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Case Report

Chronic Thromboembolic Pulmonary Hypertension Presented as Acute Heart Failure: A Case Report

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Abstract

Chronic thromboembolic pulmonary hypertension (CTEHP) according to the European Guidelines for the diagnosis and treatment of pulmonary hypertension (PH) is classified in the fourth group. CTEPH is a rare, but progressive and potentially life-threatening condition that most commonly occurs due to pulmonary artery obstruction from unresolved acute pulmonary embolism (PE). There are different data on the occurrence of CTEPH after acute PE, which is primarily due to the different factors of occurrence, sometimes due to non-specificity of symptoms and the difficulty in differentiating acute pulmonary embolism from the symptoms of pre-existing CTEPH. We present a patient with CTEPH with recurrent episodes of acute pulmonary embolism, as the cause of development of right heart failure and poor outcome.

Keywords: *Pulmonary Embolism; Pulmonary Hypertension; Chronic Thromboembolic Pulmonary Hypertension; Thrombophilia; Right Heart Failure; Dyspnea*

Introduction

Chronic thromboembolic pulmonary hypertension (CTEHP) is the cause of the development of pulmonary hypertension (PH), which is classified in the fourth group according to the latest Guideline of the European Society of Heart and Lung Diseases. CTEPH leads to pre-capillary hypertension which means combination of mPAP > 20 mmHg, PAWP < 15 mmHg and PVR > 2WU [1]. Some patients develop CTEPH after an acute PE event, which is unclear, but certain associated conditions and comorbidities are thought to be involved such as thrombophilic disorders, especially antiphospholipid antibody syndrome and high levels of coagulation factor VIII, cancer, inflammation, insufficient anticoagulation, splenectomy, devices such as implanted pacemakers, and other conditions [2-4].

In patients with CTEPH non-resolved thrombus leads to fibrous transformation of the thrombus in the pulmonary arteries, causing mechanical obstruction of flow in the pulmonary artery segment. Persistent reduction, or obstruction of the flow of the pulmonary arteries lead to redistribution of flow across the pulmonary bed and secondary remodeling of the pulmonary microcirculation with a progressive increase in pulmonary vascular resistance and development of pulmonary hypertension, which leads to right ventricular dilatation and dysfunction [1,4,5].

Case Report

A 42 old male was presented in emergency room (ER) in the University Clinic of Cardiology with complaints of dyspnea, orthopnea, marked fatigue, legs oedema and ascites. The patient was urgently hospitalized as critically ill patient in Intensive Care unit, with a symptoms and signs of acute right heart failure and signs of hemodynamic instability. His blood pressure was 90/60 mmHg, on the ECG there was atrial fibrillation with fast heart rate, average over 150 bpm (Figure 1).

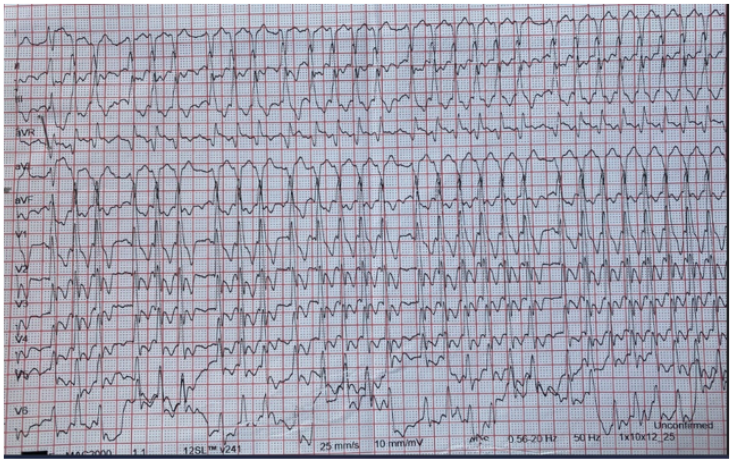

Figure 1: *ECG of the patient at the admission showing atrial fibrillation with fast heart rate, right bundle branch block and signs of right ventricular load.*

At the admission a patient had a large abdominal and legs swelling and signs of oliguria (only 800 ml diuresis for 24 hours). His blood oxygen was SaO_2 92% on ambient air. The immediate lab results showed: near normal count of blood red cells, with low level of hemoglobin (70 g/l). Hetero anamnestically we obtained information about long-term hemorrhoidal bleeding. The patient showed signs of acute deterioration of renal function with high urea and creatinine, as well as low blood protein values and coagulation status within reference ranges. Emergency bedside echocardiography was performed, which confirmed significant right ventricular (RV) dilatation, compromising left ventricular (LV) function because of the right ventricular overload, as well as marked pulmonary hypertension (Figure 2) and by the echocardiography we estimated systolic pressure of pulmonary artery (sPAP) 59 mmHg.

