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ASSOCIATION OF MULTIPLE CEREBRAL ANEURYSMS AND CEREBRAL ARTERIOVENOUS MALFORMATION: CASE REPORT AND REVIEW OF THE LITERATURE*

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SUMMARY – The incidence of aneurysmal subarachnoid hemorrhage is about 10-11 cases *per* 100,000 inhabitants. The true incidence of multiple aneurysms is not known, however, according to previous studies it may vary between 20% and 30%. The association of arteriovenous malformation and cerebral aneurysm is well documented and varies between 20% and 30%. A case is described of a 47-year-old female presenting with massive acute subarachnoid hemorrhage. Computed tomography and cerebral panangiography revealed seven saccular aneurysms (five along the left anterior cerebral artery and its branches, one at the left $M^{1/2}$ junction, and one in the anterior communicating artery), and an arteriovenous malformation involving the left frontal and parietal lobe fed mostly by the left anterior cerebral artery. Neurosurgeons clipped all seven aneurysms and then the arteriovenous malformation was extirpated.

Key words: *Intracranial aneurysm, cerebral hemorrhage; Intracranial arteriovenous malformations; Case report*

Introduction

The incidence of aneurysmal subarachnoid hemorrhage (SAH) is about 10-11 cases *per* 100,000 inhabitants[1]. The association of arteriovenous malformations (AVM) and cerebral aneurysms is well documented. There are many reports of AVMs associated with multiple aneurysms. Aneurysms have been described at typical proximal sites of AVM feeders, at abnormal distal locations along feeding vessels, and at sites unrelated to AVM supplying vessels. The true incidence of multiple aneurysms is not known. Aneurysms were detected in 10% to 11% of AVM patients[2-5]. The management of these patients remains a challenge and requires a strictly individualized approach. The most important issue is the selection and timing of therapeutic procedures from a range of recommended guidelines.

Case Report

A 47-year-old, right-handed Caucasian female with negative personal and family history was admitted to the Intensive Care Unit of a regional hospital for acute coma and cardiopulmonary arrest, which developed during sexual activity. Initial computed tomography (CT) of the head revealed extensive subarachnoid hemorrhage (SAH) and raised suspicion of arteriovenous malformation (AVM) in the left hemisphere (Fig. 1). She was not able to undergo cerebral angiography and surgery because of

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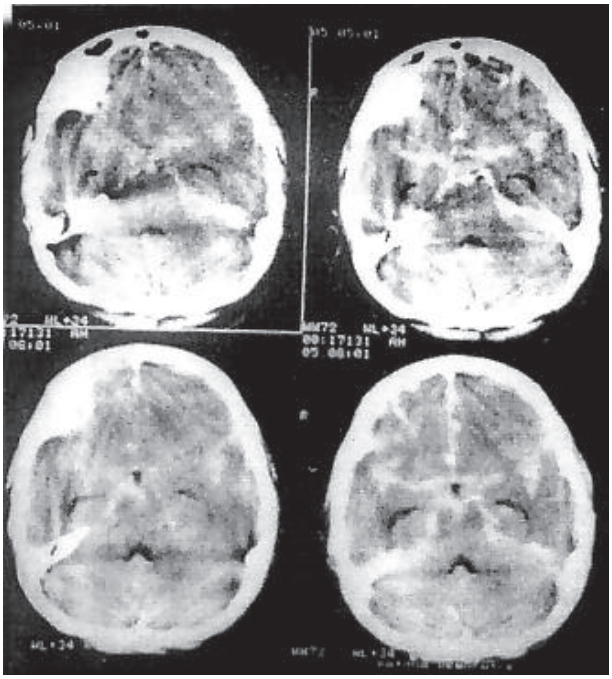

Fig. 1a. Initial CT scan: extensive subarachnoid hemorrhage.

