Online October 1, 2021
Journal of Neuroendovascular Therapy 2022; 16: 313–319
DOI: 10.5797/jnet.cr.2021-0082

Case Report

Bleb Embolization of Ruptured Cerebral Aneurysms with Coils and n-Butyl Cyanoacrylate Following Proximal Flow Control: Two Case Reports

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Objective: Morphologically challenging cerebral aneurysms cannot be treated through standard endovascular procedures. We report two cases of ruptured aneurysms treated using coils and n-butyl cyanoacrylate (NBCA).

Case Presentations: Case 1 was an 80-year-old woman diagnosed with a subarachnoid hemorrhage (SAH). An angiogram revealed a large and wide-necked basilar artery bifurcation aneurysm. Bilateral superior cerebellar and posterior cerebral arteries (PCAs) originated from the aneurysmal wall. A 3-mm-diameter bleb was detected on the aneurysmal fundus. The bleb enlarged 1 month following coil insertion. During the second treatment, we infused a small volume of 33% NBCA into the coil-framed bleb following proximal flow control of the bilateral vertebral arteries (VAs). The complete bleb obliteration was confirmed by the angiogram at 6 months later. The coil shape was followed up via plane X-ray for 5 years. No rebleeding occurred. Case 2 was a 41-year-old woman diagnosed with SAH. An angiogram revealed a dissecting aneurysm of the left PCA (P1 and P2 segments) accompanying a bleb on the P1 segment. Endovascular treatment was performed, and a coil was inserted into the bleb, infusing 33% NBCA into the coil frame following proximal flow control of bilateral VAs and the right internal carotid artery. Angiograms conducted at 3 months, 1 year, and 9 years and an MRA conducted 12 years later revealed a lack of bleb recanalization.

Conclusion: We developed a Coil and NBCA technique to obliterate ruptured blebs following proximal flow control. This technique can be considered an effective alternative for treating morphologically challenging cerebral aneurysms.

Keywords subarachnoid hemorrhage, endovascular technique, balloon occlusion, basilar artery, posterior cerebral artery

Introduction

Embolization of cerebral aneurysms with electrically detachable coils, a widely accepted endovascular treatment, was first reported by Guglielmi et al.[1] Moreover, for wide-necked and/or large aneurysms, various adjuvant therapies have been reported, such as balloon-assisted coiling, a double-catheter technique, and stent-assisted coiling.[2–5] However, morphologically challenging aneurysms cannot be effectively treated through these endovascular treatments or through direct open surgeries. Although aneurysmal embolization techniques using liquid materials, not usually used for cerebral aneurysms (such as n-butyl cyanoacrylate; NBCA), were reported even before the coiling era,[6–10] liquid materials are particularly difficult to infuse into the aneurysmal sac while avoiding liquid migration into normal vessels.

Herein, we report two cases of ruptured aneurysms, which were difficult to treat with conventional endovascular treatments or direct open surgeries. We treated these cases via Coil and NBCA embolization of aneurysmal blebs. We implemented proximal flow control using balloon catheters with a coil frame inserted into the bleb to avoid the migration of small volumes of NBCA. Our

