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Original Article

Endovascular management of multiple intracranial dural arteriovenous fistulas

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ABSTRACT

Background and purpose. – Multiply occurring intracranial dural arteriovenous fistulas (dAVFs) have been documented but rarely occur, and neither pathogenesis nor prognosis is clearly understood. This study was conducted to analyze angiographic characteristics of multiple dAVFs and to chronicle our treatment experience.

Methods. – Between April, 2002 and January, 2018, data prospectively collected from 310 patients with intracranial dAVFs were systematically reviewed, assessing clinical and anatomic outcomes of endovascular treatment in 32 patients with multiple dAVFs (≥ 2 fistulas each). Lesions were categorized as multifocal or diffuse type, depending on presentation, and further characterized as progressive or non-progressive disease.

Results. – Overall, 18 patients (56.3%) experienced aggressive presentations, including intracerebral hemorrhage or venous infarction. Cortical venous reflux (CVR) was observed in 26 patients (81.3%), and sinus thrombosis or occlusion was seen in 24 (75.0%). Clinical outcomes in patients with multifocal fistulas ($n = 11$) were excellent (100%), marked by a moderately high rate of complete occlusion (54.5%). Those with progressive disease ($n = 10$) regularly displayed certain angiographic findings, namely diffuse configuration (100%), sinus thrombosis (100%), and CVR (100%). Complete anatomic obliteration was achieved in 12 patients (37.5%), and in 26 patients (81.3%), clinical outcomes were favorable.

Conclusion. – Multiple dAVFs are typically aggressive at presentation, given strong associations with CVR and sinus thrombosis. In diffuse-type fistulas, the potential to recur or progress is high. Although definitive treatment poses a challenge, outcomes of endovascular therapeutics may be still optimized in this setting through strategic procedural modifications and careful follow-up monitoring.

Introduction

Intracranial dural arteriovenous fistulas (DAVFs) are dynamic lesions, accounting for 10-15% of all intracranial vascular malformations [1–4]. Multiply occurring intracranial dAVFs are documented but uncommon phenomena (incidence of ~6%–12.5%), described in only a few small series or isolated case reports [2–7]. Two or more anatomically separate dAVFs may thus develop synchronously or metachronously as de novo lesions during the course of follow-up monitoring [2,5].

Treatment of multiple dAVFs is often clinically difficult, complicated by assorted feeders, a proclivity for cortical venous drainage, and the inherent risk of hemorrhage [2,3,7]. Some theories on pathogenesis and mechanism have been offered, but clinical prognoses and outcomes of embolization are seldom discussed in the limited available publications. Our experience in treating multiple dAVFs is detailed herein, addressing procedural and outcome (angiographic and clinical) aspects of endovascular treatment, focusing on relation of the outcome with angiographic characteristics of multiple dAVFs.

Abbreviations: CS, cavernous sinus; CT, computed tomography; CVR, cortical venous reflux; dAVF, dural arteriovenous fistula; DSA, digital subtraction angiography; ECA, external carotid artery; ICA, internal carotid artery; ICH, intracranial hemorrhage; MRI, magnetic resonance image; MRA, magnetic resonance angiography; SRS, stereotactic radiosurgery; TAE, transarterial embolization; TVE, transvenous embolization.

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Table 1
Baseline characteristics of patients ($n = 32$) with multiple dAVFs.

Variables	Multiple dAVF ($n = 32$)
Age	53.1 ± 18.0 years
Sex	
Male	17 (53.1%)
Female	15 (46.9%)
Classification	
Synchronous	28 (87.5%)
Metachronous	4 (12.5%)
Presenting symptom	
Aggressive	18 (56.3%)
Non-aggressive	14 (43.7%)
Fistula multiplicity	
2	21 (65.6%)
3	7 (21.9%)
4	4 (12.5%)
Fistula type	
Multifocal	11 (34.4%)
Diffuse	21(65.6%)
Sinus occlusion/venous thrombosis	24 (75.0%)
CVR[a] (Borden II or III)	26 (81.3%)
Parenchymal signal change (T2/Flare)	5 (15.6%)
Embolization sessions	
1	12 (37.5%)
2	11 (34.4%)
3	4 (12.5%)
≥ 4	5 (15.6%)
Complete occlusion	12 (37.5%)
Positive final outcome	26 (81.3%)
Disease progression	
Progressive	10 (31.3%)
Non-progressive	22 (68.7%)

[a] CVR, cortical venous reflux.

Materials and methods

Study population and clinical presentation

During a 17-year period, (April, 2002 to January, 2018), 310 consecutive patients with intracranial dAVFs opted for endovascular management at our institute. A total of 32 patients (10.3%) diagnosed as multiple dAVFs (male, 17; female, 15; mean age, 53.1 years; age range, 13–79 years) were included in this study. Eight patients with bilateral cavernous sinus (CS) dAVFs were excluded. Initial clinical presentations were evaluated. Severe symptoms, such as intracranial hemorrhage (ICH), venous infarction, seizures, altered mental status, and neurologic deficits of extremities, were considered aggressive in nature [8–10]. Non-aggressive symptoms included cranial nerve palsies, visual symptoms, and tinnitus. ICH, venous infarction, and sinus thrombosis were confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) before treatment. General characteristics of these patients are summarized in Table 1.

