Safe Dose Thrombolysis in Pulmonary Embolism

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Introduction

Pulmonary embolism (PE) is a potentially lethal disease. Syncope and cardiac arrest may occur in a patient with PE. In most cases, such an episode is related to persistent, systemic hypotension or shock, which are markers of high risk for sudden death. Fibrinolysis is suitable for patients with massive acute PE or patients with submassive acute PE with clinical evidence of an adverse prognosis. Although these drugs are effective in dissolving blood clots, data summarized from randomized trials indicate a 13% cumulative rate of major bleeding and a 1.8% rate of intracranial and fatal haemorrhage.[1] Herein, we report a case of high-risk pulmonary embolism with high bleeding risk. The patient was successfully treated by thrombolysis with half-dose tissue plasminogen activator (t-PA).

Case Report

A 44-year-old woman who experienced dyspnea for 2 days presented at the emergency department of our hospital. She had a history of severe anemia caused by uterine myoma and menorrhagia. A physical examination conducted upon arrival showed that her blood pressure was 104/50 mm Hg with a regular pulse of 96 beats per minute. Her lungs and heart did not exhibit any abnormalities. There was no calf or thigh swelling or tenderness. Chest radiography images were clear, but an engorged right pulmonary artery was noted. Electrocardiography demonstrated a normal sinus rhythm and T-wave inversions across the anterior precordium; on the basis of these findings, RV pressure overload was suspected. Chest computed tomography (CT) indicated the presence of thrombus in the bilateral main pulmonary arteries, particularly on the right side (Figure 1A). Transthoracic echocardiography (TTE) confirmed a dilated right ventricle (RV) and a D-shaped left ventricle (LV) in the parasternal short-axis view. A regimen of unfractionated heparin and warfarin was initiated as anticoagulation treatment. The patient, however, still experienced dyspnea and orthostatic dizziness during hospitalization and also experienced a syncope attack on the morning of the third day after admission. To prevent further progression of the pulmonary embolism, it was recommended that the patient undergo surgical embolectomy because of the high bleeding risk of thrombolysis treatment, but she refused. After informing her family of the risk of severe bleeding or intracranial bleeding, systemic intravenous thrombolysis was performed with a half dose of tissue plasminogen activator (t-PA). Because the patient's International Normalized Ratio (INR) was 2.0 at that time, we withheld heparin and warfarin treatment for 24 h. The patient's hemodynamic status and clinical condition improved dramatically within 2 h without bleeding or other major side effects (Figure 2). On subsequent clinical follow-up, the CT was repeated to check the response to thrombolysis therapy, and a partial resolution of the thrombus was noted (Figure 1B). The patient was symptom-free and had an uneventful outcome after discharge.

Figures

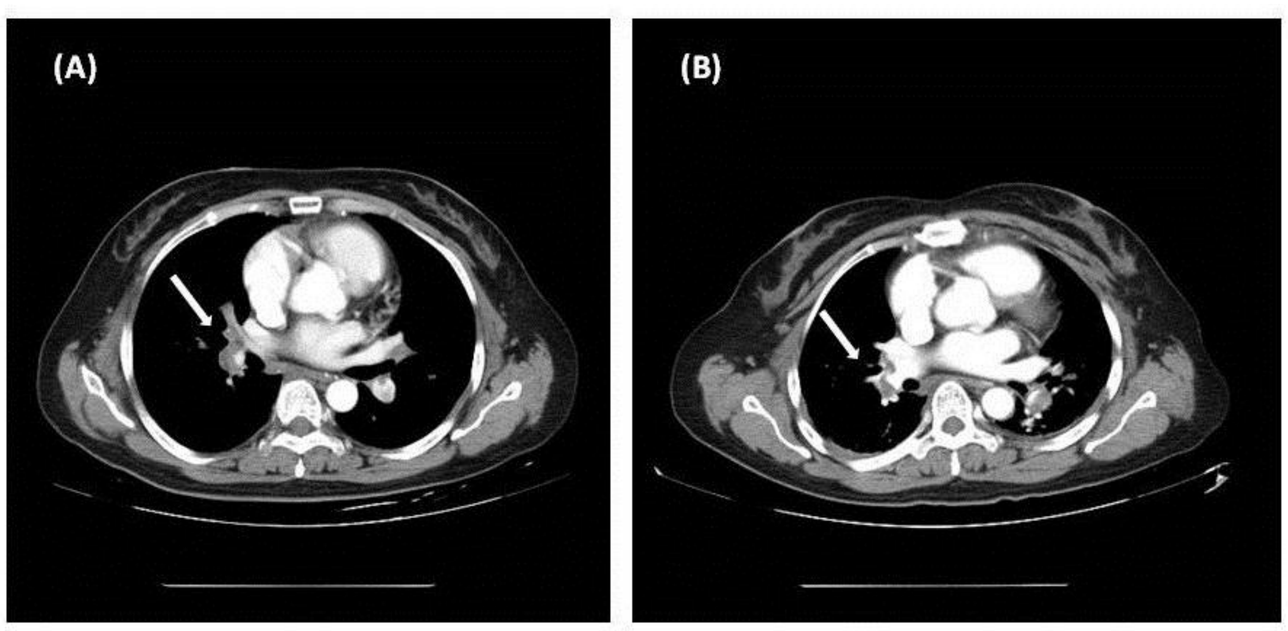

Figure 1.
(A) Chest computed tomography indicated the presence of thrombus in the bilateral main pulmonary arteries, particularly on the right side (arrow). (B) Computed tomography showed a partial resolution of the thrombus (arrow).

