Multimodality Imaging of Patent Ductus Arteriosus Complicated by Severe Pulmonary Arterial Hypertension in a Pregnant Patient

Offdan D. Narvaez-Guerra, MD, Karela B. Herrera-Enriquez, MD, Gerard P. Aurigemma, MD, FASE, Dennis A. Tighe, MD, FASE, and Bryon A. Gentile, MD, FASE, *Worcester and Boston, Massachusetts*

INTRODUCTION

Whether pregnancy adversely affects the mother with congenital heart disease (CHD) depends on the lesion. While simple lesions such as small restrictive ventricular septal defects do not represent a hemodynamic challenge during pregnancy, moderately complex lesions such as patent ductus arteriosus (PDA) carry a heightened risk of heart failure and arrhythmias.[1] On the other extreme of the disease severity, large uncorrected PDAs can be complicated by left-sided volume overload and pulmonary hypertension (PH), which appears to be flow dependent and in some cases reversible.[2] Timely identification of CHD during pregnancy can prevent the development of adverse sequelae such as heart failure as well as Eisenmenger syndrome, a severe form of PH. Eisenmenger syndrome, originally described in patients with large ventricular septal defects, is seen in sustained left-to-right shunting and leads to pulmonary vasculature remodeling and subsequent right-to-left shunting reversal; it is observed in 3% of pregnant patients with CHD.[3]

We describe a case of a patient with a previously unidentified PDA presenting during the third trimester of pregnancy complicated by biventricular dysfunction and severe PH, necessitating successful cesarean delivery and percutaneous PDA closure. Multimodality imaging was utilized to fully characterize the anatomical, physiological, and hemodynamic basis of this lesion.

CASE PRESENTATION

A 26-year-old woman, G1P0, with a medical history of seizure disorder, generalized anxiety disorder, and mild anemia was evaluated at the neurology clinic after an increase in breakthrough seizures during titration of the antiepileptic drug levetiracetam at 32 weeks of pregnancy. The patient had recently moved from South America to the United States and reported a cardiac history of a murmur in childhood accompanied by recurrent episodes of exertional dyspnea and epistaxis until the age of 18 years old, which coincided with moving from a high-altitude location to a sea-level city. The patient had not received regular cardiovascular care, was not taking any specific cardiac medications, and denied chest pain, orthopnea, palpitations, dyspnea on exertion, dizziness, and syncope. Other medications were prenatal vitamins.

Physical examination demonstrated a blood pressure of 112/54 mm Hg, heart rate 84 bpm, and oxygen saturation 96% in ambient air, which was similar in upper and lower extremities. A soft, continuous murmur was present at the left upper sternal border, left subclavicular region, and left upper back, without a thrill. There was clubbing of both hands, but not of toes. No pedal edema, cyanosis, or jugular venous distention were noted. Abdomen was gravid and nontender. A 12-lead electrocardiogram showed normal sinus rhythm, and rSR′ pattern in lead V1 with a QRS of 96 ms suggesting right ventricular (RV) conduction delay. Transthoracic echocardiography (TTE) evidenced preserved left ventricular ejection fraction (LVEF) and left ventricular (LV) dilation (three-dimensional TTE-derived LV end-diastolic volume index [LVEDVi] of 116 mL/m^2). The right ventricle (RV) was dilated with a fractional area change of 32%. There was evidence of RV pressure overload (Video 1), mild to moderate pulmonic valve regurgitation (PR) with a pressure half time >100 ms, a fairly dense spectral signal, and elevated estimated RV systolic pressure (RVSP; Figure 1). A PDA with left-to-right shunting with an estimated pressure gradient of 28 mm Hg was identified (Figure 2, Video 2).

