Vascular Anomalies and the Risk of Multiple Aneurysms Development and Bleeding

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Summary

The pathogenesis of aneurysmal subarachnoid hemorrhage is still debated and the prognosis remains severe, especially in multiple aneurysms, where the therapeutic management is complex. The aim of this study was to look for vascular anomalies and assess their relationship with aneurysm formation and bleeding in patients with multiple intracranial aneurysms. A prospective angiographical review was performed on 141 patients with multiple intracranial aneurysms seen from 1992 to 2000. Three hundred and fifty three aneurysms were studied. In 88% of the patients vascular anomalies were found.

The most common were: asymmetric caudal basilar fusion (43.2%), variations of the anterior communicating artery (AcoA) complex (31.2%), symmetric caudal basilar fusion (26.2%), antero-inferior cerebellar artery-postero-inferior cerebellar artery (AICA-PICA) (15.6%), extradural origin of the PICA (10.6%), cavernous origin of the ophthalmic artery or dorsal ophthalmic artery (dOPH) (3.5%). Some aneurysm locations were associated with a high rate of vascular anomalies, e.g.: posterior cerebral aneurysm with asymmetric caudal fusion, AcoA aneurysm with AcoA complex variation, basilar tip aneurysm with extradural PICA or symmetric caudal fusion, PI-

CA aneurysm with AICA-PICA, para-ophthalmic aneurysm with dOPH. These aneurysm locations bled proportionally more frequently when associated with the related vascular anomaly. In conclusion, these results suggest that vascular anomalies are associated with aneurysm development and bleeding.

Introduction

The pathogenesis of intracranial aneurysms remains incompletely understood and the prognosis of the bleeding is still severe. The mortality is higher in case of multiple intracranial aneurysms (MIA)^{1,2}, which are found to affect up to 34% of the aneurysms^{1,3-5}. Several studies have focused on the risk factors for subarachnoid hemorrhage (SAH)⁶⁻⁹, formation and growth of intracranial aneurysms^{9,10}. The results of these studies support the concept that cigarette smoking is one of the predominant independent risk factors for MIA, probably through a mechanism that weakens the vessel wall of the cerebral arteries¹¹.

The alteration of the arterial wall seems to be the principal mechanism of aneurysm formation, either from an acquired or congenital origin. Vascular anomalies are known to be associated with aneurysmal SAH¹²⁻¹⁴, and have been implicated in the pathogenesis of inherit-

ed intracranial aneurysms¹⁵. Assessing the congenital and environmental factors predisposing to the development of new aneurysms and their bleeding is essential to optimize the management of the patients with intracranial aneurysms. We used a prospectively collected series of patients with MIA diagnosed and followed clinically and angiographically from 1992 to 2000, to define the relationship between anatomic variation and aneurysm formation and bleeding.

Material and Methods

From a prospective database, we selected patients, with intracranial aneurysms, admitted to our institution between January 1992 and January 2000. All patients underwent angiography of the carotid arteries bilaterally and of the vertebrobasilar system. Giant, dissecting, mycotic, and fusiform aneurysms were excluded.

Angiograms performed in our institution were reviewed by a staff neuroradiologist and neurosurgeon.

The angiographic studies were analyzed for the presence of anatomic variations: cavernous origin of the ophthalmic artery or dorsal ophthalmic artery (dOPH), anterior communicating artery (AcoA) complex variations (aplasia or hypoplasia of A1 segment, bi-hemispheric anterior cerebral artery (aca), azygos aca, duplication of AcoA), extradural origin of the PICA (extradural PICA), symmetric or asymmetric basilar caudal fusion, persistent embryonic carotid-basilar anastomosis, and accessory middle cerebral artery (access mca).

A discrepancy in the rate of vascular anomalies between patients with or without aneurysms has been reported for the posterior circulation by Campos et al 16. For the anterior circulation, a control population of 49 patients with cerebral arteriovenous malformation was studied to determine the incidence of vascular anomalies in a population without intracranial aneurysms.

