De novo AVM formation following venous sinus thrombosis and prior AVM resection in adults: report of 2 cases

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Brain arteriovenous malformations (AVMs) are traditionally considered congenital lesions, arising from aberrant vascular development during the intrauterine period. Rarely, however, AVMs develop in the postnatal period. Individual case reports of de novo AVM formation in both pediatric and adult patients have challenged the traditional dogma of a congenital origin. Instead, for these cases, a dynamic picture is emerging of AVM growth and development, initially triggered by ischemic and/or traumatic events, coupled with genetic predispositions. A number of pathophysiological descriptions involving aberrant angiogenic responses following trauma, hemorrhage, or inflammation have been proposed, although the exact etiology of these lesions remains to be elucidated. Here, the authors present 2 cases of de novo AVM formation in adult patients. The first case involves the development of an AVM following a venous sinus thrombosis and to the authors' knowledge is the first of its kind to be reported in the literature. They also present a case in which an elderly patient with a previously ruptured AVM developed a second AVM in the contralateral hemisphere 11 years later. In addition to presenting these cases, the authors propose a possible mechanism for de novo AVM development in adult patients following ischemic injury.

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Brain arteriovenous malformations (AVMs) are direct, abnormal connections between arteries and veins without intervening capillary beds. Parenchymal AVMs have traditionally been considered congenital lesions, arising from aberrant vascular development during the intrauterine period. However, individual case reports published over the past 2 decades have suggested that other mechanisms may also play a role in de novo AVM development and that these lesions are both dynamic and reactive. De novo AVM formation has been documented following diagnosis of other conditions, including moyamoya disease, Bell’s palsy, cavernous malformations, dural arteriovenous fistulas, intracranial hemorrhage, seizures, hydrocephalus, and transient ischemic attacks. While cases of this kind have been well characterized in pediatric patients, reports of de novo AVM formation in adult patients are rare. Here, we present 2 cases of de novo AVM formation in adults following diagnosis of venous sinus thrombosis and a previous contralateral AVM.
Case Reports

Case 1

A 31-year-old woman initially presented with a severe headache. Magnetic resonance venography (MRV) demonstrated a left transverse sinus thrombosis with no evidence of hemorrhage, associated infarct, or other vascular abnormality (Figs. 1 and 2). A 6-month course of anticoagulant therapy was initiated, and the sinus was re-canalized. Routine MRI performed at the 2-year follow-up indicated a new $1.26 \times 0.75$–cm left temporooccipital AVM. Digital subtraction angiography (DSA) confirmed the presence of the lesion. After a detailed consultation, a conservative management strategy was undertaken and the patient was subsequently discharged to home.

Case 2

A 61-year-old man initially presented acutely with gait instability. Computed tomography angiography (CTA) and DSA confirmed a hemorrhagic left frontal AVM at the time, with no other vascular abnormalities. The patient had no history or family history of hereditary hemorrhagic telangiectasia. Microsurgical resection of the AVM was performed uneventfully, although postoperative care was complicated by seizures, which were successfully controlled by anticonvulsant medications. Follow-up CTA confirmed complete obliteration of the lesion (Fig. 3). Eleven years after the resection, the patient presented with left hemianopsia. Computed tomography angiography and DSA confirmed a right temporooccipital hemorrhage and associated de novo AVM. The patient underwent microsurgical resection of this second lesion. Follow-up imaging confirmed complete obliteration of the lesion, and the patient was subsequently discharged to home neurologically intact.

Discussion

AVM formation is believed to result from aberrant vasculogenesis and angiogenesis occurring in utero. However, limited data exist to support the congenital nature of these lesions, with only 1% being diagnosed before the age of 2 years. Koch et al. recently summarized 19 cases of de novo AVMs reported in the literature over the past 2 decades. As these lesions typically develop following either a traumatic brain injury or an ischemic event, these case descriptions have lent support to a dynamic and reactive theory of AVM development. While the underlying pathophysiology remains unclear, loss-of-function mutations in the activin receptor-like kinase 1 (ALK1) and/or the endoglin (ENG) genes have been proposed as the basis for aberrant angiogenesis and subsequent development of these lesions. The effects of these mutations occur via the vascular endothelial growth factor (VEGF) and transforming growth factor (TGF-β) pathways.

To date, only 11 de novo AVMs have been diagnosed in adult patients, with no previous reports of cases that developed following venous sinus thrombosis (Table 1). While venous sinus thrombosis has been implicated in dural arteriovenous fistula (DAVF) formation, its role in the development of parenchymal AVMs is poorly understood. In 1997 Lawton et al. demonstrated in a rat model that increased venous pressure resulting from sinus thrombosis led to an increase in angiogenesis and facial AVM formation. Aboian et al. have suggested that venous outflow occlusion and the resulting venous hypertension may induce hypoxia in neighboring parenchyma, consequently leading to increased angiogenic activity and