The patient was admitted to the hospital and underwent right heart catheterization, which showed right atrial pressure 4 mm Hg, pulmonary artery (PA) systolic pressure (PASP) 110 mm Hg, mean PA pressure 73 mm Hg, pulmonary capillary wedge pressure 9 mm Hg, pulmonary vascular resistance (PVR) 11 Woods units, and net left-to-right shunting with a pulmonary to systemic flow (Qp:Qs) ratio of 2.0 ts. After a multidisciplinary meeting, treprostinil infusion was started as an attempt to mitigate the effects of severe precapillary PH and stabilize left-to-right shunting through the PDA. Treprostinil was not tolerated, likely due a relatively sensitive PVR which led to an increase in the degree of left-to-right shunting, worsening pulmonary overcirculation, and increasing left-sided filling pressures resulting in hypoxemia. Treprostinil was discontinued in favor of sildenafil and diuretics. A noncontrast cardiovascular magnetic resonance scan (CMR) confirmed a large PDA connecting to the superior surface of the PA at the level of the bifurcation (Figure 3). Biventricular dilation and dysfunction were also confirmed with LVEF 50%, LVEDVi 159 mL/m^2, RV ejection fraction 38%, and RV end-diastolic volume index 95 mL/m^2, in addition to dilated main PA and severe PR with a regurgitant fraction of 55% (Video 3). Two days prior to a scheduled cesarean delivery, sildenafil was discontinued, which allowed for complete resolution of hypoxemia. The patient underwent an uncomplicated cesarean section delivery of a healthy child at 36 weeks under combined spinal-epidural anesthesia. The patient remained hemodynamically stable and was discharged on postpartum day 5 off sildenafil; this decision was made based on recurrence of

From the Division of Cardiovascular Medicine, Department of Medicine, University of Massachusetts Chan School of Medicine, Worcester, Massachusetts (O.D.N.-G., G.P.A., D.A.T., B.A.G.); and Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts (K.B.H.-E.).

Keywords: Cardio-obstetrics, Patent ductus arteriosus, Congenital heart disease, Pregnancy

Correspondence: Offdan D. Narvaez-Guerra, MD, University of Massachusetts Chan School of Medicine, 55 Lake Avenue North, Worcester, MA 01655. (E-mail: *offdan.narvaezguerra@umassmed.edu*).

2468-6441

https://doi.org/10.1016/j.case.2023.12.008

VIDEO HIGHLIGHTS

Video 1: Three-dimensional TTE, visualized from the apex, with corresponding two-dimensional biplane imaging from apical views, demonstrates systolic flattening of the interventricular septum, consistent with RV pressure overload.

Video 2: Two-dimensional TTE, modified parasternal short-axis view with (*right*) and without (*left*) color-flow Doppler, demonstrates a continuous flow from aorta to PA, confirming the presence of PDA with left-to-right shunting.

Video 3: Cardiovascular magnetic resonance scan, balanced steady-state free precession cine sequence at the level of the RVOT, demonstrates dilation of the main PA, and low-signal void with dephasing secondary to a centrally directed jet of PR is present. *RVOT*, RV outflow tract.

Video 4: Cardiac computed tomography of the heart and great vessels. Three-dimensional rendered image detailing the anatomy of the PDA.

Video 5: Cineangiography, RAO 0 CRAN 1 projection. Injection of iodinated contrast via a pigtail catheter in the descending aorta in close proximity to the PDA demonstrates passage of contrast into the PA territory with opacification of the PA trunk. *CRAN*, Cranial; *RAO*, right anterior oblique.

Video 6: Cineangiography, LAO 99 CAUD 0 projection. Confirmation of optimal placement of a 25 mm occluder device is visualized, without passage of contrast from descending aorta into PA. *CAUD*, Caudal; *LAO*, left anterior oblique.

Video 7: Two-dimensional TTE, apical 4-chamber view, demonstrates global LV hypokinesis with LVEF 38%, post-PDA closure.

Video 8: Two-dimensional TTE, apical 4-chamber view, LV-focused view, demonstrates normal LV systolic function, with LVEF 55%.

Video 9: Two-dimensional TTE, modified parasternal short-axis view with color-flow Doppler, demonstrates no significant flow from descending aorta into PA.

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

pulmonary edema while on pulmonary vasodilators and because the degree of physiologic postpartum rise in systemic vascular resistance did not increase left-to-right shunting.

