Reversal of Acute Ischemic Stroke After THA Using Tissue Plasminogen Activator

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abstract

Full article available online at Healio.com/Orthopedics. Search: 20130426-35

Acute ischemic stroke is a potentially catastrophic medical emergency. Recently, successful reversal of the neurologic deficits associated with major ischemic strokes has been accomplished in selected patients through the use of intravenous tissue plasminogen activator (tPA), an agent that can accomplish thrombolysis of arterial clots if given within the first few hours after the onset of stroke. Because tPA works by thrombolysis of fresh clots, a potential exists for catastrophic hemorrhage if given to acute postoperative patients. Therefore, the use of tPA has never been studied in postoperative patients, and the safety of the drug in postoperative patients is unknown.

The author describes a patient who had an acute ischemic stroke 2 days after total hip arthroplasty who was successfully treated with tPA without major complications. The patient was 51 years old and developed progressive facial droop, right arm paralysis, and dysarthria 2 days after elective hip arthroplasty. Imaging confirmed occlusion of the left middle cerebral artery. Neurologic recovery was believed to be unlikely without tPA. After tPA administration, the patient had full neurologic recovery within minutes but did develop a large (nondraining) hematoma and severe ecchymosis at the surgical site; a drop in hematocrit required 3 units of packed red blood cell transfusion. The wound did not develop skin necrosis, infection, or compartment syndrome, and the hematoma resolved within several weeks without the need for surgical intervention.

The author describes the patient’s specific circumstances, the decision-making process behind the use of tPA, and the need for contingency plans in the event that severe uncontrolled hemorrhage occurs. This information may be useful if other surgeons are faced with the dilemma of a major stroke in acute postoperative patients.

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Acute ischemic stroke is a potentially devastating, and often fatal, medical emergency that can occur in a variety of circumstances. In general, most ischemic strokes result from either cardiocerebral embolization (common in atrial fibrillation), or large or small vessel atherosclerosis. Strokes that occur without an obvious source are referred to as cryptogenic strokes. Many cryptogenic strokes are later found to be associated with unrecognized patent foramen ovale and atrial septal aneurysms.1-2

Recently, successful reversal of the neurologic deficits associated with major ischemic strokes has been accomplished in selected patients with the use of intravenous tissue plasminogen activator (tPA), an agent that can accomplish thrombolysis of arterial clots.3 Selection criteria for the use of tPA are still evolving but generally include acute onset of severe neurologic deficits secondary to acute blockage of an intracerebral artery by an arterial thrombus. Treatment needs to be initiated within the initial few hours after the onset of symptoms to be effective. Unfortunately, the use of tPA has also been associated with significant risks of bleeding, and, therefore, its use in postoperative patients has never been studied. Acute postoperative status is felt to be a relative contraindication to the use of tPA, although this is based on theoretic risks rather than quantified outcome studies.

To the author’s knowledge, no case series or case reports document the outcome of tPA in postoperative orthopedic patients. Currently, it is unknown whether the drug can be administered safely in postoperative patients. It is intuitively obvious that the further removed a patient is from the time of surgery, the safer it should be to administer tPA. However, no guidelines indicate how many hours or days after surgery constitutes a safe period to administer the drug. Therefore, for surgeons who witness an acute ischemic stroke in an immediately postoperative patient, no published data reveal how to make a decision as to whether tPA should be considered. In the current report, the author describes a patient who had an acute ischemic stroke 2 days after a total hip arthroplasty (THA) who was successfully treated with tPA with no major complications.

**Case Report**

A 51-year-old man with osteoarthritis of the right hip and congenital coxa vara was electively admitted to the author’s hospital for a right THA. His history was significant for smoking for 30 years, a contralateral THA 7 years previously, and hepatitis C, which had been in remission since treatment with interferon 6 years previously. The patient was otherwise in good health and had no known history of coagulopathy, cerebrovascular disease, venous thromboembolism, or cardiac disease. He underwent an uncomplicated primary THA with uncemented components and had an uneventful recovery on the day of surgery and postoperative day 1.

Prophylaxis against venous thromboembolism was accomplished with a 30-mg dose of enoxaparin administered subcutaneously every 12 hours beginning at 9 a.m. the morning after surgery. No wound drain was used. Antibiotic prophylaxis was accomplished with cefazolin. The patient was ambulating with physical therapy and doing well by standard postoperative measures on postoperative day 1. On the morning of postoperative day 2, the patient developed an acute right-sided facial droop, right-sided hemiplegia, and dysarthria (slurred speech). The patient was emergently evaluated by a neurologist and neurosurgeon, and a computed tomography angiogram of the head revealed occlusion of the M1 and M2 segments of the left middle cerebral artery. A definitive cause for the arterial occlusion was not evident. The patient had normal sinus cardiac rhythm, absence of carotid artery disease, and negative Doppler ultrasound of the extremities.

The patient’s neurologic deficit became more profound over the next hour, becoming aphasic and losing additional motion of the right upper extremity. Both the neurologist and neurosurgeon felt that the likelihood of permanent right-sided paralysis and loss of speech were probable outcomes from the stroke. It was believed that the best chance for neurologic recovery would be through the infusion of tPA (Activase brand of alteplase; Genentech, San Francisco, California). A literature search revealed no reports of tPA use in a patient 48 hours after major surgery. After a discussion of the risks, benefits, and uncertainties with the patient and family, they elected to proceed with tPA infusion.

