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ORIGINAL ARTICLE

Injection of N-butyl Cyanoacrylate Through a Dual-Lumen Balloon for Embolization of High-flow Intranidal Fistulas in Brain Arteriovenous Malformations: Technical Note

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Abstract

Purpose N-butyl cyanoacrylate (NBCA) glue is a valuable liquid embolic agent for the endovascular treatment of brain arteriovenous malformations (BAVM). The use of NBCA carries a risk of embolic agent reflux and distal migration with ensuing possibility of venous drainage compromise. The aim of this technical note is to describe a single center case series of high-flow intranidal fistulas embolized though a dual lumen balloon under local flow-arrest conditions.

Methods This article presents a retrospective description of a case series including five NBCA injections through a dual lumen balloon performed by a single operator in three patients with BAVM. Demographic, clinical, imaging and procedure-related data are reported.

Results The three patients presented with ruptured BAVMs. Of the patients, one underwent proximal flow-related ruptured aneurysm coiling before planned BAVM embolization. In the three patients, staged BAVM embolization as a first line treatment was decided. Preliminary embolization of high-flow BAVM fistulas by NBCA using a dual lumen balloon under local flow-arrest conditions was performed and five separate injections were carried out without any complications. No balloon entrapment or rupture was observed.

Conclusion High-flow BAVM fistulas can be treated with NBCA embolization using a dual lumen balloon under local flow-arrest conditions.

Keywords Arteriovenous malformation · Dual lumen balloon · Embolization · Fistula · N-butyl cyanoacrylate

Introduction

Brain arteriovenous malformations (BAVM) are some of the most challenging cerebrovascular disorders to manage. Rupture is the major source of morbidity and mortality [1]. Only complete and definitive nidus obliteration protects against BAVM-related hemorrhage [2]. Several strategies are available to achieve this goal, including surgical excision, stereotactic radiosurgery, embolization or a combination of these different treatment options. The choice of the treatment modality depends on a variety of factors including BAVM angioarchitecture, presentation and surgeon experience. Since the first description of BAVM embolization with methylmethacrylate particles through a carotid arteriotomy in the 1960s [3], great progress and refinement have been achieved in the field of interventional neuroradiology. Embolization can be performed as a sole treatment with a curative goal, as an adjunct before surgery or radiosurgery for nidal reduction or to target specific angioarchitectural features, such as flow-related or nidal aneurysms [4]. Embolization of high-flow intranidal fistulas can be particularly challenging. Several embolic agents have been used to embolize high-flow fistulas, including detachable balloons, glue and coils [5–8]. For several decades now, acrylic glue, originally isobutyl 2-cyanoacrylate (IBCA) and subsequently N-butyl cyanoacrylate (NBCA), has been

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widely used for BAVM embolization [9–11]. Embolization of NBCA carries a number of technical difficulties including risk of reflux, proximal embolization, glue cast fragmentation, microcatheter rupture, microcatheter adhesion and glue adhesion during microcatheter retrieval [12–14]. Distal migration of the embolic agent into the venous compartment of the BAVM prior to nidal occlusion can lead to significant hemorrhagic complications [5]. The risk of distal migration is dramatically increased in patients with high-flow intranidal fistulas. Dual lumen balloons have been used for direct coiling and injection of liquid embolic agents such as Onyx (Medtronic, Dublin, Ireland) [15–19]. Onyx and related liquid embolic agents have gained more popularity in recent times but glue injection is still relevant in a number of situations. The aim of this study was to describe a single center case series of high-flow intranidal fistulas embolized though a dual lumen balloon under local flow-arrest conditions.

Methods

Ethical Statement

This work adheres to the World Medical Association Declaration of Helsinki.

