Managing Acute Intermediate Risk Pulmonary Thromboembolism in a Patient Who Developed Heparin Induced Thrombocytopenia: Review of Current Guidelines and Literature

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Abstract

Mortality rates for pulmonary embolism differ significantly, indicating a need for escalated management. Treatment options include systemic anticoagulation, catheter-directed thrombolysis and/or thrombectomy and surgical thrombectomy. Heparin-induced thrombocytopenia is a severe complication as a result of any form of heparin which limits pharmacologic therapy with thrombolytics and anticoagulation.

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Consent Statement

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy" on the title page of the manuscript.

Declaration Statement for Conflict of Interest

The above listed authors, Drs. Asllanaj, Benge, Bhatia, and McWhorter, have no conflicts of interest to declare.

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Introduction

Acute pulmonary thromboembolism is a life-threatening cardiovascular condition with high mortality. In intermediate risk pulmonary embolism (PE), management strategy may include catheter-directed (CD) thrombolysis in addition to systemic anticoagulation. Immediate systemic thrombolysis is considered if clinical deterioration and shock ensues. When hemodynamically stable, heparin infusion is the mainstay of therapeutic anticoagulation with potential complications. Heparin-induced thrombocytopenia (HIT) is a rare but potentially fatal, antibody-mediated adverse drug reaction of heparin therapy. It occurs among 1% of hospitalized patients receiving heparin and the mortality rate is as high as 20% [1]. We present the unusual clinical course a patient with acute intermediate risk bilateral pulmonary thromboemboli who developed HIT and required additional management strategies due to rapid conditional change.

Description of Case

A 59-year-old male with a history of hypertension presented with dyspnea. Vital signs were blood pressure of 159/105 mmHg, pulse 89 beats/min and pulse oximetry of 99% on room air. Physical examination was unremarkable. Electrocardiogram showed S1Q3T3 pattern (Figure 1). Chest x-ray was notable for prominent pulmonary arteries (Figure 2). Laboratory studies revealed elevated NT pro-BNP 2737 pg/Ml, high sensitivity troponin 86 ng/L, D-dimer 55.45 mg/L, and platelet count 193,000/uL.

Chest computed tomography angiography (CTA) showed large central bilateral PE (Figure 3). Indications of pulmonary hypertension included enlargement of the main pulmonary artery (PA) and narrowing of the left ventricle compared to the right related to heart strain. Venous Doppler of the lower extremities demonstrated occlusive deep venous thrombosis (DVT) of left popliteal vein. Transthoracic echocardiogram (TTE) revealed left ventricular ejection fraction 60% without evidence of right ventricle (RV) strain.

On hospital day (HD) 2, TTE showed RV systolic pressure (RVSP) of 28 mmHg (Figure 4). Patient clinical status worsened increased oxygen requirement. Given a significant decrease in platelet count to 62,000/uL, CD thrombolysis was postponed, and an IVC catheter was placed. Unfractionated heparin was discontinued and argatroban was initiated for suspected HIT, which was later confirmed with optical density of 1.011.

On HD 12, platelet count recovered (169,000/uL). Improvement of clot burden in the left PA but increasing in the right PA with bilateral pulmonary infarct was seen on repeat chest CT (Figure 5). TTE showed RVSP of 59 mmHg. Two days following a successful CD thrombectomy and thrombolysis, he reported feeling less dyspneic. Cardiothoracic surgery was consulted due to incomplete lysis of right sided PE and recommended transfer to tertiary center. Chest CTA had shown reduction of the clot burden by 30%. Final TTE demonstrated RVSP 30 mmHg. Due to sustained clinical improvement, surgical thrombectomy referral was made on an outpatient basis and he was discharged on oral anticoagulation.

