



Syncope as the Clinical Presentation of Pulmonary Thromboembolism

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Received 27 September 2006; Accepted 28 November 2006

Abstract

Pulmonary thromboembolism (PTE) has a wide spectrum of presentations, and its cardinal manifestations include chest pain, dyspnea, and syncope. Syncope as an initial presentation of PTE occurs in 10-14% of patients and is not restricted to massive PTEs. It can also occur in the setting of non-massive cases probably due to a vasovagal mechanism or the occurrence of conduction disturbances in preexisting complete left bundle-branch block. The next point discussed here is the use of thrombolytic therapy for submassive PTE with a normal blood pressure while marked right ventricular dyskinesia or dysfunction occurs.

J Teh Univ Heart Ctr 1 (2007) 49-53

Keywords: Pulmonary thromboembolism • Deep venous thrombosis • Syncope • Echocardiography

Introduction

The cardinal manifestations of pulmonary thromboembolism (PTE) are unexplained chest discomfort (49% of patients with PTE), dyspnea (82%), and syncope (10-14%).¹

That little is known about syncope, in comparison with dyspnea and chest pain, renders an initial evaluation of patients with syncope, especially when it is not accompanied by other common PTE-related symptoms, difficult and can lead to misdiagnosis. We present a case report of a patient with syncope and pleuritic chest pain who was initially managed as suspected acute coronary syndrome.

Case study

This patient was a 65-year-old male, admitted to the emergency room (ER) with a chief complaint of chest discomfort. For seven days prior to admission, he had felt tightness in the chest and dyspnea, aggravated on exertion. The night before admission, he had been awakened by sudden chest pains, perspiration, nausea and vomiting, followed by an episode of syncope.

In the ER, he consistently had dyspnea and chest discomfort, intensified by minimal exertion. He had no history of ischemic heart disease, diabetes mellitus, hypertension, hyperlipidemia, or smoking. He was not on medication before and had never

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had major surgical procedures or immobilization.

Vital signs were: BP=100/70, in both arms; PR=104/min; and RR=28/min with oral temperature of 37 °C. Prominent S2 and a systolic murmur with II/VI intensity at the left lower sternal border were reported. Lung auscultation appeared normal. There was mild tenderness in the epigastrium. No abnormal finding was noted in the extremities.

An ECG and cardiac marker tests were requested on clinical suspicion of acute coronary syndrome. The ECG demonstrated ST-T abnormalities, but the serial cardiac markers showed no increase. The patient was declared as a case of unstable angina, and full medication with anti-ischemic and anticoagulation was commenced. On the second day of admission, the severity of the complaints was modestly reduced, and the patient was reevaluated.

The symptoms were intensified by low level activity and were characteristically pleuritic in

nature. The neck veins were prominent. The pulmonic component of S2 was accentuated. The systolic murmur, heard at the left lower sternal border, was increased by inspiration.

Severe dyspnea, pleuritic chest pain, bulging neck veins, and clear lung led us to suspect PTE. Our reexamination of the extremities to find any evidence supporting deep veins thrombosis (DVT) showed no swelling. At this juncture, the patient experienced dull ache and concurrent swelling in the left calf region, exacerbated while walking. Pain and edema gradually subsided without any special intervention. The clinical index of suspicion for PTE became stronger.

Figure 1 shows his ECG on admission.

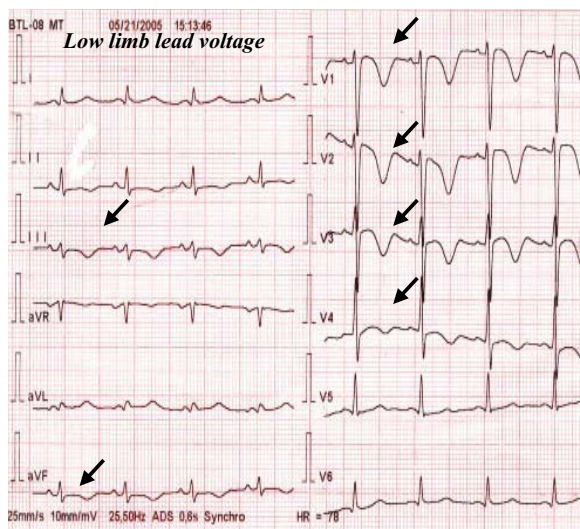


Figure 1. The patient's ECG (on admission)

The arrows denoted a T-wave inversion in V1-V4 and DIII, avF. A classic pattern of S1Q3T3 was absent.

Figure 2 shows his first chest X-Ray.