Patients and Embolization Procedures

Single center retrospective records review of patients with BAVM treated by embolization between 1 January 2015 and 30 April 2018, was performed. During this time frame, a single senior operator (NS) performed 6 NBCA injections in 4 patients using the technique described. Of the patients, two gave consent for publication and a third patient was deceased at the time of manuscript preparation. Data regarding the 4th patient who refused permission for publication are not included in this report. The three patients included presented with ruptured BAVM. The decision to embolize was taken by a multidisciplinary team including interventional neuroradiologists, neurosurgeons, and anesthesiologists based on clinical and radiological data, such as computed tomography (CT) scan, magnetic resonance imaging (MRI), digital subtraction angiography (DSA) and 3D rotational angiography. Staged embolization was planned. Treatment was delayed after rehabilitation according to standard practice at this institution. All procedures were performed in a biplane angio suite with the patient under general anesthesia with intravenous heparinization. A 6 French Envoy (Codman, Reynham MA, USA) guiding catheter was introduced through a 6 French femoral access. The guiding catheter was placed distally in the cervical vertebral artery or internal carotid artery. A long nose Eclipse 2L (Balt, Montmorency, France) 6/9 mm hypercompliant dual-lumen balloon microcatheter was navigated over a 0.014-inch microguide wire as closely as possible to the shunting point of the high-flow fistula. After balloon inflation with a 1:1 mixture of saline and contrast medium solution, a contrast injection through the balloon working lumen was performed to analyze the downstream vascular bed. The working lumen dead space was rinsed with 5% dextrose. A 1:2 NBCA Glubran 2 (GEM, Viareggio, Italy) and lipiodol (Guerbet, Villepinte, France) solution was subsequently injected under flow-arrest via balloon inflation. In cases of NBCA reflux along the distal tip of the dual lumen balloon, which was observed even with balloon inflation, the balloon was temporarily deflated, then reinflated to continue with the glue injection. Deflation was permitted by the fact that glue injection under flow-arrest is slower that under free-flow, similar to injection under wedge conditions.

Results

A total of three patients (2 female and 1 male) were included in the study. The clinical and demographic features of the patients are summarized in Table 1. In all cases, the balloon

Table 1 Patient characteristics and procedures

Case no.	Demographics	Presentation	AVM location	Spetzler-Martin grade	Previous treatment (before balloon-aided embolization)	Procedure-related (balloon embolization) complications
1	70-year-old male patient	Ruptured	Left frontal	III	None	None
2	46-year-old female patient	Rupture of a proximal (basilar) flow-related aneurysm	Right parieto-occipital	IV	Coiling of the ruptured proximal flow-related aneurysm	None
3	37-year-old female patient	Ruptured	Left internal temporal	III	None	None

