Clinical aspects, management and outcome of brain arteriovenous malformations – results with microsurgery first policy

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Abstract: We performed a retrospective study, including patients operated for brain AVMs between 1999 and 2014, in the Clinic of Neurosurgery, Emergency Clinical Hospital Bagdasar-Arseni, Bucharest. 277 patients underwent surgery for brain AVMs. Mean age was 29.82 years. 195 patients (70.40%) presented with hemorrhage and 86 cases (31.05%) were admitted with seizures. We performed total resection of AVMs in 228 cases (82.31%) and subtotal resection in 49 cases (17.69%). Regarding patients with residual nidus, 16 of them underwent second surgery, 27 stereotactic radiosurgery Gamma Knife, 3 embolization and 3 refused further treatment. Modified Rankin Scale (mRS) improved following surgery (Z = -9.248, p = 0.000). Early complications (0-30 days) were encountered in 84 patients (30.32%). We found the following risk factors for postoperative complications occurrence: motor deficit (p = 0.006), co-morbidities (p = 0.023), higher mRS (p = 0.005), lower Karnofsky score (p = 0.003), lower GCS (p = 0.016), profound nidus (p = 0.001), eloquent aria (p = 0.000), large nidus (p = 0.000), multiple arterial territory (p = 0.000), deep feeding arteries (p = 0.000), higher number of feeding arteries (p = 0.000), deep venous drainage (p = 0.000), multiple draining veins (p = 0.000), higher Spetzler-Martin grade (p = 0.006), high flow (p = 0.000), vascular steel (p = 0.000), associated aneurysms (p = 0.010) and decompressive craniectomy (p = 0.019). Mortality was 6.1%. Microsurgery is the treatment of choice for brain AVMs. Surgical results are excellent, with low morbidity and mortality. Patients with poor surgical results belonged to the group admitted with severe altered general state, state of consciousness, massive hematomas and acute brainstem dysfunction. If part of the nidus cannot be safely surgical resected, stereotactic radiosurgery can provide definitive cure of the lesion.
Key words: arteriovenous malformations, microsurgery, postoperative complications.

Introduction

Brain arteriovenous malformations (AVMs) are congenital complex network formed by dysplastic vessels (dilated arteries and enlarged arterialized veins interconnected by shunts), in which oxygenized blood flows from arteries directly into draining veins without passing through capillary bed. This network of vessels, called nidus, contains no brain tissue within.

Brain AVMs are rarely encountered, having a prevalence of 0.14%. (12) Less than 1.5 new cases/100,000 inhabitants are reported each year.(1, 9, 37, 38) AVMs represent around 6% of all brain lesions. Usually are solitary, but in 2% of the cases can be multiple.

Brain AVMs become clinically manifest in young people, mean age at diagnosis being 33 years. (27) Brain AVMs have high mortality and morbidity rates. Brain AVMs represent the most frequent cause of spontaneous cerebral hemorrhage in young adults. Onset with intracerebral bleeding is found in 50% of brain AVMs. (5, 12) Cerebral hemorrhage is a major cause of mortality, morbidity and persistent neurological deficits. Following AVMs rupture, mortality reaches 10% and morbidity accounts for 30-50%. (12, 15, 17) Brain AVMs can manifest with seizures or long-term neurological deficits.

The aim of this study is to analyze clinical aspects, management and short and long-term outcome of brain AVMs, who underwent surgery, over a period of time of 15 years, using microsurgery first policy.

Material and methods

Patient population

We performed a retrospective study, including patients who underwent surgery for brain AVMs between 1999 and 2014, in the Clinic of Neurosurgery, Emergency Clinical Hospital Bagdasar-Arseni, from Bucharest. We excluded patients who were not operated, grade VI Spetzler-Martin AVMs, spinal AVMs and patients lost at follow-up. Follow-up period varied from 3 months to 15 years.

We reviewed medical records, and we recorded: demographic data, history, previous treatment, signs and symptoms at admission, general exam, neurological exam, modified Rankin score (mRS), Karnofsky score, GCS, cerebral CT scan, MRI, angio-CT, angio-MR, four/six vessel angiography, fundoscopy, EEG, surgical details, complications, early and late outcome, complications, other treatments, and prognosis. On follow-up patients were evaluated using all or some of the followings: general exam, neurological exam, cerebral CT, MRI, four vessels angiography, fundoscopy and EEG.

