

Evaluation of Gamma Knife treatment in management of intracranial arteriovenous malformations

Thesis Submitted by

Mohamed Nawar Badr
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Under supervision of

Prof. Dr\ Mohamed Sayed Ismail

Professor of Neurosurgery
Ain Shams University

Prof. Dr\ Adel Nabeh Mohamed

Professor of Neurosurgery
Ain Shams University

Prof.Dr\ Wael Abdel Halim Reda

Professor of Neurosurgery
Ain Shams University

Dr\ Khaled Mohamed Fathy Soaud

Assistant Professor of Neurosurgery
Ain Shams University

**Faculty of Medicine
Ain Shams University
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيمًا

صِرَاقُ اللَّهِ الْعَظِيمِ

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List of abbreviations

Abbreviation	Relevant meaning
AICA	anterior inferior cerebellar artery
BAVM	Brain arteriovenous malformation
CSF	Cerebrospinal fluid
CTA	Computerized Tomographic Angiography
DSA	Digital subtraction angiography
DWI	diffusion-weighted imaging
Flair	fluid attenuation inversion recovery
fMRI	functional MRI
GKS	gamma knife surgery
GKNS	gamma knife neurosurgery
GRE	gradient- recalled echo
MCA	Middle cerebral artery
PCA	Posterior cerebral artery
PICA	posterior inferior cerebellar artery
SRS	Stereotactic radiosurgery
TOF MRA	time of flight MRA

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Introduction

Brain arteriovenous malformations (BAVMs), first described as “erectile tumors” more than 200 years ago, are defined as the direct communication of arteries to abnormally tortuous and dilated veins without interposing capillaries. The natural history of these malformations remains uncertain, as they are usually treated soon after diagnosis. Traditionally, they have been thought of as congenital lesions resulting from abnormal vascular development, and their association with well-defined genetic disorders [1].

Brain AVMs can present with intracerebral hemorrhage (ICH) or they can be unruptured, that is, with symptoms resulting from mass effect, inflammation, altered hemodynamics from direct shunting, or recruitment of dilated perinidal capillary networks (for example, progressive neurological deficits, seizures, recurrent headaches, and congestive heart failure in neonates). Despite being an uncommon disease, BAVMs account for the majority of childhood hemorrhagic strokes and represent the most common cause of isolated, nontraumatic ICH in young adults [2].

Following the advent of noninvasive imaging techniques, including the widespread availability of CT and MR imaging, there has been a significant increase in the incidental detection of unruptured BAVMs. In patients with untreated BAVMs the annual hemorrhage rates of 2–4% (major morbidity 1.7%, mortality 1%, and combined morbidity and mortality 2.7% per year); however, the vast majority (71%) of these BAVMs had ruptured at initial presentation [2].

Three therapeutic modalities for arteriovenous malformation treatment (surgery, embolization, and radiosurgery) developed in the past years with specific tools, each tool with its own qualities [3].

Controversy exists regarding the optimal treatment of cerebral arteriovenous malformations. Current management guidelines are based on case series and cohort studies, as there is yet to be a randomized trial assessing treatment modalities according to patient and AVM characteristics. Nonetheless, it is generally accepted that patients referred to radiosurgery constitute a unique AVM population [4].

Stereotactic radiosurgery (SRS) has been one of the most significant advances in the field of neurosurgery and is now available to both large and small neurosurgical practices. Although invented by a neurosurgeon and originally designed to treat functional disorders of the brain, SRS is now a multidisciplinary subspecialty that integrates the talents of neurosurgeons, radiation oncologists, and medical physicists. The treatment indications have expanded to include tumors, vascular lesions, and pain syndromes of the brain and spine. The original device, the fixed source Gamma

Knife as invented by Lars Leksell, has been joined by various linear accelerator modifications and enhanced by the latest advances in imaging, high-speed computers, and robotics [5].

The goal of stereotactic radiosurgery for cerebral AVMs is to obliterate the AVM nidus, decrease the risk of future hemorrhage, and improve seizure severity, headache, or other neurological deficits. Complete AVM obliteration following radiosurgery generally takes 1–3 years and the risk of hemorrhage during this latency period remains essentially unchanged from untreated patients. Obliteration rates following radiosurgery range from 54 to 92% [4].

