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Local Intraarterial Fibrinolysis of Thromboemboli Occurring during Endovascular Treatment of Intracerebral Aneurysm: A Comparison of Anatomic Results and Clinical Outcome

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PURPOSE: **We describe our therapeutic strategy and correlate the anatomic results and clinical outcomes in patients who received immediate fibrinolytic therapy for thromboembolic complications occurring during endovascular treatment of an intracerebral aneurysm.**

METHODS: **The medical records and angiographic examinations of 19 patients were reviewed. All endovascular procedures were performed with the patients under general anesthesia and fully heparinized. Thirteen patients received an intravenous bolus injection of aspirin. Thromboemboli occurred during catheterization or insertion of embolic material (Guglielmi detachable coils or mechanical detachable spirals) or in the first hours after the intervention. Clot distribution was within the MCA territory in 14 patients, the ACA in three patients, and the basilar trunk in two patients. A continuous intraarterial injection of urokinase was administered immediately, either superselectively distal to the thrombus or selectively within or closely proximal to the thrombus. In nine cases, chemical lysis was combined with mechanical clot fragmentation. Initial anatomic recanalization as well as clinical outcome at 3 months were evaluated.**

RESULTS: **Ten patients showed complete recanalization and nine patients showed partial recanalization. Fourteen patients had a good clinical recovery. One patient was moderately disabled and two were severely disabled according to their scores on the Glasgcow outcome scale. Two patients died, one as a consequence of the preexisting subarachnoid hemorrhage and the other because of a large intracerebral hematoma that developed after fibrinolysis. Of the 14 patients with a good clinical outcome, nine exhibited complete recanalization and five partial recanalization.**

CONCLUSION: **Pharmacological thrombolysis seems to be a safe and efficient therapy that facilitates the natural fibrinolytic process, increasing the rate of recanalization in thromboembolic events. Clot fragmentation and superselective drug infusion appear to improve the rate of recanalization. Complete recanalization increases the chance of a better clinical outcome; however, clinical outcome does not always correspond to recanalization and vice versa.**

The last decade has seen the development of new materials and advances in vascular catheterization techniques that have made it possible to treat various diseases via an endovascular approach. Of special interest is the technology to treat intracranial aneurysms by coil or spiral embolization; however, an important drawback of this technique is the risk of thromboembolic complications. Many reports have been published on intravenous and intraarterial fibrinolytic drug therapy in patients with spontaneous thromboembolism in intracranial arteries (1–5). Several of these studies suggest that fibrinolysis may be a new and safe therapeutic strategy for acute stroke (6, 7). However, reports concerning the final anatomic and clinical results of fibrinolytic treatment performed immediately after intracerebral vascular occlusion are few (8, 9). We have been treating intracranial aneurysms via the endovascular technique since 1992. In some patients, thromboembolic events occurred during therapy or in the first few hours after embolization, precipitating immediate intraarterial fibrinolysis. The iatrogenic circumstances and the tim-

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TABLE 1: Initial symptoms, aneurysmal location, and result of aneurysmal occlusion

Case	Age, y/Sex	Initial Symptoms	Location of Aneurysm	Size of Aneurysm, mm	No. of Additional Aneurysms	Interval between Symptom Onset and Therapy	Embolization Material	Degree of Aneurysmal Occlusion, %
1	33/F	SAH	R MCA, vasospasm	7	1	5 d	MDS	<90
2	52/M	Headache, vertigo	R MCA	7	3	3 mo	MDS	97
3	42/F	Aneurysmal remnant	R MCA	4	. . .	3 mo	. . .	No treatment
4	50/F	SAH, hemiparesis	R MCA, vasospasm	8	. . .	14 d	GDC	100
5	49/M	Aneurysmal remnant	L MCA	15	1	2.5 mo	MDS	100
6	59/M	TIA	L MCA	8	. . .	3 mo	. . .	No treatment
7	49/M	Headache, hemiparesis	L MCA	7	. . .	2.5 y	. . .	No treatment
8	23/F	SAH	R MCA, edema/ vasospasm	4	. . .	<7 d	GDC	100
9	58/F	Headache, fever, photophobia	L MCA, vasospasm	20	3	9 d	GDC	70
10	69/M	Neurinoma, 8th nerve	R MCA	7	. . .	>3 mo	GDC	>95
11	55/M	Seizure	AComA	20	1	4 mo	MDS	>95
12	55/M	SAH	AComA	5	. . .	6 d	Spir	100
13	57/M	Aneurysmal remnant (surgically clipped)	AComA	24	2	2.5 y	Spir	>95
14	54/M	SAH	AComA	3	. . .	3 d	GDC	100
15	61/M	Aneurysmal remnant	AComA	>25	. . .	6 mo	. . .	No treatment
16	36/M	Trauma	AComA	20	. . .	8 mo	GDC	70
17	58/F	Epistaxis	L ICA	8	1	5 mo	. . .	No treatment
18	36/M	SAH	BA	6	. . .	2 d	MDS	>95
19	45/F	Screening (PCD)	BA	4	1	>1 mo	MDS	100

Note.—MDS indicates mechanical detachable spirals; GDC, Guglielmi detachable coils; Spir, free spirals; No treatment, coiling was not initiated owing to early thromboembolic complication; PCD, polycystic kidney disease; SAH, subarachnoid hemorrhage; MCA, middle cerebral artery; TIA, transient ischemic attack; AComA, anterior communicating artery; ICA, internal carotid artery; and BA, basilar artery.

ing of the fibrinolysis were different from those in typical stroke patients (1–7). This retrospective study was designed to analyze our technique with regard to lysis of intracerebral thromboemboli in the acute phase and to correlate initial anatomic results with clinical outcome at 3 months' follow-up.

