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Reports of 2 Rare Associations of Hypoplastic Left Heart Syndrome

K. Anitha Jayakumar, MD,[a] Gouri Tilak, MD,[b] Bibhuti B. Das, MD[a]

ABSTRACT

This report describes 2 contrasting yet rare associations of hypoplastic left heart syndrome, 1 in a patient with pulmonary valve stenosis that was successfully surgically palliated and the other in a patient with an intact atrial septum and stenotic bilateral levoatriocardinal veins who was offered comfort care. These cases underscore the point that although both infants were born with hypoplastic left heart syndrome, the outcomes can dramatically differ as a result of anatomic and physiological variables. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2019;1:526–31)

We describe 2 infants with hypoplastic left heart syndrome (HLHS) who had differing physiological features from rare associations: the first had pulmonary valve dysplasia with stenosis and regurgitation, and the second had an intact atrial septum with decompressing bilateral levoatriocardinal veins.

CASE 1

HISTORY OF PRESENTATION. A full-term, nondysmorphic baby boy was born at a community hospital to a 26-year old gravida 2, para 2 mother following an otherwise uncomplicated pregnancy. There was no history of maternal diabetes or high-risk prenatal factors and no family history of congenital heart disease (CHD). At birth, the Apgar scores were 9 and 9 at 1 and 5 min, respectively. Birth weight was 4.1 kg. A loud murmur was heard on examination after birth, for which an echocardiogram was performed. Physical examination revealed oxygen saturations of 90% and a heart rate of 150 beats/min. Blood pressure in the right arm and in the lower limb were 58/35 and 56/32 mm Hg, respectively. Distal pulses in the upper and lower parts of the body were noted to be weak. Cardiac auscultation revealed a normal first heart sound, single second heart sound, systolic ejection click, systolic ejection murmur grade 3/6 at the upper left sternal border, and absence of a diastolic murmur. Results of physical examination of other systems were normal.

LEARNING OBJECTIVES

- Rare anatomic variations and comorbidities such as prematurity and IUGR are critical factors that influence clinical management choices for HLHS.
- Fetal detection of complex CHD and prenatal counseling are invaluable to set expectations regarding postnatal management for both the medical team and families.

MANAGEMENT. Echocardiogram showed HLHS for which he was immediately started on prostaglandin at 0.05 μg/kg/min at 8 h of life. His first blood gas measurements revealed the following: pH, 7.10; partial pressure of carbon dioxide, 40 mm Hg;

From the [a]Pediatric Heart Institute, Joe DiMaggio Children's Hospital, Hollywood, Florida; and the [b]Department of Radiology, Joe DiMaggio Children's Hospital, Hollywood, Florida. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Informed consent was obtained for this case.

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bicarbonate, 12.5 mEq/l; base excess, −17; and partial pressure of oxygen, 80 mm Hg. His lactic acid level was elevated at 10.1 mEq/l. He was intubated, administered intravenous vasopressors, and transferred to our cardiac intensive care unit. Echocardiography was repeated on arrival and confirmed a hypoplastic left ventricle (Figure 1A), mitral stenosis, aortic stenosis, a large patent ductus arteriosus with predominantly right-to-left shunting, moderate enlargement of the right ventricle with mildly decreased systolic function, trivial tricuspid regurgitation, pulmonary valve dysplasia (Figure 1B) with moderate stenosis (peak gradient 63 mm Hg) and moderate regurgitation, a markedly dilated pulmonary artery (PA), aortic arch hypoplasia (Figure 1C) with diastolic flow reversal into the ascending aorta, and a moderate-sized secundum atrial septal defect with nonrestrictive left-to-right shunting. Repeat blood gas values improved significantly to the following: pH, 7.35; partial pressure of carbon dioxide, 40 mm Hg; bicarbonate, 23 mEq/l; base excess, −4; and partial pressure of oxygen, 45 mm Hg. Serum blood urea nitrogen was 32 mg/dl, and creatinine was 0.7 mg/dl. A chest radiograph showed no cardiomegaly and mildly congested lung fields. Head and renal ultrasound findings were normal, as were his newborn screen results and chromosomal analysis. His cardiac function improved to normal on subsequent imaging. Recognizing the higher risk for surgical mortality posed by his native pulmonary valve disease, the options were primary heart transplantation versus Norwood palliation and potential future heart transplantation.

