Case Report

Left Thalamus Arteriovenous Malformation Secondary to Radiation Therapy of Original Vermian Arteriovenous Malformation: Case Report

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A 70-year-old gentleman with history of hypothyroidism, hyperlipidemia, hypertension, and right superior cerebellar aneurysm presented to the neurosurgery service in 2008 with vertigo. Diagnostic cerebral angiography performed that year demonstrated a vermian arteriovenous malformations (AVM). The patient underwent stereotactic proton beam radiosurgery, which resulted in a decrease in flow and size of the lesion, and the patient was lost to follow-up. Now at the age of 80, the patient presented with acute gait instability. Cerebral angiogram demonstrated his stable vermian AVM and a new 1.1 cm AVM nidus in the region of the left posterior thalamus. Although AVMs are often described as congenital lesions, there is a growing body of literature suggesting that AVMs can grow, spontaneously regress, and even arise de novo in response to some insult. Understanding what leads to the growth, remodeling, regression, and hemorrhage of AVMs is crucial in order to better direct therapeutic endeavors. We would argue that this patient's AVM is secondary to endothelial cell damage from radiation therapy. Radiation can cause endothelial cell injury and upregulation of factors, such as vascular endothelial growth factor and transforming growth factor beta expression, which are implicated in AVM development pathways. We believe that this patient's new AVM is secondary to entrance radiation dosing affecting the thalamus during radiation therapy for the original vermian AVM.

Key Words: Arteriovenous malformation—secondary arteriovenous malformation—radiation induced AVM—vermian AVM—radiosurgery—thalamus AVM

Introduction

Arteriovenous malformations (AVM) of the brain are traditionally thought to be products of maldevelopment that allow capillary connections between arteries and veins.[1] Genetic syndromes, such as hereditary hemorrhagic telangiectasia and cerebrofacial arteriovenous metameric syndromes, have been associated with the congenital formation of AVMs. However, the classic understanding that AVMs are congenital lesions arising from vascular dysgenesis has been recently disputed. There is a growing number of cases in the literature that document and support spontaneous and dynamic changes to AVMs, such as interval enlargement,[2] self-remodeling,[2] and spontaneous obliteration.[3-7] These changes can be primary or secondary to traumatic or ischemic injury.[8] In the present report, we present a case of a new, disparate thalamic AVM nidus that is found 10 years after

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radiosurgery for a vermian AVM. At the time of writing, this was the second report in the literature of an AVM developing after radiation therapy.

Case Presentation

A 70-year-old gentleman with history of hypothyroidism, hyperlipidemia, hypertension, and right superior cerebellar aneurysm presented to the neurosurgery service in 2008 after episodes of vertigo that would last 30-120 seconds. Initial evaluation with CTA and MRI/MRA demonstrated a vascular abnormality in the right posterior circulation, initially described as a distal right PCA aneurysm. Diagnostic cerebral angiography was later performed that year, which demonstrated a vermian AVM supplied by branches of the right superior cerebellar artery and venous drainage via superficial cerebellar veins to the torcula herophili and superior vermian vein (Fig 1). After multidisciplinary discussion, the patient underwent stereotactic proton beam radiosurgery for obliteration (Fig 2). Postradiosurgery the patient had no new neurologic events and serial brain imaging was performed to assess for vascular changes. The patient was lost to follow-up.

The patient presented 10 years later with acute gait instability. On exam, he experienced vertigo from lying to standing and truncal instability. Head CTA showed a new 7 mm vascular lesion in the left ambient cistern upstream relative to the vein of Galen, in addition to and separate from his previously treated vermian AVM. MRI of the brain showed no acute infarction or intracranial hemorrhage. Given the interval changes, the patient underwent a transfemoral cerebral angiogram to better define the residual AVM and new aneurysm.

The cerebral angiogram demonstrated a new 1.1 cm AVM nidus just anterior to the vein of Galen in the region of the left posterior thalamus. Arterial supply was via bilateral superior cerebellar and posterior cerebral artery branches. The nidus drained through the ectatic, 4.5 mm left basal vein of Rosenthal to the vein of Galen and straight sinus (Fig 3).

