Stereotactic Radiosurgery of 26 Intracranial Arteriovenous Malformations with Linear Accelerator

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From July 1988 through November 1991, 26 patients with inoperable arteriovenous malformations were treated with 6 MV linear accelerator at the Kangnam St. Mary's Hospital, Catholic University Medical College. There were 5 females and 21 males with median age of 29 years (range: 6~63 years) and median follow up times of 15 months (range: 4~40 months). The arteriovenous malformation volumes treated ranged from 1 cm diameter to 3.5 cm rectangular size. The prescribed doses at the isocenter varied from 15 to 30 Gy and were given as a single fraction. To date, all patients performed follow-up not only clinically but also through CT or angiography based radiologic modalities every 6 month. A complete obliteration was achieved in 6 (23%) and partial obliteration in 8 (31%) and no change in 1 (4%). We observed 14 (54%) responsiveness of arteriovenous malformations after radiosurgery by 2 years afterward. Whereas, the decision of the remaining 11 (42%) patients was considered too early to expect the therapeutic response following radiosurgery. No complications through treatment related were observed, yet. Our initial outcome in these first 26 patients with arteriovenous malformations is recommended further follow-up.

Key Words: Radiosurgery, Arteriovenous Malformation, Linear accelerator

INTRODUCTION

Standard treatment of arteriovenous malformation (AVM) is neurosurgical approach wherever it is[1~9]. However, for the management of the inoperable AVM, the radiotherapy has been used as a last assessment, despite some occasional successes until 1970. It had been considered ineffective and therefore abandoned[1,5,7,10].

Since the pioneering work of Leksell, radiosurgery (RS) has been used to treat a wide variety of benign and malignant intracranial lesions and also treat various functional disorders thereby avoiding open surgery[4,9]. He coined the term radiosurgery to differentiate this treatment from radiotherapy[5,9]. The differences between two are considerable point of treatment view. RS is used to treat relatively small volumes in only single fraction, and the beam is precisely collimated such that the dose delivered is sharply circumscribed to the target volume, wherein necrosis is tolerated. On the otherhand, radiotherapy is used to treat larger volumes, and the dose is fractionated during treatment time to take advantage of the therapeutic ratio and spare any normal tissue in the irradiated field[1,5,9]. RS has been performed with a variety of radiation sources, including the charged particle beams from the cyclotrons, the gamma unit to collimate the beams from multiple Co-60 sources onto stereotaxic target, and modifications of the conventional commercial linear accelerator[1,5,9]. One of the most successful applications of RS so far is the treatment of inoperable or inaccessible deep cerebral AVMs[1,3~9].

In this paper we report our initial results in the first 26 patients with AVM treated using 6 MV linac based RS at Catholic University Medical College in Seoul.

METHODS AND MATERIALS

From July 1988 through November 1991, 26 patients with AVM were treated using stereotactic radiosurgery at Kangnam St. Mary's Hospital. The concept and mechanical design of stereotactic radiosurgery using linac were described in many literatures[1~17].

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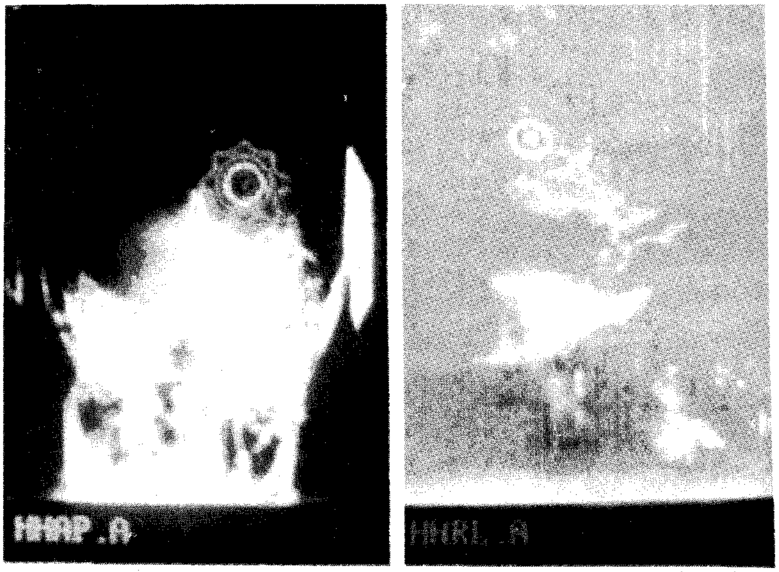

