Tissue plasminogen activator thrombolysis of a middle cerebral artery embolus in a patient with an arteriovenous malformation

Case report

JAFAR J. JAFAR, M.D., WALTER S. TAN, M.D., AND ROBERT M. CROWELL, M.D.

Department of Neurosurgery, New York University Medical Center, New York, New York; Department of Neurosurgery, University of Illinois at Chicago, Chicago, Illinois; and Neurosurgical Service, Massachusetts General Hospital, Boston, Massachusetts

A patient harboring a cerebral arteriovenous malformation (AVM) underwent angiography in an attempt to embolize the AVM. During catheterization (and prior to embolization) he became hemiplegic and aphasic. Angiography revealed a complete middle cerebral artery (MCA) occlusion by an embolus. The patient was treated with recombinant tissue plasminogen activator (t-PA), a thrombolytic agent. Restoration of MCA flow was achieved, and the patient recovered.

Immediately after MCA embolus, t-PA infusion may lead to thrombolysis and neurological recovery. The decision-making process as well as the risks associated with the use of t-PA are discussed.

KEY WORDS • tissue plasminogen activator • thrombolysis • arteriovenous malformation • embolism • angiography

ATROGENIC cerebral emboli are an infrequent but problematic complication of cerebral angiography. Berenstein specifically addressed the complication rate in 129 patients with cerebral arteriovenous malformation (AVM) who were treated with endovascular embolization (personal communication, 1989). He described a 13% rate of transient neurological complications, a 2% rate of permanent mild deficits, a 2% rate of serious permanent morbidity, and a 0.7% mortality rate. The accepted method of treatment for cerebral emboli has been emergency craniotomy and embolectomy. The time constraints of surgery are adverse, however; the longer the period of ischemia, the greater the cerebral damage, and the worse the outcome. Of 20 cases treated with emergency embolectomy at the Mayo Clinic, 35% had a good result, 35% did not improve, and 30% died poorly or died.

We present a patient with a cerebral AVM who incurred an iatrogenic middle cerebral artery (MCA) embolus during angiography prior to therapeutic embolization. The patient was treated with tissue plasminogen activator (t-PA) with flow restoration through the MCA and subsequently recovered. The advantages as well as the risks of the therapy are elucidated.

Case Report

This 37-year-old right-handed man was lifting weights when he experienced a severe frontal headache and vomiting, followed by stupor. He was taken to a local hospital where he was found to be dysphasic with a right hemiparesis. A computerized tomography (CT) scan of the brain revealed a large left frontal intraparenchymal hemorrhage with an associated AVM.

Over the next 3 weeks, the patient improved. A magnetic resonance (MR) image showed a large cigar-shaped AVM measuring 6.5 × 5 × 4 cm involving the medial aspect of the left frontal lobe accompanied by a subacute hemorrhage. Cerebral angiography revealed that the AVM was fed primarily by the left anterior cerebral artery (A1 and A2 segments) and the MCA (Fig. 1). Venous drainage from the AVM was to the superior sagittal sinus and the left middle cerebral veins.

Embolus During Angiography. Preoperative transfemoral embolization of the AVM was attempted. The strategy was to place a nondetachable occlusive balloon at the origin of the left MCA, thereby directing all the emboli to the left anterior cerebral artery territory. During the procedure, however, considerable difficulty
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![Fig. 1. Selective left internal carotid angiograms, anteroposterior (left) and lateral (right) views, showing the main arterial feeders to the arteriovenous malformation.](image1)

was encountered in floating the balloon to the MCA origin, for the balloon would not advance past the internal carotid artery bifurcation. While the delivery catheter was being flushed before any emboli were injected, the patient became completely aphasic and hemiplegic on the right with a right-sided central seventh nerve palsy. An angiogram was immediately performed revealing total occlusion of the left M, segment, presumably of embolic origin (Fig. 2). A CT scan of the brain was immediately obtained which ruled out the possibility that any new hemorrhages had occurred.

*Initial t-PA Treatment*. We considered embolectomy which would have involved the delay of first performing a craniotomy with microvascular dissection of the MCA from the overlying AVM venous drainage. We also considered using the thrombolytic agent t-PA which has the advantage of rapid intravenous administration. Although the AVM had ruptured several weeks earlier, t-PA did not effectively lyse old blood clots. Given the informed consent of the patient's family, we elected to proceed with t-PA thrombolysis. One hour after the ictus, t-PA thrombolysis was initiated. An intravenous bolus of 10 mg t-PA was administered, followed by 35 mg of continuous intravenous infusion during the 1st hour. The patient received 20 mg of t-PA during the 2nd hour, and another 10 mg was given during the 3rd hour as a continuous intravenous infusion, for a total of 75 mg over a 3-hour period. Within 30 minutes after initiation of therapy the patient started to regain speech and motor function. After the 1st hour of t-PA therapy, he improved markedly to normal motor function with minimal dysphasia. We did not want to heparinize the patient after thrombolytic therapy for two reasons. First, he still harbored an AVM with the possibility of hemorrhage. Second,

![Fig. 2. Pre-embolization angiograms, anteroposterior (left) and lateral (right) views, revealing the occluded M, and nonfilling of the middle cerebral artery branches (arrow).](image2)
he was young with no evidence of pre-existing atheroma, and the MCA was not catheterized; thus, the risk of recurrent thrombosis appeared small.

