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Cerebral Arterial Fenestrations

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Summary

Arterial fenestrations are an anatomic variant with indeterminate significance. Given the controversy surrounding fenestrations we sought their prevalence within our practice along with their association with other cerebrovascular anomalies.

We retrospectively reviewed 10,927 patients undergoing digital subtraction angiography between 1992 and 2011. Dictated reports were searched for the terms "fenestration" or "fenestrated" with images reviewed for relevance, yielding 228 unique cases. A Medline database search from February 1964 to January 2013 generated 304 citations, 127 cases of which were selected for analysis.

Cerebral arterial fenestrations were identified in 228 patients (2.1%). At least one aneurysm was noted in 60.5% of patients, with an aneurysm arising from the fenestration in 19.6% of patients. Aneurysmal subarachnoid hemorrhage or non-aneurysmal subarachnoid hemorrhage were present in 60.1% and 15.8%, respectively. For the subset of patients with an aneurysm arising directly from a fenestration relative to those patients with an aneurysm not immediately associated with a fenestration, the prevalence of aneurysmal subarachnoid hemorrhage was 66.7% vs. 58.6% (p = 0.58). Fenestrations were more often within the posterior circulation (73.2%) than the anterior circulation (24.6%), though there was no difference in the prevalence of aneurysms within these groups (61.1% vs. 60.7%, p = 1.0).

Cerebral arterial fenestrations are an anatomic variant more often manifesting at the anterior communicating arterial complex and basilar artery and with no definite pathological relationship with aneurysms.

Introduction

A fenestration is an arterial anatomic variant where a segment of a single vessel divides into at least two channels, each comprising endothelial and muscular layers (they may share the adventitia) that coalesce to a single lumen along its more distal course. Varying series from autopsy, surgical dissection, digital subtraction angiography (DSA), and cross-sectional (computed tomography (CT) and magnetic resonance (MR)) imaging have suggested a widely varying prevalence of fenestrations ranging from 0.7 to 60% [1-7]. This spacious interval largely reflects the small sample sizes, selection biases, and retrospective design of series, in addition to the sensitivity of the varying detection techniques. Advances in DSA, CT, and MR imaging have improved spatial resolution as well as the ability to manipulate anatomy in three-dimensional space with resultant higher prevalence rates of fenestrations noted in contemporary studies relative to their more dated technological equivalents [2].

The interest in fenestrations, aside from their intrinsic anatomic difference from conventional arteries, is their relationship to neurovascular pathology at large. Many studies have noted the presence of fenestrations in the setting of aneurysms, whether immediately adjacent or remote to one another. Others have noted their presence in the setting of arterial-venous malformations, ischemic stroke, and as well as other cerebrovascular anomalies, pathological or otherwise [8]. Series such as these suggest fenestrations may alter microvascular flow dynamics that may increase the risk of aneurysm formation in addition to their more generalized role as markers for any pathological vascular manifestation. Others contend that fenestrations are not benign variants, but rather pathological and as such carry a risk of subarachnoid hemorrhage independent of any other identifiable source of bleeding [9].

Given the controversy surrounding fenestrations, we sought to define their prevalence within our practice along with their varying anatomic locations, association with other cerebrovascular anomalies, and clinical presentation. We also reviewed the literature to note patterns within case series when examined collectively.

Methods

Under permission of the committee on human research (CHR 10-00936), we retrospectively reviewed our database of patients (10,927) undergoing DSA between 1992 and 2011. Dictated reports were searched for the term "fenestration" or "fenestrated". The initial query was reviewed and all duplicate medical records (18,437 examinations) removed leaving only unique cases. Three neurointerventional radiologists (DC, CS, and WK) reviewed the images from each of these cases to assess their relevance. Those considered pertinent then underwent more extensive review for demographic, clinical, imaging, and treatment variables.

A search of the Medline database <pubmed.gov> from February 1964 to January 2013 combining the terms "fenestration", "artery or arterial", and "brain or cerebral or intracranial" generated 304 citations. These were reviewed for relevance with 127 selected for analysis. Those considered pertinent were then reviewed for demographic, clinical, imaging, and treatment variables. The tabulated data were compared as proportions using the chi-squared test.

