

Embolization of a Chronic Left Ventricular Thrombus Following Thrombolytic Treatment for Acute Myocardial Infarction

Robert N. DiTrollo, DO, FACOI

Robert F. Sing, DO, FACEP, FACSM

Domenic Pisano, DO, FACOI

Kevin Pasquay, MS

Hemorrhage is a serious and sometimes fatal complication associated with the administration of thrombolytic agents for patients with an acute myocardial infarction (MI), stroke, or pulmonary emboli. Intracranial hemorrhage represents the most feared bleeding complication, carrying significant morbidity and mortality. Taking a careful history prior to the use of a thrombolytic medication is critical to determining which patients are at risk for hemorrhage. Several studies have investigated the risks and benefits of thrombolytic therapy, and guidelines have been established with indications and contraindications of such therapy. This article presents the case of a man with acute MI who was treated with thrombolytic therapy and subsequently developed embolic stroke followed by intracranial hemorrhage. The use of thrombolytic therapy in the treatment of acute MI is reviewed.

CASE PRESENTATION

Patient Presentation

A 63-year-old man presented to the emergency department (ED) with a 2-hour history of substernal chest pain, diaphoresis, and left arm pain. The patient had 2 prior episodes of chest pain over the previous 2 days, each of which lasted 2 hours in duration; these episodes were less intense than the pain that brought him to the ED.

Patient History

Past medical history was remarkable for hypertension and congestive heart failure of uncertain etiology. There also was a questionable history of apical hypertrophic cardiomyopathy. An echocardiogram performed at another institution 15 months prior to presentation described the left ventricle (LV) as dilated but with normal LV function. The apex was reported to be

hypertrophic. Outpatient medications included allopurinol, bumetanide, diltiazem CD, and metolazone.

Physical Examination

Physical examination revealed a diaphoretic man in moderate distress secondary to chest pain. Vital signs upon presentation were as follows: blood pressure, 140/96 mm Hg; heart rate, 72 bpm; respiratory rate, 24 breaths/min; and temperature, 97.2°F (36.2°C). Examination of the neck was negative for bruits or jugular venous distention. Pulmonary auscultation revealed bibasilar rales without other adventitious sounds. Cardiac rhythm was regular with a systolic murmur at the base. Abdomen was soft and nontender, with active bowel sounds. There was no hepatosplenomegaly. Rectal examination revealed no masses, and a stool sample was guaiac negative. Examination of the extremities was negative for edema, Homan's sign, and calf tenderness. Results of neurologic examination were nonfocal and essentially unremarkable.

Diagnostic Studies

Electrocardiogram showed evidence of an acute MI of the inferolateral wall (**Figure 1**). Chest radiograph showed signs indicative of congestive heart failure. An echocardiogram performed in the ED showed akinesia of the posterolateral wall of the LV and a calcified thrombus in the area of the apex (**Figure 2**).

Dr. DiTrollo is a Clinical Affiliate Instructor for the Philadelphia College of Osteopathic Medicine, and an Affiliate Professor at Temple University School of Medicine, Philadelphia, PA; and an Attending Physician in Emergency Medicine at the Crozer Chester Medical Center, Springfield, PA. Dr. Sing is Medical Director and Mr. Pasquay is an Exercise Physiologist at the Sports Science Center, Springfield, PA. Dr. Pisano is an Assistant Clinical Professor at the Philadelphia College of Osteopathic Medicine.

