—Report on Experiments and Clinical Cases—

Surgical Disconnection of Patent Paraumbilical Vein in Refractory Hepatic Encephalopathy

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Abstract

Background: Refractory hepatic encephalopathy (HE) frequently develops in patients with cirrhosis and portal-systemic shunt. Recently, patients with refractory HE associated with portal-systemic shunt have been treated with interventional radiology. We describe a promising new treatment for portal-systemic shunt, ligation of the patent paraumbilical vein (PUV) after partial splenic embolization, in patients with refractory HE.

Patients: Four patients with cirrhosis (3 women and 1 man; mean age, 56 years) and refractory HE due to a patent PUV were studied. Patency of the PUV had recurred in 1 patient after primary occlusion by interventional radiological procedures. The Child-Pugh class was B in 2 patients and C in 2. Before the present treatment, all patients had been hospitalized at least 3 times because of recurrent HE.

Surgical Procedure: Partial splenic embolization was performed in all patients to decrease portal venous pressure before surgery. Surgical ligation of the patent PUV was performed under epidural anesthesia. The patent PUV was carefully skeletonized and doubly ligated. Esophageal varices were evaluated with upper gastrointestinal endoscopy before and after surgery.

Result: The mean follow-up duration was 15.8 months. After ligation, there were no clinically significant complications. Esophageal varices were unchanged. The serum ammonia level was higher before surgery (162.3 ± 56.4 μg/dL, mean ± SD) than after surgery (41.8 ± 20.2 μg/dL; p=0.0299). No patient had symptoms of HE.

Conclusion: Ligation of the patent PUV is an effective treatment for patients with refractory HE.

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Key words: patent paraumbilical vein, hepatic encephalopathy, portal-systemic shunt

Introduction

Refractory hepatic encephalopathy (HE) frequently develops in patients with cirrhosis and portal-systemic shunt. Despite treatment with branched-chain amino acids, antibiotics, and lactulose, HE usually recurs. Recently, portal-

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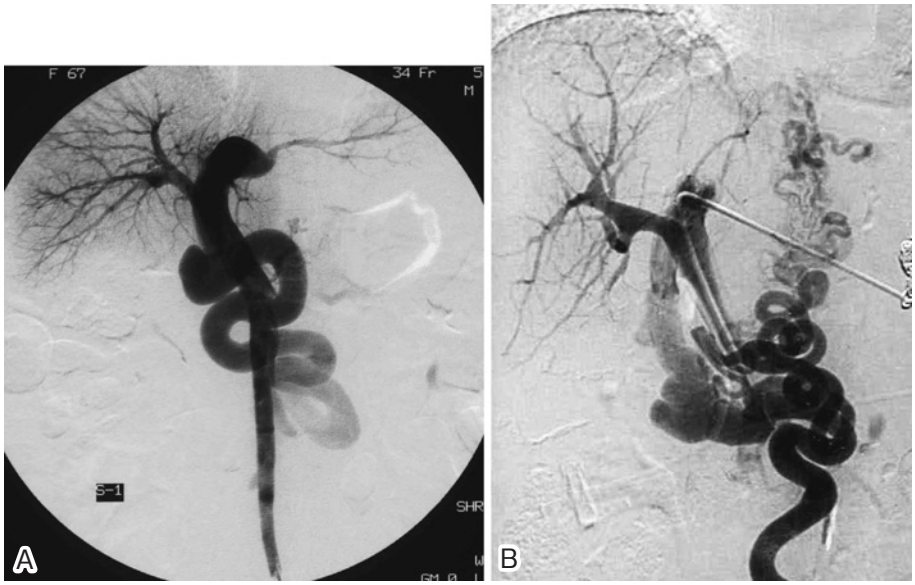

Fig. 1
A: Patent PUV connected to the external iliac vein via the superficial epigastric vein.
B: Patent PUV connected to the external iliac vein via the superficial epigastric vein and to the internal thoracic vein via the superior gastric vein.

systemic shunt associated with refractory HE has been obliterated with interventional radiologic techniques, such as percutaneous transhepatic obliteration, transileocolic vein obliteration, and balloon-occluded retrograde transvenous obliteration. We have previously described the benefits of portal-systemic shunt obliteration with partial splenic embolization[1].

We now describe 4 patients with refractory HE who responded to surgical disconnection of the patent paraumbilical vein (PUV) after partial splenic embolization.

