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BACKGROUND AND PURPOSE: **Platelet-derived thrombi may occur during intracranial aneurysm coiling. We report a series of 13 patients treated with intraarterial Abciximab for thrombus formation complicating aneurysm coiling.**

METHODS: **Four patients were treated for acutely ruptured aneurysms. Three procedures consisted of the retreatment of previously coiled aneurysms. Six patients had asymptomatic untreated aneurysms. Abciximab was administered intraarterially through a microcatheter as a bolus of 4–10 mg over a period of 10–20 minutes. All patients underwent postthrombolysis control angiography. They also underwent immediate pre- and postoperative cranial CT.**

RESULTS: **In 10/13 cases, the thrombi developed without coil protrusion into the parent artery. In one case, the thrombus was generated from the guiding catheter and embolized remote from the aneurysm site. In one case, the thrombus developed before any coil placement. In another patient, a coil loop protruded into the parent artery favoring a heightened thrombotic state. Arterial thrombi were totally occlusive in two patients, whereas in the remaining 11 cases, the thrombi were not totally obstructive. Complete recanalization was achieved in 92% (12/13) of cases within 20–30 minutes. Incomplete arterial reopening was noted in one case, in which a thrombus fragment embolized distally, causing cerebral infarction. There were no Abciximab-related intracranial hemorrhages.**

CONCLUSION: **Intraarterial Abciximab was effective in this series for the treatment of thrombotic complications occurring during aneurysm coiling.**

Thromboembolic complications, typically platelet-derived events, occur during aneurysm coiling in approximately 3% of the cases, resulting in a permanent neurologic disability in 1.7–5% of the procedures (1–3). In eloquent brain areas, thrombus disruption (of either mechanical or pharmacological origin) to reestablish arterial blood flow is mandatory when a thrombotic occlusion occurs in the absence of collateral flow. Until now, intraarterial thrombolysis with fibrinolytic agents has been widely used, but their benefit is hampered by the risk of subsequent intracranial hemorrhage (ICH), especially in the setting of acutely ruptured aneurysms. Moreover, the intraarterial administration of urokinase achieves arterial recanalization in only 47% of cases (4). Abciximab, the Fab fragment of the chimeric human-murine monoclonal antibody 7E3, binds to the glycoprotein Iib/IIIa receptor, as well as the vitronectin ($\alpha\nu\beta3$) receptor, inhibiting platelet aggregation with additional antithrombotic properties. Until now, few small series have reported the potential usefulness of Abciximab in the management of thromboembolic complications occurring in the setting of the endovascular treatment with detachable coils of intracranial aneurysms (5–8). We report our experience of intraarterial administration of Abciximab in the treatment of 13 patients for whom aneurysm coiling was complicated by thromboembolic events.

Methods

From January 2002 to October 2002, 227 aneurysms were treated by endovascular means. Ninety-eight of these 227 interventions were conducted with the balloon-remodeling technique, 14 were carried out with the assistance of a stent, and three were treated with a neck-bridge device (Trispan; Target/Boston Scientific, Fremont, CA). During the same period of time, 13 patients (eight men and five women; mean age, 49 years) developed intraprocedural thromboembolic complications during endovascular treatment of aneurysms with coils. Four patients were treated for acutely ruptured aneurysms; the delay from the onset of subarachnoid hemorrhage did not exceed 48 hours in all four cases. Three of these ruptured

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Case characteristics

Patient No./ Sex/Age (y)	Abciximab (mg/Kg)	Aneurysm Location	Acutely Ruptured	Coiling Technique	Thrombus Location	Vessel Occlusion
1/F/42	0.062	AcoA	No	Remodeling	A2 origin	No
2/F/53	0.125	Basilar tip	No	Remodeling	P1 origin	No
3/F/45	0.096	Supra ICA	No	NA	MCA	No
4/M/40	0.1	ICA Bif	No	Remodeling	MCA	No
5/F/48	0.08	PcoA	No	Std	PcoA origin	No
6/M/46	0.061	AcoA	No	Remodeling	A2 origin	No
7/F/56	0.071	AcoA	No	Std	A2 origin	No
8/M/48	0.06	AcoA	Yes	Std	AcoA A2 origin	Yes
9/M/61	0.053	MCA Bif	Yes	Remodeling	A5	No
10/M/45	0.057	MCA Bif	Yes	Remodeling	Upper trunk of MCA	Yes
11/M/47	0.065	AcoA	Yes	Remodeling	A2 origin	No
12/M/55	0.057	ICA Bif	No	Remodeling	M1 origin	No
13/M/51	0.054	MCA Bif	No	Remodeling	Upper trunk of MCA	No

