Pulmonary Artery Hypertension after Arteriovenous Fistula Creation Subsequently Resolved by Closure of the Fistula

Ryushin Matsuda¹,², Kohei Ashikaga², Yukio Sato², Keisuke Kida³, Yuki Ishibashi², and Yoshihiro J. Akashi²

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Abstract
An 83-year-old woman with end-stage renal disease (G5) received a left forearm arteriovenous (AV) shunt for vascular access 5 years before the current presentation. She had previously been hospitalized 12 times for heart failure but had not been admitted after creation of the fistula. Her renal function was maintained even with end-stage disease, and hemodialysis had been avoided. During a recent admission for heart failure treatment lasting approximately 3 weeks, an exacerbation of pulmonary hypertension (PH) was observed, and her prescriptions, including diuretics, were adjusted. Her medical condition improved, and she was discharged from the hospital under close observation. After discharge, dyspnea on effort gradually worsened. She presented again with dyspnea at rest and was readmitted for further examination and treatment for hypoxia. Transthoracic echocardiography revealed increased right ventricular systolic pressure caused by tricuspid regurgitation, suggesting exacerbation of her PH. After various examinations, we hypothesized that changes in hemodynamics resulting from the AV shunt might be affecting the onset and exacerbation of PH, so we closed the AV fistula. Right heart catheterization performed before and after shunt closure showed mean pulmonary artery pressures of 46 mmHg before closure and 37 mmHg after closure. We report a case of PH with challenging clinical management and hemodynamic changes associated with AV shunt creation.

Key words
Pulmonary hypertension, shunt, chronic heart failure, chronic kidney disease

Introduction
The Japanese guidelines for the treatment of pulmonary hypertension (PH) were revised in 2017 and divided PH into 5 categories based on the Nice classification¹. In this classification, group 5 includes PH with unclear multi-factorial mechanisms for which it is often difficult to identify the main trigger.

In the present case, the patient had suffered from chronic heart failure and kidney disease due to ischemic cardiomyopathy for more than 10 years, and an arteriovenous (AV) shunt was created for future hemodialysis. However, her renal function was maintained even in end-stage disease, and she never underwent hemodialysis. During the 5 years since AV shunt creation, PH had developed and worsened. From the clinical course and test results, we identified the AV shunt as causing increased venous return that worsened her PH. Subsequent closure of the AV shunt improved her symptoms and hemodynamics. It is quite rare for hemodialysis not to be required for more than 1 year after shunt creation. This report presents an interesting case in which an internal AV shunt is believed to have worsened PH.

1 Department of Internal Medicine, Shizuoka City Shizuoka Hospital
2 Division of Cardiology, Department of Internal Medicine, St. Marianna University School of Medicine
3 Department of Pharmacology, St. Marianna University School of Medicine
Case report

Patient: An 83-year-old woman.

Chief complaint: Dyspnea.

History of the present illness: The patient had multiple presentations for chronic heart failure associated with old myocardial infarction and chronic atrial flutter. She had been hospitalized 12 times but had not been admitted for 5 years after creation of the AV shunt. Meanwhile, her activities of daily living were impaired, and dementia had progressed, which led to gradual weight loss over several years. After 5 years without hospitalization, she was admitted for approximately 3 weeks to treat worsened hypoxemia. Exacerbation of her PH, which was diagnosed at our outpatient clinic, was confirmed. Her condition was improved by adjusting her diuretics, and she was discharged. At that time, dyspnea was observed with a walk of 50 m. Afterward, her dyspnea gradually worsened. She presented with dyspnea at rest 10 days after discharge, at which time she was readmitted for examination and treatment of hypoxemia due to her deteriorating oxygenation capacity.

Past medical history: Her medical history included a previous myocardial infarction (for which she received coronary artery bypass surgery), chronic heart failure (treated with home oxygen therapy), chronic atrial flutter, stage 5 chronic kidney disease (for which a left forearm AV shunt had been prepared 5 years previously), and type 2 diabetes mellitus.

Medications: Current medications included warfarin potassium, 2 mg; furosemide, 20 mg; tolvaptan, 15 mg; diltiazem hydrochloride, 100 mg; bisoprolol fumarate, 1.25 mg; pimobendane, 5 mg; teneligliptin hydrobromide hydrate, 20 mg; ezetimibe, 10 mg; atorvastatin calcium hydrate, 10 mg; febuxostat, 40 mg; and rabeprazole sodium, 10 mg.

Family history: Unremarkable.

