

Endovascular Treatment Using Multiple Stents for Symptomatic Intracranial Vertebral Artery Dissecting Aneurysm

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● ABSTRACT

Objective : Endovascular treatment with stent placement or stent-assisted coiling was recently introduced as an alternative to parent artery occlusion for treating intracranial vertebral artery dissections. However, complete aneurysm obliteration after single stent placement is often not accomplished. The aim of the study was to evaluate the safety and efficacy of placing multiple stents in intracranial vertebral dissecting aneurysms. **Methods :** We retrospectively reviewed 8 patients who underwent stent angioplasty with placing multiple stents for treating intracranial vertebral dissecting aneurysms. There were 5 male patients and 3 female patients with a mean age of 54 years (age range, 37-71 years). Three patients presented with subarachnoid hemorrhage (SAH), 1 presented with ischemic events and 4 presented with headache. Follow-up angiogram was performed in 8 patients within 6-12 months to determine whether or not the affected segment was occluded. **Results :** Eight patients with intracranial vertebral artery dissections were treated by placing multiple stents, 6 were treated by double stent placement and the others were treated by triple and quadruple stent placement. Although immediate complete occlusion was not shown in any cases, the follow-up angiogram revealed complete occlusion in 5 cases (62.5%) within 6-12 months. There were 2 complications (25%, temporary vasospasm during the procedure and acute thrombosis). On the modified Rankin scale applied during follow-up, 6 patients were assessed as functionally improved or of a stable clinical status, 1 patient expired due to cardiopulmonary complications, and 1 was lost to follow-up). **Conclusion :** Intracranial vertebral artery dissections can be treated by the endovascular method with placing multiple stents and the morbidity is acceptable. However, further study is needed since the treatment of patients presenting with SAH using multiple stent placement can be controversial. (*Kor J Cerebrovascular Surgery* 11(4):184-92, 2009)

KEY WORDS : Vertebral artery · Dissecting aneurysm · Stent · Endovascular treatment.

Introduction

Intracranial vertebral artery (VA) dissecting aneurysms represent approximately 3% of all intracranial aneurysms,²⁰⁾

and subarachnoid hemorrhage (SAH) from dissecting VA aneurysms is a well-known phenomenon.⁷⁾ The prompt recognition and treatment of these aneurysms is of utmost importance due to their high rate of rebleeding in the unsecured state.⁴⁾¹⁶⁾¹⁸⁾ The incidence of intracranial VA dissection is relatively low, but it has been more frequently identified due to the introduction of advanced diagnostic imaging modalities including magnetic resonance (MR) angiography and multidetector computed tomography (CT) angiography. In this report, we describe our clinical experience with VA dissections which were treated by stent angioplasty using double or multiple stents.

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Patients and Methods

Patients

A retrospective review of intracranial VA dissections managed by endovascular stent placement at our institution was performed. During the period between 2000 and 2007, 28 consecutive VA dissecting aneurysms were treated with surgical method or/and endovascular method at our institution. Among them, 20 patients were excluded including those treated with other modalities such as surgery or endovascular occlusion. The remaining 8 patients underwent endovascular treatment using multiple stent placement. Demographic and clinical presentation data of the patients are shown in Table 1. At presentation, 3 patients had SAH, 1 had ischemic events which were repeatedly presented despite antiplatelet therapy, and 4 had severe sudden-onset suboccipital headache. In all cases, it was essential to preserve the parent artery or posterior inferior cerebellar artery (PICA) due to its dominance. We retrospectively evaluated the treatment success rates, complications encountered, and patient outcomes.

Procedures

Before stent angioplasty, informed consent was obtained from patients or their relatives. The patients scheduled for elective procedures received aspirin (100 mg) and clopidogrel (75 mg) for 3 days before the stent procedure. For the patients with SAH, antiplatelet therapy was done with loading dose of clopidogrel (300 mg) through the Levin tube immediately after the procedure since they required emergency procedure.

