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CLINICAL ARTICLE - VASCULAR

Endovascular management of adjacent tandem intracranial aneurysms: Utilization of stent-assisted coiling and flow diversion

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Abstract
Background Tandem intracranial aneurysms are aneurysms located along a single intracranial vessel. Adjacent tandem aneurysms arise within the same vascular segment and their presence often suggests diffuse parent vessel anomaly. Endovascular management of these rare lesions has not been well studied. In this retrospective observational study, we describe our experience treating adjacent tandem intracranial aneurysms with endovascular embolization.
Methods We retrospectively reviewed records of patients with these lesions who underwent endovascular treatment between 2008 and 2013.
Results Thirteen patients (mean age 60.8 years; 12 women) with 28 adjacent tandem aneurysms were treated during the study timeframe. Aneurysms were located along the clinoidal, ophthalmic, and communicating segments of the internal carotid artery in 12 patients and at the basilar apex in one patient. Average size was 8.4 mm. Six patients (12 aneurysms) were treated by flow diversion via the Pipeline embolization device (PED) and seven (16 aneurysms) by stent-assisted coiling, with coils successfully placed in 11 aneurysms. Clinical follow-up was available for an average of 26.1 months; postprocedural angiography was performed for 12 patients. Complete occlusion was achieved in nine of ten (90 %) PED-treated aneurysms and eight of 11 (72.7 %) treated by stent-assisted coiling (p= 0.44). Two patients treated by stent-assisted coiling required recoiling for aneurysm recanalization. Overall, modified Rankin scale scores were 0–1 for 12 patients and 3 for one patient.
Conclusions Adjacent tandem intracranial aneurysms can be safely and effectively treated by either stent-assisted coiling or flow diversion. We prefer PED flow diversion due to better parent vessel reconstruction and lower recanalization risk.

Keywords Pipeline embolization device · Tandem adjacent intracranial aneurysms

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Introduction

Intracranial tandem aneurysms are rare vascular lesions. The term tandem aneurysms refers to multiple aneurysms located

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along a single vessel. Adjacent tandem aneurysms arise within the same or adjacent vascular segments (e.g., clinoidal and ophthalmic segments of the internal carotid artery [ICA] [30]), and their presence often suggests diffuse anomaly of the parent vessel. Although patients with connective tissue disorders such as polycystic kidney disease, Marfan syndrome, or Ehlers–Danlos syndrome have an increased risk of developing multiple intracranial aneurysms [25, 32, 34], no particular systemic disease has been associated with tandem aneurysms.

Tandem intracranial aneurysms require aggressive management, as the resulting dysplastic parent artery not only makes the existing aneurysms fragile but also is prone to de novo aneurysm development. Although no published surgical series have focused on tandem aneurysms, microsurgical exploration and clipping can be an effective treatment for such lesions. Additional interventions, such as wrapping, can also be applied during surgery to smaller aneurysmal abnormalities along the diseased vessel that are not suitable for clipping and to the parent vessel itself. Endovascular management of adjacent tandem intracranial aneurysms has not been well studied. It can be argued that adjacent tandem lesions are challenging to treat with conventional endovascular techniques because they usually require stent-assisted coiling with the need to catheterize the aneurysms multiple times. Recently, flow diversion via the Pipeline embolization device (PED; Covidien, Irvine, CA, USA) has gained notable acceptance after the publication of promising results from large multicenter clinical trials [3, 26]. The PED is a self-expanding stent composed of 48 braided strands of cobalt chromium and platinum tungsten ranging from 28 to 33 μm in diameter and is designed to hemodynamically divert blood flow away from the aneurysm dome and promote intra-aneurysmal flow stasis and thrombosis, with subsequent parent-vessel remodeling [9, 10]. Here we report our experience utilizing either stent-assisted coiling or flow diversion for the treatment of adjacent tandem intracranial aneurysms.

Materials and methods

Population, setting, and study design

A database consisting of consecutive patients with intracranial aneurysms who were treated with endovascular embolization has been maintained prospectively at our institution. Data from 2008–2013 were retrospectively reviewed to identify patients who had undergone treatment for adjacent tandem aneurysms. In accordance with an institutional review board-approved protocol, the medical records of these patients were reviewed to obtain demographic and clinical information, such as age, sex, medical comorbidities, Hunt and Hess (HH) grade (for patients with ruptured aneurysms), and results of radiographic studies. Clinical outcome was measured by modified Rankin scale (mRS) score (favorable outcome, 0–2). Radiographic results were measured by degree of aneurysm thrombosis at the time of follow-up angiography. Angiographic outcome was evaluated according to the three-point classification system established by Roy et al. [31].

