European Journal of Clinical and Experimental Medicine

ONLINE FIRST

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Article type: Original Article

Received: 22 November 2023

Accepted: 22 January 2024

Published online: 13 February 2024

eISSN: 2544-1361

Eur J Clin Exp Med

doi: 10.15584/ejcem.2024.2.7

Characteristics of patients with cerebral aneurysms and arteriovenous malformations

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ABSTRACT

Introduction and aim. Aneurysms and arteriovenous malformations (AVMs) are both vascular abnormalities that can occur simultaneously or separately and increase the risk of intracerebral hemorrhage. The aim of this research was to characterize patients with intracranial aneurysms and AVMs.

Material and methods. This retrospective research was based on analysis of Digital Subtraction Angiography. The research group consisted of 118 patients. StatSoft STATISTICA 13 was used for the statistical analysis of parameters, such as dimensions and vascularization pattern of vascular abnormalities.

Results. The total number of aneurysms described was 168. In addition, 33 patients with cerebral aneurysms were also diagnosed with cerebral AVMs. The average dimensions of the aneurysms were 6.33mm, 95% CI (5.47 7.18) × 4.76mm, 95% CI (4.09, 5.43). The abnormalities were found in the extent of circulation of ACA (anterior cerebral artery) 50 (29.76%), ICA (internal carotid artery) 48 (28.57%), MCA (middle cerebral artery) 26 (15.48%), PCA (posterior cerebral artery) 23 (13.69%). There were 76 (64%) patients with diagnosed single aneurysms and 42 (36%) with multiple.

Conclusion. Aneurysms are more likely to occur singly than multiply. The majority are located within the vascularization of the ACA. Aneurysms can coexist with AVMs, which increases the risk of rupture.

Keywords. aneurysm, arteriovenous malformation, digital subtraction angiography

Introduction

Intracranial aneurysms are defined as pathological dilatations of cerebral vessels characterized by a relatively frequent occurrence.[1] This vascular pathology affects approximately 2−5% of the adult population.[2] Although cerebral aneurysms occur in both men and women, the female gender, especially in the postmenopausal age, is thought to predispose to their formation.[3] Aneurysms within the cerebrum can be divided into congenital lesions, which are in the minority, and acquired lesions, which occur far more frequently and whose formation is particularly associated with risk factors such as older age, atherosclerosis, hypertension, smoking, alcoholism and connective tissue diseases.[4,5] In addition, the significant aspect associated with the formation of brain aneurysms are genetic factors, primarily family occurrence, hereditary diseases such as polycystic kidney disease and tuberous sclerosis, as well as some genetic syndromes such as Ehlers-Danlos syndrome and Marfan syndrome.[6-9] Brain aneurysms are also classified according to their vascular structure (angioarchitecture). A distinction is made between saccular and fusiform aneurysms.[10] The coexistence of arteriovenous malformations (AVMs) with cerebral aneurysms is another significant issue. AVMs are vascular malformations that involve the formation of fistulas between arterial and venous vessels without an intermediate capillary bed.[11] Cerebral aneurysms are more common in people diagnosed with AVMs than in those without such lesions.[12] Intracranial aneurysms are a significant medical problem because, due to rupture, they can lead to intracranial hemorrhages, potentially resulting in death or severe disability.[13] The previously mentioned coexistence of aneurysms and AVMs is a significant risk factor for such bleeding.[14] Unruptured Intracranial Aneurysms can cause nonspecific symptoms such as headache, nausea, or dizziness. Aneurysms of larger size can compress the cranial nerves, which may lead, for example, to visual impairments such as double vision, drooping of the eyelid or deterioration of visual acuity. Unfortunately, a significant number of aneurysms do not cause any symptoms for many years, which leads to many patients not being diagnosed before a life-threatening event occurs. It is only at the time of rupture that the patient experiences a sudden, very severe headache described as" the most intense headache of one's life", which may be accompanied by nausea, vomiting, nuchal rigidity, photophobia, convulsions and impaired consciousness. A great majority of cases of aneurysm rupture result in unconsciousness.[15]

