

Multimodal Treatment for Chronic Thromboembolic Pulmonary Hypertension: A Case Report

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Abstract: Chronic thromboembolic pulmonary hypertension (CTEPH) is a severe disease characterized by pulmonary thromboembolism and vascular remodeling, the pathogenesis of which has not been fully elucidated. Currently, it is believed that the disease primarily originates from the shedding of thromboemboli from the right heart system, leading to mechanical obstruction of the pulmonary artery, which in turn triggers local inflammatory reactions, endothelial damage, and vascular remodeling. This results in elevated pulmonary artery pressure, ultimately leading to right heart failure. In recent years, a multimodal treatment strategy combining balloon pulmonary angioplasty (BPA) with targeted pharmacotherapy has demonstrated significant efficacy in the treatment of CTEPH. This article reports the diagnosis and treatment process of a 68-year-old female patient with CTEPH. After undergoing BPA combined with soluble guanylyl cyclase stimulators (riociguat), the patient's clinical symptoms and hemodynamic parameters significantly improved.

Keywords: Chronic thromboembolic pulmonary hypertension; Percutaneous balloon pulmonary angioplasty; Multimodal therapy; Riociguat

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1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive and debilitating disease resulting from persistent pulmonary artery obstruction and vascular remodeling following acute pulmonary embolism^[1-4]. If left untreated, it leads to increased pulmonary vascular resistance, right heart failure, and a poor prognosis. While pulmonary endarterectomy (PEA) remains the gold-standard treatment for proximal lesions, many patients with distal or peripheral disease are deemed inoperable. For these patients, multimodal

therapy combining balloon pulmonary angioplasty (BPA) and targeted pharmacotherapy, such as the soluble guanylyl cyclase stimulator riociguat, has emerged as an effective alternative. Here, we report the case of a 68-year-old female with inoperable CTEPH who demonstrated significant clinical and hemodynamic improvement following sequential BPA procedures and riociguat treatment.

2. Clinical data

The patient is a 68-year-old female farmer. Chief complaint: breathlessness after physical activity for 9 years. Admission date: September 2019.

The patient developed asthma after a sudden activity in 2010. Pulmonary artery enhancement CT scan (CTPA) revealed pulmonary embolism, and long-term anticoagulant therapy with “warfarin” was administered. In 2013, the patient was hospitalized at a certain hospital for right heart catheterization and pulmonary angiography. The results were as follows: right atrial pressure (RAP) 10/8/8 mmHg, pulmonary artery pressure (PAP) 92/27/50 mmHg, pulmonary artery wedge pressure (PAWP) 7 mmHg, cardiac output (CO) 3.4 L/min, pulmonary vascular resistance (PVR) 12.65 Wood units, and pulmonary angiography showed multiple segmental pulmonary artery stenosis, mainly in the left upper, right upper, and right lower lungs. The patient was treated with oral rivaroxaban 20 mg/day and sildenafil 25 mg, tid for long-term therapy, but there was no significant improvement in symptoms. Past medical history: history of lower limb venous thrombosis, without treatment.

Upon admission, physical examination revealed the following: T: 36.3 °C, P: 85 beats/min, R: 20 beats/min, Bp: 105/62 mmHg, no cyanosis in lips, jugular vein engorgement, no wet rales heard in both pulmonary bases, heart rate 85 beats/min, regular rhythm, P2 accentuation, no enlargement of liver or spleen, mild non-pitting edema below the ankle joints in both lower limbs. Post-admission examinations, including blood routine, erythrocyte sedimentation rate, electrolytes, liver and kidney function tests, homocysteine, anti-streptolysin O, C-reactive protein, rheumatoid factor, immunoglobulin, thyroid function tests, interleukin-6, procalcitonin, troponin, stool routine, fibrinogen degradation products assay, D-dimer, and infectious markers, were all normal. N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) was 417.00 pg/mL, and no abnormalities were found in the autoimmune vasculitis panel. Ultrasound of the veins in both lower limbs showed the formation of atherosclerotic plaques in both lower limbs, with a widened internal diameter of the left intermuscular vein. Pulmonary function tests revealed no significant abnormalities. Computed Tomography Angiography (CTPA) showed moderate to severe stenosis in the opening of the right upper lung and a few branches of the lower lung (**Figure 1**). Cardiac Magnetic Resonance Imaging (MRI) revealed a full right ventricular end-diastolic diameter (**Figure 2**), and Ventilation/Perfusion Imaging (VQ) showed a mismatch in V/Q in both lungs, with multiple subsegmental perfusion defects in both lungs, particularly evident in the right lung, consistent with pulmonary embolism changes (**Figure 3**). The 6-minute walking distance was 275 meters. Transthoracic echocardiography revealed a left atrial anteroposterior diameter (LA) of 37 mm, a left ventricular end-diastolic diameter (LV) of 48 mm, a right atrial (RA) anteroposterior and lateral diameters of 49 mm and 41 mm, respectively, and a right ventricular anteroposterior diameter (RV) of 28 mm. The estimated pulmonary artery systolic pressure was 92 mmHg, and the tricuspid valve systolic displacement was 19 mm. Ultrasound conclusion: severe pulmonary hypertension, with enlarged right atrium and right ventricle.



