INTERNAL MEDICINE

□ CASE REPORT □

Magnetic Resonance Imaging in a Patient with Peripartum Cardiomyopathy

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Abstract

Peripartum cardiomyopathy (PPCM) is a form of heart failure that affects women late in pregnancy or early in peripartum. The present report describes a case of a patient with PPCM demonstrated by magnetic resonance imaging (MRI) with late gadolinium enhancement of the left ventricle (LV). The late gadolinium enhancement of MRI improved associated with recovery of cardiac function. Endomyocardial biopsy showed mild cell infiltration and fibrosis. Thus, MRI may be useful for the evaluation of myocardial damage and to predict the outcome of PPCM.

Key words: heart failure, myocarditis, pregnancy, lymphocyte, magnetic resonance imaging

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Introduction

Peripartum cardiomyopathy (PPCM) is a rare form of heart failure that develops in the last month of pregnancy or within 5 months of delivery in patients without preexisting heart failure (1, 2). The cause of PPCM is unknown, and its natural history is extremely variable, ranging from the spontaneous recovery of ventricular function to refractory disease. Thus, we need non-invasive tools other than the ordinary methods such as ECG and echocardiography to more precisely evaluate the severity of myocardial damage and to predict the outcome of PPCM for the treatment.

Recently, magnetic resonance imaging (MRI) is used for the diagnosis and the detection of myocardial damage in some heart diseases (3-8). However, there is no report about MRI of PPCM. The present report describes a patient with PPCM, whose myocardial damage was demonstrated by magnetic resonance imaging (MRI) with late gadolinium enhancement (LGE) of the left ventricle (LV); and LGE of MRI improved associated with recovery of cardiac function by the treatment with beta-blocker, angiotensin II receptor blocker and spironolactone.

Case Report

A 43-year-old Japanese woman without any prior history of heart disease experienced onset of recurrent precordial pain approximately 1 week after her third delivery. About 2 months later, in May 2006, she was hospitalized with congestive heart failure, and chest X-ray showed cardiomegaly and mild pleural effusion (Fig. 1), and ECG showed sinus rhythm, left axis deviation, low voltage in all limb leads, and complete left bundle branch block (CLBBB) (Fig. 2). Echocardiography demonstrated diffuse hypokinesis and dilatation of the left ventricle (LV) with an ejection fraction (LVEF) of 19% (Fig. 1). Laboratory findings are summarized in Table 1. There was a slight increase in the serum levels of aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase, C-reactive protein, and LDL-cholesterol, and triglyceride, and a marked increase of the serum level of brain natriutetic peptide although the serum level of creatine kinase was normal. The patient was started on candesartan (8 mg once daily), an angiotensin II receptor blocker, carvedilol (5 mg twice daily), a beta-blocker, and spironolactone (25 mg once daily), with good symptomatic relief. In June 2006, the patient was transferred to our hospital for specialized evaluation and treatment.

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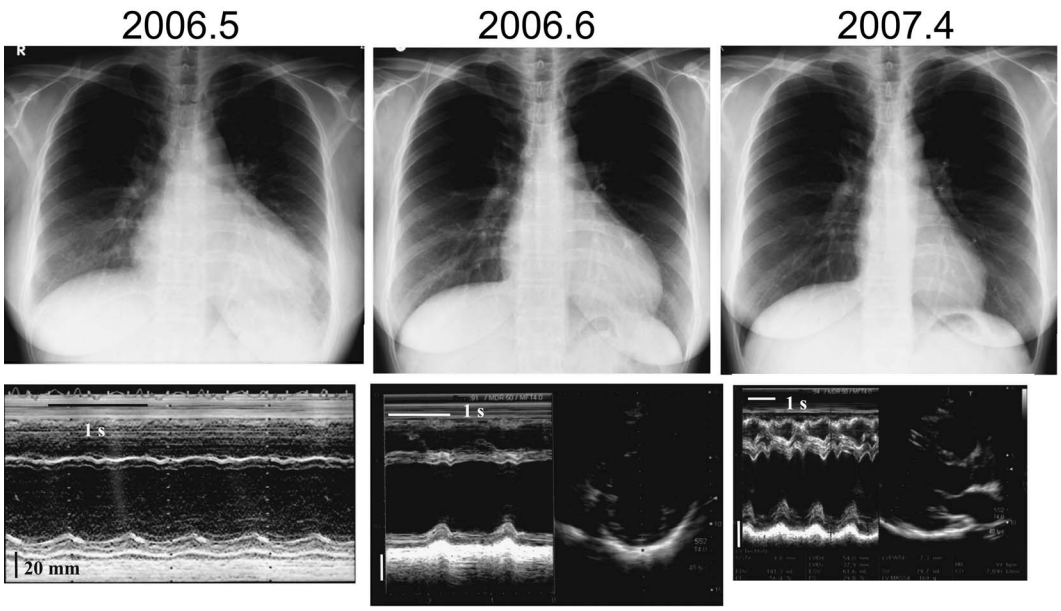

