Pulmonary Veins: Not Always Where You Expect Them

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INTRODUCTION

This case highlights (1) the use of multimodality imaging with transthoracic echocardiography (TTE), cardiovascular magnetic resonance (CMR), cardiac computed tomography (CCT), and angiography to develop a management plan and (2) a novel catheter-based approach to modify cardiac circulation in a patient with unique residual anatomic arrangement following repair of total anomalous pulmonary venous return (TAPVR). Our objective is to highlight the value of advanced cardiac imaging to guide patient management and facilitate advanced percutaneous interventions to reduce morbidity and mortality in patients with adult congenital heart disease (ACHD).

CASE PRESENTATION

A 19-year-old patient presented to establish care for history of infracardiac TAPVR after anastomosis of pulmonary venous confluence to the left atrium (LA), atrial septal defect closure, and patent ductus arteriosus ligation at 2 days of age. The patient's initial anatomy consisted of a pulmonary venous confluence, which was posterior to the LA, draining infracardiac through a vertical vein (VV) to the portal venous system (Figure 1A). During operative repair, the pulmonary venous confluence was anastomosed to the LA; however, the distal VV was not ligated, with the intention of its serving as a pressure relief system if a stenosis of the lower pulmonary venous pathway to the LA developed (Figure 2). At 13 years of age, the patient underwent CMR at an outside institution, which demonstrated a pulmonary flow (Q_p)/systemic flow (Q_s) ratio of 1.7:1 by great artery flow analysis with right-sided chamber dilation (right ventricular [RV] end-diastolic volume 107 mL/m^2) and preserved RV systolic function (RV ejection fraction [RVEF] 64%). At that time, the patient underwent right heart catheterization, which demonstrated elevated portal pressure (16-17 mm Hg) but a transhepatic gradient of 1 mm Hg. When the patient established care at our clinic 6 years after this evaluation, the patient was asymptomatic and able to live an active lifestyle. TTE demonstrated normal left ventricular size and systolic function (55%-60%) with a mildly dilated right atrium (RA) and a mildly dilated RV with normal systolic function (RVEF 49%; Figures 3A and B) and tricuspid regurgitant maximal velocity of 2.4 m/sec (Figure 3C). Only the right upper pulmonary vein (PV) was demonstrated on TTE (Figure 3D), with diastolic predominant flow. The VV drained into the inferior vena cava (IVC) with a mean gradient of 4.0 mm Hg on pulsed wave Doppler (Figures 3E and F). Hepatology evaluation was pursued given the diagnosis of portal hypertension. Hepatic elastography is used for noninvasive assessment of hepatic fibrosis or cirrhosis. This method allows mechanical excitation of the hepatic parenchyma and monitoring of tissue response. As fibrotic tissue responds differently than healthy tissue, degrees of fibrosis can be measured. Our patient's initial hepatic elastography indicated minimal fibrosis. Therefore, the patient was followed clinically for 18 months.

During subsequent follow-up, the patient continued to do well and was playing sports without limitation. The patient underwent repeat CMR, which confirmed the previously described anatomy: the right upper, right middle, and left upper PVs drained to the LA without obstruction, but the right lower and left lower PVs drained to the VV with a connection between this lower pulmonary venous confluence and the LA (Figure 4, Video 1). The study also indicated a Q_p/Q_s ratio 1.5:1 by great artery flow analysis, a moderately dilated RV (RV end-diastolic volume 126 mL/m^2), mildly depressed RV systolic function (RVEF 45%), and ventricular septal flattening in diastole. The etiology of the RV enlargement and shunt was believed to be driven by residual connection between the VV and portal venous system in combination with the significant narrowing noted between the residual lower pulmonary venous confluence and the LA. Thus, the lower PVs preferentially drained into the systemic vein via the VV as opposed to the LA. This increase in return through the systemic veins led to a volume load on the right heart. Advanced imaging was critical for defining our patient's next steps, as it delineated increasing right-sided chamber enlargement and defined the Q_p/Q_s ratio. The 2018 American Heart Association/American College of Cardiology guidelines for adults with congenital heart disease offer a Class 2A recommendation (Level of Evidence: B) for intervention in asymptomatic patients with partial anomalous pulmonary venous return, a Q_p/Q_s ratio of >1.5:1, and right-sided chamber enlargement.[1] Therefore, we were posed with the question, Does this VV require intervention?

