Arterial Occlusive Lesions Following Wrapping and Coating of Unruptured Aneurysms

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Abstract

Seven patients (mean age 57 years) developed arterial occlusive lesions following both wrapping and coating during surgery for unruptured aneurysms. Five patients had no risk factors for arteriosclerosis, and two had hypertension or diabetes mellitus. The aneurysms were located in the middle cerebral artery in four cases, and the internal carotid artery in three. Both 100%-cellulose cotton (Bemsheet®) and cyanoacrylate glue (Biobond®) were used as reinforcement materials. Postoperative angiography revealed complete clipping, and no parent artery stenoses, although one patient had a non-symptomatic diffuse narrowing in the entire carotid fork 7 days following surgery. Three patients had progressive stroke 4-5 weeks following surgery, and two had no symptoms. Both reinforcement materials were used as little as necessary in the last two patients, but they had either transient ischemic attacks or progressive stroke 2 months following surgery. Arterial steno-occlusion was confirmed angiographically in all patients. These vascular lesions were probably induced by both direct toxicity of the cyanoacrylate glue and fibrosis or granuloma formation caused by the cotton fibers. The observed angiographical reversibility suggests that the cyanoacrylate glue is more likely to be the cause of the lesions than the cotton fibers.

Key words: wrapping, coating, unruptured aneurysm, aneurysm surgery, steno-occlusion

Introduction

Cerebral aneurysms can be completely obliterated by clipping, but complete clipping cannot always be obtained when, for example, the aneurysm neck has thick atheromatous plaque or the aneurysm dome is too small to be clipped. In addition, an aneurysm may have developed because the major cerebral artery had a very thin wall. Therefore, reinforcement of the artery and aneurysm neck by wrapping and coating techniques is frequently performed.9,14,20

Cyanoacrylate glues for the reinforcement of aneurysms are inert and relatively non-toxic.2,9,14,20 However, such glues cannot provide continued reinforcement because they become friable after several months, and disappear later.19,26 On the other hand, cotton wrapping material can induce an intense fibrosis that appears within a few weeks, and progresses later.7,10 Reinforcement alone cannot be used for treating ruptured aneurysms, because only

wrapping or coating is not sufficient to prevent rebleeding.1,17,21

We describe seven cases of unruptured saccular aneurysms which developed postoperative arterial occlusive lesions following both wrapping and coating, and discuss the possible causes.

Clinical Subjects and Methods

Seven patients (mean age 57 years) presented with unruptured aneurysms (Table 1). Angiography following subarachnoid hemorrhage (SAH) showed multiple aneurysms in Cases 2, 4, and 5, who received surgery for the unruptured aneurysms 1-3 months following the first surgery for the ruptured aneurysms at different sites. Cases 1 and 7 underwent radiological examinations for headache unrelated to the aneurysms. Case 6 underwent angiography following cerebral infarction (minor stroke), and received surgery for the unruptured aneurysm 2 months following the ictus. Case 3 received a human dry dock for cerebral disorders, when magnetic resonance (MR) imaging revealed

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the aneurysm. None of the patients except Cases 6 and 7 had risk factors for arteriosclerosis, which can induce steno-occlusion in a short period. Cases 6 and 7 had a history of hypertension and/or diabetes mellitus, both of which were controlled well.

We performed both wrapping and coating of the residual neck of the aneurysms following aneurysm dome clipping, and/or on the bleb-like thin wall of the major cerebral arteries, using Bemsheet® (a non-fabric cloth of 100%-cellulose cotton fibers; Kawamoto Co., Ltd., Osaka) for wrapping, and Biobond® (methyl 2-cyanoacrylate monomer + nitrile rubber + polyisocyanate; Yoshitomi Pharmaceuticals Co., Ltd., Osaka) for coating. However, we did not perform circumferential Bemsheet wrapping around the parent arteries.

Results

Postoperative angiography, performed 4–14 days following the surgery, revealed near complete-to-complete clipping and no parent artery stenoses, except that Case 3 had a non-symptomatic diffuse narrowing in the entire carotid fork 7 days following the surgery. Right carotid angiography showed diffuse stenoses of the internal carotid artery (ICA) (C1 portion), middle cerebral artery (MCA) (M1–M2), and the horizontal part (A1) of the anterior cerebral artery (not shown), although the postoperative course was uneventful.

