Late Diagnosis of Residual Major Aortopulmonary Collateral in a Patient with Tetralogy of Fallot

Conor P. O'Halloran, MD, Jeremy Fox, MD, Andrada Popescu, MD, Matthew Cornicelli, MD, Paul Tannous, MD, and Amanda Hauck, MD, *Chicago, Illinois*

INTRODUCTION

Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease (CHD).[1] TOF is characterized by anterocephalad deviation of the conal septum, but a spectrum of disease severity exists on the basis of the degree of right ventricular (RV) outflow tract obstruction.[2] In the most severe forms of TOF with pulmonary atresia or severe stenosis, major aortopulmonary collateral arteries (MAPCAs) may develop during fetal life and provide pulmonary arterial flow either in combination with the central pulmonary arteries (PAs), or as the only pulmonary arterial supply. MAPCAs are either combined with the central PAs ("unifocalized") or in some cases eliminated during or after intracardiac repair.

Presented here is a case wherein cardiac computed tomography (CCT) diagnosed a previously unrecognized MAPCA contributing to pulmonary hypertension (PH) and right heart failure. Cardiac catheterization was performed to assess the degree of pulmonary vascular change, and after a period of medical therapy, the collateral vessel was successfully occluded, resulting in normalization of RV function and alleviation of symptoms. This allowed the patient to avoid high-risk open heart surgery.

CASE PRESENTATION

A 36-year-old man with a chromosomal microdeletion syndrome and TOF with pulmonary atresia presented to the adult CHD clinic. The patient was reportedly asymptomatic, though their lifestyle was sedentary. The patient denied chest pain, palpitations, dyspnea, or edema. Vital signs were notable for blood pressure of 121/64 mm Hg, pulse of 109 beats/min, and oxygen saturation of 93%. The physical examination was notable for both a 3/6 harsh crescendo-decrescendo systolic murmur and 2/4 holodiastolic murmur.

Prior cardiac history included initial palliation with a surgical shunt at 3 weeks of age followed by complete repair with a 16-mm aortic homograft RV-to-PA conduit placement and ventricular septal defect (VSD) closure at 3 years of age. Aortopulmonary collateral vessels were occluded at 8 years of age. All prior care had occurred at a different institution (Figure 1).

The patient underwent cardiovascular magnetic resonance imaging (CMR) 1 year previously at a different institution, which showed mildly reduced left ventricular (LV) systolic function with a LV ejection fraction of 52%. RV systolic function was moderately reduced, with an RV ejection fraction of 35%. The right ventricle was severely dilated, with an end-diastolic volume of 155 mL/m^2. There was severe pulmonary regurgitation (PR), with a regurgitant fraction of 61%. There was a significant amount of artifact from mediastinal metal, which limited a full anatomic evaluation of the aortic arch and branch PAs.

Transthoracic echocardiographic (TTE) imaging performed in the clinic was notable for moderately reduced RV function (Video 1) with mild to moderate RV-to-PA conduit stenosis (peak gradient 46 mm Hg, mean gradient 23 mm Hg) and severe regurgitation with flow reversal in the right PA (Figure 2, Video 2). There was mild tricuspid regurgitation (Video 3). RV pressure was estimated at more than 75% systemic on the basis of the tricuspid regurgitant jet, with systemic blood pressure of 121/64 mm Hg. Visualization of the left PA was limited because of patient acoustic windows. There were two small residual apical muscular VSDs with low-velocity, predominantly left-to-right flow. LV size and function were normal.

This case was reviewed at our multidisciplinary conference, and given the RV dilation and dysfunction in the setting of mixed RV-PA conduit dysfunction, the decision was made to proceed with conduit replacement. Surgical replacement was favored over transcatheter replacement given the age of the conduit and a desire to perform surgery in a good state of health, with transcatheter valve replacement in the future when the patient's overall health may be worse. CCT and cardiac catheterization were planned to fully evaluate PA anatomy and hemodynamics ahead of conduit replacement.

