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CASE REPORT

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Combination of rescue balloon pulmonary angioplasty and riociguat therapy for chronic thromboembolic pulmonary hypertension with nonsustained polymorphic ventricular tachycardia: A case report

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Abstract

We encountered a case of frequent nonsustained polymorphic ventricular tachycardia (NSPVT) due to hemodynamically unstable chronic thromboembolic pulmonary hypertension (CTEPH). A 78-year-old woman was taking anticoagulants for CTEPH. She had refused specific treatment for CTEPH, including pulmonary vasodilators, because she was then asymptomatic. She fell and sustained a femoral neck fracture, and she was referred to our hospital in anticipation of a surgical repair. Her condition on admission was complicated by respiratory failure, and electrocardiogram monitoring showed frequent NSPVT. A right heart catheterization revealed high mean pulmonary artery pressure with severely reduced cardiac output. Pulmonary angiography showed bilateral stenosis and multiple obstructions. Because NSPVT was attributed to low cardiac output syndrome caused by CTEPH, rescue balloon pulmonary angioplasty (BPA) was performed, and riociguat treatment was initiated. Afterward, the NSPVT resolved. This case suggests that the combination of rescue BPA with riociguat therapy might be an immediate and effective treatment for patients with inoperable CTEPH and severe hemodynamic instability.

KEYWORDS
balloon pulmonary angioplasty, chronic thromboembolic pulmonary hypertension, ventricular tachycardia

CASE DESCRIPTION

A 78-year-old woman was diagnosed with chronic thromboembolic pulmonary hypertension (CTEPH) after an investigation of heart enlargement on radiography. During anticoagulant treatment with apixaban for 1 year, an increase in trans-tricuspid pressure gradient to 71 mmHg on echocardiography suggested worsening pulmonary hypertension. However, she refused further examination and treatment,

including pulmonary vasodilators, because she was asymptomatic at that time.

The patient was transferred to our hospital for surgical repair of a femoral neck fracture 15 months after the diagnosis of CTEPH. On admission, her blood pressure was 129/90 mmHg, and oxyhemoglobin saturation was 96% under oxygen inhalation of 9 L/min. Electrocardiogram monitoring revealed frequent nonsustained polymorphic ventricular tachycardia (NSPVT) with a prolonged QT interval and negative T waves (Figure 1a,b; Supporting Information: Figure S1). Laboratory findings indicated an elevated B-type natriuretic peptide level (808.3 pg/mL) with normal thyroid function. The serum potassium and corrected calcium levels were 4.2 mmol/L and 8.6 mg/dL, respectively. Transthoracic echocardiography revealed right ventricular enlargement with a trans-tricuspid pressure gradient of 70 mmHg and severely reduced right ventricular function (Supporting Information: Video A). Enhanced computed tomography revealed right ventricular enlargement without fresh thrombus in the pulmonary artery (Figure 1c). The patient consented to further examinations and treatments in anticipation of an immediate and safe surgical femoral neck repair. Coronary angiography, right heart catheterization, and pulmonary angiography were urgently performed to investigate the cause of frequent NSPVT. No coronary stenoses were observed; however, right heart catheterization revealed a high mean pulmonary arterial