Therapeutic alternatives were discussed with both neurologic/neurosurgical and neurointerventional teams in a multidisciplinary decision-making process, and informed consent was obtained from all patients after careful consultation. This study was conducted with the approval of our Institutional Review Board. The requirement to obtain written informed consent for study participation was waived.

Diagnostic angiography

Prior to treatment, angio-architectural explorations were conducted via Integris V, Allura Clarity (both Philips Medical Systems, Best, The Netherlands), or Innova IGS 630 (GE Healthcare, Wauwatosa, WI, USA) biplane system, including bilateral internal and external carotid and vertebral angiographies, to assess fistulous sites (location, extent), feeding arteries, and venous attributes (drainage path/pattern). High-resolution 3D rotational angiographic images (especially source image) was also used for confirmation of the exact fistulous location and extent in recent years. Cortical venous reflux (CVR) was denoted by Borden classification (types II and III) [11]. Multiplicity was equated with more than two fistulas emerging in a single patient at anatomically separate sites [2], confirmed in each instance through careful investigation of the following:

- sequential images generated during initial conventional angiography;
- selective arterio- or venography performed immediately before each embolization, and;
- completion angiography in the immediate aftermath of each embolization.

Continuous fistulas arising from adjacent, independent venous segments were considered as single lesions and were excluded from study. For example, the ipsilateral dAVF continuously involving the transverse sinus and sigmoid sinus, or torcular lesion involving the transverse sinus was considered as single lesion, not multiple. Adjacent but non-continuous lesions of independent segments were regarded as distinct lesions.

Such lesions then qualified as synchronous (simultaneous) or metachronous (de novo) shunting, and were characterized as either multi-focal or diffuse-type depending on whether fistulous sites were limited in scope (Fig. 1A) or diffusely involved areas around sinuses (Fig. 1B) [12,13]. If at least one of the multiple shunts displayed proliferative, lengthy, or continuous sinus involvement, a diffuse designation applied; whereas all shunts with restrictive feeders and regional involvement constituted multifocal disease (see Figs. 2 and 3). All fistulas were further stratified as progressive or non-progressive disease, according to status after initial treatment. A visible increase in shunt flow or fistulous extent after achieving near-complete or partial occlusion by endovascular means or recurrent shunting following confirmed complete occlusion of fistulas at initial treatment signified progressive disease.

Endovascular procedures

All patients were treated by endovascular means after thorough investigation of angiographic anatomy. Our institutional treatment strategy in multiple dAVF as follows:

- if technically feasible, single-stage embolization was preferred;
- if not, staged embolization was recommended, monitoring of symptom change or disease progression after initial treatment;
- lesion related to symptom or lesion with cortical venous reflux was first treated;
- follow-up without emergent treatment was recommended in small-amount asymptomatic shunt lesion with antegrade drainage (Borden I);
- stereotactic radiosurgery (SRS) was also considered in residual shunt without appropriate approaching route.

The endovascular procedures performed were largely conducted under general anesthesia, applying transarterial embolization (TAE), transvenous embolization (TVE), or a combination of both initially, as permitted by existing angio-architecture (sinus patency and functionality, arterial or venous feeder accessibility, etc.). Access was typically through femoral artery or vein. Antiplatelet preparations were not routinely prescribed in advance of procedures, but after femoral sheath placement, systemic heparinization was instituted using single 2000-IU injections. Pushable fibered coils were used for TVEs, first introducing 5-Fr angiocatheters by way of external carotid artery (ECA) into main feeding

