Thrombosis of difficult intracranial aneurysms by the endovascular placement of platinum-Dacron microcoils

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Patients with symptomatic aneurysms that are not excluded from the cerebral circulation have a poor prognosis. Standard treatment is surgical exploration with direct clipping of the aneurysm. Because of their large size or relationship to the base of the skull, some aneurysms may not be suitable for direct surgical clipping and may require alternative treatment modalities. A prospective clinical and radiological study of seven patients treated with the endovascular placement of platinum-Dacron microcoils to exclude the aneurysm from the cerebral circulation is reported.

The seven patients ranged in age from 37 to 63 years; four were women. At completion of the endovascular procedure, total occlusion of the aneurysm with preservation of the parent artery had been achieved in four patients and 90% occlusion of the aneurysm in two. In the seventh patient, occlusion of the internal carotid artery resulted in the patient's death. At the 6-month follow-up review, both patients with an aneurysm less than 20 mm in size had persistent aneurysm thrombosis; however, the two patients with giant aneurysms had partial recanalization. Both required repeat thrombosis of their aneurysm with the placement of additional microcoils, one at 6 weeks and one at 6 months. These two patients have persistent aneurysm thrombosis at 12 months following their second procedure. The patient mortality rate for this study was 14%, while the procedure mortality/morbidity rate was 9%. It is concluded that thrombotic aneurysm therapy of difficult aneurysms is a safe procedure and will have a place in the treatment of selected aneurysms.

Keywords: cerebral aneurysm, thrombosis, subarachnoid hemorrhage, coil, endovascular surgery

Untreated symptomatic aneurysms have a high incidence of rupture and are associated with poor patient prognosis.

Although advances in microneurosurgery enable most aneurysms to be explored and clipped with a low rate of morbidity and mortality, some giant aneurysms with a broad atherosclerotic neck or aneurysms at the base of the skull may not be surgically treatable with an acceptable risk to the patient. Patients with these difficult aneurysms require alternative therapies to exclude the aneurysms from the circulation, thereby preventing their growth and rupture.

For many years, cervical vessel ligation of these difficult aneurysms was the mainstay of therapeutic intervention. However, carotid artery ligation requires sacrificing the parent artery, a procedure that engenders significant mortality and morbidity. Endovascular placement of detachable balloons within the aneurysm with preservation of the parent artery has been reported with variable success as a means of avoiding these disadvantages. However, not all intracranial aneurysms are suitable for endovascular balloon occlusion and other alternative endovascular therapies need to be assessed.

We report here our experience with the thrombotic endovascular intra-aneurysmal placement of thrombotic platinum-Dacron microcoils in aneurysms not suitable for direct surgical treatment. We prospectively studied all of these patients with a similar clinical and angiographic protocol in order to analyze the safety and efficacy of thrombotic endovascular therapy. This report emphasizes clinical and angiographic follow-up results in order to ascertain the long-term outcome of these patients and the difficulties encountered in treating giant aneurysms.

Clinical Material and Methods

From January, 1990, to June, 1991, seven patients were admitted to the neurosurgical service at Rhode Island Hospital with intracranial aneurysms that were considered not suitable for direct surgical clipping. All
seven patients were managed by endovascular thrombotic aneurysm occlusion utilizing platinum-Dacron microcoils.* The patients ranged in age from 37 to 63 years; four were women. Before treatment, all patients were investigated with a protocol involving magnetic resonance (MR) imaging and four-vessel cerebral angiography to assess the intracranial aneurysm. The clinical presentation and angiographic details of the aneurysms are outlined in Table 1.

The policy of the neurosurgical unit is to explore promptly all intracranial aneurysms and to clip them when appropriate. In three of the seven patients (Cases 1, 2, and 4), the aneurysm was explored but not clipped. The remaining four patients did not undergo surgical exploration because of their medical condition, refusal to consent to surgery, or the angiographic appearance of the aneurysm. All patients were managed by the neurosurgical staff and the interventional radiology staff as a coordinated team during endovascular thrombotic treatment and in the follow-up review period.

