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CASE REPORT
Congenital Heart Disease

This and that: management of Tetralogy of Fallot and pulmonary vein stenosis in an infant—a case report

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Background Tetralogy of Fallot (TOF) is the most common congenital cyanotic cardiac lesion. Pulmonary vein stenosis occurs much less commonly and remains difficult to manage. It is exceedingly uncommon for a patient to have both lesions. This case highlights the diagnostic and management difficulties in an infant with these two lesions.

Case summary The patient is a 4-month-old female infant with a history of TOF status post right ventricular outflow tract stent placement who presented after a hypoxaemic event at home to 40% SpO2. Computed tomography angiography demonstrated previously undiagnosed pulmonary vein stenosis of all four veins. She underwent multiple catheter-based palliations including balloon dilations and stent placements in each pulmonary vein in order to maximize her chances of successful definitive repair. She underwent successful repair of her TOF and pulmonary vein stenosis at ten months of age.

Discussion The combination of TOF and pulmonary vein stenosis is not common, but when these lesions co-occur, they present a significant dilemma in determining the timing of surgery in order to optimize the odds of a successful outcome. This case demonstrates that serial catheter-based procedures can be valuable tools in minimizing preoperative risk factors and highlights one strategy in determining timing of definitive surgical repair.

Keywords Tetralogy of Fallot • Pulmonary vein stenosis • Cardiac catheterization • Drug-eluting stent • Case report

ESC Curriculum 9.6 Pulmonary hypertension • 7.4 Percutaneous cardiovascular post-procedure

Learning points

- The differential diagnosis for hypoxaemia in a paediatric patient with Tetralogy of Fallot (TOF) and right ventricular outflow tract obstruction in specific can be categorized by location: pre-capillary, capillary, and post-capillary.
- Patients with both TOF and pulmonary vein stenosis require a complex and multifaceted approach to managing their atypical cardiac anatomy.
- Catheter-based interventions can palliate co-occurring lesions and increase the odds of successful definitive surgical procedures.

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Introduction

Tetralogy of Fallot (TOF) is the most common cause of congenital cyanotic heart disease with a incidence of 0.34 per 1000 live births.[1] Primary pulmonary vein stenosis (PVS) is much less common, with an estimated prevalence of 1.7 per 100 000 in children less than 2 years of age.[2] It is uncommon for TOF and PVS to occur concurrently. One large case series of patients with TOF found that 0.08% of patients with TOF also had PVS.[3] Because these lesions do not occur commonly, there is no consensus on optimal management.

Timeline

July 2019	Infant is born with prenatally diagnosed Tetralogy of Fallot (TOF). Right ventricular outflow stent placed in the third week of life.
November 2019	Patient presents after desaturation at home to 40% SpO2. Right ventricular outflow tract obstruction considered but was not demonstrated on echocardiography. Patient diagnosed with pulmonary vein stenosis via computed tomography angiography and underwent balloon angioplasty of all four pulmonary veins.
Early 2020	Repeat catheterization with balloon angioplasty and stenting of pulmonary veins in February 2020, April 2020, and May 2020.
May 2020	Patient undergoes surgical repair of TOF and sutureless repair of pulmonary vein stenosis.

Case presentation

A 4-month-old female with a history of TOF presented after a 5-min hypoxaemic event at home to 40% SpO2 on a home pulse oximeter. She was born at 36 and 1/7 weeks gestational age to a mother with type 1 diabetes. The infant carried a pre-natal diagnosis of TOF and severe right ventricular outflow tract (RVOT) obstruction which required placement of an RVOT stent shortly after birth. She had been stable at home with oxygen saturations greater than 93% on room air.

On admission, vitals were as follows: blood pressure 97/53 mmHg, heart rate 129 beats per minute, respiratory rate 28 breaths per minute, and SpO2 71% on room air. She was alert and in no distress, acyanotic, and had a normal respiratory exam. She had a III/VI holosystolic murmur, loudest at the left upper sternal border, 2+ femoral pulses, and 3–4 s capillary refill. The rest of the exam was unremarkable.

