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Natural Course of the Arteriovenous Malformations of the Brain Initially Presented by Hemorrhage: Analysis of a Clinical Series of 39 Patients

Kanama ile Kendini Gösteren AVM'lerin Doğal Seyri: 39 Olguluk Seri

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ABSTRACT

AIM: AVM because of outstanding tendency toward bleeding, even though 20 times more rare then aneurysm on the blood vessels of the brain and her own specific anatomical structure even today represents big neurosurgical challenge.

MATERIAL and METHODS: Series which is shown here consists of 39 patients which were hospitalized in the institute for neurosurgery of the Clinical Center of Serbia in the period between 1995 and 2004. This group was exposed to symptomatic therapy or it was estimated that surgery, embolization and radio surgery.

RESULTS: Combined type of venous drainage brings a high risk ($p<0.001$) from repeated bleeding. Combined artery bringing from different flows ($p<0.05$) contributes to genesis of 'steal phenomenon', in combination with deep venous drainage it presents predisposing anatomical characteristics for repeated bleeding ($p<0.001$) according to our results should present AVM with dimensions 2.5 to 5 cm localized in eloquent zone of big brain with combined type of venous drainage and cobined artery bringing from vertebro-basilar flow and carotid flow.

CONCLUSION: Perception of natural course of AVM point to certainly more benign pathology in regard to other vascular malformations. Specific anatomical structure requires planning of treatment from case to case, most often combination of embolization, radio surgery and surgical treatment

KEYWORDS: AVM, Hemorrhage, Natural course

ÖZ

AMAÇ: AVM'ler anevrizmalara göre 20 kez daha nadir görülmelerine rağmen, kanama ile kendilerini gösterebildiklerinden önemli bir nöroşirürjikal sorundurlar.

YÖNTEM ve GEREÇ: Bu seride Sırbistan Klinik Merkezinde 1995 ile 2004 yılları arasında tedavi edilmiş olan 39 olgu sunulmaktadır. Bu olgulara semptomatik tedavi veya cerrahi, embolizasyon veya radyocerrahi uygulanmıştır.

BULGULAR: Çoklu venöz drenajın tekrarlayıcı kanama gelişmesinde yüksek risk oluşturduğu ($p<0.001$) saptanmıştır. Çoklu arteriel besleyici bulunması ise çalma fenomenine yol açmaktadır ($p<0.05$). Hassas bölge yerleşimli ve boyutları 2.5 ile 5 cm arasında olan AVM'lerde eğer çoklu besleyici ve derin drenaj veni var ise, kanama riski artmaktadır ($p<0.001$).

SONUÇ: AVM'ler diğer damarsal sorunlara göre daha iyi huyludurlar. Her olgu kendi içinde değerlendirilmeli ve cerrahi, embolizasyon ve radyocerrahiden hangisinin uygun olacağına karar verilmelidir.

ANAHTAR SÖZCÜKLER: AVM, Doğal seyir, Kanama

INTRODUCTION

Arteriovenous malformations (AVM) of the brain as a separate entity were confirmed by the middle of the nineteenth century (14). AVMs represent a congenital disorder in the early differentiation of the arterial and venous blood vessels of the brain where occurs a direct contact between the arteries and veins whether in fistulous form or with inserted primordial capillary plexus (6,28). This type of circulation 'steals' the blood from the surrounding brain ('steal' phenomenon) because the normal supply of the blood is distributed inside AVM bypassing to a great extent the surrounding normal brain (6,8,10). AVM of the brain is dominantly initially presented by intracranial hemorrhage (ICH) in 30 to 55% of cases in the period from the second to the fourth decade of life, by epileptic seizures, headache and progressive neurological deficit. 95% of AVMs become symptomatic before the age of 70 (1,3,13,15).

ICH is the principal cause of morbidity and mortality, and the size of AVM, type of the venous drainage and raised blood pressure in supplying arteries are distinguished as the pathoanatomical predisposing factors for generating the bleeding from AVM (15,22,30).

Comparative studies show that annual risk for occurrence of the bleeding from AVM of the brain is 2-4% annually and it is followed by death outcome in 10% of cases and neurological deficit in 50% of cases (7,19,21,27,31).

Since AVMs of the brain do not have such a high risk of repeated hemorrhage as aneurysms and an average incidence of 0.14%, this makes possible elective approach when selecting the therapy option (surgery, embolization, radio surgery) (9,18,20,31).

