

# Gastroesophageal Variceal Bleeding Successfully Controlled by Partial Splenic Embolization

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## Abstract

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A 53-year-old male patient with a history of hepatocellular carcinoma developed gastroesophageal varices refractory to endoscopic injection sclerotherapy (EIS). He required EIS six times in 2 years for recurring variceal bleeding. After hepatic resection, he developed massive splenomegaly. Partial splenic embolization (PSE) was performed to reduce the portal pressure. Varices and variceal bleeding were not detected during 13-year follow up, until the patient died of hepatocellular carcinoma. This is a unique case of gastroesophageal varices controlled by PSE and improved portal hypertension.

**Key words:** gastroesophageal varices, partial splenic embolization

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## Introduction

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Gastroesophageal varices are common complications in patients with liver cirrhosis. Gastroesophageal varices cause severe bleeding that can lead to death. Gastroesophageal varices refractory to treatment have a poor prognosis due to recurring bleeding (1, 2). Gastroesophageal varices are associated with portal hypertension. In cirrhotic patients, intrahepatic vascular resistance increases due to fibrosis of the liver, resulting in portal hypertension. Portal hypertension changes the blood flow to the spleen, which results in splenomegaly (3). Splenomegaly increases the portal blood flow and can even worsen the portal hypertension. Patients with gastroesophageal varices with massive splenomegaly tend to be refractory to treatment due to the severe portal hypertension (4).

Partial splenic embolization (PSE) was developed as a safe and effective alternative to splenectomy to treat hypersplenism with severe thrombocytopenia in patients with chronic idiopathic thrombocytopenic purpura (5). In recent years, PSE has been performed for severe thrombocytopenia in patients with liver cirrhosis due to chronic hepatitis C infection, to safely treat these patients with interferon (6). In theory, PSE reduces portal blood flow, improving portal hypertension.

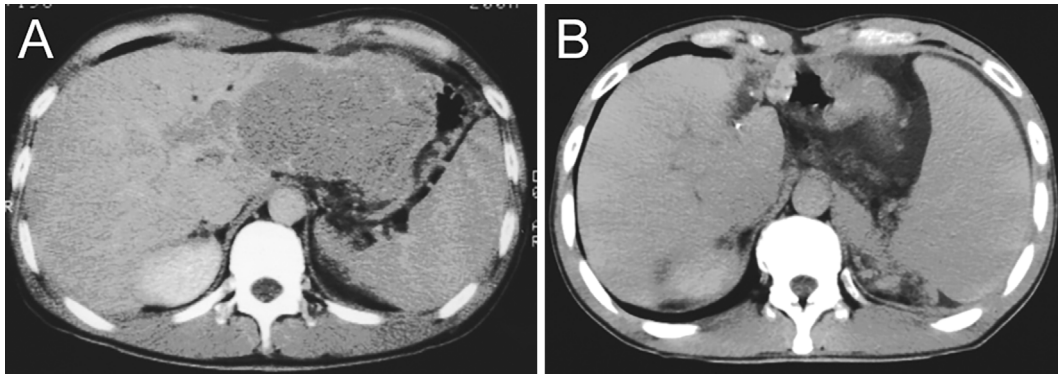
We herein report a case of refractory gastroesophageal variceal bleeding successfully controlled after performing PSE.

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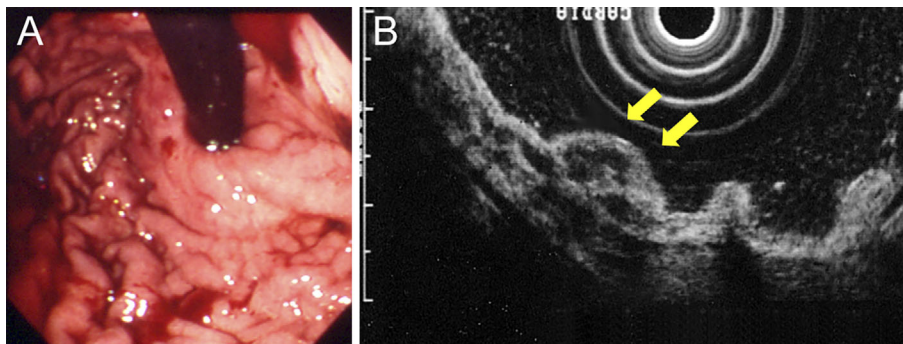
## Case Report