Treatment protocol

The treatment protocols for PED deployment and stent-assisted coiling have been published previously [15, 28]. Briefly, all patients were pretreated with a dual antiplatelet regimen of aspirin (325 mg/day orally) and clopidogrel (Plavix, 75 mg/day orally; Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, Bridgewater, NJ, and Princeton, NJ, USA). Those who underwent embolization on an emergent basis received a loading dose of aspirin (650 mg) and clopidogrel (600 mg) immediately prior to endovascular intervention. Platelet inhibition was routinely tested with goal response units of 550 for aspirin and 235 for Plavix considered therapeutic levels (VerifyNow Assay System, Accumetrics, Inc., San Diego, CA, USA). Intraoperatively, either a biaxial or a triaxial system was employed to maintain stability of the construct. A Marksman microcatheter (Covidien) was utilized for deployment of PEDs or Neuroform stents (Stryker Neurovascular, Kalamazoo, Michigan), and a Prowler Select Plus microcatheter (Codman, Raynham, MA, USA) was used to deliver Enterprise stents (Codman). When stent-assisted coiling was performed, a second microcatheter was usually jailed inside one aneurysm dome. A postoperative digital subtraction angiogram was routinely obtained at 6 months after PED placement or stent-assisted coiling. Dual antiplatelet therapy was continued for at least 3 months and could be extended if the aneurysm was giant and fusiform, thus requiring more time for endothelialization.

Statistical methods

Differences in aneurysm characteristics and treatment strategies were examined using Chi-square and two-tailed *t* tests for binary and continuous variables, respectively. Statistical significance was defined as a type I error less than 0.05. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA) and Excel 2007 (Microsoft Corp., Redmond, WA, USA).

Results

Descriptive data

Between 2008 and 2013, 13 patients were treated for adjacent tandem intracranial aneurysms at our institution. Detailed

information for each patient is listed in Table 1, and representative cases are illustrated in Figs. 1, 2, and 3. The mean age at the time of treatment was 60.8± 9.8 years (range, 45–78 years), and 12 patients were women. Eight patients had a history of tobacco use, one had coronary artery disease, six had hypertension, and four had chronic obstructive pulmonary disease. Overall, there were 28 adjacent tandem intracranial aneurysms in the study population: 11 patients were found to have two adjacent aneurysms each, and two patients were found to have three adjacent aneurysms each. Patient 1 (Table 1) presented with subarachnoid hemorrhage (SAH) from a ruptured left ophthalmic segment ICA aneurysm, whereas all other aneurysms in the cohort were unruptured.

Aneurysm characteristics and results according to treatment strategy are summarized in Table 2. The average size of the aneurysms was 8.4+2.7 mm (range, 3–14 mm). Most aneurysms (26 of 28, 92.9 %) were located along the clinoidal, ophthalmic, and communicating segments of the ICA, whereas two aneurysms were located at the basilar apex (patient 7, Table 2). Treatment strategies reflected device availability. Before 2011, seven patients with 16 tandem aneurysms were treated with stent-assisted coiling (five Enterprise, two Neuroform), and 11 of 16 aneurysms (68.8 %) were successfully coiled. Of the remaining five aneurysms, four were from the clinoidal segment of the ICA and were extradural (as determined from three-dimensional reconstructions from rotational angiography and thin-cut magnetic resonance imaging T2 sequences through the skull base); and the other was a 3-mm superior hypophyseal aneurysm that was monitored with serial noninvasive imaging studies.

Between 2011 and 2013, six patients with 12 aneurysms were treated with flow diversion: three received one PED each, and three received two PEDs each. No significant difference in aneurysm size or location was found in the treatment groups (Table 2). Coiling in conjunction with PED placement was not utilized in any patient. For the single patient with SAH (patient 1, Table 1; illustrative case 2), the ruptured ophthalmic ICA aneurysm was treated by balloon-assisted coiling initially, and the patient was readmitted later on an elective basis for stent-assisted coiling of an unruptured superior hypophyseal artery aneurysm.

