Low-Dose Thrombolysis in an Intermediate High-Risk Submassive Pulmonary Embolism With Right Atrial Thrombus: A Case Report

Joyce Karla Suero, MD | Irene Patiño, MD | Jeffrey Mendoza, MD
Philippine Heart Center, Quezon City, Philippines

Abstract

BACKGROUND: Venous thromboembolism, encompassing pulmonary embolism (PE) and deep vein thrombosis (DVT), is the third most common acute cardiovascular syndrome. It requires prompt diagnosis and risk-based treatment strategies.

CASE: A 47-year-old male, 30-pack-year smoker who recently underwent open reduction and internal fixation of the right femur presented with dyspnea. There was no hemodynamic instability. Twelve-lead electrocardiogram showed sinus rhythm with incomplete right bundle-branch block, and troponin was elevated. Chest x-ray showed dilated right descending pulmonary artery. Two-dimensional echocardiogram revealed right atrial thrombus with right ventricular dysfunction. Computed tomography of the pulmonary artery confirmed massive PE with infarct on the posterobasal segment of the right lower lobe. Venous duplex scan of the lower extremities showed an acute DVT of the right femoral vein, popliteal vein, and peroneal vein. Anticoagulation was started. With a dilemma of a recent surgery in an intermediate high-risk submassive PE, options other than guideline-recommended systemic thrombolysis were considered. A multidisciplinary consensus recommended the administration of low-dose thrombolysis, which later resulted to clinical improvement.

CONCLUSION: This is the first documented local case of successful resolution of a right atrial thrombus with pulmonary thrombus and DVT using low-dose thrombolysis, without complications of bleeding, in a patient with contraindications to thrombolysis. With more clinical experience and studies of low-dose recombinant tissue plasminogen activator in this special population, it can offer a promising treatment option.

KEYWORDS: pulmonary embolism, submassive, low-dose systemic thrombolysis, contraindication for thrombolysis, alteplase, tPA, right atrial thrombus

INTRODUCTION

Venous thromboembolism (VTE), encompassing pulmonary embolism (PE) and deep vein thrombosis (DVT), is the third most common acute cardiovascular syndrome, after myocardial infarct and stroke.[1] High clinical suspicion is of paramount importance in the diagnosis. Once PE is confirmed, treatment is done according to clinical and laboratory parameters. A clinician is faced with a problem when peculiarities are encountered, such as contraindications to standard therapy (eg, thrombolysis). Several international case reports have been published regarding low-dose thrombolysis, and very limited are found in local literature.[2–5] This is when guideline recommendations, evidence-based medicine, and sound clinical judgment with multidisciplinary approach all come into play, as will be demonstrated in this case.

CASE

A 47-year-old man with 30-pack-year smoking history and no known comorbidities presented with dyspnea. He was previously admitted at a general hospital for complete fracture of the right femur where he underwent open reduction and internal fixation. No perioperative VTE prophylaxis was administered. The procedure was uneventful, and he was discharged after 5 days.

One week after surgery, he experienced sudden-onset dyspnea and chest discomfort. He was brought to a hospital where his condition was managed as non–ST-elevation myocardial infarction. Electrocardiogram and chest x-ray were done, which were disclosed to them as normal. Unfortunately, laboratory tests done in the first hospital were not available for our review. Patient was reported to initially have hypotension and tachycardia, which later improved after fluid resuscitation. He was thereafter advised transfer to our institution.

Upon transfer to our institution's emergency room, patient had a blood pressure of 90/50 mm Hg and heart rate of 92 beats/min but was tachypneic at 27 cycles per minute with oxygen saturation at 98% at 1 to 2 L/min. Chest examination revealed no lifts, soft S1, no S4, no murmurs, and no adventitious breath sounds. He had grade 3 pedal edema and calf tenderness at the right lower extremity. Twelve-lead electrocardiogram showed sinus rhythm with incomplete right bundle-branch block. Chest x-ray revealed dilated right descending pulmonary artery. Troponin I was elevated at 0.25 ng/mL (normal, 0–0.08). Two-dimensional echocardiogram revealed right atrial thrombus (Figure 1), dilated right ventricle with free wall hypokinesia, and depressed systolic function (right ventricular fractional area change, 28%); normal left ventricular wall motion, contractility and systolic function; and moderate pulmonary hypertension (mean pulmonary artery pressure of 45 mm Hg). Computed tomography of the pulmonary artery (CTPA) revealed massive PE with infarct on the posterobasal segment of the right lower lobe (Figure 2). Duplex scan of the lower extremities revealed acute DVT of the right femoral vein, popliteal vein, and peroneal vein (Figure 3). Anticoagulation was started with unfractionated heparin at 80 U/kg bolus and then 18-U/kg per hour drip. At the medical intensive care unit, blood pressure and heart rate improved to 115/70 mm Hg and 80 to 85 beats/min. Tachypnea improved to 20 to 24 cycles/min.

