ENDOVASCULAR EMBOLIZATION OF CEREBRAL ARTERIOVENOUS MALFORMATIONS

Sarhan AA; Aidaros MA; Sobh KM* and El-Serafy TSS
Neurology Department, Faculty of Medicine, Zagazig and Al-Azhar* Universities

ABSTRACT

Background: An arteriovenous malformation is a collection of dysplastic plexiform vessels that is supplied by one or more arterial feeders and drained by one or more venous channels. Arteriovenous malformations may have a pure plexiform nidus or contain a mixed plexiform fistulous nidus. **Objective:** This work was carried out to evaluate the clinical outcome and effectiveness of the endovascular treatment of cerebral arteriovenous malformations with ethylene vinyl alcohol copolymer (Onyx). **Methods:** Twenty five patients (14 males and 11 females) with cerebral arteriovenous malformations were treated by embolization with Onyx at the Neurointervention Unit in Al-Azhar University. All patients with intracranial AVMs were subjected to preprocedural, procedural and postprocedural assessments. **Result(s):** There was significant difference in nidus diameter in all patients after embolization in comparison to before embolization. There was significant difference in Spetzler and Martin grading system before and after embolization. **Conclusion(s):** Onyx as a new embolic material, with its non-adherent properties has significantly facilitated this development.

Key Words: endovascular, cerebral, arteriovenous malformation, Onyx

INTRODUCTION

Brain arteriovenous malformations (AVMs) are complex vascular lesions in which arterial blood flow, directly into draining veins without an intervening capillary bed, through a venous conglomerate called nidus. As a consequence, blood flow is unregulated and pressure within the nidus rises exposing the veins to very high pressures.

The arteriovenous malformation detection rate is 1.1-1.2/100,000 persons/year and the incidence of arteriovenous malformation hemorrhage is 0.42/100,000 persons/year.

Spetzler and Martin proposed a simplified grading system based on the AVMS size, the eloquence of adjacent brain parenchyma and the venous drainage pattern. The AVMS size was divided into three categories: small (< 3 cm), medium (3 to 6 cm), and large (> 6 cm).

An AVM was considered to be adjacent to eloquent brain parenchyma if it was next to sensorimotor cortex, language areas, visual cortex, hypothalamus, thalamus, internal capsule, brainstem, cerebellar peduncles, or deep cerebellar nuclei.

The venous drainage was designated as superficial if all of the venous drainage emptied into the cortical venous system. If any or all of the venous drainage emptied through deep veins (internal cerebral vein, basal veins and paracentral cerebellar veins), it was categorized as deep.

Traditionally, most AVMs come into clinical attention because of hemorrhage, with epilepsy coming far behind as the second most common type of presentation. However, this pattern is gradually changing. Increasing availability of noninvasive imaging methods, mainly MRI, have led to more and more frequent detection of unruptured and even incidental AVMs.

Cerebral arteriovenous malformations are amenable to various treatment modalities which include the following either individually or in combination: surgical removal (resection), radiosurgery and endovascular embolization.

Endovascular embolization can be used for a curative embolization, nidus reduction before surgery or radiosurgery and palliative embolization. The goal of curative embolization is the complete and permanent obliteration of the AVMs nidus with the restoration of the normal arterial blood flow and the preservation of venous drainage.

The most commonly used embolic agent is the rapidly polymerizing liquid embolic agent n-Butyl Cyano-Acrylate (nBCA). The use of nBCA for brain AVMs requires experience and skill, because of the intra-nidal flow and polymerization of nBCA are both quick and largely unpredictable.

After the introduction of the Onyx liquid embolic system (EV3, Irvine, CA) which is less adhesive, more slowly polymerizing and accordingly much more advantageous than nBCA, nBCA was largely replaced as an agent for AVMs embolization.

PATIENTS AND METHODS

Between October 2010 and February 2013, twenty five patients (14 males and 11 females) with cerebral arteriovenous malformations were treated by embolization with Onyx at the Neurointervention Unit in Al-Azhar University.