MATERIAL and METHOD

Our study includes a series of 39 patients with AVM of the brain who had not been submitted to any treatment method, except for the symptomatic therapy, and who were hospitalized and AVM diagnosed at the Institute for Neurosurgery Clinical Center of Serbia in the period from October 1995 until October 2004. Arteriovenous malformation diagnosis was definitely confirmed in all cases by way of cerebral panangiography (standard or digital substraction).

During the follow-up period the patients were not submitted to any alternative manner of causal treatment, such as – surgery, embolization or radiotherapy. The patients from this series were not treated as it had been estimated that surgical procedure had a higher risk of postoperative invalidity than the natural course of the disease, or because the patient and his/her family refused treatment.

For the start follow-up time of the natural course of the disease was taken the moment when AVM was diagnosed in patients where the malformation clinically presented itself by hemorrhage.

The follow-up of the natural history of AVM was concluded at two terms: by definitely establishing the series and by starting the treatment of the same (for definitely untreated cases) and by the start term of the treatment (surgery, embolization, radiotherapy) for the patients who after the earlier foreseen follow-up period were submitted to one of the ways of causal treatment of AVM.

For representation and assessment of the clinical-anatomic AVM characteristics we used generally accepted system according to Spetzler Martin (SM index score) which means the assessment of the localization, AVM size and drainage type (superficial, deep, combined) as well as the final total value- grading (24). Neurological status and working and life capability were ranged according to values systematized in Karnofsky index (12). In order to test statistical significances and to check the hypotheses we used methods of descriptive and analytical statistics.

RESULTS

As regards the sex in the structure of the investigated patients male patients prevailed 23:16 (58.97%: 41.03%), and as regards the age, younger persons were predominant, 22 (56.4%) were under the age of 30. Mean age of all examined patients was 27.4±7.6 years.

Variation interval for age ranged from 6-64 years. Until the conclusion of the series 37 or 94.9% of patients were followed-up, and 2 or 5.1% of patients died.

The largest number of examined patients 21 or 53.8% were followed-up for longer than 36 months, i.e. over 3 years; 13-36 months 14 or 35.9% patients; and less then 12 months 4 or 10.3% of patients were followed-up. The average follow-up time of all patients was 57.2±8.7 months. The mean value of 32.0 months points to the length of the average three-year follow-up of all examined patients.

As shown in Table I, this group consists of 39 patients who had intracerebral hemorrhage (HIC) as initial sign in 22 cases or 56.4%, intraventricular (HIV) had 3 or 7.7% patients and combined type (HIC, HIV, SAH) had 5 or 12.8% of examined patients; subarahnoidal hemorrhage (SAH) as initial sign presented in 9 or 23.1% of examined patients.

Table I: Type and Total Number of Hemorrhages in Patients with Hemorrhages

Characteristic	Number	%
1.Type of hemorrhage		
HIC	22	56,4
SAH	9	23,1
HIV	3	7,7
Combined	5	12,8
2. Total number of hemorrhages		
one	15	38,5
two	18	46,2
three	3	7,7
four	2	5,1
five and more	1	2,6
Total	39	100,0

Without repeated, i.e. with one hemorrhage there were 15 or 38.5% of examined patients, and in repeated hemorrhages with 2 there were 18 or 46.2%, with 3 there were 3 or 7.7%, with 4 there were 2 or 5.1%, and with 5 hemorrhages there was only 1 patient.

Having in mind the basic aims of our investigation, as well as our hypotheses, it was of essential interest to study the site and the significance of individual risk factors that cause the occurrence of repeated hemorrhages. In order to do that we analyzed two subgroups of patients: B1-1 with one hemorrhage, i.e. without repeated hemorrhages and B1-2 with two or more hemorrhages, i.e. with repeated hemorrhages. The largest number of investigated patients in both subgroups was followed-up for more than two years. The average follow-up length in subgroup B1-1 was 49.8±14.0 months, and in subgroup B1-2 it was 70.5±9.7 months, however that was not confirmed as statistically significant difference (p>0.05), see Table II.

