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A Case of Chronic Thromboembolic Pulmonary Hypertension in Which Balloon Pulmonary Angioplasty Was Effective 6years After Disease Diagnosis

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Chronic thromboembolic pulmonary hypertension（CTEPH）is a form of pulmonary hypertension caused by persistent, widespread stenosis or obstruction of the pulmonary arteries due to thrombus organization. A 55-year-old man was diagnosed with peripheral form of CTEPH, and he received anticoagulation, vasodilatation, and home oxygen therapy. Dyspnea on exertion deteriorated 6 years after CTEPH diagnosis. Balloon pulmonary angioplasty（BPA）was performed, which resulted in improvements in clinical symptoms and the mean pulmonary pressure. Treatment with BPA should be considered in patients with the peripheral form of CTEPH receiving long-term medical treatment.

Key words: chronic thromboembolic pulmonary hypertension, balloon pulmonary angioplasty

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INTRODUCTION

Chronic thromboembolic pulmonary hypertension（CTEPH）is a form of pulmonary hypertension caused by persistent, widespread stenosis or obstruction of the pulmonary arteries due to thrombus organization［1］. Balloon pulmonary angioplasty（BPA）for the treatment of peripheral form of CTEPH shows significant improvements in the mean pulmonary arterial pressure（mPAP）, cardiac index and pulmonary vascular resistance［2］. However, to our knowledge, no report has described the interval between the diagnosis and BPA treatment for CTEPH.

Here, we report a CTEPH case in which BPA was effective, despite being performed 6 years after disease diagnosis.

CASE REPORT

A 55-year-old man presented with dyspnea on exertion. He had schizophrenia since he was 19 years old. His symptoms were suggestive of World Health Organization functional class（WHO-FC）II. Blood gas analysis showed hypoxemia（PaO2 73.1 mmHg）and his brain natriuretic peptide（BNP）level was elevated（559 pg/mL）. His D-dimer level was approximately 1.6 μg/mL. Transthoracic echocardiography revealed a D-shaped left ventricle and severe pulmonary hypertension（estimated systolic pulmonary arterial pressure［ePAP］78 mmHg）. Peripheral form of CTEPH was diagnosed based on the results of contrast-enhanced computed tomography and ventilation-perfusion scintigraphy（Fig. 1）. Even