Inclusion criteria:

- Compact AVMS.
Endovascular embolization of cerebral ..........  

- The nidus was accessible with tip of the catheter.
- Low flow rate according to the four-vessel angiography.
- Patient not fit for other modality.

**Exclusion criteria:**
- High flow cerebral AVMS.
- Small superficial cerebral AVMS located in a surgically accessible non-eloquent area.
- Patient with contraindication to radiographic contrast.
- Complicated vascular anatomy.
- Poor medical conditions that cannot withstand multiple sessions.
- Patient refusing embolization.

*All patients with intracranial AVMs were subjected to preprocedural, procedural and postprocedural assessments.*

**Preprocedural assessment:**
- Complete medical history.
- Complete general and neurological examinations.
- Laboratory investigations with stressing on complete blood picture, coagulation profile, hepatitis markers, liver function tests and renal function tests.
- Radiological investigations:
  - CT (with and without contrast) was done for all patients for diagnosis after the presentation as an investigative study, for localization of the site of the AVMS, associated infarction or hydrocephalus.
  - MRI and MRA were done for all patients and were used as good diagnostic tools in revealing pathological anatomy, edema, gliosis and associated venous varix and nidal aneurysm.
  - Intra-Arterial Digital Subtraction Angiography (IA-DSA).
  - CTA was available in some patients and not in others where it was replaced by IA-DSA.

**Procedure:**
An informed written consent was obtained from all patients. General anaesthesia was used in all patients. All sessions of Onyx embolization were carried out on a biplane angiographic unit.

A 6-French (6 F) arterial sheath was placed in the right femoral artery. Diagnostic cerebral angiography was performed and a 6 F guiding catheter was then inserted in either an internal carotid artery or a dominant vertebral artery using a standard co-axial technique.

A Dimethylsulphoxide (DMSO) compatible flow directed microcatheter (Marthon, CV3 Neurovascular) was navigated to the nidus of AVMS with an aid of 0.008-inch guide wire (Mirage, ev3 Neurovascular).

Angiography was performed to ensure that the feeding pedicle could be occluded up to 2 cm retrogradely by the reflux of Onyx along the microcatheter.

The Onyx solution must be vigorously shaken for 20 minutes to fully suspend the micronized tantalum powder. Mixing is continued until just before the embolization. Failure to do this may result in inadequate radiopacity. The microcatheter was flushed with normal saline and the dead space was loaded with pure DMSO solvent.

The Onyx mixture was drawn into a DMSO compatible 1 cc syringe. The syringe was connected to the microcatheter and a slow steady injection was begun at a rate of 0.25 ml/90 seconds to displace the DMSO in the dead space with Onyx.

The Onyx was slowly and progressively injected into the nidus under continuous visual control using biplane fluoroscopy.

As soon as reflux was noted along the microcatheter or early embolization of a draining vein was evident, the injection was stopped for 2 minutes and then resumed.

The maximum reflux to be treated was 2 cm. The microcatheter was removed using one technique of gradual increase in traction. Staged sessions were planned for partially occluded AVMs.

**Postprocedural assessment:**
- Postembolization size as detected by IA-DSA by the end of the procedure with comparison by baseline IA-DSA done before procedure.
- Immediate post-embolization angio-architectural changes.
- Immediate neurological assessment.
- Data collected as regard total ICU stay or total ward stay.
- Symptomatic improvement as regard presenting symptom.
- Postprocedural complications.
- Procedure-related permanent morbidity and mortality.
- Radiological follow up by IA-DSA and repeated scoring or Spetzler-Martin AVMS grading system were done within 6 months after embolization.
Table (1): Spetzler-Martin grading system (I-V) (Spetzler and Martin, 1986)

