Thrombolytic Therapy for Acute Left Atrial Thrombus Formation in One Patient With Heart Failure and Atrial Fibrillation

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Patients with a left atrial (LA) thrombus are considered at high risk of thromboembolic events. Reports about thrombolytic therapy are limited and optimal guidelines are lacking. In this report, a large, pedunculated, highly mobile thrombus of the LA attached via a short stalk to the LA appendage brim in a 59-year-old female with atrial fibrillation is described. The patient was treated with 100 mg intravenous tissue plasminogen activator for 2 h after the ineffective administration of heparin. The thrombus soon dissolved. However, the patient developed a transient ischemic embolism 12 h later when the post hoc heparin effect was at its nadir. Based on this and other reports, thrombolytic therapy may be effective and safe in patients with acute, non-organized LA thrombi and post hoc heparinization should be sufficient to prevent thromboembolism from rebound coagulation. (Circ J 2007; 71: 604–607)

Key Words: Atrial fibrillation; Heart failure; Left atrial thrombus; Thrombolysis

Case Report

A 59-year-old female was admitted due to aggravated dyspnea, orthopnea and abdominal fullness. One year prior to this admission, the patient was admitted for pulmonary edema. At that time, she was found to have atrial fibrillation and left ventricular (LV) dysfunction with an LV end-diastolic dimension of 53 mm and end-systolic dimension of 39 mm. The LV ejection fraction was 37% and the LA dimension was 50 mm. Since then, the patient was put on bisoprolol 5 mg/day, losartan 50 mg/day and spironolactone 12.5 mg/day. Two months prior to this admission, persistent atrial fibrillation developed and warfarin 1 mg/day was given. One month later, her prothrombin time was 11.7 s and her international normalized ratio (INR) was 1.04.

On admission, her blood pressure was 132/72 mmHg, heart rate 76 beats/min, 18 respirations/min and body temperature 36.6°C. Physical examination showed an irregularly irregular heart beat and a grade II/VI systolic murmur at the apex. A chest X-ray film demonstrated cardiomegaly and pulmonary congestion. Transthoracic echocardiography revealed a mobile elongated thrombus 26×14 mm with a stalk attached to the junction of the posterior mitral annulus and LA appendage orifice (Fig 1). The thrombus drifted and straddled the mitral leaflets in diastole and returned to the LA in systole. The thrombus was not observed through echocardiography 4 months prior to this admission. Following full discussion of all treatment options with the patient and her family, intravenous administration of heparin was accepted and initiated. Repeat echocardiography on the following day revealed no change to the thrombus. The patient and her family accepted the proposal of the use of thrombolytic therapy. Tissue plasminogen activator (tPA) (100 mg) was administered intravenously for 2 h, followed by intravenous infusion of heparin. Repeat transthoracic echocardiography 5 h after the initiation of tPA therapy indicated that the majority of the thrombus had disappeared and only a small remnant stem of the stalk remained floating at the attachment site (Fig 2). Mild gum bleeding was observed shortly after thrombolysis. Activated partial thrombin time 6 h later was 53.0 s (control, 30.6 s). Twelve hours after thrombolytic therapy, the patient was drowsy. The activated partial thrombin time was 40.2 s (control, 30.7 s). Immediate brain computed tomography demonstrated no hemorrhage or hypodense areas. The patient’s consciousness recovered without sequel on the following day. Cardiac catheterization and coronary angiography performed 2 weeks later showed that the coronary arteries were normal. The LV ejection fraction was 40%. Transesophageal echocardiography performed next day demonstrated spontaneous echo contrast in the LA and its appendage, and no thrombus was identified.
The patient was discharged with no other complications and the warfarin was given at a dose of 2.5 mg/day and the INR of prothrombin time was kept around 2.0 to 3.0. Two months later, flecainide 50 mg twice daily was administered and her atrial fibrillation was converted back to sinus rhythm 1 month later.

**Discussion**

The presence of atrial fibrillation is a risk factor for stroke and the presence of congestive heart failure increases the risk further. Presence of LA thrombus indicates a high risk of systemic thromboembolism and warrants aggressive

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Fig 1. Apical 4-chamber view of initial transthoracic echocardiography. A 26×14 mm thrombus drifted across the mitral valve during diastole (A) and returned to within left atrium (LA) during systole (B). The straddling across the mitral valve was seen on apical two chamber view (C). The thrombus was attached to the junction between the LA appendage and annulus of posterior mitral leaflet (D). AO, aortic root; AV, aortic valve; LAA, LA appendage; RA, right atrium; RV, right ventricle.

Fig 2. After thrombolytic therapy, the thrombus disappeared on apical 4-chamber view (A) and only little remnant of the stalk (Arrow) was visible on the modified short axis view (B) on echocardiography (AO, aortic root; AV, aortic valve; LA, left atrium; LAA, left atrial appendage; RA, right atrium; RV, right ventricle).
therapy. Although anticoagulant therapy is indicated for high-risk patients with atrial fibrillation, no guidelines currently exist for acute thrombus formation in the LA. In considering the high risk for systemic embolisms, acute large thrombi warrant prompt management. The prompt management options may include administration of anticoagulants, thrombolitics and surgery. In certain cases, decision making may sometimes be difficult and several issues should be considered.

