Embolic materials

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Introduction

Today, many types of embolization devices are available. Some of these devices have been developed in the fields of neuro-intervention (Onyx, Glue, and detachable coils) and vascular intervention (Stent graft), thereafter, the indication of them has been expanded to the other fields. For example, Viabahn, a self-expandable stent graft (Gore & Associates, Flagstaff, AZ, USA), developed as a recanalizing device for the treatment of limb ischemia has shown good results for the treatment of hemorrhagic vascular lesions including arterial injury and aneurysms, subsequently. These developments in new embolic devises may change the strategy and techniques in management of hemorrhagic vascular lesions in all organs.

Nowadays, it is essential for successful treatment to know the characteristics of various embolic materials and to select the most adequate embolic material for each case based upon the patient's conditions, vascular anatomy, and accessibility.
In this section, we would like to show some cases of interventional treatments for non-traumatic and non-aneurysmal hemorrhage including post-operative bleeding, GI bleeding, and pseudoaneurysms.

Embolic materials

Gelatin sponge

Gelatin sponge is an embolic material frequently used to control bleeding emergencies in pelvic fractures[1)], gynecological hemorrhage[2,3)], hemoptysis[4,5)] or blunt organ injuries[6-8)] in patients without coagulation disorders. Because gelatin sponge is a biologic substance derived from cow or pig organs （skin or bone）, there remains a potential risk of inducing allergic reaction due to heteroprotein[9,10)].In contrast, gelatin sponge, as biologic substance, is absorbable within about 2 to 6 weeks after being administered as an embolic material[I]. Therefore, it is a good candidate of the embolic material for the blunt organ injury, pelvic fractures, etc. to avoid the ischemic complications of of target area due to excessive embolization. On the other hand, in coagulation disorder cases, gelatin sponge might not be effective because gelatin sponge usually requires the patients'

coagulability to obtain efficient hemostasis. Gelatin sponges in Japanese market are made from Australian cow bone with less biological reaction due to least endotoxin than Gelform and Spongel. There are two forms of available gelatin sponges. One is a sheet form (Serescue, Nihonkayaku, Tokyo, Japan, **Figure 1a, 1b**) and the other is particle form (Gelpart, Nihonkayaku, Tokyo, Japan, **Figure 1c, 1d**). The sheet form gelatin sponge has to be prepared by the manual cutting or pumping using 3-way stopcock. This material can be used for occlusion of relatively small vessels up to a few millimeters. A particle form of gelatin sponge, a spherical 1 or 2 mm diameter gelatin sponge, does not require any preparation before embolization. In emergency situations, pre-shaped sponges reduce the procedure time of embolization and are also very helpful especially in single operator procedures.

Metallic coils, microcoils, detachable coils, and vascular plugs

These devices primarily used for isolation and/or packing of the aneurysms. Metallic coils are made of alloy including mainly platinum, nickel or cobalt[11]. There are two types of the metallic coils. One type is provided with synthetic fibers and the other without. Fibered coils may enhance the coagulation of patients to occlude the vessels. Non-fibered coils do not always require the coagulation but the dense packing in the target lesion (more than 24% of packing density in the peripheral aneurysm[12]). The delivery systems of coils are divided also into two types; one is pushable and the other is detachable. Pushable coils (**Figure 2a,b**) are provided only coil without any delivery system. They can be pushed by saline, coil pusher or guide wire. It is impossible to retrieve this type of coils after the coils are pushed beyond the tip of the catheter. The merit of pushable coils is less expensiveness compared to detachable coils. The detachable coils (**Figure 2c-f**) are attached with detachment wire. The connecting mechanisms between coils and delivery wires include mechanical, electric heating, electrolysis or hydraulic type. Due to the connecting mechanisms of detachable coils, the smoothness of the coil delivery and pushablity are different. Most of the detachable coils have stretch resistance mechanisms (SR) mainly provided by the filament. The detachable coils should be enough resistant for repetitive repositioning of coils to achieve the good packing or creating cage, otherwise the detachable coil may cause its unraveling. The coil sizes range from 1 to 32 mm in secondary diameter. The Amplatzer Vascular Plug family (Abbott, Chicago, IL, USA, **Figure 3**) is an alternative to coil embolization. AVPs are self-expanding Nitinol mesh occlusion device in plug shape with screw type detachment system, which provide the most precise positioning of themselves. AVPs, AVP II and AVP 4, are available in Japanese market, while AVP III is not launched. AVP is single layer mesh with 4 to 16 mm in diameter. The advantage of AVP is its short landing zone compare to the AVP II.