Outcome data

PED deployment and stent-assisted coiling were successfully performed for all patients. Balloon angioplasty was needed in one case to dilate a partially expanded PED stent and this was accomplished without neurological consequences. Clinical follow-up was available for an average of 23.8 months (range, 2.7–55.2 months). No deaths occurred during the periprocedural or follow-up period. Patient 5 (Table 1) discontinued Plavix against medical advice and had a right MCA embolic stroke 4 months after stent-assisted coiling. This patient made a good recovery and was asymptomatic at the latest follow-up. In addition, patient 4 developed dementia during the follow-up period and suffered from a lumbar compression fracture and was found to have an mRS score of 3; the mRS score was 0 or 1 for the other 12 patients at the latest clinical follow-up.

Postprocedural digital subtraction angiography was performed for 12 patients at a mean of 20.3 months (range, 3.5–66 months), after the initial intervention. Five of six patients treated by PED had postprocedural angiography: nine aneurysms were completely occluded and one had residual filling at the aneurysm dome. All seven patients treated with stent-assisted coiling had angiographic follow-up, and of 11 aneurysms treated, eight had complete occlusion, one had recurrent filling at the aneurysm neck, and two had residual/recurrent filling at the aneurysm dome, both of which required addition coiling during the follow-up period (Table 1, patient 7, illustrative case 3). Although flow diversion resulted in a higher rate of occlusion and a lower rate of retreatment than stent-assisted coiling, the difference was not statistically significant (p=0.08).

Discussion

Multiple intracranial aneurysms are present in approximately 15–20 % of all aneurysm patients [13, 14] and are usually in the form of bilateral or “mirror-image” aneurysms of the ICAs or MCAs [1, 18, 35]. Population studies indicate that female gender [14], smoking [17], hypertension,[29], and connective tissue disorders [25, 32, 34] are associated with the development of multiple intracranial aneurysms. Intracranial tandem aneurysms located along adjacent vascular segments of a single artery have rarely been reported [12, 23, 27], and to our knowledge, the current study of 13 patients is the largest series in the literature. The presence of multiple aneurysms along a short vascular segment could indicate underlying abnormalities of the parent vessel, such as fenestration of the supraclinoid ICA [12, 27] or basilar artery [4] although no patients in our series were found to have vascular fenestration.

Key results and interpretation

In this retrospective observational study, we evaluated 13 patients with 28 adjacent intracranial tandem aneurysms who

Table 1 Clinical characteristics and outcomes

Patient no.	Age (years), sex	Aneurysm location	No. aneurysms	Aneurysm dome (neck) size (mm)	Treatment type	No. of aneurysms treated	Aneurysm occlusion (at angiographic follow-up)	Additional treatment	Outcome (mRS) (at clinical follow-up)
1	65, F	Ophthalmic ICA	2	11 (5) 7 (5)	Enterprise stent-assisted coiling	2	Both occluded	None	0
2	66, F	Clinoidal/ophthalmic ICA	2	14 (6) 5 (4)	Enterprise stent-assisted coiling	1	Treated aneurysm occluded	None	0
3	49, F	Clinoidal/ophthalmic ICA	3	12 (6) 5 (4) 3 (2)	Enterprise stent-assisted coiling	1	Treated aneurysm occluded	None	1
4	57, F	Clinoidal/ophthalmic ICA	2	11 (4) 6 (4)	Neuroform stent-assisted coiling	1	Treated aneurysm occluded	None	3
5	57, F	Clinoidal/ophthalmic ICA	3	14 (6) 9 (5) 5 (4)	Enterprise stent-assisted coiling	2	1 occluded 1 residual aneurysm	Recoiling	0
6	49, F	Clinoidal/ophthalmic ICA	2	12 (5) 8 (5)	Enterprise stent-assisted coiling	2	Both occluded	None	0
7	73, M	Basilar	2	8 (6) 7 (4)	Neuroform stent-assisted coiling	2	1 recurrent aneurysm 1 recurrent neck	Recoiling for 1 recurrent aneurysm	0
8	67, F	Ophthalmic ICA	2	9 (5) 7 (4)	PED	2	Both occluded	None	0
9	45, F	Ophthalmic ICA	2	10 (6) 7 (4)	PED	2	1 occluded 1 residual aneurysm	None	0
10	67, F	Ophthalmic/communicating ICA	2	9 (5) 4 (3)	2 PEDs	2	Both occluded	None	1
11	78, F	Clinoidal/ophthalmic ICA	2	10 (6) 9 (5)	2 PEDs	2	Both occluded	None	0
12	55, F	Clinoidal/ophthalmic ICA	2	10 (4) 5 (4)	2 PEDs	2	Both occluded	None	0
13	62, F	Ophthalmic ICA	2	10 (5) 7 (3)	PED	2	N/A	None	0