Methods

Patients

Twenty of 352 patients with intracerebral aneurysms treated during the period from January 1992 to June 1995 suffered thromboembolic complications during endovascular coil embolization. One patient was excluded from this analysis owing to aggravation of previously known psychiatric problems, making accurate neurologic evaluation impossible. The final group thus consisted of 19 patients, 12 men and seven women, 23 to 69 years old (mean age, 44 years). The patients and the results of their clinical and angiographic examinations are summarized in Table 1.

Six patients had acute subarachnoid hemorrhage (SAH), verified by computed tomographic (CT) examination. Three patients experienced a sudden onset of clinical symptoms, such as headache, meningeal irritation, photophobia, transient hemiparesis, and so on, indicating a minor leak. Neither CT nor acute lumbar puncture showed evidence of SAH, but CT scans indicated an arterial aneurysm, which was confirmed at subsequent angiography. Four patients had previously been treated for aneurysms and were scheduled for embolization (one patient had undergone surgical clipping but had a local recurrence, and three had undergone coil embolization but a remnant of the aneurysmal neck remained). In six patients, clinical history and symptoms were vague, and the aneurysm was an incidental finding at CT.

Five of the nine patients with SAH or a suspected leak were treated in the acute stage (within 7 days after the SAH), two in the subacute phase (8 to 21 days after SAH), and the remaining two 3 months to 2.5 years after SAH. The patients without hemorrhage were treated 2.5 months to 2.5 years after the diagnosis.

Fifteen of the 19 patients were without focal neurologic deficits at the time of the procedure. Two patients presented with mild to moderate hemiparesis (cases 4 and 7). The remaining two had minor deficits from prior surgery for an acoustic neurinoma (case 10) or from aneurysmal clipping (case 13). At the time of embolization, all patients were classified according to their score on the Glasgow Coma Scale. One patient (case 18) had a score of 11 and two (cases 4 and 7) had scores of 13; all the others scored 14 or 15.

The treated aneurysms were located in the middle cerebral artery (MCA) in 10 patients, in the anterior communicating artery (AComA) in six, at the tip trunk of the basilar artery (BA) in two, and in the supraclinoidal portion of the internal carotid artery (ICA) in one. Eight patients had multiple aneurysms. Aneurysmal size was classified as small (<15 mm) (13 patients) or large (15 to 25 mm) (five patients). A giant aneurysm (>25 mm) was present in one patient. Vasospasm was observed in four patients, two who were treated in the acute phase and two who were treated in the subacute phase after SAH. Selective papaverine injection was given in one of these patients (case 9) to facilitate further catherization.

Angiography

All procedures were performed with the patient under general anesthesia, and all patients were fully heparinized by means of a biplane angiographic unit (Philip Integris, Best, the Netherlands). Diagnostic cerebral angiography was performed before or in direct connection with the therapeutic endovascular procedure. Fast subtraction rotational sequences were ini-

