Immediate postoperative thrombolytic therapy: An aggressive strategy for neurologic salvage when cerebral thromboembolism complicates carotid endarterectomy

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A 42-year-old man with a high-grade left internal carotid artery (ICA) stenosis demonstrated on a duplex scan was referred to us. A cerebral arteriogram confirmed a greater than 90% left internal carotid stenosis, but with the unexpected finding of a moderate amount of thrombus in the proximal ICA. He underwent emergent left carotid endarterectomy, but during the operation, only a small amount of thrombus was identified as adherent to the atherosclerotic plaque. He awakened in the operating room with a dense right hemiplegia and aphasia. Immediate reexploration demonstrated a patent endarterectomy site, a distal thromboembolectomy was performed without extraction of thrombus, and urokinase (250,000 units) was infused into the distal ICA. He reawakened with an unchanged right hemiplegia and aphasia. The patient then underwent an urgent postoperative carotid and cerebral arteriogram that demonstrated an embolus to the middle cerebral artery. He was treated with the superselective infusion of urokinase (500,000 units), with almost complete resolution of the clot. Over the course of the next 48 hours, the patient made a nearly complete neurologic recovery, and he was discharged from the hospital with only a slight facial droop. At 2 months' follow-up he was completely neurologically healthy. To our knowledge this is the first reported case of urokinase administered in the immediate postoperative period in the angiography suite to treat a thromboembolus complicating a carotid endarterectomy. (J Vasc Surg 2000;31:1033-7.)

Carotid endarterectomy (CEA) has become an exceptionally safe procedure in contemporary clinical practice, with a very low rate of neurologic complications.[1] Most perioperative strokes are believed to result from either intraoperative cerebral ischemia or perioperative thromboembolism.[2] Therefore, when a patient awakens in the operating room after CEA with a new neurologic deficit, immediate reexploration is indicated. In the absence of a technical imperfection at the endarterectomy site or acute thrombosis, treatment is typically conservative, and the potential for complete neurologic recovery is not good. We recently performed a CEA on a patient who awakened with a profound neurologic deficit believed to be a result of intraoperative thromboembolism. The patient was successfully treated with an immediate postoperative superselective urokinase infusion. To our knowledge this is the first case in which urokinase was administered in the immediate postoperative period in the angiography suite to reverse a neurologic deficit resulting from an intraoperative cerebral thromboembolism complicating a CEA.

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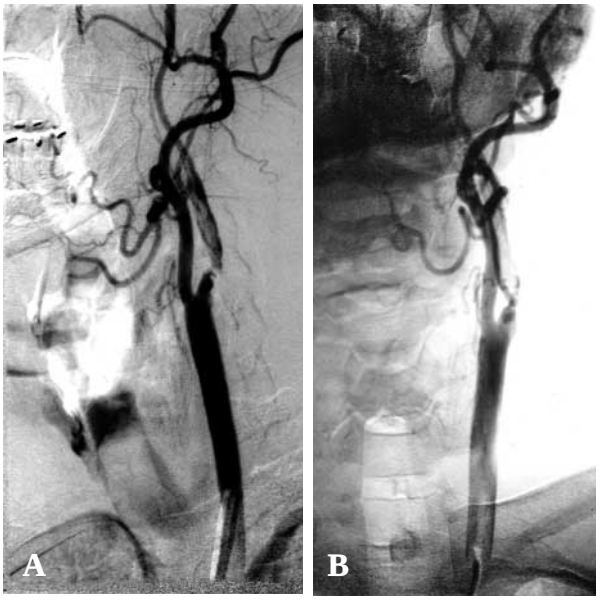

Fig 1. Preoperative carotid arteriogram demonstrating severe left internal carotid stenosis and associated intraluminal thrombus. A, Lateral view. B, anteroposterior view.

CASE REPORT

A 42-year-old construction worker went to his community hospital with the acute onset of dizziness and discoloration of the toes of both feet. His past medical history was significant for hypertension, heavy smoking, and chronic obstructive pulmonary disease; there was a strong family history of coronary artery disease. There was no prior history of neurologic symptoms or peripheral vascular disease. Pertinent findings on physical examination included palpable dorsalis pedis and posterior tibial pulses bilaterally, mild cyanotic discoloration of all 10 toes, and a left carotid bruit. He received heparin intravenously and underwent an extensive workup, including lower extremity arterial and venous Doppler scanning examinations, chest and abdominal computerized tomographic (CT) scans, and an echocardiogram. All the results were negative. However, a carotid duplex scanning evaluation revealed a high-grade left internal carotid artery (ICA) stenosis, and the patient was transferred to the Johns Hopkins Hospital 2 days after presentation for further evaluation and treatment. On presentation to our institution his toes had markedly improved, he continued to have normally palpable pedal pulses, and he was neurologically intact. The results from a transesophageal echocardiogram were negative. A carotid arteriogram demonstrated a greater than 90% left internal carotid stenosis and a moderate amount of luminal thrombus associated with the stenosis (Fig 1).