He underwent a Norwood procedure, which consisted of reconstruction of the aortic arch using pulmonary homograft with patch aortoplasty, a Damus-Kaye-Stansel anastomosis, and a 6-mm polytetrafluoroethylene ringed Gore-Tex conduit (W.L. Gore, Newark, Delaware) from the right ventricle to the central confluence of the PAs (Sano shunt). Intraoperatively the surgeon reported a tricommissural, dysplastic native pulmonary valve with thickening of all leaflets, with fusion of all 3 commissures with a short, free edge to the anterior most leaflet. Complex neoaortic (pulmonary) valvuloplasty was performed (tricommissural commissuroplasty where the commissures were brought out to the edge of the aortic wall, followed by thinning of all 3 leaflets with direct excision of the nodules along the

ABBREVIATIONS AND ACRONYMS

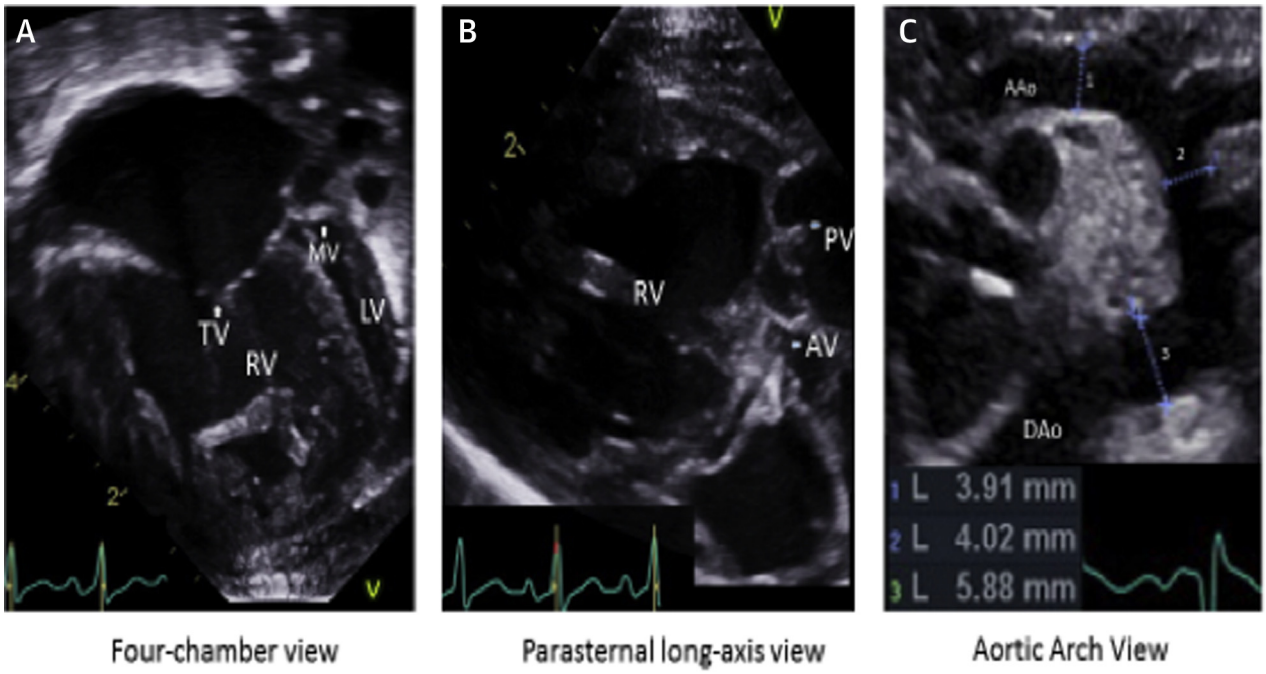
CHD = congenital heart disease

HLHS = hypoplastic left heart syndrome

IUGR = intrauterine growth retardation

PA = pulmonary artery

FIGURE 1 Findings in HLHS



Echocardiograms showing the **(A)** hypoplastic left heart syndrome (HLHS) in the first case with **(B)** a dysplastic and stenotic pulmonary valve and **(C)** a hypoplastic aortic arch. AV = aortic valve; DAo = descending aorta; LV = left ventricle; MV = mitral valve; RV = right ventricle; TV = tricuspid valve.