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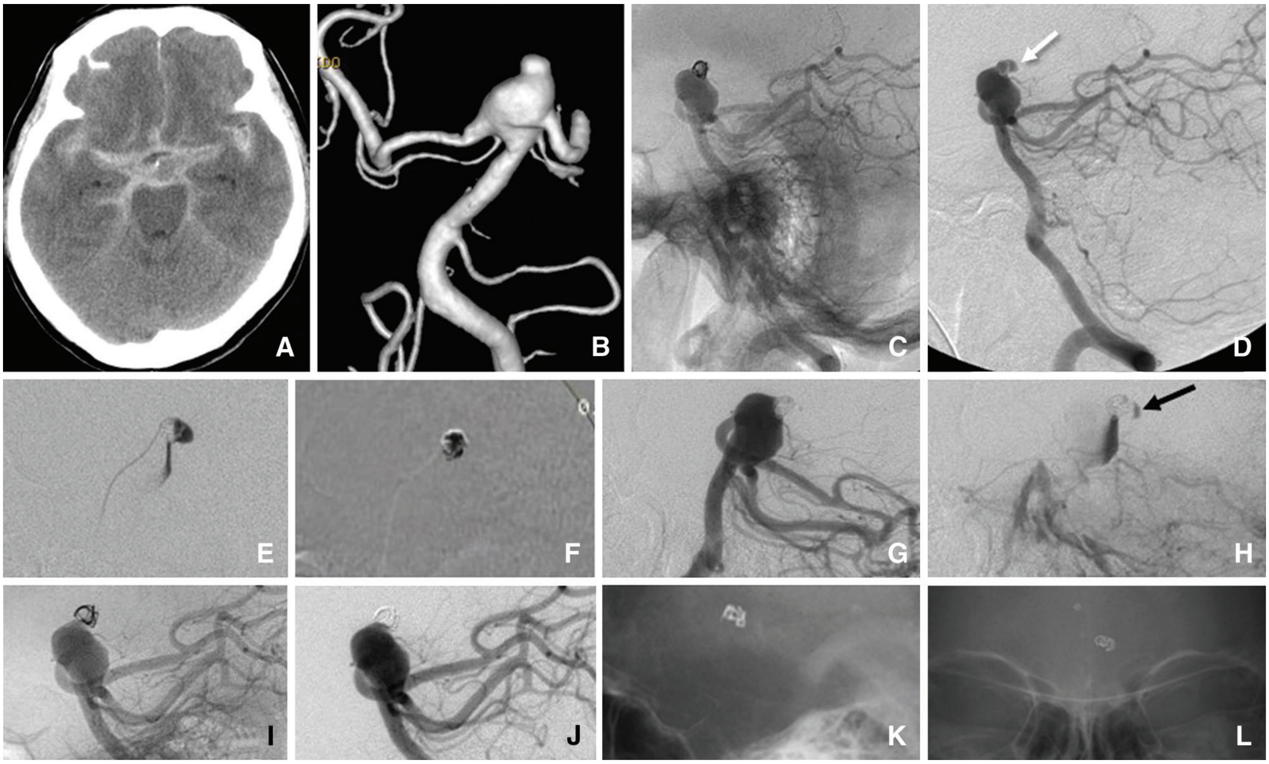

Fig. 1 The case presentation for Case 1. (**A**) A CT scan on admission revealed a diffuse SAH and a mass lesion on the prepontine cistern, indicating a large aneurysm with a partially calcified wall. (**B**) A 3D DSA of the left VA angiogram on admission showed a large and wide-necked basilar artery bifurcation aneurysm with a bleb on the aneurysmal fundus. Bilateral PCAs and SCAs originated from the aneurysmal wall, and the bilateral posterior communicating arteries were hypoplastic. (**C**) A lateral view of the left VA angiogram showing one platinum coil inserted into the bleb on the first endovascular treatment. (**D**) Bleb size (indicated with a white arrow) increased 1 month after the first endovascular treatment. (**E**) Contrast medium stagnation in the bleb following proximal flow control of bilateral VAs. (**F**) 33% NBCA injected into the coil frame, immediately after the withdrawal of the microcatheter. (**G**) Arterial phase of the left VA angiogram, after the injection of 33% NBCA. (**H**) Late venous phase of the left VA angiogram showing the contrast medium in the posterior part of the bleb (indicated with a black arrow). (**I** and **J**) Left VA angiograms at 6-month follow-up indicated the obliteration of the posterior part of the bleb (**I**, non-subtracted; **J**, subtracted) with small "neck remnant" of the bleb. (**K** and **L**) Coil X-rays at 5-year follow-up (**K**, lateral view; **L**, antero-posterior view) showing some transformation of the coil. NBCA: n-butyl-cyanoacrylate; PCA: posterior cerebral artery; SAH: subarachnoid hemorrhage; SCA: superior cerebellar artery; VA: vertebral artery

patients agreed to long-term follow-up to confirm this treatment's efficacy in terms of aneurysmal rebleeding prevention. We discuss technical points concerning polymerization time and NBCA concentrations, as well as the importance of blebs as aneurysmal bleeding points.

Case Presentations

Since NBCA is not an officially accepted material for treating cerebral aneurysms, approval for this treatment was obtained from the ethics committees of the two participating hospitals. The patient or their legal representative provided written informed consent for participating in this treatment and for anonymized publication of the resulting findings in a case report.