Prior to thrombotic therapy, patients were given 4 mg dexamethasone four times a day (tapered over 2 weeks after the procedure) and 300 mg cemadotin hydrochloride three times a day; sequential compression boots were also used. The five patients most recently treated were given 6 gm ε-aminocaproic acid every 4 hours orally for 6 weeks to enhance thrombus formation within the aneurysm. The endovascular thrombotic procedures were performed by selective catheterization of the parent intracranial artery via a transfemoral approach. During the endovascular procedure, all patients were systemically heparinized. A No. 3.2 French Tracker catheter† was navigated coaxially into the parent artery and then into the aneurysm, with the correct location confirmed angiographically. To prevent the coils from migrating from the aneurysm in patients with large aneurysm necks, a temporary balloon was positioned in the parent artery (Case 7, in the internal carotid artery) or within the neck of the aneurysm (Case 5, in the vertebral artery aneurysm).

Thrombosis of the aneurysm was achieved with the placement of multiple platinum coils interwoven with Dacron fibers via the Tracker catheter. The coils ranged in length from 10 to 30 mm and in diameter from 3 to 10 mm.

At the completion of aneurysm thrombosis, a repeat cerebral angiogram was obtained prior to removal of the catheters. The patient was then observed in the neurosurgical intensive care facility. To evaluate long-term aneurysm thrombosis, all patients underwent repeat cerebral angiography at 1, 6, 24, and 52 weeks after thrombotic therapy.

### Results

All patients were followed for periods ranging from 6 weeks to 18 months. At completion of the thrombotic endovascular procedure, cerebral angiography demonstrated 100% aneurysm occlusion with preservation of the parent artery in four patients. In two patients, 90% of the aneurysm was occluded. In one patient (Case 7), the microcoils became displaced from the aneurysm, and the internal carotid artery was inadvertently occluded. The desired aneurysm occlusion required one procedure in four patients, two procedures in two patients, and three procedures in one patient. During the 1st week after surgery, all six survivors remained neurologically normal, and the follow-up cerebral angiogram at 1 week demonstrated persistent thrombosis.

Six weeks after placement of the microcoils, thrombosis remained stable in all except one patient (Case 6). This patient required repeat thrombosis of his giant internal carotid artery aneurysm, and the aneurysm remained 90% thrombosed at 12 months. One patient (Case 3) died of a myocardial infarction at 7 weeks after the thrombotic occlusion, and histological examination revealed 90% occlusion of the aneurysm. Neurological assessment was normal in all other patients.

Follow-up review at 6 to 18 months has been obtained in four patients. Both patients with an aneurysm less than 20 mm in diameter showed persistent thrombosis of the aneurysm on follow-up cerebral angiography at 6 months. Of the two patients with giant aneurysms, one (Case 5) required repeat thrombosis at 6 months. Both of these patients have stable aneurysm

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**TABLE 1**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs) &amp; Sex</th>
<th>Presentation</th>
<th>Neurological Complications</th>
<th>Arterial Origin of Aneurysm</th>
<th>Aneurysm Size (mm)</th>
<th>Postop Aneurysmal Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37, F</td>
<td>mass effect</td>
<td>eye pain</td>
<td>internal carotid</td>
<td>9</td>
<td>nil</td>
</tr>
<tr>
<td>2</td>
<td>56, F</td>
<td>mass effect</td>
<td>headache</td>
<td>posterior carotid</td>
<td>20</td>
<td>nil</td>
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<tr>
<td>3</td>
<td>63, F</td>
<td>subarachnoid hemorrhage</td>
<td>none</td>
<td>basilar</td>
<td>8</td>
<td>nil (died at 7 wks)</td>
</tr>
<tr>
<td>4</td>
<td>52, F</td>
<td>stroke</td>
<td>hemiparesis</td>
<td>internal carotid</td>
<td>20</td>
<td>nil</td>
</tr>
<tr>
<td>5</td>
<td>63, M</td>
<td>subarachnoid hemorrhage</td>
<td>none</td>
<td>vertebral</td>
<td>25</td>
<td>extensive</td>
</tr>
<tr>
<td>6</td>
<td>48, M</td>
<td>mass effect</td>
<td>6th nerve palsy</td>
<td>internal carotid</td>
<td>30</td>
<td>extensive</td>
</tr>
<tr>
<td>7</td>
<td>52, M</td>
<td>mass effect</td>
<td>headache</td>
<td>internal carotid</td>
<td>35</td>
<td>extensive</td>
</tr>
</tbody>
</table>

* Microcoils manufactured by Cook, Inc., Bloomington, Indiana.
† Tracker catheter manufactured by Target Therapeutics, South San Francisco, California.

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FIG. 1. Case 2. A: Magnetic resonance image demonstrating a posterior circulating aneurysm embedded in the left cerebral peduncle. B: Cerebral angiogram showing the aneurysm arising from the posterior cerebral artery. C: Cerebral angiogram demonstrating total occlusion of the aneurysm following placement of the microcoils within the aneurysm. D: The aneurysm was totally occluded on this 6-month follow-up cerebral angiogram.