Given that the patient was clinically unaffected, there was no change to the Q_p/Q_s ratio or chamber dilation over 8 years, and there was only mild hepatic stiffness, we opted for continued observation. Unfortunately, the patient was noted to have progressive hepatic stiffness from minimal fibrosis (6.9 kPa) to stage III fibrosis (10.2 kPa) over 3 years on the basis of hepatic elastography (Figure 2). Therefore, through multidisciplinary discussion between cardiology and hepatology, the patient was referred for right heart catheterization for hemodynamic evaluation and consideration of percutaneous occlusion of

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VIDEO HIGHLIGHTS

Video 1: Three-dimensional CMR, whole-heart, volume-rendered reconstruction in a cinematic display, demonstrates the left upper and right upper PVs with their drainage directly into the LA and the left lower and right lower PVs as they drain into the VV.

Video 2: CCT, axial stack display from superior to inferior, demonstrates the upper and lower PVs with their drainage directly into the LA and via the narrow VV, respectively.

Video 3: CCT, sagittal stack display from left to right, demonstrates the pulmonary venous insertion into the VV, the narrowed connection to the LA, and draining of the VV into the portal venous system.

Video 4: Invasive angiography, biplane display in an anterior-posterior (*left*) and right anterior oblique (*right*) projection with contrast injection into the VV, demonstrates the stenotic connection of the lower pulmonary venous confluence to the LA.

Video 5: Invasive angiography, anteroposterior display with contrast injection into the portal vein following deployment of a vascular plug into the VV, demonstrates no residual flow across the vascular plug. The stent in the lower pulmonary venous confluence–to–LA anastomosis site can be seen as well.

View the video content online at www.cvcasejournal.com.

the VV caudal to the insertion of the right and left lower PVs as well as measurement of transhepatic gradient and liver biopsy to confirm the noninvasive measurements. To provide cross-sectional imaging and landmarks before catheterization, CCT was performed. CCT demonstrated a narrow connection (5 × 6 mm) between the VV and the LA near the left lower pulmonary venous insertion into the VV (Figure 5, Videos 2 and 3).

Cardiac catheterization access was initially obtained in the right femoral artery and right femoral vein. Hemodynamic evaluation demonstrated normal right- and left-sided filling pressures (RA pressure 5 mm Hg, RV pressure 28/6 mm Hg, pulmonary arterial pressure 26/12 mm Hg, pulmonary capillary wedge pressure 8 mm Hg, and LV end-diastolic pressure 9 mm Hg; Figure 1B). Although no intracardiac shunting was observed, the Q_p/Q_s ratio was mildly elevated (1.14:1), which was attributed to the VV draining into the IVC (oxygen saturation 97%) via the portal vein. Gradients of 4 and 3 mm Hg across the right and left PVs, respectively, were measured by reverse capillary wedge pressure. Mean pressure in the caudal segment of the VV was 10 mm Hg, compared with a mean LA pressure of 8 mm Hg. Angiography of the left pulmonary artery demonstrated rapid filling of the left lung field with return to the LA; however, there was reduced flow to the left lower lung with delayed filling of the left lower PV, draining inferior and posterior to the LA. Similar findings were present on right pulmonary angiography, with delayed flow through the right lower lung field and right lower pulmonary venous return to the VV and subsequently into the portal venous system. Angiography of the VV demonstrated an 8.5 × 8.7 mm connection between the VV and the LA (Video 4).