CCT was performed on the morning of the catheterization. The findings were notable for slight irregularity of the RV-to-PA conduit, with only mild narrowing. The conduit measured 20 × 25 mm. There was a single, large residual MAPCA measuring 9 mm in diameter from the descending aorta to the proximal left PA (Figure 3). The branch PAs were severely dilated bilaterally. There was a right aortic arch with a dilated aortic root. The coronary arteries were slightly clockwise rotated, with the left main coronary artery passing underneath the distal RV-PA conduit.

Cardiac catheterization was performed using the femoral veins and a peripheral arterial line, as there was bilateral femoral artery occlusion. Initial hemodynamics were notable for mildly reduced cardiac output (CO; 3.8 L/min). There was a step-up in saturation from 72% in the superior vena cava to 83% in the PAs, indicating an elevated pulmonary flow (Q_p)/systemic flow (Q_s) ratio. RV pressure was systemic, with only a 5 mm Hg conduit gradient. The mean

From the Division of Cardiology, Department of Pediatrics (C.P.O., J.F., M.C., P.T., A.H.), and the Department of Radiology (A.P.), Ann and Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

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Correspondence: Conor P. O'Halloran, MD, Division of Cardiology, Department of Pediatrics, Ann and Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University, 225 East Chicago Avenue, Box 21, Chicago, IL 60611-2605. (E-mail: *cohalloran@luriechildrens.org*).

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VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE imaging, RV-focused apical four-chamber view in pediatric orientation, demonstrates before intervention (*left*) that the right ventricle is moderately dilated with moderate dysfunction. Following occlusion of the MAPCA (*right*), with the transducer positioned medial to cardiac apex with decreased depth to focus on the RV free wall, a mildly dilated right ventricle is demonstrated, with increased wall thickness after volume unloading of the ventricle. RV systolic function is normal.

Video 2: Two-dimensional TTE imaging, high left parasternal view with color flow Doppler, demonstrates that RV-PA conduit valve leaflet mobility is reduced, with flow acceleration beginning at the level of the valve leaflets. There is a wide jet of PR with reversal of flow within the conduit as well as the very proximal right PA.

Video 3: Two-dimensional TTE, parasternal short-axis view with color flow Doppler focusing on the tricuspid valve, demonstrates mild tricuspid regurgitation.

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PA pressure was 52 mm Hg, and wedge pressure was 23 mm Hg. An accurate Q_p/Q_s ratio and thus pulmonary vascular resistance (PVR) could not be calculated in this physiology, because of the absence of a reliable mixing chamber distal to the shunt (collateral). The MAPCA was entered from the left PA (Figure 4), and test occlusion of the MAPCA was performed using a balloon wedge catheter. Occluded hemodynamics showed CO of 4.2 L/min, a Q_p/Q_s ratio of 1, reduction in mean PA pressure to 42 mm Hg, reduction in wedge pressure to 7 mm Hg, and thus PVR of 8.3 Wood units (WU; 11.6 indexed WU [iWU], pulmonary resistance/systemic resistance = 0.5). Next, with the test occlusion still in place, 100% fraction of inspired oxygen and 20 ppm inhaled nitric oxide were provided. CO was unchanged at 4.1 L/min, the mean PA pressure was reduced to 32 mm Hg, and wedge pressure increased to 13 mm Hg; thus PVR was 4.7 WU (6.6 iWU, pulmonary resistance/systemic resistance = 0.24).

Given the patient's age and risk for progressive pulmonary vascular disease, the decision was made not to permanently occlude the MAPCA at that time. The patient was treated with pulmonary vasodilator therapy (ambrisentan and tadalafil) and then returned to the catheterization laboratory.

With repeat catheterization and test occlusion of the MAPCA, CO was 3.9 L/min, the mean PA pressure was 29 mm Hg, and wedge pressure was 14 mm Hg; thus PVR was 3.8 WU (5.6 iWU). The conduit gradient had increased to 20 mm Hg on medical therapy. With the addition of 40% fraction of inspired oxygen and 20 ppm inhaled nitric oxide, the mean PA and wedge pressures were essentially unchanged at 28 and 13 mm Hg, respectively, but CO increased to 4.7 L/min, so PVR fell to 3.2 WU (4.7 iWU). The MAPCA was successfully occluded with a 12-mm vascular plug (Figure 4). The patient was observed overnight and discharged the following day.