Table 1 **Fenestration retrospective cohort analysis.**

Location	Cases	Male (%)	Age (±SD)	Aneurysm	Aneurysm at site [1,3]	ICH [2]	A-SAH [1]	NA-SAH [2]
Total	228	93 (40.8%)	53 (17.0)	138 (60.5%)	27 (19.6%)	117 (51.3%)	83 (60.1%)	36 (15.8%)
Anterior	56 (24.6%)	21 (37.5%)	50 (18.2)	34 (60.7%)	11 (32.4%)	26 (46.4%)	19 (55.9%)	8 (14.3%)
Posterior	167 (73.2%)	71 (42.5%)	53 (16.3)	102 (61.1%)	15 (14.7%)	90 (53.9%)	64 (62.7%)	27 (16.2%)
Multiple	5 (2.2%)	1 (20.0%)	49 (25.0)	2 (40.0%)	1 (50.0%)	1 (20.0%)	0 (0%)	1 (20.0%)
Internal carotid	3 (1.3%)	1 (33.3%)	52 (48.6)	3 (100%)	0 (0%)	1 (33.3%)	1 (33.3)	0 (0%)
Anterior cerebral	43 (18.9%)	16 (37.2%)	51 (15.4)	26 (61.9%)	10 (38.5%)	21 (48.8%)	16 (61.5%)	6 (14.0%)
Middle cerebral	10 (4.4%)	4 (40.0%)	44 (19.0)	5 (50.0%)	1 (20.0%)	4 (40.0%)	2 (40.0%)	2 (20.0%)
Vertebral	45 (19.7%)	16 (35.6%)	53 (16.6)	24 (53.3%)	2 (8.3%)	23 (51.1%)	17 (70.8%)	6 (13.3%)
Basilar	120 (52.6%)	53 (44.2%)	54 (16.4)	77 (64.2%)	13 (16.9%)	65 (54.2%)	46 (59.7%)	20 (16.7%)
Posterior cerebral	1 (0.4%)	1 (100%)	41 (NA)	1 (100%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)
PICA	1 (0.4%)	1 (100%)	62 (NA)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1 (100%)

[1] *Denominator is number of aneurysms (at given location, if applicable)*
[2] *Denominator is total patients (at given location, if applicable)*
[3] *For the subset of patients with an aneurysm arising directly from a fenestration (n = 27) relative to those patients with an aneurysm not immediately associated with a fenestration (n = 111), the prevalence of aneurysmal SAH was 66.7% vs. 58.6% (p = 0.58).*

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All analyses were performed using the software R and with a probability of significance of 0.05. To calculate 95% confidence intervals a t distribution based on sample size was employed.

Results

Review of 18,437 examinations, representing 10,927 patients yielded 228 unique fenestration cases, generating a prevalence of 2.1%. Table 1 details the general demographic and hemorrhagic details of the fenestration cohort in addition to their locations. The majority (59.2%) of these patients were female and had undergone evaluation within the sixth decade of life (53 ± 17 years). Many (60.5%) of these patients harbored at least one aneurysm at any location within the cerebral vasculature, though a smaller fraction (19.6%) manifested an aneurysm at the actual fenestration site. More than half of all patients (51.3%) presented clinically with intracranial hemorrhage, subarachnoid or otherwise, and of those patients with an aneurysm 60.1% had a history of aneurysmal rupture; 15.8% of patients had a history of a non-aneurysmal subarachnoid hemorrhage. Only five patients had multiple fenestrations.