Case 1 was an 80-year-old woman experiencing a sudden-onset headache and vomiting. She underwent a CT scan, which revealed a subarachnoid hemorrhage (SAH) accompanied by a round mass and with partial calcification on the prepontine cistern (**Fig. 1A**). Her medical history included successfully treated pulmonary tuberculosis as well as current diagnoses of hypertension and bradycardia (i.e., an implanted pacemaker). An angiogram revealed a large and wide-necked basilar artery bifurcation aneurysm associated with bilateral posterior cerebral arteries (PCAs) and superior cerebellar arteries (SCAs) originating from the aneurysmal wall. A 3-mm-diameter bleb was observed on the aneurysmal fundus (**Fig. 1B**) and the hypoplastic bilateral posterior communicating (Pcom) arteries. The first endovascular treatment was performed 3 days following SAH occurrence. Specifically, a coil (GDC10 3D, 3 mm × 6 cm; Stryker, Fremont, CA, USA) was inserted into the bleb (**Fig. 1C**). As the bleb enlarged at 39 days following the SAH (**Fig. 1D**), a second endovascular

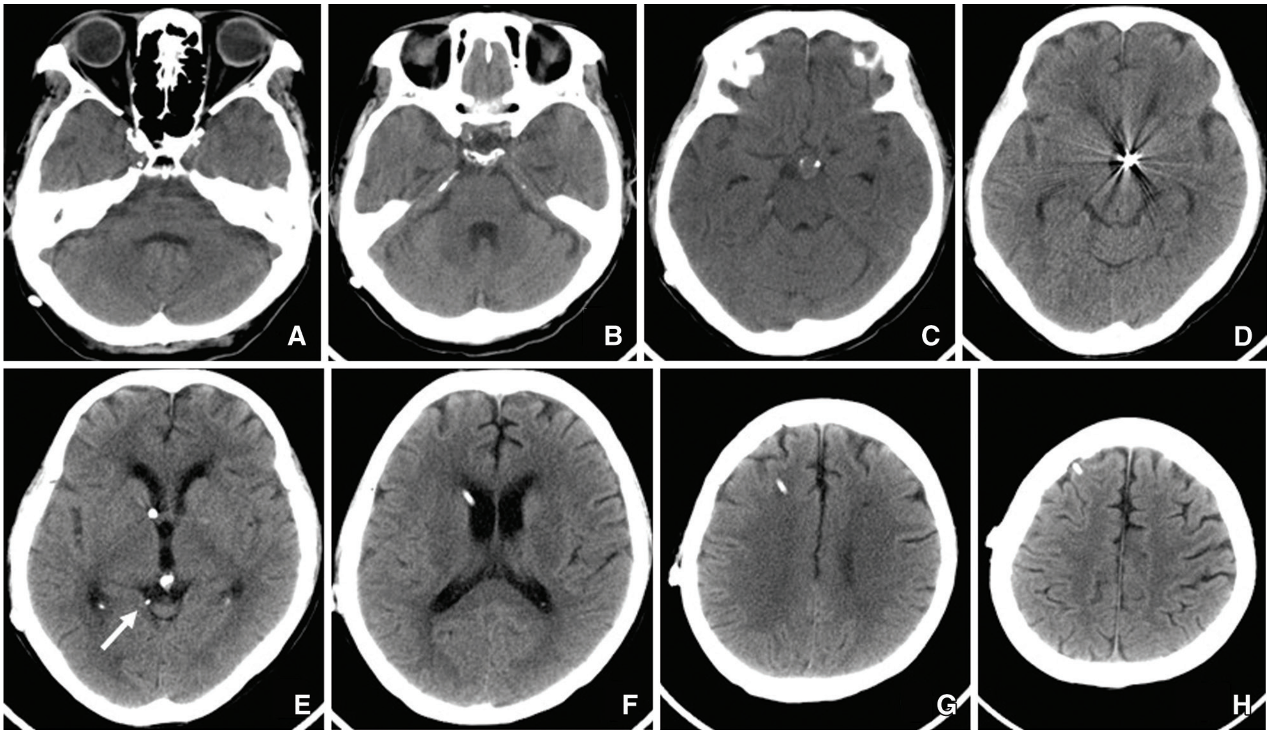

Fig. 2 (**A**–**H**) CT scans of Case 1, the day following the embolization, showing one high-density spot (**E**, indicated with a white arrow).

