Brain arteriovenous malformations

Arteriovske malformacije mozga

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dijagnoza; lečenje, ishod.

Definition

Brain arteriovenous malformation (bAVM) is a pathological arteriovenous communication 1. Morphological changes in this disease are localized on the level of blood vessel and possible changes in the surrounding parenchyma are only the consequence of changes of angioarchitecture and do not have neoplastic characteristics. Because of that, this disease terminologically has the name malformation and that is why the term angiom is incorrect since in that case it would correspond to neoplastic change 2.

Pathology

Macromorphology

Macrosopically arteriovenous malformation includes three segments: artery or arterial feeders, nidus and leading back vein or veins (Figure 1). Central part of bAVM is nidus which represents a network of vascular channels where arterioles and veins are connected directly without formed capillary network. Such nidus is on hemodynamic proximal end connected with artery and on distal end with drainage vein structures. Nidus can be of different forms and scope of its size ranges within an interval from microscopic size to the size of several centimetres 3, 4.

Etiology

During angiogenesis primitive artery forms lateral sprouts which separate from the artery and then join together into a blood vessel which shall become a vein. It is postu-
lated that defect in complete separation of the sprout from artery leads to formation of pathological communications of artery and vein which later grows into bAVM (Figure 2). Besides the stated it is probably the issue of multifactorial etiology where described embrional disorder is additionally burdened by the fact that some of genes responsible for angiogenesis are changed by separate nuclear polymorphism which represents the “second strike” on the normal angiogenesis.

Fig. 2 – Hierarchical model of development of brain arteriovenous malformations: experimental data indicate that arteries (A) and veins (V) by infusion are formed from a common precursor (1). Similarly, lymphatics (L) are derived from venous precursors. Differentiation disorder leads to arteriovenous (2) and venolymphatic (3) malformation.

Epidemiology

Basically, bAVM is a rare disease. Prevalence of bAVM in general population is difficult to determine exactly in a specific time point since there are no large post mortem studies which would also provide information on some people who have asymptomatic changes which could pass unnoticed during their lifetime. Therefore, the number of 0.94 newly discovered patients at every 100,000 inhabitants during one year should be considered as a reliable data in the context of patient number and organization of health care.

bAVM occurs more commonly in patients with Rendu-Osler-Weber syndrome where its prevalence is estimated between 4% and 13% and in rare Wyburn-Masin syndrome.

Division

bAVMs can be divided into three groups based on angioarchitecture, symptoms, prognosis and treatment.

Subpial bAVMs are the most common ones. They are localized under soft meninges, and size of nidus can range from several millimeters to several centimeters. They affect cortex and/or white matter. The form of nidus can be different, including regularly globular, ovoid, triangular, plate or completely irregular one. Arterial feeders originate from internal carotid artery branches (most commonly medial cerebral artery), vertebrobasilar branches but also branches of meningeal arteries originating from external carotid artery.

Surface pial bAVM is the most common in paediatric population and is composed of almost direct shunt. Flow is extremely strong with consequent venous dilatation. These are extremely rare lesions with great haemorrhagic potential.

Dural bAVMs are often incorrectly called dural AV fistulas. These are lesions which also include nidus localized in dural sinus. They represent about 10–15% of AVMs. Lesions of this type are most often acquired, and etiological factors are of wide spectrum including dural phlebitis, trauma, infection of paraendocranial structures (e.g. mastoiditis). Primary cause of dural bAVMs is venous hypertension. Nidus is most often small (few millimeters) and main changes which can be detected by imaging methods are located on arterial feeders and venous drainers.

Presentation

Regarding the symptoms, arteriovenous malformations can roughly be divided into hemorrhagic and non-hemorrhagic ones. There is also a group of those accidentally detected.

Hemorrhage

Intracranial hemorrhage is the most common presentation of bAVM seen in 30% to 82% of cases. This is also the most severe complication bAVMs. Blood can be found in subarachnoid space (30%), parenchyma (23%), intraventricular (16%) or in multiple mentioned locations (31%) (Figure 3). The risk of bleeding in previously non-ruptured bAVM is 2–4% per year, but in complex lesions the risks are higher.