<table>
<thead>
<tr>
<th>AVMS features</th>
<th>Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of nidus</td>
<td></td>
</tr>
<tr>
<td>Small (&lt; 3 cm)</td>
<td>1</td>
</tr>
<tr>
<td>Medium (3-6 cm)</td>
<td>2</td>
</tr>
<tr>
<td>Large (&gt; 6 cm)</td>
<td>3</td>
</tr>
<tr>
<td>Eloquence of adjacent brain</td>
<td></td>
</tr>
<tr>
<td>No eloquent</td>
<td>0</td>
</tr>
<tr>
<td>Eloquent</td>
<td>1</td>
</tr>
<tr>
<td>Venous drainage</td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>0</td>
</tr>
<tr>
<td>Deep</td>
<td>1</td>
</tr>
</tbody>
</table>

The assigned grade equals the sum of the points for all three features.

Grade I = Score 1
Grade II = Score 2
Grade III = Score 3
Grade IV = Score 4
Grade V = Score 5

Results

The mean age in our study was 34.32 years with range of 16-58 years and the standard deviation was 11.14 years. The sex distribution showed slight higher incidence in males (56%) than in females (44%) (table 2).

In our study, 10 patients (40%) were presented with weakness due to Intracranial Hemorrhage (ICH), 7 patients (28%) with epilepsy, 6 patients (24%) with headache and 2 patients with weakness as a focal neurological deficit (8%) (table 3).

The Spetzler and Martin grading of the cerebral AVMs before embolization was grade II in 3 patients (12%), grade III in 15 patients (60%), grade IV in 5 patients (20%) and grade V in 2 patients (8%) (table 4).

The majority of patients received 2-3 sessions of Onyx injection with a total number of 67 sessions (table 5).

There was marked reduction in nidus diameter after embolization in which only one patient (4%) had nidus diameter > 3 cm while 19 patients (76%) had nidus diameter ≤ 3 cm (table 6).

There was significant difference in nidus diameter in all patients after embolization in comparison to before embolization (p = 0.000) (table 7).

There was significant difference in Spetzler and Martin grading system before and after embolization (p = 0.000) (table 8).

Table (2): Age and sex distribution

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean ± SD</th>
<th>34.32 ± 11.14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Range</td>
<td>16-58</td>
</tr>
<tr>
<td>Male</td>
<td>14 (56%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (44%)</td>
<td></td>
</tr>
</tbody>
</table>

SD = Standard Deviation

Table (3): Clinical presentation of cerebral AVMs in our study

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness (ICH)</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Headache</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Weakness (focal neurological deficit)</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100</td>
</tr>
</tbody>
</table>

ICH = Intracranial Hemorrhage
Table (4): Spetzler and Martin classification of the cerebral AVMs before embolization in our study

<table>
<thead>
<tr>
<th>Spetzler and Martin grading system</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade II</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Grade III</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>Grade IV</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Grade V</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>25</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (5): Number of sessions in our study

<table>
<thead>
<tr>
<th>Number of sessions</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>25</td>
<td>100</td>
</tr>
</tbody>
</table>

Table (6): Nidus diameter of cerebral AVMs after embolization in our study

<table>
<thead>
<tr>
<th>Nidus diameter</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 3 cm</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>≤ 3 cm</td>
<td>19</td>
<td>76</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Table (7): Nidus diameter before and after embolization in our study

<table>
<thead>
<tr>
<th>Nidus diameter</th>
<th>Before embolization</th>
<th>After embolization</th>
<th>Test of significance</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>4.2 ± 0.8775</td>
<td>1.248 ± 0.8554</td>
<td>Paired t test = 26.156</td>
<td>0.000*</td>
</tr>
<tr>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>≤ 3</td>
<td>3 12</td>
<td>24* 96**</td>
<td>Z value of Wilkoxon signed ranks test = 4.89</td>
<td></td>
</tr>
<tr>
<td>&gt; 3</td>
<td>22 88</td>
<td>1 4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD = Standard Deviation
*Significant (p < 0.05)
+Five cerebral AVMs were completely occluded, while 19 cerebral AVMs had nidus diameter ≤ 3 cm.
++20% of the cerebral AVMs were completely occluded.
Table (8): Spetzler and Martin grading of the cerebral AVMs before and 6-month follow up after embolization