Illustrative Cases

Case 2
This 56-year-old woman experienced chronic suboccipital headaches. Examination revealed no focal neurological signs. Magnetic resonance imaging demonstrated a 20-mm posterior cerebral artery aneurysm with no intra-aneurysmal thrombosis (Fig. 1A); this appearance was confirmed on cerebral angiography (Fig. 1B). The aneurysm was explored via a subtemporal craniotomy, and was found to have a thick atheromatous neck with numerous perforators surrounding the body and dome of the aneurysm, which made direct surgical clipping inappropriate. The patient had an uneventful recovery following surgery. She subsequently received complete endovascular thrombotic occlusion of the aneurysm with placement of 16 platinum-Dacron microcoils within the lumen of the aneurysm (Fig. 1C). At the 6-month follow-up examination, the aneurysm remained completely occluded (Fig. 1D). The patient has had no neurological deficits.

Comment
This case illustrates the course in Cases 1 to 4, all of whom had excellent results from endovascular thrombotic treatment with no mortality or morbidity. Two of these patients have been followed for 6 months with persistent occlusion of the aneurysm. One patient (Case 3) died of a myocardial infarction at 7 weeks, and histological examination of the aneurysm revealed persistent thrombosis of the aneurysm. The results demonstrate that patients with moderate-sized aneurysms (8 to 20 mm) with no intra-aneurysmal clot have an excellent result from thrombotic occlusion. Furthermore, microcoils appropriately packed into the aneurysm will induce thrombosis that is probably associated with long-term aneurysm occlusion.

Case 5
This 63-year-old man presented following a sudden onset of headache without loss of consciousness. Computed tomography (CT) revealed diffuse subarachnoid blood. Angiography demonstrated a 25-mm vertebral artery aneurysm (Fig. 2A), and MR imaging revealed the aneurysm embedded into the brain stem with no clot within the aneurysm. The aneurysm was not explored, but was treated with a two-stage endovas-
 coils. In giant aneurysms, over a period of time the coils may be compressed within the lumen of the aneurysm or displaced into the intra-aneurysmal clot resulting in partial refilling of the aneurysm. However, the advantage of treating aneurysms by this thrombotic technique, despite this difficulty, is that the procedure can be safely repeated. Even when giant aneurysms require delayed additional procedures, they appear to be stabilized at least at the 12-month follow-up review.

**Case 7**

This 52-year-old man experienced headaches for 2 weeks. Neurological examination revealed no focal neurological signs. Magnetic resonance imaging demonstrated a 35-mm internal carotid artery aneurysm with 50% intra-aneurysmal thrombosis (Fig. 3A). Cerebral angiography confirmed the appearance of the aneurysm (Fig. 3B). Surgical exploration of the aneurysm was not performed because of its broad neck and considerable intra-aneurysmal thrombosis; the patient was treated instead with the thrombotic endovascular protocol. To prevent the microcoils from being dislodged from the aneurysm, the internal carotid artery was occluded temporarily during the first embolization. The first procedure utilized 39 microcoils and resulted in 80% occlusion of the aneurysm.

Following this procedure, the patient was neurologically normal. He returned 7 days later for the placement of more microcoils, which resulted in complete occlusion of the aneurysm (Fig. 3C). However, a final angiogram prior to removing the carotid artery catheter demonstrated that the microcoils had become displaced from the aneurysm and were occluding the internal carotid artery (Fig. 3D). The patient remained neurologically normal for 48 hours, after which he became drowsy with a left hemiparesis that initially responded to hypervolemic therapy. However, his hemiparesis worsened, and angiography demonstrated a patent internal carotid artery with filling of all the intracranial vessels and partial refilling of the aneurysm (Fig. 3E). Computerized tomography demonstrated massive cerebral edema from which he died despite aggressive therapy with hyperventilation, dexamethasone, diuretics, and barbiturate coma.

**Comment**

This patient represents the single death in this series, and illustrates the difficulty of overaggressive therapy of an aneurysm with a broad neck, for the microcoils may become dislodged and occlude the parent artery. The development of progressive raised intracranial pressure may have resulted from vasogenic cerebral edema secondary to reperfusion of the hemisphere when the carotid artery was recanalized.