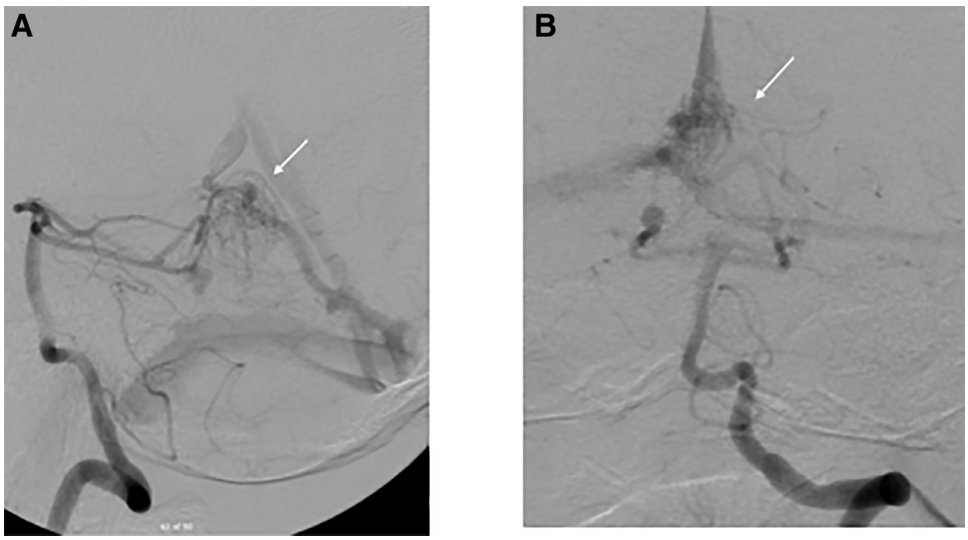

Figure 1. *(A) Lateral and (B) anterior-posterior projections of 2008 digital subtraction angiography, left vertebral artery injection, illustrating a vermian AVM supplied by branches of the right superior cerebellar artery (white arrow). AVM, arteriovenous malformations.*

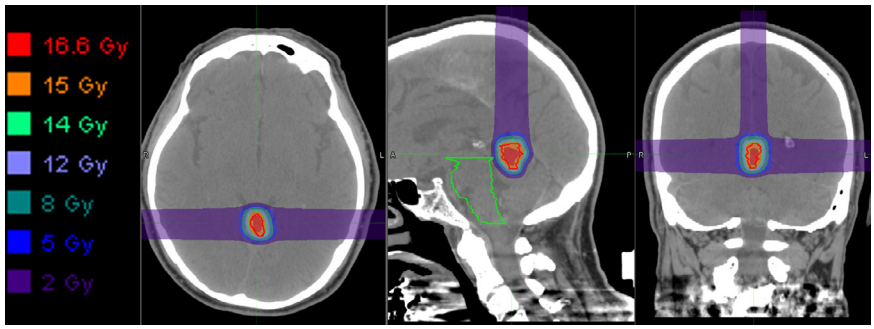

Figure 2. *Axial, sagittal, and coronal views of CT image of AVM with dosimetry planning for stereotactic proton beam radiosurgery for obliteration. AVM, arteriovenous malformations.*

