



Considerations and Literature Review for Treating Subarachnoid Hemorrhage due to Blood Blister-Like Aneurysms

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Objective: Subarachnoid hemorrhage (SAH) due to blood blister-like aneurysm (BBA) is rare but very risky during treatment. Moreover, there is no established treatment method. In this study, we performed endovascular treatment (EVT) as the first-line treatment on patients with SAH during the subacute phase, and cases were analyzed in this series.

Methods: Patients with SAH due to BBA who visited our hospital between April 2021 and March 2023 were enrolled in this study. We waited as long as possible during the acute phase and performed EVT during the subacute phase. We performed stent-assisted coiling (SAC) as the first-line treatment and performed DSA approximately 6 months after treatment.

Results: Ninety-six patients with SAH visited our hospital during the study period and six had SAH due to BBAs. There were two males and four females aged 56.2 ± 14.6 years. We performed SAC in five patients, and one died owing to rebleeding before treatment. Two patients received treatments because of rebleeding. One patient died on the day after rebleeding, whereas the other experienced rebleeding and treatments twice and achieved a good outcome. Four patients had good outcomes (modified Rankin scale [mRS]: 0). The surviving patients achieved complete occlusion at follow-up DSA. However, two patients had poor outcomes (mRS: 6).

Conclusion: Patients with SAH due to BBA treated in the subacute phase may achieve good outcomes; however, there is a risk of rebleeding during the waiting period, which often causes poor outcomes.

Keywords ► blood blister-like aneurysm, stent-assisted coil embolization, reconstructive technique

Introduction

A blood blister-like aneurysm (BBA) is considered an aneurysm by focal dissection.¹⁻³ Zhai et al. reported that hemodynamics might be involved in forming BBA owing to the unique vascular anatomy of the supraclinoid.⁴ BBA develops at the non-branching site of the supraclinoid segment of the internal carotid artery (ICA). BBAs are most

frequently located on the dorsal wall of the ICA but can also be found on the ICA's distal, medial, superior, or anterior wall.⁵ They are small aneurysms with fragile walls and necks, often not distinct. Furthermore, BBAs account for 0.9%–6.5% of ruptured aneurysms.³ Subarachnoid hemorrhages (SAHs) due to BBAs are rare, and they are often difficult to treat. The treatment risk is also high due to the above-mentioned characteristics. Microsurgery for SAH due to BBAs includes clipping, wrapping, trapping, and proximal occlusion with bypass surgery, whereas endovascular treatments (EVTs) include stent-assisted coiling (SAC), overlapping stents, flow-diversion stents, and internal trapping. However, the optimal treatment is yet to be established. Consequently, we used SAC as the first-line treatment for SAH due to BBA. As some articles have mentioned, BBAs should be treated as early as possible to avoid rebleeds^{6,7} and ruptured cerebral aneurysms should be treated within 72 h from the onset according to Japan Stroke Society guidelines for treating stroke, we waited as long as possible during the acute phase and performed

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EVT in the subacute phase. Here, we report our case series of such treatment for patients with SAH due to BBA and a literature review.

Materials and Methods

Patient selection and data collection

Patients with BBA-induced SAH who visited our hospital between April 2021 and March 2023 were included in this study. Patient information including age, sex, Hunt and Kosnic grading system, Fisher CT classification, aneurysm size, presence of blebs, increased aneurysm sizes, occurrence of rebleeding, interval from onset to treatment, degree of aneurysmal occlusion (complete occlusion [CO], neck remnant [NR], or body filling [BF]), and outcome (modified Rankin scale [mRS]) was evaluated. DSA was performed approximately 6 months after the treatment, except for fatal cases.

