e-ISSN: 2807-7970

AKSONA

Volume 3 Number 2, July 2023

Case Series: Gamma Knife Radiosurgery in Brain Arteriovenous, Is It Good Enough?

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Article info

Article History:
Received Apr 10, 2022
Revised Jul14, 2023
Accepted Jul 28, 2023
Published Jul 31, 2023

Keywords:
Brain arteriovenous malformation

Complication
Full obliteration

Gamma knife radiosurgery

Health risk

ABSTRACT

Introduction: Brain arteriovenous malformations (AVMs) are relatively uncommon. Gamma Knife radiosurgery (GKRS) is one of the AVM's therapeutic interventions, with both advantages and disadvantages. Here, we report the results of two cases of brain AVM after GKRS.

Cases:

Case 1: Non-contrast head MRI imaging of a 45-year-old man with persistent left-sided headaches revealed a 1.4 x 2.5 x 2.28 cm AVM nidus in the left parasagittal frontal lobe. After a single GKRS with a 25-Gy marginal dose, the MRI contrast showed complete obliteration, with persistent perifocal edema and headache.

Case 2: A 25-year-old woman with a history of generalized seizures. The angiograms revealed an AVM nidus with a diameter of 32.58 mm on her right posterior frontal lobe. After a single GKRS with a 22-Gy marginal dose, the MRI contrast showed full obliteration with large edema. The patient had presented with hemiparesis.

Conclusion: In these cases, the results after GKRS were full obliteration with complications of edema, headache, and hemiparesis. We also found that complications appear to be associated with adverse radiation effects.

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INTRODUCTION

Arteriovenous malformations (AVMs) are rare conditions in the vascular system that consist of a complex, tangled web of abnormal blood vessels (nidus) in which feeding arteries are directly joined to a draining vein network without an intermediate capillary bed.[1,2] AVMs are most likely congenital vascular lesions due to capillary formation failure during embryonic development.[3]

Brain AVMs are uncommon, with an incidence between 0.01-0.001% and a prevalence of < 1%, although the probability of actual cases may be higher than the data collected because many are asymptomatic cases. Furthermore, only 12% of AVMs become symptomatic, according to autopsy data.[4,5] Brain AVMs are of special concern due to the inherent high risk of bleeding from the abnormal blood vessels, which can cause neurological damage.[5] Gamma Knife radiosurgery (GKRS) is one of several therapeutic options for AVM, which also include conservative management, surgical resection, stereotactic radiosurgery (SRS), endovascular embolization, and combinations of these treatments (multimodal therapy).[6] However, Gamma Knife radiosurgery (GKRS) effectively reduces the risk of bleeding, seizure, and some neurological deficits associated with stroke. These treatments are very well known for being effective and minimally invasive.[7,8] However, there is still a risk of bleeding and radiation-induced perifocal edema and seizure before complete resolution of the nidus can be obtained with Gamma Knife radiosurgery (GKRS). Here we report the results of brain AVM therapy using Gamma Knife Radiosurgery (GKRS) in this retrospective case series, following from 2016 to 2019 in Case 1 and 2015 to 2017 in Case 2.

CASES

Case 1

A 45-year-old man with a history of headaches since July 2016 was hospitalized at Bethesda Hospital, Yogyakarta, in May 2018 with persistent left-sided headaches and a Visual Analog Scale (VAS) of 5 to 7. There was no history of seizures, nausea, or vomiting. No family member exhibited the same symptoms. The patient is an aboard employee who routinely consumes alcohol (one glass per day), does not smoke, and has a minimum of two routine workouts a week. The patient had a history of hypertension.

A physical and neurological examination revealed no abnormalities. A non-contrast head MRI showed a 1.4 x 2.5 x 2.28 cm AVM nidus in the left parasagittal frontal lobe (Figure 1). Angiography, the gold standard to diagnose AVM nidus, showed it was fed from the left anterior cerebral branch with a draining vein to the superior sagittal sinus (Figures 2a and 2b). For treatment planning and evaluation, a combination of MRI and angiography is also used. In July 2018, the patient received Gamma Knife radiosurgery (GKRS) with a 25-Gy marginal dose. The aneurysm was resected into 1 x 1.4 x 1.5 cm with perifocal edema after Gamma Knife radiosurgery, MRI, and MRA with contrast (Figures 3a and 3b). The pain patient's VAS decreased to 3 or 4 a year after the radiosurgery. The MRI contrast showed no AVM nidus, but the perifocal edema became larger (Figure 3c).

