Iranian Heart Journal; 2024; 25 (3)

Case Report

Double Jeopardy: Co-occurrence of Pulmonary Embolism and Deep Vein Thrombosis in Patients With Heart Failure

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ABSTRACT

Venous thromboembolism is a prevalent global health concern that includes 2 primary clinical manifestations: deep vein thrombosis and pulmonary embolism. In patients with heart failure, disruptions in homeostasis result from diminished cardiac output and malfunctioning cardiac chambers, leading to blood stasis. Consequently, these homeostatic abnormalities accelerate the activation of the coagulation system and fibrin formation, rendering patients with heart failure more susceptible to venous thromboembolism. This case report involves a 57-year-old woman presenting with shortness of breath following moderate exertion, such as sweeping and walking 100 meters, over the past month. The symptoms were alleviated by rest, and the patient occasionally experienced orthopnea, accompanied by pain and difficulty walking in the preceding week. The examination of the left lower extremity revealed edema, tenderness, erythema, venectasia around the left femur, and positive Homan's and Pratt's signs. Doppler imaging disclosed complete thrombosis in the popliteal veins and the left common femoral vein, partial thrombosis in the superficial femoral veins (the great saphenous vein), and subcutaneous edema in the left femur and lower extremity. Computed tomography findings for the thoracic region indicated pulmonary embolism at the bifurcation of the pulmonary artery, extending to the right and left pulmonary artery branches in the axial view. ***(Iranian Heart Journal 2024; 25(3): 85-91)***

KEYWORDS: VTE, PE, DVT, HF

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Received: January 31, 2024 **Accepted:** March 13, 2024

Venous thromboembolism (VTE) is a widespread global health concern that includes 2 primary clinical manifestations: deep vein thrombosis (DVT) and pulmonary embolism (PE). As the third and fourth most common cardiovascular diseases, PE and DVT account for 100 to 200 cases per 100,000 people. PE is the most life-threatening condition within the VTE spectrum.[1] Triggered by various factors such as physical obstruction, PE increases right ventricular (RV) afterload and pulmonary vascular resistance. The presence of heart failure (HF) in conjunction with PE results in a higher overall mortality rate (17% vs 10%).[2] Given that PE primarily originates from DVT, existing epidemiological data are primarily derived from studies on VTE. The elusive nature of PE, which can remain asymptomatic or

manifest as sudden cardiac death, adds complexity to establishing its epidemiology.[3, 4] This case report highlights the co-occurrence of PE and DVT in patients with HF.

CASE REPORT

A 57-year-old woman was referred to our department with shortness of breath following moderate exertion, such as sweeping and walking 100 meters, over the past month. The symptoms were alleviated by rest. She also occasionally experienced orthopnea, along with pain and difficulty walking in the preceding week. The patient reported swelling in the left leg over the past month.

The patient had a 1-year history of hypertension with poor medication adherence. She also had a 10-year history of diabetes mellitus, which had been treated for the preceding year with insulin (1×12 units of insulin detemir and 3×14 units of insulin aspart per day). The patient reported a history of heart swelling within the last month. No familial history of coronary heart disease, stroke, or kidney disease was reported. On physical examination, the patient had a blood pressure of 140/80 mm Hg, a heart rate of 110 beats per minute with a regular rhythm, a respiratory rate of 24 breaths per minute, and an oxygen saturation level of 98% without oxygen supplementation. The examination of the left lower extremity revealed edema, tenderness, erythema, and venectasia around the left femur, with positive Homan's and Pratt's signs. The circumference measurements were 19 cm and 23 cm for the right and left lower extremities, 29 cm and 41 cm for the right and left middle lower extremities, and 43 cm and 60 cm for the right and the mid-femur level of the left lower extremity, respectively (Fig. 1). Hematological parameters revealed elevated leukocyte (11.85 × 10^9/L) and D-dimer (>10,000 ng/mL; reference range, 0–500 ng/mL) levels. Electrocardiographic examination revealed sinus tachycardia with incomplete left bundle branch block (Fig. 2a). Doppler imaging of the lower extremities indicated total thrombosis in the popliteal veins and the left common femoral vein, along with partial thrombosis of the superficial femoral veins (the great saphenous vein) and subcutaneous edema in the left femur and the lower extremities. Ultrasonography demonstrated a noncompressible thrombus in the left femoral and popliteal veins. Duplex ultrasonography also revealed partial thrombosis from the common femoral vein to the left popliteal vein, a thrombus in the left great saphenous vein, and subcutaneous edema in the left femur region and lower extremities. Computed tomography of the thorax with axial reformatted sagittal and coronal sections revealed a PE at the bifurcation of the pulmonary artery, extending to the right and left pulmonary artery branches (Fig. 2b).