Treatment

SAC was performed as the first-line treatment. Furthermore, we waited as long as possible during the acute phase, within 14 days from the onset, while managing spasms following SAH and performed EVT in the subacute phase. During SAC, we administered 300 mg of clopidogrel and 200 mg of aspirin using a gastric tube after the induction of general anesthesia. A sheath of 8 French (Fr) was inserted into the common femoral artery, and a balloon guiding catheter was used in case of intraoperative rupture. The 8-Fr Optimo (Tokai Medical Products, Aichi, Japan) was led to the cervical ICA using the 4-Fr inner catheter. We selected a low-profile visualized intraluminal support (LVIS) stent, which is braided and has higher metal density than a laser-cut stent; the selected was expected to have a flow-diversion effect. To deploy the LVIS, a Headway 21 (MicroVention, Aliso Viejo, CA, USA) was led to the distal of BBA. Another microcatheter was led below the BBA for coil embolization. A soft coil, such as the i-ED coil Complex SilkySoft (Kaneka, Osaka, Japan), was selected because the wall of BBA was very fragile. The LVIS was partially deployed, namely the half-jail technique and the coil was placed in the parent artery. The LVIS was deployed completely as the coil was imposed on the BBA, namely the jack-up technique.

Ethics

This study was conducted in accordance with the principles of the Declaration of Helsinki, underwent inspection,

and was approved by the institutional ethics committee (approval number: 757) of Kimitsu Central Hospital. The need for written informed consent was waived because of the retrospective nature of the study, which included an analysis of routine programmatic data, and the patients were offered the opportunity to opt-out via the institutional website. Our institutional ethics committee on unapproved medical devices approved the use of a neck bridge stent for ruptured cerebral aneurysms.

Results

Ninety-six patients with SAH were admitted to our hospital during the study period and six (6.3%) had SAH due to BBAs. **Table 1** provides a summary of the patient's characteristics. A representative example is shown in **Fig. 1**. There were two males and four females, and they were aged 56.2 ± 14.5 years. Notably, all lesions were located on the right ICA. The Hunt and Kosnic grading system revealed that grade I was present in 0 cases, II in four cases, III in two cases, IV in one case, and V in one case. Fisher CT classification revealed that groups 1 and 2 were present in 0 cases, group 3 in four cases, and group 4 in two cases. The average neck length at the first examination was 3.2 ± 1.3 mm, and the average height was 2.2 ± 1.0 mm. Four aneurysms involved bleb, and two did not. We confirmed an increase in the size of aneurysms in two patients. However, the aneurysms without bleb did not increase in size. One patient did not visit a hospital at the first rupture, and one was in the subacute phase when he visited our hospital; therefore, we could not confirm whether there was an increase in the size of their BBA. One patient who died of rebleeding before the intervention became comatose (**Fig. 2**). Therefore, we could not evaluate the patient's BBA after rebleeding because the intervention could no longer be performed. The average interval from onset to intervention was 15.8 ± 7.7 days (5–26 days). Five patients were treated using SAC, and LVIS stents were used in five patients. We treated two patients in the acute phase. One patient developed rebleeding on day 5; he was treated on the same day and died the next day. Another patient was treated on day 11 owing to increased BBA size, and rebleeding occurred. We retreated the patient on day 18 due to increased BBA in size, and rebleeding reoccurred (**Fig. 3**). The remaining four patients were treated in the subacute phase. Three BBAs (60%) were BF, and two (40%) were CO immediately after treatment in five patients. Four BBAs achieved CO during the follow-up

Table 1 Characteristics of the case series

No	Sex	Age	L/R	H&K	Fisher grade	Size (mm) neck × height	Bleb	Aneurysm growth	Recurrent rupture	Treatment (day)	Results		mRS
											Immediately	6 months	
1	M	38	R	3	4	2.8 × 4.0	Yes	Not applicable	Yes	5	BF	–	6
2	F	65	R	2	3	3.2 × 1.4	Yes	No	No	14	CO	CO	0
3	M	73	R	3	4	3.8 × 2.7	No	Not applicable	No	23	BF	CO	0
4	F	42	R	4	3	1.1 × 2.3	Yes	Yes	Yes	11	BF	CO	0
5	F	68	R	2	3	5.2 × 1.5	No	Yes	No	26	CO	CO	0
6	F	51	R	5	3	3.3 × 1.5	Yes	Not applicable	Yes	–	–	–	6