All the patients underwent procedures under general anesthesia. After femoral puncture with standard Seldinger, 6-F introducer sheath was placed in the right femoral artery. After placement of 6-F guiding catheter (Envoy Max ID Multipurpose 90cm; Codmann, Johnson and Johnson Medical, Miami, FL, USA) in the proximal VA, full systemic heparinization was achieved by administering 2000~4000 IU bolus followed by hourly boluses of 1000 IU and monitoring of the activated clotting time. Stents were positioned across diseased segments to have an overlap on each side of the orifice of the dissection. We used balloon-expandable stents currently applied in interventional

cardiology such as S670 (Medtronic AVE, Santa Rosa, CA), Driver (Medtronic AVE) and Flexmaster (Jomed International, Helsingborg, Sweden) to achieve appropriate luminal diameter and sufficiently narrow strut size to occlude dissecting aneurysm. All patients underwent double or multiple overlapping stents placement in order to minimize the stent porosity. After the interventional procedure, the catheter was removed and the sheath was left in the groin. The patient was moved to the neurosurgical intensive care unit for patient monitoring and received heparin 1,000 IU/hour for the next 24 hours. Heparinization was discontinued after 24 hours post-treatment but not reversed. After the procedure, aspirin and clopidogrel were subsequently started. Aspirin 100 mg once daily was continued as permanent medication. Additionally, 75 mg clopidogrel was given once daily for 12 months.

Evaluations and Follow-Up

Digital subtraction angiography (DSA) was performed on all patients after the procedure. Angiography was assessed for lesion size, shape, location and relationship to adjacent arterial branches- PICA, anterior inferior cerebellar artery (AICA) and basilar artery. The angiographic features were classified as 1) Pearl and string; corresponding to a fusiform dilatation associated with proximal or distal narrowing, 2) String; corresponding to an isolated irregular narrowing, 3) Fusiform dilatation, and 4) Double lumen.

The grades of aneurysmal occlusion subsequent to multiple stents deployment were divided as complete (100% occluded), nearly complete ($\geq 95\%$ occluded), and incomplete ($< 95\%$ occluded). Immediate post-treatment angiogram was performed in all cases and follow-up angiographies were performed at 6~12 months in six patients. Further examination was obtained yearly if needed.

The safety of this procedure was evaluated by the incidence of any procedure-related complications, including rupture of the aneurysm or dissection of parent vessel, vasospasm and thromboembolic or hemorrhagic event during the procedure and within 30 days after the procedure. Follow-up data were collected by phone interview or from the most recent office note, and modified Rankin scale (mRS) was assigned. Overall outcomes were defined as excellent, mRS 0-1; good, mRS 2; poor, mRS 3-5; or death, mRS 6.

Table 1. Summary of the clinical characteristics in 8 patients with vertebralis dissections treated with double or multiple stents.

Patient No.	Age/Sex	Clinical presentations	MRS on admission	Angiographic Sign	Location
1	54/M	Infaction, cerebellar	1	Pearl and string sign	Left VA across PICA
2	37/M	Headache	1	Pearl and string sign	Left VA distal to PICA
3	48/F	Headache	1	Fusiform dilation	Left VA distal to PICA
4	53/M	Subarachnoid hemorrhage	3	Pearl and string sign	Left VA across PICA
5	63/F	Headache	1	Fusiform dilation	Right VA distal to PICA
6	54/F	Headache	1	Fusiform dilation	Right VA across PICA
7	49/M	Subarachnoid hemorrhage	2	Pearl and string sign	Right VA across PICA
8	71/M	Subarachnoid hemorrhage	3	Fusiform dilation	Right VA across PICA

MRS : modified Rankin Scale, VA: vertebral artery, PICA : posterior inferior cerebellar artery

Table 2. Summary of treatment options, complication related to treatment, and angiographic and clinical outcomes.