<table>
<thead>
<tr>
<th>Spetzler and Martin grading</th>
<th>Before embolization</th>
<th>After Embolization</th>
<th>Z value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Grade I</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade II</td>
<td>3</td>
<td>12</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Grade III</td>
<td>15</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade IV</td>
<td>5</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade V</td>
<td>2</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Complete occlusion</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>100</td>
<td>25</td>
<td>100</td>
</tr>
</tbody>
</table>

*Significant (p < 0.05)

DISCUSSION

As regards age and sex distribution, the mean age of the patients in our study was 34.32 years with range of 16-58 year and standard deviation as 11.14 years with higher incidence in males (56%) than in females (44%), this approximately goes with the results performed on a number of 89 patients with arteriovenous malformations, which reported that 54 (60.67%) were males and 35 (39.32%) were females. The age distribution recorded incidence peaks in the 3rd and 4th decade.

In support to our study, Hofmeister et al. reported that the mean age at diagnosis is 31.2 years, 45% of the patients are females and the cerebral AVMs are occasionally seen in the elderly but are typically diagnosed before the patient has reached the age of 40 years.

With our study, another study proved that AVMs present usually before 40 years, despite that they found in contrast to us that AVMs affect females and males equally.

Regarding the presentation of the cerebral AVMs in our study, 40% were presented with weakness due to intracerebral hemorrhage, 28% with epilepsy, 24% with headache and 8% with weakness due to AVM itself. This result goes in hand with many studies. Data from international databases and prospective population-based studies suggest that more than half of all arteriovenous malformations patients may suffer intracranial hemorrhage.

Also, in agreement with our study, Ondra et al. demonstrated that intracranial hemorrhage was also the most common recorded type of AVMs presentation, between 17% and 40% of the patients with AVMs presented with epileptic seizures. Headache was the third presentation, approximately 1% to 10% of patients with cerebral AVMs presented initially with headaches.

On the contrary, Jizong et al. proved that headache was the second common presentation following the intracranial hemorrhage and seizure was the third common presentation accounting for about 17.3%.

The Spetzler and Martin classification of cerebral AVMs among the studied patients was grade II in 3 patients (12%), grade III in 15 patients (60%), grade IV in 5 patients (20%) and grade V in 2 patients (8%).

This disagrees to some extent with Weber et al. who found in their series of 47 patients that 25 patients were grade I or II, 10 patients were grade III and 12 patients were grade IV or V.

In this work, 67 sessions of Onyx injection were done to all patients, the majority of patients received 2-3 sessions. The rate of total occlusion of brain AVMs with embolization was 20% (5 patients).

There was marked reduction in nidus diameter after embolization in which only one patient had nidus diameter > 3 cm while 19 patients (76%) had nidus diameter ≤ 3 cm. There was significant difference in nidus diameter in all patients after embolization in comparison to before embolization (p = 0.000).

The Spetzler and Martin grading of the cerebral AVMs was grade II in patients with partial occlusion (20 patients). There was
significant difference in Spetzler and Martin grading system after embolization in comparison to before embolization (p = 0.000).

These post-embolization results are similar to that obtained by van Rooij et al. who reported a series of patients undergoing embolization with Onyx, observing a cure rate of 16% (7 patients), Weber et al. who reported a complete obliteration rate of 20% alone in a series of 94 cases. Two recurrences were present at 3-month follow-up angiographic examination, resulting in a complete obliteration rate of 18%, Katsaridis et al. who demonstrated substantially higher cure rates in a consecutive series of 101 patients. Among the 101 patients, there were 52 patients in whom the treatment was completed; 28 (53.9%) AVMs were totally occluded by endovascular procedure alone, Pangiotopoulos et al. who observed a complete initial occlusion of 20 patients (24.4%) in 82 cases whereas the complete obliteration rate was 19.5% (16/82) and Xu et al. who reported in a series consisting of 86 patients that complete occlusion was 18.6% (16/86) and partial occlusion was achieved in 81.4% (70/86).

