

Two Cases of Restrictive Cardiomyopathy in Children

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Abstract

A 3-year-old girl was diagnosed with restrictive cardiomyopathy (RCM) after showing symptoms of heart failure, and a 6-year-old boy was found to have RCM after abnormal electrocardiographic findings were seen during school-based heart disease screening. Both had typical clinical features of the disease. Plasma levels of brain natriuretic peptide increased significantly in both patients, allowing us to distinguish this disease from constrictive pericarditis which has similar clinical and hemodynamic features. The early diastolic mitral annular velocity recorded by tissue Doppler echocardiography was also useful to discriminate RCM from constrictive pericarditis. The former case successfully received heart transplantation, but the latter case died suddenly prior to receiving a heart transplant. The plasma level of brain natriuretic peptide and tissue Doppler echocardiography helped us to diagnose this disease earlier and follow it more carefully, which has important implications in optimal treatment and improved prognosis of RCM in children.

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Key words: restrictive cardiomyopathy, brain natriuretic peptide, tissue Doppler echocardiography

Introduction

Restrictive cardiomyopathy (RCM) is a primary heart-muscle disease characterized by impaired ventricular filling with normal or decreased diastolic ventricular volume. Left ventricular systolic function usually remains normal, at least in the early phase of the disease, and the thickness of the left ventricle wall is within the normal range. It is a rare form of cardiomyopathy in childhood, accounting for between 2–5% of idiopathic cardiomyopathy in that age group^{1,2}. It is often difficult to distinguish RCM from constrictive pericarditis, because of similar

clinical features and similar ventricular diastolic filling hemodynamics. RCM may progress rapidly in childhood^{3,4} and heart transplantation is the only reliable treatment in such cases. We report two cases of RCM, both with rapid progression to heart failure. The plasma level of brain natriuretic peptide (BNP) and the early diastolic mitral annular velocity (e') recorded by tissue Doppler echocardiography were found to be useful for diagnosis and follow-up of RCM.

Case 1

A 3-year-old girl was referred to our hospital with

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Fig. 1A Chest radiograph shows a cardiothoracic ratio of 56%, with a double right cardiac silhouette produced by a markedly enlarged left atrium.

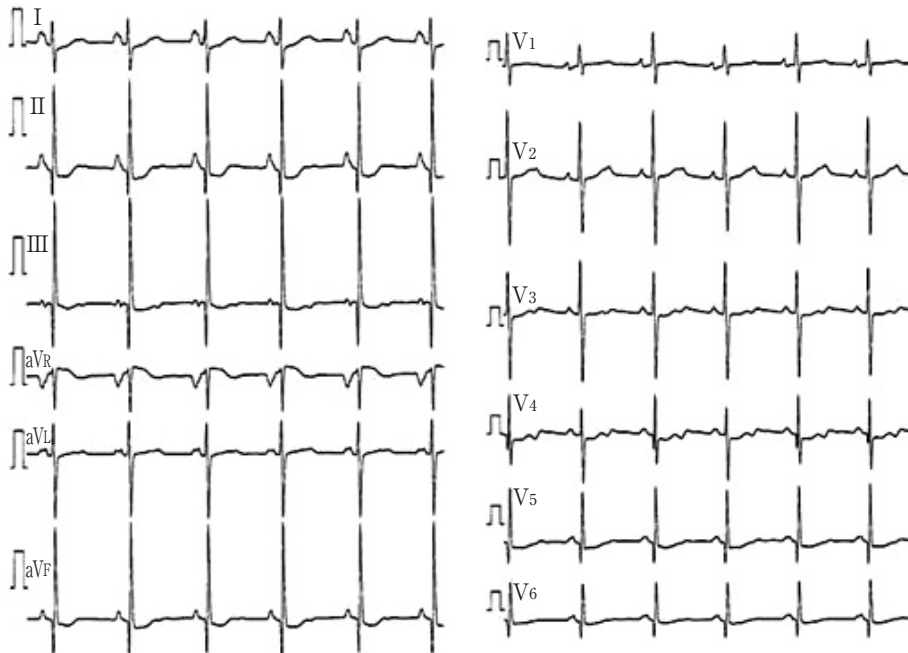
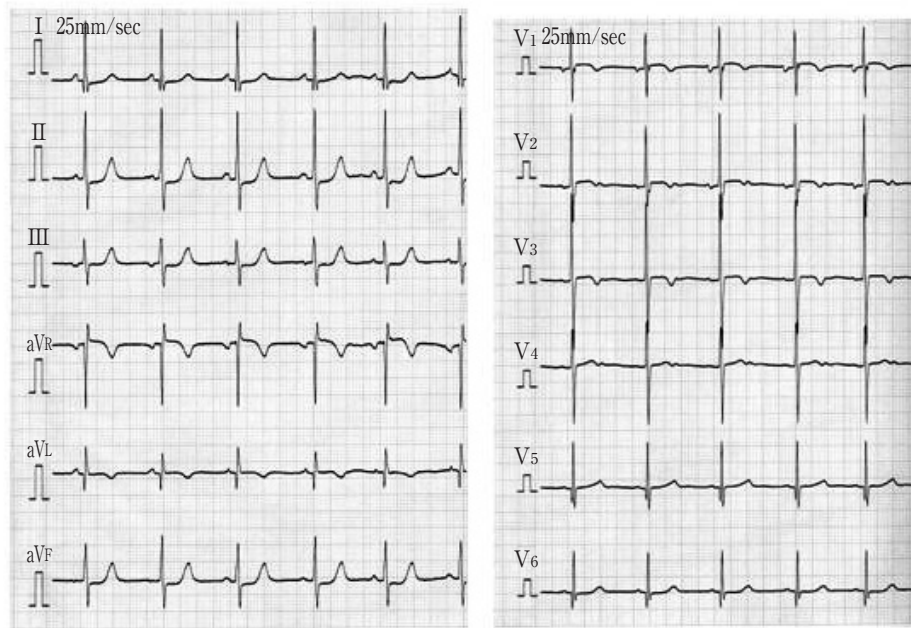


