Special Article

Direct thrombosis of aneurysms with cellulose acetate polymer

Part II: Preliminary clinical experience

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✓ The authors report the treatment of seven intracranial aneurysms in six patients with direct infusion of cellulose acetate polymer solution, a new liquid thrombotic material. These aneurysms were considered inoperable because of their size or location, or because of the patient's neurological condition. This material avoids the difficulties associated with balloon occlusion, and completely fills even irregularly shaped aneurysms. Cellulose acetate polymer solution hardens in about 5 minutes and remains solid once inside the aneurysm. Because this technique is less invasive than surgery, it can be used for high-risk patients in the acute stage of subarachnoid hemorrhage. Transient motor aphasia occurred in one patient. A small residual neck, which caused rebleeding 3 months after the treatment, remained in another patient. This article describes the new material, the procedure for direct thrombosis, and preliminary clinical results.

KEY WORDS • aneurysm • thrombotic material • endovascular technique • cellulose acetate polymer • interventional neuroradiology

IN 1974, Serbienko15 reported the successful treatment of carotid aneurysms in 82 patients by occlusion of the aneurysm with a detachable balloon. Since then, balloon thrombosis has proved to be an effective treatment for aneurysms that are difficult to reach surgically. For aneurysms with a broad or unapparent neck and those located in the cavernous portion of the carotid artery, the parent artery was occluded across the aneurysm but just proximal to it. This was done through ligation of the internal carotid artery (ICA) or occlusion with endovascular detachable balloons.16,7 With recent developments in microballoon techniques, it is now possible to enter the aneurysm directly and occlude it with a balloon while preserving the parent artery.8-12

Balloon embolization, however, cannot easily occlude the entire aneurysmal sac along with the bleb. Although rare, some reports describe the enlargement or rupture of the aneurysm, the distal propulsion of the balloon, and migration of the thrombus from the neck of the aneurysm after incomplete occlusion.13,20 These factors have led us to believe that filling the inside of the aneurysm directly with a liquid material that solidifies would be better than balloon embolization. This technique uses a liquid thrombotic material, cellulose acetate polymer. Part I of this study15 reports the experimental and histochemical results of this treatment. Here, we describe the clinical application of this thrombotic material.

Clinical Material and Methods

Patient Population

Six patients diagnosed as having intracranial aneurysms or subarachnoid hemorrhage (SAH) were admitted to our hospital over a 5-month period. The average age of these patients was 50 years (range 29 to 64 years); the female to male ratio was 1:1. Endovascular treatment using cellulose acetate polymer was considered suitable for seven of the eight aneurysms found in these patients. Overall, we employed the thrombotic procedure eight times; thrombosis was repeated in one patient.
(Case 1) because of bleeding from the residual neck of an ICA-ophthalmic artery aneurysm. One aneurysm occurred in the ICA-ophthalmic artery, one in the ICA-posterior communicating artery (PCoA), one in the intracavernous portion of the ICA, one in the basilar artery (BA)-superior cerebellar artery (SCA), and three in the bifurcation of the BA. An unruptured aneurysm of the anterior communicating artery (ACoA) was clipped in one patient (Case 2).

Indications for Treatment

Indications for treatment with cellulose acetate polymer included: 1) prior surgical procedures that failed to clip the neck of the aneurysm; 2) locations difficult to reach surgically, such as the cavernous segment of the ICA; 3) the patient's inability to tolerate general anesthesia; and 4) excessive risk in surgical clipping of the aneurysm because of its size or location or because of the patient's neurological status. Consequently, this series favored a high-risk group of patients in whom standard neuurosurgical treatment failed or who were poor candidates for surgery. All patients or a member of the family gave their informed consent before treatment began.

Occlusion Technique

All procedures were performed in the interventional neuroradiography suite using high-resolution digital subtraction angiography, the road-mapping technique, and rapid-sequence filming. Cellulose acetate polymer thrombosis was performed using local anesthesia or bilateral transfemoral approaches, and the patients were awake throughout the procedure.

