Prenatal Diagnosis and Outcome of Fetuses with Double-Inlet Left Ventricle

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ABSTRACT

The aim of this study is to characterize the in utero presentation of the subtype of double-inlet left ventricle (DILV), a rare congenital heart disease, and assess the postnatal outcome. We retrospectively studied fetuses diagnosed prenatally with DILV between 2007 and 2011. We reviewed the prenatal and postnatal echocardiograms, clinical presentations, karyotypes, and the postnatal outcomes. There were eight fetuses diagnosed with DILV with L-transposition of the great vessels (S, L, L). Mean gestational age at diagnosis was 24.7 weeks. Of these, four fetuses (50%) had pulmonary atresia. One fetus (12.5%) also had tricuspid atresia and coarctation of the aorta and died at 17 months of age. Complete heart block and long QT syndrome was present in one fetus (12.5%), who died shortly after birth. There were no extracardiac or karyotypic abnormalities. Six (75%) infants are alive and doing well. Double-inlet left ventricle with varied presentation can be accurately diagnosed prenatally. The outcome of fetuses is good in the absence of associated rhythm abnormalities with surgically staged procedures leading to a Fontan circulation.

KEYWORDS: Congenital heart disease, double-inlet left ventricle, fetal echocardiography, single ventricle

Double-inlet left ventricle (DILV) is a form of univentricular atrioventricular connection. It is a rare congenital cardiac anomaly with an incidence of 0.05 to 0.1 per 1000 live births.[1] It accounts for 1% of all congenital cardiac anomalies and is seen in 4% of neonates with congenital cardiac disease.[2] Double-inlet ventricle exists when the greater part of both atrioventricular (AV) junctions is supported by a single ventricular chamber.[3] It comprises a heterogeneous group of cardiac anomalies that can involve several combinations of morphological and functional variation at the level of the AV valves, ventriculoarterial connection, and systemic or pulmonary outflow obstruction. The varying arrangements lead to a single functioning ventricular chamber, more commonly the left ventricle.

The aim of this study was to characterize the in utero presentation of the subtype of DILV and assess the postnatal outcome.

METHODS

This was a retrospective study performed at the University of Minnesota, Minneapolis. It was approved by the University of Minnesota Institutional Review Board. Eight fetuses with DILV were identified from the fetal echocardiography database from July 2007 to February 2011. DILV was identified on the basis of a single large

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morphological left ventricle containing two AV valves that were separated from the small underdeveloped right ventricle by the bulboventricular foramen. The reason for referral for fetal echocardiography was abnormal cardiac structures found during an obstetric ultrasound examination. Prenatal echocardiography and Doppler interrogation were obtained at 20 to 34 weeks of gestation. Maternal prenatal and postnatal medical records were reviewed for gestational age (GA) at diagnosis and at delivery, karyotypic abnormalities, extracardiac anomalies, growth restriction, and fetal and neonatal clinical course. All fetal and transthoracic echocardiograms were performed at the University of Minnesota hospital as part of routine clinical care. Examinations included two-dimensional fetal and transthoracic echocardiography with pulse wave and color Doppler imaging using variable frequency transducers. The studies were performed using Hewlett-Packard 5500 (Hewlett-Packard, Andover, MA). All prenatal and postnatal echocardiograms were reviewed retrospectively by a single examiner. Tei index or myocardial performance index was measured using pulsed-wave Doppler technique on the prenatal and the first postnatal echocardiographic stored images. The degree of AV valve insufficiency was recorded prenatally and postnatally. Cardiothoracic ratios were calculated prenatally. Delivery information including GA at delivery, mode of delivery, birth weight, and Apgar scores were also reviewed. The number and type of staged surgical palliative procedure were recorded for each infant with associated morbidity and mortality. Confirmation of prenatal diagnosis was obtained from postnatal transthoracic echocardiography, angiography, and subsequent operations.