Statistical analysis

We used IBM® SPSS® Statistics 20 for statistical analysis. We performed uni- and bivariate analysis.

Results

From 1999 to June 2014, in the Clinic of Neurosurgery a total number of 820 patients were admitted with brain AVMs, but only 277 patients (33.78%) underwent surgery.
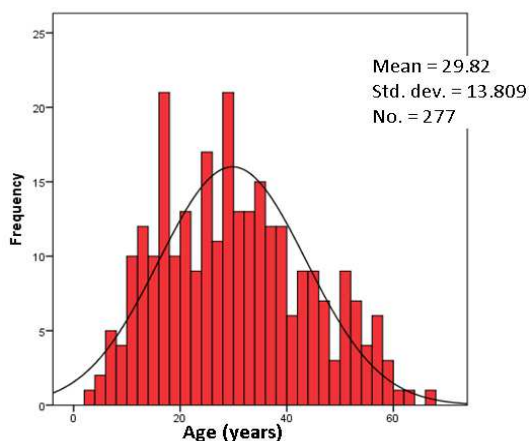
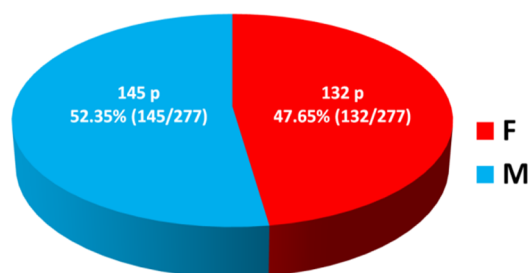Figure 1 - Histogram for age distribution

Figure 2 - Sex distribution

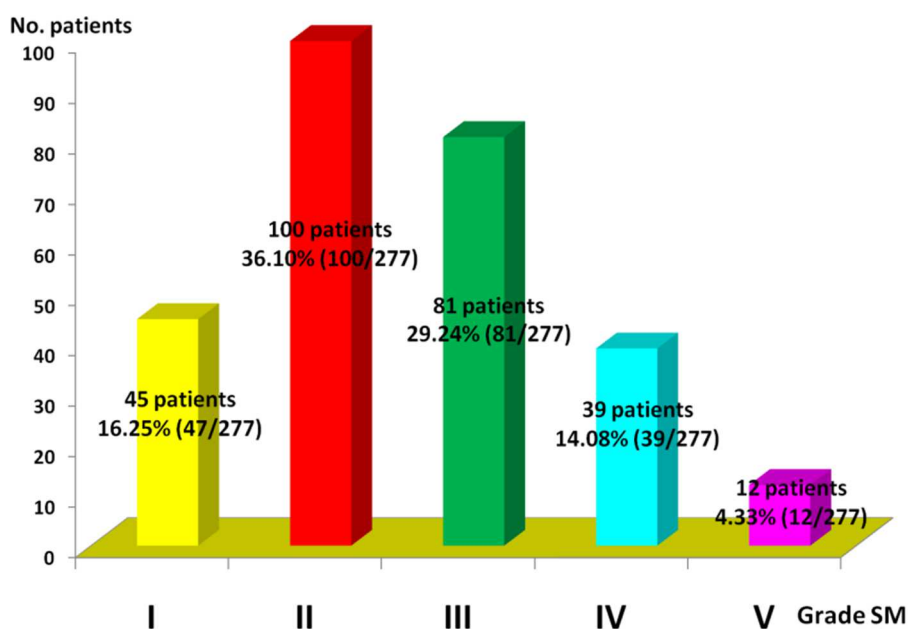Age varied from 3 to 67 years (mean age 29.82 years, median age 29 years). Sex ratio was 1.098.