At most recent follow-up, TTE imaging showed improved RV size and normalized RV function (Video 1), with an increased gradient across the RV-PA conduit (peak/mean 64/33 mm Hg vs 46/23 mm Hg at presentation). The patient described significantly improved energy and no new symptoms. Conduit revision is not being actively pursued at this time given the patient's good clinical status and borderline indications.

DISCUSSION

Described here is the case of a 36-year-old man with TOF/PA/MAPCA repaired with a RV-PA conduit and later reported occlusion of residual MAPCAs. The patient had developed mixed conduit dysfunction over time with evidence of elevated RV pressure with reduced RV function. The presumptive diagnosis of symptomatic conduit failure was called into question when a previously undiagnosed MAPCA was identified on CCT. Catheterization showed an elevated Q_p/Q_s ratio, PH, no significant conduit gradient, and elevated PVR. The patient was treated medically with pulmonary vasodilators, leading to reduction in PVR and allowing closure of the MAPCA in the catheterization laboratory. Subsequently RV function normalized, and symptoms were diminished.

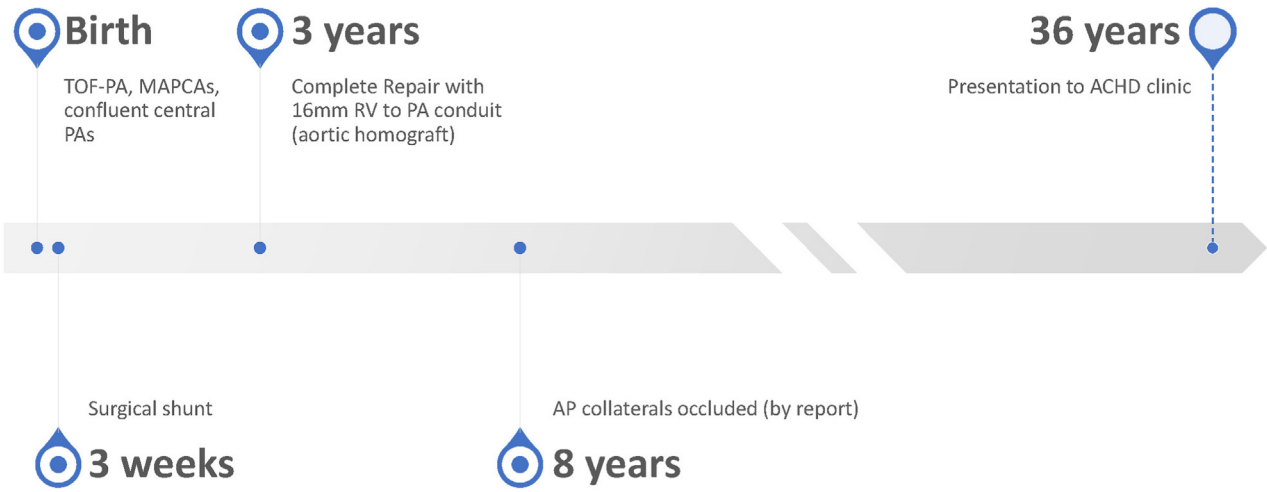

Figure 1 Major cardiac intervention before presentation to the adult CHD (ACHD) clinic. All prior care occurred at a different institution.