treatment was performed 45 days following the SAH. Following 7F femoral and 5F right brachial sheaths insertion, systemic heparinization was initiated until reaching an activated clotting time longer than twice that during pre-heparinization. A Patlive occlusion balloon catheter (7F; Terumo Clinical Supply, Gifu, Japan) was inserted in the left vertebral artery (VA) for proximal flow control. A HyperForm occlusion balloon (7 mm × 4 mm; Medtronic, Minneapolis, MI, USA) was inserted in the right VA. We employed an Excelsior SL10 microcatheter (Stryker) with a steam-shaped tip in an S form for stabilization inside the bleb. The head position was tilted (vertex down) to fix the bleb angle. Balloon test occlusion of the bilateral VAs resulted in the stagnation of the infused contrast medium passing through the microcatheter into the bleb (**Fig. 1E**). Following microcatheter irrigation with a 5% glucose solution, bilateral balloon occlusion of the VAs was initiated, and 33% NBCA (Hystoacryl; B. Braun, Melsungen, Germany) diluted with Lipiodol (Guerbet, Villepinte, France) was infused into the coil frame within 5 s using a 1-mL syringe (**Fig. 1F**). The quick withdrawal of the microcatheter was performed following an additional 30 s of proximal flow control. Blood flow of bilateral VAs was restarted by deflating the balloons. NBCA migration was not detected during the procedure, and the bleb was obliterated (**Fig. 1G**), except the small posterior portion of the bleb (**Fig. 1H**, black arrow). The patient was transferred to a rehabilitation hospital; at that time, she presented with an estimated modified Rankin Scale score of 3.[11] Six months following the second embolization, an angiogram revealed maintained bleb occlusion (**Fig. 1I** and **1J**). The coil shape was observed for >5 years via plane X-ray (**Fig. 1K** and **1L**); although some transformation of the coil was detected, no aneurysm rebleeding was found during the follow-up period. **Figure 2A**–**2H** shows the CT scan performed the day following the embolization, which indicated one small high-density spot suspected as the migrated NBCA (**Fig. 2E**, white arrow) without any additional neurological deficit.

Case 2 was a 41-year-old woman experiencing a sudden-onset headache. She was diagnosed with SAH (**Fig. 3A**) and was referred to our medical center 3 days later. The CT scan on admission indicated a small remnant clot on the prepontine cistern (**Fig. 3B**). Her medical history included hypothyroidism, diabetes mellitus, and depression. The angiogram on admission revealed a dissecting aneurysm involving the P1 and P2 segments of the left PCA and a pearl-and-string sign. The P1 segment was curved, and a bleb was associated with the aneurysmal wall (**Fig. 3C**–**3F**). The left Pcom artery was of the adult type