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In 1995, a 53-year-old male patient with chronic hepatitis B received left lobectomy for a 12-cm hepatocellular carcinoma (HCC) in the left lobe of the liver (Fig. 1A). The pathology showed moderately differentiated HCC (Edmondson II) and there was no evidence of cirrhosis in the surrounding liver. In 1997, 2 years after the resection, he received esophago-gastro-duodenoscopy (EGD) because of anemia. Esophageal varices that had not been identified before the hepatic resection were found. The varices were located in the lower esophagus and the cardia of the stomach, and were described as Li F<sub>2</sub> Cb RC<sub>2</sub> and Lg-c F<sub>1</sub> Cw RC<sub>0</sub> according to the Japanese Research Society of Portal Hypertension classification (7). The esophageal varices were moderately enlarged and beady, and were blue-colored with obvious red color signs. He received endoscopic injection sclerotherapy (EIS), in which 5% monoethanolamine oleate (EO) was injected directly into the esophageal varices until the variceal space was filled with the sclerosant. Esophageal varices or gastric varices recurred six times in 2 years, and EIS was performed each time. In July 2000, he was admit-



**Figure 1.** Abdominal computed tomography (CT). (A) CT before hepatic resection for hepatocellular carcinoma. (B) CT before partial splenic arterial embolization.



**Figure 2.** Images of esophago-gastro-duodenoscopy (EGD) and endoscopic ultrasonography (EUS) before partial splenic arterial embolization. (A) An EGD image of the gastric variceal bleeding. (B) EUS. Arrows, gastric varices.

ted to our hospital for massive hematemesis. Emergency EGD revealed a large amount of fresh blood in his stomach, but the source of the bleeding was unclear (Fig. 2A). Endoscopic ultrasonography (EUS) was performed and gastric varices were detected as vessel-like echoic-free spaces, 2 mm in diameter, in the fornix of the stomach (Fig. 2B). EIS was performed by injecting 5% EO directly into the varices. After EIS, EUS showed that the vessel-like echo-free spaces had disappeared, indicating that EIS was effective.

The hepatic resection had initiated the development of portal hypertension, which led to the splenomegaly. However, the greatly increased portal blood flow due to the splenomegaly was thought to be aggravating the portal hypertension of the patient, resulting in the development of gastroesophageal varices and variceal bleeding. Indeed, as measured using computed tomography (CT) volumetry, the splenic volume of the patient increased 3.25-fold compared with the volume before hepatic resection (Fig. 1B, Tables 1 and 2). The ruptured gastric varices in this patient were very small and difficult to distinguish from gastric folds. The varices were identified only by EUS (Fig. 2B). In dynamic CT (Supplemental material 1), a distended and tortuous splenic vein was detected but there were no major vessels in the gastric mucosa to suggest existence of typical large gastric varices with port-systemic shunts such as a splenorenal shunt or a gastrosplenic shunt to be treated with

Balloon-occluded Retrograde Transvenous Obliteration. Reduction of portal pressure was considered necessary to prevent recurrence of recurring variceal bleeding. Trans-jugular intrahepatic portosystemic shunts (TIPS) can reduce portal hypertension markedly but may also induce hepatic encephalopathy and impair liver function; thus, TIPS is considered a bridge to liver transplantation (8). We decided to perform PSE to decrease the portal hypertension by reducing the portal blood flow, thus preventing a recurrence of variceal bleeding.

Written informed consent was obtained from the patient before the procedure. A prophylactic dose of gentamycin was administered prior to performing PSE. The celiac arteriogram showed massive splenomegaly with a cephalocaudal length of 23.5 cm (Fig. 3A, B). The catheter was placed in the splenic artery and embolization was performed using a 2-mm-square gelatin sponge via the blood flow until the splenic arterial flow was completely stopped (Fig. 3C). Gentamycin was continuously administered until 14 days after PSE. After PSE, the patient showed low-grade fever and mild left upper abdominal pain that were controlled with an antipyretic analgesic. Seven days after PSE, a massive infarcted area was observed in the spleen (Fig. 4A) with 70% of the total spleen volume analyzed by CT volumetry (Table 2). The platelet count increased from 57,000/ $\mu$ L to 153,000/ $\mu$ L in 7 days (Table 2).

**Table 1. Clinical Characteristics.**

	before HR	before PSE	5 yrs after PSE
White blood cells ( $\mu\text{L}$ )	5,300	1,600	2,600
Red blood cells ( $\times 10^3/\mu\text{L}$ )	4,590	3,410	4,170
Hemoglobin (g/dL)	13.7	9.1	12.0
Platelet ( $\times 10^3/\mu\text{L}$ )	154	57	82
Prothrombin time (%)	100	58	76
Total bilirubin (mg/dL)	0.7	1.2	1.2
AST (IU/L)	42	15	23
ALT (IU/L)	36	23	27
LDH (IU/L)	354	402	411
ALP (IU/L)	210	215	266
$\gamma$ -GTP (IU/L)	242	13	39
Choline esterase (IU/L)	486	128	214
Total protein (g/dL)	7.3	6.0	7.2
Albumin (g/dL)	4.2	3.7	4.3
Total cholesterol (mg/dL)	233	128	183
Triglyceride (mg/dL)	166	39	49
Urea nitrogen (mg/dL)	16	26	18
Creatinine (mg/dL)	0.5	0.6	0.6
Sodium (mEq/L)	141	143	142
Potassium (mEq/L)	4.1	3.9	4.3
Chloride (mEq/L)	103	106	105