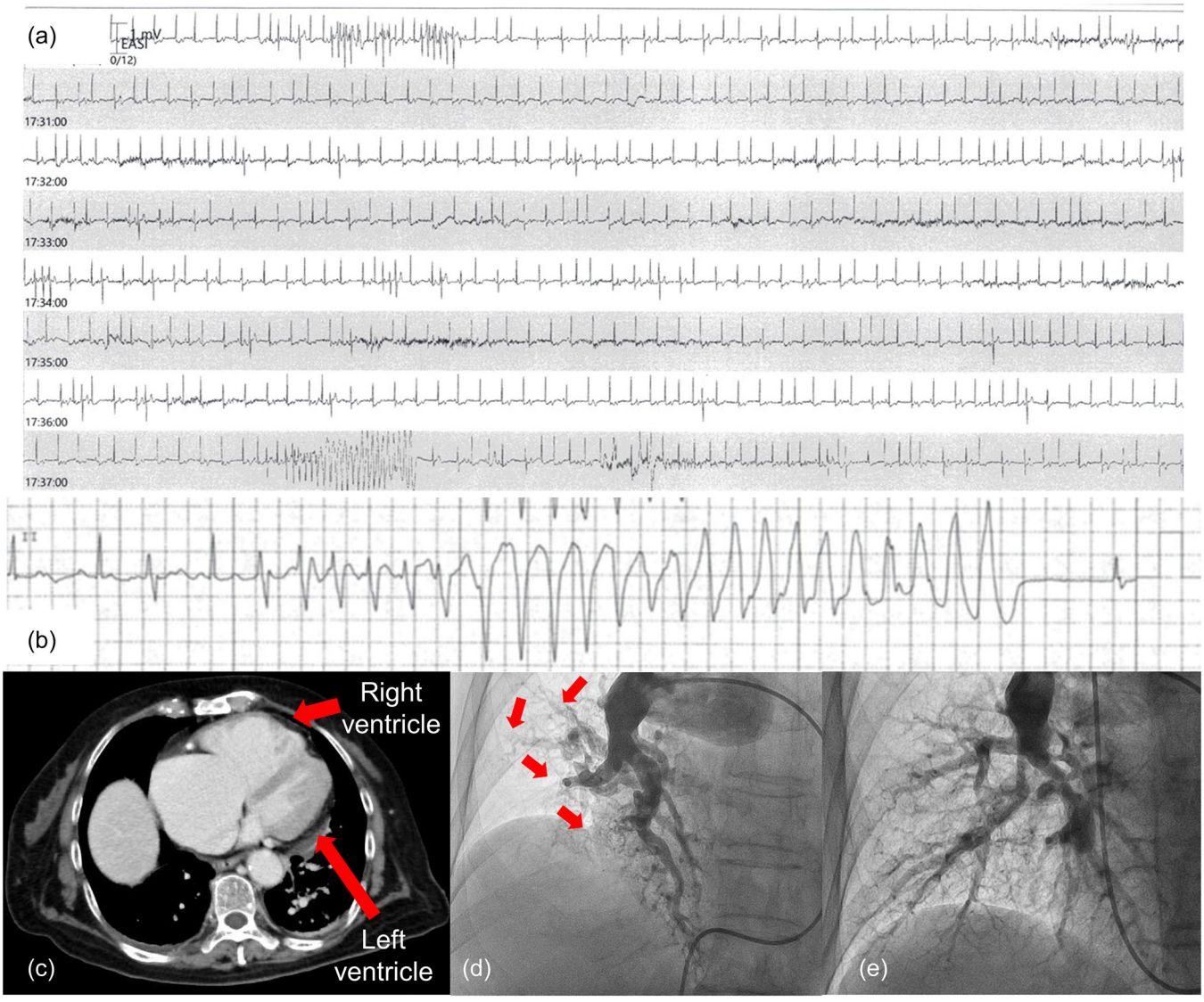

FIGURE 1 (a) Electrocardiogram (ECG) monitoring shows frequent nonsustained polymorphic ventricular tachyarrhythmias. (b) Magnified view of a section of ECG monitoring. (c) Enhanced computed tomography shows significant right ventricular enlargement. (d) Pulmonary angiography (PAG) before balloon pulmonary angioplasty (BPA) shows multiple occlusions in the right lung (red arrow). (e) PAG after the four BPA procedures shows that the treated vessels have been opened.

pressure of 34 mmHg with severely reduced cardiac output of 1.5 L/min estimated by the Fick method. Pulmonary angiography revealed multiple subtotal and total occlusions in both lungs (Figure 1d). NSPVT was assumed to be mainly a result of low cardiac output syndrome due to CTEPH. Therefore, rescue balloon pulmonary angioplasty (BPA) was successfully performed for three right segmental pulmonary arteries (A7, A8, A9) without complications. Immediately after BPA, NSPVT completely resolved, and the patient recovered well.

On Day 2 of hospitalization, a 12-lead electrocardiogram revealed improvement in negative T waves (Supporting Information: Figure S2). Oral riociguat 3.0 mg was initiated and titrated to a dose of 7.5 mg daily. Three additional BPAs were administered on hospitalization Days 6, 9, and 10; nine segments of the right lung and five of the left were treated with four BPAs. The patient's respiratory condition gradually improved, and nasal oxygen inhalation was reduced to 1 L/min by Day 15. Transthoracic echocardiography after four BPAs showed improvements in right ventricular function and enlargement (Supporting Information: Video B). On Day 17, total left hip arthroplasty was performed, and her hemodynamic and respiratory status remained stable both intraoperatively and postoperatively. A 12-lead electrocardiogram showed improvement in the prolonged QT interval on Day 22 (Supporting Information: Figure S3). Follow-up right heart catheterization and pulmonary angiography were performed on Day 49 (Figure 1e). The patient's hemodynamic parameters improved: mean pulmonary arterial pressure and cardiac output were 35 mmHg and 4.62 L/min, respectively (Supporting Information: Table S1). The patient was transferred to another hospital on Day 50 for further rehabilitation.

