Case Report

VOLUME STAGED RADIOSURGERY FOR LARGE ARTERIOVENOUS MALFORMATION - A CASE STUDY

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ABSTRACT

Introduction: *Large Arteriovenous malformations (AVMs) are challenges in management because of outcomes and adverse affects. Volume Staged Radiosurgery has been an appropriate approach when removal resection and embolization are not recommended.*

Case presentation: *A 53 year-old gentleman was diagnosed with a large intracranial AVM with persistent headache and short-term seizure. Brain MR and angiograph showed a bulky volume of AVM nidus. Removal resection and embolization were not recommended because of high risk of adverse affects. Patient was treated by volume staged radiosurgery.*

Management and outcome: *Radiosurgery was divided into two stages. First stage was 15 Gy to the anterior half, and second one was 13 Gy to the posterior half of whole AVM, interval time was 5 months. 5 months post-treatment, there was still remained shunts for right internal carotid artery (ICA), completely obliteration for right external carotid artery (ECA). One year post-treatment, obliteration for right ICA was completed.*

Discusion: *Volume Staged Radiosurgery is a potential treatment option for large AVM with controlled and obliteration efficacy, especially to AVMs which are not appropriate for removal surgery and embolization.*

Key words: *large arteriovenous malformation, volume staged radiosurgery*

I. INTRODUCTION

Arteriovenous malformations (AVMs) are congenital vascular anomalies comprised of an abnormal number of blood vessels that are abnormally constructed. The blood vessels directly shunt blood from arterial input to the venous system without an intervening capillary network to dampen pressure. The annual incidence of AVM recognition is thought to be 10,000 patients per year in the United States [1].

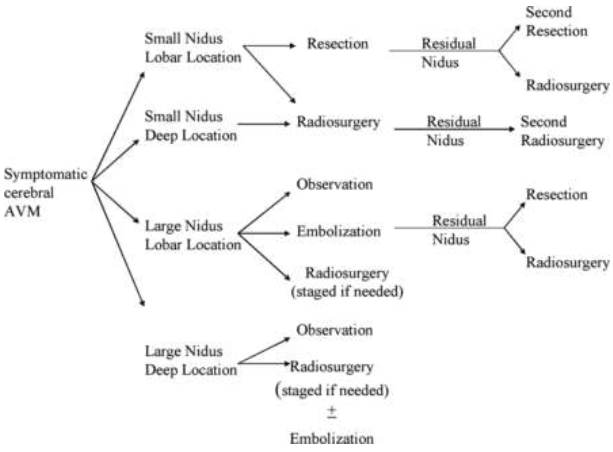

Figure 1: Treatment strategy for AVM [15]

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In making a decision for management strategies, we often employ a decision tree algorithm as shown in *Figure.1*.

Surgical removal is arguably the best option for small- to medium- sized lesions, defined as Spetzler-Martin (SM) (Table 1) grades I - III, occurring in noneloquent and superficial regions of the brain, particularly those with a history of hemorrhage [2]. Complete resection is curative and eliminates the risk of hemorrhage without a latent period. Large lesions, usually SM Grades IV and V, have substantially higher surgical complication rates and remain a therapeutic challenge. The overall prevalence or natural history of large AVMs is not well known, but such lesions have also been associated with increased rates of hemorrhage [3]. In most reports, lesion size is defined by the greatest maximal dimension of the AVM nidus, and the incidence of AVMs larger than 2.5–3 cm varies from 30% to 62% in natural history studies [4].

Table 1: Spetzler-Martin Scale

Spetzler-Martin AVM Grading Scale	**Points**
Size	
0-3 cm	1
3.1-6.0 cm	2
> 6 cm	3
Location	
Noneloquent	0
Eloquent *	1
Deep venous drainage	
Not present	0
Present	1
AVM Total Score	**1-5**

(*) Eloquent locations- areas of sensorimotor, language, visual, thalamus, hypothalamus, internal capsule, brain stem

For larger volume AVM (average diameter 4–5 cm), observation may be the only reasonable strategy in view of the risks of even multimodality management [5]. This may be especially true for patients who have never bled previously.

