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Transarterial Onyx Embolization of Cranial Dural Arteriovenous Fistulas: Long-Term Follow-Up

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ABSTRACT

BACKGROUND AND PURPOSE: Endovascular therapy with liquid embolic agents is a common treatment strategy for cranial dural arteriovenous fistulas. This study evaluated the long-term effectiveness of transarterial Onyx as the single embolic agent for curative embolization of noncavernous cranial dural arteriovenous fistulas.

MATERIALS AND METHODS: We performed a retrospective review of 40 consecutive patients with 41 cranial dural arteriovenous fistulas treated between March 2006 and June 2012 by using transarterial Onyx embolization with intent to cure. The mean age was 57 years; one-third presented with intracranial hemorrhage. Most (85%) had cortical venous drainage. Once angiographic cure was achieved, long-term treatment effectiveness was assessed with DSA and clinical follow-up.

RESULTS: Forty-nine embolization sessions were performed; 85% of cranial dural arteriovenous fistulas were treated in a single session. The immediate angiographic cure rate was 95%. The permanent neurologic complication rate was 2% (mild facial palsy). Thirty-five of the 38 patients with initial cure underwent short-term follow-up DSA (median, 4 months). The short-term recurrence rate was only 6% (2/35). All patients with occlusion at short-term DSA undergoing long-term DSA (median, 28 months) had durable occlusion. No patient with long-term clinical follow-up (total, 117 patient-years; median, 45 months) experienced hemorrhage.

CONCLUSIONS: Transarterial embolization with Onyx as the single embolic agent results in durable long-term cure of noncavernous cranial dural arteriovenous fistulas. Recurrence rates are low on short-term follow-up, and all patients with angiographic occlusion on short-term DSA follow-up have experienced a durable long-term cure. Thus, angiographic cure should be defined at short-term follow-up angiography instead of at the end of the final embolization session. Finally, long-term DSA follow-up may not be necessary if occlusion is demonstrated on short-term angiographic follow-up.

ABBREVIATIONS: cDAVF = cranial dural arteriovenous fistula; CVD = cortical venous drainage

Endovascular therapy is commonly used for the treatment of noncavernous cranial dural arteriovenous fistulas (cDAVFs). Cyanoacrylates, ethyl alcohol, coils, and particles can be used alone or in combination via transarterial, transvenous, or occasionally direct percutaneous treatment routes. There is no US

Food and Drug Administration–approved liquid embolic agent for the treatment of cDAVFs. The ethylene-vinyl alcohol copolymer liquid embolic system (Onyx; Covidien, Irvine, California) is FDA-approved for the presurgical embolization of brain arteriovenous malformations. Since Onyx has become available, transarterial embolization of cDAVFs by using Onyx as the sole endovascular embolic agent has become our preferred treatment strategy. This endovascular treatment approach represents an “off-label” use of the Onyx liquid embolic system.

The immediate occlusion rate in large cohort studies of patients treated with transarterial Onyx embolization ranges from 62% to 92%, and short-term durable occlusion has been demonstrated.^{1–4} We have previously reported our short-term experience using Onyx in these patients⁵ and have compared the success of this technique with embolization using *n*-butyl cyanoacrylate.⁶ However, there currently remain no published data on the long-term effectiveness for embolization of cDAVFs by using Onyx, to

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Table 1: Baseline characteristics of study cohort (n = 40 patients with 41 cDAVFs)

Characteristic	No. of Patients
Age (mean; range)	57 (30–79)
Male (%)	21 (53%)
Presentation	
Tinnitus	14 (35%)
Hemorrhage	13 (33%)
Incidental/nonspecific headache syndrome	10 (25%)
Seizure	2 (5%)
Superficial siderosis	1 (2%)
Cognard grade	
I	5 (12%)
IIA	3 (7%)
IIB	3 (7%)
IIA+B	4 (10%)
III	15 (37%)
IV	11 (27%)
Borden grade	
I	8 (15%)
II	7 (22%)
III	26 (63%)

our knowledge. Here we report our long-term angiographic occlusion rate and clinical follow-up in a cohort of noncavernous cranial DAVFs that were treated by using transarterial Onyx embolization with the intention of complete cure.

MATERIALS AND METHODS

Patient Cohort

Between March 2006 and June 2012, forty consecutive patients with 41 noncavernous cDAVFs treated by using transarterial Onyx embolization as the single embolic agent with the intention of complete cure were retrospectively identified. Baseline characteristics of the study cohort are described in Table 1. This retrospective analysis was approved by the institutional review board of Massachusetts General Hospital.