**Discussion**

Untreated symptomatic aneurysms have a high incidence of rupture, associated with a poor prognosis. The natural history of symptomatic giant aneurysms is
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Fig. 3. Case 7. A: Magnetic resonance image demonstrating an intracranial aneurysm with extensive intra-aneurysmal thrombosis. B: Angiogram illustrating the large broad-necked internal carotid artery aneurysm. C: Angiogram showing complete obliteration of the aneurysm following placement of multiple microcoils within the aneurysm, with preservation of the internal carotid artery. D: Follow-up angiogram, obtained before removal of the carotid artery catheter, revealing displacement of the microcoils into the lumen of the internal carotid artery, resulting in its occlusion. E: Repeat angiogram on Day 3 illustrating a patent internal carotid artery, patent distal arteries, and partial refilling of the aneurysm.

less well documented, but reports suggest that they are more lethal than smaller aneurysms, with approximately 80% of patients dying or becoming incapacitated within 5 years of diagnosis. The optimum treatment of a cerebral aneurysm is total occlusion of the aneurysm, preservation of the parent artery, with minimum operative morbidity and mortality. Due to modern advances in microneurosurgical techniques, these aims can be achieved with excellent results in the majority of patients. However, for some patients with giant aneurysms or aneurysms at the base of the skull, direct clipping of the aneurysm may not be achieved with the same low mortality and morbidity rates.

Hunterian Ligation

For many years the management of difficult aneurysms has involved modifications of the Hunterian ligation, such as proximal parent occlusion or proximal and distal trapping of the aneurysm. If the cerebral collateral circulation was insufficient to maintain adequate cerebral perfusion, carotid artery ligation had to be supplemented with external carotid artery to internal cerebral artery anastomosis. However, Hunterian ligation of intracranial aneurysms is hazardous because of the risk of early or delayed cerebral ischemia, and long-term protection from rebleeding is not optimum in all cases. The Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhage reported a 49% incidence of acute ischemic complications following internal carotid artery occlusion, a 28% incidence for all patients with common carotid artery occlusion, but only a 12% incidence for unruptured aneurysms. These results are supported by Kak, et al., who described ischemic complications ranging from 4% to 40% depending on the grade of the patient and timing of carotid artery ligation after the subarachnoid hemorrhage. To decrease the incidence of cerebral ischemic complications, Miller, et al., selected patients with a cerebral blood flow greater than 40 ml/100 gm/min, and reported a 5% incidence of ischemia following carotid artery ligation. Long-term delayed cerebral ischemic complications are reported with an incidence of approximately 8%. Similarly, the Cooperative Study reported that among 233 patients five
had delayed ischemic complications with an onset between 11 months and 4 years after carotid artery ligation. The delayed ischemia was probably embolic from the terminal clot in the internal carotid artery.4,8

Another disadvantage of proximal ligation is that the early protection of the aneurysm against rebleeding is lost over long follow-up periods. Kak, et al.,25 who reviewed the literature from 1953 to 1973, found an overall rebleed rate of 3.0% to 8.4% at variable times after carotid artery ligation. Similarly, the Cooperative Study29 reported a rebleed rate of 6.8% at long-term follow-up review. Miller, et al.,21 reported a more favorable outcome, with only one rebleed in 72 patients treated with carotid artery ligation.

Endovascular Detachable Balloons

Endovascular therapies have recently been investigated in an attempt to overcome the limitations of direct surgical exploration and carotid artery ligation to treat difficult aneurysms. Endovascular treatment of aneurysms utilizing detachable balloons was first described in 1974 by Serbilenko.31 This innovative technique has since been reported by numerous authors4,8,12,15,19,20 and includes both intra-aneurysmal balloon occlusion and proximal parent artery occlusion. Higashida, et al.,20 reported endovascular treatment of 25 posterior circulation aneurysms, with intra-aneurysmal balloon occlusion accomplished in 15 patients. The aneurysm was subtotally occluded in six of these 15, and five patients died of delayed aneurysm rupture. Fox, et al.,12 reported occlusion of the parent artery in 65 of 68 patients, with an overall aneurysm occlusion rate of 76.9%; however, occlusion of supraclinoid aneurysms was only 50%. There were cerebral complications in nine patients; however, all except one was temporary (1.5% morbidity). These reports suggest that endovascular balloon techniques successfully occlude only the aneurysm in a limited number of cases.