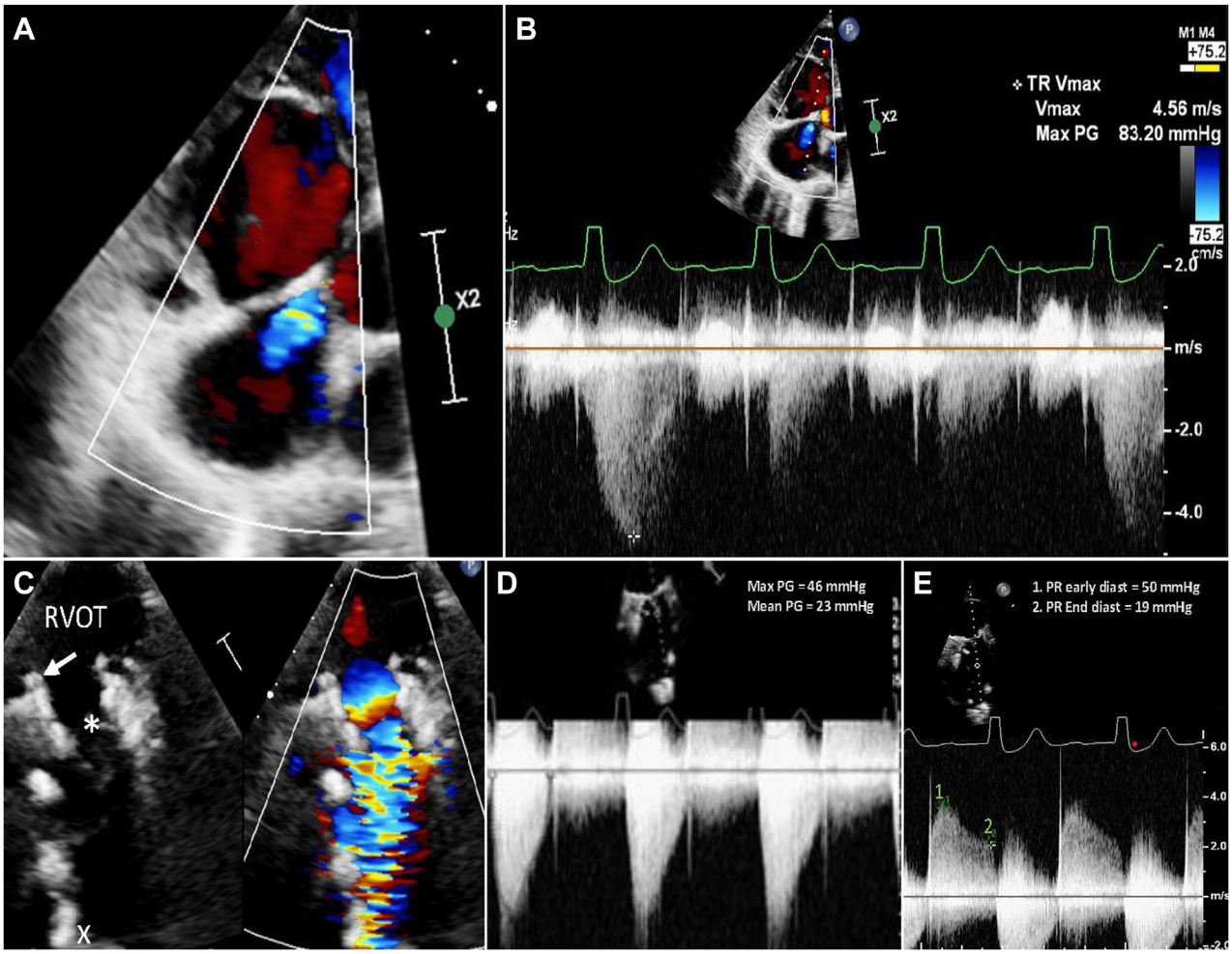

Figure 2 **(A)** Two-dimensional TTE imaging, parasternal short-axis with color flow Doppler, demonstrates mild tricuspid regurgitation. **(B)** Continuous-wave spectral Doppler interrogation of the most complete tricuspid regurgitation envelope demonstrates a peak velocity of 4.6 m/sec (83 mm Hg). **(C)** High left parasternal view with transducer slid up a rib space from standard location to focus on the proximal RV-PA conduit (*arrow*) and valve leaflets (*asterisk*) demonstrates flow turbulence beginning at the valve annulus. **(D)** Continuous-wave spectral Doppler of the conduit demonstrates a peak gradient (PG) across the conduit of 46 mm Hg and a mean gradient of 23 mm Hg. **(E)** Continuous-wave spectral Doppler of the conduit regurgitant jet demonstrates elevated peak and end-diastolic PR gradients. *RVOT*, RV outflow tract; *TR*, tricuspid regurgitation; *Vmax*, maximal velocity.

