Superselective intranidal delivery of platinum-based high-density packing coils for treatment of arteriovenous malformations

Kirthi S. Bellamkonda, MSc,^a Arash Fereydooni, MD, MS,^a Kiley Trott, MD,^{b,c} Yan Lee, MD,^{b,c} Saral Mehra, MD, MBA,^{b,c} and Naiem Nassiri, MD,^{a,c} New Haven, Conn

ABSTRACT

Arteriovenous malformations (AVMs) classically feature an intervening nidus of poorly differentiated endothelium. The pillar of modern AVM treatment is intranidal delivery and deposition of various liquid embolic agents such as n-butyl cyanoacrylate, ethylene vinyl alcohol copolymer, and ethanol. These agents are cumbersome to prepare, deliver, and deploy and have been associated with complications related to limited delivery control, nonretrievability, frequent microcatheter exchanges, and nontarget embolization. Coils and other proximal occlusive agents have not been traditionally recommended as sole embolic agents for AVM treatment given the inherent lack of adequate AVM nidus penetration with previous coil technologies. In the present report, we have described a series of three patients with AVMs in whom newer generation, platinum-based, packing coils were used safely and effectively as the primary agent for superselective nidal penetration and embolization. (J Vasc Surg Cases and Innovative Techniques 2021;7:230-4.)

Keywords: Arteriovenous malformation; AVM; Embolization; Nidus; Platinum coils

Arteriovenous malformations (AVMs) represent pathologic low-resistance connections between arteries and veins that form proximal to high-resistance distal capillary beds.^{1,2} Left untreated, they can cause venous hypertension-mediated pain, bleeding, ulceration, and disfigurement. More severe, chronic cases can rarely cause distal steal and high-output heart failure.³ AVMs classically feature an intervening nidus of various angioarchitectural configurations.⁴ This is an extremely low-resistance region with poorly differentiated endothelium and neither an arterial nor a venous designation. The pillar of modern AVM treatment is nidal obliteration using various polymerizing and nonpolymerizing liquid embolic agents such as n-butyl cyanoacrylate (n-BCA), ethylene vinyl alcohol copolymer (Onyx; Medtronic, Dublin, Ireland), and ethanol. These can be associated with potentially devastating complications related to nontarget distribution and embolization, especially in

https://doi.org/10.1016/j.jvscit.2021.01.005

less experienced hands.⁵ Although coils have been used to obliterate direct fistulous arteriovenous connections and as adjunct embolic agents to seal proximal nidus arterial feeders and distal venous drainers, coiling has not been used routinely for intranidal embolization owing to the technical limitations and the coils' inability to induce endothelial cell disruption. In the present report, we have demonstrated that superselective intranidal embolization using the latest generation, platinum-based packing coils as a first-line embolic agent is safe and effective in treating certain configurations of AVMs. All the patients provided written informed consent for the report of their cases.

CASE REPORT

Patient 1. A 44-year-old, healthy male patient with a medical history of squamous cell cancer of the lip had been referred for further evaluation and treatment of a large, symptomatic, left anterolateral proximal chest wall mass. The findings from examination of an incisional biopsy by the referring service had suggested a vascular malformation. The patient reported that the mass had been present for "quite some time" but could not provide further details. His symptoms included pain, swelling, discomfort, and limited range of motion at the shoulder joint. The mass was partially compressible and tender and warm to palpation, with visible overlying venous tributaries. Mild ipsilateral arm swelling was present, with no evidence of acral steal. We detected a high-flow, low-resistance signal using handheld Doppler ultrasound interrogation. Using T2-weighted, fatsuppressed, contrast-enhanced magnetic resonance imaging (MRI) series, the mass showed enhancement within the subcutaneous tissues with no invasion of the intercostal musculature or thoracic cavity.⁶ Multiple flow voids were detected, confirming the presence of an AVM.

From the Division of Vascular Surgery and Endovascular Therapy,^a and Division of Otolaryngology,^b Yale School of Medicine; and the Vascular Malformations Program, Yale New Haven Hospital.^c

Author conflict of interest: N.N. has been on the speakers' bureau and served as a consultant for Penumbra, Inc. K.S.B., A.F., K.T., Y.L., and S.M. have no conflicts of interest.