Is It a Thrombus, Vegetation or Tumor?
Differentiating between a thrombus and tumors or infective vegetations may be difficult in some cases. Furthermore, the thrombus may be formed and superimposed onto the vegetations or tumors or vice versa and therefore, the thrombus may be formed and superimposed onto the LA might occur and this severed thrombus could block the mitral orifice and result in sudden death.11

Anticoagulation with heparin or warfarin may be appropriate for sessile, immobile thrombi that are typically considered less risky than pedunculated and floating ones. For example, in this case, the pedunculated thrombus drifted into the LV inflow tract in diastole and returned to the LA in systole and, therefore, it was difficult to differentiate from a myxoma. Fortunately, the likelihood of a myxoma in this case could be excluded based on its absence on echocardiography 4 months previously. Also, an absence of signs of infection and its attachment site at a low-flow atrial wall helped us rule out the possibility of vegetation.

What Shape Does the Thrombus Have?
Anticoagulation with heparin or warfarin may be appropriate for sessile, immobile thrombi that are typically considered less risky than pedunculated and floating ones. For example, in some cases, anticoagulants can be prescribed to dissolve the thrombus prior to percutaneous intervention for patients with mitral stenosis. Although there is no definite guideline for riskier pedunculated thrombi, they may need quicker management and closer monitoring to reduce the risk of embolization.

Is the Thrombus Organized?
Organization or partial organization within a thrombus may indicate that the thrombus has existed longer than an unorganized one. The response of an organized thrombus to anticoagulant therapy may be unpredictable. Parts of the thrombus may dissolve quicker than other parts and, thus, fragments may be shed during therapy and result in embolization. When the echo quality is adequate, hyperechogenic areas with or without calcification may be observed in organized thrombi. Sometimes the appearance of a cyst or a crescent lamellar echo signals could be seen in larger ones.

Fang et al described recurrent cerebral embolism in a 65-year-old female patient with transient ischemic attack, nonvalvular atrial fibrillation and an immobile LA thrombus when she was being treated with anticoagulant therapy. The follow-up transesophageal echocardiography showed that the thrombus decreased in size and became pedunculated and mobile, with detachment impending 8 days after initiation of anticoagulant therapy. Wrisley et al reported a detached large LA thrombus that was successfully retrieved surgically. Fraser et al reported a case of sudden death because of the detachment of an immobile LA thrombus following the initiation of anticoagulant therapy. Sometimes, spontaneous severance of the stalk of a pedunculated thrombus in the LA might occur and this severed thrombus could block the mitral orifice and result in sudden death.11

When is Thrombolytic Therapy Indicated?
Thrombolytic therapy has been shown to be effective in patients with mitral prosthesis with thrombosis.12 Thrombolytic therapy is another option for treating an LA thrombus. In this case, thrombolysis for this 2.6 x 1.4 cm thrombus was quick and complete. During the administration of thrombolytics, the patient only experienced minor gum bleeding and no embolism resulted from shedding fragments.

However, the effectiveness and risk of thrombolytics for an organized or partially organized thrombus or thrombi of longer duration is not known clinically. In consideration of fragment shedding after partial resolution, it is advised to check the echo characteristics of the thrombus carefully before initiating thrombolytic therapy. In the present case, the thrombus was thought to be homogeneous and soft as we saw it moving within the LA and drifting into the mitral orifice (Fig 1). These features suggested that this thrombus was fresh and unorganized. Therefore, the thrombus dissolved soon after the administration of tPA.

Although tPA therapy worked quite well in our patient, this is just one case. Theoretically, the detachment of a large LA thrombus after thrombolytics could occur if the stalk was dissolved first. Therefore, the compilation of more clinical experience is needed in order to establish a correct guideline to treat such patients.

Post Hoc Anticoagulation
The episode of disturbed consciousness was deemed a transient ischemic attack 12 h after thrombolytic therapy was completed and when the activated partial thrombin time was at its nadir of 40.2 s (control, 50.7 s). Inadequate maintenance of anticoagulation may have caused this episode. Although anticoagulation and coagulation after administration of anticoagulants is like a tug of war. Coagulation may surpass anticoagulation when the effect of anticoagulation is on the wane. A rebound thrombosis after discontinuing anticoagulant therapy was reported by Kadoi et al.13 Therefore, maintaining sufficient anticoagulation may be crucial following thrombolytic therapy for LA thrombus.

For those with non-valvular atrial fibrillation, warfarin is often used for the prevention of thromboembolism. Hylek et al reported that anticoagulation that produced an INR of ≥ 2 reduced the occurrence of ischemic stroke and in-hospital mortality. Therefore, lower INR target levels cannot be recommended. Previous insufficient anticoagulation in our case confirms this point of view.

Thrombolysis vs Surgery
The indications for thrombolysis or surgical removal of an LA thrombus may be complex, especially for acute large thrombi. However, when a thrombus is organized or when suspicion of tumor or an infective mass exists, surgery is indicated. In cases in which the acute LA thrombus is very large and thrombolysis will likely increase risk of thrombus fragmentation, surgical intervention may be a conservative modality and thrombolytic therapy should only be limited to patients with high perioperative risk or contraindication for operation.

References
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