Discussion

Natural History of Emboli

The true natural history of acute MCA occlusion is difficult to determine. Spontaneous recanalization from presumed lysis of the embolus over time has been reported. A poor neurological outcome, however, has been documented in patients undergoing recanalization. Meyer, et al. reported that patients with acute profound deficits secondary to proximal MCA occlusion, such as our patient, fared poorly due to loss of flow in the lenticulostriate arteries which are functional end arteries.

Pharmacology of t-PA

Recombinant t-PA is a naturally occurring protein that catalyzes the conversion of inactive plasminogen into active plasmin, the main fibrinolytic enzyme. It is distinguished from other plasminogen activators, such as streptokinase and urokinase, by its enzymatic activity, which is greatly enhanced in the presence of fibrin.

The initial half-life of t-PA in plasma is 3.6 to 4.6 minutes and its terminal half-life ranges from 39 to 57 minutes. In practice, the action of t-PA outlasts its apparent half-life due to its binding to thrombi and because of the effects and longer half-life of its product plasmin. Tissue plasminogen activator has no hemodynamic effects and, since it is a naturally occurring substance, it is generally not considered immunogenic, unlike streptokinase. In pharmacological doses, t-PA (like other thrombolytic agents) cannot distinguish between a cerebral embolus and a protective hemostatic plug elsewhere. For this reason, all patients receiving t-PA should be monitored for bleeding from sites of catheter insertion. It is therefore advisable not to remove intravascular angiography sheaths prior to or for a few hours after t-PA administration.

Treatment Rationale

Tissue plasminogen activator has been used effectively in the treatment of patients with acute coronary and peripheral vascular thrombosis. The clinical use of thrombolytic therapy in acute stroke is still under investigation. Studies of experimental t-PA treatment have demonstrated re-establishment of cerebral circulation and blood flow, improvement in neurological and pathological outcome, and a reduction in mortality rate.

Urgent re-establishment of flow to the ischemic area is essential in preventing infarction. Experimental studies in regional ischemia have shown a critical period of 4 to 6 hours beyond which re-establishment of flow is of no benefit due to irreversible cerebral infarction. In our patient, thrombolytic therapy with t-PA was started 1 hour after the MCA embolic occlusion. The ease with which t-PA can be given through a peripheral...
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intravenous infusion system expedites the treatment process and decreases the ischemic time. Also, intravenous administration of t-PA alleviates the need to maintain the catheter tip near the embolus.

The decision to institute thrombolysis in our case was based on the need for immediate reperfusion and the angioarchitecture of the AVM. It was obvious that more than 4 hours would elapse from the time of the MCA occlusion to the actual re-establishment of flow by an embolectomy. Moreover, the major AVM drainage was via the sylvian veins, obscuring the MCA and rendering an attempted embolectomy tedious and dangerous. Although the patient had presented with an intracranial hemorrhage, that was 3 weeks before and t-PA-mediated thrombolysis is less effective as the clot ages. 19,24,25

The present case shows that immediate intravenous t-PA followed by heparinization can lyse an MCA embolus and lead to the resolution of a severe deficit. Since the embolus occurred in the angiographic suite, the time lag and diagnostic problems usual in the management of an MCA embolus were not encountered. 2 When a symptomatic MCA embolus occurs in the angiographic suite, t-PA therapy may be considered an important treatment option.

Potential Complications

Hemorrhage. A major potential complication of t-PA thrombolysis is hemorrhage. Even though t-PA is relatively clot-specific in pharmacologically effective doses, it is not exclusively fibrin-selective. In actual fact, no thrombolytic agent, including t-PA, can differentiate between an MCA thrombus (a clot) and a hemostatic plug at another vascular site, such as in a gastric ulcer. This complication seems to be dose-dependent. A low dose such as the 80 mg used for thrombolysis in the Myocardial Infarction Trial 1 was associated with a lower incidence of intracerebral hemorrhage. We based our patient’s dosage on that study. The incidence of intracranial hemorrhage in thrombolytic therapy for acute stroke secondary to an embolus is less than 1%. 7

Reocclusion. Another major problem associated with acute t-PA administration is reocclusion. Twenty-four percent of the patients in the Myocardial Infarction Trial developed reocclusion. 2 Due to reocclusion of the MCA in our patient, we had to give two 75-mg doses of t-PA, each over 3 hours and separated by a treatment-free period of 3 hours. The patient recovered 1 hour after initiation of the second course of t-PA. After heparin anticoagulation for the next 3 days, the patient did not develop further problems. A predischarge cerebral angiogram revealed complete patency of the MCA. We did not believe at first that heparinization was warranted because of the patient’s young age and the angiographically healthy-looking MCA prior to the embolization attempt. We are still hesitant to advocate anticoagulation for such a problem. A second dose of t-PA is even more potent; however, it is possible that a large dose given over a longer duration might be preferable to heparinization. Alternatively, administering an antiplatelet agent such as aspirin concomitant with thrombolytic therapy might be effective. 4

Summary

This case establishes three points: 1) within 1 hour after symptomatic MCA embolic occlusion, t-PA can effect recanalization and recovery; 2) t-PA thrombolysis can be achieved without hemorrhage 3 weeks after AVM bleeding; and 3) for persistent patency of a previously normal MCA, heparinization after t-PA thrombolysis may be required to avoid reocclusion.

References


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Address reprint requests to: Jafar J. Jafar, M.D., Department of Neurosurgery, New York University Medical Center, 560 First Avenue, New York, New York 10016.