Case Report

Cerebral Embolism as a Rare Complication of Balloon-Occluded Retrograde Transvenous Obliteration for Gastric Varices: A Case Report

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Abstract

We report a case of cerebral embolism caused by balloon-occluded retrograde transvenous obliteration (BRTO) for gastric varices in a 77-year-old woman with liver cirrhosis. Balloon-occluded retrograde venography demonstrated multiple collaterals between the efferent and systemic veins, and some of them could not be embolized with metallic coils. Therefore, they were embolized with ethanol, 50% glucose solution, gelatin sponge particles, and ethanolamine oleate, and BRTO was completed. After BRTO, however, the patient complained of mild aphagia and paralysis of the right fingers, and magnetic resonance imaging demonstrated cerebral embolism. The symptoms gradually improved after the administration of ozagrel sodium and rehabilitation. The varices were also completely thrombosed. Patent foramen ovale was suspected as a cause of cerebral embolism.

Key words: balloon-occluded retrograde transvenous obliteration, cerebral embolism, patent foramen ovale

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Introduction

Balloon-occluded retrograde transvenous obliteration (BRTO) for gastric varices has become accepted worldwide as a minimally invasive, relatively safe, and highly effective treatment. The complication profiles of BRTO can be divided into early procedural-related complications and late physiologic complications related to an expected increase in portal hypertension. According to a large meta-analysis including 1,016 patients treated with BRTO, the incidence of a major early complication rate was 2.6%, including pulmonary embolism (n = 4), portal or splenic vein thrombosis (n = 11), renal vein thrombosis (n = 3), extravasation of sclerosant (n = 5), and death within 24 hours of BRTO (n = 2, one patient with advanced hepatocellular carcinoma [HCC] invading the portal vein and one Child-Pugh C class patient with HCC) [1].

We encountered a case of cerebral embolism that occurred as a complication of BRTO for gastric varices. To our knowledge, cerebral embolism caused by BRTO has not been reported. In this report, we present our case and discuss the mechanism of cerebral embolism caused by BRTO.

Case Report

A 77-year-old woman with an unknown etiology of liver cirrhosis had growing gastric varices. Contrast-enhanced computed tomography (CT) showed large gastric varices draining into the left inferior phrenic vein (**Figs. 1A** and **1 B**). The varices were indicated for BRTO, and written informed consent was obtained from the patient before the procedure.

After local anesthesia, a 6-F sheath was placed in the

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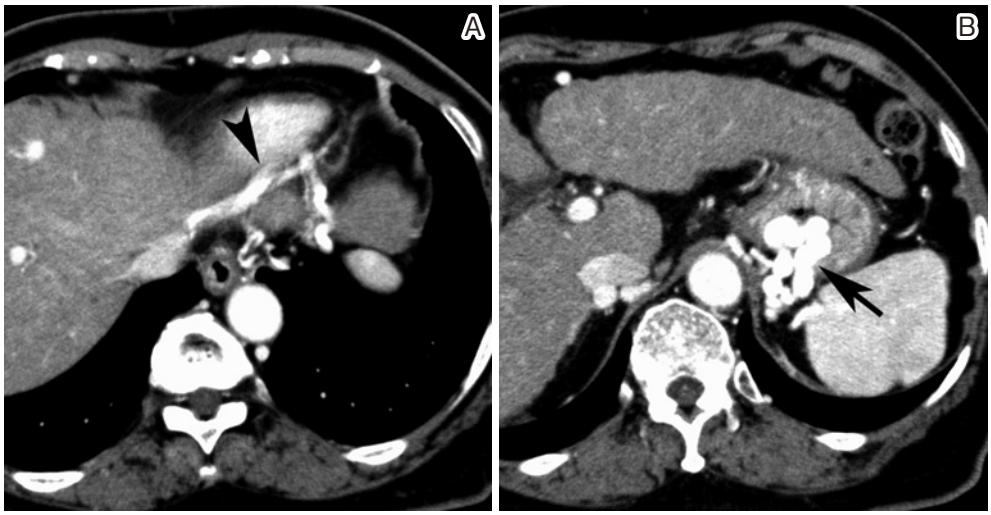

Fig 1. A: Contrast-enhanced CT shows the dilated subphrenic portion of the left inferior phrenic vein (arrowhead). B: Large gastric varices are also seen (arrow).