DISCUSSION

The optimal treatment of patients with severe CTEPH and hemodynamic instability remains an area of debate. Pulmonary endarterectomy (PEA) is a potentially curative treatment for operable CTEPH.[1] Thus, PEA should be considered for operable patients, even those with severely compromised hemodynamics. However, our patient had predominantly distal lesions, and our institution's surgeons had less experience treating such patients with severely compromised hemodynamics in emergencies. In addition, using riociguat alone, excessive time may be required to achieve hemodynamic improvements sufficient for surgical femoral neck repair. Therefore, we decided to perform BPA first and then initiate combination therapy with riociguat.

The efficacy and safety of rescue BPA in patients with severely compromised hemodynamics remain unclear. Previous reports demonstrated that rescue BPA effectively improved hemodynamics and facilitated withdrawal from extracorporeal membrane oxygenation in CTEPH patients with severely compromised hemodynamics.[2,3] In contrast, another article reported that two of three patients with CTEPH after PEA died after rescue BPA for persistent severe pulmonary hypertension.[4] Because BPA can be a high-risk procedure, rescue BPA for patients with CTEPH and severely compromised hemodynamics should be performed only at well-experienced BPA centers after a thorough indication evaluation by a multidisciplinary team. In this case, we attempted to treat a limited number of simple lesions with undersized balloons to avoid pulmonary vascular injury during the first and second BPAs. The only complication was a tiny pulmonary vascular injury that did not affect the patient's respiratory condition during the fourth BPA.

In this case, NSPVT resolved immediately after BPA without administration of antiarrhythmics, including magnesium. Considering the suppression of NSPVT with a left bundle branch block pattern, indicating an origin from the right ventricle, and the subsequent electrocardiogram changes, NSPVT and the prolonged QT interval on admission may have reflected hemodynamic instability due to CTEPH. In addition, we should consider all routine oral medications; quetiapine fumarate could have been related to the prolonged QT interval. In the present case, the combination of rescue BPA and riociguat therapy was effective for an inoperable patient with frequent NSPVT due to low cardiac output syndrome caused by CTEPH. However, the mechanism of this rapid and favorable therapeutic response is speculative. While hemodynamic improvements have been reportedly observed a few weeks after BPA,[5,6] some reports have indicated improvement in cardiopulmonary exercise testing and cardiac output within a few days after BPA.[7,8] Although hemodynamic parameters could not be evaluated immediately after BPA in our patient, some subsequent hemodynamic improvements, especially in cardiac output, may be attributed to the greater synergistic effect of the combination of BPA and riociguat compared with the effects of BPA or riociguat alone.

In this case, the combination of rescue BPA and riociguat therapy immediately and effectively alleviated NSPVT due to low cardiac output syndrome caused by CTEPH and stabilized hemodynamic parameters, suggesting that it could be a treatment option for such patients ineligible for PEA. However, because BPA can

be a high-risk procedure, it should be performed only at well-experienced BPA centers.

AUTHOR CONTRIBUTIONS

Yoshitake Fukuda was the attending physician and wrote the first draft of the manuscript. Hiroto Shimokawahara determined the indication for BPA and performed all BPAs. He revised the manuscript and contributed much to the second draft of the manuscript. Shunsuke Chikama examined the patient on admission, conducted echocardiography, and was involved in post-BPA care. Atsuyuki Watanabe reviewed and revised the manuscript, especially regarding ventricular arrhythmias. Hiromi Matsubara assisted with the first BPA. He also reviewed and revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

Dr. Hiroto Shimokawahara received lecture fees from Bayer Yakuhin and Nippon Shinyaku, and received research funding from Bayer Yakuhin. Dr. Hiromi Matsubara received lecture fees from Bayer, Nippon Shinyaku, Janssen, Mochida Yakuhin, Kaneka Medix, and Merck Sharp and Dohme. Dr. Hiromi Matsubara is involved in collaborative research with Nippon Shinyaku.

ETHICS STATEMENT

Written consent was delivered by the patient to publish patient information and images.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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