Discussion

Mortality intermediate PE remains exceedingly high despite thrombolytic and anticoagulation therapy. At present, clinical effectiveness of fibrinolysis on mortality has not been clearly established beyond 90 days [2]. Despite initial encouraging results, thrombectomy and CD thrombolysis have not been considered as the first choice of treatment in the current European Guidelines for high risk PE, even in cases of major contraindication to thrombolysis [3]. Given the variability in PE mortality, risk stratification of low, intermediate, and high risk PE has been adopted by all major guideline committees including the American College of Cardiology. Risk stratification is used to navigate treatment modalities. Patients with low risk PE (normotensive, normal biomarkers) are typically treated with direct oral anticoagulants in the outpatient setting. High risk PE (hypotension with systolic blood pressure <90 mmHg for >15 minutes, syncope, cardiac arrest) warrant immediate thrombolytic therapy, with or without mechanical hemodynamic support. Intermediate risk PEs can present in a normotensive patient with imaging indicative of RV strain, elevated biomarkers, Pulmonary Embolism Severity Index (PESI) class III-IV and its simplified version, sPESI >1. Systemic thrombolysis, CD therapy, and surgical embolectomy with mechanical support, plus anticoagulation are all considered in the treatments for both high and intermediate risk PE.

Systemic thrombolysis for intermediate risk PE has shown to reverse hemodynamic compromise by improving RV dilatation, PA pressure and pulmonary perfusion [4]. Unlike high risk PE, systemic thrombolytic therapy in intermediate risk PE has not shown to reduce mortality and recurrence [5]. Given the risks of systemic thrombolysis including major bleeding and intracranial hemorrhage (ICH), CD approaches are used in patients with relative contraindications to thrombolytic therapy. CD delivery of fibrinolytic agents or mechanical fragmentation of a thrombus have lower risk of ICH (0.35%) when compared to systemic thrombolysis (3%) [6]. Surgical embolectomy is an option after failed thrombolytic therapy or absolute contraindications to thrombolytics. In recent years, the perioperative mortality for surgical embolectomy has decreased from 29% to 3.6% [7]. In cardiogenic shock or refractory PE, mechanical circulatory support is considered to decrease RV afterload and improve RV function [8].

First-line treatment for high risk PE has been systemic thrombolysis due to more than 90% of patients responding within 36 hours [9]. In comparison, CD thrombolysis also showed a reduction in the mean RV distention within 48 hours. For CD therapy, the rates of major bleeding ranged from 0% to 4%, and less than 1% experienced ICH [10]. The rate of major bleeding from systemic thrombolysis was 19%, and 5% was intracranial [11]. In general, bleeding rates vary among studies, and the rates comparing interventional bleeding risk after 48 hours are lacking in literature. Considering our patient presented 5-days after symptom onset, systemic heparinization was initiated as the benefits and risks were similar to systemic thrombolysis after one week of onset [12]. Additionally, the patient's PESI score was 69 (Class II low risk) and sPESI was 0, which supported use of heparin over thrombolysis in the setting of intermediate risk PE. Due to ongoing dyspnea, CD thrombolysis was performed after platelets recovered. The ULTIMA trial compared CD thrombolysis plus anticoagulation and anticoagulation alone which showed improvement of RV distension in the former; thus supporting a hemodynamic benefit in the CD therapy group [13].

The presence of HIT antibodies and decrease of more than 50% in platelet count warranted cessation of heparin and initiation of argatroban. Platelet count of 100,000/L was considered adequate for thrombolysis as indicated by Srinivias et. al. in a study comparing thrombolysis and anticoagulation in management of DVT [14]. Small studies have shown success with CD thrombectomy for high risk PE [15]. One common theme shared with the management of intermediate risk PE was that CD thrombectomy was an option only when systemic thrombolysis was contraindicated. With more advancement in the field, CD therapy could become first-line treatment for intermediate PE.

Conclusion

Intermediate-high risk PE remains a challenging clinical scenario due to potential clinical deterioration as a result of treatment failure and relative contraindication to life-saving procedures. Thrombectomy and CD thrombolysis remain as invaluable tools providing improvement in clinical outcomes.

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