Disadvantage of AVP is longer occlusion time due to the single layer and less density of the mesh. AVP II is multi-layered and multi-segmented design with 3 to 22 mm in diameter. The merit of AVP II is its shorter occlusion time compared to AVP's because of multi-layered and multi-segmented mesh. The demerit of AVP II is its longer landing zone however the landing zone could be controllable with compression method. Both AVP and AVP II require 6Fr or larger guiding catheter or sheath for delivery. AVP 4, an alternative choice with low profile flexible mesh, only requires the diagnostic catheter with more than 0.038 inches inner diameter for delivery. The size of AVP 4 ranges from 4 to 8 mm in diameter. The advantage of these materials is the precise occlusion of the vessels because of the detachment system with self-expanding plug design. AVP III, the other lineup of the AVP family, is not available in Japanese market. AVP III is provided in Oblong cross-sectional shape with multiple layers of Nitinol mesh. According to the producer site, AVP III might provide the fastest occlusion of all the AVPs. Because of its unique design and detachment system, the AVP family can be positioned more precisely than coils, and it can be a coil or catheter anchor[13].

***N-2-butyl cyanoacrylate (NBCA) glue* (Figure 4)**

NBCA is a liquid embolic material including cyanoacrylate adhesion[14,15]. Among three cyanoacrylates available before, N-2-butyl cyanoacrylate (so called NBCA or glue) is now widely available because of its usefulness and safety[16]. Cyanoacrylates chain reaction of polymerization occur in anion condition[17]. Because the pure NBCA is radiolucent and reacts very quickly, it usually used as a mixture with ethiodized oil (Lipiodol, Guerbet, France) or Tantalum powder to obtain the radio-opacity and to control the polymerization time. NBCA is widely used for embolization procedures in patients with coagulation disorders because of its adhesive characteristics[18,19]. Once NBCA is injected in the blood vessels, NBCA started to polymerize due to anions trigger NBCA chain reaction[17]. NBCA polymerization causes inflammatory damage of the endothelium, finally leading to the permanent occlusion of the target vessels[20]. The catheter should be rinsed with glucose to eliminate the anions in the catheter lumen and to avoid NBCA adhesion before starting the injection of NBCA-Lipiodol mixture. Lipiodol is usually mixed with NBCA to control the polymerization time[3] with the NBCA:Lipiodol ratio as 1:1 to 1:5. A higher NBCA content has a shorter polymerization time, while higher Lipiodol content provides a longer despite of a higher viscosity. It is important to select an appropriate mixture ratio for successful embolization, because the mixture with high NBCA ratio may not reach the bleeding point due to immediate polimerization. The most popular injection method is the continuous column injection[21], in which NBCA mixture is injected continuously like a column without a reflux. Sandwich injection is an alternative method of the NBCA

injection. Some amount of the NBCA mixture loaded in the catheter is pushed out by glucose consecutively. To switch the NBCA mixture and glucose smoothly, 3-way stopcock is useful. The pumping injection is another injection method, in which NBCA mixture is injected as a droplet. The wedged injection method can provide a longer polymerization time. In this method, catheter tip is wedged into the small artery before the NBCA injection. Subsequently, both the catheter and the wedged artery are filled by glucose. Because of the hemostasis of the wedged artery, the anion in the blood can be eliminated. Therefore, NBCA does not polymerize until it reaches the target lesion or meets with the collateral blood flow. The balloon assisted NBCA injection, B-Glue technique, has been reported by Hamaguchi et al[22]. as an alternative to wedged injection. It utilizes a micro-balloon catheter with a low profile and high trackability. B-Glue technique is especially useful in torturous feeding arteries, which are not suitable to the wedge injection technique. Some physicians use very low concentrated NBCA solutions with 1:9 or 1:10 mixture ratios which shows similar hemodynamic behaver to 100% Lipiodol, flowing into the target lesion. In my personal experience, postpartum hemorrhage is the best candidate for very low concentrated NBCA.

