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SEQUENTIAL SYSTEMIC THROMBOLYSIS FOR CLOT-IN-TRANSIT AFTER THROMBOLYTIC FAILURE IN MASSIVE PULMONARY EMBOLISM

Evans MacCready, Sanaa Afriyie-Ansah, Ama Owusuaa Kwakye, Romeo Boaheng

Department of Internal Medicine, Cape Coast Teaching Hospital, Cape Coast, Ghana

Corresponding author's e-mail: e.maccready@ccth.gov.gh

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ABSTRACT

Introduction: A clot-in-transit (CIT) is a mobile thrombus within the right heart associated with acute pulmonary embolism (PE) and high mortality. Although systemic thrombolysis remains the standard treatment for massive or high-risk PE, management of thrombolytic failure and associated CIT remains challenging, particularly when surgical embolectomy and catheter-directed thrombectomy are unavailable. Sequential systemic thrombolysis represents a practical therapeutic option in these high-risk scenarios.

Case description: A 54-year-old woman with hypertension presented with progressive dyspnoea and pleuritic chest pain. Computed tomography pulmonary angiography confirmed massive bilateral PE, and she was treated with intravenous tenecteplase. Despite initial hemodynamic improvement, hypoxemia persisted, and echocardiography revealed a large CIT within the right atrium. In the absence of surgical or catheter-directed options, she received repeat systemic thrombolysis with alteplase, achieving complete thrombus resolution and rapid clinical recovery without bleeding complications. Further evaluation revealed large uterine fibroids compressing the iliac veins as the likely source of extensive deep vein thrombosis.

Discussion: This case demonstrates the potential role of sequential systemic thrombolysis in managing thrombolytic failure and CIT when advanced interventions are unavailable. Switching to alteplase after unsuccessful thrombolysis with tenecteplase may enhance thrombus dissolution due to pharmacological differences in fibrin affinity and duration of fibrinolytic activity. Early reassessment following thrombolysis is critical to detect persistent thrombus and guide timely intervention.

Conclusion: Sequential systemic thrombolysis can serve as a safe, effective, and practical rescue strategy for clot-in-transit complicating massive PE, particularly in low-resource settings where surgical or catheter-based interventions are not available.

KEYWORDS

Clot-in-transit, pulmonary embolism, thrombolytic failure, sequential thrombolysis

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LEARNING POINTS

- Sequential systemic thrombolysis can be a safe and effective rescue option following thrombolytic failure in massive pulmonary embolism.
- Early echocardiographic reassessment is essential to detect treatment failure and guide further therapy.
- Large uterine fibroids can cause iliac vein compression and predispose to extensive deep vein thrombosis.

INTRODUCTION

Pulmonary embolism (PE) is a potentially fatal condition that requires timely diagnosis and intervention. Systemic thrombolysis remains the standard treatment for massive or high-risk PE, with alteplase recommended as the preferred fibrinolytic agent[1]. Tenecteplase has demonstrated comparable efficacy and safety, supporting its use as an alternative fibrinolytic agent in settings where alteplase is unavailable[2]. However, thrombolytic failure occurs in a subset of patients, requiring prompt reassessment and rescue therapy[3].

A clot-in-transit (CIT) is a mobile thrombus within the right heart reported in 3 to 4% of patients with acute PE, and carries a mortality rate approaching 45%, underscoring its clinical significance and need for rapid intervention[4]. The occurrence of CIT following unsuccessful thrombolysis poses a complex therapeutic challenge. While current European Society of Cardiology (ESC) guidelines recommend surgical embolectomy or catheter-directed interventions as rescue strategies, these are often unavailable in resource-limited settings. In such cases, repeat systemic thrombolysis may offer a practical alternative. However, evidence supporting this approach, particularly with an alternative fibrinolytic agent, is limited to small case series and is not addressed in the current guidelines[4,5].

This report describes a patient with massive PE who developed CIT and persistent hypoxemia despite systemic fibrinolysis with tenecteplase. In the absence of advanced interventional options, she was successfully treated with repeat systemic thrombolysis using alteplase. This case underscores the importance of early reassessment after thrombolysis and highlights sequential systemic thrombolysis as a practical rescue strategy in low-resource settings.

CASE DESCRIPTION

A 54-year-old woman with well-controlled hypertension presented with a 5-day history of progressive dyspnoea, pleuritic chest pain, and dry cough. On initial evaluation, she was tachypnoeic with oxygen saturation of 86% on room air which improved to 94% with 5 l/min oxygen via nasal cannula. Her blood pressure was 130/88 mmHg.

A Wells score of 7.5 indicated a high pretest probability for PE, and anticoagulation with enoxaparin was initiated. Computed tomography pulmonary angiography (CTPA) confirmed multiple bilateral segmental emboli. The next day, blood pressure dropped to 84/50 mmHg consistent with massive PE, necessitating thrombolysis with intravenous tenecteplase, the only available agent at the time. A dose of 45 mg was given as she weighed 82 kg. Although her blood pressure normalized post-thrombolysis, she remained hypoxemic with persistent dyspnoea.

She was referred to our hospital 6 days after initial thrombolytic therapy. On arrival, she was in respiratory distress requiring high-flow oxygen but haemodynamically stable. Electrocardiogram showed sinus tachycardia with a heart rate of 112 bpm, S1Q3T3 pattern, and T wave inversions in leads V1, V2 and aVF *(Fig. 1)*, consistent with right heart strain.

Transthoracic echocardiography demonstrated a large clot-in-transit within the right atrium *(Fig. 2)* measuring 5.4 × 1.9 cm with right atrial and ventricular dilatation, and tricuspid annular plane systolic excursion of 15.3 mm.