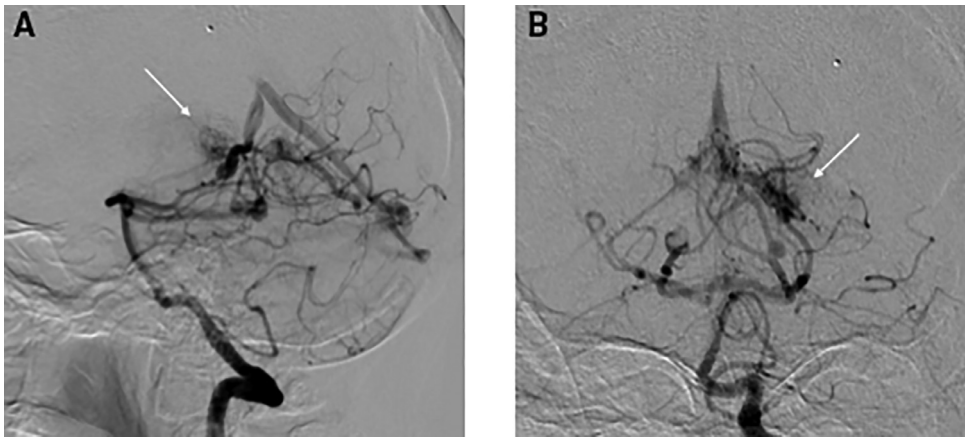

Figure 3. *(A) and (B) 2018 digital subtraction angiography, left vertebral artery injection, illustrating new 1.1 cm AVM nidus supplied with bilateral superior cerebellar and posterior cerebral artery branches (white arrow). AVM, arteriovenous malformations.*

Follow-Up

In this patient, nidal obliteration was never achieved. Nevertheless, there was a decrement in flow through the nidus and nidal size, and the lesion has not ruptured after 10 years since the procedure. However, the patient now presents with a neurological deficit in the setting of a radiographic changes which angiography revealed to be a second nidus. Others have proposed using the classification of "secondary" as part of the nomenclature in AVMs.[8] Due to the growing use of cranial imaging, there have been more cases published that show that these lesions are not formed congenitally but rather "spontaneously" (Table 1). At the time of writing, there were 33 cases in both adult and pediatric populations.

Discussion

Understanding what leads to the growth, remodeling, regression, and hemorrhage of AVMs is crucial in order to better direct therapeutic endeavors. There is a complex interplay between the structural and hemodynamic properties that lead to the dynamic changes of AVMs. Impaired autoregulation has been described as a potential root cause for the formation of AVMs.[9] Several forces, including vascular injury, abnormal endothelial signaling, and microshunt formation, have all been identified as potential mechanisms of impaired autoregulation.[10-12] We would argue that this patient's AVM is secondary to endothelial cell damage from radiation therapy.

Stereotactic radiosurgery (SRS) is an established treatment method for the treatment of brain arteriovenous malformations. Radiosurgery is often chosen over other modalities like surgery or embolization for lesions smaller than 3 cm in diameter or less than 10 cm^3 in volume that are located in an eloquent area where surgery is likely to cause a neurologic deficit.[13-16] SRS involves using precise, single fraction dose of radiation to create a desired biological response within a specific region in the brain while minimizing radiation exposure to the surrounding tissue (IRSA Guideline). In the case of AVMs, the goal of SRS is to gradually occlude the vessels of the malformation over time.[14] Obliteration of the AVM ranges from less than 50% to greater than 90%, with lower cure rates associated with lesions greater than 3 cm in diameter.[13,17-20]

Adverse effects of radiosurgery include short-term problems such as headache from the frame, nausea from pain medication, and perhaps a small acute increased risk of seizure in patients with cortical lobar AVMs, particularly if a prior history of episodic seizures is present.[21] Late complications after radiosurgery, include hemorrhage, edema, or necrosis.[21] Hemorrhage is the most common and feared late complication. Because of this, 1 disadvantage of the procedure is that there is a risk of hemorrhage during the lag period from the time of treatment to the time of occlusion of vessels.[22]

Radiation has been shown to cause endothelial cell injury, thereby inducing vessel remodeling and vascular endothelial growth factor and transforming growth factor beta expression.[8,23-27] These growth factors have been associated as part of the pathway of AVM formation. Therefore, this raises the theoretical possibility that AVMs could arise from radiation therapy.[12,28,29] We theorize that there have been some entrance radiation dosing affecting the thalamus during the radiosurgery for the original vermian AVM. Given the new symptoms with relatively unchanged structural lesions, we believe that an AVM secondary to radiation is the most likely explanation in this presentation.