With the presence of massive PE in CTPA and evidence of right ventricular dysfunction and myocardial injury but with no hemodynamic instability, clinical diagnosis was intermediate high-risk submassive PE based on the 2019 European Society of Cardiology guidelines for the diagnosis and management of PE. Several options were considered because of the relative contraindications for thrombolysis (recent surgery): systemic thrombolysis, percutaneous catheter-directed treatment, and surgical embolectomy. After a multidisciplinary approach, the patient was offered low-dose thrombolysis. Upon clearance

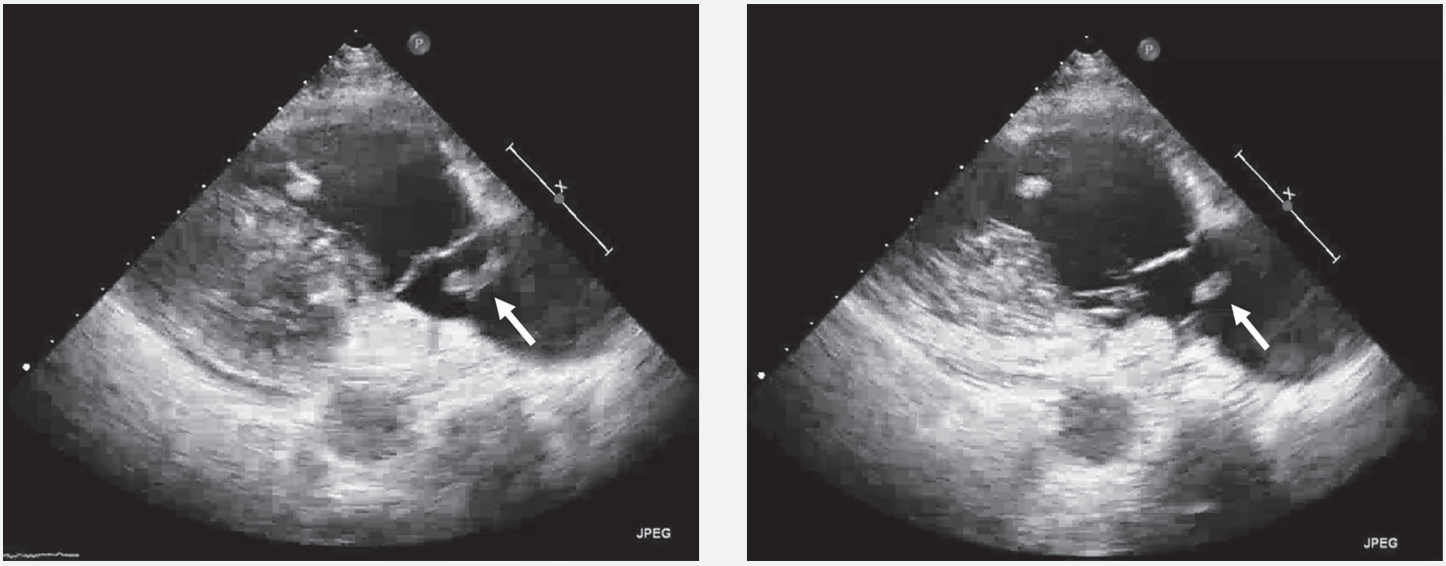

Figure 1. Echocardiogram in a right ventricular inflow view showing right atrial thrombus (white arrow)

