Myotonic Dystrophy Associated with QT Prolongation and Torsade de Pointes

YUJI UMEDA, M.D., UICHI IKEDA, M.D., PH.D., JUN YAMAMOTO, M.D., HIROSHI FUKAZAWA, M.D., YUJI HAYASHI, M.D.,
HIDEYUKI FUJIKAWA, M.D., PH.D., KAZUYUKI SHIMADA, M.D., PH.D.

Department of Cardiology, Jichi Medical School, Tochigi, Japan

Summary: A rare case of myotonic dystrophy (MD) with congestive heart failure, associated with QT prolongation and torsade de pointes (TdP) is reported. A 53-year-old woman was admitted to the hospital because of congestive heart failure. Electrocardiograph (ECG) showed first-degree atrioventricular block and QT prolongation. During hospitalization, TdP appeared but returned to sinus rhythm spontaneously. As the patient had quadriplegia, a myopathic face, cataracts, diabetes mellitus, and an increased number of cytosine-thymine-guanine (CTG) repeats (760 repeats), she was diagnosed as having MD. Electrocardiographic analysis of her family also revealed abnormal QT(U) prolongation in her daughter and brother who both had MD, while ECG findings of other family members without MD were normal. Thus, the presence of QT(U) prolongation was associated with MD in this family.

Key words: myotonic dystrophy, QT prolongation, torsade de pointes, heart failure

Introduction

Myotonic dystrophy (MD) is a multisystem autosomal dominant disease and the most common form of adult muscular dystrophy. This disease is characterized by myotonia and progressive muscle weakness, and also by other multiple systemic effects such as cataracts, diabetes mellitus, frontal baldness, premature aging, and gonadal involvement.¹ Myo-

cardial impairments sometime become overt with signs and symptoms of congestive heart failure or arrhythmia. The incidence of electrocardiographic (ECG) abnormalities in this disease ranges from 37 to 80%,² predominantly in the form of conduction disturbances. There have been several case reports regarding ventricular tachycardia in patients with MD, but there have been no reports of MD complicated with torsade de pointes (TdP). Here, we report a rare case of MD with congestive heart failure, also associated with TdP due to QT prolongation.

Case Report

A 53-year-old woman was admitted to our hospital in August 1997 with increasing shortness of breath. She had a son and a daughter, as well as four brothers (Fig. 1). Her daughter had quadriplegia and mental weakness. One of four brothers had died suddenly at the age of 39 and another had been diagnosed as having MD. She had a lensectomy for cataracts on both eyes at the age of 30 and developed insulin-dependent diabetes mellitus at the age of 39. At the age of 45, she began to feel stiffness in the shoulder and weakness of grip and had difficulty walking. In February 1997, she was admitted to a local hospital because of dyspnea and was diagnosed with congestive heart failure. During hospitalization, ventricular tachycardia and fibrillation occurred once and direct-counter shock was performed. She was transferred to our hospital for the evaluation of congestive heart failure.

The patient's initial temperature was 37.3°C, blood pressure was 164/63 mmHg, and pulse was 63 beats/min. Her jugular veins were distended. There were no heart murmurs, but a galloping rhythm was audible. Coarse crackles were heard over the entire right lung field. No hepatomegaly or leg edema was noted.

Admission laboratory data were as follows: red blood cell count $293 \times 10^4/\text{ml}$, hemoglobin 8.5 g/dl, hematocrit 25.5%, white blood cell count 10,000/ml, glutamic oxaloacetic transaminase 77 mU/l, glutamic pyruvic transaminase 102 mU/l, lactic dehydrogenase 694 mU/l, blood urea nitrogen 36 mg/dl, creatinine 1.05 mg/dl, blood sugar 207 mg/dl, and glycated hemoglobin A1c 8.2%. Arterial blood gas analysis revealed severe hypoxia (PO_2 of 52.8 mmHg) and hypercapnia (PCO_2

Address for reprints:

Uichi Ikeda, M.D., Ph.D.
Department of Cardiology
Jichi Medical School
Minamikawachi-Machi
Tochigi 329-04, Japan

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FIG. 1 Pedigree of the patient's family. Arrow indicates the patient, † indicates deceased. Underlined numbers indicate the number of cytosine-thymine-guanine repeats. MD = myotonic dystrophy, HCC = hepatocellular carcinoma, YO = years old.

of 53.5 mmHg) under an oxygen supply of 5 l/min. Other laboratory data were within normal limits.

