

## Clinical Article

# Multi-Modality Treatment for Intracranial Arteriovenous Malformation Associated with Arterial Aneurysm

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**Objective :** Intracranial arteriovenous malformation (AVM) associated with aneurysm has been infrequently encountered and the treatment for this malady is challenging. We report here on our clinical experience with AVMs associated with arterial aneurysms that were managed by multimodality treatments, including clipping of the aneurysm, microsurgery, Gamma-knife radiosurgery (GKS) and Guglielmi detachable coil (GDC) embolization.

**Methods :** We reviewed the treatment plans, radiological findings and clinical courses of 21 patients who were treated with GKS for AVM associated with aneurysm.

**Results :** Twenty-seven aneurysms in 21 patients with AVMs were enrolled in this study. Hemorrhage was the most frequent presenting symptom (17 patients : 80.9%). Bleeding was caused by an AVM nidus in 11 cases, aneurysm rupture in 5 and an undetermined origin in 1. Five patients were treated for associated aneurysm with clipping followed by GKS for the AVM and 11 patients were treated with GDC embolization combined with GKS for an AVM. Although 11 associated aneurysms remained untreated after GKS, none of them ruptured and 4 aneurysms regressed during the follow up period. Two aneurysms increased in size despite the disappearance of the AVM nidus after GKS and then these aneurysms were treated with GDC embolization.

**Conclusion :** If combined treatment using microsurgery, GKS and endovascular treatment can be adequately used for these patients, a better prognosis can be obtained. In particular, GKS and GDC embolization are considered to have significant roles to minimize neurologic injury.

**KEY WORDS :** Arteriovenous malformation · Aneurysm · Radiosurgery · Endovascular treatment · GDC embolization.

## INTRODUCTION

The coexistence of intracranial aneurysms and arteriovenous malformations (AVMs) are rare complex vascular lesions and intracranial aneurysms coexist with approximately 15% of all AVMs<sup>1,3,31</sup>. The risk of hemorrhage in patients with AVMs and associated aneurysms was reported to be 7% per year, which is higher than the 3% risk of hemorrhage for patients with only AVMs<sup>3</sup>. Moreover, the risk for hemorrhage in patients with AVMs with intracranial aneurysms has been reported to be 9.8%-per-year<sup>31</sup>.

Management of a patient suffering AVMs and associated aneurysms is challenging because of the complex AVM-aneurysm hemodynamic relationship. It has been recom-

mended that associated aneurysms should be treated initially or simultaneously with the AVMs<sup>1,4,35</sup>. Although one stage operation for treating both lesions is ideal and the recently advanced microsurgical techniques facilitate successful surgery, the complications related to this surgery can be fatal. The recent consensus for the management of complex cerebrovascular lesions emphasizes that safety is more important than efficacy when surgery is used to treat these combined lesions. Following the recent developments, AVMs and aneurysms have been successfully treated not only by craniotomy, but also by non-surgical treatment modalities including radiosurgery and embolization with Guglielmi detachable coil (GDC). Therefore, a proper combination of multiple treatment modalities in accordance with the clinical presentation and the angio-architectural relationship is helpful to achieve reliable clinical outcomes. This report represents the authors' experiences with 21 patients who had AVMs and associated arterial aneurysms, and we suggest that radiosurgery and GDC embolization can be an effective option to minimize the complications.

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## MATERIALS AND METHODS

The authors retrospectively reviewed the medical records and the angiographic findings of 21 patients who were diagnosed with AVMs and accompanying intracranial arterial aneurysms between March 2001 and December 2005. The patients who presented with AVM associated with pseudoaneurysms or venous aneurysms were excluded from this analysis. All the patients were treated by Gamma-knife radiosurgery (GKS) for their AVM, and the accompanying aneurysms were managed by multi-disciplinary treatment methods.

### Radiosurgery for an AVM

After attaching a Leksell stereotactic instrument to a skull, cerebral angiography and magnetic resonance imaging were done in all cases. A GKS (Leksell Gamma Knife Type 2,3004B) was used for the treatment of the nidus of the AVM. The mean volume of the nidus was 4,029 mm<sup>3</sup>

(165-25,308 mm<sup>3</sup>) and the mean marginal radiation dose was 22.6 Gy (16-25 Gy) and the mean maximum dose was 37.1 Gy (28.6-41.7 Gy). In case of a feeding pedicle aneurysm, we didn't include this type of aneurysm in the radiosurgical target. Coexistence of arterial aneurysms did not influence the radiosurgical planning of AVMs. So, radiosurgery for AVMs with arterial aneurysms was identical to AVMs without aneurysms.

