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CASE REPORT

Pulmonary hypertension in stiff left atrial syndrome: pathogenesis and treatment in one

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Abstract

We present the rare case of a patient with pulmonary hypertension in the context of the stiff left atrial syndrome after extensive catheter ablation, a unique constellation characterized by high pulmonary artery and pulmonary artery wedge pressures due to left atrial dysfunction but normal left ventricular end-diastolic pressure, normal mitral valve, and absence pulmonary vein stenosis. This patient was surprisingly oligosymptomatic, however, which may have been due to a persistent post-puncture atrial septal defect, which may have allowed for controlled left atrial decompression, which is in line with the novel concept of the catheter-based creation of an intracardiac shunt as a treatment for heart failure.

Keywords Pulmonary hypertension; Post-capillary; Left atrium; Catheter ablation

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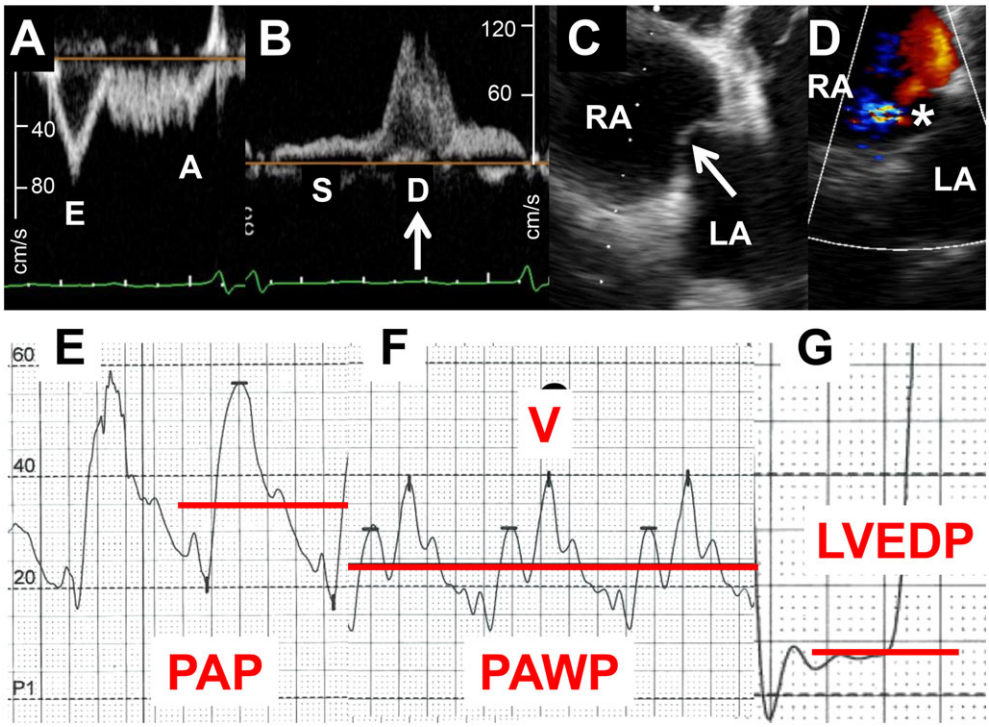
Introduction

In patients with suspected pulmonary hypertension (PH), confirmation of the diagnosis by right heart catheterization and an exact definition of the underlying haemodynamic constellation by findings from cardiac catheterization and non-invasive imaging are a prerequisite for an appropriate management.[1] Pulmonary arterial hypertension (PAH) is a rare disease, and the majority of PH patients have PH in the context of left heart disease.[1] Importantly, administration of specific PAH therapies in patients with PH due to left heart diseases even can cause harm.[2] Herein, we present the case of a patient with PH in the context of the stiff left atrial syndrome.[3–5] The aim of this case presentation is, on the one hand, to describe this rare disease and, on the other hand, to highlight the importance of a systemic diagnostic approach to the patient with suspected PH using a combination of invasive haemodynamics and non-invasive imaging.