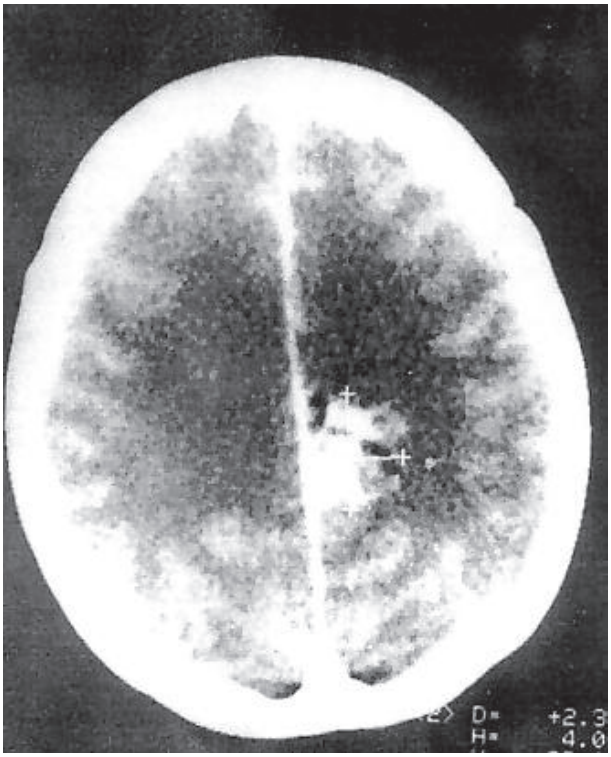

Fig. 1b. Initial CT scan: arteriovenous malformation in the left frontal lobe.

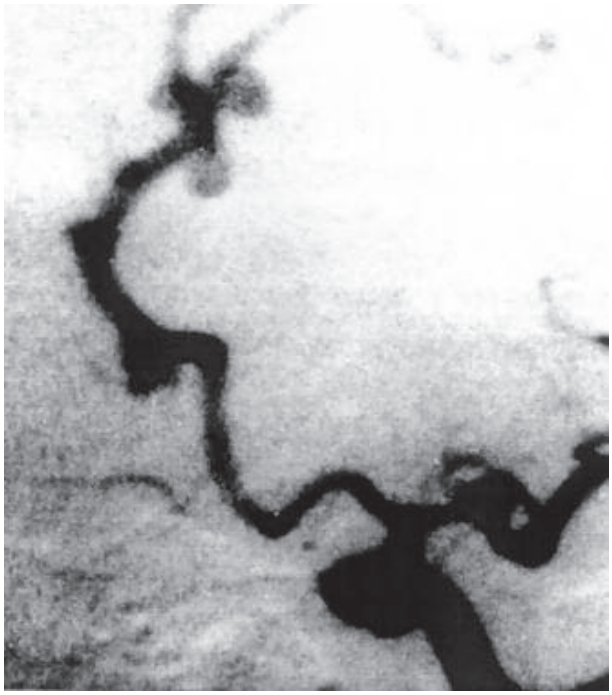

Fig. 2a. Cerebral angiogram: multiple aneurysms on the left anterior cerebral artery and its branches.