Figure 3 - Distribution according to Spetzler-Martin grading system

Intraparenchymatal hematoma
174 p (89.23% - 174/195)
Intraventricular hemorrhage
82 p (42.05% - 82/195)
Subarachnoid hemorrhage
23 p (11.79% - 23/195)
Subdural hematoma
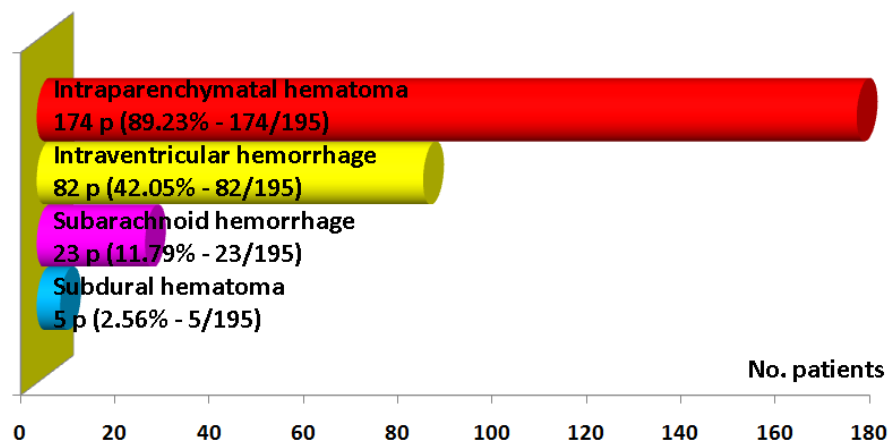**5 p (2.56% - 5/195)**

No. patients

Figure 4 - Bleeding site in patients with cerebral hemorrhage

According to Spetzler-Martin grade, we found 45 patients (16.25%) with grade I, 100 patients (36.10%) with grade II, 81 patients (29.24%) with grade III, 39 patients (14.08%) with grade IV and 12 patients (4.33%) with grade V.

The two main pattern of AVMs presentation were onset with hemorrhage or seizures. In our series of patients 195 cases (70.40%) presented with cerebral hemorrhage and 86 (31.05%) were admitted with seizures. Analyzing only the group with hemorrhage, we found that 174 patients (89.23%) had intraparenchymatal hematoma, 82 cases (42.05%) presented intraventricular bleeding, 23 cases (11.79%) had subarachnoid hemorrhage and 5 patients (2.56%) had subdural hematoma.

Altered mental state was encountered in 115 patients (41.52%). All patients presented with altered mental state came from the group with cerebral hemorrhage. One hundred eleven patients (40.07%) presented motor deficits.

According to location, most of brain AVMs were found in the supratentorial compartment, 250 cases (90.25%), compare with 27 cases (9.75%) with infratentorial lesions. In 169 AVMs (61.01%) the whole nidus or part of it was located in eloquent areas and in the rest of 108 cases (38.99%) the nidus was seated in noneloquent areas. AVMs were superficial in 230 cases (83.03%) and deep in 47 patients (16.97%).

