Andrew Latimer, MD, Jeffrey Bell, RN, BSN, CEN, NREMT-P, Elizabeth Powell, MD, and Peter V.R. Tilney, DO, EMT-P, FACEP

A 77-Year-Old Man With Large Vessel Acute Ischemic Stroke

A 77-year-old man with a past medical history significant for hypertension, coronary artery disease on aspirin, congestive heart failure, a remote history of deep vein thrombosis formerly on warfarin (noncurrently), and an old right-sided ischemic stroke with residual tremor in his left lower extremity for which he takes levetiracitam presented to a rural emergency department after developing acute-onset left-sided hemiplegia. Local emergency medical services was called to the patient's home after his family noted the deficits shortly after dinner. He was found sitting on the couch in the family living room after having shared an evening meal with the rest of his family. The paramedic noted complete left-sided hemiplegia, including left-sided facial droop and gaze deviation to the right, and marked dysarthria. During transport, the ground team reported stable vital signs and a blood glucose level of 158 mg/dL.

Upon arrival to the emergency department, the patient was "last seen normal" 1 hour 15 minutes before. On examination, he was awake and alert but had 0/5 strength to his left upper and lower extremities, including significant left-sided facial droop. He had a rightward gaze deviation with dense left-sided neglect and significant dysarthria with aphasia. His National Institutes of Health Stroke Scale score was 18. He was rapidly taken for a noncontrasted head computed tomographic (CT) scan and a CT angiogram of the head and neck. The noncontrasted head CT scan showed a right-sided hyperdense area of ischemia noted to be a middle cerebral artery (MCA) sign (Fig. 1) suggestive of large proximal MCA thrombus with no evidence of acute hemorrhage. The CT angiogram showed a right-sided M1 distribution occlusion or cutoff (Fig. 2).

Laboratory values were obtained, and an electrocardiogram showed new-onset atrial fibrillation. The regional stroke team was consulted using a telemedicine robot terminal with bidirectional cameras and speakers. The patient was deemed a candidate for thrombolytic therapy and was treated with an intravenous (IV) tissue plasminogen activator (tPA) bolus followed by a 1-hour infusion 1 hour 53 minutes from "last seen normal." Rotor wing critical care transport was contacted to transport the patient to a neurointervention suite at the receiving facility. The patient spent a total of 1 hour 17 minutes in the emergency department before helicopter emergency medical services (HEMS) transport.

On HEMS arrival, the patient was found to be hemodynamically stable with a blood pressure of 143/66, a heart rate of 67, and an oxygen saturation of 96% on a 2-L nasal cannula. The patient was placed on the transport stretcher, transferred to the transport monitor, and tPA infusion was continued. The patient's systolic blood pressure remained under 180 systolic, and no blood pressure management was required throughout the flight. The patient was taken directly to angiography, and care was transferred without incident.

Upon arrival to the receiving facility, the patient had aspiration thrombectomy of the right M1 artery occlusion with reperfusion shown intraprocedure at 3 hours 58 minutes from the "last seen normal" time (Figs. 3 and 4).

The patient initially had some improvement in his neurologic examination demonstrated by some movement in his left upper and lower extremity but went on to have a hospital course complicated by left-sided anterior cerebral artery ischemic stroke and a urinary tract infection. He was discharged to a skilled nursing facility on hospital day 13.

Discussion

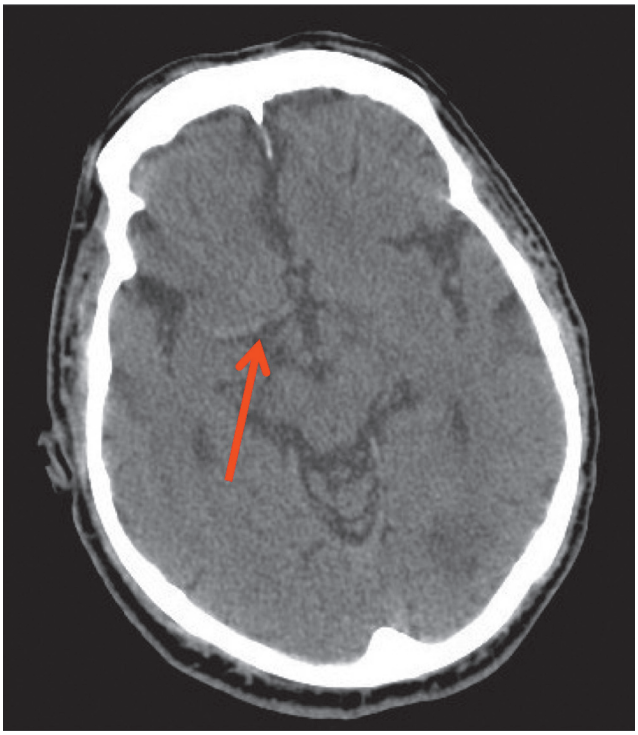
Epidemiology

Stroke is a leading cause of morbidity and mortality worldwide and is the fourth leading cause of death in the United States, affecting close to 750,000 people and resulting in greater than 120,000 deaths annually.[1] The burden of disability directly resulting from stroke is also significant, resulting in more than 74 billion dollars in economic costs as well as untold social costs.[1] Acute ischemic stroke (AIS), caused by occlusion of the intracranial arteries, represents more than 85% of acute stroke, the remainder of which are mostly hemorrhagic strokes.[2]