TOF exists on a spectrum based on the degree of anterior deviation of the conal septum and RV outflow tract obstruction. In the more severe forms of TOF, MAPCAs develop during fetal life to provide supplemental or exclusive pulmonary blood flow. In this disease spectrum, the central PAs can range from absent to normal in size. MAPCAs may provide the only blood supply to a particular lobe or segment ("single supply") or supply segments also supplied by the central PAs ("dual supply"). In repair of TOF, MAPCAs can either be incorporated into the central PA supply ("unifocalized") or eliminated by coiling or clipping. In either case, the pulmonary vascular tree may be abnormal after repair and require PA interventions.

Mortality among patients with TOF has declined over time because of improved operative techniques and lifetime medical management.[3] Echocardiography, CCT, CMR, and cardiac catheterization are used in follow-up after repair of TOF.[4] Echocardiography provides information on ventricular size and function, valve function, and estimation of intracardiac pressures. CMR is useful in quantifying ventricular size and function, valve regurgitation, and differential pulmonary blood flow. CCT is used primarily to assess the pulmonary arterial vasculature, which is commonly abnormal. Cardiac catheterization provides CO, RV and PA pressure, and PVR data. When used correctly, this multimodal assessment of repaired TOF provides the care team with a robust understanding of the patient's anatomy and physiology, allowing early recognition and mitigation of residual lesions.[5]

There are several important lessons gleaned from this case. First is the utmost importance of fully defining the anatomy of adult patients with CHD, before making management decisions. As patients age, their care is commonly transitioned among multiple institutions. Obtaining a full anatomic history and survey can be challenging because of limitations in the medical record and challenges transferring images among institutions. In many cases, cross-sectional imaging is required to define the current anatomy. CMR is recommended at least every 3 years in young adults with repaired TOF to evaluate RV size and function and PR severity.[5] In this case, metallic artifact limited the utility of CMR. CMR was performed at an outside