A No. 8 French sheath was placed into each femoral artery, and a No. 6.5 French tapered catheter was inserted through each femoral artery. A four-vessel cerebral angiogram was obtained to assess the size and shape of the aneurysm, route of access, the relationship of the aneurysmal neck to the parent vessel, and the collateral blood flow. During occlusion of aneurysms in the anterior circulation, angiography was performed through one catheter and a Tracker-18 infusion catheter was inserted into the other catheter. The tip of the Tracker-18 catheter was gently guided into the aneurysm and precisely positioned at the deepest part of the sac. For aneurysms in locations unfavorable to navigation via the parent vessel, a Tracker-18 catheter can be steamed-formed into an appropriate shape and used in conjunction with a 0.014-in. steerable guide wire to help place its tip directly in the aneurysm. To prevent cellulose acetate polymer from washing into the distal artery through the neck of the aneurysm, the carotid artery was compressed using Matas' method to reduce the main circulation to the aneurysm. Because Matas' method effectively reduces blood flow, a part of the contrast material injected into the aneurysm via the Tracker-18 catheter remains inside the aneurysm. For aneurysms in the posterior circulation, a No. 8 French nontapered guiding catheter was placed into the proximal vertebral artery. The microballoon catheter was then advanced through the guiding catheter into the midportion of the BA. This method was used in place of Matas' method to reduce blood flow. The other No. 6.5 French tapered catheter, including the Tracker-18 catheter, was placed into the opposite proximal vertebral artery. The tip of the Tracker-18 catheter was then gently guided into the sac of the aneurysm.

Dimethyl sulfoxide (DMSO) (0.37 ml) was injected to irrigate the lumen of the catheter. The DMSO was then replaced with cellulose acetate polymer prepared as described in Part I of this study. Cellulose acetate polymer was infused slowly over a period of 3 to 5 minutes until the lumen of the aneurysm was impermeable.

*Tracker-18 infusion catheter manufactured by Target Therapeutics, San Jose, California.
Thrombosis with cellulose acetate polymer in patients

Fig. 2. Case 2. A: Left internal carotid artery angiogram, lateral projection, demonstrating an irregularly shaped aneurysm originating from the internal carotid artery (ICA), and an unruptured aneurysm of the anterior communicating artery (arrow). The tip of the catheter is in the sac of the ruptured aneurysm. B: Angiogram after injection of cellulose acetate polymer into the aneurysm. The aneurysm is totally occluded; normal filling of the ICA and posterior communicating artery remains. C: Angiogram taken 6 months after the procedure. The aneurysm is still obliterated by cellulose acetate polymer. D: Skull x-ray film demonstrating the solidified polymer within the aneurysmal sac. The sac retains the same size and configuration it had immediately after injection of the thrombotic material.

Case Reports

Case 1

This 61-year-old right-handed man suddenly lost consciousness on February 25, 1991. At admission, he was semicomatose and unresponsive to commands. Cerebral angiography demonstrated an ICA-ophthalmic artery aneurysm measuring 8 × 11 mm, originating from the dorsal wall of the left ICA (Fig. 1A). Computerized tomography revealed mild hydrocephalus and dilated ventricles. A continuous spinal drainage tube was inserted into the subarachnoid space of the lumbar region.

Operation. We treated the aneurysm using cellulose acetate polymer and a Tracker-18 catheter 17 hours after the onset of SAH. The tip of the catheter was carefully introduced into the sac of the aneurysm. Matsa's method was used to compress the left carotid artery. During compression, a small amount of contrast material injected through the catheter remained in the lumen of the aneurysm, and a faint retrograde flow of contrast medium was observed in the proximal ICA (Fig. 1B). Cellulose acetate polymer (0.47 ml) was slowly injected into the aneurysmal sac. On the angiogram obtained after treatment, a small crescent of contrast medium lying along the anterior portion of the lumen of the aneurysm was visible during the early arterial phase (Fig. 1C).

Postoperative Course. After treatment, the patient showed no neurological change but gradually recovered consciousness over the next several weeks. An angiogram obtained 5 weeks after thrombosis showed that the size of the residual neck and cellulose acetate polymer had not changed.

On May 31, the patient suddenly sustained another SAH. An angiogram demonstrated a growing crescent of residual neck measuring 2.5 × 12 mm (Fig. 1D). Through a transfemoral route, a Tracker-18 catheter was directed into the aneurysm and 0.14 ml cellulose acetate polymer was slowly infused into the sac of the aneurysm. After treatment, angiography demonstrated that the aneurysm was obliterated and the parent vessel was preserved (Fig. 1E). A follow-up angiogram 5 months after the procedure showed continued obliteration of the aneurysm and normal filling of the intracranial circulation. At 8 months after the procedure, the patient is neurologically intact except for a mild gait disturbance.