The earliest occlusive lesions were observed 7 days following wrapping and coating (Table 1). Three of the first five patients had progressive strokes at 4–5 weeks following surgery. We used as little Biobond and Bemsheet as necessary in the last two patients. However, they had either transient ischemic attacks (TIAs) or progressive major stroke 2 months following surgery. The other two patients had non-symptomatic lesions. Angiography of several patients confirmed that the M1 stenosis had progressed at 7 weeks following surgery, and had improved at 6 months to 1 year following surgery. Smaller arteries, such as the anterior choroidal artery and MCA branches (M2), were sometimes occluded, and the ICA was occluded in one patient.

Representative Case Reports

Case 2: A 49-year-old female developed SAH in May 1992. Ruptured anterior communicating artery (AcomA) and unruptured left MCA aneurysms were clipped, and the small residual neck of the MCA aneurysm was wrapped and coated. The postoperative course was uneventful. Bilateral carotid angiography 17 days after surgery showed complete clipping and no vasospasm (not shown), and she was discharged with no deficits. Preoperative angiography had also shown an unruptured right MCA aneurysm (Fig. 1A), so she received surgery for this remaining aneurysm 43 days following SAH in June 1992. The small residual neck and the bleb-like thin wall in the distal end of the MCA horizontal part (M2) were wrapped and coated. Postoperative right carotid angiography showed no problems (Fig. 1B), and she was discharged with no deficits.

She experienced a TIA causing left hemiparesis 38
days following the second surgery. Right carotid angiography showed a 50% stenosis of the distal part of the right M1 (Fig. 1C). She received antiplatelet therapy, although she had had several TIAs in the 51 days following the second surgery. Angiography showed a progressive stenosis of the right MCA (Fig. 1D), and a stenosis of the left MCA (M1-M2) (not shown). Computed tomography (CT) 57 days following the second surgery showed a fresh infarction in the right corona radiata. Despite intensive medical care, mild left hemiparesis persisted even after she was discharged. Follow-up right carotid angiography showed improvement of the MCA stenosis (Fig. 1E).

**Case 4:** A 59-year-old female suffered SAH in February 1994. A ruptured ICA aneurysm was clipped successfully. Very small aneurysms on the left M1 bifurcation and the left superior cerebellar artery (SCA) origin were reinforced with wrapping and coating. Angiography 10 days following surgery showed complete clipping, and disappearance of the left MCA small aneurysm and mild stenosis of the adjacent anterior trunk origin (not shown). The patient was discharged with no deficits.

Preoperative carotid angiography had also shown an unruptured right MCA aneurysm (Fig. 2 left). She underwent surgery for this remaining right MCA aneurysm in June 1994. Part of the neck remained because of atheromatous plaque, so was wrapped and coated (Fig. 3). Postoperative angiography showed complete clipping and no residual neck (Fig. 2 center). Repeat angiography in July 1995 performed to confirm possible aneurysm growth from the residual neck showed 70% stenoses in both right M2 trunks (Fig. 2 right). Complete disappearance of the left SCA small aneurysm and mild stenosis of the SCA origin were observed, and an AcomA aneurysm was also seen (not shown). She received antiplatelet medication, and was followed up with strict blood pressure control. She hoped to receive surgery for the AcomA aneurysm, and was admitted to our hospital 24 months following the second surgery.

**Fig. 1 Case 2.** Right carotid angiograms, anteroposterior view, showing the middle cerebral artery aneurysm (A: arrowhead), disappearance of the aneurysm and no arterial stenosis at 9 days following the second surgery (B), M1-M2 stenosis at 39 days (C: arrow), worsening of the stenosis at 53 days (D), and improvement at 1 year (E).
Angiographical findings were the same as those of the previous study (not shown). The AcomA aneurysm was completely clipped through the right pterional approach that was used in the previous craniotomy, so the right MCA aneurysm could be observed. The arachnoid membrane around the aneurysm had thickened, although there was no granuloma around the Bemsheet. The Bemsheet was not firmly adhered to the aneurysm and vessel walls, and could be easily removed. Part of the Bemsheet was removed with the aneurysm dome for histological study. The outer surface of the M2 walls at the location of the angiographical stenoses appeared normal, suggesting that proliferative pathology had progressed centripetally to induce the stenoses. She was discharged with no deficits. Histological study showed that there had been an intensive inflammation in the past, although whether cause was Bemsheet or Biobond was unclear (Fig. 4).
Case 4: Photomicrographs of the specimens obtained at the third surgery showing cell infiltration in the wall of the aneurysmal dome (left: arrows; HE stain, ×10), mostly consisting of lymphocytes, with plasma cells, polymorphonuclear histiocytes (or macrophages), and a reactive neo- vessel indicating inflammation in the chronic stage (center: HE stain, ×100), and wrapping and coating materials around the dome (right: Masson-trichrome stain, ×120). The cut surfaces of Bemsheet fibers appear as oval or round, amorphous, light blue materials with diameters of 20–40 μm, and Biobond appears as round, amorphous, dark-colored particles with diameters of 0.5–20 μm. There is no collagen fiber or fibrosis.

