Use of Intracranial Stenting to Secure Unstable Liquid Embolic Casts in Wide-Neck Sidewall Intracranial Aneurysms

BACKGROUND: Onyx HD 500 (eV3, Irvine, CA) is a high-viscosity liquid embolic agent that has recently been approved in the United States as a humanitarian use device for the treatment of wide-neck sidewall intracranial aneurysms. Preliminary evidence suggest that liquid embolic agents can provide improved angiographic results with a lower incidence of recanalization compared to coil embolization.

OBJECTIVE: To report unstable Onyx casts and how to deal with them.

METHODS: We report 4 cases of intracranial aneurysms treated with Onyx HD 500 in which, after the aneurysm was successfully obliterated, the Onyx cast was noted to have 1 of 2 types of embolic cast instability. In all 4 cases, an intracranial stent or vascular reconstruction device (VRD) was placed across the Onyx cast at the aneurysm orifice and the cast was stabilized.

CONCLUSION: This series is the first published description of Onyx HD 500 aneurysm cast instability. It is also the first report of using a stent or vascular reconstruction device rescue technique to secure an unstable Onyx cast and represents a new indication for these devices.

KEY WORDS: Aneurysm embolization, Endovascular aneurysm occlusion, Intracranial stenting, Liquid embolic agent, Onyx HD 500, Wide-necked intracranial aneurysm, Unstable aneurysm cast

Onyx (eV3, Irvine, CA) is an endovascular liquid embolic agent that is a combination of ethylene-vinyl alcohol copolymer, dimethylsulfoxide, and tantalum. Onyx 18 and 34 are low-viscosity versions that have become important agents for embolization of arteriovenous malformations in the brain. A high-viscosity type of Onyx, Onyx 500 HD, has been designed to treat intracranial aneurysms. Preliminary data suggest that Onyx HD 500 might provide improved angiographic results for embolization of certain wide-neck sidewall intracranial aneurysms and possibly decrease recanalization rates compared with other embolization techniques.

In the United States, Onyx HD 500 has recently been approved as a humanitarian use device for sidewall aneurysms with a wide neck (>4 mm or with a dome-to-neck ratio <2) that are not amenable to treatment with surgical clipping (http://www.fda.gov/cdrh/nda/docs/H060003.html).

Recently, intracranial stents and vascular reconstruction devices (VRDs) have also been approved as humanitarian use devices and are used for wide-neck intracranial aneurysms to keep coils from herniating into the parent artery. Other authors have described augmenting Onyx embolization with intracranial stenting before the injection of Onyx as a method to improve long-term angiographic results in giant intracranial aneurysms. We present 4 cases of aneurysms treated with Onyx HD 500 in which the Onyx cast was noted to be unstable at the conclusion of the procedure, and a stent or VRD was placed as a rescue technique to secure the Onyx cast. In this study, we encountered 2 types of cast instability: movement of the entire solid Onyx cast and pulsatility of a small protrusion or “tail” of Onyx in the parent artery that fails to laminate or tack against the endothelium. This pulsatility corresponds with...
the arterial pulsations. Individual cases and types of instability are described below (Table 1).

This series represents the first published description of Onyx HD 500 aneurysm cast instability. It is also the first report of using a stent or VRD rescue technique to secure an unstable Onyx cast and represents a new indication for these devices.

Illustrative Cases

Patient 1

A 64-year-old woman initially presented with subarachnoid hemorrhage. Digital subtraction angiography revealed 2 intracranial aneurysms: a large left dorsal variant ophthalmic segment aneurysm and a small ventral variant ophthalmic segment aneurysm. The ventral aneurysm was more difficult to treat because the dome was shallow and the neck was wide (Fig. 1, A and B). The dorsal variant aneurysm was thought to be the aneurysm that ruptured because of its larger size, irregular shape, and associated large daughter aneurysm (i.e., Murphy’s teat), and therefore this aneurysm was coiled first. After the patient recovered from the subarachnoid hemorrhage, the patient returned for elective treatment of her second adjacent and more difficult aneurysm. At the time of this follow-up angiogram, there was already recanalization of the initially coiled larger dorsal variant aneurysm (Fig. 1).

The patient was administered aspirin and Plavix (Sanofi Aventis, Bridgewater, NJ), and her smaller ventral variant aneurysm was successfully occluded with Onyx, delivered with multiple cycles of balloon inflation, injection, and reperfusion. After the microcatheter was removed, immediate angiography demonstrated that the Onyx cast was migrating out of the aneurysm lumen (Fig. 1C). The balloon was reinflated, pushing the cast back into the aneurysm. The balloon was left inflated for an additional 10 minutes in an attempt to secure the cast into the aneurysm, but this was unsuccessful.