Despite feeling well and maintaining euvolemia 2 weeks postdelivery, the patient was readmitted with acute decompensated heart failure 4 weeks later. A TTE showed worsening biventricular dysfunction (LVEF of 46%), severe tricuspid regurgitation with hepatic vein systolic flow reversal, and RVSP of 106 mm Hg. Diuretics and sildenafil were reinitiated resulting in symptomatic and hemodynamic improvement. A cardiac computed tomography (CCT) was obtained for preprocedural planning of PDA closure (Figures 4 and 5, Video 4), which confirmed presence of a large PDA (14 mm in diameter and 18 mm in length) and did not show evidence of coronary artery disease. Ten days after admission (8 weeks postpartum), a repeat cardiac catheterization revealed a PASP of 110 mm Hg, which decreased to 62 mm Hg during a transient balloon occlusion test, without increase in right atrial pressure, and an aortic pressure of 132/87 mm Hg, which suggested favorable hemodynamic conditions for shunt closure; therefore the patient underwent successful percutaneous PDA closure with a 25 mm occluder (Videos 5 and 6). Three days later, a repeat TTE showed LVEF of 38% and diffuse RV hypokinesis (Video 7). Guideline-directed medical therapy (GDMT) was begun with beta-blockers, angiotensin-converting enzyme inhibitors, mineralocorticoid antagonist, and subsequently SGLT2 inhibitors and ARNI therapy. One year following PDA closure and treatment with GDMT, the patient remained asymptomatic (Figure 6). A TTE performed at that time showed normal biventricular function LVEF 55%, LVEDVi 54.6 mL/m^2, RV fractional area change 41%, RVSP 26 mm Hg, and a PDA closure device without evidence of residual shunting (Videos 8 and 9).

DISCUSSION

Globally, PDAs occur in 1 in 2,000 births, and account for 5% to 10% of all CHD, with an incidence inversely related to gestational age and weight and directly related to high altitude.[4,5] In high-altitude dwellers such as our patient, PDAs have a tendency toward larger ductal diameters and higher PA pressures than those living at low altitude.[6] While some believe ductal patency persists due to lower arterial oxygen tension, it is still unknown whether certain phenotypic adaptations to chronic hypobaric hypoxia can lead to variable degrees of PDAs among those at high altitude.[5,7]

In light of severe PH, our patient was considered to be in World Health Organization pregnancy risk category IV, which translates into a high risk of maternal and fetal morbidity and mortality.[1] "Silent" PDAs, diagnosed by imaging in asymptomatic patients, can be seen in approximately 1 in 20 births.[4] Our patient, who previously experienced symptoms, was not overly dyspneic or fatigued during pregnancy prior to identifying a large PDA. Pregnancy can affect the clinical expression of a PDA by modifying the ratio between the pulmonary and systemic flows primarily driven by an increase in total blood volume, since the mean PA pressure and the PVR stay relatively stable in the third trimester.[1] Additionally, there is an increased risk of thromboembolic events in the third trimester, which may predominantly affect the pulmonary arterial circulation in the case of PDA, due to an increase in hypercoagulable proteins seen during this period.[8]

Normal changes in total blood volume and cardiac output seen in pregnancy can lead to increases in all chamber sizes and generally begin at 12 weeks' gestation, with a return to baseline values within 3 to 6 months postpartum.[9] These increases in chamber size do not constitute dilation, although it should be noted that normative values for chamber sizes in pregnancy are not firmly established. In an observational echocardiographic study including 121 women, LVEF significantly increased in the second trimester compared with in nonpregnant controls (68% vs 63%, $P < .03$) and normalized in the third trimester. This study also showed that there was no significant change in LV diastolic function during pregnancy.[10,11] Our patient met the criteria for LV dilation by three-dimensional TTE volumetric method, which was later confirmed by CMR. The subsequent increase in PR was likely the result of initiation of pulmonary vasodilator therapy, which directly increased the Qp:Qs ratio by lowering the PVR and leading to higher end-diastolic pressures due to increased shunting through the PDA. Pressure gradients in healthy pregnant women may be affected by a normal increase in blood flow and volume.[9]

