Texas Heart Institute Journal

Case Reports

Fetal Left Ventricular Apical Aneurysm Progressing to Dilated Cardiomyopathy Due to Glycogen Storage Disease

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Fetal dilated cardiomyopathy is a rare anomaly characterized by ventricular dilation and dysfunction. Its causes are diverse, and its outcomes are generally dismal. We describe a rare case of prenatally diagnosed left ventricular apical aneurysm that progressed rapidly to dilated cardiomyopathy. At age 2 months, the infant underwent heart transplantation. Pathologic examination of the explanted heart revealed that the cause of the dilated cardiomyopathy was glycogen storage disease. This case highlights the crucial roles of timely diagnosis, frequent close monitoring, and multidisciplinary care in achieving a successful postnatal outcome. ***(Tex Heart Inst J 2022;49(4):e207364)***

Citation:
Challapudi G, Boyle GJ, Rodriguez ER, Komarlu R. Fetal left ventricular apical aneurysm progressing to dilated cardiomyopathy due to glycogen storage disease. Tex Heart Inst J 2022;49(4):e207364. doi: 10.14503/THIJ-20-7364

Key words:
Cardiomyopathy, dilated/diagnosis; delivery rooms/organization & administration; fetal diseases/diagnosis/diagnostic imaging/etiology/pathology/physiopathology; glycogen storage disease; heart ventricles; infant, newborn; prenatal diagnosis; treatment outcome; ultrasonography, prenatal

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Fetal dilated cardiomyopathy (DCM) is a rare form of cardiomyopathy associated with varying degrees of ventricular dilation and dysfunction. Fetal DCM can be caused by viral infections, tachycardia, or genetic, metabolic, and idiopathic factors. It affects 0.4% to 3.6% of high-risk pregnancies[1-3] and is fatal in 70% to 80% of cases. Fetal DCM is associated with a high rate of spontaneous intrauterine or neonatal death, especially death related to hydrops fetalis.[1,4]

We report a case of left ventricular (LV) apical aneurysm with rapid progression to fetal DCM, caused by glycogen storage disease (GSD).

Case Report

A 21-year-old woman, pregnant for the first time, presented for routine obstetric ultrasonography with the fetus at 24 weeks' gestation. The patient had had an upper respiratory tract infection at 6 weeks' gestation. Test results for cytomegalovirus, parvovirus, *Toxoplasma gondii*, and anemia were negative.

The fetal ultrasonogram incidentally revealed LV dilation. A fetal echocardiogram at 26 weeks' gestation revealed normal segmental cardiac anatomy; however, a portion of the LV apex was thin-walled, dilated, and dysfunctional, suggesting an aneurysm (Fig. 1). A small circumferential pericardial effusion was noted, but no mitral regurgitation (MR) was observed. The fetal heart rate and rhythm were normal. The cardiovascular profile score (a composite score of cardiomegaly, ventricular and valvar function, umbilical arterial and venous Doppler imaging, and effusions) was 9.0/10.0.[5]

At 32 weeks' gestation, a follow-up echocardiogram revealed worsening dilation and thinning that encompassed almost the entire LV, raising concern about progression to DCM (Fig. 2). There was moderately decreased LV systolic function. The small circumferential pericardial effusion persisted, and severe MR was now apparent.

At 34 weeks' gestation, the fetus developed polyhydramnios of unclear cause and underwent amnioreduction. Subsequent fetal echocardiograms at 34 to 36 weeks' gestation revealed a persistent severely dilated, thin-walled, dysfunctional LV with severe MR (Fig. 3); the cardiovascular profile score had declined to 2.0/10.0. Fetal magnetic resonance images revealed adequate lung volumes and no intracranial abnormality.

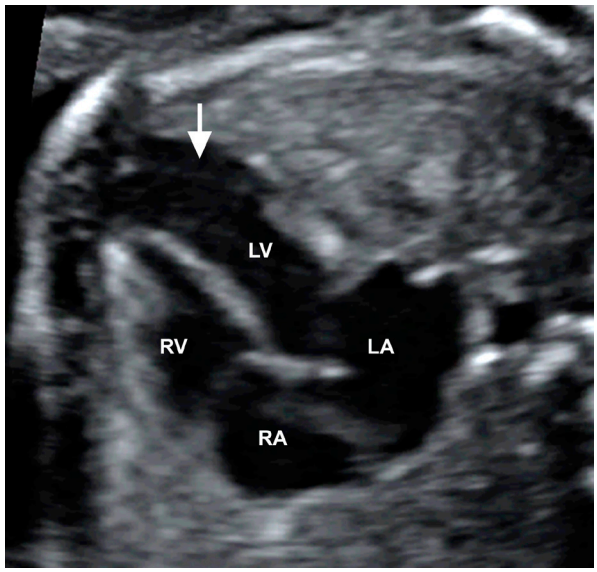

Fig. 1 *Fetal echocardiogram at 26 weeks' gestation (4-chamber view) shows a left ventricular (LV) aneurysm (arrow).*