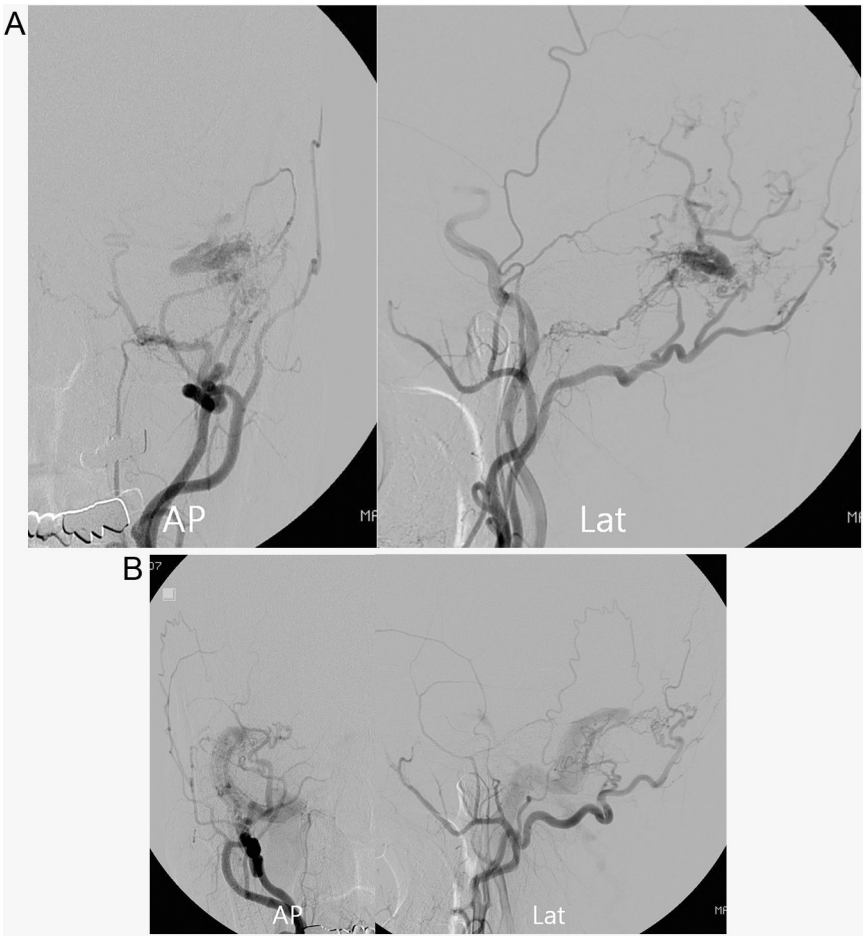

Fig. 1. Illustration of focal (A) versus diffuse-type (B) in dAVF.

arteries, and then navigating 6-Fr guiding catheters into main draining (i.e., jugular) veins. Micro-catheters for pushable coil delivery were placed in mural channels of fistulas or nearest culprit draining veins (or sinuses). Once the AVF angioanatomic configurations were defined via selective angiography, embolizations were then performed. Most TAEs involved n-butyl cyanoacrylate (n-BCA) or Onyx 18 use, placing 6-Fr guiding catheters in ECA (or rarely internal carotid artery [ICA]) and navigating micro-catheters for delivery of embolic materials into main feeding arteries (as far as feasible) under micro-guidewire guidance. Again, angioanatomic configurations were delineated through selective angiography, excluding any dangerous anastomoses, and embolizations were performed.

Angiographic and clinical outcomes

Immediate angiographic results after endovascular embolization were classified by degree of shunting as follows: complete occlusion (no shunt), near-complete occlusion (minor residual shunt, with marked volume and velocity reductions), or partial occlusion (major residual shunt, with slight reduction or no change in volume and velocity). If all fistulas appeared completely occluded, clinical follow-up 1–6 months after treatment was advised. Only in patients with aggravated clinical symptoms were further imaging studies, such as digital subtraction angiography (DSA) or magnetic resonance angiography (MRA), recommended. In patients with residual shunting but much reduced flow after initial treatment, DSA at the 1-month follow-up point was recommended to assess any further need of treatment. In patients whose multiple high-flow shunts could not be successfully occluded through single-stage embolization, staged embolizations were arranged at 4–12 weeks after first treatment, depending on patient status and extent of residual shunt or CVR. Clinical outcomes were gauged by degree of symptomatic abatement after treatment as follows: improved, no change, or aggravated. Assessments were done during hospitalization periods and in outpatient clinics at months 1 and 6 after final treatment.

Results

Study population

All data of baseline characteristics, initial presentations, multiplicity of fistulas, and treatments in the 32 patients studied is provided as Supplemental Table 1, and summarized in Table 1. The dAVFs were multifocal in 11 patients (case No. 1–11) and diffuse in 21 patients (case No. 12–32). Overall, 10 patients (case No. 23–32) experienced progressive disease, the other 22 harboring non-progressive lesions. Aggressive presenting symptoms were manifested in 18 patients (56.3%), CVR (Borden type II or III) was observed in 26 patients (81.3%), and 24 patients (75.0%) suffered sinus thrombosis or occlusion. Parenchymal signal change on MRI (T2/Flare) prior to the treatment was observed in 5 patients. Most patients (case No. 1–28) had synchronous multiple shunts at initial diagnosis. Only four de novo (metachronous) fistulas developed in four patients (case No. 29–32) during the follow-up interval (Fig. 4). All patients underwent endovascular treatments at least once for multiple dAVFs. One patient (case No. 18) relied on conservative