In addition to symptomatic therapy primarily to stabilize heart rhythm, inotropes and vasopressors were administered as a continuous infusion, with invasive monitoring of hemodynamic parameters with a Swan-Ganz catheter. Hemodynamic parameters we got were: mean pressure in pulmonary artery (mPAP) 60 mmHg, pulmonary artery wedge pressure (PAWP) 13 mmHg, pulmonary vascular resistance (PVR) 11WU and central venous pressure (CVP) 33 mmHg. He also got low molecular weight heparin (LMWH), blood transfusion and substitution with albumen.

We got an information that the patient had a previous history of recurrent venous thromboembolism (VTE), with a first episode of deep venous thrombosis (DVT) and pulmonary thromboembolism (PE) 7 years ago, followed by a relapse one year ago. He has been diagnosed with a right ventricular failure (RVF) and pulmonary hypertension (PH) and treated for 7 years, mostly as an outpatient, with a chronic therapy for heart failure. He was also diagnosed before with a positive thrombophilia test for LA, ITGA2, MTHFR1298, MTHFR677 and MTRR, PAI-1.

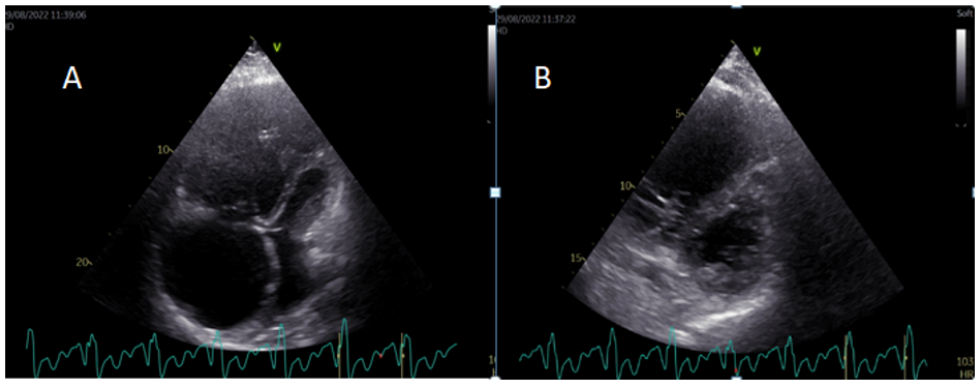

Figure 2: *Four chamber view on transthoracic echocardiography showed dilated RV with small LV (A) and D-shape of the LV due to RV overload (B).*

Computed tomography pulmonary angiography (CTPA) showed signs of CTEPH (Figure 3) and also acute pulmonary embolism. After stabilization of the general condition of the patients, a comprehensive echocardiography assessment was performed. Echocardiography in addition to dilated right heart cavities, impaired left ventricular function and pulmonary hypertension, showed reduced right ventricular function (global longitudinal strain GLS - 7.4%, tricuspid annular plane excursion - TAPSE 11 mm). CTPA and comprehensive echocardiography were performed also in order to refer to a PH specialized center for pulmonary endarterectomy (PEA), or balloon pulmonary angioplasty (BPA). Unfortunately, the general condition of the patient suddenly deteriorated, he went into shock and died. Resuscitation measures were unsuccessful.

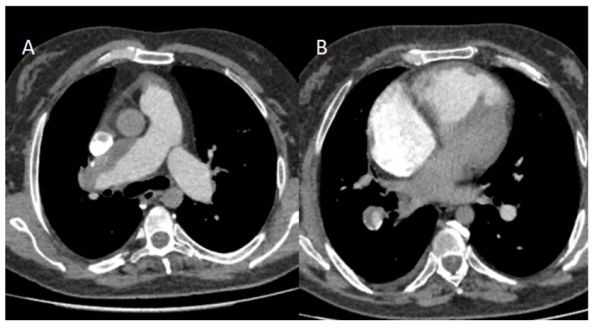

Figure 3: *CTPA showed extensive peripheral thromboembolic filling defects in the right pulmonary artery (A) and peripheral thromboembolic filling defects at the level of the bifurcation of the right lobar arteries for the middle and lower lobe (B).*