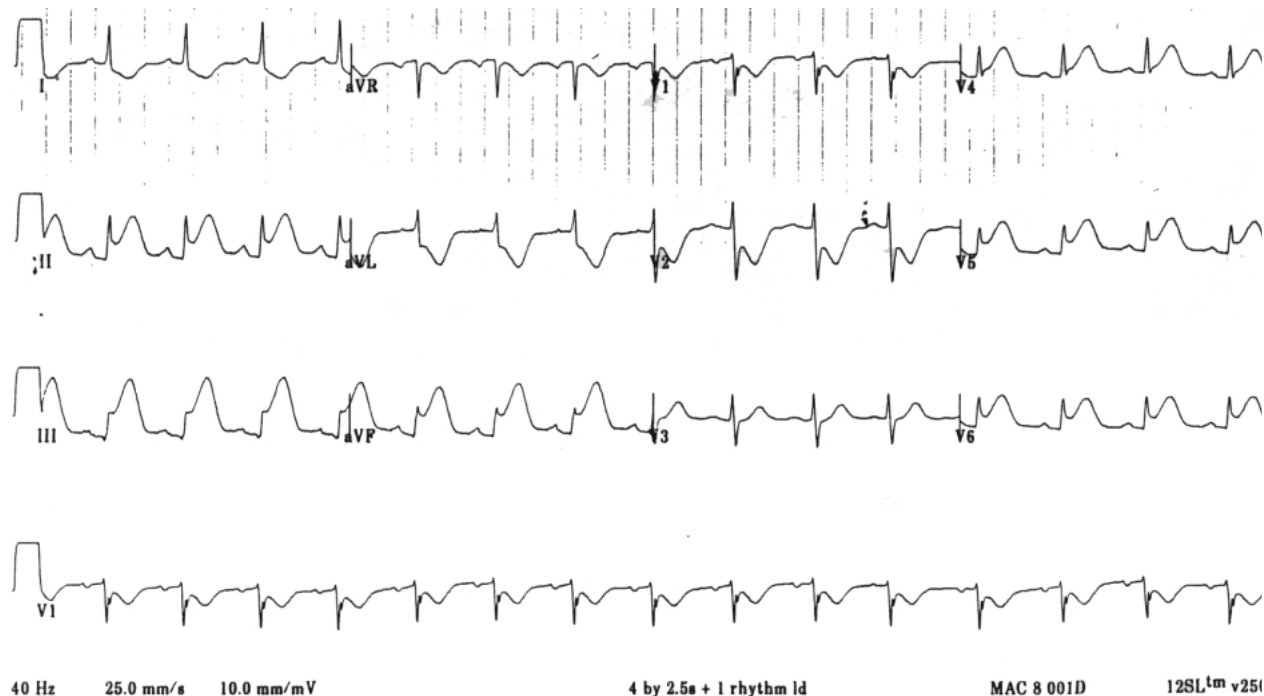


Figure 1. Electrocardiogram demonstrating the case patient's acute inferolateral wall myocardial infarction.

Initial Treatment and Clinical Course

The patient was treated with tissue plasminogen activator (t-PA) and heparin along with oxygen, morphine, and intravenous nitroglycerin. He experienced progressive relief of pain with improvement of ST segment abnormalities seen on electrocardiogram. Toward the end of the infusion of t-PA, the patient developed expressive aphasia and a right-sided hemiparesis. The heparin was stopped, as was the remaining t-PA. Computed tomography (CT) of the brain was negative for evidence of hemorrhage, and the consulting neurologist felt that the neurologic changes were secondary to an acute embolic episode.

Approximately 5 hours after the t-PA infusion was stopped, the patient was noted to have focal seizure activity of the left upper extremity along with progressive deterioration in his level of consciousness. A repeated CT scan of the brain revealed a large amount of brain edema on the left side with a moderate-size posterior parietal hemorrhage. There also was a small right-sided parietal hemorrhage and a small left-sided subdural hematoma. The patient's clinical status continued to deteriorate, and serial CT scans of the brain showed increasing amounts of blood with mass effect, ultimately requiring emergency neurosurgical evacuation of the subdural hematoma.

Approximately 24 hours after the initial develop-

ment of aphasia and hemiparesis, the patient's lower extremities became cold and cyanotic, and arterial Doppler examination revealed no distal pulses bilaterally. The patient underwent progressive changes consistent with acute arterial occlusive disease. No further invasive intervention was performed at the request of the family. Subsequent echocardiogram showed that the previously demonstrated thrombus in the LV apex was no longer present (**Figure 3**). The patient died several days later.

