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Percutaneous Transluminal Angioplasty Adjunct to Thrombolysis for Acute Middle Cerebral Artery Rethrombosis

Fong Y. Tsai, Bruce Berberian, Violet Matovich, Mark Lavin, and Kenneth Alfieri

PURPOSE: To report three patients, each of whom had acute rethrombosis of a reopened middle cerebral artery after urokinase treatment for proximal stenosis (percutaneous transluminal angioplasty of the stenosis was performed adjunctive to the thrombolytic treatment to preserve the success of the thrombolysis), and a fourth patient who had percutaneous transluminal angioplasty right after the completion of thrombolysis and had no rethrombosis despite a partial dilatation of the severe stenosis. **METHODS:** Thrombolytic treatment was carried out by a coaxial technique with a Tracker 18 catheter through a 5-F angiographic catheter; 80 000 U in 5 mL of urokinase were intermittently injected every 15 minutes after an initial dose of 250 000 U. All patients were given 3000 U of heparin with a booster dose of 1000 U every hour. Angioplasty was performed with a Stealth catheter balloon, 2 to 3 mm × 1.5 cm. **RESULTS:** Three patients recovered without hemorrhage after percutaneous transluminal angioplasty and thrombolytic treatment. Percutaneous transluminal angioplasty was unsuccessful in one patient because of the inability to pass a 2-mm Stealth balloon catheter, and the result was a second rethrombosis. This patient had a poor recovery. **CONCLUSION:** Acute thrombosis of the middle cerebral artery may be associated with severe proximal stenosis. Rethrombosis may occur even after complete thrombolysis. Percutaneous transluminal angioplasty may be safely performed to prevent rethrombosis.

Index terms: Arteries, cerebral, middle; Arteries, stenosis and occlusion; Arteries, transluminal angioplasty; Thrombolysis; Thrombosis, arterial

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Acute thrombosis of the middle cerebral artery may result in severe neurologic sequelae. Early recanalization, improving blood flow, is necessary to minimize severe complications. Intraarterial local thrombolysis has been used in patients with acute thrombosis of the middle cerebral artery. Recently, we noted immediate rethrombosis in the middle cerebral artery after complete thrombolysis. We report our experience using urokinase and adjunctive percutaneous angioplasty in four patients.

Methods

We have treated 31 patients with middle cerebral artery occlusion over the past 7 years. Exclusionary criteria included intracranial hemorrhage and duration of symptoms beyond 6 hours. All patients were treated within 6 hours of the onset of symptoms. (If a patient had progressive deterioration, thrombolysis could be delayed up to 8 hours.) Thrombolysis was performed through a Tracker 18 catheter (Target Therapeutics, San Jose, Calif) advanced to the occluded segment of middle cerebral artery coaxially through a 5-F catheter. The tip of the Tracker catheter was placed as close to the clot as possible and advanced as thrombolysis progressed. The maximum dose of urokinase was 1.75 million IU except in case 3, in which 2 million IU total was required because of rethrombosis.

In our early experience with the first 11 patients, we assayed fibrinogen levels before, during, and hourly after urokinase infusion. No patient had a level below 250 mg/dL even after 1.75 million IU of urokinase. We now only assay fibrinogen levels before, during, and at the completion of thrombolysis.

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Urokinase was initially injected as a 250 000-IU bolus followed by 80 000 IU injected over 2 to 3 minutes every 15 minutes. All patients were given 3000 U of heparin intravenously and an hourly booster of 1000 U. Heparinization was not reversed after thrombolysis. The femoral sheath was left in place for 2 to 3 hours. Anticoagulation and antiplatelet therapy continued for 3 months. Angioplasty was performed with a Stealth (Target Therapeutics) angioplastic catheter with balloon sizes either 2 mm \times 1.5 cm or 3 mm \times 1.5 cm. Nitroglycerin (100 mg) was given intraarterially before the Stealth catheter was advanced to the stenosis.