Case 2

A 25-year-old woman with a history of generalized seizures was admitted to Bethesda Hospital, Yogyakarta, in June 2015. This was her first seizure since birth. The patient was a dental student with no history of hypertension, diabetes melitus, or any medical issues. The patient has regular workouts such as bicycling and running. Babinski was positive on the left on the neurological and physical examinations; motor, sensory, and cranial nerve exams were normal. Angiograms showed a 32.58 mm diameter AVM nidus on the right posterior frontal lobe (Figures 4a, 4b, and 5). In July 2015, she had Gamma Knife radiosurgery (GKRS) with a 22-Gy marginal. Five months after radiosurgery, the patient developed left-sided hemiparesis, and an MRI showed large edema in the right posterior frontal lobe (Figure 6a). The AVM nidus was totally resected two years after Gamma Knife radiosurgery (GKRS) (Figure 6b), although encephalomalacia and gliosis perifocal remained in the right posterior frontal lobe.

DISCUSSION

Arteriovenous malformations of the brain are focal abnormalities of arteriovenous shunts that may be connected to each other by one or more fistulas, with feeding arteries and draining veins in the brain parenchyma. This direct connection of arteries and veins (lack of a capillary bed) causes low-resistance pulsation and turbulent high-velocity blood flow, creating high-pressure vascular channels within both the AVM and the venous drainage, especially in veins with fibromuscular thickening and inadequate elastic lamina, making them more likely to rupture, which increases the risk of hemorrhage.[6,9] High blood

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flow can also trigger the blood steal phenomenon, in which the AVM steals blood from normal cerebral tissue, causing focal neurologic signs and symptoms referable to the area of the brain where effective flow is stolen, such as seizures and focal neurological deficits. Furthermore, mass effects due to direct compression of brain tissue or swelling related to the AVM result in focal neurological deficits.[10,11]

AVM's clinical presentation might vary depending on size and the quantity of arteriovenous shunting inside these lesions, which can include signs of intracranial hemorrhage (focal deficits, nausea, vomiting, and so on), seizures, and headaches.[4] Many cases had been reported in which the most frequent location was on the frontal, followed by the parietal, temporal, and occipital lobes.[9] Both locations in the first case had a 1.4 x 2.5 x 2.28 cm nidus in the parasagittal frontal lobe, and the patient in the second case had a 32.58 mm diameter AVM in the right posterior frontal lobe. Based on size, Gamma Knife radiosurgery (GKRS) is ideal for small AVMs (< 3 cm).[12]

Decisions on the management of cerebral AVMs are still being debated due to a lack of data on the risk of hemorrhage as well as predictors and treatment complications.[13] The main goal of treatment for brain AVM is complete nidus obliteration to prevent rebleeding and potential neurological deterioration.[14,15] Gamma Knife radiosurgery (GKRS) itself is intended to induce progressive occlusion of an AVM by using high-dose targeted radiation. A radiation source, such as a Gamma Knife, delivers precise, focused treatment using a navigation system. Radiation causes endothelial damage and intimal layer thickening in the AVM, which leads to nidal vessels thrombosis. This progressive obliteration of the AVM takes about 2–3 years, with a median of about 20 months. The radiation dose interval to achieve 90% or higher full obliteration is over 20-Gy, 60–70% for AVM margin doses of 15-Gy, and 70–80% for AVM margin doses of 18-Gy. After 3-5 years, Gamma Knife radiosurgery (GKRS) has a 70–85% obliteration rate and a low morbidity rate. Regardless, the key factors influencing the risk of delayed radiation-related complications are the AVM dose (≥ 12 Gy), brain volume, and AVM location. Our patient in Case 1, received a 25-Gy marginal dose of Gamma Knife radiosurgery; full obliteration was reported one year later, and 22-Gy was reported three years later in the second patient. As seen in Case 1, the Pollock-Flickinger score indicated excellent outcomes in smaller volumes of nidus.[16–20]