DISCUSSION

Embolization and Stroke Following Acute MI

The case patient presented with an inferolateral wall acute MI, and echocardiographic findings indicated the presence of a large, organized, calcified thrombus in the apex of the LV. Studies indicate that although one third of patients with acute MI have LV thrombi, only a small percentage of these are likely to embolize.¹ Tamarin and associates studied the effect of warfarin versus control for the treatment of LV thrombi after acute MI, and their results clearly showed that anticoagulant treatment hastened LV thrombus resolution.² Stratton and Resnick studied embolic risk in patients with LV thrombi and concluded that the increased embolic risk is not restricted to the immediate post-infarction period, documenting that chronic thrombi

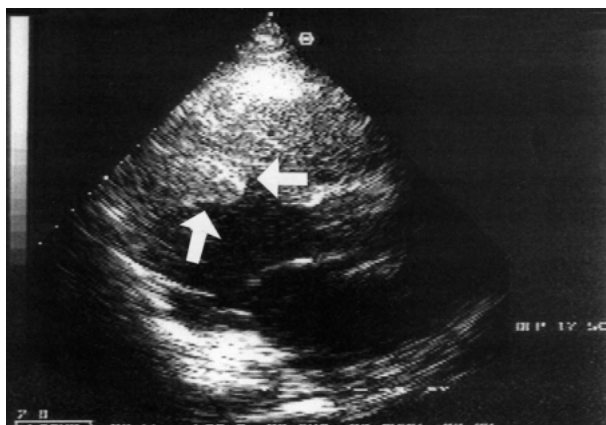


Figure 2. Echocardiogram of the case patient showing a calcified thrombus in the left ventricle (arrows).

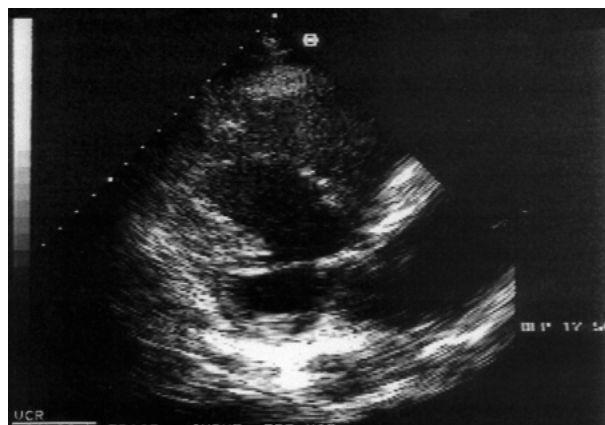


Figure 3. Echocardiogram of the case patient subsequent to thrombolytic therapy and the development of progressive neurologic deterioration. The previously visualized calcified thrombus has disappeared.

continue to embolize.³ Their study did not investigate the possible outcomes of established thrombi treated with thrombolytic agents (as in the case patient).

Stroke is a well-known complication of acute MI. The etiology of stroke in this case was thought to be due to emboli from a cardiac origin. The case patient developed neurologic symptoms consistent with a left hemispheric stroke believed to be secondary to an embolic source originating in the LV. Cerebral embolism of cardiac origin is a common cause of stroke, accounting for nearly one third of all cerebral infarctions.⁴

Anticoagulant therapy for acute MI is complicated by central nervous system hemorrhage in 0.05% to 0.14% of treated patients.⁵ As a complication of thrombolytic therapy for acute MI, intracranial hemorrhage may be due to parenchymal intracranial hemorrhage, hemorrhagic transformation of cerebral infarction, or subdural hematoma.⁶ In several studies, intracerebral hemorrhage has been reported to occur during infusion or fewer than 24 hours after infusion of a fibrinolytic agent.⁵⁻⁹

The case patient's progressively deteriorating neurologic status and evidence of hemorrhage on subsequent CT scan support the conclusion that he sustained a hemorrhagic infarction of the left hemisphere and possibly one in the right hemisphere. The patient developed hemorrhagic conversion of the embolic stroke 8.5 hours after the initial negative CT scan. Another possibility may have been a primary central nervous system bleed given the findings of bilateral parietal hemorrhage along with left-sided subdural hematoma; however, due to the concurrent findings of systemic embolization to the lower extremities, it is this author's conclusion that the events were a result of emboli rather than just hemorrhage per se.