Case report

In 2016, a 68-year-old man with previous catheter ablation procedures for atrial fibrillation and flutter including extensive ablation within the left atrium in 2006 and 2008 was referred for cardiac catheterization because of an elevated systolic pulmonary artery pressure (PAP). The patient was oligosymptomatic (New York Heart Association functional class I–II). Specifically, he was able to perform hikes in the mountains with elevation gains up to 1000 m without major problems. Still, serial echocardiograms had revealed a continuously rising systolic PAP over a period of 3 years (2014, 40 mmHg; 2015, 55 mmHg; and 2016, 65 mmHg). Plasma B-type natriuretic peptide (BNP) was 25 ng/L. Transthoracic and transesophageal echocardiography showed normal left ventricle size (left ventricular end-diastolic diameter, 50 mm) and ejection fraction (left ventricular ejection fraction, 55%) and dilated atria (left atrial volume index, 37 mL/m^2; right atrial volume index, 38 mL/m^2). The ratio of the peak early (E) to atrial (A) transmitral velocities (E/A) was 1.8 (*Figure 1A*), the average (medial and lateral annulus) peak early mitral annular velocity was 8 cm/s, and E/e′ was 10. A diastolic-dominant pulmonary venous flow (systolic to diastolic peak flow ratio: 0.2; *Figure 1B*) and a very pronounced atrial septal bulge to the right throughout the cardiac cycle (*Figure 1C*) suggested high left atrial pressure. The right ventricle was mildly dilated (basal diameter 45 mm), and right ventricular function was normal (tricuspid annular plane systolic excursion, 24 mm; right ventricular peak systolic

Figure 1 (A) Transesophageal echocardiography with pulsed-wave Doppler signal of mitral inflow: there is no significant left ventricular diastolic dysfunction, and there is no evidence of mitral stenosis. E, peak early transmitral velocity; A, peak atrial transmitral velocity (also see text for more detailed description). (B) Transesophageal echocardiography showing abnormal pulmonary venous flow: there is predominantly diastolic (D) forward flow (arrow), while normally systolic (S) flow predominates. (C) Transesophageal echocardiography showing atrial septal bulge to the right (arrow) indicating higher pressure in the left atrium (LA) than in the right atrium (RA) throughout the cardiac cycle. (D) Transesophageal echocardiography showing colour Doppler (asterisk) with flow from the left atrium (LA) to the right atrium (RA). (E–G) Pressure tracings from right and left heart catheterization. (E) Pulmonary artery pressure (PAP). (F) Pulmonary artery wedge pressure (PAWP) with high V waves (V). (G) Left ventricular end-diastolic pressure (LVEDP); same scale in millimetre of mercury for E–G. Please note that zeroing in the LVEDP tracing seems not to be perfect. Thus, we assume an LVEDP of 12 mmHg.



annular velocity, 14 cm/s). Transesophageal echocardiography revealed a small post-puncture atrial septal defect (ASD) with continuous left-to-right shunt (*Figure 1D*), but no significant mitral valve pathology (mean diastolic gradient, 1 mm; minimal regurgitation). Left and right heart catheterization (*Figure 1E–G*) performed via a right radial artery/right brachial vein access revealed a mean arterial pressure of 97 mmHg, a mean right atrial pressure of 10 mmHg, a mean PAP of 35 mmHg, and a mean pulmonary artery wedge pressure (PAWP) of 24 mmHg with large V waves of 40 mmHg, but a left ventricular end-diastolic pressure (LVEDP) of only 12 mmHg, i.e. isolated post-capillary PH with a significant discordance between PAWP and LVEDP. Oxygen saturations in the aorta and pulmonary artery were 97 and 74%, respectively. Based on the Fick principle, this would result in a cardiac output of 5.0 L/min (cardiac index 2.5 L/min/m^2) if the ASD would be ignored. The coronary arteries were normal. Pulmonary vein stenosis was excluded by computed tomography. Integration of the non-invasive and invasive findings (*Figure 2*) led to the diagnosis of PH in the context of a 'stiff left atrial syndrome'. Treatment with anticoagulation and a beta-blocker was continued, and the patient remained stable with normal exercise tolerance during a follow-up of 1 year.

Discussion

The stiff left atrial syndrome is a relatively rare phenomenon (1.4% in the best documented series reported by Gibson *et al.*[3]) typically occurring several years after catheter ablation due to scarring with reduction or loss of left atrial compliance and contractility.[3–5] This complication occurs after extensive ablation also within the left atrium[3] and surgical maze procedures.[4] The stiff left atrial syndrome is defined as the combination of heart failure symptoms, PH, and left atrial dysfunction (typically with large V wave in the PAWP tracing) in the absence of a significant mitral valve pathology.[5] The present case is an excellent example to illustrate the diagnostic challenges sometimes encountered in patients with suspected PH. Right heart catheterization clearly revealed isolated post-capillary PH, which, in the presence