All data are presented as the mean $\pm$ standard deviation with ranges.

RESULTS

Eight patients were prenatally diagnosed with DILV. All eight fetuses were live-born. The mean GA at diagnosis was 24.7 ± 5 (range 20 to 34) weeks. Three fetuses were referred in the third trimester. Seven fetuses (87.5%) were referred to the fetal cardiologist for abnormal cardiac anatomy on obstetric ultrasound. One fetus (12.5%) was referred for increased nuchal translucency. The mean maternal age was 27.8 ± 3.3 (range 21 to 31) years. No maternal risk factors were present. None of the infants had any major extracardiac or karyotypic abnormalities. Two fetuses (25%) had one minor anomaly. One had a single umbilical artery and, the other had increased nuchal translucency.

All eight fetuses were of (S, L, L) form of DILV with anterior and leftward aorta arising from the outlet chamber and the pulmonary artery (PA) arising from the left ventricle. From the four-chamber view, both AV valves are seen opening into the large smooth-walled left ventricle (Figs. 1A and 1B). The outlet hypoplastic right ventricle was L-looped (left side of the larger left ventricle). Most patients (87.5%) had two AV valves. Anatomic features and clinical data of the prenatal and postnatal outcomes are presented in Table 1. Four fetuses (50%) had pulmonary atresia, of which one fetus had severe subpulmonary stenosis at 29 weeks that evolved into pulmonary atresia at 34 weeks of GA. Three had membranous pulmonary atresia. One fetus (12.5%) with no pulmonary outflow obstruction was diagnosed with a right aortic arch postnatally. One fetus (12.5%) had tricuspid hypoplasia at 22 weeks, which evolved into tricuspid atresia at 32 weeks of gestation. This same fetus was diagnosed postnatally with coarctation of the aorta.

One fetus (12.5%) with no pulmonary outflow obstruction presented with congenital complete heart

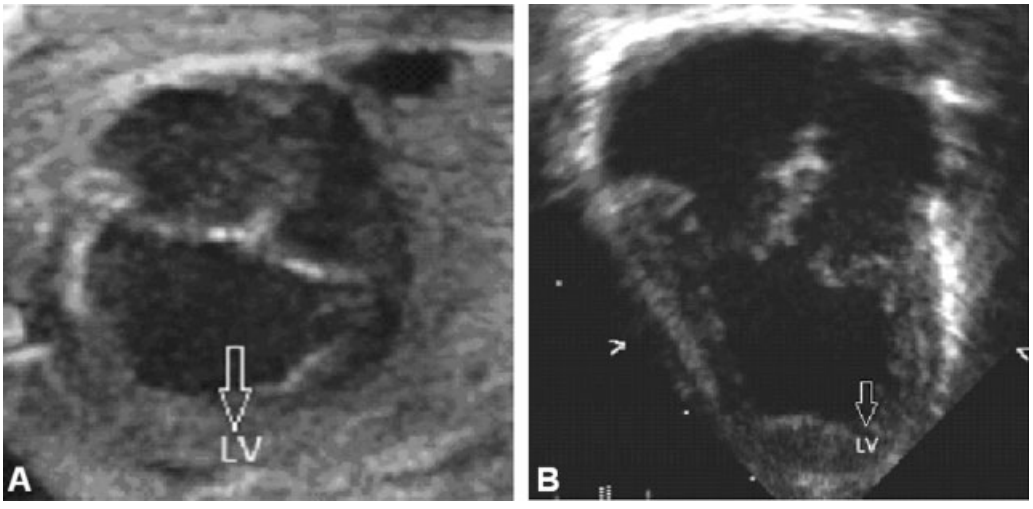

Figure 1 (A) Two-dimensional fetal echocardiogram at 24 weeks of gestation. (B) Two-dimensional transthoracic echocardiogram at birth. Both images demonstrate double-inlet left ventricle (two atrioventricular valves empty in a smooth walled left ventricle).