As to the distribution within the intracranial circulation, nearly three quarters (73.2%) of fenestrations were located within the posterior circulation with the basilar artery being the most frequently (52.6%) affected vessel. Fenestrations were found at other locations, including the internal carotid (1.3%), middle and posterior cerebral (4.4% and 0.4%, respectively), and posterior-inferior cerebral (0.4%) arteries, though certainly more seldom than vertebral, anterior cerebral, and basilar arteries. Those fenestrations found within the anterior cerebral artery, defined as its primary and secondary segments and anterior communicating artery complex, most frequently (38.5%) had intimate aneurysmal association while the basilar artery less often (16.9%) showed such a relationship. For the subset of patients with an aneurysm arising directly from a fenestration (n = 27) relative to those patients with an aneurysm not immediately associated with a fenestration (n = 111), the prevalence of aneurysmal SAH was 66.7% vs. 58.6% (p = 0.58).

Collectively, the mean aneurysm size (Table 2) was 6.74 mm (5.98, 7.50) identical to those arising at the fenestration specifically (mean 6.74 mm 5.31, 8.17). Posterior circulation aneurysms (5.52 mm 3.86, 7.18), in particular those from basilar artery (5.22 mm 3.71, 6.73), were smaller than those within the anterior circulation. As previously stated, fenestrations were more often within the posterior circulation than the anterior circulation (24.6%), though there was no difference in the prevalence of aneurysms within these groups (61.1% vs. 60.7%, p = 1.0).

Table 2 **Aneurysm size mm [95% CI].**

Mean overall	6.74 (n=121) [5.98, 7.50]
Mean A-SAH	6.58 (n=74) [5.77, 7.39]
Mean aneurysm at site	6.74 (n=27) [5.31, 8.17]
Location	
Mean of anterior	6.63 (n=52) [5.71, 7.56]
Mean of posterior	5.52 (n=25) [3.86, 7.18]
Mean of basilar	5.22 (n=18) [3.71, 6.73]

Discussion

The fenestration cohort herein described is the largest of its kind. The prevalence of fenestrations within our retrospective cohort was 2.1%. This is more than the 0.7% prevalence from a series using a comparable DSA technique, though fewer than other series using MR (2.8 – 3.0%), DSA (22.9 – 28%), and CT (3.5 – 12.9%) and significantly less than those reported from autopsy series [3,4,6,7,9-12].

To help put our results in an historical context we compiled a comparable number (204) of cases (Table 3) from the literature. These individual and serial reports span more than four decades and reflect the technological changes in kind. They also reflect reporting bias selecting for cases less frequently seen in practice as evidenced by the higher fractions relative to our cohort of fenestrations of the internal carotid (10.3% vs. 1.3%, p-value <0.001), and middle (11.3% vs. 4.4%, p-value 0.01) and posterior (2.0% vs. 0.4%, p-value 0.3) cerebral arteries, and lower fractions within the anterior cerebral (13.7% vs. 18.9% p-value 0.19), basilar (44.1% vs. 52.8%, p-value 0.1), and vertebral (11.8% vs. 19.7%, p-value 0.03) arteries. And just as such exotic locations are over represented so are the relative associations with other pathologies, namely hemorrhage and aneurysms. Within the meta-analysis nearly three quarters (72.5%) of patients had an aneurysm, 60.3% had an aneurysm arising at the site of the fenestration, and 72.1% manifested aneurysmal rupture.

Fenestrations and aneurysms

The relationship between fenestrations and aneurysms is controversial with many series, including our own, reporting a high prevalence of aneurysms in patients with fenestrations, and with other series noting no such relationship [2,4,6]. Excluding our series, the prevalence of an aneurysm in the setting of a fenestration ranges from 2.5 to 17% [2,6,10,12,13]. The distinction should be made regarding fenestrations and aneurysms as to whether the two are anatomically associated or remote relative one another [2]. In the setting of fenestrations distant from aneurysms, a higher prevalence of aneurysms might suggest the fenestration represents a marker of more generalized vascular dysfunction, though there is no evidence describing alterations in genetic expression unique to patients with fenestrations that might put them at such risk. Furthermore, though the number of patients was small [5], we did not see a trend whereby patients with multiple fenestrations had more aneurysms, suggesting that more fenestrations are not an indicator of more vascular pathology.

