Complication Analysis of 469 Brain Arteriovenous Malformations Treated with N-Butyl Cyanoacrylate

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Summary

We independently assessed the frequency, severity and determinants of neurological deficits after endovascular embolization with NBCA of brain arteriovenous malformations (BAVMs) to have a better basis for making treatment decisions. All the charts of 469 BAVMs patients who underwent embolization with NBCA were reviewed. We analyzed the complications and their relation to angiographic features. The 469 patients were treated with 1108 endovascular procedures. Each met one to eight times, average 2.3 times. Eleven patients showed treatment-related complications, including four haemorrhagic and seven ischemic complications. Of these 11 cases, two died, two had persistent disabling deficits, and another seven suffered transient neurological deficits.

Our finding suggests a low rate of disabling treatment complications for embolization of brain AVMs with NBCA in this center. The management of AVM patients who have high risk of embolization therapy should be treated by special strategy.

Introduction

Treatment decisions for patients with brain arteriovenous malformations (BAVMs) are based on natural-course risk estimates weighed against outcome data from invasive interven-

tion. At present, both remain incompletely defined. Over the last decade, advances in the superselective microcatheterization technique have established endovascular techniques as an integral and indispensable tool in the treatment of BAVMs. To date, the risk and determinants of complications from endovascular treatment have not been well described^{1,3}.

Retrospectively studying our 469 BAVMs patients who underwent embolization with NBCA, we analyzed the risk of complications and the determinants of treatment-related neurological deficits.

Patients and Techniques

Since 1988, a series of 469 brain AVM patients were treated by endovascular embolization with NBCA at our institute. They comprised 296 male and 173 female patients with a mean age of 33.1 years (range 7-63 years). 278 patients sought medical advice for a sudden intracerebral haemorrhage, 47 for headache, 106 for epilepsy and 38 for gradual neurological deficit or other symptoms. According the Spetzler-Martin Grading Scale, there were seventy-one cases of grade I, 97 of grade II, 192 of grade III, 82 of grade IV, and 27 of grade V. The 469 patients were treated with 1108 endovascular procedures. Each met one to eight times, average 2.3 times. With the patients under local anesthesia and sedation, the nidus was reached

with a 1.5-Fr or 1.8-Fr Magic microcatheter (Balt, France) and sometimes assisted by a Terumo 0.010" guide wire. During the procedure, systemic heparinization was added to the treatment protocol, and the whole coaxial system was continuously flushed with saline via an infusion pump. Under real-time road-mapping or DSA, NBCA injection was performed only when the tip of the microcatheter was wedged into the nidus of the AVMS with no reflux of contrast proximally. Embolization was performed in all cases and then surgical resection in 32 patients or radiosurgery in 117 patients.

For this study, all the charts of 469 BAVMs patients who underwent embolization with NBCA were reviewed, and 11 patients who suffered complications associated with NBCA embolization were identified. The complications included ischemia and haemorrhagic (within two weeks after embolization). Based on the clinical situation three months after embolization, complications were classified as transient, minor permanent, severe permanent neurological deficit, vegetative state, and death.

Results

One hundred and fifty-six patients (33%) were cured with embolization alone, 198 achieved 80%-99% volume reduction, and 104 achieved 60%-79% reduction, and 11 below 60%. Eleven patients showed treatment-related complications, including four haemorrhagic and

seven ischemic complications. Among four bleeding patients, two died—one was in a vegetative state, and one fully recovered in three months. Among seven ischemic patients, one developed permanent neurological deficit, another six patients had a transient neurological deficit that disappeared within three months. Because cranial CT scan was not performed routinely for every patient after embolization, patients who suffered a slight haemorrhage without obvious symptoms may have been neglected.

Severe complications included death, vegetative state, and major permanent neurological deficits. Mild complications included minor permanent and transient neurological deficits. So the severe complication rate resulting from embolization was 0.7%, the mortality was 0.5% and the mild complication rate was 1.4%. The total complication rate was 2.4%.