### Classification of the associated arterial aneurysms

Because of the complex aneurysm-AVM blood flow relationship, classifying the associated aneurysms according to the angio-architectural relation between the feeding artery to the AVMs and the aneurysm location is mandatory for planning treatment. We defined the type of the associated arterial aneurysms according to the location of the artery harboring the aneurysm relative to the feeding artery of the AVM according to the categories established by Perata et al.<sup>27)</sup> (Table 1). The type of aneurysm was

**Table 1.** Angiographic findings and treatment of aneurysm

Case No.	Age / Sex	AVM				Aneurysm			Neurological outcome (mRS <sup>†</sup> )
		Location	Nidus volume (mm <sup>3</sup> )	S-M grade	Feeding artery	Location	Classification	Treatment	
1	32/M	Parietal <sup>‡</sup>	4,320	3	PCA	PcoA	Proximal	Clip	2
2	51/M	Temporal <sup>‡</sup>	4,189	2	AchoA	ACA	Remote	Clip	3
3	60/M	Frontoparietal <sup>‡</sup>	6,776	3	MCA	PcoA	Proximal	Observation	2
4*	49/M	Corpus callosum <sup>‡</sup>	3,240	1	ACA, SCA	AcoA/SCA	Proximal/Feeding pedicle	Clip GDC	2
5	56/M	Parietal <sup>‡</sup>	3,249	2	MCA	AcoA	Proximal	Clip	2
6	39/M	Occipital	165	1	MCA	AcoA	Proximal	GDC	1
7	46/M	Frontoparietal <sup>‡</sup>	7,600	3	MCA, ACA	MCA	Feeding pedicle	GDC	0
8	54/M	Cerebellum	400	1	AICA	AICA	Feeding pedicle	Observation	0
9*	70/F	Frontal <sup>‡</sup>	3,000	4	MCA	ICA/MCA	Proximal/Feeding pedicle	GDC/Observation	3
10	43/M	Cerebellum	1,500	1	PCA, SCA	SCA	Feeding pedicle	GDC	1
11*	42/M	Corpus callosum <sup>‡</sup>	2,300	4	ACA, AchoA	ACA/MCA	Feeding pedicle/Remote	GDC/Clip	2
12	57/M	Corpus callosum <sup>‡</sup>	2,600	3	ACA, PCA	AcoA	Proximal	Observation	3
13	48/F	Frontal	1,300	2	ACA, MCA	AcoA	Proximal	GDC	0
14	24/M	Frontotemporal <sup>‡</sup>	1,000	3	MCA	MCA	Feeding pedicle	GDC	2
15	61/F	Frontoparietal <sup>‡</sup>	4,500	3	ACA	ACA	Feeding pedicle	Observation	2
16	21/F	Corpus callosum <sup>‡</sup>	11,000	4	ACA, PCA	ACA	Feeding pedicle	Observation	1
17*	58/M	Cerebellum	25,308	2	PCA	Basilar top/PCA	Proximal/Feeding pedicle	GDC/Observation	1
18	43/M	Cerebellum	300	1	PICA	PICA	Feeding pedicle	GDC	1
19	29/F	Frontal	1,014	1	ACA	ACA	Feeding pedicle	GDC	1
20	71/M	Thalamus <sup>‡</sup>	450	2	PCA	ICA	Remote	Observation	4
21*	32/M	Temporal	400	2	PCA	PcoA (2)/ PTA (1)	Proximal (2)/ Feeding pedicle (1)	GDC (2)/ Observation (1)	2