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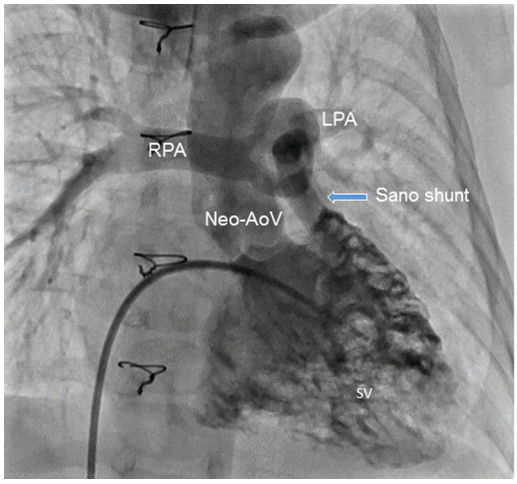
FIGURE 2 Angiography Before a Glenn Procedure



A right ventricular angiogram in the cranial left anterior oblique view showing a competent neoaortic valve (Neo-AoV) with no significant stenosis and normal-size branch pulmonary arteries before a Glenn procedure. LPA = left pulmonary artery; RPA = right pulmonary artery.

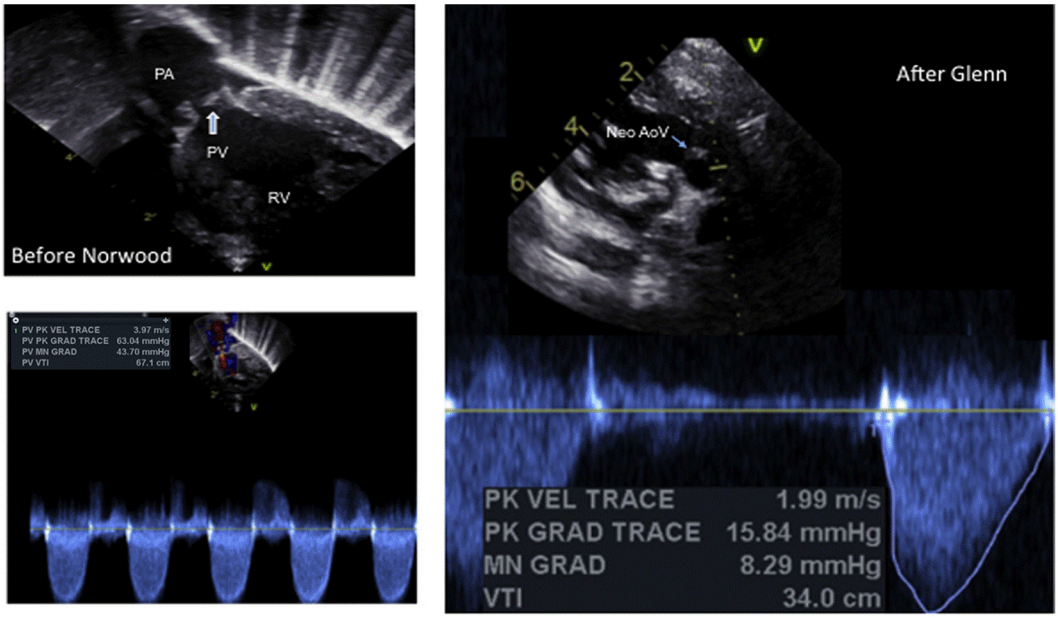
ventricular surface of the leaflets using a Beaver blade; the free edge of the anteriormost leaflet was divided in the middle, and a triangular piece of 2-ply extracellular matrix patch was sutured in place using running 7-0 polypropylene suture (Johnson and Johnson Medical Devices, New Jersey) to extend the midportion of this leaflet). Total cardiopulmonary bypass time was 227 min, and total aortic cross-clamp time was 71 min. He required temporary atrial pacing for junctional rhythm. He underwent delayed sternal closure on post-operative day 5 shortly after which he was successfully extubated. Post-operative transesophageal echocardiography demonstrated a peak gradient of 12 mm Hg across the neoaortic valve with moderate regurgitation and normal right ventricular systolic function. His post-operative course was otherwise uncomplicated. Because of concerns for aspiration, a G-tube was placed, and he was discharged home on day of life 42 with aspirin, enalapril, furosemide (Lasix), and pantoprazole. He was jointly monitored as an outpatient by the single-ventricle home monitoring program and the transplant service. He continued to do well clinically, with excellent growth and stable cardiac function. Serial interstage echocardiograms demonstrated mild neoaortic valve stenosis, but the regurgitation improved with time and was mild before stage 2 palliation. At 4 months of age he underwent cardiac catheterization (Figure 2) in preparation for stage 2 single-ventricle palliation. His hemodynamics values were as follows: mean right atrial pressure, 8 mm Hg; ventricle, 89/8 mm Hg; ascending aorta, 76/39 mm Hg with mean 56 mm Hg; and descending aorta pressure, 68/39 mm Hg with mean 52 mm Hg. Right PA diameter was 9.4 mm, and left PA diameter was 6.7 mm. He successfully underwent a bidirectional Glenn operation. His post-operative clinical course was uncomplicated, and he was discharged home 5 days after Glenn surgery. He was removed from the transplant waiting list at the time of discharge after the Glenn procedure. At last follow-up his neoaortic valve had mild stenosis (mean gradient 8 mm Hg) and regurgitation by echocardiogram compared with moderate stenosis (mean gradient 44 mm Hg) and regurgitation before the Norwood procedure (Figure 3). He is thriving, with normal growth and development, as of the writing of this report.