Fig. 3 – Hemorrhagic presentation of brain arteriovenous malformations (bAVM): a) intracerebral hematoma; b) isolated intraventricular hematoma resulting from rupture of intraependymal bAVM; c) combined intracerebral and intraventricular hematoma; d) intracerebellar hematoma.
Factors facilitating hemorrhagic risk

Aneurysms

Aneurysms combined with bAVM appear in large series in 7–23% of cases. The reason of possible sub-detection can lay in the fact that not all patients are submitted to digital subtraction angiography (DSA), method regarded as the golden standard.

By definition, aneurysms are located on arteries while vein dilatations would be terminologically correctly to call varices or vein dilatations. However, in medical terminology, all dilatations of blood vessels in correlation with bAVM are called aneurysms.

Generally, aneurysms are divided into prenidal, nidal and postnidal ones. Prenidal aneurysms are further divided into: aneurysms independent of flow (aneurysms of arterial branches which bAVM does not belong to), distant flow dependent aneurysms (arterial aneurysms which belong to branches which vascularize bAVM but are at least one segment distant from nidus), close flow dependent aneurysms (aneurysms of branches that vascularize bAVM in close vicinity of nydus) (Figure 4). Vein aneurysms are the most common source of bleeding.

There is also a possibility of existence of pseudoaneurysms in nydus itself.

It is highly probable that aneurysms represent a weak point in angioarchitecture of bAVM and great number of studies analyzing the risk of hemorrhage in bAVMs have come to the conclusion that existence of aneurysms increases the risk of hemorrhage.

Nidus size

Many studies have tried to analyze nidus size as a risk factor of hemorrhage, but this issue has remained the matter of controversy until today. Significant number of studies show that hemorrhagic complications are more common with small niduses than with bigger ones. In this context two facts are to be mentioned for better understanding of the problem. Firstly, (against the theory that smaller bleed more often) bigger bAVMs more often give non-hemorrhagic symptoms and are being detected this way, so the share of hemorrhagic presentations with big bAVMs is significantly smaller than with small bAVMs which rarely give non-hemorrhagic manifestations and are more commonly detected due to bleeding. Secondly, (in favour of the theory that smaller ones bleed more often) blood pressure in small bAVMs is significantly higher than in big ones.

Deep venous drainage

Anatomy and subsequently hemodynamics are different in surface and deep venous drainage. In the external system, anastomosis of veins are better, thus the possibility of compensation of increased inflow of blood volume and higher pressure is increased. Unlike this well developed vessel network, internal veins without anastomoses direct blood only towards Galen’s vein and straight sinus. Such system has reduced capability of adaptation to hemodynamic factors which contribute to development of bleeding and because of that bAVMs with deep venous drainage are more prone to bleeding than those with surface drainage. Researches support the thesis that the risk of bleeding in cases of deep venous drainage is higher.

Venous stenosis

Reduction in diameter of draining veins results in increase of pressure in proximal vascular bed of bAVM causing higher risk of rupture. Increased risk of bleeding in cases of stenosis of drainage veins is confirmed in several studies.

Non-hemorrhagic manifestations

Epilepsy

This is the second most common symptom of bAVM. Most often it is the consequence of cortically located bAVMs in temporal zones in middle aged patients. These seizures may occur within nonhemorrhagic manifestations, in case of draining vein thrombophlebitis, but also due to hemorrhage and edema of surrounding brain tissue. According to frequency, it is an initial symptom in 16–53% of cases. They mostly present as partial attacks, while attacks of grand mal type occur in 27–35% of cases.
Headache

Headache is an initial symptom in 7–48% of cases. These headaches are not specific and distinction between typical migrainous attacks and headaches of bAVM origin cannot be made.

Focal neurological deficit

Effects that can cause focal neurological deficit are blood stealing phenomenon, venous hypertension and mass effect.

Regarding the stealing phenomenon, bAVM are lesions which recruit significantly greater quantities of blood per volume unit compared to brain parenchyma. Upon breaking compensatory mechanisms of intracranial circulation of surrounding zone of brain parenchyma due to blood deficit they become the source of focal neurological deficit. Characteristics of this deficit are in direct relation with localization of bAVM and function of surrounding brain parenchyma.