Patient No.	No. of stents	Stent type and size (mm)	Complications	Immediate AO	Follow-up AO at 6-12 Months	Follow-up MRS
1	2	AVE S670 3.0x 9 AVE S670 3.0x12	None	Incomplete	Complete	1
2	2	AVE S670 3.0x12 AVE S670 3.5x12	None	Incomplete	Complete	0
3	2	AVE Microdrive 3.0x12 AVE Microdrive 3.5x12	None	Incomplete	Complete	1
4	2	JOSTENT Flexmaster 2.75x19 AVE Microdrive 2.75x24	Temporary vasospasm	Incomplete	Complete	1
5	2	MEDTRONIC Driver 4x24 GUIDANT Zeta 4x33	None	Incomplete	ND	ND
6	3	JOSTENT Flexmaster 2.75x26 JOSTENT Flexmaster 2.75x23 MEDTRONIC Driver 3x24	None	Incomplete	Incomplete (stable)	0
7	4	JOSTENT Flexmaster 3 x19 JOSTENT Flexmaster 3.5x19 MEDTRONIC Driver 3x30 GUIDANT Zeta 3x38	None	Incomplete	Complete	1
8	2	BS Neuroform 4.5x20 JOSTENT Flexmaster 3.5x16	Acute thrombosis	Incomplete	ND	6

AO : angiographic outcome, MRS : modified Rankin Scale, AVE : Arterial Vascular Engineering, BS : Boston Scientific, ND : not done

Results

Stent type and size, complication related to treatment, and angiographic and clinical outcomes were summarized in Table 2. There were 5 men and 3 women in the study group, with age ranging from 37 to 71 years (mean age, 54 years). The follow-up period ranged from 18 to 92 months, with median period of 37 months.

Stent placements were technically successful preserving parent artery and PICA in all cases. We performed double stent replacement in 6 patients, triple stent replacement in 1 patient, and quadruple stent replacement in 1 patient. We decided the method that could be applicable to each case by considering the clinical manifestations, size, location and relationship with adjacent arterial branches. Immediate angiographic findings were incomplete occlusion in all cases

(8 patients). Follow-up angiogram showed complete occlusion in 5 cases within 6~12 months and incomplete occlusion in one patient (all aneurysms were stable), and there was no evidence of in-stent-thrombosis or stenosis.

Despite the risk of rebleeding, 3 patients with subarachnoid hemorrhage were treated only with multiple stenting to preserve the parent artery or posterior inferior cerebellar artery (PICA) due to its dominancy. Regardless of initial incomplete occlusion, no recurrent hemorrhage occurred during the follow-up period. Although various degrees of contrast filling of the aneurysms were visible at the end of the procedure, follow-up angiogram clearly revealed beginning thrombosis, which continued and resulted in a substantial reduction of the aneurysmal size, that was observed after 4 weeks. Six month control angiogram revealed total occlusion of the aneurysms except one case (case No. 6). In 4 patients with headache, 3 patients

