CLINICAL STUDY

Embolizing intracranial arteriovenous malformations with Onyx: experience at a single center with 250 patients

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ABSTRACT

Objective The aim of this study is to evaluate the embolization techniques, as well as the effects and complications, using the non-adhesive liquid embolic material Onyx in intracranial arteriovenous malformations (AVMs).

Methods The study comprises a retrospective analysis of 250 patients with intracranial AVMs treated with Onyx in Guangdong General Hospital from Jan 2010 to Dec 2017. The therapeutic strategies, as well as embolization effects and complications, of Onyx are summarized.

Results Of 250 cases, 170 were male and 80 were female. Following the Spetzler–Martin (S-M) grading system, there were 35 cases of grade I, 77 of grade II, 72 of grade III, 39 of grade IV, and 27 of grade V. All cases were treated with Onyx. In addition, 69 cases were treated with Glubran glue. The injected volume of Onyx per patient ranged from 1 mL to 10 mL. The largest volume of Onyx injected in one procedure was 10 mL. The cure rate was 67.9% (76/112) of grade I–II patients, 15.0% (11/72) of grade III patients, 7.7% (3/39) of grade IV patients, and 0% (0/27) of grade V patients. The total cure rate was 36.0% (90/250). The average number of targeted vascular branches per patient was 2.28. The microcatheter broke off in two cases. There were two patients who suffered an intracranial hemorrhage during the embolic procedure; in one of these two patients, the microcatheter also broke off. There were two patients who suffered an intracranial hemorrhage after the embolic procedure; one of them died. Seven cases suffered new-onset neurological deficits or their original symptoms deteriorated. Six of them improved or recovered within 3–6 months. The total complication rate was 5.2% (13/250).

Conclusion The application of Onyx in intracranial AVMs is flexible, effective and safe, and may also reduce the complications.

Keywords: intracranial arteriovenous malformations; embolization treatment; treatment outcome; complication; Onyx.

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INTRODUCTION

Intracranial arteriovenous malformations (AVMs) account for more than 90% of the cerebrovascular malformations. The incidence has been estimated to be almost 1 in 100,000 people (1). The annual risk of cerebral bleeding is on average 2 to 4% (2), with a mortality rate of almost 1% (1) and the peak age of bleeding between 20 and 39 years (3). The liquid embolic agent Onyx (MTI, USA), available since 1999, has been used in Europure water. The development of Onyx was a landmark for the treatment of AVMs, and it became a commonly used embolic agent in everyday endovascular practice around 2004/2005 (4). Onyx is supplied in ready-to-use vials (5). After more than 10 years of clinical application, Onyx is known to be effective, but there are also related complications (4,6-8). Meanwhile, with increasing knowledge of Onyx, the application strategies are changing. We have retrospectively analyzed the clinical data of 250 cases in which Onyx embolization was applied following different treatment strategies in order to treat intracranial AVMs.

PATIENTS AND METHODS

The retrospective study was conducted in Guangdong General Hospital. From Jan 2010 to Dec 2017, 250 patients with intracranial AVMs treated with Onyx were included. All 250 AVMs were confirmed by experienced neuroradiologists and neurosurgeons by magnetic resonance imaging (MRI) and angiograms. Ethical approval was obtained from the hospital. Written informed consent was obtained from each patient or his/her immediate family.

Of these patients, 170 were males and 80 were females, the median age was 34 years (range: 2–73 years). They were classified following the Spetzler–Martin (S-M) grading system; 35 cases were grade I, 77 cases were grade II, 72 cases were grade III, 39 cases were grade IV, and 27 cases were grade V. In 235 patients, the AVM was located supratentorially; in the other 15 patients, it was located subtentorially. The initial symptoms included the following: hemorrhage in 91 patients, headache in 57, seizure in 54, focal neurologic deficits in 9, and other symptoms in 33 patients; the AVMs in the remaining 6 patients were found serendipitously.

ENDOVASCULAR EMBOLIZATION PROCEDURE

Patients received intratracheal intubation anesthesia. Vascular assessment was carried out via a transfemoral approach by using a 6F MPC or MPD (Johnson, USA) guiding catheter. After having performed diagnostic angiography to delineate the architecture of the lesions, we evaluated the therapeutic options for each individual, i.e., treatment with Onyx only or treatment with Onyx combined with Glubran glue (NBCA-MS, GEM, Viareggio, Italy). We used two types of microcatheters: 1.5F Marathon and 1.7F Echelon-10 (Medtronic, USA).