Our results seem to indicate that curative embolization of AVMs can achieve high rates of total and near total occlusion with acceptable complications.

CONCLUSION

The endovascular treatment of the cerebral AVMs is safe, efficient and can achieve high rates of total and near total occlusion. Onyx as a new embolic material, with its non-adherent properties has significantly facilitated this development.

REFERENCES

انصمام التشوهات الشريانية الوريدية المخية

تتكون التشوهات الشريانية الوريدية المخية من تجميعات مرکبة من الأوعية الدموية التي تتغذى عن طريق شريان أو أكثر و يتم صرفها وردياً عن طريق قناة ورديه أو تلقى دون شعاعات دموية بينهما.

وحض و معدل اكتشاف التشوهات الشريانية الوريدية المخية هو 1 إلى 2 لكل مئة ألف شخص.

و يعتبر أعراض التشوهات الشريانية الوريدية المخية هي الأكثر حدوثاً و تصل نسبةها إلى خمسين في المائة من الحالات، أما الأعراض الأخرى فهي متصلة في تشنجات صرعية و صداع و عوارض الخلل العصبي.

و تعتبر أشعة تصوير الشريان والأوردة المخية بالصبغة من أهم الوسائل المستخدمة لتشخيص التشوهات الشريانية الوريدية المخية.

و قد ساهمت التقنيات الحديثة في مجال صناعة القسطرة في ظهور العلاج التداخلي للتشوهات الشريانية الوريدية المخية.

و و يهدف انصم تشوهات الشريانية الوريدية المخية باستخدام القسطرة إلى علقتها غلفاً كاملاً أو تصميم حجماً من أجل تسهيل التدخل الجراحي أو الأشعاعي.

و الهدف من البحث هو تقييم فاعلية العلاج التداخلي للتشوهات الشريانية الوريدية المخية.

و اشتملت هذه الدراسة على عدد خمسة و اثني عشر مريضاً بالتشوهات الشريانية الوريدية المخية بعد أخذ موافقة كتابية من المرضى تم إجراء الأتي لهم:

1. مرحلة ما قبل العلاج التداخلي:
   - التاريخ المرضي مع الفحص الطبي.
   - الفحص العصبي الكامل.
   - تحايل عملية و تشمل: صورة دم كاملة و ودلالات زمن تاخمر الدم و نسبة الوريدية نتريوجين و الكرياتيني بالدم و ودلالات الفيروسات الكبدية في وس. و
   - أشعة مقطعية و أشعة مقطعية على المخ.
   - أشعة مقطعية و أشعة مقطعية على شرايين المخ.
   - أشعة بالصباية على شرايين المخ الأربعة باستخدام القسطرة.

2. مرحلة العلاج التداخلي:
   - تحديد عدد الجلسات.
   - التغيير الفيسيفي المخفي في التشوهات الشريانية الوريدية المخية بعد عملية الانصم مباشرةً.

3. مرحلة ما بعد العلاج التداخلي:
   - تقييم الودالة الإكلينيكية للمريض.
   - عمل أشعة تداخلية بالصبغة على شرايين المخ باستخدام القسطرة في خلال ستة أشهر من عملية الانصم و مقارنتها بالأشعة التي تم إجرائها قبل عملية الانصم.

أظهرت النتائج الآتي:

- انصم التشوهات الشريانية الوريدية المخية كلياً في نسبة 20% من الحالات.
- انصم التشوهات الشريانية الوريدية المخية إلى حجم يمكن معه استخدام العلاج الإشعاعي بواسطة سكينة جاما في نسبة 80% من الحالات.

و لقد خلصنا من هذه الدراسة أن انصم التشوهات الشريانية الوريدية المخية باستخدام مادة الأونكس أمن و فعال و يؤدي إلى انصم التشوهات الشريانية الوريدية المخية كلياً في بعض الحالات و جزئياً في البعض الآخر.