The patient was diagnosed with PE and managed collaboratively by the Thoracic, Cardiac, and Vascular Surgery Department. The RIETE Score for this patient was 1 point, indicating an intermediate risk with a 2.8% risk of significant bleeding. She exhibited stable hemodynamics with a PESI Score of 67, classified as Class I and low risk. Subsequently, an inferior vena cava (IVC) filter was implanted in the patient. Based on these findings, the patient was diagnosed with PE and DVT in the left popliteal and common femoral veins.

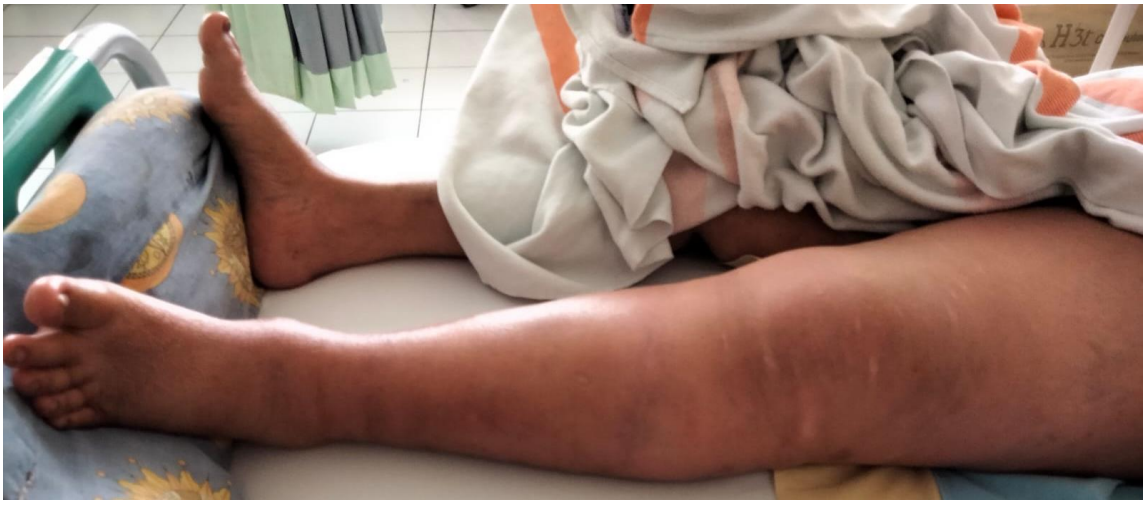

Figure 1: The image documents the patient's left leg swelling.

