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Does hemorrhagic presentation in cerebral arteriovenous malformations affect obliteration rate after gamma knife radiosurgery?☆

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Abstract

Objectives: Radiosurgery has been widely adopted for the treatment of cerebral AVMs. However radiosurgical treatment of patients with hemorrhagic presentation is fraught with risk of rebleed during latency period. The present study intends to analyze the obliteration rate, time to obliteration and chances of rebleed in patients with hemorrhagic versus non-hemorrhagic clinical presentation in cerebral arteriovenous malformations (AVMs) treated with gamma knife radiosurgery (GKS).

Patients and methods: Of all the patients with cerebral AVMs treated from May 1997 to Jun 2006, 157 patients with neuroimaging follow up with digital subtraction angiography harboring 160 AVM nidii formed the study group. The mean age of presentation was 28 years (range, 6–58 years); mean nidus volume being 3.64 cm^3 (range, 0.011–36.6 cm^3). The mean follow up period was 70 months (range, 13–121 months). All the patients were treated predominantly by primary GKS with use of adjunctive pre-GKS embolization in selected patients.

Results: A total of 103 (64%) patients presented with hemorrhage. There was no difference in the obliteration rate (69% versus 67%, $p = 0.672$), mean latency period to obliteration (30 months versus 32 months, $p = 0.1989$) and chances of hemorrhage (4.8% versus 3.5%, $p = 0.690$) in patients with hemorrhagic as compared to non-hemorrhagic presentation.

Conclusion: Prior hemorrhage does not affect the outcome after GKS in terms of obliteration rate, latency to obliteration as well as chances of hemorrhage during latency period. Gamma knife appears equally efficacious irrespective of the mode of clinical presentation in the management of cerebral AVMs; a concomitant use of pre-GKS embolization/surgery may be needed in patients with hemorrhagic presentation in selected cases, however.

Keywords: Arteriovenous malformations; Gamma knife; Hemorrhage; Outcome; Stereotactic radiosurgery

1. Introduction

Arteriovenous malformations of the brain can present with intracerebral hemorrhage, seizures, progressive neurological deficit or headache [1,2]. With an annual risk of hemorrhage varying from 2 to 4%, the management of AVM is primarily based on eliminating this risk of hemorrhage [1,3–7]. The role of radiosurgery has increased over the past few years with various studies quoting an obliteration rate varying from 60 to 90% after GKS [2,8–11]. However, the effects of radiosurgery on AVMs are delayed and as complete obliteration generally occurs over a period of 2–5 years, the patient is exposed to risk of hemorrhage during this latent period, the Achilles heel of radiosurgical treatment of cerebral AVMs, especially in patients who present with an intracerebral hemorrhage [1–3,7]. The authors have evaluated their results of radiosurgical management analyzing the efficacy of GKS in

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patients with hemorrhagic versus non-hemorrhagic clinical presentation.

2. Material and methods

A total of 511 patients with cerebral AVMs underwent radiosurgical treatment (including those who underwent repeat GKS for failed primary GKS) at the All India Institute of Medical Sciences, New Delhi using Leksell Gamma Knife Model B^{TM} (Elekta Instruments AB, Stockholm, Sweden) between May 1997 and June 2006. Of these 511 patients, 157 patients harboring 160 AVM nidii who had available neuroimaging follow up consisting of at least one check digital subtraction angiography (DSA) formed the study group. The mean age of presentation was 28 years (range, 6–58 years); mean nidus volume being 3.64 cm^3 (range, 0.011–36.6 cm^3). The mean follow up period was 70 months (range, 13–121 months).

