Onyx In Brain Arteriovenous Malformation Embolization

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Abstract

Keywords:

Introduction

Embolization has long been used as an adjunct to surgical resection in the treatment of brain arteriovenous malformation (bAVM). The most commonly used embolic material, n-butylcyanoacrylate glue, requires experience and skill to handle its quick and unpredictable flow and polymerization. A new liquid embolic agent, ethylene vinyl alcohol copolymer (Onyx), is less adhesive and polymerizes slowly, which provides better control for radiologists performing embolization.

Objective

To report our experience in embolization using Onyx alone or in combination with histoacryl for bAVM embolization in our tertiary referral center.

Methods

We retrospectively reviewed the anatomy, technical conditions, complications and clinical outcome of all bAVM patients embolized at our center using Onyx alone or in combination with n-butylcyanoacrylate glue.
Results

Between 2010 and 2013, 13 patients [6 (46.2%) male; 7 (53.8%) female; aged, 14–57 years] were included, and a total of 31 embolizations were performed. Clinical presentation included hemorrhage [9 (69.2%)], seizures [2 (15.4%)], and headache [2 (15.4%)]. Most AVMs were located in the brain hemispheres [12 (92.3%)] and measured <3 cm [7 (53.8%)]. Complete occlusion of the AVM was obtained in 2 (15.4%) patients; 11 (84.6%) patients had partial occlusion [6 (54.5%) had <50% nidus occlusion]. Complications occurred in four procedures involving 3 patients (morbidity, 23.1%). This resulted in the death of 1 patient (mortality, 7.7%) and complete recovery with no disability in 2 patients.

Conclusion

The total nidal occlusion achieved herein is comparable to other similar studies. Our morbidity and mortality were higher compared to other studies which may be attributed to the small number of patients. More data is being collected which may better reflect on our experience.

Keywords: therapeutic embolization; arteriovenous malformations; angiography; butylcyanoacrylate; Onyx copolymer

Introduction

An arteriovenous malformation (AVM) is a tangled cluster of vessels (known as nidus) in which feeder arteries connect directly to draining veins without any intervening capillary bed. The most common presenting symptom is hemorrhage (71%), followed by seizures [24%] (1). The goal of treatment is to prevent hemorrhage; seizure control and stabilization of neurological deficits are also occasionally a goal of treatment (2).

Embolization has been used as an adjunct to surgical resection. The goal of embolization is to reduce the size of the nidus by occluding the arterial feeders and the nidus itself. Several different embolic materials have been used in endovascular embolization, such as balloons, polyvinyl alcohol particles, and most commonly, n-butylcyanoacrylate (n-BCA) glue. The intranidal flow and polymerization of n-BCA glue are quick and unpredictable, requiring experience and skills to handle it (3). A new liquid embolic agent, ethylene vinyl alcohol copolymer (Onyx; Covidien/ev3, Irvine, CA, USA) is less adhesive and polymerizes slowly, which provides better control for the radiologist performing the embolization. Herein, we describe our experience using Onyx alone or in combination with n-BCA glue for embolization of brain AVM (bAVM).

Research Methodology

The current study was a retrospective review of medical records and previous imaging of all patients with bAVM that underwent embolization between January 2010 and January 2013 at our tertiary referral center. A total of 115 embolizations were performed at our center during this period for a variety of indications, including treatment of cerebral and spinal vascular disorders and pre-operative embolization of tumors. Thirty-eight embolizations were done for bAVM. Patients with incomplete pre-embolization images archived in our hospital’s picture archiving and communication system (PACS) were excluded. These were patients who had imaging done at another hospital and were referred to our center for embolization. The pre-embolization images may have been kept by the patient and not archived into the PACS.

Patient demographics and number of embolizations were recorded. Other variables reviewed included image evaluation completed by a neuroradiologist and an interventional neuroradiologist and AVM anatomy, which was evaluated by cross-sectional imaging and digital subtraction angiogram. The outcome of embolization was assessed by evaluating the percentage of nidal occlusion post-embolization based on digital subtraction angiogram images. Any recorded complications that occurred and steps taken to remedy them were also reviewed. Each patient’s clinical status post-embolization recorded in their medical record was also reviewed using the Modified Rankin Scale.

Results

The current results are presented based on the BRAVO study (4). Our review included 13 patients [6 (46.2%) male; 7 (53.8%) female] aged 14 to 57-years-old treated for bAVM by embolization at our hospital between January
2010 and January 2013. The majority of patients presented with intracranial hemorrhage [9 (69.2%)], while the rest presented with seizure [2 (15.4%)], and headache [2 (15.4%)]. No patient presented with neurological deficit or was an incidental finding. Table 1 summarizes the anatomy of AVM among our patients.