Mass effect is one of controversial issues related to bAVM. There are statements that these lesions do not produce mass, but targeted research proved its existence. This data is significant in explaining both the symptom of focal neurological deficit and for radiological differential diagnosis of intracranial lesions.

Accidental findings

There is a possibility of accidental detection of bAVM in patients referred to imaging for other reasons. In such cases, bAVM can be asymptomatic or the symptoms were not recognized. Such lesions account for about 25%.

Imaging methods

Aims of imaging methods are: diagnosis of bAVM in different clinical settings; pretherapeutic evaluation of bAVM facilitating easier decision making on the therapy type; treatment of bAVM by interventional radiology as an independent method or within multidisciplinary approach; posttherapeutic evaluation.

Computed tomography (CT)

Nonenhanced CT examination

CT is most often the first imaging method of evaluation of bAVM especially in cases of hemorrhagic presentation. This is mostly consequent to the organization of radiological service and usage of CT as the first diagnostic tool in brain emergencies. On CT scans, bAVM nidus can be slightly to moderately hyperdense. Calcifications may be observed as the consequence of previous minor bleedings. Surrounding zone of hypodensity may be present, corresponding to gliosis or, in case of breakthrough of compensatory mechanisms, edema.

In hemorrhagic presentation a characteristic image of subarachnoid, intracerebral and intraventricular hemorrhage is observed in different combinations, typically in the region around bAVM. When bAVM is suspected on nonenhanced CT, CT angiography (CTA) is performed.

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Computed tomography angiography (CTA)

CTA is a method able to analyze morphology of vascular network of bAVM. The principle of arterial visualization by CT is the same for all body regions, and always include administration of contrast agent. Contrast fills the lumen of vascular structures and allows visualization of feeding and draining vessels, as well as nidus itself, presented as conglomerate of tubular structures of contrast agent density.

As with all imaging methods there is a limit in diameter of a blood vessel which CTA can present. Therefore, small vascular structures cannot be visualized. This poses a problem in the treatment planning, since after embolization and change of hemodynamic properties, diameter of previously undetected feeders can increase and have impact on further change in morphology and dynamics of bAVM.

Another significant limitation of CTA, and all multi-phase CT examinations in general, is high irradiation dose.

Magnetic resonance imaging (MRI)

Basic MRI

Basic sequences (T1W, T2W, FLAIR, GRE) provide information similar to nonenhanced CT, about localization and characteristics of surrounding parenchyma and compartments. On T2W sequence blood vessels are presented as hypointense due to flow void phenomenon. The role of MRI in urgent protocol can be in revealing minimal acute subarachnoid hemorrhagic collections which are presented as hyperintense on FLAIR sequence. It is important to emphasize that, in non urgent protocols, hemosiderin deposits on GRE that are presented as hypointense are the sign of earlier hemorrhage. In this context differential diagnosis is important, however, comparison of former CT scan, which is in most cases available, makes the distinction possible.

Tissue specificity and better presentation of brain parenchyma are important advantages in analysis of surrounding brain tissue and especially in evaluation of edema which may originate as the consequence of hemorrhage or venous hypertension.

MR angiography

Time of flight and phase contrast MR angiography

Time of flight (TOF) and phase contrast MR angiography are methods which display lumen of bAVM blood vessels but they face numerous limitations. In many cases they are not capable of precise detection of anatomic change, measuring of nidus size is prone to errors, intranidal aneurysms are often invisible, and presentation of small drainage veins and blood vessels of small caliber in general is not uniformly good. As with other static methods, great disadvantage is incapability of lesion blood flow dynamics analysis.

4D MR angiography

4D MR angiography (4DMRA) is noninvasive imaging method with the goal to, besides morphology change, analyze dynamics of its blood flow by adding the fourth dimension (time) to the three dimensionality of the method of MR diagnostics by successive quick high number of acquisitions. Until appearance of 4DMRA the only method by which this dynamics could be evaluated was invasive angiography which, despite of its quality, has three negative characteristics which absolutely cannot be overcome: invasive nature, application of iodine agent and radiation risk. 4DMRA originated in the attempt to find the method similar to digital subtraction angiography but without above mentioned disadvantages. Preservation of temporal and spatial resolution is satisfactory and 4DMRA represents a method which shows great efficiency in diagnostics and anatomic analysis of bAVM with good interobserver and intermethod agreement.