Fig. 1. Isodose distributions superimposed on two orthogonal angioprojection images. Doses are calculated and summed for four arcs with equall arc spacing and 1.0 cm diameter beam size. The 80, 40, 20, 10% isodose curves are shown.

The radiosurgical procedures consist of three steps: target localization using stereotactic frame (Hitchcock's), dose planning with 386 personal computer (and digitizer) (Fig. 1), and finally treatment in terms of linear accelerator adapting with head frame and special collimator[2~10,14,15].

An important problem in radiosurgery is the utilization of the proper irradiation parameters such as isocenter position, collimator size, arc position and weights to optimize dose distributions. The current standard technique utilize single isocenter with standard arc arrangements (4~7 arcs with the arc length from 30° through 130°) especially for spherical lesions. However, for irregular shapes, weighting arcs were utilized to change treatment volume shape. Multiple isocenter approach can be considered after verification test. Depending on the size and location of AVM, isocenter position and collimator size were chosen to cover the target volume within sharply decreasing isodose surface[1,14,15] (*i.e.* 70~90% *in single isocenter*).

Depending on the size and location of AVM, prescribed doses were determined and varied from 15 to 30 Gy. The tumor dose was prescribed at the target margin of isodose curve (e.g. 80%). The collimator size varied from 1 cm diameter to 3.5 cm rectangular one.

Stereotactic brain CT scan and/or stereotactic angiography were carried out prior to stereotactic radiosurgery. Clinical objectives are to achieve changes in the intracranial hemodynamic condition resulting in a decrease in frequency of hemorrhages, in neurologic deficiencies, subjective complaints including headache or in frequency of seizures[1,4]. Radiologic objectives are to achieve hemodynamic changes, that is, decrease in blood flow through AVM with decrease in the size of AVM until total disappearance[1,4]. The follow up of patients were performed not only through clinical aspect but also CT or angiography based radiological methods every 6 month intervals after RS.

Our patients consisted of 5 females and 21 males with median age of 29 years (ranging from 6 ~63 years, double peaks; 20s & 40s). All patients were assessed by a radiosurgical team consisting of a neurosurgeon, a radiation oncologist, a neuroradiologist and a physicist. The median follow-up time post-radiosurgery was 15 months (ranging from 4~40 months).

RESULTS

Of the 26 patients (M:F=21:5) with AVMs, eight (30.8%) were sustained of complicated AVMs of which symptomes were related to prior hemor-

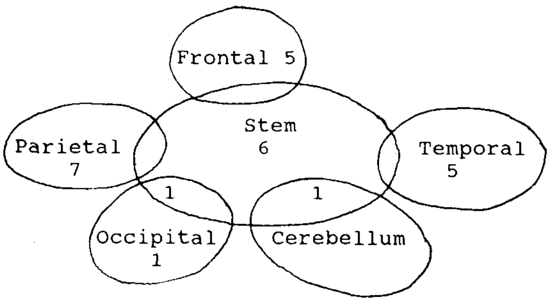

Fig. 2. Sites of 26 AVMs Treated by Radiosurgery. (hemorrhage: 8 26)

Table 1. Relationship between the Outcome after RS and the AVM Size

size (cm)	<1	1≤ <3	3≤
total 0. (n=6)	2	4	
Partial 0. (n=8)	1	5	2
No Change (n=1)			1
Not checked (n=11)	5	6	