\*Case No. 4, 9, 11, 17, 21 patients had multiple arterial aneurysms, <sup>†</sup>The modified Rankin Scale (mRS) is a measure of function, grades are defined as follows: 0-no symptoms; 1-no significant disability despite symptoms, able to carry out all usual duties and activities; 2-slight disability, unable to carry out all previous activities but able to look after own affairs without assistance; 3-moderate disability, requiring some help but able to walk without assistance; 4-moderately severe disability, unable to walk without assistance and unable to attend to own bodily needs without assistance; 5-severe disability, bedridden, incontinent, and requiring constant nursing care and attention; 6 represents death, <sup>‡</sup>AVMs located on eloquent area (total 13). ACA: anterior cerebral artery, AcoA: anterior communicating artery, AchoA: anterior choroidal artery, AICA: anterior inferior cerebellar artery, GDC: intra-aneurysmal embolization with Guglielmi detachable coil, ICA: internal cerebral artery, MCA: middle cerebral artery, PCA: posterior cerebral artery, PcoA: posterior communicating artery, PICA: posterior inferior cerebellar artery, PTA: posterior temporal artery, SCA: superior cerebellar artery, S-M Grade: Spetzler-Martin Grade

defined as “a feeding pedicle” if the aneurysm was located on a direct feeding vessel to the AVM, as “proximal in location” if it had arisen from the circle of Willis origin of an artery supplying to the AVM and as “remote” if the artery harboring the aneurysm was not involved in the AVM supply.

The majority of associated aneurysms in this analysis were incidentally recognized during angiography. Yet, 4 patients presented with spontaneous subarachnoid hemorrhage or a ruptured aneurysmal sac that was identified on the operative field. For these patients, the initial treatment was concentrated on the symptomatic aneurysms. We discriminated between the ruptured and unruptured aneurysms among multiple aneurysms in the cases of aneurysmal rupture at the time of the initial clinical presentation based on the location of the hematoma as related to the conventional angiographic findings and the operative findings.

**Follow up**

Follow-up lasted for a mean of 48 months (range : 24-84 months). All patients were monitored by means of conventional angiography at 24-36 months after the last treatment to identify the obliteration of the nidus or the size change of the associated aneurysms. Neurological outcomes were based on the modified Rankin Scale (mRS) at the last follow up date.

**RESULTS**

**Clinical presentation and the associated arterial aneurysms**

The hemorrhage was the most frequently presented finding (17 of the 21 patients) treated with GKS (Table 2). The bleeding focus was determined by the location and distribution of the hematoma on the computed tomography (CT) and this was correlated with the angiography and the operative findings. Bleeding was caused by an AVM nidus in 11 cases, by aneurysm rupture in 5 cases and by an undetermined origin in 1. Interestingly, one patient presented with simultaneous bleeding at both an aneurysm and an AVM. Four patients had no history of

hemorrhage, and three of these suffered seizure and the other complained of third nerve palsy due to compression from a posterior communicating artery aneurysm, which was then treated by clipping.

There were a total of 27 aneurysms in 21 patients and five patients had AVMs with multiple arterial aneurysms. The associated aneurysms were the feeding pedicle type for 13 aneurysms (48.2%), the proximal in location type for 11 (40.7%) and the remote type for 3 (11.1%).

**Radiosurgical outcome of the AVMs**

All 21 patients underwent GKS, either as the initial treatment modality (14 patients) or as an adjuvant therapy following the treatment of aneurysms (7 patients). On the follow-up angiography, sixteen irradiated AVMs (76.2%) showed complete obliteration, 3 (14.3%) partial obliteration and 2 (9.5%) subtotal obliteration. In these case series, two patients (case No. 16, 17) had large AVMs (10 cm<sup>3</sup> or more in volume). Our strategy of radiosurgery for large AVMs were as follows : 1) marginal dose lower than 20 Gy, 2) optimal treatment planning for minimizing superfluous irradiation (If enlarged draining veins often occupying nidus on angiography are precisely excluded, pure volume of nidus may be smaller than the volume simply estimated based on imaging studies, and 3) in case of AVM which is larger than 14 cm<sup>3</sup> in volume and has several hemodynamically remote feeding arteries, the staged volumetric radiosurgery is considered to be the option. Therefore, in these two patients, the marginal dose was each 19 Gy and 20 Gy. Although case No. 17 was 25308 mm<sup>3</sup> in volume, he underwent the single session radiosurgery because the nidus was supplied by single vessel (PCA). In the present study, despite the mean 22.6 Gy-marginal dose and the mean 37.1 Gy-maximum dose, there was no radiosurgical complication, such as adverse radiation effects and post-treatment hemorrhage. We think that these results may be attributed to precise measurement of the target volume and the optimal planning is no less critical than the low-dose radiation to protect normal surrounding structures. However, the number of these cases is too small to discuss which is more potent factor to avoid the radiosurgical complications between the optimal planning and low radiation dose.