Table 1: Anatomy of AVM

<table>
<thead>
<tr>
<th>Location</th>
<th>Total no. of patients: 13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
</tr>
<tr>
<td>Right</td>
<td>7 (53.8)</td>
</tr>
<tr>
<td>Left</td>
<td>6 (46.2)</td>
</tr>
<tr>
<td>Hemisphere</td>
<td>12 (92.3)</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Corpus Callosum</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Eloquent</td>
<td>7 (53.8)</td>
</tr>
<tr>
<td>Non eloquent</td>
<td>6 (46.2)</td>
</tr>
</tbody>
</table>

A total of 31 embolizations were done on these 13 patients (median, 2 embolizations per patient) and a range of one to five procedures per patient (Table 2).

Table 2: Technical Results

<table>
<thead>
<tr>
<th>Total embolisations performed</th>
<th>31</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of embolisations/patient</td>
<td>Median = 2</td>
</tr>
<tr>
<td>Embolic materials used:</td>
<td>Range: 1-5</td>
</tr>
<tr>
<td>Onyx</td>
<td>17 (54.8)</td>
</tr>
<tr>
<td>Glue</td>
<td>6 (19.4)</td>
</tr>
<tr>
<td>Onyx &amp; Glue</td>
<td>2 (6.5)</td>
</tr>
<tr>
<td>None (embolisation attempted but abandoned)</td>
<td>6 (19.4)</td>
</tr>
</tbody>
</table>
In reviewing the number of embolizations performed, we included those which were attempted but abandoned for various reasons, but mainly due to spontaneous nidal occlusion or failure to cannulate feeder arteries. In six procedures (19.4%), no embolic agents were used (Table 2). We included these procedures because in our opinion, these embolizations were indicated in order to achieve as much nidal occlusion as possible and are reflected in the number of embolizations needed per patient. Embolization outcomes are described in Table 3, in the death of 1 patient (mortality, 7.7%) and complete recovery with no disability in 2 patients (Table 4).

**Table 3:** Outcome of AVM treatment

<table>
<thead>
<tr>
<th>Nidal occlusion</th>
<th>Size &lt;3cm</th>
<th>Size 3-6cm</th>
<th>Total n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>1</td>
<td>1</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>75 – 99%</td>
<td>1</td>
<td>0</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>50 – 74%</td>
<td>1</td>
<td>3</td>
<td>4 (30.8)</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>4</td>
<td>2</td>
<td>6 (46.2)</td>
</tr>
</tbody>
</table>

**Complementary treatment for partially embolised AVM = 11 patients n(%)**

- Awaiting radiosurgery: 4 (36.4)
- Refused further intervention: 1 (9.1)
- Lost to follow up: 6 (54.5)

Complications occurred in four procedures involving 3 patients (morbidity, 23.1%). This resulted

**Table 4:** Complications from embolisations

<table>
<thead>
<tr>
<th>Patient</th>
<th>Procedure</th>
<th>Type of complication</th>
<th>Treatment for complication</th>
<th>MRS post treatment</th>
<th>Outcome post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>Intra-op perforation of feeder artery</td>
<td>Embolisation of perforated artery</td>
<td>0</td>
<td>Achieved &lt;50% nidal occlusion</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Post op Intracranial haemorrhage – treatment related</td>
<td>Decompression surgery</td>
<td>5</td>
<td>Death</td>
</tr>
<tr>
<td>B</td>
<td>3</td>
<td>Post op Intracranial haemorrhage – disease related</td>
<td>Conservative</td>
<td>0</td>
<td>Regression of AVM without further intervention, refused further treatment</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>Cortical venous thrombosis with no venous infarct</td>
<td>Conservative</td>
<td>0</td>
<td>Total nidal occlusion without further intervention</td>
</tr>
</tbody>
</table>
Discussion

An AVM is a tangled cluster of vessels known as nidus in which feeder arteries connect directly to draining veins usually via arteriovenous shunting without any intervening capillary bed. Due to its rarity and presence of asymptomatic patients, establishing a true prevalence rate is difficult. The prevalence of detected AVM inferred from incidence data is <10.3 per 100,000 people (5). The mean age of presentation is 33.7 years (1), and it affects men and women equally. The most common presenting symptom is hemorrhage (71%), followed by seizures [24%] (1). This is similar to our current data, where 69.2% presented with hemorrhage. The annual risk of hemorrhage is 1.3%-4.0% per year and 1.0% results in mortality per year (1, 6); mortality after initial rupture is 10%–17.6% (6).