Of the 31 patients we have treated, 14 were women and 17 were men. Their ages ranged from 42 to 67 years with an average age of 54 years. Nine of our 31 patients had middle cerebral artery stenosis. Three patients had acute rethrombosis of the middle cerebral artery distal to the stenosis, requiring repeat thrombolysis followed by angioplasty. A fourth patient who had percutaneous transluminal angioplasty immediately after thrombolysis did not have rethrombosis. Of the 31 patients, 2 in our early experience using continuous urokinase infusion had massive intracranial hemorrhages and died. One patient had multiple petechial hemorrhages without neurologic sequelae.

Five patients with mild to moderate stenosis were treated with thrombolysis before we started performing adjunctive percutaneous transluminal angioplasty. Four recovered well without rethrombosis. One patient worsened 12 hours after thrombolysis. A repeat computed tomographic (CT) scan showed only edema, which at that time we thought was caused by failure of urokinase. An angiogram was not performed, because early in our experience we did not consider the possibility of rethrombosis. The remaining patients recovered without complications or neurologic sequelae.

Results

Case 1 (Fig 1)

A 46-year-old man presented to the emergency department with acute onset of global aphasia and dense right hemiparesis starting about 2 hours before his arrival. CT findings were normal with the exception of slight asymmetry of the sylvian fissures. Emergency cerebral angiography showed total occlusion of the left middle cerebral artery with poor collateral flow to distal branches. The initial dose of 250 000 IU of urokinase was given through a Tracker catheter about 4.5 hours after the onset of the clinical deficit. After an additional 750 000 IU of urokinase, digital subtraction angiography showed complete thrombolysis, very good distal circulation, and focal stenosis in the

proximal middle cerebral artery. After the initial improvement, the patient's clinical symptoms worsened while he was awaiting transfer back to the intensive care unit. After repeat CT scan, hemorrhage was excluded. Repeat angiography showed rethrombosis of the middle cerebral artery at the focal stenosis. Urokinase was restarted, and the middle cerebral artery was reopened with an additional 500 000 IU. Percutaneous transluminal angioplasty was performed to prevent recurrent thrombosis. A Stealth 3 \times 1.5-mm angioplastic balloon catheter was advanced to the stenotic segment, which was dilated. After the percutaneous transluminal angioplasty and urokinase, no evidence of rethrombosis was seen. The patient recovered very well and, 6 months later, had only numbness of his right hand and occasional difficulty finding words. Magnetic resonance imaging demonstrated residual infarcts in the posterior parietal lobe. He has been stable for more than 2 years.

Case 2

A 52-year-old man had acute onset of slurred speech and right hemiparesis during hospitalization for a cardiac problem. An emergency CT scan done approximately 3 hours after the onset of symptoms showed a small old infarct in the left basal ganglia, but findings were otherwise normal. Emergency cerebral angiography showed total occlusion of the left middle cerebral artery. Urokinase and heparin were started about 6 hours after the onset of symptoms. The thrombus dissolved completely with 1.25 million U of urokinase given over 3.5 hours, and a segmental stenosis was discovered in the proximal middle cerebral artery. He relapsed to a prethrombolysis state after the initial improvement. Repeat angiography showed rethrombosis of the M2 segment of the middle cerebral artery, just distal to the stenosis. We decided to dilate the stenosis to avoid a second rethrombosis using a 2.5-mm \times 1.5-cm Stealth angioplastic balloon catheter. The middle cerebral artery was reopened completely after an additional 375 000 U of urokinase were given over 1.5 hours. The patient recovered with persistent right-leg weakness. Follow-up magnetic resonance imaging showed residual infarction in the basal ganglia and parietal lobe. One and a

