Rapid Progression of Neuromuscular Disorder Related Cardiomyopathy in a Young Patient

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Abstract

An 11-year and 3-month-old boy with a neuromuscular disorder was admitted for dyspnea. Echocardiography revealed severe left ventricular dysfunction with an ejection fraction (EF) of 17%. However, the EF had been 57% when the patient was 10 years and 9 months old. The patient’s clinical condition became refractory, and he died on the 155th day of hospitalization. Speckle-tracking analysis was retrospectively performed, which demonstrated that the global radial strain was within the normal range; however, the global longitudinal and circumferential strains were lower than normal 10 years and 9 months of age. Adult neuromuscular disorder-related secondary cardiomyopathy generally progresses slowly, although progression depends on the age of onset of cardiomyopathy.

Key words: cardiomyopathy, echocardiography, heart failure, speckle-tracking, neuromuscular disorder

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Introduction

Cardiomyopathies caused by neuromuscular disorders such as Duchenne/Becker and Emery-Dreifuss muscular dystrophy and myotonic dystrophy, are classified as secondary cardiomyopathies (1). The organs most frequently clinically or sub-clinically affected by this genetic defect include with skeletal muscle, brain, and heart (1, 2). Cardiac involvement is a frequent finding in neuromuscular disorders and comprises rhythm abnormalities, hypertrophic and dilated cardiomyopathies and left ventricular (LV) noncompaction cardiomyopathy (1-3). Adult neuromuscular disorders related cardiomyopathy generically presents as a slowly progressive disorder over several years (1, 4, 5). This case report concerns the rapid progression of neuromuscular disorder related cardiomyopathy in a boy just over 11 years of age.

Case Report

An 11-year and 3-month-old boy with a difficulty stepping, developmental delay and mental deterioration was admitted to our institution with a complaint of general fatigue and dyspnea. Although he was not provided a definitive diagnosis some three years and two months earlier, when he was 8 years and 1 month of age, he was diagnosed with an unidentified neuromuscular disorder based on the findings of a genetic test, and biopsy of the left rectus femoris muscle. Since then, he had regularly visited our institution. An echocardiographic examination performed in November 2010, when he was 10 years and 9 months old, showed a normal LV function with an ejection fraction (EF) of 57% without LV dilatation (LV end-diastolic and systolic diameters of 38 mm and 28 mm, respectively) (Fig. 1A, Supplementary File 1). Four months later, in March 2011, when the patient was 11 years and 1 month old, an echocardiographic examina-
Figure 1. (A) Transthoracic echocardiography from the mid-left ventricular (LV) short-axis view performed in November 2010 (the patient was 10 years and 9 months old) showed a normal LV ejection fraction (EF) calculated using the modified biplane Simpson’s rule of 57% and LV end-diastolic and -systolic diameters of 38 mm and 28 mm, respectively. (B) Transthoracic echocardiography from the mid-LV short-axis view performed in May 2011 (the patient was 11 years and 1 month old) showed slight LV dysfunction of the LV EF at 46% calculated using the modified biplane Simpson’s rule, with LV end-diastolic and -systolic diameters of 45 mm and 36 mm, respectively. (C) Transthoracic echocardiography from the mid-LV short-axis view performed on admission showed severe LV dysfunction with an LV EF of 17% calculated using the modified biplane Simpson’s rule, and dilated LV end-diastolic and systolic diameters of 50 mm and 44 mm, respectively.

On admission, the patient was 139 cm tall and weighed 22 kg (<-3SD). His blood pressure was 88/60 mmHg, his heart rate was 112 beats per minute, his oxygen saturation was 96% on room air and his body temperature was 36.0°C. The jugular veins were distended. Auscultation revealed a third heart sound and a Levine II/VI systolic murmur at the left lower sternal border, while coarse crackles were detected in both lower lung fields. The laboratory findings were as follows: brain natriuretic peptide, 643 pg/mL; aspartate aminotransferases, 204 U/L; alanine aminotransferases, 267 U/L; lactic acid, 19.8 mg/dL; pyruvic acid, 1.35 mg/dL; white blood cells, 6,700/μL; C-reactive protein, <0.1 mg/dL;
Creatine kinase, 235 U/L; troponin-1, 0.16 ng/mL. Chest radiography showed a cardiothoracic ratio of 55% with pulmonary congestion (Fig. 2A), while electrocardiography disclosed a normal sinus rhythm and first-degree atrioventricular block, similar findings to those of previous electrocardiograms (Fig. 2B). An echocardiographic examination revealed severe LV dysfunction with an EF of 17% calculated using biplane Simpson’s rule, while the septal and posterior wall thickness values were 7.4 mm and 9.6 mm, respectively (Fig. 1C, Supplementary File 3). The LV end-diastolic and systolic diameters were 50 mm and 44 mm, respectively. Mild-to-moderate functional mitral regurgitation was observed, however, there was no evidence of moderate tricuspid regurgitation. An endomyocardial tissue biopsy and cardiac magnetic resonance imaging were not performed.