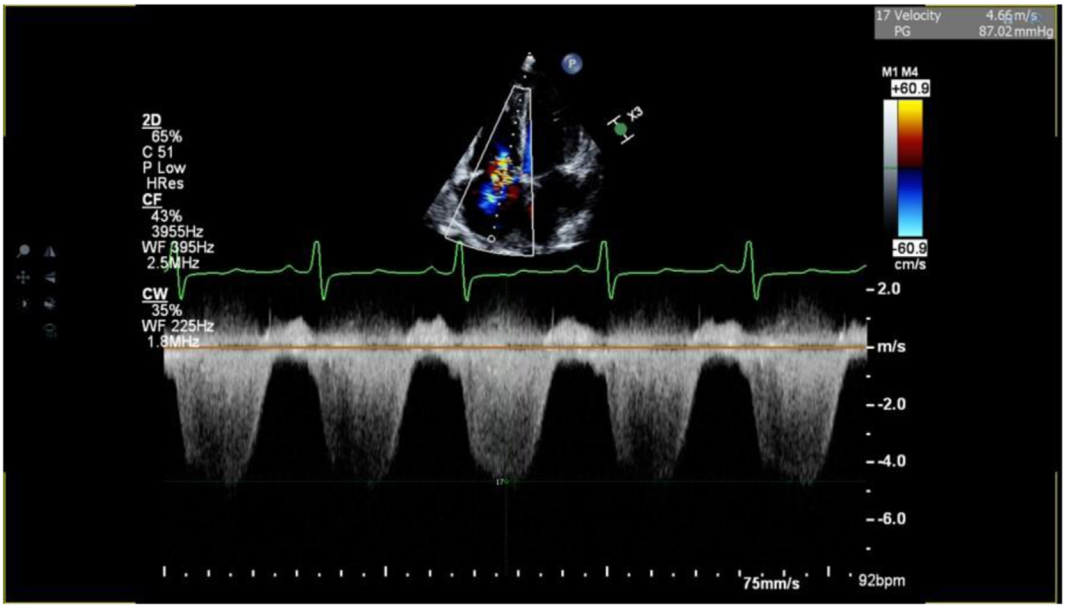

Figure 1 Two-dimensional TTE, color-flow Doppler at the tricuspid valve level, demonstrates a regurgitant jet with a maximum velocity of 4.7 m/sec and a pressure gradient of 87 mm Hg.

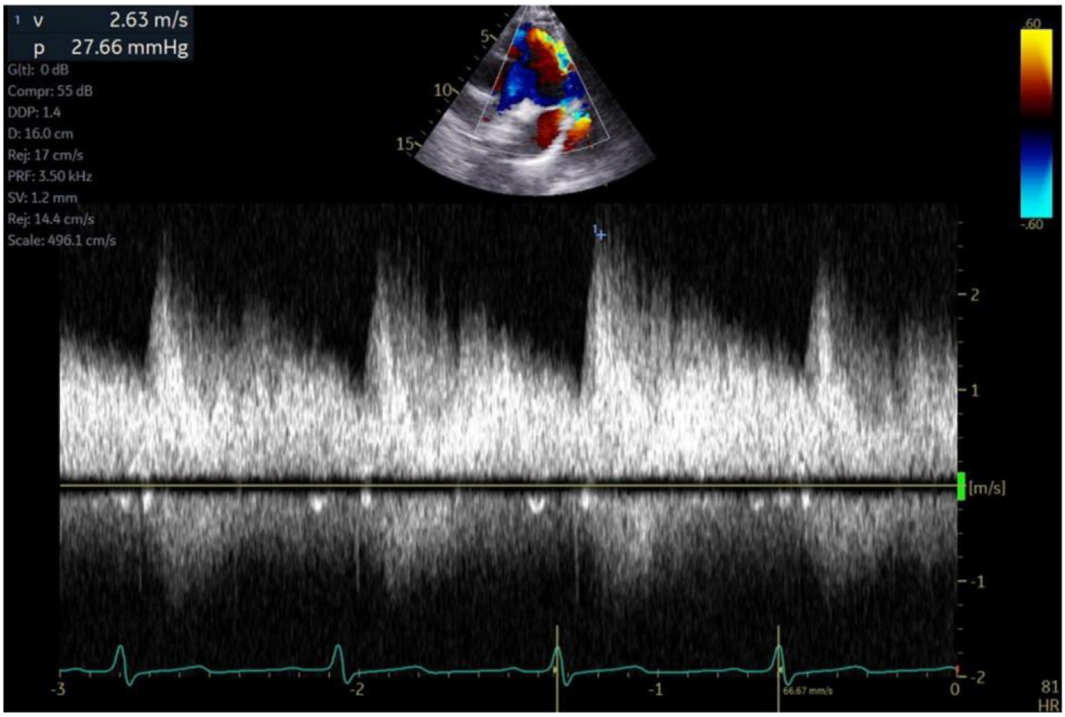

Figure 2 Two-dimensional TTE, modified parasternal short-axis view at the level of great vessels, with color flow–guided, continuous-wave Doppler spectral signal of PDA, shows a systolic pressure of 28 mm Hg through the PDA, which correlates with an estimated RVSP of 83 mm Hg, considering a systemic blood pressure of 110/80 mm Hg at the time of the study.

