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【 CASE REPORT 】

Peripartum Serial Echocardiographic Findings in a Patient with Life-threatening Peripartum Cardiomyopathy

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Abstract:

A 35-year-old woman was referred to our hospital for the management of acutely decompensated heart failure due to peripartum cardiomyopathy (PPCM). Generally, cardiac examinations are performed after the manifestation of heart failure in patients with PPCM. Thus, reports of serial cardiac examinations before the onset of PPCM are scarce. In this case, we were able to document the serial echocardiographic findings before the onset of life-threatening PPCM. We found that the left ventricular systolic function was preserved at 35 weeks of gestation but declined acutely after delivery at 38 weeks. Although speculative, these findings suggest that left ventricular dilation might precede the onset of PPCM.

Key words: peripartum cardiomyopathy, echocardiography, predictor

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Introduction

Peripartum cardiomyopathy (PPCM) is characterized by systolic cardiac dysfunction and presents in the last month of pregnancy or within five months of delivery in women without pre-existing cardiac disease (1). A diagnosis of PPCM is confirmed by the exclusion of other underlying disorders and strict echocardiographic indications of left ventricular (LV) dysfunction, defined as an LV ejection fraction (LVEF) less than 45% (2). The reported incidence of PPCM varies globally and ranges from 1 in 1,421 to 1 in 9,861 deliveries (3). While half of the patients regain a normal LVEF, some patients require inotropes and mechanical circulatory support and may even require a heart transplant to survive (4). However, the etiology of PPCM remains unknown, and it is difficult to predict the onset of PPCM before the disease becomes apparent.

Case Report

A 35-year-old woman (gravida 1, para 1; uneventful pregnancy with history of first delivery at 32 years of age) was referred to our cardiac emergency department for the management of heart failure due to PPCM. The patient had a benign medical history before the current delivery of twin pregnancy. Her blood pressure had been within the normal range throughout the pregnancy, ranging from 111/64 to 129/75 mmHg in the absence of antihypertensive agents, and she had not developed proteinuria during the pregnancy. She was admitted to the obstetric hospital for the management of her pregnancy at 32 weeks of gestation. On admission, she was asymptomatic. However, chest radiography showed cardiac enlargement [cardiothoracic ratio (CTR), 54%] (Fig. 1A), and transthoracic echocardiography showed a slightly dilated cardiac chamber and preserved LV function [LV end-diastolic dimension (LVDd)/LV end-systolic

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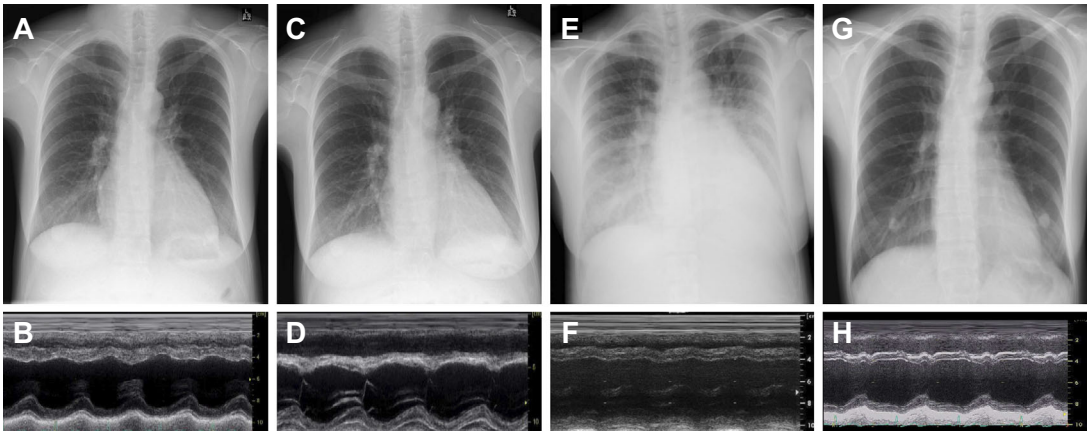

	At 32 weeks of gestation	At 35 weeks of gestation	Immediately after delivery (38 weeks)	6 months after delivery
LVDd	51 mm	54 mm	58 mm	44 mm
LVDs	34 mm	36 mm	53 mm	29 mm
LVEF	54%	62%	24%	53%
BNP	138 pg/mL	154 pg/mL	2696 pg/mL	9 pg/mL