Although our patients experienced full obliteration, the possibility of adverse radiation effects (ARE) as a complication was there since, in both cases, they were given ≥ 12-Gy. Possible complications reported during long-term follow-up after GKRS are hemorrhage, radiation-induced necrosis, perilesional edema, delayed cyst formation, seizures, psychiatric abnormalities, cranial neuropathy, arterial stenosis, radiation-induced tumor, and symptomatic post-radiosurgery neurological sequelae. Bir *et al.* also reported that a few patients suffered from persistent clinical symptoms following GKRS, such as neurological deficits (1.7%), seizures (1.7%), and headaches (2.3%), but most patients had good clinical outcomes.[17] Both subjects in this case had cerebral edema, including headaches in Case 1 and hemiparesis in Case 2. The formation of edema may be associated with cerebrovascular impairment, disruption of the blood-brain barrier, or radiation-induced damage to microglia and astrocytes. This is similarly related to the encephalomalacia and gliosis perifocal that occurred in Case 2. As a result of direct compression of brain tissue or swelling caused by the AVM, it results in focal neurological deficits such as hemiparesis, as in Case 2.[21] Yen *et al.* also reported hemiparesis, presumably because of the mass effect, or steal phenomenon. This phenomenon also activates trigeminovascular nerve afferents, resulting in headaches.[15] Other theories explain Cortical Spreading Depression (CSD), a slowly propagating wave of depolarization that is accompanied by massive transmembrane ion fluxes and is followed by suppression of brain activity and changes in regional cerebral blood flow (rCBF), which can cause headaches.[19]

CONCLUSION

In each of these cases, Gamma Knife radiosurgery (GKRS) provided complete obliteration. Some side effects, such as cerebral edema, headache, and hemiparesis, may develop.

Acknowledgement
Thank you to all committees and assessors of the 22nd Continuing Neurological Education (CNE) scientific meeting, Surabaya, Indonesia.

Conflict of Interest
The authors have no conflict of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contribution
All authors made a significant contribution to the study.

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TABLES AND FIGURES

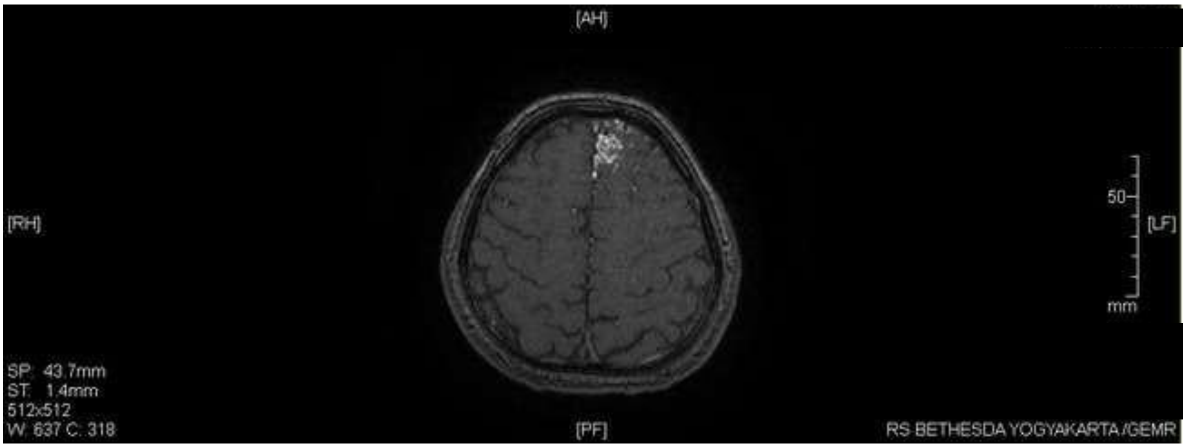

Figure 1. Head MRI showed a 1.4 x 2.5 x 2.28 cm AVM nidus in the left parasagittal frontal lobe