***Stent graft (Viabahn)* (Figure 5)**

Stent graft is the covered stent with PTFE or other membrane. There are self-expandable stent graft and balloon-expandable in the world market. Viabehn (Gore), which is the heparin bonded self-expandable stent graft, is available for both peripheral vascular lesions and traumatic or iatrogenic arterial injuries in thoracic or abdominal regions. However, it is not indicated to the vessel injuries in the aorta, the coronary arteries, the brachiocephalic trunk, the carotid arteries, the vertebral arteries, and the pulmonary arteries and true aneurysms by health insurance in Japan. In patients with massive bleeding, arterial spasm is often observed. Because the diameter of arteries with spasm may be narrower than usual, it is difficult to select adequate size of the stent grafts. Moreover, the delivery system of the stent grafts which usually needs 6Fr or wider caliber may present problems in emergency practice. If the arterial injury is located on the proximal portion of the major aortic branches, the delivery is not very difficult. However, if it occurs on the distal portion, stent graft delivery is more complicated. Additionally, dual antiplatelet therapy (DAPT) is required after stent graft deployment to reduce the risk of its thrombotic occlusion, but it may be problematic in traumatic patients. The costs of the stent graft and the placement procedure are high.

Choice of embolic materials

The most important information to guide the selection of embolic devices is patient's

coagulation status and the size of target vessel. A Japanese Society of Interventional Radiology survey found that the majority of interventional radiologists would choose NBCA as the embolic material for patients with coagulation disorders. Accurate measurement of the target vessel diameter before the procedure is also important. The correct diagnosis (e.g. to distinguish the pseudoaneurysms from the true aneurysms), and the accurate knowledge of the available devices including embolic materials and delivery systems are the most important factors to design an adequate treatment method. In this section, the principle of the embolic materials is presented. Through the case presentation, the proper use of each embolic material according to specific condition of each case will be shown.

Conclusion

In this section, the most common embolic materials and devices have been introduced. To select embolic devices, the best alternative for the patient at that moment must be considered.

a | b
c | d

Figure 1: Gelatin sponges in Japanese market

a: Photo of Serescue (Nippon Kayaku, Tokyo, Japan). Its size is about 2.5 x 2.5 cm with 1cm thickness.

b: Gelatin sponge particles after manual cutting of Serescue. Particle size is controllable by each physician. To prepare the particle, it takes about 1 to 5 minutes. In emergency situations, the preparation might be time consuming.

c: Photo of Gelpart (Nippon Kayaku, Tokyo, Japan). The spherical gelatin sponge particle distributed in a Vial in 1 and 2 mm in diameter.