LA = left atrium; RA = right atrium; RV = right ventricle

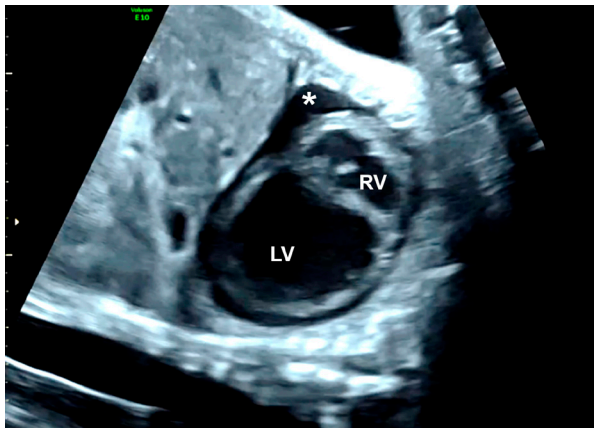

Fig. 2 *Fetal echocardiogram at 32 weeks' gestation (short-axis view) shows moderate left ventricular (LV) dilation and a small pericardial effusion (asterisk).*

RV = right ventricle

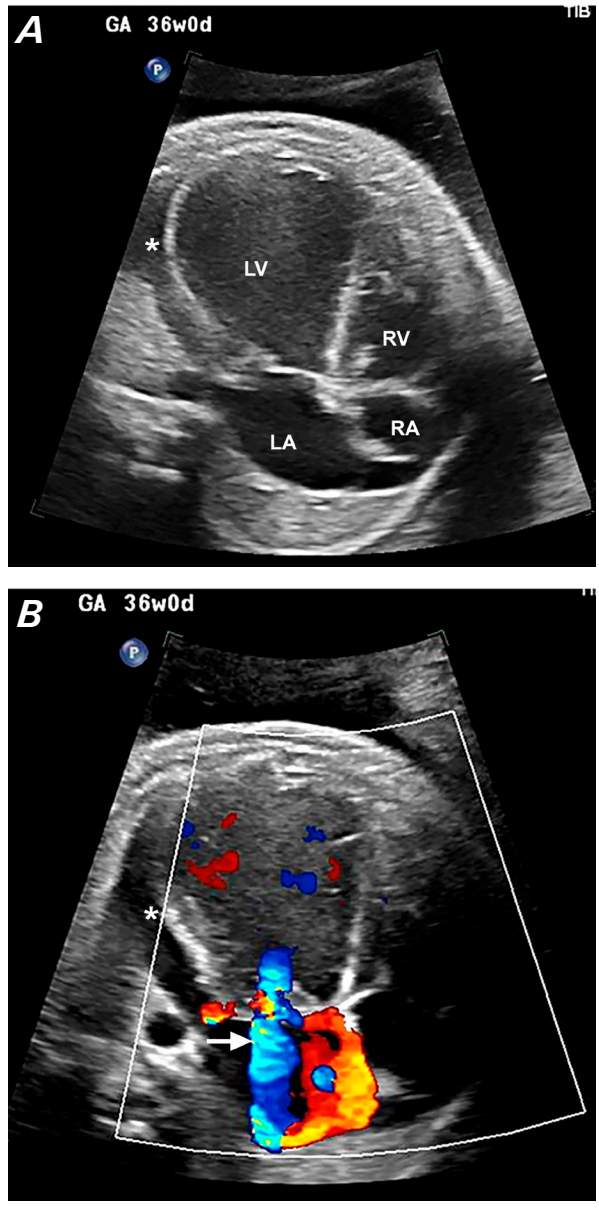

Fig. 3 *Fetal echocardiograms at 36 weeks' gestation (4-chamber views) show **A**) a thin-walled, severely dilated left ventricle (LV) and compressed right ventricle (RV) with a small pericardial effusion (asterisk), and **B**) severe mitral regurgitation (arrow) and pericardial effusion (asterisk).*

LA = left atrium; RA = right atrium

Supplemental motion image is available for Figure 3B.