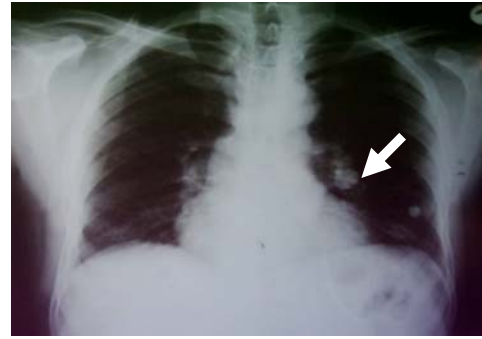


Figure 2. The patient's first chest X-Ray. The arrow denotes tapering of the pulmonary artery after the enlarged portion

Cardiothoracic ratio was in the upper limit of normal. There were prominent left pulmonary artery and distended descending branch with tapering to the peripheral. Other findings included bibasilar cystic-like lucencies and calcified foci in the hilum of both lungs and at the peripheries of the left lung.

The first transthoracic echocardiography was performed (figure 3).

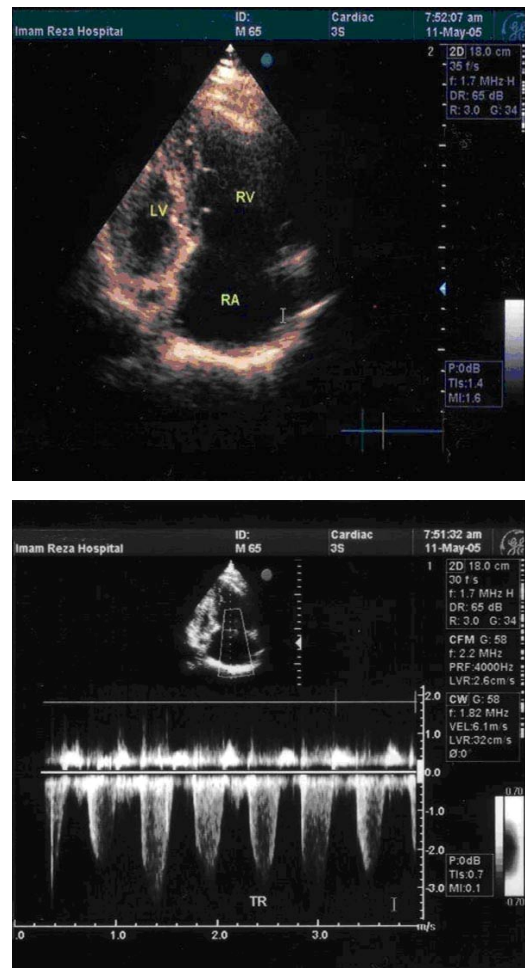


Figure 3. The patient's first transthoracic echocardiography



RV was markedly enlarged. The IVS was displaced toward the left ventricle. There was moderate RV hypokinesia (with sparing of the apex), no visible clot in dilated pulmonary trunk, TR with PG of 40 mmHg, and decreased inspiratory collapse of IVC. The estimated PAP was 55 mmHg.

The plasma D-dimer ELISA increased to 25000 microgram per liter.

The liver enzymes were normal. We were not able to find any clinical clues denoting the presence of malignancies. The sedimentation rate was also in normal range.

A venous ultrasound examination of the left lower extremity and pelvic vessels showed no evidence of thrombosis as a possible source of PTE.

UFH (unfractionated heparin) via intravenous infusion began with dosing adjusted on the base of body weight and titrated by controlling PTT.

A multidetector-row CT scan of the chest was not performed (due to the inaccessibility of this equipment), so the patient was referred for perfusion lung scanning (figure 4).

It showed multiple large and moderate segmental defects, consistent with high- probability PTE.

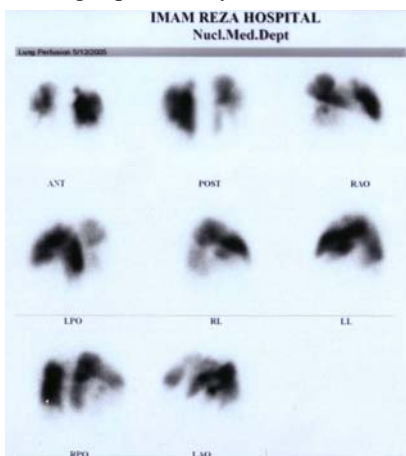


Figure 4. The patient's first lung perfusion scan

On the sixth day of admission, the patient still had marked dyspnea on minimal exertion, but his hemodynamics were stable.

