Capability of cerebral autoregulation assessment in arteriovenous malformations perinidal zone

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Abstract

Background: Cerebral autoregulation (CA) in the region of an intracranial artery involved in blood supply of arteriovenous malformations (AVM) is impaired. This could be due to pathologic shunting, disguising real state of CA, or brain lesion in perinidal area. It is quite difficult to define the influence of both factors on CA. The purpose of this study was to assess dynamics of CA in patients with AVM in perioperative period.

Methods: The radicality of AVM embolization (Hystoacryl or Onyx) was evaluated in 47 patients by cerebral angiography and blood flow index in precerebral arteries with a Vivid E ultrasound scanner. We monitored blood flow velocity (BFV) in basal cerebral arteries with Multi Dop X and blood pressure (BP) with Finapres-2300. CA was assessed with cuff test (autoregulation index – ARI) and phase-shift (PS) between spontaneous oscillations of BP and BFV within the range of Mayer’s waves.

Results: Preoperative values of ARI and PS were 1.8±0.7 and 0.3±0.2 rad, respectively. In 15 cases with total embolization a significant (p<0.005) increase of rate of CA (ARI: 6.0±1.1, PS: 0.9±0.1 rad) was noted. In other two cases with total embolization, CA didn’t change significantly after operation. In 14 cases with subtotal embolization postoperative ARI and PS were 3.6±0.5 and 0.7±0.1 rad, respectively (p<0.05), and in cases with partial elimination were 2.1±0.6 and 0.4±0.1 rad (p>0.05).

Conclusion: CA assessment could be used for detection of its real impairment in perinidal zone of AVM during the staged endovascular treatment and for prognostication of postoperative complications.

Keywords: Cerebral autoregulation, Cerebral blood flow volume, Arteriovenous malformation, Embolization.
Introduction

Comprehension of specific hemodynamic features in cerebral arteriovenous malformations (AVM) is a key to good treatment outcome. Cerebral autoregulation (CA) is an important adaptive mechanism of cerebral hemodynamic stability [1–4]. Introduction of transcranial Doppler (TCD) in clinical practice improved timely diagnosis of cerebral hemodynamic disorders and prognosis of outcome in patients on different stages of endovascular treatment [5–7]. Continuous multichannel monitoring of blood flow velocity (BFV) in intracranial arteries and systemic arterial blood pressure (BP) using advanced TCD technique makes possible noninvasive assessment of CA with cross-spectral analysis as well as thigh-cuff test [8–11].

AVM is a congenital deformity which is characterized by the absence of capillary network and high rate of arteriovenous shunting. The occurrence of AVM is estimated at 18 per 100,000 population per year. The main symptoms of AVM are intracranial hemorrhage and epileptic seizures. Superselective embolization with different kind of embolizing materials (Histoacryl, Onyx) is one of the main methods of AVM treatment aiming at exclusion of abnormal vessels of AVM from circulation.

Due to the absence of normal resistive component in the structure of AVM, the major pathogenic mechanism of disease progression is low vascular resistance, as well as absence of regulation in afferent vessels of AVM and its network. This causes formation of pathologic blood flow shunting through AVM, which is its specific hemodynamic feature.

The vasomotor reactivity and rate of CA has been shown to decrease in cerebral arteries, predominantly in the arteries feeding cerebral AVM [12, 13]. Major cerebral arteries are more accessible for noninvasive insonation of BFV than arteries of second and third order. Hence all used methods allow detection of decreased rate of CA, mostly in a major cerebral artery, which feeds both the shunting structure (nidus) through hypertrophic afferent vessels of an AVM and surrounding brain (perinidal zone) perfused by this artery. Decrease of CA rate in a territory perfused by a major cerebral artery happens due to significant shunting and total CA impairment in AVM’s vessels and possible decrease of CA rate in the arteries of perinidal zone. In case of significant shunting process, AVM may disguise true value of CA rate in zones of brain nearby AVM network. In case of less prominent shunting, the data of CA assessment in the region of a major artery would reflect rather true functional value of resistive vessels feeding brain adjacent to AVM.

Thus, investigation of CA in major arteries feeding AVM in staged exclusion of AVM from circulation by embolization (decrease of shunting flow) will promote detection of true impairment of CA in the perinidal zone. The latter will make natural disease progression, surgery, and postoperative period more predictable.

The purpose of this study is to assess the dynamics of CA in patients with cerebral AVM in perioperative period.

Methods

Forty seven (47) patients (age range 22–63 years) with cerebral AVM were studied. All patients were divided into groups according to the Spetzler-Martin classification [14]. In 12 patients AVM corresponded to I–II grades, in 24 patients had grade III AVM, and 11 patients had grade IV AVM. AVMs were embolized either with Hystoacryl or Onyx through afferent vessels originated from the middle cerebral artery (MCA) and the anterior cerebral artery (ACA). All patients had a standard preoperative workup including CT angiography, cerebral MRI with MR angiography, ultrasound Doppler of cerebral arteries, as well as additional methods of CA evaluation and extent of AVM embolization.