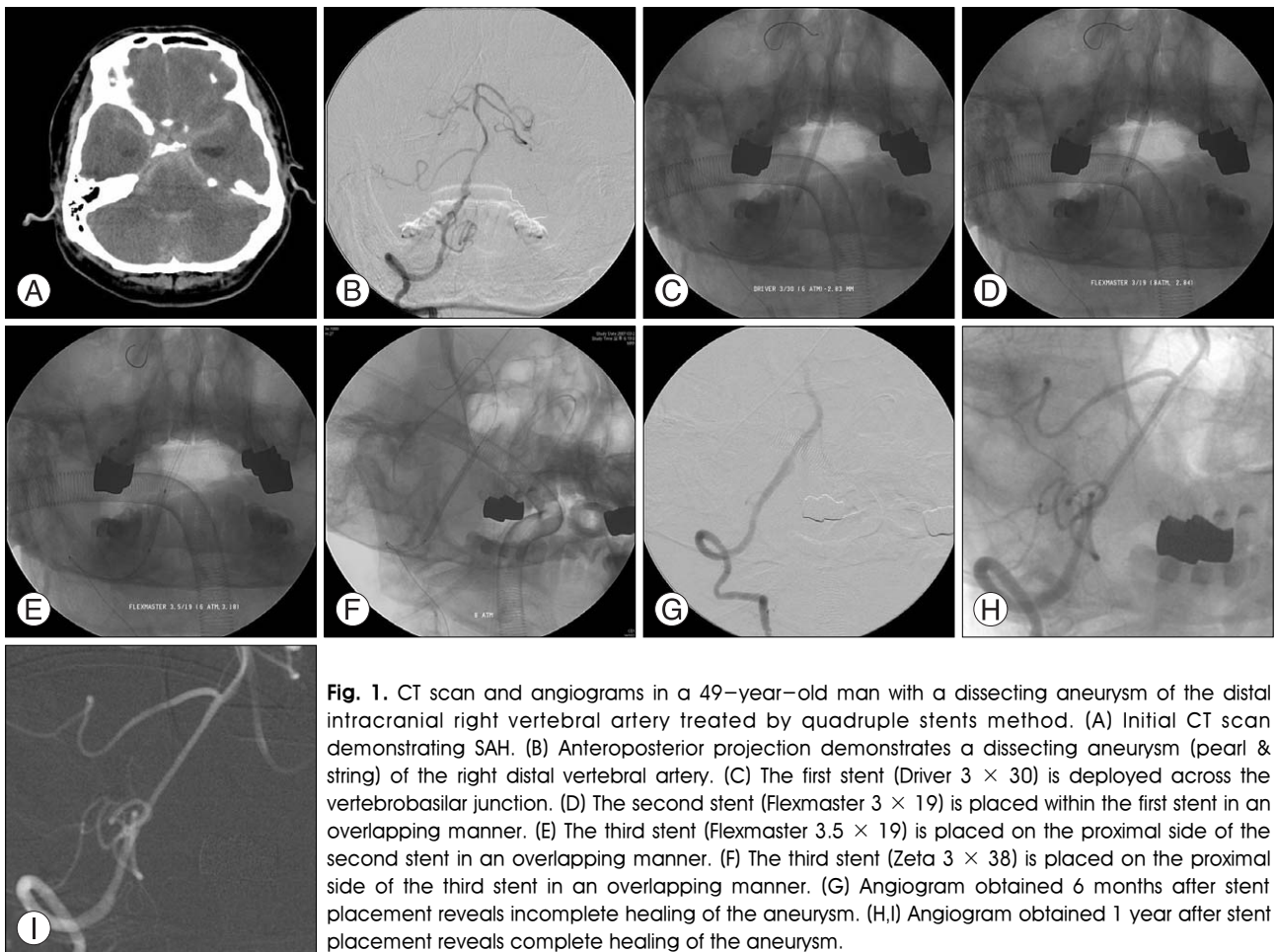


Fig. 1. CT scan and angiograms in a 49-year-old man with a dissecting aneurysm of the distal intracranial right vertebral artery treated by quadruple stents method. (A) Initial CT scan demonstrating SAH. (B) Anteroposterior projection demonstrates a dissecting aneurysm (pearl & string) of the right distal vertebral artery. (C) The first stent (Driver 3 × 30) is deployed across the vertebrobasilar junction. (D) The second stent (Flexmaster 3 × 19) is placed within the first stent in an overlapping manner. (E) The third stent (Flexmaster 3.5 × 19) is placed on the proximal side of the second stent in an overlapping manner. (F) The fourth stent (Zeta 3 × 38) is placed on the proximal side of the third stent in an overlapping manner. (G) Angiogram obtained 6 months after stent placement reveals incomplete healing of the aneurysm. (H,I) Angiogram obtained 1 year after stent placement reveals complete healing of the aneurysm.

(75%) were improved and 1 patient was not evaluated due to follow-up loss. In 1 patient with ischemic stroke, there was no instance of new ischemic attack, new neurologic deficit, and new minor or major stroke after the procedure.

There were 2 complications(25%). One patient (case No. 4) had temporary vasospasm during the procedure, which resulted in underestimation of the dissection area and required a longer second stent positioning within the first. Another patient (case No. 8) had acute thrombosis. The patient initially presented with SAH (Hunt-Hess grade III, Fisher grade III) due to ruptured right VA dissecting aneurysm, which was treated using two stents [Neuroform (4.5 × 20) Flexmaster (3.5 × 16)]. Immediate post-treatment angiogram showed acute thrombosis of stent placement site. After intra-arterial injection of urokinase 100,000 U and Tirofiban 2.5 mg, thrombosis was resolved and stent lumen was intact.

On the modified Rankin scale applied in follow-up, 6 patients were assessed as functionally improved or stable

clinical status except 2 patients. One patient was expired due to cardiopulmonary complications 1 month after the procedure, and another patient could not be assessed due to loss to follow-up.