Nonetheless, this does not seem to apply to pregnant patients with pathologic hemodynamic derangements such as in our patient in whom the echocardiographic estimation of PASP and mean PA pressure were later confirmed invasively.

Additional imaging modalities are available to adequately characterize PDA during pregnancy. The safety of CMR during pregnancy is well established and appears to have the risk of producing a loud tapping noise during the study, which in theory could lead to

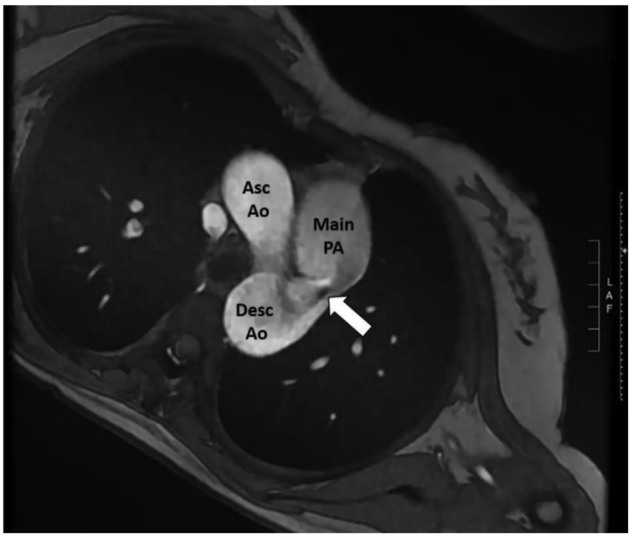

Figure 3 Cardiovascular magnetic resonance scan, balanced steady-state free precession cine, axial plane at the level of the great vessels, demonstrates dephasing of flow going through the PDA (*arrow*) from the descending aorta into the main PA during midsystole. *Asc Ao*, Ascending aorta; *Desc Ao*, descending aorta.

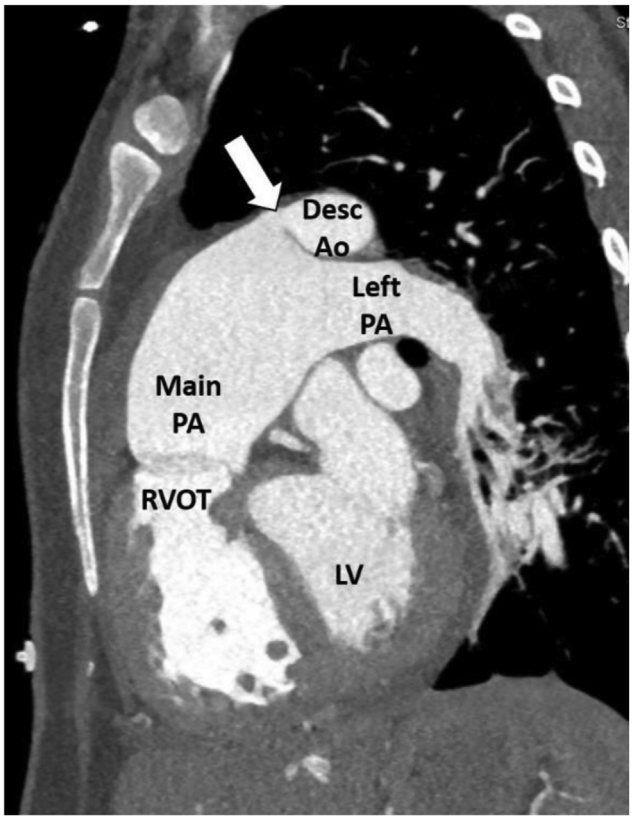

Figure 4 Cardiac computed tomography of the heart and great vessels, sagittal plane, demonstrates communication between the PA and the descending aorta through the PDA (*arrow*). To visualize PDA, CCT was performed using the automatic bolus triggering technique for a region of interest placed in the distal main PA. *Desc Ao*, Descending aorta; *LV*, left ventricle; *RVOT*, RV outflow tract.

