Endovascular Treatment of Cerebral Aneurysm with Coils and Onyx

in-vivo experiment

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Summary

We investigated endovascular treatment of cerebral aneurysm by coil and Onyx in vivo experiment in order to promote the advantages of coil embolization. The aim of this study was to clarify the advantages and problems of coil and Onyx embolization and to evaluate its potentials for application in clinical medicine.

We set experimental aneurysms made of external jugular vein to bilateral carotid arteries of 10 Beagle dogs and embolized aneurysm with coils and Onyx. Two months later, the dogs were sacrificed and took out the experimental aneurysms and examined them histologically.

We have experienced Onyx migration into the vessel at the beginning of our experiment. Technical problems were as follows; Onyx was not easily visible on DSA monitor particularly in tight coil packing. Catheter tip was often stuck to the Onyx in the aneurysm. Protect balloon could not completely protect the Onyx leakage into the vessel. Microscopic examinations were as follows; The aneurysm was filled with Onyx, coils, and inflammatory reactants. The orifice of the aneurysm was packed with augmented fibrous tissue.

1. This method increased contact between the aneurysm wall and coils.

2. Onyx filled the intra-aneurismal space more tightly.

3. Coils prevented Onyx from flowing out into the vessel.

4. In Onyx, intimal layer was more rapidly formed at the neck of the aneurysm than coils only.

5. The most important problems during Onyx embolization is how to prevent Onyx migration into the vessel. We should like to propose the guideline for Onyx embolization.

Introduction

We have presented the mechanism underlying the prevention of aneurysm rupture by coil embolization¹. The mechanism has two points, the one is Guglielmi detachable coil (GDC)^{2,3} obstructs intra-aneurismal flow and facilitates thrombus formation in the aneurysm, and the second is by anchoring the wall, coils depress the pulsating motion of the aneurysm wall and decreases the stress of the aneurismal wall that is to say reinforces the aneurismal wall.

But, as long as there is left intra-aneurismal flow and incomplete intra-aneurismal solidification, there remains risk of coil compaction and aneurysm re-growth⁴.

In order to preserve the effects of aneurismal wall enforcement and flow restriction by coils and to promote intra-aneurismal thrombus formation and solidification, we investigated endovascular treatment of cerebral aneurysm by

Figure 1 A series of coils and Onyx embolization. A) The micro-catheter was at the bottom of the aneurysm and the neck was protected with Equinox. B) Intra-aneurysm injection of contrast medium. C) CAG from guiding-catheter. D) Completion of coil and Onyx embolization. The lumen of the carotid artery was intact.

coil and Onyx (Micro Therapeutics, Inc., Irvine, CA) in vivo study.

The aim of this study was to clarify the advantages and the problems of coil and Onyx embolization in vivo experiment and to evaluate its potential for application in clinical medicine.

Material and Methods

We produced an experimental aneurysm in the common carotid artery of a dog using a

pouch of its extrajugular vein. We investigated the method of coil and Onyx embolization, the condition of precipitation of Onyx, and the ability to visualize Onyx by fluoroscopy. Finally, we removed the experimental materials from the aneurysm in the dog, and carefully examined them histologically.

Experimental Aneurysm

We used 10 Beagle dogs weighing about 10 kgs. After setting up a drip of physiological

saline solution and parenterally injecting anesthetic drugs (ketaral 1.5 cc+ serectal 1.5 cc I.M. nembutal 1.0cc I.V.), we connected the dog to the respirator for assisted ventilation. Iopamiron 300 was used as a contrast medium for the study. The Beagle dog was fixed on the experimental table in a supine position, and a linear incision was made in the middle of the neck. After subcutaneous dissection, the external jugular vein was exposed and was extracted out about 5 cm for the venous pouch. We then exposed the common carotid artery and sutured the venous pouch measuring about 5 mm in diameter to the common carotid artery bilaterally with 7-0 nylon sutures.

Onyx Infusion Study

We introduced two 6F guiding catheters, one for the micro-catheter and the other for the balloon catheter (Equinox: Micro Therapeutics, Inc., Irvine, CA), through the femoral arteries of both sides into the same common carotid artery.

We infused 0.3~0.5cc DMSO and 16% Onyx slowly into the one aneurysm with the infusion tool for Onyx, while monitoring their entry into the aneurysm by DSA. During the infusion, we protected the neck of the aneurysm with the balloon catheter (Equinox) (figure 1). Into the other aneurysm, we first inserted two coils (ED coil: Kaneka Medics, Inc, Japan) for framing, and then infused DMSO and Onyx as described above. We made the endpoint of Onyx infusion just before the line of the neck when the aneurysm cavity was no longer visible on fluoroscopy.

Histological Examination

Two to six months after the infusion experiment, we checked the patency of the common carotid artery by DSA. Then we took out the aneurysm model in the common carotid artery under general anesthesia. We examined it macroscopically and microscopically.

Results

We experimented ten Beagle dogs. In the first four dogs, we could not infuse Onyx properly. Onyx flowed out into the vessels and obstructed them (figure 2). The other two dogs were dead because of their physical conditions.