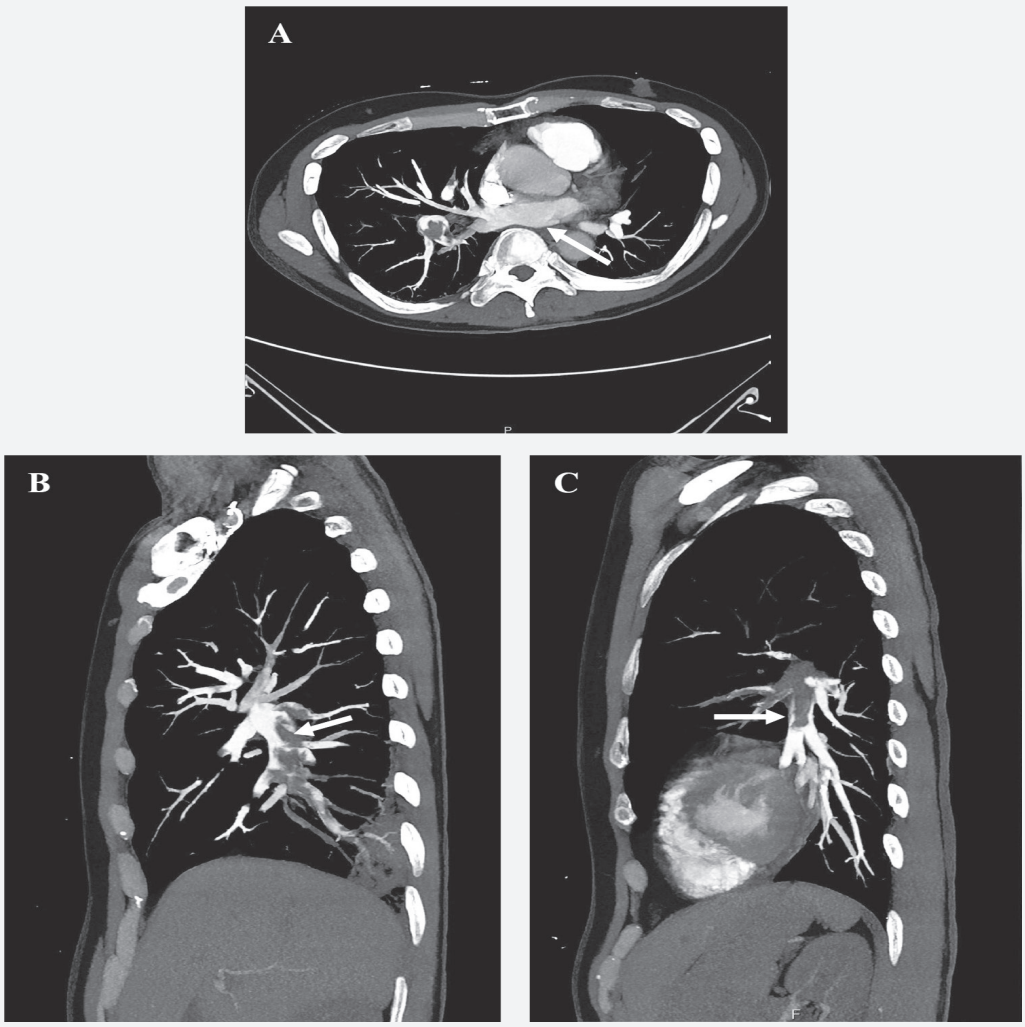

Figure 2. Computed tomography of the pulmonary artery showing multiple filling defects (white arrow) starting from the main pulmonary artery (A) and propagating to the right (B) and left (C) main pulmonary arteries