IVS (mm)	8	8	10
LVPW(mm)	10	8	7
LVDD(mm)	59	59	54
LVDS(mm)	54	48	38
LVEF (%)	19	33	56
LVFS (%)	8	18	30

Figure 1. **Time course of chest X-ray and echocardiography. Cardiomegaly and cardiac function gradually ameliorated.**

Table 1. **Laboratory Data**

2006	May	June	2006	May	June
WBC (/μl)	4860	4000	Glu (mg/dl)	112	71
Ht (%)	36	39	LDL-C (mg/dl)	150	97
BUN (mg/dl)	14	13	HDL-C (mg/dl)	42	33
Cr (mg/dl)	0.8	0.78	TG (mg/dl)	191	95
TP (g/dl)	6.9	7.7	CRP(mg/dl)	0.80	0.03
T Bil (mg/dl)	0.8	0.7	BNP (pg/ml)	555	24.5
AST (IU/l)	54	30	ANA	n.e.	x40
ALT (IU/l)	127	39	RF (IU/ml)	n.e.	<9.5
LDH (IU/l)	221	152			
γ-GTP (IU/l)	47	19			
CK (IU/l)	95	70			
troponin T (ng/ml)	n.e.	<0.01			

WBC , white blood cell count; Ht, hematocrit; BUN, blood urea nitrogen, Cr, serum creatinine; TP, total protein; T Bil, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase ; CK, creatine kinase; γ-GTP, γ-glutamyltransferase; Glu, glucose; LDL-C, LDL-cholesterol ; HDL-C, HDL-cholesterol; TG, triglyceride; CRP, C-reactive protein; BNP, brain natriuretic peptide; ANA, anti-nuclear antibody; RF, rheumatoid factor; n.e., not examined

On admission, physical examination revealed height of 156 cm, weight of 55 kg, blood pressure of 90/60 mmHg, and a regular pulse rate of 60 beats/min. The lungs were clear, and there was no significant murmur or extra-systolic heart sound appreciated. Neither hepatomegaly nor edema of lower extremities was seen. The patient's cardiovascular

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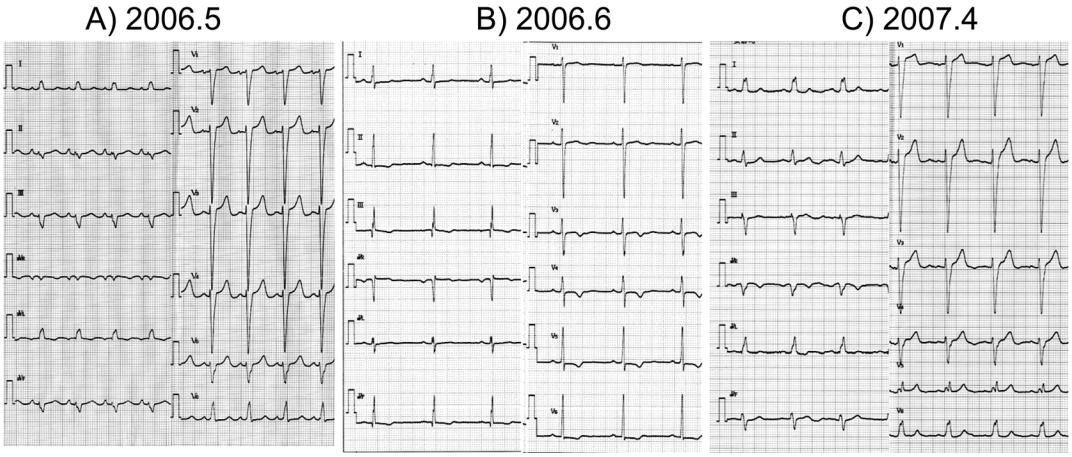