Figure 1. Serial chest radiograph and transthoracic echocardiogram from 32 weeks of gestation to 6 months after delivery. (A) Chest radiograph at 32 weeks of gestation. (B) Transthoracic echocardiogram at 32 weeks of gestation. (C) Chest radiograph at 35 weeks of gestation. (D) Transthoracic echocardiogram at 35 weeks of gestation. (E) Chest radiograph at referral to our hospital (38 weeks of gestation). (F) Transthoracic echocardiogram at referral to our hospital (38 weeks of gestation). (G) Chest radiograph 6 months after delivery. (H) Transthoracic echocardiogram 6 months after delivery. BNP: B-type natriuretic peptide, LVDd: left ventricular end-diastolic dimension, LVDs: left ventricular end-systolic dimension, LVEF: left ventricular ejection fraction

dimension (LVDs), 51/34 mm; LVEF calculated using Teichholz's formula, 54%] (Fig. 1B). Her plasma B-type natriuretic peptide (BNP) level was elevated at 138 pg/mL. At 35 weeks of gestation, she unexpectedly gained body weight, and chest radiography showed further cardiac enlargement (CTR, 58%) and left pleural effusion (Fig. 1C). Her LV dimensions and BNP level also showed slight increases (LVDd/LVDs, 54/36 mm; BNP level, 154 pg/mL), while the LVEF was still preserved (62%) (Fig. 1D). Although her ratio of mitral valve inflow velocity to left ventricle wall tissue velocity was within normal range (E/e': 9.4), the trans-tricuspid pressure gradient was mildly elevated (34 mmHg), suggesting a certain degree of diastolic dysfunction had caused her pleural effusion. Her electrocardiogram did not change during pregnancy.

She subsequently underwent usual vaginal delivery, and healthy twin neonates were born at 38 weeks. Immediately after delivery, progressive malaise and dyspnea developed. Chest radiography revealed pulmonary congestion and increased bilateral pleural effusion. Transthoracic echocardiography revealed a severely reduced LV systolic function and increased LV dimensions. Thus, the patient was diagnosed with heart failure, and PPCM was suspected as the underlying etiology. The patient was referred to our tertiary medical center for further management.

On referral to our hospital, the patient's pulse rate was 103 beats/minute, her blood pressure was 150/97 mmHg, respiratory rate was 29 breaths/minute, and room air oxygen saturation was 94%, with a New York Heart Association (NYHA) functional class III. Her BNP level was elevated at 2,696 pg/mL. Chest radiography showed further cardiac enlargement (CTR, 64%) and pulmonary congestion (Fig. 1E). On transthoracic echocardiography, LVDd/LVDs was 58/53 mm, and LV wall motion exhibited severely reduced contraction, with an LVEF of 24% (Fig. 1F) and only mild mitral regurgitation.

Emergency right heart catheterization indicated progressive heart failure with a high pulmonary capillary wedge pressure (25 mmHg), high pulmonary arterial pressure (40/23/30 mmHg), normal right atrial pressure (2 mmHg), and normal cardiac index (4.6 L/min/m^2). We then detected an increased heart rate (from 95 to 138 beats/minute) and a gradual decrease in her cardiac index (down to 2.8 L/min/m^2). Considering her low stroke volume index (20 mL/m^2), we initially administered inotropes, but her heart failure continued to worsen. Thus, intra-aortic balloon pumping (IABP) was used for circulatory support. Cabergorine, which is a potent dopamine receptor agonist, was

