Right Heart Failure in a Patient with Critical Pulmonary Stenosis, Absent Right Pulmonary Artery, and Lung Cancer

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: **Female, 67-year-old**
Final Diagnosis: **Absence of right pulmonary artery • lung cancer • pulmonary stenosis**
Symptoms: **Abdomen distension • dyspnea • fatigue • right heart failure**
Medication: **—**
Clinical Procedure: **Percutaneous pulmonary valve implantation • radiation therapy • right heart catherization**
Specialty: **Cardiology • Pulmonology**

Objective: **Rare disease**
Background: Unilateral absence of a pulmonary artery (UAPA) is a rare congenital cardiovascular malformation. More than half of UAPA cases have other cardiac lesions such as tetralogy of Fallot or septal defects. Clinical manifestations are diverse and range from heart failure after birth to an incidental finding on chest imaging during adulthood. Whereas early surgical revascularization is recommended in infancy, this is usually not feasible in the adult population. Management in these patients is aimed at treating the complications of UAPA.
Case Report: A 67-year-old woman was evaluated for subacute right heart failure. An echocardiogram revealed pulmonary stenosis, tricuspid regurgitation, and depressed right ventricular function. Chest computed tomography (CT) showed absence of the right pulmonary artery. Additionally, there was a lung tumor in the right upper lobe. Right-heart catheterization confirmed a critically obstructed pulmonary orifice shown by hemodynamic collapse when crossing the pulmonary valve with the catheter. The patient underwent pulmonary valve balloon dilatation with right ventricular outflow tract stenting followed by percutaneous implantation of a balloon-expandable stent-valve. The clinical course was complicated by a complete heart block. Oncologic management consisted of stereotactic radiotherapy.
Conclusions: The combination of UAPA, pulmonary stenosis, and lung cancer is rare. Pulmonary stenosis worsens prognosis in adult patients with UAPA, but also constitutes a therapeutic target. The decision to treat the pulmonary stenosis should be based on the severity of stenosis, the degree of pulmonary hypertension, and individual anatomy. We chose percutaneous pulmonary valve implantation because our patient had a critical pulmonary stenosis with normal pulmonary pressures.

Keywords: **Catheterization, Swan-Ganz • Heart Defects, Congenital • Heart Failure • Pulmonary Valve Stenosis • Atrioventricular Block**
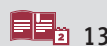
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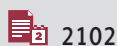
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Background

Congenital unilateral absence of a pulmonary artery (UAPA) is a cardiovascular anomaly with an estimated incidence of 1 in 200 000 individuals [1]. It is caused by involution of the proximal sixth aortic arch, which is destined to become the proximal portion of the pulmonary artery (PA). In contrast, the distal intrapulmonary portion of the PA develops normally and connects to the ductus arteriosus in fetal circulation. After birth and ductal closure, the connection to the extrapulmonary PA is impeded by the proximal interruption, giving rise to a high-pressure, aorto-pulmonary collateral circulation to supply the affected lung. UAPA can occur as an isolated defect, but is frequently combined with other anomalies such as tetralogy of Fallot (TOF), septal defects, coarctation of the aorta, transposition of the great arteries, and pulmonary stenosis (PS) [2]. Isolated UAPA can present with exertional dyspnea, recurrent lung infections, or hemoptysis, but is often diagnosed as an incidental finding in adulthood. Congestive heart failure usually develops at an earlier stage if UAPA is accompanied by other congenital lesions. Early revascularization during infancy, either by a primary anastomosis between the main PA and the intrapulmonary PA or by a surgical shunt, is recommended because it prevents complications of UAPA. However, adults with UAPA are generally not good candidates for revascularization. Management strategies in this patient population are mainly symptom-based and consist of pharmacological treatment for pulmonary hypertension, selective embolization of collateral arteries, and lobectomy or pneumonectomy [3].

