Case Report

CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: HOW TO DIAGNOSE? A CASE REPORT

Sidhi Laksono¹,², Hillary Kusharsamita³

¹Faculty of Medicine, Universitas Muhammadiyah Prof Dr Hamka, Tangerang, Indonesia
²Department of Cardiology and Vascular Medicine, Pertamina Central Hospital, South Jakarta, Indonesia
³Pertamina Central Hospital, South Jakarta, Indonesia

Corresponding Author: sidhilaksono@uhamka.ac.id

ABSTRACT

Background Chronic thromboembolic pulmonary hypertension (CTEPH) is a pulmonary embolism (PE) complication that is a primary cause of pulmonary hypertension (PH) and may lead to right heart failure and significant mortality especially when left untreated. Although CTEPH is the only cause of PH that is curable without needing to resort to lung transplant, it is often misdiagnosed due to the absence of diagnostic instruments and the absence of specific presenting symptoms. This also complicates the process of distinguishing between acute thromboembolic disease and the acute embolic event worsening of undiscovered CTEPH.

Objective A better understanding of CTEPH is crucial, therefore we discuss a diagnosis rare case of CTEPH.

Case Description A 44-year-old man presenting with syncope and chest discomfort who had no previous episodes of acute PE.

Conclusion Computed Tomography Pulmonary Angiography (CTPA) is a significant test for identifying CTEPH. Oral anticoagulants may provide patients with CTEPH a safe and beneficial life-long treatment.

Keywords: Chronic Thromboembolic Pulmonary Hypertension, Computed Tomography Pulmonary Angiography, Diagnosis, Pulmonary Embolism.
CASE DESCRIPTION

Patient Information
A 44-year-old man presents to the emergency department complaining of epigastric pain and a history loss of consciousness. One hour before arriving at the hospital, the patient was discovered unconscious while praying. The patient was unconscious for approximately ten minutes and when he awoke, he complained of epigastric pain and chest discomfort. There was no prior medical history, and the reported symptoms were unprecedented. He had no history of PE or deep vein thrombosis. The patient's occupation is described as a software engineer. The patient was a regular smoker, consuming 5–10 cigarettes each day. A family history of hypertension was noted.

Clinical Findings
In ER the patient is alert, his chest discomfort persists, and vital sign showed a cardiogenic shock. Physical examination revealed blood pressure of 70/54 mmHg, pulse rate of 115 beats/min, respiration rate of 26 breaths/min. No murmurs or gallops were detected. No jugular venous distention was found. Vesicular breath sounds were present in both lungs, and there were no rales or wheezing. The extremities were warm, and no peripheral cyanosis was observed. A dobutamine infusion of 5 mcg/kg/min and a 5mg isosorbide dinitrate (ISDN) was given.

Diagnostic Assessment
The electrocardiogram (ECG) shows sinus tachycardia with a complete right bundle branch block (CRBBB). His blood gas analysis are all within normal limits. A significant elevation of troponin T of 788.50 was also found. Therefore, the working diagnosis was acute myocardial infarction with new RBBB, and loading 300mg of clopidogrel and 160 mg of aspirin was also given. The patient was then consulted to an interventional cardiologist and advised to do the primary percutaneous coronary intervention (PPCI). During the procedure, the coronary angiography (CAG) result shows coronary artery disease involving 3 vessels (CAD3VD) with a spontaneous lysis. The stenosis was found 40% in LAD, 40% in LCX, and 30% in RCA.

Therapeutic Intervention
A subcutaneous injection therapy of Enoxaparin sodium 0.8 cc was added, two times daily. The patient was then observed in the intensive care for further evaluation. One day after the observation in the intensive care, the patient experienced dyspnea, a follow up ECG was done. On the ECG, S1T3 pattern, T inverted on anterior leads (V1-V4) and right axis deviation (RAD) was found (Figure 1). The patient was then suspected of having a thromboembolic PH. An immediate Computed Tomography Pulmonary Angiography (CTPA) was then performed. On CTPA, a large thrombus is seen in a. right pulmonary to the base of the superior & inferior lobar segments (severe stenosis in the inferior segment ±70-80%). An extensive thrombus is also seen in a. left pulmonary to base of superior & inferior lobar segments (severe stenosis at ±60-70%). Furthermore, a mild fibrosis was found in the right and left inferior lobes (Figure 2). A significant elevation of D-dimer of 22.34 mg/dl was also found. An echocardiography was also done, with a result of positive McConnell, positive D-Shaped left ventricle (LV), moderate PH with a mPAP 46 mmHg. The patient was confirmed to have a CTEPH, a rivaroxaban of 20mg once daily was added to the therapy.