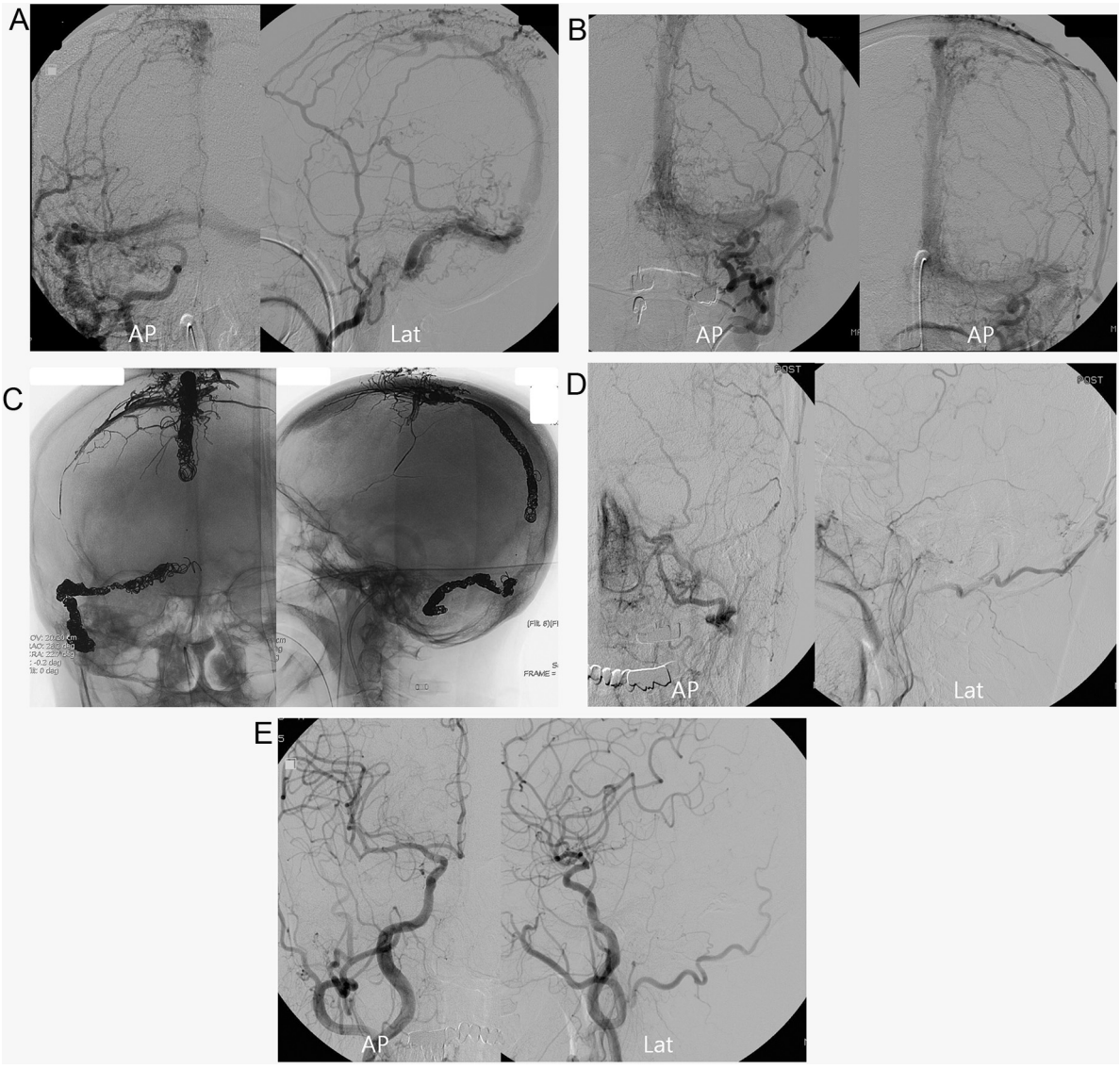

Fig. 2. Demonstrative case of focal-type in multiple dural AVF. A. Left external carotid angiographic image of left transverse sinus dAVF with cortical reflux in patient with ICH of left occipital lobe; B. Right external carotid angiographic image of right transverse-sigmoid junctional dAVF with antegrade venous drainage. Both fistulous sites were limited in scope; C. Transarterial embolization using NBCA (glue) for the left side fistula; D. Disappearance of fistula confirmed by completion angiography; and, E. Spontaneous regression of the untreated right side fistula in 3-month follow-up angiography.

treatment, having failed initial transvenous obliteration. His symptoms remained unchanged thereafter.

Endovascular and clinical outcomes

Endovascular embolization sessions averaged 2.3 (range, 1–9; median, 2). Embolization was undertaken more than twice in 20 patients, generally in patients with diffuse (15/21, 71.4%) or progressive (10/10, 100%) disease. All patients were followed clinically and by imaging, the mean duration being 41.3 months (range, 6–120 months). During post-embolization follow-up, complete obliteration of multiple fistulas was achieved in 12 patients (37.5%). Three patients needed further stereotactic radiosurgery (SRS) for residual fistulas, ill-suited for endovascular technique. Twenty-six patients (81.3%) had favorable clinical outcomes (symptom free or much improved). One patient (3.1%) died, despite multiple attempts at embolization. Unfavorable outcomes (aggravated symptoms or severe neurologic deficits) resulted in three patients (9.4%) (see supplemental Table 1). In Table 2, both clinical and angiographic attributes of multifocal and diffuse fistulas are contrasted. Patients with multifocal (vs. diffuse) lesions fared much better clinically (100% vs. 71.4%), achieving a higher rate of complete anatomic occlusion (54.5% vs. 28.6%). In Table 3, progressive and non-progressive categories of multiple dAVFs are compared. Progressive (vs. non-progressive) disease was more aggressive

Table 2
Attributes of multifocal and diffuse dAVFs.