The method provides characterization of not only important anatomic features such as size, localization and vascular feeding and draining components but also the analysis of blood flow. Also it is possible to obtain velocity-dependent mapping of brain blood flow with the possibility of marking blood vessels with different colors in correlation with the blood flow velocity. However, in comparison with digital subtraction angiography (DSA), it has a sensitivity of 73.7%, specificity of 100%, positive predictive value of 100% and negative predictive value of 78.3%, due to which DSA is still the golden standard.

Fig. 6 – Invasive digital subtraction angiography (DSA) and 4D magnetic resonance angiography (4D MRA) studies of the same patient. Arterial (a) and venous (b) phase of DSA examination. The arrow marks the nidus, and the arrow pointers the venous drainage. Arterial (c) and venous (d) phase 4D MRA examinations. Arrow indicates nidus. Significantly better display on the DSA method than the 4D MRA. However, the 4D MRA provides an overview of hemodynamics that, prior to its development, could be achieved only by using invasive angiographic techniques.

Functional MRI

Functional MRI is a method for determining activity of brain parenchyma during performance of certain activities.
such way, zones of brain parenchyma responsible for execution of certain activities are determined for every single examinee. This method is also applicable in analysis of brain parenchyma related to bAVM and determination of its eloquence. The eloquence of surrounding parenchyma is one of the risk factors in further therapy which shall be mentioned further in the text within the section on Spetzler-Martin classification.

**Digital subtraction angiography**

Digital subtraction angiography is invasive method which comprises catheterization of certain blood vessel, transcatheter application of iodine contrast agent and subsequent acquisition of x-ray images. During image processing all structures except administrated contrast agent are subtracted and deleted. In this method endocranial vascular structures are underlined and their presentation is obtained without contamination of images with surrounding structures. Despite development of non invasive imaging methods (CT, MRI) the quality of data about anatomy and hemodynamics of bAVM obtained by DSA is still superb.

Based on all mentioned, nowadays diagnosis of most bAVMs is based on non invasive imaging methods, while treatment planning is based on information obtained by DSA.

DSA is the invasive method bearing risk of ionizing radiation and iodine contrast. Also there are risks for medical staff due to the nature of the method, with possibility of contamination by patient’s blood and above mentioned ionizing radiation. Due to all mentioned, the rigorous protocol of the method must be fully respected.

Routinely, catheterization of external and internal carotid artery, as well as vertebral arteries is performed. Acquisition of images is performed in anteroposterior, profile and oblique position. Number of acquisitions in a second (f/s) should be adjusted to higher value (desired 7 f/s) due to improvement of possibilities for analysis of dynamics of vascular flow. However, one should bear in mind that greater number of acquisitions per second means greater exposure of a patient to ionizing radiation so that these values in circumstances when it is not absolutely necessary should be reduced to the level of 3 f/s.

The method also has certain disadvantages. Detection of aneurysms or intervascular communications within nidus is not perfect, neither is the possibility of analysis of nidus division into compartments in correlation with their vein drainage. The last mentioned occurs mostly due to application of contrast agent into big blood vessels thus imbibing the whole nidus with contrast and preventing analysis of bAVM. Overcoming of these deficiencies is tried by using superselective DSA during which catheterization of separate arteries nidus feeders is carried out. This allows for better analysis of nidus compartments as well as better analysis of vascular structures of nidus regarding aneurysms and intervascular communications in order to reduce superposition with surrounding vascular structures. Moreover, superselective DSA is the introduction into embolization of bAVM.