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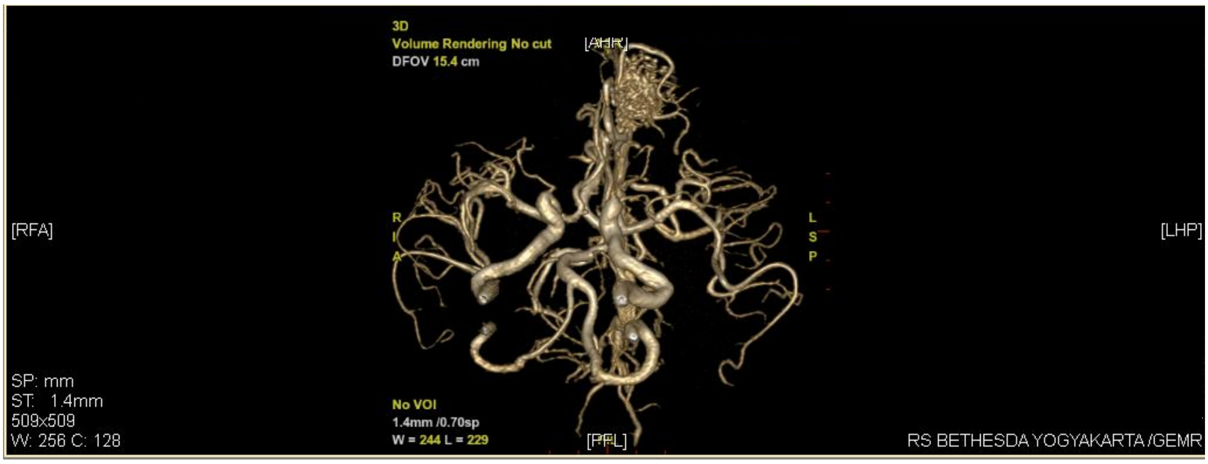

Figure 2a. AVM in the left parasagittal frontal lobe gets feeding from the left anterior cerebral branch with draining vein to the superior sagittal sinus (posterior view)

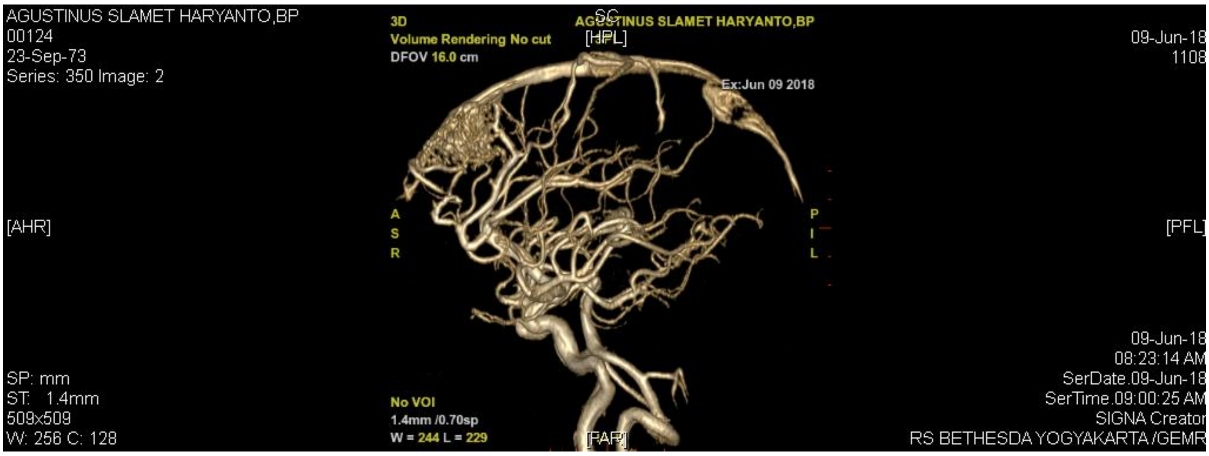

Figure 2b. AVM in the left parasagittal frontal lobe gets feeding from the left anterior cerebral branch with draining vein to the superior sagittal sinus (lateral view)