A multidisciplinary approach consisting of surgery, endovascular embolization, and stereotactic radiosurgery is used to treat bAVM. Surgical resection is the definitive treatment for eradication of lesions (7). However, stereotactic radiosurgery and embolization have been increasingly used for inoperable lesions. Embolization has also been used as an adjunct to surgical resection. The goal of embolization is to reduce the size of the nidus by occluding the arterial feeders and the nidus itself. This facilitates surgical resection, prevents further hemorrhage, and/or reduces signs and symptoms associated with steal phenomenon, venous hypertension, and seizures (7). Typically, embolization is done in stages. At our center, the number of embolizations per patient ranges from one to five (median, 2). Unfortunately, complete obliteration of AVM by embolization alone is low [13%] (8). Thus, it is usually used in a multidisciplinary treatment program.

Several different embolic materials have been used in endovascular embolization, such as balloons, polyvinyl alcohol particles, and n-BCA glue. The intranidal flow and polymerization of n-BCA glue are quick and unpredictable, requiring extensive experience and skill when handling it (3). The embolic agent Onyx is less adhesive and polymerizes slowly, which provides better control during the embolization procedure.

Our data shows 2/13 patients (15.4%) achieved total occlusion, which is similar to other studies. van Rooij et al. reported total occlusion in 16% of their 44 patients (3), while Pierot et al. reportedly achieved total occlusion in 23.5% of their 117 patients, and Katsaridis et al. attained total occlusion in 53.9% of their 52 patients (4, 9). In our opinion, the number of total occlusions achieved herein was not directly due to the embolic material used or the technical aspects of embolization. As seen in Table 3, 54.5% of our patients were lost to follow-up. We might have achieved a higher number of total occlusions if we were able to continue embolization in these patients.

The safety and efficacy of Onyx has been reported in several studies. In a study of 44 patients with a total of 52 embolizations, van Rooij et al. reported a morbidity and mortality of 4.6% and 2.3%, respectively (3). In the BRAVO study on 117 patients by Pierot et al., 5.1% morbidity and 4.3% mortality were reported (4). Katsaridis et al. also reported similar results in 52 patients where the morbidity and mortality were 8% and 3%, respectively (9).

In the present study, morbidity (23.1%) and mortality (7.7%) were higher than what has been reported previously. This is likely due to the small number of patients included in our study. We have one death which resulted from the treatment. Herein, a 51-year-old man underwent his fourth embolization. The AVM nidus measured 3-6 cm and had been partially embolized previously, achieving <50% occlusion. The latest embolization was uneventful, and three vials of Onyx were used to achieve 50%-75% occlusion. He was extubated with full GCS recovery, and no neurological deficit was noted while in the angio suite. However, his GCS dropped 6 h later. A computed tomography scan showed a left temporoparietal intra parenchymal bleed with mass effect and midline shift, likely due to a venous infarct. Onyx cast was seen within the draining vein (Figure 1).
There were also smaller Onyx casts seen in the internal cerebral and cortical veins, and he underwent decompression surgery to treat the intracranial bleed. However, the patient eventually lost his brainstem function and passed away. We postulate that the presence of Onyx in the draining vein contributed towards the venous thrombosis, which subsequently resulted in venous infarct and intra parenchymal hemorrhage. Due to the inhomogeneity of the radio-opacity of Onyx, it is difficult to visualize, particularly when it is not in the targeted site.

**Conclusion**

The total nidal occlusions achieved in our center is comparable to other similar studies. However, this number can certainly be improved, not only with respect to technical aspects, but also by improving our patients’ commitment to their treatment and preventing their loss to medical follow-up. We also hope to improve our morbidity and mortality. More data is being collected which may better reflect on our experience with this procedure and new embolic agent.

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**Conflict of Interest**

None

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None

**Authors Contribution**

Conception and design, Analysis and interpretation of the data, Drafting of the article, Statistical expertise, Collection and assembly of data: HH

Conception and design, Analysis and interpretation of the data, Critical revision of the article for important intellectual content, Final approval of the article, Provision of study materials or patients: ASM

Provision of study materials or patients, Collection and assembly of data, Final approval of the article, Administrative, technical, or logistic support: AAA & ZAH

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