Patients

Thirty-one patients received a diagnosis of portal-systemic encephalopathy and underwent interventional radiology or surgery at our center from 1987 through 2006. This report describes 4 (14.8%) of these patients who had refractory HE due to a patent PUV. Three women and 1 man with a mean age of 56 years are described. Cirrhosis was attributed to hepatitis C virus infection in 1 patient, nonalcoholic steatohepatitis in 1, and alcoholic cirrhosis in 2. The Child-Pugh class was B in 2 patients and C in 2. The Model for End-Stage Liver Disease (MELD) score ranged from 9 to 11 (median, 10.5). PUV patency was diagnosed on the basis of computed tomography and Doppler color-flow ultrasonography. The patent PUV was classified into four types according to the criteria of Yeh et al[2]. In 3 patients, the patent PUV was connected to the external iliac vein via the superficial epigastric vein. In the remaining patient, the patent PUV was connected to the external iliac vein via the superficial epigastric vein and to the internal thoracic vein via the superior gastric vein (**Fig. 1**). The characteristics of the patients and patent PUVs are shown in **Table 1**. The patients underwent routine physical examinations and laboratory investigations, including a complete blood count, liver function tests, and measurement of serum ammonia levels. In addition, all patients had been previously screened with upper gastrointestinal endoscopy for the presence of esophageal varices. Esophagogastric varices were present in 3 of the 4 patients (mild esophageal varices in 2, and moderate esophageal varices and moderate gastric varices without red color signs in 1).

Table 1

Case	1	2	3	4
Age	35	69	70	49
Sex	Male	Female	Female	Female
Etiology of cirrhosis	Alcoholic	Alcoholic	HCV	NASH ***
Child-Pugh grade	B	C	B	C
Type of PUV* connected to	external iliac vein	external iliac vein	external iliac vein	external iliac vein and internal thoracic vein
Varices				
Esophageal varices	mild	mild	—	moderate
Gastric varices	—	—	—	moderate
HE** appearance	9 months ago	12 months ago	14 months ago	10 months ago
Times of admission with HE**	3	4	4	3
Portal venous pressure (mmH_2O)				
Pre → Post	416 → 481	312 → 351	—	—
Serum ammonia level (μg/dL)				
Pre → Post	230 → 45	110 → 25	187 → 28	122 → 69
HE** recurrence	12 months no recurrence	19 months no recurrence	22 months no recurrence	10 months no recurrence

PUV *: paraumbilical vein
HE**: hepatic encephalopathy
NASH***: nonalcoholic steatohepatitis

Partial Splenic Embolization

Before surgical disconnection of the patent PUV, all patients underwent partial splenic embolization to prevent portal hypertension after surgery. The procedures and clinical courses have been described in detail elsewhere[1]. The femoral artery approach was used for superselective catheterization of the splenic artery. The catheter tip was placed as distally as possible in either the hilus of the spleen or an intrasplenic artery. Embolization was achieved by injecting a gelatin sponge cut into 2-mm cubes and suspended in saline solution containing antibiotics. With this procedure, 50% to 70% of the splenic parenchyma was embolized. Simultaneously, portal-phase superior mesenteric arteriography was performed to reconfirm the form of the patent PUV.

Surgical Procedure

The surgical procedure was performed with the patient in the supine position during epidural anesthesia. A short median incision was made in the upper abdomen. It is very important to decide which incision provides the shortest route to the point where cutting and ligation would be most effective. The optimal approach should be decided preoperatively with Doppler color-flow ultrasonography.

The patent PUV was carefully skeletonized, and 10-French rubber catheters were passed behind the skeletonized vein, without the abdomen being opened **(Fig. 2)**. In the first 2 patients, portal venous pressure was measured via the ileocolic vein before and after ligation. The catheter was advanced into the portal venous system via the ileocolic vein through a small abdominal incision. The PUV pressure was measured before and after ligation by means of the tip of the catheter advanced into the portal venous system via the patent PUV through the operative incision. In the other 2 patients, clamp tests were performed instead. The patent PUVs were doubly ligated at both the hepatic and umbilical sides with 3-0 absorbable threads. The patent PUV was then cut between the ligations, and the skin was sutured. For follow-up, all patients underwent computed tomographic scanning within 4 months of the procedure; serum ammonia levels were measured monthly.

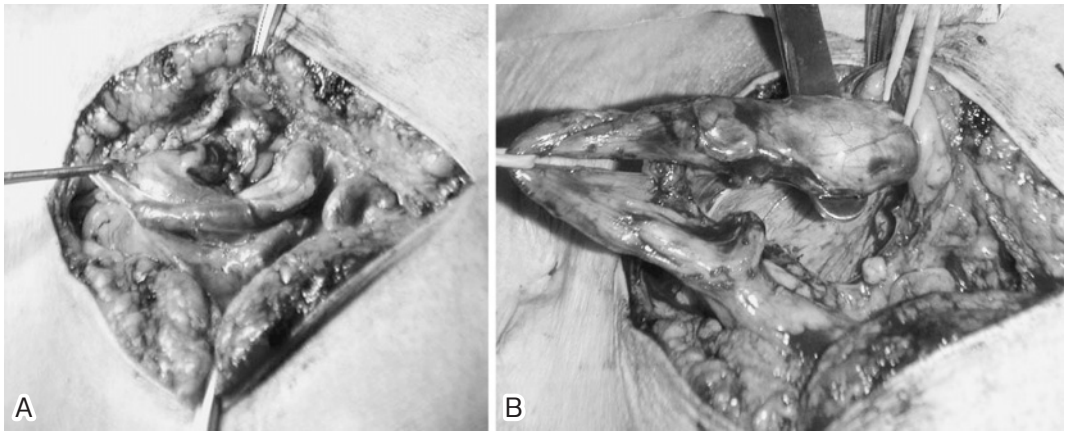

Fig. 2
A: Portal hypertension increased the number and caliber of patent PUVs.
B: Ten-French rubber catheters were passed behind the skeletonized PUV.