BF: body filling; CO: complete occlusion; F: female; H&K: Hunt and Kosnic grading; L: left; M: male; mRS: modified Rankin scale; R: right

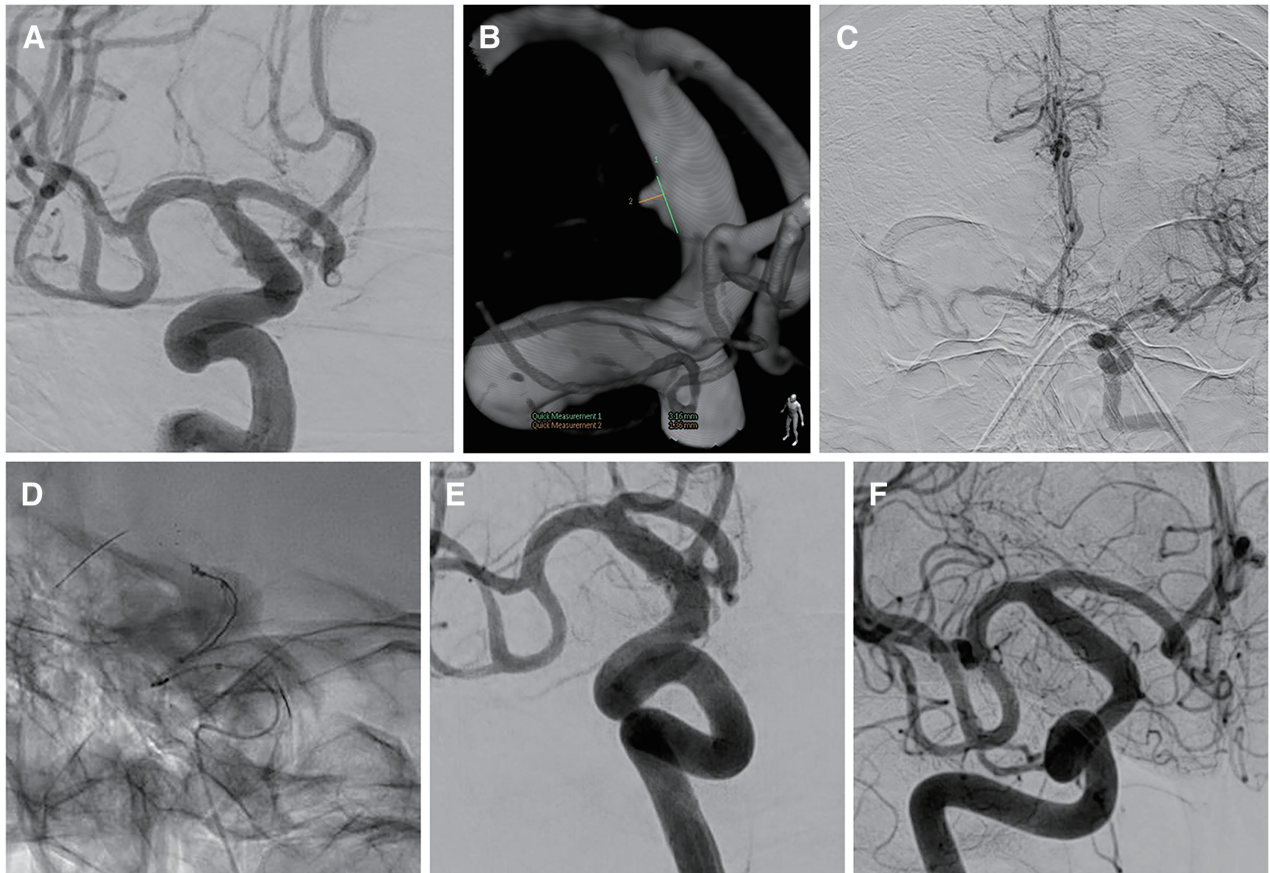


Fig. 1 Case 2. A 65-year-old female. She was transported to our hospital following complaints of sudden headache and nausea. (A) BBA was observed on the right ICA C2 portion. (B) A three-dimensional rotational angiography revealed that the BBA had a 3.2 mm neck length and 1.4 mm height. (C) The manual Matas test showed a developed collateral circulation. Parent artery occlusion was considered depending on the situation. (D) An LVIS of stent 4.5 mm × 17 mm was deployed using the half-jail technique. SAC was performed using the jack-up technique. An iED coil silky soft of 1.0 mm × 3 cm was used. (E) CO was achieved just after SAC. (F) A follow-up DSA after 6 months revealed no recurrence. BBA: blood blister-like aneurysm; CO: complete occlusion; ICA: internal carotid artery; LVIS: low-profile visualized intraluminal support; SAC: stent-assisted coiling