We assembled a multidisciplinary care team of subspecialists who would be involved in the care of the mother and the newborn, including a pediatric cardiac intensivist, pediatric cardiologist, pediatric cardiac interventionalist, pediatric cardiothoracic surgeon, pediatric cardiac anesthesiologist, neonatologist, fetal surgeon, obstetrician, maternal fetal medicine physician, and maternal anesthesiologist; delivery personnel in the special delivery unit, pediatric cardiac intensive care unit, and neonatal intensive care unit; extracorporeal membrane oxygenation personnel; and cardiac catheterization laboratory personnel. A comprehensive care plan and checklist were devised (Fig. 4). Delivery in the special delivery unit was planned, with potential "exit to extracorporeal membrane oxygenation" as one of the management options. Several practice runs were completed before the anticipated delivery, to minimize time delays in performing each task.

However, the mother went into labor earlier than planned and delivered a male infant at 37 weeks' gestation by cesarean delivery (birth weight, 3.5 kg). The newborn was stabilized, intubated, and placed on inotropic support with prostaglandin, epinephrine, and dobutamine infusions promptly after umbilical venous

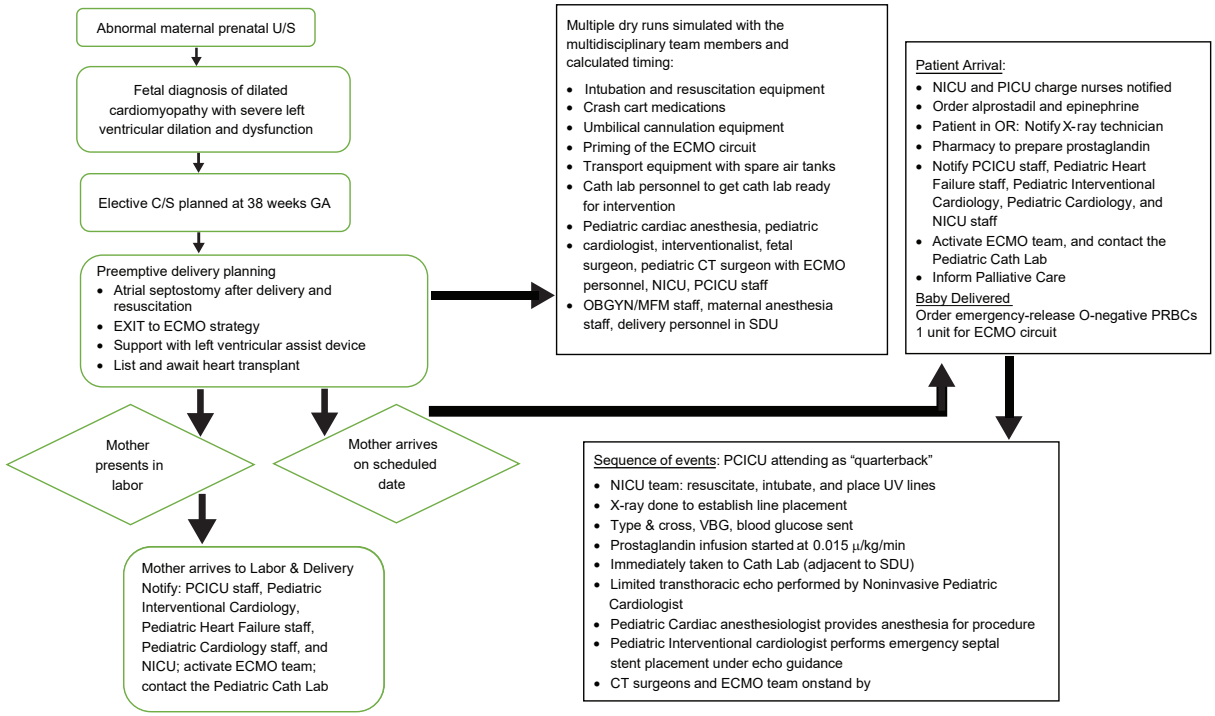

Fig. 4 *Diagram shows the planned care-path algorithm for delivery and management.*
C/S = cesarean delivery; cath = catheterization; CT = cardiothoracic; echo = echocardiogram; ECMO = extracorporeal membrane oxygenation; EXIT = ex utero intrapartum treatment; GA = gestational age; lab = laboratory; MFM = maternal fetal medicine; NICU = neonatal intensive care unit; OBGYN = obstetrics and gynecology; OR = operating room; PCICU = pediatric cardiac intensive care unit; PICU = pediatric intensive care unit; PRBC = packed red blood cells; SDU = special delivery unit; U/S = ultrasound; VBG = venous blood gas