Discussion

With advances in superselective microcatheterization techniques and advanced knowledge on the angioarchitecture of BAVMs, endovascular embolization has gained a significant role in the multimodality treatment of brain AVMs⁴. Since 1988, we have performed embolizations on 469 patients by the following treatment strategy⁵⁻⁷. Achieving a true cure by embolization alone. In our group, about 33% of patients were cured by embolization alone. Presurgical embolization achieved by blocking

Figure 1 A,B, Lateral left ICA angiograms before embolization. A) Arterial phase showed a Spetzler grade II AVM in the parietal region. B) Venous phase demonstrated the stenoses of the main draining vein. C,D) Lateral left ICA angiograms after embolization. C) Arterial phase showing the nidus significantly reduced. D) Venous phase demonstrating the main drainage vein is completely occluded (arrow). E) Lateral skull films showed the glue cast after embolization. F) Twenty-four hours later, CT scan revealed intracerebral haematoma in the left parietal lobe.

the problematic feeders as well as the collateral supply to dry the surgical fields. Embolization to permanently reduce the nidus volume or eradicate various types of weak angioarchitectural elements, and diminish the high flow of the vascular malformation, in an effort to reduce the risk of haemorrhage so that radiosurgery can be performed with high curative

rate and low risk. Palliative embolization used in symptomatic large AVMs (6 cm) which usually had a high treatment risk with any treatment modality, to ameliorate the clinical condition or reduce the potential risk of haemorrhage.

Notwithstanding the considerable strides made in the field of endovascular embolotherapy of brain AVMs, the embolization of

Figure 2 A) CT scan showed SAH. B) Lateral right ICA angiograms demonstrated an ICA-PcoA aneurysm and a Spetzler grade IV AVM. C) Post-embolization angiograms showed that parts of the nidus were glued, but the ICA-PcoA aneurysm was untreated. DD CT scan revealed severe SAH and intracerebral haematoma.

BAVMs, as currently practiced, continues to carry a significant intrinsic risk of transient or permanent neurological deficits or death². The rate of treatment-related permanent neurological deficits and death culled from the literature ranges from 2.6% to 18%, depending on the

material used to obliterate the malformation, the means of delivering the occlusive agent, and patient selection. In our group, the complication rate was 2.4%, which was lower than published data.

Haemorrhage during or after embolization is

the most life-threatening sequela of endovascular embolotherapy for BAVMs. In our group, four patients suffered peri- or post-embolization intracranial haemorrhage. The mechanisms that result in peri- and post-embolization include^{8,10}: venous outflow obstruction; intranidal and extranidal rerouting of blood flow; 'normal perfusion pressure breakthrough'; traumatic microcatheter or microguidewire manipulation; and cementing of the catheter in the vessel.

Occlusion of the draining venous outlet during embolization of AVMs with NBCA can be devastating^{8,10}. Hademenos GJ et Al¹¹ employed a biomathematical AVM model using electrical network analysis and noted that impairment of total drainage of AVM induced a rapid redistribution of blood into the weak plexiform vessels of the residues of the nidus, causing a haemodynamic overload and an increased of rupture. In our group, a 45-year-old woman was diagnosed with a Spetzler grade II AVM of the left lobe within the motor cortex. The main feature of the lesion was that the main draining vein was stenosed at the junction as it entered the superior sagittal sinus (figure 1A,B). Angiogram after embolization with 1.0 ml of 50% NBCA showed that a piece of glue was blocked at the stenosis point and the draining vein was occluded (figure 1C to E). We realized the danger of impairment to the main drainage system, so the patient was sedated and transferred to the neuro-ICU for monitoring, and the systolic blood pressure kept to below 90 mmHg. Unfortunately, although we had taken these measures, the patient suffered a large volume intracerebral haemorrhage identified by CT scan 24 hours later (figure 1F). The haematoma was evacuated in emergency, but the patient suffered second haemorrhage two days later and became comatose. After another operated to evacuate the hematoma and remove the residues of AVM, the patient remained comatose and had maintained a vegetative state one year later.