**Outcome of the associated arterial aneurysms**

Of all 27 aneurysms in this study, 5 aneurysms were treated with clipping and 11 were treated with GDC embolization. Nine associated aneurysms remained untreated because of their broad neck or the small sized sac of the aneurysms. Two cases inevitably remained untreated because of unsuccessful GDC embolization. The changes

**Table 2.** Initial clinical presentation of 21 patients

Symptoms	Number of patients
Bleeding	17
Headache	11
Mental deterioration	4
Dizziness	2
Non-bleeding	4
Seizure	3
3rd nerve palsy	1

in the size of these eleven aneurysms in 11 patients that were treated conservatively after the GKS for the AVMs were analyzed with a follow-up angiography. Equivocal change was seen in 5 patients and regression was seen in 4 (disappeared 3, decreased 1). The all spontaneous regressed aneurysms (4 of 11) were the feeding pedicle type. In two patients, even though their aneurysms were located in feeding pedicular artery and their AVMs were complete obliterated after GKS, the size of the aneurysmal sac was increased, and both patients were treated with GDC embolization without delay. There were no hemorrhagic events during the follow up periods.

## DISCUSSION

The mechanisms of the AVM associated with aneurysm can be explained with several hypotheses<sup>2,11,24,26,36</sup>. At first, the aneurysm may occur due to hemodynamic stress related to the AVM. Second, both lesions are congenital malformations of vascular development. Third, these associations can accidentally exist together<sup>19</sup>. Among these hypothesis, the hemodynamic stress secondary to the increased blood flow of AVMs plays a significant role to provoke this coexistence of lesions<sup>1,5,7,10-13,15,17,18,21,23,25</sup>. This hypothesis is supported by a report showing that the associated aneurysms tend to be concentrated in feeding arteries which supply AVMs<sup>25</sup> and the associated aneurysms may shrink in proportion to the occlusion of the AVMs<sup>6,14,17,18,22,31,35,37</sup>.

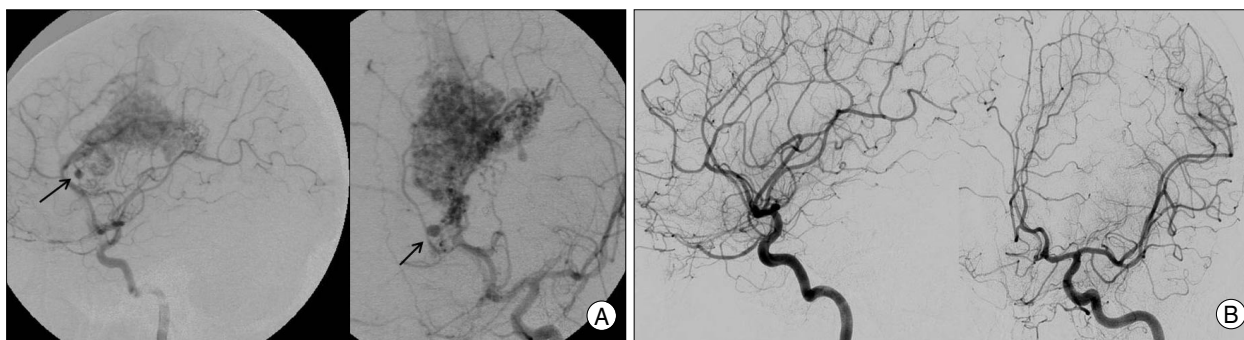
In spite of an incomplete understanding of the hemodynamic relationship between AVMs and their associated aneurysms, the hypothesis that decreased blood flow through the feeding artery following an AVM's obliteration might induce shrinkage or complete obliteration of the associated aneurysms has permitted treating the AVMs first, except for a patient whose initial clinical presentation is SAH. Even though there are opinions that elimination of AVMs may increase the intra-aneurysm pressure and the associated aneurysm may be prone to impending rupture<sup>1,10</sup>, as the AVMs are gradually occluded, the risk for aneurysmal rupture decreases because the blood flow and shear stress through the feeding artery are more critical hemodynamic factors than the arterial pressure<sup>12</sup>.