DISCUSSION. The first description of HLHS was provided by Dr. Bardeleben in Germany (1). In classical HLHS, there is hypoplasia of the left-sided heart structures, and the hypoplastic left ventricle cannot sustain systemic cardiac output. The common variants are mitral atresia and aortic stenosis, mitral and aortic atresia, and a rare variant where both mitral and aortic valves are small (2). Without intervention, HLHS is universally fatal, usually within the first weeks of life. Surgical treatment is staged palliation, consisting of a Norwood procedure in the neonatal period, followed by a superior cavopulmonary anastomosis (Glenn operation) between 4 and 6 months of age, and then conversion to the Fontan circulation achieved around the age of 3 years.

The combination of HLHS and pulmonary valve dysplasia is extremely rare, with a frequency of 0.4% among 230 autopsy cases of HLHS (3). One hypothesis for this finding is that during embryogenesis, the foramen ovale narrows, forcing flow from the inferior vena cava through the tricuspid valve into the pulmonary trunk, thus causing turbulence in the developing pulmonic region with subsequent pulmonary valve dysplasia or stenosis.

The successful outcome in our case may reflect the infant's greater body weight, no restriction of atrial-level shunting, normal right ventricular systolic function, minimal atrioventricular regurgitation, mitral stenosis, and aortic stenosis with some prograde blood flow through the native aortic valve. Prior reports of this rare association are limited (3–5), and they painted a dismal prognosis, with most patients not surviving except in 1 case where surgical palliation was also successful (6).

FIGURE 3 Doppler Findings Before and After Valve Repair



Doppler study of the dysplastic and stenotic pulmonary valve (PV) before the Norwood operation and the neoaortic valve after the Glenn procedure. GRAD = gradient; MN = mean; PA = pulmonary artery; PK = peak; VEL = velocity; VTI = velocity-time integral.