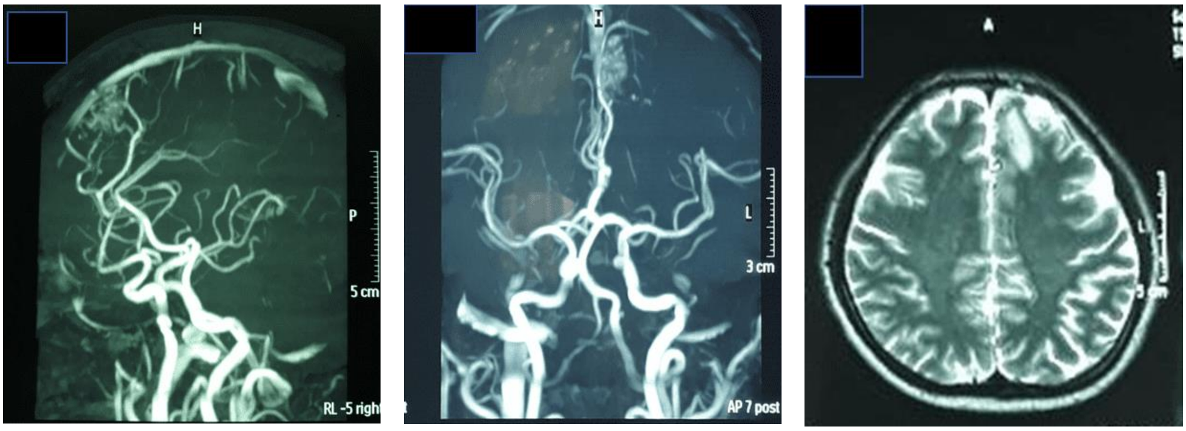

Figure 3a and b. Head MRA with contrast post Gamma Knife radiosurgery showed resected AVM nidus to 1x 1.4x 1.5 cm, c. Head MRI with contrast showed perifocal edema

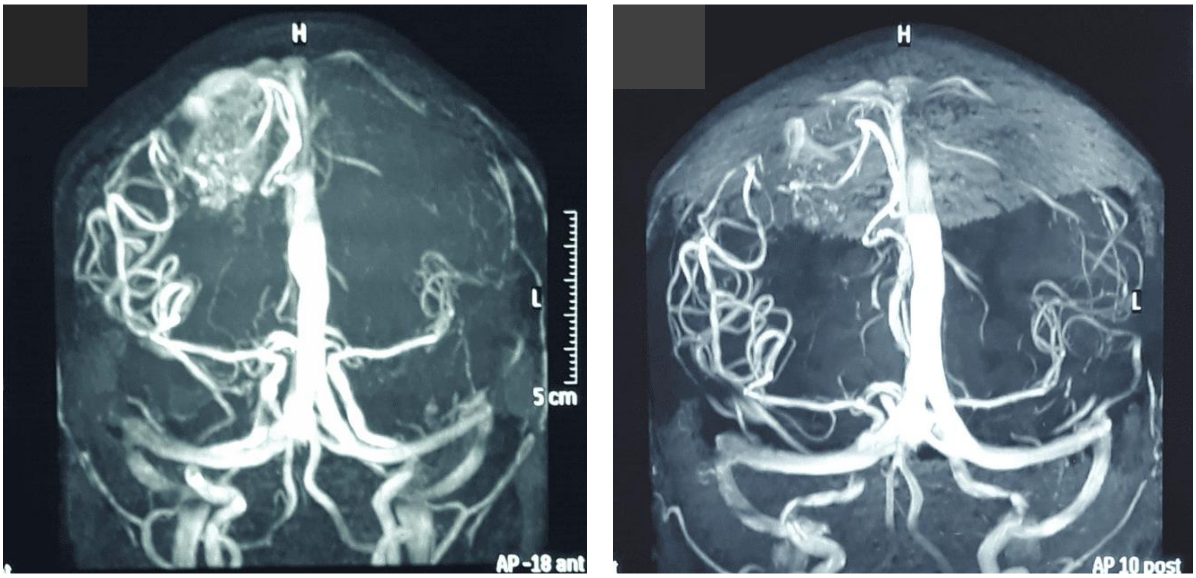

Figure 4a. MRA showed 32.58mm diameter of AVM nidus, b. MRA 2 years post Gamma Knife radiosurgery (GKRS) showed full obliteration

