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Clinical features of Neonatal Cardiomyopathy

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Abstract

Background: Neonatal cardiomyopathy is a rare disease that ranges from being asymptomatic to abruptly lethal and is not well characterized [1]. We investigated the clinical features of five neonates with cardiomyopathy in our hospital to determine key clinical characteristics.

Methods: We retrospectively reviewed the records of five newborns who were diagnosed with cardiomyopathy between January 2000 and December 2018. The primary evaluation included reasons for diagnosis, underlying diseases, therapy, and turning point.

Results: Patients with hypertrophic cardiomyopathy (HCM) or left ventricular noncompaction (LVNC) were diagnosed on the basis of cardiac murmur, while the patient with dilated cardiomyopathy (DCM) was diagnosed on the basis of sucking failure. Underlying diseases included Noonan syndrome and LEOPARD syndrome. All patients had received β-blockers, and those with DCM and LVNC were also administered diuretics and angiotensin-converting enzyme inhibitors. The two patients with HCM underwent follow-up as out-patients. One patient with HCM died at 3 years old because of arrhythmia. The patient with DCM died due to heart failure 38 days after birth. The patient with LVNC exhibited severe heart failure after birth, requiring follow-up while considering heart transplantation.

Conclusions: Noonan syndrome and LEOPARD syndrome, which is RAS/MAPK-related diseases, should be considered in patients diagnosed HCM. Because heart failure progresses rapidly in patients with neonatal DCM and those with LVNC, planned therapy should include consideration of heart transplantation.

Keywords

Neonate; Hypertrophic Cardiomyopathy; Dilated Cardiomyopathy; Left Ventricular; Noncompaction; RAS/MAPK

Case-1

The baby was born by caesarean section at 38 weeks of gestation because of a breech presentation. The infant weighed was 2940 g at birth and her Apgar scores were normal. Her family histories were unremarkable. She was transferred to our hospital because of a cardiac murmur. Echocardiography on admission showed hypertrophy of the interventricular and posterior left ventricular walls (**Fig-A**). The pressure gradient at the left ventricular outflow tract

(LVOT) was 40 mmHg. We diagnosed hypertrophic cardiomyopathy and started bisoprolol (0.1 mg/kg/day). Heart failure did not occur, but the patient died suddenly at 3 years old because of arrhythmia.

Case-2

The patient was a female weighing 2520 g who was born transvaginally at 39 weeks of gestation. Initial physical examinations showed **o**cular hypertelorism, loose skin, and low-set ears, leading to a diagnosis of Noonan syndrome. Echocardiography on admission showed hypertrophic cardiomyopathy (**Fig-B**) and pulmonary valve stenosis, and bisoprolol (0.1 mg/kg/day) was administered. She was transferred to our hospital at three months old because of atrial tachycardia. The arrhythmia was treated with flecainide (25 mg/m^2/day) and sotalol (25 mg/m^2/day). After beginning treatment, the atrial tachycardia resolved. The patient is now 1 year old without the occurrence of heart failure.

Case-3

The patient was a male weighing 3100 g who was born transvaginally at 40 weeks of gestation. He was transferred to our hospital because of a cardiac murmur at 1 day old. Echocardiography on admission showed hypertrophy of the interventricular and posterior left ventricular walls (**Fig-C**). Noonan syndrome was diagnosed because of typical clinical manifestations, including HCM. During follow-up, multiple lentigines were observed. Genetic analysis at the age of 12 years indicated a point mutation in *PTPN11* exon 13, indicating LEOPARD syndrome. The pressure gradient at the LVOT was 100 mmHg. Bisoprolol (0.1 mg/kg/day) did not improve the HCM. The patient is now 18 years old, without occurrence of heart failure or arrhythmia. The patient requires