At the average length of the follow-up time which was 4.8 years, new hemorrhages occurred in 24 or 61.5% patients, with 58 episodes and with the hemorrhage/year rate 28.5%. On the average in 3.5% annually a new hemorrhage occurred in relation to the total number of the investigated patients, without statistically significant difference in relation to sex. Prevalence of the new hemorrhage episodes in investigated patients who were longitudinally followed-up up to 24 months was 37.5%, from 25-48 months it was 61.5%, and in patients who were followed-up for 49 months and more it was 72.2%. Statistical analysis did not confirm this rising trend as statistically significant (X2=2.821; p>0.05), see Table III.

In both investigated patient subgroups the persons of male sex were dominant, however the participation of these investigated patients was somewhat greater in the subgroup with repeated hemorrhages (62.5%: 53.3%), in the subgroup with repeated hemorrhages slightly prevailed participation of younger people (58.3%: 53.3%).

Statistical testing did not define significant differences between the investigated subgroups as regards the distribution of findings of the investigated characteristics (p>0.05), Table IV.

On admittance Karnofsky index of 80 and more was more frequent in patients with repeated hemorrhages (25.0%: 6.7%), but without statistically significant difference (p>0.05). However, mean value of Karnofsky index was statistically significantly higher in investigated patients who had repeated hemorrhages (66.6±2.9; 56.0±3.7; p<0.035), Table V.

Table II: Length of Longitudinal Follow-up of Investigated Patients

Follow-up length	Group	
	B1-1	B1-2
Up to 6 months	2	-
7-12	-	2
13-24	3	1
25-36	5	5
37-48	-	3
49-60	1	1
61 i >	4	12
Total	15	24
X	49,8	70,5
SE	14,0	9,7
Mann-Whitney U-test Z = 1,791 ; p>0,05		

Table III: Prevalence of Repeated Hemorrhages in Reference to Longitudinal Follow-Up Length (31 Patients had Repeated Haemorrhage)

Follow-up length		Repeated hemorrhages	
	N	n	%
Up to 24 months	8	3	37,5
25 - 48	13	8	61,5
49 and more	18	13	72,2
Total	31	24	61,5

$X^2 = 2,821$; DF = 2 ; p >0,05

The occurrence of new hemorrhages, as well as the rate of hemorrhage episodes/year was higher in investigated patients with index 80 and more (85.7%: 56.2%), i.e. (38.5: 25.5%), but without statistically significant difference (p>0.05). In relation to the Karnofsky index level at the end of the follow-up period no significant differences were found in the investigated parameters (p>0.05), Table VI.

At shorter average follow-up time the rate hemorrhage/yrs was statistically significantly higher in arterial supply from VB confluence in relation to ACM (45.8%: 10.6%; p<0.01) also statistically significant was the supply from ACA confluence in relation to ACM confluence as a predisposing factor for hemorrhage (51.4%: 10.6%; p<0.01). Multiple supply arterial network confirmed statistically significant place in

Table IV: Demographic and Anamnestic Characteristics in Patients with One (B1-1) and Two and More (B1-2) Repeated Hemorrhagies

Characteristic	Group				P
	B1-1		B1-2		
	N	%	n	%	
1. Sex					
M	8	53,3	15	62,5	> 0,05
F	7	46,7	9	37,5	
2. Age					
Up to 30 yrs.	8	53,3	14	58,3	> 0,05
31 <	7	46,7	10	41,7	
3. Associated diseases					
■ Hypertension and diabetes	2	13,3	7	29,2	>0,05
■ others	2	13,3	3	12,5	
Total	15	100,0	24	100,0	

B1-1: *with one hemorrhage;* ***B1-2:*** *two and more hemorrhages*

Table V: Karnofsky Index on Admittance in Patients with One (B1-1) and Two and More (B1-2) Repeated Hemorrhages

Characteristic		Group				P
		B1-1		B1-2		
		N	%	n	%	
Karnofsky index	≤ 70	14	93,3	18	75,0	>0,05
	80 ≥	1	6,7	6	25,0	
	X	56,0		66,6		<0,035
	SE	3,7		2,9		

B1-1: *with one hemorrhage;* ***B1-2:*** *two and more hemorrhages*

Table VI: Bleeding Incidence in Reference to Karnofsky Index at the end of Longitudinal Follow-Up

Characteristic	N	Occurrence of new hemorrhages		Rate hemorrhage / yrs	Mean follow-up time (years)	Xep Annual
		n	%			
Karnofsky index						
Up to 70	3	18 (40)	56,2	25,5%	4,89	3,9
80 and >	2	6 (18)	85,7	38,5%	6,67	2,6
	7					

p>0,5 *( ) number of hemorrhage eppisodes* predisposition for bleeding from AVM. In examined patients with three types of arterial supply the rate hemorrhage/yrs was significantly higher in relation to two types of supply present (52.0%: 23.2%; p<0.05). In Table VII is shownt neuroradiological findings by conventional angiography.