DSA, except for one treated but fatal case. No ischemic complication occurred during the perioperative period, and no intraoperative rupture was observed. Four patients (67%) achieved good outcomes (mRS:0), whereas two patients (33%) died. The patients experienced rebleeding and showed deterioration before the intervention. An overview of the case series is shown in **Fig. 4**.

Discussion

In this study, we reported our case series of using SAC as the first-line treatment for SAH due to BBA. BBAs exhibit a loss of the internal elastic lamina and vascular intima and media, sometimes appearing only as a fragile fibrous layer and are associated with arterial dissections.^{1,4)} BBAs are at

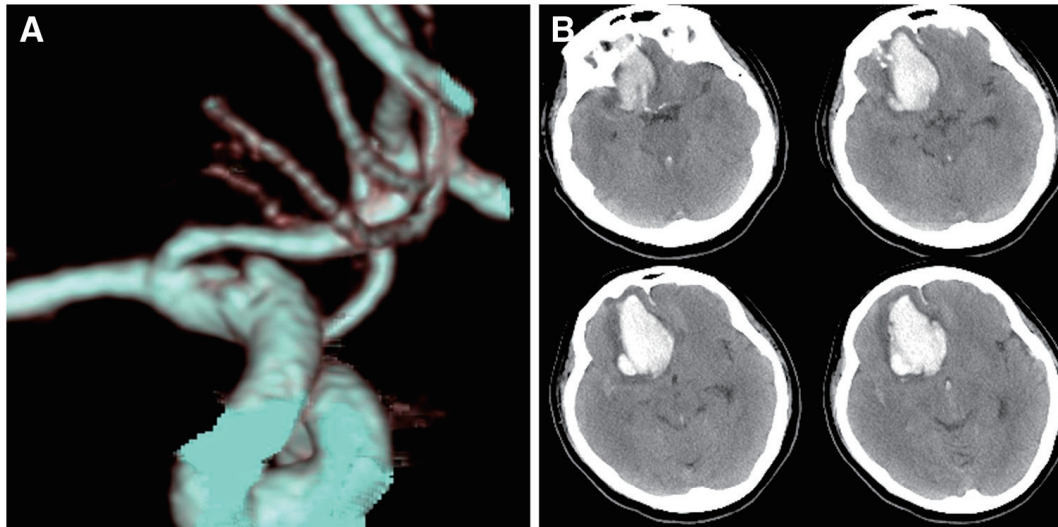


Fig. 2 Case 6. A 51-year-old female. She was transported to our hospital owing to headache, nausea, and consciousness disturbance. The Hunt and Kosnic grading system showed grade 5. Consciousness disturbance improved after admission; we planned to perform SAC during the subacute phase. (A) 3D CTA revealed BBA on the right ICA C2 portion. The neck was 3.3 mm, and the height was 1.5 mm. (B) Sudden deterioration of consciousness and bilateral dilation of the pupils occurred on day 14. CT revealed rebleeding. She died 5 days after rebleeding. BBA: blood blister-like aneurysm; ICA: internal carotid artery; SAC: stent-assisted coiling

