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Long-term outcome after endovascular treatment of cavernous sinus dural arteriovenous fistula and a literature review

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Abstract

Background: The long-term efficacy of endovascular treatment (EVT) for cavernous sinus dural arteriovenous fistulae (CS-dAVF) was assessed with a special focus on residual shunts after initial EVT.

Patients and Methods: This retrospective survey included 50 patients who had undergone EVT and were followed for one month or longer (median follow-up 56 months).

Results: Common preoperative symptoms were chemosis (78%), extra-ocular motor palsy (72%), exophthalmos (66%), and tinnitus (26%). CS-dAVF were addressed by transvenous embolization (tVE, n = 48), tVE only was used in 43 instances and tVE plus transarterial embolization (tAE) in 5. Two patients underwent tAE only. Procedure-related morbidity (brainstem infarction) was recorded in one patient (2%) and transient symptom exacerbation (paradoxical worsening) in 12 patients (24%). Postoperative digital subtraction angiography showed no major retrograde shunt or cortical venous reflux in any of the 50 patients. Anterograde or minor retrograde residual shunt was observed in 17 patients (34%); 3 of these underwent additional tVE and 4 had gamma-knife surgery. The shunt flow disappeared in all 17 patients 12.6 ± 13.4 (mean ± SD) months after initial EVT. At the latest follow-up, 65.7 ± 52.6 months after the initial operation, no shunt flow was observed in any of the 50 patients. None had remaining or newly developed chemosis or tinnitus on follow-up. The rate of persistent cavernous sinus symptoms at the latest follow-up was higher in patients with- than without post-procedural paradoxical worsening (5/12, 41.7% vs 2/38, 5.3%, p=0.0059 by Fisher's exact test).

Conclusion: Long-term follow-up showed that EVT, especially tVE, is an efficient and safe treatment for CS-dAVF. It resulted in the eventual disappearance of shunt flow. Residual shunt without major retrograde flow or cortical venous reflux can be monitored without additional treatment.

KEY WORDS: arterio-venous fistula, cavernous sinus dural AVF, endovascular treatment, transvenous embolization, coil

Introduction

Dural arteriovenous fistulae (dAVF) are pathological shunts between dural arteries and adjacent venous sinuses and veins in the dura mater [2, 21, 39]. They represent 10 - 15% of all cerebral vascular malformations [22]. The reported annual incidence is 0.29 - 0.51/100,000 adults [19, 29]. While dAVF can arise anywhere in the dura mater, they more frequently {43.6% [13] - 45.9% [19]} involve the cavernous sinus (CS-dAVF) in the Japanese population than the European population. The differences in the intracranial distribution of dAVF among various ethnic groups have also been reported although no specific reasons as to their different incidences have been provided. [8].

CS-dAVF elicit various symptoms, e.g. exophthalmos, chemosis, pulsatile bruit, ocular motor palsy, and symptoms due to cerebral bleeding and/or infarction attributable to cortical venous reflux [16, 21, 32, 38]. Treatment is indicated in the presence of severe symptoms, symptomatic progression, and cortical venous reflux [12, 14-16, 21, 27].

Endovascular treatment (EVT) is widely used to address these lesions [6, 15, 17, 21, 32, 44, 45]. Although its goal is complete disappearance of the major venous shunt, residual retrograde and/or anterograde venous shunts can remain [14]. There are few studies on the long-term outcome of endovascularly treated CS-dAVF. We assessed the long-term (mean 5.5 years) effectiveness of EVT for CS-dAVF with a special focus on residual shunts observed immediately after the operation.

Materials and Methods

Patients

From 1996 to 2013, 62 patients with CS-dAVF were referred to Kagoshima University Hospital and two affiliated hospitals for EVT due to the existence of cortical venous reflux or severe or progressive symptoms. The interval between symptom onset and referral ranged from 0 to 48 months with a mean of 5.3 ± 7.4 months (SD). Of the 62 patients, 4 rejected EVT due to fear and/or tolerability of their symptoms. Among the other 58 patients who underwent EVT, 8 underwent less than one-month follow-up. As these 12 patients were excluded, 50 patients, 8 men (16%) and 42 women (84%), were

included in this retrospective study (**Table 1**). Their ages ranged from 30 to 87 years (median 66, mean 66.2 years). Clinical and radiological data were extracted from the patients' charts and a neuroimaging data base.

Indication for EVT

Cortical venous reflux was observed in 29 patients and considered a primary indication for active treatment. Of the other 21 patients, 15 presented with severe ophthalmic symptoms including severe chemosis, exophthalmos, and visual impairment and 6 had less severe symptoms that had grown worse in the course of several months.

Of the 50 patients, 5 had undergone manual compression of the cervical carotid artery before referral; it had failed to ameliorate their symptoms.

Operative procedure

EVT was performed in 50 patients under the supervision of a senior author (K.A.).

We primarily aimed to obliterate shunts through trans-venous routes. In cases where it was not possible to introduce the microcatheter into the cavernous sinus via any venous routes, we used the arterial route. Trans-arterial embolization (tAE) was added when major shunt flow remained after trans-venous embolization (tVE).