We recorded data regarding feeding arteries and venous drainage. In 209 cases (75.45%) arterial supply came exclusively from superficial feeding arteries and in 68 malformations (24.55%) from deep feeding arteries. Deep arterial feeders were represented by all feeding arteries coming from perforating or choroidal arteries. Feeding arteries came from a single arterial territory in 156 cases (56.32%) and in 121 lesions (43.68%) from multiple arterial territories. An arterial territory was represented by all branches arising from one major cerebral artery.
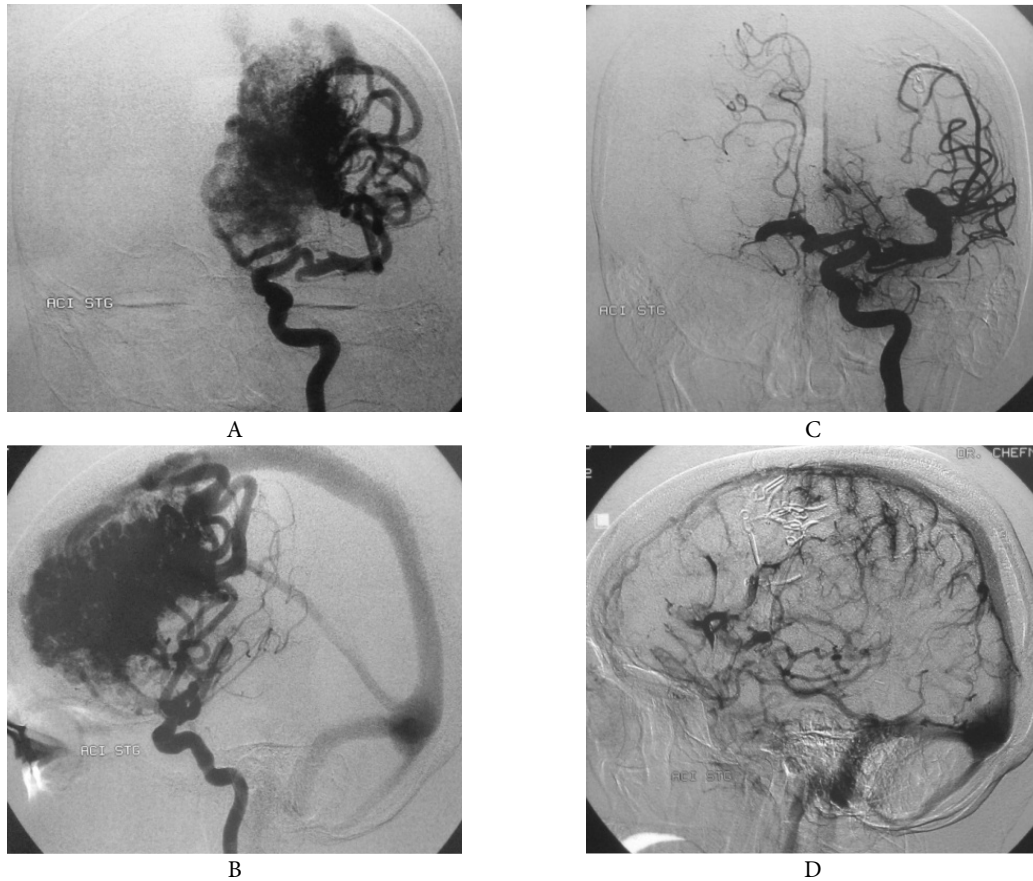
A

C

B

D

Figure 5 A, B - Giant left frontal AVM, feeding arteries from left MCA, left ACA, right ACA, left PCoA and left PCA. Venous drainage in straight sinus via SSS and SSI; C, D. Postoperative aspects: complete resection

Anterior circulation territories were represented by ACA and MCA territories and posterior circulation territories were PCA, PICA, AICA and SCA territories. One hundred and sixty-eight AVMs (60.65%) had only superficial venous drainage, while 109 (39.35%) had deep venous drainage. One hundred thirty-four lesions (48.38%) had a single draining vein and 143 cases (51.62%) had multiple draining veins. Vascular steel was noted in 118 cases (42.60%). Thirty two patients (11.55%) also had one or multiple intracranial aneurysms.

We performed total resection of AVMs in 228 cases (82.31%). The rest of 49 patients (17.69%) had residual nidus. In patients with grade I Spetzler-Martin we were able to performed total resection in all 45 cases (100%). In patients with grade II, we were able to achieve total resection in 93 cases (93%) and we left a residual nidus in 7 patients (7%). In grade III we performed total resection in 59 patients (72.94%) and subtotal resection in 22

cases (27.16%). From the total number of cases with grade IV, we were able to perform 21 total resections (53.85%) and 18 subtotal resections (46.15%). In grade V we succeeded total resection in 10 cases (83.33%) and in the other 2 cases (16.67%) we left a residual nidus.

Regarding patients with residual nidus, 16 of them underwent second surgery, 27 stereotactic radiosurgery Gamma Knife, 3 endovascular embolization and 3 refused further treatment.

Decompressive craniectomy was performed in 70 cases (25.30%).

We compared modified Rankin Scale (mRS) before and following surgery, and we found that in 202 patients (72.92%) mRS improved, in 41 cases (14.80%) it remained unchanged and in 34 patients (12.28%) mRS got worse. Statistical analysis, using Wilcoxon test, showed that mRS improved after surgery statistically significant ($Z = -9.248$, $p = 0.000$).

