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# Reperfusion Injury Following Catheter Directed Thrombolysis of Pulmonary Embolism

**Ari Friedman[1], Seth Sokol[2], Amit Kakkar[2], Mark Guelfgaut[3], Jincy Thankachen[2]**

[1]Department of Medicine, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, USA
[2]Division of Cardiology, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, USA
[3]Department of Radiology, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, USA
*Corresponding author: friedmaa7@nychhc.org

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**Abstract** Catheter directed thrombolysis (CDT) is a growing field of intervention to treat pulmonary embolism (PE) and restore physiologic circulation. Reperfusion injury (RI) is a well-documented phenomenon seen post-thrombolysis. To date there are no reported cases of this phenomena following CDT. We present a patient with bilateral PE treated with CDT who subsequently developed RI.

***Keywords:*** *reperfusion injury, pulmonary embolism, catheter directed thrombolysis*

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## 1. Introduction

Catheter directed thrombolysis (CDT) is a growing field of intervention to treat pulmonary embolism (PE) [1] and restore physiologic circulation. Reperfusion injury (RI) is a well-documented phenomenon seen post-thrombolysis, most commonly with reperfusion of the heart and brain [2,3]. To the best of our knowledge, reperfusion injury in the setting of thrombolytic therapy for pulmonary embolism has been described only twice in the literature [4,5], and never with the use of CDT. We present a case of RI following treatment with CDT for bilateral PE.

## 2. Case Series

A 42-year-old female with metastatic breast cancer undergoing active treatment with chemotherapy presented to the emergency department with tachycardia and tachypnea and acute onset shortness of breath.

The patient had a past medical history significant for Stage IV triple positive breast cancer, locally advanced metastatic disease to bone, lung, and hilar lymph nodes, being treated with Paclitaxel, Trastuzumab, and Pertuzumab. The patient began experiencing dyspnea during chemotherapy (cycle 3), where while seated had an oxygen saturation of 88% but resolved without further treatment. After completion of the chemotherapy infusion the patient returned home where she felt progressively worsening dyspnea, and then an acute worsening in shortness of breath while climbing a flight stairs, prompting her to go to seek medical attention. Review of system was negative for any other infectious signs. She had a negative personal history of any previous blood clots, miscarriages, or skin manifestations of a clotting disorder.

Due to the history of active malignancy and acute onset shortness of breath, an ultrasound of the lower extremities was performed and found an acute deep venous thrombosis in the left popliteal vein. Subsequent computerized tomography (CT) scan with angiogram was done and showed extensive bilateral acute pulmonary emboli (Figure 1-A) with no additional consolidation, pleural effusion or pneumothorax, and no congestion on CT or Chest X-ray (CXR) (Figure 1, B,D). Transthoracic echocardiography (TTE) was significant for moderately dilated right ventricle (RV) with normal systolic function, peak systolic pressure of 51mmHg, and interventricular septum flattening consistent with right ventricular volume and pressure overload. The patient was transferred to the cardiac care unit and started on anti-coagulation therapy with enoxaparin 150 mg twice daily. The patient remained persistently tachycardic to 125 BPM at rest, as well as dyspneic with speaking and minor exertion. Troponin was elevated to 0.056 ug/L and Pro-BNP to 560pg/mL, and a Pulmonary Embolism Severity Index (PESI) score of 92. Given the elevated biomarkers, PESI score, and patient's submassive PE with signs of right heart strain, the patient underwent bilateral catheter directed thrombolysis on day six of hospitalization with Ekos catheter (Boston Scientific, Marlborough, MA). An initial 4mg of tissue plasminogen activator (tPA) bolus was delivered to right lung and 3mg to the left lung, with subsequent bilateral infusion of 1mg/hr for 12 hours.

Approximately 1 hour after completion of tPA infusion, the patient developed worsening tachypnea, hypoxia with an oxygen saturation of 87-88% on room air, associated pleuritic chest pain, and a fever to 101.9 Fahrenheit. There

was no hemoptysis or productive cough, no leukocytosis, procalcitonin was low (0.16 mg/mL), and hemoglobin unchanged from the patient's baseline.