Right ventricular outflow tract (RVOT) obstruction or PS is classified according to the level of obstruction (subvalvular, valvular, and/or supravalvular), etiology (usually congenital, rarely acquired) and presence of associated lesions. It can remain asymptomatic or manifest with exertional dyspnea, chest pain, or syncope. Transcatheter balloon valvuloplasty is the first-choice intervention in valvular and supravalvular RVOT obstruction in patients with suitable anatomy [4]. Limitations of pulmonary balloon dilatation are recoil in resistant lesions and need for re-intervention due to residual stenosis. Percutaneous pulmonary valve implantation (PPVI) with RVOT pre-stenting was originally approved for dysfunctional pulmonary conduits in surgically-corrected congenital heart disease. In recent years, this technique is increasingly used to treat native RVOT obstruction [5]. Periprocedural complications such as coronary artery compression or RVOT rupture are rare. Stent fracture and infective endocarditis are the main concerns during follow-up [6].

In this article, we present a unique case of an absent right PA combined with valvular PS and lung malignancy in a patient presenting at an older age. We show that PPVI is a non-invasive therapeutic option for these complicated patients.
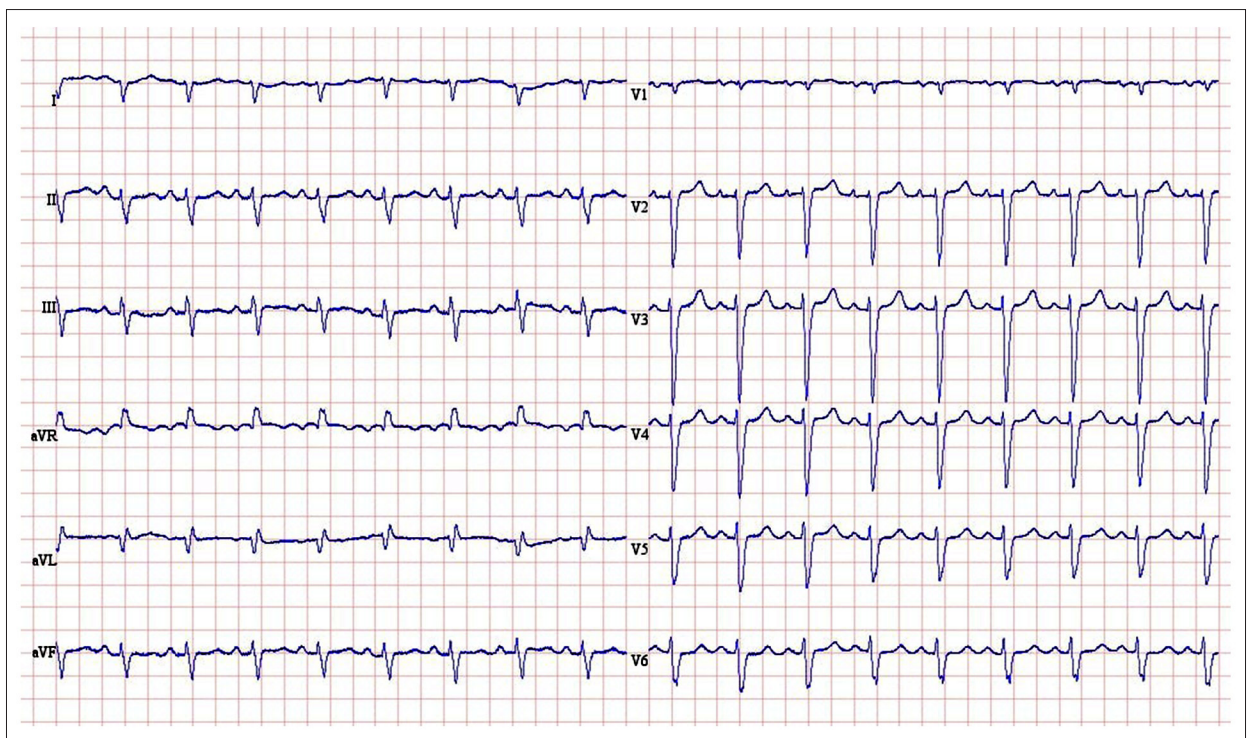