Consequently, intravascular treatment was via the transvenous route in a total of 48 patients; 43 underwent tVE only; 5 underwent additional tAE. Two patients were treated by tAE only. Both tVE and tAE were performed using digital subtraction angiography (DSA) under local anesthesia and sedation with pentazocine (15 mg), diazepam (5 mg), and the continuous intravenous administration of propofol (1 - 2 mg/kg/hr). An intravenous bolus of heparin (1000-2000 units) was given before the endovascular procedure.

First, we obtained common carotid and external carotid artery angiographies to identify the shunt site and the shunt-flow outlets.

For tVE, a 6-Fr sheath was inserted into the right femoral vein. The access route was the inferior petrosal sinus (IPS) in 44 patients and the superior ophthalmic vein in 4. A 4.2-Fr coaxial catheter was positioned in the IPS through a 6-Fr guiding catheter lodged in the jugular vein. The tip of the 1.7/2.4-Fr tapered microcatheter was advanced over a 0.014-inch guidewire into the fistulous point. Platinum coils, mainly "Target coils" (Stryker, Fremont, California) sized 2-10 mm, were placed via the microcatheter to

obliterate the venous orifice leading to cortical venous reflux and the ophthalmic veins with retrograde flow. Then, the affected cavernous sinus was packed with coils. We usually terminated the tVE procedure upon the disappearance of major retrograde- and cortical venous reflux flow irrespective of the existence of minor residual antegrade shunt flow.

For tAE, the arteries involved in shunting were obliterated using N-butyl-cyanoacrylate (NBCA) and/or bare platinum coils delivered through microcatheters positioned in the middle meningeal artery and/or the internal maxillary artery.

Statistical analyses

The Statflex® version 6.0 software program (Artech Co., Osaka, Japan) was used for statistical analysis of the results. Depending on the characteristics of the data sets, data were analyzed with Fisher's exact test or the Mann-Whitney *U*-test. Differences of $p < 0.05$ were considered statistically significant.

Results

Symptoms at diagnosis

Among the 50 patients, the affected side was on the right in 20 patients and on the left in 21; in 9 patients there was bilateral involvement. Based on the classification of Barrow et al. [2], 4 patients were recorded as type B, 3 as type C, and 43 as type D (**Table 1**).

Of the 50 patients, 39 (78%) presented with chemosis, 36 (72%) with double vision, 33 (66%) with proptosis, 6 (12%) with visual impairment, 11 (22%) with orbital pain, and 13 (26%) with tinnitus. Cranial nerve palsy involving the abducens nerve was observed in 33 (66%), the oculomotor nerve in 11 (22%), and the facial nerve in one patient (2%). The duration from onset to diagnosis was 0 - 48 months (median 2 months). DSA revealed cortical venous reflux in 21 patients (42%).

Neuroimaging findings

Immediate post-procedural DSA showed no shunt flow in 33 patients (**Figure 1**). Minor residual shunt flow was observed in 17 patients (**Figure 2**); none of these

manifested cortical venous reflux. Residual shunt flow was seen mainly in the inferior petrosal vein (IPS) in 8 patients and in both superior ophthalmic veins (SOVs) and the IPS in the other 9 patients.

Among the 17 patients with a residual shunt, 3 underwent a second tVE procedure due to persistent severe ophthalmic symptoms; the procedure obliterated the shunt flow. Stereotactic radio-surgery using a gamma-knife unit was performed in 4 patients. The other 10 underwent no additional procedures; they were followed up using neuroimaging studies including magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and computed tomography (CT) scans one month after the initial procedure and then every 3 - 4 months. The shunts eventually disappeared in all 17 patients at 1 - 42 months after the operation (median 4, mean 12.7 ± 13.3 months) (**Figure 3**).

These observations indicate that complete obliteration of the shunt flow was achieved by a single EVT in 43 of the 50 patients (86%).

Postoperative changes of symptoms

Surgical morbidity and mortality

Among the total of 58 patients who underwent EVT, the rate of severe morbidity related directly to the procedure was 1.7% (1/58). There was no mortality.

Early postoperative period

Among the 50 patients followed more than one month postoperatively, paradoxical worsening, [15, 18, 24] was observed in 12 (24%), i.e. in 7 of 33 (21.2%) with total shunt disappearance and in 5 of 17 (29.4 %) with a residual shunt (**Table 2**); the symptoms gradually improved in both groups.

A 72-year-old woman with a 2-month history of left chemosis, orbital pain, and facial nerve paresis developed right hemiplegia 4 hours after successful EVT that resulted in total shunt flow disappearance. MRI showed a venous infarct in the brain stem ipsilateral to the affected cavernous sinus (**Figure 4**). Her modified Rankin score (mRS) was 4 at 6 months after the procedure and she remained dependent.

A 78-year-old woman with a history of untreated hypertension presented with residual shunt flow exclusively toward the IPS. She developed a small left putaminal hemorrhage ipsilateral to the affected cavernous sinus 3 months after the initial treatment,

suffered from right hemiplegia, and became dependent (mRS 4).