The scenario of anatomically associated fenestrations and aneurysms, however, has been explored, particularly as to the changes in fenestrated arterial wall organization and alterations of flow around the fenestration and how both may be involved in aneurysm formation [3,14-16]. Thinning or absence of the media has been noted at the proximal and distal margins of fenestrations, though similar histological arrangements are noted at other conventional anatomic arterial bifurcation locations. That saccular aneurysms tend to form at such branch points, fenestration-based or otherwise, is well-

Table 3 **Fenestration meta-analysis.**

Location	Cases	Male	Age (SD)	Aneurysm	Aneurysm at site	ICH	A-SAH	NA-SAH	p-value [a]
Total	204	103 (50.5%)	48 (16.8)	148 (72.5%)	123 (60.3%)	116 (56.9%)	106 (71.6%)	1 (0.5%)	
Anterior [45-96]	72 (35.3%)	33 (45.8%)	52 (16.2)	45 (62.5%)	39 (86.7%)	33 (45.8%)	33 (73.3%)	0 (0%)	
Posterior [80,95,97-161]	122 (59.8%)	67 (54.9%)	46 (16.4)	94 (77.0%)	78 (83.0%)	75 (61.5%)	66 (70.2%)	1 (0.8%)	
Multiple [48,49,51,70,95, 122,136, 162,163]	9 (4.4%)	3 (33.3%)	37 (19.9)	7 (77.8%)	5 (71.4%)	7 (77.8%)	6 (85.7%)	0 (0%)	
Internal carotid [45,47,52, 56,57,64,73,75,77-79,84-86,93,164-166]	21 (10.3%) [a]	6 (28.6%)	45 (13.9)	14 (66.7%)	13 (92.9%)	7 (33.3%)	7 (50.0%)	0 (0%)	< 0.001
Anterior cerebral [46,51, 53,54,59,61,63,65,68-71,74,80,87,90, 91,94,167,168]	28 (13.7%) [a]	15 (53.6%)	53 (14.5)	22 (78.6%)	19 (86.4%)	17 (60.7%)	18 (81.8%)	0 (0%)	0.19
Middle cerebral [50,55, 60,62,67,72,76,81-83,92,96]	23 (11.3%) [a]	12 (52.2%)	56 (18.5)	9 (39.1%)	7 (77.8%)	9 (39.1%)	8 (88.9%)	0 (0%)	0.01
Vertebral [80,95,101,114,119,121, 132,133,139,145,148,149,154,159,169]	24 (11.8%) [a]	13 (54.2%)	42 (18.6)	9 (37.5%)	3 (33.3%)	13 (54.2%)	8 (88.9%)	0 (0%)	0.03
Basilar [80,97-100,102,104-106, 108-113,115-117,120,123-126,128-130, 134,135,140,141,143,144,146,147, 150-152,154,155,157,158,161,170,171]	90 (44.1%) [a]	48 (53.3%)	48 (15.3)	79 (87.8%)	72 (91.4%)	59 (65.6%)	56 (70.9%)	1 (1.1%)	0.1
Posterior cerebral [88,103, 118,127,142,160]	4 (2.0%) [a]	3 (75.0%)	26 (10.8)	3 (75.0%)	3 (100%)	2 (50.0%)	2 (66.6%)	0 (0%)	0.30
PICA [107,137,138,153]	4 (2.0%) [a]	3 (75.0%)	56 (13.4)	3 (75.0%)	0 (0%)	1 (25.0%)	0 (0%)	0 (0%)	0.30