Figure 2 Onyx migration into the parent vessel.

To the last four dogs we infused coils and Onyx successfully and extracted the specimens from them.

We have found the following technical problems. It was difficult to recognize clearly the precipitated Onyx in the aneurysm cavity by fluoroscopy. There was a time lag between the infusion and the precipitation of Onyx. It was impossible to stop or control the Onyx infusion promptly. It was possible to change the direction of Onyx precipitation by intermittent infusion. But, the catheter tip often got stuck to the Onyx in the aneurysm during withdrawal of the micro-catheter. It was impossible to completely block the influx of Onyx into the parent vessel with the protective balloon alone.

Macroscopically epithelialization at the neck was observed even when the Onyx was near it but not quite reached it microscopically (figure 3). On the other hand, with coils only, there was a mere fibrous band without epithelialization at the neck of the aneurysm (figure 4).

Microscopic findings were as follows. The aneurysm cavity was filled with Onyx, coils and inflammatory reactants. There was no blood influx into the aneurysm cavity (figure 5). Onyx accumulation was observed in patches. Infiltration with neutrophils, macrophages, and neovascularities were observed around these patches.

The orifice of the aneurysm was packed with augmented fibrous tissue (figure 6). On the

Figure 3 With coils and Onyx, epithelialization was observed almost over the neck.

Figure 4 With coils only, there were a mere fibrous band and clot at the neck.

other hand, the wall of the aneurysm was thinned at areas where it came in contact with DMSO and Onyx was sometimes exposed to the outer layer of the aneurysm wall due to the toxic effects of DMSO on the wall.

Discussion

GDC embolization for cerebral aneurysm³ is a less invasive therapeutic procedure than clipping surgery, because cerebral aneurysms can be managed without direct contact with the brain. But, there are some problems that remain to be resolved regarding coil compaction

or re-growth⁴ and incomplete neck packing. The neck protect technique (re-modeling technique) advocated by Moret is effective for the broad neck aneurysm⁵. But in case of large or giant aneurysms, it is not sufficient for coil compaction.

Murayama et Al reported a "Bioabsorbable polymeric material coil" for promoting intra-aneurysm solidification^{6,7}. Iwata et Al tried bFGF or VEGF coating of the coil to promote intra-aneurysm solidification and epithelialization of the aneurismal neck. Both the coil coating methods were aimed at inducing more effective solidification of the aneurysm.

Figure 5 Microscopic findings of the aneurysm cavity. The aneurysm cavity was filled with Onyx, coils, and inflammatory reactants. There was no blood influx into the aneurysm cavity.

Figure 6 The orifice of the aneurysm was packed with augmented fibrous tissue.

Mawad et Al presented the effective embolization with stent and Onyx for giant cerebral aneurysm. He concluded that the anatomical results and clinical outcome in his small series (11 cases) were very encouraging⁸.

On the other hand, coil and Onyx embolization is aimed at solidifying and reinforcing the aneurismal wall as efficiently as possible, and preventing coil compaction and re-growth of the aneurysm.

The most important problems encountered during Onyx embolization are how to prevent Onyx migration into the vessel and how to embolize the whole aneurysm up to the neck. Murayama et Al reported the relatively poor control of migration of Onyx into the parent artery with coils, microstents, and balloons⁹. But, based on the results of our studies, we think that the migration of Onyx into the vessel might be prevented by careful combined use of coils, stents and balloon.

Based on the results of our study, we would like to propose the following guidelines for Onyx embolization.

- 1) It is important to monitor Onyx infusion by obtaining subtraction image which is masking the coils and balloon just before Onyx infusion (figure 7). And, DSA must be repeated to confirm the extension of Onyx into the aneurysm.

- 2) The concentration of Onyx should be more than 18 or 20% to ensure instant precipitation in the aneurysm.

- 3) The endpoint of Onyx infusion should be just before the line of the neck when the aneurysm cavity is no longer visible on fluoroscopy.

- 4) The tip of the micro-catheter should not be bent excessively in order not to be stucked into the Onyx, and the neck of the aneurysm should be protected with a balloon or stent during the catheter withdrawal.

- 5) In order to minimize the toxicity of DMSO on the aneurysm wall, DMSO should be infused carefully through a micro-catheter at a volume of 0.2 to 0.3 ml, not exceeding the dead space volume of the catheter.

Onyx is an advantageous material for inducing epithelialization at the neck. Flow reduction in the aneurismal cavity and epithelialization at the neck induced by Onyx infusion will facilitate organization of the aneurysm.

Figure 7 The monitoring of Onyx infusion with a subtraction images by masking the coils and balloon just before Onyx infusion.

But, in order to prevent the complications, careful management of Onyx infusion must be necessary.

Conclusions

1. We studied the endovascular treatment for embolization of cerebral aneurysm with coils and Onyx in vivo.

2. Coils and Onyx embolization is a very useful method for reinforcing the aneurysm wall, promoting intra-aneurysm solidification, and preventing coil compaction and aneurysm re-growth.

3. To prevent Onyx migration into the vessel and to ensure embolization of the whole aneurysm up to the neck, some technical guidelines must be followed.

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