Figure 1. CTPA: Peripheral branches of the pulmonary artery are thin and occluded.

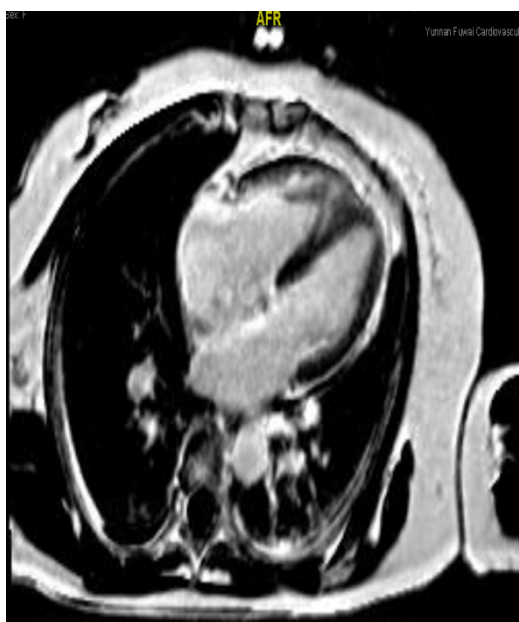


Figure 2. Cardiac MRI: The right ventricular diameter is full, with moderate to severe stenosis in the opening of some branches, particularly on the right side.

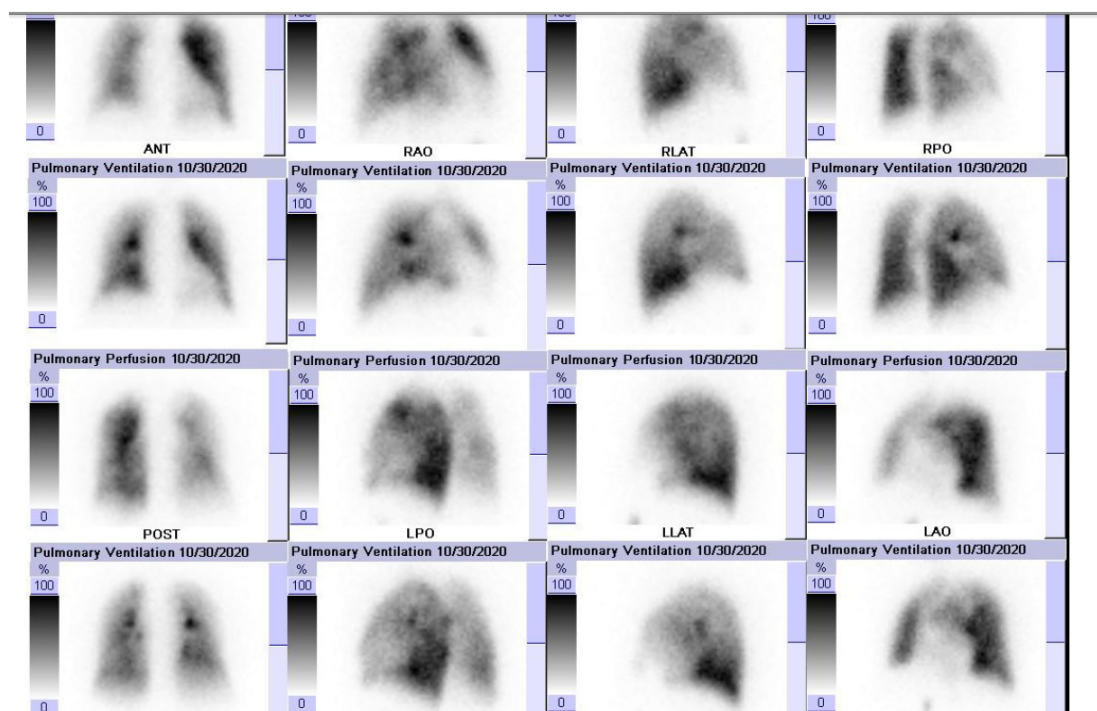


Figure 3. Lung perfusion: Bilateral pulmonary V/Q mismatch, multiple subsegmental impaired blood perfusion in both lungs, with marked impairment in the right lung.