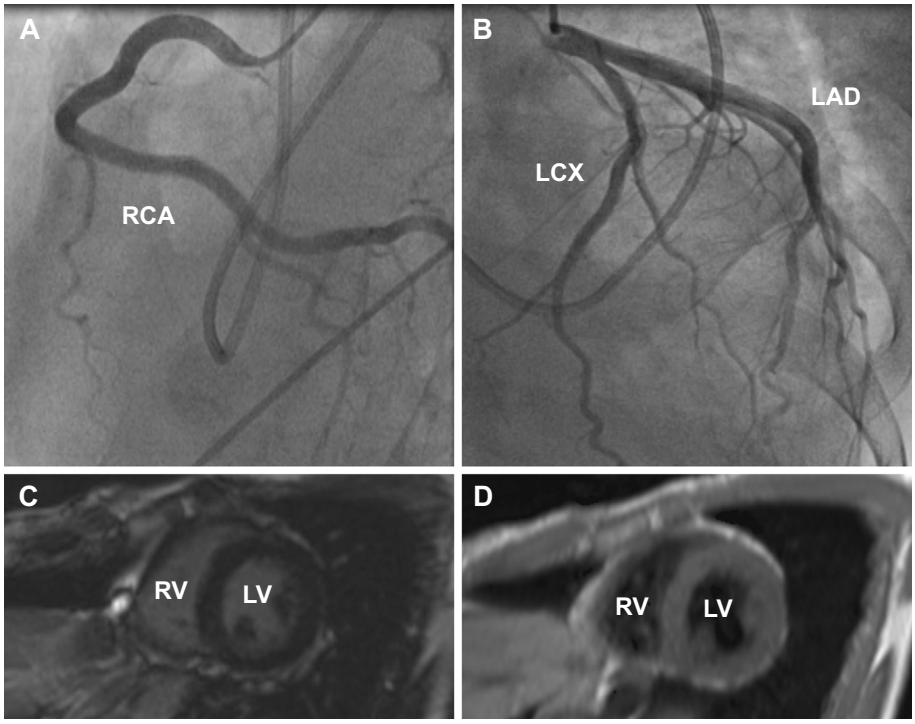

Figure 2. **Coronary angiography, and cardiac magnetic resonance imaging. (A) Right coronary angiography showed a normal right coronary artery. (B) Left coronary angiography showed a normal left coronary artery. (C) The myocardium was not enhanced on late gadolinium-enhanced cardiac magnetic resonance imaging. (D) The myocardium had no high-signal-intensity areas on T2-weighted cardiac magnetic resonance imaging. LAD: left anterior descending coronary artery, LCX: left circumflex artery, LV: left ventricle, RCA: right coronary artery, RV: right ventricle**

prescribed at a dose of 1 mg for the suppression of lactation, due to the high metabolic demands of lactation and breastfeeding. Bromocriptine was not administered for the treatment of PPCM because the available data were insufficient to recommend its routine use. Her hemodynamic parameters improved with these multidisciplinary treatments. Her heart failure gradually improved, allowing for the removal of IABP 9 days after the insertion and the discontinuation of inotropes 15 days after infusion.

Her hemodynamic state remained stable after weaning from inotrope therapy, and she was transferred to the ward with the following medications: 1.25 mg/day enalapril, 5 mg/day carvedilol, 20 mg/day furosemide, and 25 mg/day spironolactone. Pre-discharge laboratory tests, chest radiography, and transthoracic echocardiography showed significant improvements: CTR, 50%; LVDd/LVDs, 49/40 mm; and LVEF, 42%. Her plasma BNP level normalized to 10.2 pg/mL. During hospitalization, we excluded other causes of heart failure based on laboratory tests, coronary angiography, and cardiac magnetic resonance (Fig. 2). An endomyocardial biopsy performed one month after the onset of PPCM revealed no infiltrative disorders and showed that the interstitial fibrosis and interstitial edema were mild, without inflammatory cell infiltration, myocardial necrosis, or degeneration (Fig. 3). We therefore diagnosed the patient as having PPCM. She was discharged 45 days after admission with an NYHA class I. Six months later, her BNP level decreased to 9.3 pg/mL, CTR decreased to 49% (Fig. 1G), LVDd/LVDs decreased to 44/29 mm, and LVEF improved to 53% (Fig. 1H).

Discussion

PPCM is a life-threatening disease, but its precise etiology and progression remain largely unknown. Cardiac examinations in patients with PPCM are usually performed after the manifestation of heart failure. Thus, reports of serial cardiac examinations before the onset of PPCM are scarce. In our case, we were able to document serial cardiac examinations before the onset of life-threatening PPCM. The major findings in our report were as follows: First, the LV systolic function was preserved (LVEF, 62%) at 35 weeks of gestation but declined acutely (LVEF, 24%) after delivery at 38 weeks. Serial echocardiography revealed that the deleterious effects on the systolic function occurred within 3 weeks. Second, LV dilation (LVDd/LVDs, 51/34 mm at 32 weeks; 54/36 mm at 35 weeks) and an elevated BNP level (154 pg/mL at 35 weeks) might precede the onset of PPCM.

The causes of PPCM are reportedly multifactorial, including inflammatory cytokines (5), cleavage of prolactin to an angiostatic N-terminal 16 kDA prolactin fragment (6), cardiac angiogenic imbalance (7), and genetic susceptibility (2). In addition, some investigators have suggested acute myocarditis as a possible cause of PPCM based on endomyocar-