Fig. 1B Electrocardiogram shows left and right atrial enlargement, ST-segment depression, and low-voltage T waves in the inferior and lateral leads.

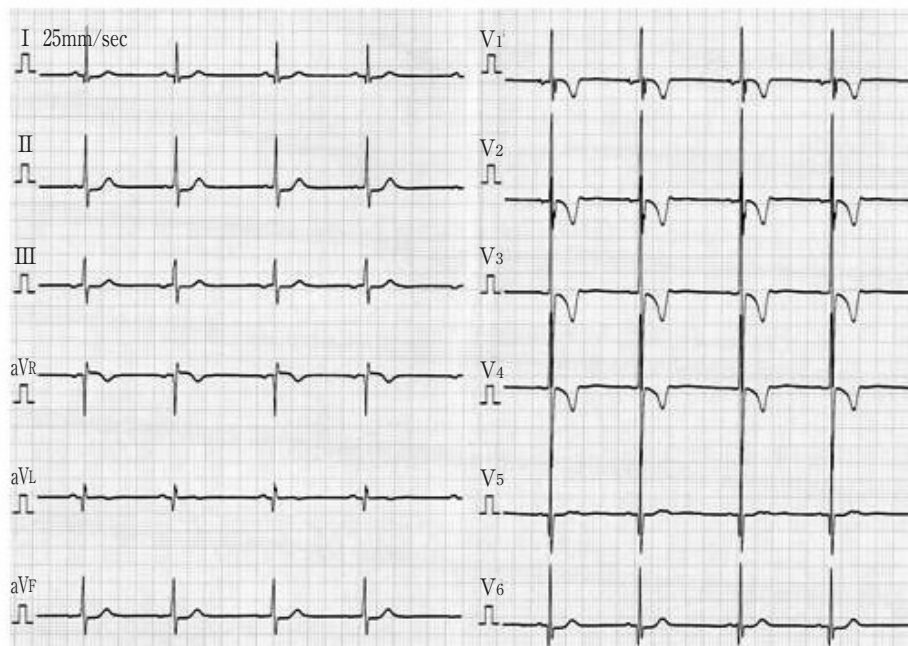
symptoms of cough, dyspnea on exertion, and hepatomegaly. At the age of 2 years 8 months, a bout of pneumonia led to chest radiography, which revealed cardiomegaly. Echocardiography suggested the diagnosis of RCM. At the time of referral, she was being treated with diuretics, β -blocking agents, angiotensin-converting enzyme inhibitors, isosorbide dinitrate, and aspirin. On physical examination, height was 92.8 cm, weight was 12.2 kg, systolic blood pressure was 92 mm Hg, and pulse was 78

beats per minute. No abnormal heart sounds were detected, and no significant heart murmur was audible. The liver edge was palpable 3 to 4 cm below the right costal margin, and the spleen was palpable 2 cm below the left costal margin. The plasma level of BNP was markedly elevated to 1,290 pg/mL. Chest radiography showed cardiomegaly (cardiothoracic ratio, 56%), a double silhouette along the right cardiac border indicating left atrial enlargement, and mild pulmonary congestion (**Fig. 1**



EKG (6y1m)

Fig. 2A Electrocardiogram shows left atrial enlargement, deep Q and low-voltage T waves in leads V5 and V6 and a 2.0-mV R wave in lead V1.



