Balloon Pulmonary Angioplasty in Chronic Pulmonary Thromboembolic Pulmonary Hypertension

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INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease, caused by obstruction and incomplete resolution of thrombus and further remodeling of the pulmonary artery. The treatment of CTEPH depends on the location of the obstruction and its surgical accessibility.1 In operable CTEPH, pulmonary endarterectomy (PEA) remains the treatment of choice.1 In the authors’ experience, PEA may be conducted safely with a relatively low risk, and patients who undergo successful PEA have a significant improvement in their clinical status and hemodynamic data.2 However, in patients with inoperable CTEPH, lifelong anticoagulant use is recommended, as well as riociguat. In addition, balloon pulmonary angioplasty (BPA) is emerging as a promising alternative treatment option, with hemodynamic and functional improvement and acceptable complication rates.1 The present study reports the first case of inoperable CTEPH receiving BPA treatment in Taiwan.

CASE REPORT

In September 2013, a 58-year-old man presented with exertional dyspnea, which had continued for 6 months. Initially, exertional chest tightness was found, however it progressed to chest pain with palpitations. The patient also reported having varicose veins across bilateral legs for several years previously but was otherwise healthy before the documented acute pulmonary embolism episodes. There was no family history of genetic disease or relevant coagulation disorders.

The patient visited the National Taiwan University Hospital outpatient clinic for evaluation, and a series of examinations were performed. During the physical examinations, engorged jugular vein and right ventricular heave were noted, however in auscultation the breath sounds were clear. The patient’s heartbeat was regular with an accentuated S2 and grade II/VI mid-systolic murmur heard at the left lower sternal border. Chest radiography showed a dilated right atrium (RA) and right ventricle (RV) with an enlarged hilar shadow (Figure 1A). Electrocardiogram revealed normal sinus rhythm with right axis deviation, clockwise rotation, increased p wave amplitude in lead II, and T-wave inversion in the inferior and precordial leads (Figure 1B). Echocardiography showed dilated RA and RV with moderate tricuspid regurgitate and a peak pressure gradient (TRPG) of 96 mmHg. (Figure 1C and D). Right heart catheterization also confirmed the diagnosis of severe pulmonary hypertension with a pulmonary artery pressure (PAP) of 102/45 mmHg (mean 61 mmHg).

Contrast enhanced computed tomography (CT) showed small filling defects in the RA and bilateral inferior segmental pulmonary arteries (Figure 1E and F). A lung ventilation/perfusion (V/Q) scan revealed multiple large segmental or lobar mismatched perfusion defects in both lungs (Figure 1G and J).

Laboratory data, including virology (human immunodeficiency virus, hepatitis B and hepatitis C virus) and rheumatology (anti-nuclear antibody, anti-ribonucleoprotein, anti-centromere protein, anti-topoisomerase I and anti-Smith antibodies) profiles, all showed negative results.
When a diagnosis of CTEPH was reached, the patient received warfarin 2mg HS. Following assessment by a multidisciplinary CTEPH team, it was determined that the patient was not a good PEA surgical candidate, due to poor surgical accessibility and the patient’s willingness.

Sildenafil 25 mg Q12H was administered from December 2013. However, the patient’s symptoms still progressed under medication. Repeat right heart catheterization revealed persistent severe pulmonary hypertension with a PAP of 106/40 mmHg (mean 62 mmHg) and a pulmonary vascular resistance (PVR) of 1,265 dyn·s·cm⁻⁵.

The patient first received BPA on December 30th 2014. Selective pulmonary angiography from the left basal trunk is shown in Figure 2A and B. A 6Fr multipurpose guiding catheter (Mach 1 peripheral MP; Boston Scientific, Natick, MA, USA) was engaged to the left basal trunk, and a 0.014 inch Sion guidewire (Asahi Intec, Aichi, Japan) was advanced to the left posterior basal segmental artery (A10), which was selected as the intervention target. Intravascular ultrasound (IVUS) (Boston Scientific, Marlborough, Massachusetts) was used to determine the vessel size. BPA was performed to the left A10 with a 3.0 × 15 mm Sapphire II balloon catheter (Orbus Neich, Fort Lauderdale, FL, USA) and a 6.0 × 20 mm Sterling balloon catheter (Boston Scientific Medi-Tech, Miami, Florida) (Figure 2C and D). After intervention the pulmonary angiography revealed improved flow at the capillary phase and increased venous return (Figure 2E and F).