The type of arterial supply was not statistically significantly different between the investigated groups of patients (X2=0.942; p>0.05), although the frequency of multiple supplies was higher in group B1-2 (62.5%: 46.7%). Also in group B1-2 AVMs localized in the left cerebral hemisphere are considerably more frequent (50.0%), and in group B1-1 in the right hemisphere (66.7%). However, in the manner of presentation of the distribution of findings they did not show statistically significant difference (X2=2.310; p>0.05).

The size of AVM and the value of Martin-Spetzler score did not show significant differences in the distribution of findings between patients without and with repeated hemorrhage episodes (p>0.05). However, as regards the drainage, differences in distribution of findings showed statistically significant difference (X2=7.764; p<0.020). Namely, in patients where new hemorrhage episodes did not occur AVMs with deep drainage were dominant (80.0%), and in patients with repeated hemorrhage episodes combined drainage predominated (58.3%). In AVMs that presented with one hemorrhage episode, although the difference exists, combined drainage is more frequent and it is statistically considerably less significant (subgroup B1-1) Table VIII.

In accordance with the earlier mentioned findings, we have found that hemorrhages occur significantly more frequent in combined drainages (87.5%: 42.8%; p<0.01), as well as the hemorrhage episode/yrs rate (33.6%: 22.6%; p<0.05), in relation to findings in deep drainages. The size of AVM, as well as the finding of Martin-Spetzler score did not show significant differences in frequency of the occurrence of new hemorrhages in investigated patients, as well as the hemorrhage episode/yrs rate. However, we need to stress that the average number of hemorrhage episodes per year is considerably greater when the size of AVM is from 2.6-5.0 cm (3.7) and 5.1 and more cm (3.8), also in deep drainages (4.4) in relation to superficial (2.5) and combined ones (3.0), Table IX.

Analyzing the variance of the investigated characteristics statistically significant difference between the patient subgroups without and with present repeated hemorrhage episodes showed Karnofsky index on admittance (p=0.0307) and the drainage type (p=0.0115).

Analyzing discriminatively we arrived at a statistically significant function with the following parameters (canonical r = 0.5191; r2 = 0.2694; Wilks Lambda 0.7305; X2=11.304; p<0.0035).

From the obtained function, convincingly greatest discriminative value shows drainage variable, where the correlation with the discriminative factor amounts to 0.71997, then Karnofsky index upon admittance with correlation of 0.60833 and Martin-Speltzer index with correlation of 0.49438. Less discrimination, but still with a significant influence, showed AVM size and the length of longitudinal follow-up. All the other characteristics have no influence on dividing these two sets of investigated patients.

Investigated variables were included into the model of multivariant logistic regression, also with the aim to define

Table VII-A: Bleeding Incidence in Reference to the Type of Arterial Supply and Localization of Change

Characteristic	N	Occurrence of new hemorrhagies		Rate hemorrhage / yrs	Mean follow-up time (years)	Xep Annual
		n	%			
1. Type of arterial supply						
VB	7	4 (13)	57,1	45,8%*	4,06	2,2
ACM	5	2 (4)	40,0	10,6%*	7,55	9,4
ACA	4	3 (6)	75,0	51,4%*	2,92	1,9
ACI	1	-	-	-	2,17	-
Total	17	9 (23)	52,9	28,7%	4,71	3,5
Two	16	10 (23)	62,5	23,2%**	6,19	4,3
Three	6	5 (12)	83,3	52,0%**	4,04	2,0
Total	22	15 (35)	68,2	28,4%	3,49	3,5

***p<0,01 *****p<0,05 ******p<0,001*

those variables that contribute to frequency – the occurrence of the new hemorrhage episodes. Analysis results have shown that the drainage has the greatest contribution, then comes Karnofsky index on admittance, slightly less the condition graded by Martin-Spetzler score and AVM size.