EKG (10y8m)

Fig. 2B Electrocardiogram shows left atrial enlargement and left- and right-ventricular hypertrophy. It also shows negative T waves in leads V1 to V4, low-voltage T waves in leads V5 and V6, ST-T depression in leads II and V6, and deep Q waves in leads V5 and V6.

A). Electrocardiography revealed sinus rhythm, left and right atrial enlargement, ST-segment depression, and low-voltage T waves in inferior and lateral leads (**Fig. 1B**). Echocardiography showed a

anatomically normal heart with marked left atrial dilatation, a left atrial/aortic ratio of 3.48, mild mitral valve regurgitation, no tricuspid valve regurgitation, and mild left ventricular dysfunction with an

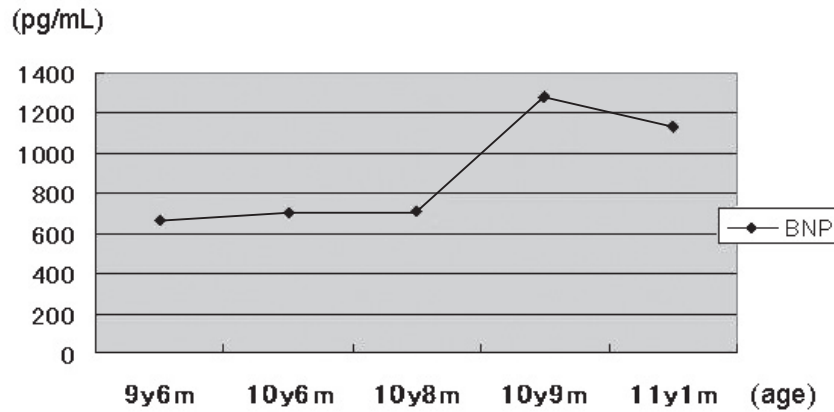


Fig. 3 This figure shows the time course of plasma levels of BNP in case 2. Elevated BNP indicates a clinically critical condition.



Fig. 4 Chest radiograph shows cardiomegaly with a cardiothoracic ratio of 54% and double right cardiac silhouette produced by a markedly enlarged left atrium.

Table 1 Hemodynamic Data of Case 1

position	pressure	position	pressure
SVC	11/6 (6)	RV outflow	50/EDP10
RA mid	11/6 (6)	RV inflow	52/EDP10
IVC	11/(6)	LV	97/EDP28
rt-PA branch	48/18 (31)	AsAo	96/41/(64)
rt-PA wedge	28/22 (20)		
lt-PA branch	52/20 (32)		
m-PA	51/18 (32)		

SVC: superior vena cava, IVC: inferior vena cava, RA: right atrium, PA: pulmonary artery, RV: right ventricle, LV: left ventricle, AsAo: ascending aorta EDP: end-diastolic pressure. Numbers in brackets indicate mean pressure

ejection fraction of 56%. The left ventricular end-diastolic dimension was 39.6 mm (reference range: 24–42 mm), and the left ventricular end-diastolic wall thickness was 4.4 mm (reference range: 5–7 mm). The patient also underwent cardiac catheterization. Hemodynamic measurements revealed an elevated end-diastolic pressure of 28 mm Hg in the left ventricle and 10 mm Hg in the right ventricle (**Table 1**), a systolic pressure of 51 mm Hg in the main pulmonary artery, and a wedge pressure of 20 mm Hg in the right pulmonary artery. Magnetic resonance imaging showed no increase in pericardial thickness. These findings were consistent with RCM.

The patient was initially treated with an intravenous catecholamine (dobutamine), and then with phosphodiesterase III inhibitors. Consequently, she underwent heart transplantation in the United States at the age of 4 years.

Case 2

A boy was referred to our hospital at 6 years of age because of cardiomegaly and an abnormal electrocardiogram, detected in a school-based heart disease screening. Chest radiography showed a 54.5% cardiothoracic ratio. Electrocardiography revealed left atrial enlargement and left ventricular hypertrophy (**Fig. 2A**). Echocardiography showed enlargement of the left atrium and mild left ventricular dysfunction. A diagnosis of dilated cardiomyopathy was made at that time, and the

Table 2 Hemodynamic Data of Case 2

position	pressure	position	pressure
SVC	11/8 (9)	RV outflow	41/EDP10
RA mid	11/7 (9)	RV inflow	42/EDP11
IVC	11/8 (9)	LV	93/EDP22
rt-PA branch	40/20 (27)	AsAo	94/62/(76)
rt-PA wedge	26/24 (22)		
lt-PA branch	41/21 (27)		
m-PA	41/20 (26)		

Abbreviations see in Table 1

patient visited our hospital once a year thereafter.