For AVM lesions of S-M grade I or II, the aim was to apply therapeutic embolization during Onyx injection. If vessels were small or could not be embolized completely, we added Glubran glue to accelerate the embolization process. For S-M grade III AVMs, if there was a high bleeding risk, caused for instance by a high blood flow through an arteriovenous fistula or by a nidus in an aneurysm, we performed targeted embolization. Subsequently, we removed the microcatheter, we assessed the risk of postoperative cerebral hemorrhage (caused by a change in hemodynamics after the embolization), and we completed the treatment. Two patients' catheters were removed fast, and the others' were removed slowly.

We also found that the vessels of some patients could not be embolized completely, so in some cases a partly AVM remained after the first operation. Depending on the remaining lesion, we could choose between further embolization, stereotactic radiotherapy (SRT), microsurgery, or conservative treatment (5,9-13).

POSTOPERATIVE MANAGEMENT

For AVMs of S-M grade I or II, we performed fluid replacement, hormone therapy, and symptomatic treatment, whether the embolization was completed or not. For AVMs of S-M grade III

and above, additional to the above treatments, the patients underwent electrocardiogram and blood pressure monitoring for 6–12 hours (until the blood pressure was reduced to 80% of the preoperative blood pressure).

RESULTS

Application of Onyx with Glubran glue and the treatment effect

We used a combination of Onyx and Glubran glue for embolization in 69 cases. Each patient required vascular embolization of one to five branches, with an average of 2.28 branches. Of all patients, 56.8% (142/250) underwent multiple embolization treatment. The injected volume of Onyx was 1–10 mL per patient. The largest volume of Onyx injected in one procedure was 10 mL. The cure rate was 67.9% (76/112) of grade I–II patients, 15.0% (11/72) of grade III patients, 7.7% (3/39) of grade IV patients, and 0% (0/27) of grade V patients. The total cure rate was 36.0% (90/250) (see Table 1). Of all 108 patients who underwent only one embolization treatment, 30 (27.8%) patients were cured, i.e., 11 S-M grade I, 17 S-M grade II, and 2 S-M grade III patients.

Perioperative complications and follow-up

Intravascular microcatheter indwelling did not occur. General complications occurred in 5.2% of the cases (13/250). The microcatheter broke in two cases, an intraoperative hemorrhage occurred in two cases (in one of which a microcatheter also broke during the operation), postoperative hemorrhage occurred in two cases (one resulting in death), and new-onset neurological deficits or aggravation of the original symptoms occurred in seven cases. Follow-up care for these seven patients was performed by phone, clinic observation, or hospitalization. Six patients improved symptoms or recovered fully in the 3–6 months postoperation, and in one patient improvement was not obvious.

Typical case

A 24-year-old man suffered dizziness and headache for 7 days. He was treated with endovascular interventional treatment with Onyx. After embolization, DSA showed there were several lesions that had remained untreated. After a second embolization treatment, 4 months later, DSA showed that the residual AVM had disappeared completely (Figure 1).

DISCUSSION

The advantages and problems of Onyx embolization for intracranial AVMs

Compared to the traditional liquid embolic agent NBCA, Onyx has the advantage of slow injection, and it does not easily adhere to a pipe (12,14). Therefore, we could inject Onyx and observe the embolus structure in the vascular malformation at the same time, so we could meanwhile adjust the strategy of embolization and choose an appropriate time of extubation. Onyx was once considered to make the endovascular treatment of intracranial AVMs enter a new era, when it was initially used in clinic (15,16).

Table 1 Imaging data and treatment results of different S-M grades of intracranial AVM patients.

S-M grade	Total	The number and rate of other changes in deformity (%)		Therapeutic strategy	Total (%)	
		Blood flow-related aneurysm	High flow arteriovenous fistula		Complication	Curative embolization
Grade I	35	0	1 (2.9)	Curative embolization	2 (5.7)	26 (74.3)
Grade II	77	4 (5.2)	7 (9.1)	Curative embolization	3 (3.9)	50 (64.9)
Grade III	72	5 (6.9)	9 (12.5)	Increase embolization rate	5 (6.9)	11 (15.3)
Grade IV	39	6 (15.4)	6 (15.4)	Targeted or palliative	3 (7.7)	3 (7.7)
Grade V	27	5 (18.5)	6 (22.2)	Targeted or palliative	0	0
Total	250	20 (8.0)	29 (11.6)		13 (5.2%)	90 (36.0%)

Note: Targeted or palliative treatment is targeted at an aneurysm, an arteriovenous fistula, the drainage of venous stenosis, or the reduction of the lesion size in the vascular malformations.