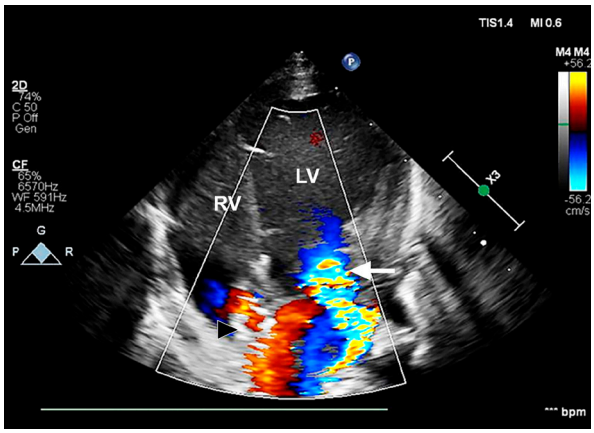

Fig. 5 *Postnatal transthoracic echocardiogram shows a severely dilated and thin-walled left ventricle (LV), severe mitral regurgitation (arrow), and left-to-right flow through the atrial stent (arrowhead).*

RV = right ventricle

Supplemental motion image is available for Figure 5.

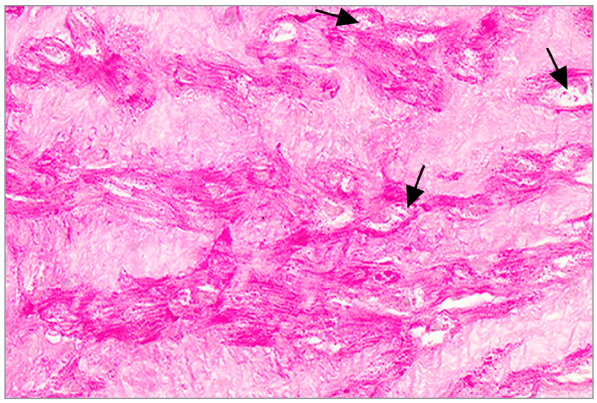

Fig. 6 *Photomicrograph shows glycogen granules (deep pink) in the sarcoplasm of the myocytes (arrows) (periodic acid–Schiff staining, orig. ×1,000).*

line placement. He was immediately taken to the cardiac catheterization laboratory, where a rapidly obtained postnatal echocardiogram confirmed the prenatal findings and also identified elevated left atrial pressure and a restrictive patent foramen ovale. An emergency balloon atrial septostomy with atrial septal stent placement was performed to reduce the left atrial pressure (Fig. 5).

The newborn was rapidly transported to the intensive care unit. Because he was critically ill and needed hemodynamic stabilization, no coronary or aortic root angiography was performed. After heart transplant evaluation that day, the newborn was listed for transplantation (United Network for Organ Sharing 1A) on hospital day 4. On day 12, he underwent Berlin LV

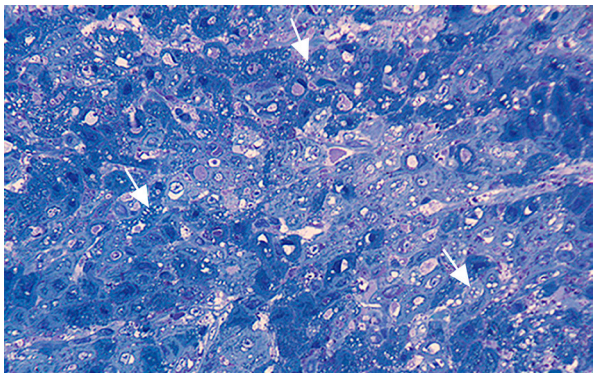

Fig. 7 *Photomicrograph shows plastic-embedded tissue, indicating abundant sarcoplasmic inclusion of glycogen (arrows) (toluidine blue stain, orig. ×1,000).*

assist device placement as a bridge to heart transplantation. The transplant was successfully completed when he was 2 months old.

More than 6 months after transplant, the infant's allograft function was preserved. Pathologic analysis of the explanted heart revealed abundant myocardial glycogen accumulation, consistent with primary storage disorder involving glycogen metabolism (Figs. 6 and 7). Accordingly, the fetal DCM was attributed to GSD. The infant continued to show no signs of hepatosplenomegaly at the most recent follow up, 26 months after transplantation.

