We present the results of treatment of 15 patients with brain arteriovenous malformation initially presented by epilepsy in Neurosurgery, Clinical Center of Serbia in Belgrade, in the period 2004-2010 year. 

Results: Most of the patients had a grand mall type of epilepsy, 14 of them, while one was present petit mall epilepsy. The attacks are manifested individually in 14, and in 1 case series. Response to treatment was good in 11 and 4 patients with refractory. In 26.7% of cases, seizures alternated with bleeding. Anatomical features of malformations did not show a significant difference in the predisposition to epilepsy treatment response.

Conclusion: Good control of epilepsy by medication supports the view that there is no need for urgent surgical treatment of brain AVM so we can generally conclude that brain AVM in relation to a wide range of neurosurgical patients are in benign lesions, which requires patience and good workmanship and strategic therapeutic approach.

Key words: AVM of the brain, epilepsy, the natural course

INTRODUCTION

AVM represent a set of abnormal direct communication between the cerebral arteries and veins and are congenital in origin. They emerge in the third week of gestation, with the development of primitive blood vessels. Termination in the development of primitive blood vessels results in the formation of direct communication between arteries and veins by inserting a primordial capillary plexus between them. They consist of a central angiomatous nidus, feeding arteries and drainage veins. When the AVM is projected into the ventricle, the vessels which protrudes into the ventricle are covered only with ependymal tissue. AVM is usually fed by the branches of the middle cerebral artery, and then the anterior and posterior cerebral artery. AVM in 50-75% of cases is presented by hemorrhage, which is usually parenchymal and is more common in small malformations (Parkinson et al. 1980, Cohen et al. 1982). The risk of hemorrhage in AVM is 3-4% per year while the risk of re-hemorrhage slightly higher in the first year and is about 6%. Mortality from hemorrhage 10-15%, and the morbidity is about 30% after each episode of bleeding. Epileptic seizures (EPI) is the second significant aspect of the presentation of AVM and they are the initial symptom in 24.2%, AVM has equal frequency in men and women and they occur most often between 10 and 40 years of age. Most often focal seizures occurred and they are generalized in 55.8% of cases. In 27% cases grand mall seizures (GM) are refractory to medical therapy. The risk of hemorrhage in patients with epilepsy as the initial symptom is about 1 to 2.3% per annum. Every fourth patient with seizures as an initial symptom will have hemorrhage.

MATERIALS AND METHODS

We present a group of 15 patients with AVM of the brain in which the malformations was initially presented by epilepsy and CT/NMR findings of brain pointed to cerebral localization of the AVM could cause epileptic seizures, and excluded the second pathological substrate that could cause epilepsy. Patients were treated at the Clinic of Neurosurgery (NHK), Clinical Center of Serbia in the period from October 2006 to May 2012. The analysis classifies patients with AVM of the brain that have not been subjected to any of the modes of treatment: surgery, embolization and/or radiotherapy, excluding symptomatic therapy. The diagnosis of cerebral AVM is set panangiography (standard or digital subthreshold). The patients were not treated because the the Collegium of Neurosurgeons lesion assessed inoperable or unsuitable
for other forms of causal treatment, because the patient or his family refused treatment or because it is estimated that surgical treatment is burdened higher risk of postoperative disability than if left to the natural course disease, and the AVM unsuitable for other therapeutic modalities. The criterion for inclusion in the study was the moment of diagnosis, in which single attacks GM type dominate. All patients were followed for an average of four years. Clinical follow-up completed with the definitive establishment of the series and the start of data processing definitely untreated cases or the time of initiation of the causal treatment of AVM. To evaluate the clinical and anatomical characteristics of the AVM was used widely accepted system according to Spetzler-Martin (SM index-score). For each AVM was made the following assessment: measuring the size, estimation of general and neurological status, as well as working and living skills of patients with AVM was performed according to Karnofsky index.

RESULTS

The group with epilepsy as the initial mode of clinical presentation AVM included 15 patients, of whom 7 or 46.7% were male and 8 or 53.3% were female. The youngest patient was 11 years old and the oldest 54, the average age of all patients was 32.8 ± 11.5 years. The largest number of patients studied had a grand mall (GM) type of epilepsy, 14 of them or 93.3%, and in one patient or 6.7% was present petit mall (PM) epilepsy. Seizures are individually manifested in 14 or 93.3%, and in 1 case series, or 6.7%. Response to treatment was good in 11 or 73.3% and the refractory at 4 or 26.7% of the subjects (Table 1). Karnofsky index was lower in patients with refractory response to therapy and significantly lower at the end of follow-up (p<0.05). Type of blood supply and the manner of presentation (right-left) showed no significant difference between patients with good and refractory response to therapy. Patients who had a refractory response to treatment had higher values of total AVM Martin-Spetzler's score compared to patients whose epilepsy is well controlled by medication, and in these patients the combined type of drainage was dominated. During follow-up in 4 patients there was bleeding from the AVM, which made 26.7% of all patients with epilepsy as an initial sign, representing an annual risk of 0.14%. One (6.67%) patient who had AVM MS index 5 died two days after hemorrhage due to developed infarction of cerebrum hemisphere, due to thrombosis of the internal carotid artery at the level of the cavernous sinus. Other three patients had the following values of the index MS: 2 in one patient, 3 in one patient and 1 patient had a value of MS index 5. The first two patients were operated on one patient registered absence seizures during the three years of operation, while were in another epileptic seizures occurred with the same frequency as before surgery.