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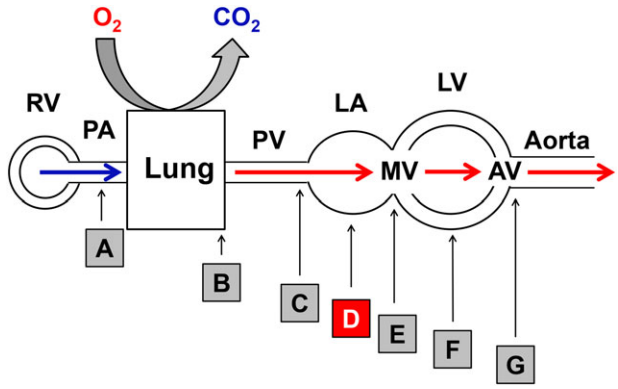
Figure 2 Schematic representation of the anatomic levels of 'obstruction' (A–G) in different forms of pulmonary hypertension, each characterized by a distinct haemodynamic profile (modified from Maeder *et al.*[1]). (A) Pulmonary arterial hypertension or pulmonary hypertension associated with lung disease: high mean pulmonary artery pressure (mPAP), low mean pulmonary artery wedge pressure (mPAWP), and low left ventricular end-diastolic pressure (LVEDP). (B) Pulmonary veno-occlusive disease: high mPAP, normal mPAWP, and low/normal LVEDP. (C) Pulmonary vein stenosis: high mPAP, high mPAWP, low/normal LVEDP, normal left atrial size, and evidence of pulmonary vein stenosis. (D) (Present situation, red), stiff left atrium: high mPAP, high mPAWP, low/normal LVEDP, dilated left atrium, normal mitral valve, and exclusion of pulmonary vein stenosis. (E) Mitral stenosis: high mPAP, high mPAWP, low/normal LVEDP, dilated left atrium, and abnormal mitral valve. (F) Heart failure with reduced or preserved ejection fraction: high mPAP, high mPAWP, high LVEDP, and no aortic valve pathology. (G) Aortic stenosis: high mPAP, high mPAWP, high LVEDP, and aortic valve stenosis. Abbreviations: AV, aortic valve; LA, left atrium; LV, left ventricle; MV, mitral valve; PA, pulmonary artery; PV, pulmonary vein; RV, right ventricle.



of a normal left ventricular ejection fraction, typically would have led to a diagnosis of heart failure with preserved ejection fraction (HFpEF) if no measurement of LVEDP would have been undertaken. The observed discrepancy between PAWP and LVEDP clearly rejected a diagnosis of HFpEF, and the non-invasive findings (borderline e′ and E/e′, low BNP but clearly abnormal pulmonary venous flow, and impressive atrial bulge to the right) were well in line with the invasive haemodynamic data in that they suggested high left atrial pressure but no significant left ventricular diastolic dysfunction. This case highlights the fact that sometimes both right and left heart catheterization is required during the workup of a patient with suspected PH. The classical cause of a high PAWP/low LVEDP constellation is severe mitral stenosis (*Figure 2E*), which was not present in this case, however. We have not performed simultaneous measurement of PAWP and LVEDP, which is a limitation. However, 2D and Doppler echocardiography did not reveal any evidence of mitral stenosis. The second classical cause of this constellation is pulmonary vein stenosis, another well-known complication of previously used techniques for pulmonary vein isolation (*Figure 2C*). Therefore, computed tomography was essential to exclude pulmonary vein stenosis. The combination of history, non-invasive findings, and the haemodynamic information then allowed the diagnosis of a stiff left atrial syndrome (*Figure 2D*). We have not proven the presence of atrial fibrosis by cardiac magnetic resonance imaging. However, the patient's history of extensive ablation also within the left atrium and the detailed non-invasive and invasive haemodynamic assessment were highly suggestive of the presence of a fibrotic non-compliant left atrium. Notably, the left atrium was only mildly dilated, which may indicate that the ablation procedures had led to 'shrinkage' of the left atrium with reduced capacitance.[5]

