Mitral valve dysplasia syndrome: A unique form of left-sided heart disease

Lindsay S. Rogers, MD,[a] Amy L. Peterson, MD,[a] J. William Gaynor, MD,[b] Jonathan J. Rome, MD,[a] Paul M. Weinberg, MD,[a] and Jack Rychik, MD[a]

Background: Mitral valve dysplasia syndrome is a unique form of left-sided heart disease characterized by aortic outflow hypoplasia, dilated left ventricle, dysplastic/incompetent mitral valve, and a restrictive/intact atrial septum. Patients with this constellation of abnormalities have been managed in a variety of ways with overall poor outcomes.

Methods: We performed a retrospective review of all patients with mitral valve dysplasia syndrome to identify fetal echocardiographic markers predictive of outcomes.

Results: Mitral valve dysplasia syndrome was identified in 10 fetuses. Fetal left heart dilation and abnormal pulmonary venous flow were associated with increased mortality. Seven fetuses had abnormal pulmonary venous Doppler patterns; 3 had a unique ''double-reversal'' flow pattern. Severe fetal left heart dilation (left heart/right heart area ratio > 1.5) was present in 5. Prenatal intervention was performed on 3 fetuses: balloon aortic valvuloplasty (n = 2) and balloon atrial septostomy (n = 1). Of the 3, one died in utero and neither survivor underwent a 2-ventricle repair. Five patients required an immediate postnatal intervention to open the atrial septum. The overall mortality was 50%.

Conclusions: Mitral valve dysplasia syndrome is a unique form of congenital heart disease with severe aortic stenosis but normal or enlarged left ventricle secondary to primary mitral valve disease. Increased left heart size and pulmonary vein Doppler patterns are predictive of postnatal outcome. Despite the presence of a dilated left ventricle, postnatal management with staged single ventricle palliation may be the most effective strategy. (J Thorac Cardiovasc Surg 2011;142:1381-7)

Critical left-sided obstructive heart disease can manifest within a wide spectrum of anatomic variability. Aortic outflow obstruction in the presence of an intact ventricular septum can be associated with a diminutive left ventricle and is then referred to as hypoplastic left heart syndrome (HLHS). In this anomaly, a left ventricle of inadequate size dictates management toward the strategy of staged palliation for single ventricle reconstruction, culminating in a Fontan procedure. In contrast, aortic outflow obstruction with valvular aortic stenosis (AS), an intact ventricular septum, and a normal or dilated left ventricle usually represents critical aortic valve disease. In this anomaly, balloon aortic valvuloplasty (BAV) or aortic valve surgery to relieve outflow obstruction is performed in an attempt to recruit the left ventricle as the systemic ventricle. Fetal echocardiography can accurately diagnose and distinguish between different forms of critical left-sided congenital heart disease in utero, which allows for proper prenatal counseling and preparation for specific postnatal management strategies.

We describe a distinct form of critical left-sided heart disease that does not easily fall into the categories described herein. In this anomaly, there is severe aortic outflow obstruction and an intact ventricular septum, but a normal-sized or dilated left ventricle in the presence of severe mitral regurgitation (MR). The left atrium is enlarged and the atrial septum is either severely restrictive or intact. Inasmuch as mitral valve disease with significant MR is a distinctive feature, we refer to this entity as the ''mitral valve dysplasia syndrome'' (MVDS). This anomaly differs from other forms of critical left-sided heart disease, having discrete pathophysiologic features and a distinct set of findings discernible on fetal echocardiography. Patients with a prenatal diagnosis of the aforementioned constellation of anatomic abnormalities have previously been reported to have an extremely poor prognosis, some dying in utero.[1-3] Management of MVDS as either a form of isolated critical AS or conventional HLHS can lead to decisions that lack full consideration of the uniqueness and complexity of this disease.

We report our experience with prenatally diagnosed MVDS, including prenatal progression of disease, management strategies applied, and their variable outcomes. We aim to identify prenatal echocardiographic features of MVDS that are predictive of postnatal outcomes and may guide future management decisions for these patients. By

From the Divisions of Cardiology[a] and Cardiothoracic Surgery,[b] Children's Hospital of Philadelphia, Philadelphia, Pa.

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Address for reprints: Jack Rychik, MD, Cardiac Center at The Children's Hospital of Philadelphia, 34th St and Civic Center Blvd, Philadelphia, PA 19104 (E-mail: Rychik@email.chop.edu).

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Abbreviations and Acronyms

AS = aortic stenosis
BAV = balloon aortic valvuloplasty
HLHS = hypoplastic left heart syndrome
MR = mitral regurgitation
MVDS = mitral valve dysplasia syndrome
OHT = orthotopic heart transplant

recognizing this constellation of cardiovascular findings as a distinct disease entity, we can devise novel strategies to improve outcomes for this patient population.