DISCUSSION

Crawford and associates in 1986 based on the results of twenty years of follow-up of patients with AVM found that the risk of bleeding, 42%, 18% of epilepsy, neurological deficit, 27%, and death is about 29%. They also present a model of a patient with brain AVM with generally poorer prognosis. This is a man older than 40 years, which has significant neurological deficit on admission, as well as large and deep placed AVM previously presented subarachnoid hemorrhage as well as AVM localized in the functional zone of the brain. Forster making a cross-section in the treatment of AVM of the brain at the Karolinska Hospital, University of Stockholm, in the period 1930-1965. [1] year, found that there is hemorrhage as the initial symptom of brain AVM in 71% of cases, epilepsy in 47% of cases, a simultaneous presentation of epilepsy and hemorrhages in 23% of cases. The average age of patients at the time the initial bleeding was 30 years old, and epilepsy 25 years. Patients with epilepsy as an initial sign of having a chance to bleed 25% over the next 15 years, while patients who experienced one hemorrhage have a chance to re-bleed of 25% over the next four years. Postoperatively, there was a reduction in the frequency of epileptic seizures in 14% of cases, while in 22% of patients postoperatively developed epilepsy, and that they had preoperatively. Guidetti and Delitala summarize their experience in 145 patients with AVM treated conservatively or surgically. [2] The follow up period was 2-25 years. Male to female ratio was 1.6: 1. Age of the respondents ranged from 5-6 years, with a peak incidence between 20 and 30 years. Overall operative mortality was 6.3%. The mortality rate among conservatively treated patients was 20%. These authors emphasize that the operation showed no therapeutic effect on epilepsy, but epilepsy maintained postoperatively, and that in four cases occurred immediately after the operation so that they came to the conclusion that conservative treatment is reserved for patients with epilepsy that is well controlled by medication, elderly patients and patients with unacceptably high surgical risk. Mingrino states hemorrhage as a cause of hospitalization for brain AVM in 5.8% of cases, while 21.6% is the tendency to rehemorrhage [3]. Hemorrhage associated with seizures register as an initial symptom in 5.8% of patients, whereas the coma as the initial symptom is registered in 17.2% of cases. Epilepsy as an initial symptom in large AVM in 26.7% in secondary AVM at 17.6% in small AVM in 10.2% of cases. Parkinson gives absolute priority to the surgical treatment of AVM of the brain compared to conservative treatment [4]. Of the 100 patients diagnosed with brain AVM, 90 were operated with direct operative mortality of 12%. 8% of patients who did not have epilepsy preoperatively gained epilepsy postoperative, and neurological deficit were present in 35%. Pelletier indicates that superficially localized AVM are mainly present by epileptic seizures while deep have a greater tendency to bleed [5].
Also, he first describes the phenomena of retrograde flow ("back-flow") from the drainage vein AVM in the veins of the normal brain, which is more common in veins with a large shunt (high flow), and this very phenomenon reduces the tendency to bleed from the AVM. The problem of postoperative epilepsy is attributed to direct intraoperative manipulation. It is believed that it is occurring in an average of 7% of patients who did not have epilepsy before surgery, while patients who had preoperative epilepsy in 54%, the improvement of the status remains unchanged 32%, and worse finding is registered in 12% of cases'. Janicicjevic and colleagues suggest that the current AVM surgery involves the use of microsurgical techniques, and the only surgical procedure that leads to a definitive cure is complete excision of the malformation without residues. Any residue of the malformation, which may not be greater than 1/10 of the total volume of the lesion in terms of propensity to re- and perhaps catastrophic hemorrhage is as dangerous as the whole malformation. The significance of the supplying artery was highlighted in the literature, because the feeding arteries easily identified on arteriography. These arteries are abnormal in terms of anatomical and physiological characteristics, and can be related to the AVM in three forms: as the terminal arteries that end at the AVM, the transit arteries undergoing AVM giving branches participating in its irrigation and transient arteries passing through the malformation is not taking part in its architecture. Yasargil analyzing AVM states that there are 60 possible combinations of arterial feeder vessels for each lesion. Biggest drop in system pressure comes when the supplying arterial vessels are crossing in the AVM, and as a sure indication of the presence of stealing blood ("steal" phenomenon) identifies the length of the arterial supply is greater than 8 cm, measured from the level of Wilis's hexagon. Arterial supply in the context of the results of our series could not be singled out as a factor that affects the quality of regulation of epileptic seizures. Patients who had a refractory response to treatment had higher values of total AVM Spetzler-Martin score compared to patients whose epilepsy is well controlled by medication, and in these patients dominated the combined type of drainage. Drainage veins have 6-10 times greater distensibility of the supplying artery and may contain three times the volume of blood from the artery, and the compliance of their 18-30 times higher than in the arteries. Patients with epilepsy refractory to treatment, while higher values of Spetzler Martin's index and combination with venous drainage predominantly found in poor treatment response. A good medication control of epilepsy supports the view that there is no need for urgent surgical treatment of brain AVM so we can generally conclude that brain AVM in relation to a wide range of neurosurgical patients fall into benign lesions, which requires patience and strategic good workmanship in therapeutic approach.