Case 2

This 42-year-old woman came for medical evaluation of confusion, severe headache, right hemiparesis, and a stiff neck on March 15, 1991. Cerebral angiography demonstrated rupture of a left ICA-PCoA aneurysm, measuring 9 × 11 mm, as well as an unruptured aneurysm in the ACoA (Fig. 2A).
Operation. A Tracker-18 catheter was immediately inserted into the ruptured ICA-PCoA aneurysm. The aneurysm had a cloverleaf configuration, and 0.275 ml cellulose acetate polymer was injected using Matas' procedure under fluoroscopy. Injection was continued slowly until the polymer completely filled the aneurysm, preserving the ICA (Fig. 2B). Four days later, the ACoA aneurysm was surgically clipped. During the clipping of this aneurysm, the surface of the sac of the first aneurysm was exposed, revealing a small black thrombus and the white cellulose acetate polymer within the aneurysmal sac (Fig. 3).

Postoperative Course. Six months later, a follow-up arteriogram showed complete clipping of the ACoA aneurysm and continued total occlusion of the ICA-PCoA aneurysm with cellulose acetate polymer (Fig. 2C). A plain skull x-ray film showed the polymer to be the same size as it had been at the time of thrombosis (Fig. 2D). After thrombosis, the patient's neurological deficit gradually improved, but she had mild right hemiparesis.

Case 4

This 29-year-old man suffered from gradually increasing weakness of his extremities and dysarthria. Vertebral angiography showed a giant aneurysm containing a thrombus at the basilar bifurcation (Fig. 4A). The left posterior cerebral artery (PCA) emerged from the sac of the aneurysm; thus, complete obliteration of the sac of the aneurysm would also occlude the proximal PCA.

Operation. We used a Tracker-18 catheter to infuse cellulose acetate polymer and a microballoon catheter to preserve the parent artery. These catheters were directed up the posterior circulation, through the BA, and into the aneurysm (Fig. 4B). The microballoon was filled with 0.03 ml contrast material and inflated to preserve the PCA; 6.0 ml cellulose acetate polymer was infused into the sac of the aneurysm through the Tracker-18 catheter.

Postoperative Course. An angiogram obtained immediately after treatment showed that the basilar bifurcation aneurysm was obliterated and the PCA was preserved. Faint contrast material was seen around the cellulose acetate polymer (Fig. 4C). The patient was in stable neurological condition during this procedure. An angiogram 1 month after the procedure showed that the area of faint contrast material had disappeared, and another at 5 months after treatment proved that the PCA was preserved (Fig. 4D).

Case 5

This 53-year-old man presented with SAH and severe headache. His neurological condition was classified as Grade III according to the scale of Hunt and Kosnik. A cerebral angiogram showed aneurysms at the basilar bifurcation and the BA-SCA (Fig. 5A). Surgical exploration had been unsuccessful because of the location of the aneurysms and the acute effects of the hemorrhage, and the aneurysms were considered inoperable. The patient suddenly lost consciousness 21 days after SAH.

Operation. Emergency endovascular occlusion of the aneurysms using cellulose acetate polymer was performed. A Tracker-18 catheter was gently advanced into the basilar bifurcation aneurysm. The BA was catheterized with a nondetachable microballoon catheter to reduce the blood flow of the parent artery, and cellulose acetate polymer was infused into the sacs of both the basilar aneurysm (0.58 ml) and the BA-SCA aneurysm (0.47 ml). The basilar bifurcation aneurysm was completely thrombosed (Fig. 5B), but the BA-SCA aneurysm was incompletely thrombosed to preserve both the PCA and the SCA originating from the dome of the aneurysm (Fig. 5C).

Postoperative Course. An angiogram obtained immediately after the treatment showed complete occlusion of the basilar bifurcation aneurysm and about 90% occlusion of the BA-SCA aneurysm. The patient was neurologically unchanged during this procedure. Six days after treatment, he died as a result of primary brain damage caused by the two episodes of SAH.