Correspondence: Naiem Nassiri, MD, Division of Vascular Surgery and Endovascular Therapy, Yale University School of Medicine, 333 Cedar St, Boardman 204, New Haven, CT 06510 (e-mail: naiem.nassiri@yale.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

²⁴⁶⁸⁻⁴²⁸⁷

^{© 2021} The Authors. Published by Elsevier Inc. on behalf of Society for Vascular Surgery. This is an open access article under the CC BY-NC-ND license (http:// creativecommons.org/licenses/by-nc-nd/4.0/).



Fig 1. A (top row), Intraoperative imaging studies from patient 1 (from left to right): pre-embolization angiography of lesion, superselective microcatheterization of feeding vessel, nidal coil deposition, and postembolization angiogram depicting lesion devascularization. **B** (middle row), Intra- and postoperative imaging studies from patient 2 (from left to right): pre-embolization angiogram of lesion, postembolization angiogram depicting lesion devascularization, external appearance of lesion preoperatively, and external appearance of lesion postoperatively. **C** (bottom row), Intraoperative imaging of patient 3 (from left to right): pre-embolization angiogram of lesion, intermediate results of coil embolization, and final results of embolization.

Based on these findings, transfemoral left subclavian angiography with embolization was offered. Angiography revealed a Yakes IIA AVM fed by branches of the thoracoacromial trunk and lateral thoracic artery, with rapid shunting into the axillosubclavian venous system (Table). A 2.7F, 150-cm Lantern microcatheter was placed at the terminal branches of the thoracoacromial trunk feeding the AVM nidus. Three 60-cm Ruby packing coils (Penumbra, Inc, Alameda, Calif) were advanced and delivered, with appropriate nidal deposition and no evidence of migration or nontarget embolization. The completion angiogram demonstrated near-total obliteration of the AVM nidus with cessation of venous arterialization (Fig 1, *A*). No complications developed. The patient reported an immediate improvement in local pain. His postoperative course ≤18 months was uneventful, with sustained symptom relief and devascularization of the AVM confirmed using duplex ultrasound surveillance.

Patient 2. A 28-year-old male patient had presented with a chronically symptomatic submental vascular malformation that had been treated 9 years previously with resection and 5 years previously with embolization but with limited success. The patient complained of throbbing, pulsatile pain, and cosmetic disfigurement. Physical examination demonstrated a protuberant, irregular, skin-colored, right submental mass with a cobblestone overlying appearance. A contrast-enhanced, T2-weighted, fat-suppressed MRI series revealed an enhancing, 3-cm subcutaneous lesion overlying the mental protuberance with multiple flow voids suggestive of an AVM. Pre-operative

Post-operative



Fig 2. Left: Preoperative appearance of patient 3's lesion. **Right:** Appearance of lesion after embolization and surgical reconstruction.

Selective bilateral cervicocerebral angiography confirmed the presence of a Yakes IIA AVM that was fed predominantly by terminal branches of the right facial and submental arteries. During the course of two separate sessions, superselective microcatheterization of the nidus was performed as described, and a total of three coils (one Ruby packing [15 cm; Penumbra, Inc] and two SMART extrasoft coils [1 mm \times 3 cm and 2 mm \times 4 cm; Penumbra, Inc]) were delivered terminally into the nidus. Completion angiography demonstrated obliteration of nidal flow and diminished venous enhancement. At \sim 90 days after embolization, the patient underwent successful resection and local reconstruction with no major bleeding complications (Fig 1, *B*). At the 6-month follow-up examination, the patient had remained asymptomatic with no further recurrence of the lesion or symptoms.

Patient 3. A 22-year-old female patient had presented with a longstanding history of a lower lip vascular malformation, previously treated unsuccessfully with laser ablation. She noted pain, swelling, ulceration, bouts of projectile hemorrhage, severe

cosmetic disfigurement, and psychosocial impairment that limited employment and activities of daily living. The physical examination revealed an exophytic, fungating mass affecting the right lower lip with mucosal involvement and ulceration. Overlying ulcerations were present that were extremely tender to palpation. Doppler ultrasound interrogation confirmed a high-flow, low-resistance signal. Topical and oral analgesics had provided little to no relief.

