Case Report

Symptomatic de novo arteriovenous malformation in an adult: Case report and review of the literature

Jayson A. Neil, Daphne Li, Michael F. Stiefel, Yin C. Hu

Department of Neurological Surgery, New York Medical College, Valhalla, New York, USA

E-mail: Jayson A. Neil - jayson.neil@gmail.com; Daphne Li - daphne.li@gmail.com; Michael F. Stiefel - StiefelM@wmcm.com; *Yin C. Hu - HuY@wmcm.com

*Corresponding author

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INTRODUCTION

Cerebral arteriovenous malformations (AVMs) are abnormal vascular connections that form between arteries and veins, without an intervening capillary bed or neural tissue. They are a heterogeneous group of vascular lesions varying in locations, sizes, and venous drainages. The incidence of cerebral AVMs in the general population is less than 1%. AVMs may be clinically silent or present with hemorrhages, often in the second or third decade of life. Less commonly, AVMs may manifest other symptoms such as seizures and those related to mass effect or ischemic steal. The pathogenesis of AVMs remains incompletely elucidated and has traditionally been thought to be congenital. We present a case of symptomatic de novo cerebral AVM in a patient with an initial negative magnetic resonance imaging (MRI) of the brain at the age of 15, but 9 years later developed a left parietal AVM.

CASE REPORT

History and presentation

The patient is a 24-year-old right-handed male with a past medical history significant for a seizure disorder. He experienced his first seizure at age 15, resulting in a severe facial burn after falling on a home heater. An initial MRI of the brain was performed, which was negative [Figure 1]. He continued to have intermittent seizures until age 17 when he was placed on antiepileptic medications. At the age of 24, he suffered a 4-min generalized tonic-clonic seizure. Further workup including an MRI of the brain revealed a 2 × 1.7 × 1.8 cm left parietal AVM [Figure 2], which was not present...
on the MRI 9 years ago. Digital subtraction cerebral angiogram (DSA) showed a Spetzler–Martin grade II AVM in the left parietal region with arterial feeders from the left middle cerebral artery (MCA) and the left posterior cerebral artery (PCA) and early venous drainage into the superior sagittal sinus [Figure 3].

**Procedure**

After a thorough discussion about the natural history and treatment options (observation, microsurgical, and radiosurgery), the patient elected to have the AVM resected. The patient underwent presurgical Onyx (eV3 Neurovascular Inc., Irvine, CA) embolization of the AVM followed by a left parietal craniotomy and resection of the AVM without complication or morbidity. Postoperative cerebral angiography demonstrated no residual AVM nidus or early venous drainage. The hospital course was unremarkable and the patient was discharged home on postoperative day three. At 6 months follow-up, the patient remained seizure free and not on antiepileptic medications.

**DISCUSSION**

Although cerebral AVMs have traditionally been considered congenital lesions, there is an increasing number of case reports of *de novo* AVMs [Table 1]. To date, there are nine other cases that have reported these phenomena. Of these nine cases, seven reported the occurrence of *de novo* AVMs in patients that had other vascular pathology, such as prior resection of AVMs in different locations during childhood.[1,3,4,13,16‑18] The majority of those cases were documented in pediatric patients. The literature review yielded five cases that reported *de novo* AVM development in patients without vascular pathology on prior MRI, as is the case in this patient.[5,9,11,14,20] Of these *de novo* AVM cases, only two of the reported cases involved adult patients.[5,14] Together, with the case we have presented in this paper, these reports comprised a very small, but growing body of literature that challenged the traditional view of the pathogenesis of cerebral AVMs.

The pathogenesis of AVMs remains ill defined. It is a widespread belief that AVMs are congenital, arising between weeks 4‑8 of embryological growth.[8] The symptomatic presentation of AVMs in adults before the age of 40, in addition to the *de novo* AVMs reported in children, support the concept of the temporal vulnerability of vascular elements to a physiologic or environmental trigger.[20] These triggers, which can be mechanical, inflammatory, thrombogenic, ischemic/hypoxic, or hormonal, generally lead to hemodynamic stress.[5,20] Disturbances of the venous drainage system may contribute to the formation of cerebral AVMs. Venous stenosis, occlusion, or agenesis during embryology or chronic venous hypertension during childhood and adulthood can result in tissue hypoxia and drive the impetus for angiogenesis.[12,15,1,22,23] However, the role of the venous hypertension in the growth of an AVM remains indeterminate. Other vascular lesions such as dural or pial arteriovenous fistula in the brain and spine can develop after trauma, infection, or inflammation further support the notion of environmental influences stimulating angiogenesis. Many of these injuries result in the release or increased expression of transforming growth factor (TGF) and vascular endothelial growth factor (VEGF), which play important roles in angiogenesis. The overstimulation of angiogenesis due to these stressors leads to vascular remodeling and other changes resulting in the maturation of AVMs.[24]
Table 1: Previously reported cases of de novo AVM formation