Results

Table 1 summarizes the complications, follow-up results, and outcomes in this series of seven aneurysms in six patients. All aneurysms were thrombosed to a degree ranging from 80% to 100% using cellulose acetate polymer. Occlusion was incomplete in some aneurysms to preserve the normal vessel originating from the aneurysm. Complications associated directly with treatment occurred in two patients (Cases 1 and 3). Case 1 is reported fully above. In Case 3, the intracavernous aneurysm was ectatic without a well-defined neck. Test occlusion of the proximal cervical ICA was...
Thrombosis with cellulose acetate polymer in patients

well tolerated for 30 minutes, and the patient developed no focal neurological problems. Therefore, the carotid artery was occluded with cellulose acetate polymer infused into the ICA just proximal to the neck of the aneurysm, as well as into the aneurysmal dome. The contralateral carotid angiogram obtained after the thrombotic procedure showed enough blood supply in the ipsilateral hemisphere. The presenting symptom was considered to be correlated with the hemodynamic change after the treatment. After the procedure, the patient developed mild motor aphasia, which resolved in 5 days. No permanent neurological deficits occurred in this series. The single death (Case 5) was due to primary brain damage caused by two episodes of SAH.

Discussion

Cellulose acetate polymer is widely employed as a component of membranes contained in renal dialyzers. Dimethyl sulfoxide has been used to reduce intra-

Fig. 4. Case 4. A: Vertebral angiogram demonstrating a large aneurysm at the basilar bifurcation. B: Diagram illustrating the tip of the Tracker-18 catheter as it is positioned in the dome of the aneurysm. A microballoon catheter is located in the neck of the aneurysm to preserve the posterior cerebral artery (PCA). SCA = superior cerebellar artery. C: Angiogram obtained after the procedure showing obliteration of the dome of the aneurysm. The proximal sac (arrow) has been maintained to preserve the origin of the PCA. D: Conventional subtraction angiogram obtained 5 months after the procedure showing the PCA still preserved. The opacified irregular mass representing cellulose acetate polymer (arrows) can be clearly seen.

Fig. 5. Case 5. A: Vertebral angiogram, anteroposterior view, demonstrating a basilar artery (BA) bifurcation and a BA-superior cerebellar artery (SCA) aneurysm. The tip of the catheter (arrowhead) is seen in the dome of the aneurysm. A partially inflated balloon (arrow) was temporarily placed in the mid-basilar artery to reduce blood flow. B: Angiogram obtained after thrombosis of the basilar bifurcation aneurysm showing that the aneurysm is obliterated. Cellulose acetate polymer impinges slightly on the proximal posterior cerebral artery (PCA). C: Angiogram obtained after thrombosis of the BA-SCA aneurysm. Thrombosis is incomplete to preserve the SCA and PCA. The tip of the catheter (arrowhead) is seen in the aneurysm. A balloon (arrow) is placed at the origin of the aneurysm.

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TABLE 1
Clinical summary of six patients treated with cellulose acetate polymer (CAP) embolization*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs.)</th>
<th>Sex</th>
<th>Presenting Symptoms</th>
<th>Aneurysm Location</th>
<th>Aneurysm Size (mm)</th>
<th>Amount of CAP (ml) &amp; Date of Embolization</th>
<th>Complications</th>
<th>Dates of Follow-Up Study</th>
<th>Results</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61</td>
<td>M</td>
<td>SAH (2/25/91)</td>
<td>ICA-ophthalmic art</td>
<td>8 x 11</td>
<td>0.47, 2/26/91 growth of residual neck</td>
<td>2/27/91, 4/1/91</td>
<td>90% occlusion, rebleed from residual neck</td>
<td>good</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>F</td>
<td>SAH (5/31/91)</td>
<td>ICA-ophthalmic art</td>
<td>2.5 x 12</td>
<td>0.14, 6/8/91 none</td>
<td>7/24/91</td>
<td>100% occlusion</td>
<td>good</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>F</td>
<td>mass effect</td>
<td>intracavernous</td>
<td>17 x 27</td>
<td>2.65, 5/13/91 transient aphasia (resolved in 5 days)</td>
<td>control angiogram refused</td>
<td>100% occlusion</td>
<td>good</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>M</td>
<td>mass effect</td>
<td>BA bifurcation</td>
<td>29 x 56</td>
<td>6.0, 5/21/91 none</td>
<td>10/9/91</td>
<td>95% occlusion to preserve PCA</td>
<td>good</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>M</td>
<td>SAH (5/6/91)</td>
<td>BA bifurcation</td>
<td>4 x 6</td>
<td>0.58, 5/27/91 none</td>
<td>-</td>
<td>100% occlusion</td>
<td>died†</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>52</td>
<td>F</td>
<td>SAH (5/31/91)</td>
<td>BA bifurcation</td>
<td>17 x 23</td>
<td>0.45, 6/7/91 none</td>
<td>7/1/91</td>
<td>80% occlusion to preserve perforating arteries</td>
<td>good</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations: SAH = subarachnoid hemorrhage; ICA = internal carotid artery; art = artery; PCoA = posterior communicating artery; AC0A = anterior communicating artery; BA = basilar artery; PCA = posterior cerebral artery; SCA = superior cerebellar artery.
†Death caused by primary brain damage from two episodes of SAH.