Table 1 Data of Patients with DILV

Case	Fetal Echo (GA wk)	CT Ratio	Prenatal Diagnosis	Postnatal Diagnosis	LV Tei		AV Valve Insufficiency		GA at Delivery (wk)	Birth Wt (g)	Surgical Outcome	Survival
					Prenatal	Postnatal	Prenatal	Postnatal				
1	34	0.4	DILV, L-TGA pulmonary atresia (membranous)	DILV, L-TGA, pulmonary atresia (membranous)	34 wk: 0.2	0.2	No	No	39	3370	1. central shunt (14 DOL)	Male; alive (12 mo)
											2. Glenn (6 mo)	
2	22	0.5	DILV, L-TGA, tricuspid hypoplasia, no PS, mild right AV valve insufficiency, LV mildly dilated	DILV, L-TGA, tricuspid atresia, coarctation of aortic arch, no PS, mild right AV valve insufficiency, LV mildly dilated	22 wk: 0.68	0.33	Mild right AV valve	Mild right AV valve	39	3160	1. PA banding, coarctation repair (7 DOL)	Female; died (17 mo)
	27				27 wk: 0.64						2. CHB pacemaker placed at 4.5 mo	
	32				32 wk: 0.62						3. RSV myocarditis resulted in heart failure needing heart transplant (17 mo)	
3	20	0.5	DILV, L-TGA, No PS, mild right AV valve insufficiency	DILV, L-TGA	20 wk: 0.2	0.37	Mild right AV valve	No	38	3080	Glenn and PA banding (6 mo)	Male; alive (23 mo)
	24				24 wk: 0.2							
	30				30 wk: 0.3							
4	29	0.5	DILV, L-TGA, severe PS evolved into pulmonary atresia with retrograde flow in the PDA	DILV, L-TGA, pulmonary atresia	29 wk: 0.35	0.56	No	No	38	3300	1. central shunt (4 DOL)	Male; alive (32 mo)
	34				34 wk: 0.37						2. Glenn (3.3 mo)	
											3. Fontan (2 y)	
5	25	0.5	DILV, L-TGA, pulmonary atresia (membranous)	DILV, L-TGA, pulmonary atresia (membranous)	25 wk: 0.21	0.6	No	No	38	3520	1. central shunt (7 DOL)	Male; alive (33 mo)
											2. Glenn (6 mo)	
											3. Fontan (2 y)	
6	20	0.3	DILV, L-TGA, no PS	DILV, L-TGA, no PS, right aortic arch	20 wk: 0.3	0.56	Mild right AV valve	Mild right AV valve	39	3770	1. PA banding (7 DOL)	Male; alive (41 mo)
	24				24 wk: 0.37						2. Glenn (6 mo)	
	34										3. Fontan (2.5 y)	
7	28	0.5	DILV, L-TGA, pulmonary atresia (membranous)	DILV, L-TGA, pulmonary atresia (membranous)	28 wk: 0.33	0.47	No	No	40	3380	Central shunt (5 DOL)	Female; alive (2 mo)
	32				32 wk: 0.53							

Table 1 (*Continued*)

Case	Fetal Echo (GA wk)	CT Ratio	Prenatal Diagnosis	Postnatal Diagnosis	LV Tei		AV Valve Insufficiency		GA at Delivery (wk)	Birth Wt (g)	Surgical Outcome	Survival
					Prenatal	Postnatal	Prenatal	Postnatal				
8	20	0.5	DILV, L-TGA, CHB, long QT syndrome, hydrops	Neonatal death	20–24 wk: 2	n/a	No	n/a	28	1170	Neonatal death	Male; Neonatal death
	24											

AV, atrioventricular; CHB, complete heart block; CT, cardiothoracic ratio; DILV, double-inlet left ventricle; DOL, day of life; GA, gestational age; L-TGA, L-transposition of the great arteries; LV, left ventricle; n/a, not applicable; PA, pulmonary artery; PS, pulmonary stenosis; RSV, respiratory syncytial virus; Wt, weight.