Latest follow-up

The follow-up period ranged from 1 - 176 months (median 56, mean 65.7 ± 52.6 (SD) months). At the latest follow-up, 43 patients had no shunt-related symptoms. The time to the disappearance of symptoms after the initial treatment was shorter in patients with no- than in patients with residual shunts (4.5 ± 5.7 vs. 10.8 ± 11.5, p = 0.0441, Mann-Whitney *U*-test) (**Table 2**). In 7 patients (14%) we observed persistent shunt-related symptoms; they were 4 of 33 patients with immediate post-procedural shunt disappearance and 3 of 17 patients with residual shunts. There was no difference in the probability of residual shunt-related symptoms at the latest follow-up between the two groups (p = 0.677, Fisher's exact test). The residual shunt-related symptoms included abducens nerve palsy in 6 and oculomotor nerve palsy in one patient.

On the other hand, the rate of shunt-related symptoms was significantly higher in patients with- than without paradoxical worsening (5/12, 41.7% vs 2/38, 5.3%, p=0.0059 by Fisher's exact test).

None of the patients complained of orbital pain, chemosis, exophthalmos, or tinnitus at the latest follow-up.

All but the 2 patients with hemiplegia (4%) were independent; another patient died of procedure-unrelated colon cancer. The mRS was 0 in 37 patients, 1 in 4 patients, 2 in 6 patients, and 4 in 2 patients among 49 survivors.

Literature review

We reviewed 13 reported series of CS-dAVF including more than 20 patients that were published since 2000 [6, 13, 14, 15, 16, 21, 24, 32, 35, 36, 42, 43, 45]. The total number of patients was 1361. Their and our 50 patients' clinical presentation and treatment results are summarized in Tables 3 and 4.

Discussion

According to our literature review and our current findings (Table 3), CS-dAVF primarily affected women (998 of 1361 patients, 73.3%) and middle-aged individuals (their mean age ranged from 55 to 67 years). These epidemiologic data were concordant

with ours. The most frequent symptom was red eye (conjunctival congestion); the incidence ranged from 77-93% (median: 90%), followed by chemosis (incidence: 32-100%; median: 78%), proptosis (incidence: 14-96%; median: 66.5%), visual impairment (incidence: 11-33%; median: 25%), and diplopia (incidence: 34 - 72%; median: 51%).

Because it was considered to be a benign entity due to the abundant extracranial drainage and occasional shunt subsidence, some recommended that CS-dAVF should be treated conservatively [3, 30, 39]. In case series, 10 - 73% of patients experienced the spontaneous remission of CS-dAVF [23, 30, 39] . In a longitudinal follow-up study of Sasaki et al. [30], 19 of 26 patients (73%) with "relatively low-pressure, low-flow shunts" showed spontaneous symptom disappearance. The time to the disappearance of symptoms tended to be longer than 12 months (mean 19.6 ± 20.2 months) and the disappearance of the fistula was angiographically confirmed in only 4 patients. Patients with low shunt flow not directed into cerebral veins, and patients with mild, non-worsening symptoms can be conservatively managed for a period with intermittent manual compression under regular MRI follow-up [3, 6, 30, 31] .

The risk for serious intracerebral events due to cortical venous reflux and for irreversible impairment of visual and other cranial nerve function may necessitate quick intervention [4, 5, 7, 11, 15, 21, 27, 38, 39]. The coexistence of cortical venous reflux affects the prognosis negatively; 15% of such patients suffered serious central nervous system events during follow-up [9]. Consequently, patients with cortical venous reflux, 42% in our series, are considered to be the primary subset for treatment, as are patients with serious ocular and progressive symptoms [12, 14, 15, 16, 21, 27] or with hemorrhagic presentation [34].

Drainage patterns can be expected to change during long-term follow-up due to intimal thickening of the downstream venous sinus and veins receiving high-speed shunt inflow [32]; this is called high-flow venopathy [33]. Some patients without cortical venous reflux will eventually manifest reflux during follow-up due to progressive occlusion of downstream sinuses and veins [31]. Therefore, CS-dAVF without cortical venous reflux may also become a target for active intervention in the course of the

disease. Similar changes in drainage pattern can occur after incomplete occlusion, which may result in changes of symptoms. Understanding longitudinal changes in drainage patterns and its symptomatic evolution after tVE should be the target of future studies. Although EVT has been the first choice (Table 4), there are few reports on its long-term outcomes [16, 21]. Ours is the longest follow-up series (over 5 years). The shunt flow completely disappeared in 30 - 100% (median: 72.5%) of reported series immediately after the initial procedure; in up to 70% (median 21%) residual shunt was observed. Changes in the residual shunt were reported in only one earlier publication [6]; it had disappeared in 16 of 19 patients (84.2%) at the final follow-up 26 months after the procedure. Our literature review showed that CS-dAVF-related symptoms had completely disappeared in 47 - 95% (median 83.5%) of patients at the final follow-up 25.2 months (median) after the initial treatment (Table 4).