Note.—AcoA, anterior communicating artery; ICA bif, bifurcation of the internal carotid artery; MCA bif, bifurcation of the middle cerebral artery; NA, not applicable; PcoA, posterior communicating artery; Std, standard coiling technique; Supra ICA, supraclinoid internal carotid artery.

aneurysms were coiled with the remodeling technique by using a balloon microcatheter that was temporarily inflated across the aneurysm neck during coil delivery. Three of 13 interventions consisted of the retreatment of partially recanalyzed previously coiled aneurysms; all three of these interventions were conducted at least 1 year after the initial coiling. These three aneurysms were retreated with the remodeling technique. Six of the 13 patients harbored an asymptomatic aneurysm, three of which were coiled with the remodeling technique. All patients were given an initial bolus of 5000 IU of heparin followed by the continuous infusion of 2500–3000 IU/h to maintain an activated clotting time (ACT) between 200 and 300 seconds. In accordance with our anticoagulation protocol, a 250-mg intravenous bolus of aspirin was administered to the patients for whom the aneurysm was not ruptured or was in the setting of a retreatment. Abciximab (ReoPro; Centocor, Malvern, PA) was administered intraarterially through the coil delivery microcatheter (Excelsior; Boston/Target, Fremont, CA) with its distal tip inserted in the occluded artery adjacent to the thrombus. The catheter tip was located just proximal to the aneurysm neck in 11 of 13 cases. In the remaining two cases (patients 3 and 9), the catheter tip was navigated distally up to the thrombus, which was located remote from the aneurysm site. Abciximab, diluted in saline to achieve a concentration of 0.2 mg/mL, was administered as a bolus of 4–10 mg over a period of 10–20 minutes, depending on how fast thrombus resolution was achieved while preventing injections exceeding 10 mg. In two cases, a concomitant local intraarterial bolus of 4 mg of Nimodipine was administered to resolve an associated vasospasm. All patients underwent postthrombolysis control angiography. They also underwent immediate pre- and postprocedural cranial CT in the angiographic room as we routinely do in the setting of endovascular treatment of cerebral aneurysms. Relevant data of all the 13 cases are summarized in the Table.

Results

In 10/13 cases (78%), the thrombi originated and were in contact with the coil mesh without any angiographically apparent coil protrusion into the parent artery. In one case of a right middle cerebral artery bifurcation aneurysm, the thrombus was located distally in the right anterior cerebral artery, as the embolus was generated from the guiding catheter totally irrespective of the aneurysm location. In another case, the thrombus developed before any coil placement; this patient was later shown to have an elevated factor VIII and a short ACT (30 seconds). Abciximab was administered and successfully dissolved the complicating clot, although no coils were placed. In another patient, a coil loop protruded into the parent artery, favoring a heightened thrombotic state. Seven patients had broad-neck aneurysms in which the coil-blood interface was large, thus increasing the thrombotic risk. Arterial thrombi were totally occlusive in two patients (Fig 1) whereas in the remaining eleven cases, the thrombi were small and not completely obstructive but compromising downstream arterial flow (Fig 2). Complete recanalization was achieved in 92% (12/13) of cases. In these patients, the thrombus dissolution was achieved within 20–30 minutes after the end of the Abciximab perfusion. Incomplete arterial reopening was obtained in one case in which a thrombus fragment embolized distally; Abciximab failed to completely dissolve the thrombus and a CT scan revealed a cerebral infarct in the territory of the compromised arterial branch (patient 9). This patient presented on admission with a ruptured aneurysm associated with a cerebral hematoma and a left hemiplegia; he subsequently died at day 4 from intracranial vasospasm. The deleterious effect of the vasospasm was augmented by the cerebral infarct secondary to the distal embolus. No evidence of postthrombolysis ICH or other developments of aggregated neurologic deficits related to the thrombotic events were present.

Discussion

Abciximab is a potent glycoprotein receptor inhibitor capable of preventing thrombosis. It is indicated as an adjunct to percutaneous coronary intervention for the prevention of cardiac ischemic complications. The standard dose of Abciximab in coronary angioplasty is an intravenous bolus of 0.25 mg/kg followed by a 12-hour infusion of 0.125 μg/kg/min. There are several reports in the literature of the thrombolytic