Echocardiogram demonstrated a widely patent RVOT stent with reduction in the Doppler gradient and flow acceleration in the pulmonary veins (*Figure 1*). Computed tomography angiography demonstrated severe PVS of all the veins as they entered the left atrium, with the left lower, right upper, and right middle being the worse affected with near atresia (*Figure 2*). Diagnostic cardiac catheterization was significant for elevated pulmonary vascular resistance (PVR) of 12.58 iWU and stenosis of all pulmonary veins.

At that time, surgical intervention was felt to be associated with unacceptably high risk of mortality. The decision was made to return to the cardiac catheterization lab for intervention. The pulmonary veins were subjected to balloon angioplasty. Her clinical improvement was short lived, and she underwent repeat cardiac catheterization at 5 months of age with stenting of her pulmonary veins with drug-eluting stents and dilation of the RVOT stent (*Figure 3*). Multiple cardiac catheterizations with ballooning and stenting followed on a regular 4- to 6-week schedule with improvement in pulmonary pressures and PVS.

The discussion about optimal timing for surgical intervention required weighing the risk of surgery in a patient with severe PVS and improving moderate-severe pulmonary vascular resistance vs. the need for recurrent intervention and continuing cyanosis. After a subsequent cardiac catheterization at nine months of age, the patient's post-intervention pulmonary pressure and PVR had improved, with the latter decreasing to 3.87 iWU. The decision was made then to proceed with surgical repair. At 10 months of age, the patient underwent resection of bilateral PVS via a surture-less technique: the stented pulmonary veins were incised longitudinally into upstream regions without stenosis, and then the atrial wall was sewn to the pericardium around the resected areas. The TOF was repaired with resection of the RVOT stent, closure of the ventricular septal defect (VSD), tricuspid commisuroplasty, atrial septal defect reduction, and aortic homograft in the pulmonary position. The homograph was placed per surgeon preference, with the goal that the patent conduit would improve anterograde flow and improve the odds of pulmonary artery patency. Due to the potential for pulmonary hypertension post-operatively, she was left with a 3 mm VSD fenestration; she was unstable when attempting to come off bypass and the fenestration was enlarged to 6 mm.

In the immediate post-operative period, there was no obstruction across the RVOT and PVS was alleviated. However, within the next 3 months, PVS was observed in all veins. She continued to require frequent angioplasty and stenting of her pulmonary veins every 1–2 months (*Figure 4*, *Table 1*). She did well for a period with minimal complications including gastrostomy tube dependence due to oral aversion and mild developmental delay. At 16 and then 17 months of life respectively, she developed a left and then a middle cerebral embolic stroke post-interventionally with subsequent right hemiplegia and seizures which resolved on anti-epileptic medications. She continues to rehabilitate after these events and to regain her motor and neurodevelopmental skills.

Discussion

This patient's complex presentation led to questions as to the possible causes for her cyanosis; the differential diagnosis of cyanotic spells in a patient with an RVOT stent can be categorized as pre-capillary, capillary, or post-capillary. Pre-capillary causes include any cause of decreased pulmonary blood flow: in-stent thrombosis, relative stenosis of a fixed stent in a growing patient (an issue particularly