Bedside ultrasound showed minimal basilar atelectasis and a left posterior subpleural consolidation. CXR was significant for mildly increased vascular congestion (Figure 1,C). A subsequent CT scan showed wedge-shaped peripheral regions of consolidation in the bilateral lower lobes consistent with pulmonary infarcts corresponding geographically to the previously seen bilateral pulmonary emboli, as well as a trace left pleural effusion and no other signs of congestion (Figure 1, E-G). Blood cultures drawn during the post-thrombectomy period showed no microbial growth. Repeat TTE showed preserved LV function and mild signs of RV strain which were improved from pre-intervention TTE, and RV systolic pressure improved to 25-33mmHg. The patient was treated with intravenous furosemide with improvement of dyspnea and oxygen saturation.

The patient did not require any further thrombolysis post initial intervention and was able to be discharged within a few days. The patient has been on long term anticoagulation and done remarkably well through the 30 days and 6-month follow-ups, with improvement in symptoms.

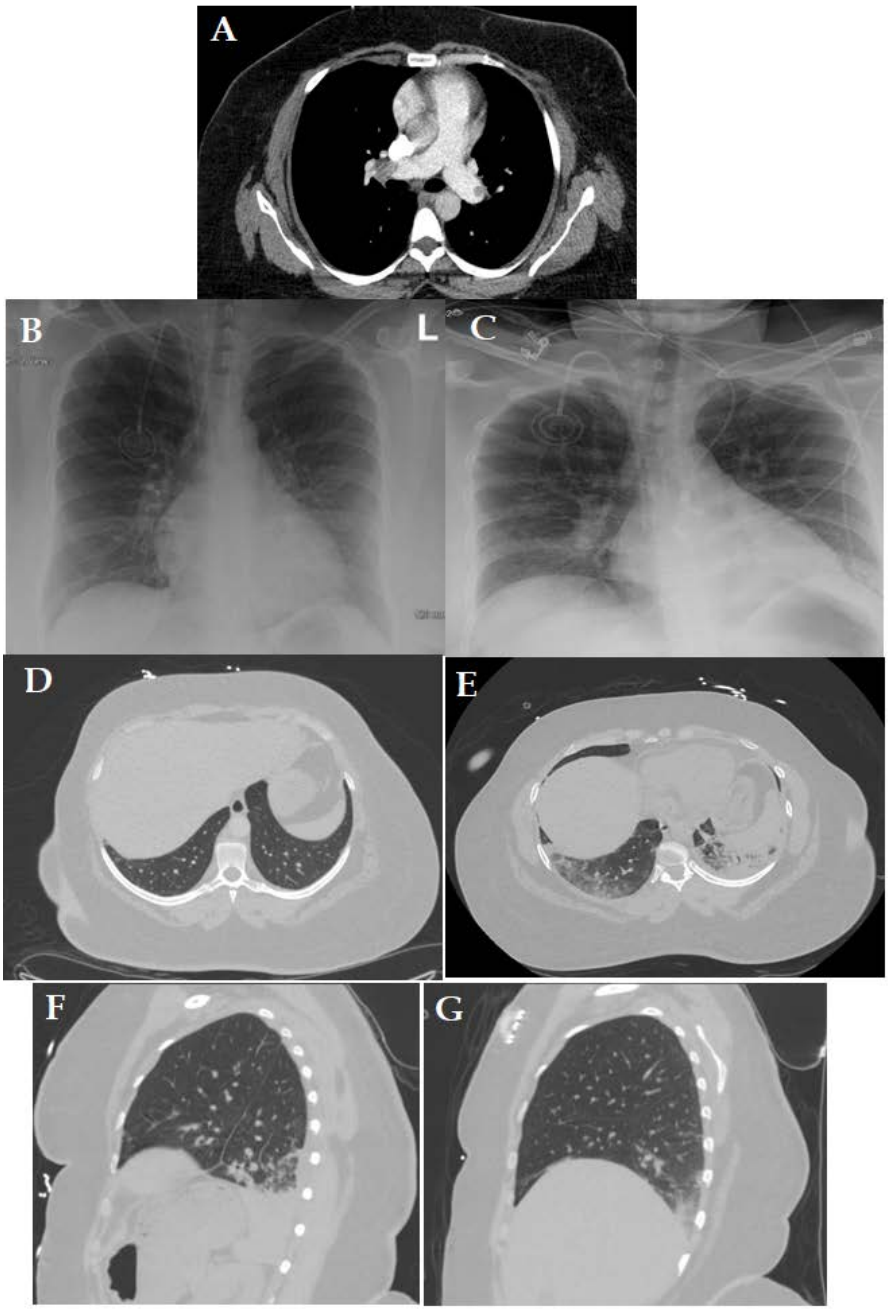


**Figure 1.** A: Computed tomography (CT) of the showing origin of a large filling defect of the right pulmonary artery (white arrow) extending into the superior lobar, posterior segmental, interlobar, lateral basal segmental, and posterior basal segmental arteries. Additionally seen is the origin of a smaller filling defect of the left pulmonary artery (white arrow) with extension into the apical segmental, superior lingular, inferior lingular, medial basal segmental, lateral basal segmental, and posterior basal segmental arteries. B. Chest X-ray (CXR, Posterior-Anterior view) on admission with no evidence of airspace disease or edema. C. Portable CXR post catheter directed thrombolysis with new mild bilateral airspace disease and mild pulmonary vascular congestion. D. CT Chest at baseline (pre-catheter directed thrombolysis). E. CT of the base of lungs post thrombolysis revealing bibasilar atelectasis, areas of consolidation in both posterior bases and a small left pleural effusion. F. Sagittal view of the left lower lobe with a wedge shaped consolidation. G. Sagittal view of the right lower lobe with a wedge shaped consolidation

## 3. Discussion

Other differentials for the onset of fever and respiratory distress included infectious causes and diffuse alveolar hemorrhage (DAH). The patient's negative blood cultures, improvement with diuretics, and resolution of fevers without antibiotics, made an infectious etiology unlikely. Similarly, given the patient's lack of hemoptysis, no observed drop in hemoglobin, and CT scan without evidence of diffuse alveolar infiltrates, the diagnosis of DAH was deemed unlikely as the cause of the symptoms.