Table VII-B: Neuroradiological Findings (Angiography & CT) of AVM

Patient (Initials and age)	Sex	Diametar (cm)	Localisation	Arterial supply	Drainage
AV 26	M	6	Left cerebellar hemisphere	VB	deep
GB 45	F	2.7	Right parietal paraventricular	MCA, AP	combined
DjB 64	M	2.5	Right basal ganglia	ACA bill.	deep
IS 38	F	4.2	Right parietal lobe	ACA, MCA	combined
LA 29	F	4.2	Left insula	MCA	superficial
MM 55	M	3.7	Pons	PCA, PICA	deep
Mm 40	M	4.3	Left basal ganglia	MCA, ACA, AChoA	deep
MG 35	M	4.5	Left basal ganglia and III ventricle	AChoA, AChoP	deep
PM 17	F	3.2	Corpus callosum	ACA, MCA	deep
RK 50	F	1.1	Brainstem	VB	deep
SV 50	M	2.7	Right occipital lobe	PCA, A.calosomarginalis	superficial
TA 18	M	5.8	Right basal ganglia	MCA, AP, ACE	combined
AV 25	M	2.5	Brainstem	ACP bill et AchoP	deep
BB 26	F	3.5	Left parietal lobe	AChoP, MCA ACoA	deep
Blj 32	F	6.2	Corpus callosum	MCA bill, AP, PCA	deep
IG 23	M	6.3	Left frontal lobe	ACA bill, PCA	combined
LS 25	F	4.1	Corpus callosum	AP, ACHoP	deep
MM 22	F	5.7	Right temporal lobe	AchoA, SCA, ACA	deep
MG 55	M	2.8	Right basal ganglia	MCA, ACA	deep
MJ 20	F	3	Right cerebellar hemisphere	PICA bill	deep
MD 35	M	2.7	Right temporoparietal	ACA	combined
SS 22	M	2.5	Basal ganglia and III ventricle	AChoA, AP	deep
SV 36	M	3	Right motor cortex	MCA, ACA	deep
SN 57	F	2.6	Right parietooccipital	MCA, ACA	deep
HI 33	F	5.9	Right motor cortex	MCA, ACA, AChoP	combined
MD 63	M	4.7	Right parietooccipital	ACA, PCA	combined
SV 35	M	3.7	Left motor cortex	MCA, ICA, AChoP	combined
JV 55	F	5.8	Left motor cortex	ACA bill	combined
BB 13	M	4.2	Right frontal lobe	MCA	combined
EN 45	M	3.7	Right motor cortex	AP, MCA	deep
DjD 44	M	6.3	Right motor cortex and basal ganglia	MCA, PCA, AP	combined
HR 21	F	6.9	Cerebellum	VB	deep
KG 25	M	2.3	Right parietal lobe	MCA	combined
MD 36	M	4.3	Left motor cortex	MCA,ACA bill, AChoP	combined
KB 24	M	5.7	Left thalamus and mesencephalon	MCA, AP, PCA	combined
SZ 22	F	4.2	Pineal region	AP bill, PCA	deep
PJ 34	M	2.3	Right cerebellar hemisphere	PICA, AICA	deep
LS 22	F	6.2	Left motor cortex	ACA, MCA, PCA	combined
ZD 46	M	5.7	Corpus callosum	ACA, MCA, PCA	deep

Table VIII: Anatomical Characteristics of AVM in Patients with One (B1-1) and Two and More (B1-2) Repeated Hemorrhages

Characteristic	Group				P
	B1-1		B1-2		
	N	%	n	%	
1. Size of AVM					
Up to 2,5 cm	4	26,7	9	37,5	> 0,05
2,6 - 5,0	8	53,3	7	29,2	
5,1 and more	3	20,0	8	33,3	
2. Drainage					X^2=7,764 ; DF=2
Superficial	1	6,7	1	4,2	p<0,020
Deep	12	80,0	9	37,5	LR=8,450 ; p<0,015
Combined	2	13,3	14	58,3	C=0,407; p<0,02
3. M-S score					
1	-	-	-	-	> 0,05
2-3	5	33,3	9	37,5	
4-5	10	66,7	15	62,5	
Total	15	100,0	24	100,0	

B1-1: *with one hemorrhage;* ***B1-2:*** *two and more hemorrhages*

Table IX: Bleeding incidence in reference to the size of AVM, drainage type and Martin-Spetzler score