neonatal hearing damage; however, no adverse fetal consequences have been reported.[1,11] Despite the safety of gadolinium use during the second or third trimester when organogenesis has completed, the American College of Radiology recommends avoidance when other imaging modalities are sufficient for diagnosis.[1] As such, gadolinium was not utilized in this patient's care. Conversely, CCT provides excellent assessment of the vascular anatomy but has the disadvantage of exposing the mother and fetus to ionizing radiation with the risk of pregnancy termination, teratogenesis, growth restriction, cognitive abnormalities, and malignancy.[1] Cardiac catheterization is key in assisting important therapeutic decisions and quantifying the degree of PH and/or shunting but has the risk of fetal radiation exposure.[1]

The immediate postpartum period is characterized by increased preload due to decompression of the vena cava with augmented venous return leading to increased cardiac output and transiently elevated mean arterial pressure; this increase in output and pressure gradually declines over the following 2 weeks.[1] Current guidelines issue a IIb recommendation for PDA closure in adults with net left-to-right shunt if PASP is 50% or greater than systemic pressure, and/or PVR is greater than one-third systemic.[12] This was achieved with excellent results in our patient. Pulmonary vasodilators were utilized to lower PA pressures to reduce the risk of RV failure following PDA closure. In the largest series of adults with PDA treated with percutaneous closure devices, complications included obstruction of the aorta or branch PAs, residual leaks, transient hemolysis if very large PDAs were present, device embolization, and transient LV systolic dysfunction.[13] A preclosure LVEF <62% has been identified as the best predictor of postclosure LV dysfunction.[14] A nearly 20% reduction in LVEF was seen in our patient after percutaneous PDA closure, which was the result of preload reduction and a sudden afterload increase, most commonly described among patients with large shunts, preexisting LV dysfunction, and PH.[13] Education on medication compliance and treatment with GDMT were fundamental in achieving a normal biventricular function 1 year after PDA closure in our patient.

CONCLUSION

Large uncorrected PDAs complicated by PH can be identified during pregnancy. Timely identification is key in planning optimal delivery strategies under the guidance of a multidisciplinary team. Multimodality imaging is used to identify various aspects of this condition, from vascular characterization and hemodynamic consequences to adequate intraprocedural and postprocedural assessment. Percutaneous closure of PDA can be successfully pursued when there are no anatomical or hemodynamic constraints.

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.