d: Magnified image of the Gelpart in 2 mm in diameter

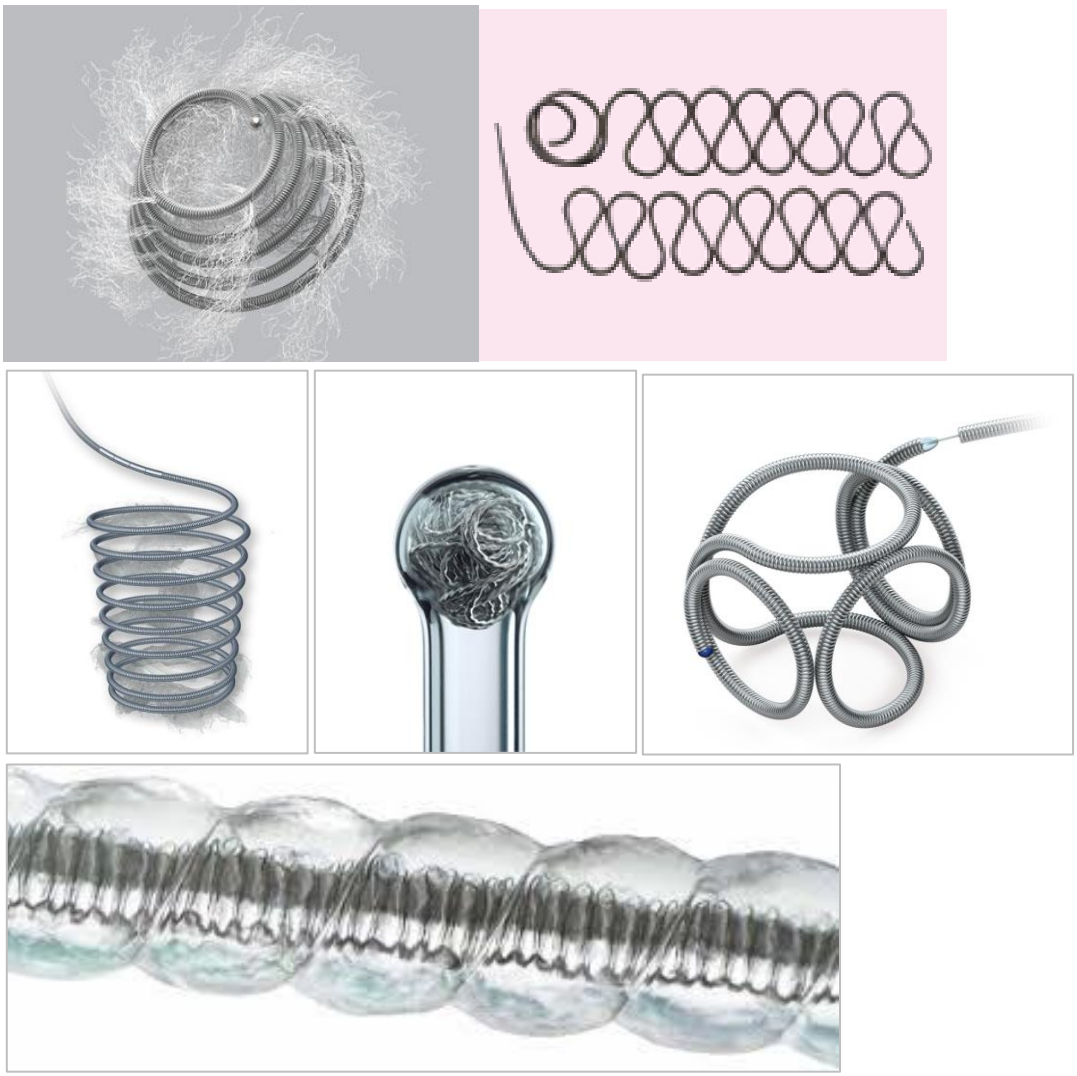

Figure 2: Metallic coils in Japanese market

a: Tornado coil (COOK medical, Bloomington, Indiana, USA). Pushable coil with fiber fixed in tornado shape.

b: C stopper (Piolax medical device, Yokohama, Japan). Pushable coil without fiber.

c: Fibered IDC (Boston scientific, Marlborough, MA, USA). Detachable coils with mechanical detachment system. There are fibered and non-fibered types available.

d: Deltamaxx (Johnson and Johnson, New Brunswick, New Jersey, USA). Detachable coils with electric heating detachment system. Delta shape coils.

e: Target coils (Striker, Kalamazoo, MI, USA). Detachable coil with electrolysis detachment system.

Figure 2f: Azur (Terumo, Tokyo, Japan) after hydrogel expanded. Detachable coils with electric heating detachment system. Expandable hydrogel covers coils or fill inside the coils. The hydrogel around coil expand 4 to 5 times more than original size of coils distribute the wider filling volume.

Figure 3: Amplatzer Vascular Plug family (Abbott, Chicago, IL, USA).
AVP, AVP II and AVP 4 are available in JApan.

Figure 4: NBCA. Liquid embolic material in plastic tube.

Figure 5: Viabahn (W. L. Gore & Associates, Inc., Flagstaff, Arizona, USA).
Stentgraft with heparin bonding inside the stentgraft now only available in Japanese market for vascular lesions.

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