CLINICAL STUDY

Endovascular treatment of blood blister-like aneurysms in the internal carotid artery using a Willis covered stent

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ABSTRACT

Background Despite the current availability of flow diverter devices (FDD), problems remains regarding optimal endovascular treatment (EVT) for blood blister-like aneurysms (BBAs) of the internal carotid artery (ICA).

Objective To evaluate the safety and efficacy of EVT of BBAs in the ICA with a Willis covered stent.

Methods 20 consecutive patients (5 men and 15 women) with ruptured BBAs underwent EVT using a Willis covered stent in two institutions from March 2013 to March 2018. Clinical observations, angiographic characteristics, and procedural and follow-up outcomes were retrospectively evaluated.

Results 20 consecutive patients (5 men and 15 women) with ruptured BBAs underwent EVT using a Willis covered stent in two institutions from March 2013 to March 2018. Clinical observations, angiographic characteristics, and procedural and follow-up outcomes were retrospectively evaluated.

Conclusion Our initial results demonstrate that reconstructive EVT using a Willis covered stent provides a viable approach to treat ICA BBAs. However, an expanded clinical evaluation and larger cohort are needed to confirm the results.

Keywords: blood blister-like aneurysm; endovascular treatment; Willis covered stent.

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Conflict of interest: The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Funding: This work was financially supported by the National Natural Scientific Fund of China (grant number 81771951), and the Science and Technology Commission of Shanghai (grant number 14DZ1941204).

Ethical approval: The study was approved by the two institutional review boards.

Informed consent: All patients gave their written informed consent to participate.

Journal of Interventional Medicine 2018, Vol. 1, No. 3, pp. 157–163

http://www.j-i-m.net/
INTRODUCTION

Blood blister-like aneurysms (BBAs) are challenging entities, which arise from non-branching sites on the supraclinoid internal carotid artery (ICA), and are suspected to originate from dissections. They are particularly rare, representing approximately 0.9%–6.5% of all ICA aneurysms and 0.5–2% of all ruptured aneurysms (1,2). Morphologically, BBAs are small and hemispherical with an extremely fragile wall and bulge from non-branching sites on the ICA. BBAs are difficult to detect, dangerous to treat, prone to spontaneous re-rupture, and carry a high rate of morbidity and mortality (2-4).

Although a few recent systematic reviews attempted to clarify the optimal management of BBAs (1,5-8), their treatment in the ICA is challenging and no randomized controlled trials, whether microsurgery, or endovascular treatment (EVT), or a combination of the two, have been published. Microsurgery results in aneurysm obliteration rates superior to EVT techniques, but come with a higher risk of intraoperative bleeding. EVT seems to offer lower morbidity and mortality, but has an increased retreatment rate due to incomplete aneurysm obliteration and subsequent regrowth. In short, it may be said that the ideal methodology for the management of BBAs in the ICA has not yet been determined. Recently, multiple stent-assisted coil embolization and flow diverter devices (FDD) have been observed to be a safe and effective therapeutic modality for ICA BBAs (9-13).

In the English language literature, there have only been two studies that examined covered stents for BBAs in the ICA (2,14). The Willis covered stent (MicroPort, Shanghai, China) has become available for intracranial ICA pseudoaneurysms, aneurysms, recurrent aneurysms, and traumatic carotid cavernous fistulas (15-19). In this retrospective study, we present our initial observations of 20 ICA BBAs that have undergone EVT using the Willis covered stent.

MATERIAL AND METHODS

Patients

Between March 2013 and March 2018, 20 consecutive patients (5 men, 15 women; mean age, 50.6 years) with ruptured BBAs underwent EVT using a Willis covered stent in two institutions. The study was approved by the two institutional review boards, and all patients gave their written informed consent to participate. The decision to proceed with EVT using a Willis covered stent was determined by two experienced interventional neuroradiologists (W.W., with over 15 years of experience; JQ.W., with over twenty years of experience), based on patient status, location of the BBAs, composition of the related vessels, and collateral circulation. All patients and family members consented to the treatment. In the event of unsuccessful placement of a Willis covered stent, multiple stent-assisted coil embolization was used as an alternative treatment option.

Willis covered stent placement

Willis covered stent placement and periprocedure management have been described in detail previously (15-19). Briefly, the stent consists of three parts: a bare stent, expandable polytetrafluoroethylene (ePTFE) membrane, and balloon catheter. The stent has been approved by China’s Food and Drug Administration subject to the improvement of the stent and the accumulation of more clinical data.