The patient was taken immediately from the angiography suite to the operating room and underwent CEA with an indwelling shunt under general anesthesia. During the operation, a high-grade stenosis was confirmed in a long atherosclerotic plaque, but there was only a minimal amount of thrombus associated with an ulcer. The patient

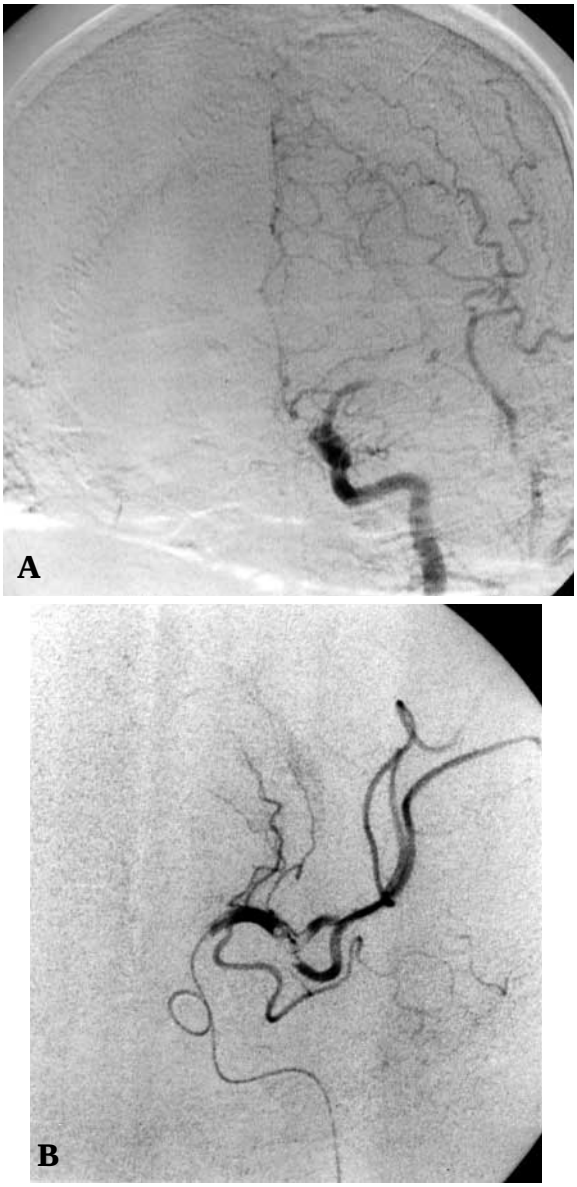

Fig 2. Postoperative selective left carotid arteriogram. Note occlusion of the left MCA (A). After gentle catheter manipulation of the occluding thrombus, partial antegrade flow is restored (B).

immediately awakened and exhibited a dense right hemiplegia and apparent aphasia. He underwent immediate reoperation, and the vessel was found to be patent, without technical deficit or thrombus. There was brisk backbleeding from the distal ICA. A balloon thromboembolectomy procedure was performed, but no thrombus was extracted. An intraoperative arteriogram was performed that confirmed ICA flow into the brain, but with inadequate visualization of the intracerebral vessels. Urokinase (250,000 units) was infused into the distal ICA, and the incision was closed over a closed-suction

drain. The patient again awakened in the operating room with a dense right hemiplegia and aphasia.

