Becker Muscular Dystrophy with Early Manifestation of Left Heart Failure

Hiroshi Miyashita, Uichi Ikeda, Kazuyuki Shimada, Takashi Natsume* and Kiichi Arahata**

We encountered a case of dystrophin-verified Becker muscular dystrophy which exhibited left heart failure as an initial symptom but no subjective muscle weakness. Severe cardiac involvement has been thought to rarely occur in the early stage of this disease, however accurate diagnosis was limited until the dystrophin diagnosis became available. This case suggests that some cases of dilated cardiomyopathy might be Becker muscular dystrophy, and that dystrophin tests should be added to the conventional investigation of patients with dilated cardiomyopathy.

(Key words: dystrophin test, secondary cardiomyopathy, endomyocardial biopsy, skeletal muscle biopsy)

Introduction

In recent years, the nature of Becker muscular dystrophy has been significantly clarified owing to the discovery of dystrophin (1). This disease has been known to show varied clinical features including secondary cardiomyopathy. In addition, until the dystrophin diagnosis was available, nonfamilial cases could never be conclusively diagnosed. There have been few reports on cardiac involvement in dystrophin-verified cases of Becker muscular dystrophy. We report here a dystrophin-verified case accompanied with severe cardiomyopathy, but with the absence of noticeable muscle weakness.

Case Report

A 16-year-old boy visited to our hospital suffering from transient anterior chest oppression and dyspnea which occurred suddenly during exercise. Until then, he had never been aware of difficulties. He weighed 49 kg and was 163 cm in height. His blood pressure was 140/90 mmHg and his pulse rate was 70 bpm with some irregularity. No evident heart murmur or rale was audible. Proximal muscles of the limbs seemed to be mildly atrophic, whereas calf muscles showed pseudohypertrophy. However, the manual muscle test revealed only minimal muscle weakness (4/5 or more). No significant family history of muscular ailments was determined.

The chest roentgenogram showed cardiomegaly (cardiothoracic ratio = 59%) and slight pulmonary congestion. The ECG exhibited relatively high R waves in V1-2, and deep Q waves in V4-6 and aVL. A tendency of right axis deviation and low voltage in limb leads was also recognized.

The laboratory examinations showed high myogenic enzyme levels and myoglobinemia; creatine kinase 10,450 U/L (MM 95.8%), aldolase 24.6 IU/L, and serum myoglobin 920 ng/ml. Serum levels of hepatic isozyme of lactic dehydrogenase (total activity 2,003 U/L, lactic dehydrogenase5 (LD5) 25.4%) and alanine aminotransferase (136 U/L) were also increased. Inflammatory reactions and viral titer were negative.

The two-dimensional and M-mode echocardiograms (Fig. 1) revealed a moderately dilated left ventricular cavity with diffuse hypokinesis. Left ventricular wall thickness was normal. The 201Tl myocardial imaging at rest showed attenuation of radionuclide uptake in the apical portion of the anterior septum, and the inferoposterior and lateral walls.

In cardiac catheterization, mean pulmonary capillary wedge pressure and pulmonary artery pressure were 10 mmHg and 25/10 mmHg, respectively. Cardiac output was 6.0 L/min by thermodilution. A left ventriculogram showed left ventricular dilatation and diffusely hampered contraction (ejection fraction = 38%). The histological findings of the right ventricular biopsy showed mild fibrosis without evident inflammation (Fig. 2a).

An electromyogram showed a myogenic pattern. The quadriceps muscle biopsy exhibited a myopathic appearance (Fig. 2b). The immunofluorescence localization of dystrophin in the skeletal muscle [the methods were previously described (2)] showed a faint and patchy fluorescence pattern (Fig. 3).
Becker Dystrophy with Heart Failure

Fig. 1. Echocardiograms. The upper panel shows two-dimensional echocardiograms of the left ventricular long axis view. The lower panel is a M-mode echocardiogram of the left ventricle. Both panels indicate a dilated left ventricular cavity with severely reduced contraction (end-diastolic left ventricular dimension = 61 mm, ejection fraction = 35% by the Teichholz equation). IVS: interventricular septum, LV: left ventricular cavity, PW: left ventricular posterior wall.

therefore the diagnosis of Becker muscular dystrophy was made. His left ventricular function deteriorated gradually, and he died of congestive heart failure 17 months after the initial observation despite intensive medical treatment for heart failure.