Clinical findings on admission: The patient’s level of consciousness was clear. Her height was 143 cm and weight was 56.3 kg. Blood pressure was 138/62 mmHg with a heart rate of 65 bpm, and her body temperature was 36.4°C. Her respiratory rate was 24/min and peripheral artery oxygen saturation was 84% on O₂ at 2 L/min by nasal cannula. A jugular venous pulse was palpable, and wet rales were heard on auscultation. Systolic murmurs of Levine Grade 2 were heard at the third intercostal space at the left sternal border. Pitting edema was observed in both lower legs.

Laboratory findings on admission: Hematological examinations included white cell count (8,900/μL), red cell count (365×10⁶/μL), hemoglobin (11.2 g/dL), hematocrit (40.4%), platelet count (157×10⁴/μL), total protein (5.8 g/dL), bilirubin (0.9 g/dL), aspartate aminotransferase (23 IU/L), alanine aminotransferase (16 IU/L), lactic acid dehydrogenase (292 IU/L), alkaline phosphatase (194 IU/L), γ-glutamyl transpeptidase (20 IU/L), creatinine (2.43 mg/dL), blood urea nitrogen (72.2 mg/dL), Na⁺ (134 mEq/L), K⁺ (3.6 mEq/L), Cl⁻ (102 mEq/L), creatine kinase (33 IU/L), cardiac troponin (0.087 ng/mL), C-reactive protein (0.69 mg/dL), and N-terminal pro b-type natriuretic peptide (22528 pg/mL).

Arterial blood gas analysis on O₂ at 4 L/min via face mask revealed pH = 7.305, PCO₂ = 38.5 mmHg, PO₂ = 76.1 mmHg, HCO₃⁻ = 18.6 mmol, actual base excess = −6.7 mg/dL, and standard base excess = −6.6 mg/dL. Chest X-ray findings included a 66% cardiothoracic ratio, cardiac dilatation, protrusion of the right pulmonary artery, and a blunted right costophrenic angle (Figure 1A). Standard 12-lead electrocardiograms revealed a heart rate of 76 bpm, 4:1 common atrial flutter, and intraventricular conduction disturbance (Figure 1B). Transthoracic echocardiograms showed reduced wall motion in the left ventricular lower wall and dilatation of the right atrium and ventricle; the left ventricular ejection fraction (LVEF) was 44.7%. Mild to moderate aortic valve stenosis, functional mitral regurgitation, and moderately tricuspid regurgitation were also observed. Right ventricular systolic pressure (RVSP) estimated from tricuspid regurgitation was 86 mmHg. The inferior vena cava diameter was 29 mm with no changes during respiration.

Clinical course: The patient’s weight observed 19 days before admission was 52.7 kg, with a rapid subsequent increase to 56.3 kg on admission. Therefore, a presumptive diagnosis of biventricular heart failure was made. As an initial treatment, carperitide and additional diuretics were administered, but no significant improvement was observed. On the 6th hospital day, transthoracic echocardiograms revealed a RVSP of 119 mmHg and LVEF of 30%, suggesting deterioration of PH and reduced left ventricular systolic function. Result of indwelling right heart catheterization results included mean pulmonary artery pressure (mPAP) = 46 mmHg, pulmonary artery wedge pressure (PAWP) = 14 mmHg, and pulmonary vascular resistance (PVR) = 9.0 (Table 1). To evaluate PH-associated left heart disease (group 2 by Nice classification), a water loading test was considered; however,
Figure 1. Chest X-ray and standard 12-lead electrocardiograms on admission.
A: Chest X-ray shows a cardiothoracic ratio of 66%, cardiac dilation, protrusion of the right pulmonary artery, and a dull right costophrenic angle.
B: Standard 12-lead electrocardiograms revealed a heart rate of 76 bpm, 4:1 normal atrial flutter, and intraventricular conduction disturbance.

Figure 2. Transthoracic echocardiograms on admission.
Flattening of the interventricular septum was observed.

her low oxygen level while on O\textsubscript{2} at 8 L/min precluded performance of the test. The patient was under-diuresed and overhydrated. Because her PAWP was not underestimated, group 2 by Nice classification (left heart disease) was not a likely main cause. Therefore, we considered the possibility of pulmonary arterial hypertension, group 1 by Nice classification. She had no remarkable family history, and connective tissue disease markers (antinuclear antibodies and various autoantibodies) were negative. No findings of portal hypertension or congenital heart disease were observed, and an idiopathic cause could not initially be ruled out. Then, taking the AV shunt into consideration, we presumed that reversible improvement might be achieved by shunt intervention. There were no other specific findings suggesting PH of group 1 by Nice classification. Moreover, there were no obvious findings suggestive of pulmonary disease on chest computed tomography or reduced accumulation on pulmonary blood flow scintigrams.
Accordingly, PH of groups 3 and 4 by Nice classification was ruled out. As her RVSP had been elevated ever since creation of the AV shunt 5 years before, and her general condition was consistent with the time course of PH, we presumed that increased venous return due to the AV shunt might be affecting the PH. Because her left ventricular function was decreasing, we concluded that the AV shunt was no longer usable. Thus, on the 13th hospital day, we performed AV shunt closure. After closure, her RVSP gradually decreased to 74.3 mmHg on the 27th hospital day (Figure 3). On the 26th hospital day, right heart catheterization revealed a decreased mPAP (37 mmHg) and improvement her PH. Diuretic doses were also reduced, and her PAWP was 8 mmHg and PVR was 9.4 (Table 1). Following confirmation of the improvement of her PH and oxygenation level, we discharged her on the 39th hospital day.