TCD with bilateral monitoring of BFV in basal cerebral arteries, as well as thigh-cuff test were performed by MultiDop X, DWL (Germany). Monitoring of BP by CNAP (Austria) was performed parallel to BFV monitoring. CA was assessed by thigh-cuff test (autoregulation index – ARI) and phase shift (PS) in cross-spectral analysis of spontaneous oscillations of BP and BFV in basal cerebral arteries within the range of Mayer's waves. Data were processed with conventional statistical programs (Statistica 7.0 for Windows, Excel). Parametric (Student) and non-parametric (Kolmogorov-Smirnov) tests were used. Difference was considered to be statistically significant if p<0.05.

Extent of embolization was evaluated by intraoperative cerebral angiography. 16 patients had color Doppler of both internal carotid arteries (ICA) and vertebral arteries (VA) before and after surgery with evaluation of total flow index by ultrasound scanner Vivid E (USA). Thus, in patients with cerebral AVMs, flow velocity index (FVI_{norm}) was calculated. We also investigated 26 healthy volunteers (13 men and 13 women) with color Doppler of both ICA and VA to assess normal total flow index (FVI_{norm}), which was 661±91 mL/min for males and 560±82 mL/min for females. Then shunting blood flow was calculated as FVI_{shunt} = FVI_{total} - FVI_{norm}. FVI_{norm} was put in accordance with patients’ gender.

All patients were divided into three groups depending on the extent of embolization based on angiographic images. Seventeen (17) patients were included in the group with total AVM embolization, in whom 75–100% of AVM volume was excluded. Subtotal embolization (50–75%) was achieved in 14 patients. Partial occlusion of AVM (up to 50%) was performed in 16 patients.

Results

Preoperative study in all patients revealed decreased CA in basal cerebral artery feeding AVM. ARI was 1.8±0.7, PS was 0.3±0.2 rad.
Endovascular intervention and early postoperative period in all patients were without complications. In general, postoperative investigation showed positive dynamics of CA, the degree of which was different in groups. Patients with total exclusion of AVM from circulation in 15 cases (12 patients – I, II grades, 3 patients – III grade by Spetzler-Martin) had significant (p<0.05) increase of CA (ARI after surgery was 6.0±1.1, PS was 0.9±0.1 rad). Other 2 patients with total AVM occlusion (grade III by Spetzler-Martin) did not have significant changes in CA after surgery. Mean values of ARI and PS in entire group of total embolization were 4.6±1.4 and 0.9±0.2 rad respectively (p<0.05).

The dynamics of CA in patients with subtotal embolization (14 patients with AVM grade III) was also significant (p<0.05): postoperative ARI and PS were 3.6±0.5 and 0.7±0.1 rad, respectively.

Partial embolization was achieved in 5 patients with grade III AVM and in all patients with grade IV AVM (n=11). Changes of CA rate were insignificant (p>0.05) in these cases: ARI was 2.1±0.6, PS was 0.4±0.1 rad.

CA dynamics in relation with extent of AVM embolization is shown on the Figure 1. In patients with total AVM embolization much more considerable changes in PS and ARI (Figure 1b) were observed. A clear dependence was revealed in 16 patients comparing PS and shunting flow indexes obtained during preoperative investigation: in cases with a higher shunting flow PS in basal cerebral artery on the AVM side was less (Figure 2a). The same dependence during investigation of PS on the contralateral side was less significant (Figure 2b).

Results of investigation of a female patient (44 years old) with AVM in left frontal lobe fed through perforating vessels of left ACA are presented on the Figure 3. Before surgery PS was 0.4 rad, ARI was 2, FVI total was 947 mL/min. Both PS and ARI increased up to normal values (1.0 rad and 6, respectively) after total AVM embolization in one session of embolization by Onyx. FVI in left ICA decreased from 458 to 233 mL/min.

Results of investigation of a female patient (40 years-old) with AVM in left frontal lobe fed by left ACA are presented in Figure 4. Before surgery PS was 0.2 rad, ARI was 1, FVI total was 733 mL/min. PS did not change (0.5 rad) after total AVM occlusion in one session of embolization by Onyx. ARI was also 2. FVI total decreased insignificantly – to 618 mL/min. FVI in left MCA was reduced to 0.5 rad, ARI was 2, FVI total was 1221 mL/min. PS did not change after surgery (0.5 rad), ARI was 2. FVI total decreased significantly, to 920 mL/min. FVI in the right ICA decreased from 493 to 395 mL/min.