We experienced EVT-related morbidity in one case (1.7%); in the previously reported series it was 7% (median). However, the rate of residual shunt was slightly higher in our- than earlier series [34% vs. 21% (median)]. This may be attributable to our concern that excessive coil packing of the cavernous sinus may lead to irreversible cranial nerve damage. In our patient with a venous infarct in the brain stem, we suspect that insufficient packing of the posterior part of the cavernous sinus resulted in reopening of the orifice leading to the deep venous system. This case alerts to the importance of occluding the entrance leading to intracranial veins when preoperative DSA shows cortical venous reflux. In addition, the peripheral facial palsy preoperatively seen in this patient may be a warning sign indicating brain stem dysfunction attributable to cortical venous reflux. In such patients secure occlusion of the entrance leading to intracranial veins is essential and close monitoring of the postoperative course is warranted for the early detection of fistular re-opening that may require immediate re-intervention to re-occlude the orifice. In the patient with putaminal bleeding seen 3 months after the initial treatment the causative relationship between dAVF and putaminal bleeding is ambiguous; nonetheless, the primary prevention for stroke is warranted in patients with dAVF.

The effect of intravascular coiling is generally thought to be derived from thrombogenesis surrounding the coils rather than the direct packing effect [10, 20].

Shunt flow eventually disappeared in all 50 of our patients. There was no difference in the probability of residual shunt-related symptoms at the latest follow-up between the 33 shunt-free- and the 17 patients with residual shunt on immediate post-procedural DSA (Table 2). However, at the latest follow-up, the rate of shunt-related symptoms was significantly higher in 12 patients with- than 38 patients without paradoxical worsening. Nishino et al. [24] reported that at the end of 30-month (mean) follow-up, 15% of the patients with *de novo* or exacerbated cranial nerve palsy after EVT continued to suffer from cranial nerve palsy. The time to the disappearance of symptoms was shorter in our patients with no residual shunts than those with residual shunt. But, considering the delay was only six months and tight coil packing may result in irreversible damage to cranial nerves, our practice to terminate the EVT procedure when the major shunt flow and cortical shunt flow disappears seems rational.

Some patients require additional treatment after the initial EVT such as a second EVT and gamma-knife surgery [9]. Of our 50 patients, 4 underwent gamma-knife surgery as a second-line modality; total shunt obliteration was seen 2 - 41 months thereafter. Although gamma-knife treatment alone is non-invasive and relatively safe its cure rate is unsatisfactory, 70 - 75%, within 2 years [5, 43]. We suggest that this treatment modality should be considered a second-line option after tVE which provides a quick resolution of symptoms and complete shunt obliteration in the long term.

In our series, follow-up imaging studies of 10 patients with post-EVT residual shunts showed their eventual disappearance without additional treatment at a mean of 11.4 months (median 5.5 months) after the initial treatment. This finding may justify withholding additional tVE or gamma-knife surgery until 6 months after unsuccessful tVE on the condition that cortical venous reflux and clinical severe or exacerbated symptoms are absent.

At present, NBCA is the only liquid adhesive whose use for CS-dAVF is approved in Japan. Problems associated with its use are nontarget embolization, gluing of the catheter, and migration of the material to the venous side. We used NBCA in only 4 patients in our series. Dimethylsulfoxide (DMSO) soluble liquid embolic materials, Onyx and PHIL, have been introduced to address CS-dAVF. While Wenderoth reported a high obliteration and low complication rates after embolization with Onyx and PHIL

mainly through trans-orbital transvenous routes [42], others encountered serious morbidity, unexpected migration of the material, and profound trigeminal cardiac reflex [1, 26, 40]. It remains to be determined whether DMSO is neurotoxic to intra-cavernous cranial nerves [41], and some performed TAE with DMSO-soluble liquid material only after tVE embolization had failed [25, 28, 37, 41] . We suggest that until the safety of the materials and the appropriate delivery techniques are established, transvenous coil embolization should be the first-line treatment in patients with CS-dAVF.

The retrospective nature of our study prohibits uniform treatment-related judgments including the proper timing of EVT or its withdrawal, the method and timing of additional treatments, and the timing and modality used for follow-up studies. Especially due to the lack of regular angiographic follow-up studies, we could not elucidate the particular changes in residual shunt flow leading to the improvement of symptoms and its timing. Therefore, prospective, multicenter studies using identical treatment and regular follow-up protocols are needed to identify the best strategy to address CS-dAVF and to assess long-term clinical outcomes.

Conclusion

Our long-term follow-up of 50 patients with CS-dAVF who underwent EVT showed that shunt flow disappeared in the course of 5-year follow-up. In approximately half of our patients with residual shunts immediately after the initial EVT, shunt flow disappeared 5.5 months after the procedure without additional treatment. Paradoxical worsening of cavernous sinus symptoms after EVT was related to permanent cranial nerve impairment. Therefore, EVT for CS-dAVF should aim at eliminating cortical venous reflux and major retrograde shunt flow rather than at complete shunt disappearance elicited by tight coil packing of the cavernous sinus.

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Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the

subject matter or materials discussed in this manuscript.