A TTE was performed again. RV dysfunction and hypokinesia intensified. The peak gradient of TR increased to 57 mmHg.

Despite the well-preserved blood pressure readings, our findings prompted us to prescribe thrombolytic agents. Available thrombolytic streptokinase (SPK) was, therefore, selected with 250,000 units' intravenous infusion over a 30-minute period, followed by 100,000 units per hour, continued up to 24 hours. At this point, the patient was on the 6th day of admission (nearly 13 days after the onset of symptoms).

The initialization of thrombolytic therapy was followed by a dramatic response. On the second day, dyspnea markedly reduced. The global function of the right ventricle improved and PAP decreased (figure 5 & 6).

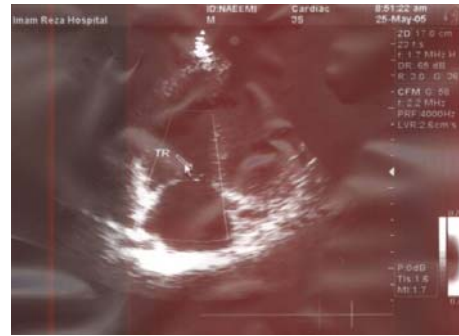


Figure 5. Transthoracic echocardiography after thrombolytic therapy, showed global function of right ventricle improved (with TAPSE of nearly 2.49cm); tricuspid regurgitation was barely detectable in color Doppler with PG of 23 mmHg; estimated PAP was 33mmHg

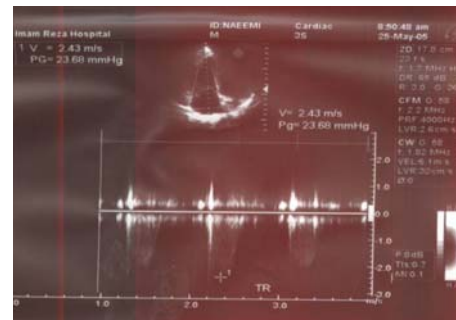


Figure 6. Transthoracic echocardiography, M-mode view after thrombolytic therapy, showed reduced tricuspid regurgitation

One week after thrombolytic therapy, the systolic function of the right ventricle (on the basis of echocardiographic findings) became normal with near normal PAP and decreased gradient of TR.

Figure 7 show his lung perfusion scan after SPK

It showed three moderate and few small segmented perfusion defects, consistent with resolving PTE.

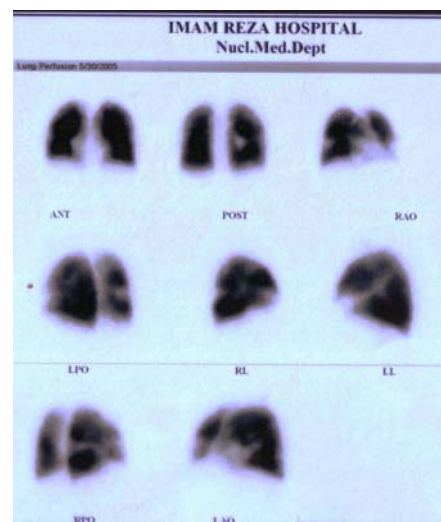


Figure 7. Lung perfusion scans after thrombolytic therapy

The patient was discharged from the hospital with good

general health on oral anticoagulant (warfarin) with a target INR of 2-3. One month later, we visited him at the clinic. He continued to be free of symptoms and the RV function remained normal. His full-intensity anticoagulation will be continued for up to 6 months, and the patient will be monthly followed-up.

The most important step in the management of such patients is the identification of the cause of the clot. As several of the diagnostic tests that need to be done are affected by an existing or recent blood clot and by any anticoagulant therapy that is given, we had to order a few tests (CBC for ruling out essential thrombocythemia, liver enzymes, PT, and aPTT) and treat the person's existing blood clots first. After six months of full-intensity anticoagulation, follow-up testing will be done to help us determine our patient's risk of developing recurrent blood clots.

The testing may include: Activated Protein C Resistance (APCR), Factor V Leiden mutation assay (when APCR is abnormal), Homocysteine, Anticardiolipin antibodies, and a Prothrombin 20210 mutation test. If the aPTT testing is prolonged, Lupus anticoagulant testing may be carried out later, along with Protein C, Protein S, and Antithrombin (III). If no abnormalities can be detected, low-intensity (target INR of 1.5-2) anticoagulation will be continued indefinitely.

Discussion

Pulmonary thromboembolism has a wide clinical spectrum of presentations via numerous abnormalities and, as a result, is often difficult to be certainly diagnosed.