AVM arteriovenous malformation

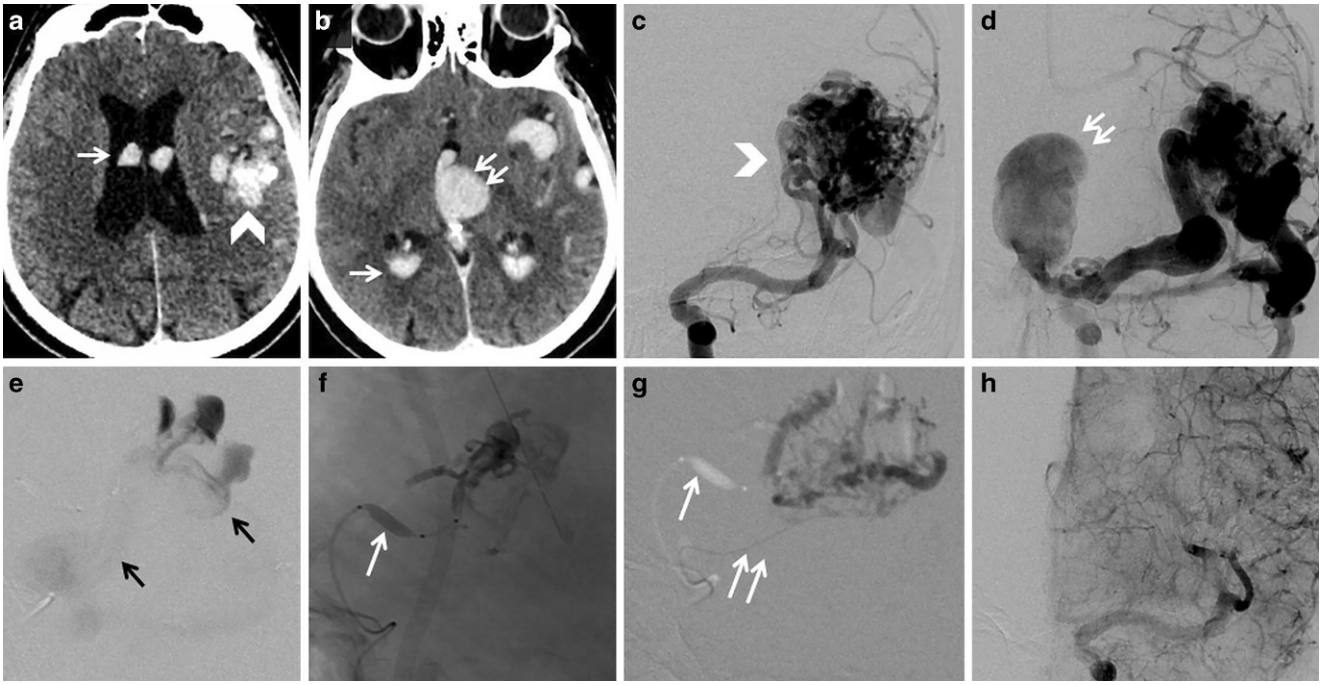

Fig. 1 Balloon-aided N-butyl cyanoacrylate (NBCA) embolization of a high-flow intranidal arteriovenous shunt in a left frontal brain arteriovenous malformation (BAVM). **a** and **b** Patient 1 was admitted for spontaneous intra-ventricular hemorrhage (*white arrow*) related to a left frontal BAVM (*white arrowhead*) draining in a deep venous varix (*double white arrows*) as demonstrated on a head angio-CT scan. **c** and **d** Anteroposterior projection of the left carotid artery digital subtraction angiography (DSA) confirmed the presence of a left frontal BAVM (*white arrowhead*) draining in a deep venous varix (*double white arrows*). **e** After initial accessory arterial feeder embolization through a flow-guided Magic 1.2 (Balt) microcatheter, the main feeder artery was catheterized with a long nose Eclipse 2L (Balt) 6/9 mm dual lumen balloon microcatheter. Selective angiography after balloon inflation demonstrated a high-flow intranidal arteriovenous fistula with immediate venous opacification (*black arrows*). **f** Balloon inflation (*white arrow*) allowed local flow arrest and NBCA injection without inopportune venous progression. **g** Glue cast showing both fistula embolization and adequate nidal progression after removal of the Eclipse 2L balloon (Balt) (*white arrow*). Note that a second flow-guided Magic 1.2 (Balt) microcatheter (*double white arrows*) was previously positioned to complete nidal occlusion from another pedicle. **h** Final control showing near complete BAVM obliteration and disappearance of the large varicose draining vein

could be navigated over a 0.014-inch Traxcess microguide wire (Microvention, Aliso Viejo, CA, USA) through an arterial feeder close to the shunt point. A total of five balloon-aided NBCA injections into high-flow arteriovenous fistulas were performed. In all cases, balloon inflation allowed local flow-arrest. All injections through the dual lumen balloon led to definitive occlusion of the intranidal high-flow arteriovenous fistula. No distal migration threatening the venous outflow occurred during the five injections under flow-arrest conditions. No microcatheter entrapment or balloon rupture occurred. All five injections and related procedures were uneventful. Figs. 1 and 2 demonstrate NBCA injections through a 6/9 mm Eclipse dual lumen balloon. A long nose balloon microcatheter (7 mm distal tip beyond the balloon) was chosen to decrease the risk of NBCA reflux and contact with the balloon surface.

Patient 1 was a 70-year-old male, admitted for spontaneous intraventricular hemorrhage related to a left frontal Spetzler-Martin III BAVM draining in a deep venous varix (Fig. 1). It was decided to treat the ruptured BAVM by embolization after rehabilitation but early intraventricular rebleeding on day 24 prompted rapid intervention. The intervention allowed successful high-flow fistula occlusion and near complete BAVM obliteration and disappearance of the large varicose draining vein. The patient died a few months later of an unrelated cause.