Ethical considerations

This retrospective study was approved by the Ethics Committee of Kagoshima University Hospital (reference No. 25-38, URL: http://com4.kufm.kagoshima-u.ac.jp/information/department/015/015-02.html). The authors certify that this study was conducted in accordance with the Helsinki declaration (revised in 2000) and the Ethical Guidelines for Medical and Health Research Involving Human Subjects (effective February 9, 2015) promulgated by the Ministry of Health, Labor and Welfare, Japan. Informed consent for the treatment was obtained from all patients. Study-specific informed consent was waived due to the retrospective and noninvasive nature of the investigation using information contained in medical charts and records. An opt-out method was used. To protect patient privacy, all data were collected and analyzed under anonymization in an unlinkable fashion.

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Figure Legends

Figure 1:

A 74-year-old woman with a 3-month history of left chemosis, double vision, and exophthalmos.

A: Pre-treatment MRI scan showing engorgement of the left ophthalmic vein (white arrow heads).

B: DSA of the left common carotid artery showing shunt flow into the superior ophthalmic vein (SOV) (arrow heads).

C: Post-treatment DSA showing coils placed in the left SOV and the left cavernous sinus (arrows). Shunt flow completely disappeared.

Figure 2:

A 64-year-old woman with a 4-month history of left chemosis, orbital pain, and double vision.

A: Pre-treatment DSA of the left internal carotid artery showing shunt flow in the left SOV and inferior petrosal vein.

B: Post-treatment DSA showing coils placed in the left cavernous sinus (arrows). Minor shunt flow into the inferior petrosal vein persisted (arrow heads).

C: DSA performed one month later disclosed spontaneous disappearance of the shunt flow without additional treatment.

Figure 3:

Follow-up of 17 patients whose shunt flow remained immediately after initial endovascular treatment.

tVE : trans-venous embolization, tAE: trans-arterial embolization, NAT: no additional treatment

Encircled numerals indicate the interval from initial to additional treatment.

Uncircled numerals indicate the interval from initial treatment to the timing of neuroimaging studies confirming shunt disappearance. Numerals in

parentheses indicate the duration of total follow-up after the initial treatment. ↑ : timing of gamma-knife treatment. ▲: timing of tVE, ▽: time of putaminal bleeding

Figure 4:

A 72-year-old woman with a 2-month history of left chemosis, orbital pain, and facial nerve paresis.

A: Pre-treatment DSA of the left external carotid artery showing shunt flow in the left superior ophthalmic vein (SOV), inferior ophthalmic vein, inferior petrosal sinus, and basal vein (arrow heads).

B: Post-treatment DSA showing total shunt flow disappearance.

C: Diffusion-weighted MRI showing a left paramedian high-intensity area in the pons indicating venous infarction. She suffered right hemiplegia.

Table 1. Clinical summary of our 50 patients

Characteristics	number (%)
total number	50
sex (%)	male: 8 (16), female 42 (84)
age	66.2 ± 11.3 (mean±SD), 66 (median)
affected side (%)	right: 20 (40), left: 21 (42), bilateral : 9 (18)
Barrow's type	A, n = 0; B, n = 4; C, n = 3; D, n = 43
Cognard classification	Ⅰ, n=0; Ⅱa, n=21; Ⅱb, n=0; Ⅱa+b, n=29; Ⅲ, n=0; Ⅳ, n=0; Ⅴ, n=0
mRS (%)	1, n = 15 (30), 2, n = 35 (70)
duration of symptoms (months)	6.9 ± 20.3 (mean ± SD), 2 (median)
symptoms (%)	chemosis: 39 (78), diplopia: 36 (72), proptosis: 33 (66), tinnitus: 13 (26), orbital pain: 11 (22), visual impairment: 6 (12)
procedure (%)	tVE: 43 (86), tVE + tAE:5 (10), tAE: 2 (4)
follow-up (months)	65.7 ± 52.6 (mean ± SD), median 56

SD: standard deviation, tVE: transvenous embolization, tAE: trans-arterial embolization; mRS, modified Rankin score

Barrow's type of carotid cavernous fistulae: A, direct carotid-cavernous fistula; B, fed from the internal carotid artery only; C, fed from the external carotid artery only; D, fed from both internal and external carotid arteries, n: number of patients

Table 2. Post-procedural changes of symptoms

	Total	Total shunt-disappearance	Shunt residual
Immediate DSA findings (%)	50	33 (66)	17 (34)
Immediate follow-up (< 1 month)			
improved (%)	35	24 (72.7)	11 (64.7)
static (%)	3	2 (6.1)	1 (5.9)
paradoxical worsening (%)	12	7 (21.2)	5 (29.4)
procedure related morbidity (%)	1	1 (3) [a]	0
mRS >2 (%)	1	1 (3)[a]	0
Latest Follow-up			
complete recovery (%)	43	29 (87.8)	14 (82.4)
time to complete recovery (months)	6.3 ± 8.3	4.5 ± 5.7*	10.8 ± 11.5*
residual symptom (%)	7	4 (12.1)	3 (17.6)
mRS >2 (%)	2	1 [a] (3)	2 [b, c] (5.9%)

mRS : modified Rankin scale, *: p = 0.0441, Mann-Whitney *U*-test

[a]: brain stem infarct, [b]: putaminal bleeding 3 months after the initial treatment, [c]: died of colon cancer