The previous published studies have suggested that the simultaneous surgical approach for treating both lesions in a single operation is the best option<sup>1,4,35</sup>. If a ruptured aneurysm is close to the nidus, then a one stage operation can be performed with a high success rate because the parenchymal hemorrhage from the aneurysm contributes to easy accessibility. The close anatomical relationship

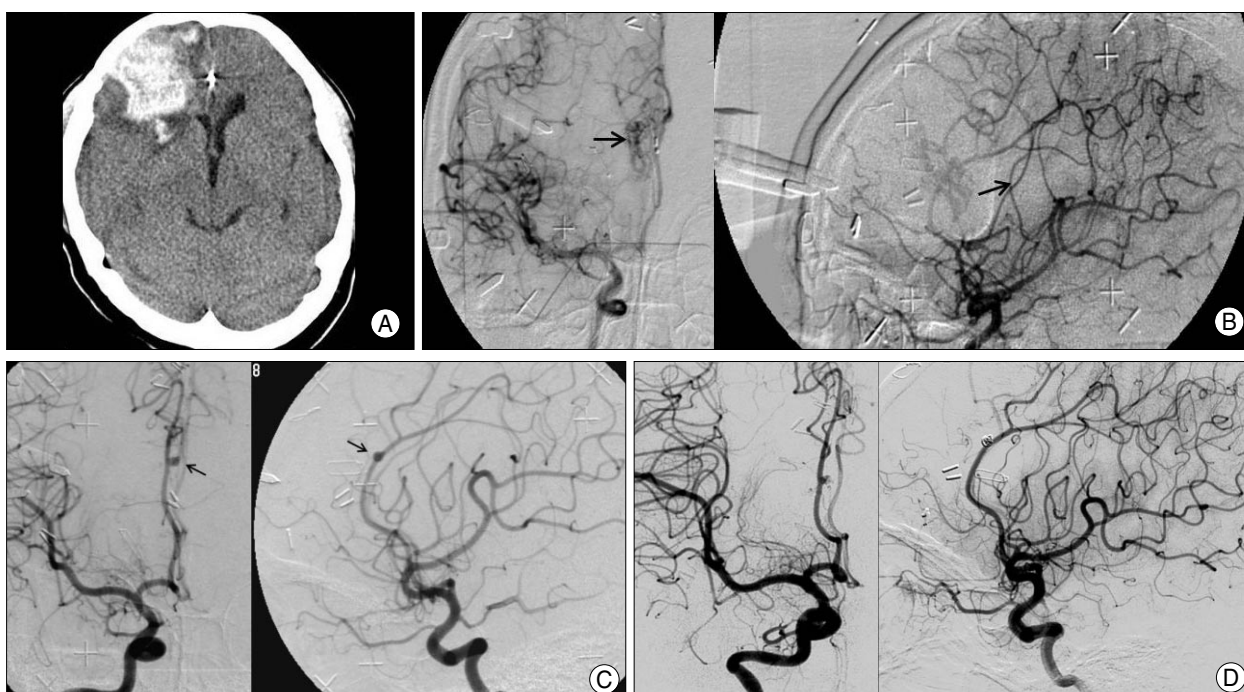
between the lesions facilitates eliminating both the nidus and the aneurysm simultaneously. Other reports have suggested that the associated aneurysm must be preventively eliminated because the mortality and morbidity related to aneurysmal rupture that is higher than for AVM's rupture<sup>6,20,28</sup>. Moreover, there is a low chance of rebleeding from an AVM compared to that from an aneurysm. However, the abrupt change of the hemodynamics due to the resection of an AVM may cause massive hemorrhage from the associated aneurysms<sup>1</sup>, and the intraoperative hemorrhage from a ruptured aneurysm may be fatal if proximal control of the artery harboring the aneurysm is not feasible.