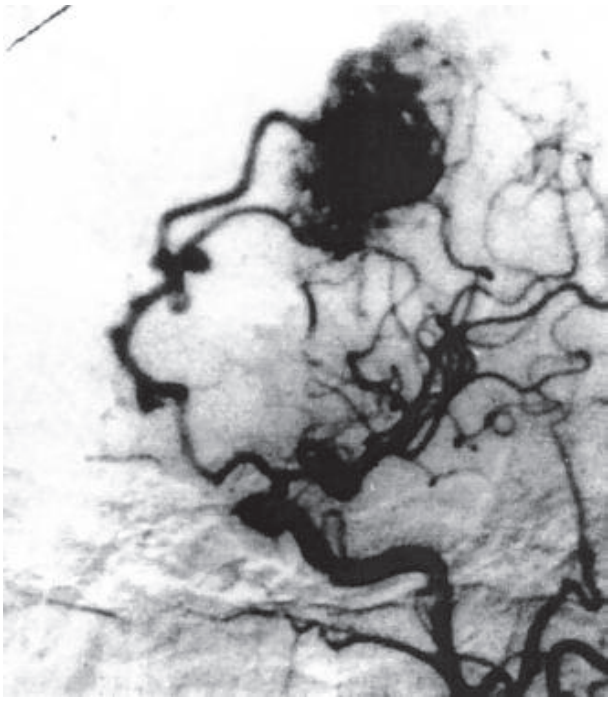

Fig. 2b. Cerebral angiogram: arteriovenous malformation, Martin-Spetzler scale grade III.

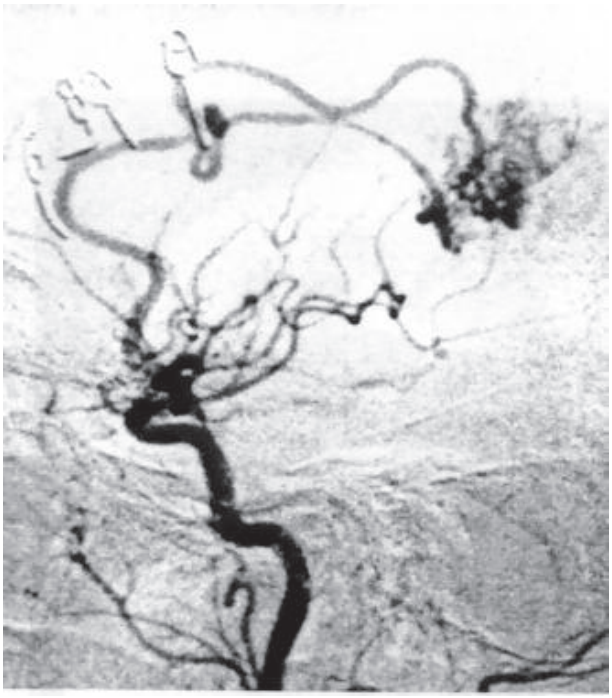

Fig. 3. Cerebral angiogram: condition after first surgery with clipping of four aneurysms along the left anterior cerebral artery. There is still one aneurysm left.

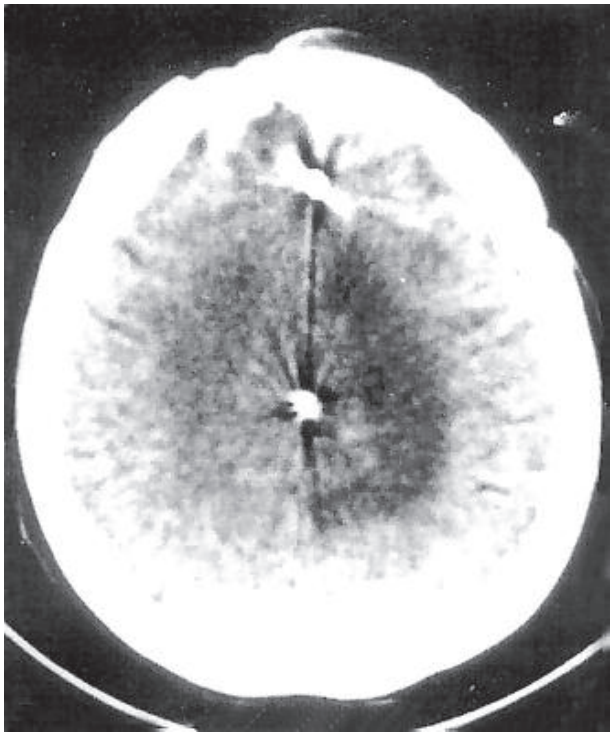

Fig. 4. CT scan: postoperative edema after AVM extirpation.

a generally poor condition (Hunt-Hess scale grade V). After three weeks of intensive therapy, she was conscious, disoriented, partially dysphasic, with slight right-sided hemiparesis (Hunt-Hess scale grade III). Then she was transferred to our hospital to undergo angiographic examination, which revealed an AVM (Martin-Spetzler scale grade III) in the left frontal and parietal lobe fed by branches of the left anterior cerebral artery (ACA) and middle cerebral artery (MCA) (Fig. 2). Five aneurysms along the left ACA, one in the left MCA trifurcation, and one in the anterior communicating artery (AcoA) were also found.