Figure 2. Electrocardiographs. ECG showed sinus rhythm, left axis deviation, low voltage in all limb leads, and complete left bundle branch block (CLBBB) at hospitalization with congestive heart failure (A). And left axis deviation decreased and the voltage of all limb leads increased after 11 months (C). Only ECG on admission in our hospital showed narrow QRS without CLBBB, and it showed inverted T waves in leads II, III, $_aV_F$, and V_{3-6} (B).

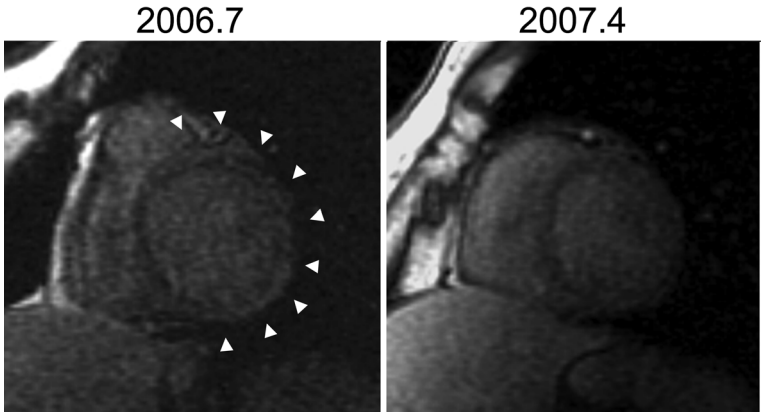

Figure 3. MRI with gadolinium showed late enhancement of the midwall and subepicardium in the anteroseptal, lateral, and posterior walls of LV (arrow heads), and this change decreased about 10 months after the first MRI.

status was determined as New York Heart Association (NYHA) class II.

Repeat chest X-ray showed only mild cardiomegaly (Fig. 1). Only ECG on admission showed narrow QRS without CLBBB, and it showed sinus rhythm and inverted T waves in leads II, III, $_aV_F$, and V_{3-6} (Fig. 2). Other ECGs showed LBBB. Echocardiography demonstrated diffuse hypokinesis of the LV and dilatation of the LV with an LVEF of 33% (Fig. 1). There was no abnormal data except for a slightly low level of HDL-cholesterol of 33 mg/dl and a slight increase of the serum level of brain natriuretic peptide.

Coronary angiography showed no significant stenosis of the coronary arteries. Right ventricular catheterization revealed normal pulmonary artery pressure (PAP) of 26/9 (mean 15) mmHg and mean pulmonary capillary wedge pressure (PCWP) of 4 mmHg. Cardiac index (CI) was 2.71 l/min/m^2. Left ventriculogram showed diffuse hypokinesis of the LV and an LVEF of 36%. MRI with gadolinium was performed about 2 months after the onset of heart failure, in July 2006, and it showed LGE mainly in the mid wall and the subepicardium in the anteroseptal, lateral, and posterior walls of LV (Fig. 3).

Endomyocardial biopsy (EMB) of LV was performed in July 2006, and it demonstrated that cell infiltration and interstitial fibrosis were mild without myocardial necrosis, degeneration or interstitial edema (Fig. 4). Immunohistochemical staining indicated that infiltrating cells were mainly T cells (Fig. 5). The Dallas criteria indicated borderline myocarditis.