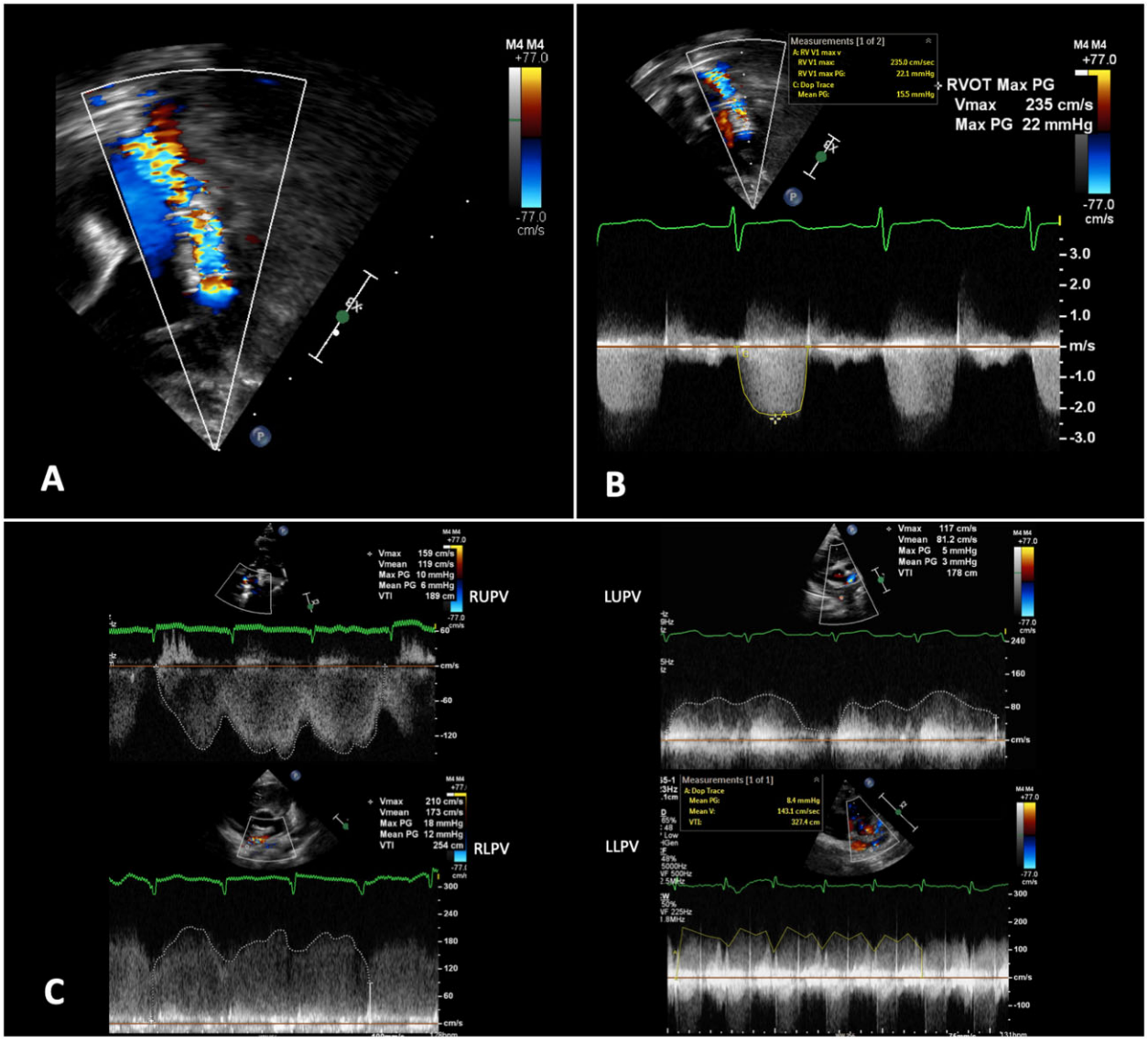

Figure 1 Echocardiogram: (*A*) Apical four chamber view of the heart showing the stent within the right ventricular outflow tract in 2D and in colour with minimal turbulence of flow across the stent. (*B*) Continuous wave Doppler across the stent estimates a peak gradient of 22 mmHg and a mean gradient of 15.5 mmHg. (*C*) Evidence of pulmonary vein stenosis noted on Doppler in four pulmonary veins.

pertinent in paediatric patients), and anatomical obstruction of the RVOT from fibrosis or muscle bundles in the RV. Capillary causes include airway-related disorders such as interstitial lung disease, acute respiratory infection causing airway obstruction, and subsequently low Qp:Qs, or capillary bed changes causing pulmonary hypertension. Post-capillary causes include downstream obstruction such as PVS or elevated left atrial pressure which could impede pulmonary venous drainage.