After angiography and hemodynamic assessment, it was determined that the patient might benefit from stent relief of the pulmonary venous obstruction and subsequent VV occlusion. Radiofrequency perforation was performed to gain transeptal access, under transesophageal echocardiographic (TEE) guidance, with balloon dilation of the transeptal puncture and subsequent wire pass transeptally into the LA to access the VV and eventually in the portal vein. Portal venous access was then obtained with the assistance of interventional radiology. Venous ultrasound was used to identify a right posterior portal venous branch, and a micropuncture needle was

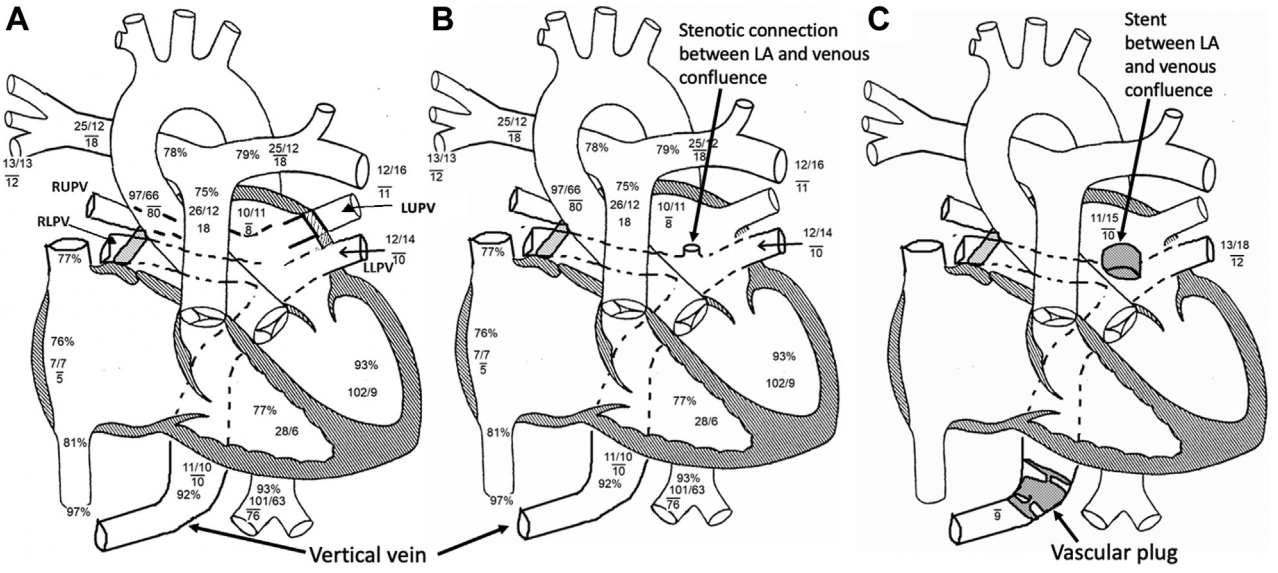

Figure 1 Diagrams demonstrating the original anatomy with pulmonary venous confluence posterior to the left atrium (LA) with the VV draining into hepatic vein **(A)**, anatomy and hemodynamics at the time of cardiac catheterization with stenotic entry of lower PVs to the LA and VV intact **(B)**, and hemodynamics following interventions **(C)**. *LLPV*, Left lower PV; *LUPV*, left upper PV; *RLPV*, right lower PV; *RUPV*, right upper PV.