The patient received other interventions in the following two years (2015-2016), and his medication was also switched to riociguat in May 2015, due to its ready availability. The 2nd BPA was performed to the left A9 and A10 on January 27th 2015; the 3rd BPA was performed on December 14th 2015 to the right A7 and A8; and the 4th BPA was performed to the right A9 and A10 on January 9th 2016. After serial interventions, the hemodynamic data showed great improvements (Table 1). The mean PAP decreased from 62 mmHg to 29 mmHg, and the PVR decreased from 1,225 dyn·s·cm⁻⁵ to 328 dyn·s·cm⁻⁵. NT-pro-BNP decreased from 523 pg/mL to 26.38 pg/mL, and 6MWD improved from 120 m to 462 m. The NYHA FC also improved from class III to I. Serial echocardiography follow-up also showed decreased RA and RV size and improved pulmonary hypertension (TRPG from 96 mmHg on November 12th 2013 to 29 mmHg on April 7th 2016). The follow-up lung V/Q scan on April 19th 2016 revealed improved perfusion on the bilateral lower lobes. Furthermore, the nuclear first-pass cardiac function dis-
closed improved right ventricle ejection fraction (RVEF) from 38% (December 18th 2013) to 58% (June 15th 2016).

**DISCUSSION**

The present study presents a case of inoperable CTEPH treated by BPA. The first intervention was performed in December 2014. To the best of our knowledge this is the first attempt of BPA in a patient with inoperable CTEPH in Taiwan.

Pulmonary hypertension is a serious disease with a grave prognosis. CTEPH is classified by the World Health Organization (WHO) as a group 4 pulmonary hypertension, and is caused by remodeling due to persistent pulmonary vascular obstruction by thromboembolic material. In operable CTEPH, PEA is the treatment option of choice, however, PEA is still a very uncommon procedure in Taiwan. In the present case the disease location, as estimated by CT and pulmonary angiography, was between level II and III (closer to level III) according to the University of California, San Diego classification system. This presents a more challenging surgical situation, although operating is still a treatment option in an experienced surgical center. In the present case, the team discussed the treatment options with the patient several times, and he selected the non-surgical pathway to treat his disease. A low PEA rate is common in Asia, even in proximal disease; a lack of disease awareness by physicians, misclassification, lack of experienced surgical centers, and personal choices may be some of the reasons for this situation.

The goal of CTEPH treatment is to unload the right ventricle to improve the patient’s clinical symptoms and
quality of life, and to prevent disease progression. However, in cases of inoperable CTEPH there is an unmet need despite state-of-the-art medical therapy that effectively treats the disease. In the Chest 1 clinical trial sub-group analysis of inoperable CTEPH patients revealed that the baseline PVR was 867 ± 471 dyn·sec·cm⁻⁵ and the mean change after 16 weeks riociguat treatment was -257 ± 279 dyn·sec·cm⁻⁵. Only ~31% of patients moved to the lower WHO functional class. This indicates that the majority of patients were still symptomatic with limited exercise tolerance. Therefore, there are still unmet medical needs following the treatment of inoperable CTEPH.

BPA is an emerging treatment for inoperable CTEPH. The first case report of BPA as a treatment for CTEPH was documented by Voorburg et al. in 1988. A case series involving 18 inoperable CTEPH patients was published by Feinstein et al. in 2001, which demonstrated the effectiveness of BPA. However, despite the observed hemodynamic improvements, the complication rate was high. Among 47 episodes of intervention in 18 patients, 11 patients developed reperfusion pulmonary edema and 3 patients required mechanical ventilator support. Recently, Mizoguchi et al. refined the BPA method by using an appropriate balloon size via IVUS guidance and limiting the balloon dilatation to 1-2 pulmonary segments per session, as a staged procedure.

In conclusion, BPA appears to be effective and safe in patients with inoperable CTEPH if performed cautiously as a staged procedure.

LEARNING POINTS
1. The treatment choice for CTEPH depends on the location of the obstruction and the patient’s clinical condition. In operable CTEPH, pulmonary endarterectomy (PEA) is the treatment of choice.
2. In inoperable CTEPH, there is an unmet medical need for an effective medical therapy. Balloon pulmonary angioplasty (BPA) is the emerging choice with promising hemodynamic and functional outcomes.
3. Following refinement of the procedure, and advances in skills and equipment, the complication rate of BPA has reduced. It is an effective and safe treatment option for inoperable CTEPH when performed cautiously as a staged procedure.

DECLARATION OF CONFLICT OF INTEREST
All the authors declare no conflict of interest.
REFERENCES