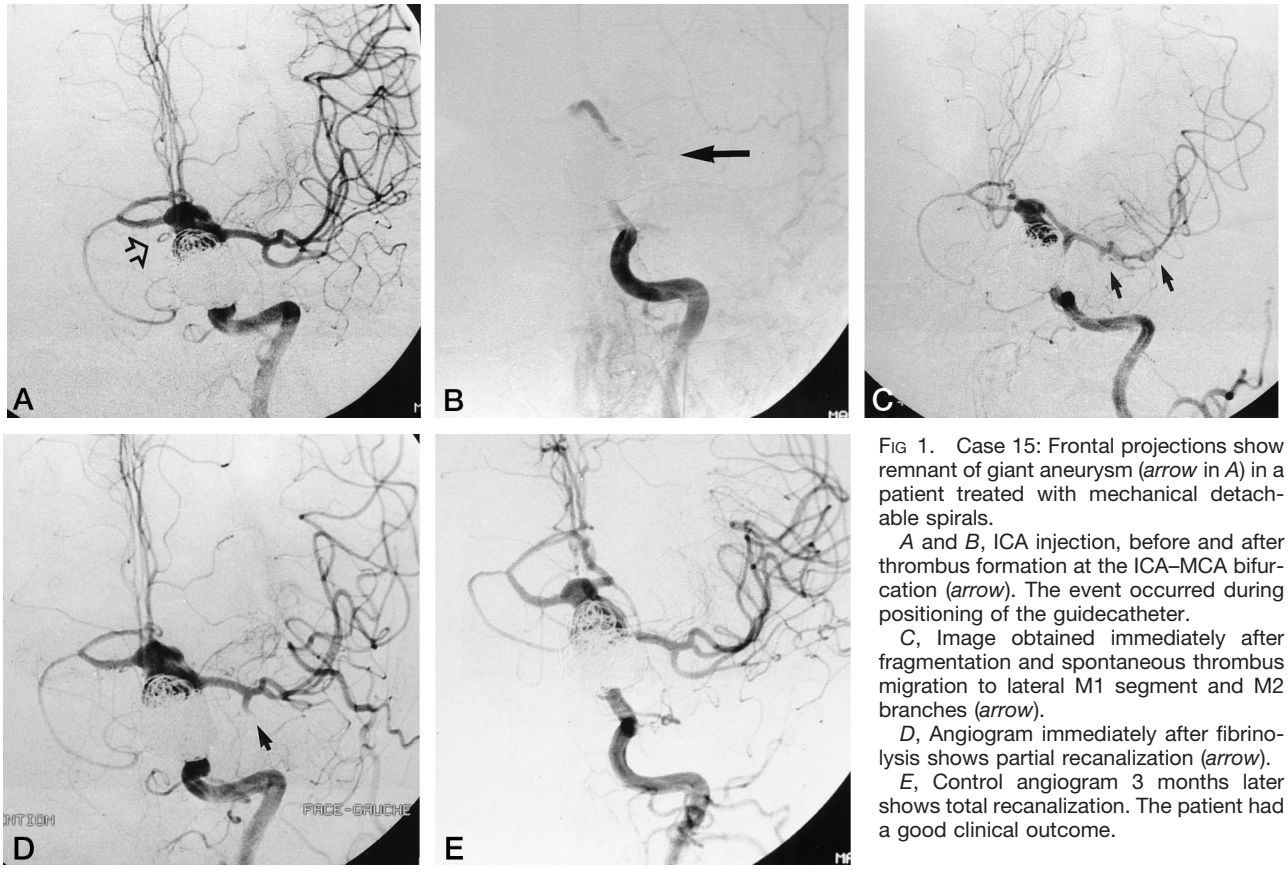

FIG 1. Case 15: Frontal projections show remnant of giant aneurysm (*arrow* in *A*) in a patient treated with mechanical detachable spirals.

A and *B*, ICA injection, before and after thrombus formation at the ICA–MCA bifurcation (*arrow*). The event occurred during positioning of the guidecatheter.

C, Image obtained immediately after fragmentation and spontaneous thrombus migration to lateral M1 segment and M2 branches (*arrow*).

D, Angiogram immediately after fibrinolysis shows partial recanalization (*arrow*).

E, Control angiogram 3 months later shows total recanalization. The patient had a good clinical outcome.

tially performed to define the optimal projection for visualization of the aneurysmal neck. A nonionic, low-osmolar contrast agent was used (Omnipaque, Nycomed, Olso, Norway).

Embolization Technique

The microcatheters used included the MAG 3F/2F (Balt, Montmorency, France) for mechanical detachable spirals and free spirals (both manufactured by Balt) and the Tracker 10 (Target Therapeutics, San Jose, Calif) for Guglielmi detachable coils (Target Therapeutics). Most frequently, Terumo guidewires (Terumo, Tokyo, Japan) were used to navigate the microcatheters.

Heparinization Regime

Heparin was given as soon as the 6F introducer sheat was inserted. From 1992 to 1994, a dose of 50 IU/kg body weight was given as a bolus followed by a continuous infusion of 30 IU/kg per hour during the endovascular procedure) (mean dose, a bolus of 3500 IU followed by 2100 IU/h). This was later changed, and from the beginning of 1994, a bolus of 5000 IU followed by a continuous infusion of 2500 to 3000 IU/h has been used. The aim of anticoagulation was to keep the activated clotting time (ACT) at a level two to three times above normal during catheterization and coil embolization. In addition, 200 to 250 mg of aspirin was given intravenously as a single dose in most patients, the exceptions were those treated in the acute phase. No heparin was added to the catheter flush solutions. Heparinization by continuous infusion was continued for 48 hours after treatment, with a dose that maintained the activated partial thromboplastin time (APTT) two to three times above the normal level. In case of complications, heparinization was sometimes prolonged and intensified (APTT elevated three to four times above normal).

Thromboembolic Complications

Angiographic criteria for thromboembolism were reduced flow and absence of opacification on previously seen vessels or intraarterial filling defects. All the thromboembolic episodes occurred during the interventional procedure (18 patients) or within the first hours thereafter (one patient). In four patients (cases 3, 15, 16, and 17) intracranial emboli were noted when the 6F guidecatheter was placed within the lumen of the ICA (Fig 1, case 15). In the majority of cases (14 patients), the thromboembolic event occurred either when the microcatheter was maneuvered into or out of the aneurysmal sac or during insertion of the coils/spirals. In three of these patients (cases 2, 5, and 8), obstruction of the parent vessel (MCA bifurcation or trifurcation) was probably caused by coil protrusion with additional local thrombus formation (Fig 2, case 5). In one patient (case 10), signs of thromboembolism (transient episodes of hemiparesis) developed 2 hours after the intervention, and coil migration with local thrombus formation at the aneurysmal neck was observed on the emergency control angiogram.

The occurrence and distribution of thromboemboli were within the trunk and/or distal branches of the MCA in 14 patients (the M2 branches were involved in 13), in the segments of the anterior cerebral artery (ACA) in three patients and at the trunk and/or tip of the BA in two patients (Table 2). In two patients included in the MCA group (cases 3 and 15), the thrombus initially appeared at the ICA-MCA bifurcation but migrated spontaneously into the lateral portion of the MCA before fibrinolysis had started.

Fibrinolytic Therapy

In all patients, fibrinolytic therapy started immediately after control angiography produced signs of thromboembolism. The thrombus was mechanically fragmented before fibrinolysis in