Case 7: A 59-year-old female with diabetes mellitus experienced headache, nausea, and vomiting in October 1995. CT showed no abnormality, but angiography at another hospital showed aneurysms of the right MCA and basilar artery. She was admitted to our hospital. The unruptured aneurysms were

Fig. 5 Case 7. Left carotid angiograms, lateral view, showing the internal carotid-posterior communicating artery aneurysm (left: arrow), disappearance of the aneurysm and no occlusive lesions at 10 days following the second surgery (center), and internal carotid artery occlusion at 68 days (right).
clipped through a right pterional approach. The residual neck of the MCA aneurysm was wrapped and coated. SAH was not observed. Postoperative angiography showed no problems, although a small aneurysm at the bifurcation of the left ICA and posterior communicating artery was observed (Fig. 5 left).

The last aneurysm was clipped through left pterional approach 37 days following the initial surgery. A very thin wall at the MCA bifurcation was also identified. Both the residual neck of the aneurysm and the thin wall of the MCA were reinforced using a small amount of Bemsheet and Biobond. The patient complained of eyelid ptosis and double vision due to left oculomotor nerve paresis 6 days following the second surgery, although CT and MR imaging did not show any cause. Angiography showed no problems (Fig. 5 center), and she was discharged with left oculomotor nerve paresis.

She developed speech disturbance and right upper extremity weakness 60 days following the second surgery, and was admitted to another hospital. Angiography showed a left ICA occlusion (Fig. 5 right), and a mild stenosis of the right M1 distal segment (not shown). Her deficits progressed to global aphasia and right hemiplegia, and CT showed an extensive infarction in the left MCA area.

**Discussion**

The present series suggests that cyanoacrylate glue and cotton fiber can induce arterial occlusive lesions and resultant cerebral stroke. Two similar cases have been recently reported.12) Experimental and clinical studies have shown that cyanoacrylate glues have a direct vascular toxicity, and can induce vascular steno-occlusion,3,5,6,10,11,13,17,22-25) These glues can increase the production of superoxide anions in polymorphonuclear leukocytes, resulting in oxidation and destruction of cell membranes, and cell toxicity.6,11) Experimental studies have shown that these glues induce necrosis and inflammatory reactions in the adventitia and media of blood vessels.3,5,6,10,22-25) The vascular wall is replaced by dense fibrosis, and intimal proliferation can occur.10) Both these effects may cause vessel steno-occlusion. Autopsy of a patient who died of rebleeding from a ruptured MCA aneurysm that had been coated with a cyanoacrylate glue 3 days before showed recent acute necrosis of the wall of the aneurysm because of a marked inflammatory reaction.17) We observed chronic inflammatory reaction in the aneurysm wall in Case 4. Similar reactions may possibly occur in the wall of parent arteries.

Glue-induced pathology resulting in occlusive lesions is progressive to some extent, but some changes may reverse later.6,10,23) Similar reversible phenomena were observed in several cases in our present series. In addition, small arteries react to the glue differently from large arteries as the former tend to occlude.5,10) Our present series also indicates this tendency. These observations suggest that Biobond is one of the causes for the observed postoperative occlusive lesions.

Cyanoacrylate glues also cause neural toxicity.3,6,11,25) Our Case 7 suffered ipsilateral oculomotor nerve paresis 6 days following wrapping and coating for an aneurysm at the bifurcation of the ICA and posterior communicating artery. Oculomotor nerve palsy has been caused by a muslin-induced granuloma 7 months after wrapping for a small unruptured ICA aneurysm at the anterior choroidal artery origin.12) Compared with our Case 7, the paresis took longer to appear following surgery. Therefore, it is reasonable to consider that the oculomotor nerve paresis in our case was not caused by Bemsheet, but by Biobond toxicity.

Cotton fibers are chemically stable and there are no reports of direct toxicity to any tissue. The fibers themselves remain unchanged in the tissue for years,7) as seen in our Case 4. Bemsheet may allow Biobond to contact with vessels for a longer period, thereby causing the glue to have toxic effects on the surrounding tissue. However, cotton fibers can induce marked fibrosis and granuloma, which are progressive.7,8,15,16) Aneurysm wrapping with only cotton can result in occlusive lesions following granuloma formation.8) Therefore, cotton fibers may be a cause of occlusive lesions. In fact, it is unlikely that the major artery (ICA) occlusion in our Case 7 was induced by Biobond alone.