Chest radiography revealed bilateral pulmonary congestion and cardiac enlargement (cardiothoracic ratio of 0.58). Electrocardiograph (ECG) showed first-degree atrioventricular block and prolongation of corrected QT interval (QTc; 670 ms) (Fig. 2). Echocardiography showed mild left ventricular hypertrophy, lower normal systolic function (ejection fraction of 58%), and moderate diastolic dysfunction [the ratio of mitral flow peak early (E) wave velocity to peak atrial (A) wave velocity = 0.77, deceleration time (DT) = 267 ms, isovolumic relaxation time (IVRT) = 126 ms (normal values in our laboratory;³ E/A = 1.45 ± 0.26 , DT = 192 ± 13 , IVRT = 72 ± 6)].

On the first day of admission, TdP occurred but spontaneously returned to sinus rhythm (Fig. 2). Serum electrolyte

levels were within normal range. She had received no medications known to affect ECG features before or during this episode. After treatment was initiated with lidocaine, nicorandil, and magnesium, TdP did not occur again, but the QTc interval remained prolonged during hospitalization and also after discharge. Congestive heart failure improved after treatment with diuretics and dopamine.

As the patient had quadriplegia, a myopathic face, cataracts, and diabetes mellitus, we suspected that she had MD and performed a genotypic analysis for her and her family. DNA extracted from peripheral blood leukocytes was analyzed for the size of the cytosine-thymine-guanine (CTG) repeat using Southern blotting. The number of CTG repeats for the patient and her daughter was 760 and 1,133, respectively, while the number for her son was less than 50.

In the ECG analysis of the patient's family, abnormal increases in U wave amplitude close to the end of the T wave were observed in her daughter (QUc = 549 ms) and her brother (QUc = 584 ms) who had MD, while ECG findings of other family members, including her son, were normal. The affected members had no deafness to suggest an association with the Jervell and Lange-Nielsen syndrome, nor did they take medications known to affect QT interval.

Discussion

Previously, we and others have reported the presence of left ventricular systolic and diastolic dysfunction in patients with MD.³⁻⁵ We speculate that the etiology of congestive heart failure in this patient was a combination of systolic and diastolic dysfunction associated with MD. The presence of anemia and infection might exaggerate heart failure. A coronary arteriogram was not performed in this case, but there were no history of angina pain, no abnormal laboratory data showing myo-

FIG. 2 (A) Twelve-lead electrocardiogram (ECG) on admission showing first-degree atrioventricular block and prolonged QTc interval (670 ms). (B) ECG just before the episode of torsade de pointes (TdP) showing marked QTc prolongation (730 ms). (C) ECG showing TdP.

cardial injury, no asynergy in echocardiogram, and no ischemic findings in thallium 201 single-photon emission computed tomography, suggesting that myocardial ischemia was not involved in her heart failure.

In this family, the presence of QT(U) prolongation seemed to be associated with MD. On the other hand, there have been some reports on QT prolongation associated with diabetic neuropathy,⁶ thus this possibility must be ruled out in this patient. However, the degree of QT prolongation in diabetic neuropathy is usually mild (a longest reported QTc interval was 500 ms^{6,7}) and the patient's daughter and brother with prolonged QT(U) did not have diabetes mellitus. QT prolongation persisted even after her heart failure improved, but the heart failure may have triggered Tdp.

The genetic mutation associated with MD has been reported to be the expansion of the CTG trinucleotide repeat in the 3' untranslated region of a protein kinase gene located on the q13.3 band of chromosome 19.^{7,8} The trinucleotide repeat, which is present 5 to 37 times in the normal population, has been found to be amplified up to 3,000 times in patients with MD.^{8,9} In families with MD, symptoms appear at an early age and become more severe in successive generations; this phenomenon is known as anticipation.¹ The degree of expansion of the CTG repeat correlates with the anticipation as seen in this patient and her daughter. However, we and others have reported that the expansion of the CTG repeat does not correlate with the degree of cardiac involvement, such as left ventricular dysfunction and conduction disturbances,³ although their relationship remains controversial.¹⁰ We have not investigated the defect in the channel proteins to account for QT prolongation in the affected members, but it is most likely that they had two separate genetic defects which are in close proximity on the same chromosome.

Several investigators have proposed ventricular tachycardia as a potential cause of sudden death in patients with

MD. We experienced a rare case of MD with congestive heart failure, also associated with QT prolongation and Tdp. Physicians should be aware that MD may be complicated by such cardiac involvements.

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