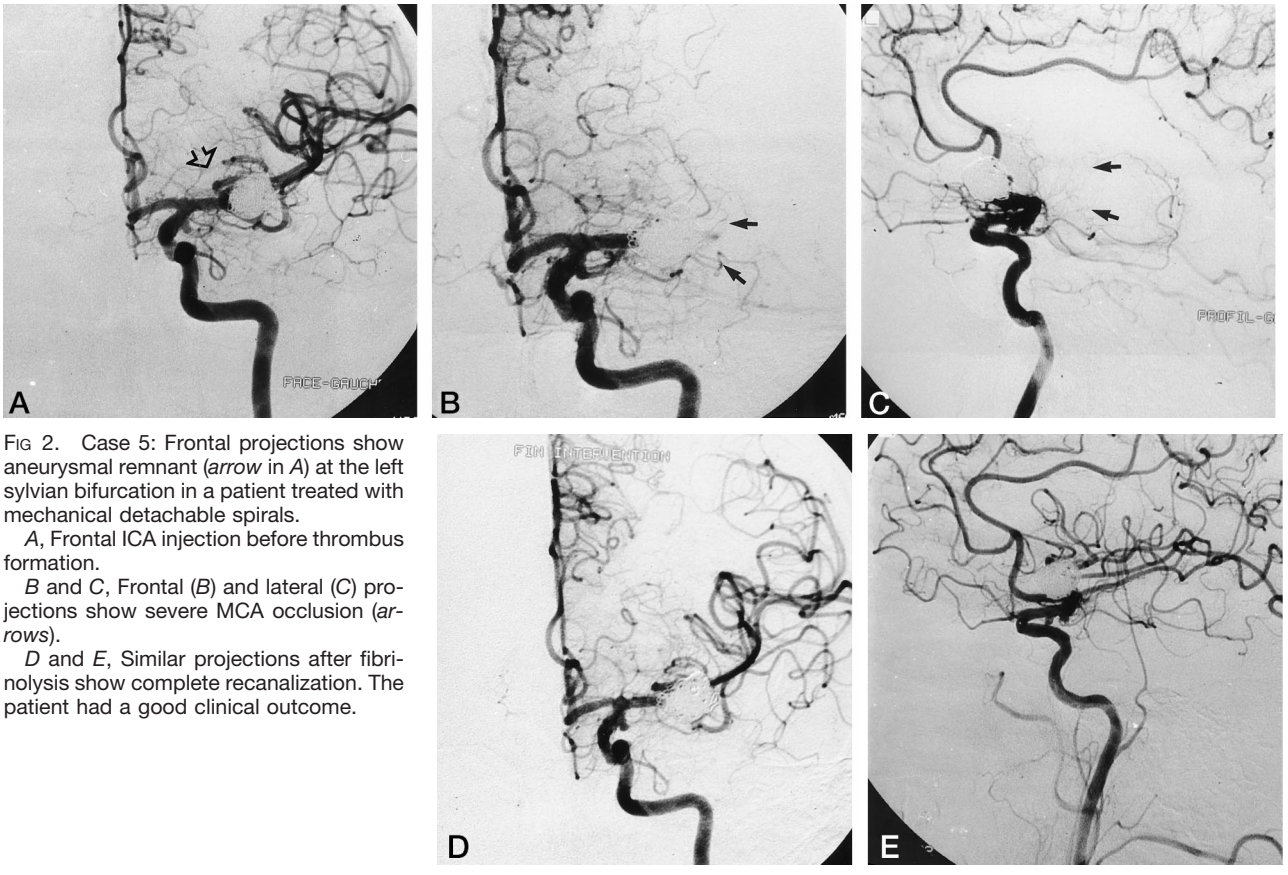

FIG 2. Case 5: Frontal projections show aneurysmal remnant (*arrow* in *A*) at the left sylvian bifurcation in a patient treated with mechanical detachable spirals.

A, Frontal ICA injection before thrombus formation.

B and *C*, Frontal (*B*) and lateral (*C*) projections show severe MCA occlusion (*arrows*).

D and *E*, Similar projections after fibrinolysis show complete recanalization. The patient had a good clinical outcome.

nine patients, for whom it was possible to pass through the thrombotic mass using the guidewire and/or the microcatheter with a simultaneous injection of saline solution. In these patients, the tip of the catheter was positioned superselectively, distal to the thrombus, before the fibrinolytic drug was administered. Clot fragmentation and superselective catheterization were not possible in the remaining 10 patients owing to the vascular anatomy or coil protrusion in these patients, the catheter had to be positioned selectively within or just proximal to the thrombus.

Urokinase infusion at a concentration of 15 000 to 20 000 IU/mL was then started by continuous manual injection. The mean dose used was 975 000 IU (range, 450 000 to 1 300 000 IU) and the infusion rate was approximately 20 000 IU/min. The infusion lasted 30 to 60 minutes and was repeatedly interrupted by control angiography. Once perfusion had been reestablished, the fibrinolytic treatment was stopped. Even if perfusion was not achieved, treatment was stopped at the maximum dose of 1 300 000 IU. Final control angiography was performed in one or more of the main arteries (ICA, VA) to evaluate the canalization and the existence of a possible collateral blood supply. Heparinization was continued throughout the procedure according to the normal routine. A mandatory ACT and fibrinogen test were conducted in all patients before starting fibrinolysis and repeated 3 hours after cessation of fibrinolysis. Postoperative heparinization was conducted as described above.

CT examinations were performed in seven patients immediately after lysis or within the first days after embolization. Control angiograms were obtained in three patients within the first days after fibrinolysis, and 13 patients had repeat angiography at long-term follow-up.

Evaluation of Anatomic Results and Clinical Outcome

The results were based on the degree of recanalization observed on the angiograms obtained immediately after fibrinolytic therapy and at neurologic examination performed at approximately 3 months.

We defined complete recanalization as normal opacification of all previously occluded vessels and partial recanalization as recanalization of one or more but not all occluded arteries. Those with almost complete recanalization were included in this group (4) (ie, patients with flow reduction remaining in the periphery of the vessels involved). We defined no recanalization as the condition in which all vessels remained occluded.

Neurologic examinations were performed during the first 24 hours after the embolization and fibrinolytic procedures, at the time the patient left the hospital, and again after 3 months. Patients were divided into five groups depending on their score on the Glasgow Outcome Scale (GOS) (10): GOS 5 indicated good recovery (resumption of normal life despite minor deficits); GOS 4, moderate disability (disabled but independent); GOS 3, severe disability (conscious but disabled, dependent for daily care); GOS 2, persistent vegetative state (unresponsive and speechless); and GOS 1, death.

Results

Anatomic results, clinical outcome characteristics, and complications are summarized in Table 2.