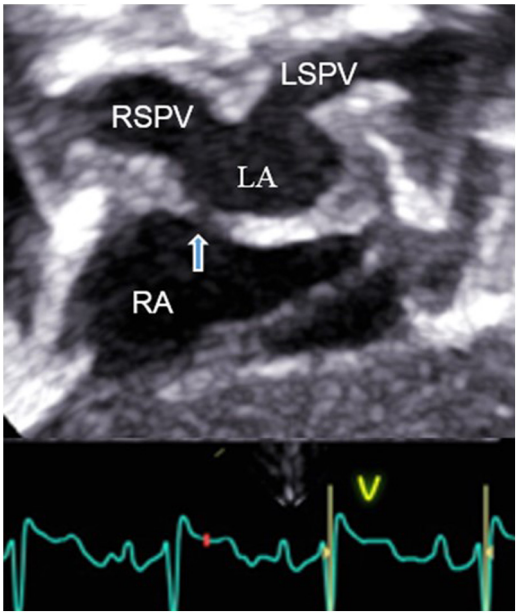
CASE 2

HISTORY OF PRESENTATION. A pre-term baby girl was born to a 30-year-old gravida 3 para 1 mother at 34 weeks of gestation secondary to fetal distress. Birth weight was 1.38 kg (severe intrauterine growth retardation [IUGR]), and Apgar scores were 6 and 7 at 1 and 5 min, respectively. Pregnancy was complicated by gestational diabetes, hypertension, and chlamydial infection. No family history of CHD was present. Fetal echocardiography at an outside facility had reportedly revealed HLHS, and the parents were reportedly counseled regarding staged single-ventricle surgical palliation. She was intubated immediately after birth as a result of poor respiratory effort and hypotonia. Her cardiac examination was notable for a single first heart sound and no appreciable murmurs. A chest radiograph showed pulmonary venous congestion with a ground-glass appearance of both lung fields. An echocardiogram after birth confirmed HLHS with mitral and aortic atresia, an intact atrial septum (Figure 4), dilated main PA, and a large, tortuous patent ductus arteriosus with potentially 2 decompressing levoatriocardinal veins.

MANAGEMENT. She was administered a prostaglandin infusion and remained on positive-pressure ventilation with initially stable hemodynamic values. A computed tomography angiogram was performed to define pulmonary venous anatomy and demonstrated the following. The 2 right-sided and 2 left-sided pulmonary veins each formed a confluence and drained into the left atrium. In addition, the right superior pulmonary vein that was formed from a confluence of the middle and upper lobe veins also continued to a markedly tortuous and stenotic vertical vein that eventually drained to the right brachiocephalic vein-superior vena cava confluence. The left inferior pulmonary vein continued into a possibly stenotic left levoatriocardinal vein that eventually drained to the left brachiocephalic vein (Figures 5A to 5C).

The infant developed progressive pulmonary venous congestion and severe acidosis. After much deliberation among the care team, it was decided that surgical intervention was not a viable option because of the recognized dismal clinical outcomes in view of her comorbidities, including prematurity, severe IUGR, an intact atrial septum, obstructed pulmonary venous egress, and recognized pulmonary vascular disease. The family declined an autopsy.