| Literature                                                                 | Patient gender | Age at time of initial imaging | Reason for initial imaging                                                                 | Type of imaging performed | Age at AVM diagnosis | Presenting symptoms at time of AVM diagnosis | Type of imaging performed for AVM diagnosis |
|---------------------------------------------------------------------------|----------------|-------------------------------|-------------------------------------------------------------------------------------------|----------------------------|----------------------|---------------------------------------------|--------------------------------------------|
| No prior vascular pathology                                               | Female         | 26 years old                  | Multiple cranial nerve deficits and ataxia a few days after a streptococcal throat infection, Exclusion of vasculitis | Cerebral angiogram        | 32 years old         | Severe headache, nausea and vomiting         | CT, MRI, cerebral angiogram               |
| Bulsara KR, Alexander MJ, Villavicencio AT, Graffagnino C: De novo cerebral arteriovenous malformation: Case report. Neurosurgery 50:1137-40; discussion 1140-1, 2002 | Female         | 3 years old                  | Struck by car suffering mild head injury and experiencing posttraumatic epilepsy          | CT and MRI                | 7 years old          | Intractable epilepsy                        | MRI, MR angiography, cerebral angiogram   |
| Gonzalez LF, Bristol RE, Porter RW, Spetzler RF: De novo presentation of an arteriovenous malformation: Case report and review of the literature. J Neurosurg 102:726-729, 2005 | Female         | 6 years old                  | Bell's Palsy                                                                            | MRI                       | 9 years old          | Increased seizure activity, behavioral changes, ataxia, aphasia after minor head injury | CT, MRI                                   |
| Stevens J, Leach JL, Abruzzo T, Jones BV: De novo cerebral arteriovenous malformation: Case report and literature review. AJNR Am J Neuroradiol 30:111-112, 2009 | Female         | 16 years old                 | Evaluation of seizures leading to diagnosis of epilepsy treated with phenytoin           | Cerebral angiogram        | 30 years old         | 5 year history of complicated migraines and 1 episode of seizure | CT post-contrast, MRI, bilateral carotid angiography |
| Mahajan A, Manchandia TC, Gould G, Bulsara KR: De novo arteriovenous malformations: Case report and review of the literature. Neurosurg Rev 33:115-119, 2010 | Male           | 25 years old                 | Cerebral infarctions, seizures                                                          | CT, angiogram-moyamoya    | 11 years old         | Follow-up                                    | MRI, cerebral angiogram                   |
| Ozsarac M, Aksay E, Kiyani S, Unek O, Gulera FF: De novo cerebral arteriovenous malformation: Pink floyd's song "brick in the wall" as a warning sign. J Emerg Med 43:e17-20, 2012 | Female         | 10 years old                 | Intraventricular hemorrhage                                                             | CT, cerebral angiogram, post-operative angiogram confirming complete AVM resection | 27 years old | Sudden headache, right-sided numbness | CT, bilateral carotid angiography, post-operative angiogram confirming complete AVM resection |
| Prior vascular pathology                                                  | Female         | 3 years old                  | History of sickle cell disease and associated moyamoya arteriopathy                     | MRI                       | 6 years old          | Incidental finding                           | MRI, CT angiography, cerebral angiogram   |
| Schmit BP, Burrows PE, Kuban K, et al. Acquired cerebral arteriovenous malformation in a child with Moyamoya disease: case report. J Neurosurg 84:677-80, 1996 | Female         | 2 years old                  | Cerebral infarctions, seizures                                                          | CT, angiogram-moyamoya    | 11 years old         | Follow-up                                    | MRI, cerebral angiogram                   |
| Akimoto H, Komatsu K, Kubota Y. Symptomatic de novo arteriovenous malformation appearing 17 years after the resection of two other arteriovenous malformations in childhood: case report. Neurosurgery 52 (1):228-232, 2003 | Female         | 10 years old                 | Intraventricular hemorrhage                                                             | CT, cerebral angiogram, post-operative angiogram confirming complete AVM resection | 27 years old | Sudden headache, right-sided numbness | CT, bilateral carotid angiography, post-operative angiogram confirming complete AVM resection |
| O'Shaughnessy BA, DiPatri AJ Jr, Parkinson RJ, Batjer HH. Development of a de novo cerebral arteriovenous malformation in a child with sickle cell disease and moyamoya arteriopathy. Case report. J Neurosurg 102 (2 Suppl):238-243, 2005 | Female         | 3 years old                  | History of sickle cell disease and associated moyamoya arteriopathy                     | MRI                       | 6 years old          | Incidental finding                           | MRI, CT angiography, cerebral angiogram   |

Contd...
Genetic etiologies for cerebral AVMs are also currently being explored. AVMs have been known to occur in the context of certain genetic disorders, such as hereditary hemorrhagic telangiectasia (HHT), Wyburn–Mason syndrome, and Sturge–Weber syndrome. Through studies of knockout mice modeled after the loss-of-function mutations found in HHT, a genetic two-hit mechanism has been proposed for the development of AVMs.\(^1\) In this two-hit model, a loss-of-function mutation of various receptors in the TGF-\(\beta\) family or a dysregulation of nitric oxide synthase activity results in vascular destabilization. This leaves the vasculature more vulnerable to a second hit by environmental factors.

The growing number of sporadic cases of cerebral AVMs still warrants an explanation. Some studies suggest that germ-line mutations of certain proteins may be involved in AVM development.\(^10,19\) Potential target proteins include endothelial angioprotein receptor Tie-2, TGF-\(\beta\), nitric oxide synthase, vascular endothelial growth factor (VEGF), and fibroblast growth factor. A recent study has also suggested an association between single nucleotide polymorphisms and sporadic cerebral AVM susceptibility, implicating proteins, and cytokines involved in the inflammatory cascade, angiogenesis, vascular remodeling, and stabilization.\(^23\)

Thus the pathomechanism of cerebral AVMs remains incompletely elucidated. The theory of congenital formation of all cerebral AVMs is being challenged as de novo AVMs are increasingly being reported. This case report documents a rare occurrence of a symptomatic de novo AVM in an adult male with no prior vascular cerebral pathology with an initial negative MRI at age 15 who subsequently developed an AVM on later imaging, providing further evidence that not all cerebral AVMs are congenital.

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