right femoral vein, and a 5.2-F 9-mm diameter balloon catheter (Selecon MP catheter II, Terumo Clinical Supply, Kakamigahara, Japan) was advanced into the left inferior phrenic vein. Retrograde venography under balloon occlusion of the left inferior phrenic vein demonstrated the pericardiophrenic vein and the left internal thoracic vein through the anastomosis, without opacification of the main efferent vein (**Fig. 2A**). After balloon deflation, more distal advancement of the balloon catheter was attempted, but it was impossible due to the friction of the catheter and vessel wall at the orifice of the left inferior phrenic vein. Therefore, the balloon was re-inflated and the collateral vein connected to the left internal thoracic vein was embolized with metallic coils (Tornado embolization microcoil and Micronester embolization coil, Cook, Bloomington, IN, USA) using a 2.2-F tip microcatheter (Progreat β^3, Terumo, Tokyo, Japan) advanced through the balloon catheter. Venography after coil embolization performed through the more distally advanced microcatheter revealed the left intercostal vein (**Fig. 2B**), and it was also embolized with coils. However, venography at the more distal level revealed several collateral veins connecting with the paravertebral venous plexus (**Figs. 2C-E**). One collateral vein could have been selected by the microcatheter, but coil embolization resulted in failure because the microcatheter became dislodged after deployment of one microcoil. Catheterization into the other veins was also impossible because of the severe angulation of their orifices. To embolize these collaterals, 2 mL of absolute ethanol was infused through the microcatheter placed near their orifices. During ethanol injection, however, the patient complained of pain, and an analgesic (Pentagin, Daiichi-Sankyo, Tokyo, Japan) was administered intravenously. Thereafter, the patient was sedated. The collateral veins still flowed after ethanol injection. Therefore, two injections of 5 mL of 50% glucose solution and an infusion of 3 mL of 5% ethanolamine oleate with iopamidol (EOI) (a mixture of 10% ethanolamine oleate [Oldamin, Takeda, Osaka, Japan] and the same amount of iopamidol [Iopamiron 300, Bayer, Osaka, Japan]) for 10 min were added, but the veins still flowed. Occlusion of the collateral veins was finally achieved by infusion of gelatin sponge particles (Gelfoam, Upjohn, Kalamazoo, MI, USA) cut into approximately 2-mm cubes, followed by 3 mL of 5% EOI for 10 min. However, repeated venography revealed the paraesophageal vein (**Fig. 2F**), and it was embolized with the combination of gelatin sponge particles and 3 mL of EOI because of unsuccessful catheterization. During embolization of these collaterals, the nurse asked the patient about her condition. The patient awoke and falteringly replied that she was sleepy. The procedure was continued because we believed that she might be speaking inarticulately due to the administration of ethanol and analgesia. Thereafter, the patient slept again.

Finally, all collateral veins disappeared, and 12 mL of EOI was infused into the varices for 30 min. After the aspiration of EOI, 10 mL of EOI was additionally infused for 30 min (**Fig. 2G**). Further infusion of EOI was attempted but ceased because the varices were filled with EOI and clots, and additional EOI did not fill the varices. In total, 32 mL of EOI was used, and the catheter and sheath were withdrawn after the removal of residual EOI.

Four hours after BRTO, the patient awoke and complained of mild aphagia and paralysis of the right fingers. The saturation of percutaneous oxygen was 97%, and it was stable before, during, and after BRTO. Diffusion-weighted magnetic resonance imaging showed acute small infarctions in the left frontal and right parietal lobes, and cerebral embolism was suspected (**Fig. 3**). Therefore, 60 mg of ozagrel sodium (Xanbon, Kissei, Matsumoto, Japan) was administered for 7 days, and rehabilitation was simultaneously started. The symptoms gradually improved, and contrast-enhanced CT performed 1 week after BRTO showed complete thrombosis of the varices (**Fig. 4A**). No portoplumonary venous anastomoses (PPVAs), pulmonary arteriovenous malformations (AVMs), or vessel dilatations were demon-