block at 20 weeks of gestation. The atrial rate was 120 to 130 beats per minute and the ventricular rate was 40 to 50 beats per minute. There was a family history of long QT syndrome among two maternal second-degree relatives, and there was concern for coexisting fetal long QT syndrome. Fetal magnetocardiography was performed at a research laboratory, which diagnosed long QT syndrome with QTc interval at 600 to 700 milliseconds. Steroids for fetal lung maturity were administered, and the fetus was closely monitored by serial echocardiography. Hydrops developed at 24 weeks. There was continuous deterioration of fetal cardiac function with a Tei index of 2 and nonreassuring fetal heart status. At 28 weeks, the baby was delivered liveborn but died shortly after birth.

Mild AV valve insufficiency was present in 37.5% of fetuses, but was only present postnatally in 25% of infants. All fetuses had a normal cardiothoracic ratio, with a mean of 0.46 ± 0.07 (range 0.3 to 0.5). The mean GA of delivery was 37.3 ± 3.8 (range, 28 to 40) weeks and the mean birth weight was 3093 ± 805 (range 1170 to 3770) g. Apgar scores for seven neonates at 5 minutes were 8 or more. None of the neonates required intubation. Prostaglandin infusion was required for maintaining ductal patency in cases of systemic or pulmonary obstruction.

The outcome of the fetuses with DILV was variable. One fetus with heart block and long QT syndrome died shortly after birth. Of the remaining seven fetuses, postnatal follow-up is available for a period ranging from 2 to 41 months. All seven infants had staged surgical palliation. Four infants with pulmonary outflow obstruction underwent a central shunt in the first few days of life (range 3 to 14 days), of which, one infant has had bidirectional Glenn and three have had Fontan completion and all infants are doing well.

One infant had PA banding with no pulmonary outflow obstruction in the first week of life. This was followed by bidirectional Glenn and Fontan completion, and the infant is doing well. One infant had mild pulmonary stenosis requiring PA band and Glenn at 6 months of age, and the infant is doing well. The infant with associated tricuspid atresia and coarctation of the aorta underwent PA band and repair of the coarctation of the aorta. This infant developed complete heart block and required a permanent pacemaker at 4.5 months of age. At 6 months of age, this infant developed respiratory syncytial myocarditis resulting in heart failure and was placed on the heart transplant list. The infant died postoperatively after a heart transplant at 17 months of age. Overall survival was 75%.

DISCUSSION

DILV can be associated with a variable neonatal outcome depending on the associated cardiac anomalies.

Common morphological patterns seen are a left anteriorly located ascending aorta from the right ventricle and pulmonary trunk arising right posteriorly from the dominant left ventricle (74%), obstruction to the aortic arch (12%), and pulmonary stenosis (40%).[4] DILV has been associated with AV valve abnormalities (mainly AV insufficiency) in 39% of cases.[5] Our study showed findings with (S, L, L) in all fetuses (100%), with pulmonary atresia in 50% and aortic arch obstruction in 12.5%. Mild AV valve insufficiency was present in 37.5% prenatally and 25% postnatally.

Prenatal diagnosis was accurate in seven of the eight fetuses. One fetus with coexisting coarctation of the aorta was diagnosed postnatally. Detection of coarctation of the aorta is challenging prenatally. It can be a progressive lesion in utero with relative worsening of the distal arch hypoplasia in later gestation,[6] due to continual decrease in the amount of blood flow traversing the isthmus as pregnancy advances. Quantitative distal aortic arch hypoplasia and ventricular and great artery size discrepancy have been observed and may facilitate the diagnosis during serial echocardiographic evaluation.