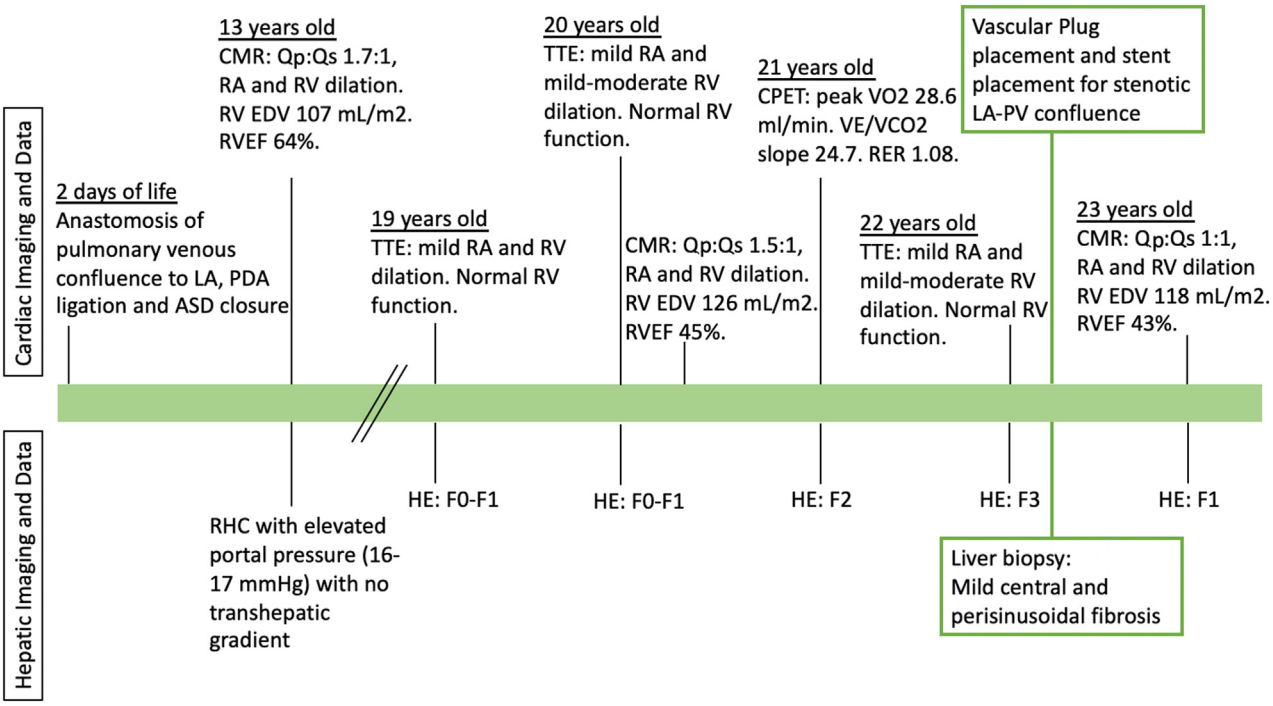

Figure 2 Timeline demonstrating key data points from clinical, cardiac imaging, and hepatic evaluations. *ASD*, Atrial septal defect; *CPET*, cardiopulmonary exercise testing; *EDV*, end-diastolic volume; *HE*, hepatic elastography; *LA*, left atrium; *PDA*, patent ductus arteriosus; *RA*, right atrial; *RER*, respiratory exchange ratio; *RHC*, right heart catheterization; *VCO2*, carbon dioxide production; *VE*, minute ventilation; *VO2*, oxygen uptake.

advanced into the portal vein with ultrasound guidance. A glide wire was advanced into the portal vein, and the needle was exchanged for a vascular sheath. The wire (right femoral vein → IVC → RA → LA → VV → portal vein) in the portal vein was snared through the portal venous sheath to provide wire stability for sheath positioning across the stenotic entry point of the lower PVs into the LA. A 26-mm stent was positioned across the stenotic LA-PV site and deployed with serial balloon dilation to provide stenotic relief. Consideration was then