HR: hepatic resection, PSE: partial splenic embolization, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase,  $\gamma$ -GTP:  $\gamma$ -glutamyl transpeptidase

**Table 2. Changes of Splenic Volume and Platelet Count.**

	before HR	before PSE	PSE 1 week	PSE 1 year	PSE 5 year
Splenic volume (mL)	271	811	264	327	359
Platelet ( $\times 10^3/\mu\text{L}$ )	154	57	153	81	82

HR: hepatic resection, PSE: partial splenic embolization

The patient's recurring variceal bleeding ceased after PSE. Two years after PSE, EGD showed no sign of recurring gastroesophageal varices (Fig. 5). The splenic volume analyzed by CT volumetry showed a small increase in size 5 years after PSE, but it remained within 40% of the initial volume (Fig. 4, Table 2). The platelet count, which transiently increased after PSE (to 153,000/ $\mu\text{L}$ ), decreased to 81,000/ $\mu\text{L}$  at 1 year after PSE and was maintained at that level thereafter. In 2007, the patient was started on entecavir 0.5 mg/day for the treatment of chronic hepatitis B. During the 13-year follow up, until the patient died of recurrent HCC, the patient had shown no recurrence of variceal bleeding or gastroesophageal varices.

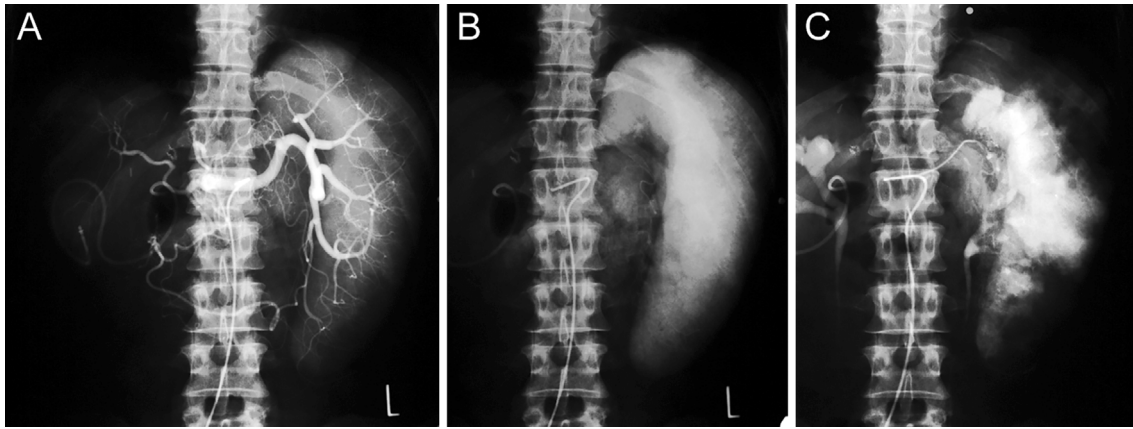
## Discussion

Despite improvements to therapies for gastroesophageal varices, the mortality rate is 20% at 6 weeks after variceal bleeding (9). Even when the bleeding is controlled and the varices are successfully treated, varices have a high recurrence rate, which is associated with a poor prognosis in cir-

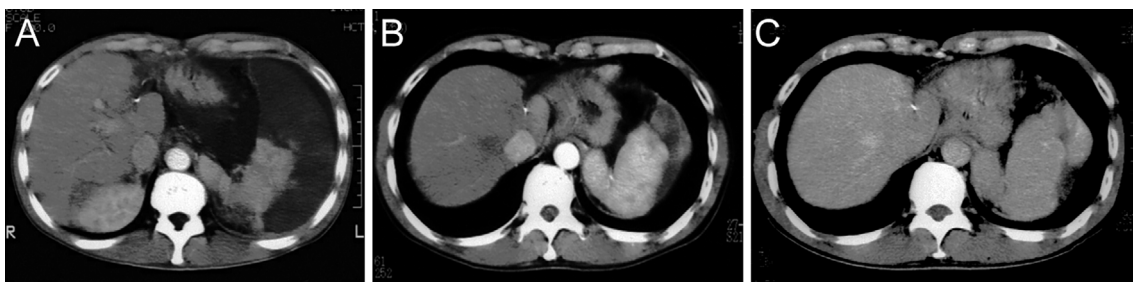
rhotic patients.