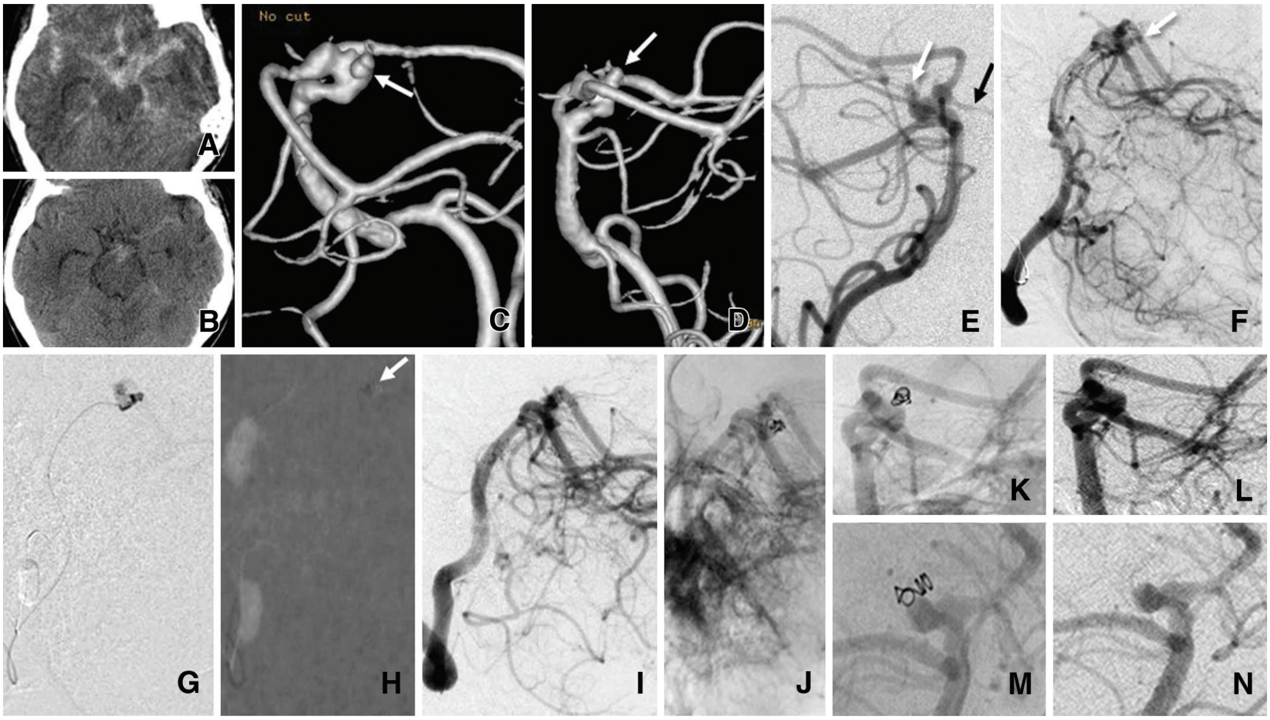

Fig. 3 The case presentation for Case 2. (**A**) A CT scan on the day of SAH occurrence revealed a diffuse subarachnoid clot. (**B**) A CT scan 3 days after SAH occurrence showing a small remnant clot on the prepontine cistern. (**C** and **D**) Right VA 3D DSAs showing the dissecting aneurysm involving the P1 and P2 segments of the left PCA and the bleb (indicated with a white arrow) on the P1 segment of the aneurysm (**C**, left-posterior-oblique view; **D**, left-lateral view). (**E** and **F**) Right VA angiograms indicating the bleb (indicated with white arrows) and the left posterior communicating artery (indicated with a black arrow) (**E**, right-anterior-oblique view; **F**, left-lateral view). (**G**) Contrast medium stagnation infused through the microcatheter following proximal flow control of bilateral VAs and the right internal carotid artery. (**H**) 33% NBCA (indicated with a white arrow) within the coil frame after the balloon deflation. (**I** and **J**) Right VA angiograms (lateral view) immediately after the embolization indicate the complete obliteration of the bleb (**I**, subtracted; **J**, non-subtracted). (**K**–**N**) Right VA angiograms at 9-year follow-up show no bleb recanalization (**K** and **L**, left lateral view; **M** and **N**, right anterior oblique view; **K** and **M**, non-subtracted; **L** and **N**, subtracted). NBCA: n-butyl cyanoacrylate; PCA: posterior cerebral artery; SAH: subarachnoid hemorrhage; VA: vertebral artery

and was connected with the aneurysmal dome of the P2 segment (**Fig. 3E**). Endovascular treatment was performed 5 days after the SAH. After general anesthesia, a 6F sheath was inserted in the right femoral artery, and two 5F sheaths were inserted in the left femoral artery in tandem. Similar to Case 1, following systemic heparinization, a 6F occlusion balloon catheter was placed on the right VA, and micro-occlusion balloons were placed on the left VA and the right internal carotid artery for proximal flow control. Balloon test occlusion revealed contrast medium stagnation in the bleb following injection of the contrast medium from a pre-shaped microcatheter (**Fig. 3G**). Thereafter, a GDC detachable coil (US/SR 2 mm × 3 cm; Stryker) was inserted into the bleb (making a coil frame), and 33% NBCA infusion was performed via the same maneuver as in Case 1 (**Fig. 3H**). Complete bleb obliteration was obtained (**Fig. 3I** and **3J**), and the patient was discharged 3 weeks later without any neurological deficits. During follow-up, angiograms at 1 and 9 years (**Fig. 3K**–**3N**) and MRI at 12 years revealed persistent bleb obliteration. Although the CT scan the day after the embolization revealed one high-density spot suspected as the migrated NBCA (**Fig. 4A**, white arrow), the diffusion-weighted MRIs at 4 days after the embolization indicated no ischemic lesions (**Fig. 4B**–**4H**).

Discussion

Case 1 had a large and wide-necked basilar artery bifurcation aneurysm; bilateral PCAs and SCAs originated from the aneurysm. Owing to its shape, branches, and partially calcified wall, clipping surgery and endo-saccular coil embolization were judged to be difficult procedures. Despite a coil-mediated attempt for bleb embolization, bleb size had increased at follow-up 1 month later. Bleb enlargement indicated a ruptured point, and bleb rebleeding was deemed urgent.