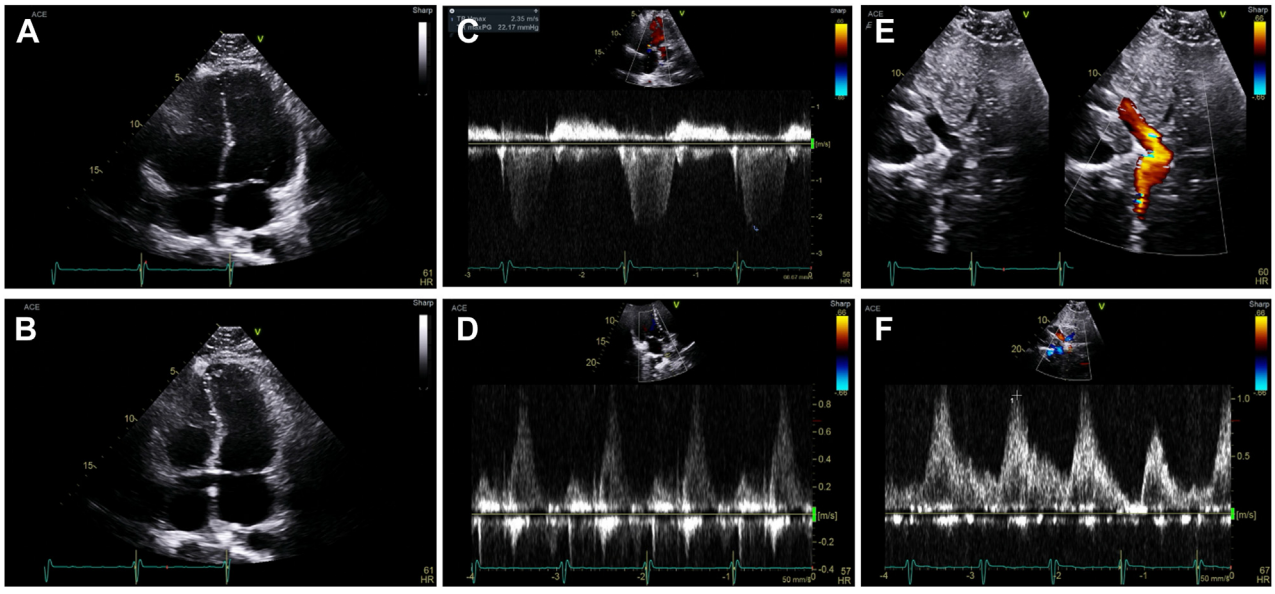

Figure 3 TTE images from the patient's first study demonstrate normal left ventricular size and function and mild RV enlargement (RV length 8.3 cm, RV basal diameter 6.4 cm, RV midcavitary diameter 5.3 cm) and normal systolic function (RVEF 49%). Apical four-chamber views in diastole **(A)** and systole **(B)**. Right upper PV Doppler captured in apical three-chamber **(C)** and four-chamber views **(D)**. Subcostal view demonstrates the VV draining directly into the hepatic vein, with a minimal gradient of 4 mm Hg **(E, F)**.

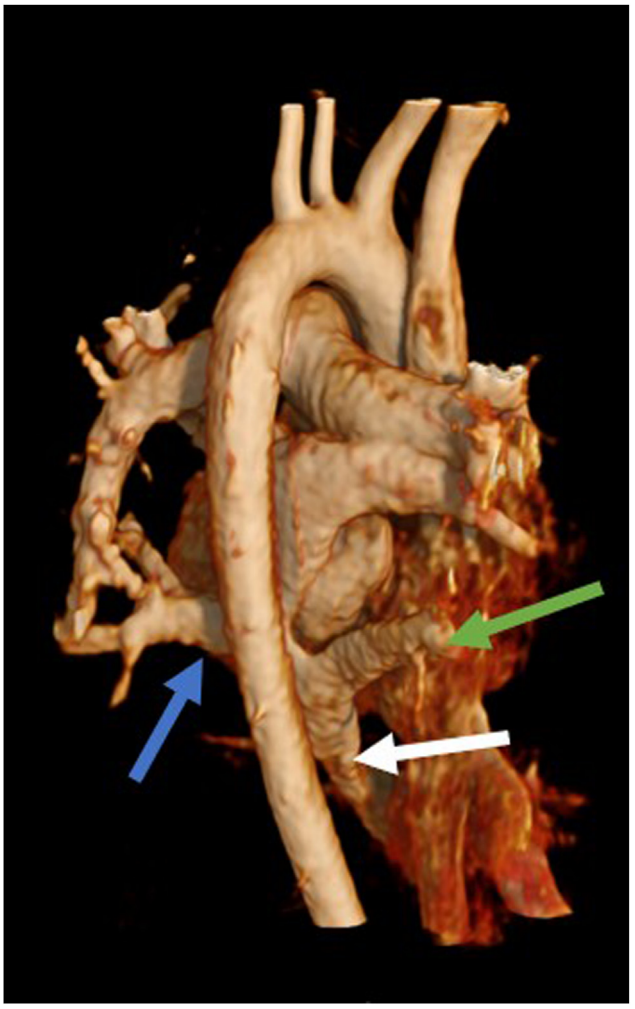

Figure 4 Three-dimensional CMR, whole-heart, volume-rendered reconstruction, demonstrates the left (*blue arrow*) and right (*green arrow*) lower PVs draining to the VV (*white arrow*), which descends caudally to the portal venous system.

given to the VV. Balloon occlusion of the VV caudal to the lower pulmonary venous insertions demonstrated no significant gradient across the stented area. Thus, it was decided to occlude the VV distally to eliminate left-to-right shunting. A vascular plug was introduced via the portal venous access site, positioned in the VV, and deployed successfully, with angiography demonstrating no residual flow through the VV (Video 5, Figure 1C) and no obstruction of the left or right hepatic vein. A 2 mm Hg gradient was measured across the stented PV-LA entry at the conclusion of all interventions.