ICA, internal carotid artery; *mRS*, modified Rankin scale; *N/A*, not available; *PED*, Pipeline embolization device

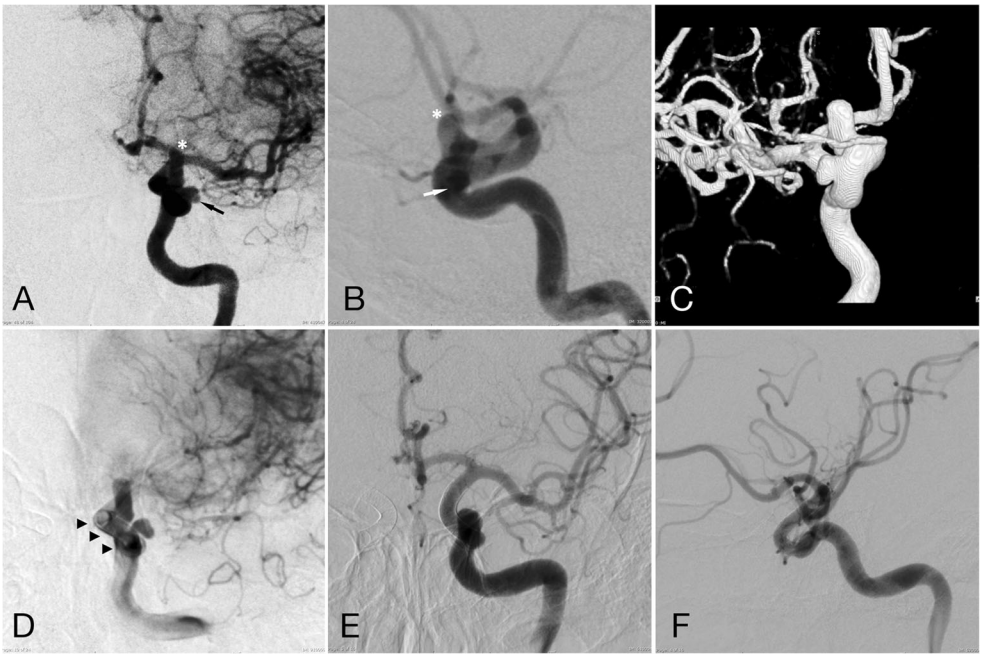

Fig. 1 Illustrative case 1 (patient 12, Table 1). This patient presented with chronic headache and was found to have multiple intracranial aneurysms. Specifically, there were adjacent tandem aneurysms along the clinoidal and ophthalmic segments of the left internal carotid artery (ICA) 1**a**, **b**), with one pointing superiorly (*asterisk*) and the other pointing laterally (*arrow*). A reconstruction of 3-D rotational angiogram showed that the paraclinoid segment of the left ICA was diffusely irregular (**c**). The patient was treated with 3.75 mm×18 mm and 3.75 mm×20 mm Pipeline embolization devices (PEDs; Covidien, Irvine, CA) (**d**, *arrowheads*) through a Marksman microcatheter (Covidien), and a control angiogram obtained after deployment of the PEDs demonstrated significant stasis of contrast material within both aneurysms (**d**). Follow-up angiogram at 3 months showed no residual filling in either aneurysm and good reconstruction of the parent vessel (**e**, anteroposterior (AP) view; **f**, lateral view)