Anatomic Results

At the end of fibrinolytic infusion, complete recanalization was achieved in 10 patients and partial re-

TABLE 2. Location of thromboemboli, fibrinolytic strategy, anatomic result, and clinical outcome

Case	Neurologic Deficits	Thrombus Distribution (n)	Microcatheter Position	Fragmentation	Urokinase, ×10 000 IU	Complications	Anatomic Result	Findings at Long-Term Control Angiography	Glasgow Outcome Scale Score (GOS 1–5)		
									24 h	4–7 d	>3 mo
1	0	R M1–2 (all)	S	No	120	Rehemorrhage, aneurysmal rupture	PR (collaterals)	PR	3	4	5
2	0	R M2 (1)	S	No	90	. . .	PR (collaterals)	CR	3	4	5
3	0	R M1	S	No	90	. . .	CR	CR	4	5	5
4	0	R M1–2 (4)	SS	Yes	95	. . .	CR	CR	5	5	5
5	0	L M1–2 (1)	S	No	90	. . .	CR	CR	5	5	5
6	0	L M2 (1)	SS	Yes	100	. . .	CR	. . .	5	5	5
7	0	L M2 (1)	SS	Yes	70	. . .	CR	CR	5	5	5
8	0	R M2 (3)	S	No	90	ICH	PR (collaterals)	. . .	2 (ICH/op)	1	1
9	0	L M2 (2)	SS	Yes	100	. . .	PR	CR	2	3	3 (aphasia, mild hemiparesis)
10	7th nerve palsy (postop)	R M2 (2)	S	No	45	Infarct	PR (collaterals)	. . .	3	4	5
11	0	A1–2	S	No	105	Infarct	CR	. . .	3	3	4 (mild hemiparesis, algoneurodystrophia)
12	0	A1–2	S	No	90	Spasm	PR	. . .	4	2	1
13	Hemiparesis (postop)	A1–2	S	No	82.5	. . .	CR	CR	5	5	5
14	0	L M1–2 (3)	SS	Yes	105	Rehemorrhage, aneurysmal rupture	PR (collaterals)	CR	2	3	3 (aphasia)
15	0	R M1–2 (3)	SS	Yes	130	. . .	PR (collaterals)	CR	4	5	5
16	0	A2–3	SS	Yes	100	. . .	CR	CR	5	5	5
17	0	R M2 (2)	SS	Yes	110	. . .	CR	CR	5	5	5
18	0 Hydrocephalus	BA (4)	S	No	120	Infarct	PR	CR	4	5	5 (quadrant hemianopia)
19	0	BA (2)	SS	Yes	120	. . .	CR	. . .	5	5	5

Note.—S indicates selective; SS, superselective; CR, complete recanalization; PR, partial recanalization; GOS 5, good recovery; GOS 4, moderate disability; GOS 3, severe disability; GOS 2, persistent vegetative state; GOS 1, death; and ICH, intracerebral hemorrhage, and op, followed by immediate operation (surgical evacuation).