Discussion

Endovascular treatment is now considered as one of the efficient treatment options in symptomatic vertebral dissecting aneurysms.¹⁷⁾²¹⁾ Endovascular treatment of dissecting aneurysms of the intracranial VA artery can be divided as being deconstructive and reconstructive.¹⁾ Deconstructive endovascular techniques include proximal occlusion of the parent artery and occlusion of the dissected segment of the vessel with coils and/or balloons. Deconstructive procedures alone can be sufficient if important branch vessels are not incorporated in the segment of the vessel to be occluded, and collateral blood flow to the remainder of the posterior circulation is adequate. However,

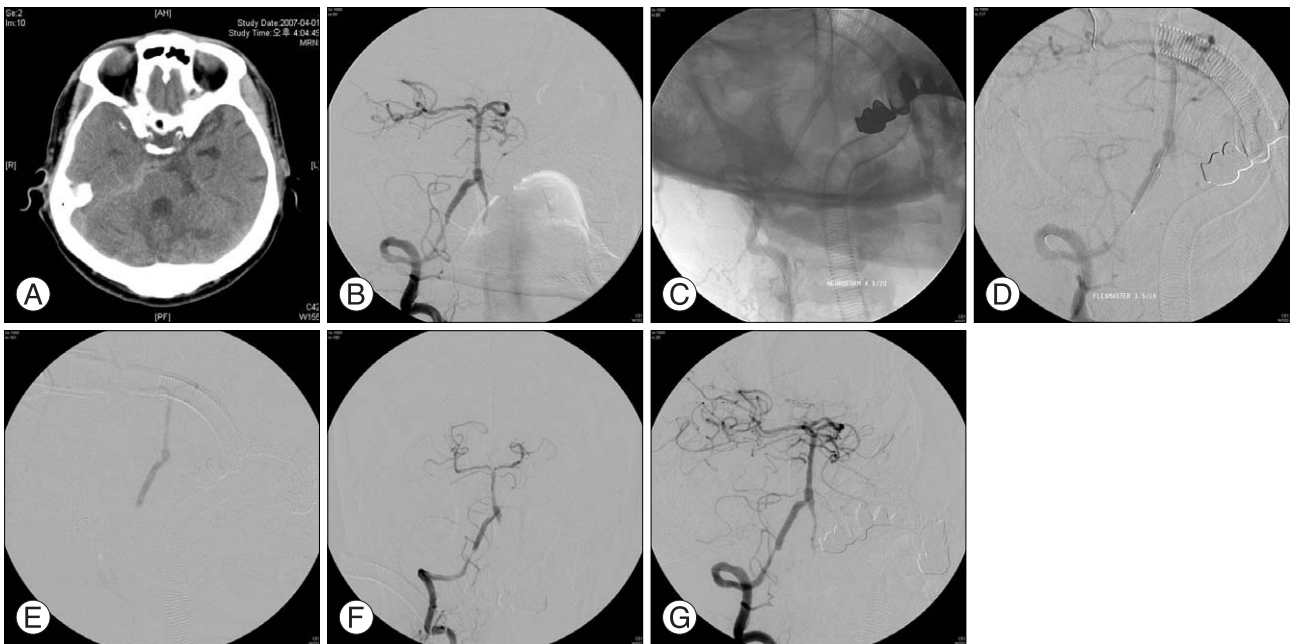


Fig. 2. CT scan and angiograms in a 71-year-old man with a dissecting aneurysm of the distal intracranial right vertebral artery treated by double stents method. (A) Initial CT scan demonstrating SAH. (B) Anteroposterior projection shows a fusiform dilatation of the right distal vertebral artery and vertebrobasilar junction with severe stenosis on the free posterior inferior cerebellar artery segment. (C) The first stent (Neuroform 4.5 × 20) is deployed across the vertebrobasilar junction. (D) The second stent (Flexmaster 3.5 × 16) is placed on the proximal side of the first stent in an overlapping manner. (E) Acute thrombosis is developed at the second stent deploying site. (F) Angiogram obtained immediately after the intraarterial infusion of urokinase 100,000 U and Tirofiban 2.5 mg demonstrates complete recanalization of the right vertebral artery. (G) Angiogram obtained 8 days after stent placement reveals stable incomplete healing of the aneurysm.