were treated endovascularly at a single institution. We found that 17 of 21 treated aneurysms (80.9 %) were completely occluded at midterm follow-up of 20.3 months, and 12 patients (92.3 %) had favorable outcome (mRS of 0–2) at an average of approximately 2 years after the intervention. There were no periprocedural neurological complications or deaths during the follow-up period. These results were consistent with case studies reported by Ichikawa et al. [12] and Ng et al. [27], both of whom described the treatment of adjacent tandem aneurysms associated with fenestration of the supraclinoid ICA. In one case, two aneurysms (a superior hypophyseal aneurysm and an anterior choroidal aneurysm) were located at the proximal and distal ends of the fenestrated segment and both were coiled [12]. In the other case, two aneurysms arose from both limbs of the fenestration, one of which was clipped and the other of which was treated with stent-assisted coiling [27]. In a third case, reported by Mut et al. [23], two tandem aneurysms along the cavernous ICA were treated with PEDs, and both aneurysms occluded at 9 months after intervention. These results collectively suggest that stent-assisted coiling and flow diversion can be utilized safely for the treatment of intracranial tandem aneurysms and can achieve clinical outcomes similar to those associated with conventional endovascular therapies for unruptured intracranial aneurysms [31].

Generalizability

Although the natural history of intracranial tandem aneurysms, as compared to other cerebral aneurysms, has not been well understood, some reports suggest that patients harboring multiple intracranial aneurysms have an increased risk of suffering SAH. Aneurysms associated with vascular fenestration were also thought to have a higher incidence of rupture [2, 16]. Moreover, with the presence of multiple aneurysms, the dysplastic parent artery not only makes the existing aneurysms fragile but also is likely prone to new aneurysm development. As a result, tandem intracranial aneurysms require aggressive management.

The available treatment options for these lesions include microsurgical clipping and/or wrapping, primary coiling, stent-assisted coiling, and flow diversion. Surgical treatment is usually challenging due to the dysplastic nature of the parent vessel, and the aneurysms in our cohort were mostly located at the paraclinoid ICA segment or basilar apex, which also favors endovascular therapy. Conversely, we believe that flow diversion via PEDs is uniquely suited for obliterating