Different treatment paradigms for large inoperable AVMs include single-stage Stereotactic RadioSurgery (SRS), embolization (definitively, pre-SRS, or post-SRS), SRS with planned salvage of surgery or repeat SRS, proton-based SRS, fractionated SRS, dose-staged SRS, and volume-staged (VS)-SRS, which is an alternative approach where the nidus is divided into separate volumes and treated in separate sessions while minimizing overlap between stages [2].

Outcomes after radiosurgery may be predicted based on volume, location, age, angioarchitecture, and dose delivered [6]. SRS is an excellent management strategy for patients with AVMs 30 mm in average diameter (for a single procedure). Staged procedures are used for larger vascular malformations or for those that were incompletely obliterated 3 years or more after an initial procedure.

VS-SRS has been described as a way to potentially improve rates of obliteration and decrease the normal tissue 12-Gy volume by 27.3% and the overall 12-Gy volume by 11% compared with a hypothetical single session of SRS [7].

In this study, we introduce a 53 year-old gentleman with large AVM diagnosis, AVM at eloquent site, affected functionally. Removal surgery and endovascular intervention were not available.

II. CASE REPORT

A 53 year-old gentleman presented persistent headache in 2 years. He had previously hypertension history, treated permantly by calcium blocker, without history of vision blur and seizure. He came Neurosurgery Department because of increasing headache and short-term seizure. Brain MRI showed a large AVM at right brain lobular, maximum diameter of AVM's nidus was 6.48 cm *(Figure.2)*. In DSA, there were many large and high flow supplying arteries (the largest was right internal carotid artery-ICA) *(Figure.3a,b)*. The diagnosis was inoperative large AVM, Spetzler-Martin grade V, inappropriate for embolization. We decided to use Volume Staged Radiosurgery with interval time was 3-6 months. The AVM had been divided into two halves (anterior and posterior) based on a land mark as posterior edge of anterior clinoid. Dose to anterior half was 15 Gy and posterior half was 15 Gy after calculated doses for coverage and organs at

risk. PTVs were defined as GTV+2mm *(Figure.4*). Simulation was performed by using specific radiosurgery thermomask, CT simulation and MRI were recorded by 1mm slice thickness; plans were calculated by dosimetrists and software Monaco 5.1. MRIs and DSA were taken before treatment, between 2 stages and 3, 6, 12, 18 months after the second stage. Following up time was 24 months at time of report.

First fraction (1st stage) was on September 28th of

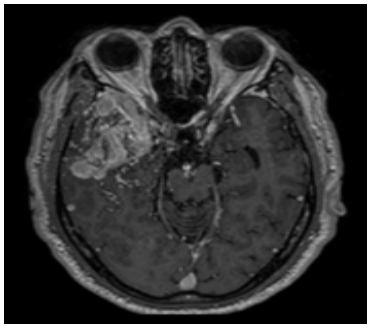
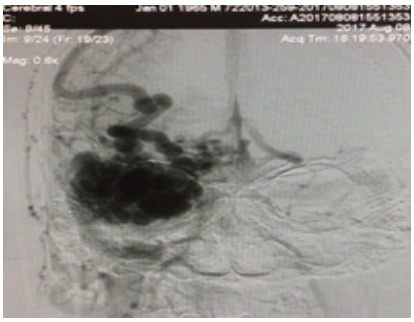
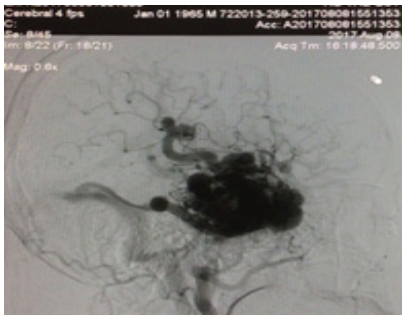