Early complications (0-30 days) were encountered in 84 patients, leading to a morbidity rate of 30.32%. Normal perfusion pressure breakthrough was noted in 17 cases (6.14%). Secondary intraparenchymatal hematoma required emergent surgery in 16 cases and in one case it was limited, with no mass effect, the patient presented no additional neurological deficits and it was treated conservatively with good outcome.

TABLE 1

Early complications (0-30 days following surgery)

| Complications	No. patients*	% complications
IPH ← NPPB	17	6.14%
IPH ← rebleeding from residual nidus	2	0.72%
Malignant brain swelling	3	1.08%
Ischemia	2	0.72%
Acute brainstem dysfunction	6	2.17%
EDH	2	0.72%
SDH, subdural hygroma	3	1.08%
Infections	8	2.89%
Seizures	17	6.14%
Hydrocephalus	12	4.33%
CSF fistula	2	0.72%
Arachnoiditis	2	0.72%
Motor deficit	21	7.58%
Aphasia/dysphasia	7	2.53%
Other neurological deficits	5	1.80%
Pulmonary complications	5	1.80%
Thrombocytopenia, coagulopathy, DIC	1	0.36%
Wound dehiscence	1	0.36%

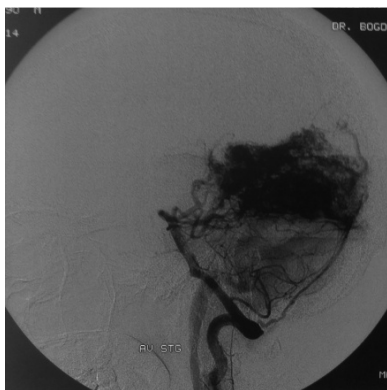*one patient may present more than one complication
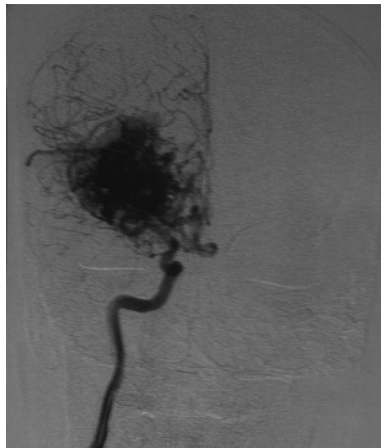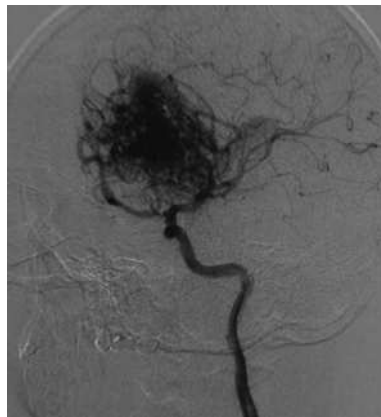
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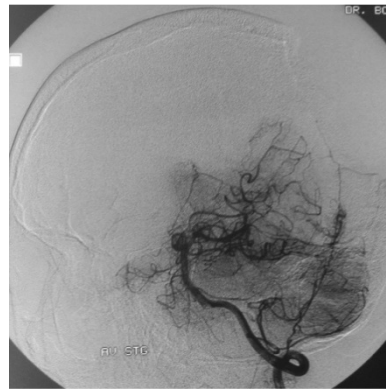
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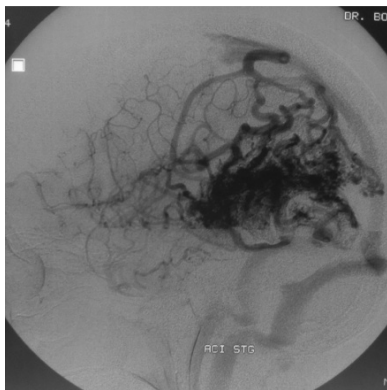
B

E

C

F

Figure 6 A, B, C - Giant left TPO AVM, feeding arteries from left MCA, left pericallosal artery, left PCA (P3 segment), left middle meningeal artery, left posterior meningeal artery, both occipital arteries.

