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CASE REPORT

Left Ventricular Noncompaction: A Rare Cause of Hydrops Fetalis

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Abstract We present a case of isolated left ventricular noncompaction (LVNC), a severe congenital cardiomyopathy, which presented in the neonatal period as fetal hydrops. To our knowledge, this is the first child with LVNC presenting with hydrops fetalis to survive infancy. Once considered a uniformly fatal and extremely rare form of cardiomyopathy, LVNC has recently been shown to be more common than previously reported, with a varying range of clinical severity. Although long-term morbidity and mortality are not clearly known, recent work suggests better survivability than once reported.

Keywords Ventricular noncompaction · Cardiomyopathy · Hydrops fetalis · Newborn

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Left ventricular noncompaction (LVNC), also known as spongy ventricular myocardium, is a rare cardiomyopathy occasionally presenting with congestive heart failure and hydrops fetalis in the neonatal period. Ventricular noncompaction is believed to result from an insult during fetal development that causes an arrest of normal compaction of ventricular myocardium [1]. LVNC has been previously reported in an infant who presented at birth with congestive heart failure and severe hydrops fetalis. That infant died of heart failure on the second day of life [5]. We present here a child with isolated LVNC that presented with profound hydrops fetalis in the newborn period and has now survived into toddlerhood.

Case Report

A female infant was born at 33 weeks' gestation to a 31-year-old G_3P_2 Caucasian mother with a prenatal course complicated by gestational diabetes type A2 and positive Group B streptococcus carrier status. A 22-week ultrasound performed at an outside facility was reportedly normal. The mother presented with regular uterine contractions and decreased fetal movement. Ultrasound revealed hydrops fetalis with large pleural effusions and severe bradycardia, prompting an emergent cesarean section. At delivery, the infant remained bradycardic despite intubation and positive pressure ventilation. Emergent pleurocentesis was performed, with a significant improvement in heart rate. Apgar scores were 4 and 7 at 1 and 5 min, respectively.

Physical examination revealed a severely edematous neonate with no obvious dysmorphic features. Birth weight was 3940 g. Initial oxygen saturations were 61% on 100% oxygen. Chest X-ray revealed diffuse opacification of both

lung fields; oxygenation improved after placement of bilateral chest tubes and surfactant administration. Laboratory studies were significant for a hematocrit of 38.3%, total protein of 2.2 g/dL, albumin of 1.3 g/dL, total bilirubin of 1.5 mg/dL, 4+ protein on urine dipstick, prothrombin time >50 s, and D-dimer of 3.2 μg/mL. Initial management to correct coagulopathy and support blood pressure included red blood cell, cryoprecipitate, and fresh-frozen plasma transfusions, albumin administration, and initiation of dopamine and dobutamine drips.

Initial electrocardiogram demonstrated normal sinus rhythm without abnormalities. Repeat electrocardiogram on day of life 4 after improvement of edema showed biventricular hypertrophy with massive QRS voltages (Fig. 1). An echocardiogram performed during the first hour of life showed decreased contractility and mild pericardial effusion. The heart and great vessels appeared structurally normal, although the exam was suboptimal due to severe anasarca. Serial echocardiograms over the following days revealed extensive trabeculations in the left ventricle with regional hypokinesis consistent with isolated LVNC (Fig. 2 and Supplements 1–3). Laboratory evaluation to identify causes of fetal hydrops, including hemolysis, chromosomal and metabolic abnormalities, congenital nephrotic syndrome, and infection, were unremarkable. Ultimately, the cause of hydrops fetalis was determined to be congestive heart failure secondary to isolated LVNC. The infant's cardiac function was initially stabilized on dopamine and dobutamine, resulting in shortening fractions of 29–42%. She was subsequently transitioned to oral digoxin, enalapril, and furosemide, with a shortening fraction of 19% at the time of discharge.

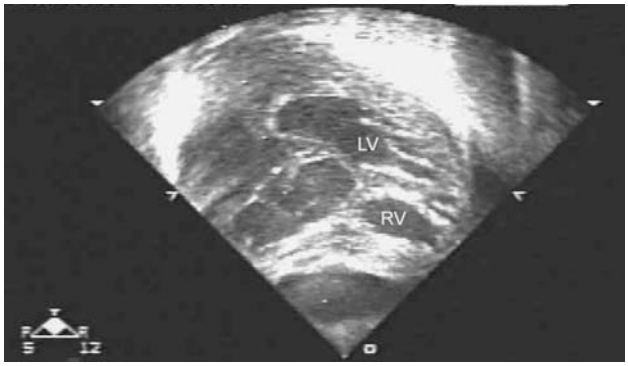

Fig. 2 Still image from echocardiogram completed on day of life 4 demonstrating extensive trabeculations in the left ventricle. See Electronic Supplements 1–3 for video clips. *LV* left ventricle; *RV* right ventricle