We then navigated a 4 × 22-mm Enterprise VRD (Cordis Neurovascular, Inc., Miami Lakes, FL) across the inflated balloon overlying the aneurysm neck without difficulty. We were planning to partially deflate the balloon to allow passage of the microcatheter, but, to our surprise, this was not necessary. Digital subtraction angiography revealed that the Onyx cast was secured in the aneurysm with the VRD, and there was no further instability (Fig. 1, D and E). Unfortunately, the VRD was inadvertently deployed with its terminal tines landing exactly in the ostium of the ophthalmic artery (Fig. 1D). This caused slow angiographic filling of the ophthalmic artery and most likely resulted in a thromboembolism to the retina. The patient awoke from the procedure with decreased vision ipsilaterally (initial visual acuity 20/200, which improved to 20/40 in 1 month). Follow-up angiography 9 months later revealed durable occlusion of the Onyx-embolized aneurysm with no recanalization, but further recanalization and coil compaction in the coiled larger dorsal variant aneurysm, which was embolized again. The patient’s vision continued to improve at subsequent ophthalmology follow-up visits.

Patient 2

A 48-year-old woman presenting with dizziness was found to have a right medial variant clinoidal segment intracranial aneurysm with a wide neck (Fig. 2, A and B). As in the previous case, we believed that liquid embolic agents might provide a better chance for complete aneurysm obliteration, especially at the neck, and thus a lower risk of recanalization compared with standard embolization techniques. Therefore, the aneurysm was embolized with 0.4 mL of Onyx using multiple cycles of balloon inflation and injection.

On the final digital subtraction angiography after microcatheter removal, a small string protrusion or “tail” of Onyx was present in the parent artery with cardiac-gated pulsations (Fig. 2C). Typically, a small amount of Onyx in the parent artery adjacent to the aneurysm cast will laminate along the endothelium of the parent artery, and the high cohesiveness of the Onyx prevents dislodgment. However, in this case, the Onyx did not laminate or tack down to the endothelium, and the unstable pulsatile string was thought to represent a long-term risk. Therefore, a 4.5 × 37-mm Enterprise VRD was placed across the neck of the aneurysm and over the Onyx string, securing it against the wall of the parent vessel (Fig. 2, D and E).

The patient awoke without symptoms and was discharged on post-procedure day 1 with no complications. She is awaiting follow-up angiography.

### Table 1. Cases of Unstable Onyx Casts Secured With Intracranial Stents

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y/sex</th>
<th>Institution</th>
<th>Presentation</th>
<th>Location</th>
<th>Size, mm</th>
<th>Neck: Dome</th>
<th>% of Final Occlusion</th>
<th>Type of Instability</th>
<th>Stent</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64/F</td>
<td>Vanderbilt</td>
<td>Unruptured</td>
<td>Ophthalmic segment, ventral variant</td>
<td>5 × 5.5</td>
<td>1:1</td>
<td>100</td>
<td>Entire cast migrating out of aneurysm</td>
<td>Enterprise (4.5 x 28mm)</td>
<td>Temporary vision loss in ipsilateral eye</td>
</tr>
<tr>
<td>2</td>
<td>49/F</td>
<td>Vanderbilt</td>
<td>Unruptured</td>
<td>Superior hypophyseal</td>
<td>6 × 7</td>
<td>0.8:1</td>
<td>100</td>
<td>Portion of cast in parent artery pulsating</td>
<td>Enterprise (4.5 x 37mm)</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>51/F</td>
<td>Vanderbilt</td>
<td>Unruptured</td>
<td>Ophthalmic Segment</td>
<td>4 × 6</td>
<td>2:3</td>
<td>100</td>
<td>Portion of cast in parent artery pulsating</td>
<td>Enterprise (4.5 x 37mm)</td>
<td>Temporary decrease in visual acuity in ipsilateral eye</td>
</tr>
<tr>
<td>4</td>
<td>59/F</td>
<td>Rush</td>
<td>Unruptured</td>
<td>Cavernous carotid</td>
<td>14 × 17</td>
<td>3:4</td>
<td>100</td>
<td>Entire cast moving during microcatheter removal</td>
<td>Neuroform (4.5 x30mm)</td>
<td>None</td>
</tr>
</tbody>
</table>
Patient 3

A 57-year-old woman presenting with headaches and a family history of aneurysmal subarachnoid hemorrhage was discovered to have a right superior hypophyseal aneurysm with a wide neck (Fig. 3, A and B). Based on our previous experience, we believed that a liquid embolic agent could provide superior neck coverage and possibly a lower risk of recanalization. Therefore, we embolized the aneurysm with Onyx, delivered with multiple cycles of balloon inflation and injection.

At the conclusion of the procedure, after the microcatheter was removed, we noted a small string of Onyx protruding into the parent artery with cardiac-gated pulsations, similar to patient 2 (Fig. 3C). An Enterprise VRD was placed to secure the string to the endothelium (Fig. 3, D and E).