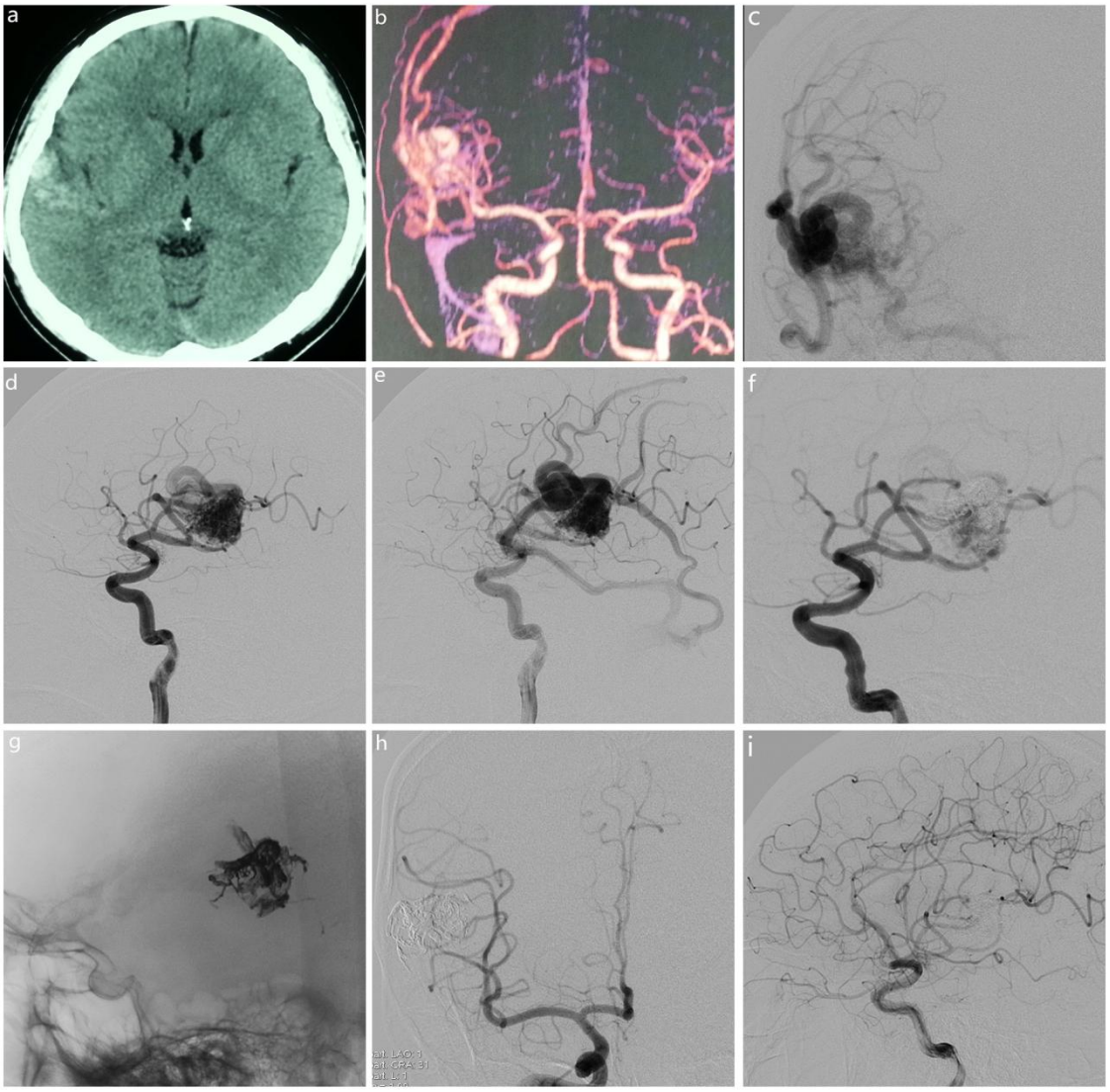

Figure 1 Image data before and after embolization. (a) CT scan showing the change of mixed density of the right temporal lobe. (b) CTA showing that the AVM was located in the right temporal lobe. (c)–(e) DSA showing feeding arteries, an AVM nidus, and draining veins. The AVM was supplied by multiple vessels of the middle cerebral artery. (f) There were several residual lesions that had remained untreated. (g) Onyx formed a mold in the nidus. (h)–(i) DSA showing that the residual AVM had disappeared completely.

The aim of the Onyx treatment of the patients included in this study was curative embolization of intracranial AVMs, so the early cases resulted in a higher incidence of complications. Katsaridis et al. (8) used Onyx to embolize 101 cases of intracranial AVMs. Their results showed that there were three (3%) deaths, and eight (8%) patients suffered permanent neurological deficits. Common issues with Onyx include increasing the embolization rate of intracranial AVMs and decreasing the complication rate (17).