	Multi-focal type	Diffuse type
Cases numbers	11	21
Non-sinus type shunts	4	2
Sinus occlusion/thrombosis	5 (45.4%)	19 (90.5%)
Aggressive presentation[a]	4 (36.4%)	14 (66.7%)
CVR[b] (Borden II or III)	7 (63.6%)	19 (90.5%)
Parenchymal signal change (T2/Flare)	2 (18.2%)	3 (14.3%)
Embolization sessions (mean)	1.5	2.7
Final complete occlusion	6 (54.5%)	6 (28.6%)
Favorable clinical outcome	11 (100%)	15 (71.4%)

[a] ntracranial hemorrhage, venous infarction, seizure, neurologic deficits.
[b] CVR, cortical venous reflux.

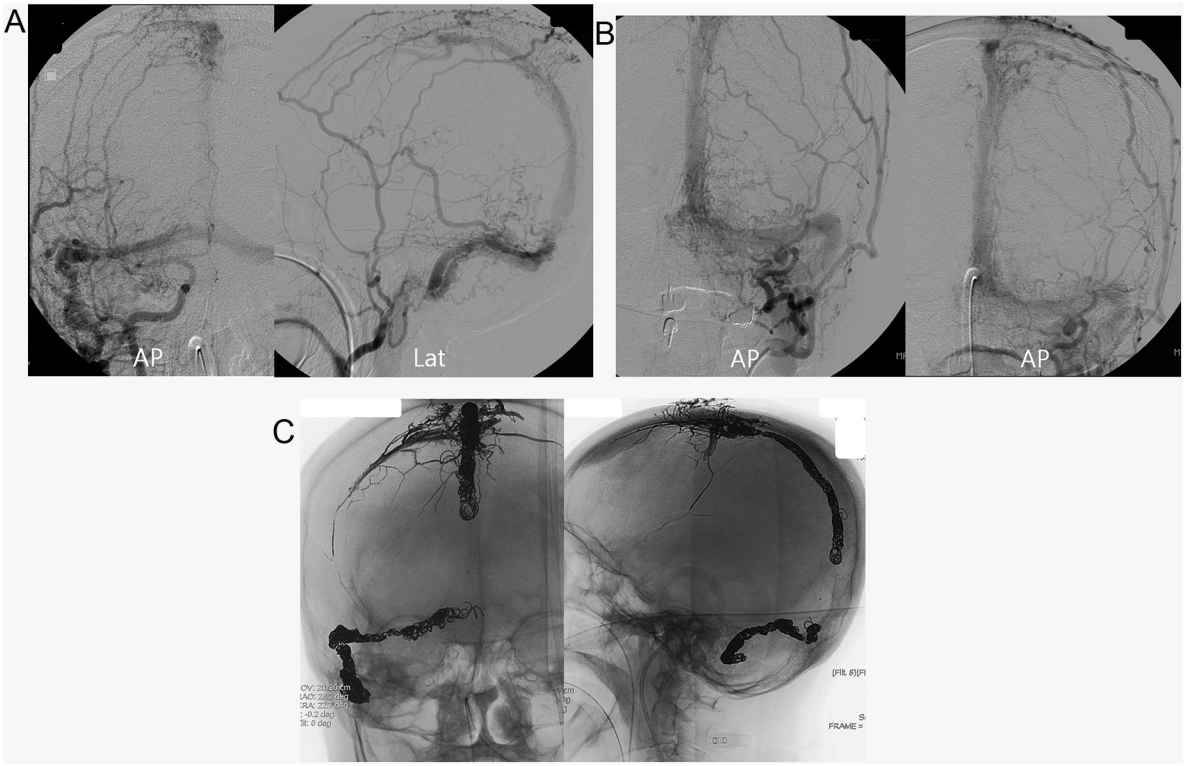

Fig. 3. Demonstrative case of diffuse-type in multiple dural AVF. A. Right common carotid angiographic image of right transverse-sigmoid and superior sagittal sinus dAVF with cortical reflux in patient with recurrent seizure; B. Left external carotid angiographic image of torcula (left) and superior sagittal sinus (right); C. Transarterial and transvenous embolization using Onyx and pushable coils. All of the fistulas diffusely involved areas around sinuses.

Table 3
Comparison of progressive and non-progressive disease subsets.