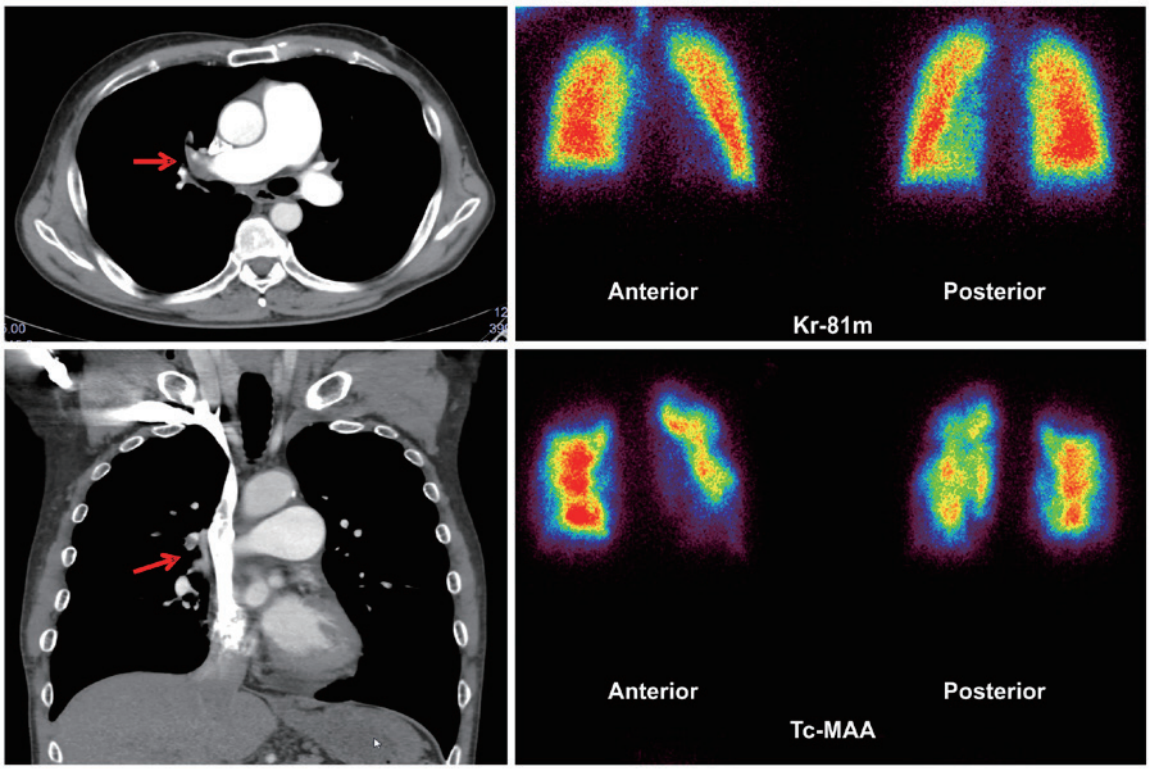

Fig. 1. Contrast-enhanced computed tomography shows a contrast defect in the right upper pulmonary artery. Ventilation-perfusion scintigraphy shows no abnormalities in ventilation, but segmental blood flow defects were observed mainly in the right upper lobe, right middle lobe, and left upper lobe.

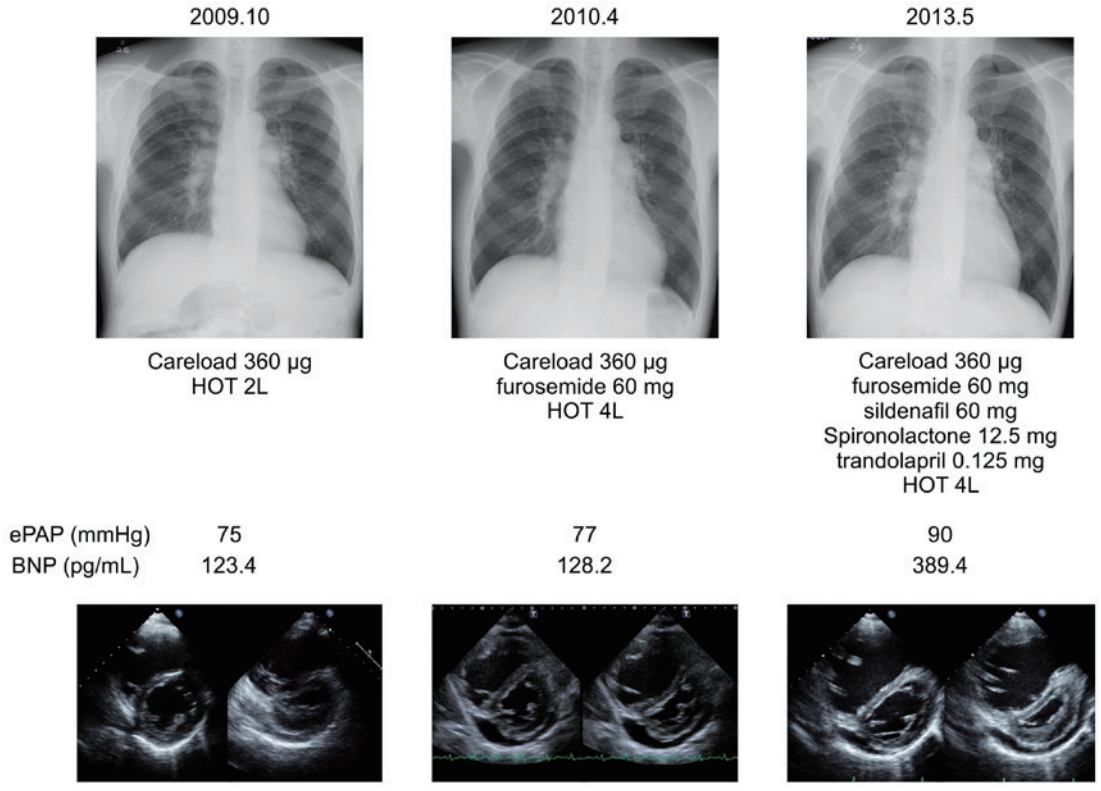

Fig. 2. Time-course progression of the disease. Even after anticoagulation, vasodilatation, and other treatments, including loop diuretic administration and home oxygen therapy, the patient has time-dependent elevations in estimated pulmonary arterial pressure and brain natriuretic peptide, as well as progression of right-sided cardiac enlargement.