Follow-up protocol

Follow-up protocols included clinical and angiographic follow-ups, head computed tomography angiography (CTA), and magnetic resonance angiography (MRA). DSA follow-up was recommended every year thereafter, and CTA follow-up was also acceptable as long as the result of the previous DSA follow-up was satisfactory. Follow-up studies were then conducted at 1 month, 3 months, 6–12 months, and 12 months post-procedure and annually thereafter. Clinical follow-ups included observing changes in the preliminary clinical presentation and adverse events related to the device, procedure, or other diseases.

Postoperative outcome evaluation

Data on the technical success, the initial and final angiographic results, mortality, morbidity, and final clinical outcomes were collected and estimated at the time of patient death, or at the end of follow-up. Technical success was defined as the covered stent being appropriately placed in the targeted artery without major complications. Major complications were defined as vascular rupture, endoleak and
thrombotic events, vascular occlusion, and minor complications such as vasospasm, etc. The angiographic results were categorized as complete occlusion and no endoleak, or incomplete occlusion with endoleak. Outcome data were classified into good (0–2) and disabled (3–5), according to the modified ranking scale (mRS) (20). Patients were clinically assessed before and after EVT and follow-up occurred every 3–6 months after discharge from the hospital. Each patient’s clinical status at the last clinical follow-up was defined as the final outcome. Patients who were not followed at our institution were interviewed by telephone.

RESULTS

| Patients No./Sex/Age (y) | Onset | H & H grade | Location | Size, mm (Neck & Height) | Stent Size, mm | Immediate angiographic result | Complication | Follow-up time | Final angiographic result | mRS |
|-------------------------|-------|-------------|----------|--------------------------|----------------|-------------------------------|--------------|----------------|--------------------------|-----|
| 1/F/39                  | SAH   | II          | R        | 2.5 x 3.0                | 3.5 x 100      | Complete occlusion            | No           | 36            | Complete occlusion        | 0   |
| 2/F/43                  | SAH   | III         | L        | 3.0 x 2.8                | 3.5 x 100      | Complete occlusion            | No           | 32            | Complete occlusion        | 0   |
| 3/F/50                  | SAH   | IV          | L        | 3.3 x 4.0                | 3.5 x 100      | Complete occlusion            | Spasm        | 26            | Complete occlusion        | 3   |
| 4/M/28                  | SAH   | II          | R        | 1.7 x 3.5                | 3.5 x 70       | Complete occlusion            | No           | 12            | Complete occlusion        | 0   |
| 5/F/44                  | SAH   | III         | L        | 4.0 x 3.3                | 3.5 x 100      | Complete occlusion            | No           | 12            | Complete occlusion        | 0   |
| 6/F/58                  | SAH   | III         | L        | 4.5 x 7.0                | 3.5 x 100      | Complete occlusion            | No           | 12            | Complete occlusion        | 1   |
| 7/F/60                  | SAH   | II          | L        | 1.4 x 2.2                | 3.5 x 100      | Complete occlusion            | No           | 16            | Complete occlusion        | 0   |
| 8/F/29                  | SAH   | IV          | L        | 3.5 x 4.2                | 3.5 x 100      | Complete occlusion            | No           | 7             | Complete occlusion        | 1   |
| 9/F/60                  | SAH   | III         | L        | 4.0 x 4.5                | 3.5 x 100      | Complete occlusion            | No           | 7             | Complete occlusion        | 1   |
| 10/F/67                 | SAH   | II          | L        | 5.0 x 6.4                | 3.5 x 100      | Incomplete occlusion          | Endoleak     | 3             | Complete occlusion        | 1   |
| 11/M/60                 | SAH   | III         | L        | 6.5 x 10.2               | 3.5 x 100      | Incomplete occlusion          | Endoleak     | 6             | Complete occlusion        | 1   |
| 12/M/62                 | SAH   | III         | L        | 2.0 x 8.5                | 3.5 x 70       | Complete occlusion            | No           | 6             | Complete occlusion        | 1   |
| 13/F/36                 | SAH   | III         | L        | 3.1 x 5.2                | 3.5 x 100      | Complete occlusion            | No           | 6             | Complete occlusion        | 1   |
| 14/M/32                 | SAH   | III         | L        | 3.0 x 2.2                | 3.5 x 70       | Incomplete occlusion          | Endoleak Rebleeding | -   | -             | 6   |
| 15/M/80                 | SAH   | III         | R        | 3.1 x 10.0               | 3.5 x 100      | Complete occlusion            | No           | 6             | Complete occlusion        | 3   |
| 16/F/52                 | SAH   | IV          | R        | 3.5 x 5.3                | 3.5 x 100      | Complete occlusion            | Spasm        | 6             | Complete occlusion        | 3   |
| 17/F/68                 | SAH   | IV          | L        | 4.0 x 4.6                | 3.5 x 100      | Incomplete occlusion          | Endoleak Severe Spasm | -   | -             | 6   |
| 18/F/40                 | SAH   | III         | L        | 4.0 x 6.0                | 3.5 x 100      | Complete occlusion            | Spasm        | 6             | Complete occlusion        | 0   |
| 19/F/53                 | SAH   | II          | L        | 2.8 x 4.0                | 3.5 x 100      | Complete occlusion            | No           | 6             | Complete occlusion        | 0   |