**Radiological report**

Diagnosis of bAVM is mostly determined on the basis of noninvasive radiological methods. Report of radiological CT or MR examination should include the following key elements: 1) size – nidus dimensions (depth, width, height) and, if possible, its volume in mm³ (attention should be paid to the distinction between nidus and vein component of BAM so that the last one is not included in calculation of nidus size; 2) localization – lobe and gyrus, depth (cortically and subcortically); supraor infratentorial; 3) venous drainage – one or more veins; deep or surface (cortical); 4) afferent arterial system: anterior, middle or posterior cerebral artery – branches of external carotid artery; 5) classification according to Spetzler-Martin – allows certain quantification of the degree of therapeutic risk; 6) signs of lesion complexity – recent or old hemorrhage; mass effect; perifocal edema; intranidal or distant thrombophlebitis; venous “aneurysms”, possible signs of venous thrombosis; arterial aneurysms.

**Classification**

Classification systems are made to stratify and classify bAVM into groups according to the desired factor. Factors by which classifications are determined are surgical risk (Spetzler-Martin) and individual risk from bleeding (Nataf).

**Classification according to Spetzler-Martin**

Numeric value is scored for each category. Size: small (less than 3 cm) – 1 point; medium (between 3 cm and 6 cm) – 2 points; big (bigger than 6 cm) – 3 points; Eloquency of surrounding brain parenchyma: non-eloquent zone – 0 points; eloquent zone – 1 point; venous drainage: surface only – 0 points; deep – 1 point.

Score obtained by this classification is within interval from 1 to 5 where higher values correspond to higher surgical risk.

**Classification according to Nataf**

Based on the study of 250 patients treated by radiotherapy this classification divides patients into five groups according to risk from bleeding which is determined by hemodynamic characteristics of bAVM: Grade 1 – without risk factor, divided in two subgrades (1a – with venous engagement, and 1b – without venous engagement); Grade 2 – venous stenosis or venous reflux; Grade 3 – only deep venous drainage, and Grade 4 – intranidal-ependymal aneurysms. Higher grade corresponds to higher risk from bleeding and distribution of bleeding according to grades is as follows: 13% for grade 1a, 38% for grade 1b, 48% for grade 2 and 90% for grades 3 and 4.

**Therapy**

Therapy for bAVM is complex, and absence of a single therapeutic method which would offer the cure makes the...
situation even more demanding. Therapeutic approaches are endovascular embolization, radiotherapy and surgery. Decision on the treatment modality depends on a large number of factors, the analysis of which should be performed by an experienced multidisciplinary team composed of diagnostic neuroradiologist, interventional neuroradiologist, radiation oncologist and neurosurgeon.

**Surgical therapy**

In urgent protocol with hemorrhagic presentation a surgical treatment may be indicated with the aim of removing life-threatening hematoma. In case of surface localization and small dimensions of bAVM it can be removed during this urgent procedure.

In elective surgery the aim of operation is complete recovery from AVM. The standard microscopic technique is used, and strategy is that the treatment of arteries is performed first, followed by nidus and drainage veins treatment. The success of the procedure is evaluated by postoperative imaging where complete absence of AVM is expected. In case of residual lesion, the decision on further therapy is brought multidisciplinary.

The outcome of surgical treatment on the basis of 25 series with 2,452 patients is as follows: mortality ranges from 0% to 15%, while postoperative morbidity from about 1% to 18%.

**Radiotherapy**

Radiotherapy is a noninvasive radiation method which cause proliferation of blood vessels endothelium with the aim of their obliteration by applying high energy beams on bAVM. This effect is not instant – it takes about six months for the first results to be detected, while the whole process lasts two to three years on average. It is proved that equal safety is achieved by using gamma knife, cyclotron or linear accelerator as the source of radiation.

Degree of obliteration is mostly connected with the nidus size, and with changes less than 15 mm it is 77%, with changes between 15 and 25 mm it is 62%, while for bigger than 25 mm it is 44%.

In radiological follow-up it is important to determine and analyze possible residue of the lesion and also to determine the existence of early and late radiation complications, such as disturbance of blood-brain barrier, edema and necrosis.

**Endovascular embolization**

Endovascular treatment of aneurysms is a part of therapeutic arsenal in multidisciplinary approach to the treatment of bAVM. Basically, it is a method where transcatheteric application of embolizing agent is delivered to bAVM with the aim of its occlusion.