Discussion

Here, we describe a case of dystrophin-verified Becker muscular dystrophy with the precocious manifestation of severe cardiomyopathy. Serological tests and histological findings of myocardium excluded acute viral myocarditis. Persistent high myogenic enzyme levels made it necessary to differentiate dystrophic cardiomyopathy from dilated cardiomyopathy with coincidental myopathy. Histological findings of the skeletal muscle were consistent with muscular dystrophy. Absence of a distinctive family history made it difficult to determine the specific form of muscular dystrophy, however, Becker muscular dystrophy was conclusively diagnosed based on dystrophin anomalies regarded as the essential entity of X-linked muscular dystrophy (1, 2). Electrocardiographic findings approximated those reported in Duchenne muscular dystrophy and in some Becker muscular dystrophy cases (3–5).

It is very atypical, however, that Becker muscular dystrophy would display heart failure as an initial symptom. It is generally believed that muscle weakness is the initial symptom in Becker muscular dystrophy, and that as the disease stage proceeds, ECG abnormalities and other cardiac problems become manifest. According to a previous epidemiological study (4), advanced cardiomyopathy is rare in Becker muscular dystrophy patients under the age of 20. The study also showed that 50% of Becker muscular dystrophy cases were nonfamilial. Only several cases accompanied with severe cardiomyopathy have been reported in the past and cases with an early onset of cardiac failure are even rare. According to our investigation, only 2 dystrophin-verified cases were reported to have developed heart failure in the absence of problematic skeletal muscle symptoms (5, 6).

Becker muscular dystrophy, especially nonfamilial or female cases, have been missed or misdiagnosed in the past before the dystrophin-based diagnostic method became available. Dystrophin diagnosis is essential for a distinctive diagnosis of Becker muscular dystrophy (1). Even in a familial case with X-linked recessive inheritance, a different gene, such as in the Emery-Dreifuss type, might be involved. Therefore, the knowledge obtained from patients without dystrophin analysis has to be reassessed in the light of dystrophin-verified cases.

The dystrophin gene is expressed in skeletal muscles, cardiac muscles, smooth muscles, and the brain. In skeletal and cardiac muscles, dystrophin is present in the same isoforms (7), suggesting that cardiac involvement in Becker muscular dystrophy may evolve from the same mechanism as skeletal myopathy. Recently, Anan et al (6) demonstrated that the myocardium of a Becker muscular dystrophy patient with cardiomyopathy exhibited a patchy pattern of immunostaining for dystrophin, just like skeletal muscles.

Because of widely varying anomalies concerning dystrophin, Becker muscular dystrophy including its cardiac involvement may have a broad spectrum. Berko et al (8) reported X-linked dilated cardiomyopathy cases with increased creatine kinase (isozyme MM) but without skeletal muscle weakness or myopathy. The relation of such cases to Becker muscular dystrophy is unknown because dystrophin analyses were not carried out. There is, however, a possibility that some of the dilated cardiomyopathy cases are Becker muscular dystrophy or that some Becker muscular dystrophy cases present cardiac manifestations without associated muscle weakness, as seen in our case.

In conclusion, this case of dystrophin-verified Becker muscular dystrophy which exhibited left heart failure in the absence of muscle weakness suggests that dystrophin analysis should be
Fig. 2. Micrographs of (a) the right ventricular biopsy and (b) muscle biopsy obtained from the quadriceps muscles, stained with hematoxylin and eosin. a: Mild fibrosis of the myocardium is observed. No evident cell infiltrate is seen. Bar indicates 50 μm. b: Marked variety of muscle fiber size, including regenerated fibers with central nuclei, disruption of muscle fibers, are shown. Pyknotic nuclear clumps, proliferated collagenous fibers and adipose cell infiltration are also noted. Bar indicates 100 μm.

References

6) Anan R, Higuchi I, Ichinari K, et al. Myocardial patchy staining of dystrophin in Becker’s muscular dystrophy associated with...
Fig. 3. Immunofluorescence localization of dystrophin in the patient’s skeletal muscle specimen. In contrast with the normal control (a) showing continuous immunofluorescence along the sarcolemma, the patient’s specimen (b) exhibits faint and patchy fluorescence pattern. Bars indicate 100 μm.