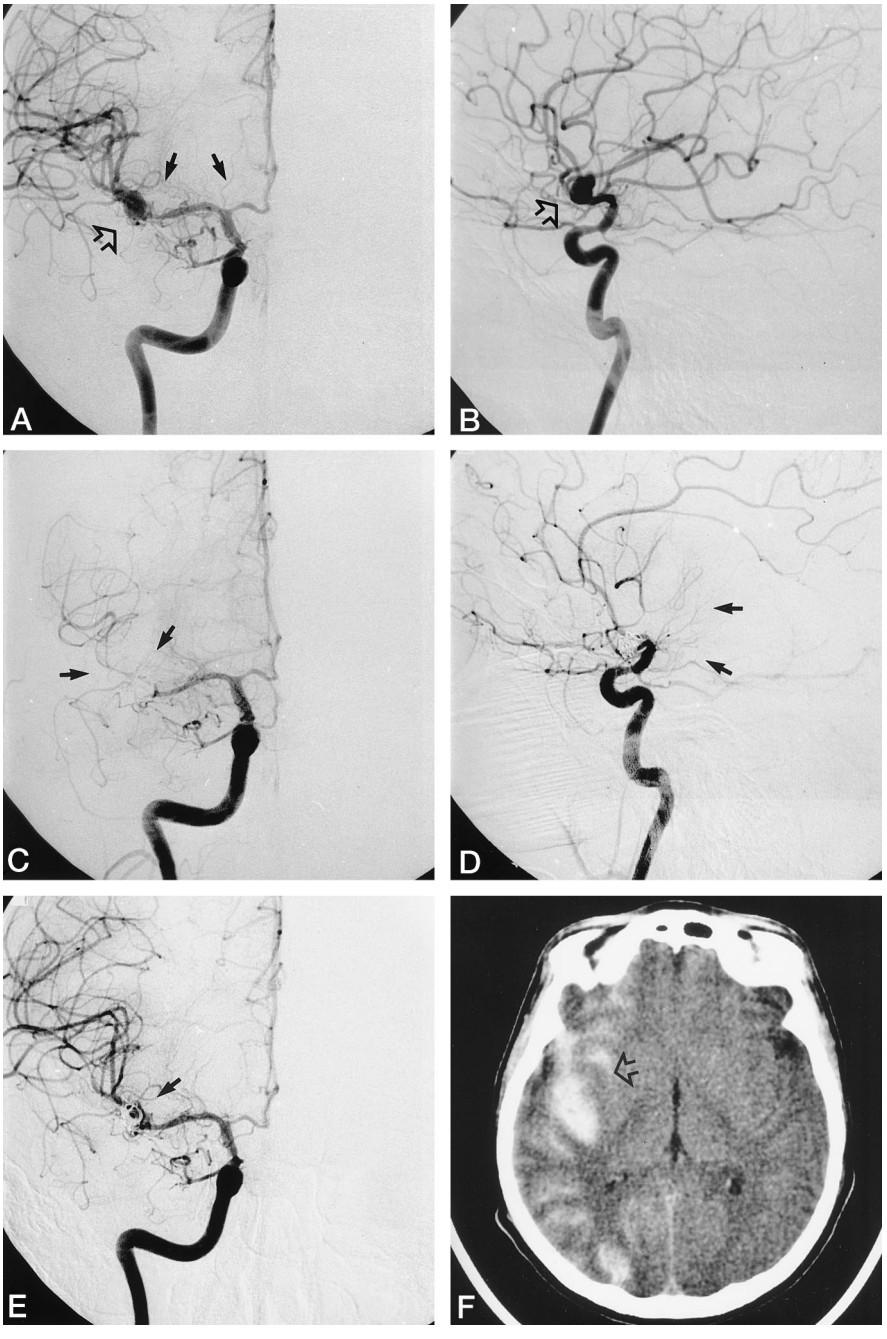

FIG 3. Case 1: Patient with an acute SAH.

A and *B*, Frontal (*A*) and lateral (*B*) projections show a small MCA aneurysm (*open arrow*) and moderate vasospasm (*closed arrows*).

C and *D*, Thrombosis developed during coiling. Images obtained after fibrinolysis show partial recanalization and several of the MCA branches that remained unopacified (*arrows*).

E, Control angiogram (frontal projection) 3 days later shows almost complete recanalization.

F, CT scan obtained immediately after fibrinolysis due to aneurysmal rupture during the procedure. Blood is seen within the right sylvian fissure (*open arrow*). No neurologic deficits were noted at long-term follow-up.

canalization was obtained in nine patients. Of the former, the vessels affected were the BA in one, the ACA in three, and the MCA in six (one or more of the M2 branches were engaged in five of these six). In nine patients in whom partial recanalization was achieved, four had almost complete recanalization, with only a modest flow reduction in peripheral vessels (cases 2, 9, 10, and 12). A collateral, leptomeningeal blood supply was noted in most of the patients with partial recanalization. Seven of these patients had thromboemboli located in the MCA territory (in several, two or more of the M2 segments were involved). In one of these patients, most of the M2 segments showed no opacification after thrombolysis (case 1, Fig 3). One patient had thrombus in the ACA region, and the remaining patient had thrombus within the vertebrobasilar junction and at the tip of the BA (case 18, Fig 4).

In three of these patients, control angiograms, obtained during the first days after treatment, showed complete recanalization in one patient (case 18), almost complete recanalization in one patient (case 1), and an unchanged pattern in the third patient (case 14). Of the 13 patients who underwent control angiography after a long time interval, six belonged to the group with partial recanalization. All six showed angiographic improvement, and five patients had completely normal vascular morphology.

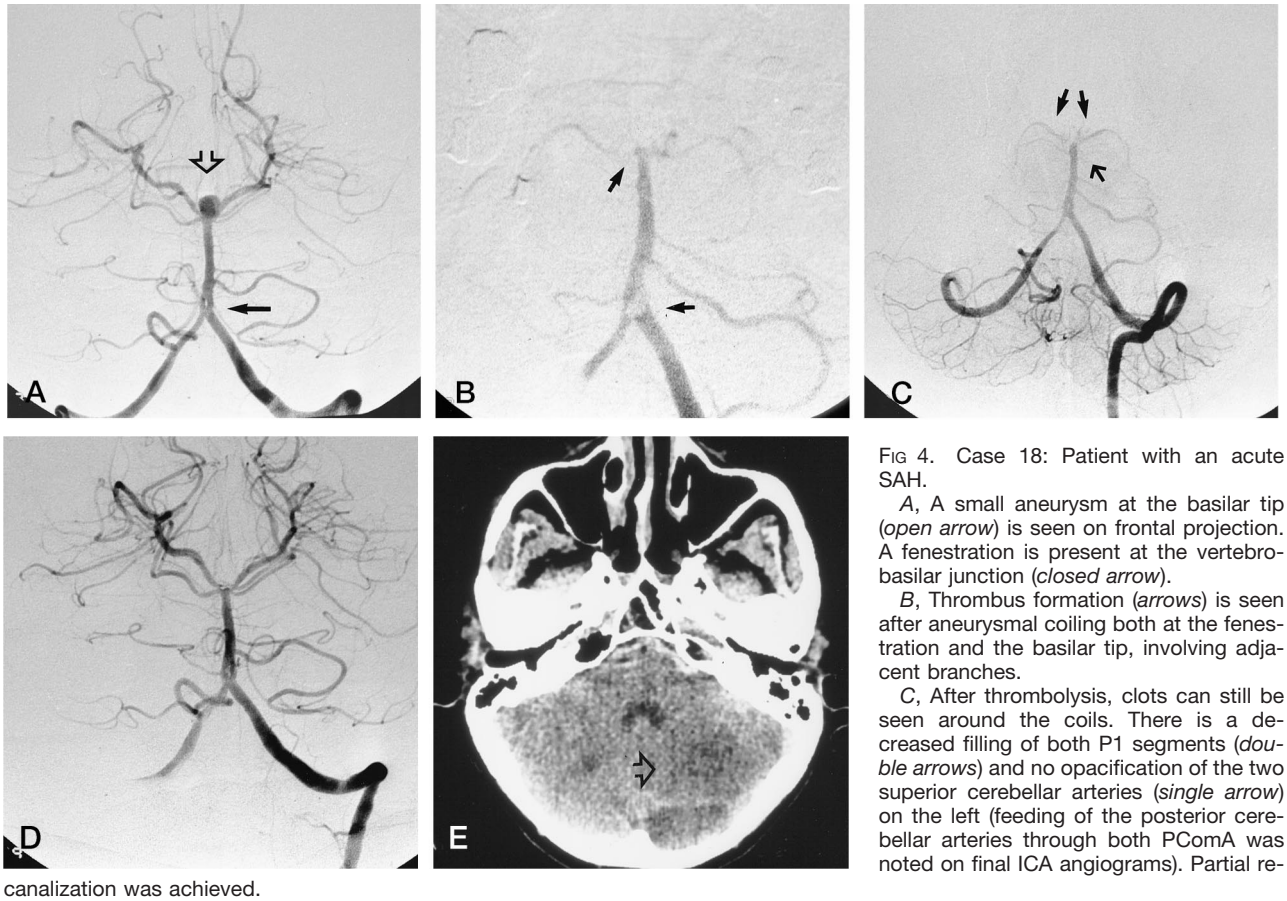

FIG 4. Case 18: Patient with an acute SAH.