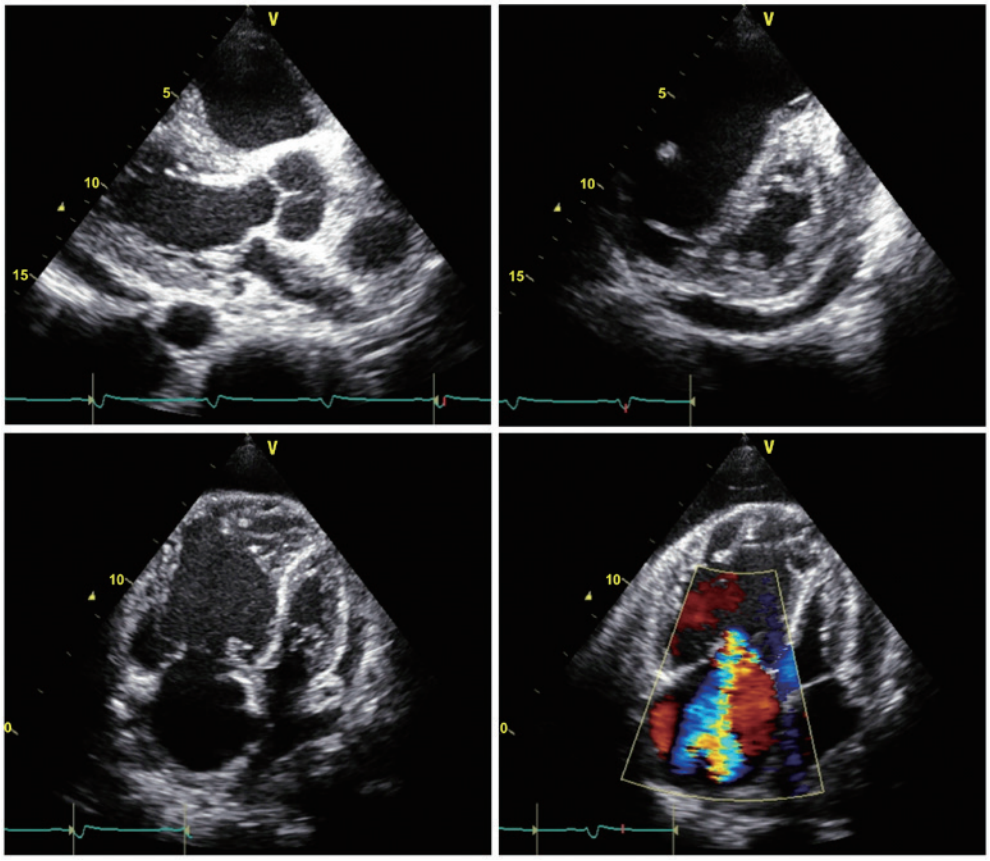

Fig. 3. Transthoracic echocardiography shows pulmonary arterial pressure elevation (estimated pulmonary arterial pressure, 94/25 mmHg) and right-sided cardiac enlargement. The left ventricle shows D-shape over the entire cardiac cycle.

after anticoagulation therapy with warfarin, vasodilatation therapy with beraprost sodium and sildenafil, and other treatments including loop diuretic administration and home oxygen therapy, he experienced time-dependent elevations in ePAP and BNP as well as the progression of right-sided cardiac enlargement (Fig. 2). Although we suggested BPA, he did not want it. We continued medical treatment.

He was reviewed owing to ongoing dyspnea and edema in the lower legs 6 years after CTEPH diagnosis, and his vital signs were follows: body temperature, 36.1 ℃; blood pressure, 95/59 mmHg; heart rate, 66 beats/min; respiratory rate, 20 breaths/min; and peripheral oxygen saturation (SpO2), 93% (with a nasal cannula delivering oxygen at a rate of 5 L/min). His symptoms were suggestive of WHO-FC IV. Blood gas analysis indicated hypoxemia (PaO2 57.1 mmHg), and marked BNP elevation (1953.6 pg/mL) was noted. The D-dimer level was not elevated (0.5 μg/mL). Electrocardiography showed complete right bundle branch block and ST-segment depression in leads II, III, aVF and V1- 4 during sinus rhythm. Transthoracic echocardiography indicated pulmonary arterial pressure elevation (ePAP, 94 mmHg) and the left ventricle had a D-shape over the entire cardiac cycle. The echocardiographic data were as follows: left ventricular diastolic dimension, 44mm; left ventricular systolic dimension, 21mm; left ventricular ejection fraction, 84%; right ventricular end-diastolic area, 50.0cm2; and right end-systolic area, 41.6cm2 (Fig. 3). Ventilation-perfusion scintigraphy revealed new perfusion defects in the lower lungs bilaterally, indicating CTEPH exacerbation (Fig. 4). Although we noted clinical improvement in his symptoms of right heart failure, such as leg edema, with the introduction of a furosemide, his breathing condition did not improve. Further medical intervention, including treatment with riociguat, was considered, but was ultimately not employed owing to concern regarding