Given the known risks of intracerebral hemorrhage with tPA infusion after stroke, the neurosurgeon remained ready for emergency neurologic surgery if needed. From an orthopedic standpoint, there was a risk of life- or limb-threatening hemorrhage from the surgical site, compartment syndrome, and an infection if an unstable wound conditions should develop. The orthopedic surgical team remained on site and ready for emergent orthopedic intervention if any of the above should occur. Because the effect of tPA on a 48-hour postoperative surgical site is unknown and given the short half life of the drug (5 minutes), the orthopedic team was prepared, if necessary, to take the patient to the operating room, evacuate the hematoma, achieve hemostasis if possible, and hold pressure sponges on the surgical field (manually) for as long as necessary until bleeding subsided and the infusion completed.

With the above contingencies in place, the infusion was initiated approximately 2 hours after the onset of the stroke. An initial bolus of 7.4 mg of tPA was administered, followed by a 1-hour infusion of 67.3 mg of tPA. Within minutes of the infusion, the patient had minor bleeding from his gums and tongue, and within 5 to 10 minutes, minor bloody oozing occurred from the surgical site of the hip. Minor bleeding was also noted around the intravenous catheter sites. The hip and thigh were wrapped in a compression dressing and observed. Prophylactic antibiotics were
administered to minimize the risk of infection should an unstable hematoma develop. External bleeding from the hip never became severe. Significant thigh edema did occur within 1 to 2 hours of the infusion, but the thigh compartments remained soft. Substantial ecchymosis developed around the hip, buttock, and thigh. The patient required 3 units of packed red blood cells to maintain a stable hemoglobin/hematocrit.

Within minutes of the infusion, the patient’s right sided hemiparesis resolved, as did his aphasia and dysarthria. Although major bleeding from the surgical site never occurred, mild serosanguinous drainage from the underlying hematoma persisted for 3 to 4 days after the infusion and then resolved without sequelae. The patient experienced full neurologic recovery before leaving the hospital. He was discharged to home on postoperative day 6 (4 days after the stroke). The patient was prescribed clopidogrel (Plavix, Bristol Meyers Squibb/Sanofi partnership; New York, New York) for the prevention of a recurrent stroke and used pneumatic compression pumps for 7 days after discharge to minimize the risk of venous thromboembolism because it was necessary to discontinue taking enoxaparin after the stroke.

When neurologically stable, the patient underwent echocardiography that demonstrated a large patent foramen ovale and an atrial septal aneurysm, both of which were believed to be risk factors for cryptogenic stroke. He later underwent successful closure of the patent foramen ovale. It was hypothesized that the cryptogenic stroke was most likely caused by a venous thromboembolism that passed from the right atrium to the left atrium through the patent foramen ovale and then passed to the cerebral circulation.

**Discussion**

Prompt evaluation of patients with an acute ischemic stroke by members of a stroke treatment team can delineate treatment options. Although a general discussion of patient selection for tPA is beyond the scope of this case report and outside the field of orthopedic surgery, it is clear that some patients could potentially benefit from tPA. Because no guidelines or case reports are available regarding the use of tPA in postoperative orthopedic patients, surgeons are forced to make a decision as to whether to leave a patient permanently paralyzed or undertake a potentially risky treatment without any empirical evidence to make such a decision.

In this case, after frank discussion with the patient, the decision was made to administer the drug despite the risks and the lack of literature to guide the decision-making process. It is likely that orthopedic operations may be more at risk for major hemorrhage than other types of surgeries because it is not possible to achieve solid hemostasis of bone bleeding intraoperatively. Fortunately, the current patient had the best possible outcome, with resolution of the stroke without permanent neurologic deficit and without permanent complications related to the drug. The current findings may aid other surgeons faced with similar circumstances, although each case is different and generalizations can not be made based on a single case.

A surgeon must take several important considerations into account if confronted with the dilemma of a massive stroke in an acute postoperative patient. First, one should consider how far removed from surgery the patient is. The closer the patient is to the time of surgery, the greater the risk of a hemorrhagic catastrophe. Second, how stable was the hemostasis at the time of closure and did the patient have a stable hemoglobin prior to the consideration of giving tPA? Third, how tolerant is the particular surgical site at accommodating a potentially large hematoma? For example, sites such as the hip can tolerate a larger hematoma than the knee. A vital organ that was operated on may not tolerate a large hematoma. Fourth, is the surgical team immediately available with an available surgical suite if severe bleeding occurs? Fifth, are adequate blood transfusion products typed, crossed, and immediately available for transfusion through a large bore catheter if needed? It is also important to recognize that this drug has a short half-life but is typically given over a 1-hour long infusion process.

If severe bleeding occurs, consideration for shutting off the infusion should be given. A small case series of postoperative cardiac patients who received thrombolytic therapy for stroke has been described. The authors reported that 13 strokes in postoperative cardiac patients within 1 week of surgery were treated with intra-arterial thrombolysis at a mean of 4.3 days postoperatively; 1 patient developed hemothorax, but no reoperations were required. The patients in that study were generally further removed from surgery than the current patient.

**Conclusion**

The authors describe a patient who experienced a profoundly disabling stroke on postoperative day 2 after THA that was successfully treated with tPA without a major incident. Because no case reports describe the use of this drug so soon after major orthopedic surgery, the author believes that the current single case is noteworthy. If other surgeons faced with similar circumstances choose to use this drug in the future, it would be beneficial to report the outcomes (positive or negative) so that the surgical community can try to ascertain in what instances the benefits of treatment outweigh the risks.

**References**