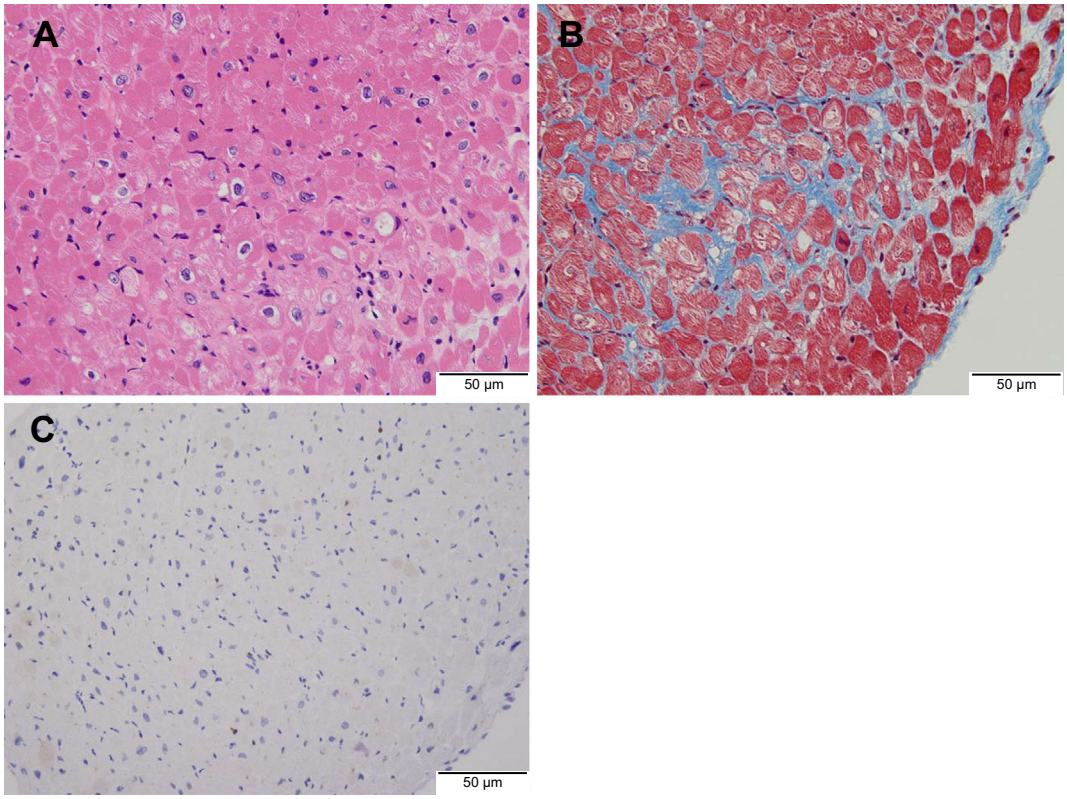

Figure 3. **Microphotographs of right ventricle endomyocardial biopsy specimens. (A) Interstitial edema was mild without inflammatory cell infiltration, myocardial necrosis, or degeneration (Hematoxylin and Eosin staining). (B) Interstitial fibrosis was mild (Masson's trichrome staining). (C) There were no CD3-positive lymphocytes (immunohistochemical staining for CD3-positive T-cells).**

dial biopsy specimens demonstrating high prevalence of inflammatory cells (8). Although endomyocardial biopsy specimens in our patient demonstrated no inflammatory cells, the procedure was performed one month after the onset of PPCM. Considering the acute decline in the LV systolic function, acute inflammation and/or acute autoimmune response may be a possible cause of PPCM in our patient to some extent.

As described above, a number of potential factors in addition to myocarditis are indicated to be involved in the onset of PPCM. Genetic variants in patients with PPCM are reported to be remarkably similar to those found in patients with dilated cardiomyopathy (9); thus, a genetic susceptibility to PPCM and/or pathophysiology similar to dilated cardiomyopathy have been indicated (10). In our patient, the LVDd gradually increased, and the BNP level was elevated, as is the case in dilated cardiomyopathy, before the decline in the systolic function and the onset of PPCM. Although LV dilation and BNP elevation are influenced by pregnancy, we considered their changes in the present case to be beyond the normal range in pregnancy, based on previous reports. For example, Savu et al. suggested that the LVDd is dilated to 47±3 mm in normal pregnancy (11), but the LVDd in our patient was dilated to 54 mm at 35 weeks. Another report showed that the LVDd increases with gestational age, reaching its peak at 32 weeks (12). However, in our patient, the LVDd increased from 32 to 35 weeks of gestation (from 51 to 54 mm). With regard to BNP, the median BNP level during pregnancy reportedly increases to 26 pg/mL (range, 10-142 pg/mL) in the third trimester (13). Although a twin pregnancy differs considerably from a singleton pregnancy in many aspects, a report showed that N-terminal pro BNP only increased to 72±49 pg/mL in twin pregnancy (14). In our patient, the BNP level was 154 pg/mL at 35 weeks, which seems to be beyond the normal range even for a twin pregnancy. The literature regarding the LV size in twin pregnancy is lacking. However, we speculate that the patient's LV size of 54 mm might be slightly dilated, as Japanese women are generally relatively lean and small, based on the findings of a report on the cardiac function in twin pregnancy from Western countries (15).

LV dilation and BNP elevation beyond the normal range in pregnancy (although the twin pregnancy might have influenced these changes) preceded the decline in the LVEF in our patient. Our case suggests that LV dilation and BNP elevation may precede heart failure decompensation and might be predictors for the development of PPCM. Further studies are required to test this hypothesis.

Conclusion

Our case demonstrated serial cardiac changes before the onset of PPCM. We found that the LVEF declined acutely after 35 weeks of gestation, and LV dilation might have preceded the decline in the LVEF, suggesting that LV dilatation

might be a predictor for the development of PPCM. Further studies are warranted to investigate the underlying mechanism, natural course, and predictors of PPCM.

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

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