However, this grading system has recently been subject to criticism. Specifically, in terms of size malformations neurosurgeons are likely to preoperative diameter malformations and overall value SM recent estimates higher compared to neuroradiology. Disagreement also manifest in assessing the type of drainage, especially in cases of malformation, which has a small deep drainage vein and commanding extensive superficial vein. Localization of the AVM is also difficult to assess in borderline cases, ie, in areas that are in the immediate vicinity so. eloquent areas - the somatosensory and motor cortex, a center for speech, visual cortex, hypothalamus, thal the brainstem, internal capsule, and deep central nuclei. Interestingly, the age of the patient at the time of diagnosis of AVM initially presented epilepsy has no impact on the frequency and type of attack and on the therapeutic response. On the other hand the results of surgical treatment does not favor surgery as the method of choice for the treatment of epilepsy was under AVM brain or genuine epilepsy. In large AVM epilepsy occurs in 26.7%, secondary 17.6% and 10.2% of small. Radiosurgical treatment of brain AVM smaller than 3 cm in diameter initially presented by epilepsy, only after three years of treatment suggests that the 65% can expect a good medication control epilepsy and its cure. The unreliability of these results is reflected in the method itself (complete occlusion of the AVM can be expected only after 4 years of treatment, gamma knife included), disadvantages of the proposed classification system AVM (especially for AVM localized in the basal ganglia and brain stem) and a tough and long selection of symptoms, due to the tendency that patients with AVM initially the presented later epilepsy may experience bleeding and vice versa.  

CONCLUSION

Our results indicate that epilepsy as an initial symptom of AVM of the brain in most cases, ie, 93.3% presented a GM type and in 73.3% of cases had a good therapeutic response to one of the AEDs. In 26.7% of cases, GM attacks are coupled combination of several antiepileptic drugs. In 26.7% of cases of epileptic seizures took turns with bleeding, with direct annual risk of 0.14%. Poorly controlled epilepsy accompanied by a reduction of working ability, Karnofsky index was significantly lower in patients with epilepsy refractory to treatment, while higher values of Spetzler Martin's index and combination with venous drainage predominantly found in poor treatment response. A good medication control of epilepsy supports the view that there is no need for urgent surgical treatment of brain AVM so we can generally conclude that brain AVM in relation to a wide range of neurosurgical patients fall into benign lesions, which requires patience and strategic good workmanship in therapeutic approach.
SUMMARY

EPILEPSIA KAO INICIJALNI FAKTOR KLINIČKE PREZENTACIJE ARTERIOVENSKIH MALFORMACIJA MOZGA – PRIRODNI TOK I FAKTOR RIZIKA


Rezultati: Najveći broj ispitivanih bolesnika imao je grand mal tip epilepsije, njih 14, dok je kod jednog bila je prisutna petit mall epilepsija. Napadi su se pojedinačno ispoljavali kod 14, a u serijama kod 1 bolesnika. Odgovor na terapiju bio je dobar kod 11 i refraktna kod 4 ispitnika. U 26,7% slučajeva epileptički napadi su se smenjivali sa krvarjenjem. Anatomske karakteristike malformacije nisu pokazale značajnu razliku u pogledu predispozicije za terapijski odgovor epilepsije.

Zaključak. Dobra medikamentozna kontrola epilepsije podržava stav da nema potrebe za urgentnim hirurškim lečenjem AVM mozga tako da generalno možemo zaključiti da moždanje AVM u odnosu na širok spektar neurohirurških bolesti spadaju u benignije lezije, što zahteva strpljiv i strategijski dobro obradjen terapijski pristup.

Ključne reči: AVM mozga, epilepsija, prirodni tok

BIBLIOGRAPHY