At the age of 10 years 10 months, the boy's heart dysfunction rapidly worsened. The left ventricular ejection fraction decreased from 53% to 46%. The plasma BNP level increased from 712 to 1,280 pg/mL (**Fig. 3**). Because the patient complained of occasional chest pain, he was referred to our hospital for cardiac catheterization. Chest radiography showed cardiomegaly (cardiothoracic ratio, 54%), with a double silhouette along the right cardiac border indicating left atrial enlargement (**Fig. 4**). Electrocardiography revealed sinus rhythm, left atrial enlargement, left- and right-ventricular hypertrophy, and ST-T depression (**Fig. 2B**). Twenty-four-hour electrocardiography showed no significant arrhythmia. Echocardiography showed an anatomically normal heart with left atrial dilatation (left atrial/aortic ratio, 1.70), no tricuspid valve regurgitation, and mild left ventricular dysfunction (ejection fraction, 46%). The left ventricular end-diastolic dimension was 48 mm (reference range: 24–42 mm), and the left ventricular end-diastolic wall thickness was 7.3 mm (reference range: 5–7 mm). The early diastolic mitral annular velocity (e') recorded with tissue Doppler echocardiography was 3.78 cm/sec. The hemodynamic measurements revealed an elevated end-diastolic pressure of 22 mm Hg in the left ventricle and 10 mm Hg in the right ventricle, along with a systolic pressure of 41 mm Hg in the main pulmonary artery and wedge pressure of 22 mm Hg of right pulmonary artery (**Table 2**). Mild mitral valve regurgitation was revealed by left ventriculography. A diagnosis of RCM was made. The patient was treated with diuretics, β -blocking agents, angiotensin-converting

enzyme inhibitors, and digoxin. Two months later, he died suddenly prior to receiving a heart transplant.

Discussion

Because RCM and constrictive pericarditis share similar clinical and hemodynamic features, including altered ventricular diastolic filling, it is often difficult to distinguish these two conditions by means of clinical examination and conventional testing. Recently, it has been reported that in adults BNP levels are significantly higher in RCM (825.8 ± 172.2 pg/mL) than in constrictive pericarditis (128.0 ± 52.7 pg/mL)⁵. Therefore, the plasma BNP level might be used as a tool for differential diagnosis. In our 2 cases in children, the plasma levels of BNP were higher than 500 pg/mL, consistent with the previous report on cases in adults. Moreover, the plasma levels of BNP paralleled the clinical condition. In both of our patients, the BNP levels were around 700 pg/mL when their conditions were stable but increased markedly (to 1,290 and 1,280 pg/mL, respectively) when the patients' conditions deteriorated. Thus, monitoring the plasma BNP level might be useful not only for diagnosis but also for evaluation of disease status in children with RCM.

The early diastolic mitral annular velocity (e') recorded with tissue Doppler echocardiography has been reported to accurately discriminate between RCM and constrictive pericarditis^{6–9}. In the second of our 2 patients, e' decreased to 3.78 cm/sec (normal range: 8.0–16.0 cm/sec), indicating altered ventricular relaxation due to primary myocardial disease. The combination of plasma BNP and e' measured with tissue Doppler echocardiography could allow the more precise, noninvasive diagnosis of RCM.

The clinical course after a diagnosis of RCM in childhood has been reported to be an accelerated deterioration in comparison with that seen in adults³⁴. Medical treatment of these patients has not been effective over time, and only heart transplantation seems a reliable treatment. However, it is difficult to decide the timing of heart transplantation because of the variability of each individual's natural history. Moreover, no consistent

predictors for progression of RCM have yet been identified. According to one report, RCM patients at risk of sudden death often have symptoms such as chest pain or syncope without ongoing heart failure¹⁰. The authors conclude that these symptoms are caused by ischemia and suggest immediate evaluation including electrocardiography. However it has been reported by others that ST depression in RCM patients with abnormal ST-T segments at rest is not necessarily related to myocardial ischemia, but is rather characteristics of RCM¹¹. So far there is no simple reliable method for evaluating myocardial ischemia in pediatric RCM patients. We recommend that these patients be followed up more carefully using not only conventional examinations but also new methods, such as plasma BNP levels and tissue Doppler echocardiography. We expect that the evaluation of clinical state by a suitable combination of these methods will have important implications in improved prognosis of RCM in children.

The young girl in our first case above was listed for heart transplantation just after symptoms of heart failure appeared and was successfully conducted to transplant. The boy in our second case, in retrospect, might have benefitted by being followed and treated more aggressively, perhaps by implanting a cardioverter-defibrillator and by being listed earlier for transplant. These two cases show that careful and frequent monitoring of electrocardiograms, accurate evaluation of myocardial ischemia, suitable management of heart failure, and proper timing of listing for heart transplantation are critical aspects of the management of pediatric RCM. Evidence is mounting that plasma BNP levels and tissue Doppler echocardiography are important tools that may lead to more accurate diagnosis and more effective treatment of RCM in children.

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