Figure 2: Pre-treatment MRI



(a)



(b)

Figure 3a,b: Pre-treatment DSA

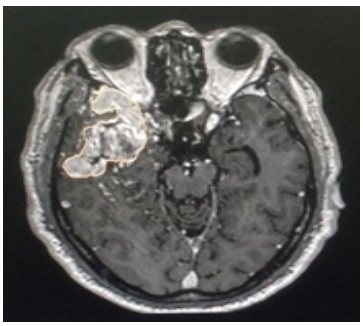


Figure 4: Whole AVM nidus contouring

Structure	Volume [...	Min. Dose [c...	Max. Dose [...	Mean Dose ...	Cold Ref. [...	Volume < [...	Volume < [...	Hot Ref. [c...	Volume > [...	Volume > [...	% in Vol...	Is in ...	Heterogeneity Ind...	Conformity Index
GTV T 1ST	30.544	1105.2	2020.6	1760.8				1500.0	30.496	99.84	100.00	yes	1.16	0.41
PTV1SA	46.888	988.7	2020.6	1704.4				1500.0	44.988	95.95	100.00	yes	1.24	0.85
R OPTIC	0.600	410.7	988.7	657.9				800.0	0.120	20.00	100.00	yes	2.07	0.00
CHIASMA	0.584	219.0	976.3	509.2				800.0	0.048	8.22	100.00	yes	3.41	0.00
skin(Unsp.Tiss.)	3539.416	2.3	634.8	99.5							100.00	no	15.29	
BRAIN	1447.832	8.7	2015.2	221.9							100.00	yes	25.89	
BRAIN STEM	27.152	67.5	415.4	155.5							100.00	yes	2.96	
L COCHLEA	0.344	124.6	216.1	166.0							100.00	yes	1.51	
L EYE	6.864	59.8	195.7	119.5							100.00	yes	2.16	
L LEN	0.144	94.0	143.5	117.7							100.00	yes	1.48	
L OPTIC	0.592	80.5	215.6	136.4							100.00	yes	2.02	
R COCHLEA	0.328	175.7	387.9	269.7							100.00	yes	1.97	
R EYE	7.184	90.8	618.7	265.8							100.00	yes	3.41	
R LEN	0.208	131.2	268.3	171.9							100.00	yes	1.40	

Figure 5: Dose Volume Histogram (DVH)

2017, delivered 15 Gy to the anterior half of whole AVM. Coverage were >95% prescriptive dose to 100% of volume, maximum dose was 1847 cGy (<140% prescriptive dose) *(Figure.5).*

48 hours after first fraction, he felt mild headache, without seizure or dizzy, symptom disappeared after 24 hours treated by steroid (dexamethasone 8mg BID).

After 4 months, he came for continous treatment. MRI before second stage showed reduction of whole AVM toward treated half by 20% *(Figure.6*). We decided to make some modifications:

- Alleated borderline between two halves anteriorly (toward treated half) by 2mm.

- Decreased dose for second stage at posterior half to 13 Gy, due to assure protection to organs at risk (chiasm, right optic nerve).

The second stage was performed on February 26th, 2018 (5 months apart).