[a] *Chi-square test comparing retrospective cohort vs. meta cohort.*

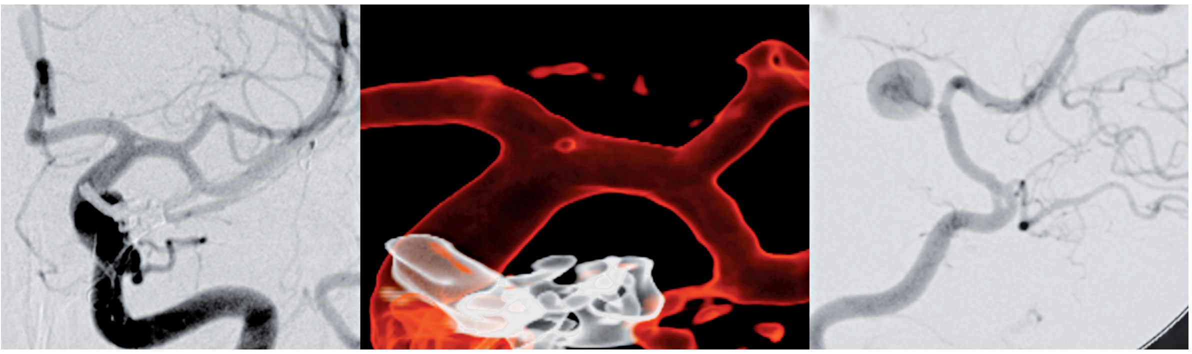

Figure 1 High magnification oblique 2D DSA (A) and 3D rotational angiographic (B) images of an internal carotid artery terminus fenestration. C) Lateral 2D DSA image of a cavernous internal carotid artery fenestration. Note the M1 middle cerebral segment aneurysm.

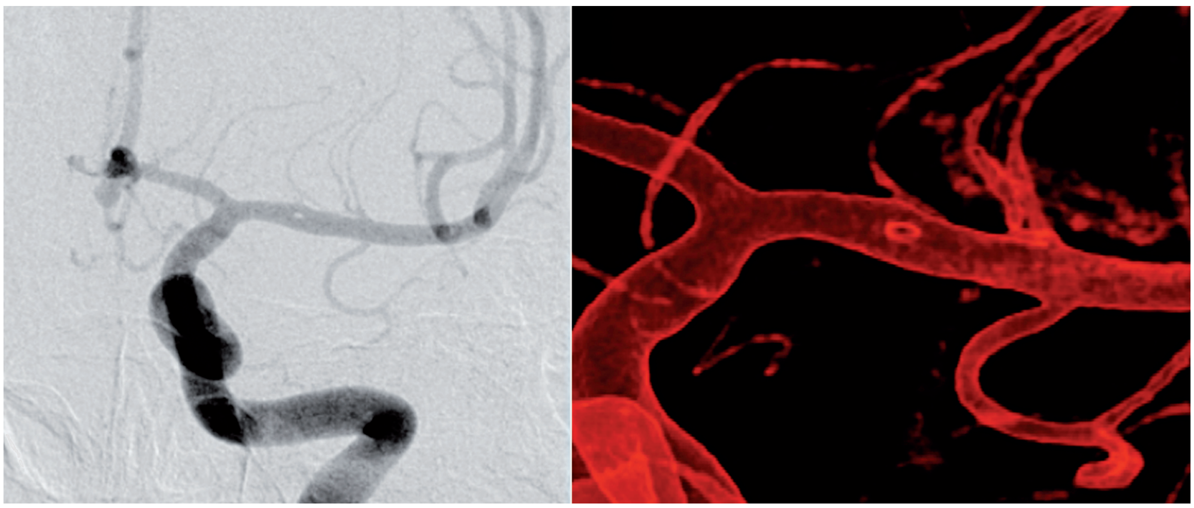

Figure 2 High magnification oblique 2D DSA (A) and 3D rotational angiographic (B) images of a middle cerebral artery fenestration. Note the anterior communicating artery aneurysm.

described, though there may be additional risks added by a fenestration such as changes in pressure and flow. Such hemodynamic alterations may not only predispose to aneurysm formation, but also to dissection and/or thromboembolic events [3,17-26]. Ischemic injury may be related to an absence of anterograde filling of a more expansive distribution or to occlusion of small perforating arteries arising from a fenestrated segment. Arterial perforators are often occult on DSA, though need to be considered if occlusion of the limb of the fenestration is considered part of treatment [27,28]. These small branches, best visualized on microsurgical dissection, are variable in their origins and may arise from either the smaller or larger of the fenestration limbs.