Though they co-exist very infrequently, the co-occurrence of TOF and PVS presents a challenging clinical question: when is it best to stop catheter-based interventions of PVS in favour of definitive surgical repair? The answer likely lies in striking a balance between the risks of hyper-cyanotic spells and the benefits of improved surgical outcome with older age. Right ventricular outflow tract stents can help in the interim by keeping the RVOT widely patent and by significantly reducing the chance of hyper-cyanotic spells, allowing for definitive repair at a later stage. Despite technical advancements, PVS recurs frequently and mortality remains high.[4–6] Catheter-based interventions for PVS can serve as a palliation by relieving downstream obstruction and minimizing cyanotic events until more definite treatments are undertaken. Such interventions have shown good results immediately post-operatively, although ballooned vessels

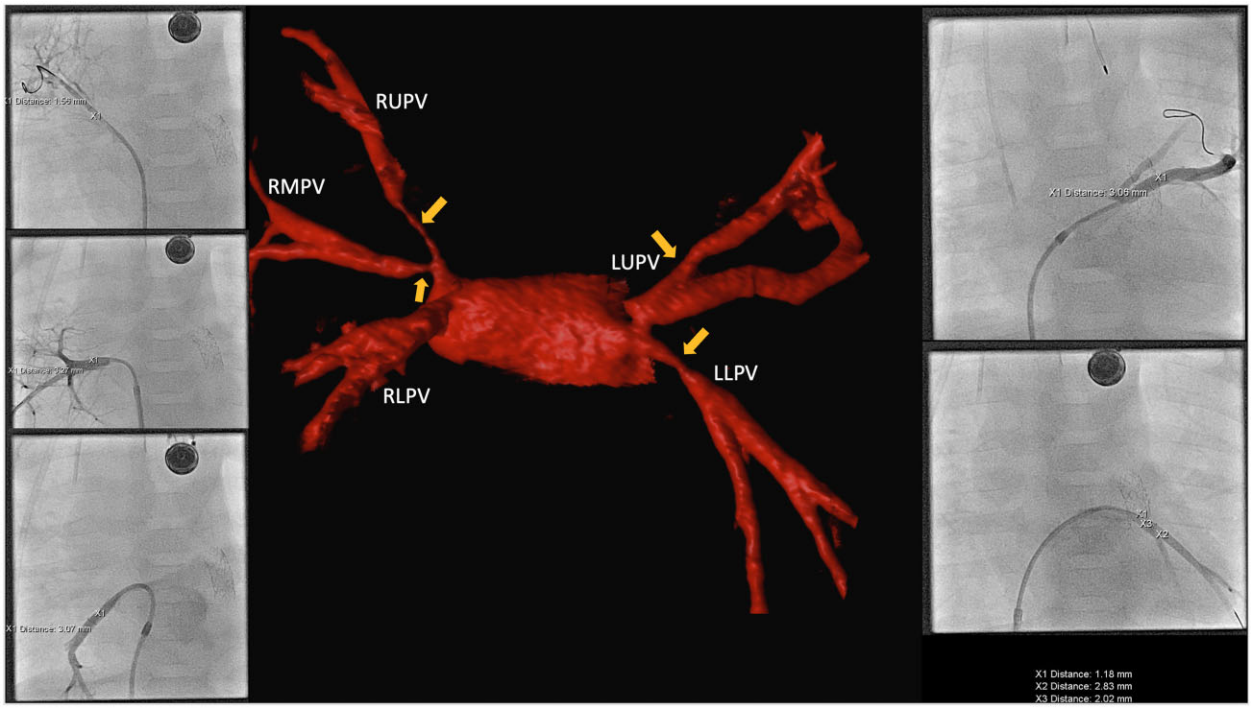

Figure 2 Computed tomography angiography reconstruction: the central image is a computed tomography angiography reconstruction showing stenotic pulmonary veins emptying into the left atrium. The orange arrows denote areas of stenosis. The image next to each pulmonary vein corresponds an angiographic image of that vein taken during a subsequent cardiac catheterization. LLPV, left lower pulmonary vein; LUPV, left upper pulmonary vein; RLPV, right lower pulmonary vein; RMPV, right middle pulmonary vein; RUPV, right upper pulmonary vein.