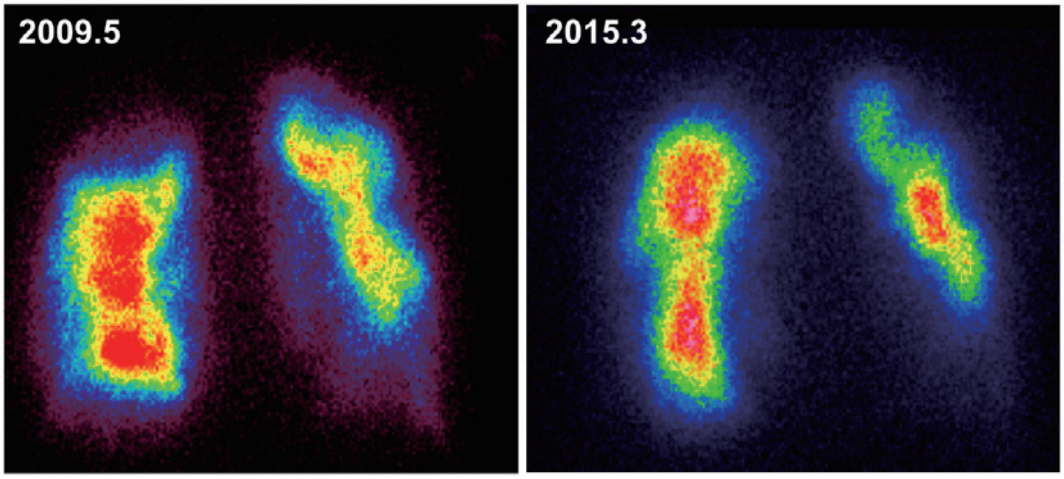

Fig. 4. Ventilation-perfusion scintigraphy shows new perfusion defects in the lower lungs bilaterally, indicating chronic thromboembolic pulmonary hypertension exacerbation.

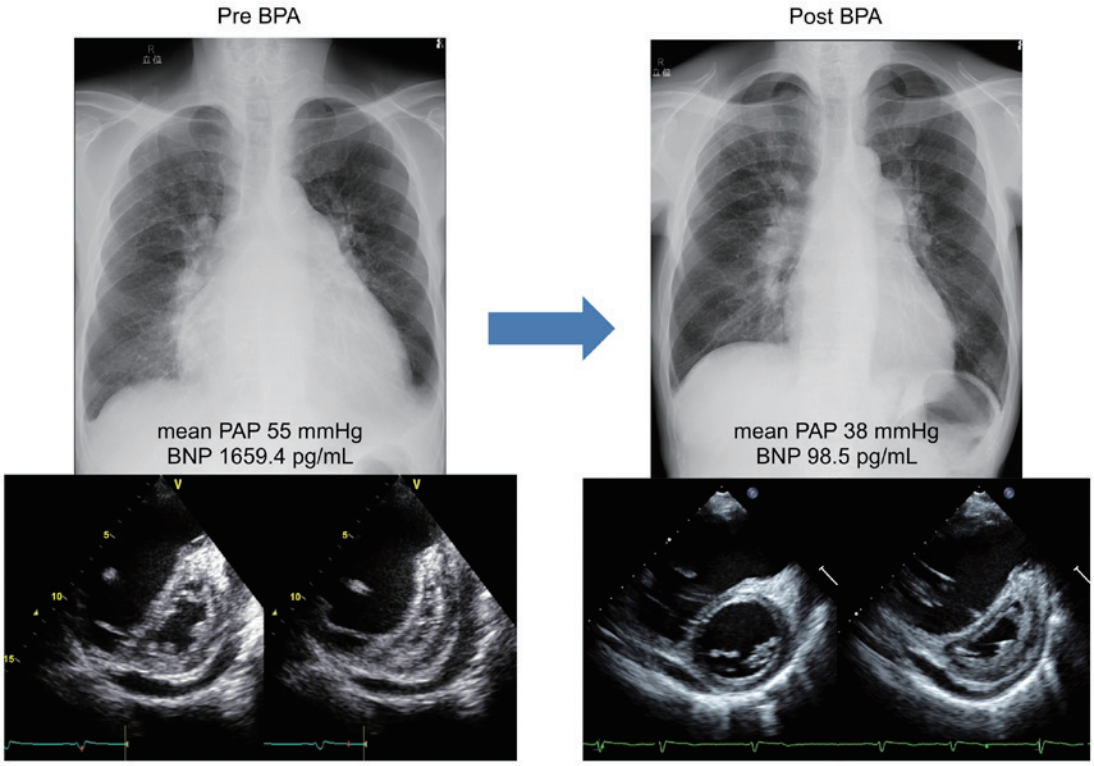

Fig. 5. Improvements in the pulmonary arterial pressure and brain natriuretic peptide level are seen at the end of 7 balloon pulmonary angiography sessions.