Aim of the study

The aim of this work is:

- 1) Reviewing the literature regarding intracranial arteriovenous malformation, pathology, diagnosis, and management using Gamma Knife radiosurgery.
- 2) Evaluation of Gamma knife radiosurgery as a modality of treatment of intracranial arteriovenous malformation.

Anatomy and Pathology of brain arteriovenous malformation

The etiology of BAVM remains unknown. Recent studies have suggested a role for genetic factors in the pathogenesis of sporadic BAVM which is further supported by reports of familial occurrence of BAVM [97] and the association of BAVM with known systemic genetic disorders (such as Osler-Weber-Rendu disease, Sturge-Weber disease, and Wyburn-Mason syndrome) [6].

Molecular characterization of BAVM tissue demonstrates a highly angiogenic milieu with evidence of increased endothelial cell turnover and inflammatory cell-mediated vascular remodeling. Taken together with a number of reports of de novo BAVM formation, radiographic growth after initial BAVM diagnosis and regrowth after successful treatment of BAVM these findings challenge the long-held assumption that BAVMs are static lesions of congenital origin. As such, future studies are needed that explore new paradigms in BAVM pathogenesis, including the possibility that BAVMs might represent benign slowgrowing vascular tumors (not just static congenital lesions), could result from acquired somatic mutations (not just congenital/germline mutations), and may represent aberrant adult vasculogenesis (not just persistent neonatal angiogenesis) [6].

I. Location and Angioarchitecture:

Cerebral AVMs are encountered throughout the central nervous system. They seem to predominate in areas supplied by the middle cerebral artery. Ninety-three percent are located supratentorially in the frontotemporal lobes. Intracranial dura may be affected, leading to the formation of dural vascular malformations. Angiography remains the gold standard method for diagnosing and evaluating AVMs and provides invaluable information about their angioarchitecture. Analysis of vascular patterns is useful in understanding the pathology of this disease [7].

II. Arterial Supply:

Cerebral AVMs typically receive their blood supply from intracranial branches of the internal carotid artery and vertebrobasilar systems. Arterial feeders are often multiple, but may sometimes be unique in arteriovenous fistulas. Valavanis in 1996 proposed a classification of arterial feeders based on embryological studies. The first type of arterial feeder is termed a terminal or dedicated type that ends in the nidus itself and corresponds to primitive penetrating vessels. The second type is the

pseudoterminal “functional” type or vessels “de passage,” which supply the brain beyond the nidus. These vessels are hypothesized to have initiated growth at a later stage or have developed from an established arterial source [8].

The last type is the indirect type and represents “satellite” branches from an artery in close proximity to the nidus. They correspond to vessel ingrowth after final structural development of the brain has been completed. Other sources of blood supply to AVMs may exist, such as those emerging from the choroid plexus or meningeal branches of the external carotid artery. The frequency of meningeal arterial contribution is significantly higher in superficial AVMs, especially in the temporal, parietal, and occipital regions [8].

Larger AVMs and lesions with higher degrees of angiographic arteriovenous shunting with steal phenomena are also factors that favor meningeal arterial development. Meningeal feeders were previously thought to be congenital, but recent evidence suggests that they may develop during growth of the AVM. Stenosis of the feeding arteries to cerebral AVMs has been reported in approximately 20% of cases. It is possible that if these stenosis progress, thrombosis of the AVM may occur [8].

III. Nidus Architecture:

The nidus is best conceived as a functional unit rather than a pathoanatomic entity. Yasargil described two types of arteriovenous connections within the lesion nidus: a direct fistulous connection between arteries and veins, and a plexiform pattern with ramifications existing between afferent and efferent vessels. Houdart et al. in 1993 proposed three types of niduses based upon hemodynamic and radiological features: the arteriovenous fistula, where direct communications exist between arteries and veins; the arterioloovenous fistula that exists between several arterial branches and a vein; and the arterioloovenulous fistula, which is the most classical type and is marked by ramifications between arteries and venules [8].

IV. Venous Drainage:

Venous blood from the AVM can drain through a single or multiple channels toward the superficial or deep venous systems. In high flow fistulas, an aneurysmal dilatation of the great vein of Galen can be observed [8].