**Note:** Targeted or palliative treatment is targeted at an aneurysm, an arteriovenous fistula, the drainage of venous stenosis, or the reduction of the lesion size in the vascular malformations. BBAs = Blood blister-like aneurysms; F = female; M = male; mRS = modified ranking scale.
Figure 1 Case 7: A 60-year-old female suffering from SAH. (a) Brain CT showing SAH with H&H grade II. (b) Working projective angiogram shows a blister aneurysm located at the dorsal wall of C6 segment of ICA. (c) Under roadmap, a Willis covered stent (3.5 × 100 mm) was implanted at the target position guided by microwire. (d) Immediate angiogram post EVT showed the complete occlusion of the BBA and the reconstruction of the ICA. (e, f) The 3-month and 16-month angiographic follow-up showed the complete occlusion of the BBA and the patency of ICA.

BBA = blood blister-like aneurysm; EVT = endovascular treatment; ICA = internal carotid artery.

The initial angiographic results demonstrated that the complete occlusion rate was 79% (Figure 1). Endoleak and vasospasm were observed in 4 patients. All BBAs with endoleak were retreated with balloon reinflation to eliminate these endoleaks. Two BBAs with vasospasm were treated with transarterial Nimodipine injection. Although there was no rebleeding and no iatrogenic dissection, two patients experienced severe complications. One patient died early due to rebleeding the second day after EVT, while another patient died due to severe vasospasm on the seventh day.

Angiographic follow-up data were available for the remaining 17 patients, who showed complete occlusion (100%) for 3 to 36 months (median, 12.1 months). Mild asymptomatic in-stent stenosis was found in 2 patients during the follow-up period. No patients experienced rerupture, retreatment, or recurrence of the aneurysm. According to the mRS, good clinical outcomes were achieved in 14 patients (74%).

DISCUSSION

Despite the advances in endovascular and microsurgical fields, BBAs frequently present tremendous therapeutic challenge because of their unfavorable characteristics. Patients are typically afflicted with SAH, which is especially common in
younger female patients, as well as a right-sided ICA predominance, and hypertension. All patients in our study had ruptured ICA BBAs, were mostly female, and an average of 50.6 years of age, which is consistent with study populations that have been previously reported. However, a left-sided ICA predominance was rare (12). BBAs have typically been viewed as a subtype of dissecting aneurysms, classically with small, bleb-like and ill-defined neck lesions at non-branching sites of the dorsal wall of the ICA. Generally, an ICA BBA is diagnosed based on the following characteristics: (1) aneurysms located at nonbranching sites of the supraclinoid segment of ICA projecting anteriorly, (2) initially small (maximum diameter <10 mm), (3) SAH corresponding to the aneurysm, (4) a newly developing or rapidly growing lesion (<2 weeks) on repeated angiograms, and (5) irregular aneurysm or ICA wall (7,9,10).