Figure 1. Baseline ECG. ECG shows a sinus tachycardia with normal AV conduction (PR interval 162 ms) and broad QRS complex (116 ms), suggesting an intraventricular conduction delay. The extreme axis deviation (223 degrees), the dominant S-waves in leads I, II, and III ("S1S2S3 pattern"), and the deep S-waves in leads V5 and V6 are consistent with RV disease.
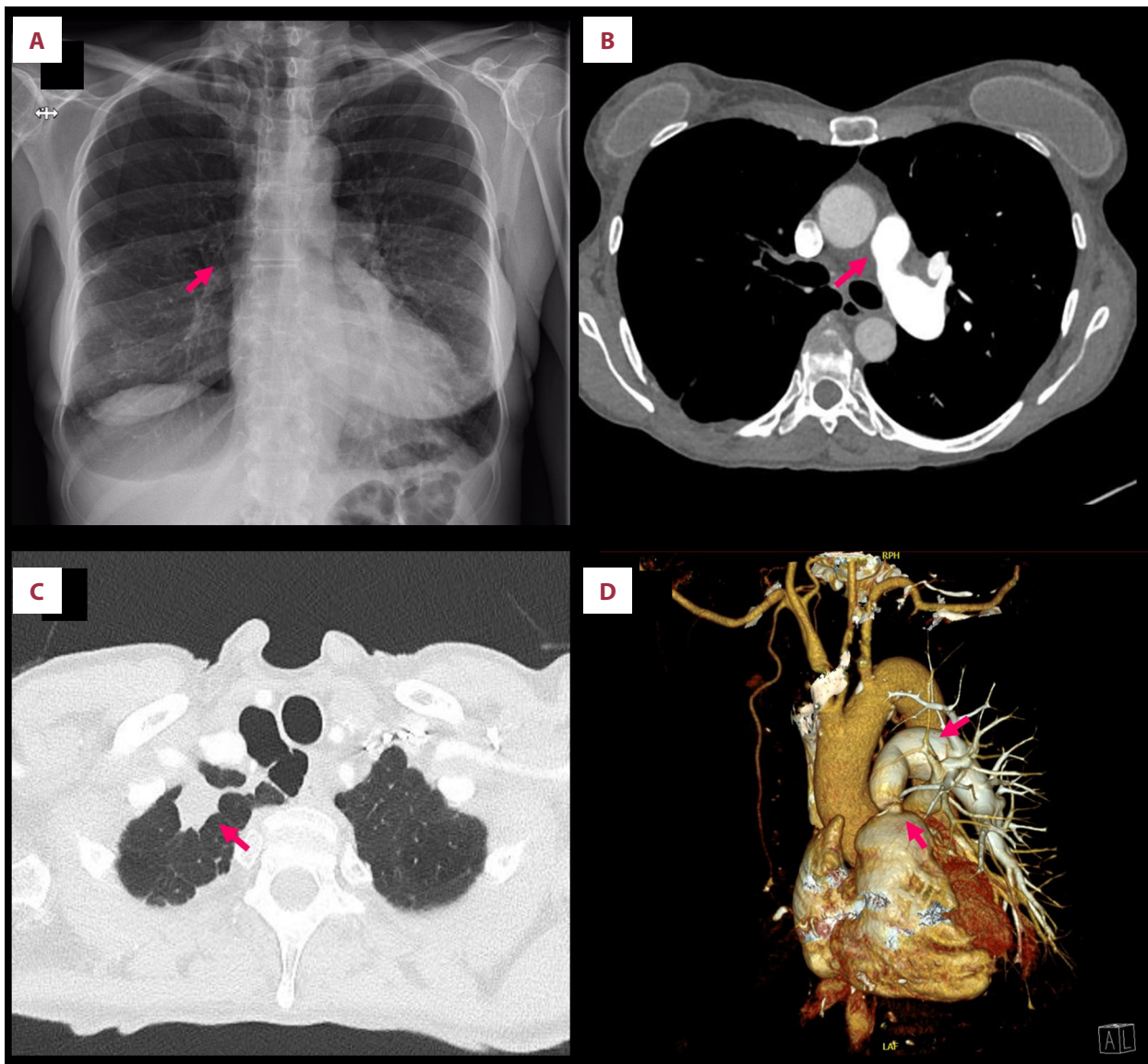
Figure 2. Radiological findings. (**A**) Arrow shows the hypoplastic aspect of the right lung hilum on chest X-ray. (**B**) Arrow shows absent right PA. (**C**) Arrow shows a spiculated mass in the right upper lobe. (**D**) 3D volume-rendering reconstruction showing RVOT obstruction and solitary left PA.