Intravenous tPA for Stroke

The emergency treatment for AIS witnessed a paradigm shift in the mid-1990s after the publication of the NINDS trial. The NINDS trial suggested that patients treated with tPA were 30% more likely to have minimal or no disability at 3 months with a 6.4% risk of intracerebral hemorrhage within 36 hours of treatment versus a 0.6% risk of hemorrhage in patients given placebo.[2,3] There was a suggested mortality benefit in those who received tPA that was not statistically significant in the sample size of the trial. The NINDS trial prompted the Food and Drug Administration to approve tPA for the treatment of AIS within 3 hours of symptom onset.[2,3] A series of later studies, the ECASS I, II, and III, and the ATLANTIS trials showed a time dependency to the administration of tPA and outcome and suggested that the administration of tPA up to 4.5 hours from the onset of symptoms could be both safe and efficacious.[2-4] Further studies

Figure 1. Hyperdense MCA sign on noncontrasted head CT scan.



have corroborated these findings, leading the most recent American Heart Association/American Stroke Association guidelines to support the use of tPA in AIS in certain patients up to 4.5 hours from symptom onset.[4] The decision to administer IV tPA up to 4.5 hours from symptom onset is typically done in consultation with specialists. There are certain inclusion and exclusion criteria for the administration of IV tPA (Table 1), and the dosing is calculated as an initial bolus and then a 1-hour infusion (Table 2).

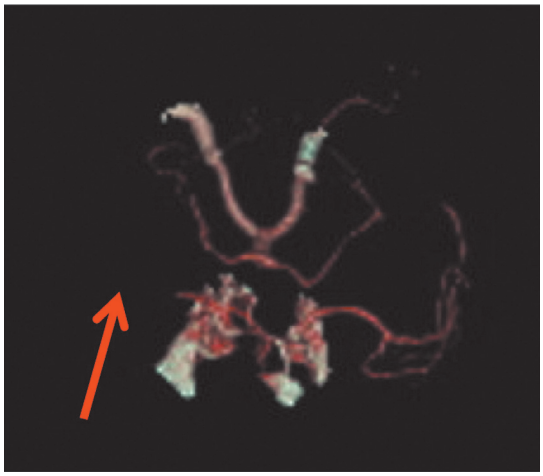
Time Is Brain Concept

Further analysis of the growing body of data has led to the "time is brain" concept in the treatment for AIS. As time from symptom onset increases, so does the number needed to treat to achieve a favorable outcome and the risk of intracerebral hemorrhage.[2,3,5] As such, it is imperative to diagnose AIS (in part by ruling out intracerebral hemorrhage, hypoglycemia, and other AIS mimics) and to proceed with treatment as soon as possible to allow for the best possible outcome.

Large Vessel Occlusion

Some evidence has suggested that the administration of IV thrombolytics is not particularly effective in patients with large or proximal artery occlusions causing AIS when compared with patients with smaller or more distal clots.[6] These patients with large vessel occlusion (LVO) have a higher rate of death, severe disability, and significantly lower rates of recanalization after IV thrombolytics.[7] The patient in our case, presenting with a National Institutes of Health Stroke Scale score of 18 and proximal MCA thrombus, fits this category of

Figure 2. CT angiogram showing large right MCA territory cutoff. Note the occlusion or cutoff on the patient's right side.



AIS patients. In an attempt to treat patients like these as well as patients presenting outside of the 3- to 4.5-hour tPA window, neurointerventional intra-arterial techniques have been developed to recanalize these obstructed cerebral vessels. Critical care transport services are often used to transport these patients to facilities with these capabilities.

Endovascular Therapies

Endovascular therapies have prolonged the treatment window of AIS for many patients. There are a number of interventional techniques with a variety of devices that largely fit into 2 categories: intra-arterial administration of thrombolytics up to 6 hours after the onset of symptoms and mechanical thrombectomy up to 8 hours after the onset of symptoms.[2,8] These are typically done only at specialized stroke centers with the necessary facilities and expertise. Recanalization of the occluded vessel is the ultimate goal and portends the best neurologic outcome for the patient.[8,9] There have been a number of trials examining the administration of guided intra-arterial tPA after administering IV tPA in patients with LVO coined "bridging therapy," and these have suggested benefit without reaching statistical significance.[8,9] Further trials are currently ongoing.

Mechanical Thrombectomy

Mechanical thrombectomy, which was performed in our patient, was first approved by the Food and Drug Administration in 2004. Since that time, a variety of devices have been approved for this purpose; however, there have been no randomized placebo controlled trials to support its use as of yet.[8-10] Using mechanical thrombectomy after IV tPA administration as a form of "bridging therapy" has been shown to be safe and does improve recanalization rates, which correlate with the best outcomes, suggesting a benefit.[9-14] Further trials are currently ongoing to show a concrete benefit to mechanical thrombectomy after IV tPA, but this has become a largely preferred method to treat LVO in AIS.[13-16]