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Figure 5. Digital Substraction Angiography (DSA) before Gamma Knife radiosurgery

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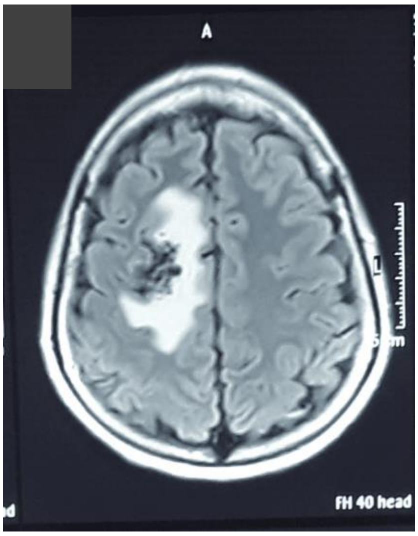

Figure 6a. Five months post Gamma Knife radiosurgery (GKRS) showed cerebral edema in right posterior frontal lobe

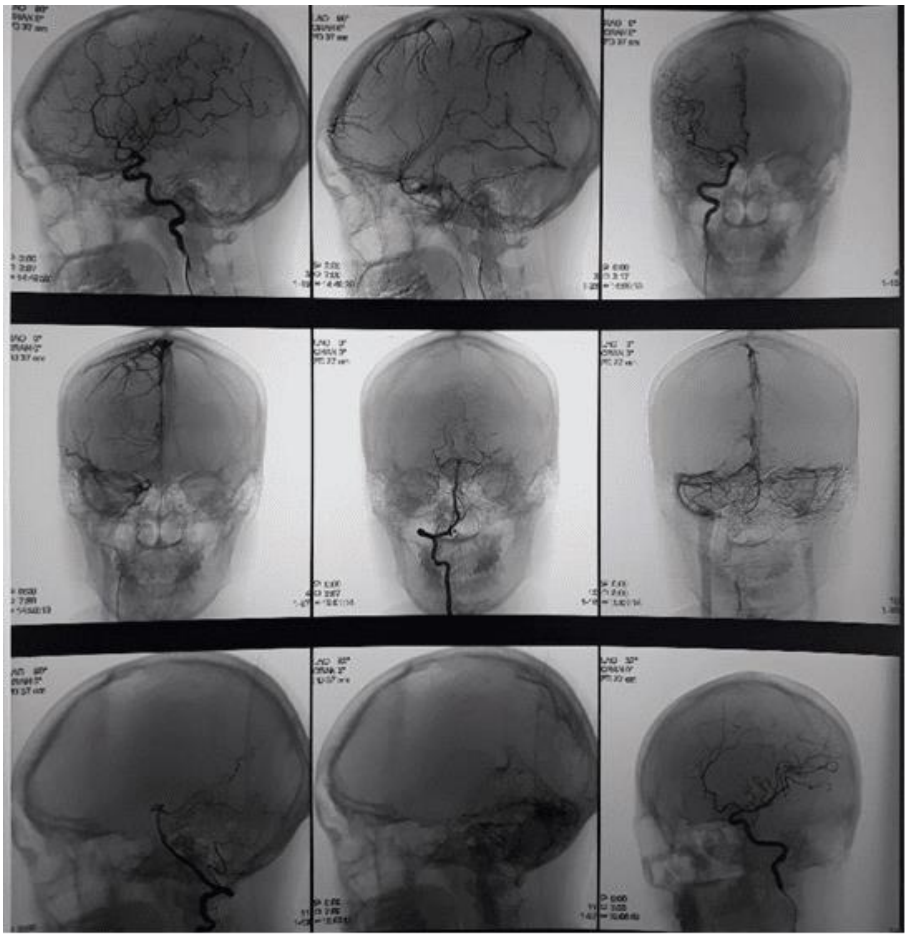

Figure 6b. CT Angiograph 2 years post Gamma Knife radiosurgery (GKRS) showed full obliteration