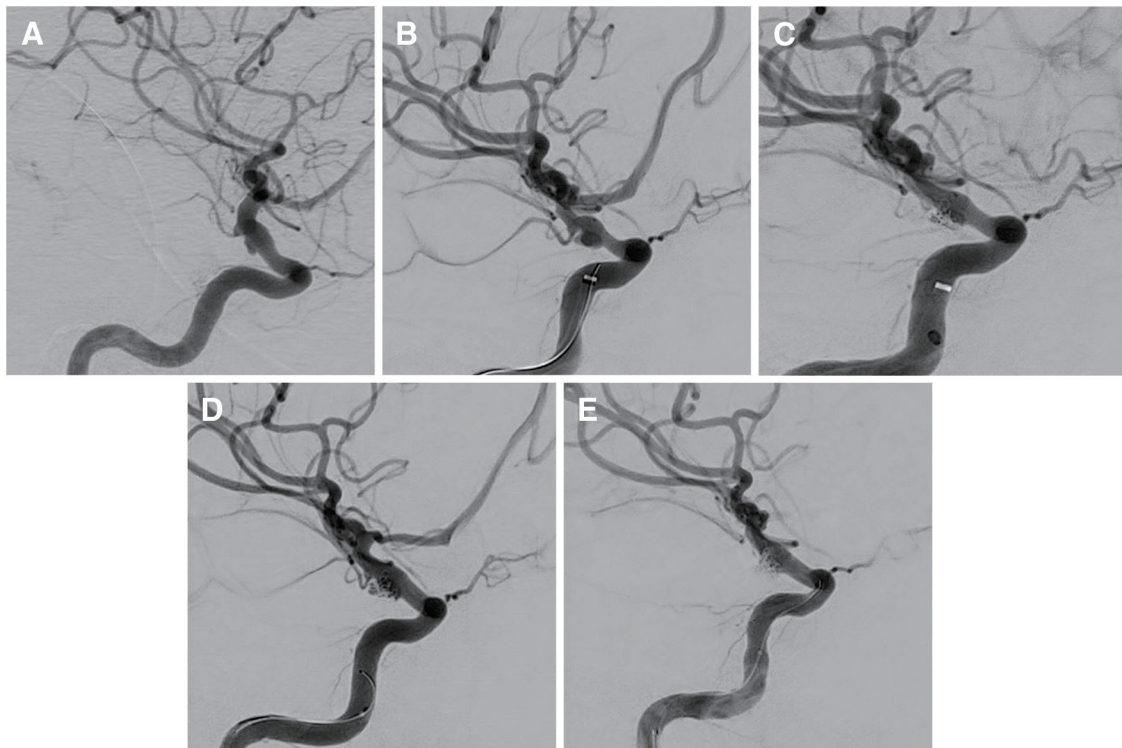


Fig. 3 Case 4. A 42-year-old female. She was transported to our hospital owing to a sudden headache and vomiting. CT revealed SAH. (A) BBA was revealed on the right ICA C2 portion on day 1. We planned to wait during the acute phase and perform SAC during the subacute phase. (B) Rebleeding occurred on day 11. BBA size increased on DSA. (C) SAC was performed on the same day. (D) Rebleeding occurred again on day 18, and the aneurysm relapsed. (E) SAC was performed using the trans-cell technique. BBA: blood blister-like aneurysm, ICA: internal carotid artery; SAC: stent-assisted coiling; SAH: subarachnoid hemorrhage

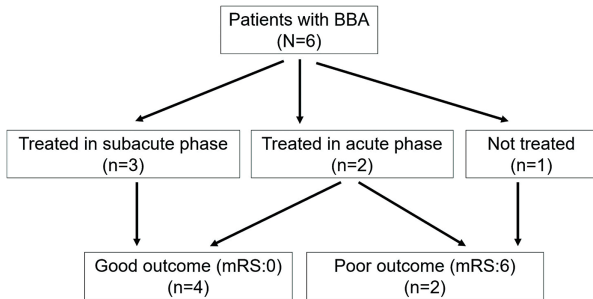


Fig. 4 An overview of this case series. BBA: blood blister-like aneurysm; mRS, modified Rankin scale

