Intra-arterial urokinase for treatment of retrograde thrombosis following resection of an arteriovenous malformation

Case report

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Retrograde thrombosis of feeding arteries is a potentially catastrophic complication occasionally reported following resection of arteriovenous malformations (AVM's). No successful therapy for this condition, which causes postoperative stroke, has previously been reported. A case of retrograde thrombosis of the left middle cerebral artery immediately following resection of a parietal AVM is reported in a patient with a retained intra-arterial catheter from preoperative embolization. The administration of urokinase within 4 hours of surgery resulted in dramatic clinical and angiographic improvement without hemorrhagic complications. While urokinase is considered highly experimental in this setting, this case demonstrates that thrombolytic agents should be viewed as therapeutic options worthy of further investigation.

KEY WORDS - arteriovenous malformation - embolization - retrograde thrombosis - thrombolytic therapy - urokinase

Complications following surgical resection of arteriovenous malformations (AVM's) include normal perfusion pressure breakthrough, cerebral edema, brain swelling due to venous insufficiency, postoperative hemorrhage, and cerebral infarction due to retrograde thrombosis of a feeding artery. In the only reported series that specifically addresses retrograde thrombosis, this phenomenon occurred in five (6.6%) of 76 patients. No successful therapy for this potential catastrophe has been described. The present report documents the successful use of local thrombolytic therapy for recanalization of a thrombosed arterial feeder following AVM resection surgery.

Case Report

This 30-year-old right-handed woman presented to another hospital with a sudden severe headache, slurred speech, and right arm and leg paresthesia. A computerized tomography (CT) scan revealed a cerebral hemorrhage, and she was referred to our hospital for further study and definitive therapy.

Examination. Angiography revealed a left parietal wedge-shaped AVM with a 5-cm retrorolandic conical nidus and a complex pattern of superficial and deep draining veins (Fig. 1).

Operations. Three months after presentation, the patient underwent successful embolization of the AVM using N-butylcyanoacrylate polymer. However, during this procedure, the intra-arterial catheter became fixed within the AVM and could not be retrieved. In order to prevent vascular injury, the catheter, which extended from the AVM to the bifurcation of the left common carotid artery, was left in place. Despite this complication, the patient did well and returned home within 8 days. Aside from a right superior quadrant visual field cut, she had no neurological deficits. Four weeks later, she was readmitted for resection of the AVM. A preoperative angiogram showed a significantly smaller AVM nidus. The main arterial feeder was nearly completely thrombosed, and a secondary feeder was dilated (Fig. 2). Surgery was uneventful, with no intraoperative or anesthetic complications.
Intra-arterial urokinase therapy for retrograde thrombosis

FIG. 1. Initial selective left internal carotid arteriograms, lateral (left) and anteroposterior (right) views, demonstrating a 5-cm retrorolandic conical arteriovenous malformation nidus with a complex pattern of superficial and deep draining veins. The primary arterial feeder is the left middle cerebral artery.

FIG. 2. Selective left internal carotid arteriograms obtained 4 weeks after embolization and 1 day before surgery, lateral (left) and anteroposterior (right) views. A significant reduction in the size of the arteriovenous malformation nidus is seen. The retained catheter in the partially thrombosed left middle cerebral artery is marked by arrows.

An emergency CT scan showed no evidence of an intracranial hemorrhage. A selective left internal carotid artery (ICA) angiogram obtained 4 hours after surgery revealed complete occlusion of the left middle cerebral artery (MCA). Several lenticulostriate arteries and the left anterior choroidal artery were visualized. The anatomy of the left anterior cerebral and left pericallosal arteries was normal (Fig. 3 left).

After obtaining informed consent for thrombolytic therapy from the patient's husband, 125,000 U urokinase (Abbokinase) was infused into the left ICA over a period of 20 minutes. During the following 20 minutes, the patient showed neurological improvement, saying a few words and moving her right leg. A second dose of 125,000 U urokinase was infused during the next hour. Repeat angiography demonstrated collateral circulation from the anterior choroidal artery filling distal branches of the MCA. By this time, the patient was moving her right leg more briskly and her speech was improved but still limited to a few one-word responses; however, she was unable to move her right arm.

In order to infuse urokinase directly into the thrombus, a microcatheter* was advanced into the M1 segment of the MCA and a local infusion of urokinase, 1000 U/min, was administered until flow was obtained through the MCA 1 hour later. At that time, there was partial recanalization of the MCA and its distal branches (Fig. 3 right). Although the patient was markedly hemiparetic and aphasic, she had regained movement in her right arm and leg and was no longer mute. Heparin therapy, with an initial intravenous dose of 5000 U followed by an infusion of 800 U/hr, was begun in order to achieve an activated partial thromboplastin time that was prolonged 1.5 to 2 times the normal control. There was no blood loss and no decline in hematocrit.