Basic rules of endovascular treatment are as follows:
1) decision on therapy should always be brought by multidisciplinary team; 2) objective of treatment is to be determined: complete or partial occlusion or prevention of bleeding or improvement of clinical symptoms; 3) procedure must be explained to the patient and/or family or custodians in detail; 4) the procedure can be carried out only by experienced neurological team (neuroradiologist, neuroanesthesiologist and instrument staff); 5) a patient shall be monitored in the intensive care unit during 24 hours after the treatment; 6) today most of interventions are performed under general anesthesia.

**Intervention technique**

The basic concept of embolization is nidus and drainage veins occlusion. Arteries are allowed to be occluded on the level of distal arterioles. The principle of intranidal embolization assumes placement of microcatheter top into arterioles as close as possible to drainage veins in practically occlusive position. Catheterization has to be as distal as possible. Then, after control angiogram, where expected route of embolization agent is evaluated, the embolization itself is carried out with above mentioned objective of nidus and drainage veins occlusion (Figure 7).

**Fig. 7 – Endovascular embolization of brain arteriovenous malformations (bAVM).** (a) Digital subtraction angiography (DSA) catchment of the internal carotid artery; brain arterial malformations (bAVM) presentation occipital with demarcated arterial artery, nidus and drainage vein. (b) Superselective catheterization of the arteries of the feeder; the tip of the microcatheter in the embolization position. Phases of the embolisation application: before the first (c) and the last (d) control; (e) Targeted DSA region of BAM; displaying complete occlusion of nidus; (f) Control DSA of the carotid artery after the procedure.
**Material**

Rough division of materials is on catheters needed for catheterization of blood vessels and reaching desired location in bAVM and embolization material itself which is applied transcatheterically.

**Catheters**

Catheters are further divided into leading catheters, common catheters and microcatheters.

The function of common catheters, prior to intervention, is to make images of endocranial vasculature by catheterization of extracranial segments of carotid and vertebral arteries and then in some cases they serve as support for bringing the leading catheter. Common catheters are mostly of a diameter of 5F and according to the type of their distal end they are most often vertebral or SIM catheters.

Leading catheters are most often of a diameter of 6F and their function is to provide stability for microcatheter apparatus which is placed through them. Top of the leading catheter should be brought as close as possible to endocranium and with that goal their design is a compromise of hardness and elasticity – hardness because microcatheter needs strong support first of all on the long road from the location of puncture in femoral region to endocranium and then in endocranium where it acts without external support but its point of support for further progress it finds in the hardness of the leading catheter which is placed by its top just under endocranium. Elasticity of the leading catheter is needed to overcome demanding and often winding anatomy of aorta and aorta’s arch where it is often required to pass through curves of vascular structures whose angulation is in interval from blunt to extremely sharp angles. During embolization itself another role of the leading catheter is application of contrast agent with the aim of making control angiograms from which information about course of intervention in its different phases are obtained.

Microcatheters are the smallest of sets of catheters and their function is to reach nidus itself with the support of leading catheter in order to prevent embolization. Their diameter at distal end is most often 1.5 to 1.7 F and in the market microcatheters with top of diameter up to 1.3 F can be found. These are soft catheters, of extremely small diameter which are capable to catheterize even distal parts of curved intracranial vascular network by experienced hand using leading wires. Besides the fact that catheters are soft and atraumatic, their wall is equipped most often by nitinol strengthening which gives them certain rigidity thus preserving lumen width of microcatheter which is of key significance for application of embolization agent. Internal wall of microcatheter is such as to support the application of contrast agent and the whole design of some types is such that it helps blood flow in vascular bed. Top of a catheter can be fixed firmly to the rest of the catheter and according to type it can also have appropriate top which can be left glued to embolization material in order to enable pulling out of the rest of catheter after intervention.

**Embolization material**

Dominant embolization agent in practice today is Onyx. Generically, it is a mixture of ethylene-vinyl alcohol polymer (EVOH) and dimethyl sulfoxide (DMSO). EVOH dilutes in DMSO in different concentration from 6%, 6.5% and 8% thus obtaining substances of different viscosity which have different roles in embolization of bAVM. Radiological opacification required for performing the procedure under control of x-rays is achieved by application of tantalum powder. Just because of that later CT images are significantly contaminated by artifacts so that noninvasive imaging diagnostic follow up of patients treated by Onyx is directed to MRI.