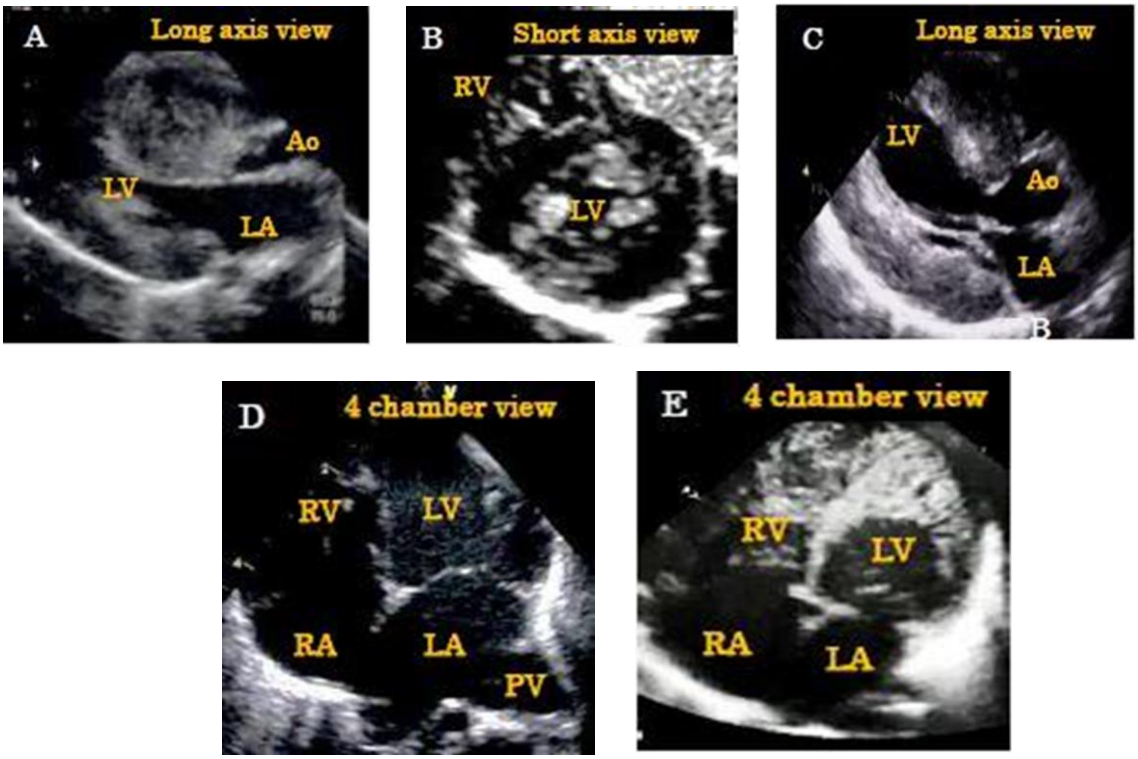

Fig-A: *Transthoracic echocardiography shows hypertrophic cardiomyopathy on the parasternal long-axis view in case*

Fig-B: *Parasternal short axis view in case*

Fig-C: *Parasternal long-axis view in case*

Fig-D: *Dilated cardiomyopathy on the 4-chamber view in case*

Fig-E: *Left ventricular noncompaction on the 4-chamber view in case*

LV: Left Ventricle; RV: Right Ventricle; LA: Left Atrium; RA: Right Atrium; Ao: Ascending Aorta; PV: Pulmonary Vein

myocardial resection because of severe LVOT stenosis.

Case-4

The baby was born by caesarean section at 37 weeks of gestation because of a breech presentation. The infant weighed was 2470 g at birth and her Apgar scores were normal. Her family histories were unremarkable. She came to our hospital because of respiratory failure at 10 days old. Echocardiography on admission showed a dilated left atrium, left ventricle, and pulmonary veins (**Fig-D**). She was diagnosed with DCM and cardiogenic shock, and intensive care therapy including mechanical ventilation, catecholamines, and diuretic agents was started. However, heart failure did not improve, and the patient died at 37 days old.