The determination of the aneurysm which bled was based on CT and angiographic findings. The aneurysm responsible for the hemorrhage was verified whenever possible by intra-operative or autopsy information. Data were collected prospectively in a database. Chart re-abstraction was used for verification of data correctness and completeness. All data records were checked for missing values and logical inconsistencies.

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Table 1 Incidence of the different vascular anomalies

Vascular anomaly	Number of patients	%
Asym caudal	61	43.2
AcoA complex	44	31.2
Sym caudal	37	26.2
AICA-PICA	22	15.6
Extradural	15	10.6
PICA		
dOPH	5	3.5
Access MCA	1	0.7
Trigeminal	1	0.7
None	17	12

Asymmetric caudal basilar fusion (Asym caudal), variations of the anterior communicating artery complex (AcoA complex), symmetric caudal basilar fusion (Sym caudal), antero-inferior cerebellar artery-postero-inferior cerebellar artery (AICA-PICA), extradural origin of the PICA (Extradural PICA), cavernous origin of the ophthalmic artery origin or dorsal ophthalmic artery (dOPH), accessory middle cerebral artery (Access MCA), persistent trigeminal artery.

Results

A total of 141 patients with 353 saccular MIA were studied. The mean age of the 141 patients was 46.4 years (range from 12 to 77 years). The male: female ratio was 41:59. Fourteen percent of the patients with MIA had hypertension, 4.9% had polycystic kidney disease, 1 had fibromuscular dysplasia, and 1 had Ehlers-Danlos disease. Among all the patients analysed, 112 (79.4%) had a SAH and 29 (20.5%) had no history of SAH (incidental: 21; mass effect: 2; transient ischemic attack/stroke: 2; and screening: 4).

One hundred and twenty four patients (88%) had vascular anomalies. Within these vascular anomalies, the most frequent findings were: asymmetric caudal fusion (43.2%), AcoA complex variations (31.2%), symmetric caudal fusion (26.2%), AICA-PICA (15.6%), extradural PICA (10.6%) (table 1).

The analysis of the anterior circulation in the control group of 49 patients revealed 8.1% of AcoA complex variations without any other

vascular anomalies. For the posterior circulation, the data already reported by Campos et al, suggested that there is a significant increase in symmetrical caudal fusion in aneurysm group of patients¹⁶.

Common locations for MIA were: the middle cerebral artery (MCA), the para-ophthalmic (para-opht) and the posterior communicating arteries (PcoA) (table 2). Some locations were always associated with vascular anomalies. Indeed, it was the case for basilar tip (bas tip) and posterior cerebral artery (PCA) aneurysms (table 3). PCA aneurysms were always associated with asymmetric caudal fusion. For each vascular anomaly, the pattern of aneurysm locations was different from the general one (table 2). Patients with AcoA and carotid terminaison (car term) aneurysms had in proportion more AcoA complex anomalies, 47.5 % and 40 % respectively (table 4). In patients with symmetric caudal fusion bas tip aneurysms were more frequent. The same association was noticed for AICA-PICA with PICA aneurysms and extradural PICA with bas tip aneurysms (table 4).

In our series, MCA was the location with the highest rate of aneurysm rupture (table 5). But this rate changed if we consider specifically

Table 2 Incidence of the different aneurysmal locations

	Number of aneurysms	%
MCA	121	34.2
PcoA	52	14.7
Para-opht	50	14.1
AcoA	40	11.3
Car term	20	5.6
Bas tip	18	5
ACA	14	3.9
PICA	12	3.3
Cavernous	12	3.3
SCA	7	1.9
Ant chor	6	1.6
PCA	4	1.1

Middle cerebral artery (MCA), posterior communicating artery (PcoA), para-ophthalmic (para-opht), anterior communicating artery (AcoA), carotid terminaison (Car term), basilar tip (Bas tip), anterior cerebral artery (ACA), postero-inferior cerebellar artery (PICA), superior cerebellar artery (SCA), anterior choroidian artery (Ant chor), posterior cerebral artery (PCA).