Marshall and colleagues reported satisfactory control of ICP after injecting 10% to 20% DMSO at a dose of 1 gm/kg in six patients with hypertension due to severe head injury and cortical venous thrombosis. Doses up to 8 gm/kg/day of 10% to 20% DMSO are well tolerated by primates and yield no evidence of long-term toxicity, hemolysis, or coagulopathy. Our patients required a maximum dose of only 0.5 to 1 gm DMSO. We selected DMSO as the solvent for cellulose acetate polymer because it diffuses rapidly upon contact with physiological saline or blood, so that only the polymer remains. A small amount of bismuth trioxide was added to the material as a radiopaque agent. The mixture of 250 mg cellulose acetate polymer, 3 ml DMSO, and 900 mg bismuth trioxide was appropriate to yield liquid of a viscosity that flowed smoothly through a No. 27 needle or a Tracker-18 catheter.

In many aneurysms treated with intravascular balloon embolization, parts of the neck may not be filled. When this happens, circulatory flow and turbulence often cause the aneurysm to grow and form a thrombus around the balloon. In few cases growth and rupture of an aneurysm after incomplete treatment with balloons have been reported. These complications arise from the difficulties of completely obliterating aneurysms with any one balloon or combination of balloons and from the obvious potential consequences of leaving even a small portion of an aneurysm intact. It is unlikely that any balloon, regardless of its size or shape, perfectly matches the shape of an aneurysmal sac without leaving a remnant of neck. Therefore, we developed a liquid solution that conforms to the contours of even irregularly shaped aneurysms.

When infused through the tip of a catheter positioned in the deepest part of the aneurysmal sac, cellulose acetate polymer begins to solidify upon contact with the blood within the aneurysmal sac. It then hardens and advances to the aneurysmal neck until it is flush with the lumen of the parent vessel. A fragment of solidified polymer cannot wash into the distal vessel because blood flow is controlled through carotid compression or microballoon inflation during the procedure.

In our Case 1, a small residual neck or anterior portion of the aneurysmal sac was not filled because the amount of cellulose acetate polymer infused was insufficient to fill the aneurysmal sac. Although we expected thrombosis to occur and completely occlude the aneurysm, a growing residual neck bled 3 months later. If a residual neck is observed in an aneurysm, the patient's condition should be assessed continuously to monitor further changes and to see if repeated treatment is necessary. Follow-up studies must assess subtotal occlusion and hemodynamic changes occurring within the residual neck, particularly for patients in whom a normal vessel originating from the aneurysm was preserved.

It is probable that aneurysms in the ACoA and middle cerebral artery could also be treated with endovascular thrombotic therapy using cellulose acetate...
Thrombosis with cellulose acetate polymer in patients

dehydrated. This could be done with temporary occlusion of either the A1 or M1 segments with a nondetachable balloon while the polymer is being injected; however, it would significantly increase the complexity of the procedure.

The technique using cellulose acetate polymer offers significant advantages over complicated procedures such as balloon embolization, in which detachment sometimes causes subsequent rupture. The solution remains hard within the aneurysm and conforms to the individual shape of each lesion. Nevertheless, long-term clinical and radiographic follow-up study is necessary to ensure continued occlusion.

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References


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