	Progressive group	Non-progressive group
Cases numbers	10	22
Diffuse type	10 (100%)	11 (50.0%)
Sinus occlusion/thrombosis	10 (100%)	14 (63.6%)
Aggressive presentation[a]	9 (90.0%)	9 (40.9%)
Bilateral feeders	8 (80.0%)	14 (63.6%)
CVR[b] (Borden II or III)	10 (100%)	16 (72.7%)
Parenchymal signal change (T2/Flare)	2 (20%)	3 (13.6%)
Embolization sessions (mean)	3.9	1.4
Final complete occlusion	2 (20.0%)	10 (45.5%)
Favorable clinical outcome	7 (70.0%)	19 (86.4%)

[a] Intracranial hemorrhage, venous infarction, seizure, neurologic deficits.
[b] CVR, cortical venous reflux.

upon initial presentation, linked consistently with diffuse-type fistulas (100%), sinus occlusion or thrombosis (100%), and CVR (100%). In addition (and not surprisingly), more embolization sessions (3.9 vs. 1.4) were required, with less chance of complete obliteration (20.0% vs. 45.5%) or favorable outcome (70.0% vs. 86.4%). However, six patients with progressive disease did suffer recurrences after complete or nearly complete embolization, emerging sporadically over much time (2–40 months) after therapeutic success.

Endovascular complications

Procedural complication was occurred in 7 patients (21.9%), and complication rate per embolization session was 9.6% (7/73 embolization session). Three patients suffered facial nerve palsies during staged TAE, with two recovering completely and one partially 6 months later. In four patients, ICH occurred after TVE or TAE, and one patient (case No. 15) suffered venous infarction (with small ICH) 3 days after a second TVE session. In the latter instance, recovery was nearly complete 2 weeks later through conservative management. Another patient (case No. 27) developed subarachnoid and intraventricular hemorrhages after a third TAE session. Although improvement was notable, residual right-sided deficits (weakness, blindness) persisted. A third 70 year-old female (case No. 26) with multiple proliferative dAVFs of CS bilaterally, right transverse sinus, and right jugular bulb, experienced paradoxical worsening of cranial nerve palsy upon complete obliteration of the bilateral CS fistulas. The right-sided transverse and jugular fistulas were also completely occluded after multistage embolizations. However, the right transverse sinus fistula recurred 1 year later and again 2 years after repeated TAE and TVE procedures. The last embolization attempt was complicated by immediate post-operative intraventricular hemorrhage, with obstructive hydrocephalus, and the patient died 1 month later. One patient (case No. 29) also developed a de novo dAVF at right transverse sinus 3.5 years after complete obliteration (in six sessions) of multiple, left-sided diffuse dAVFs. Three months after three subsequent embolization sessions, a large ICH occurred, presenting as seizures and leading to coma. Ultimately, hemiplegia persisted after interventional craniectomy.

Discussion

Multiple intracranial dAVFs are uncommon, with only a few small series [2,3,5] and sporadic case reports in publication. To our knowledge, the present aggregate of 32 patients with multiple dAVFs is the largest of any reported series. Heretofore, only 79 cases of multiple intracranial dAVFs have been formally documented in the literature [2–5,7,14–42]. All of these were fully reviewed and tabulated in a Supplemental Table 2.

Patients with multiple dAVFs are more apt to suffer hemorrhage, venous infarction, and neurologic deficits at presentation, due to a higher frequency of CVR [2,3,21]. Available data indicate