the dissected segment cannot be occluded in patients with involvement of PICA and/or a dominant feeding pedicle to the anterior spinal artery in the dissected segment. Reconstructive endovascular treatments that consist of stent placement including multiple stent method and stent-assisted coil embolization are considered, in theory, as more reasonable treatment options than destructive procedures because we cannot predict the destiny of collateral vessels.¹⁾

VA dissecting aneurysms may present with varied symptoms and signs, including headache, neck pain, transient ischemic attacks, cerebellar and brain stem infarcts, and subarachnoid hemorrhage. Ischemic symptoms occur in a large proportion of patients with VA dissections. Approximately 10% of VA dissections extend intracranially and can present with SAH.¹⁹⁾ In cases presenting with SAH, the surgical or endovascular treatment was considered helpful due to the high rebleeding rate during the acute stage.⁴⁾¹⁵⁾ High mortality rates have been reported in patients presented with SAH. Reported rebleeding rates in these patients have ranged from 24% to 71%.⁴⁾¹⁶⁾ Aggressive treatments including internal trapping have been implemented due to their tendency for early rebleeding and a fatal natural course.¹⁶⁾ Early intervention to prevent rebleeding may improve overall outcome of patients. However, it is not always possible to accomplish immediate obliteration of dissecting aneurysm when it involves the dominant PICA or when the contralateral VA is not functionally competent.¹¹⁾ Some authors advocate using double stents as overlapping or stent-within-a stent technique.⁶⁾¹⁴⁾

Non-hemorrhagic type of VA dissections are considered to be benign in nature, so the therapeutic management of non-hemorrhagic type of VA dissections remains controversial.⁷⁾¹⁷⁾ But, the patients who have persistent symptoms of ischemia despite adequate anticoagulation or dangerous lesions liable to rupture are generally considered to be the indication of the surgical and endovascular treatment. In this analysis, we even treated patients with severe sudden-onset suboccipital headache using multiple stents due to liability to rupture.

Multiple stent placement may be a relatively simple technique to more effectively change intra-aneurysmal flow and achieve subsequent thrombosis. The influence of stent porosity on changing the local hemodynamics between the aneurysm and the parent vessel was shown in the experimental studies.¹²⁾²⁴⁾ Findings of experimental studies have shown that a metallic stent, bridging the aneurysmal neck, may alter the flow pattern within the aneurysm, promoting thrombus formation and aneurysmal occlusion.⁶⁾²⁴⁾ Stent placement affects regionally on the arterial wall, and it leads to neo-intimal formation through transient and regional proliferation and migration of smooth muscle cells mixed with various degrees of connective tissue matrix.⁵⁾ In addition, flow remodeling through the stent may promote intra-aneurysmal thrombosis through immediate intimal repair or reduced porosity, decreasing intra-aneurysmal inflow and flow velocity, as demonstrated in aneurysm flow models and animal experiments.¹²⁾²⁴⁾ Double stent method can reduce the porosity and permeability of stent and alter inflow into dissected zone or aneurysmal sac.¹²⁾ This method can