Embolization Procedure

All procedures were performed with the patient under general anesthesia by using biplane angiographic units (Neurostar, Axiom Artis, and Artis zee; Siemens, Erlangen, Germany). Informed consent included the off-label use of Onyx as the primary embolization agent. All procedures were performed via the transfemoral approach by using coaxial techniques with continuous flushing of the catheters with heparinized saline (4000 U of heparin per liter). After initial diagnostic angiography, standard guide catheters were placed into the external carotid artery and dimethyl-sulfoxide-compatible microcatheters were directed into the target arterial pedicle. In most cases, a Marathon microcatheter (Covidien) was placed through a 5F MPC Envoy guide catheter (Codman & Shurtleff, Raynham, Massachusetts) and navigated over an X-Pedion-10 (Covidien) or Mirage 0.008 microwire (Covidien) to reach the distal aspect of the target arterial pedicle. After microcatheter angiography confirmed an optimal position, the microcatheter was flushed with 5 mL of normal saline. The dead space of the microcatheter was subsequently filled with dimethyl-sulfoxide, and Onyx was injected during 90 seconds to fill the microcatheter and replace the dimethyl-sulfoxide in the dead

Table 2: Procedural characteristics of study cohort (n = 41 DAVFs)

Characteristic	No.
No. of feeding pedicles (mean, range)	4 (1–10)
Total No. of embolization procedures	49
No. of embolization procedures per patient (mean; range)	1.2 (1–3)
No. of single-stage embolizations	35 (85%)
Complications (n = 49 embolization procedures)	
Technical events	5 (10%)
All clinical events	7 (14%)
Transient neurologic	1 (2%)
Permanent neurologic	1 (2%)
Death	0

space. Under continuous fluoroscopic guidance, Onyx was slowly infused into the target arterial pedicle by using a “thumb-tapping” technique to form an initial “plug” at the microcatheter tip. Excessive reflux was avoided to minimize challenges related to subsequent microcatheter removal and the risk of nontarget embolization. Once sufficient antegrade flow of Onyx was established, prolonged injections were performed. Intermittent injection pauses of between 30 and 120 seconds were used to avoid Onyx migration into nontarget areas and to facilitate redirection of newly injected Onyx to desired areas. In general, Onyx-34 was used for plug formation with subsequent injection of Onyx-18. Intermittent angiography through the guide catheter was occasionally performed during embolization to assess the extent of residual flow or areas of nontarget embolization. Angiographic cure was defined as formation of an attenuated Onyx cast in the target fistula and the proximal draining venous structures with no residual arteriovenous shunting. In 2 cases, Gelfoam (Phadia, Uppsala, Sweden) was injected into the superficial temporal and occipital arteries to further promote thrombosis of the scalp arteries after Onyx embolization.

Follow-Up

All patients were scheduled for short-term (3-month) follow-up angiography to confirm persistent occlusion of the cDAVF following the endovascular treatment course. If complete occlusion of the shunt was not achieved, further treatment (endovascular or surgical) was planned. No patients underwent radiosurgical treatment. Long-term (>12-month) angiographic follow-up was left to the discretion of the neurointerventionalist; early in the study period, 3-year angiography was scheduled.

RESULTS

Patient Cohort

Mean age was 57 years (range, 30–79 years), and one-third of patients presented with intracranial hemorrhage. Thirty-five (85%) had cortical venous drainage (CVD); the classifications of Cognard et al⁷ and Borden et al⁸ are reported in Table 1.

Embolization Safety Results

Forty-nine embolization sessions were performed for 41 cDAVFs in 40 patients. The procedural characteristics are described in Table 2. Although the cDAVFs had multiple arterial feeding pedicles (mean, 4; range, 1–10), the mean number of embolization ses-

Table 3: Procedural effectiveness at time of treatment, short- and long-term follow-up

Procedural Effectiveness (No. of patients)	Angiographic Cure (No.)
At end of final treatment (40)	35 (95%)
Short-term angiographic follow-up ^a (35)	33 (94%)
Long-term angiographic follow-up ^b (24)	24 (100%)

^a Short-term follow-up occurred at a median of 4.2 months (2–12 months).

^b Long-term angiographic follow-up occurred at a median of 28.2 months (12–63 months).

sions per patient was 1.2 (range, 1–3). Thirty-five (85%) cDAVFs were treated to cure in a single embolization session.

Technical procedural complications without clinical consequence occurred in 5 (10%) of 49 embolization sessions—1 vertebral artery dissection, 1 occipital artery perforation during Onyx embolization that sealed, 1 microcatheter rupture in the middle meningeal artery, 1 instance of nontarget nonocclusive embolization into a superior sagittal sinus leaflet, and a single episode of intraprocedural thrombosis in the external carotid circulation during a treatment session despite heparinization, which raised the suspicion of heparin-induced thrombocytopenia. This particular procedure was aborted, and the cDAVF was cured on the third embolization session.