Benefits and Risks of Thrombolytic Agents

Multiple studies and case reports have looked at the impact of thrombolytic therapy as a treatment modality for intracardiac thrombus and the complications of peripheral or recurrent embolization associated with its use. Kremar and associates used urokinase to successfully lyse LV thrombi in 10 of 16 patients, as documented by echocardiography.¹⁰ They found no evidence of embolic events in any of the 16 patients studied. Kemennu and Riggs published a case report showing successful lysis using t-PA of a right ventricular thrombus in a patient with congestive cardiomyopathy.¹¹ Krogmann and associates had similar successful results using t-PA to lyse a LV thrombus in a 2-year-old boy with cardiomyopathy. The thrombus was completely resolved in 72 hours without complication.¹²

Other reports have shown the dangers of peripheral embolization and the resultant complications. Blazer and associates reported a case of peripheral embolization during streptokinase therapy for a left atrial thrombus. In fact, the patient had emboli present in both femoral arteries requiring embolectomy on the third day of therapy.¹³ In a case reporting the use of t-PA in the treatment of cardioembolic stroke, during treatment, the patient embolized to the left internal and external carotid arteries as well as the left middle cerebral artery, originating from a mobile thrombus in the LV discovered by echocardiogram.¹⁴ These cases highlight the possible risk of fragmentation of intracardiac thrombi to various locations of the circulation. What has not been elucidated from these studies is whether the risk of fragmentation of intracardiac

thrombi from the use of thrombolytics is related to the age of the thrombus.

Several studies, including GISSI-1⁵, ISIS-II⁸, AIMS,¹⁶ and GUSTO¹⁷ have shown mortality benefits with the use of thrombolytic therapy in the setting of an acute MI. The GUSTO investigators concluded that accelerated t-PA given with intravenous heparin provided a survival benefit over previous standard thrombolytic regimens.¹⁷ There was, however, a significant excess of hemorrhagic strokes with accelerated t-PA as compared with streptokinase therapy.

Contraindications to the use of t-PA in patients with acute MI include history of stroke, recent (within 2 months) intracranial surgery, intracranial neoplasm, arteriovenous malformation, and cerebral aneurysm (Table 1). None of these contraindications were present in the case patient. Additional risk factors for intracranial hemorrhage following thrombolytic therapy include age (> 70 years), hypertension, higher dosage of the thrombolytic agent, concomitant medications (calcium channel blockers), and cardiopulmonary resuscitation.⁶ Combined fibrinolytic and anticoagulant treatment also has been shown to be a potential cause of intracranial hemorrhage following thrombolytic therapy.⁶ The case patient had several of these risk factors, which in combination, likely led to lysis and embolization of the LV thrombus followed by subsequent hemorrhage into the embolized area.

Assessing Risks of Thrombolytic Therapy in Acute MI Patients

The goal with thrombolytic therapy is to give the medication to appropriate patients as soon as possible after their arrival in the ED. This is most often initiated prior to obtaining an echocardiogram. The technology of echocardiography is becoming increasingly available in the ED and other settings where thrombolytic therapy is being initiated. The ability to perform echocardiography in the ED could not only assist in the selection of qualified patients to receive thrombolytic therapy, but also identify the rare patient with a previously unknown intracardiac thrombus. This would alert the treating physician to the presence of the thrombus and the potential complication of systemic embolization. Research into the frequency of LV thrombus in the setting of acute MI would contribute to establishing the overall risk of embolization involved in using these agents. In addition, research to assess whether the risk of embolization of LV thrombi is affected by the age of the thrombus would help to predict which patients are more likely to be affected by this life-threatening complication.

Table 1. Contraindications to Thrombolytic Therapy

Contraindications

- Active internal bleeding (excluding menstruation)
- Current blood pressure > 180 mm Hg systolic or > 110 mm Hg diastolic
- Intracranial neoplasm
- Previous stroke (hemorrhagic or other) or other cerebrovascular event within 1 year
- Suspected aortic dissection

Relative contraindications

- Active diabetic retinopathy
- Active peptic ulcer disease
- Blood pressure > 180/110 mm Hg at presentation
- Current use of anticoagulants (INR > 2.0-3.0)
- History of severe hypertension
- Known bleeding diathesis
- Noncompressible puncture sites
- Other intracerebral pathology not listed as a contraindication
- Pregnancy
- Prior allergic reaction or exposure to streptokinase anistreplase
- Prolonged (> 10 min) or traumatic cardiopulmonary resuscitation
- Recent internal bleeding (within 2-4 weeks)
- Recent major surgery (within 3 weeks)
- Recent trauma (within 2-4 weeks)

INR = international normalized ratio.