Table 3. Clinical characteristics of previously-reported and our patients with cavernous sinus dural arterio-venous fistulae

author	year	total number	male	female	mean age (years)	symptoms (%)
Meyers et al. [21]	2002	135	36	99	60	red eye (93), chemosis (87), proptosis (81), visual impairment (31), diplopia (68), tinnitus (49), pain (34)
Cheng et al. [6]	2003	27	3	24	60	chemosis (96), proptosis (96), visual impairment (26), cranial nerve palsy (19), tinnitus (11)
Suh et al. [35]	2005	58	8	50	57	ocular pattern (64), orbital pattern (53), cavernous (71), cerebral pattern (5)
Satomi et al. [32]	2005	65	14	51	66	chemosis (32), proptosis (18), diplopia (35), ptosis (11), tinnitus (11)

Kim et al. [15]	2006	56	11	45	57	chemosis (32), proptosis (21), visual impairment (13), diplopia (34), ptosis (13), orbital pain (34), headache (21)
Wu et al. [43]	2006	155	50	105	59	red eye (90), chemosis (47), proptosis (29), visual impairment (33), diplopia (44), bruit (25), pain (25)
Kirsch et al. [16]	2006	141	29	112	67	chemosis (94), proptosis (87), visual impairment (28), cranial nerve palsy (54), diplopia (51), ptosis (13), bruit (19)
Nishino et al. [24]	2008	31	9	22	62	red eye (77), proptosis (71), abducens palsy (68), oculomotor palsy (42), tinnitus (35), trigeminal nerve dysfunction (6), pain (29)
Yoshida et al. [45]	2010	44	13	31	66	chemosis (100), proptosis (14), visual impairment (11), abducens palsy (30), oculomotor palsy (7)
Jung et al. [14]	2011	76	25	51	59	chemosis (71), proptosis (67), visual impairment (24), diplopia (62), trigeminal nerve dysfunction (8)
Hiramatsu et al. [13]	2014	469	120	349	67	n.m.
Thomas et al. [36]	2015	22	n.m.	n.m	55	ocular and orbital (82), cavernous (36), cortical (18)
Wenderoth [42]	2016	32	15	17	62	n.m.

Present series	2017	50	8	42	66	chemosis (78), proptosis (66), visual impairment (12), diplopia (72), tinnitus (26), pain (22)
Total		1361	341	998		

pain: including orbital pain, retro-orbital pain, and headache

n.m.: not mentioned

cavernous: dysfunction or palsy of nerves in cavernous sinus,

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Meyers et al. [21]	2002	135	101 / 32	0	2	6	n.m.	n.m.	56	no: 90%	90)

			n.m.								
Cheng et al. [6]	2003	27	26 / 0 / 1	0	0	4	7	30 / 70	26	no: 89%	96)
Satomi et al. [32]	2005	17	0 / 11 / 0	0	6	5	n.m.	n.m.	9	no: 35%	cure (47), improved (53)
Kim et al. [15]	2006	56	45 / 0 / 11	0	0	9	11	52 / 48	13	n.m.	cure or improved (91)
Wu et al. [43]	2006	155	n.a.	146	0	2	11	n.a.	22	no: 75%	cure (50-81)#, improved (15-46) #, static (0-4) #
Kirsch et al. [16]	2006	141	106 / 0 / 32	0	3	9	3	81 / 19	52	n.m.	cure (95), residual (6)
Nishino et al. [24]	2008	31	22 / 0 / 11	0	0	n.m.	39	79 / 21	30	n.m.	cure (85), improved (15)
Yoshida et al. [45]	2010	44	42 / 2 / 0	0	0	7	14	82 /18	17	n.m.	
Jung et al. [14]	2011	76	40 / 28 / 8	0	0	7	13	47 /53	20	no: 70%, improved: 25%	cure (70), improved (18), static or worse (12)

Thomas et al. [36]	2015	22	12 / 3 / 2, open: 1	0	4	n.m.	n.m.	n.m.	9	n.m.	cure (73), incomplete resolution (27)
Wenderoth [42]	2016	32	27 / 3 / 2	0	0	6	3	100 / 0	6	no: 100%	n.m.
present series	2017	50	43 /2 / 5	0	0	2	24	66 / 34	66	no: 100%	cure (86), residual (14)

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No.: number, EVT: endovascular treatment, tVE: transvenous embolization, tAE: transarterial embolization, GK: gamma knife, Tx: treatment, PW: paradoxical worsening, n.m.: not mentioned, n.a.: not applicable, open: craniotomy for cavernous sinus surgery