How to improve the cure and embolization rate of Onyx embolization for intracranial AVMs

Our goal is to improve the embolization rate and the cure rate and to control the complications at the same time. For the patients of S-M stage I–II, the complete embolization rate was 67.9%, and the total cure rate was 36.0%. Compared to previous reports, the cure and embolization rates are obviously improved. We hypothesize that the reasons behind

this improvement include the following. 1) After DSA examination, we chose to treat the lesions that were superficial or had a certain amount of hematoma by microsurgery. For some deep AVMs with slim supply arteries, we chose stereotactic radiosurgery treatment. 2) The Onyx application skills include the selection of the working angle, the timing and number of injections, the embolization strategy adjustment during the surgery process, the application of different amounts and concentrations of Onyx, and the optional combination with Glubran glue. The ideal embolization effect usually appeared after waiting patiently. Moreover, the surgeon must keep in mind the fact that Onyx can diffuse through the lesion or reach the drainage vein. The excessive or insufficient application of Onyx can deteriorate the operation outcome. 3) For the patients of S-M grade III–V, in order to improve the embolization rate, we chose to embolize multiple blood vessels, after fully assessing the risk of postoperative complications. 4) As we gained experience applying Onyx, we learned not to worry unnecessarily about the microcatheter being entrapped in the Onyx; fear to fail can cause low embolization and cure rates. In fact, even if the microcatheter was entrapped by Onyx, this did usually not cause any complications (18,19).

How to reduce the complication rates of Onyx embolization for intracranial AVMs

The aim of the present study, i.e., to improve the cure rate of treatment of intracranial AVMs, also resulted in a higher complication rate than previously reported. In our work, the overall complication rate is 5.2%, including one death. Seven patients suffered new-onset nerve dysfunction or aggravation of the original symptoms after embolization. Six of these seven obviously improved or recovered fully in the postoperative 3–6 months. The complications obviously decreased; we observed better embolization treatment effects than before.

We summarize our experience as follows. 1) It is necessary to precisely understand the characteristics of Onyx to prevent the erroneous embolization of normal blood vessels and draining veins. 2) For S-M grade III–V, especially grade IV and V, vascular malformations, we still believe that fractionated embolization would reduce the related complications (20). For high-grade AVMs with no hemorrhage, the patients can be observed, after eliminating dangerous factors. For S-M grade III cases, the elimination of the lesions is still the aim of the treatment, although the embolization rate is not very high. 3) For high-flow vascular malformations or arteriovenous fistulae in malformations, we can choose to use Onyx 34 and, additionally, Glubran glue of a high concentration in order to avoid erroneous embolization of draining veins and to decrease the intraoperative and postoperative risk. 4) If it is difficult to allow Onyx to diffuse in a small residual arteriolar deformity, we can combine Onyx treatment with the application of Glubran glue to form emboli. It is not necessary to cure the patient with only Onyx, which would increase the risk of hemorrhage and erroneous embolization. 5) It is necessary to be cautious when choosing Onyx for the embolization treatment of vascular malformation, as it is applied by perforating an artery branch. 6) It is better not to use Onyx for vascular malformations if the feeding artery is tortuous and slender. When the head of the microcatheter can be taken off (e.g., the Sonic microcatheter), we can choose Onyx for embolization (20). 7) Intraoperative angiography and multi-angle observation help to observe the diffusion of Onyx in malformations, which helps to prevent diffusion to other blood vessels and erroneous embolization. 8) For fistulae or high blood flow in grade III–IV AVMs, the patients' postoperative blood pressure must be controlled, in order to prevent the occurrence of blood vessel perforations. 9) The way of withdrawing the microcatheter is also important. We chose quick withdrawing for only two patients during an early stage of the surgery. For the other patients, we withdrew the tube slowly. There are many factors that affect the withdrawal of the microcatheter, including the extent of vascular tortuousness, the reflux length, the Onyx concentration, and the Onyx injection time. We used intermittent strength and continuous traction. If it was difficult to withdraw the microcatheter, we could use a little DMSO to dissolve solidified EVOH on the head of the microcatheter. In this work, the longest extubation time was nearly 20 min. The microcatheter was pulled off in two cases. The patients did not suffer any extubation-related complications.

In short, Onyx, a new type of non-adhesive liquid embolization agent, has the big advantage that it is more easily controllable than the other available embolization agents. Due to its versatile application strategies and the relatively easy visualization of the

embolization during the surgery, Onyx provides the opportunity to adjust the treatment to each individual patient. As long as we fully understand the characteristics of Onyx and we practice enough patience and caution, we can safely and effectively embolize intracranial AVMs and reduce the complication rate.

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