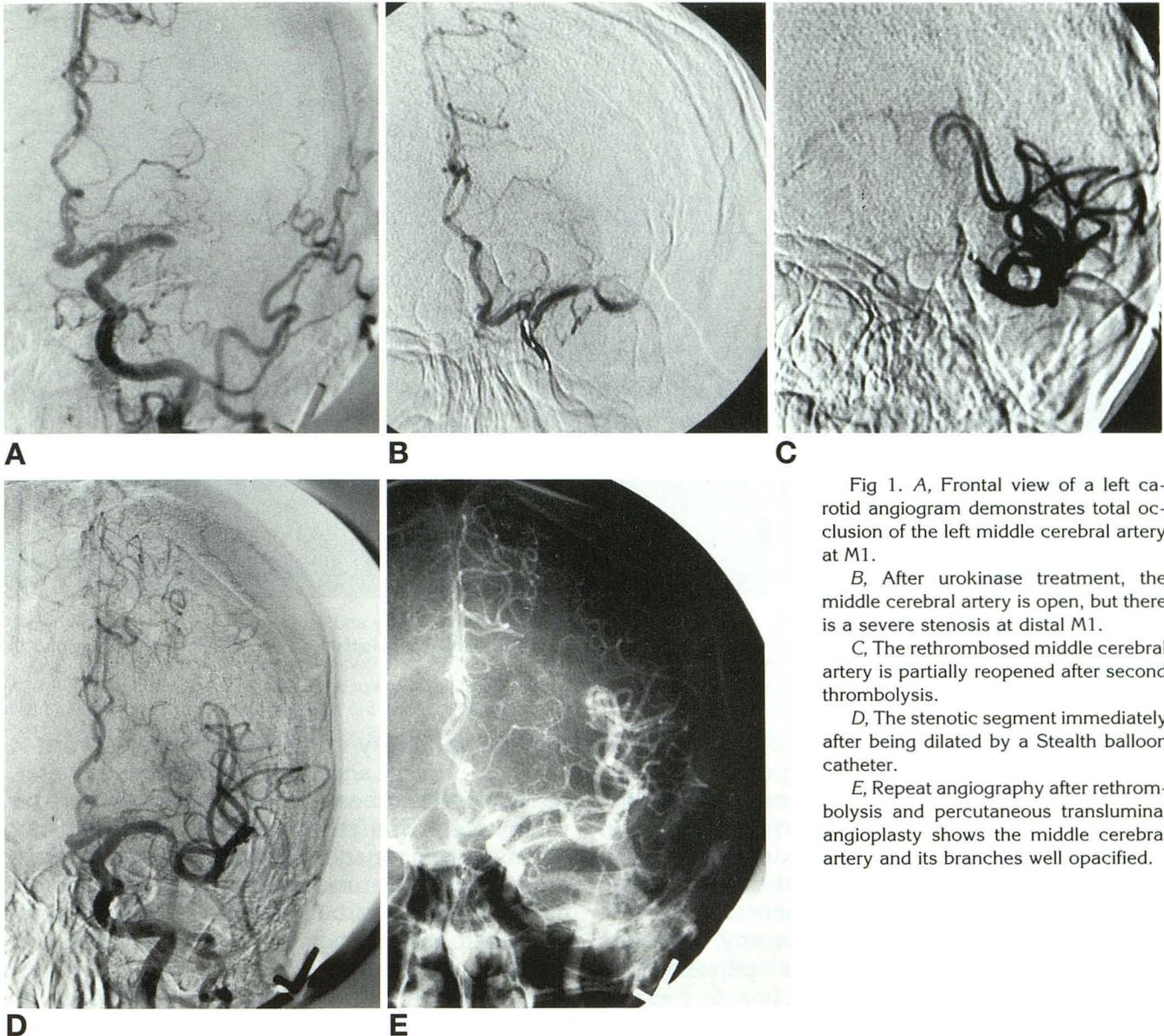


Fig 1. *A*, Frontal view of a left carotid angiogram demonstrates total occlusion of the left middle cerebral artery at M1.

B, After urokinase treatment, the middle cerebral artery is open, but there is a severe stenosis at distal M1.

C, The rethrombosed middle cerebral artery is partially reopened after second thrombolysis.

D, The stenotic segment immediately after being dilated by a Stealth balloon catheter.

E, Repeat angiography after rethrombolysis and percutaneous transluminal angioplasty shows the middle cerebral artery and its branches well opacified.

half years later, he had persistent mild right-leg weakness.