However, embolization of a draining vein does not always lead to complications. The risk of bleeding after the drainage system is impaired depended on the dynamic importance of the occluded draining vein and flow changes through the nidus^{11,12}. If NBCA embolization is chosen, the risk is minimized by using diluted glue, injecting slowly, and employing the technique of pausing for two or three seconds if glue passes into the draining vein. In AVM associat-

ed with a marked venous outflow obstruction, the initial embolization is aimed at diminishing the flow through the nidus compartment draining through the stenosed or ecstatic vein. In the unwanted instance of venous outflow occlusion during embolization, the patient should be sedated and monitored carefully, and blood pressure maintained below 90 mmHg for 48-72 hours. If the total drainage is severely impaired, emergency surgical excision of the residues of the nidus may be a wise choice.

Extranidal and intranidal rerouting of haemodynamics from embolization of BAVMs is responsible for some iatrogenic haemorrhagic complications^{12,14}. Handa et Al¹³, investigating the pressure in 47 arteries feeding 21 BAVMs during transarterial embolization using microcatheters, found that systolic pressure increased by 22 mmHg on average, and that feeding artery pressure increased significantly more in well-embolized than in poorly embolized vessels. Also, Gao et Al¹⁴ noted that partial nidus embolization causes more proximal elevation of pressure within arterial feeders. Intranidal rerouting of blood flow and pressure elevation in artery caused by embolization may result in the fragile part of AVM, such as the aneurysms situated within the nidus or feeders.

In our experience, two patients died from the rupture of associated aneurysms peri- or post-embolization. One case was a 15-year-old male. His cerebral angiogram showed multiple associated aneurysms situated either in close proximity to the nidus or within the nidus. The vessel harboring the aneurysm was selected for embolization first, in an attempt to include the aneurysm in the glue cast. Although the aneurysm within the nidus was glued at the same time, the aneurysm on the feeding artery was missed. Another embolization was tried to occlude the aneurysm, but failed. Two hours after the embolization, the patient suffered severe intracerebral haemorrhage and died two days later. Another case was a 40-year-old man who presented with SAH (figure 2A). Right ICA angiography revealed a large AVM in the right brain accompanied by an ICA-PcoA aneurysm (figure 2B). Because of the mistaken therapy tactics, we performed the endovascular embolization of the nidus of the AVM with NBCA. Just after the embolization, the patient's blood pressure suddenly rose significantly and emergency CT scan showed a more massive SAH and ICH (figure 2D). Although

prompt therapy was instituted, the patient died.

About 10% to 20% brain AVMs accompany associated aneurysms¹⁵⁻¹⁷. The treatment strategy was described by Meisel et al¹⁸ who observed shrinkage of arterial aneurysms after endovascular treatment of AVM and concluded that the aneurysms should not be the primary targets compared with AVMs. On the contrary, Piotin and Moret¹⁹, who considered that proximal aneurysms with AVMs have a greater propensity to rupture when compare with aneurysms in patients without AVM, suggested proximal AVM-associated aneurysms should be treated first, especially when the aneurysm has been identified as a source of haemorrhage. Intranidal or feeding artery aneurysms are the fragile part in BAVMs. On the basis of our experience, as the increasing flow and pressure in the residual nidus and feeding artery after partial embolization raise the risk of fragile structure rupture, the aneurysm and other fragile parts should be embolized first. In the case of intranidal aneurysm or flow-related feeder aneurysms in close proximity to the nidus, the vessel harboring the aneurysms is the vessel selected first for embolization, in an attempt to include the aneurysms in the glue cast. In a feeder aneurysm that is not in close proximity to the nidus or a flow-related aneurysm in the circle of Willis, coil occlusion should be undertaken before embolizing the nidus^{12,14-17}.

Despite the significance of normal perfusion pressure breakthrough being in question and its pathophysiological basis yet to be substantiated, there are several reported series in which this complication constitutes the major cause for morbidity and mortality unrelated to technical error²⁰. The NPPB is considered to occur when the high-flow shunt of the AVM is occluded and nearby normal brain and its capillary bed are exposed to normal perfusion pressure⁸⁻¹⁰. These nearby structures have lost the ability of autoregulation as a result of chronic hypoperfusion and may be incapable of responding to the tremendous rise in local flow. This results in edema formation and possibly in haemorrhage. One case in our series suffered post-embolization intracranial haemorrhage because of NPPB, the diagnosis was derived by the process of excluding reasonable alternative explanations for haemorrhage. No direct evidence for the existence of NPPB was derived from this case. After active treatment, the patient was discharged without neurological deficits.