While RI has been described as early as the 1960s [6], the underlying mechanism is not fully elucidated, although several key cellular pathways that mediate the damage have been identified [7]. These injuries are more commonly seen in the brain and heart, and while reperfusion therapy is cornerstone in the treatment of ischemic insult for both tissues, reperfusion associated injury remains a clinically significant complication. With cardiac reperfusion, reversible forms of myocardial injury such as stunning and reperfusion arrhythmias are observed, as well as irreversible reperfusion induced necrosis that can contribute to the size of the myocardial infarct [8]. For the brain as well, RI can cause significant complications including fatal edema and intracranial hemorrhage [2].

Previously, RI secondary to a PE has been described only twice in the literature, one English publication following the treatment of a PE with systemic thrombolysis [5], and another Korean publication in the treatment of chronic PE with pulmonary endarterectomy [9]. Following reperfusion therapy with systemic thrombolysis, the patient developed dyspnea, fever, impaired oxygenation on arterial blood gas, CXR with new fluffy alveolar infiltrates in same area of the diffusion impairment, and subsequent ventilation perfusion (V/Q) scan revealed reperfusion and decreased ventilation in the same area. Infectious workup was negative, and a right heart catheterization revealed preserved RV function. The patient required a second course of thrombolysis at which point the edema spontaneously resolved and the patient improved clinically with a repeat V/Q scan showing resolution of the ventilatory defect [5].

Our case follows a similar presentation with acute onset of dyspnea, impaired oxygenation, and non-infectious fevers, and new radiologic evidence of pulmonary injury in the same area of reperfusion without any evidence of residual venous thrombosis.

## 4. Conclusion

RI following CDT is a rare clinical entity that can present as acute dyspnea, hypoxia, pyrexia, and pulmonary edema. This case report highlights the importance of recognizing RI among the differentials of respiratory distress post-CDT therapy. Early recognition and treatment prevented further respiratory sequalae in our patient. RI post thrombolysis, although a rare complication, requires further epidemiological study to document the true prevalence of this entity.

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