V. Multiplicity and Associated Lesions:

Multiple intracranial AVMs are exceptional. The occurrence of multiple AVMs in one patient should raise the diagnosis of hereditary hemorrhagic telangiectasia. The association of intracranial and intraspinal AVMs is also rare. Other unusual associations include AVM and multiple congenital cardiac defects or tumors. Oligodendrogliomas and metastases have been reported to occur in proximity to AVMs, raising the question of whether there is a pathophysiological relationship between the two entities. Associated aneurysms are reported to occur with AVMs in 3% to 28% of patients in most case series. Three types of aneurysms have been described in relation to the location of the nidus: those related to vessels feeding the AVM, those remote from the AVM, and those that are intranidal. Perata et al. classified aneurysms associated with AVMs into four categories [8].

Type of the associated Aneurysm	location
Type 1	dysplastic lesions located on the circle of Willis independent from the nidus
Type 2	located on the circle of Willis on the same artery supplying the AVM
Type 3	related to a vessel feeding the AVM
Type 4	intranidal

Table 1: classification of aneurysms associated with AVMs

VI. Gross Pathology:

Autopsy analysis provides valuable information about the macroscopic features of AVMs. The postmortem appearance of an AVM is often less impressive than its intraoperative appearance because of the collapse of previously distended vessels. The living appearance of an AVM can in some measure be restored by the postmortem intravascular injection of a suitable medium. The most typical gross appearance is that of a “bag of worms” (Fig. 1). The mass is often wedge shaped, extending from the leptomeningeal surface deep into the parenchyma, frequently reaching or entering the ventricular system. This configuration accounts for the occurrence of bleeding within the intracranial compartment with the potential of extension toward the ventricles or the subarachnoid space. The vessels vary in size and may exceed one centimeter in diameter [8].

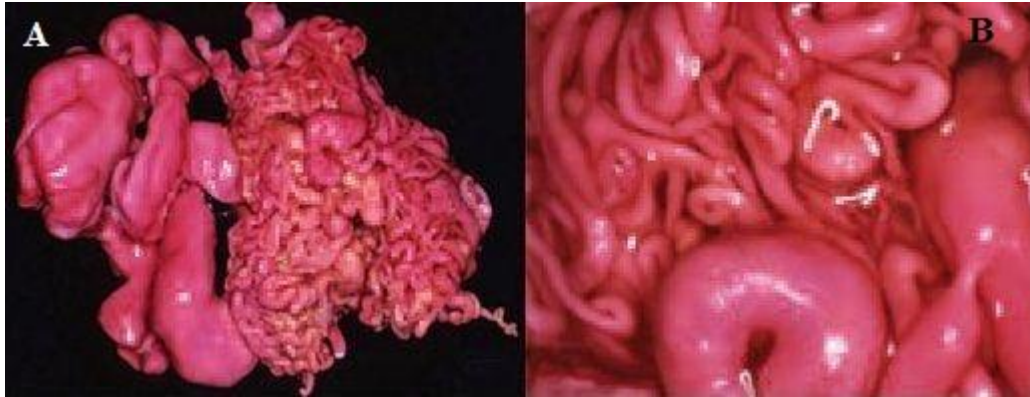


Figure 1: A large sylvian AVM in a 30-year-old woman. **A:** cast of the resected nidus showing that the nidus is a conglomerate of venous tangles and loops. **B:** cast surface at higher magnification [9]

Conversely, very small AVMs can be totally missed on pathologic examination even with thin slices. These malformations are typically cryptic or angiographically occult. They may be responsible for intraparenchymal hemorrhage where no etiology is found on angiographic or even intraoperative examinations. The vessel walls are variably thickened, and atheroma or calcification may be encountered macroscopically. Associated aneurysms may be observed on feeding or intranidal vessels. The arachnoid covering is usually discolored and thickened, while adjacent convolutions show variable degrees of atrophy as a result of chronic ischemia. Pigmentation from previous hemorrhage may be present in the adjacent brain, with loss of normal distinction between gray and white matter [8].

VII. Histopathological Features:

Cerebral AVMs exhibit mature vessel-wall characteristics and high flow profiles that predispose to vascular recruitment, arterialization of venous structures, and gliosis of intervening and adjacent brain tissues. High flow and hemodynamic stress can induce alterations to the mature vessel wall phenotype and normal structural integrity. Immunohistochemical studies show that cerebral AVMs exhibit similar features to normal vessels and show actin and myosin heavy chain staining within the media of vessel walls [10].