Endovascular Thrombotic Occlusion

Thrombotic aneurysm occlusion is a recent extension of endovascular therapy for aneurysms. The concept of intra-aneurysmal thrombotic occlusion was first reported by Gallagher13 in 1964. He reported 15 patients in whom the aneurysm was explored via a craniotomy; he injected hog hair into the lumen of the aneurysms of these patients through a pilojector gun. Gallagher achieved complete occlusion of the aneurysm in nine patients; two of the nine died postoperatively, one from raised intracranial hypertension secondary to cerebral swelling and the other from internal carotid artery occlusion. Similarly, Mullan28 utilized copper electric thrombosis with a stereotactic technique to induce aneurysm thrombosis. He reported on 61 patients, of whom 47 had satisfactory thrombosis; three postoperative deaths were attributed to the procedure. Alksne and Smith1 stereotactically injected an iron-acrylic compound to successfully induce thrombosis of an anterior communicating artery aneurysm. The first investigators to utilize the endovascular route to induce aneurysm thrombosis was Hilal, et al.,22 who placed platinum coils interwoven with Dacron fibers into the aneurysm. Subsequently, Dowd, et al.,9 reported three patients with posterior fossa aneurysms who were similarly treated with good results. Also, Higashida, et al.,21 reported the use of microcoils to obtain thrombosis of a giant intracranial aneurysm. Guglielmi, et al.,15 reported a combination of detachable coils placed in the aneurysm followed by electrothrombosis in 15 patients; they achieved thrombosis of the aneurysms varying from 70% to 100%.

Complications

Our results demonstrate the significant promise of endovascular thrombotic therapy in the treatment of difficult aneurysms; however, both the early potential complications and long-term prognosis require critical assessment. In our series, one patient developed thrombosis of the parent artery when the coils inadvertently occluded the internal carotid artery; this experience cautions against the overaggressive placement of multiple microcoils in an aneurysm with a broad neck. However, we have not experienced propagation of thrombosis or distal embolization from the induced thrombosis when the coils remained within the aneurysm. A review of the literature suggests that propagation of clot from an occluded aneurysm is rare. There are only two reported cases of spontaneously occluded giant aneurysms resulting in parent artery occlusion.2,36 Distal thromboembolism from a clotted aneurysm has been described in 5% to 59% of cases in reported series.36 In our patients, the likelihood of distal embolism is small because the platinum-microcoil-induced thrombosis is intermeshed with Dacron fibers. In this series, the single death was secondary to reperfusion vasogenic cerebral edema that occurred when the occluded internal carotid artery was recanalized. Reperfusion cerebral ischemia is characterized by early cytotoxic edema and later vasogenic edema resulting in expansion of the extracellular space.11 Vasogenic edema characteristically occurs following restoration of cerebral blood flow after an ischemic period. Ito, et al.,24 demonstrated a marked increase in the water content of the brain after 3 to 6 hours of cerebral ischemia followed by 21 hours of reperfusion of the hemisphere; they also showed that the edema resulted from leakage of plasma constituents from the blood through the damaged blood-brain barrier. Another potential etiological factor for cerebral edema is the induced inflammatory reaction within the brain that may follow rapid thrombosis of the aneurysm. Heros and Kolluri14 reported massive cerebral edema following spontaneous thrombosis of two intracranial aneurysms. Similarly, in a series of 25 patients, Whittle, et al.,36 presented CT evidence of cerebral edema surrounding the aneurysm in two patients.
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Long-Term Outcome

The long-term outcome of patients with endovascular intra-aneurysmal thrombosis is not known. Aneurysms that are partially spontaneously thrombosed bleed at a rate not dissimilar to that of nonthrombosed aneurysms. In his original series treated by pilection, Gallagher found that three of the four partially thrombosed aneurysms had ruptured. In the series reported by Mullan, all eight patients whose aneurysm was partially thrombosed died of a ruptured aneurysm. The significant aneurysm hemorrhage rate reported above is less likely to apply to our patient series because the platinum-Dacron microcoils produce an extensive fibrotic intra-aneurysmal thrombosis that may prevent long-term rupture of the aneurysm.

Conclusions

This study demonstrates the potential usefulness of endovascular thrombotic therapy utilizing platinum-Dacron microcoils to treat difficult aneurysms. The technique is relatively safe, with a procedure mortality rate of 9%. We demonstrated persistent thrombosis in smaller aneurysms (10 to 20 mm) for at least 6 months. However, repeat endovascular treatment may be needed before stable thrombosis occurs in giant aneurysms or aneurysms containing intra-aneurysmal clot. Intra-aneurysmal thrombosis may protect against future rupture, but further long-term follow-up review is required.

Acknowledgments

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