Since unruptured brain aneurysms may not cause any symptoms, their diagnosis is significantly more difficult. For this reason, they are often diagnosed incidentally. Imaging examinations such as computed tomography (CT), digital subtractive angiography (DSA) or magnetic resonance imaging (MRI) are used in detecting both aneurysms and AVMs.[16-17] Considering the severe consequences of ruptured aneurysms and AVMs, there are attempts to look for other diagnostic methods that would help detect these vascular pathologies in the prodromal period. Among the potential options for early diagnosis of aneurysms are biomarkers from blood or cerebrospinal fluid (CSF) samples. In the process of aneurysm formation and rupture, inflammatory and cell adhesion molecules, enzymes or hormones are involved. Some of those that are associated with the inflammatory process, such as MPO, GM-CSF, MCP-1 and other cytokines could potentially be used in the future as biomarkers for the diagnosis of cerebral aneurysms.[18] A potential inflammatory parameter that could be useful in the diagnosis of brain aneurysms is interleukin-6, which is increased in the cerebrospinal fluid of patients with unruptured cerebral aneurysms.[19] Another example of such biomarkers could be proteins that build the walls of blood vessels. In the study titled: Intracranial Aneurysm Biomarker Candidates Identified by a Proteome-Wide Study, researchers observed increased levels of the ORM1 glycoprotein in a group of patients with unruptured aneurysms.[20] There is reason to suspect that ORM1 shows potential to be used as a biomarker in future screening of unruptured aneurysms.[20] The inflammatory process, as in the case of aneurysms, has an important role in the pathogenesis of the formation of AVMs. Significant activity of proinflammatory cytokines can be observed, resulting in overexpression of cell adhesion molecules. It leads to the recruitment of leukocytes secreting metalloproteinase-9, which damages the walls of AVMs, finally causing the rupture of vascular pathology. Because of this, it can be assumed that there is a possibility of using inflammatory parameters, such as proinflammatory cytokines or metalloproteinase-9, as biomarkers for the diagnosis of AVMs.[21] In addition, with the progressive development of technology, the opportunity to use artificial intelligence (AI) in the diagnostic process of intracranial aneurysms is being recognized.[22] Given the high risk of death or injury from hemorrhage caused by ruptured aneurysms, patients diagnosed with aneurysms must be qualified for intervention. Several treatment approaches can be identified. First of all, surgical techniques and percutaneous embolization procedures are distinguished. The choice of the type of therapy depends on many factors, such as the morphology of the vascular lesion, the patient's medical condition and preferences.[23] In addition to surgery, other forms of treatment for aneurysms are being investigated. Pharmacological treatment may be considered as one of the options. A number of research suggests that some of the commonly used drugs for cardiovascular disease (statins, calcium channel blockers and angiotensin receptor antagonists) may have a application in the preventive treatment of unruptured intracranial aneurysms.[24] A significant clinical problem involving the treatment of patients with cerebral aneurysms is the issue of SARS-CoV-2 virus infection. Due to the high infectivity that SARS-CoV-2 virus has, many patients with vascular disease are at risk of coronavirus infection, including its severe course. SARS-CoV-2 enters cells through angiotensin-converting enzyme 2 (ACE2), which serves as a receptor for the virus. SARS-CoV-2 attacks epithelial cells and induces inflammation, leading to damage of the vascular endothelium. For this reason, people with cerebral aneurysms have a risk of developing vascular complications. Because of this danger, people with such vascular pathologies, should be especially considered as a group at higher risk for a more severe course of SARS-CoV2 virus infection.[25]

Aim

To characterize and compare vascular abnormalities in patients diagnosed with intracranial aneurysms. To investigate whether aneurysm diameter depends on the presence of AVMs.

Material and methods

The research was based on analysis of anonymized archival data obtained by digital subtractive angiography (DSA) imaging performed by multi-row CT scanner (GE Optima CT 660) with usage of Seldinger wire technique. All examinations were performed at the University Hospital in Krakow. The data was collected from descriptions provided by experienced radiologists. The data included age and gender of patients, the size of diagnosed intracranial aneurysms, considering the maximum and minimum dimensions of vascular lesions, the presence of single and multiple aneurysms, their vascularization and the presence of arteriovenous malformations.