a high risk of complications and recurrence. The treatment of SAH due to BBAs involves microsurgery and EVT. The advantage of microsurgery is the non-use of antiplatelet drugs. An operator directly observes the lesions, which may be used to clarify the etiology. However, the surgical approach showed an increased incidence of intraoperative rupture compared with EVT (28.8% vs. 3.2%).¹⁾ When intraoperative rupture occurs, ischemic complications also increase. Tan et al.⁸⁾ reported that more patients achieved good outcomes with EVT than with microsurgery (72.7% vs. 28.6%). Moreover, the mortality rate was higher with microsurgery (32.1% vs. 11.4%).⁸⁾ Peschillo et al.⁹⁾ reported that the rates of good outcomes with mRS0-2 were 67.4% and 78.9% with microsurgery and EVT, respectively. The rates of perioperative complications were 7.0% and 20% in the EVT and microsurgery groups, respectively. Perioperative death occurred in 9.0% and 10.7% of EVT and microsurgery cases, respectively.⁹⁾

For EVT, antiplatelet drugs are essential for avoiding ischemic complications when stents are used. However, ischemic complications have become a problem even with the prevalent use of antiplatelet drugs. In Japan, insurance does not cover using stents in the acute phase. Although there are some problems with using EVT, as mentioned above, we performed SAC as a first-line treatment in patients with SAH due to BBA. Yu et al.⁵⁾ reported 13 patients with BBA between 2004 and 2010 treated using SAC: 6 had no deficit, 3 had ischemic complications, 3 died from rebleeding, and 1 died from a central nervous system infection.⁶⁾ Recent articles have also reported the efficacy and safety of SAC. Roh et al.¹⁰⁾ reported, using pooled analysis, that the rates of good outcome were 89.9%, rebleeding was 7.94%, recurrence was 24.2%, and the mortality rate was 7.7%. Ye and Lv¹¹⁾ treated eight patients with SAC; all aneurysms achieved CO, and all patients had good outcomes. Using a meta-analysis, Scerrati et al.¹²⁾ reported that 687 patients were treated with EVT and 258 were treated using SAC.

SAC had a higher rate of immediate occlusion (63.4%) than stand-alone stent placement (42%) and flow diverters (FDs; 53.7%); however, the occlusion rate at the final follow-up was comparable between the different techniques.

Notably, all the stents used in our case series were LVIS stents. Aihara et al.¹³⁾ reported on 12 patients with 13 aneurysms whose BBAs were only treated with SAC LVIS stents. Twelve aneurysms (92%) were CO during the follow-up DSA, and no rebleeding occurred. A study that compared SAC using an LVIS stent with microsurgery reported that no retreatment was performed in the LVIS group; the mean mRS in the LVIS group was significantly lower than in the microsurgery group, and adverse outcomes were significantly lower in the LVIS group than in the microsurgery group.¹⁴⁾ Combining a coil and stent reduces the risk of rebleeding and prevents the migration or shortening of the stent, compared with using the stent alone.

The efficacy of overlapping stents has been reported in case reports or treatment results of single institutions by Suzuki et al.⁶⁾ and Ji et al.⁷⁾ Lim and Song¹⁵⁾ treated 16 patients with overlapping stents and 1 with SAC. Three of the patients died, whereas 14 achieved CO during the follow-up DSA. Eight patients had good outcomes, five did not, and one died of SAH due to another reason. Our case series did not include this technique; however, it should be considered when the BBA is very shallow and performing an SAC becomes dangerous.