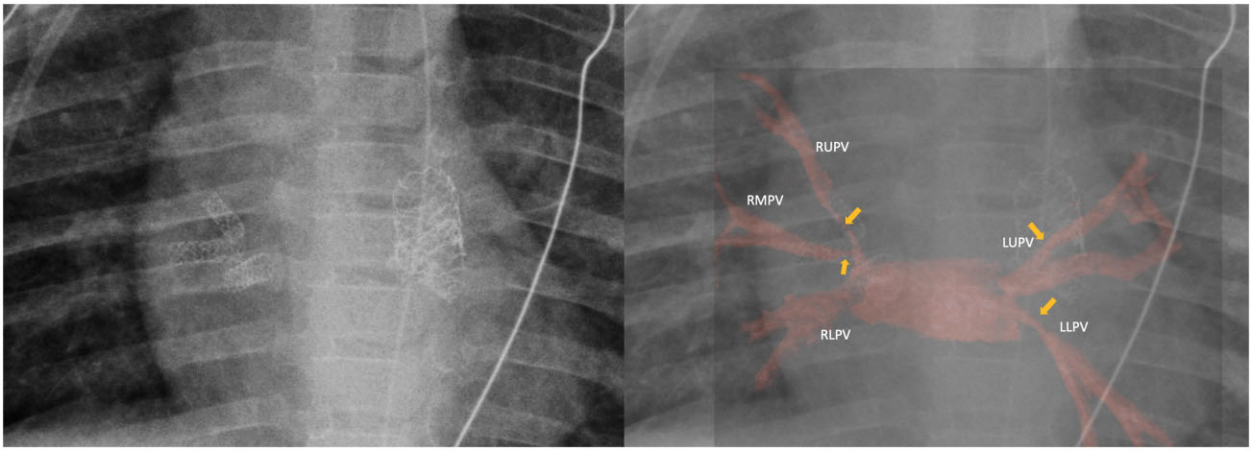

Figure 3 Fluoroscopic demonstration of stents: **t**he fluoroscopic image on the left demonstrates the five pulmonary vein stents. Note the stents in all of the pulmonary veins, as well as the larger stent in the right ventricular outflow tract. The second image on the right demonstrates the stents superimposed on the computed tomography reconstruction of the pulmonary veins.