Table 3 Aneurysm location and associated vascular anomalies (%)

	Asym Caudal	AcoA Complex	Sym caudal	AICA PICA	Extra dural PICA	DOPH	None
MCA	42.9	28	22.3	14	86.6	1.6	18.1
AcoA	42.5	47.5	25	15	20	2.5	10
PcoA	42.3	21.1	21.1	17.3	60	3.8	7.6
Para-opht	46	22	30	16	13.3	6	12
Bas tip	44	16.6	44	16.6	33.3	5.5	0
PICA	58.3	16.6	16.6	25	6.6	0	16.6
Car term	20	40	20	10	33.3	0	6
SCA	85.7	57.1	0	0	0	0	42.8
PCA	100	25	0	25	0	0	0

Middle cerebral artery (MCA), anterior communicating artery (AcoA), posterior communicating artery (PcoA), basilar tip (Bas tip), para-ophthalmic (para-opht), carotid terminaison (Car term), anterior cerebral artery (ACA), postero-inferior cerebellar artery (PICA), superior cerebellar artery (SCA), posterior cerebral artery (PCA), asymmetric caudal basilar fusion (Asym caudal), variations of the anterior communicating artery complex (AcoA complex), symmetric caudal basilar fusion (Sym caudal), antero-inferior cerebellar artery-postero-inferior cerebellar artery (AICA-PICA), extradural origin of the PICA (Extradural PICA), cavernous origin of the ophthalmic artery origin or dorsal ophthalmic artery (dOPH).

each vascular anomaly. In fact, in presence of AcoA complex variation, the AcoA aneurysms bled proportionally more. For the posterior circulation, symmetric caudal and extradural PICA were associated with a higher rate of bleeding of bas tip aneurysms. This link was also noticed for AICA-PICA with PICA aneurysms. In presence of dOPH, para-opht or AcoA aneurysms bled proportionally more (table 4).

Discussion

The results of our study suggest that vascular anomalies are highly common in patients with MIA, and are associated with aneurysm development and rupture. This link between vascular anomalies and aneurysm locations was found for: asymmetric caudal fusion and PCA aneurysm, AcoA complex anomalies and car term or AcoA aneurysms, symmetric caudal fusion or extradural PICA and bas tip aneurysms, AICA-PICA and PICA aneurysms, dOPH and para-opht aneurysms. Furthermore, within these vascular anomalies, some were associated with a higher rate of bleeding: symmetric caudal fusion or extradural PICA and bas tip aneurysms, AICA-PICA and PICA aneurysms, AcoA complex anomalies and AcoA aneurysms.

Even though the MCA was the most frequent aneurysm location with the highest overall bleeding rate, it wasn't the most frequent site for aneurysm rupture for each vascular

anomalies. In case of AcoA complex anomalies AcoA aneurysms bled proportionally more than MCA ones (table 4). Moreover, MCA aneurysms were one of the locations with a high rate of no associated vascular anomaly.

The significance of these results is limited as they come from multiple subgroups of small sizes.

These data reflect one population of one center and may not be applicable for other centers. Infact, certain aneurysm locations appear to be under- (AcoA and PcoA) or over-represented (MCA, para-ophtalmic) relative to the distribution reported for aneurysms overall¹⁷. We found that MCA, AcoA and PICA were more frequently responsible for SAH. The results are not completely in agreement with the information provided by Nehls¹⁸ who described AcoA, PICA and basilar locations with a high probability of rupture, and MCA with a low risk. This discrepancy could be explained by the fact that patients with multiple aneurysms are fundamentally a different population, with different genetic or environmental factors predisposing to multiplicity.

Both environmental and genetic factors have been implicated in the pathogenesis of cerebral aneurysms. For multiple aneurysms, cigarette smoking seems to be the only factor, among the environmental ones, to be consistently identified in all the populations studied^{8,10,19,20}. The concept of a congenital predisposition is supported by several lines of evidence including