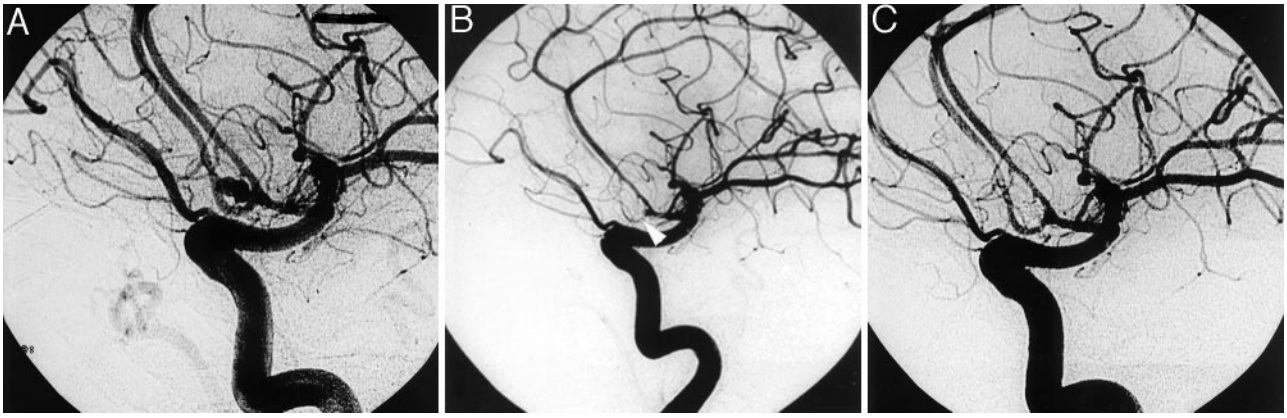

FIG 1. Case 8.
A, Left ICA (best projection), showing a ruptured anterior communicating artery (AcoA) aneurysm before the embolization treatment.
B, Left ICA (best projection) after aneurysm coiling, showing an obstructive thrombus (*arrowhead*) at the origin of the AcoA.
C, Left ICA (best projection) 20 minutes after the local delivery of 4 mg of Reopro, showing the restoration of the arterial flow in the AcoA and the right A2 segment.

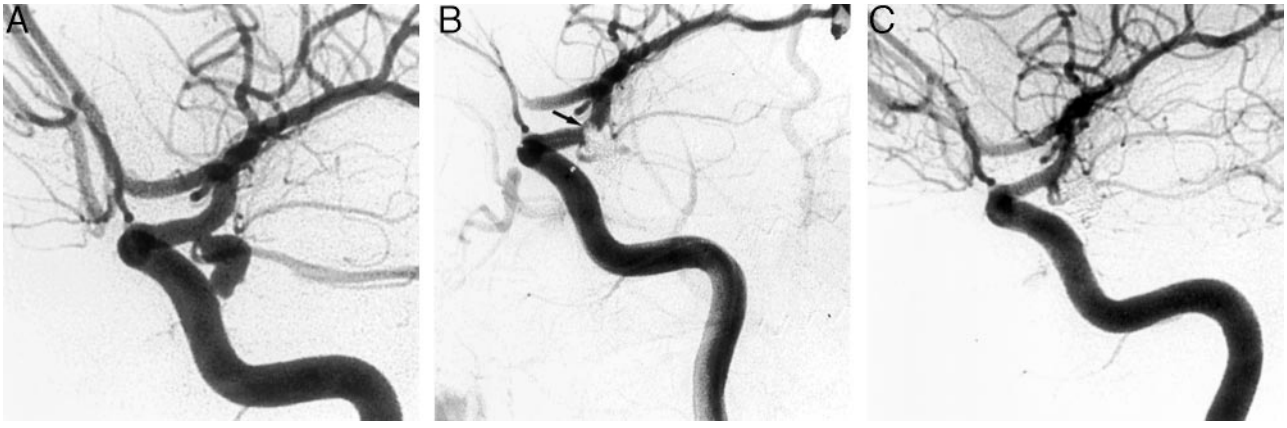

FIG 2. Case 5.
A, Left ICA (best projection), showing a ruptured supraclinoid ICA at the origin of the posterior communicating artery.
B, Left ICA (best projection) after aneurysm, coiling showing a nonocclusive thrombus (*arrow*) into the ICA lumen (*arrow*).
C, Left ICA (best projection) 30 minutes after the local delivery of 4 mg of Reopro, showing that the thrombus has been desegregated.