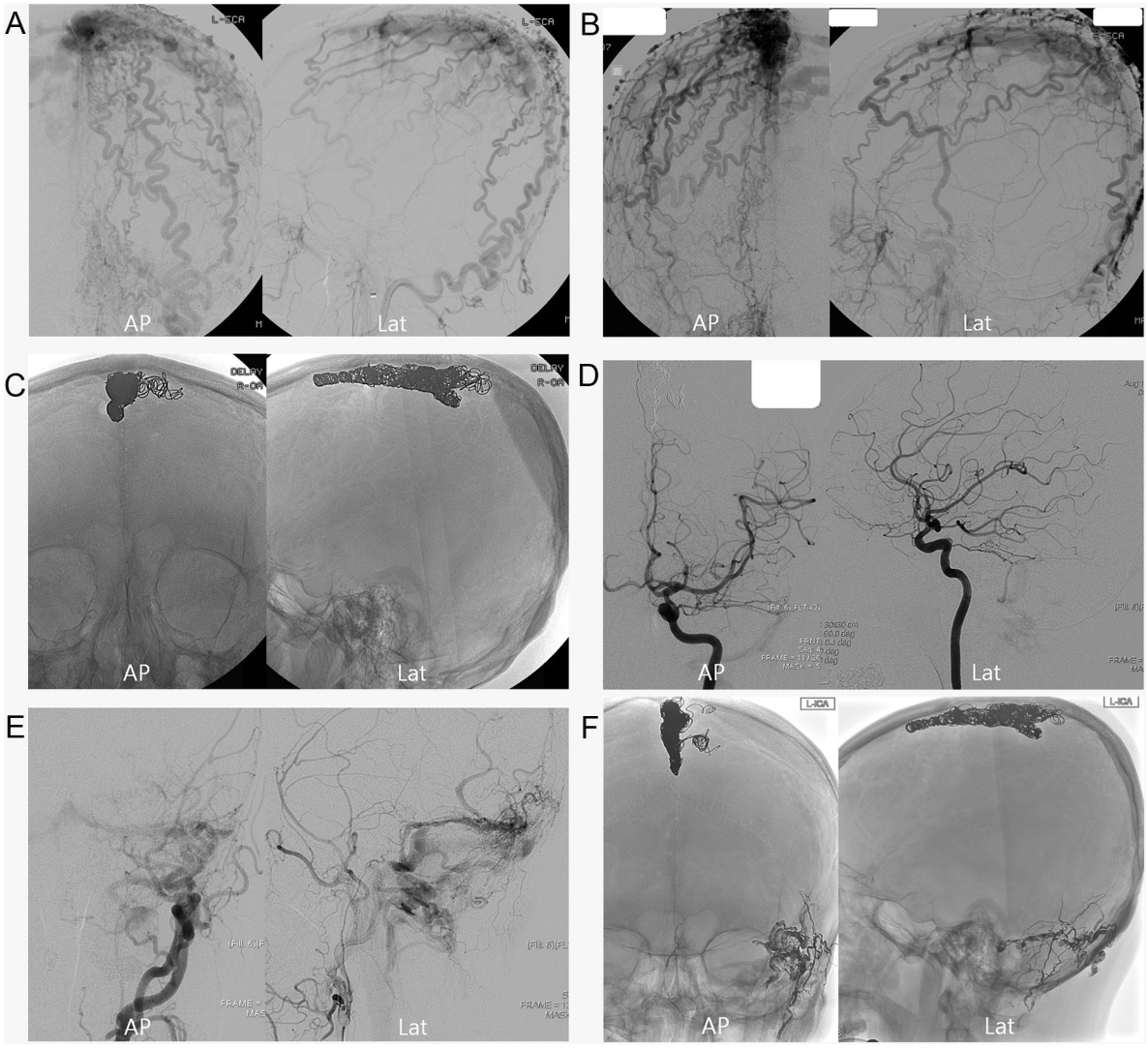

Fig. 4. Demonstrative case of metachronous dural AVF. A and B. Both external carotid angiographic image of superior sagittal sinus dAVF; C. Transvenous embolization using pushable coils; D and E. De novo dAVF on left tranverse-sigmoid sinus confirmed by left internal (D) and external carotid angiography after 11 years (E); and (F) Staged transarterial embolization using Onyx.

that such aggressive symptoms develop in 65–89% of patients with multiple dAVFs, most accompanied by CVR (84–93%, Borden II/III) [2,3,5,7,23]. Van Dijk et al. [2] have cited an 89% rate of CVR in patients with aggressive clinical presentations of multiple dAVFs, reflecting a 3-fold increase beyond that of solitary dAVF. Our findings are in agreement, having observed CVR in 94.4% of patients with aggressively presenting (56.3%) multiple dAVFs.

Although the etiopathology of such lesions remains obscure, evidence is mounting that cyclical sinus thrombotic occlusion and recanalization are at fault, coupled with venous hypertension. These fistulas may arise (via angioneogenesis) as micro-shunts within dura, perhaps under varied conditions, such as congenital anomalies, venous sinus thrombosis, head trauma, transcranial surgery, trans-sinus procedures [38,41], hyper-coagulative states, hormonal fluctuations (pregnancy, menopause, oral contraceptive use), tumors, otitis, or sinusitis [25,28,43]. Stemming from excess arterial flow to dural sinus, mechanical obstruction develops, causing retrograde drainage into cortical veins. Venous hypertension also ensues, due to progressive venous thrombosis and CVR [4,5,19,23,26]. Left unchecked, high-flow shunting results from the enlarging channels [8,32]. Within a partially recanalized sinus, a growing fistula of diffuse nature recruits more blood from parenchymal vessels, creating a network of multiple feeders and numerous AV shunts that are readily identified by angiography [3,4,26,28,30,44]. Venous hypertension may also prompt intracranial hypoperfusion, thus triggering angiogenic growth factor [i.e., vascular endothelial growth factor (VEGF)] release to further spur neovascularization and evolving dAVFs [28,45,46]. Hence, multiple dAVFs or distal de novo shunts, situated far from sites of origin, and even spinal dAVFs have been noted in pertinent case reports [5,25,26,36,38,41].

In the context of multiple dAVFs, sinus thrombosis and occlusion have been encountered at high rates, both in our study (24/32, 75.0%) and in other publications (71.4%). Based on above hypotheses and supported by our data, multiplicity and diffuseness of lesions then imply late-stage development, involving more numerous feeder vessels, greater risk of recurrence and proliferation, and particularly complex treatment. By comparison, focal-type fistulas signify early-stage development, marked by fewer and more localized feeders that are potentially easier to treat. Indeed, for patients in our series with multifocal fistulas, excellent clinical outcomes (100% vs. 71.4%) and a higher rate of complete occlusion (54.5% vs. 28.6%) were achieved in fewer embolization sessions (1.5 vs. 2.7). Multiple localized fistulas are more easily treated and may even

spontaneously regress on occasion, as noted in some publications [6,7,14,18]. Actually, several of our patients with focal-type AVFs (case No. 4, 5, 7, 10) did present aggressively with high-flow fistulas and high-grade CVR. However, the cure rate and outcomes of endovascular treatment were still good. Such high-grade yet focal lesions could represent instances of marginal or no flow into dural venous sinus or solely retrograde cortical venous drainage. Consequently, the favorable treatment responses reflect limited involvement well-suited for TAE, especially for Onyx filling [6].