adverse drug reactions such as a decreased blood pressure. Improvement with medical treatment alone was not expected. Because he wanted BPA this time, he underwent it. Prolonged pulmonary hypertension tends to advance pulmonary vascular remodeling, increase the complexity of BPA procedures and the number of treatments. BPA was performed for lesions in 8 segments in the right lung and 3 segments in the left lung. At the end of 7 BPA sessions, improvements were noted in mPAP (55 mmHg to 39 mmHg) and BNP level (1659 pg/mL to 98 pg/mL). His caridothorathic ratio assessed using chest radiography reduced from 60% to 49% (Fig. 5). Furthermore, his symptoms improved from

WHO-FC IV to II. He is scheduled to undergo further BPA sessions.

DISCUSSION

This case shows that BPA is effective for patients with CTEPH persisting for a long time after disease diagnosis.

CTEPH reportedly develops in 3.8% of patients who have survived acute pulmonary thromboembolism [3]. On the other hand, approximately 30% of CTEPH patients have no history of acute pulmonary thromboembolism, while 45%, have a history of venous thrombosis. However the pathogenesis and epidemiology of CTEPH remain largely unknown [4,5].

The 5-year survival rates in patients with CTEPH were found to decrease to 50%, 30% and 10% with increases in the mPAP to 30 mmHg, 40 mmHg, and 50 mmHg, respectively [6]. In addition, a recent study reported 1- and 3-year survival rates of 82% and 70%, respectively [7]. These observations indicate that CTEPH has a poor prognosis.

The medical treatment for CTEPH consists of lifelong anticoagulant administration to prevent recurrence and secondary thrombus formation and oxygen therapy for the management of hypoxemia. Moreover, some previous reports evaluated the efficacy of pulmonary vasodilators for pulmonary arterial hypertension (PAH) in patients with CTEPH [8-10] and suggested that sufficient hemodynamic improvements, or even prognostic improvements, would be difficult to achieve in CTEPH cases [7].

First-line options for the fundamental treatment of CTEPH include pulmonary endarterectomy (PEA), because these patients, unlike those with PAH, have physical stenosis or obstruction of the pulmonary arteries caused by thrombus organization and therefore show limited responsiveness to vasodilators, even when administered to expand blood vessels. However, perioperative mortality rates with PEA range from 5 to 10%, indicating that the surgeon's skill and institutional experience have major impacts on whether PEA is successful [11-13]. In addition, the prognosis after PEA among patients with the peripheral form of CTEPH is poor, with a perioperative mortality rate of 25% [14].

For these reasons, since the mid-2000s, BPA has been performed instead of administering medications that do not have sufficient efficacy in CTEPH patients who are not suitable candidates for PEA. Mizoguchi et al. reported significant improvements in the mPAP, pulmonary vascular resistance, 6-minute walking distance, and BNP level during a maximum of 7 years of follow-up after 255 BPA sessions in 68 patients with CTEPH [2]. Pulmonary hypertension does not become symptomatic until there is substantial progression of pulmonary lesions, due to numerous pulmonary vascular beds. However, once patients reach the symptomatic stage, pulmonary arterial pressure increases precipitously. On the other hand, with even a slight increase in the number of pulmonary vascular beds, a decrease in pulmonary arterial pressure can reasonably be expected after symptoms onset.

BPA is a relatively new technology, and no report has described the interval between the diagnosis of CTEPH and BPA treatment for CTEPH. In our patient, with the peripheral form of CTEPH, who was considered eligible for BPA owing to no expectation of improvement with medications, BPA was performed. This treatment, despite being performed 6 years CTEPH diagnosis, resulted in improvements in the mPAP BNP level, and clinical symptoms. In our patient with peripheral form of CTEPH, further additional BPA sessions are scheduled with the an aim of maintaining mPAP of 30 mmHg in order to improve the prognosis [6]. Treatment with BPA should be considered in patients receiving long-term medical treatment for the peripheral form of CTEPH.

In conclusion, we experienced a patient with the peripheral form of CTEPH. BPA was confirmed to be effective in this patient, despite being performed 6 years after disease onset. BPA should be considered as a treatment option for the peripheral form of CTEPH.

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None

CONFLICTS OF INTEREST

The authors declare that there is no conflict of

interest.

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