The patient was treated with oxygen inhalation, furosemide and dobutamine for congestive heart failure (Fig. 3). His condition was somewhat stabilized, and the administration of low-dose losartan and carvedilol was started. Furthermore, we used amiodarone because ventricular tachycardia (Torsade de pointes) was observed on the 20th day of hospitalization. Since liver dysfunction caused by amiodarone was observed, landiolol was used instead, and the ventricular tachycardia disappeared. However, the patient’s
clinical condition was refractory to these pharmacological therapies and continued to deteriorate, especially after the 120th day of hospitalization, at which time he required the addition of dopamine, and tolvaptan. His family rejected the implantation of a ventricular assist device, and he died of heart failure on the 155th day of hospitalization. Unfortu-
nately, his family did not consent to an autopsy study.

Discussion

The case reported here concerns a young patient with neuromuscular disorder-related cardiomyopathy that exhib-
ted rapid progression over a 2-month period, leading to fa-
tal drug refractory heart failure.

Cardiac involvement, including hypertrophic and dilated cardiomyopathy, is a frequent complication of neuromuscu-
lar disorders (1-3). Cardiac involvement leads to impulse generation defects, a impulse conduction defects, thickened myocardium, LV hypertrophy, dilatation of the cardiac chambers, secondary valve insufficiency, reduction of the coronary vasodilative reserve, intracardiac thrombus forma-
tion, and heart failure with systolic and diastolic dysfunc-
tion. Cardiac involvement has been observed in patients with Duchenne/Becker muscular dystrophy, Emery-Dreifuss mus-
cular dystrophy, myotonic dystrophy, mitochondrial myopa-thy and so on. Neuromuscular disorder-related cardiomyopa-thy in adults generally progresses slowly over the years, however, the progression depends on the age of onset of cardiomyopathy (1, 4, 5). Although the precise reason for the rapid progression and refractoriness to conventional medical therapy observed in this case was unclear, previous investigators have reported that the cardiac function of young patients with neuromuscular disorder related cardio-
myopathy, especially those less than 30 years of age, dete-
riorates rapidly, being associated with a poor overall progno-
sis and mortality rate of approximately 70% (4). Therefore, physicians should pay special attention to the appearance of cardiac involvement in young patients with neuromuscular disor-ders. In this case, two-dimensional speckle-tracking strain analysis was retrospectively performed for a more de-
tailed assessment of the LV myocardial function with the aid of three different types of speckle-tracking strains using a dedicated software program (EchoAgent; Toshiba Medical Systems, Tochigi, Japan). Radial and circumferential strains were assessed from the basal, mid and apical LV short-axis views, and the longitudinal strain was assessed from the ba-
sal, mid and apical levels in the apical four-chamber, two-
chamber, and long-axis views, after which each global strain was calculated by averaging the peak global strain of the three views. The global radial strain was within the normal range (58.4% vs. 51.4±8.0%), whereas the global longitudi-
nal (-10.7% vs. 19.9±2.4%) and circumferential strains were

**Figure 4.** Results of two-dimensional speckle-tracking strain analysis. The global radial strain was within the normal range, whereas the global longitudinal and circumferential strains were lower-
than-normal.
lower-than-normal (-14.3% vs. -30.5±3.8%) (Fig. 4) (6) in November 2010 (the patient’s EF was 57%).

We have detected early minor LV endocardial dysfunction caused by neuromuscular disorders, even in patients with a preserved global LV systolic function, which can eventually lead to impaired global LV performance. The EF is the most extensively investigated echocardiographic systolic function and has been established to be a powerful predictor of mortality in patients with heart failure (HF). However, the LV systolic function is a complex, coordinated action involving longitudinal contraction, circumferential shortening, and radial thickening (7). LV myocardial damage begins with longitudinal shortening, which occurs at an earlier stage of HF, while the impairment of circumferential shortening develops at a later stage of HF (8, 9). Therefore, multidirectional speckle-tracking strain analyses have been found to be useful for the early detection of minor LV myocardial dysfunction associated with neuromuscular disorders in maintaining the EF and may thus prove clinically useful for the prediction of the possible occurrence of global LV dysfunction.

In conclusion, physicians should pay special attention to the appearance of cardiac involvement in young patients with neuromuscular disorders. Furthermore, speckle-tracking strain analyses may prove to be useful for evaluating subtle early LV myocardial changes in such patients. Patients who develop cardiac involvement should be provided special care (e.g. frequent out-patient treatment or early and aggressive supportive treatment) in order to enhance their chances of survival.

The authors state that they have no Conflict of Interest (COI).

References


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