Venous drainage in SSS, left transverse sinus, herophili torcula and straight sinus;
D. E. F - Postoperative aspects: complete resection
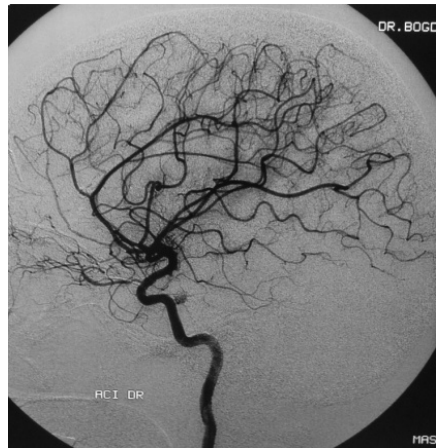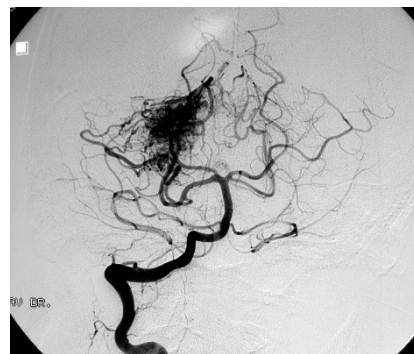
A

B

C

D

Figure 7 A, B - Right frontal AVM, feeding arteries right ICA, right ECA (← STA), left ICA (←ACoA) and VBS (← PCoA). Multiple enlarged draining veins; C, D - Postoperative aspects: complete resection

A

B

C

D

Figure 8 A, B - Infratentorial AVM right cerebellar
hemisphere, feeding arteries from SCA and PCA.
Deep venous drainage in Galen vein and superficial
in torcular Herophili and lateral sinus;
C, D - Postoperative aspects: complete resection

We used bivariate analysis to see which risk factors for early complications occurrence are. Analyzing clinical data, we found the following risk factors: motor deficit (p = 0.006, OR = 2.069, 95% CI 1.229-3.482), co-morbidities (p = 0.023, OR = 2.288, 95% CI

1.103-4.744), higher mRS (U = 6427.500, p = 0.005), lower Karnofsky score (U = 6294.500, p = 0.003) and lower GCS (U = 6786.000, p = 0.016). Age, sex, hemorrhage, seizures and altered mental state were not risk factors for developing postoperative complications. Analyzing imaging findings, we found the following risk factors: profound nidus (p = 0.001, OR = 2.957, 95% CI 1.554-5.625), eloquent aria (p = 0.000, OR = 3.590, 95% CI 1.965-6.558), large nidus (U = 4686.000, p = 0.000), multiple arterial territory (p = 0.000, OR = 5.410, 95% CI 3.083-9.492), deep feeding arteries (p = 0.000, OR = 4.901, 95% CI 2.736-8.779), higher number of feeding arteries (U = 2338.000, p = 0.000), deep venous drainage (p = 0.000, OR = 5.724, 95% CI 3.278-9.995), multiple draining veins (p = 0.000, OR = 11.661, 95% CI 5.799-23.448), higher Spetzler-Martin grade (U= 3006.000, p = 0.006), high flow (p = 0.000, OR = 5.050, 95% CI 2.701-9.442), vascular steel (p = 0.000, OR = 4.945, 95% CI 2.842-8.605) and associated aneurysms (p = 0.010, OR = 2.603, 95% CI 1.233-5.495). Supra/infratentorial location was not a risk factor for developing postoperative complications. Analyzing surgical data we found that decompressive craniectomy was a risk factor (p = 0.019, OR = 1.955, 95% CI 1.109-3.446), while total resection/residual nidus were not associated with postoperative complications occurrence.

There were 17 deaths, resulting a mortality rate of 6.1%.

Long-term outcome was favorable and slowly favorable in 241 patients (87.01%), unfavorable in 15 cases (5.42%) and 4 patients (1.44%) headed to vegetative state. Patients

with poor surgical results belonged to the group admitted with severe altered general state and state of consciousness, massive hematomas and acute brainstem dysfunction.

Discussions

Brain MAVs become clinically manifest and are diagnosed in young people. In our series of patients mean age was 29.82 years. Literature review showed a mean age at onset of 33.7-35 years (2, 13). Relevant literature shows either a slight male distribution of the disease (13) or an even gender ratio (2), in our study sex distribution slowly favored men.