A, A small aneurysm at the basilar tip (*open arrow*) is seen on frontal projection. A fenestration is present at the vertebrobasilar junction (*closed arrow*).

B, Thrombus formation (*arrows*) is seen after aneurysmal coiling both at the fenestration and the basilar tip, involving adjacent branches.

C, After thrombolysis, clots can still be seen around the coils. There is a decreased filling of both P1 segments (*double arrows*) and no opacification of the two superior cerebellar arteries (*single arrow*) on the left (feeding of the posterior cerebellar arteries through both PComA was noted on final ICA angiograms). Partial recanalization was achieved.

D, Control angiogram obtained a few days later shows complete recanalization.

E, Left-sided cerebellar (*arrow*) and occipital infarctions are seen on CT scan obtained shortly after fibrinolysis. Clinical outcome was good, despite a persistent quadrant hemianopia.

Clinical Outcome

Eleven patients had made a good recovery when discharged from the hospital 4 to 7 days after treatment. In another three patients, further recovery was documented over the following months. A good recovery (GOS 5) was thus achieved in 14 patients (74%) on a long-term basis. Two of these patients had minor persistent neurologic deficits; one was left with arthralgia and the second with a minor lateral quadrant hemianopia. One patient had moderate disability after 3 months, exhibiting a mild leg and brachial hemiparesis with severe algoneurodystrophia (reflex sympathetic dystrophy syndrome). Another two patients were severely disabled (GOS 3). Both patients had persistent and severe aphasia, one with an additional minor hemiparesis. Two patients died. One patient (case 8) who had severe cerebral edema on a CT scan obtained before the intervention, also had vasospasm and endured a prolonged therapeutic procedure necessitated by coil migration. This patient was initially in good condition but 2 hours after the endovascular session she suddenly became comatose with bilateral mydriasis. CT revealed a massive, ipsilateral, intracerebral hematoma, which was immediately evacuated. She did not recover, and died some days later. The other patient (case 12) was initially in good clinical condition but severe vasospasm developed 3 days after treatment. CT revealed a large ischemic lesion and death followed some days later.

In two patients, the aneurysms ruptured during fibrinolytic therapy, prompting immediate reversal of heparinization. CT showed bleeding into the sylvian fissure in one patient (case 1, Fig 3) and into the interhemispheric fissure in the other patient (case 14). The first patient made a good recovery but the second was left with a severe disability. Cortical infarctions were apparent on CT scans in three patients (cases 10, 11, and 18).

Comparison of Anatomic Results and Clinical Outcome

Of the 14 patients who had a good clinical outcome, nine were in the group in whom complete recanalization was achieved and five were in the group with partial recanalization. The two patients in whom minor deficits persisted were among those with partial recanalization. The patient with moderate disability had complete recanalization whereas recanalization was classified as partial in the two patients with a GOS score of 3. In the two patients who died, only partial recanalization was obtained. In the three patients with a good clinical outcome and partial recanalization, a well-developed collateral blood supply

was noted. The patient (case 1) who had poor initial thrombus resolution but almost complete recanalization 3 days later had a good clinical outcome. Of the nine patients who had undergone clot fragmentation and superselective microcatheter location (ie, placed beyond the thrombus), complete recanalization was achieved in six. Seven of these nine patients made a good recovery and two were severely disabled. Four of the 10 patients who had the catheter positioned proximal to the thrombus made a good recovery. In three of these, complete recanalization was noted.

Discussion

Thrombotic complications during endovascular treatment of aneurysms occurred in 5.6% of our patients. In treating these complications, we used fibrinolytic drugs restrictively. Our contraindications to treatment were similar to those generally accepted for stroke patients, but were always balanced by the possible risk of a permanent ischemic brain lesion caused by the reduced blood supply. The decision to perform thrombolysis was based on the vascular territory involved and the blood flow pattern, including possible collateral supply. In all events in which a large clot formed and vascular occlusion persisted, fibrinolysis was initiated according to the technique described. Patients treated during the acute phase of SAH or following a recent rupture were given fibrinolytic drugs only if the aneurysm was sufficiently embolized.

Whenever possible, clot disruption by fragmentation is carried out before and in combination with chemical thrombolysis; clot fragmentation alone is never used as the sole solution. (L. Picard et al, "Thrombo-Embolic Complications of Intracranial Endovascular Procedures: Therapeutic Protocol," presented at the annual meeting of the American Society of Neuroradiology, Chicago, Ill, April 1995). The purpose of fragmentation is twofold: to establish flow beyond the thrombus, permitting passage of the fibrinolytic drug, the heparin, and the intrinsic fibrinolytic factors into the occluded area, and to increase the surface of the clot accessible to the drug (11). In this study, we found that complete recanalization was obtained in six of the nine patients who had been treated with a combination of clot fragmentation and fibrinolysis. In comparison, only four among the 10 patients in whom the catheter was positioned proximal to the thrombus belonged to the group in which recanalization was complete. These results suggest that fragmentation and superselective drug infusion may improve the rate of recanalization.