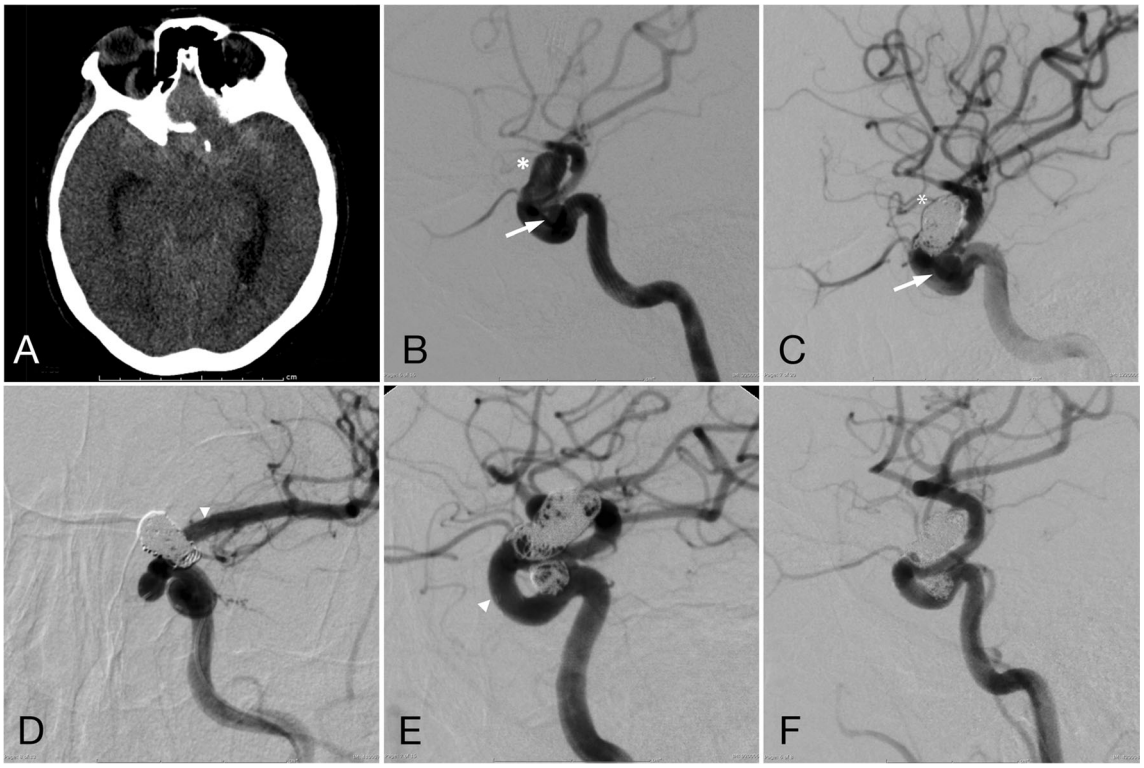

Fig. 2 Illustrative case 2 (patient 1 Table 1). This patient presented with obtundation and was found to have diffuse subarachnoid hemorrhage (SAH) and hydrocephalus (**a**). Diagnostic cerebral angiography (**b**, AP view; **c**, lateral view) demonstrated a large left ophthalmic ICA aneurysm (**b** and **c**, *asterisk*) and an adjacent superior hypophyseal aneurysm (**b** and **c**, *arrow*). The ophthalmic ICA aneurysm was considered the source of hemorrhage and was secured by performing balloon-assisted coiling (**c**), whereas the superior hypophyseal aneurysm was untreated. The patient recovered well from the SAH and required ventriculoperitoneal shunting prior to discharge. One month later, elective stent-assisted coiling of the left superior hypophyseal aneurysm (**d**-AP, **e**-lateral) was performed with a 4.5-mm × 28 mm Enterprise stent (Codman, Raynham, MA, USA) (*arrowhead*). Follow-up angiogram at 9 months showed no residual filling in either aneurysm and a patent left ophthalmic artery (**f**, lateral)

intracranial tandem aneurysms. Despite the relatively brief availability of the PED for clinical use, a multitude of reports have demonstrated its distinct versatility,[3, 6–11, 19–22, 24, 26, 33] and its utilization as a primary treatment for intracranial aneurysms has gained increasing acceptance. Endoluminal therapy with a flow diverter such as the PED provides better reconstruction of the aneurysm neck and results in lower recanalization rates, as demonstrated by the current study and in Ref. [5]. Moreover, PEDs can theoretically induce repair of the dysplastic and diseased parent vessel and therefore offer durable, long-term cure of adjacent tandem intracranial aneurysms. In our series, the risk of perioperative and long-term complications was similar for patients treated with stent-assisted coiling and with flow diversion; and stent-assisted coiling for multiple aneurysms within a short vascular segment is technically more complex because of the need for repeated catheterization of the aneurysm. This type of technical challenge applies to both open-cell (i.e., Neuroform) and closed-cell (i.e., Enterprise) intracranial stents. Further, computational fluid dynamics analyses by Mut et al. [23] demonstrated a decreased energy content within the proximal and distal aneurysms and supported the notion that PEDs established an environment conducive to vessel healing and aneurysm occlusion.

Limitations

Several limitations should be considered while interpreting the results presented in this paper. We conducted a single-center, retrospective, observational study, and therefore there is inherent selection bias associated with the study. The rate of perioperative complications associated with PED deployment or stent-assisted coiling in our series was low, which could be due to the small sample size. Furthermore, although midterm follow-up data in our study showed a high occlusion rate for aneurysms treated by PEDs (90 %), the relatively recent adoption of PED in clinical use implies that the long-term durability of the treatment, especially its potential protective effect on the dysplastic parent artery, remains unclear. Nevertheless, our data demonstrated that endovascular therapy, especially flow diversion via PEDs, is a safe and effective form of treatment for intracranial tandem aneurysms.