Case-5

The patient was a female weighing 3100 g who was born transvaginally at 40 weeks of gestation. She was transferred to our hospital due to cardiac murmur and tachypnea at seven days old. On admission, echocardiography showed bilateral ventricular noncompaction (**Fig-E**). The patient was diagnosed with LVNC and heart failure, and oral medication including furosemide (final dose; 3 mg/kg/day), enalapril (final dose; 0.2 mg/kg/day), carvedilol (final dose; 0.2 mg/kg/day), and aspirin (5 mg/kg/day) was administered. However, heart failure did not improve, and the patient was transferred to a cardiac transplantation institution at four months old.

Discussion

Clinical results from our hospital are summarized in **Table-1**. Cases 1-3 were diagnosed with HCM. Case-2 exhibited Noonan syndrome and case-3 exhibited LEOPARD syndrome, which is similar to Noonan syndrome. Cases 4 and 5 exhibited DCM and LVNC, respectively. Patients exhibited poor body weight gain and their turning points were death or reliance on a ventricular assist device. The patients with HCM used β-blockers, while patients with DCM and LVNC used furosemide and enalapril.

Cardiomyopathy presents a high risk for sudden cardiac death in pediatric patients, and patients

Table-1: Summary of Five Neonates with Cardiomyopathy

Case	Reasons for reaching a diagnosis	Underlying disease	Body weight gain	Arrhythmia	Turning point
Case-1 HOCM	Heart murmur	None	Good	None	Death (3 y.o.)
Case-2 HCM, PS	Heart murmur	Noonan syndrome	Good	Atrial tachycardia	Alive (1 y.o.)
Case-3 HOCM	Heart murmur	LEOPARD syndrome	Good	None	Alive (18 y.o.)
Case-4 DCM	Respiratory failure	None	Poor	None	Death (37 d.o.)
Case-5 LVNC	Heart murmur	None	Poor	None	VAD (4 m.o.)

HOCM: Hypertrophic Obstructive Cardiomyopathy

HCM: Hypertrophic Cardiomyopathy

PS: Pulmonary Valve Stenosis

LVNC: Left Ventricle NonCompaction

VAD: Ventricular Assist Device

diagnosed as infants, children and young adolescents show worse prognosis than those diagnosed as adults [2]. A single-center study from America showed the transplant-free survival rate to be only 46% at 1 year, whereas registry data from the UK showed a transplant-free 1-year survival rate of 66% in children requiring hospitalization after an episode of heart failure [3].

Recent studies reported therapies for end-stage DCM including cardiac resynchronization therapy, restrictive atrial septal defect (ASD) creation, and pulmonary artery banding [4]. Transcatheter ASD creation reduced left atrial pressure and brain natriuretic peptide levels [5]. Restriction of the interatrial communication preserves adequate filling pressure for diastolic and/or systolic dysfunctional systemic ventricle while altering clinical symptoms related to the 'out-of-proportion' left atrial and pulmonary pressures. Pulmonary artery banding (PAB) is effective if right ventricular function is preserved, and was introduced on the following hypotheses: geometric rearrangement of LV dimension achieved by reestablishing the interventricular septal position with gradual restoration of LV ejection fraction, and cardiac improvement with the potential for regeneration reciprocal to patient' age, and promoted by PAB-induced right ventricular hypertrophy [6]. In our cases, the patient with DCM did not undergo therapy and died at 37 days old because her parents did not consent to progressive treatment. The patient with LVNC did not undergo therapy because of rapid heart failure, which required progression a ventricular assist device.

Conclusions

Noonan syndrome and LEOPARD syndrome, which are RAS/MAPK-related diseases should be considered in neonates diagnosed with HCM. Because heart failure progresses rapidly in patients with neonatal DCM and LVNC, planned therapy should include consideration of CRT, ASD creation, PAB, and heart transplantation.

Disclosures

Conflict of Interest: None

Author contributions

All other authors contributed to data collection and interpretation, and critically reviewed the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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