Prior to usage of Onyx it is required to mix it at least 20 minutes to prevent tantalum powder settling thus resulting in weak opacification of agent. Catheters through which Onyx can be applied must be compatible with dimethyl sulfoxide (DMSO).

Advantage of Onyx in relation to other embolization agents and above all in relation to cyanoacrylic glues is that the risk from catheter gluing is reduced. This allows for greater quantity of embolization agent to be applied without replacement of the catheter. Also, Onyx behaves as liquid column without formation of drops independent from the main one.

**Complications**

Complications are divided to technical complications related to the procedure itself and clinical complications.

**Technical complications**

The most important technical complication is gluing the top of catheter to embolization agent and impossibility of its pulling out after intervention. Such scenario occurs in 4% of cases and can result in post embolization acute hemorrhage described below. There are two way of extraction: catheter traction by application of continually strengthening force until catheter is unglued or sudden strong traction of catheter. These methods are clearly related to different risks. With the aim of overcoming this issue catheters which are capable of separation of proximal end have been developed which remains confined to embolization agent but the rest of catheter can be pulled out.

Moreover, rupture of microcatheter by wire lead is possible, which must be recognized since through perforation made proximally from the top of catheter, embolization agent may be applied unwantedly thus causing ischemic complications.

Also, plugging of catheter lumen by embolization agent is possible when the whole catheter must be taken out and embolization is continued by application of a new catheter.

**Clinical complications**

Major risk of embolization of bAVM is post embolization acute bleeding. This can be the complication with mild but also devastating consequences and cause of its occurrence is embolization of drainage vein, postponed venous thrombosis, breakthrough of the level of normal perfusion...
pressure, rupture of intranidal aneurysm or breaking of the wall during manipulation or extraction of catheter 5.

In the study carried out on 564 patients who were treated in 1,569 procedures, acute bleeding after embolization occurred in 1% of embolizations or 3% of patients 40.

Some of angiographic characteristics can predict development of bleeding: occlusion or slow contrast flow in drainage vein, contrast stagnation in nidus, almost complete occlusion of small bAVM with persisting small nidus and occlusion of big direct fistula in nidus. With the aim of preventing bleeding, the treatment of bAVM should be divided into several interventions except for grade 1 where whole lesion can be embolized in one act. If the vein has to be preserved then application of embolization agent should be stopped for several seconds when it reaches the vein and then continue with nidus filling. Also in the first act, weak points of the lesion are treated in 1,569 procedures, acute bleeding after embolization occurred in 1% of embolizations or 3% of patients 40.

Another complication is ischaemia of brain parenchyma caused by embolization of arteries proximally from nidus. It occurs rarely and clinical consequences are milder 5.

Results of endovascular embolization

The results of embolization of AVM by usage of embolization agent Onyx were evaluated in the study carried out from 2005 to 2007 which included 117 patients. Complete occlusion was achieved in 23.5% of cases, occlusion 75–99% of the lesion in 33.9% of cases, occlusion 50–75% of the lesion in 27.8% of cases, and occlusion less than half of the lesion in 14.8% of cases. Total perioperative mortality was 4.3%. Additional treatment was carried out in 82.3% of cases of incomplete embolization and mostly by usage of radio-surgical methods 41.

Conclusion

Brain arteriovenous malformation is a rare disease of endocranialvascular system with complex morphology and hemodynamics. The most difficult complication is intracranial bleeding which is a major cause of mortality and morbidity as the consequence of bAVM. Noninvasive imaging diagnostics (CT and MRI) offers excellent possibilities of presentation of complications and acceptable possibilities in diagnostics of vascular morphology of bAVM. Golden standard in diagnostics of vascular anatomy of bAVM is invasive angiography (DSA). Therapy of a lesion is multidisciplinary and is carried out by endovascular embolization, radiotherapy and surgical intervention.

REFERENCES

21. Spotlger RF, Hazravas RW, McCormick PW, Zahranakis JM, Filan RA, Zimmerman RA. Relationship of perfusion pressure and


27. Stojanovic S. Computerized abdominal and pelvic tomography. 1st ed. Novi Sad: Simbol; 2016. (Serbian)


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