Case Report

A 67-year-old woman with a past medical history of hypothyroidism presented with progressive dyspnea on exertion (New York Heart Association [NYHA] functional class III). She reported fatigue, abdominal discomfort, and swollen legs but did not experience chest pain or syncope. Her symptoms began only a few weeks ago. She was a former tobacco user and had smoked 8 pack-years. Clinical examination was remarkable for a wide split of second heart sound, bilateral lower-limb edema, and jugular venous distension. Body height and weight were 165 cm and 50 kg, respectively. Oxygen saturation was 91% on room air and blood pressure was 125/80 mmHg. An

electrocardiogram (ECG) showed sinus tachycardia with a normal PR interval and RV hypertrophy (**Figure 1**). Laboratory tests showed elevated D-dimers of 1196 ng/ml and N-terminal pro-brain natriuretic peptide of 6271 ng/l with mild renal impairment (glomerular filtration rate of 52 ml/min) and mildly elevated liver function test results. Echocardiography revealed a depressed right ventricular (RV) function with a tricuspid annular plane systolic excursion (TAPSE) of 10 mm. There was increased RV wall thickness, dilatation of right-sided heart chambers, D-shaping, severe tricuspid regurgitation, (TR) and a dilated inferior vena cava with reduced respiratory variation. Chest X-ray (**Figure 2A**) showed a hypoplastic right lung hilum, signs of chronic obstructive bronchial disease, and a small
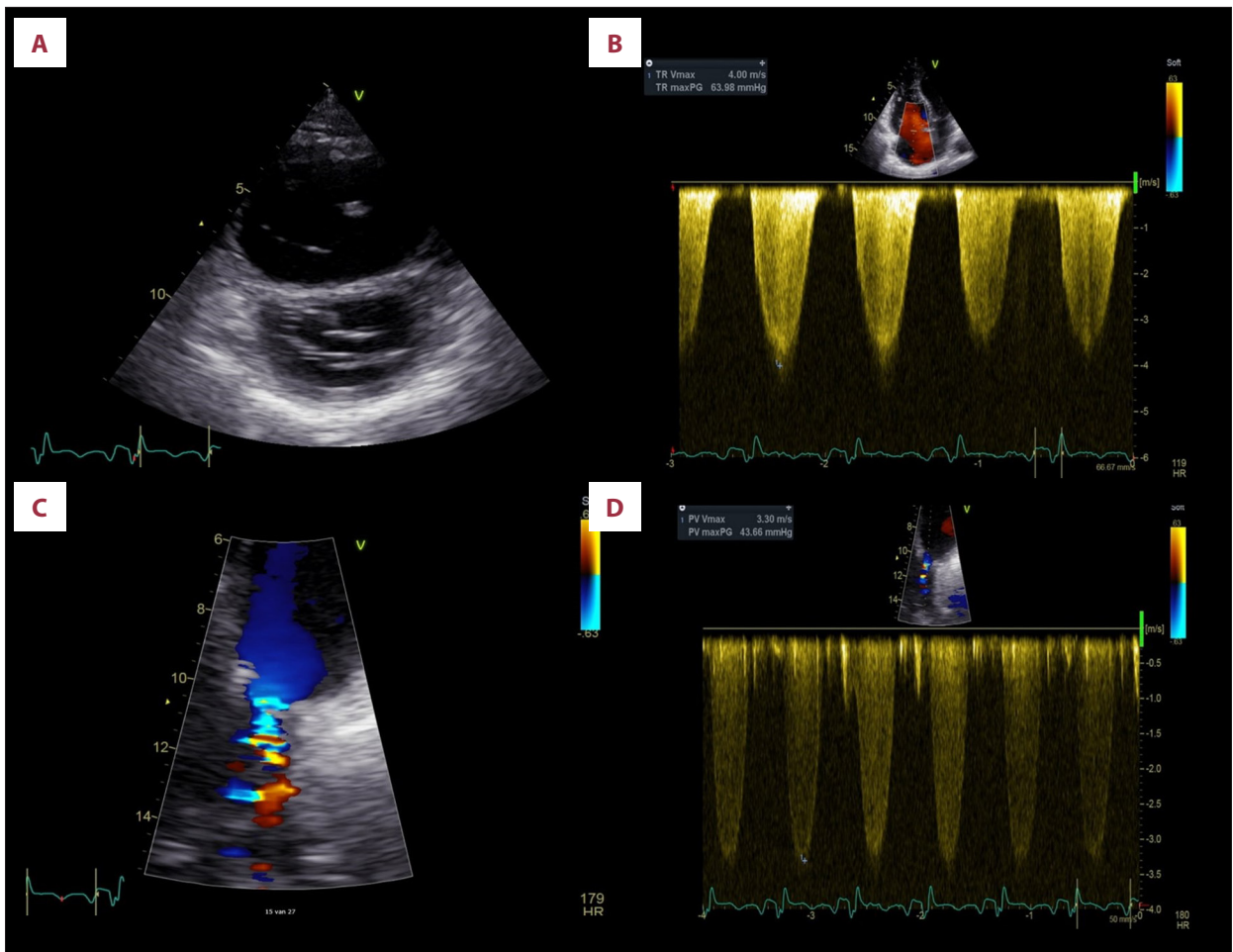
Figure 3. Transthoracic echocardiography on admission. (**A**) RV dilatation and D-shaped interventricular septum during diastole, consistent with RV volume overload. (**B**) Severe tricuspid regurgitation with TR gradient of 64 mmHg. 2D vena contracta was 7.6 mm and hepatic vein systolic flow reversal was present. RA pressure was 10-20 mmHg. (**C**) Flow acceleration at the level of the pulmonary valve. (**D**) Moderately increased peak transpulmonary gradient of 44 mmHg. Subtracting the gradient across the pulmonary valve from RV systolic pressure yields the PA systolic pressure. In this case, the calculated PA systolic pressure is 30-40 mmHg.