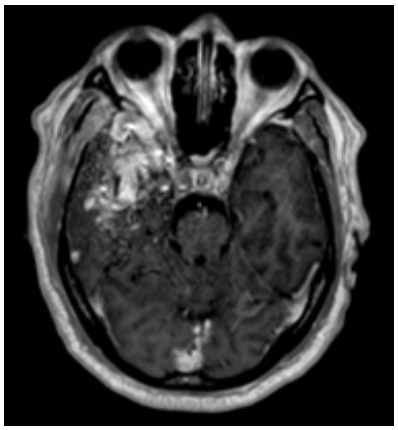
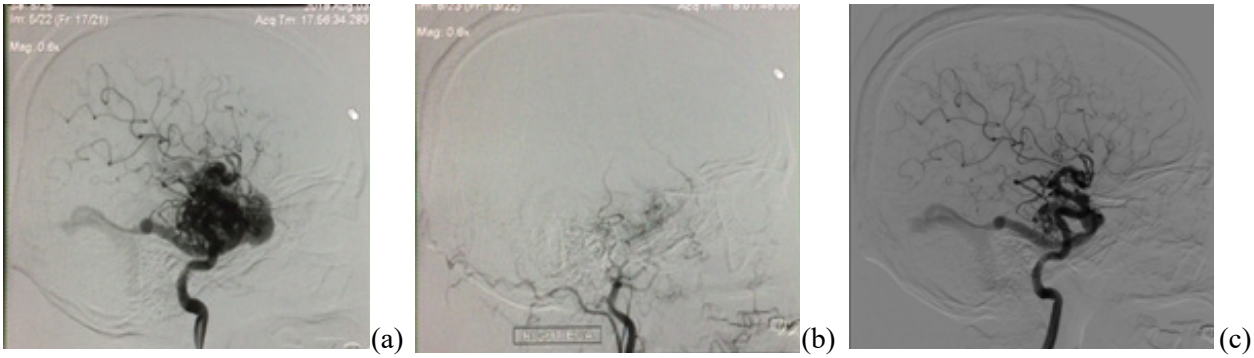


Figure 6: MRI before second stage



(a) (b) (c)

Figure 7: (a) Remained shunts for right internal carotid artery, (b) Completely obliteration for right external carotid artery and (c) Completely obliteration for right internal carotid artery

III. DISCUSSION

The Spetzler-Martin AVM Grading Scale is based on size, location, and venous drainage of intracerebral AV malformation. The scale is calculated by adding the points for each category. The range is 1 to 5. The lower the score, the better the outcome. In our case, other indications such as removal surgery and embolization were not available, because high risk of hemorhage and Spetzler-Martin grade V. Decision on staged volume radiosurgery was appropriate. Volume and maximum diameter of AVM nidus were massive, unsafe to adjacent organs at risk if using either single fraction radiosurgery or fractionated routine radiotherapy.

In a subgroup of 48 patients with AVMs larger than 15 ml, Pan et al found an obliteration rate of 25% after 40 months. In their single radiosurgery strategy, the average margin dose was 17.7 Gy and 16.5 Gy for AVMs with volumes 10 to 20 ml and more than 20 ml, respectively. In their follow-up examinations, they observed 37% moderate and 12% severe adverseradiation effect in patients with AVMs larger than 10 ml [8]. Miyawaki et al. reported that the obliteration rate in patients with AVMs larger than 14 ml treated using LINAC-based radiosurgery was 22% [9]. Inoue et al. reported an obliteration rate of 36.4% and hemorrhage rate of 35.7% in the subgroup of AVMs larger than 10 ml treated by radiosurgery [10].

The probability of developing post radiosurgery imaging changes depends on marginal dose and treatment volume. The volume of tissue receiving 12 Gy or more (the 12-Gy volume) is the single factor that seems to have the closest correlation with the probability of developing imaging changes [11]. Location does not seem to affect the risk of developing imaging changes but has a marked effect on whether or not these changes are associated with symptoms. Post- radiosurgery imaging changes (new areas of high T2 signal in brain surrounding the irradiated AVM nidus) develop in approximately 30% of patients 1-24 months after radiosurgery [12].

In the present case, post radiosurgery imaging change was at 4 months after first stage treatment (whole volume reduced 20%) without symptoms (Fig.6). This is appropriate due to dose of 15 Gy at anterior half.

Delayed complications of radiosurgery include the risk of hemorrhage despite angiographically documented completely obliteration AVMs, the risk of temporary or permanent radiation injury to the brain such as persistent edema, radiation necrosis, and cyst formation, and the risk of radiation-induced tumors. Cyst formation after AVM radiosurgery was first reported by Japanese investigators who reviewed the outcomes of patients initially treated in Sweden [13]. Delayed cyst formation has been reported in other recent long-term follow-up studies [14].