Given these findings, we decided to forego MRI in favor of selective angiography. Bilateral selective examinations confirmed the presence of a large Yakes IIA and IV AVM affecting the right mental and submental regions. Arterial feeders were predominantly from the terminal branches of the right facial and submental arteries. Using a similar technique, superselective nidus microcatheterization and coil deposition was performed in two separate sessions spanning 2 months. A total of 20 Ruby packing, SMART wave, and SMART extra soft coils (Penumbra, Inc) ranging from 2 to 4 mm in diameter and 4 to 10 cm in length were deployed (Fig 1, C). The Yakes IV component of the AVM was not conducive to transarterial microcatheterization of the dispersed, interstitial nidus and was, therefore, treated successfully with a single session of direct stick embolization with one vial of n-BCA. No bouts of nontarget embolization occurred, and no perioperative complications had developed. After each session, the patient had recovered uneventfully and experienced a segmental reduction in symptoms. After the first session of embolization, the hemorrhagic bouts had ceased. Within 1 month after the final procedure, the patient had undergone successful resection of the malformation with local reconstruction and wound healing at 4 months postoperatively. At the last follow-up examination, she remained largely asymptomatic with satisfactory cosmesis. Also, she had returned to work and no longer required analgesic pharmacotherapy (Fig 2).

DISCUSSION

Although used occasionally as an adjunctive method for proximal inflow or distal outflow occlusion when paired with Onyx (Medtronic), n-BCA, or ethanol, coils have traditionally not been the primary embolic agent of choice for AVM treatment, given their limited capability for nidal penetration. Despite the popularity of ethanol among certain experts, we have tended to use a more conservative approach to AVM embolization, relying on less potent embolic agents such as n-BCA, Onyx (Medtronic), and coils. Yakes pointed out that "proximal occlusion of the feeding arterial supply will never effectively treat an AVM."7 Without obliteration of the nidus itself, the AVM is likely to recruit collateral feeding vessels and recur with time.^{1,2} Older generation coils placed in proximal feeding arteries were never adequate for sustained AVM obliteration. We have, however, demonstrated in the present case series that newer generation, low-profile, platinum-based packing coilsnicknamed "liquid metal"-can safely and effectively be used as first-line and primary embolic agents of choice

Table. Summary of Yakes classification system for arte-riovenous malformations

| Yakes classification | Description |
|-------------------------|--|
| 1 | Arteriovenous fistula without intervening nidus, with one inflow artery and one outflow vein |
| Π | Arteriovenous malformation with poorly differentiated nidus with multiple contributory arteries and (a) multiple outflow veins, which can be aneurysmal or (b) a solitary aneurysmal outflow vein |
| III | Arteriovenous malformation without a nidus, containing multiple contributory arteries and arterioles connecting directly into an aneurysmal vein and (a) one solitary outflow vein or (b) multiple outflow veins |
| IV | Arteriovenous malformation with nidus containing a large number of arterioles shunting into many venules, with extensive tissue infiltration |

for AVM nidus obliteration with satisfactory short- to midterm outcomes. Their use requires careful angiographic interrogation and classification of the AVM nidus because not all angioarchitectural varieties-such as Yakes IV AVMs-will be conducive to this technique. Yakes described the Yakes IV AVM as "innumerable microfistulae" interspersed with capillary beds. Thus, transarterial approaches will not be selective enough to both obliterate pathologic microfistulas and also spare the capillary beds, leading to inevitable tissue necrosis.⁸ Classification schemes, such as those championed by Yakes and Houdart, therefore, remain essential component of therapeutic strategies (Table).9,10 It is essential to highlight that superselective, third and fourth order, branch microcatheterization is needed-with microcatheters as low profile as 1.6F-for adequate terminal access of the nidus such that premature and proximal nontarget embolization is avoided. With certain anatomic constraints, however, in which direct intranidal microcatheter access might not be feasible or safe, these "liquid metal" coils can be advanced antegradely to penetrate the nidus from a more proximal location, given their low resistance to flow and premature coiling on exiting from the microcatheter tip. Given these flow properties, these coils have traditionally been used as "fillers" to enhance packing of a previously scaffolded space and not as an initial deposition. By deploying these coils as the first deposition, we are taking advantage of their inherent resistance to coiling to maximize distal penetration and intranidal flow.

The fully detachable nature of these coils allows for total expulsion from the microcatheter and evaluation of the deposited configuration before deployment commitment without time restriction or other such limitations. Furthermore, total retrieval back into the delivery apparatus and even back outside the patient is possible, which helps to maximize deployment precision and minimize the risk of nontarget embolization. These maneuvers are not possible with liquid embolic agents, lethal which can have catastrophic—even consequences.⁵ Furthermore, the inert, noninflammatory nature of platinum is beneficial for subsequent surgical debulking or resection of the treated AVM. We have used Doppler ultrasound studies for follow-up imaging, because the presence of coils results in prohibitive artifacts on computed tomography or MRI.