bilateral pleural effusion. A contrast-enhanced CT scan of the thorax (**Figure 2B-2D**) revealed absence of the right PA with a collateral circulation from intercostal and bronchial arteries and normally developed right-lung parenchyma. There was focal narrowing at the proximal pulmonary trunk. A spiculated nodular mass with a maximal diameter of 2.5 cm was visible in the apex of the right lung. The CT scan did not show any pulmonary emboli. The patient was admitted for oxygen supplementation, intravenous loop diuretics, and diagnostic work-up.

Echocardiography was repeated and confirmed a valvular PS, which was missed in the first ultrasound examination. The pulmonary valve was dome-shaped with turbulent flow starting at the level of the valve and a moderately increased peak instantaneous gradient without pulmonary regurgitation (**Figure 3**). During right-heart catheterization, advancement

of the Swan-Ganz catheter into the pulmonary trunk abruptly interrupted blood flow and led to a marked drop in arterial blood pressure and respiratory arrest. Pullback of the catheter into the right atrium restored systemic blood pressure, confirming a critical PS (**Figure 4**). RA, systolic RV, and systolic PA pressures were 9 mmHg, 68 mmHg, and 26 mmHg, respectively. Pulmonary capillary wedge pressure (PCWP) could not be measured due to the hemodynamic collapse as soon as the catheter crossed the RVOT. Consequently, pulmonary vascular resistance (PVR) in the contralateral PA could not be calculated. Arterial oxygen saturation was 94% and mixed venous oxygen saturation was 72% without a step-up. On cardiac MRI, the RV ejection fraction was 17%, RV end-diastolic volume was 104 ml/m^2, and end-systolic volume was 86 ml/m^2. There was no late gadolinium enhancement. ^{18}FDG/PET-CT demonstrated very high metabolic activity in the apical lung
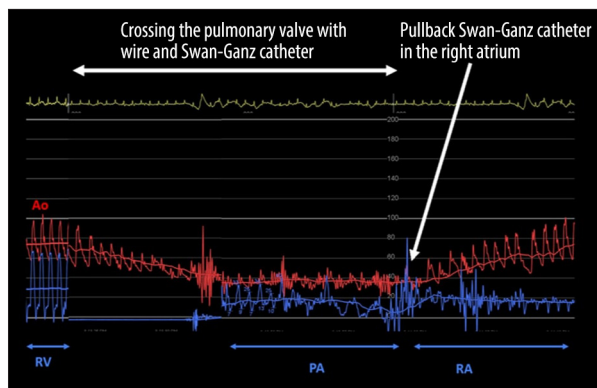
Figure 4. Baseline hemodynamic data during right-heart catheterization. Aorta (Ao), right ventricle (RV), pulmonary artery (PA), and right atrium (RA) pressure tracings. Note the clear fall in systemic pressure when crossing the pulmonary valve and subsequent pressure recovery after catheter pullback. This can be explained by mechanical obstruction of a narrowed pulmonary orifice and relief of this obstruction after catheter withdrawal. This is similar to Carabello's sign in critical aortic stenosis.