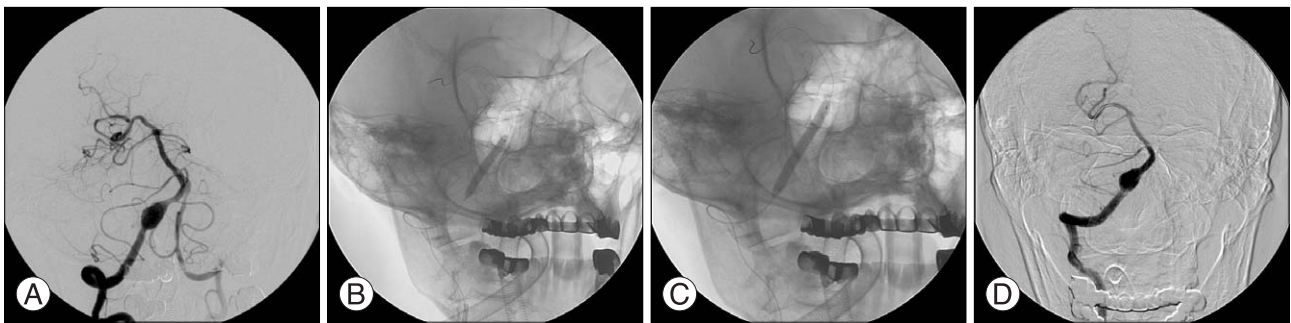


Fig. 3. Angiograms in a 63-year-old woman with a dissecting aneurysm of the distal intracranial right vertebral artery treated by double stents method. (A) Anteroposterior projection demonstrates a fusiform dilatation of the right distal vertebral artery (B) The first stent (Driver 4 × 24) is deployed across the dissecting aneurysm. (C) The second stent (Zeta 4 × 33) is placed in an overlapping manner. (D) Angiogram obtained immediately after stent placement reveals incomplete healing of the aneurysm.

further alter the inflow within the aneurysm, promoting stasis and immediate thrombosis and safely allowing subsequent neointimal endothelial formation.¹⁵⁾ Dissecting aneurysms might be good candidates for multiple stent method, because a stent might effectively tack down the torn vessel, resulting in occlusion of aneurysm and no regrowth.⁶⁾⁸⁾

There have been several reports for treatment of the dissecting aneurysms with stent placement.¹⁾²⁾³⁾⁶⁾⁹⁾¹⁰⁾¹¹⁾¹⁵⁾¹⁹⁾²²⁾²³⁾ Placement of a porous stent across the inflow zone alters the dynamics of blood flow, often reducing flow into the aneurysm. However, the single stent placement showed complete occlusion of the aneurysm in a few cases. Lanzino et al. reported 4 patients were treated with single stent placement. In these patients, no one showed complete occlusion of the aneurysm during 3 months follow-up periods.¹¹⁾ Ahn et al. reported 5 patients were treated with single stent placement alone. None of them showed complete occlusion of the aneurysm on post-treatment and follow-up angiograms.²⁾ Mehta et al. reported 1 patient was treated with single stent placement. The case has shown

incomplete occlusion of the aneurysm during 2 months follow-up, so it was retreated with another stent placement.¹⁵⁾ In our study, 8 patients were treated with double or multiple stents placement; all cases showed incomplete obliteration in immediate post-treatment angiogram, but follow-up angiogram showed 5 cases (62.5 %) of complete obliteration of vertebral artery dissecting aneurysms within 6~12 months. Regrowth of the vertebral artery dissecting aneurysm after single stent replacement was also reported in several cases. Shin et al. reported 1 patient was treated with single stent placement.²¹⁾ The case showed regrowth of the vertebral artery dissecting aneurysm 12 months after the treatment. Ahn et al. reported 1 case of regrowth of the vertebral artery dissecting aneurysm after single stent placement. The patient underwent proximal occlusion with coils after balloon occlusion test.¹⁾ In our study, 1 case showed regrowth of the dissecting aneurysm one year after the treatment although it was treated with double stent placement. One more stent was deployed in an overlapping manner, so finally triple stent placement was done. The Angiogram obtained 6 months after the additional stent