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Figure 1

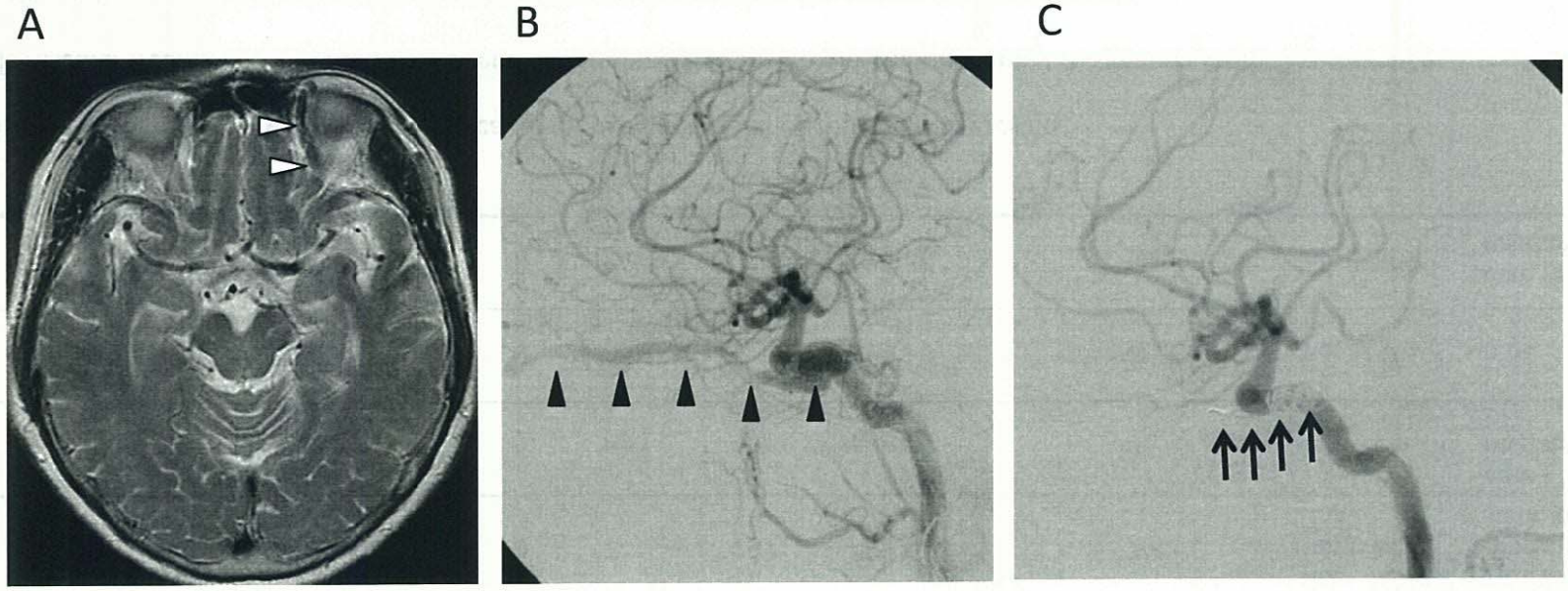

Figure 2

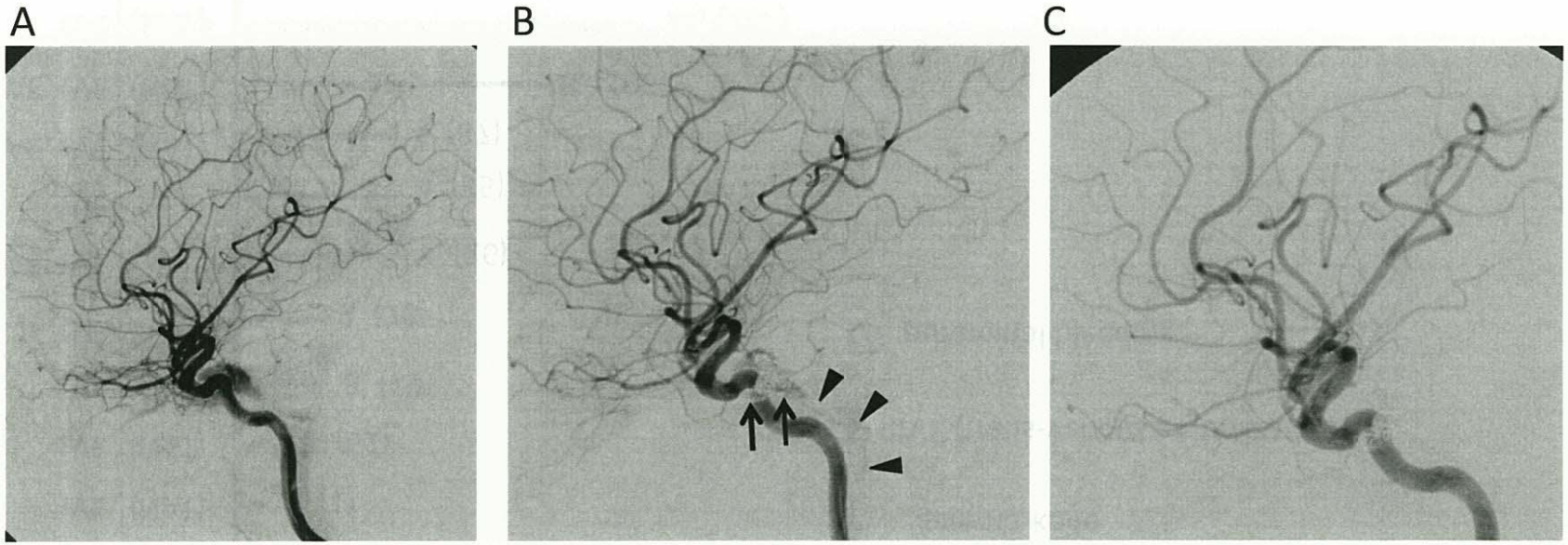

Figure 3

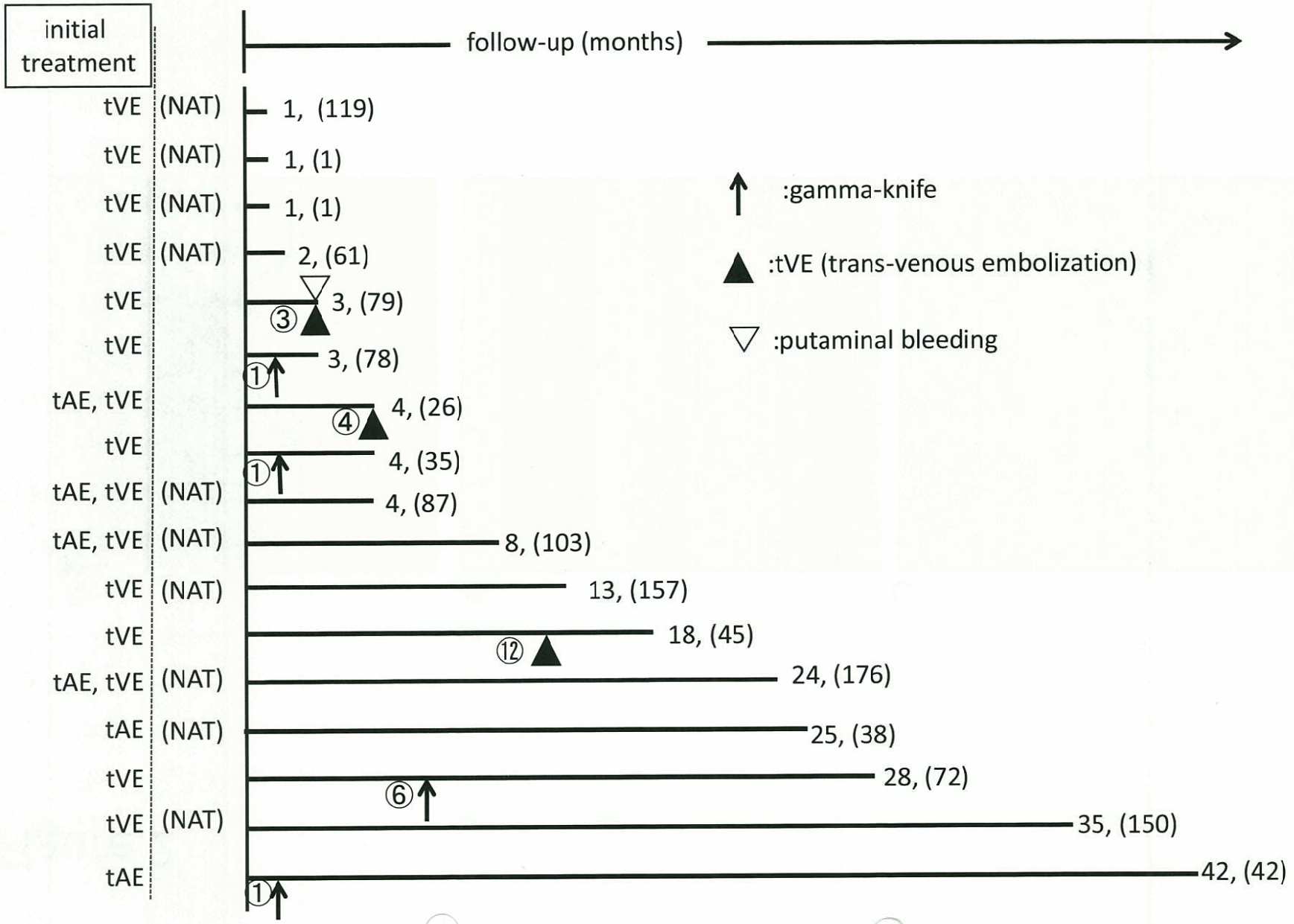
initial treatment
follow-up (months)
tVE (NAT) 1, (119)
tVE (NAT) 1, (1)
tVE (NAT) 1, (1)
tVE (NAT) 2, (61)
tVE 3, (79)
③
tVE 3, (78)
①
tAE, tVE 4, (26)
④
tVE 4, (35)
①
tAE, tVE (NAT) 4, (87)
tAE, tVE (NAT) 8, (103)
tVE (NAT) 13, (157)
tVE 18, (45)
⑫
tAE, tVE (NAT) 24, (176)
tAE (NAT) 25, (38)
tVE 28, (72)
⑥
tVE (NAT) 35, (150)
tAE 42, (42)
①
:gamma-knife
:tVE (trans-venous embolization)
:putaminal bleeding

Figure 4