Adverse clinical events occurred in 7 (14%) of 49 embolization sessions: focal alopecia from radiation injury, transient orbital chemosis of unclear etiology that resolved within 24 hours, 2 cranial nerve palsies (partial facial and maxillary nerve palsies) with near-complete and complete resolution in these 2 patients, transient intraprocedural bradycardia progressing to brief self-resolving asystole without clinical consequence during embolization through the artery of the falx cerebelli for a Cognard III cDAVF at the torcula, and an episode of immediate postextubation respiratory distress leading to secondary asystolic arrest. The patient was resuscitated and recovered without clinical consequences. The final event was pulmonary embolism occurring 4 days after embolization of a ruptured Cognard IV cDAVF in a 71-year-old man. The only permanent neurologic complication was in the patient with partial facial palsy. There were no procedure-related cerebral ischemic or hemorrhagic complications, nor procedural mortality.

Embolization Effectiveness Results

The effectiveness of the embolization procedure at the end of the final treatment, and at short- and long-term angiographic follow up is summarized in Table 3.

Immediate Results. At the end of the final session, angiographic cure was achieved in 38 of 40 (95%) patients. Two patients were not cured after transarterial Onyx injection. A 72-year-old man with an incidental Cognard III cDAVF draining into a single cortical vein had minimal residual arteriovenous shunting at the end of 2 embolization sessions. His second embolization session was complicated by partial left maxillary and facial nerve palsies, and he underwent surgical closure of the shunt. His cranial nerve palsies had recovered by his 6-month clinical follow-up. The second patient, a 54-year-old woman, presented with pulsatile tinnitus from an extensive transverse-sigmoid sinus junction Cognard IIa cDAVF. Although significant reduction in shunting volume was

achieved, her second embolization session was complicated by partial facial nerve palsy. Her pulsatile tinnitus became tolerable; thus, no further treatment was performed. Her facial nerve function recovered to almost normal, with only minimal residual palsy.

Short-Term Follow-Up. Thirty-five (92%) of the 38 patients with immediate angiographic occlusion underwent short-term follow-up DSA at a median of 4.2 months (range, 2–12 months). Two patients (6%) had recurrence of their cDAVF. One patient with recurrence of his Cognard IV cDAVF located at the torcula underwent an additional uncomplicated embolization session to angiographic cure, which was durable at repeat angiography at 10 months posttreatment. The second recurrence occurred in a patient with a Cognard IV cDAVF supplied by the right superficial temporal artery, which was treated with surgical occlusion.

Long-Term Follow-Up. Twenty-four (73%) of the 33 patients with short-term angiographic occlusion underwent long-term (>12-month) DSA at a median of 28.2 months (range, 12–63 months). All patients (100%) had durable occlusion of their cDAVF at 59 patient-years of follow-up. Long-term clinical (>12-month) follow-up was available for 32 patients at a median of 44.8 months (12–80 months). No patient experienced intracranial hemorrhage during 117 patient-years of long-term follow-up.

DISCUSSION

Our results demonstrate the effectiveness of transarterial Onyx embolization as the single embolic agent for achieving long-term durable cure of noncavernous cDAVFs. In addition, in a cohort of patients in which one-third presented with intracranial hemorrhage and 85% demonstrated CVD, clinical outcomes were favorable, with minimal permanent complications and no patient experiencing intracranial hemorrhage during 117 patient-years of long-term follow-up.

Transarterial Onyx embolization has provided a new treatment paradigm for the care of patients with cDAVFs. The characteristics of the compound allow it to penetrate the multiple arterial branches that supply these lesions and occlude vascular passages into the proximal venous component, the ultimate treatment goal. Several large cohort studies by using transarterial Onyx as the primary embolization method have reported high initial cure rates and durable short-term angiographic occlusion. Immediate postembolization or short-term DSA cure rates range from 62% to 92%.^{1–4} Angiographic follow-up varied per series, with a median of 3–6 months. In 2 large cohort series, the short-term DSA occlusion rate was 100%.^{1,2} Therefore, these data provide satisfactory evidence that effective short-term occlusion with Onyx is readily achievable.

However, longer term angiographic and clinical follow-up data have not been published to validate the long-term effectiveness of this treatment strategy. In addition, there have been reports of recurrence of cured cDAVFs after transarterial treatment.⁹ Our data demonstrate that angiographic cure is only definitively confirmed after interval short-term angiography demonstrates cDAVF occlusion. In our cohort, 2 of 35 patients with immediate posttreatment angiographic occlusion had recurrence at short-term (median, 4.2 months) DSA. These recurrences

could be potentially related to intraprocedural vasospasm, which could obscure residual areas of arteriovenous shunting, persistent microfistulas not visible immediately following the initial treatment, or insufficient penetration of Onyx into the proximal draining venous structures. However, once occlusion is demonstrated on short-term DSA, all patients had durable angiographic occlusion at a median of 28.2 months (range, 12–63 months).