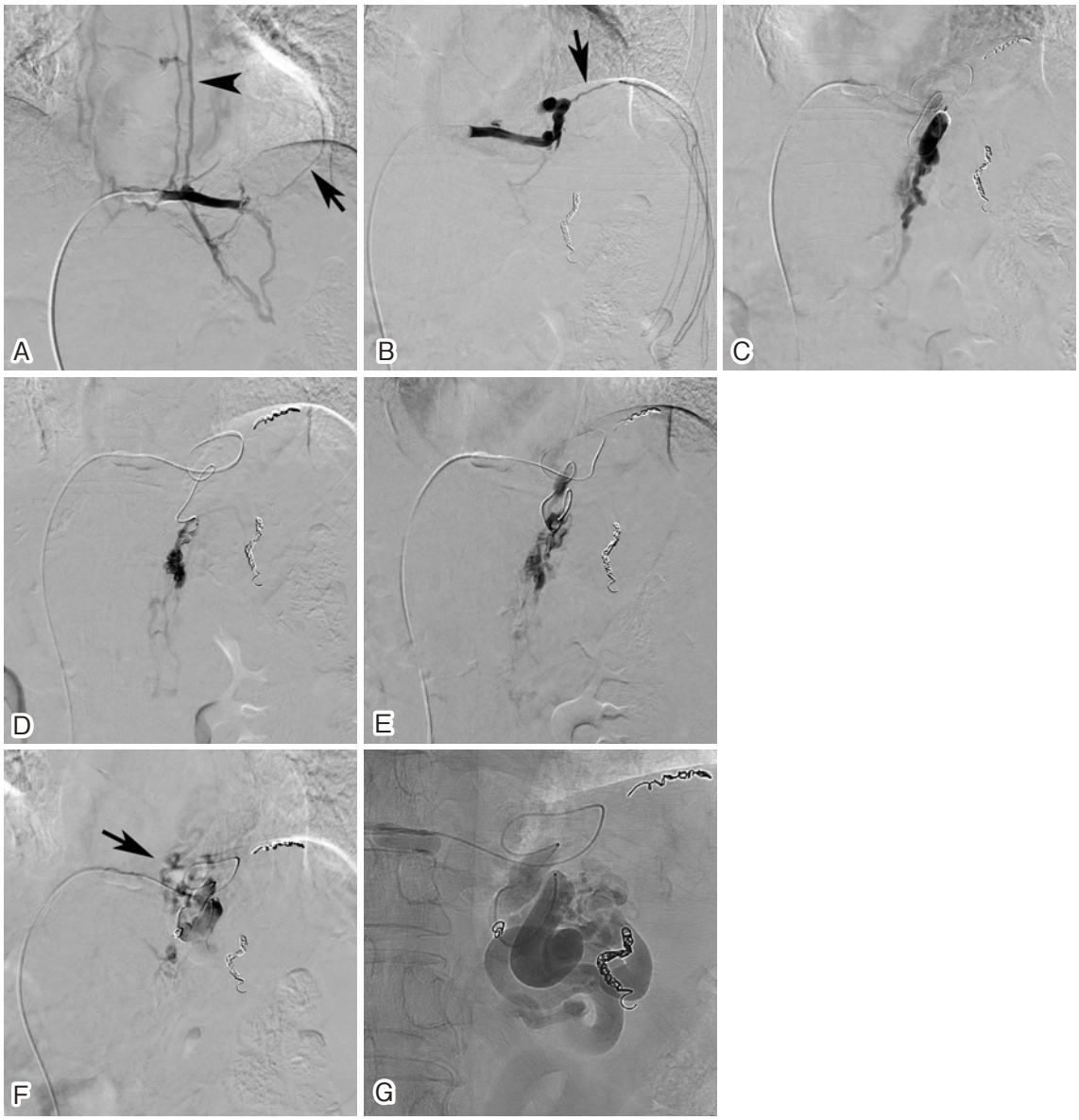

Fig 2. A: Retrograde venography under balloon occlusion of the left inferior phrenic vein demonstrates the pericardiophrenic vein (arrow) and the left internal thoracic vein (arrowhead) through the anastomosis, without opacification of the main efferent vein. B: Venography at the distal level after embolization of the collateral vein connecting with the left internal thoracic vein shows the left intercostal vein (arrow). C-E: Repeated venography at the more distal level after coil embolization of two veins shows several collateral veins communicating with the paravertebral venous plexus. F: Venography after embolization of multiple collateral veins shows the paraesophageal vein (arrow). G: After embolization of the collateral veins, EOI filled the entire varices.

strated. Enhanced transesophageal echocardiography was not performed. The patient is currently alive 4 years after BRTO without recurrence of gastric varices or induction of other varices (**Fig. 4B**). The symptoms related to cerebral embolism have almost disappeared, although she has untreatable multiple HCCs due to a poor hepatic function reserve.