The patient had a head CT scan, which ruled out an intracerebral hemorrhage. He then underwent a cerebral arteriogram, which demonstrated an abrupt occlusion of the left middle cerebral artery (MCA) (Fig 2, *A*). Through a 6-French introducer sheath in the right femoral artery and after the administration of heparin (5000 units), a 6-French Envoy MPC–guiding catheter (Cordis Corp, Miami, Fla) was advanced in the proximal left common carotid artery, and a Turbotracker-18 microcatheter (Boston Scientific, Natick, Mass) was advanced coaxially to the left MCA over a Transcend-14 guide wire (Boston Scientific) under fluoroscopic control using road map guidance. The tip of the guide wire was then carefully advanced through the clot, and gentle mechanical disruption of the clot was performed, allowing immediate reperfusion of distal MCA branches (Fig 2, *B*). The tip of the catheter was then placed within the clot, and then the superselective injection of urokinase (500,000 units) was performed. The completion arteriogram, which was performed approximately 6 hours after the patient awakened from surgery with his deficit, demonstrated reperfusion of the left MCA territory with only minimal delayed filling of some temporal branches (Fig 3). After this, the patient was appropriately following commands and exhibited good strength in the right leg, but had persistent paralysis of the right arm. He received an intravenous drip of heparin (1000 U/h) and was taken to the intensive care unit for monitoring.

Over the next 8 hours the patient began to move his right arm, manifested normal strength in the right leg, and was speaking with some dysarthria. During the next 72 hours the patient exhibited normal right-sided strength and was speaking coherently. On his sixth postoperative day the patient was ambulating independently, tolerating a regular diet, and speaking normally. With symmetric upper and lower extremity strength and sensation and with only a slight facial asymmetry, he was discharged on warfarin. Before discharge, a head CT scan confirmed a small infarct involving the left lentiform nucleus. On the advice of our hematology consultants and in view of the necessity for ongoing anticoagulation that might confound the analysis, a hypercoagulability workup was deferred. At 2 months' follow-up the patient was neurologically healthy. No anatomic etiology for the patient's "blue toes" was identified, and his peripheral arterial perfusion remains normal.

DISCUSSION

Over the past two decades thrombolytic therapy has assumed a role in the management of acute arterial occlusive disease, primarily involving the lower extremities. Although interest in the treatment of patients with acute stroke with systemic thrombolysis dates back to the 1950s, the efficacy of this approach has largely been limited by high rates of cerebral hemorrhage.[3] Over the last decade, however, there has been a renewal of interest in the management of patients with acute ischemic stroke using the selective intra-arterial infusion of thrombolytic agents, and the results have improved when compared with systemic administration. It is clear from this experience that the direct infusion of the thrombolytic agent into the occluding thrombus as soon as possible after the onset of symptoms is the key to limiting ischemic brain injury and minimizing the risk of hemorrhagic complications.[4] One may therefore reasonably infer that the patient who experiences an acute thromboembolic complication of CEA would be an ideal candidate for catheter-directed thrombolysis and that intraoperative administration would be the most expeditious strategy.[5]

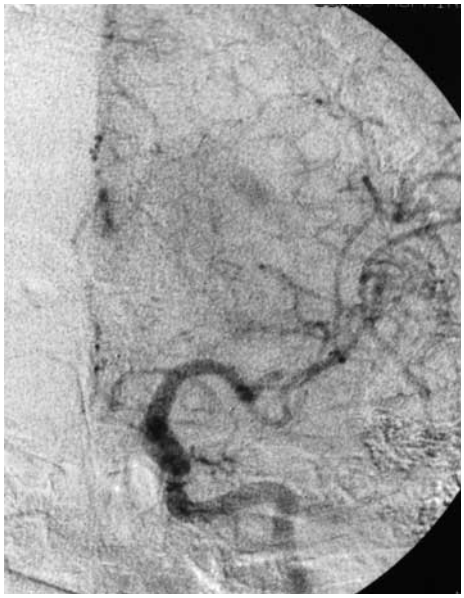

Fig 3. Completion of left carotid arteriogram after superselective administration of urokinase (500,000 units) into the MCA thrombus. Note nearly complete recanalization.

Although intraoperative thrombolysis has assumed an increasingly accepted role in the management of patients undergoing surgery for acute limb ischemia, experience with intraoperative intracerebral thrombolysis is scant. Barr et al[5] reported the first successful case in 1995, in which 500,000 units of urokinase was infused through a microcatheter that was placed into an MCA clot under fluoroscopic control to treat an embolus detected during a CEA, with complete clot resolution and full neurologic recovery. Subsequently, Comerota and Eze[6] reported the case of a 65-year-old man who awakened with a right hemiplegia resulting from acute thrombosis of the left anterior cerebral artery during CEA. The man was treated intraoperatively with an infusion of urokinase (1 million units) that was delivered through the side-