Results

During the operations, the estimated blood loss was minimal (less than 50 mL). The postoperative laboratory data showed no noteworthy abnormalities in any patient. Because partial splenic embolization had been performed, portal venous pressure increased slightly after ligation. There were no postoperative complications or deaths. The HE improved after ligation of the patent PUV in all patients. The postoperative courses were uneventful. No marked changes in the esophagogastric varices were detected after treatment. The mean follow-up duration was 14 months. The serum ammonia level was higher before surgery (162.3 ± 56.4 μg/dL; mean ± SD) than after surgery (41.8 ± 20.2 μg/dL; p= 0.0299; **Table 1**).

Discussion

The pathogenesis of HE is complex but is thought to involve hyperammonemia. Ammonia produced by intestinal bacteria enters the systemic circulation from the bowel through portal collateral vessels, thereby bypassing the liver[3]. Thus, portal-systemic shunt is considered a cause of HE. Portal-systemic shunt develops in patients with portal hypertension due to cirrhosis, and a patent PUV is a common cause of portal-systemic shunt. In classic cases of Cruveilhier-Baumgarten syndrome, there is hepatofugal flow via a patent PUV to the veins of the anterior abdominal wall[4]. However, the etiology of patent PUVs remains controversial and requires further investigation[4–7].

In the present study, esophagogastric varices were present in 3 of the 4 patients (mild esophageal varices in 2, and moderate esophageal varices and moderate gastric varices without red color signs in 1). Esophagogastric varices were not severe because portal-systemic shunt had developed. Obliteration of the portal-systemic shunt sometimes increases portal venous pressure and worsens esophageal varices. Partial splenic embolization, an interventional radiological method for the treatment of hypersplenism, is considered necessary to prevent increased portal venous pressure[8]. We have previously reported the benefits of portal-systemic shunt obliteration followed by partial splenic embolization. While the portal venous pressure was monitored, partial splenic embolization reduced the portal venous pressure to a level similar to that before obliteration[1]. In the first 2 patients, we measured portal venous pressure via the ileocolic vein before and after ligation. The postoperative portal venous pressure did not differ appreciably from the preoperative level. On the basis of this experience, increased portal venous pressure after ligation was prevented by preoperative embolization of 50% to 70% of the splenic parenchyma. Thus, measurement of portal venous pressure via the ileocolic vein was considered unnecessary in the 2

more recently treated patients.

In 1 of our patients PUV patency recurred after primary occlusion. Complete obliteration of the patent PUV via the transileocolic vein had been performed with metallic coils and absolute ethanol, but HE recurred after 1 year. A new hepatofugal flow was detected through the new patent PUV, which had not been patent after the first treatment.

Hypothetically, the most important reason for recurrence is that interventional radiological procedures can obliterate only one patent PUV, even though the normal falciform ligament contains 1 to 3 tiny collapsed PUVs. The number and caliber of patent PUVs are increased by the presence of portal hypertension[5]. In contrast to interventional radiological procedures, surgical treatment involved ligation as well as cutting the atretic patent PUVs. Our results suggest that ligation is more reliable than interventional radiological procedures for obliteration of patent PUVs.

Liver transplantation is the treatment of first choice for cirrhosis with refractory HE, but the worldwide shortage of donor organs remains a serious problem. To ensure that donor livers are properly allocated, the United Network of Organ Sharing has recommended the MELD score for assigning priorities. However, the MELD score does not take into account encephalopathy, ascites, or esophageal variceal hemorrhage. Although patients with refractory HE who have a patent PUV require liver transplantation, their MELD score would not be high enough to put them at the top of the waiting list for liver transplants. Our patients did not have severe liver cirrhosis but did have portal-systemic shunt and a patent PUV.

Patients with HE frequently require emergency hospital admission, and the onset of HE interferes with patients' daily lives. Our experience indicates that surgical disconnection of patent PUVs can improve HE and enhance patients' activities of daily living within a short period. In the longer term, liver transplantation should be considered in patients undergoing surgical disconnection, because a new portal-systemic shunt, leading to HE, is very likely to develop in a different direction. Unless the shortage of donors is eased in the future, procedures designed to obliterate portal-systemic shunt, such as surgical disconnection of patent PUVs, will probably play an important role in maintaining the quality of life of patients with liver cirrhosis. In conclusion, we consider surgical disconnection an effective treatment for patent PUVs associated with refractory HE.

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