· RS: radiosurgery
· AVM: arteriovenous malformation
· O: obliteration

Table 2. Relationship between the Outcomes after RS and the Lapsed Times (%)

years	Total 0 (n=6)	Partial 0 (n=8)	No Change (n=1)	Not Checked (n=11)
3≤	4 (67)	3 (37.5)		
1≤ <3	2 (33)	6 (62.5)	1 (100)	
1<				11 (100)

· RS:radiosurgery · 0: obliteration

rhage. The sites of involvement were shown in Fig. 2, representing deep seated inoperable AVMs. Table 1. listed the outcomes after radiosurgery in relation to the size of AVM.

By 2 years following RS, complete obliteration was seen in 6 (23%), partial obliteration (residual abnormal vessel) in 8 (31%) and no change in 1 (4%) (Fig. 3). One who had no radiologic interval change untill 30 months after treatment showed stationary clinical courses. The relationships between the clinical outcomes and the lapsed times after RS were shown in Table 2. We observed 14 (54%) responsiveness of the treated AVM by 2 years afterward.

Follow-up time of eleven (42%) patients with under 1 year were considered too short to evaluate the response of treatment. There was no treatment related complications so far observed, yet.

DISCUSSION

AVMs are congenital abnormalities which develop from aberrant connections within the primitive arterial and venous plexus overlying the developing cortical mantle. During embryologic maturation this region of abnormal vasculature is incorporated into the brain parenchyma. Initially, the cerebral vasculature adjacent to the AVM develops normally. However, because AVMs lack a normal capillary bed, local blood flood through the AVM is *increased, and vascular dilatation gradually* ensues. This shunting of blood through the AVM may result in a steal phenomenon. The lack of a normal capillary bed implies that the vessels of an AVM provide no nutritive function. Therefore, tissue deep within an AVM may be nonfunctioning and sclerotic, whereas immediately adjacent tissue usually retains its normal integrity and function[5].

Histologic examination of AVM usually shows evidence of microscopic or gross hemorrhage. Gliotic neural parenchyma are frequently found between component vessels, and hemosiderin-laden macrophages are usually found. Varying degree of spontaneous thrombosis within vessels of AVM is common and may lead to occasional obliteration of the AVM[16].

AVM demonstrate a large range in number, size and location of feeding arteries and draining veins and it is uncertain whether they represent a single disorder or a family of disorders. Their natural history is poorly understood since their incidence is low, although incidental, unruptured AVMs are seen with increasing frequency at CT and MRI[1,4]. Autopsy series suggest that a fairly large number of deep AVMs escape diagnosis. Deep AVMs comprise up to 35% of all intracranial AVMs. Intraventricular and brain stem AVMs comprise 20% of deep AVMs and inoperable deep AVMs comprise 27% of all intracranial AVMs. In children deep AVMs can comprise as much as 1% of neuropediatric hospital admissions. About one third of all deep AVMs are in the posterior fossa[4,5]. Deep AVMs appear most frequently in male and about 75% of patients with deep AVMs develop symptomes before 40 years of age[4,5]. In our cases, all but one were supratentorially involved along with male preponderance and dual peak prevalance at their 20s and 40s. Five (19%) out of 26 patients were in the pediatric age group (below 15 years of