In our study, one fetus had a coexistent congenital complete heart block. There was also a strong maternal family history of long QT syndrome, and this was suspected in the fetus. The diagnosis was confirmed with fetal magnetocardiography. The ventricular rate in the fetus was less than 50 beats per minute, which progressed to hydrops, resulting in preterm delivery and subsequent neonatal death. The presence of a complete AV block along with complex congenital heart defect has been associated with poor prognosis. A ventricular rate of less than 60 beats per minute and the presence of hydrops are associated with a survival rate of 20%.[7] Fetal magnetocardiography is a noninvasive technique to monitor spontaneous electrophysiological activity of the fetal heart through extremely weak variations of the associated magnetic fields, located outside the maternal abdomen by superconducting sensor arrays.[8] It can be recorded reliably from the 20th week of gestation and can be used to classify arrhythmias.[8] It has also been used to diagnose prolonged QT syndrome.[9,10] Long QT syndrome is inherited as an autosomal-dominant form with variable presentation. It is a rare, but potentially life-threatening condition and can lead to ventricular flutter in utero.[11] In our study, fetal magnetocardiography facilitated the diagnosis of long QT syndrome allowing appropriate counseling to the family regarding the severity of the complex heart defect.

Assessment of fetal cardiac function is of critical importance in some high-risk fetuses. Tei index has been described as an easily measured Doppler-derived index of left or right ventricular myocardial performance combining systolic and diastolic time intervals.[12] It is a combined index of global myocardial function and is independent of heart rate and ventricular geometry.[12,13] The fetus with heart block, long QT syndrome, and hydrops had significantly elevated Tei index (2.0) at 24 weeks, and died shortly after delivery at 28 weeks.

Infants with DILV who have no pulmonary outflow obstruction tend to develop congestive heart failure within the first few months of life due to the increased blood flow and require PA banding early in the neonatal period. In cases of pulmonary outflow obstruction, a systemic-to-PA shunt is required to provide adequate blood flow for oxygenation. The timing of this procedure depends on the degree of the pulmonary stenosis. Infants with severe obstruction require this palliative surgery earlier compared with those with moderate restriction who remain well compensated for a longer time. In neonates with severe systemic outflow obstruction, repair of the same is needed prior to the closure of the ductus arteriosus, to maintain adequate systemic flow. The neonatal course depends on the presence of associated malformations, especially of the AV valves and outflow tract obstruction. The most common approach to the surgical management is a staged approach that usually culminates in a modified Fontan operation.[14] The initial surgery is aimed to limit the pulmonary blood flow and repair the aortic arch obstruction if present, as in our series. None of the infants required Norwood or Damus-Stansel-Kaye operation; however, regular surveillance echocardiography is being performed to detect any systemic outflow obstruction. Although the initial palliative surgery with PA banding compares favorably with Norwood results, lower morbidity and mortality are seen in Clark series.[15] Fontan is the ultimate procedure of choice for patients with DILV. Early mortality has decreased to 3% and survival is 97 and 88% at 5 and 10 years after surgery, respectively.[16] Vigilant follow-up is needed to monitor the development of systemic outflow obstruction after the Fontan operation.

CONCLUSION

Prenatal diagnosis of DILV has increased over the last decade.[17] DILV, L-transposition of the great arteries, and associated evolving outflow obstruction can be diagnosed prenatally due to an abnormal four-chamber and outflow tract views with serial fetal echocardiography. Prenatal diagnosis allows delivery to be planned at a tertiary care facility with optimal postnatal management and early interventions including administration of prostaglandins and availability of neonatology, cardiology, and pediatric cardiac surgery. Prenatal diagnosis helps with the opportunity to discuss and counsel the complex situation with parents and prepare them for the likely course of their newborn.

The limitations of the study include a small number of patients identified, which is not unusual due to the rarity of this complex congenital heart defect. The strength of our study is that all patients were from a

single institution, which relates to uniformity of care including surgical techniques, and pre- and postoperative management.

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