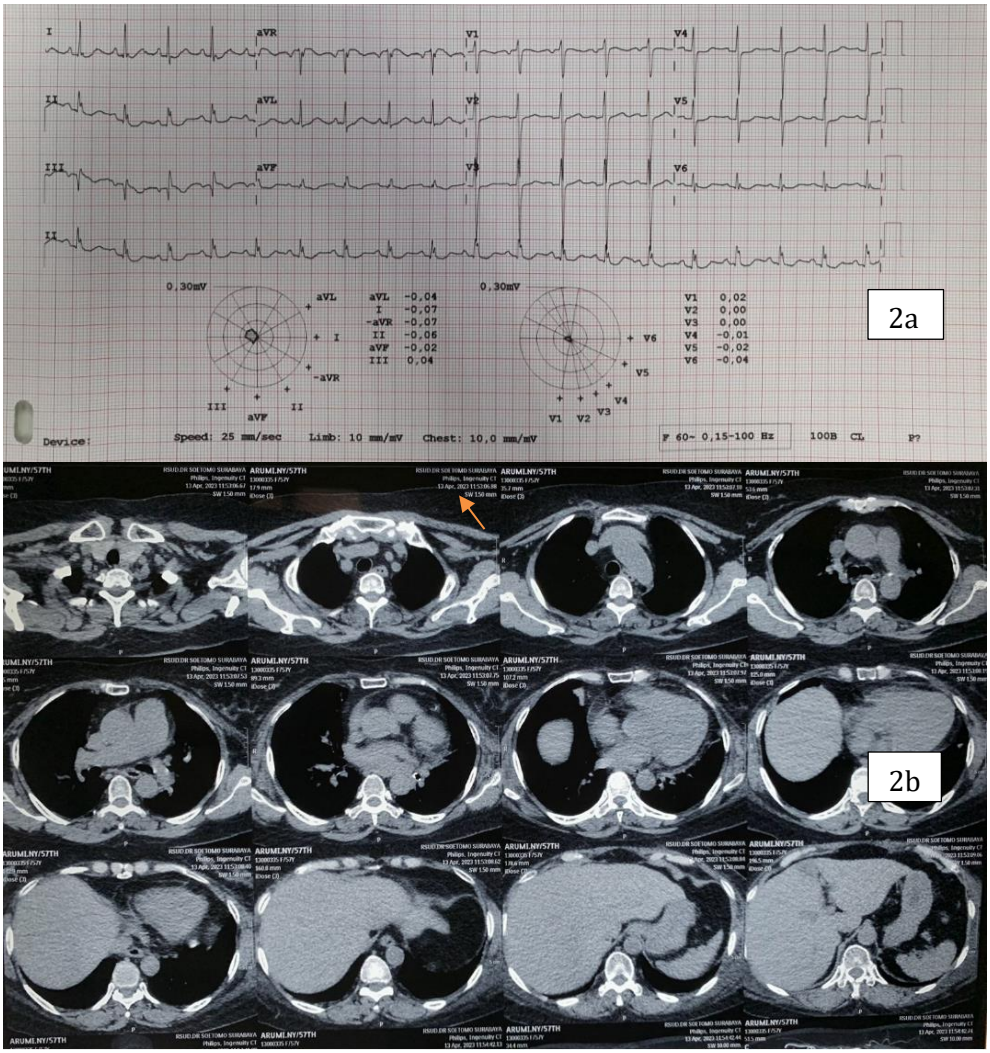

Figure (2a): The images showcase ECG examination results and **(2b)** computed tomography of the thorax results.

DISCUSSION

Diagnosing PE and HF in patients with shortness of breath can be extremely challenging. Proficient history-taking and thorough clinical examinations are indispensable for precise diagnosis and optimal management.[2] In the presented case, the patient had a history of hypertension and diabetes mellitus. It is noteworthy that HF is primarily attributed to coronary heart disease, hypertension, and diabetes mellitus, all of which originate from endothelial damage. This damage disrupts pro- and anti-coagulant functions, increasing susceptibility to thrombosis.

Previous studies have shown that individuals with congestive heart failure (CHF) have an elevated risk of experiencing PE, the most severe and life-threatening form of VTE. The risk of PE increases with worsening left ventricular (LV) systolic performance in patients with CHF. In acute PE cases, CHF independently predicts higher mortality rates.[2, 5] Conversely, in patients with HF, PE independently predicts death or rehospitalization. Numerous conditions, such as aging, male sex, cancer, prolonged immobility due to stroke or recent surgery, prior VTE, CHF, acute infection, pregnancy or puerperium, estrogen hormone therapy, varicose veins, various rheumatologic diseases, obesity, factor V Leiden, antiphospholipid syndrome, and nephrotic syndrome, are significant risk factors for VTE. VTE poses a potentially high risk for patients with CHF. The clinical features of HF and PE are similar, as are their pathophysiological mechanisms and risk factors.[4] The increased prevalence of VTE in patients with CHF has been associated with LV systolic dysfunction. Patients with a left ventricular ejection fraction (LVEF) below 20% had a significantly increased risk of thrombosis in a prior study.[6]

Several risk factors contribute to the occurrence of thromboembolism in patients with HF. The pathophysiology underlying HF and VTE (including PE and DVT) involves multiple factors.[2] These factors include blood stasis in both the lower extremities and the heart, resulting in increased blood coagulability (or hypercoagulable states) and endothelial dysfunction due to hypoperfusion and systemic inflammation. Thrombogenesis is associated with the upregulation of tissue factor, tumor necrosis factor-α, interleukin, vascular endothelial growth factor, and C-reactive protein, as well as a decrease in endothelial nitric oxide synthase activity. These patients also face an increased risk of arterial thrombosis, particularly LV endocardial thrombosis in the presence of apical akinesis or dyskinesis, and an elevated susceptibility to stroke, often associated with atrial fibrillation.[6, 7]

Conversely, PE can cause RV dysfunction (acute cor pulmonale), potentially leading to a rapid rise in pulmonary pressures and triggering HF.[8] PE-induced RV pressure overload may result in diastolic interventricular septal deviation toward the LV and impaired RV systolic performance, restricting LV filling and left-sided cardiac output. Moreover, RV pressure overload may increase wall stress and cause ischemia by raising myocardial oxygen demand and decreasing supply.[9]

DVT often causes PE as a complication, originating from a concealed or apparent thrombosis in the lower or upper limbs. Despite comprehensive venous evaluation, over 40% of patients with PE have no prior or ongoing diagnosis of peripheral thrombosis.[10] Obesity is associated with various risk factors that may precipitate a thromboembolic event, such as venous stasis and reduced mobility.[4] The risk of DVT is higher in obese women than in obese men.[9] DVT results from localized endothelial injury and immobility following traumatic limb injuries. Even minor lower extremity

injuries unrelated to surgery, limb casting, or immobility can increase the risk of DVT up to 5 times compared to subjects without such trauma. In the presented case, the patient experienced sudden pain and difficulty walking throughout the previous week without a history of trauma.