After admission, right heart catheterization, pulmonary angiography, and percutaneous balloon pulmonary angioplasty were performed under local anesthesia. Details are as follows: RAP 10/8/8 mmHg, PAP 68/34/41 mmHg, PAWP 11 mmHg, CO 3.70 L/min, CI 2.1 L/min/m², PVR 8.92 Wood U, radial artery oxygen saturation 84.6%. Pulmonary angiography showed moderate to severe stenosis in the branch opening of the apical segment of the right upper lobe, severe stenosis in the opening of the internal and external basal segments of the right lower lobe, and severe stenosis in the posterior basal segment of the right lower lobe. Moderate stenosis in the middle segment of the inferior lingual artery of the left upper lobe, moderate to severe stenosis in the opening of the posterior pulmonary artery of the left lower lobe, moderate to severe stenosis in the lateral branch opening of the left lower lobe, and moderate to severe stenosis in the anterior pulmonary artery of the left lower lobe. Based on clinical history combined with right heart catheterization, the final diagnosis was chronic thromboembolic pulmonary hypertension, chronic pulmonary heart disease with cardiac enlargement, tricuspid insufficiency, and cardiac function class III (NYHA classification). After completing the right heart catheterization, BPA treatment was administered: balloon angioplasty was performed on the posterior pulmonary artery of the left lower lobe, the lateral branch of the left lower lobe, the inferior lingual artery of the left upper lobe, and the anterior pulmonary artery of the left lower lobe. Post-discharge treatment: oral administration of lioxapine 1 mg TID, gradually titrated to 2.5 mg TID, and rivaroxaban 20 mg/day.

The patient was admitted to the hospital again in October 2020 for another BPA procedure. The cardiac ultrasound examination revealed pulmonary hypertension, with a left atrial anteroposterior diameter of 40 mm, a left ventricular end-diastolic diameter of 41mm, a right atrial superior-inferior × lateral-medial diameter of 55 × 50 mm, a left atrial superior-inferior × lateral-medial diameter of 59 × 40 mm, and a right

ventricular anteroposterior diameter of 26 mm. TAPSE was 23 mm. On November 5, 2020, the patient underwent right heart catheterization, pulmonary angiography, and percutaneous pulmonary balloon dilatation. Details are as follows: RAP 15/14/13 mmHg, PAP 76/29/44 mmHg, PAWP 13 mmHg, CO 5.05 L/min, CI 2.94 L/min/m², PVR 6.14 Wood U. Pulmonary angiography showed grid-like stenosis in the apical segment of the right upper lobe, grid and cord-like stenosis in the medial and lateral basal segments of the right lower lobe, and local annular stenosis in the posterior basal segment of the right lower lobe. Balloon dilatation was performed on the aforementioned vascular lesions. Post-procedure, the patient continued to take leosilva 1 mg TID and gradually titrated up to 2.5 mg TID, as well as rivaroxaban 20 mg/day. After half a year, a follow-up examination showed significant symptom relief, with NT-pro-BNP at 135.00 pg/mL and 6MWD at 410 meters.

3. Discussion

The pathogenesis of CTEPH is not fully understood. Most scholars believe that its main mechanism involves thrombosis obstructing the pulmonary artery, leading to abnormal blood flow. This process also involves pulmonary artery lumen remodeling and local inflammatory response after thromboembolism, ultimately resulting in right heart failure. For patients with CTEPH, if the thrombus is located in the pulmonary lobe or above the pulmonary segment, pulmonary endarterectomy (PEA) is the preferred treatment. However, for a thrombus located in the pulmonary subsegment or below the subsegment, PEA is not feasible. Multimodal therapy (BPA + medication) is the standard treatment for such cases of CTEPH. In this case, due to extensive peripheral pulmonary artery disease, PEA is not feasible, and fractional BPA has become the preferred treatment ^[5–10].

In this case, despite anticoagulant therapy, the patient's symptoms continued to progress. Through CTPA, VQ, and pulmonary angiography, combined with right heart catheterization, CTEPH was finally diagnosed. Before the second BPA treatment, a follow-up right heart catheterization was performed, and the mean pulmonary artery pressure (PAP) did not decrease. However, considering the clinical symptom improvement and the increase in 6-minute walking distance (6MWD) from 275 meters to 386 meters, as well as the decrease in pulmonary vascular resistance (PVR) from a baseline of 8.92 Wood U to 6.14 Wood U, it indicated that one BPA treatment could still reduce the right heart afterload. However, the pulmonary artery remained high. Six months after the second BPA procedure, the patient's clinical symptoms significantly improved (including endurance, NT-pro-BNP, and 6MWD), indicating that multimodal therapy (targeted drugs and two BPA procedures) had achieved significant clinical improvement in the patient.

4. Conclusion

This case study indicates that for CTEPH patients who are not suitable for PEA treatment, the multimodal treatment regimen combining BPA with targeted drugs is a safe and effective treatment option. However, the treatment plan should be individualized and implemented with long-term follow-up. Due to the short follow-up period in this case, long-term follow-up is needed to observe the efficacy of the treatment.

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Disclosure statement

The authors declare no conflict of interest.

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