Notably, several studies have reported the efficacy and safety of FDs. In their systematic review, Kan et al.¹⁶⁾ referred to using a Pipeline (Medtronic Neurovascular, Irvine, CA, USA) in treating BBAs. FD targets the diseased vessel wall more effectively compared with surgery, and the operator avoids manipulating the fragile vascular wall. Möhlenbruch et al.¹⁷⁾ reported the efficacy and safety of using a Flow Redirection Endoluminal Device (FRED) (MicroVention). Thirty patients were treated using FRED, and 23 (77%) achieved an mRS of 0–2. Immediate CO was achieved in 10 patients (10%), and 24 (92%) achieved CO at the final follow-up. A major stroke or death occurred in 17% of the patients. Zhu et al.¹⁸⁾ reported in their meta-analysis that the treatment of BBA with FD achieved good outcomes in 83% of the patients and mentioned the efficacy and safety of FD. Recurrence occurred in 13% of the patients, rebleeding occurred in 3%, and treatment-related morbidity and mortality occurred in 3%. Yan et al.¹⁹⁾ used FD to treat 13 patients who experienced recurrence after SAC. Twelve of these patients achieved a CO, and there were no perioperative complications and

rebleeding. A meta-analysis by Sanchez et al.²⁰ compared the safety and efficacy of surgical, flow-diverting stents (FDS) and other endovascular approaches for treating ruptured BBA. The FDS subgroup achieved significantly reduced rates of perioperative retreatment compared with the surgical ($P = 0.025$) and non-FDS endovascular ($P < 0.001$) subgroups. Patients in the FDS subgroup also achieved a significantly lower incidence of perioperative rebleeding ($P < 0.001$), perioperative hydrocephalus ($P = 0.012$), postoperative infarction ($P = 0.002$), postoperative hydrocephalus ($P < 0.001$), and postoperative vasospasm ($P = 0.002$) than patients in the open surgical subgroup. They concluded that flow diversion seems to be effective for ruptured BBA. Bounajem et al.²¹ reported the safety and efficacy of the Pipeline Flex embolization device with Shield Technology (PED-Shield; Medtronic Neurovascular) for treating ruptured ICA pseudoaneurysms. PED-Shield has a phosphoryl-choline surface modification, resulting in lower material thrombogenicity in vitro. Of the 33 patients included in their analysis, no thromboembolic complications occurred. Among patients with a 3-month follow-up, 93.8% had mRS of 0-2. CO at follow-up was observed in 82.6% of patients. They mentioned that the reduced material thrombogenicity appeared to improve the safety of the PED-Shield.

Therefore, FD is useful for BBA even with the insurance problem in Japan. It is possible that FD outcomes have improved and cases have increased in recent years. Our case series did not include this technique partially because no operator could use FD in our institution; however, it is currently worth considering.

Internal trapping is a deconstructive technique with a high hemostatic effect. Rebleeding can be prevented; however, ischemic complications may occur. It is unclear whether the patient overcomes the vasospasm due to SAH if it is performed in the acute phase. Rouchaud et al.³ reported that the rate of initial CO was higher with the deconstructive technique than with the reconstructive technique. (77.3% vs. 33.0%, $P = 0.003$); however, perioperative stroke occurred more frequently (29.1% vs. 5.0%, $P = 0.04$). Peitz et al.²² also mentioned that the deconstructive technique is associated with a higher complication rate than the reconstructive technique. Hayashi et al.²³ reported a case where a parent artery occlusion was performed for BBA rupture. The patient recovered completely despite minor ischemic complications. They concluded that rebleeding from BBA should be prevented first, and ischemic complications are avoided secondarily. Nagao et al.²⁴

reported a case in which occlusion of a parent artery of the ICA was performed after the stent was deployed from the right middle cerebral artery to the posterior cerebral artery through the posterior communicating artery to secure the anterior circulation. Consequently, it may be difficult to evaluate consciousness and collateral circulation in a patient with SAH. However, a balloon occlusion test measuring stump pressure and the Matas and Alcock tests may be useful. The deconstructive technique should be considered when a reconstructive technique cannot be performed for some reason, during a BBA relapse after the reconstructive technique, and when sufficient collateral flow is expected, or hemostasis should be prioritized in the state of emergency.