Patient 2 was a 46-year-old female with a right parietooccipital Spetzler-Martin IV BAVM, admitted for spontaneous subarachnoid hemorrhage related to a proximal basilar flow-related aneurysm rupture. The aneurysm was treated by coiling in the acute phase. After rehabilitation, the staged BAVM embolization was decided. High-flow fistulas were successfully targeted by embolization as demonstrated in Fig. 2 with final control showing residual shunting. A third embolization session by standard flow-guided NBCA injection was complicated by distal migration of the embolic material, venous drainage compromise and subsequent postprocedural hematoma. Further treatment will be discussed after rehabilitation.

Patient 3 was a 37-year-old female with a left temporal Spetzler-Martin III BAVM, admitted for isolated intraventricular hemorrhage. After rehabilitation, the patient under-

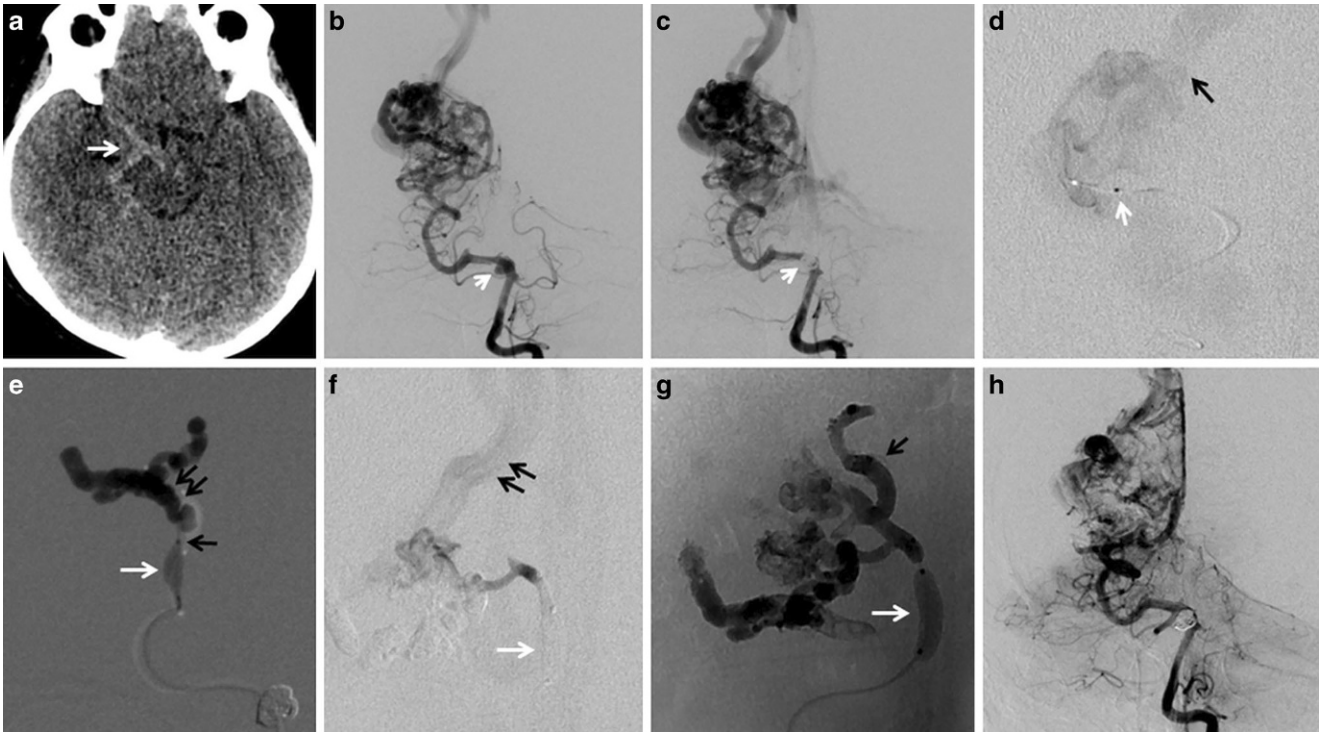

Fig. 2 Balloon-aided N-butyl cyanoacrylate (NBCA) embolization of a high-flow intranidal arteriovenous shunt in a right parietooccipital brain arteriovenous malformation (BAVM). **a** Patient 2 was admitted for spontaneous subarachnoid hemorrhage (*white arrow*) as demonstrated on a head CT scan. **b** Anteroposterior projection of the left vertebral artery digital subtraction angiography (DSA) demonstrated a right parietooccipital BAVM with a ruptured proximal basilar artery flow-related aneurysm (*white arrow*). **c** Acute phase aneurysm coiling was undertaken without complications (*white arrow*). **d** Selective catheterization and DSA through a flow-guided Magic 1.2 (Balt) microcatheter (*white arrow* showing the microcatheter tip) demonstrated a high flow intranidal arteriovenous fistula with minimal plexiform nidal interposition and rapid venous opacification (*black arrow*). **e** A long nose Eclipse 2L (Balt) 6/9 mm dual lumen balloon microcatheter was navigated distally. Balloon inflation (*white arrow*) allowed NBCA injection (*double black arrows*) under local flow-arrest conditions without inopportune venous progression. The *black arrow* shows the nose beyond the inflated balloon. **f** A second arterial branch was catheterized distally with an Eclipse balloon and selective angiography under local flow-arrest with the inflated balloon (*white arrow*) demonstrated a second high-flow intranidal arteriovenous fistula with minimal plexiform nidal interposition and rapid venous opacification (*black arrow*). **g** Unsubtracted image showing the inflated balloon (*white arrow*) and glue cast (*black arrow*). **h** Final control showing residual shunting

went a first embolization session allowing successful occlusion of high-flow fistulas. A later embolization session, using standard flow-guided embolization was complicated by NBCA reflux in the left posterior cerebral artery, leading to an occipital infarction with symptomatic hemianopia. The residual nidus was treated by stereotactic radiosurgery and the patient is awaiting MRI control.

Discussion