nodule, without evidence of metastatic disease. A tumor biopsy could not be obtained safely. A 24-hour urine collection showed normal levels of 5-hydroxyindoleacetic acid (5-HIAA). The patient lost 4.5 kg of body weight with diuretics and her symptoms significantly improved. She was discharged with bumetanide 1 mg and spironolactone 25 mg. Subsequently, she underwent stereotactic radiation therapy. Follow-up PET-CT 1 month after completing radiotherapy showed decreased FDG uptake of the lung nodule.

The PS was treated with a two-staged procedure (**Figure 5**). First, a balloon valvuloplasty and pre-stenting of the RVOT was performed. Postprocedural echocardiography showed a transvalvular peak gradient of 12 mmHg, mean gradient of 5 mmHg, and a free pulmonary regurgitation with early termination of regurgitant flow. The diuretics were continued and phenprocoumon was initiated with an INR target of 2-3. Three weeks later, the patient presented on an early outpatient control because of increased dyspnea on exertion for 1 week. ECG showed a total atrioventricular (AV) block with ventricular escape rhythm of 40/min, which was managed with a dual-chamber pacemaker. The ventricular lead was placed in the RV apex. Six weeks after the balloon dilatation, a PPVI was successfully performed using an Edwards SAPIEN 3 valve. Manipulation of the sheath was performed with caution to avoid dislocation of a pacemaker wire. On follow-up one and a half month later, the patient was in NYHA functional class II. Her main concerns were low blood pressure (office measurement was 91/56 mmHg) and nycturia. On echocardiography, RV function improved (TAPSE 17 mm) but the pulmonary pressure was moderately increased (peak systolic PA pressure measured 57 mmHg).

For this reason, the diuretic strategy was not altered. She is now being monitored by both the Cardiology and Respiratory Oncology Departments.

Discussion

We describe a case of subacute right heart failure in a woman with absent right PA, valvular PS, and lung cancer.

PS is usually present at birth, but the setting of malignant disease raises suspicion for carcinoid heart disease. This possibility is unlikely because of the absence of other symptoms of carcinoid syndrome and negative urinary 5-HIAA. The spiculated border and intense ^{18}FDG uptake of the lung nodule are more consistent with a carcinoma. Echocardiography did not show pathognomonic endocardial carcinoid plaques, primary tricuspid valve disease, or any degree of pulmonary regurgitation. Isolated PS in carcinoid heart disease is uncommon [7]. Therefore, we believe our patient's PS was congenital. This is supported by the abnormal valve mobility on 2D echocardiography, and the concomitant absent right PA. UAPA with RVOT obstruction detected in an adult patient is very rare, but has been reported before [8]. The level of obstruction in these cases was supravalvular in the peripheral PA branch. Our patient had a valvular obstruction with a dome-shaped pulmonary valve. The absence of other intracardiac defects allowed the PS to remain silent until adulthood. The advanced age at clinical presentation reflects the RV's ability to adapt to chronic abnormal loading conditions.