Case 3

A 60-year-old woman was brought to the emergency room by a family member who stated that the patient, on awakening that morning, showed right-side weakness and an inability to express herself. The family member noticed that the patient had had mental status changes for 3 days. Physical examination showed aphasia and right hemiparesis. Non-contrast head CT findings were normal. Ap-

proximately 6 hours after the onset of symptoms, digital subtraction angiography showed total occlusion of the left middle cerebral artery. A 3-F Tracker catheter was advanced to the occluded segment coaxially through the angiographic catheter. Thrombolysis occurred with 1 million U of urokinase over 3 hours. The patient's clinical status deteriorated after transfer to the intensive care unit. Repeat CT was normal, and repeat angiography showed rethrombosis of the proximal left middle cerebral artery. Another 1 million U of urokinase was infused, and repeat angiograms demonstrated a highly stenotic proximal left middle cerebral artery.

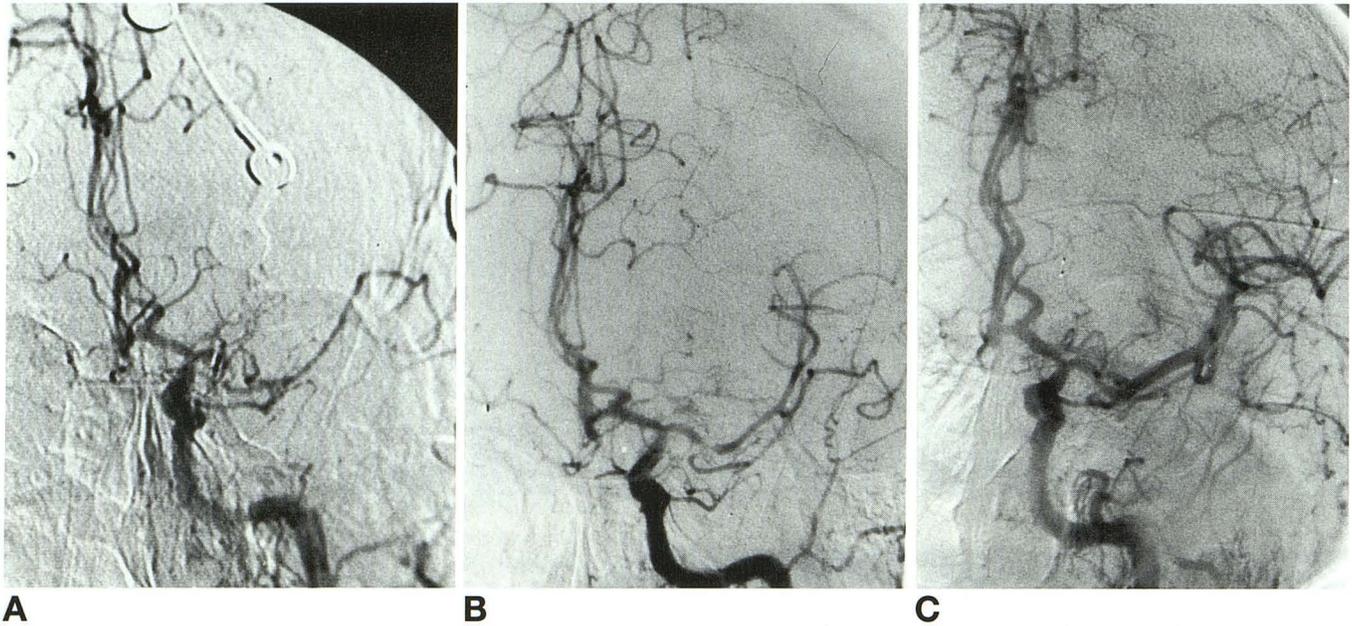


Fig 2. A, Left carotid angiography shows complete occlusion of the left middle cerebral artery just distal to bifurcation of the internal carotid artery.

B, Repeat angiography shows rethrombosis of branches of the left middle cerebral artery and stenosis of M1.