Routine blood tests (including inflammation markers), abdominal sonography, and transthoracic echocardiography were negative. Transcranial Doppler ultrasonography showed high velocity and low resistance on A_1 segments of both ACAs (Table 1). The patient was treated at the Department of Neurosurgery, Olomouc University Hospital. On April 6, 1998, parasagittal frontal craniotomy and clipping of the four of five aneurysms along the left ACA branches were performed (Fig. 3). An attempt was then made to embolize the AVM, however, it had to be aborted due to severe vasospasm during the application of contrast agent. Vasospasms persisted for another seven days, and thus the decision was made to clip the last ACA aneurysm and to extirpate the AVM in a second operation on May 5 (Fig. 4). We decided against a follow-up angiogram because of the patient's history of severe vasospasms during the embolization attempt. In third operation on June 6, the ACoA aneurysm (which was bigger than seen on the angiogram and was partially occluded by a thrombus) was clipped. It was the suggested source of bleeding. The patient's general and neurologic condition did not change after these three operations and embolization attempt. She was transferred to the Department of Rehabilitation. To the best of our knowledge, she is now able to walk, however, she has slight left hemiparesis and aphasia (Hunt-Hess scale grade III).

Transcranial Doppler ultrasonography performed after the operations revealed major differences between the mean velocities (V_{mean}) before and after AVM extirpation (Table 2). The differences in the mean velocities before and after AVM extirpation in the left MCA, left ACA and right ACA were 30.4%, 120% and 40%, respectively. This fact indicates that the AVM was fed from the opposite carotid bed *via* ACoA, in which another aneurysm was situated.

Table 1. Flow parameters before arteriovenous malformation surgery

	V_{syst} (m/s)	V_{diast} (m/s)	V_{mean} (m/s)	PI	RI
Left MCA	1.31	0.69	0.94	0.66	0.47
Left ACA	1.13	0.71	0.87	0.48	0.37
Right MCA	0.87	0.45	0.59	0.71	0.48
Right ACA	1.06	0.64	0.80	0.52	0.61

V_{syst} = systolic velocity; V_{diast} = diastolic velocity; V_{mean} = mean velocity; PI = pulsatility index; RI = resistance index; MCA = middle cerebral artery; ACA = anterior cerebral artery

Table 2. Flow parameters after arteriovenous malformation surgery

	V_{syst} (m/s)	V_{diast} (m/s)	V_{mean} (m/s)	PI	RI
Left MCA[f]	1.09	0.50	0.70	0.84	0.54
Left ACA[g]	0.85	0.21	0.35	1.83	0.75
Right MCA[f]	0.99	0.37	0.55	1.13	0.63
Right ACA[g]	1.00	0.29	0.48	1.48	0.71

V_{syst} = systolic velocity; V_{diast} = diastolic velocity; V_{mean} = mean velocity; PI = pulsatility index; RI = resistance index; MCA = middle cerebral artery; ACA = anterior cerebral artery

Discussion

Perret and Nishioka have reported on 34 cases of coincidence of AVM and aneurysms among 545 patients with AVM. Twenty-six patients had one aneurysm, six patients had two aneurysms, and two patients had three aneurysms associated with AVM. Also, in these 34 patients, there were 29 cases of subarachnoid hemorrhage, whereas the remaining five patients were free from bleeding[6].