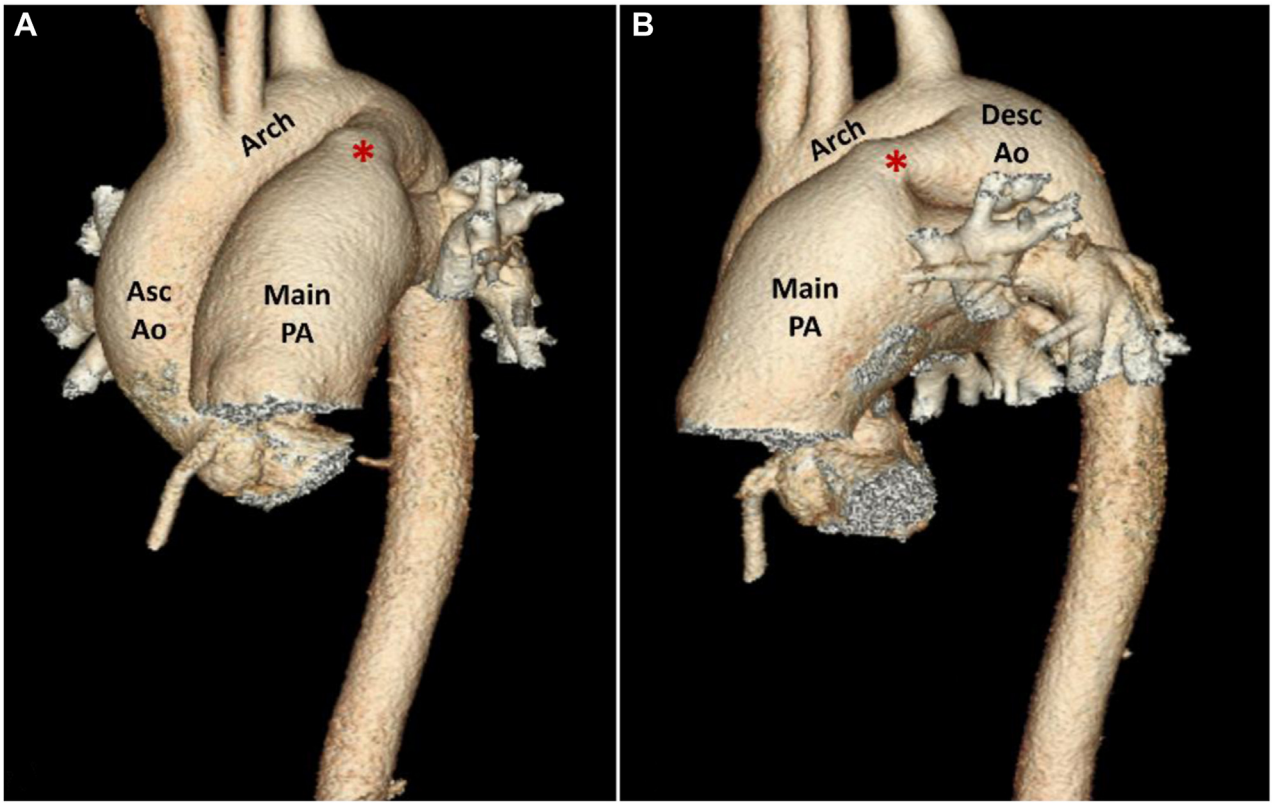

Figure 5 Cardiac computed tomography, three-dimensional volume-rendered images, demonstrates an anteroposterior view **(A)** and left lateral view **(B)** of the great vessels, which detail the presence of the PDA (*red asterisk*) and the surrounding anatomy. *Asc Ao*, Ascending aorta; *Desc Ao*, descending aorta.