The infant's inpatient course was complicated by an isolated perforation of the lesser curvature of the stomach

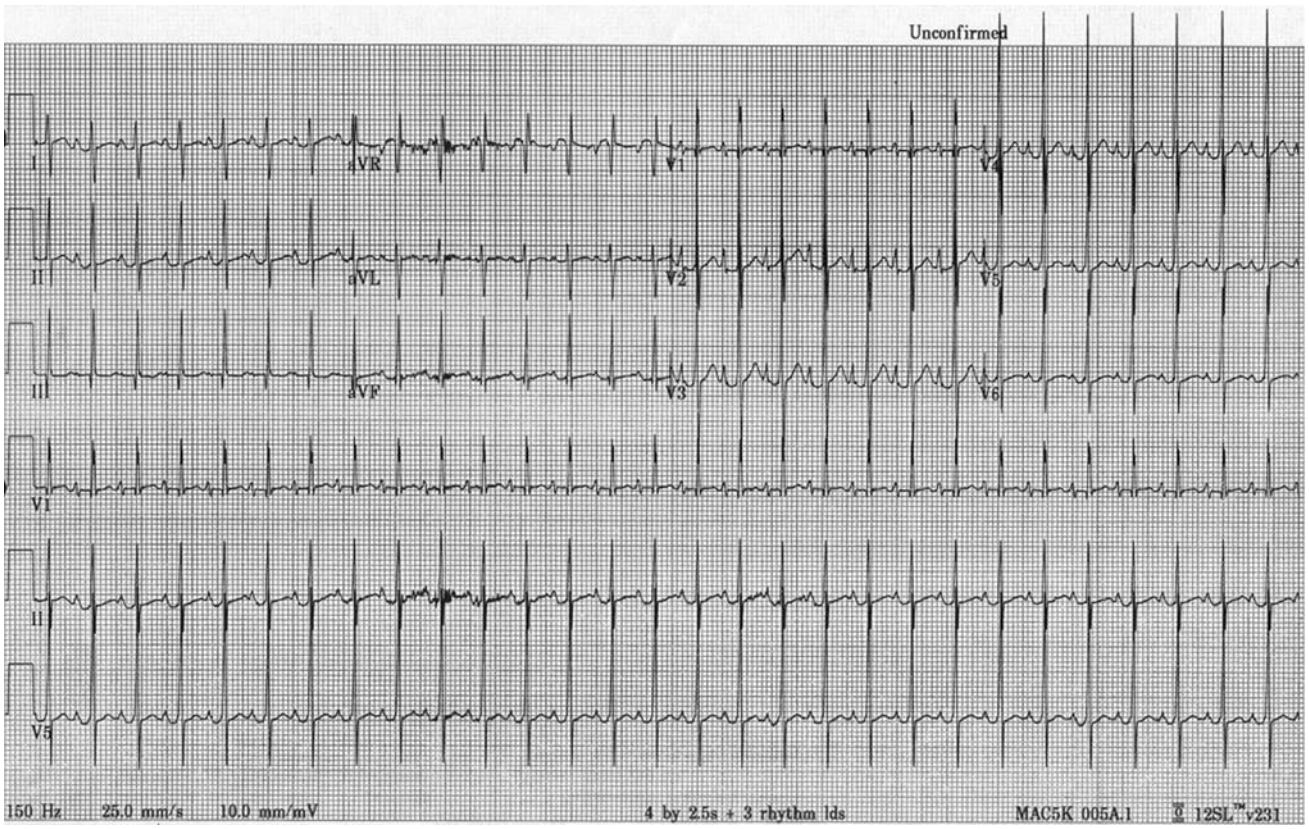

Fig. 1 Electrocardiogram completed on day of life 4 demonstrating biventricular hypertrophy and massive QRS voltages

that was surgically repaired. She developed significant direct hyperbilirubinemia. Extrahepatic biliary atresia and other pathologic causes of direct hyperbilirubinemia were ruled out, and the hyperbilirubinemia resolved spontaneously after discharge. She had difficulty tolerating oral feedings, so she was discharged on gastrostomy feedings.