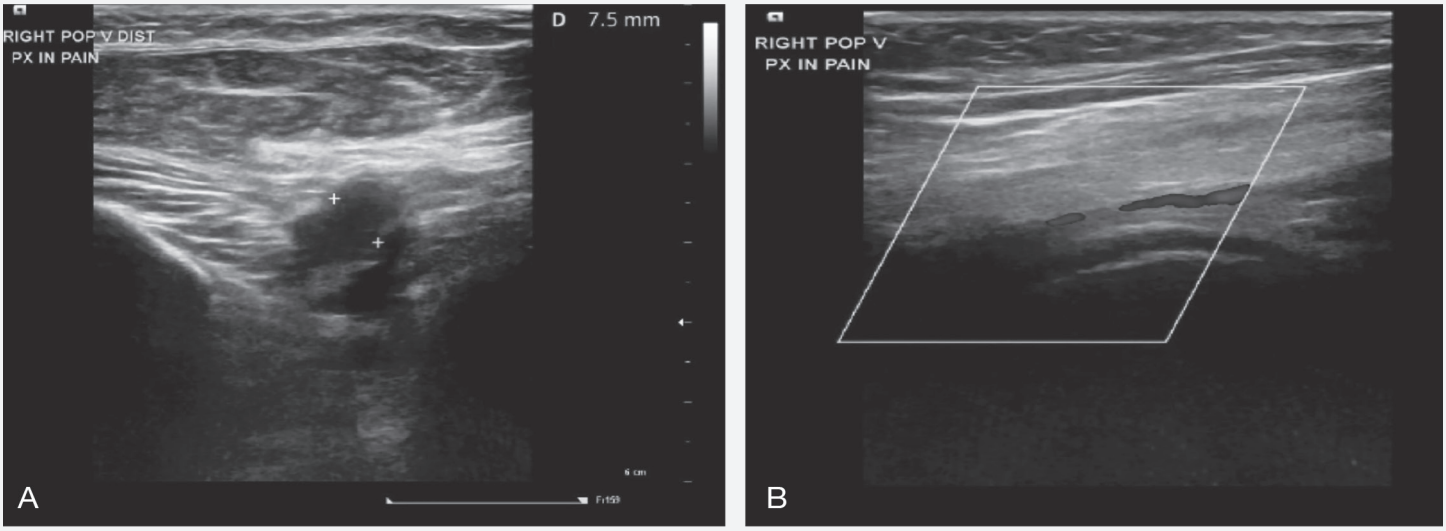

Figure 3. Venous duplex scan of lower extremities showing heterogeneous hypoechoic intraluminal density with partial compressibility (A) and partial color flow (B) along the right popliteal vein consistent with deep vein thrombosis

by orthopedic surgery, alteplase 50 mg was given (alteplase 10 mg intravenously [IV] over 1 minute and the remaining alteplase 40 mg as infusion for 2 hours). Patient had significant improvement of dyspnea and right leg pain thereafter. There were no reports of bleeding, hemodynamic instability, or need for mechanical ventilation.

On the ninth hospital day, follow-up CTPA revealed decrease in the number and size of the filling defects and decrease in the degree of pulmonary artery dilatation. Duplex surveillance scan of the lower extremities revealed partial resolution and recanalization. Repeat two-dimensional echocardiogram revealed resolution of right atrial mass and normalization of the right ventricular systolic function and pulmonary artery pressure.

The patient was discharged improved on the 14th day. He was given rivaroxaban 20 mg daily. On follow-up after 3 months, he was reported to be asymptomatic with good functional capacity.

DISCUSSION

Our patient is a 47-year-old male smoker with recent orthopedic surgery, who presented with sudden-onset dyspnea. He was initially diagnosed as having non–ST-elevation myocardial infarction in the first hospital of consult, but when assessed in our hospital, he was diagnosed as otherwise. He was clinically stable with no hemodynamic instability or need for mechanical ventilation. Workup revealed massive PE via CTPA. Additional tests showed acute DVT, elevated troponin, and right atrial thrombus. With data suggesting intermediate high-risk submassive PE (Pulmonary Embolism Severity Index I, HESTIA score 2, positive troponin, and right ventricular dysfunction), reperfusion treatment was warranted. However, there was a dilemma in choosing the most appropriate reperfusion strategy for the patient: systemic thrombolysis, catheter-directed thrombolysis, or embolectomy.[6]

Systemic thrombolysis is the recommended treatment for massive PE and has been considered in intermediate-risk PE with right ventricular dysfunction and/or myocardial damage[6] such as in our case. However, the patient had a relative contraindication to recent surgery.[7] Catheter-directed thrombolysis and surgical embolectomy were relatively contraindicated as well, due to the presence of right atrial thrombus.[8,9] And in line with recommendations, surgical embolectomy was the last resort in a patient who is hemodynamically stable and has not undergone any reperfusion strategy.[6]

After a multidisciplinary consensus meeting involving representatives from the specialties of vascular medicine, pulmonary medicine, vascular surgery, interventional cardiology interventional radiology, and orthopedic surgery, low-dose thrombolysis was deemed the best strategy. The patient was given alteplase 50 mg (alteplase 10 mg IV over 1 minute and the remaining alteplase 40 mg as infusion for 2 hours), which is half of the standard dose of 100 mg.[6]