Table 1. *Reported cases of secondary AVM formations*

Study	Age (years), sex	AVM location	Detection interval (years)	Associated primary condition	Imaging modality
Schmit et al. (1996)	11, M	Left posterior parietal	9	Moyamoya disease−parietal infarct	MRI and digital subtraction angiography
Friedman et al. (2000)	61, M	Right cerebellum	2	Tentorial dural AV fistula	Digital subtraction angiogram
Bulsara et al. (2002)	32, F	Right posterior temporal	6	Inflammatory/demyelinating disease	MRI and digital subtraction angiography
Akimoto (2003)	27, F	Cingulate gyrus, corpus callosum	17	Previously resected AVM (splenium, occipital lobe)	CT and digital subtraction angiography
Miyasaka et al. (2003)	50, F	Multiple AVMs	8	Right parietal ICH	CT and digital subtraction angiography
O'Shaughnessy et al. (2005)	6, F	Right sylvian	3	Sickle Cell and Moyamoya disease	CTA, MRI and digital subtraction angiogram
Gonzalez et al. (2005)	7, F	Right posterior temporal	4	Trauma—left frontal ICH Intractable seizures	MRI
Song et al. (2007)	2.5, F	Left CPA	2.5	Hemangiomatosis	MRI
Stevens et al. (2009)	9, F	Left temporal-occipital	3	Seizures	MRI and digital subtraction angiography
Jeffree and Stoodley (2009)	5, M	Right insula, Basal ganglia	5	Previous ICH	CT and digital subtraction angiography
Jeffree and Stoodley (2009)	15, M	Right temporal-parietal	5	Previous ICH	Digital subtraction angiogram
Jeffree and Stoodley (2009)	18, M	Left parietal-occipital	10	Previous ICH	CT and digital subtraction angiography
Mahajan et al. (2010	30, F	Left frontal-parietal	14	Bell's palsy, seizure	CT and MRI
Alvarez et al. (2012)	8, M	Posterior third ventricle (vein of Galen)	2	Cavernous malformation, DVA	CT and MRI
Ozsarac et al. (2012)	50, M	Left temporoparietal	25	Epilepsy	CT
Mathon et al. (2013)	9, M	Right Sylvian fissure	4	Medulloblastoma	MRI and digital subtraction angiography
Kilbourn et al. (2014)	18, M	Pons	7	Congenital hydrocephalus, absence seizures	CTA
Fujimura et al. (2014)	14, F	Right occipital	4	Moyamoya disease	MRA
Morales-Valero et al. (2014)	35, F	Left parietal-occipital	4	Unknown, no history of cerebrovascular disease	MRI and digital subtraction angiography
Morales-Valero et al. (2014)	56, M	Left temporal	14	TIA	Digital subtraction angiogram
Miller et al. (2014)	12, F	Left parietal	6	Left traumatic subdural hematoma	MRI and digital subtraction angiography
Neil et al. (2014)	24, M	Left parietal	9	Seizures	MRI and digital subtraction angiography
Yeo et al. (2015)	7, M	Left cerebellar	6	Seizures	MRI
Yeo et al. (2015)	16, F	Left anterior temporal	9	Seizures	MRI
Nakamura et al. (2016)	53, M	Left frontal	3	Left frontal ICH	Digital subtraction angiogram
Markham and Hollingworth (2016)	4, M	Left posterior superior temporal gyrus	4	Unknown, no history of cerebrovascular disease	MRI and digital subtraction angiography
Shimoda et al. (2016)	5, M	Right parietal	4.5	HHT	MRI and digital subtraction angiography

Table 1 (*Continued*)

Study	Age (years), sex	AVM location	Detection interval (years)	Associated primary condition	Imaging modality
Pabaney et al. (2016)	52, F	Left basal frontal	8	Ischemic stroke	CTA and digital subtraction angiography
Koch et al. (2016)	24, F	Left medial temporal (left choroidal)	5	Radiation therapy	MRI and digital subtraction angiography
Shi et al. (2017)	33, F	Left temporal-occipital	2	Left transverse sinus thrombosis	CTA
Shi et al. (2017)	72, M	Right temporal-occipital	11	Previous left frontal AVM	MRI
Santos et al. (2018)	7, M	Left thalamic	3	Right hemispheric stroke, cerebral aneurysm	MRI
Present Case	80, M	Left posterior thalamus	10	Radiation therapy	CTA and digital subtraction angiography

Abbreviations: AVM, arteriovenous malformations; HHT, hereditary hemorrhagic telangiectasia; CTA, computed tomography angiography; MRA, magnetic resonance angiography.

Addendum: References of reported cases of secondary AVM

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