On postoperative visual examination, we discovered a small area of decreased vision in her ipsilateral visual field. Ophthalmological consultation revealed retinal edema suggestive of emboli and visual acuity of 20/25 in that eye. The patient’s vision returned to baseline before discharge the next day. Follow-up angiography performed 6 months later revealed durable occlusion of her aneurysm with no change.

Patient 4

A 59-year-old woman presented with a right third nerve palsy. Further workup revealed a wide-neck cavernous segment internal carotid artery aneurysm (Fig. 4, A and B). The patient was administered aspirin and Plavix, and her aneurysm was embolized with Onyx.

The microcatheter was shaped into a “J” and was curved deep within the aneurysm dome, which in retrospect should have been avoided. After the aneurysm was obliterated with Onyx HD 500, while removing the curved microcatheter, the entire Onyx cast was noted to rotate approximately 20 degrees clockwise, secondary to the resistance of the overly shaped microcatheter. The cast was secured within the aneurysm with a 4.5 × 30-mm Neuroform Stent (Boston Scientific, Natick, MA) (Fig. 4,
C and D). The patient awoke without symptoms and was discharged home on postoperative day 1 with no complications.

**DISCUSSION**

Traditional coil embolization of intracranial aneurysms only fills approximately 34% of the aneurysm lumen volume with embolic material, and coils are not capable of providing complete coverage across the neck of an aneurysm. If an intracranial stent or VRD is added, a maximum of 45% occlusion can be achieved. Secondary to these limitations, there is an average recanalization rate of 20% after coiling intracranial aneurysms, and these limitations are more pronounced in wide-neck aneurysms. Stent-assisted coiling can increase the neck coverage and the number of coils, but the same limitations exist. Liquid embolic agents, however, offer the possibility of 100% volumetric filling of the aneurysm with embolic material as well as complete neck coverage at the parent artery interface. This could decrease the risk of subsequent aneurysm recanalization. There are some preliminary data to suggest improved angiographic results with Onyx HD 500 and a lower incidence of recanalization compared with coils. Therefore, in our practice, we consider the use of liquid embolic agents for most sidewall wide-neck carotid and vertebral aneurysms.

We have treated 47 aneurysms in 46 patients with Onyx HD 500 embolization at our 2 institutions, and we have encountered cast instability at the conclusion of the procedure 4 times (4 of 47 [9%]). Only 2 of the 46 patients presented with subarachnoid hemorrhage. Neither Onyx nor intracranial stent-assisted coiling is an ideal choice for acutely ruptured aneurysms because of the need for antiplatelet therapy before embolization. Our experience with Onyx HD 500 has revealed 2 types of instability, and both types can be successfully treated with an intracranial stent or VRD. The first type of instability has been encountered twice (patients 1 and 4) and is characterized by movement of the entire cast.
The rate of postoperative visual symptoms raises the question of whether Onyx HD 500 is more likely to lead to visual symptoms or retinal artery ischemia than traditional coiling, stent-assisted coiling, or clipping of paraclinoid intracranial aneurysms. Thromboembolic events have been detected on magnetic resonance imaging after coiling in as many as 60% of patients.\textsuperscript{10} The 9% complication rate in this small series is not outside the published ranges (3%–32%) for paraclinoid aneurysm treatment.\textsuperscript{11–19} More specifically, visual disturbance after treatment with either clipping or coiling of ophthalmic segment artery aneurysms is well described, and our rate is within the reported range (0%–29%).\textsuperscript{11–19}

**CONCLUSION**

Deployment of an intracranial self-expanding Neuroform stent or Enterprise VRD should be considered as an effective strategy after Onyx embolization of a wide-neck aneurysm if instability of the aneurysm cast is identified.

**Disclosure**

Demetrios K. Lopes, MD, and Robert A. Mericle, MD, perform physician training and physician proctoring for Onyx HD 500, for which they receive compensation from ev3. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

**REFERENCES**

The liquid embolic Onyx HD 500 offers the potential to achieve 100% aneurysm filling with remodeling of the aneurysm neck flush to interface with the parent vessel, resulting in possible reduced recurrence rates compared to coiling with or without stent assistance.\(^1,2\) In CAMEO there were 9 delayed parent vessel occlusions though evidence of Onyx migration associated with these was not reported and the incidences were felt to be related to inadequate antiplatelet therapy.\(^1\) Cikirge et al consider stent use to be essential for adequate Onyx embolization of large and giant aneurysms.\(^2\) This report highlights the possibility of direct Onyx cast compromise of the parent vessel, either by a strand of Onyx leaking into the vessel or by displacement of the entire cast, and demonstrates how this potentially dire complication can be rescued by emergent stent deployment across the aneurysm neck. Whether these aneurysms should be preemptively treated with stent assistance will emerge with greater experience.