In four patients, occlusion of the major vessels occurred when the guidecatheter was inserted into the ICA. In these cases, catheterization was performed by a neuroradiologist who was undergoing endovascular training (ie, with limited experience in the use of these devices). This consequence underlines the necessity of thorough education and training. In the other 15 patients, tromboemboli occurred during or shortly after coil embolization. We consider this rate of thromboembolic complications, even though low, to be unsatisfactory. Thrombi formation may have been a consequence of our ambition to achieve a dense and complete occlusion of the aneurysmal sac, a goal that may have increased the risk of the coil mass extending toward the parent artery and adjacent branches. It definitely increases the duration of the endovascular procedure. However, this risk has to be balanced with the possibility of future growth or rerupture of the aneurysmal sac. To reduce periprocedural clot formation, the heparinization regime was changed in 1994, with the new dose based on the experiences of our cardiovascular surgeons. Since then, our rate of thromboembolic complications has decreased dramatically.

In all our patients, acute vascular occlusion developed during or within the first hours after the interventional procedure. Local intraarterial fibrinolytic drug therapy was administered within minutes after diagnosis. The fibrinolytic therapy was angiographically effective in all 19 patients. Complete recanalization was observed in 53% and partial recanalization in 47% of patients immediately after fibrinolysis. This rate of success is high compared with the rate of recanalization reported in the majority of publications, with the exception of that by Zeumer et al (12), who obtained recanalization in 96% of their patients. Barnwell et al (11) reported an overall recanalization rate of 77%, Mori et al (7) 45%, and Hacke et al (6) achieved 44% recanalization in treating vertebrobasilar occlusive disease. Sasaki et al (4) realized complete or partial recanalization in 74% of patients by using local intraarterial infusion. However, a true comparison of our results with respect to those published in other studies is not possible. Most reported studies used different treatment protocols, different definitions of recanalization, and involved patients suffering from an acute stroke due to cardiac fibrillation or atherosclerotic vascular disease. In our study, the general circumstances were entirely different, as were the patients. Nevertheless, our rate of recanalization indicates that the early administration of a fibrinolytic drug increases the chances of favorable clot dissolution.

The long-term follow-up angiograms in our series showed further improvement in five of six patients; results consistent with previous reports on the rate of spontaneous recanalization in a stroke population. Spontaneous thrombolysis has been estimated to be 20% during the first 24 hours and 80% within the first week after ictus (13). Even if not fully proved by our study, we believe that clot dissolution and recanalization are accelerated by therapeutic fibrinolysis. In this context it should be emphasized that the clinical progress was most obvious during the first week after therapy, but also that four of our patients improved during the following months (Table 2).

No major angiographic differences were evident between the patients in whom neurologic deficits developed and those in whom they did not, but complete recanalization seems to increase the chances of a better clinical outcome. The reasons these patients had different clinical outcomes are multifactorial. In

most cases, we believe that fibrin or thrombus formation was induced at the tip of the catheter or around the coil. However, on some occasions, the occlusive material may have been an embolus from a preexisting thrombosis within the aneurysmal sac that was dislodged during coil maneuvering. Consequently, these emboli originate from thrombotic material a long time before anticoagulant therapy is given, resulting in clots with different characteristics. As has been thoroughly discussed by Zeumer et al (12) aging thrombi lose their bound plasminogen, leading to less proteolytic reactivity.

Another factor that must be considered is the different vulnerability to ischemia found in different regions of the brain. In a study performed by Baired et al (14) using single-photon emission CT, some patients were found to exhibit reperfusion without angiographically verified recanalization, and vice versa. Further research into, and a deeper understanding of the circumstances leading to ischemic brain lesions is needed. In our opinion, the risks of clotting do not correlate with the size of the aneurysm but rather with its location and with the extent of experience of the doctor in charge.

Most thromboemboli in our series occurred in the MCA territory, which was also the most frequent location of the aneurysms. We regard this location as a region of special concern and interest, because it was in this region that we most often failed to obtain complete recanalization and a satisfactory clinical outcome, particularly if the more distal branches were involved. This result is in accordance with the experience of others (11). One explanation may be that placing the catheter in a position suitable for fibrinolytic therapy is often difficult because the branches originate in close relationship to the aneurysmal sac. Thrombosis is more likely in cases in which coils protrude from the aneurysm into the lumen of the main artery. This was the case in four of our patients.

Complications related to fibrinolytic therapy were seen in three patients. Two suffered aneurysmal rebleeding, in both instances the patients underwent embolization during the acute phase of an SAH. To prevent or minimize the risk of such a complication, we believe fibrinolysis should be considered only if the aneurysm has been sufficiently embolized. In the third patient, one of the two patients who died, a huge intracerebral hematoma developed, probably representing a hemorrhagic transformation of an ischemic lesion. It is likely that the fibrinolytic therapy contributed to this complication (1, 13). Asymptomatic bleeding was not seen in any of the other four patients who had CT examinations shortly after the intervention. No other adverse reactions to urokinase were noted.

In the one patient in whom severe vasospasm developed some days after fibrinolytic therapy, we regard the death as being related to and caused by the natural history of the subarachnoid hemorrhage rather than being related to the thromboembolism or the fibrinolysis that followed.

Conclusions

Only 20 (5.7%) of 352 patients treated with coil/spiral embolization in our department had thromboembolic complications followed by acute fibrinolysis. Nineteen of these 20 patients were included in this analysis. Twelve patients had a good clinical outcome after therapy. Seven patients were left with some neurological deficit or died. In six of these patients (1.7%), the neurologic sequelae were considered to be the result of the thromboembolic complication or the fibrinolytic therapy.

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