Follow-Up And Outcomes
On three consecutive days, there was relief of the symptom accompanied by a notable and significant decrease in D-dimer levels to 1.6 mg/dl (dropping from 22.34 mg/dl). The patient was then prescribed with a continuous treatment of rivaroxaban as the lifelong anticoagulation for his CTEPH condition.

DISCUSSION
The diagnosis of CTEPH may be difficult to make since patients often show no symptoms while having severe pulmonary artery occlusion. Many of the individuals did not have a history of PE, hence the diagnosis is often neglected. Dyspnea, hypoxemia, and right ventricular (RV) dysfunction are symptoms that become evident as PAH worsens, ultimately
resulting in mortality from decompensated right heart failure.\textsuperscript{3} Current research has shown that 25\% of patients do not have a history of PE.\textsuperscript{4} This poses a difficulty in differentiating between a de novo acute event and an acute embolic event worsening of undetected CTEPH. Even though PH has started, most people do not have any symptoms during the "honeymoon period".

Figure 1. Follow-up ECG. Showing S1T3 pattern, inverted-T on anterior leads (V1-V4) and right axis deviation (RAD).

Picture 2. Computed Tomography Pulmonary Angiography (CTPA). Large right and extensive left pulmonary thrombus.
As a result, CTEPH is generally not identified until the patient develops severe PH characterized by dyspnea, hypoxemia, edema, and/or indications of right heart dysfunction such as fatigue, chest pain, and syncope. Patients with inflammatory diseases, malignancy, or coagulopathy are at a higher risk for developing CTEPH. Following a comprehensive history and physical examination, individuals with symptoms and signs of PH and a clinical history consistent with PH of unexplained etiology should be tested for persistent thromboembolic pulmonary hypertension. Initial ECG results on PH often include right atrial enlargement, RAD, and right ventricular enlargement, frequently with a strain pattern. Anterior precordial leads often show T wave inversion, which represents repolarization irregularities associated with right ventricular hypertrophy. Although there may not be a consistent correlation between ECG findings and the severity of pulmonary PH, a study involving 47 patients reported that a R wave amplitude in V1 greater than 1.2 mV or an R/SV1 ratio exceeding 7 can indicate a pulmonary artery systolic pressure surpassing 90 mm Hg. The sensitivity of this indicator was found to be 94%, while the specificity was 47%. While the exact cause of CTEPH is unknown, acute PE is a known precipitating factor. In our patient, there was no recorded incident of an acute PE episode before he was taken to the hospital. His symptoms began with a sudden chest tightness and syncope episode and worsened with dyspnea after he was evaluated in intensive care following a PPCI treatment for acute myocardial infarction condition in the emergency department. ECG test when the patient experienced dyspnea showed normal sinus rhythm, RAD, S1T3 pattern with marked T inversion, which were compatible of suspected thromboembolic PH. A marked elevation of D-dimer was also noted, indicating hypercoagulability as the risk development of CTEPH. Furthermore, on an echocardiogram, signs of elevated pulmonary pressure include an enlarged right atrium and ventricle, RV hypertrophy, globally decreased RV systolic function, pulmonary artery dilatation, interatrial septal bowing to the left, and a D-shaped LV. Additionally, Echocardiography is helpful because it may identify secondary conditions including left-sided heart disease, valvular abnormalities, chamber mass, or intracardiac shunt. A diagnosis of CTEPH was made after the patient’s echocardiogram indicated positive McConnell, positive D-Shaped left ventricle, moderate PH with a mPAP of 46 mmHg. Growing research has examined the CTPA’s diagnostic accuracy for CTEPH. The sensitivity and specificity were shown to be reduced when the emboli were found in more peripheral areas. Study shows a pooled sensitivity for total arteries, main-lobar arteries, and segmental arteries was 88%, 95%, and 88%, respectively, while pooled specificity was 90%, 96%, and 89%, respectively. Depending on the severity of PH and vascular blockage, the imaging results in individuals with CTEPH might be very different. CTPA has the highest sensitivity for identifying abnormalities in the main and lobar pulmonary arteries and progressively lower sensitivity in the segmental and subsegmental arteries. In our case, a large and extensive thrombus with severe stenosis, also a mild fibrosis was found, which confirms the diagnosis of CTEPH and rule out the acute thromboembolic disease. Recent research has brought attention to an increased prevalence of coronary artery disease in persons diagnosed with CTEPH in comparison to those who have survived an acute pulmonary embolism. This link may occur via several mechanisms, including inflammation, systemic and local hypercoagulability, and endothelial damage. These variables are also essential components in the mechanistic route that contribute to the process of arterial stiffness. The elevated arterial stiffness observed in CTEPH patients may increase the susceptibility to atherosclerosis-related diseases. Consequently, there is a potential reduction in blood flow to the coronary arteries, leading to the occurrence of myocardial ischemia.
Among the 679 patients in a recent investigation of the European CTEPH registry, 12.7% had a concurrent diagnosis of cancer, 11.8% had cardiovascular disease and/or myocardial infarction, and 9.5% had chronic obstructive pulmonary disease. This leads us to the conclusion that, regardless of any other known cardiopulmonary condition, CTEPH should be taken into consideration in all individuals exhibiting symptoms consistent with the disease. In our case, treating acute myocardial infarction was crucial and needed as a live saving. However, taking it a step further and being proactive in evaluating CTEPH could have added significant outcome. Given its consistent symptoms and prevalence, initiating an early CTPA could have been a game-changer. This approach would have facilitated the initiation of timely and proactive treatment, hence guaranteeing a more complete and comprehensive treatment strategy for CTEPH.