Characteristic	N	Occurrence of new hemorrhages		Rate hemorrhage / yrs	Mean follow-up time (yars)	Xep annual
		n	%			
6. Size of AVM						
do 2,5 2,6-5,0 5,1 >	1 3 1 5 1 1	9 (20) 7 (16) 8 (22)	69,2 46,7 72,7	33,8% 27,0% 25,9%	4,55 3,95 7,70	2,9 3,7 3,8
7. Drainage						
surface deep combined	2 2 1 1 6	1 (2) 9 (22) 14 (34)	50,0 42,8* 87,5*	40,0% 22,6%** 33,6%**	2,50 4,63 6,32	2,5 4,4 3,0
8. M - S score						
1 2 - 3 4 - 5	- 1 4 2 5	- 9 (18) 15 (40)		- 30,4% 27,7%	- 4,55 5,77	- 3,5 3,6
Total	3 9	24 (58)		28,5%	5,21	3,5

DISCUSSION

Initial presentation by bleeding was recorded in 39 patients. The average age of all investigated patients was 27.4±7.6 years. Prevalence of the new hemorrhage episodes in patients longitudinally followed-up up to 24 months was 37.5%, from 25-48 months 61.5% and in patients followed-up for 49 months and more 72.2% ($X2=2.821$; $p>0.05$), and the presence of associated systemic diseases had no influence on the increase of the tendency to bleeding. American and Swedish authors point to homogeneity of the results of the natural course of AVM of the brain regardless of the nationality (2,5). Parkinson points out that initial presentation of AVM of the brain by hemorrhage occurs between 20 and 40 years of age, with a slight predominance of males, without increasing the incidence of bleeding due to associated systemic diseases, and that the risk from bleeding is constant in the course of the follow-up period, regardless of age (19). During the cumulative follow-up period of 953 months for the patients . With this manner of presentation, 24 episodes of repeated bleeding were recorded, and that represents a cumulative risk of 3.33% per year. Namely, patients who once experience bleeding from an arteriovenous malformation are under constant risk of 3.33% annually to experience a repeated bleeding. The arrived at value is in accordance with results of Forster – 3% and Martin and Spetzler 2-3% (5,23). Nusbaum cites that the risk from hemorrhage is identical both in AVM that presented with bleeding and in those that had no hemorrhage, and that risk amounts to 3-4% annually (17).

After initial hemorrhage our patient population had significant neurological deficit that in 82% of cases was presented by the value of Karnofsky index less than 70, meaning that these patients could take care of themselves with effort or with significant assistance from another person but that deficit did not get worse until the end of the follow-up interval, regardless of the number of repeated hemorrhages. However, significant recovery was recorded in the group of patients who experienced more episodes of repeated bleeding. Statistical confirmation ($p<0.035$) that mean value of Karnofsky index is considerably higher in the group with repeated hemorrhages is in accordance with the results of Brown who presented a series of patients with AVM of the brain treated at the Mayo Clinic and stressed that an average of 12 months was needed for the recovery of the pyramidal deficit and cognitive functions, and that seemingly easy recovery may dissuade the patient from the proposed surgery (20).

According to our results the predisposing factors for hemorrhage from AVM are: arterial supply from the vertebrobasilar confluence with absolute statistical confirmation ($p<0.01$), multiple arterial supplies from different arterial confluences ($p<0.05$) with a remark that statistically significantly higher hemorrhage rate is from the confluence of the anterior cerebral artery than from the confluence of the middle cerebral artery ($p<0.01$). The significance of supply arteries is specially stressed in literature, as the supply arteries are easily identified by arteriography (1). These arteries are abnormal both anatomically and physiologically and they may be in connection with AVM in three forms: as terminal arteries – ending in AVM, transit arteries – passing through AVM and giving branches that participate in its irrigation and transient arteries – that only pass through the malformation not participating in its architecture (25,26). Analyzing AVM, Yasargil mentions the existence of 60 possible combinations of arterial supply blood vessels for each lesion (31). The greatest decrease of the systemic pressure happens where the supply arteries pass into AVM, and as the certain indicator of the presence of 'steal' phenomenon is distinguished the length of arterial supply longer than 8 cm measured from the level of Wilis hexagon (16). Obtained statistical values ($p<00.1$) that point to the location domination of the left hemisphere as the factor, which favors the occurrence of bleeding, has not been confirmed by literature and we think it occurred as a result.