Although numerous treatment techniques have been suggested, the optimal management of the lesions remains controversial. Some of the treatment methods that have been proposed include microsurgery including clipping techniques; titanium vascular miniclip ICA repair; vessel graft wrapping reinforced by clips; trapping; ICA occlusion; revascularization; and EVT. EVT can be performed with coils, coils and stent placement, multiple stents, stent placement alone, or internal coiling trapping. Recent systematic reviews and reports have attempted to clarify whether multiple stent-assisted coil embolization and FDD are a safe and effective modality in the treatment of ICA BBAs (9-13). Song et al. (9) reported the use of triple enterprise stents for 7 BBAs and double stents for 3. The angiographic follow-ups (mean, 12.2 months) revealed total occlusion in all 10 patients. Clinical data revealed 8 patients with mRS scores of 0–2 and 2 patients with mRS scores of 3–5. Zhu et al. (10) reported that using overlapped LVIS stents combined with coiling is a feasible and safe method to treat BBAs. Overall, the use of the LVIS stent was shown to be less likely to lead to recurrence and is approved as effective and safe in treating BBA compared with other stents. This may be due to the high degree of metal coverage, which provides better flow diversion. The greater the strut density and thickness, the more easy was the neointima formation promoted. Therefore, multiple stents provide not only immediate protection from hemorrhage by flow redirection with the disruption of intra-aneurysmal flow and dispersion of the inflow jet, but also provide angiographic improvement and long-term durability by promoting further stent endothelialization. Because of the purely endoluminal arterial reconstruction, FDD represents an appealing option for BBA repair. Yoon et al. (13) reported a total of 12 BBAs in the ICAs of 11 patients from 6 institutions in the United States. Nine (75%) were treated with a single Pipeline Embolization Device (PED); One was treated with 2 PEDs; One was treated with coils and 1 PED; and 1 was treated with coils and 2 PEDs. Three (27%) had major perioperative complications. Seven patients demonstrated complete obliteration. Early clinical outcomes were favorable in all 10 survivors. Linfante et al. (12) successfully treated 9 out of 10 patients (8 ICA and 2 MCA) with SAH secondary to BBAs with PEDs in two institutions. Placement of a single PED resulted in immediate occlusion or near occlusion of the BA in 9 out of 10 patients. In the surviving nine patients with favorable clinical outcomes there was complete occlusion of the BBAs on long-term follow-up angiography (mean 15 months). In 2018, Mokin et al. (11) reported the largest multicenter study using FDD for BBAs in the ICA at 14 institutions in the United States from 2011 to 2017. 43 patients with 45 BBAs of the ICA were treated with PED. Angiographic follow-up data were available for 30 patients. 87.5% of BBAs were eliminated, 9.4% showed reduced filling, and 3.1% showed persistent filling. Clinical follow-up data were available for 38 of the 43 patients. 68% of patients had a good clinical outcome at 3 months. There were 7 (16%) immediate procedural and 2 (5%) delayed complications, with 1 case of fatal delayed re-rupture after the initial treatment. Their data support the use of flow diversion technique as a safe and effective therapeutic modality. However, complications associated with BBAs using PED such as intraprocedural and delayed re-rupture of BBAs, and intra procedural thrombus, cannot be underestimated, and resulted in an in-hospital mortality rate of 19%, according to the largest report.

In the English language literature, there have only been two studies the reported the use of covered stents (2,14). In 2009, Lee et al. (2) reported 4 patients with BBAs treated with Jostent, 3 of whom showed permanent aneurysm occlusion. ICA rupture occurred in 1 patient. In 2017, Fang et al. (14) evaluated the safety and feasibility of the Willis covered stent in 13 patients with ruptured ICA BBAs. Immediate DSA showed complete aneurysm occlusion in 12/13 patients. Angiographic follow-up of 4–6 months
showed complete exclusions without aneurysm recurrences in all patients, indicating covered stents might offer a promising therapeutic option.

In the current retrospective study, we present initial data from 20 BBAs of the ICA that underwent EVT using the Willis covered stent. The technical success rate was 95%. Initial angiographic results demonstrated that the complete occlusion rate was 79%. The major complication rate was 21% and the mortality rate was 10.5%. Angiographic follow-up data (median, 12.1 months) were available for all surviving patients that showed complete occlusion (100%). Although mild in-stent stenosis was found in 3 patients during the follow-up period, there was no further treatment due to the absence of clinical symptoms. Clinical outcomes were favorable in 14 patients (74%). Our results are comparable to those reported in the literature, whether multiple stent-assisted coiling or FDD were used as the EVT technique for ICA BBAs.

All stents have the following common issues: (1) How should dual antiplatelet medication be managed when EVT of ruptured BBAs with different stents is in the acute stage? (2) How should intraoperative and postoperative thromboembolism, associated with stent-related thromboembolism, be managed before the complete occlusion of BBAs? (3) How should re-bleeding of BBAs after EVT be managed? (4) How should the stenosis of the stented parent artery during long-term follow-up be managed? To date, there are no unifying guidelines to help us in answering the above questions. Various neurointerventional radiologists have put forward different strategies. For instance, some proposed reduced perioperative antiplatelet protocols to prevent regrowth or rebleeding of the BBAs. There is some controversy regarding the proper method for the treatment of thromboembolism and rebleeding of ICA BBAs.

In our study, the Willis covered stent failed to implant in one case, with endoleak being a major complication, which may be related to the characteristics of the covered stent. We have reduced the cover rate of the metal and improved the attributes of the membrane of the covered stent, in order to reduce endoleak and failure rate.

INNOVATIONS AND LIMITATIONS

The results are encouraging, though some limitations are associated with. First, the number of cases is limited due to the rarity of the indicated cases; second, there is a possibility of retrospective design and patient-selection bias in the study; and third, the most important limitation is that the study is a non-randomized case series.

CONCLUSIONS

Our preliminary data show that reconstructive endovascular Willis covered stents appear to be a safe and effective treatment alternative for BBAs in the ICA and are associated with a good occlusion rate and favorable clinical outcomes. However, an expanded clinical evaluation and larger cohort are needed to confirm these results.

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