Suzuki and Onuma report on 9 cases of coincidence of AVM and intracranial aneurysms among 140 AVM patients. Four of the 9 aneurysms were situated on main feeders, 3 were located at the origin of a main feeder, and 2 did not have any hemodynamic relation[7]. Tamaki *et al.* describe a small, 'low-flow' AVM and aneurysm in the distal bed of MCA in an 8-year-old boy. In this case, the cause of their coexistence was more likely to be a congenital anomaly than the hemodynamic stress[8]. Recently, an extensive publication has described 45 patients with aneurysms among 600 patients harboring an AVM[9].

There are numerous conditions described in the literature as risk factors for developing AVM and berry aneurysms. The most commonly encountered conditions are polycystic kidney disease, aortic coarctation[3,10], moyamoya disease, Takayasu's arteritis, Marfan's syndrome, and fibromuscular dysplasia[11].

Observation of sporadic cases revealed an association of AVM and multiple aneurysms with other syndromes. For example, the case of a 68-year-old woman with a history of surgical removal of cardiac myxoma has been described. Cerebral angiography performed due to multiple intracerebral hemorrhages showed multiple fusiform and berry aneurysms one year later. Histologic examination confirmed that the lesions were associated with vessel wall infiltrations of the myxoma[12].

Schievink *et al.* have published a case report of a boy with progressive hemifacial atrophy (Parry-Romberg disease), who was treated for a giant aneurysm on the left cavernous part of the internal carotid artery at the age of five. Seven years later, he was treated for the same problem on the other side, and another six years later he suffered from an aneurysm on the left PCA[13].

Another interesting association has been described by Erbengi and Inci, who found multiple cerebral aneurysms in conjunction with pheochromocytoma. The authors

speculate about the etiopathogenetic relations between acute fluctuation of blood pressure, and development and rupture of aneurysms[14].

Other syndromes and diseases that have been described in coincidence with multiple cerebral aneurysms are Recklinghausen's disease[15,16], Ehlers-Danlos syndrome[17], meningiomas and angiolipomas[18-20], sickle cell disease[21,22], lymphomatoid granulomatosis[23], alkaptonuric ochronosis[24], systemic lupus erythematosus[25], multiple endocrine neoplasia – Wermer's syndrome[26], Klippel-Trenaunay syndrome[27], anomalies in origin, number or course of cerebral arteries[28,29], or persistence of primitive trigeminal arteries[30], and multiple systemic aneurysms[31,32]. For the time being, there is no clear explanation of the etiopathogenesis of these phenomena.

According to the available literature, one can consider three different theories that have been proposed to explain such a pathology: 1) hemodynamic stress; 2) conjunct congenital anomaly of vessel wall development; and 3) accidental coexistence. The first theory assumes that aneurysms may develop on AVM feeders under stress caused by increased flow velocity and blood volume. This hypothesis is supported by findings on vessels that are usually spared from developing aneurysms (lenticulostriate arteries, terminal branches of pericallosal artery, anterior choroid artery, cerebellar arteries). The hemodynamic relationship between elevated blood flow and development of aneurysms has also been supported by Schenkin *et al.* They describe aneurysm regression after AVM resection and three cases of aneurysm development on the internal carotid artery after occlusion of the opposite one[33].

Turjman *et al.* performed superselective microcatheter angiography of AVM pedicles in 100 AVMs before their embolization. Aneurysms were revealed in 58 patients, 24 of them with single aneurysm and 34 with multiple aneurysms[34].

Impaired vessel wall development may be another etiopathogenetic factor in the AVM – aneurysm association[35]. This would provide an explanation for the occurrence of aneurysms in vessels hemodynamically unrelated to AVMs as well as for those in correlation with 'low-flow' AVMs. Rhoten *et al.* demonstrated preproendothelin-1 gene (ppET-1) local repression in AVM lesions (as compared to controls) as well as to normal vasculature distal to the lesions in the same patient. Recognition of ppET-1 gene regulation may be the first step in understanding the pathophysiology of AVMs[36].