The ultimate clinical goal of treatment of cDAVFs is to alter the natural history, particularly with regard to the risk of intracranial hemorrhage. Large population studies reveal that approximately 30% of patients with cDAVF with CVD present with hemorrhage.¹⁰ The risks of early rebleeding can be high—in an earlier cohort of 20 patients with intracranial hemorrhage from cDAVFs, 7 patients (35%) had radiologically confirmed rebleeding within the first 2 weeks after presentation.¹¹ Long-term morbidity and mortality rates are elevated in patients with persistent CVD. In a cohort of 20 patients with persistent long-term CVD followed for a mean of 4.3 years, 7 patients (35%) bled and 9 patients (45%) died.¹² Five of the 20 patients initially presented with intracranial hemorrhage—3 of these 5 patients rebled; 5 of 15 remaining patients developed hemorrhage. The hemorrhages during follow-up occurred at a median of 2.3 years (range, 0.3–5.4) after the initial presentation. Despite treatment, cDAVFs with CVD are associated with excessive long-term mortality,¹³ making long-term clinical follow-up prudent. In our treated cohort, one-third presented with intracranial hemorrhage and 9 of these 13 patients had long-term (>12-month) clinical follow-up (median, 44.5 months; range, 12.3–81.3 months; total, 34 patient-years). All are alive, and none experienced rebleeding.

It has been reported that patients presenting with benign (incidental/pulsatile tinnitus/orbital phenomena) symptoms from cDAVFs with CVD may be at lower annual risk for intracranial hemorrhage (approximately 1.5%) compared with those presenting with aggressive neurologic symptoms.^{14–16} However, these estimates are based on small patient numbers or short follow-up periods. In the series by Strom et al,¹⁵ 1 of 17 patients presenting with benign symptoms from persistent CVD bled 13 years later. In another series by Söderman et al,¹⁴ a complicated “time-at-risk” period was calculated by combining the time between symptom onset/nonangiographic diagnosis, the time between diagnostic angiography and treatment, and clinical follow-up. In the cohort of 53 patients who did not present with intracranial hemorrhage, 1 patient bled during a time-at-risk period of 67.1 patient-years, conferring an annual 1.5% risk for intracranial hemorrhage. Despite the complex methodology and limitations,¹⁷ the per-patient follow-up period of 1.3 years is relatively short. In the most recent publication evaluating this patient cohort, 1 in 24 cDAVFs with benign presentation bled during a total of 23 patient-years of untreated follow-up, leading to an annual hemorrhage rate of 4.3%.¹⁸ Of note, the range of follow-up for the entire cohort of 70 patients was 1 day to 13 years.

Most (24 of 40) of the patients in our cohort had benign presentation—pulsatile tinnitus, nonspecific headache syndrome, or incidental. Eighteen of 24 patients with benign presentation had CVD. In this cohort, the long-term risks of intracranial hemorrhage need to be balanced against the treatment risks. In the entire cohort, only 1 permanent neurologic complication (partial facial

palsy) occurred in 40 patients who underwent 49 embolization sessions. This is within the (0%–7.5%) permanent complication rate in the larger published cohorts treated with transarterial Onyx.^{1,3,4,19} While the natural history of patients with benign symptoms from cDAVFs with CVD remains unclear, we think that the high success rate coupled with a low morbidity rate from transarterial Onyx embolization mandates treatment to angiographic cure once CVD is discovered, for long-term hemorrhage protection.

Our study adds unique and important long-term effectiveness data supporting the use of transarterial Onyx for the embolization of cDAVFs. The strengths of our study include the long-term angiographic and clinical follow-up, the use of DSA to confirm durable occlusion, and the homogeneous and relatively large cohort of noncavernous cDAVFs treated with transarterial Onyx. The limitations are the retrospective study design and the 9 patients with cure on short-term follow-up DSA who did not undergo long-term DSA. This limitation reflected a change in our practice as we gathered experience during the study period. The presence of long-term durable angiographic occlusion in all patients with occlusion on short-term DSA follow-up during the study period led some of our neurointerventionists to perform MR angiography after short-term DSA follow-up.

CONCLUSIONS

Transarterial embolization with Onyx as the sole embolic agent results in durable long-term cure of noncavernous cranial DAVFs. Recurrence rates are low on short-term follow-up, and all patients with angiographic occlusion on short-term DSA follow-up have durable long-term cure. Thus, angiographic cure should be defined at short-term follow-up angiography instead of at the end of the final embolization session. Finally, long-term DSA follow-up may not be necessary if occlusion is demonstrated on short-term angiographic follow-up.

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