There is no evidence to guide treatment of RVOT obstruction in adult patients with UAPA due to the rarity of this condition. RVOT obstruction in a patient with UAPA is usually detected during infancy, combined with TOF or other cyanotic congenital heart disease. Data of UAPA patients with TOF suggest that relief of the RVOT obstruction is beneficial [9]. Our patient's RVOT obstruction was proven to be hemodynamically critical during right-heart catheterization, similar to the Carabello sign described in critical aortic stenosis. Therefore, our patient had a clear indication for treatment of the RVOT obstruction. PPVI was the preferred method because of high surgical risk. We chose a two-step approach to reduce the risk of rupture of the RVOT, which was mildly calcified, and to create a stable landing zone. Before the intervention, the pulmonary circulation was protected from high pressures by the reduced transpulmonary blood flow due to the stenotic RVOT. On follow-up after PPVI, development of pulmonary hypertension due to increased RV stroke volume and vascular remodeling was a concern. However, studies of single-lung physiology after pneumonectomy show that postoperative pulmonary hypertension is relatively uncommon and, if present, not severe [10]. Our patient's pulmonary pressure was moderately
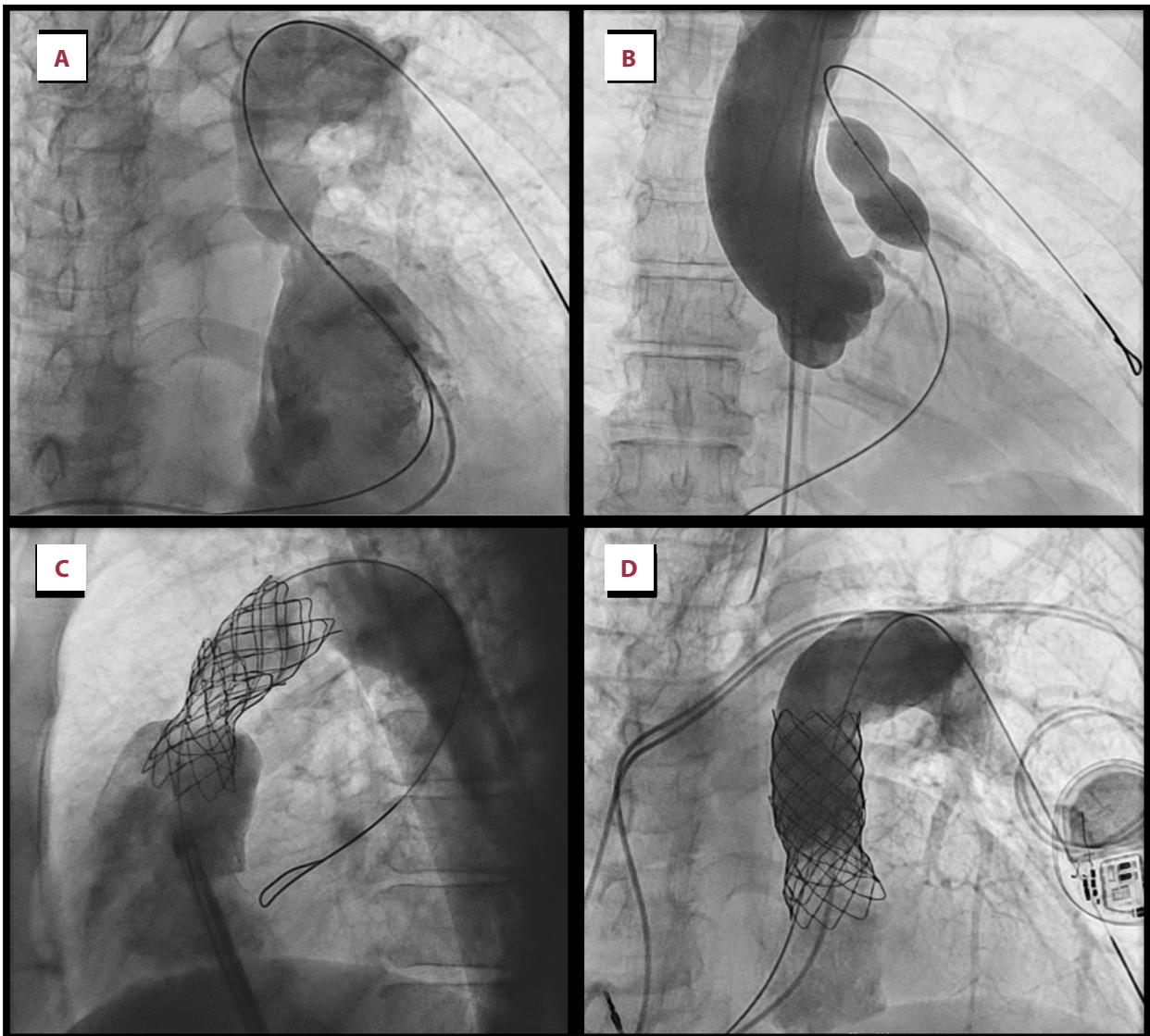
Figure 5. **Percutaneous pulmonary valve implantation (PPVI).** (**A**) Valvular RVOT obstruction and a single left PA. (**B**) RVOT balloon inflation (Tyshak II PDC 523 17.0×33 catheter) with simultaneous aortic root angiography (Pigtail 5 French catheter) to exclude coronary artery compression. (**C**) Three stents deployed in the RVOT with consequent free pulmonic regurgitation, visible as reflux of contrast into the RV. Two Covered 8 Z 45 stents and 1 Optimus AT 43 XL stent premounted on BIB BB 10 and 11 French catheters were used. The stents were placed in a diabolo configuration to limit diastolic backflow. Post-dilatation of the first stent with a PTS 306 30.0×30 8 French catheter. (**D**) Angiography after 23 mm Edwards SAPIEN 3 valve implantation shows competent valve function.

