CASE REPORT

A case of pregnancy complicated with dilated cardiomyopathy 1X

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Abstract

Dilated cardiomyopathy 1X (CMD1X) is characterized by dilated cardiomyopathy (DCM) with mildest limb-girdle muscle symptoms and normal intelligence. Compound heterozygous mutation in fukutin gene is known as its genetic cause. Here, we report a pregnancy case complicated with CMD1X. A 25-year-old primiparous woman, who had been diagnosed as CMD1X at the age of 19, was referred to our hospital at 6 weeks of gestation. In early pregnancy, the evaluation of her cardiac function showed ejection fraction 47% and NYHA class II. Worsening of cardiac function was observed from 30 weeks, manifesting reduced cardiac load with left ventricular dilatation and in-hospital bed rest was necessary. Elective cesarean section was performed at 35 weeks to prevent deterioration of cardiac function. The parameters of her cardiac function returned to the pre-pregnancy status in a month after delivery, whereas she realized persistent worsening of muscular weakness at postpartum.

INTRODUCTION

A series of Japanese cases characterized by dilated cardiomyopathy (DCM) and hyper-CKemia with no or minimal limb-girdle muscle symptoms and normal intelligence caused by a compound heterozygous mutation of 3 kb retrotransposal insertion and missense mutation in fukutin (FKTN) were first described by Murakami et al. [1]. Currently, it is designated ‘cardiomyopathy dilated 1X (CMD1X: #611615)’ in the OMIM database. Only eight cases limited to the Japanese family have been reported so far. This is the first report describing a pregnancy case complicated with CMD1X.

CASE REPORT

A 25-year-old primiparous woman who had been diagnosed as CMD1X at the age of 19 was referred to our hospital at 6 weeks of gestation. Prior to the genetic diagnosis, she had manifested with exertional dyspnea and mild muscular weakness at neck and proximal extremities. DCM was confirmed in her echocardiogram showing systolic dysfunction with ventricular dilatation and left ventricular ejection fraction (EF) of 41%. Diffuse muscle atrophy and mild necrosis-regeneration process had found in biceps brachii muscle biopsy. Immunohistochemical analysis of biopsied muscle sample had shown a reduced α-dystroglycan staining and a normal pattern of the distribution and expression of β-dystroglycan. As previously reported [2], the analysis of her genomic DNA using the polymerase chain reaction technique had revealed a compound heterozygous mutation of 3 kb retrotransposal insertion. In addition, a direct sequencing of all the exons and adjacent introns of FKTN had shown a missense mutation (c.302G>T, p.Cys101Phe).

In the first trimester of her pregnancy, echocardiography demonstrated diffused left ventricular hypokinesis accompanied

Received: July 23, 2015. Revised: August 24, 2015. Accepted: September 18, 2015

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with left ventricular dilatation. EF was 47% and left ventricular
diastolic dimension (LVDd) was 53 mm. Her clinical
findings at 10 weeks of gestation are demonstrated in Table 1. The limitation
level of her physical activity was class II in New York Heart Asso-
ciation (NYHA) functional classification. Mild muscular weak-
ness at neck, rhomboids and gluteus medius along with
bilateral calf hypertrophy was demonstrated in her neuromuscu-
lar evaluation and a waddling gait was observed. Her tendon re-
flexes in biceps, brachioradialis and triceps were suppressed. She
and her husband opted to continue pregnancy after our counsel-
ing about the risk for maternal cardiac failure at term and post-
partum and the possible adverse outcome in the fetus.
Medication with β-blocker to prevent the progression of DCM
was continued during pregnancy. From 28 weeks of gestation,
she was hospitalized for a concern of increase in the cardiac
load in the third trimester and received intensive evaluation for
her cardiac function. From 30 weeks of gestation, cardiothoracic
ratio on chest X-ray and LVDd on echocardiogram increased pro-
gressively together with gradual elevation of peripheral concen-
tration of brain natriuretic peptide (BNP; Fig. 1). Although
subjective symptom related to cardiac failure was not obvious
at bed rest, allowing pregnancy to continue until term could
cause irreversible deterioration of cardiac function. Therefore,
she underwent an elective cesarean section at 35 weeks of gesta-
tion and gave birth to a healthy male baby (birth weight: 2306 g,
Apgar score 8 point at 5 min).
A transient elevation of peripheral BNP was found at post-
operative day (POD) 7 and was normalized at POD 14 (Fig. 2). In
two weeks after delivery, the parameters of cardiac function on
echocardiogram and the level of daily activity both recovered to
the conditions comparable to those before pregnancy. At post-
partum, she realized worsening of muscular weakness and had
some difficulty in climbing stairs and holding her baby. She
was discharged with her baby at POD 17.