port of the indwelling carotid shunt, with complete clot lysis and significant neurologic improvement. In another report, a patient with an acute cervical ICA thrombosis and an MCA embolism underwent simultaneous CEA and intraoperative intracerebral thrombolysis with 500,000 units of urokinase.[7] Eckstein et al[8] have recently reported a series of four men and one woman, ranging in age from 55 to 72 years, who underwent CEA and intraoperative thrombolysis with 500,000 units of urokinase for treatment of thromboembolic occlusions of the MCA (n = 4) and anterior cerebral artery (n = 1). Two of these patients received the thrombolytic infusion during an emergency reexploration after new neurologic deficits developed 2 and 3 hours after the initial CEA. There was one postoperative death due to stroke, two patients made complete neurologic recoveries, and two patients were discharged with mild neurologic deficits.[8]

In this case report, imaging limitations in the operating room precluded our ability to adequately visualize the intracerebral vasculature. Nevertheless, according to the preoperative arteriogram (Fig 1) and the relative paucity of thrombus found in the patient's ICA, a distal thromboembolus was the most likely explanation for the patient's profound neurologic deficit. In view of the location of the embolus, as depicted during the selective postoperative carotid arteriogram (Fig 2), it is not surprising that the intraoperative administration of 250,000 units of urokinase into the distal cervical ICA did not achieve the desired clinical outcome. In the absence of this imaging capability, we believed it was more appropriate to obtain a formal carotid arteriogram in the angiography suite in the hopes of performing a superselective infusion of urokinase postoperatively, rather than persisting with an infusion of a much higher dose, as others have reported.[6]

Previous work has indicated that the risk of cerebral hemorrhage increases if the thrombolytic infusion is initiated more than 6 hours after the onset of the ischemic insult,[9] and we could treat our patient within that window. Furthermore, we believed the risk-benefit ratio clearly supported an aggressive attempt at thrombolysis in view of the patient's young age, his profound neurologic deficit, and the potential for neurologic recovery if complete recanalization of the MCA could be achieved, as demonstrated in previous angiographically controlled trials.[6] Although we recognized the potential for bleeding into the surgical wound, we believed the likelihood of that complication was small because of the short half-life (14 minutes) of urokinase and the relatively low dose delivered over a short duration by selective catheter infusion. Furthermore, a drain had been left in place after the CEA, and the patient was closely monitored after thrombolysis in the intensive care unit.

To our knowledge, this is the first report of a patient undergoing immediate postoperative superselective urokinase infusion in the angiography suite for a thromboembolic complication of CEA. On the other hand, Katzan et al[10] reported on 6 patients who were treated with intra-arterial thrombolysis for ischemic strokes developing from 2 to 14 days (mean, 6 days) after major cardiac surgical procedures. Four patients were treated with urokinase (40,000-500,000 units), and two patients received tissue plasminogen activator (25 and 50 mg). Recanalization of the intracerebral thrombus was complete in one case, partial in three cases, and minor in two cases. Four patients improved clinically, and one died of cerebral edema. No patient experienced a significant systemic bleeding complication, and only one patient had a small asymptomatic cerebellar hemorrhage.[10] Mechanical manipulation of the clot to allow recanalization of the affected vessel with the lowest thrombolytic drug dose (Fig 2) was carried out in each patient, as in our patient.[10]

In summary, although the patient undergoing CEA, who may be a potential candidate for catheter-directed thrombolysis administered intraoperatively or immediately postoperatively, will most likely be encountered infrequently in the practice of most busy carotid surgeons, this strategy does offer an opportunity for dramatic recovery of neurologic function and should be part of our therapeutic armamentarium. Our case and the experience of others indicate that this treatment is most appropriate for the patient in whom one suspects a thrombotic intracerebral arterial occlusion. It is unlikely that atheroembolic debris, which is the more common cause of intraoperative embolic stroke, would likely respond to lysis. In other words, the decision to attempt intracerebral thrombolysis in the patient who experiences an apparent intraoperative stroke is a clinical judgment that should be made on a case-by-case basis. As in the management of a patient who is seen with an ischemic stroke de novo, precise angiographic localization of the offending thrombus and selective lytic infusion at the earliest possible hour will offer the greatest chance for successful lysis and minimize the risk of hemorrhagic transformation. If that imaging capability is available in the operating room, intraoperative thrombolytic therapy will allow the most expeditious treatment. On the other hand, in the absence of this capability and if an interventional

neuroradiology team is available, rapid transfer of the patient to the angiography suite, as in the present case, is a viable option with the potential for achieving a gratifying neurologic recovery.

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