Fenestrations and location

We recognize the limitation of endowing equal meaning to all fenestrations. These variants may arise in multiple locations and can have vastly different apertures, limb lengths, and relationships with perforating vessels to which they might give rise. It may be that only a subset(s) of fenestrations carry greater risk of bleeding and/or aneurysmal formation. We noted fenestrations at multiple locations throughout the cerebral vasculature, though with more limited representation at the internal carotid (0.03%; Figure 1), middle cerebral (0.9%; Figure 2), posterior cerebral (0.01%; Figure 3), vertebral (0.4% (Figure 3) and posterior-inferior cerebellar (0.01%) arteries. Given such scarci-

Figure 3 A) High magnification lateral 2D DSA image of a cervical segment vertebral artery fenestration. B) High magnification Waters projection 2D DSA image of a left P1 posterior communicating artery fenestration. C,D) High magnification Waters 2D DSA and 3D rotational images of a basilar artery terminus fenestration.

ty, we focused our discussion on the two most frequently encountered fenestration locations: the anterior communicating arterial complex (Figure 4) and the basilar artery (Figure 5).

As with other morphological variations, arteries closer to the anatomic midline more frequently manifest fenestrations, namely the anterior communicating and basilar arteries [3,5,8,16,24,29-32]. Fenestration of the anterior cerebral artery is rare with only 0.4% prevalence within our cohort and with other case series ranging from 0.1 to 7.2% [11,19,27,30,33-35], though if the anterior communicating artery is included the prevalence increases significantly rising up to 40% by some accounts. The increased prevalence of fenestrations within the anterior communicating artery mirrors the relatively higher rate of fenestration within the basilar artery, both midline vascular structures, and supporting their etiology as one of abnormal embryonic arterial fusion [2-4,8,11,19,33-39]. The anterior cerebral-anterior communicating artery complex was the most common site within our cohort to have an aneurysm arise directly from the fenestration (38.5%) with a similar fraction (27.6%) reported by others for aneurysms arising from A1 fenestrations [31]. The relatively increased aneurysm-fenestration co-location may in part be related to the manner in which the anterior communicating region is interrogated during 2D DSA. The standard anterior-posterior and lateral projections used in DSA are limited in their ability to resolve aberrant anatomy of the anterior communication region. In the setting of an aneurysm within this region, a finding easier to make on such routine AP and lateral projections, additional oblique projections (Figure 1) are performed to better delineate the aneurysmal architecture often facilitated by 3D rotational angiography [11,33]. It is these tailored projections that will more often reveal such anatomic variants. For those fenestrations arising from the A1 segment special consideration must be paid to the presence of perforating branches supplying the basal ganglia and optic chiasm if vessel sacrifice is necessitated. Autopsy series have noted the predilection for perforators to arise from the more lateral aspects of the A1, though these vessels may arise from either or both limbs of a fenestration [27].

Fenestrations of the basilar artery are thought to arise from congenital non-fusion of the paired longitudinal neural arteries and are rare with only 1.1% prevalence within our cohort and from other case series ranging from 0.3 to 6.0% [2-4,7,8,14,16,40-43]. Of all locations within our cohort, the basilar artery occurred most frequently (52.6%) with a similar relationship noted within the literature reviewed herein (44.1%). This finding is thought to be in part related to the relative ease of their detection using standard DSA projections. Juxtaposed against the difficulty in resolving the anterior communicating complex with routine 2D DSA, the basilar artery is nearly always larger in diameter and, more importantly, in a more orthogonal relationship with the image intensifier using either Townes or Waters projections