Ten of the 32 patients in this study suffered progressive or recurrent dAVFs after initial embolizations, most or all of them displaying diffuse-type fistulas (100%), bilateral feeders (80.0%), sinus thrombosis (100%), and CVR (100%) as angiographic findings. Progression or recurrence of dAVFs occurred in 71.4% (10/14) of patients with above features. Upon review of the literature, only 7 patients were reported to progress after treatment. Arai et al. [17] described multiple diffuse dAVFs of superior sagittal sinus and posterior fossa in one patient, all lesions supplied bilaterally and associated with sinus thrombosis (transverse, straight, superior sagittal). Goto et al. [7] also documented three recurrences, all involving transverse sinus bilaterally, with diffuse sinus occlusion and CVR. Watanabe et al. [20] similarly reported a patient with dAVFs of cavernous and superior petrosal sinuses, supplied bilaterally, showing progressive CVR and bilateral inferior petrosal sinus occlusion. In a patient with superior sagittal and transverse sinus thrombosis, reported by Saito et al. [4], multiple bilateral shunts of superior sagittal, transverse, and straight sinus were repeatedly embolized (eight times), but recurrence and rebleeding developed 7 years later. Finally, Bai et al. [26] published an account of AVF at left jugular bulb. After complete embolization, multiple dAVFs with bilateral feeders and CVR were evident 4 years later, ultimately involving superior sagittal, transverse, and straight sinuses. TAE was again applied, using Onyx. However, 1 month later, straight sinus occlusion and a new tentorial dAVF had developed. Typically, fistulas that share these angiographic features may progress or recur anywhere from 2–40 months after initial treatment, requiring other treatment modalities, an average of 4.1 (range, 2–9) embolization sessions, and careful long-term follow-up monitoring.

Despite the gravity of initial presentations in this setting, rendering treatment more complex and heightening the risk of recurrence, therapeutic results still proved acceptable overall. As in most (80.5%) of the cases previously published [2,7,23,26,30], clinical outcomes in the patients we studied were largely favorable (81.3%), although complete anatomic obliteration was far less often achieved (37.5%). By substantially reducing flow and relieving venous hypertension, exceptional clinical results were attained in some patients with residual lesions. Even in those with progressive disease, stabilization of remnant fistulas through staged and repeated embolizations yielded good results in a majority (70.0%) of patients.

Nevertheless, the procedural complication rate was not low (9.6% of complication rate per embolization session). Three patient suffered CN palsy related to TAE. All the patients were partially or fully recovered. However, the other 4 patients underwent ICH developed after multisession embolization. The precise reasons that ICH or venous infarction after procedure are more common in multiple dAVF are not known, but it may be affected by aggressive treatment with multisession of TVE or TAE (or combined), because majority of multiple fistulas were proliferative and diffuse lesions or disease progressed despite of staged embolization. In our series, all patients with ICH after procedure were diffuse-typed dAVF, and 3 patients were in progressive group.

Our investigation is limited in that it is a nonrandomized retrospective observational study with a small study population. Thus, there is a potential for bias in choice of treatment strategy, including staged embolization. In addition, line between focal and diffuse-type might be not clear, although we tried to define the fistulous area or point using 3D source image. Therefore, subjective judgement of the observer might intervene.

Conclusion

Many patients with multiple dAVFs present initially with aggressive symptoms, given a high association with CVR. In general, such lesions are difficult to completely obliterate, tending to readily progress or recur. Multifocal lesions respond well to endovascular treatment, with impressive clinical outcomes. However, in patients with diffuse-type fistulas, demonstrating sinus thrombosis, CVR, and bilateral feeders, the risk of recurrent or progressive disease is comparatively greater. Nevertheless, outcomes of even complex scenarios may be optimized through long-term follow-up monitoring, multimodal management, and staged endovascular treatments.

Ethics approval

This study was conducted with the approval of the Seoul National University Hospital.

Ethical standards

We declare that all human and animal studies have been approved by our Institutional Review Board and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This study was approved by our Institutional Review Board.

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No funding was received.

Authors' contribution

Guarantor of integrity of the entire study – Young Dae Cho.
Study concepts and design – Moon Hee Han.
Definition of intellectual content – Ching-Chang Chen.
Literature research – Won-Sang Cho/Jeong Eun Kim/Ching-Chang Chen.
Clinical studies – Moon Hee Han/Young Dae Cho/Hyun-Seung Kang.
Experimental studies/data acquisition and analysis – Dong Hyun Yoo/Jeongjun Lee/Jusun Moon.
Statistical analysis – Won-Sang Cho/Jeong Eun Kim.
Manuscript preparation – Ching-Chang Chen/Young Dae Cho manuscript editing- Hyun-Seung Kang/Moon Hee Han.
Manuscript review – all authors.

Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at https://doi.org/10.1016/j.neurad.2018.10.010.

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