We did not perform revascularization surgery for subsequent cerebral ischemia considering the surgical risks in our series. Medical therapy was given using antiplatelet, anticoagulant, or thrombolytic agents, low-molecular dextran, dobutamine, steroid, and thromboxane synthetase inhibitor. However, we could not stop the stroke processes in all patients. We now try not to use Biobond and Bemsheet for aneurysm reinforcement because we want to avoid the complications described in this paper. We have had no patient with later complications. However, there are no ideal materials for wrapping and coating, and this issue remains for further investigation.

This study suggests that occlusive vascular lesions may result from the direct toxicity of cyanoacrylate glues and marked fibrosis or granuloma formation caused by cotton fibers. Some occlusive lesions are reversible, and the absence of fibrosis suggests that
the glues are more likely than cotton as the cause of the lesions. Patients who receive wrapping or coating should be monitored for the complications of cerebral ischemia due to vascular occlusive lesions.

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References


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Commentary

The authors have presented seven well documented cases of arterial intracranial stenosis after wrapping aneurysms with cellulose cotton and cyanoacrylate glue. Although the precise mechanism of induction of stenosis is not elucidated by this study, several fea-
tures of the reported patients lend insight into the pathophysiology and suggest that more than one mechanism may be responsible for the observed angiographic changes. One patient (Case 3) developed asymptomatic diffuse narrowing of the carotid, middle, and anterior cerebral arteries within 7 days of surgery followed by spontaneous resolution. This may simply represent a case of cerebral vasospasm, perhaps unrelated to the wrapping. Of the five patients that underwent follow-up angiography, two improved, two were unchanged, and one worsened. Those patients with persistent or progressive arterial stenosis following wrapping may well have developed an arteriopathy induced by direct toxicity of the wrapping agents, most likely the cyanoacrylate glue, as suggested by the authors and documented by the pathological material. Given the relative ineffectiveness of wrapping aneurysms, this article should serve to further dampen any enthusiasm for this modality as a definitive treatment for intracranial aneurysms.

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Dr. Kawamura and collaborators have presented an interesting paper on arterial occlusive lesions following wrapping and coating of unruptured aneurysms using either Bemsheet, a non-fabric cloth of 100% cellulose cotton fibers, and/or Biobond, methyl 2-cyanoacrylate monomer + nitrile rubber + polyisocyanate. Although this technique is not performed in our service when we are dealing with unruptured aneurysms, there is no doubt about the usefulness of the information brought up by this paper. Seven cases with arterial occlusive lesions were presented, however, both the total and the partial rate of arterial occlusion by using these materials could be better evaluated if the authors could provide the total number of patients who underwent this treatment.

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The authors describe seven patients with delayed narrowing of a cerebral artery occurring after wrapping with Bemsheets and also with Biobond for unruptured aneurysms. Five cases showed ischemic symptoms 1 to 2 months following surgery and their angiographic findings clearly demonstrate arterial occlusive lesions at the site of the reinforcement procedure. It is interesting that some of the angiographic stenosis is reversible and histological study suggests inflammatory cell infiltration, not granuloma formation. The authors speculate the etiology of the “angitis” as the direct toxicity of the glue. I have similar experience with two such cases associated with circumferential wrapping with Bemsheets and coated with Biobond (ref. 12 of this article). Both cases showed neurological deterioration 3 and 6 months after aneurysm surgery. The difference of the temporal profile is probably due to wrapping technique and it might suggest an intense fibrotic response is also responsible for developing occlusive lesions.

The complication pointed out by the authors indicates an important technical aspect of the aneurysm obliteration procedure. Complete clipping of the aneurysm is not always possible and residual thinning in the neck or in the parent artery has been considered to have some risk of regrowth, but the necessity for reinforcement and the ideal procedure remains unknown. Especially for incidentally found unruptured aneurysms, strict neck clipping is not preferred for fear of parent artery occlusion or stenosis. The suggestion of the authors that wrapping and coating procedures may carry the potential risk to induce delayed vasculopathy seems important for both operative procedure and patient follow-up.

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This paper describing focal arterial narrowing after wrapping and coating of unruptured aneurysms is an important and very interesting contribution. As the authors described, several reports have indicated that both cyanoacrylate glue and cotton might cause arterial narrowing if used for aneurysm wrapping. Nevertheless, their analysis of seven cases provides important information related to the problems occurring following aneurysm wrapping. Although they did not report the occurrence rate of arterial narrowing among the aneurysms wrapped with cyanoacrylate glue and cotton, this article calls our attention to the urgent need for a more safe and reliable material for aneurysm wrapping.

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