The research group consisted of 118 patients who were diagnosed with intracranial aneurysms, 33 of whom also had coexisting cerebral arteriovenous malformations. All patients were hospitalized in the University Hospital of Krakow between 2015 and 2022. The patients were divided into two groups:

Group 1 – patients diagnosed only with intracranial aneurysms,

Group 2 – patients diagnosed with both aneurysms and AVMs.

In addition, the relationship of aneurysm vascularization to AVMs was analyzed in Group 2. Group 2 was divided into subgroups as follows:

Subgroup 2.1 intranidal aneurysms,

Subgroup 2.2 flow-related aneurysms,

Subgroup 2.3 aneurysms unrelated to the shunt flow to the AVM.

Intranidal aneurysms are those located inside the boundaries of the AVM nidus. Flow-related aneurysms are those occurring along the course of arteries implicated in the perfusion of the nidus and, as such, are hemodynamically related to the AVM. The last group involves aneurysms unrelated to the shunt flow to the AVM, meaning they are located beyond the arteries vascularizing the AVM.

Since coexistence of AVM and aneurysm is well documented, it is very important to evaluate whether there is correlation between size of aneurysm and the coexistence with AVM.[12] Therefore, a comparison of the dimensions of the aneurysms between Group 1 and Group 2 was analyzed.

StatSoft STATISTICA 13 software was used to statistically analyze the collected data regarding the investigated cerebral vascular abnormalities. Significance level was set at 5% ($p<0.05$). Nonparametric test was used due to uneven sample size.

Results

The structure of analyzed population is presented in Table 1. The dimensions of the aneurysms analyzed in the research are presented in Table 2.

Table 1. Structure of analysed population

Characteristics	Group 1		Group 2		All patients	
Patients, n (%)	85 (72%)		33 (28%)		118	
Gender, n (%)	Women	Men	Women	Men	Women	Men
	53 (62%)	32 (38%)	20 (61%)	13 (39%)	73 (62%)	45 (38%)
Age in years, means	60		44		55	
	61	58	42	45	56	54

Table 2. The dimensions of the aneurysms analyzed in the research

Characteristics	Cases, n	Maximum dimension (millimeters)	95% CI	Minimum dimension (millimeters)	95% CI
All patients	168	6.33	5.47, 7.18	4.76	4.09, 5.43
Group 1	119	6.22	5.26, 7.19	4.65	3.89, 5.41
Group 2	49	6.51	4.68, 8.34	5.12	3.68, 6.56

The prevalence of single and multiple aneurysms was one of the factors investigated. The whole research group included 76 (64%) patients with single aneurysms detected and 42 (36%) patients diagnosed with multiple aneurysms. There were 56 patients (66%) in the group 1, and 20 (61%) patients with diagnosed single aneurysms in the group 2. In contrast, patients with multiple intracranial aneurysms were 29 (34%) in the group 1 and 13 (39%) in the group 2.

In the overall studied population, multiple aneurysms were more common in women (22% of all women) than men (14% of all men).

In group 1, 119 aneurysms were diagnosed in patients. Of these, 24 patients had 2 aneurysms and 5 patients had 3 aneurysms.

In group 2, 49 aneurysms were diagnosed in patients. Of these, 10 patients had 2 aneurysms and 3 patients had 3 aneurysms coexisting with AVMs. The number of intranidal aneurysms (Subgroup 2.1) was 11 (22.5%), flow-related aneurysms (Subgroup 2.2) was 27 (55%) and aneurysms unrelated to the AVM's vasculature (Subgroup 2.3) was 11 (22.5%).

The next feature analyzed was the vascularization of the aneurysms. The vascular abnormalities investigated had their arterial supply among the following vessels:

- anterior cerebral artery (ACA),
- middle cerebral artery (MCA),
- posterior cerebral artery (PCA),

- cerebellar arteries,
- internal carotid artery (ICA),
- other arterial vessels.

Among the entire group of patients, the most common arteries that provided aneurysmal vascularization were the anterior cerebral artery (50 aneurysms vascularized) and the internal carotid artery (48 aneurysms vascularized). Other aneurysms were found in the extent of circulation of MCA (26 aneurysms vascularized), PCA (23 aneurysms vascularized), cerebellar arteries (19 aneurysms vascularized) and other arterial vessels (2 aneurysms vascularized). Also in the group 1, both the ACA and ICA were the most numerous arterial supplies (40 and 39 vascularized aneurysms, respectively). In contrast, in the group 2, the cerebellar arteries (12 vascularized aneurysms) and the ACA (10 vascularized aneurysms) were the most common arterial supplies.