elevated after PPVI. Invasive reassessment of PCWP and PVR was not conducted.

Our patient's clinical course was complicated by a complete heart block after pulmonary balloon dilatation. She did not have a pre-existing left bundle branch block or AV conduction abnormalities. However, the baseline QRS complex was wide, suggesting an intraventricular conduction delay (**Figure 1**). Iatrogenic conduction disturbances are a known complication of transcatheter aortic valve implantation due to the anatomical proximity of the balloon to the conduction system. Traumatic AV block after pulmonary valvuloplasty is a rare event because of the longer distance between the AV node and the pulmonary valve compared to the aortic valve. If it occurs, it usually manifests shortly after balloon inflation. Right-heart catheterization prior to balloon valvuloplasty is more likely to cause direct injury to the AV node. In addition, AV node dysfunction is more prevalent in patients with idiopathic pulmonary hypertension. Remodeling of the AV node's ion channel transcriptome has been observed in an animal model of pulmonary

hypertension, which could explain the increased susceptibility to AV conduction disorders in this population [11]. A similar pathophysiology in our patient with right-heart remodeling due to RVOT obstruction may hypothetically have increased the risk of AV conduction disturbances. The reason why she developed a delayed total AV block is unclear. Although the exact time of onset cannot be established with certainty, the heart block was not present during the two-day observation following valvuloplasty. It may have developed soon after hospital discharge, but was only diagnosed 3 weeks later based on increased dyspnea for 1 week.

The co-occurrence of UAPA and lung malignancy is very rare. Our patient has a history of smoking, which is an independent risk factor. We found only 10 cases of UAPA associated with lung cancer in the literature. None of these had additional PS. Pathologic examination revealed non-small cell lung cancers in most cases, and 70% of lung cancers appear to occur on the ipsilateral side of the absent PA [12]. Most cases of ipsilateral lung cancer were treated surgically with lobectomy or pneumonectomy. Ito et al reported a patient treated with radiotherapy performed on a contralateral lung tumor [13]. Despite the ipsilateral tumor location in our patient, we opted for radiotherapy because of the prohibitive surgical risk.

Conclusions

We describe a case of absent right PA associated with critical PS and lung cancer in the right upper lobe in a 67-year-old patient presenting with right heart failure. Determining appropriate treatment in UAPA with a coexistent heart or lung condition remains difficult and should be tailored individually. The balance between PS severity and the degree of collateral flow and pulmonary hypertension may guide therapeutic strategy for PS in patients with UAPA. Radiation therapy is a non-invasive treatment option for lung cancer in UAPA patients not amenable to surgery.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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