Eight months following intervention, CMR was performed and demonstrated a Q_p/Q_s ratio of 1:1 and slight reduction in RV size (118 mL/m^2), with unchanged mildly depressed RV systolic function (RVEF 43%). Residual RV dysfunction was presumed to be secondary to volume unloading of the RV following shunt elimination, as there was no evidence of valvular disease, pulmonary hypertension, or intrinsic cardiomyopathy. Follow-up imaging demonstrated a small thrombus on the vascular plug device; therefore, apixaban and aspirin were started, and the thrombus resolved on serial imaging. Additionally, hepatic elastography 1 year following this procedure demonstrated regression to only mild fibrosis (stage I). The patient has done well since the procedure and remains asymptomatic.

DISCUSSION

The case presented demonstrates a unique residual anatomy following repair of TAPVR. There are four primary anatomic subtypes of TAPVR: supracardiac, infracardiac, cardiac, and mixed. In supracardiac TAPVR, the pulmonary venous flow eventually returns to the RA via the superior vena cava. In this case, the pulmonary venous confluence typically drains into the innominate vein or superior vena cava. In infracardiac TAPVR, the pulmonary venous flow eventually returns to the RA via the IVC. In cardiac TAPVR, the pulmonary venous return drains either directly into the RA or into the RA via the coronary sinus. Mixed TAPVR is a combination of any of the three aforementioned types.[2] These typically coincide with the presence of an atrial communication. The severity of neonatal presentation is dependent on the presence of obstruction of the pulmonary venous return. This can happen secondary to (1) compression of the VV by other intrathoracic structures or the diaphragm, (2) an intrinsic narrowing or stenosis of the VV, or (3) narrowing of the ostium of the VV as it enters the systemic vein or RA. An inadequately sized atrial-level communication can also lead to inadequate systemic output. Infracardiac TAPVR carries the highest risk for obstruction.[3] The presence of pulmonary venous obstruction leads to eventual pulmonary edema, tachypnea, and hypoxemia, necessitating urgent surgical correction.

Our patient had initial repair as a neonate given significant pulmonary overcirculation and respiratory distress. The VV was left intact without ligation because of concern for the development of stenosis of the lower pulmonary venous pathway to the LA in the future following repair. As the clinical course and workup evolved, ligation of the VV was indicated given the presence of RV dilation, increased Q_p/Q_s ratio, and mildly depressed RV function even though the patient remained asymptomatic. Intervention was initially delayed given the lack of symptoms, but with rapid progression of hepatic fibrosis, intervention was believed to be appropriate. Although there are a handful of case reports describing VV ligation or plug (surgical or transcatheter) in asymptomatic patients, most interventions are prompted by RV dilation, and no patients have been described with rapid fibrosis. Additionally, no prior cases of concomitant plugging of the VV with stenting of the stenotic venous confluence to the LA have been described.

The current guidelines emphasize the importance of multimodality imaging for anatomic characterization, functional assessment, and procedural planning (Class 1, Level of Evidence: B) in patients with unrepaired and repaired anomalous pulmonary venous return.[1] In our patient, TTE, CMR, CCT, and TEE were all critical in the arc of care and helped deliver a favorable outcome. Especially in patients with congenital heart disease, acoustic windows are not always ideal, and given prior surgical procedures, the anatomy of interest is not always readily available in the usual acquisition windows. Additionally, in patients with predominantly posterior defects, such as those with anomalous pulmonary venous connections, cross-sectional imaging with CCT, CMR, and TEE is critical to defining anatomy. CMR is of particular importance for evaluating Q_p/Q_s ratio and clearly delineating RV size and function (characterization on TTE is often suboptimal), as alterations to these parameters often prompt intervention in asymptomatic patients. Alternative approaches include preoperative TEE to further classify the gradients across the stenotic VV-LA connection; however, given the need for physiologic data, we opted for CMR instead.