C, Repeat angiography after the second thrombolysis and percutaneous transluminal angioplasty. The middle cerebral artery and its branches are patent.

Percutaneous transluminal angioplasty was unsuccessful, because the high degree of stenosis prohibited passage of even the smallest Stealth catheter. The patient had speech deficits and right hemiparesis. MR showed extensive infarction in the left basal ganglia and the temporal and parietal lobes. Although there was some improvement after physical therapy, speech deficits and right hemiparesis persisted 9 months later.

Case 4 (Fig 2)

A 46-year-old woman who had had a stroke 2 years earlier with residual mild right-side sensory deficit suddenly had progressive aphasia and right-side weakness the morning of discharge from our hospital. She had an episode of syncope 3 days earlier. CT findings were normal except for two small old infarcts in the left basal ganglia. Emergency cerebral angiography approximately 8 hours after the onset of symptoms showed complete thrombosis of the left middle cerebral artery just distal to segmental stenosis of the main trunk. One million units of urokinase dissolved the thrombosis. We thought the stenosis was severe and rethrombosis very likely, so we performed percutaneous translu-

minal angioplasty immediately with a 2-mm \times 1.5-cm Stealth angioplastic balloon catheter. Neither rethrombosis nor recurrent symptoms were noted. She recovered with very minimal right-side sensory deficits and no aphasia. Magnetic resonance imaging showed no definite cortical infarction, but there was a small infarct at the left basal ganglia.

Discussion

Thromboembolus from the heart or an atherosclerotic carotid bifurcation may dislodge distally into the intracranial circulation. The thrombus may be small and result in transient ischemia, without residual deficit. A bigger thrombus may obstruct a major branch and result in total occlusion. Although spontaneous lysis of thromboembolus occurs, the process may not be sufficient to restore circulation in time to preserve brain function (1-5). Heparin enhances spontaneous lysis and has been used to treat acute stroke, but as many as 37% of these patients deteriorate because of thromboembolus propagation. Local intraarterial thrombolysis has proved to be safe and effective for those patients with acute-onset middle cerebral artery occlusion (6-11). The infusion technique