Discussion

Cardiomyopathies account for 8% to 11% of cardiovascular disorders detected in utero.[1-4] Primary fetal cardiomyopathy is an etiologically heterogeneous condition that can be caused by intrinsic fetal pathologic status or by extrinsic factors.[1] In a large prenatal series by Pedra and colleagues,[1] fetuses with DCM had significantly lower right and left ventricular shortening fractions and a tendency toward a larger cardiothoracic ratio. Systolic and diastolic dysfunction and atrioventricular valve regurgitation were identified as risk factors for death, because they were more prevalent in nonsurvivors. Compared with hydrops fetalis and systolic dysfunction, diastolic dysfunction was associated with an 8-fold–higher mortality rate.[1] In another study,[6] hydrops fetalis was associated with an 18% survival rate and a high rate of spontaneous intrauterine and early neonatal death. The absence of hydrops fetalis despite worsening cardiac function and progressive atrioventricular valve regurgitation most likely contributed to our patient's survival and safe delivery.

Fetuses and infants with DCM have extremely poor overall outcomes. More than 80% will die or will need cardiac transplantation[1]; however, some milder forms of DCM can have better outcomes.[7] The fetus in our case was diagnosed initially as having an LV aneurysm that progressed to DCM within a 6-week period, highlighting the need for close serial monitoring to evaluate the natural history and progression to potential cardiomyopathy.[6,8] A complete diagnostic workup for fetal DCM should include a detailed maternal and family history, hematologic indices, autoimmune antibody testing, a detailed fetal anatomic survey, infectious studies, and genetic counseling to determine treatable causes; nonetheless, in our case, prenatal workups for all of these potential causes were negative.

Serial fetal echocardiography with close monitoring of ventricular function and rhythm is crucial to assist with and tailor management plans. Donofrio and colleagues[9] elegantly outlined steps for achieving successful outcomes in complex prenatal conditions, including individualized care plans and algorithms, multidisciplinary expert teams, simulations, checklists, and debriefing—all of which were done in our case (Fig. 4). Although a cesarian delivery was planned to reduce the risk for fetal compromise, the mother unexpectedly went into early labor. Because of careful planning and multiple simulations, the postnatal transition was smooth and uneventful.

Dilated cardiomyopathy is most often idiopathic in origin; only 4% of cases are caused by inborn errors of metabolism (vs 27% of hypertrophic cardiomyopathy cases).[10] Cardiac involvement can occur in GSD type II (acid maltase deficiency, Pompe disease), type III (debranching enzyme deficiency, Forbes disease), type IV (branching enzyme deficiency, Andersen disease), type V (myophosphorylase deficiency), and type IX (cardiac phosphorylase kinase deficiency); types II, III, and IX usually present with hypertrophic cardiomyopathy.[11] Patients with storage diseases typically present with coarse or dysmorphic facial features, hepatosplenomegaly, and skeletal deformities.[10,12] In this case, an abdominal ultrasonogram showed no hepatosplenomegaly.

Cardiomyopathy is the chief reason for heart transplants in infants younger than one year of age, who have some of the worst pediatric cardiology outcomes.[13] Presentations of cardiomyopathy in infants and young children depend on the cause and degree of myocardial dysfunction and include symptoms related to heart failure, such as grunting, tachypnea, trouble breathing, failure to thrive, poor weight gain, hepatomegaly, and pedal edema. Life-threatening arrhythmias or unexplained syncope due to LV outflow tract obstruction can be an ominous indication of Pompe disease.

Our case highlights that DCM can indeed be caused by GSD. This is a rare event, because GSD is more often associated with hypertrophic cardiomyopathy. A few reports have described the cases of adults with LV apical aneurysm and DCM caused by GSD type IV, but this also is a rarity, given that children with DCM have a poor prognosis and will probably need a heart transplant within a few years of diagnosis.[13-15]

Conclusion

In this patient, prenatal LV apical aneurysm progressed rapidly to DCM, impaired ventricular function, and MR. Our case highlights the importance of serial monitoring for the progression of adverse conditions and the role of multidisciplinary care in achieving successful outcomes, from delivery to postnatal heart transplant.

Acknowledgment

We thank Neha Chellu for her help in editing this manuscript.

Published: 25 August 2022

Conflict of Interest Disclosure: None

Funding/Support: None

Meeting Presentation: This work was presented orally at the 10th annual Phoenix Fetal Conference; Scottsdale, Arizona, 11 November 2019.

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