Table 4 Vascular anomalies and ruptured aneurysm location

Vascular anomalies	MCA	PcoA	Para-opht	AcoA	Car term	Bas tip	PICA	SCA	PCA
Asym caudal	23%	14.7%	5%	10%	0%	1.6%	5%	1.6%	0%
AcoA complex	20%	11%	4.5%	25%	4.5%	2.2%	4.5%	0%	0%
Sym caudal	13.5%	10.8%	2.7%	13.5%	0%	8.1%	0%	0%	0%
AICA-PICA	13.6%	9%	13.6%	9%	0%	4.5%	13.6%	0%	0%
Extradural PICA	13.3%	16.6%	0%	6.6%	0%	13.3%	0%	0%	0%
dOPH	0%	0%	20%	20%	0%	0%	0%	0%	0%

Middle cerebral artery (MCA), anterior communicating artery (AcoA), posterior communicating artery (PcoA), basilar tip (Bas tip), para-ophtalmic (Para-opht), carotid terminaison (Car term), postero-inferior cerebellar artery (PICA), superior cerebellar artery (SCA), posterior cerebral artery (PCA), asymmetric caudal basilar fusion (Asym caudal), variations of the anterior communicating artery complex (AcoA complex), symmetric caudal basilar fusion (Sym caudal), antero-inferior cerebellar artery-postero-inferior cerebellar artery (AICA-PICA), extradural origin of the PICA (Extradural PICA), cavernous origin of the ophthalmic artery origin or dorsal ophthalmic artery (dOPH).

the presence of aneurysms in the infant²¹, their familial occurrence²², or their association with heritable connective tissue disorders²³. Vascular anomalies have also been described to be associated with aneurysm SAH¹², and their incidence in the circle of Willis is correlated with the occurrence of intracranial aneurysms^{24,25}. The majority of the studies report vascular anomalies of the following arterial segments: the AcoA complex²⁶, embryonic origin of the PCA^{15,24}, PcoA infundibulum^{15,27,28}, persistent trigeminal arteries^{13,29}, and the vertebral artery (fenestration or anomalous termination)^{14,15,30,31}. There is a great difference in the incidence related by these different authors concerning the same vascular anomaly. This point may be related to the fact that the populations studied are different or to incomplete angiogram studies.

In our study, we show a link between vascular anomalies and aneurysm location for several vascular segments: AcoA, carotid termination, basilar tip, PICA. These aneurysm locations bled proportionally more often when associated with a specific vascular anomaly. This point may stress the fact that not all aneurysms bleed, but they probably require conditions or triggers, which could be environmental and/or congenital like vascular anomalies. For AcoA, basilar tip, PICA, the location of the aneurysm takes place in the same vascular segment of the vascular anomaly. For the association between extradural PICA and basilar tip aneurysms, the site of the aneurysm differs from the arterial segment of the vascular anomaly.

This anomaly may not be a direct effect on the wall of the parent vessel's aneurysm but could be a marker of abnormal development, and therefore relate to the same defect in time. The anomaly of the vessel wall responsible of the aneurysm may correspond to a segmental vulnerability whereas the vascular anomaly remains a marker. Therefore, the vascular anom-

Table 5 Bleeding rate of the different aneurysm location

	Number of	%
MCA	26	23.2
AcoA	17	15.1
PcoA	14	12.5
Para-opht	7	6.25
Bas tip	7	6.25
PICA	6	5.3
Car term	2	1.7
SCA	2	1.7
ACA	1	0.8
unknown	30	26.7

Middle cerebral artery (MCA), anterior communicating artery (AcoA), posterior communicating artery (PcoA), basilar tip (Bas tip), para-ophthalmic (para-opht), carotid termination (Car term), anterior cerebral artery (ACA), posterior-inferior cerebellar artery (PICA), superior cerebellar artery (SCA), posterior cerebral artery (PCA).

alies could be a time marker of a weakness of congenital origin.

Intracranial aneurysms may develop over a short period of time and either rupture immediately or remain stable without rupturing³²⁻³⁴. As the natural history of asymptomatic intracranial aneurysm is still unclear, the indications for screening remain controversial except for patients with family history of intracranial aneurysm associated or not with autosomal dominant polycystic kidney disease³⁵. The challenge is to define screening programs targeting the patients at higher risk for the development of an aneurysm and SAH. Therefore, complete angiogram studies should be performed to detect multiple aneurysm and vascular anomalies, which we believe to be implicated in aneurysm development and bleeding.

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