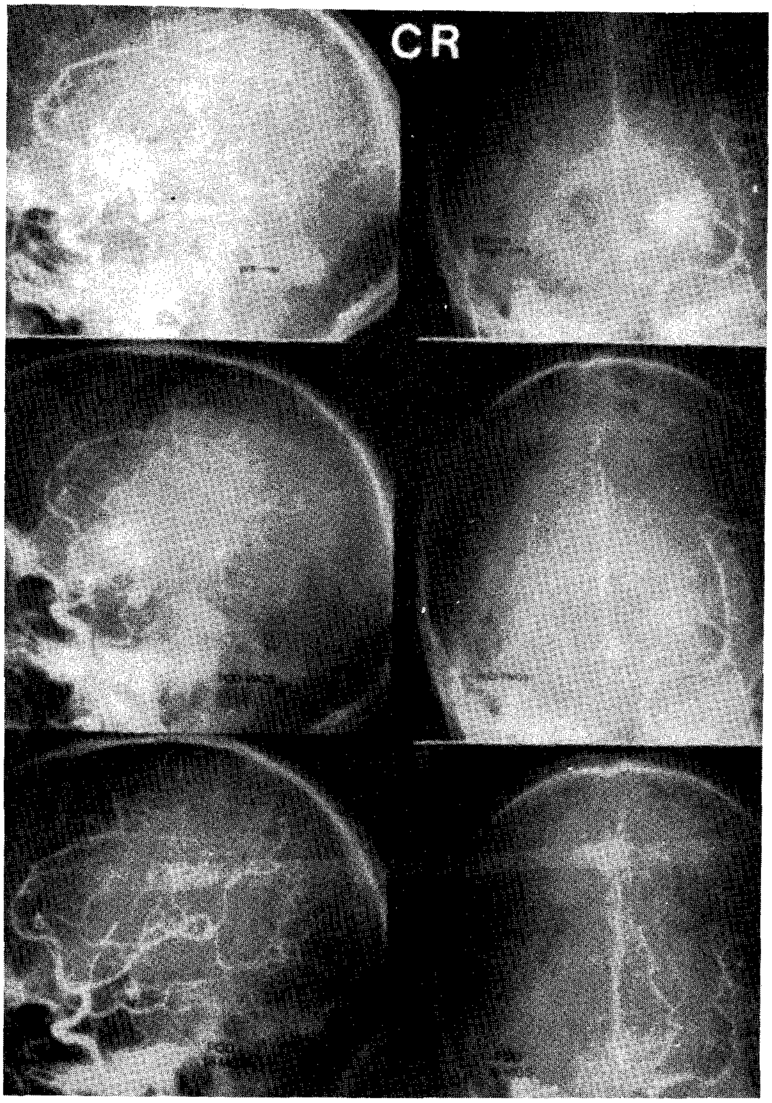

Fig. 3. This 41-year old man presented with headache, stupor and right sided weakness, followed by cerebral angiograms (lateral and anteroposterior). He underwent radiosurgical treatment with 19 Gy to 80% isodose line which corresponded to the periphery of the lesion. Angiography 18 months later revealed complete thrombosis of the lesion.

age).

Mortality for all AVMs approaches 15%[4]. That of deep AVMs is much higher, perhaps approaching 25%, owing to the more dangerous sites and the higher frequency of bleeding. Morbidity, including hemorrhage, neurological disability, paresis, ataxia, brain stem dysfunction, coma and seizure is often severe since deep AVMs are almost always located close to important brain structures. Hemorrhage occurs in up to 25% of patients[4,5]. In our small series, hemorrhagic strokes were observed in 30.8%(8/26) of the patients.

Several factors make comparision of the results of treatments between various groups difficult: 1) grading systems for AVM are not used, although their use has been suggested; 2) patient selection factors vary; 3) AVM location within the brain is important; 4) concomitant medical problems may play a role; and 5) brain exposed to prior injury such as stroke or open excision may have decreased tolerance to therapy including RS. In addition, RS outcomes may vary for technical reasons; 1) There is no consensus on the minimum volume beyond the nidus that should be treated or on the minimum dose required in whatever volume is selected. 2) Although angiography is usually used to define the treatment volume, small outlying AVM vessels may exist which are beyond the resolution and detection of current angiography, and could eventually hemorrhage even though follow-up angiography is completely normal. The likelyhood of this occurance may depend on how generously the treatment volume was selected. 3) Orthogonal angiographic studies do not allow determination of the three dimensional structure of an AVM nidus; if the nidus is irregularly shaped, a spherical isodose surface which encloses it may needlessly enclose a substantial amount of normal tissue. In a few special cases this problem can be overcome by using multiple isocenters in conjunction with an imaging technique which allows determination of conjuction with an imaging technique which allows determination of the shape of the nidus such as multiple stereoscopic angiographic pairs or possibly MRI[15]. There is some evidence that MRI can be used to seperate the nidus from the rest of the AVM.