Discussion

There is no consensus in the literature concerning impairment of CA and cerebral perfusion in brain adjacent and distant to AVM, as well as significance of this impairment for presenting clinical symptoms, disease progression and prognosis of complications in the postoperative period.

There are studies in which authors assessed cerebral blood flow in patients with AVM with Xe133 inhalation using single photon-emission tomography. Signs of hypoperfusion in structurally intact zones of the brain distant to AVM have been revealed. The reason for decrease of blood flow in the perinidal zone and the contralateral side was explained by decrease of BP in proximal parts of afferent vessels, due to the presence of significant shunt through AVM and consequently a decrease of pressure on the level of arterial cerebral circle of Willis [15–17]. The latter in turn causes decrease of pressure in intact perinidal arteries and on the contralateral side, which in case of impairment of CA and cerebrovascular reactivity may be accompanied by reduction of cerebral blood flow. Young W.L. et al. [18] suggested that chronic hypotension in normal vascular zones adjacent to AVM induces adaptation of lower limit of CA, which provides constancy of blood flow. There is opinion that CA in the afferent vessel’s territory feeding both AVM and adjacent brain initially impaired since own AVM vessels lack CA ability due to altered histological structure of the vessel wall [19, 20].

Nowadays endovascular surgery is the preferred method of AVM treatment. Technology improvements, new types of embolizing materials in particular, make embolization more manageable. As a result, multi-stage opera-
Figure 2. Relations between shunting flow and phase shift (PS) (a) on the side of arteriovenous malformations (AVM), (b) contralateral side.

Figure 3. Carotid angiograms and results of color Doppler in the left internal carotid arteries (ICA) with calculation of flow index before (a) and after (b) total arteriovenous malformations (AVM) embolization by Onyx in a 40 year old patient (case 1) with AVM in the left frontal lobe.
flow in both AVMs. In case 1, FVI_{total} before embolization was increased by 2 times in comparison with normal values, which indicates high shunting flow through AVM nidus. In case 2, FVI_{total} before operation differed from normal values much less but was also higher. In case 1, AVM was supplied by MCA, in case 2 by ACA. Possible difference in AVM structure cannot be excluded as reason of dissimilarity of FVI_{total}. The aforementioned differences may have various mechanisms of influence on the vascular territory where AVM and perinidal zone are located, which in turn could lead to difference in CA rate dynamics in these cases: full recovery in case 1, and no change in case 2. It is not clear why in latter case CA didn’t improve after total embolization of AVM and still may affect state of CA postoperatively.

Further investigations should be directed to pathologic mechanisms determining circulation both in AVMs. In case 1, FVI_{total} before embolization was increased by 2 times in comparison with normal values, which indicates high shunting flow through AVM nidus. In case 2, FVI_{total} before operation differed from normal values much less but was also higher. In case 1, AVM was supplied by MCA, in case 2 by ACA. Possible difference in AVM structure cannot be excluded as reason of dissimilarity of FVI_{total}. The aforementioned differences may have various mechanisms of influence on the vascular territory where AVM and perinidal zone are located, which in turn could lead to difference in CA rate dynamics in these cases: full recovery in case 1, and no change in case 2. It is not clear why in latter case CA didn’t improve after total embolization of AVM. Possibly there are other factors besides shunting compromising circulation of perinidal zone (e.g. persistent ischemia due to inadequate collateral flow), which are not eliminated after total embolization of AVM and still may affect state of CA postoperatively.

Further investigations should be directed to pathologic mechanisms determining circulation both in AVMs.
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and surrounding brain. Detailed analysis of clinical symptoms, hemodynamics, CA dynamics in these patients in the perioperative period will explain causes of different treatment outcomes. The obtained results may be used for determination of surgical strategy, management of patients in the postoperative period, and prognosis of possible neurologic complications.

Conclusion

Assessment of the CA in AVM major feeding arteries, during staged exclusion of AVM from circulation (stepwise decrease of shunting process), will help to reveal true impairment of CA in the perinidal zone, to find the optimal surgical strategy, and to better predict treatment outcomes.

Abbreviations

ACA: Anterior cerebral artery; ARI: autoregulation index; AVM: Arteriovenous malformations; BFV: Blood flow velocity; BP: Blood pressure; CA: Cerebral autoregulation; FVI: Flow velocity index; ICA: Internal carotid arteries; MCA: Middle cerebral artery; PS: Phase shift; TCD: Transcranial Doppler; VA: Vertebral arteries

Competing interests

The authors declare no conflict of interest.

References

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Figure 4. Carotid angiograms and results of color Doppler in the left internal carotid arteries (ICA) with calculation of flow index before (a) and after (b) total arteriovenous malformations (AVM) embolization by Hystoacryl in a 45 year old patient (case 3) with AVM in the right temporal lobe.