The thrombus's morphology and the size of the blocked vessel are used to distinguish between acute thromboembolic disease and CTEPH. In contrast to the central position of acute pulmonary embolism, the symptoms of chronic thromboembolism appear as eccentric filling defects generating obtuse angles with the wall. In contrast to the retraction and reduced diameter of occluded arteries seen in CTEPH, acute emboli tend to enlarge the occluded artery. Fibrotic webs or bands are also common in patients with CTEPH. Chronic thrombus organization also may induce localized stenosis of arteries followed by regions of dilation and calcification.

Initiating anticoagulant medication as soon as possible is the primary step in treating CTEPH. Most individuals with persistent thromboembolic pulmonary hypertension will be treated on anticoagulation medication. The goal is to stop further episodes of venous thromboembolism and pulmonary artery thrombosis from happening. Lifelong anticoagulation has decreased the risk of recurrent venous thromboembolism in individuals with unprovoked or idiopathic pulmonary embolism.

Recent studies show that lifelong anticoagulation is the most important part of the treatment for CTEPH, whether it's combined with pulmonary endarterectomy, balloon pulmonary angioplasty, or medical treatment only. In individuals with CTEPH, direct oral anticoagulants may be a viable option for lifetime anticoagulant treatment because of their low risk of side effects and high efficacy. Notably, most of the anticoagulants that were prescribed were mostly warfarin and rivaroxaban. As compared to rivaroxaban, warfarin has been linked to a greater risk of bleeding and mortality from bleeding complications. For this reason, we use rivaroxaban as a lifelong treatment for preventing raising thromboembolic risk without raising bleeding events.

**CONCLUSION**

CTEPH is an uncommon but significant complication, with high rates of morbidity and death. Thus, it necessitates awareness and vigilance about symptoms, which, if present, should trigger an appropriate diagnostic examination by differentiating acute thromboembolic disease and CTEPH. CTPA is an essential examination in determining CTEPH. Oral anticoagulants may provide CTEPH patients with a safe and effective option to lifelong anticoagulant treatment.

**CONFLICT OF INTEREST**

The author states no conflict of interest.

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