properties of Abciximab and of its benefits during endovascular intracranial procedures. These reports have shown that Abciximab has a potential indication as a rescue agent after failed thrombolysis (6, 9, 10) in the management of thrombotic complications of intracranial angioplasty (11), in the treatment of complications occurring during carotid angioplasty (5, 12, 13), and in aneurysm coiling (5–8). Abciximab has also been used in combination with fibrinolytic agents to enhance thrombolysis (6, 14). Abciximab was administrated intraarterially in only three of these reports (6, 12, 15). In experimental studies, rapid and complete resolution of preformed thrombi was achieved after early administration of Abciximab in a dose-dependent manner. This dose-dependent dispersion of platelet aggregates back to single cells was observed with Abciximab concentration well above the recommended dose used in coronary procedures (16). The mechanism of this effect was shown to be due to partial displacement of platelet-bound fibrinogen by Abciximab. In addition to its ability to disperse platelet aggregates, Abciximab has properties that impede the formation and stability of clot structure. It has been shown to allow the penetration of both endogenous and parenteral fibrinolytic agents into the clot, thereby promoting more rapid and extensive thrombolysis (17). The latter property is of significant importance particularly in older clots (ie, those consisting of platelets as well as fibrin and red blood cells).

Dose and Administration of Abciximab

We chose to deliver a 4-mg bolus of Abciximab intraarterially, up to a maximum of 10 mg. The abovementioned experimental data showed that early administration of Abciximab (within a minute of thrombus formation) at high concentrations led to rapid desegregation of the thrombus. We observed that clot resolution began within 20 minutes and was complete within 30 minutes in 92% (12/13) of the cases. It is likely that the local and immediate intraarterial administration of low doses of Abciximab effectively

produced high concentrations at the site of the thrombus.

To our knowledge, only three reports of intraarterial administration of Abciximab in the cerebral circulation exist in the literature. In two cases of acute distal embolization associated with carotid angioplasty, Abciximab was successfully used in a selective internal carotid bolus injection of 5 mg followed by an intravenous bolus of 5 mg (15). In three other cases of ischemic cerebrovascular events complicating carotid stent placement procedures, Abciximab bolus (0.25 mg/kg) was injected into the common carotid artery, followed by the standard coronary intravenous infusion of 0.125 μg/kg/min for 12 hours. Symptoms resolved in all three cases within 5 hours (12). Kwon et al (6) recently reported three cases of intraarterial use of Abciximab as a bailout procedure after failure of urokinase therapy for acute thrombosis of cerebral arteries. Abciximab was injected intraarterially at doses of 4 mg, 5 mg, and 10 mg, respectively, achieving a rapid flow restoration without hemorrhagic complications.

In our series, because the intraarterial route was chosen, a reduced partial bolus of 4–10 mg was used, representing a small fraction of the dose used for prophylactic administration of Abciximab in percutaneous coronary procedures (eg, 20 mg Abciximab bolus in an 80-kg adult). The standard recommended 12-hour Abciximab infusion, after bolus administration, maintains a platelet blockade during the highly thrombogenic phase within the first hours after coronary angioplasty and stent placement. In our cases, the procedure consisting of aneurysm embolization, with coils and any possible thrombi forming downstream of the aneurysm, would occur at a site without current vessel wall damage. Therefore, we did not consider that there was a need for prolonged antithrombotic coverage once the thrombus had dissolved.

Risk of Intracranial Hemorrhage

The main and potentially serious concern with Abciximab is bleeding. Abciximab is recommended to be used with low-dose heparin ($\leq$70 IU/kg) in conjunction with aspirin. No increase of major bleeding was observed as compared with that of heparin administration alone. It is important to note that the incidence of ICH in patients receiving Abciximab was not different from placebo in more than 8500 patients from the combined analysis of four major trials (18). There was, however, an insignificant trend toward increased ICH when Abciximab was used in combination with a high dose of nonweight-adjusted heparin (bolus >10,000 IU). Furthermore, in a randomized double-blind, placebo-controlled study designed to evaluate the safety of Abciximab in acute ischemic stroke, the rate of ICH was not increased as compared with that of placebo, despite enrollment of patients up to 24 hours after stroke onset (19). However, minor bleeding (3–5 g/L of hemoglobin loss) was increased by Abciximab, although most occurred at the vascular access site. Our patients underwent full heparinization, obtaining an ACT between 200 and 300 seconds. Patients in whom ICH was ruled out received an additional 250 mg of aspirin at the beginning of the procedure. We did not observe any ICH with this pharmacological combination; however, the amount of platelet-bound circulating Abciximab was certainly negligible in our patients. The absence of ICH in our series compares favorably with the risk of ICH when urokinase is used as a thrombolytic agent.

Conclusion

In our series, Abciximab proved a safe and effective rescue agent for thromboembolic complications during aneurysm coil placement. As a result, we no longer administer urokinase in the management of thrombotic complications in neurovascular procedures. The selective intraarterial administration of Abciximab allows significantly reduced dosing while providing a favorable safety profile and lowered costs.

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