FIGURE 4 Intact Atrial Septum



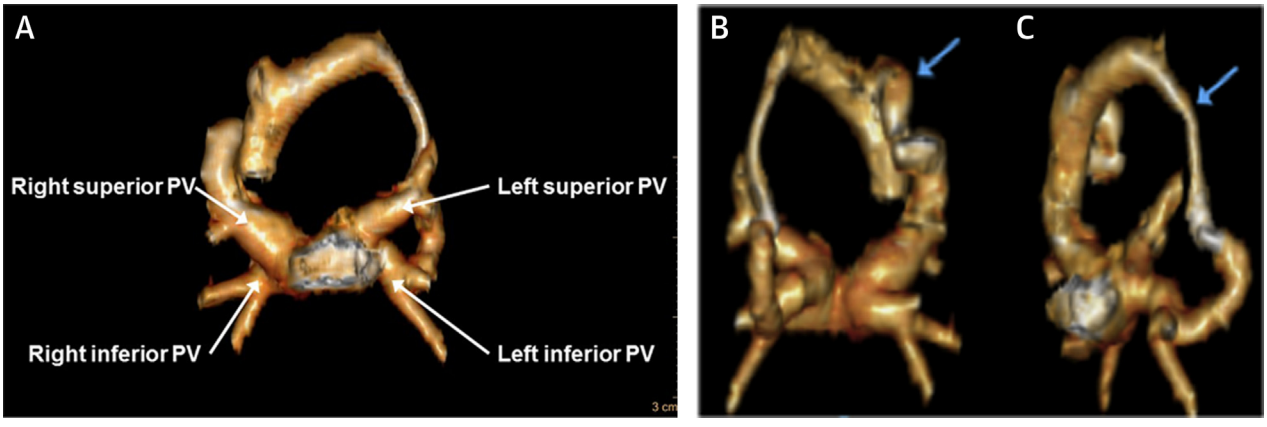
Echocardiogram showing an intact atrial septum **(arrow)** in the second case of hypoplastic left heart syndrome. LA = left atrium; LSPV = left superior pulmonary vein; RA = right atrium; RSPV = right superior pulmonary vein.

DISCUSSION. HLHS with an intact atrial septum is a rare finding, although it has been reported that in 23% of HLHS surgical specimens from patients who had a Norwood procedure, the foramen ovale was found restrictive or closed (7). In this variant of HLHS, there is no effective egress from the left atrium without decompressing levoatriocardinal veins, and this has been previously described in left-sided obstructive lesions (8). Decompressing levoatriocardinal veins are thought to result from the persistence of anastomotic channels that connect the capillary plexus of the embryonic foregut to the cardinal veins, which are often complex and stenotic, as was described in this case. The prognosis in this cohort remains poor despite advances in prenatal detection and postnatal management (9). Levoatriocardinal veins are rare even among patients with severe left-sided heart obstructive disease and provide egress of pulmonary venous return only in those patients without any significant interatrial communications. This rare anomaly has been described unilaterally, and we are also unaware of any published reports of bilateral channels. A potential possibility is that cases with bilateral channels such as that case described here are severe, and either these fetuses die in the womb or the infants who are born alive do not survive the immediate postnatal period.

CONCLUSIONS

In neonates with HLHS and significant pulmonary valve dysplasia, despite the potential future need for neoaortic valve repair and/or replacement, surgical Norwood palliation with neoaortic valvuloplasty is a reasonable therapeutic option versus primary heart transplantation. In stark contrast to the first case, in the second case, because of the stated cumulative

FIGURE 5 Abnormal Pulmonary Venous Drainage



Computed tomography angiogram showing the abnormal pulmonary venous (PV) drainage in the second case of hypoplastic left heart syndrome. **(A)** Pulmonary veins seen from the posterior aspect of the left atrium. **(B)** The right superior pulmonary vein continues as the right levoatriocardinal vein **(arrow). (C)** The left inferior pulmonary vein continues as the left levoatriocardinal vein **(arrow).**

comorbidities, we pursued a "do nothing" approach by recognizing the futility of staged surgical palliation and/or heart transplantation. These 2 disparate but rare cases of HLHS highlight the complex decision-making processes that often confront clinicians even in the current era of improved outcomes for HLHS. These scenarios are not dissimilar from morbidities recognized more often in clinical practice such as pulmonary vein stenosis, tricuspid valve regurgitation, prematurity, growth retardation, and genetic syndromes. Recently, it was observed in Sweden that with enhanced imaging techniques, prenatal detection of HLHS has increased with a proportionate rise in staged surgical palliation, although simultaneously the fetal termination rates for this diagnosis have also increased (10).

ADDRESS FOR CORRESPONDENCE: Dr. K. Anitha Jayakumar, Joe DiMaggio Children's Hospital Heart Institute, 1005 Joe DiMaggio Drive, Fourth Floor, Hollywood, Florida 33021. E-mail: KaJayakumar@mhs.net.

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