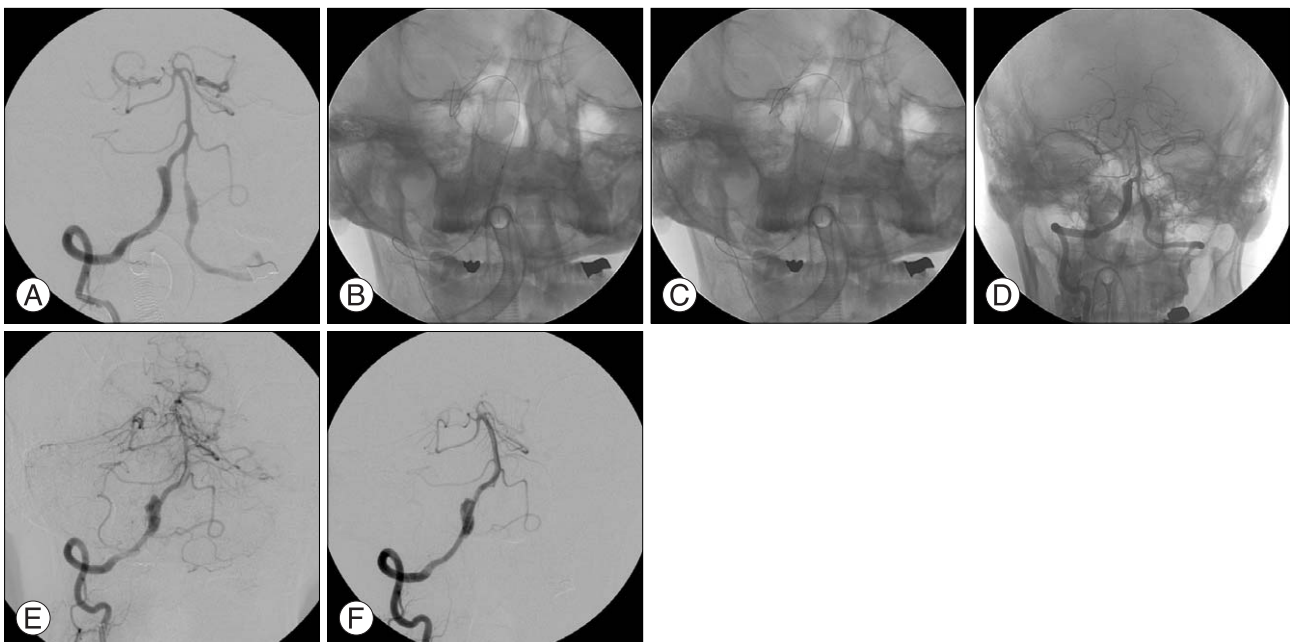


Fig. 4. Angiograms in a 54-year-old woman with a dissecting aneurysm of the distal intracranial right vertebral artery treated by triple stents method. (A) Anteroposterior projection demonstrates a fusiform dilatation of the right distal vertebral artery (B) The first stent (Flexmaster 2.75 × 26) is deployed across the dissecting aneurysm. (C) The second stent (Flexmaster 2.75 × 23) is placed on the proximal side of the first stent in an overlapping manner. (D) Angiogram obtained 1 year after the stent placement reveals regrowing of the aneurysm. (E) The third stent (Driver 3 × 24) is placed in an overlapping manner. (F) Angiogram obtained 6 months after the third stent placement reveals stable incomplete healing of the aneurysm.

placement reveals stable incomplete healing of the aneurysm.

Reducing the porosity and permeability of stent by multiple stent placement technique may contribute to the complete obliteration of the dissecting aneurysm and the prevention of the regrowth of the aneurysm. There are some limitations in treatment for dissecting aneurysm with double or multiple stents method. Stent placement across the aneurysm can alter the inflow within the aneurysm, promoting intra-aneurysmal stasis. However, immediate postprocedural angiograms after double or multiple stent placement did not reveal complete obliteration of the dissecting aneurysm in many reports.²⁾⁶⁾¹⁵⁾ Theoretically, stent-grafts or pipeline stents are the ideal implants for covering dissecting aneurysms, but at present, they are still in technical development. They also have several disadvantages, such as increased thrombogenicity and inflammatory reaction with subsequent intimal hyperplasia. Of a particular importance in the intracranial circulation is that they are less flexible than are bare stents.⁶⁾¹⁴⁾ The limited flexibility is a prominent drawback of the stent-grafts.¹⁴⁾

In our study, there was also no case that showed complete obliteration of dissecting aneurysm immediately after the multiple stent placement. Furthermore, it took a long time for the aneurysm to be completely obliterated. Although a sufficient hemodynamic protection is at least anticipated, it may not completely prevent the ruptured dissecting aneurysm from rebleeding. However, by reducing the porosity and permeability of the stent, multiple stent placement are considered more effective for the complete occlusion of dissecting aneurysms and the prevention of the regrowth of dissecting aneurysm than single stent placement.

Conclusion

Intracranial vertebral artery dissections can be treated by endovascular method using multiple stent placement with acceptable morbidity. Reconstructive treatment using multiple stents may be an alternative for VA dissection aneurysm with involvement of major artery. However, further study is needed since treatment of patients presenting with SAH using multiple stent placement can be controversial.

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