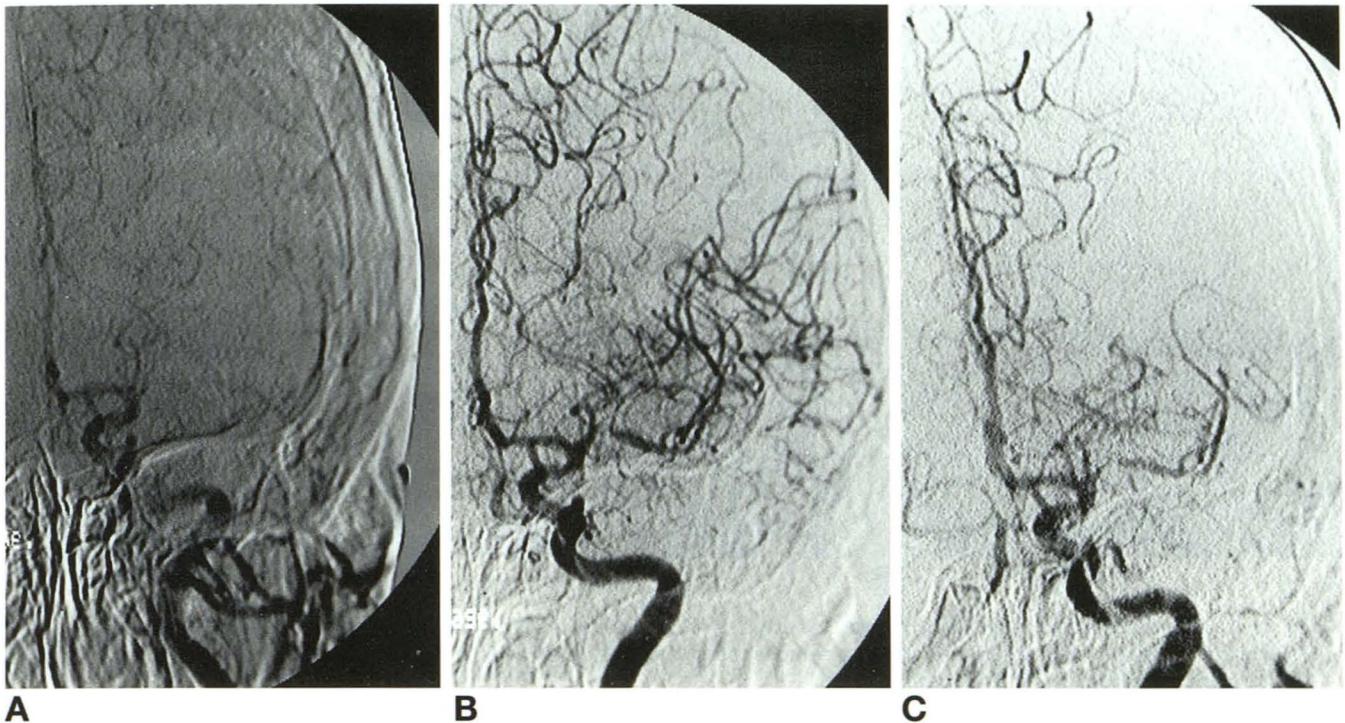


Fig 3. A, Left carotid angiogram shows total occlusion at the origin of the left middle cerebral artery. B, The Tracker catheter is advanced to the distal middle cerebral artery after reopening of the proximal middle cerebral artery. The distal middle cerebral arterial branches are partially reopened, but severe stenosis is noted at proximal M1. C, Repeat angiography demonstrates rethrombosis of the middle cerebral artery distal to the stenosis.

for thrombolysis varies; most investigators report using slow continuous infusion with urokinase or tissue plasminogen activator. Thrombolysis with continuous infusion may take longer than intermittent injection and may delay reopening of the occluded middle cerebral artery, leading to reperfusion hemorrhage (6–12). Two patients had hemorrhagic complications in our early experience with continuous infusion. We have had no such complications since changing to intermittent injection. This technique also tends to minimize the severe body shaking caused by urokinase.

The middle cerebral artery is the most frequent site of acute thrombosis from thromboembolus and is also a frequent site of stenosis (Figs 3 and 4) (1–5, 7–11, 13, 14). Stenosis may be obscured by a large embolus and may promote thrombus propagation. Angiography may demonstrate only total occlusion, not the stenosis. From our small series of patients, we believe that the femoral sheath should be kept in place even when thrombolysis is complete and especially if there is stenosis. The patients need to be observed closely, and if the clinical symptoms worsen, reangiography should be

performed immediately (after a CT scan to rule out hemorrhagic complication) with or without percutaneous transluminal angioplasty, because immediate rethrombosis may occur. Over 7 years, we have treated 31 patients with acute middle cerebral artery occlusion; 9 had stenosis. Three of these patients (as seen in cases 1, 2, and 3) had acute rethrombosis of the middle cerebral artery distal to the stenosis requiring immediate angioplasty. One patient had percutaneous transluminal angioplasty before rethrombosis occurred, as seen in case 4. Retrombosis in our 3 patients occurred distal to the stenosis. The degree of stenosis in these patients was very severe. In case 1 the middle cerebral artery was rethrombosed just distal to the stenotic M1 segment. Case 2 had rethrombosis distal to the M2 segment. The middle cerebral artery in case 1 was more tortuous than in case 2, so we chose to perform thrombolysis before percutaneous transluminal angioplasty in case 1 to avoid the guide wire and catheter and risking injury to the arterial wall. We think rethrombosis occurring in mildly or severely stenotic vessels may account for at least a portion of failures with urokinase.