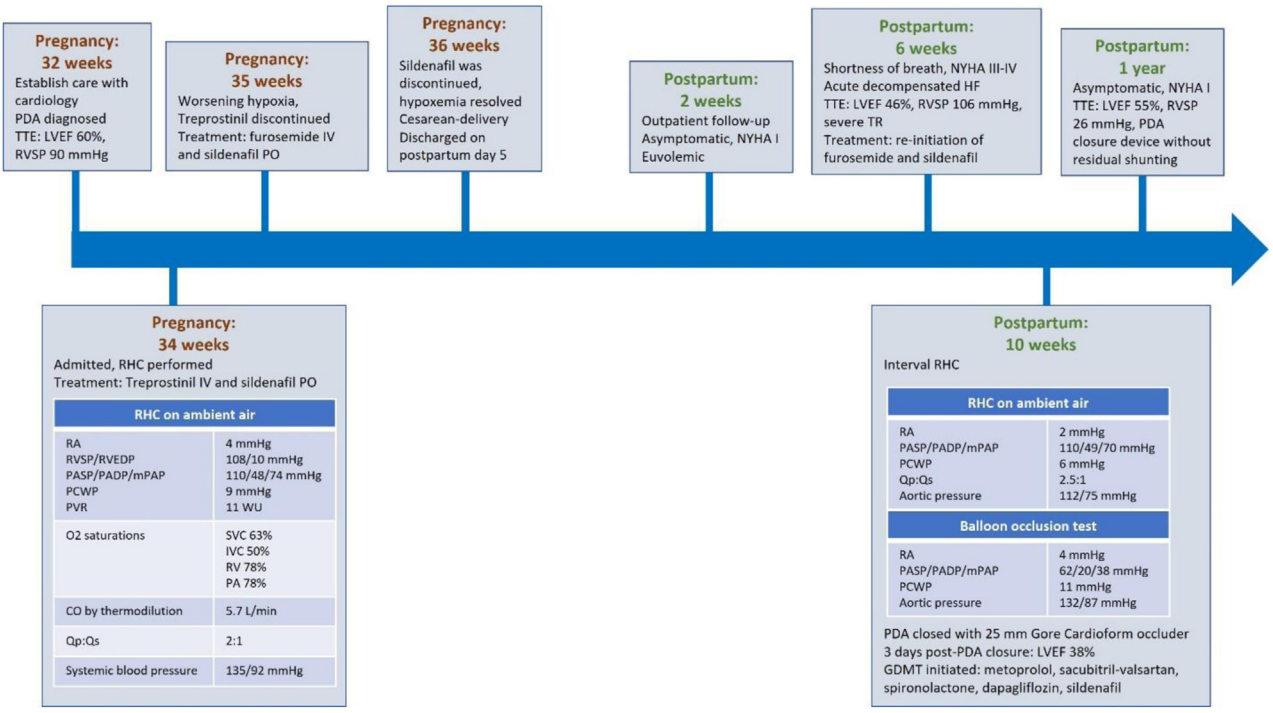

Figure 6 Timeline of events since first contact with cardiology, to follow-up 1 year after delivery. *CO*, Cardiac output; *IV*, intravenous; *mPAP*, mean PA pressure; *NYHA*, New York Heart Association class; *PO*, oral; *PADP*, PA diastolic pressure; *PCWP*, pulmonary capillary wedge pressure; *Qp*, pulmonary flow; *Qs*, systemic flow; *RA*, right atrium; *RHC*, right heart catheterization; *RVEDP*, RV end-diastolic pressure; *RVSP*, RV systolic pressure; *TR*, tricuspid regurgitation; *WU*, Woods units.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflicts of interest.

ACKNOWLEDGMENTS

We thank Andrea Sweeney-Walsh, RDCS, Brittany O'Neill, RDCS, Jennifer Bragg, RCS, and Abbey Bryant, RDCS, for acquisition of images.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.12.008.

REFERENCES

1. Canobbio MM, Warnes CA, Aboulhosn J, Connolly HM, Khanna A, Koos BJ, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American heart Association. Circulation 2017;135:e50-87.
2. Fadel BM, Mohty D, Husain A, Dahdouh Z, Al-Admawi M, Pergola V, et al. The various hemodynamic profiles of the patent ductus arteriosus in adults. Echocardiography 2015;32:1172-8.
3. Yuan SM. Eisenmenger syndrome in pregnancy. Braz J Cardiovasc Surg 2016;31:325-9.
4. Backes CH, Hill KD, Shelton EL, Slaughter JL, Lewis TR, Weisz DE, et al. Patent ductus arteriosus: a contemporary perspective for the pediatric and adult cardiac care provider. J Am Heart Assoc 2022;11:e025784.
5. Hasan A. Relationship of high altitude and congenital heart disease. Indian Heart J 2016;68:9-12.
6. Białkowski J, Głowacki J, Zabal C, Garcia-Montes A, Bermudez-Canete R, Flores-Arizmendi R, et al. Patent ductus arteriosus at low and high altitudes: anatomical and haemodynamic features and their implications for transcatheter closure. Kardiol Pol 2011;69:431-6.
7. Narvaez-Guerra O, Herrera-Enriquez K, Medina-Lezama J, Chirinos JA. Systemic hypertension at high altitude (Dallas, Tex: 1979). Hypertension 2018;72:567-78.
8. Mendelson MA. Pregnancy in women with left-to-right cardiac shunts: any risk? Int J Cardiol Congenit Heart Dis 2021;5:100209.
9. Curtis SL, Belham M, Bennett S, James R, Harkness A, Gamlin W, et al. Transthoracic echocardiographic assessment of the heart in pregnancy—a position statement on behalf of the British Society of echocardiography and the United Kingdom maternal cardiology Society. Echo Res Pract 2023;10:7.
10. Tso G, Lee J, Lui G, Trivedi H, Cohen M, Bernstein P, et al. Range of echocardiographic parameters during normal pregnancy. J Am Coll Cardiol 2012;59:E1301.
11. Prokšelj K, Brida M. Cardiovascular imaging in pregnancy. Int J Cardiol Congenit Heart Dis 2021;5:100235.
12. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of cardiology/American Heart Association task force on clinical practice guidelines. Circulation 2019;139:e698-800.
13. Wilson WM, Shah A, Osten MD, Benson LN, Abraha N, Breitner D, et al. Clinical outcomes after percutaneous patent ductus arteriosus closure in adults. Can J Cardiol 2020;36:837-43.
14. Jeong Y-H, Yun T-J, Song J-M, Park J-J, Seo D-M, Koh J-K, et al. Left ventricular remodeling and change of systolic function after closure of patent ductus arteriosus in adults: device and surgical closure. Am Heart J 2007;154:436-40.