![FIG. 1. Case 1. A: Magnetic resonance venography image indicates the presence of a left transverse sinus thrombosis. B: Coronal MR image confirms a venous thrombosis (white arrow) without evidence of a left temporooccipital AVM. C: Coronal MR image obtained 2 years later demonstrates resolution of the thrombosis and indicates the presence of a de novo AVM on the ipsilateral hemisphere. D: Image obtained with DSA confirms an AVM fed by the left distal middle cerebral artery.](image1)

![FIG. 2. Case 1. Left: Contrast-enhanced MR image shows a draining vein in the left temporooccipital region (arrowhead). Right: Contrast-enhanced MR image obtained 2 years later confirms an AVM emanating from the region where the draining vein had been previously visualized (arrow).](image2)
lesion formation. In the presence of the aforementioned genetic abnormalities, these conditions may result in uncontrolled vascularization of the tissue. Morales-Valero et al. proposed that once a nidus develops and supports rapid blood flow, shear stress on the endothelial lining of the newly formed, fragile vessels can serve as the stimulus for further angiogenic activity. We theorize that a draining vein in Case 1, which was visible on MRI at the time of

**TABLE 1. Literature review of adult de novo intracranial AVMs**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Initial Presentation</th>
<th>De Novo AVM Formation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age at Baseline Imaging (yrs), Sex</td>
<td>Symptoms</td>
</tr>
<tr>
<td>Friedman et al., 2000</td>
<td>61, M</td>
<td>Vertigo, vomiting, rt arm dysmetria, nystagmus</td>
</tr>
<tr>
<td>Bulsara et al., 2002</td>
<td>26, F</td>
<td>Gait ataxia, nystagmus, dysmetria, myoclonic jerks</td>
</tr>
<tr>
<td>Akimoto et al., 2003</td>
<td>10, F</td>
<td>Intraventricular hemorrhage</td>
</tr>
<tr>
<td>Jeffree &amp; Stoodley, 2009</td>
<td>8, M</td>
<td>Headache, facial droop, speech deficit, vomiting, decreased consciousness</td>
</tr>
<tr>
<td>Mahajan et al., 2010</td>
<td>16, F</td>
<td>Facial paralysis</td>
</tr>
<tr>
<td>Ozsarac et al., 2012</td>
<td>&lt;25, M</td>
<td>Seizures</td>
</tr>
<tr>
<td>Morales-Valero et al., 2014</td>
<td>31, F</td>
<td>Obtunded, confused</td>
</tr>
<tr>
<td>Neil et al., 2014</td>
<td>42, M</td>
<td>TIA</td>
</tr>
<tr>
<td>Kilbourn et al., 2014</td>
<td>7, M</td>
<td>Absence seizures</td>
</tr>
<tr>
<td>Koch et al., 2016</td>
<td>&lt;2, F</td>
<td>Ventriculomegaly, balance loss, inability to sit upright</td>
</tr>
<tr>
<td>Present cases</td>
<td>31, F</td>
<td>Headache</td>
</tr>
<tr>
<td>&amp;</td>
<td>61, M</td>
<td>Gait instability, hemorrhage</td>
</tr>
</tbody>
</table>

Dx = diagnosis; NA = not available; TIA = transient ischemic attack.
* Exact age of patient unknown.
† Patient age was 16 months at time of initial presentation.
De novo AVM formation

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The average incidence of multiple cerebral AVMs is reported to be 1.9%. Only one previous case involving de novo AVM formation following previous AVM resection in a separate location has been reported. Our second case demonstrates de novo AVM formation in an adult patient following resection of a previously ruptured AVM in the contralateral hemisphere. It is unlikely that the de novo AVM was radiologically occult, as DSA, CTA, and MRI following resection of the first AVM did not show a contralateral AVM. Furthermore, a moderately sized contralateral hematoma would be unlikely to completely occlude an existing AVM. While recurrence of completely resected AVMs has been reported in the pediatric literature, reports of de novo AVM formation in adults in different anatomical locations following resection of previous AVMs are extremely rare. This case further substantiates the notion that AVM development is a dynamic process.

Limitations

In Case 1, only MRV was performed to visualize the venous sinus thrombosis, rather than DSA, which is more sensitive and specific for the detection of AVMs. Therefore we cannot rule out the presence of a radiologically occult, small AVM beyond the resolution of MRI. However, the lesion was easily detected on routine MRI at 2 years, adding weight to the notion of de novo AVM formation. In Case 2, a complete DSA was performed 11 years prior to diagnosis of the patient’s first AVM. Unfortunately, because of the amount of time that had elapsed, the imaging was subsequently expunged from the institution’s records. However, the neuroradiology report confirms that no abnormalities on the contralateral side were seen at the time that the DSA was performed.

Conclusions

We report 2 cases of de novo AVM formation in adults, which challenge the traditional belief that all parenchymal AVMs are congenital and provide support for the theory that AVMs may be acquired in some cases. These cases further establish the dynamic nature of AVMs and suggest that de novo AVM formation can occur in adult patients as well as in pediatric patients. We theorize that venous sinus thrombosis-induced hypertension and outflow occlusion may lead to parenchymal ischemia, increased angiogenic activity, and eventual AVM formation. Further studies are required to elucidate the exact pathophysiology involved in this process.

References


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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