AVMs are more likely to present with hemorrhage (3). The rate of hemorrhage is 3% per year, with initial bleeding rate of 2.2% per year and rerupture rate of 4.5% per year (13). In patients with increased risk factors for rupture, such as previous hemorrhage (16, 39), exclusively deep venous drainage (8, 16, 18, 28, 39), large size lesions (16, 40) or nidus less than 3 cm in diameter (8, 21), deep (16, 21, 39, 40) and infratentorial locations(8, 16, 18, 21, 29), feeders originating in perforating arteries (28), single feeding artery (21), single draining vein (21), combined deep and superficial venous drainage (21), varix of the draining veins (21), associated aneurysms (18, 21) and increasing age (39), the hemorrhage rate increases significantly. In our study the majority of patients, 70.40%, presented intracerebral hemorrhage. The most common pattern of bleeding was intraparenchymal hematoma, followed by intraventricular. Less common AVMs bled into the subarachnoid or subdural space. Regardless of bleeding site, hemorrhagic onset is associated with altered mental state and neurological deficits (19, 25). Sturiale et al. showed that intraparenchymatal hematoma and intraventricular hemorrhage are associated with severe clinical state at admission. (41) In our series of cases all patients admitted with altered mental state and the majority of patients with motor deficits came from the group with ruptured AVMs.

Seizures were encountered in 31.05% of cases. Other studies found a seizure rate of 29% (10, 42). Sturiale et al. found predisposal factors for seizure occurrence, such as size > 4 cm, dilated feeding arteries, cortical location, feeding vessels arising from middle and posterior cerebral arteries (42). Garcin et al. found that masculine sex, large size, location in the frontal lobe, location in the border area of arterial territories, superficial venous drainage, venous ectasia are predictive for occurrence of secondary epilepsy (10). Shankar et al. reported that AVM location, fistulous nidus, venous stenosis, long pial course of draining veins correlated with seizure occurrence (33).

Ideally, complete angioarchitecture of AVMs must be known before surgery. For that, patients with good neurological status are investigated using four or six vessels angiography, the gold standard imaging study. But in some cases, with comatose patients, with ruptured AVMs and life-threatening intracranial hematoma, emergent surgery is required for surgical evacuation of the blood clot. Hemorrhagic presentation is usually ictal, patients, sometimes without history of previous diseases, are admitted with profound altered mental state and new onset

neurological deficits. In comatose patients CT scan shows intraparenchymatal hematoma, with mass effect, midline shift and cerebral herniation. These patients also present respiratory failure and rapid neurological deterioration. In such cases, the best option is emergent life-saving surgery for hematoma evacuation and decompressive craniectomy, in order to decrease intracranial pressure. After neurological recovery the patient is further investigated for rest of nidus and elective surgery in order to cure the AVM can be performed with good results (30). Superficial, small AVMs can be completely removed at first surgery once hematoma is evacuated, and postoperative angiography shows no abnormal vessels. Patients with good neurological state can be thoroughly investigated before operation and elective surgery is performed.

In a young patient presenting a primary intracranial hematoma the surgeon must always suspect a ruptured AVM, and must be prepared accordingly. The bone flap should be large enough to control a possible AVM. The abnormal dilated vessels on the brain surface draw attention to the possibility of this lesion. After blood clot evacuation the cavity must be inspected for abnormal vessels and the nidus must be resected, in accordance with AVM surgery principles. (6, 11, 20, 22) In spite of poor neurological status, emergent life-saving surgery, with hematoma evacuation and decompressive craniectomy is mandatory, and many patients may experience good neurological recovery (30, 34).

Over the time, the outcome of AVM surgery had improved. Morbidity and mortality correlates with Spetzler-Martin grading system. (31, 35) Nowadays, low grade AVMs can be safely removed, with low complication rate. Morbidity and mortality increases in higher grades. The higher the grade, the lower is the rate of complete resection. Literature review shows that besides Spetzler-Martin scale, hemorrhagic presentation (19), location (4), eloquent area (31), size (4, 23, 31), diffuse nidus (7), deep perforanting arteries (7) and deep venous drainage (31) influence the rate of complications and outcome.