Her outpatient course has been significant for pathologic gastroesophageal reflux requiring Nissen fundoplication as well as pulmonary hypertension of unknown etiology, postulated to be secondary to chronic microaspiration. Her cardiac function has remained stable on furosemide, digoxin, spironolactone, and enalapril, with recent shortening fractions measuring 25–30%. Developmentally, she is within normal limits along language streams but mildly delayed along motor streams and does not display any obvious dysmorphic features at 2 years of age.

Discussion

First described in 1990, LVNC is a congenital cardiomyopathy characterized by gross autopsy findings of dysplastic and thinned-appearing myocardium with excessive trabeculations not communicating with any structures other than the left ventricular cavity [1]. Ventricular noncompaction is believed to result from a defect during endomyocardial morphogenesis occurring at 5 to 8 weeks of gestation, at which time a gradual compaction of myocardium normally occurs. The apparent arrest of compaction results in the persistence of prominent trabeculations and deep intertrabecular recesses. Ventricular noncompaction can be isolated, most commonly involving the left ventricle, or associated with other congenital heart defects. The exact prevalence of LVNC is unknown, but recent research suggests that it may be underdiagnosed. Patients commonly present with signs and symptoms of heart failure during infancy; however, some patients have been identified in late childhood, adolescence, or adulthood, suggesting a spectrum of clinical severity [9, 12]. LVNC has been previously reported in a neonate who presented at birth with congestive heart failure and hydrops fetalis; the infant died on the second day of life [5].

The recognition of ventricular noncompaction requires a strong index of suspicion. Many patients have electrocardiographic abnormalities, with marked biventricular hypertrophy and extreme QRS voltages, T wave inversion, and pre-excitation, including Wolff-Parkinson-White syndrome [7, 11]. Two-dimensional echocardiography, angiography, or cardiac magnetic resonance imaging can be used to make the diagnosis. Depressed systolic function, prominent ventricular trabeculations with deep intertrabecular recesses, regional hypokinesis, and color Doppler demonstrating blood flow through the recesses in continuity with only the ventricular cavity are suggestive of ventricular noncompaction; however, debate exists regarding specific diagnostic criteria [2, 4]. The differential diagnosis of isolated LVNC includes prominent trabeculations as a normal variant, other cardiomyopathies with prominent trabeculations, and cardiac metastases [1, 7]. Comorbid conditions such as chromosomal abnormalities, metabolic diseases, and mitochondrial disorders, in particular, Barth syndrome, have all been associated with ventricular noncompaction and should be ruled out during the evaluation.

LVNC was previously considered an unclassified cardiomyopathy by the World Health Organization; however, the American Heart Association reclassified LVNC as a genetic primary cardiomyopathy in 2006 [6]. Kindred studies demonstrate an 18% to 50% inheritance among first- or second-degree relatives [12]. X-linked inheritance has been associated with mutations in the G4.5 gene on chromosome Xq28, which encodes a protein family called tafazzins. This defect has been identified in patients with Barth syndrome and muscular dystrophies [3]. Cases of autosomal dominant inheritance have been associated with defects in the ZASP gene on chromosome 10q22 [10], α-dystrobrevin gene on chromosome 18q12 [3], and candidate genes muscle LIM protein and SOX6 on chromosome 11p15 [8]. No specific genes have been identified with a purely autosomal recessive or mitochondrial inheritance pattern.

Once the diagnosis of LVNC is established, management strategies are tailored toward clinical and echocardiographic findings and known comorbidities. The only definitive treatment is heart transplantation. Patients with systolic dysfunction and heart failure are treated with anticongestive therapy [7, 11]. Some institutions have used "metabolic cocktails" with coenzyme Q10, carnitine, riboflavin, and thiamine in patients with suspected mitochondrial or metabolic syndromes [7]. Confounding clinical factors, especially cardiac arrhythmias and thromboembolism, should be identified and addressed, although the prevalence of these complications is much higher among adults with noncompaction. In a case series of 36 pediatric patients with noncompaction, only 25% had cardiac arrhythmias and none had a history of thromboembolic events [7]. The long-term clinical outcome of patients with noncompaction is poor, with death ultimately occurring from heart failure or sudden cardiac death. Two recent case series of 58 children with ventricular noncompaction demonstrated 5-year survival rates of 70–75%, with 10% of patients requiring heart transplantation [7, 11].

In summary, LVNC is a congenital cardiomyopathy that can present with hydrops fetalis in the newborn period. Recent literature suggests that LVNC is more prevalent than previously thought and should be considered when evaluating a child with cardiomyopathy. More research is needed to better understand the pathophysiology of

ventricular noncompaction, but modern congestive heart failure interventions and advances in heart transplant medicine have improved outcomes.

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