Based on the reported data, complete obliteration rates at 2 years were 84%[7], 75%[10], and 65%[4] respectively. Whereas, Partial response rates at 2 years were 30% and 25% using helium ion[4]. The reported complete response rate obtained with helium ions and protons are lower, although this may be related to patient selection or other factors. By the outcome of our 26 AVMs with median follow up of 15 months, complete response in 6 (23%) and partial response in 8 (31%) were obtained with the doses ranging from 15 to 30 Gy and collimator size from 1 cm diameter to 3.5 cm rectangular one.

It is still not clear how well patients are protected from subsequent hemorrhage. Before any protection is conferred, there may be a long latency period of 1~2 years between RS and obliteration during which patients are at risk for hemorrhage[1,5].

Occasional acute reactions have been reported, including headache, elevated temperature, or increased risk of seizure. According to the early series of data, there were 3 to 15% of the neurologic deficits or delayed radionecrosis following RS only to decrease by way of changing the doses and field size[5].

No complications have been reported as a result of dose deposition outside the brain during RS. Typical measured doses delivered to various organs during RS are as folows;[5] isocenter=100%, lens=0.1%, thyroid=0.2%, liver=0.05%, gonads=0.02%.

The pathological changes after irradiation have been recognized intimal proliferation and vascular occlusion. Small vessels are occluded more easily than large ones, in part because small vessels have less latitude for endothelial changes to occur before patency is compromised. Nilson observed late intimal thickening following gamma unit irradiation of the basilary arteries in the cat and noted occlusion of small arteries in the surrounding brain tissue[17]. RS of AVMs may lead to an intense gliosis around the malformation, possibly producing an endarteritis obliterance[16]. Kjellberg observed an endotheleitis with small vessels of AVMs irradiated with protons with associated subendothelial deposition of collagen and hyaline and inferred that normal capillaries were unaffected at the dose level used[6]. Usually, obliteration of AVMs after RS is not complete for 1~2 years[1~12,16,17]. The exact mechanism of damage of AVMs or to normal brain tissue following high dose small volume irradiation is not yet completely understood and further animal stuies may provide the information on dose-volume relationships for RS in normal brain.

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= 국문초록 =

뇌동정맥기형 26예의 선형가속기를 이용한 뇌정위다방향 단일방사선치료

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가톨릭의대 강남성모병원 치료방사선과에서는 1988년 7월부터 1991년 11월 사이 40개월 동안에 26명의 수술 불가능한 뇌동정맥기형 환자에 대하여 6 MV 선형가속기를 이용하여 뇌정위다방향 단일 방사선치료를 실시하였다.

환자연령은 6세부터 63세였고(중앙값 29세), 남녀의 비는 21:5였다. 치료 종료 후 추적기간은 4개월~40개월 간이었다(중앙값 15개월). 뇌동정맥기형의 크기는 직경 1 cm부터 43 cm^3까지였으며 환자 연령, 병소의 크기 및 뇌내 위치에 따라 4~7회의 부분회전 조사를 실시하여 15~30 Gy를 단일 조사하였다.

모든 환자는 임상적 그리고 CT 또는 MRI나 뇌혈관조영술을 병행하여 방사선치료 전 및 후 6개월 간격으로 뇌동정맥기형의 크기변화를 추적 분석하였다. 2년 이상된 예의 추적검사를 분석한 결과 완전 관해 6(23%), 부분관해 8(31%), 무변화 1(4%)명 씩으로 분석되었다. 11(42%)명은 방사선치료한지 1년 미만의 무반응군으로 간주되었다. 이상으로 치료후 2년째 반응율은 54%(14예)였다. 치료에 따른 부작용은 아직 관찰되지 않았다.