Time was a factor contributing to response and obliteration capacity evaluation. Though two stages of treatment had been accomplished, DSA at 6 months still remained shunts *(Figure.7a),* while MRI showed completely response. Obliteration evidence presented in DSA only at 12 months after treatment *(Figure.7b,c).*

IV. CONCLUSION

Volume Staged Radiosurgery is a potential treatment option for large AVM with controlled and obliteration efficacy. However, indication should be made after very careful discussion by neuro-surgeons, endovascular specialists and radio-oncologists, requires many experiences before applying to treatment.

REFERENCES

1. Deruty R, Pelissou-Guyotat I, Morel C, Bascoulergue Y, Turjman F. Reflections on the management of cerebral arteriovenous malforma- tions. Surg Neurol 1998; 50(3):245–255, discussion 55–56.
2. Stefani MA, Porter PJ, Brugge KG, Montanera W, Willinsky RA, Wallace MC: Large and deep brain arteriovenous malformations are associated with risk of future hemorrhage. Stroke 33:1220–1224, 2002.
3. Flickinger JC, Kondziolka D, Maitz AH, Lunsford LD: Analysis of neurological sequelae from radiosurgery of arteriovenous malformations: how location affects outcome. Int J Radiat Oncol Biol Phys 40:273-278, 1998.
4. Lawton MT: Spetzler-Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. Neurosurgery 52:740–749, 2003

5. Han PP, Ponce FA, Spetzler RF. Intention-to-treat analysis of Spetzler– Martin grades IV and V arteriovenous malformations: natural history and treatment paradigm. J Neurosurg 2003; 98(1):3–7.
6. Pollock BE, Flickinger JC, A proposed radiosurgery-based grading system for arteriovenous malformations. J Neurosurg 2002; 96(1):79-85.
7. Mathis JA, Barr JD, Horton JA, Jungreis CA, Lunsford LD, Kondziolka DS, et al: The efficacy of particulate embolization combined with stereotactic radiosurgery for treatment of large arteriovenous malformations of the brain.
8. Pan DH, Guo WY, Chung WY, Shiau CY, Chang YC, Wang LW: Gamma knife radiosurgery as a single treatment modality for large cerebral arteriovenous malformations. J Neurosurg 93 Suppl 3:113-119, 2000.
9. Miyawaki L, Dowd C, Wara W, Goldsmith B, Albright N, Gutin P, et al: Five year results of LINAC radiosurgery for arteriovenous malformations: outcome for large AVMS. Int J Radiat Oncol Biol Phys 44:1089-1106, 1999.
10. Inoue HK, Ohye C: Hemorrhage risks and obliteration rates of arteriovenous malformations after gamma knife radiosurgery. J Neurosurg 97:474-476, 2002
11. Friedman WA, Bova FJ, Bollampally S, Bradshaw P: Analysis of factors predictive of success or complications in arteriovenous malformation radiosurgery. Neurosurgery 52:296-307; discussion 307-298, 2003.
12. Flickinger JC, Kondziolka D, Lunsford LD, Pollock BE, Yamamoto M, Gorman DA, et al: A multi-institutional analysis of complication outcomes after arteriovenous malformation radiosurgery. Int J Radiat Oncol Biol Phys 44:67-74, 1999.
13. Hara M, Nakamura M, Shiokawa Y, Sawa H, Sato E, Koyasu H, et al: Delayed cyst formation after radiosurgery for cerebral arteriovenous malformation: two case reports. Minim Invasive Neurosurg 41:40-45, 1998.
14. Izawa M, Hayashi M, Chernov M, Nakaya K, Ochiai T, Murata N, et al: Long- term complications after gamma knife surgery for arteriovenous malformations. J Neurosurg 102 Suppl: 34-37, 2005
15. Kalash R, Engh Johnathan A., Amankulor N, “Brain Radiosurgery” in “Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy (SBRT), 2018.