METHODS

Patients

Retrospective review of The Fetal Heart Program database at the Children's Hospital of Philadelphia identified fetuses with a diagnosis of MVDS syndrome between January 2002 and December 2009. Inclusion criteria were presence of a normal or dilated left ventricle in the face of aortic hypoplasia (aortic annulus diameter < 2 standard deviations for gestational age) and hemodynamically significant MR (moderate or greater) determined by original report and confirmed by our review. All had at least 1 prenatal echocardiogram and documentation of subsequent clinical course. The study was approved by the Institutional Review Board at The Children's Hospital of Philadelphia (CHOP IRB# 10-007559).

Fetal Echocardiography

Fetal echocardiograms were performed using a Siemens Sequoia system (Siemens Medical Solutions, Inc, Mountain View, Calif) using curvilinear 6-MHz probe. Standard imaging was performed using the American Society of Echocardiography protocol.[4] Digital images were acquired as 3-second loops and reviewed with measurements made blinded to clinical outcome using a syngo Dynamics version 8.0 (Siemens Medical Solutions, Inc) analysis workstation. An optimal 4-chamber view was identified and the cardiothoracic area ratio was measured. Right atrial, left atrial, right ventricular, and left ventricular cavity areas were individually traced at end-diastole. The sum of the left atrial and left ventricular area was compared with that of the right atrial and right ventricular area and an index of the ratio of left-sided/right-sided area was calculated as a measure of overall relative left-sided enlargement. The atrial septum was inspected with 2-dimensional imaging and interrogated with color Doppler flow mapping in multiple planes with notation made of the presence or absence of a defect. Spectral tracings of pulsed-wave Doppler interrogation of the pulmonary veins were analyzed, and patterns of flow were identified.

Prenatal and Neonatal Clinical Course

All diagnoses were confirmed, when possible, by a complete postnatal echocardiographic evaluation. In 2 patients, the left ventricular area was obtained by tracing the left ventricular cavity in end-diastole, both before and after initial palliative surgery. Charts were reviewed to obtain data concerning prenatal and neonatal clinical course. When applicable, pathology reports were reviewed and the heart specimens were examined in conjunction with a cardiac pathologist (P.W.).

Data Analysis

Echocardiographic data of left-sided/right-sided area ratio and pulmonary venous flow patterns were correlated with need for immediate postnatal intervention and outcome. Cardiac nonsurvival was defined as not alive or receiving a heart transplant. Progressive change in echocardiographic parameters from initial diagnostic fetal echocardiogram until last prenatal assessment was noted.

RESULTS

Subjects

Ten patients received a prenatal diagnosis of MVDS between 2002 and 2010. Data are summarized in Table 1. One family opted for nonintervention at birth (patient 9) and 9 patients were followed serially. Forty-two fetal echocardiograms were performed (range, 1-9 per fetus). Gestational age at initial diagnosis ranged from 21 to 35.7 weeks. Mean gestational age at last fetal echocardiogram was 34 $\pm$ 4.3 weeks. Three of the 10 gestations were twin. Three patients had hydrops fetalis: 1 (patient 1) had spontaneous resolution of hydrops without intervention, another (patient 8) had stabilization of hydrops on initiation of maternal oral digoxin, and the third (patient 10) died at 29 weeks during fetal intervention. Gestational age at delivery ranged from 33.7 to 39 weeks; birth weight ranged from 1600 to 3300 g.

Echocardiographic Findings

Echocardiographic data are reported (Table 1) from the last fetal echocardiogram in 9 patients (incomplete images in patient 6) performed at a range of 24.9 to 39 weeks of gestation.

Heart size. Six of the 9 patients had cardiomegaly noted on fetal echocardiogram with cardiothoracic area ratios greater than 0.33 (Figure 1). Left heart/right heart area ratio was predictive of cardiac mortality; no patient with a left heart/right heart area ratio of more than 1.5 at final assessment had cardiac survival beyond the neonatal period. Figure 2 demonstrates the change in left heart/right heart area ratio during gestation. Patient 1 had a ratio of 2.9 at initial presentation at 27.7 weeks of gestation and had a steady decline to 0.99 at 39 weeks, surviving beyond the neonatal period.

Atrial septum. One patient (no. 10) had an intact atrial septum and the remainder had a restrictive atrial septum on initial fetal echocardiogram. Three patients progressed from a restrictive atrial septum on fetal echocardiogram to an intact atrial septum at birth. Patient 7 had an intact atrial septum on the final fetal echocardiogram at 34 weeks. The remaining 2 patients had a restrictive atrial septum on the final fetal echocardiogram but an intact atrial septum on the initial postnatal echocardiogram. All patients with an intact atrial septum at birth had a left heart/right heart ratio of 1.5 or more on fetal echocardiogram.

Pulmonary venous Doppler flow patterns. Two patients had normal pulmonary venous Doppler patterns (Figure 3, *A*). Four patients had blunting of peak velocity of the systolic wave and significant atrial systolic flow reversal (Figure 3, *B*), a pattern similar to that previously described