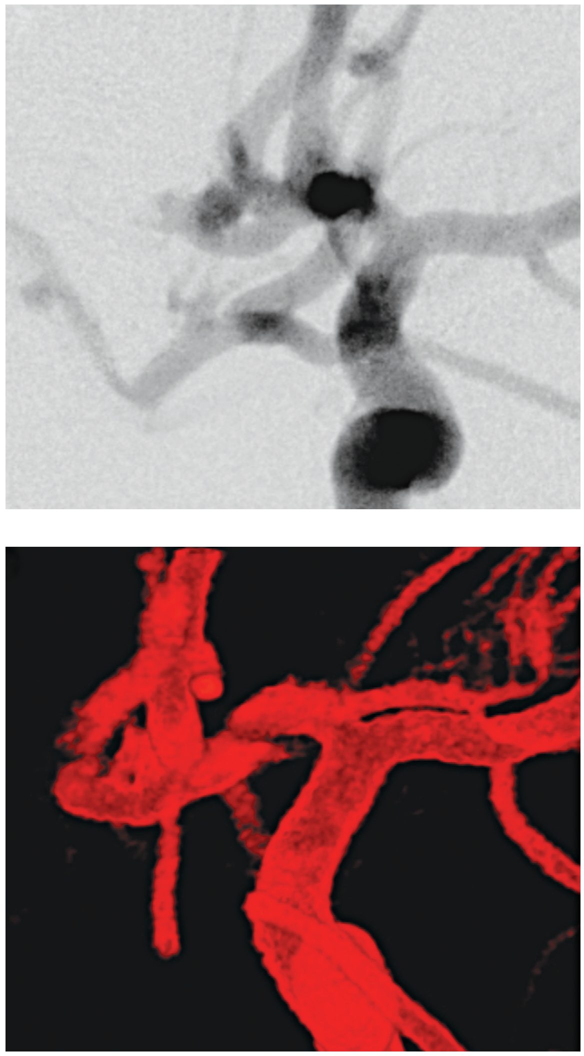
A
B

Figure 4 High magnification oblique 2D DSA (A) and 3D rotational angiographic (B) images of an anterior communicating artery fenestration.

(Figure 2). Fenestrations may occur anywhere along the length of the basilar artery, though they are most frequently noted at the proximal extent adjacent to the vertebral-basilar junction [8]. As such this location has been noted as a hotspot for aneurysm formation, with up to 70% of vertebral-basilar junction aneurysms having an associated fenestration, though such aneurysms remain rare overall with fewer than 80 reported in the literature [3,28,44].

There are limitations to this descriptive review imposed by its retrospective methodology. The source population, patients undergoing DSA (primarily 2D) at a large tertiary care medical center, certainly introduces bias and in turn limits any conclusion regarding the fenes-