In our study 17 patients developed normal perfusion pressure breakthrough. Normal perfusion pressure breakthrough, first described by Spetzler in 1978 (36), characterized by hemorrhage and edema occurring in spite of complete resection of AVM, is caused by loss of auto regulation of cerebral vessels from the surrounding brain. The high flow of the AVM steals most of the blood, leaving only a small amount for neighboring areas. Vessels supplying surrounding brain try to compensate the chronic hypoperfusion through vasodilatation and capillary network formation (32). After blood flow redistribution, arterioles cannot constrict, as a consequence of prolong vasodilatation, because they had lost the capacity of autoregulation and capillary break down, leading to hemorrhagic foci and edema. After AVM removal, blood flow is redistributed through dilated arteries to a hypoperfused brain area. Although, the exact pathophysiological mechanism of normal perfusion pressure breakthrough occurrence remains unknown, distant manifestations

being reported (14). Factors predictive for normal perfusion pressure occurrence are: large size, high flow, vascular steal seen on angiography by paucity of filling with contrast agent of surrounding vessels supplying vicinity brain and filling of the AVM from distant major arteries, feeders from the external carotid artery, clinical vascular steal, objected by fluctuating or progressive neurological deficits (22).

Patients with residual nidus or recurrence can be reoperated or can be referred to Gamma Knife stereotactic radiosurgery. Our policy regarding residual nidus is particular to each case. If residual nidus was found on postoperative angiography and the nidus is located into a surgical suitable area, we preferred second surgery. But residual nidus can originate from AVMs extending into eloquent areas or from particular angioarchitecture, with presence of passing thorough arteries. Passing arteries must be spared because they supply normal brain and their inadvertent occlusion leads to ischemic stroke in distal vascular territories. In cases with nidus surrounding passing through arteries, if you cannot identify and spared the passing through artery, is better to leave a residual nidus. In order to indentify passing through arteries the nidus must be dissected opposite to the arterial supply in order to see which arterial branch passes the tangle of vessels. Passing through arteries usually can be found around middle cerebral artery and pericallosal arteries. We had no recurrence in our series of patients, but it was described in the literature and was associated with young age and deep venous drainage (24).

Flow-related unruptured associated aneurysms remained untouched and control angiography confirmed their disappearance after AVM surgery.

In patients with long-term seizures, surgery allows progressive and significant reducing of doses of antiepileptic drugs.

Social and professional reintegration is extremely important in patients with AVMs, because they are young and active people.

Although available in our hospital, our policy is not to use preoperative embolization, because embolization harbors some week points: it is not a curative treatment, recanalization of the AVM quickly occurs, therefore surgery must be performed within 3-30 days (12), it can mask arterial feeders, which cannot be seen and secured intraoperatory and may reopen after surgery, it cannot remove the AVM and therefore symptoms secondary to increased intracranial pressure and pseudotumor mass linger, and embolization carries all risks, including rupture, normal perfusion pressure breakthrough, retrograde venous thrombosis, stroke, neurological deficits. Morbidity related to preoperative embolization is 4-8.9%. (4) Yet, advantages of preoperative embolization must not be ignored: it facilitates surgery, decreases intraoperatory blood loss and allows selective embolization (26, 43). We used it in 3 patients with residual nidus, with suitable angioarchitecture.

So, our policy in AVMs is surgery first, followed by, in cases with residual nidus, reoperation or stereotactic radiosurgery Gamma Knife. We do not favor endovascular embolization.

Conclusions

Microsurgery is the treatment of choice for brain AVMs. Surgical results are excellent, there are low morbidity and mortality rates. Motor deficit, co-morbidities, higher mRS, lower Karnofsky score, lower GCS, profound nidus, eloquent aria, large nidus, multiple arterial territory, deep feeding arteries, higher number of feeding arteries, deep venous, multiple draining veins, higher Spetzler-Martin grade, high flow, vascular steel, associated aneurysms and decompressive craniectomy were risk factors for complications occurrence following surgery. Patients with poor surgical results belonged to the group admitted with severe altered general state, state of consciousness, massive hematomas and acute brainstem dysfunction. If for any reason a part of the nidus cannot be safely surgical resected, stereotactic radiosurgery can provide definitive cure of the lesion.

Acknowledgement

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