Treatment options for the dissecting aneurysm (Case 2) were left P1 and P2 segment trapping followed by bypass surgery of the left PCA and internal trapping of the P1

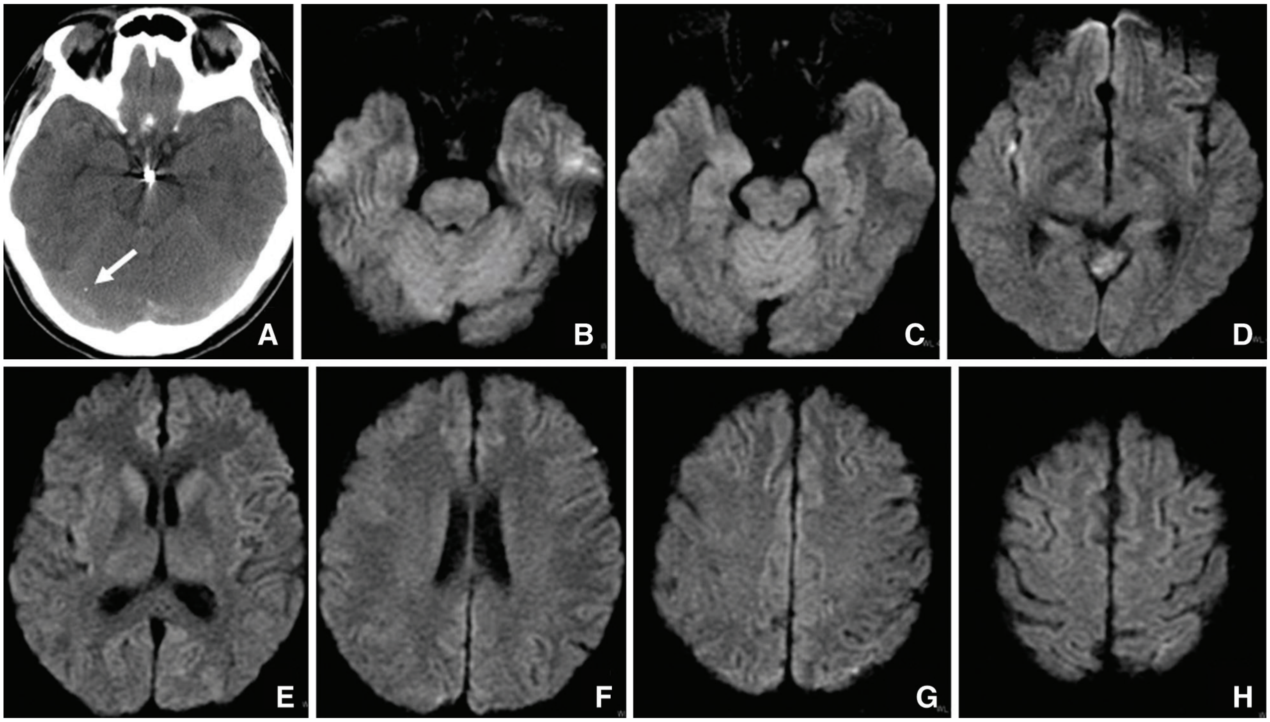

Fig. 4 (**A**) CT scan at the day after embolization of Case 2, showing one white spot (white arrow) of right cerebellar hemisphere. (**B**–**H**) Diffusion-weighted MRIs 4 days following the embolization of Case 2, showing no ischemic lesions of the brain.

segment, with consideration of the collateral flow via the left Pcom artery. However, trapping P1 and P2 segments implies sacrificing the perforators originating from the PCA. Moreover, it was unclear from the current case examinations whether the left Pcom artery could provide sufficient blood flow to the regions perfused by the left PCA.

The two ruptured aneurysms were considered difficult to treat via conventional treatments. Both aneurysms were accompanied by blebs diagnosed as rupture points. Thus, we developed the Coil and NBCA technique to obliterate blebs on the acutely ruptured phase. The goal of this technique is to prevent NBCA migration using proximal flow control, a coil frame in the bleb, and infusing a small volume of NBCA into the coil frame within 5 s.