The treatment with beta-blocker, angiotensin II receptor blocker, and spironolactone were continued and the patient's cardiac function gradually recovered. Chest X-ray showed no cardiomegaly, and echocardiography demonstrated that LVEF was 56% about 1 year after occurrence of heart failure (Fig. 1). ECG showed CLBBB, but the voltage of all limb leads was increased (Fig. 2). LGE of MRI was also decreased about 10 months after the onset of heart failure, in

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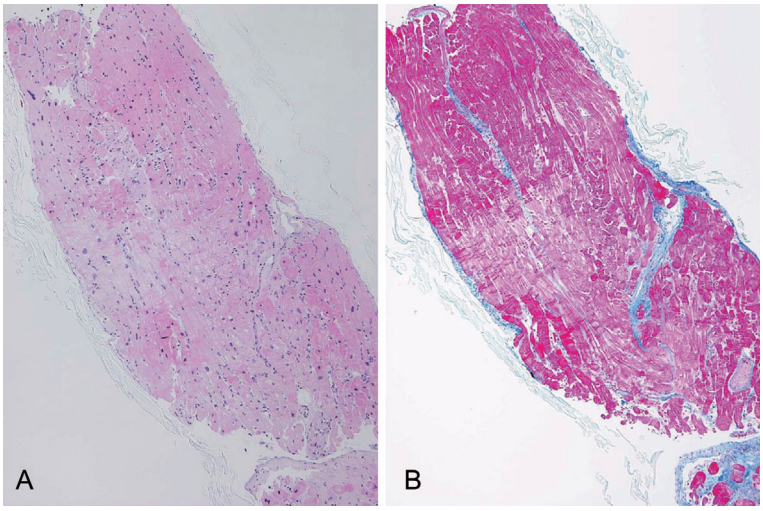

Figure 4. **Microphotographs of emdomyocardial biopsied left ventricle (A, Hematoxylin and Eosin staining, ×100; B, Azan stain, ×100).**

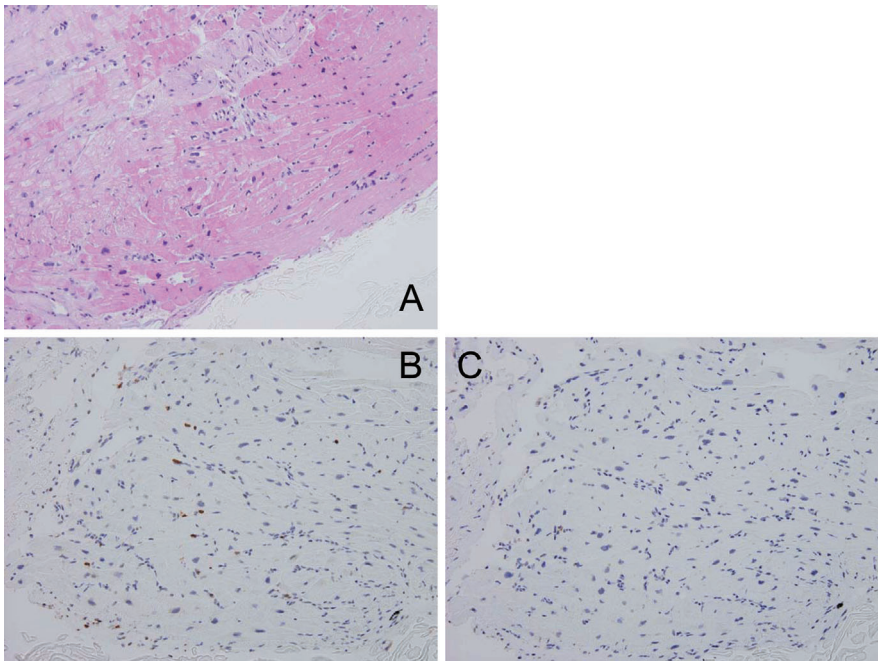

Figure 5. **Microphotographs of Hematoxylin and Eosin staining and immunostaining of infiltrating cells in emdomyocardial biopsied left ventricle. A) Hematoxylin and Eosin staining (×200). Cell infiltration was seen in the interstitium of myocardium. B) Immunostaining using anti-CD 3 antibody for T cell (×200). Most of infiltrating cells were CD3-positive. C) Immunostaining using anti-CD79a antibody for B cell and plasma cell (×200). There are few CD79a-positive cells in the interstitium of myocardium.**

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Discussion

In the present case, EMB demonstrated cell infiltration confirmed by immunohistologic staining and replacement fibrosis and MRI showed LGE mainly in the mid wall and subepicardial layer in the anteroseptal, lateral, and posterior walls of LV, which indicates myocardial damage. These suggest that myocardial inflammation may contribute to disease process in the present patient with PPCM.