In this case, the differential diagnosis includes PTE, pneumonia, and MI. In the elderly, pneumonia must be considered with presentations such as chest pain especially on inspiration, dyspnea, tachypnea, and low-grade fever. However, the diagnosis of pneumonia can be ruled out on the basis of the course of symptoms, clear lung on physical examination, no lung parenchymal involvement in CXR, and a normal white blood cell (WBC) count.

As another differential diagnosis, MI should be considered. An ECG shows a T-wave inversion in V1-V4, which can be due to right ventricular strain from progressive right heart failure, anterior septal ischemia caused by primarily coronary artery involvement, or the secondary effects of the PTE. Nevertheless, MI rapidly loses its importance as a diagnosis due to normal serial cardiac markers.¹

Syncope is a possible but little known presenting manifestation of acute PTE.^{2,3} Its presence causes difficulty in making an appropriate diagnosis. The occurrence of syncope during PTE may result from different possibilities: the first possibility is acute right ventricular failure, caused by massive embolism consequent to a reduction in the cross-sectional pulmonary vascular area and pulmonary arterial hypertension. This failure could trigger a significant decrease

in left ventricular filling, with concomitant tachycardia, arterial hypotension, and low cerebral flow,⁴ which may be the most probable mechanisms of syncope in the presence of acute PTE.⁵ In addition to the hemodynamic alterations, respiratory disorders such as bronchoconstriction, an increase in the dead space, and a reduction in the pulmonary surfactant contribute to the clinical finding in these patients.⁶ In some cases, syncope progresses to cardiac arrest; in others, it is brief. In the latter, the embolic occlusion of the pulmonary artery may change to a partial occlusion.

The second possibility is the reflex syncope due to a vasovagal mechanism triggered by pulmonary thromboembolism.^{4,5,7-10} The third possibility is complete atrioventricular block in the presence of preexisting complete left bundle-branch block. The development of acute right bundle-branch block due to pulmonary embolism supposedly accounts for complete A.V. blockage and syncope in these individuals.^{4,9,11,12}

Syncope as an initial presentation of pulmonary embolism occurs in 10% of patients. In one study, patients with syncope showed a more pronounced tendency to present with main pulmonary artery embolus than patients without syncope (contingency coefficient= 0.301, $P<0.04$, one tailed).⁷

Syncope is not uniformly restricted to massive PTE. It can occur in the setting of non-massive cases by way of the second or third mechanism mentioned above.^{7,12}

In this case, a high-probability lung perfusion scan is sufficient to diagnose PTE and justify the institution of anticoagulant treatment.¹³

The next point is the choice between anticoagulation with heparin alone and thrombolytic plus heparin.¹⁴

We decided to administer SPK due to the progressive course of RV dysfunction and hypokinesia detected by serial TTE studies and also the persistence of severe dyspnea. Elevated cardiac biomarkers such as troponin can also be used for risk stratification, which was not increased in our patient.

In 1977, the FDA approved the use of thrombolytic therapy for PE associated with hypotension and significant hypoxemia despite oxygen supplementation.¹⁵ In massive PE, many specialists strongly recommend primary therapy with thrombolytic.^{6,15,16} In submassive PTE, however, it is difficult to decide. Data suggest that patients with hemodynamically stable PTE but moderate to severe RV dysfunction may benefit from thrombolytic therapy. Some trials have offered echocardiographic data, suggesting that the detection of RV hypokinesia is associated with a 2-3 fold increase in mortality.¹⁷

In 1997, one multicenter, prospective study (Management strategy and prognosis of pulmonary embolism registry of MAPPET) supported the use of thrombolytic therapy in submassive PE with stable hemodynamics. According to this registry, a thrombolytic-therapy group had a reduced 30-day mortality rate (4.7% VS 11.1%, $P=0.016$) and reduced risk for recurrent venous thromboembolism (7.7% VS 18-7%, $P<0.001$) compared to the heparin group; major bleeding



complications were significantly higher in the thrombolytic-treated patients (21.9% VS 7.8%).

On the basis of these data, thrombolytic therapy in submassive PE with RV dysfunction should be considered on an individual basis.¹⁷

The patient's age, symptoms, physical examinations, level of hypoxemia, and severity of RV dysfunction should be studied. In cases of dyspnea, hypoxemia, and evidence of moderate to severe RV hypokinesia, we can consider thrombolytic therapy.

Until further studies confirm the available preliminary data, exact guidelines for this clinical scenario cannot be proposed.

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