To minimize the risk of NPPB, patients with large high-flow AVM and multiple large feeding vessels should be embolized in stages, and the systolic arterial pressure maintained at 15% to 20% below baseline during the first 24 hours after embolization. Subsequent embolizations are performed at approximately three to four week intervals. The rationale for this is to allow stabilization of the altered cerebral haemodynamics that occurs after embolization.

In our group, no vessel perforation occurred, that was the benefit of flow-directed microcatheters which can advance through the vasculature into the nidus without the guiding of guidewire.

Gluing the tip of the microcatheter in the nidus of AVM is a problem specific to the use of glue. The abrupt withdrawal of the guide catheter and magic is mandatory for if the microcatheter is glued within the nidus, abrupt withdrawal will break the microcatheter in its middle to distal segment and decrease the risk of rupture of the nidus¹⁰. Also, the risk of gluing can be minimized by ensuring that the catheter tip is wedged, preventing glue reflux, and using diluted glue mixture¹⁰. We had glued one microcatheter in our series, and the microcatheter was broken and the distal segment retained in the cerebral vasculature. By six months anticoagulation, no permanent neurologic sequelae had been observed during six years follow-up.

First and foremost, when an intracranial haemorrhage occurs, anticoagulation must be reversed immediately. If the bleeding point is identified by angiography, immediate occlusion of the ruptured vessel using coil or glue is necessary. Then emergency cranial CT scan is mandatory. Depending on the CT result and the clinical status, evacuation of the hematoma or conservative therapy can be chosen¹⁰.

Ischemic complications mainly occur from nontarget occlusion². There were five cases of cerebral ischemia for this reason. In three of those patients, the microcatheter tip wedged in the distal aspect of the feeder and not directly within the nidus. Although no normal vessel branches were found in superselective angiography, some small normal parenchymal branches originating from the feeder were opacified and cast by glue when injecting NBCA. These three patients had transient neurological deficit, and they recovered completely within three months.

Figure 3 A) Lateral oblique view of a right ICA angiogram demonstrated an ischemic area in the right frontal lobe. B) Postembolization oblique angiogram showed the callomarginal artery demonstrated in figure A (arrowhead) was occluded. C,D) A day later, CT demonstrated the cast of nidus and the cast of the callomarginal artery. Also the low density infarct lesion was noted in the anterior callosomarginal region of the right frontal lobe.

Reflux of NBCA into normal cerebral vasculature during embolization occurred in another two patients. One patient had complete hemianopia that was evident three months after embolization. The other had a mild hemiparesis

that cleared up one week later (figure 3A-D). Wedge positioning of the microcatheter at or within the nidus of the AVM, with more diluted NBCA, allows for longer injection times and greater control of the injection. If wedge posi-

tioning is not possible, only when no normal parenchymal vessels are opacified with the test injection and the AVM is located in a noneloquent area or functional testing is negative, can embolization proceed. If a passage feeding artery is due to be embolized, the tip of the microcatheter should be wedged in the feeder at least 5 mm distal to the branch point with the vessel of passage. These measures can minimize the risk of nontarget occlusion^{2,21}.

Cerebral ischemia also may occur from catheter-induced thrombotic emboli. Systemic heparinization and continuous flush of the whole coaxial system with saline, can minimize the risk of catheter-induced thrombotic emboli². When a larger feeder is occluded and leaving the huge trunk from which it is supplied to only a small normal branch or two, heparinization should be

maintained for 48 to 72 hours to prevent retrograde thrombosis.

Conclusions

In our group, 33% of patients with brain AVMs were cured by embolization by NBCA alone with a severe morbidity of 0.7% and a mortality of 0.5%. Our findings suggest a low rate of disabling treatment complications in this center for endovascular brain AVM treatment. Also, our study showed that high-grade stenosis of draining veins, flow-related aneurysms, and passage feeder, etc, were high risk angioarchitectural elements to embolization of BAVMs with NBCA. In these patients, a special treatment strategy should be adopted according to the angioarchitectural features.

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