DISCUSSION

Genetic diseases associated with FKTN gene defect include
Fukuyama congenital muscular dystrophy, Walker-Warburg
syndrome, limb-girdle muscular dystrophy type 2M (LGMD2M)
and CMD1X. A gene product of FKTN participates in glycosylation
of α-dystroglycan, which controls the linkage between extra-
cellular and intracellular proteins [3]. Defect of the FKTN gene
could lead to muscular dystrophy, a developmental disturbance
of central nervous system and eye anomalies [4]. Murakami
et al. [1] first identified a compound heterozygous FKTN mutation,
showing DCM with no or minimal LGMD symptom and normal
intelligence. This genetic disease was currently categorized as
CMD1X. Similar to Fukuyama congenital muscular dystrophy,
muscle biopsy of patients with CMD1X indicated altered glycosy-
lation of α-dystroglycan, although minimal dystrophy was his-
tologically detected in skeletal muscle. A molecular mechanism
for cardiomyopathy-dominant disease phenotype with mildest
skeletal muscular dystrophy in CMD1X is not clari-
fied.
Clinical cases of CMD1X have been limited to eight Japanese so
far. To our knowledge, there is no preceding report on pregnancy
of a patient with CMD1X. Pregnancy has a negative impact on
the cardiac function in the women with DCM [5]. A previous

Table 1: Clinical findings at 10 weeks of gestation

| Clinical laboratory data | Echocardiography |
|-------------------------|------------------|
| WBC 5.4 × 10^3/μl | IVS/PWth 6/5 mm |
| Hb 12.3 g/dl | LVDd/Ds 51/42 mm |
| Pt 20.5 × 10^4/μl | EF 47% |
| PT-INR 0.93 | AoD 25 mm |
| APTT 26.9 s | LAD 36 mm |
| Fbg 304 mg/dl | Asynery Posterior wall |
| Cre 0.26 mg/dl | |
| Na 140 mEq/l | |
| K 4.1 mEq/l | |
| CK 1873 U/l | |
| CK-MB 52 U/l | |
| BNP 45.3 pg/ml | |
A prospective study found that adverse maternal cardiac event occurred in 39% of pregnancies complicated with DCM [6]. In addition, the incidence of the cardiac event was significantly higher if any of three risk factors, moderate or severe LV dysfunction (EF <45%), NYHA functional class III or IV and/or a previous cardiac event was present. In this context, the present case was at moderate risk, showing borderline values of EF, 41% prior to pregnancy and 48% in the first trimester. Generally, it is known that the increase in intravascular volume and cardiac output in the third trimester elevates the risk for adverse cardiac event in pregnant women with DCM [5]. In the present case, the pregnancy period can be extended until 35 weeks without irreversible exacerbation of cardiac failure at postpartum, although the progress of cardiac dysfunction was manifested from 30 weeks. Regarding the prenatal management conducted in this case, the medication with β-blocker and the prophylactic hospitalization for bed rest might contribute to preservation of cardiac function, leading to the extension of pregnancy without severe adverse cardiac event.

She recognized the worsening of muscular weakness at postpartum. According to a previous study on pregnancy outcome in women with hereditary neuromuscular disorders, persistent worsening of muscular symptoms was experienced in 54% of LGMD pregnancies, whereas walking ability was maintained in nearly all women who had been ambulant before pregnancy [7]. Therefore, the progression of muscular dystrophy during pregnancy is possible in the present case. However, the influence of disuse syndrome should be considered, since long-term bed rest might have additional negative impact on the disease-specific muscular dysfunction.

The design of this work has been approved by the University of Tokyo ethical committee. Informed patient consent has been obtained. T.N. accepts full responsibility for this work.

CONFLICT OF INTEREST STATEMENT

None declared.

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