Gamma knife was offered to patients with AVM in an eloquent area, deep-seated AVM, residual AVM after surgery, embolization or conventional radiotherapy, large AVM not suitable for any other modality of treatment, patient's preference and residual AVM after failed radiosurgery. Decision regarding the best form of treatment was made after detailed discussion with our neuroradiological colleagues and based on clinical presentation. However, patient's choice and financial concerns formed an important parameter where all modalities of treatment were possible as in cases of low grade AVMs (Spetzler Martin (SM) grade I–II). Pre-GKS embolization was performed in patients with hemorrhagic presentation with presence of high risk features on angiograms like venous hypertension, arterial aneurysms, venous pouch, periventricular location, etc. or in patients with non-hemorrhagic presentation with higher grade/larger volume AVMs and the procedure was deemed possible by the neuroradiologists. Radiosurgery was performed using 201 source ^{60}Co Gamma Knife (Model B, Elekta Instruments AB, Stockholm, Sweden). The stereotactic frame was fixed to the patient's head under local anesthesia (general anesthesia was used in children below 8 years of age or uncooperative patient) and the position of the frame was adjusted on the head so as to bring the AVM nidus as close to the centre of the frame as possible. All patients underwent angiography along with a MRI brain for the stereotactic localization of the AVM. The software used for dose planning was Leksell Gamma Plan (Elekta Instruments, Inc.). The dose applied to the margin in majority of cases was 25 Gy using 50% isodose lines. Lower doses were given for lesions located in critical locations like basal ganglia/thalamus and for large volume AVMs.

Patients were advised clinical evaluation every six months after the treatment. MRI/CT in the follow-up period was done only in symptomatic patients. Hemorrhage was defined as clinically symptomatic event as sudden headache, seizure, focal deficits, death or a combination of these along with sign of fresh bleed from the previously diagnosed AVM detected by means of MRI or CT. Follow up angiography was performed at 2 years and yearly thereafter in the presence of residual AVM till 4 years. Presence of a residual AVM in an angiogram even after 4 years of GKS was considered as radiosurgical failure and second radio surgical treatment/embolization as deemed necessary was considered. As the time of cessation of AVM flow cannot be determined exactly, the no flow method was used which considered the time of cessation of AVM flow as occurring immediately before the time patient visit at which no flow was observed, thus theoretically maximizing the period of time during which the patient population would be at risk for hemorrhage. Data for patients with incomplete angiographic follow up was censored till their last follow up.

Statistical analysis was carried out using STATA 9.0 (College Station, TX, USA). Data were presented as number (%) and median (Range) as appropriate. The differences in medians were compared using Wilcoxon Rankum test and proportions were compared using Chi Square/Fisher Exact test. Kaplan-Meier method was used to calculate the obliteration free survival rate. The p-value < 0.05 was considered statistically significant.

3. Results

A total of 160 nidii were treated in these 157 patients. All the patients with angiographic follow up after the radiosurgical treatment were included in the present analysis. This does not involved any selection bias because angiography was the only routine follow up imaging study done in all patients starting two years after GKS and a MRI/CT was done only in very few of them mainly in patients with fresh deficits due to financial constraints. The clinical presentation of the patients is depicted in Table 1; hemorrhage being the most common mode of presentation. (64%) A hemorrhagic presentation was more common in patients with age <24 ($p = 0.0005$), nidus volume <3 cm^3 ($p = 0.026$) and deep location of AVM ($p < 0.001$).

AVM characteristics viz. location, SM grade along with radiation dosimetry parameters are summarized in Table 2. The volume of the AVM ranged from 0.011 to 36.6 cm^3 (mean 3.72 cm^3). The dose rate ranged from 3.629 to 1.253 Gy/min during the treatment period.

Previous surgery in the form of microsurgical resection of the AVM (3), hematoma evacuation (10), ventriculoperitoneal shunt (2) and external ventricular drainage (1) was

Table 1
Clinical summary of 157 patients with 160 arteriovenous malformations

Clinical presentation	No. of patients (%)
Hemorrhage	103 (64)
Seizure	47 (29)
Neurological (motor/sensory deficit, visual field defects)	53 (33)
Headache	26 (17)