And finally, Boyd-Wilson has reported on the incidence of aneurysms to be the same in both normal and AVM population, thus leading him to a conclusion that their coexistence was merely coincidental[37].

The above mentioned theories have both opponents and advocates. Each of the theories has a logical and/or statistical supporting background. In our patient, the pathology could be explained by the first theory. All aneurysms were situated on AVM feeders and blood flow in these arteries fell immediately after AVM extirpation.

Selection of the best management for such patients remains a very important issue. Auxiliary methods usually do not answer the question as to which lesion is the source of bleeding. Therefore, the selection, timing and sequence of therapeutic procedures represent the most challenging problem in AVM – aneurysm patients. One can expect spontaneous involution of aneurysms after decrease of blood flow towards the feeder[38], but Hodgson *et al.* have reported that none of the aneurysms on proximal parts of feeders disappeared after stereotactic radiosurgical AVM obliteration in their group[39].

In a recent study of 305 AVM – aneurysm cases, proximal aneurysms were not considered to be the source of bleeding, and therefore were not primary targets for treatment as AVMs were. Moreover, no bleeding was observed from either proximal or intranidal aneurysms after AVM embolization, and a 50% aneurysm shrinkage was recorded in more than a half of cases[40].

On the other hand, resection of a 'high-flow' AVM is usually followed by an abrupt increase in vascular resistance and an extreme risk of aneurysmal rupture[41,42]. Therefore, we chose an alternative method recommended and clipped all aneurysms on the main feeder first, and only then extirpated the AVM. Transcranial Doppler ultrasonography confirmed our presumption of dramatic flow velocity and vascular resistance changes after AVM extirpation (Tables 1 and 2). Our findings are similar to those reported by Manchola *et al.*[43].

In conclusion, coexistence of multiple cerebral aneurysms and AVM remains one of the most challenging problems in vascular neurology and neurosurgery. The neurologist must exclude various disorders that have similar appearance, possibly leading to this diagnosis and hazardous association; the neurosonologist and neuroradiologist have to describe the aneurysm character and blood supply to the AVM. Detailed information on the anatomy and blood circulation of the pathologic structures help the neurosurgeon choose the best management. Close cooperation among these specialists is the only way to manage such complicated cases successfully.

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Sažetak

UDRUŽENOST VIŠESTRUKIH MOŽDANIH ANEURIZMA I MOŽDANE ARTERIOVENSKE MALFORMACIJE: PRIKAZ SLUČAJA I PREGLED LITERATURE

B. Křupka, M. Vaverka, S. Buřval, R. Herzig i I. Vlachová

Incidencija aneurizmatskog subarahnoidnog krvarenja iznosi oko 10-11 slučajeva na 100.000 stanovnika. Stvarna incidencija višestrukih aneurizma nije poznata, no prema prethodnim ispitivanjima ona bi se mogla kretati između 20% i 30%. Udruženost arteriovenske malformacije i moždane aneurizme dobro je dokumentirana i kreće se između 20% i 30%. Autori izvješćuju o slučaju 47-godišnje žene koja je došla s opsežnim akutnim subarahnoidnim krvarenjem. Kompjutorizirana tomografija i cerebralna panangiografija otkrile su sedam sakularnih aneurizma (pet duž lijeve prednje moždane arterije i njezinih ogranaka, jednu na lijevom spoju $M^{1/2}$ i jednu u prednjoj komunikacijskoj arteriji) i arteriovensku malformaciju koja je zahvaćala lijevi frontalni i parijetalni režanj koji se uglavnom opskrbljuje putem lijeve prednje moždane arterije. Neurokirurzi su štipaljkama učvrstili svih sedam aneurizama, nakon čega je uklonjena arteriovenska malformacija.

Ključne riječi: *Intrakranijska aneurizma, moždano krvarenje; Intrakranijske arteriovenske malformacije; Prikaz slučaja*