Drainage veins have 6-10 times greater distensibility than supply arteries and they can contain blood volume three times greater than the arteries, and their compliance is 18-30 times greater then in arteries (4). Obtained results confirmed the significance of the vein type of drainage from AVM as predisposing factor for the occurrence of bleeding. In patients with one bleeding during the follow-up statistically significant domineers the form of deep venous drainage, while in patients with repeated bleeding domineers the combined venous drainage ($X2=7.764$, $p<0.02$) with significant predomination of the combined drainage ($p<0.5$). Distribution of values of the Spetzler Martin index did not show statistically significant difference between the patients without and those with repeated hemorrhages, but the average number of annual hemorrhage episodes is considerably greater if the size of AVM is over 2.5 cm in diameter ($p<0.01$). Kader in the series of 449 patients find hemorrhage as initial symptom in AVMs smaller than 2.5 cm in 90% of cases, in lesions of 2.5-5 cm in 52% of cases, while in lesions larger than 5 cm in 50% of cases (11).

Spetzler-Martin grading system represents statistical confirmation that neurosurgeons and neuroradiologists have coordinated attitudes as regards the anatomical characteristics of AVM of the brain that would be predictors of the bad outcome for the patient if left to the natural course of the disease. However, this grading system has recently been submitted to criticism. Analyzing the series of 224 patients with AVM of the brain Rose points out that errors are present from subjective as well as objective reasons. Namely, as regards the size of the malformation neurosurgeons are more inclined to preoperatively assess diameter of malformation and the total value of SM score bigger than the neuroradiologists. The disagreement is also manifested in the assessment of the type of the drainage, especially in cases of malformation that has a small, deep drainage vein and a dominant, wide superficial vein (1). It is also difficult to estimate the localization of AVM in border cases, i.e. in zones that are in the immediate vicinity of the so called eloquent zones – somatosensor and motor cortex, speech center, visual cortex, hypothalamus, thalamus, capsula interna, brain stem, cerebelar pedunculi and deep central nuclei (29).

CONCLUSIONS

The results of our investigations that refer to the natural course of the disease in 39 patients with AVM enable us to draw the following conclusions. Demographic characteristics of the patients, as well as the presence of associated diseases have not shown statistically significant influence on the occurrence of new episodes of the disease (p>0.05).

The condition of patients at the start of the disease estimated through average Karnofsky index showed significant interdependence with the occurrence of the new episodes of the disease (p<0.035). Namely, the patients in excellent condition with or without minor neurological deficit – seemingly healthy after the first attack showed considerably more frequent tendency to have repeated episodes of the disease as regards the patients who during the initial phase of the presentation of the disease suffered considerable neurological deficit.

The combined type of the venous drainage within anatomical characteristics of AVM has significant influence on the occurrence of new episodes of the disease (p<0.01) and on the incidence of the hemorrhage/yrs rate, which means that the type of malformation where the combined type of drainage is represented may be considered as the predominant, predisposing factor for the presentation of AVM by bleeding.

The type of arterial supply (p<0.01) and the presence of several arterial supplies from different confluences (p<0.05) represent statistically significant factors in the prevalence of bleeding from AVM. As the dominant, predisposing factor for the bleeding from AVM turned out to be the supply from vertebrobasilar confluence.

In a specific situation of relatively small series of investigated patients as ours (39), the value of Martin-Spetzler index did not turn out to be statistically significant predisposing factor for the manner of initial presentation of AVM, as well as for the weight of expected morbidity and mortality, however it should be stressed that the average number of annual hemorrhage episodes is considerably greater when the size of AVM is 2.5 cm and more.

Generally we may conclude that AVM of the brain as regards the entire range of neurological diseases pertain to benign lesions, and that demands patient and strategically well-prepared therapy approach.

Analyzing our series of 39 patients during the average follow-up of 5 years and 4 months we may propose the following model of the natural course of AVM:

After the initially presented bleeding there remains 3.33% annual risk of repeated bleeding, with remark that repeated hemorrhages are statistically significantly more frequent in patients with higher Karnofsky index value. The total mortality during this follow-up period is 5.3% with cumulative survival probability of 0.9217 after 30 months. Hemorrhages are considerably more frequent from a medium sized AVM (2.5-5 cm), localized in the eloquent zone of the brain, with combined type of the venous drainage, arterial supplies from the vertebrobasilar confluence, confluence of the anterior cerebral artery or even combined arterial supply.

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