HF causes homeostasis issues by decreasing cardiac output, leading to blood stasis in malfunctioning cardiac chambers. This disruption of homeostasis accelerates the activation of the coagulation system and fibrin formation, making patients with HF more susceptible to VTE.[2, 3] In patients with HF, increased plasma viscosity, platelet activation, thrombin formation, and elevated levels of circulating coagulant factors and thrombin agents (eg, fibrinogen and D-dimer), as well as decreased soluble thrombomodulin, may contribute to thrombogenesis. The pathophysiological processes linking VTE and HF remain unclear. Key factors include impaired protein C pathway, particularly the downregulation of the endothelial protein C receptor by inflammatory cytokines increased in patients with HF, which impairs protein C pathway-mediated anticoagulation; augmented procoagulant responses resulting in hypercoagulability; PAR activation; neurohormone activation; stasis due to decreased cardiac output; and endothelial dysfunction caused by hypoperfusion and systemic inflammation. Tumor necrosis factor and interleukin-6 levels are elevated in patients with HF; the former is associated with coagulation system activation, while the latter is linked to procoagulant tissue factor.[2] Patients with CHF who are younger than 60 years old have a significant relative risk of PE, DVT, and venous thromboembolism.[4] Patients with normotensive HF exhibiting signs of right HF, such as increased jugular venous pressure, tricuspid regurgitation, and an amplified sound of pulmonic closure (P2), should be evaluated for submassive PE. However, even without PE, patients with HF often present with symptoms of RV dysfunction. Lower extremity edema, hepatomegaly, and increased jugular venous pressure without substantial pulmonary rales may indicate subacute or chronic PE, suggesting new or exacerbated right-sided HF.[9]

Previous studies have demonstrated that greater mean LV wall thickness, relative wall thickness (a measure of LV concentricity), and LA volume index (a barometer of chronic LV filling pressure) are associated with an increased risk of incident VTE in patients with clinical comorbidities and before incident HF. This finding suggests that stage B HF (symptomatic LV remodeling) may be a risk factor for VTE. Given that the prevalence of stage B HF is estimated to be 4 times higher than that of stages C and D HF combined, increased VTE awareness based on additional risk factors may be necessary.[11]

Laboratory assessment of patients with suspected acute PE is challenging, as cardiac biomarkers (eg, NT-proBNP) and D-dimer levels can be abnormally elevated in HF alone or HF with VTE. Nonetheless, patients with HF who exhibit elevated cardiac biomarkers and signs of new or worsening RV failure should undergo additional PE testing. In the context of PE, RV dysfunction is a strong independent predictor of early mortality, correlating with elevated cardiac biomarkers.[9]

In the presented case, the patient opted for IVC filter implantation. Although a limited number of studies suggest that IVC filters can reduce PE risk without promoting DVT or severe bleeding and decrease overall mortality, anticoagulation therapy remains the first-line treatment for PE. IVC filters are often used for patients after assessing the risks and benefits of PE occurrence and in cases with contraindications to

anticoagulation therapy, such as injury or a high risk of bleeding.[12]

CONCLUSIONS

PE is a potentially life-threatening condition that often presents asymptomatically and is associated with DVT, posing significant diagnostic challenges. Proficient history-taking skills and comprehensive clinical examinations are crucial for accurate diagnosis. This case study provides valuable insights into the symptoms and patient descriptions in instances of PE and DVT in patients with HF, aiming to enrich the existing knowledge on PE management and contribute to a more comprehensive understanding for future reference.

Acknowledgments
We extend our sincere appreciation to the dedicated and skilled staff of the Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga - Dr Soetomo General Academic Hospital, Surabaya, East Java, Indonesia.

Ethical Approval and Consent to Participate
We declare that this case report adheres to ethical standards and guidelines. Appropriate permissions, including written informed consent, were obtained.

Conflict of Interest
The authors declare no conflicts of interest.

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