Discussion

The present case shows PH caused by blood flow changes due to AV shunt deployment. This case is quite rare because hemodialysis had not been performed for 5 years after the AV shunt was created. Because results of right heart catheterization under overhydration did not meet the criteria for post-capillary PH (PAWP <15 mmHg), we suspected main causes other than PH associated with left heart disease. These other mechanisms of PH and the other causative diseases met the criteria for group 5 by Nice classification, particularly tumor embolism, fibrous mediastinitis, chronic renal failure, and segmental PH. The focal point of this case was how to consider the influence of PH in this patient with Group 2 left heart failure based on her past medical history and cardiac function. In this case, diastolic pressure gradients (DPG; diastolic PAP – PAWP) before and after the shunt closure procedure were 8 mmHg and 22 mmHg, respectively. These values did not meet the criteria of PH due to elevated pulmonary venous pressure (post-capillary PH), which is a DPG of < 7 mmHg2). In PH with left heart failure, the concept of combined pre- and postcapillary PH, which includes precapillary PH due to pulmonary artery remodeling, is recognized. However, the PAWP in this case did not meet the criteria. Thus, we identified from the clinical course that the main pathophysiology of PH might be due to pulmonary artery remodeling following creation of the AV shunt rather than the effect of left heart failure.

Internal shunt creation increases venous return. When venous return increases, right ventricular output also increases, leading to elevation of the systolic pulmonary artery pressure. To date, several case reports have suggested the possible onset of PH in patients with AV shunts who are undergoing maintenance hemodialysis; however, no significant differences in the onset of PH were identified in those studies3–5). A significant correlation between blood flow in a shunt and pulmonary arterial pressure has been reported6). Blood flow in our patient’s shunt was sufficient (1200 mL/min; general value: 500–1000 mL/min7). Accordingly, we presumed that right heart overload might be associated with the onset of PH. Pulmonary intimal thickening and vascular wall remodeling of the peripheral small pulmonary arteries might have

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Table 1. Right Heart Catheter Findings

| 6th hospital day  | 26th hospital day  |
|------------------|-------------------|
| (before shunt closure) | (after shunt closure) |
| BP (mmHg) | 111/58 | 106/70 |
| CI (L/min/m²) | 2.3 | 2.0 |
| CO (L/min) | 3.5 | 3.0 |
| PAWP (mmHg) | 14 | 8 |
| PAP (mmHg) | 78/22 (46) | 56/30 (37) |
| RA (mmHg) | 14 | 8 |
| PVR (Wood units) | 9.0 | 9.4 |

BP: blood pressure, CI: cardiac index, CO: cardiac output, PAWP: pulmonary artery wedge pressure, PAP: pulmonary artery pressure, RA: right atrial pressure, PVR: pulmonary vascular resistance.
gradually progressed due to the long-term overload on the pulmonary artery, leading to elevation of the PVR. In this case, PH had slowly worsened over the 5 years after the AV shunt creation, and during that time, remodeling had also progressed that had elevated her PVR. The mechanism of onset of PH caused by long-term overloading in a shunt is quite similar to that of portal hypertension or pulmonary arterial hypertension due to congenital heart disease. An elevated PVR in those conditions suggests poor prognosis. Our patient’s elevated PVR was a result of pulmonary artery remodeling, and thus, PVR did not improve after the shunt closure. In the discharge assessment, our patient’s mPAP was 27 mmHg and PH was still evident; therefore, we estimated that her prognosis would be poor. This case suggests that the use of pulmonary vasodilators should be considered in patients with pulmonary arterial hypertension when right heart failure worsens.

**Conclusion**

In this case, PH was initiated by AV shunt creation and was improved after shunt closure. Based on the patient’s clinical course and hemodynamic evaluation, more than sufficient blood flow in the shunt triggered overload in the right heart, and over the long clinical course, it had also induced pulmonary artery remodeling, which appeared to be the main causes of her PH.

**Conflicts of Interest**

The authors have nothing to disclose.
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