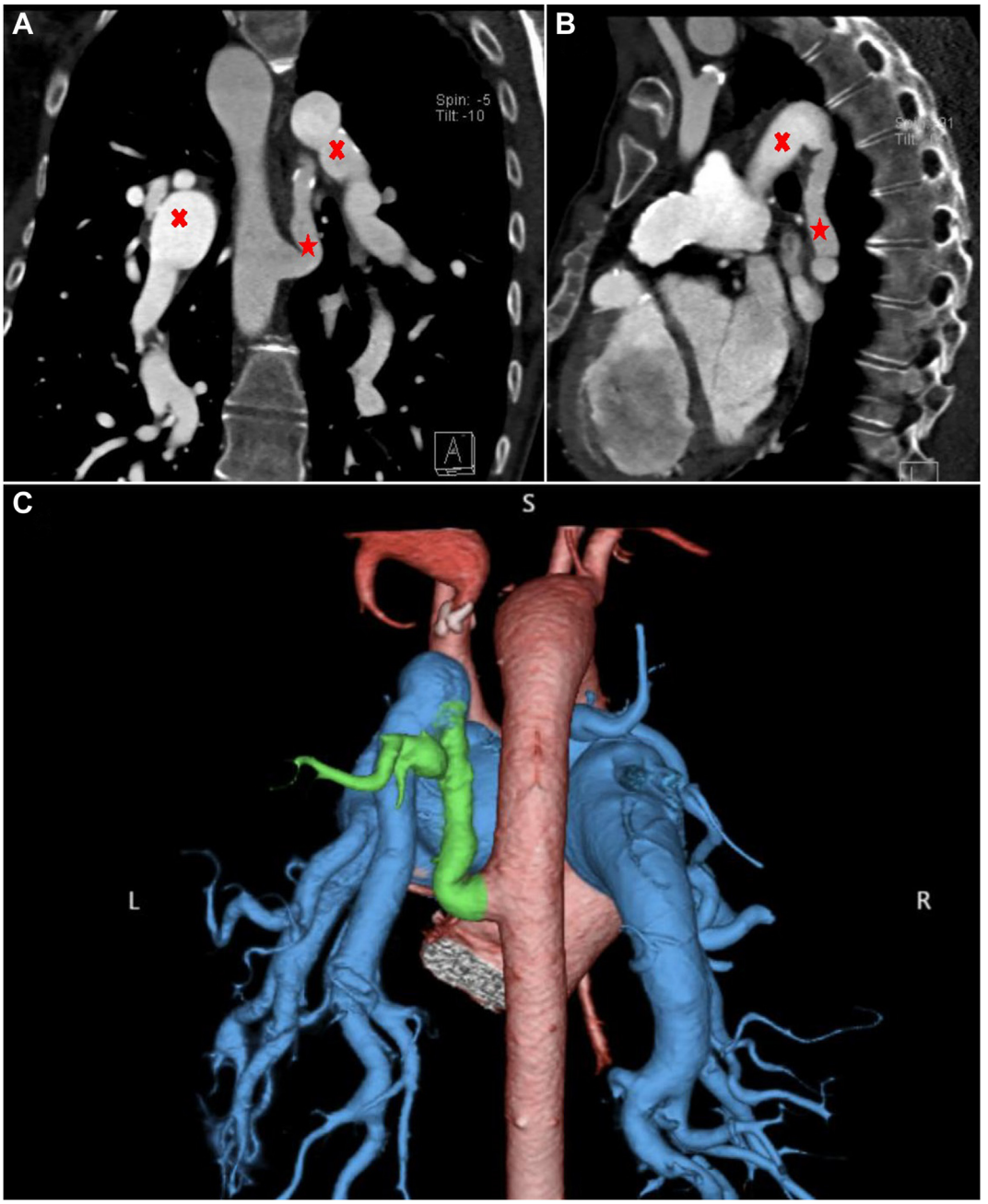

Figure 3 CCT, coronal **(A)** and sagittal **(B)** views, demonstrates a large collateral vessel (*asterisk*) originating from the descending thoracic aorta and entering the proximal left PA (LPA) (X). The right and left lower PAs (X) are also seen and are dilated and tortuous. **(C)** CCT, three-dimensional reconstruction, displayed from a posterior perspective, demonstrates the full course of the residual MAPCA (*green*) from the aorta (*red*) to the LPA (*blue*).

institution, and differential flows were not measured. The typical sequences and CMR techniques to eliminate these metallic artifacts (black-blood imaging or use of a contrast agent such as ferumoxytol) could not be performed post hoc. In cases such as this, CCT is an important adjunct to improve visualization of the vasculature.

Initially, the lack of clear anatomic understanding led to the incorrect presumptive diagnosis of conduit failure leading to RV dysfunction. By TTE imaging, there was evidence of RV hypertension on the basis of a tricuspid regurgitant jet, but there were other findings indicating that RV hypertension was not fully explained by conduit stenosis. The low-velocity VSD shunt suggested near systemic RV pressures, but the mean conduit gradient was only 23 mm Hg. Importantly, the peak PR velocity estimated a mean PA pressure of 50 mm Hg above the right atrial pressure, which should have raised suspicion for elevated PA pressure rather than conduit stenosis as the cause of elevated RV pressure.[6] In this case, the presence of significant MAPCA shunt contributed to the appearance of flow reversal in the PA and increased the volume of PR. The inability to optimally visualize the branch PAs complicated the interpretation of these Doppler measures, as branch PA stenosis, a common residual lesion in TOF,