Nevertheless, the timing of the intervention remains controversial. There are reports that BBAs should be treated as early as possible to avoid rebleeds,^{6,7} and the Japan Stroke Society guideline for stroke treatment recommended that ruptured cerebral aneurysms should be treated within 72 h from the onset; however, we waited as long as possible during the acute phase and performed the EVT during the subacute phase. Fujimori et al.²⁵ reported treating 11 patients using EVT in the acute phase. Two patients experienced rebleeding on postoperative day 1, whereas retreatments were performed in 5. Wen et al.²⁶ compared short-term progressive BBAs and non-progressive BBAs pathologically: 26 BBAs were progressive, and 55 were non-progressive. Progressive BBAs were diagnosed significantly earlier using angiography (3.36 ± 0.61 days vs. 6.53 ± 1.31 days, $P < 0.05$) and revealed a higher rate of bleb presence (61.5% vs. 38.2%, $P < 0.05$). Notably, both progressive and non-progressive BBAs revealed pseudoaneurysms. However, non-progressive BBAs were more histologically destroyed. This may mean that different phases of BBA development were shown.²⁶ BBA may no longer increase in size when tissue destruction is complete.

We are concerned regarding rebleeding, and as much as we would have liked to treat earlier, we waited as long as possible during the acute phase and performed EVT during the subacute phase. It has been reported that if BBAs are treated in the late phase, they may be covered by a thick clot, which improves the stability of the BBA wall and leads to a better outcome.⁷ Patients in our case series who were able to wait until the subacute phase achieved good outcomes, and the BBAs achieved CO. Patients must be treated in the acute phase if rebleeding occurs; however, there is a possibility that recurrence may be decreased by treating during the subacute phase. However, there is

a risk of rebleeding during the waiting period. As mentioned earlier, the early phase from the onset, including a bleb, is associated with a high risk of increased BBA size. Moreover, patients with high Hunt and Kosnic grades are reportedly at risk of recurrence.⁷⁾ In our case series, five of six BBAs experienced rebleeding or increase in size, and three of four, including a bleb, experienced rebleeding or increase in size. Two BBAs without blebs increased in size but did not experience rebleeding. Patients with high Hunt and Kosnic grades tended to experience rebleeding. Hence, we should be careful while waiting, especially in the early phase from the onset, including blebs and high Hunt and Kosnic grades. Other problems with waiting during the acute phase are the fact that fasudil or clazosentan cannot be used, and hypertension cannot be maintained to deal with cerebral vasospasm because the source of bleeding is not treated. The efficacy of FD was reported, and devices have improved in recent years, as mentioned earlier. Three of six patients (50%) experienced rebleeding in our case series, and the rebleeding rate cannot be ignored. Two of them achieved good outcomes; however, this may only be not fatal because of the small sample size. Two of the three patients received follow-up experienced aneurysm growth. Frequent detection during the acute phase may allow for treatment before rebleeding could occur. There are key benefits in treating SAC during the subacute phase mentioned above. Tanoue et al.²⁷⁾ reported a case in which a BBA was treated after becoming a saccular aneurysm in the late phase. However, treating with FD in the acute phase may also be considered.

This study had some limitations. First, it had a small sample size because of the rarity of the disease and the single institution used; however, this limitation also resulted in a relatively unified treatment plan or device. Second, this was a retrospective study. Articles on BBA tend to be case reports or original articles dealing with small sample sizes, and many systematic reviews have been written. Therefore, a prospective multicenter study is warranted.

Conclusion

There is no established treatment method for SAH due to BBA; however, we performed SAC as the first-line treatment in the subacute phase. The outcome was good when treatment was performed before rebleeding and deterioration. However, the outcomes were often poor when rebleeding occurred before the intervention. We should recognize that the rate of rebleeding while waiting is not low: three

of six patients (50%) experienced rebleeding in our case series. Caution concerning rebleeding before intervention should be taken when patients are in the early phase, BBA includes a bleb, and the Hunt and Kosnic grades are poor. There is a risk of rebleeding in the acute phase; however, recurrence may decrease after treatment in the subacute phase. Given the risk factors listed above, FD in the acute phase may be selected; however, our case series did not include this treatment.

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Disclosure Statement

The authors declare no conflict of interest.

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