Aneurysms dimensions were compared between group 1 (49 observations) and 2 (119 observations). Neither of them were proven to be statistically significant different using Mann-Whitney U test, z(dimension 1)=-0.434, p(dimension 1)=0.6657, z(dimension 2)=0.687, p(dimension 2)=0.4942.

Discussion

According to the existing knowledge on the epidemiology of aneurysms, females predominate also among the research group, especially in the postmenopausal age.[3,5] In both analyzed groups, the distribution of patients by gender is similar, with a female predominance. The patients with coexisting aneurysms and AVMs had a lower age of lesion detection. This may indicate a predisposition to aneurysm formation among patients with AVMs. In this study, there was a correlation between the presence of an aneurysm and arteriovenous malformation to a significant extent (77.5% of aneurysms associated with AVM vascularization), which is also confirmed by other studies. [26] It is worth noting that the size of aneurysms in patients with AVMs is not statistically larger than those without. However average age of people in this group is significantly lower than in the group without AVMs, which may lead to the conclusion that there is a particular cause such as a genetic component that lowers the age of developing an aneurysm. There is also a theory that increased blood flow to the AVM results in the creation of an aneurysm.[27] Greater dimensions of aneurysms may potentially affect higher risk of their rupture.[28] There is a significant proportion of individuals with multiple aneurysms in the research population, which could indicate the presence of specific syndromes that predispose to aneurysm formation. In addition, the incidence of multiple aneurysms in the group with malformations is only slightly higher than in the group without malformations. This raises the observation that the presence of malformations significantly increases the size of aneurysms, but not necessarily the number of aneurysms. Multiple aneurysms pose a significant problem because with each subsequent aneurysm the risk of rupture and thus hemorrhage increases.[29] Among the group 1, the most common arteries associated with aneurysms were the internal carotid artery and the anterior cerebral artery (which the research also included the anterior communicating artery), which may be related to the tendency for aneurysms to form at the bifurcations.[30] Also notable is the higher proportion of cerebellar artery aneurysms in people with arteriovenous malformations. This may be related to a greater susceptibility to changes in the structure of this artery in people with a concomitant tendency to form malformations. The study highlights the increased prevalence of multiple aneurysms compared to other studies, which may raise further questions about the reasons for this prevalence in the study population.[31] Higher number of multiple aneurysms were present both in women and men. It shows that it is important to search for more aneurysms if one is detected. Moreover, the paper points out the need to follow-up people with AVMs because of the risk of future aneurysms.

There are limitations to this study, which are mainly due to the lack of access to clinical data of the patients included in the analysis and the lack of follow-up. Part of the reason for this is the fact that patients who have imaging examinations performed at the Radiology Department of the University Hospital are not necessarily being hospitalized there while referrals for examinations rarely include detailed clinical data of the patient.

Conclusion

Intracranial artery aneurysms are one of the most common vascular abnormalities of the brain. Rupture of an aneurysm can cause serious complications, primarily being a life-threatening condition due to subarachnoid hemorrhage. Aneurysms occur in a variety of locations and sizes. These abnormalities more often occur singly than multiply, however the amount of multiple aneurysms is significant. The majority of aneurysms are located within the vascularization of the ACA and ICA. With advances in radiology, there are increasing numbers of opportunities for early detection of aneurysms and appropriate management before developing complications, especially in patients at greater risk of their development. However, more research is needed to specifically focus on early detection of patients at risk of vascular abnormalities and their proper treatment.

Declarations

Funding

No financial support was received.

Author contributions

Conceptualization, J.O. and M.S.; Methodology, J.O., M.S. and M.W.; Software, M.W.; Validation, J.O. and M.S.; Formal Analysis, J.O.; Investigation, J.O., M.S. and M.W.; Resources, J.O.; Data Curation, M.S.; Writing – Original Draft Preparation, J.O., M.S., M.W. and S.S.; Writing – Review & Editing, J.O. and S.S.; Visualization, J.O.; Supervision, J.O.; Project Administration, J.O.

Conflict of interest

The authors declare no conflict of interest.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

Not applicable.

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