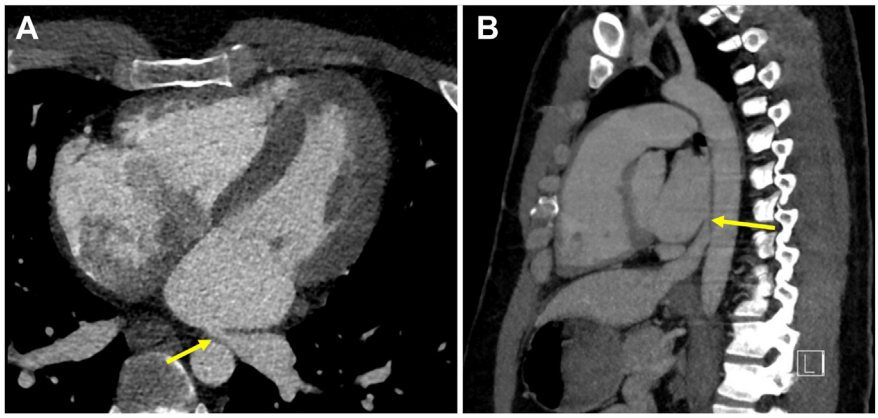

Figure 5 CCT, multiplanar reconstructions, axial **(A)** and sagittal **(B)** displays, demonstrates the stenotic insertion of the VV into the LA.

In symptomatic and asymptomatic patients, guidelines indicate surgery as the method for repair. Recently, transcatheter occlusion of the VV in partial anomalous pulmonary venous connection with dual return to the LA and a VV has begun to gain favor in the congenital cardiology community, as indicated in multiple case studies and our center's unpublished experience.[4-12] Although TTE remains the initial imaging modality of choice, often further evaluation of posterior structures requires TEE or cross-sectional imaging. In our case, the entry of the VV was severely narrowed as visualized on CCT, with secondary findings of increased Q_p/Q_s ratio and right-sided chamber dilation on CMR in the absence of an intracardiac shunt. This case highlights the challenge to both relieve the VV-LA stenosis and occlude the VV though traditional venous access sites in combination with portal venous access and provides a template for unique circumstances. The multidisciplinary approach involving our imaging, ACHD, hepatology, interventional radiology, and interventional cardiology teams led to a cohesive plan and allowed our patient to avoid redo sternotomy and postsurgical intensive care unit and hospital stays. With limited recovery time, our patient was able to resume their occupation with limited disruption.

As an imaging and ACHD community, multimodality imaging is necessary for continued care for our patients, especially continued use of echocardiography and increasing uptake of CMR to help reduce the radiation exposure associated with CCT in younger patients. Specifically for patients with initial TAPVR including a persistent VV, these modalities are important for monitoring RV size and function and extracardiac shunting. During initial operative repair for TAPVR, when the supracardiac veins are reanastomosed and lower veins drain into the LA through a VV, it is common to leave the VV unligated, as this can reduce early postoperative mortality.[13,14] The long-term impact of this has been evaluated only in small case series. The available data indicate that 50% to 80% of patients had patent VVs at 5 years following initial surgery. Of those patients, 15% to 60% ultimately had to undergo VV ligation because of large shunts.[15] As described in a few case reports, transcatheter approach may be successful at centers with ACHD expertise. However, most of these reports have minimal follow-up, and therefore, the durability of this solution remains unknown. On the basis of the physiology and longevity of vascular plugs in other vessels, we anticipate this to be a permanent solution, but long-term data are needed.

CONCLUSION

In patients with anomalous pulmonary venous return with dual connection to the LA and an anomalous vessel, a percutaneous approach can be taken. A LA–to–pulmonary venous confluence dilation with balloon angioplasty or stent deployment in combination with VV occlusion with a vascular plug can mitigate morbidity and mortality for patients with ACHD. Multimodality imaging and multidisciplinary discussions can aid in deciding which patients may benefit from such an approach.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient for the publication of this study and accompanying images.

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DISCLOSURE STATEMENT

The authors report no conflict of interest.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.12.015.

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