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Simon et al present their experience with 4 cases in which Onyx HD 500 was used to treat an aneurysm, with subsequent instability of the Onyx requiring the placement of a stent or vascular reconstruction device as a rescue maneuver. The authors treated a total of 47 aneurysms in 46 patients with Onyx HD 500, and instability of the liquid embolic cast occurred in 4 (9%) of these cases, with 2 being further complicated by retinal ischemia. This complication rate seems to be relatively higher than the thromboembolic complication rate associated with coil embolization of unruptured aneurysms (which was the case in all but 2 of the authors’ 46 patients); therefore, one has to wonder if there were any other thromboembolic issues in this group of patients. One must be very careful when reading the authors’ comparison of their retinal ischemic events with those found in the published literature regarding the treatment, surgical or endovascular, of paracilnoid aneurysms. Many of the studies they cite deal with larger aneurysms; and in 1 of the studies, a full quarter of the unruptured aneurysms were extradural.\(^1\) One must also be careful not to be confused with a comparison between magnetic resonance imaging-detected thromboembolic events with actual clinical ischemic events. If the patient experiences no untoward neurologic sequelae related to a magnetic resonance imaging finding of thromboembolism, does it truly matter? The visual complication rates in the series presented here may very well fall in the range of that reported in the literature for all paracilnoid aneurysms, but it would seem that this novel technique is associated with at least 2 highly technical steps (balloon occlusion and the controlled injection of a liquid embolic agent) that require a fairly steep learning curve.

On a different note, the authors are to be commended for their creative use of intracranial stents in the treatment of this technical complication. Without either the Enterprise or Neuroform stent, the complications could have been truly disastrous. It is hoped that readers will see the value and relative safety associated with intracranial stents and not overlook them when treating complex cerebrovascular disorders. We wish the authors well and look forward to further publications related to the use of Onyx in the treatment of intracranial aneurysms.

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In the paper by Simon et al the authors report on 4 patients with wide-necked intracranial aneurysms treated with the newly FDA approved Onyx HD500 embolic. The 4 cases described were complicated by unstable movement of the embolic during the procedure, necessitating emergent stent placement (3 Enterprise and 1 Neuroform) across the aneurysm neck, which resulted in angiographic improvement in all patients. Three of the 4 patients had no neurologic sequelae from the procedure and 1 patient suffered ipsilateral decreased vision.

The paper is important in that Onyx HD recently received FDA approval for use in wide-necked intracranial aneurysms and this appears to be the first report of stent salvage for unstable or herniating Onyx HD500 embolic. Interestingly, it is also the first report of any kind on Onyx HD500 usage for intracranial aneurysms in this country. Prior reports from outside the United States using Onyx HD500 for aneurysms have documented embolic Onyx herniation with and without parent vessel occlusion. In fact, this complication was the most common major complication during the European (CAMEO) trial.\(^1\) Of note, there was also a significant rate of visual deficits perhaps related to multiple balloon inflations, thromboembolic occlusions or both.

As part of their efforts to obtain FDA approval in this country, the eV3 company ran 2 separate trials between 2001-2004, the first of which was terminated prematurely because of an unacceptably high rate of parent artery embolic herniation (26.3%), thromboembolic occlusion (18.4%) and resultant morbidity. It was felt that inappropriate and non-standardized use of antiplatelet agents, attempts to “remodel” the neck of the
aneurysm and/or lack of preembolization stent placement may have contributed to these complications. The results were improved considerably in the second trial in which there was a standardized antiplatelet regimen and aneurysm neck/parent vessel "remodeling" was not permitted, yielding an embolic herniation rate of 17.9% and a parent vessel occlusion rate of 3.6% (unpublished data, "Instructions for Use" insert for HD500). I suspect some of the thromboembolism/occlusions from these trials were in fact embolic cast instability that was simply not recognized or described as such. There is probably a fine line between cast instability and thromboembolism/occlusion, particularly in large or giant aneurysms where the aneurysm mouth is poorly visualized. The Neuroform and Enterprise stents were in their infancy during those initial trials making preembolization stent placement or stent-rescue a much more attractive option presently.

It is an interesting commentary on the way new embolic agents are rolled out in this country in that the first publication on Onyx HD500 use is a complications paper. There is little data comparing the risks and benefits of this agent to the other routinely used techniques for treating wide-neck aneurysms (stent-coiling, multiple catheter coiling, balloon-assisted coiling). The reported rate by Simon et al of this complication (9%) is somewhat concerning, despite the fact that the bailout procedure was mostly successful. The long-term and even midterm effects of aneurysm stents are still not well defined. Longer term follow-up of these 4 patients as well as a more general reporting on the authors’ accumulating experience with this new agent for intracranial aneurysm therapy would be a welcome addition to the literature.

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