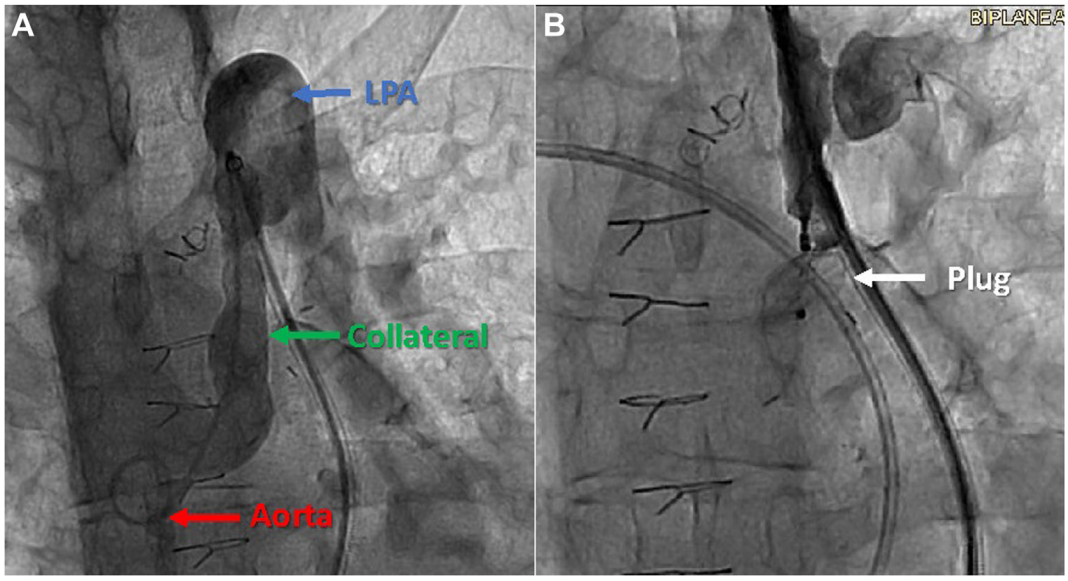

Figure 4 Results of cardiac catheterization. **(A)** Anterior-posterior fluoroscopy demonstrating a long sheath from the femoral vein passing through the right heart into the left PA (LPA). Through the long sheath, a pigtail catheter crosses the MAPCA to the aorta. Power injection via the pigtail demonstrates the MAPCA originating from the aorta and entering the proximal LPA. Coils are present in the mediastinum from prior collateral vessel occlusion. **(B)** In the same view at the next catheterization, a 12-mm vascular plug is used to occlude the MAPCA. Contrast injection via the long sheath on the pulmonary side of the collateral demonstrates that the collateral vessel is occluded.

could result in similar findings of elevated peak PR velocities. It should be noted that the PR Doppler pattern shown in Figure 2 was inconsistent with the CMR finding of severe regurgitation (regurgitant fraction 61%), as the flow velocity did not rapidly return to baseline but at the time did not raise suspicion for a residual shunt. PH in the setting of TOF with a lifelong history of pulmonary stenosis would be extremely rare, so an alternative etiology such as an unrepaired left-to-right post-tricuspid shunt should have been suspected.

The residual MAPCA provided a large, post-tricuspid left-to-right shunt. Years of increased PA flow and pressure resulted in elevated PVR. Severe elevation of the PVR without adequate response to pulmonary vasodilator therapy may suggest that irreversible and progressive pulmonary vascular disease has occurred, and removal of the shunt may result in worse outcomes in that context, as it eliminates a possible right-to-left shunt, which can be used as a "pop-off" during times of very high PVR, similar to a reversed Potts shunt.[7] Fortunately, in this case, the PVR was reduced with months of outpatient medical therapy such that the collateral vessel could be safely eliminated in the catheterization laboratory.

This case highlights the need for a multidisciplinary approach in the management of adults with residual CHD. Close collaboration among the adult CHD, radiology, cardiac imaging, PH, and interventional cardiology teams was required to appropriately care for this patient.

CONCLUSION

A complete physiologic and anatomic understanding is required to properly manage adults with repaired or palliated CHD. A multimodal imaging approach is often required to complete this understanding. The management of adults with complex CHD, particularly with residual lesions, requires a team approach, leveraging expertise of clinical cardiology, advanced imaging techniques, interventional cardiology, and cardiac surgery.

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

The authors declare that informed patient consent was not provided for the following reason: informed consent is not required for case reports without identifiable patient information.

FUNDING STATEMENT

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DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.12.017.

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