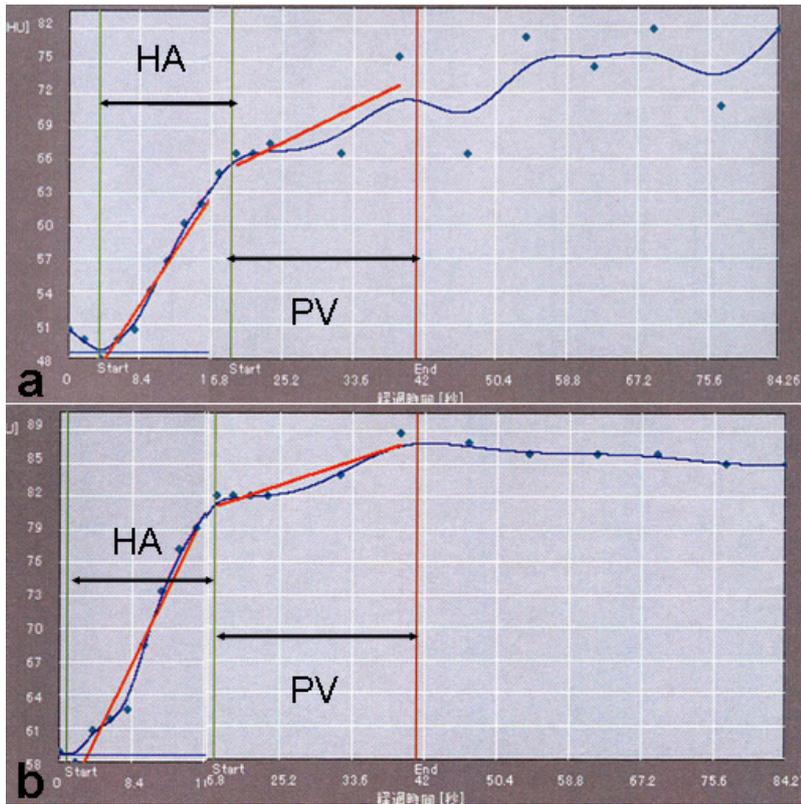
Fig. 6 Perfusion CT scans before and after B-RTO.
a. Prior to B-RTO.
b. Post B-RTO.
The graph shows time density curves where the ordinate represents the liver parenchymal contrast effect. The data were analyzed using the maximum slope method. The area between the green vertical bars shows data for the hepatic arterial (HA) phase and that on the right side data for the portal vein (PV) phase. The portal vein pressure values before and after the B-RTO were 0.35 and 0.92, respectively, hence indicating an increase in intrahepatic portal blood flow after the B-RTO.

treatment produced an increase in hepatopetal portal blood flow evidenced both morphologically and quantitatively by imaging and qualitative analysis, with consequent noticeable improvements in hyperammonemia and hepatic encephalopathy.

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