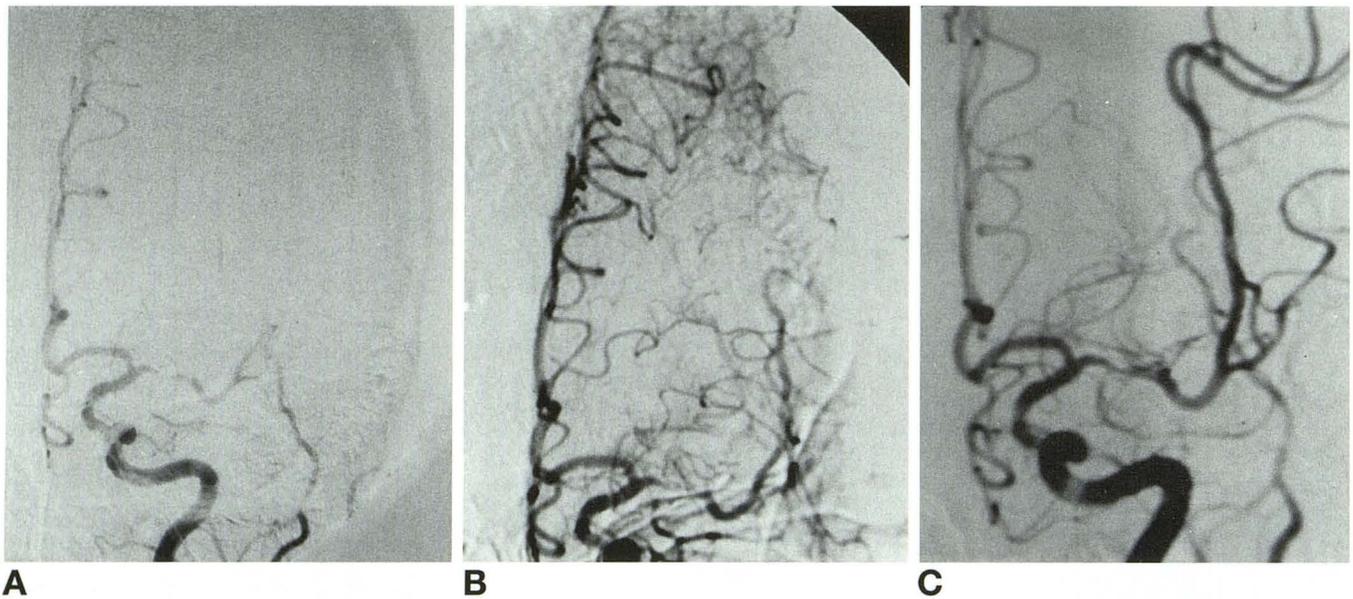


Fig 4. A, Left carotid angiography shows severe stenosis of M1 and distal occlusion of the left middle cerebral artery. B, Repeat angiography after thrombolysis again demonstrates a segmental stenosis at M1. C, After partial angioplasty, M1 is better opacified.

We need further experience to establish the safety of percutaneous transluminal angioplasty of intracranial stenosis. The potential risks associated with the intracranial percutaneous transluminal angioplasty include arterial rupture, spasm, and distal embolization (14–17). We minimize these risks by underdilating the stenosis, because cerebral blood flow may be restored to normal with 50% of normal vessel caliber (15–17). We also pretreat with nitroglycerin to avoid spasm. In case 3 the patient had a poor recovery because percutaneous transluminal angioplasty failed after rethrombolysis and rethrombosis. This case illustrates that percutaneous transluminal angioplasty after thrombolysis may be needed, if it can be performed safely, to avoid rethrombosis of the middle cerebral artery in patients with severe stenosis. Percutaneous transluminal angioplasty may not be required if the middle cerebral artery is not severely stenotic. We do not have sufficient experience from our series to suggest percutaneous transluminal angioplasty should be routinely performed after thrombolysis if no rethrombosis occurs. The prognosis of middle cerebral artery occlusion or stenosis is not favorable, with approximately 9% of patients having strokes each year and a mortality rate of 2.6% per year (13). The poor prognosis of middle cerebral artery stenosis and potential rethrombosis may increase the need for percuta-

neous transluminal angioplasty in patients with severe stenosis noted after urokinase treatment, as in case 4.

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