This case series supports the feasibility of embolization of high-flow intranidal fistulas with NBCA using a dual lumen balloon under local flow-arrest conditions. The use of balloons in endovascular procedures has a longstanding history [20]. New generation dual lumen balloons have one lumen dedicated to balloon inflation and a second dimethyl sulfoxide (DMSO) compatible, termed the working lumen, dedicated to the microguide wire. A side benefit is that the working lumen can be used for stent or coil deployment [15, 19] and liquid embolic agent injection [15–18]. Over the last few years Onyx embolization of BAVMs, spinal AVMs, cervical AVMs, dural arteriovenous fistulas and aneurysms using dual lumen balloons has been extensively described in the literature [15, 17, 18, 21, 22]. The injection of NBCA is a valuable technique for BAVM embolization [9, 10]; however, flow-dependent injection is limited by poor control over NBCA distribution and progression. Several parameters including microcatheter design, blood flow, blood vessel caliber, temperature and operator experience determine the success of the procedure [12]. The NBCA is usually mixed with iodized oil which imparts radio-opacity to the embolic mixture and thus greatly enhances control over injection [23]. Varying the ratio between the two components modifies polymerization dynamics with an increased iodized oil concentration generating a buffer that delays contact with blood and increases polymerization time [24]. The NBCA can also be injected without iodized oil, fur-

ther accelerating polymerization. In such cases, tantalum powder is added for radio-opacity [25]. Using highly concentrated NBCA in high-flow fistulas has the drawback of increasing the risk of microcatheter entrapment [26]. This seems less likely when using hydrophilically coated microcatheters [27]. Alternatively, distal progression and penetration of NBCA can be enhanced by continuous flushing of the guiding catheter with dextrose 5% solution during NBCA injection, limiting the risk of proximal occlusion [28]. Also, because an increasing iodized oil concentration also increases viscosity, adjunction of titrated quantities of acetic acid to the glue mixture has been proposed to prolong polymerization time without increasing glue viscosity [23]. Increased control over NBCA progression into high-flow arteriovenous shunts can sometimes be obtained by inducing hypotension to limit distal embolization [26]. An interesting alternative to flow-dependent embolization is the wedging technique where the microcatheter is advanced to such a distal position that it occludes the arterial lumen [29, 30]. The arterial pedicle beyond the microcatheter becomes a virtual extension of the lumen and facilitates both delivery of the liquid embolic agent across the fistula site in flow-arrest conditions and permeation of the perifistulous collateral network [12]; however, it is not always possible to navigate the microcatheter to reach such a distal position. Additionally, arterial pedicles of high-flow fistulas may be too large to wedge a microcatheter.