Discussion

According to Kiyosue's classification [2], the feature of gastric varices in the present case is classified into type B-3 contiguous with gastrocaval shunt and high-flow collateral vessels between the main efferent vein and multiple systemic veins. Small clots or particles might migrate into the systemic circulation through these collaterals and cause cerebral embolism. The patient was sedated during the procedure by the administration of an analgesic; therefore, the discovery was delayed until the patient fully awoke, although the patient's faltering reply to the call from the nurse during collateral embolization might indicate mild motor aphasia. Therefore, we determined that cerebral embolism developed during collateral embolization, but we could not

determine when it developed or its causative agent.

Cerebral embolism is a severe complication of neurointerventions, but it can be caused by transarterial interventions below the aortic arch. Cerebral embolism of iodized oil (Lipiodol 480, Guerbert Japan, Tokyo, Japan) is a well-known severe complication of transarterial chemoembolization for HCC, mainly caused by the injection of a large volume of iodized oil (mean, 25.9 ± 14.7 mL; maximum, 50 mL) [3]. Paradoxical cerebral embolism also develops through venous interventions, mainly via thrombolysis for a clotted hemodialysis access [4]. Clot migration to the systemic circulation also causes symptoms such as angina pectoris if it enters the coronary artery.

A PPVA is a collateral vessel that can develop after portal hypertension, and the frequency of the condition varies widely, from less than 1% to 30% [5]. PPVA can cause paradoxical cerebral embolism during portal vein intervention, including BRTO; therefore, the presence of PPVA should be carefully checked before the injection of embolic agents and sclerosant. In a report by Miura et al. [5], PPVA was identified in 3/21 (14%) patients who had no gastrorenal shunts. Although the present case also had no gastrorenal shunts, PPVA was not demonstrated on the venography of each collateral vein performed before embolization. However, the presence of PPVA could not be completely excluded because it is a very small vessel ranging from 2 mm to 7 mm in size [5].

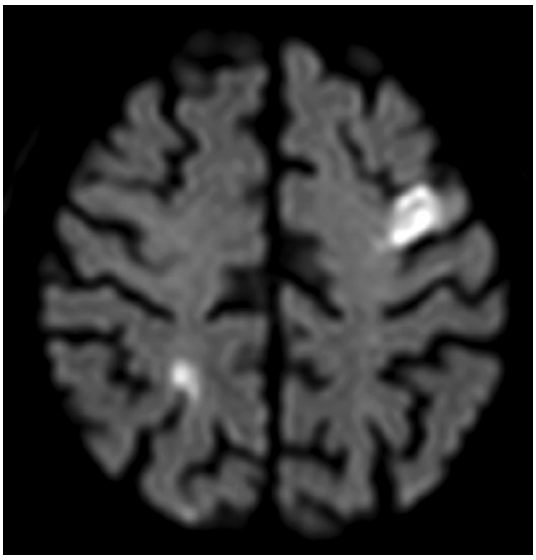

Fig 3. Diffusion-weighted magnetic resonance imaging performed 4 hours after BRTO shows small infarctions in the right parietal and left frontal lobes.

There are two other possible routes of clot migration from the vein into the systemic circulation: a patent foramen ovale (PFO) and pulmonary AVM or shunts. A patent foramen ovale, which is common and found in nearly 25% of healthy individuals, may serve as a persistent tunnel that allows clots to pass from the right to the left atrium and enter the systemic circulation [6]. Pulmonary AVMs are abnormal communications between pulmonary arteries and veins and are also a common cause of paradoxical cerebral embolism. Moreover, patients with end-stage cirrhosis and/or portal hypertension present with arterial hypoxemia associated with intrapulmonary vasodilatation, called hepatopulmonary syndrome (HPS). The diameter of the dilated vessels in HPS patients varies from 15 μm to 100 μm and, in some cases, to 500 μm, whereas it normally ranges between 8 μm and 15 μm [7]. High-resolution CT can identify large, dilated pulmonary vessels in the lower lung zones [8]. The clot can pass through severely dilated intrapulmonary vessels and cause cerebral embolism [9]. In our case, thoracic CT showed no pulmonary AVMs or dilated intrapulmonary vessels, as well as PPVA. Therefore, the presence of PFO was suspected as a cause of cerebral embolism, although enhanced transesophageal echocardiography was not performed.