Postoperative Course. The patient was brought to the neurosciences critical care unit for postoperative care. Upon arrival, she was awake, followed commands briskly, spoke in appropriate two-word phrases, and moved all limbs equally. Her vital signs remained stable, with a mean arterial blood pressure of 80 to 90 mm Hg. Thirty minutes after arrival, she suffered an acute neurological event that resulted in complete right hemiplegia. She remained awake but was somnolent and mute. She sluggishly followed commands to move her left arm and leg but did not follow central commands (for example, to open and close her eyes, to put out her tongue, and to smile). She had no stiffness of the neck and there had been no clinically apparent seizures.

* Microcatheter manufactured by Target Therapeutics, Inc., Los Angeles, California.
Follow-up CT 10 days postoperatively showed a left MCA distribution infarct involving the left basal ganglia and the left parietal region. Angiography 2 weeks after surgery showed complete recanalization of the left MCA and its distal branches. A follow-up angiogram obtained 6 months after surgery revealed no residual nidus of the AVM (Fig. 4).

The patient returned home from the hospital 19 days after surgery. Her facial weakness had resolved and she was walking, having regained normal strength in her right leg proximally and distally. Her right arm strength returned to nearly normal; however, she had a residual apraxia characterized by difficulty in initiating and coordinating movements with her right arm and hand. Her speech, although much improved, was still marked by a primarily expressive (Broca's) aphasia.

Discussion

Retention of an intra-arterial catheter is an infrequent complication of AVM embolization with N-butylcyanoacrylate, having occurred in seven (2.3%) of 300 patients treated in this fashion (G DeBrun, unpublished data). Of these seven, only the patient described in this report had any adverse sequelae; the other six patients were asymptomatic with a minimum follow-up period of 2 years. Two of these six patients underwent surgical resection of the AVM without complications, despite the retained catheters.

An infrequent but recognized complication following AVM removal is postoperative retrograde thrombosis of a feeding artery. The phenomenon occurred in five (6.6%) of the 76 patients reported recently by Miyasaka, et al., who presented three factors contributing to the development of retrograde thrombosis: 1) advancing age of the patient; 2) large AVM size; and 3) markedly elongated and dilated feeding vessels. It is impossible to know whether this complication would have occurred in our patient following embolization and surgical resection of her large AVM if the embolization catheter had not been left within the MCA preoperatively. One must, however, presume that this complication contributed to the sluggish postoperative flow through this former feeding vessel, thus predisposing to retrograde propagation of thrombus to the origin of the MCA.

Because of the devastating consequences of a dominant hemisphere MCA stroke due to retrograde thrombosis and the lack of acceptable alternative therapeutic options, the unprecedented use of thrombolytic therapy in a patient only a few hours after AVM surgery was chosen. This resulted in complete recanalization of the occluded vessel with dramatic neurological recovery.

The administration of systemic thrombolytic agents for the treatment of acute strokes has generally been met with an unacceptably increased risk of intracerebral hemorrhage, however, more favorable results using urokinase systemically have been reported from Japan. Recent advances in interventional neuroradiological techniques and endovascular instrumentation have led to the experimental use of local intra-arterial thrombolytic therapy in acute carotid distribution strokes.

Selectively infusing thrombolytic agents directly into the thrombosed vessel has been successful in salvaging neurological function and reducing cerebral infarction volume. By limiting the time interval between clinical onset and arterial recanalization, the risk of intracerebral hemorrhage may be minimized. The importance of minimizing this time interval is stressed by Jafar, et al., in their report of the successful use of tissue plasminogen activator to recanalize the MCA of a patient who suffered an embolic stroke during angiography. The time factor is most important when the lenticulostriate arteries are involved, since prolonged occlusion of these terminal arteries may result in an increased incidence of hemorrhage following reperfusion. In the series reported by Theron, et al., the only hemorrhagic complications occurred in patients treated more than 6 hours after clinical onset.

Given the volume of infarcted brain and the potential for postoperative bleeding in our otherwise healthy young patient, the decision to use local urokinase therapy was made with trepidation. Because of the devastating impact of a dominant-hemisphere MCA stroke, the risk was thought to be warranted. Our patient's favorable outcome demonstrates that thrombolytic agents in this setting should be viewed as a therapeutic option worthy of further investigation. The use of this approach for the treatment of retrograde thrombosis of a feeding artery following AVM resection requires caution and the collaborative efforts of neurosurgeons, interventional neuroradiologists, and neuroanesthesiologists in a critical-care setting with a skilled nursing staff experienced in the care of neurosurgical patients.

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References


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