A precedent exists for successful coil-only treatment of type II renal AVMs, for which liquid agents have a high risk of causing infarct.¹¹ We found 1 described case of coil-only embolization and 23 cases of coil-and-ethanol therapy in a study of 192 Yakes II AVMs.¹²

We, too, required the adjunctive use of n-BCA despite successful coil embolization in the Yakes IV nidus we encountered in one patient. This finding highlights the importance of a comprehensive, multifaceted approach to AVM treatment. The relatively short follow-up remains a limitation of our small series. Late complications and recurrence are concerns that require ongoing surveillance. We have continued to follow up these patients to better understand the long-term durability of our approach.

CONCLUSIONS

Historically, AVM nidus embolization has been accomplished via direct stick or transarterial delivery of liquid embolic agents, which can be associated with limited control and the risk of irreversible nontarget embolization. We have demonstrated in the present series of three patients that superselective transarterial microcatheterization and intranidal delivery of platinum-based, highdensity packing coils is technically feasible, safe, and effective in treating peripheral AVMs in the short term and as a bridge to surgical excision. Longer term follow-up is needed to better ascertain treatment durability.

REFERENCES

- 1. Rosen RJ, Nassiri N, Drury JE. Interventional management of high-flow vascular malformations. Tech Vascular Interv Radiol 2013;16:22-38.
- Rosen RJ, Nassiri N. Visceral and extremity arteriovenous malformation. In: Handbook of Interventional Radiologic Procedures. Philadelphia: Lippincott, Williams, & Wilkins; 2010.
- Carlson TR, Yan Y, Wu X, Lam MT, Tang GL, Beverly LJ, et al. Endothelial expression of constitutively active Notch4 elicits reversible arteriovenous malformations in adult mice. Proc Natl Acad Sci 2005;102:9884-9.
- Fereydooni A, Dardik A, Nassiri N. Molecular changes associated with vascular malformations. J Vasc Surg 2019;70: 314-26.e1.

- Yakes WF, Yakes AM, Vogelzang RL, Ivancev K. Endovascular treatment of vascular malformation: an overview. In: Kim Y-W, Lee B-B, Yakes WF, Do Y-S, editors. Congenital Vascular Malformations: A Comprehensive Review of Current Management. Berlin, Germany: Springer; 2017. p. 197-209.
- 6. Lidsky ME, Spritzer CE, Shortell CK. The role of dynamic contrast-enhanced magnetic resonance imaging in the diagnosis and management of patients with vascular malformations. J Vasc Surg 2012;56:757-64.el.
- 7. Yakes W, Huguenot M, Yakes A, Continenza A, Kammer R, Baumgartner I. Percutaneous embolization of arteriovenous malformations at the plantar aspect of the foot. J Vasc Surg 2016;64:1478-82.
- Yakes WF, Yakes AM. Classification of arteriovenous malformation and therapeutic implication. In: Mattassi R, Loose DA, Vaghi M, editors. Hemangiomas and Vascular Malformations: An Atlas of Diagnosis and Treatment. Berlin, Germany: Springer; 2015. p. 263-76.
- 9. Houdart E, Gobin Y, Casasco A, Aymard A, Herbreteau D, Merland J. A proposed angiographic classification of

intracranial arteriovenous fistulae and malformations. Neuroradiology 1993;35:381-5.

- Yakes WF, Vogelzang RL, Ivancev K, Yakes AM. New arteriographic classification of AVM based on the Yakes classification system. Berlin, Germany. In: Kim Y-W, Lee B-B, Yakes WF, Do Y-S, editors. Congenital Vascular Malformations: A Comprehensive Review of Current Management 2017:63-69.
- Lee SY, Do YS, Kim CW, Park KB, Kim YH, Cho YJ. Efficacy and safety of transvenous embolization of type II renal arteriovenous malformations with coils. J Vasc Interv Radiol 2019;30:807-12.
- 12. Bouwman FC, Botden SM, Verhoeven BH, Kool LJS, van der Vleuten CJ, de Blaauw I, et al. Treatment outcomes of embolization for peripheral arteriovenous malformations. J Vasc Interv Radiol 2020;31:1801-9.

Submitted Oct 25, 2020; accepted Jan 21, 2021.