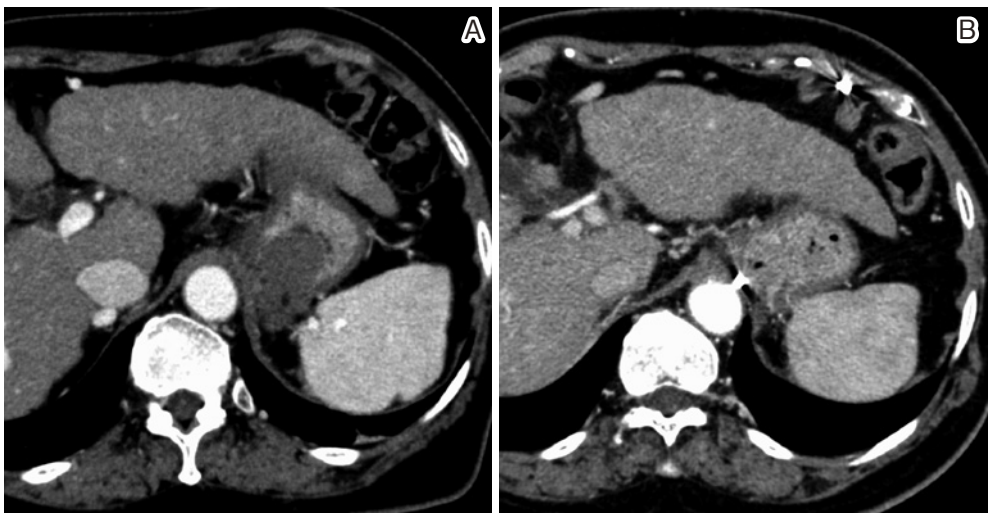

Fig 4. A: Contrast-enhanced CT performed 1 week after BRTO shows complete thrombosis of the varices. B: Contrast-enhanced CT performed 4 years after BRTO shows disappearance of the varices.

For embolization of the abovementioned collateral veins that could not be selected by a microcatheter, we used absolute ethanol, 50% glucose solution, gelatin sponge particles, and EOI. However, such embolic agents have no immediate occlusive effects, and embolic effects on a relatively large vessel are also limited. Therefore, small clots formed by sclerosants or gelatin sponge particles can enter the right atrium through the collateral veins. We used gelatin sponge particles approximately 2 mm in diameter to prevent passing through the collaterals; however, the shape and size of gelatin sponge particles can readily change in a vessel. Therefore, the possibility that gelatin sponge particles might cause cerebral embolism cannot be excluded. The injection of gelatin sponge particles >2 mm in diameter using a high-flow microcatheter followed by EOI infusion might prevent clot or particle migration into collateral veins that cannot be embolized with a metallic coil. N-butyl-2-cyanoacrylate (NBCA) might be another option to embolize the collaterals; however, we hesitated to use it because we wished to keep the microcatheter in the main efferent vein, as it had been deeply advanced there with marked efforts. Additionally, NBCA might involve a risk of systemic embolization and inadvertent occlusion of the main efferent vein.

During venous interventional procedures, we should keep in mind that clot migration into the right atrium is associated with a risk of not only pulmonary embolism but also systemic embolization, because the presence of PPVA, PFO, and occult pulmonary AVMs or shunts in a treated patient cannot be excluded. For the same reason, the use of small-sized gelatin sponge particles should be avoided to prevent paradoxical cerebral embolism. Additionally, deep sedation during the procedure should be avoided when the procedure carries a risk of paradoxical cerebral embolism. Furthermore, in the BRTO procedure, balloon indwelling time is another key to prevent clot migration. It ranged from 30 min to 50 min in the original technique [2]; however, overnight balloon occlusion has become popular, although it has other potential risks of increased access bleeding, higher infection rates, and patient inconvenience [5, 10]. Balloon occlusion should be continued at least until additional EOI injection into the varices is impossible due to filled clots.

In summary, we report a case of cerebral embolism related to the BRTO procedure. It is important to be aware that venous interventions are also associated with a risk of cerebral embolism through PPVA, PFO, pulmonary AVMs, or shunts.

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