Repeat CTPA confirmed increased thrombus burden with new filling defects in both pulmonary arteries. Doppler ultrasound of the lower limbs revealed bilateral femoral deep vein thrombosis. Pelvic ultrasound identified multiple large uterine fibroids compressing the iliac veins, thought to be the risk factor for thrombosis, as further evaluation for additional risk factors, including thrombophilia screening and malignancy work-up, was negative.

Given her persistent hypoxaemia and clot burden, and the unavailability of surgical or catheter-based interventions, repeat systemic thrombolysis with alteplase (100 mg over two hours) was pursued as the only available option. Echocardiography post-thrombolysis confirmed complete resolution of the intracardiac thrombus as shown in *Figure 3*.

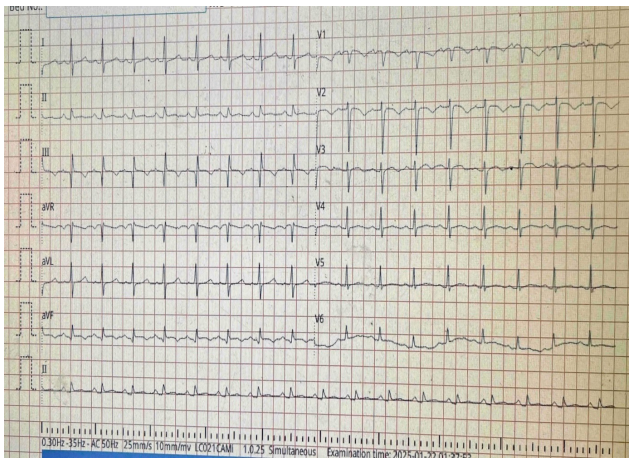


Figure 1. *Electrocardiogram showing sinus tachycardia, S1Q3T3 pattern and T-wave inversions in leads V1, V2, and aVF.*

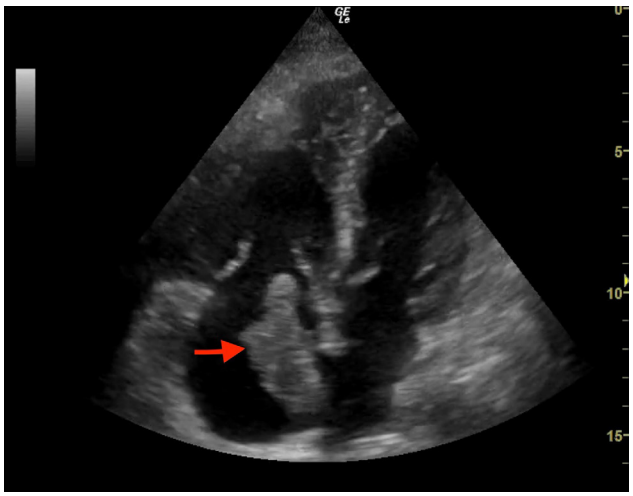


Figure 2. Transthoracic echocardiogram (apical four-chamber view) demonstrating a large clot-in-transit within the right atrium (red arrow) and associated right heart dilatation.



Figure 3. Post-thrombolysis transthoracic echocardiogram showing complete resolution of the previously visualized clot-in-transit.

The patient's symptoms improved rapidly; she was weaned off oxygen within 24 hours and discharged 5 days later on oral anticoagulation. She was subsequently referred for an elective hysterectomy to address the underlying risk factor.

DISCUSSION

CIT is a rare but critical finding in the context of acute PE, often associated with rapid deterioration and high mortality. Its presence signifies an actively migrating embolus and mandates urgent therapeutic intervention. Management options are dictated by resource availability[4,6].

Systemic thrombolysis remains the first-line treatment for massive or high-risk PE[1]. However, failure of thrombolysis occurs in approximately 8% of cases, leaving clinicians with limited evidence-based options, particularly in resource-limited settings where surgical embolectomy or catheter-directed thrombolysis, as recommended in the 2019 ESC Guidelines, are unavailable[3].

Our case highlights the successful use of sequential systemic thrombolysis with two different fibrinolytic agents—tenecteplase followed by alteplase—to achieve complete thrombus resolution in a patient with massive PE who developed CIT following initial unsuccessful thrombolysis. While tenecteplase offers practical advantages such as single-bolus administration, its shorter half-life and limited duration of fibrinolytic activity may be insufficient in cases with a large or persistent thrombus burden[2]. Alteplase, given as a continuous infusion, may provide more sustained clot dissolution, making it a reasonable rescue agent when initial therapy fails[1,5].

The current ESC Guidelines emphasize initial thrombolysis in high-risk PE but provide limited direction on managing thrombolytic failure or CIT, especially with sequential fibrinolysis[1,5]. Our case report contributes to the limited literature supporting sequential thrombolysis in these scenarios[4,5]. This report also underscores the importance of early post-thrombolysis reassessment to detect persistent clot and guide timely intervention.

Finally, this case draws attention to underlying anatomical risk factors, in this instance, large uterine fibroids compressing the iliac veins, consistent with previous reports linking fibroid-induced venous stasis to thromboembolic events[7]. Addressing such structural causes is essential to prevent recurrence and improve long-term outcomes.

In summary, sequential systemic thrombolysis may represent a safe, effective, and pragmatic rescue strategy for CIT complicating massive PE in settings where advanced interventional options are unavailable. Further studies are needed to define optimal treatment protocols and inform future guideline recommendations for managing thrombolytic failure and CIT in PE.

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