Cardiac MRI with LGE can identify areas of myocardial damage in myocardial infarction (3) as well as in hypertrophic and dilated cardiomyopathy (4, 5). Recent studies have demonstrated that this modality may also be useful for the non-invasive recognition of myocardial inflammation in patients with acute and chronic myocarditis (6-8). In the present patient, diffuse and mainly mid wall and subepicardial distribution of LGE was observed in LV, which is consistent with patterns previously observed in the context of

myocarditis (6-8).

Although the causes of peripartum cardiomyopathy (PPCM) remain unclear, previous studies have suggested that myocarditis may contribute to the pathogenesis of PPCM by demonstrating a dense lymphocyte infiltrate with variable amounts of myocyte edema, necrosis, and fibrosis (9-13).

EMB is the only tool that may provide a definite diagnosis of myocarditis. The Dallas criteria are the only widely accepted guideline for the histological diagnosis of myocarditis. According to the Dallas criteria, myocarditis was classified as active if myocardial necrosis or degeneration associated with inflammatory infiltration was present, and as borderline if necrosis or degeneration is absent (14). In the present case, myocarditis was classified as borderline by the Dallas criteria. The time interval between onset of symptoms and EMB correlated with the histological diagnosis. Because EMB was performed about 2 months after symptoms occurred in the present case, myocardial necrosis might have been seen if EMB were performed earlier.

Although the cause of myocarditis in the present patient remains unclear, some studies have investigated the relationship between autoimmune mechanisms, inflammation, and PPCM. A viral trigger for the development of PPCM has previously been postulated and investigated (15). Further, abnormal immune responses against fetal cells or myometrial antigens have been proposed to be important mechanisms of PPCM (1, 16-18).

A previous report demonstrated that LGE becomes diffuse over a period of days and weeks in myocarditis (19). The mechanism of LGE in myocarditis has been discussed (20). Gadolinium chelating agents are extracellular contrast agents that are inert and cannot cross the myocyte cell membrane. Acute necrosis in the myocarditis is characterized by ruptured sarcolemmal membranes and surrounding interstitial edema, allowing the contrast agent to accumulate in the intertsitium, and to diffuse into the intracellular spaces. Fibrosis expands the interstitial space and it also leads to an increase in LGE. In the present case, LGE was seen in diffuse and mainly mid and subepicardial myocardium although EMB did not show myocardial necrosis and interstitial edema although there was mild fibrosis, and there was no significant increase of serum level of creatine kinase. Thus, mechanism of myocardial damage of PPCM may be different from that of ordinary viral myocarditis. Recently, it was reported that membrane damage and inadequate membrane repair may participate in the pathogenesis of cardiomyopathy (21). Lamparter et al (22) reported that circulating autoantibodies to cardiac tissue including anti-sarcolemmal antibodies were observed in patients with PPCM. We hypothesized that myocyte membrane dysfunction or damage without myocyte necrosis may have been induced by an autoimmune mechanism and may have altered the membrane permeability causing cardiac dysfunction at least about 2 months after the onset of heart failure in the present case with PPCM. The altered membrane permeability might allow contrast agent of MRI to diffuse into the intracellular space, which induces LGE.

We also demonstrated that late gadolinium enhancement of MRI decreased about 10 months after the onset of heart failure in the present case with medical treatment. In myocarditis, late gadolinium enhancement decreases during healing and may become invisible after recovery. And the large scar area may still be visible after healing causing a distinctive linear mid wall pattern of LGE (6). Thus, healing, a natural course of myocarditis may have been related to the decrease of LGE in the present case.

The present case was treated with angiotensin II type 1 receptor antagonist, beta-blocker, and spironolactone. Previous reports suggested that angiotensin II type 1 receptor antagonist and beta-blocker are useful for the treatment of myocarditis (23-25). These data suggest that the treatment with these medicines may advance myocardial healing in PPCM. In conclusion, MRI may be useful for diagnostic, pathogenic, and prognostic considerations in patients with PPCM.

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