Utilizing an inflatable balloon for flow-arrest aided NBCA injection is a relatively old idea. In 1979 Kerber et al. reported using a single lumen balloon with a custom-made distal valve, allowing balloon inflation for flow-guided navigation and subsequent flow control [9]. Additional pressure by the operator then delivered the embolic agent into the BAVM through the single lumen balloon. More recently, several authors have reported the use of single lumen balloons for proximal high-flow control, subsequently facilitating NBCA injection through a second microcatheter navigated more distally [5, 31]. The concept was further refined by Hamaguchi et al. who demonstrated in a swine model the feasibility of NBCA injection through the working lumen of a dual lumen balloon microcatheter under flow-arrest conditions [12]. This was termed the B-glue technique. In their study, a 50% NBCA (Histoacryl®, Aesculap, Tuttlingen, Germany) mixture with iodized oil was used [12]. The B-glue technique demonstrated a significantly better control of the embolus range with less fragmentation and reflux in a swine model of intercostal artery embolization [12]. The B-glue technique was also successfully used to treat a traumatic pseudoaneurysm arising from a small branch of the deep femoral artery without reflux [32]. More recently, Takao et al. reported successful embolization of a severe intrahepatic arterioportal shunt prior to chemoembolization of a hepatocellular carcinoma [33]. To the best of our knowledge, the present case series is the first description of NBCA embolization through a dual lumen balloon under local flow-arrest conditions in the setting of BAVM. This technique widens the armamentarium of the interventional neuroradiologist for the management of BAVM and is particularly useful for embolizing high-flow arteriovenous fistulas which have been reported as presenting a particular challenge for stereotactic radiosurgery, surgery and embolization [34].

Significant limitations may hinder the generalizability of the technique described here. First of all, dual lumen balloons are more difficult to navigate distally in cerebral arteries with a higher risk of navigation-related complications when compared to low-profile flow-dependent microcatheters usually used for NBCA embolization. Specific potential complications related to distal balloon inflation include arterial dissection and arterial rupture. Further development is required to make dual lumen balloons specifically tailored for this indication. Additional concern comes from a recent report by Park et al. regarding possible incompatibility between lipiodol and balloon microcatheters [35]. Park et al. reported a case of Hyperglide (Covidien, Irvine, CA, USA) single lumen balloon rupture upon contact with a 21% NBCA-lipiodol liquid embolic agent solution during a preoperative hemangiopericytoma embolization procedure [35]. Subsequent in vitro testing with several commercially available single and dual lumen balloon microcatheters demonstrated tolerance to NBCA [35]. Conversely, adding lipiodol to inflated balloons resulted in rupture. Moreover, scanning electron microscopy of balloon surfaces exposed to lipiodol solution for 10 s demonstrated surface cracks [35]. This particular concern must be addressed if the technique is to be widely applied by using dedicated balloons compatible with lipiodol; however, it is noteworthy that no balloon rupture was recorded in this short case series due to the contact with the NBCA-lipiodol mixture. When the glue refluxed too close to the distal aspect of the balloon, it was gently deflated to help the progression of the glue cast then the balloon was re-inflated for further NBCA injection.

Conclusion

High-flow BAVM fistulas can be treated with NBCA embolization using a dual-lumen balloon under local flow-arrest conditions.

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N.-A. Sourour; drafting the work: E. Shotar, A. Al Raaisi, F. Clarençon, N.-A. Sourour; critical revision of the work for important intellectual content: all co-authors; final approval of the version to be published: all co-authors; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: all co-authors.

Conflict of interest F. Clarençon: consultant for Truffle Capital, Penumbra, Guerbet and Stryker. N.-A. Sourour: consultant for Balt. E. Shotar, A. Al Raaisi, S. Lenck, K. Premat, V. Degos and B. Mathon declare that they have no competing interests.

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