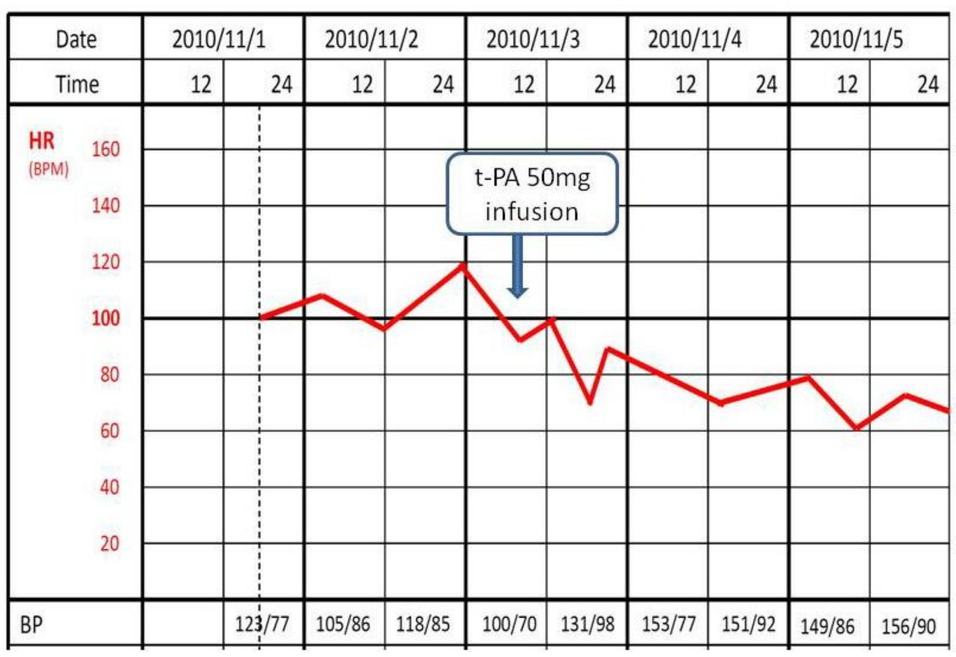

Figure 2.
(The Temperature, Pulse and Respiration Record showed the hemodynamic status improved dramatically. Systolic blood pressure rose again from 100 mmHg to 153 mmHg and heart rate descreased from 110 bpm to 70 bpm within 2 h after t-PA infusion.

Discussion

PE is a relatively common cardiovascular emergency. Occlusion of the pulmonary arterial bed may be acutely life-threatening. Alternatively, the patient may present with syncope or systemic hypotension, which may progress to shock and death as a result of acute RV failure. Analysis of the International Cooperative Pulmonary Embolism Registry (ICOPER) data demonstrated a 90-day all-cause mortality rate of 52.4% (95% CI, 43.3–62.1%) in patients with systolic blood pressure (SBP) < 90 mm Hg compared with 14.7% (95% CI, 13.3–16.2%) in normotensive patients.[2] According to data from Management Strategy and Prognosis of Pulmonary Embolism Registry (MAPPET), the in-hospital all-cause mortality was 15.2% in hypotension patients and 24.5% in the patients with shock status.[3]

Syncope in the setting of pulmonary embolism can be the result of 3 possible mechanisms. First, massive pulmonary arterial obliteration could cause RV failure and impaired LV filling, leading to a reduction in cardiac output, reduced cerebral blood flow, and ultimately syncope. The second mechanism involves the appearance of arrhythmias associated with RV overload. In the third mechanism, the embolism can trigger a vasovagal reflex that leads to neurogenic syncope. Although the prognostic value of syncope has not been specifically addressed, it has generally been considered a poor indicator in the diagnosis of pulmonary embolism. Physicians and other healthcare professionals must be vigilant with patients who have syncope, because this symptom may be a "forgotten sign" of life-threatening pulmonary embolism.[4]

The PAIMS 2study (Akeplase Combined With Heparin Versus Heparin in the Treatment of Acute Pulmonary Embolism. Plasminogen Activator Italian Multicenter Study 2) concluded that t-PA administration resulted in a greater and faster improvement of angiographic and hemodynamic variables compared with heparin treatment.[5] Approximately 92% of patients can be classified as responders to thrombolysis on the basis of clinical and echocardiographic improvement within the first 36 h.[6] The 2008 American College of Chest Physicians' guidelines include fibrinolysis as an option for patients with submassive PE who are judged to have a low risk of bleeding.[7] However, some physicians are understandably reluctant to use thrombolysis regimens because of the life-threatening complications associated with the administration of full-dose t-PA; data summarized from randomized trials revealed a 13% cumulative rate of major bleeding and a 1.8% rate of intracranial and fatal haemorrhage.[1] We believe that there is a safer manner in which t-PA can be administered.

The present case involves a patient with PE who presented with low CO symptoms and signs, high bleeding risk, and no response to medical treatment. The patient was recommended to undergo a surgical embolectomy, but she refused. We believe that thromboembolus in pulmonary arterial circulation is very sensitive to thrombolysis, and the pulmonary blood flow is equal to the entire cardiac output. Different from cases of acute stroke and acute myocardial infarction, cerebral blood flow is typically 15% of the CO, and approximately 5% of the total CO flows through the coronary arteries. Almost all t-PA molecules converge in the lungs. We therefore adjusted the t-PA dosage to half the regular dose because of the high bleeding risk. The patient's hemodynamic status and clinical condition improved dramatically within 2 h without any bleeding or other major side effects.

In conclusion, this is the first case to show that use of a lower t-PA dose can be safe and effective for patients with pulmonary embolism. We further suggest that pulmonary embolism can be more aggressively and safely managed with what we call "safe-dose t-PA."

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