Two known randomized controlled trials utilizing low-dose alteplase in submassive PE have been published. Both studies randomized subjects into low-dose tissue plasminogen activator (tPA) group (50% of the standard dose) and anticoagulation-alone group and excluded patients with recent surgery or trauma. In a prospective randomized controlled trial by Sharifi et al[2] in Arizona (MOPETT trial) involving 121 patients, there was significantly less pulmonary hypertension and less recurrent PE in the tPA group, and there was no bleeding noted. In the prospective observational study by Mi et al[3] in China involving 136 patients, there was greater echocardiographic improvement and less clot burden in the first group; however, more minor bleeds were noted. Alteplase infusion was done differently in both trials. Whereas the former administered 10-mg bolus by an intravenous bolus followed by infusion of the remaining 40 mg within 2 hours, the latter administered 50 mg as infusion over 2 hours. Patient was given alteplase as done in the MOPETT trial.[2]

In a case series by Layman et al[4] in the United States, five patients were given low-dose tPA for submassive PE. All subjects showed improvement of symptoms. Three showed improvement of right ventricle function and size, and no patient had any bleeding during or after tPA administration.

No known local studies have been found for submassive PE as our case. But in a case report by Seguban et al,[5] low-dose alteplase (50 mg IV infusion over 2 hours) was given to a patient with massive PE in a setting of an acute anterior wall STEMI, who had just undergone PCI and had high risk for bleeding. There was clinical improvement with no bleeding episodes noted.

As of this writing, this is the first reported local case to have utilized low-dose alteplase in a setting of intermediate high-risk submassive PE with a relative contraindication to systemic thrombolysis. Patient had significant improvement of dyspnea and right leg pain. There were no reports of bleeding, hemodynamic instability, or need for mechanical ventilation. Resolution of echocardiographic right atrial thrombus, right ventricular dysfunction, and temporal resolution of pulmonary infarcts and DVT were noted. On follow-up after 3 and 6 months, patient was noted to be asymptomatic with good functional capacity.

CONCLUSION

This is the first documented local case of successful resolution of a right atrial thrombus with pulmonary thrombus and DVT using low-dose thrombolysis, without complications of bleeding, in a patient with contraindications to thrombolysis. With more clinical experience and studies of low-dose recombinant tPA in this special population, it can offer a promising treatment option.

REFERENCES:

1. Zipes D, Libby P, Bonow R, Mann D, Tomaselli G, Braunwald E. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.* 11th ed. Elsevier; 2019:1681–1698.
2. Sharifi M, Bay C, Skrocki L, et al. Moderate pulmonary embolism treated with thrombolysis (from the "MOPETT" trial). *Am J Cardiol* 2013;111:273–277.
3. Mi YH, Liang Y, Lu YH, et al. Recombinant tissue plasminogen activator plus heparin compared with heparin alone for patients with acute submassive pulmonary embolism: one-year outcome. *J Geriatr Cardiol* 2013;10:323–329.
4. Layman SN, Guidry TJ, Gillion AR. Low-dose alteplase for the treatment of submassive pulmonary embolism: a case series [published online June 19, 2019]. *J Pharm Pract* 2019;897190019855164. doi:10.1177/0897190019855164.
5. Seguban JM, Alajar E, Isidro J, Pestaño N, Punzalan FE, Castillo R. Concurrent massive pulmonary embolism with emboli in transit and anterior ST elevation myocardial infarction with increased bleeding risk successfully treated with low-dose systemic alteplase: a case report. *Cardiol Cardiovasc Med* 2019;3:352–359.
6. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Respir J* 2019;54(3):1901647.
7. Martin C, Sobolewski K, Bridgeman P, Boutsikaris D. Systemic thrombolysis for pulmonary embolism: a review. P T. 2016;41(12):770–775.
8. Aggarwal V, Nicolais C, Lee A, Bashir R. Acute management of pulmonary embolism. October 24, 2017. https://www.acc.org/latest-in-cardiology/articles/2017/10/23/12/12/acute-management-of-pulmonary-embolism.
9. Sabri SS, Saad WEA, Turba UC, Park AW, Angle JF, Matsumoto AH. Percutaneous pulmonary embolectomy: indications, techniques and outcomes. *Vasc Dis Manage* 2010;7:E223–E229.