In this case series, 16 of all 21 patients (76.2%) were managed by non-surgical treatment modalities such as GKS and GDC embolization with a relatively low complication rate. The efficacy and safety of radiosurgery for AVMs have been verified<sup>19,16,30,33,38</sup> and GDC embolization is considered to be a useful treatment for aneurysms associated with the AVMs treated by radiosurgery<sup>8</sup>. For patients presenting with SAH and incidental AVMs, the symptomatic aneurysms were treated first and the AVMs were next treated with radiosurgery. We tried to treat the incidentally encountered aneurysms by GDC embolization or surgical clipping when possible. Nevertheless, in nine cases, the aneurysms were too small and broad necked that the best course was simply to observe them on follow-up. In 2 cases, GDC embolization failed because the location of the associated aneurysm was too distal. Therefore, 11 aneurysms were kept under clinical observation after GKS. On the follow up angiography, we found that 9 cases of aneurysm were decreased or stable after the complete obliteration of the nidus of the AVM. These clinical courses of the unsecured aneurysms can be attributed to the radiosurgical effect on the aneurysm, which is secondary to the decreased blood flow into the nidus.

The rate for spontaneous regression of untreated feeding pedicular aneurysm after GKS for AVMs was 50% (4 of 8) and these regressed aneurysms were mainly located on the distal portion of the feeder to the nidus. Redekop et al.<sup>31</sup> reported on the effect of AVM treatment on the aneurysm and they estimated the spontaneous regression rate of the feeding artery aneurysms that were between the proximal and distal pedicular artery. They revealed that the associated aneurysms on the distal pedicular feeder are easier to regress than those on the proximal pedicular feeder. This result suggests that associated aneurysms are more susceptible to regression in response to decreased blood flow into the nidus by the radiosurgical effect in the case that a distal branch of the artery harboring the associated aneurysm



**Fig. 1.** Pre-radiosurgical and post-radiosurgical angiography show spontaneous regression of untreated feeding pedicular aneurysm after GKS. A : On angiographic examination of GKS, an aneurysm is detected at the distal feeding pedicular artery. B : Fifty months after irradiation, angiography demonstrating obliterated nidus of AVM and related aneurysm. AVM : arteriovenous malformation, GKS : Gamma-knife radiosurgery.



**Fig. 2.** Case of AVM with newly developed aneurysm after radiosurgery. A 21-year-old female patient with previous microsurgery for AVM nidus presented with intracranial hemorrhage on right frontal lobe on CT scan (A). On angiographic examination (B), remained nidus is detected and treated by Gamma knife (marginal dose 22 Gy). On follow-up angiographic examination, nidus of AVM is obliterated but de novo aneurysm (arrow) is detected at the previous feeding artery (C). This aneurysm was treated with GDC embolization and demonstrating of complete obliteration of nidus and coiled aneurysm after 2 years follow-up (D). AVM : arteriovenous malformation, GDC : Guglielmi detachable coil.

supplies only the nidus (Fig. 1).

Yet, in this case series, two untreated feeding pedicular aneurysms were rather enlarged in size despite complete obliteration of the AVMs and both of these aneurysms were occluded by GDC embolization without delay. One of these two cases is illustrated in Fig. 2. This case implies that if the stepwise obliteration of the nidus induces the diversion of blood flow from the nidus to the neighboring brain tissue, then the blood flow through the branching arteries of the direct feeder supplying the nidus may increase and the blood flow through the proximal portion of the direct feeder supplying the nidus may paradoxically increase.

Consequently, the flow-related aneurysm located on the proximal portion of the feeding artery has a chance to increase in size in spite of AVM obliteration.

For the cases of remote aneurysms, their coexistence with AVMs can be explained by coincidental theory rather than by hemodynamic stress theory, and managing remote aneurysms in a fashion similar to general aneurysms that are without AVMs may be reasonable<sup>25,32</sup>. The fate of unsecured aneurysms with partial or complete obliterated AVMs remains unpredictable and the regression, enlargement and de novo aneurysm formation after substantial AVM therapy have been illustrated<sup>17,29,31,34</sup>.

Therefore, close follow up of an unsecured aneurysm is mandatory, and complementary treatment should be provided for the associated aneurysm with their increased size after radiosurgery for the AVMs.

## CONCLUSION

AVMs associated with aneurysm have the characteristics of a low incidence, a high bleeding tendency and they are difficult to manage. Treatment with GKS and GDC embolization is considered to have a significant role to minimize the neurologic injury. Furthermore, radiosurgery may be valuable as an initial single treatment modality for the AVMs associated with flow-related aneurysms, except for aneurysmal rupture. However, there is a chance that flow-related aneurysms will increase in size according to the unpredictable change of hemodynamics after curative treatment for an AVM, and so angiographic follow up and complementary treatments are important.

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