Treatment of patients with the stiff left atrial syndrome is very challenging and essentially consists of diuretics.[3–5] Interestingly, this patient was oligosymptomatic despite impressive haemodynamics. We assume that the patient benefitted from the fact the he had remained in sinus rhythm (*Figure 1*). Second, the persistence of a small post-puncture ASD may have allowed for controlled left atrial decompression in the presence of a large left-to-right atrial pressure gradient. The herein observed haemodynamics are likely to worsen significantly during exercise with increased venous return to the non-compliant left atrium,[6] and controlled left-to-right atrial shunting may become important particularly on exertion. Notably, the latter principle represents the pathophysiological basis for a promising novel interventional therapy for heart failure, i.e. the catheter-based creation of a 'neo-ASD'.[7,8] In a recent study, this treatment has been shown to attenuate the exercise-associated rise in PAWP and thereby to improve exercise capacity and quality of life in patients with HFpEF,[8] a condition characterized by chronically or periodically (exercise) increased left atrial pressure due to left ventricular diastolic dysfunction.[9] The shunt device used in this trial created an ASD with a diameter of 8 mm,[7] and this led to a left-to-right shunt with a pulmonary to systemic flow ratio of 1.3:1.0 and mild dilation of right-sided chambers after 6 months.[8] Very recently, this principle has, for the first time, been applied to a patient with stiff left atrial syndrom.[10] In this patient with refractory symptoms, atrial septostomy was performed to create a defect of 1.5 × 0.7 cm, which led to a significant clinical improvement but no right heart failure after 1 year.[10] At this time, a left-to-right atrial gradient of 7 mmHg was recorded.[10] In the present case, the relatively high oxygen saturation in the pulmonary artery and the dimensions of the right-sided cavities would fit a certain ASD. However, we have not performed a shunt calculation to prove the presence and to demonstrate the size of a left-to-right shunt. Thus, although the pathophysiological considerations regarding the role of the ASD are plausible, the exact role of the ASA in the present case remains speculative. Still, due to the unique constellation of a patient with few symptoms but strong evidence of a stiff left atrial syndrome, we suspect that the patient suffered from a condition where both its pathophysiology and its treatment were related to the same procedure.

Conflict of interest

None declared.

References

1. Maeder MT, Schoch OD, Kleiner R, Joerg L, Weilenmann D. Pulmonary hypertension associated with left-sided heart diseases. *Swiss Med Wkly* 2017; **147** w14395. doi: https://doi.org/10.4414/smw.2017.14395.
2. Maeder MT, Kleiner R, Weilenmann D. Severely worsening dyspnea after initiation of macitentan therapy for pulmonary arterial hypertension. *Int J Cardiol* 2016; **202**: 244–245.
3. Gibson DN, Di Biase L, Mohanty P, Patel JD, Bai R, Sanchez J, Burkhardt JD, Heywood JT, Johnson AD, Rubenson DS, Horton R, Gallinghouse GJ, Beheiry S, Curtis GP, Cohen DN, Lee MY, Smith MR, Gopinath D, Lewis WR, Natale A. Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors. *Heart Rhythm* 2011; **8**: 1364–1371.
4. Welch TD, Coylewright M, Powell BD, Asirvatham SJ, Gersh BJ, Dearani JA, Nishimura RA. Symptomatic pulmonary hypertension with giant left atrial v waves after surgical maze procedures: evaluation by comprehensive hemodynamic catheterization. *Heart Rhythm* 2013; **10**: 1839–1842.
5. Yang Y, Liu Q, Wu Z, Li X, Xiao Y, Tu T, Zhou S. Stiff left atrial syndrome: a complication undergoing catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2016; **27**: 884–889.
6. Urey MA, Darden D, Stoller D, Drazner MH, Horn V, Sarma S, Levine BD. Stiff left atrial syndrome after multiple percutaneous catheter ablations. Role for invasive hemodynamic exercise testing. *Circ Heart Fail* 2017; **10** e003885.
7. Sondergaard L, Reddy V, Kaye D, Malek F, Walton A, Mates M, Franzen O, Neuzil P, Ihlemann N, Gustafsson F. Transcatheter treatment of heart failure with preserved or mildly reduced ejection fraction using a novel interatrial implant to lower left atrial pressure. *Eur J Heart Fail* 2014; **16**: 796–801.
8. Hasenfuss G, Hayward C, Burkhoff D, Silvestry FE, McKenzie S, Gustafsson F, Malek F, Van der Heyden J, Lang I, Petrie MC, Cleland JG, Leon M, Kaye DM. REDUCE LAP-HF study investigators. A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial. *Lancet* 2016; **387**: 1298–1304.
9. Maeder MT, Thompson BR, Brunner-La Rocca HP, Kaye DM. Hemodynamic basis of exercise limitation in patients with heart failure and normal ejection fraction. *J Am Coll Cardiol* 2010; **56**: 855–863.
10. Chandrashekar P, Park JY, Al-Hijji MA, Reddy YNV, Zack CJ, Reeder GS, Rea RF, Borlaug BA. Atrial septostomy to treat stiff left atrium syndrome. *Circ Heart Fail* 2017; 10e004160.