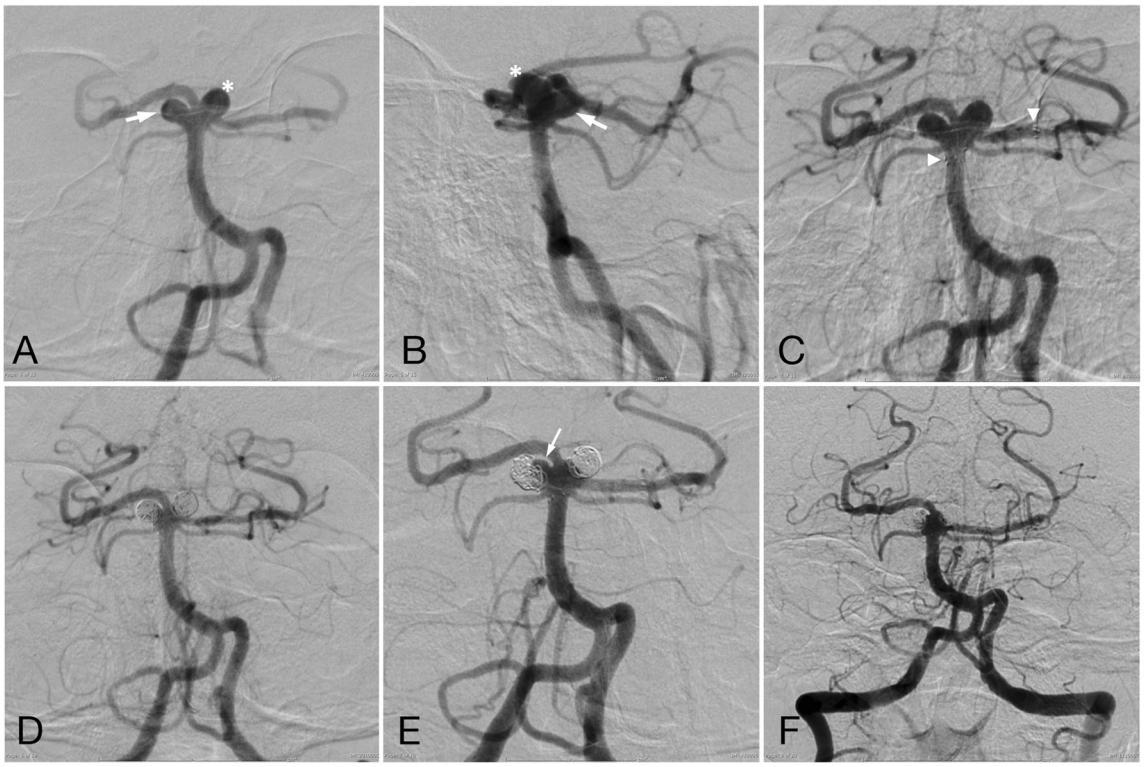

Fig. 3 Illustrative case 3 (patient 7, Table 1). This patient had a history of pituitary macroadenoma and was found to have multiple incidental intracranial aneurysms at the top of the basilar artery. Diagnostic angiogram (**a**, AP view; **b**, lateral view) demonstrated a broad-based saccular aneurysm at the basilar apex (**a**, **b**, *asterisk*) and another between the right posterior cerebral artery and right superior cerebellar artery (**a**, **b**, *arrow*). The patient underwent stent-assisted coiling of both aneurysms (**c**, **d**), with a 3.5-mm×20 mm Neuroform stent (Stryker Neurovascular, Kalamazoo, MI, USA) placed from the left posterior cerebral artery to the basilar artery (**c**, *arrowheads*). The patient had follow-up with annual brain MR angiograms. The right superior cerebellar artery aneurysm was found to have recanalized 5 years after the initial embolization (**e**, *arrow*) and was successfully re-coiled (**f**)

Table 2 Aneurysm characteristics and results according to treatment strategy

Characteristic	PED only (n=12)	Stent-assisted coiling (n=16)	p value
Aneurysm size (mm)			
Mean (SD)	8.1 (2.0)	8.6 (3.1)	0.27
Range	4–10	3–14	
Aneurysm location			
ICA	12	14	0.13
Posterior circulation	0	2	
Aneurysms treated	12	11	0.02
Rupture status			
Unruptured	12	15	0.21
Ruptured	0	1	
Follow-up angiography			
Complete occlusion	9	8	0.44
Residual neck	0	1	
Residual aneurysm	1	2	
Retreatment	0	2	0.08

ICA, internal carotid artery; *PED*, Pipeline embolization device; *SD*, standard deviation

Conclusions

Adjacent intracranial tandem aneurysms are rare vascular lesions and are located most commonly along the ICA. Although they can be safely and effectively treated by either stent-assisted coiling or flow diversion, PED is the preferred modality at our center due to better parent vessel reconstruction and lower risk of recanalization. Further investigation with long-term angiographic and clinical follow-up is needed to further elucidate the durability of PED treatment for obliterating these aneurysms.

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Contributorship statement Lin and Levy are responsible for concepts and design. All authors contributed intellectually. All authors acquired, analyzed, and interpreted the data. Statistical analysis was performed by Lin. Manuscript was prepared by Lin and Brouillard. All authors reviewed and made critical revisions to the manuscript.

Data sharing statement Additional data from this study (case series) may be made available upon request directed to the corresponding author.

Ethics approval This study was approved by the University at Buffalo Institutional Review Board (Project 578913-2).

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