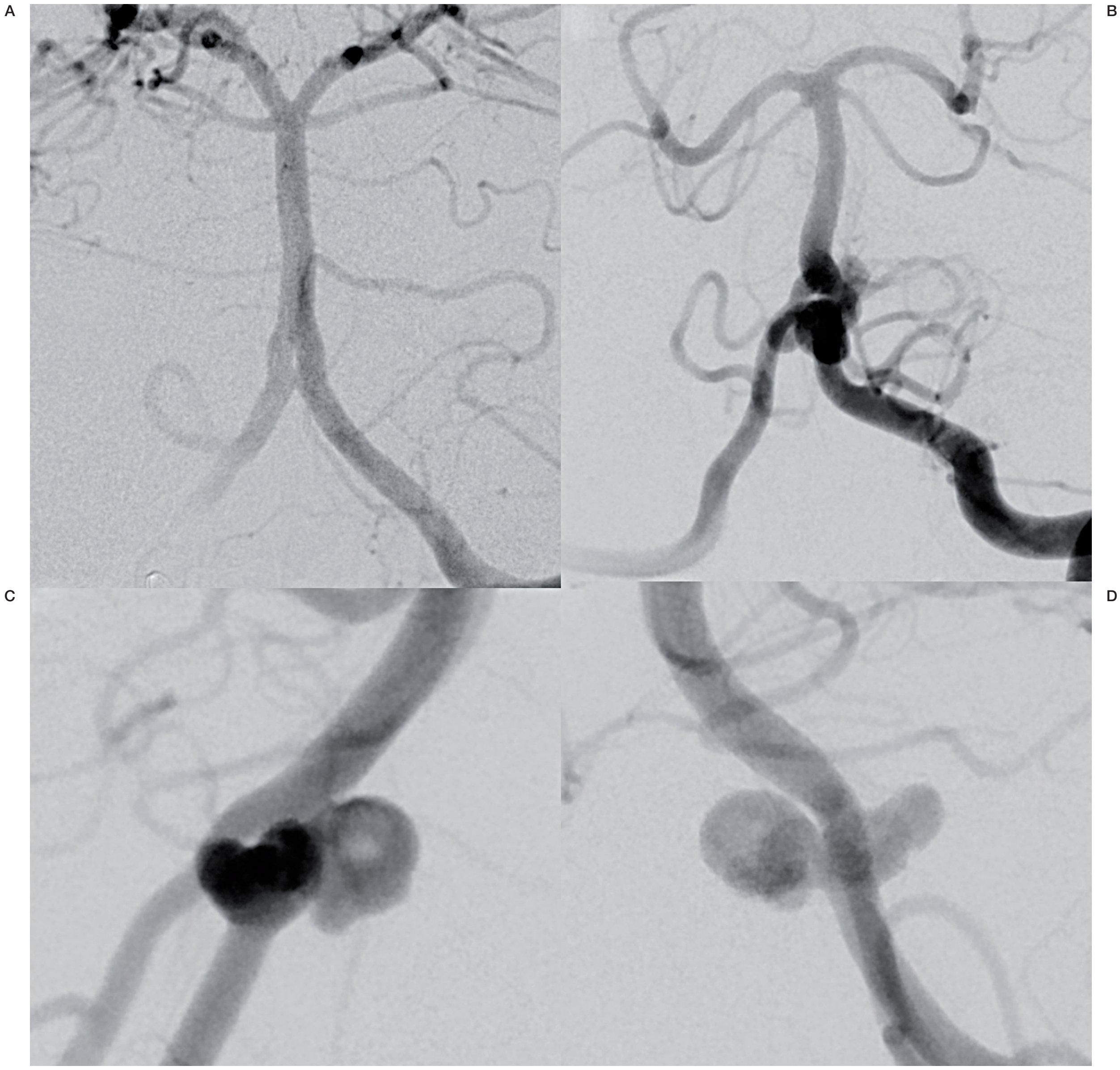

Figure 5 A) Waters projection 2D DSA image of a proximal basilar artery fenestration. B) Townes projection 2D DSA image of a proximal basilar artery fenestration with anteriorly and posteriorly directed aneurysms arising from the fenestration. C,D) High magnification oblique 2D DSA images of the fenestration-related aneurysms.

tration prevalence within the general population. Furthermore, the use of document review to screen for cases, as opposed to prospectively reviewing all angiograms, ensures many fenestrations will have been missed. Given the controversy surrounding fenestrations, operators may have made note of them more frequently in the setting of hemorrhagic or aneurysmal pathology, while more permissive in documentation of cases where no such pathology existed. We certainly see such reporting bias within the literature. Collectively, these case series (Table 3) do not reflect the natural history of fenestrations, but rather the attention to an incompletely understood phenomenon at extreme clinical spectra. No doubt some of that reporting bias is here as well and as such no conclusions of causation are made between fenestrations, aneurysms, and/or intracerebral hemorrhage.

Future studies on the topic would ideally be prospective in nature and from large, more generalized populations (e.g. patients undergoing cross-sectional imaging in an emergency department setting). Such studies have been performed, though with cohorts of hundreds of patients leaving them relatively underpowered to answer questions concerning such rare phenomena. As it stands, declarations of causation are invalid, though we would be remiss to not stress the value in identifying and reporting fenestrations as part of clinical practice particularly when an aneurysm is in play as it may affect treatment. Neuroradiologists and neurointerventional surgeons are encouraged to note fenestrations in practice given the associations described herein and, if for no other reason, to help improve our overall understanding of neurovascular pathology.

Conclusions

Cerebral arterial fenestrations are a relatively rare anatomic variant and remain one of indeterminate and likely heterogeneous clinical significance. They more often manifest in the anterior communicating arterial complex and basilar artery and have no definite pathological relationship with aneurysms.

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