We utilized contrast medium stagnation to confirm flow control inside the bleb. The patient's head position was tilted (vertex down) to adjust the bleb angle to the floor. In both cases, we could position the head accordingly. Proximal flow control was achieved via occlusion of the bilateral VAs in Case 1 and via occlusion of the bilateral VAs and the right internal carotid artery in Case 2.

Systemic heparinization for balloon flow control was mandatory until an activated clotting time longer than twice that during pre-heparinization was achieved. We selected an over-the-wire (not flow-directed) microcatheter for this technique because the steam shape helps to better stabilize the microcatheter's tip in the bleb. Although over-the-wire microcatheters are not usually used to inject NBCA, its hydrophilic microcatheter coating (reported to diminish NBCA adhesion[12]), trackability, and high burst pressure are useful for the Coil and NBCA technique.[13] We used a 1-mL syringe to infuse a small NBCA volume (approximately 0.03 mL) into the blebs, with careful consideration of the high pressure in the microcatheter.

The coil frame in the bleb plays an important role in preventing NBCA migration. Raymond et al. reported coil protection against NBCA migration in a canine aneurysm model.[14] They described improved NBCA delivery through a single coil positioned at the aneurysm neck and assumed a mechanism based on flow pattern modification inside the sac and the neck, possible coil function as a skeleton for NBCA polymerization, and formation of a physical barrier. Further, Suh et al. also reported that coil frames protect from NBCA spillage.[15]

Mixture ratios of NBCA and Lipiodol are recommended as 25%–33% NBCA because of contrast definition on angiography and polymerization time. Mean polymerization times for 33% NBCA (NBCA: Lipiodol at a 1:2 ratio) and

25% NBCA (1:3 ratio) have been reported as 4.7 and 7.5 s, respectively.[16] Therefore, when using 33% NBCA, the interval between the initiation of NBCA infusion into the bleb and microcatheter withdrawal should be around 5 s to avoid sticking between the microcatheter and NBCA. Nishihori et al. reported focal internal trapping of a large VA aneurysm using coils and NBCA (25% NBCA), with uneventful microcatheter withdrawal 30 s following infusion.[17] In our case, owing to the blebs' morphology, the migration of coils or NBCA could have easily occurred because of glue application; therefore, we considered a short NBCA infusion time of 5 s.

Because we used the 300 mgI/mL contrast medium (specific gravity [SG], 1.326, 37°C) diluted to 60% by heparinized saline (SG, 1.004, 20°C), the SG of the diluted contrast medium was estimated to be higher than blood (SG, standard values, 1.05–1.06). Therefore, the stagnation of the contrast medium occurred in the bottom of the bleb following successful flow control by proximal occlusion of parent arteries. The SG of Lipiodol is 1.270–1.292 and 33% of NBCA (SG, 1.00–1.02, 20°C) contains 67% of Lipiodol; therefore, the SG of 33% NBCA was estimated to be close to that of the diluted contrast medium. However, unlike the contrast medium, 33% NBCA was trapped within the coil frame after injection following the proximal flow control in both cases. We assume that the mechanism of this phenomenon is due to the adhesion between coils and small volumes of 33% NBCA.

Short- and long-term aneurysm rebleeding were prevented in both cases by bleb obliteration using the Coil and NBCA technique. However, we could not confirm that the blebs were the precise bleeding points, nor could we confirm why bleb obliteration prevented rebleeding for 5–10 years or more.

Recent studies on computational fluid dynamics determined aneurysmal rupture points. Cebral et al.[18] and Salimi Ashkezari et al.[19] indicate that blebs form at or adjacent to regions of high wall-share stress. These reports indicate the importance of blebs as rupture points. The long-term protection against rebleeding achieved by complete obliteration of the bleb using the Coil and NBCA technique in our cases appears to indicate the importance of blebs as sites for the origin of bleeding. Raymond et al. reported that coil and NBCA embolization improves neointimal sealing of the aneurysmal neck in wide-necked aneurysms in dogs.[20] Based on that, we assume that neointimal formation over the bleb orifice plays a role in long-term rebleeding prevention after applying the Coil and NBCA technique on these patients.

Conclusion

Although we found that the Coil and NBCA technique obliterates bleeding points originating from blebs, this is not the first-line treatment for ruptured aneurysms. Our case report indicates that this treatment could be considered a useful and effective alternative for treating aneurysms that are morphologically challenging to treat and are accompanied by a bleb that can be flow-controlled.

Acknowledgments

The authors thank Dr. Hiroki Tomita for his support and valuable advice.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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