Discussion

Chronic thromboembolic pulmonary hypertension (CTEHP) is a rare but progressive and potentially life-threatening disease. It occurs most commonly as an uncommon sequel to acute pulmonary embolism (PE). Why in some patients fail to resolve the thrombus

after acute PE is unclear, but certain conditions and comorbidities are thought to be involved, such as thrombophilic disorders, especially antiphospholipid antibody syndrome and high levels of coagulation factor VIII, cancer, inflammation, insufficient anticoagulation, splenectomy, devices such as implanted pacemakers and other conditions [2,3,5]. Thrombophilia's are inherited and acquired hypercoagulable or a prothrombotic state, which can lead to an abnormality of blood coagulation that increases the risk of thrombosis. Such abnormalities can be identified in 50% of people who have an episode of thrombosis. A significant proportion of the population has a detectable thrombophilic abnormality, but most of these develop thrombosis only in the presence of an additional risk factor [6-8]. Our patient was positive on thrombophilia test, with recurrent episodes of PE despite anticoagulation therapy with NOAC and developed right ventricular failure and pulmonary hypertension.

NOAC are recommended in preference to vitamin K antagonists for the acute phase treatment of PE, but yet there is no specific guidance for the use of these drugs in patients with inherited thrombophilia [3]. Several case reports and post-hoc analyzes of clinical trials have shown positive results of DOACs in patients with hereditary thrombophilia and VTE, but there is still no substantial evidence to support widespread use of NOACs [9]. Dabigatran has been analyzed in the RE-COVER and RE-COVER II studies for acute symptomatic venous thromboembolism compared with warfarin, and in Re-MEDY study for secondary prevention of venous thromboembolism. Still, little is known about the potential effects on thrombophilic factors and clinical outcome in patients with VTE treated with dabigatran. In the studies, RE-COVER, RE-COVER II and RE-MeDY a high percentage of those analyzed for thrombophilia were positive for thrombophilia, and only a small percentage were with known antiphospholipid syndrome. The presence of thrombophilia did not significantly affect the efficacy or safety of dabigatran in preventing recurrent VTE. In patients with antiphospholipid antibody syndrome, is mandatory to use vitamin K antagonist in patients with VTE [6,10]. Further research in this area is needed to confirm the safety and utility of the type of anticoagulant in the resolution of VTE, particularly in the recurrence of VTE and the development of CTEPH.

In patients with CTEPH non-resolved thrombus leads to fibrous transformation of the thrombus in the pulmonary arteries, causing mechanical obstruction of flow in the pulmonary artery segment. Persistent reduction, or obstruction of the flow of the pulmonary arteries lead to redistribution of flow across the pulmonary bed and secondary remodeling of the pulmonary microcirculation with a progressive increase in pulmonary vascular resistance and development of pulmonary hypertension, which leads to right ventricular dilatation and dysfunction [1,8,11,12]. In the early stages of the development of pulmonary hypertension, dyspnea on exertion, fatigue, palpitations and atypical chest pain may occur. Due to the progressive worsening of the disease, the symptom of dyspnea occurs with less and less effort. The diagnosis of CTEPH is based on evidence of pre-capillary pulmonary hypertension assessed by right heart catheterization (RHC), associated with at least one segmental perfusion defect evident on ventilation/perfusion scan (V/Q scan) or newer modalities for perfusion as computered tomography pulmonary angiography (CTPA) or pulmonary angiography (annular stenosis, chronic lesions and/or complete occlusions) [1]. Echocardiography is widely used method as the initial diagnostic tool when PH is suspected, or whenever there are symptoms after acute PE.

Transthoracic comprehensive echocardiography (TEE) can give useful information about the hemodynamic changes on the RV and LV that occur in CTEPH: RV dilatation, hypertrophy of the RV wall, RV/LV ration bigger than 1, eccentricity index bigger than 1, D-shape of the LV with small LV end-diastolic dimension due to RV overload and dilated vena cava inferior, with non collapsibility more than 50%. Also, by echocardiography PH can be detected and evaluated by the maximal velocity of tricuspid regurgitation and the present other signs suggesting pulmonary hypertension [12-14].

Disease progression is associated with the development of right heart failure and deterioration of LV function due to RV load [15,16]. In our patient, there was the development of marked dilatation of the right ventricle with significant compression of the LV and impaired expansion of the LV, as well as the development of pulmonary hypertension. Patients with PH who develop RV dysfunction and compromised LV function have poor quality of life and poor outcome. Early detection of the disease is important for prompt indication of PEA or BPA.

Conclusion

CTEPH is a late complication of pulmonary embolism, which can be successfully treated with BPA or PEA. Certain other conditions such as thrombophilia and comorbidities can cause non-resolved thrombus after PE and can be reason for development of CTEPH. Timely diagnosis CTEPH and detection of the overload of the right ventricle and the development of pulmonary hypertension can prevent deterioration of the condition of these patients and a poor outcome.

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