Adapted from Massie BM, Amidon TM. Heart. In: Tierney LM, McPhee SJ, Papadakis MA. Current medical diagnosis and treatment 2003. 42nd ed. New York: McGraw-Hill; 2001:312-408.

CONCLUSION

This case illustrates an uncommon but potentially devastating complication of thrombolytic therapy. Increased utilization of echocardiography early in the evaluation of patients with MI may reveal a higher incidence of LV thrombus. When a thrombus is present, the risk of embolization must be weighed against the potential benefit of thrombolytic treatment. **HP**

REFERENCES

1. Meltzer RS, Visser CA, Fuster V. Intracardiac thrombi and systemic embolization. *Ann Intern Med* 1986;104:689-98.
2. Tramarin R, Pozzoli M, Febo O, et al. Echocardiographic assessment of therapy efficacy in left ventricular thrombus post myocardial infarction [abstract]. *Circulation*

- 1983;68(Suppl 3):331.
3. Stratton JR, Resnick AD. Increased embolic risk in patients with left ventricular thrombi. *Circulation* 1987;75:1004-11.
 4. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: a prospective registry. *Neurology* 1978;28:754-62.
 5. Assessment of short-anticoagulant administration after cardiac infarction. Report of the Working Party on Anticoagulant Therapy in Coronary Thrombosis to the Medical Research Council. *Br Med J* 1969;1:335-42.
 6. Sloan MA, Gore JM. Ischemic stroke and intracranial hemorrhage following thrombolytic therapy for acute myocardial infarction: a risk-benefit analysis. *Am J Cardiol* 1992;69:21A-38A.
 7. Rovelli F, De Vita C, Feruglio GA, et al. GISSI trial: early results and late follow-up. Gruppo Italiano per la Sperimentazione della Streptochinasi nell'Infarto Miocardico. *J Am Coll Cardiol* 1987;10(5 Suppl B):33B-39B.
 8. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. *Lancet* 1988;2(8607):349-60.
 9. Sloan MA, Price TR, Terrin ML, et al. Ischemic cerebral infarction after rt-PA and heparin therapy for acute myocardial infarction. The TIMI-II pilot and randomized clinical trial combined experience. *Stroke* 1997;28:1107-14.
 10. Kremer P, Fiebig R, Tilsner V, et al. Lysis of left ventricular thrombi with urokinase. *Circulation* 1985;72:112-8.
 11. Kemennu L, Riggs TW. Tissue plasminogen activator lysis of a right ventricular thrombus. *Am Heart J* 1992;123(4 Pt 1):1057-8.
 12. Krogmann ON, von Kries R, Rammos S, et al. Left ventricular thrombus in a 2-year-old boy with cardiomyopathy: lysis with recombinant tissue-type plasminogen activator. *Eur J Pediatr* 1991;150:829-31.
 13. Blazer D, Degroat T, Kotler MN, et al. Peripheral embolization during thrombolytic therapy for left atrial thrombus. *Am J Cardiol* 1986;58:554-5.
 14. Yasaka M, Yamaguchi T, Yonehar T, Moriyasu H. Recurrent embolization during intravenous administration of tissue plasminogen activator in acute cardioembolic stroke. A case report. *Angiology* 1994;45:481-4.
 15. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). *Lancet* 1986;1(8478):397-402.
 16. Effect of intravenous APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. AIMS Trial Study Group. *Lancet* 1988;1(8585):545-9.
 17. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. The GUSTO Investigators. *N Engl J Med* 1993;329:673-82.

Copyright 2003 by Turner White Communications Inc., Wayne, PA. All rights reserved.