In general, the two main treatments for varices are therapies that reduce portal pressure and endoscopic local therapies. Portal pressure is associated with portal inflow and vascular resistance (10). Non-selective  $\beta$ -blockers such as propranolol or nadolol, which are used for portal hypertension, act by decreasing the cardiac output ( $\beta$ 1-blockade) and inducing splanchnic vasoconstriction ( $\beta$ 2-blockade). However, these drugs are not approved for the treatment of gastroesophageal varices or portal hypertension in Japan. Shunt procedures connecting the portal system to systemic veins such as shunt surgery (distal splenorenal shunts) or TIPS effectively decompress the portal pressure, but these procedures lead to short survival, especially in cirrhotic patients, and increase the risk of encephalopathy (11).

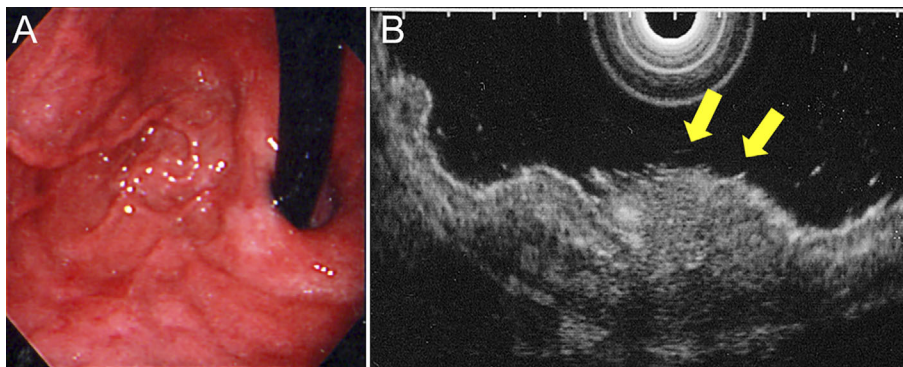
Endoscopic local therapies such as EIS and endoscopic variceal ligation (EVL) can achieve obliteration of the varices. EIS is considered more effective than EVL because it can embolize the feeding vessels of varices supplied by the portal system. EIS has been reported to prevent variceal bleeding and the recurrence of developing varices after the



**Figure 3.** Angiography. (A) image of arterial phase before partial splenic embolization (PSE). (B) image of late phase before PSE. (C) image of arterial phase after PSE.



**Figure 4.** Abdominal computed tomography after partial splenic embolization. (A) Image at 7 days. (B) Image at 1 year. (C) Image at 5 years.



**Figure 5.** Esophago-gastro-duodenoscopy (EGD) and endoscopic ultrasonography (EUS) 5 years after partial splenic embolization. (A) EGD. (B) EUS. Arrows, treated gastric varices.

treatment (12, 13). In the present case, EIS was effective at each treatment, and the disappearance of variceal vessels was confirmed by EUS. However, the patient developed recurring varices and variceal bleeding in a short period.

Gastroesophageal varices refractory to treatment such as EIS or EVL is thought to be associated with extreme portal hypertension (2). Portal hypertension alters the blood flow to the spleen, causing splenomegaly (14). Splenomegaly is reported as a risk factor for rebleeding of esophageal varices after endoscopic treatment (4). Splenomegaly also increases the risks of bleeding in gastroesophageal varices that develop in patients with liver cirrhosis (14). A normal spleen

supplies 19% of the total portal venous inflow, but in patients with chronic hepatitis and cirrhosis, 48% of the portal venous inflow is supplied by spleen (15). An increased portal inflow in patients with splenomegaly could make the portal hypertension even worse.

In the present case, the patient developed massive splenomegaly after hepatic resection. The hepatic resection had increased the intrahepatic vascular resistance, which may have led to the development of massive splenomegaly. The massive splenomegaly probably increased the portal flow resulting in severe portal hypertension.

PSE is an interventional radiology procedure originally

developed for the treatment of thrombocytopenia due to hypersplenism (5). However, advances in interventional radiology techniques widely extended its indication such as for portal hypertension with hypersplenism, hereditary spherocytosis, thalassemia, splenic trauma and pretreatment for interferon therapy in chronic hepatitis C (16, 17).

PSE has been shown to improve portal hypertension by reducing splenic and portal venous pressure (18, 19). PSE reduces the flow volume of the splenic vein decreasing the portal venous inflow and portal pressure (18). In the present case, the decreased splenic volume after PSE reduced the portal venous inflow, improving the portal hypertension. This may have contributed to preventing a recurrence of bleeding from gastroesophageal varices.

In conclusion, PSE could be an effective treatment option in patients with portal hypertension accompanied by splenomegaly associated with variceal bleeding refractory to endoscopic therapies.

**The authors state that they have no Conflict of Interest (COI).**

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