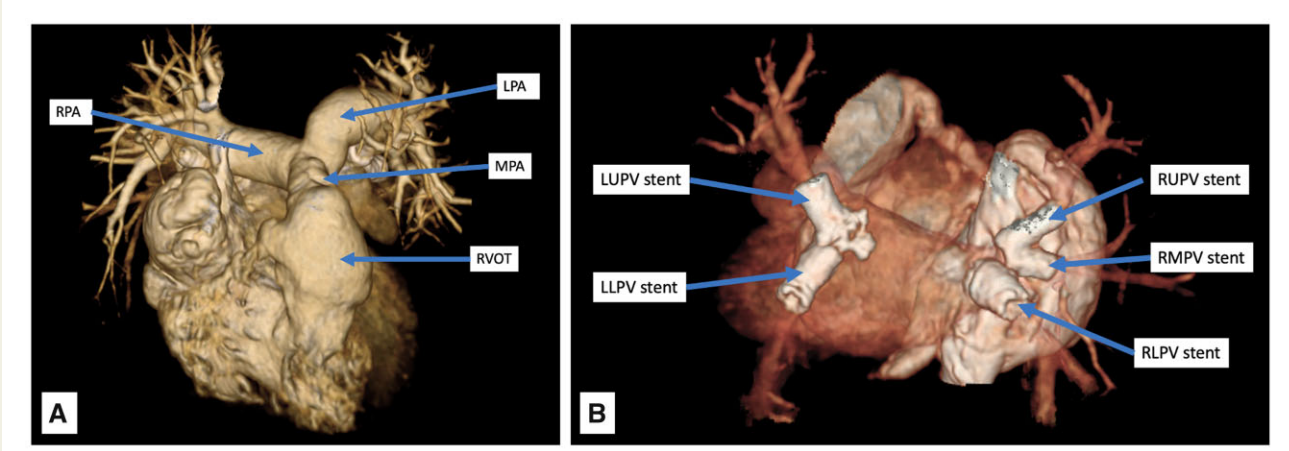

Figure 4 Computed tomography reconstruction: the computed tomography reconstructions demonstrate the patient's post-operative anatomy and stent locations. (*A*) Computed tomography angiography reconstruction highlighting the postoperative pulmonary artery anatomy. LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery; RVOT, right ventricular outflow tract. (*B*) Computed tomography angiography reconstruction of pulmonary veins, with the stents highlighted. LLPV, left lower pulmonary vein; LUPV, left upper pulmonary vein; RLPV, right lower pulmonary vein; RMPV, right middle pulmonary vein; RUPV, right upper pulmonary vein.

Table 1 Description of pulmonary vein stenosis

Vessel	Description of anatomy at diagnosis	Description of current anatomy
Left upper pulmonary vein	Angiography not performed at diagnosis as the vessel appeared atretic on initial CTA. Measured 1.4 mm × 1.9 mm on CTA.	Stented, stent measures 3.6 mm × 3.3 mm. The vein measures 5.4 mm × 4.3 mm.
Left lower pulmonary vein	Nearly atretic on angiography. Severely stenotic, distal vessel measuring 3.6 mm on catheterization. Decompressing vessel seen draining into innominate vein. Measured 1.8 mm × 1.9 mm on CTA.	Stented, stent measures 3.6 mm × 3.3 mm. The vein measures 4.6 mm × 4.1 mm.
Right upper pulmonary vein	Small and stenotic. Measured 1.5 mm distally on catheterization. Stenosis distal to left atrium. Measured 1.8 mm × 2.2 mm on CTA.	Stented, stent measures 3.2 mm × 2.4 mm. The vein measures 4.5 mm × 3.1 mm.
Right middle pulmonary vein	Significant proximal stenosis distal to confluence of the left atrium. Distal vessel measuring 2.9 mm on angiography. Measurement not recorded on CTA.	Stented, stent measures 3.3 mm × 3.0 mm. The vein measures 3.2 mm × 3.1 mm.
Right lower pulmonary vein	Proximal stenosis prior to joining the left atrium. Distal vessel measuring 3.0 mm on angiography. Measured 2.2 mm × 3.8 mm on CTA.	Stented, stent measures 4.6 mm × 3.7 mm. The vein measures 4.8 mm × 3.7 mm.

The left column notes the pulmonary vein of interest. The middle column describes the pulmonary vein anatomy when the stenosis was first described at 4 months of life. These initial descriptions are based on catheterization and CT angiography. The right column describes the anatomy at 17 months of life and is based on CT angiography.

tend to re-stenose, especially in younger patients, and implanted stents can stenose or impede future surgical interventions.[6–8]

The answer to the question of optimal timing of repair in a patient with both PVS and TOF will likely be patient-dependent and will be influenced by the presence of hyper-cyanotic spells and the severity of PVS and PVR and the need for recurrent intervention. In our patient, the decision was made to move ahead with surgical treatment only after her PVR had decreased significantly, despite requiring multiple catheter-based interventions in the interim. This proved to be a wise decision as the patient almost succumbed to rebound pulmonary hypertension post-operatively despite PVR optimization prior to surgery.

Patient perspective

A palliative strategy was discussed with the patient's family after the diagnosis of PVS in the context of shared decision-making. Her parents were informed of risks and benefits and selected a treatment course with full curative intent.

Lead author biography

Christopher P. Scott, M.D. is a PGY3 pediatrics resident at Children's Wisconsin and the Medical College of Wisconsin. After residency, he intends to pursue a fellowship in pediatric cardiology.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

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Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that witnessed verbal consent for submission and publication of this case report including images and associated text has been obtained from the patient's next-of-kin. This has been discussed with the editors.

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