Unsuccessful Tissue Plasminogen Activator Treatment of Acute Stroke Caused by a Calcific Embolus

John I. Halloran, MD
Ivo Bekavac, MD, PhD

ABSTRACT

Intravenous (IV) administration of tissue plasminogen activator (tPA) given to patients during acute cerebral ischemia according to National Institute of Neurological Disorders and Stroke (NINDS) guidelines improves clinical outcome by 11% to 14%. The success of IV tPA stroke therapy is dependent on several previously reported factors. The authors suggest that the presence of calcification within an embolus may represent an additional important factor. This report describes a patient with an acute stroke secondary to a spontaneous calcific cerebral embolus who had a negative outcome despite receiving proper thrombolytic therapy.

Key words: Stroke, thrombolysis, tPA, embolus.

Halloran JI, Bekavac I.
Unsuccessful tissue plasminogen activator treatment of acute stroke caused by a calcific embolus.
DOI: 10.1177/105122804205748

Intravenous (IV) tissue plasminogen activator (tPA) is an effective treatment for acute stroke when administered according to reported guidelines. This case report describes a patient with acute stroke secondary to a spontaneous calcific embolus who had a negative outcome despite receiving proper IV thrombolytic therapy. The case suggests a calcific embolus may be relatively resistant to effective treatment with IV tPA.

Case Presentation

A 74-year-old left-handed woman presented to the emergency room physician with acute onset of expressive aphasia. She had no weakness, numbness, or change in her vision. According to her family, no episode of syncope was observed. There was no history of cardiac disease or respiratory failure. She showed no improvement in her condition during her evaluation in the emergency room.

Her past medical history was remarkable for left hemispheric ischemic infarct and complete recovery of right hemiplegia 5 years earlier and an episode of transient encephalopathy 6 months prior to this event. At that time, she had a workup that included a head computed tomography (CT) that revealed an old left hemispheric infarct and no intravascular calcification, a negative electrocardiogram, and Holter monitor evaluation. Carotid color duplex examination revealed no hemodynamically significant disease. Thoracic aorta was not evaluated.

Physical examination revealed a blood pressure of 178/74 and regular heart rate of 80. There was no ocular or carotid bruit. The cardiac examination was normal, without murmur. Peripheral arterial pulses were present, and no peripheral edema was appreciated. Neurological examination revealed Broca's aphasia, left facial hypesthesia, and bilateral hyperreflexia with extensor plantar responses. The patient had completely preserved comprehension. The National Institutes of Health Stroke Scale score was 5.

Laboratory findings were unremarkable. No metabolic abnormality was identified. Electrocardiogram revealed normal sinus rhythm without evidence of acute ischemia. Transthoracic echocardiogram was essentially normal, without evidence of mass or thrombus. A transesophageal echocardiogram was not performed. A carotid ultrasound did not identify significant stenosis or atherosclerotic plaque in the extracranial carotid arteries.

The head CT showed no evidence of acute ischemia. There was a focal calcification, 2 mm in diameter, within the right Sylvian fissure (Fig 1) that was not present on a head CT performed 6 months earlier (Fig 2).

The patient met inclusion criteria for IV thrombolytic treatment with tPA, and informed consent was obtained. The drug was administered according to National Institutes of Health protocol.

Approximately 1 hour after the infusion of tPA was completed, the patient became less responsive and developed left hemiplegia with conjugate eye deviation to the right. She still had intact comprehension. Her speech was not fluent, and she was unable to repeat words. A repeat head CT performed this time with CT angiography (CTA) of the circle of Willis revealed a hypodense area within the M2 territory of the right middle cerebral artery. CTA demonstrated quite distinctly a calcific atheroembolus within a proximal M2 segment of the right middle cerebral artery (Fig 3). There was no intracranial hematoma.

Heparin was started intravenously 24 hours after tPA was given. The patient subsequently developed generalized tonic-clonic seizures well controlled with phenytoin. Neurological status remained unchanged. Her comprehension remained intact. Several days later, her general condition deteriorated due to acute renal failure and aspiration pneumonia. She died 10 days after the onset of neurological symptoms because of aspiration pneumonia and renal failure. No autopsy was performed as per the request of the patient's family.
Fig 1. Axial noncontrast head computed tomography (CT) image reveals calcification in right Sylvian fissure. It was not present on head CT examination performed 6 months earlier (see Fig 2). Incidental calcification in right globus pallidus.

Fig 2. Axial noncontrast head computed tomography image reveals no evidence of a calcific embolus. Again evident is calcification in right globus pallidus.

Fig 3. Computed tomography angiogram clearly demonstrates the intravascular location (proximal M2 branch of right middle cerebral artery) of the right Sylvian fissure calcification (arrow).
Discussion

A calcific embolus is a rare cause of stroke and usually follows an invasive procedure. These emboli may originate from the aortic valve, aortic arch, carotid arteries, or cardiac mural thrombus.1,2

Spontaneous embolization is less frequent.4

Thrombolytic therapy has been a remarkable development in the treatment of acute stroke. Inclusion criteria exist as do several options for administration (ie, IV, intra-arterial [IA], combined IV and IA). To the best of the authors' knowledge, there has been no reported case of tPA therapy for an acute stroke caused by a calcific embolus and no reports whether IV tPA is efficacious in treatment of it.

Plasminogen activators have proven effective in the treatment of acute thrombus. The embolus in this case was, at least in part, atheromatous. An atheroembolus consists of a combination of cholesterol and calcium, and one would expect tPA therapy to be ineffective in treatment of the atheroma unless fibrin was adherent to it. IV thrombolysis may effectively treat an intravascular clot that forms proximal or distal to the embolus.

Intra-arterial thrombolysis offers several potential advantages in stroke treatment including higher concentration of fibrinolytic agent delivered to the site, decreased systemic exposure and dose of thrombolytics, and, more important, an opportunity for mechanical disruption of the embolus with the delivery catheter or guide wire. In open clinical series, IA thrombolysis had higher early recanalization rates than did IV therapy (60%-80% for IA and 20%-60% for IV).3

A disadvantage of IA thrombolysis is a limited time window for action (3-6 hours after stroke onset). Despite proven efficacy, patients with a large artery intracranial occlusion who present inside 3 hours from symptom onset are candidates for only IV thrombolysis.6 Combined intra-arterial and intravenous thrombolysis regimens are rapidly evolving.7 Suction thrombectomy has been described recently as another option for clot removal in acute stroke patients.8 This type of mechanical therapy may have been a more effective treatment in this case.

Conclusion

A calcific embolus is a rare source of acute stroke and usually follows an invasive procedure. The authors are aware that the majority of patients who receive IV tPA for acute stroke do not improve clinically, but no clinical data were available to us at the time of treatment of this patient (nor subsequent to it) regarding the comparative success rate of tPA in the treatment of calcific versus noncalcific cerebral embolus. In fact, to the authors' knowledge, there is no reported case of IV thrombolytic treatment of acute stroke caused by a calcific embolus. Treatment regimen change is not justified based on a single case report. Further studies addressing the efficacy of IV tPA in treatment of calcific versus noncalcific embolic stroke as well as comparative efficacy of other modes of therapy (eg, suction embolectomy) may be justified.

References