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EMERGENCY DEPARTMENT EVALUATION AND MANAGEMENT OF PERIPARTUM CARDIOMYOPATHY

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□ Abstract—Peripartum cardiomyopathy (PPCM) affects 1000–1300 women in the United States each year. We present three cases of PPCM seen in our Emergency Department (ED) that cover the entire spectrum of disease from mild heart failure to sudden cardiac death. Without previous heart disease, these women develop cardiomyopathy with impairment of left ventricular function in the last month of pregnancy, or during the first 5 months postpartum. The etiology of PPCM is not clear, although various mechanisms have been proposed, including infection, autoimmune response, prolonged tocolysis during labor, and maladaptive responses to the hemodynamic changes of pregnancy. The initial presentation of these patients is frequently to the ED. The differential diagnosis and key characteristics of PPCM are discussed. ED management should focus on three elements: reduction in pre-load, reduction in afterload, and increase in inotropy. Key differences between the antepartum and postpartum states are highlighted.   © 2009 Elsevier Inc.

□ Keywords—cardiomyopathy; peripartum; heart failure; pregnancy; postpartum

INTRODUCTION

Postpartum or peripartum cardiomyopathy (PPCM) is a clinical entity whose etiology remains unclear. PPCM is associated with 1 of every 3000–4000 live births in the United States (US), thereby affecting 1000–1300 women annually (1). The prognosis of women who develop PPCM varies, with an alarmingly high mortality rate of 20–50% (2,3). In those who survive, 50% will have improvement of left ventricular (LV) function, and of these women, 10% to more than 50% will have complete recovery (3–6). Women with PPCM may present to the Emergency Department (ED) for initial evaluation and management of their acute symptomatology. A review of the emergency medicine literature noted few reports on the evaluation and management of this disease entity within the past two decades (7–10). Here, three cases of women presenting to the ED with PPCM are discussed, followed by the diagnosis and management of this potentially life-threatening disease.

CASE REPORTS

Case 1

A 23-year-old, previously healthy woman, gravida 3 para 2 (2 full-term live births, 1 medical abortion), 28 days postpartum, presented to the ED with the initial complaint of a headache. The headache was frontal, throbbing, and consistent with similar headaches in the past. On further review of systems, she reported intermittent episodes of dyspnea. The dyspnea began late in the third

trimester, and was thought to be within the spectrum of normal third trimester dyspnea. However, over the 2 days before ED evaluation, she developed increased orthopnea, new paroxysmal nocturnal dyspnea (PND), and worsening dyspnea on exertion. She denied any chest, left arm, neck, or jaw pain. She had not noted any peripheral edema or swelling. She did not have any hemoptysis.

The prenatal history was notable for normal blood pressures and no proteinuria. She had gone into labor at term, and had had an uncomplicated spontaneous vaginal delivery without tocolytics. Family and social history were non-contributory.

On ED presentation, the temperature was 36°C (96.4°F), pulse was 119 beats/min, blood pressure was 148/91 mm Hg, respiratory rate was 18 breaths/min, and oxygen saturation was 96% on room air. The physical examination was significant for bilateral diffuse rales and an S4 gallop. There was no jugular venous distention or peripheral or periorbital edema. The neurological examination was normal. A chest radiograph revealed cardiomegaly and bibasilar consolidations consistent with pulmonary edema (Figure 1). Table 1 lists pertinent laboratory studies, all of which were within normal limits, including cardiac enzymes, liver function tests, and uric acid. The electrocardiogram (ECG) demonstrated

Table 1. Relevant Laboratory Studies

Laboratory Test	Patient #1	Patient #2	Patient #3
Hematocrit (36–48%)	44.4	33.7	38.7
Platelets (K/μL)	371	291	203
Creatinine (0.7–1.3 mg/dL)	0.7	0.5	1.1
AST (9–30 U/L)	17	68	314
ALT (7–52 U/L)	12	47	188
Alk Phos (36–118 U/L)	110	174	88
Uric Acid (1.8–6.7)	5.4	*	*
CK (27–218 U/L)	100	213	147
CK-MB (0–5 ng/mL)	ND	1.7	4
Troponin-I (< 0.1 ng/mL)	0.04	0.16	< assay
BNP (< 100 pg/mL)	†	894	*
Urine protein (0–15 mg/dL)	19	NP	*

* Test not performed.
† Test not available to be performed at time of patient presentation. Normal values are included in parentheses.
ND = not done (laboratory does not run if total CK is low normal); NP = test not performed because urine dip was negative for protein.

sinus tachycardia and left atrial enlargement with lateral T wave inversions (Figure 2). In consultation with the cardiology service, the patient was admitted to the ED observation unit, placed on a cardiac monitor with supplemental oxygen, and given intravenous furosemide.

The following day, an echocardiogram revealed an ejection fraction (EF) of 40–45%. The patient was then admitted to the cardiology service and diuresed with increasing doses of furosemide, yet the urine output remained low. A right heart catheterization indicated she was intravascularly volume depleted. She was gently hydrated and started on digoxin and captopril to improve the cardiac output. Given her predisposition to clot formation in the setting of a low EF, she received enoxaparin, and was gradually shifted to warfarin. She was discharged from the hospital 1 week later on captopril, digoxin, warfarin, and metoprolol. On 6-month followup, the echocardiogram showed a recovered EF (now
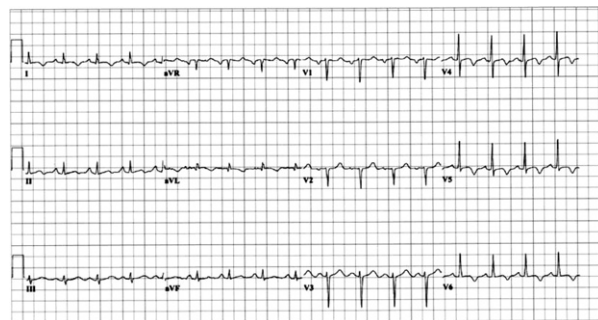

Figure 1. Chest X-ray study from Case 1 revealing cardiomegaly and pulmonary edema.

Figure 2. Electrocardiogram from Case 1 demonstrating sinus tachycardia, left atrial enlargement, and lateral T-wave inversions.

55%). One year later, she was maintained on lisinopril and metoprolol XL.

Case 2

A 36-year-old previously healthy woman, gravida 7, para 4 (4 full-term live births, 3 medical abortions), 5 days postpartum, presented to the ED with shortness of breath. On the day before ED presentation, the patient developed dyspnea that worsened with exertion. She noted orthopnea and peripheral edema in both lower extremities. She reported chest pain that increased with exertion and inspiration, but denied fever, chills, visual changes, right upper quadrant pain, and leg pain. She also complained of an intermittent headache over the last several days.

The prenatal history was notable for normal blood pressures and no proteinuria. She went into labor at term, and had a vacuum-assisted delivery without tocolytics. She was discharged on hospital day #2. The patient was a tobacco smoker until the beginning of this pregnancy. Family history and social history were non-contributory.

On ED presentation, the temperature was 36.5°C (98°F), pulse was 64 beats/min, blood pressure was 158/102 mm Hg, respiratory rate was 24 breaths/min, and oxygen saturation was 97% on room air. She was in mild respiratory distress. She had a jugular venous pressure of approximately 7 cm. The cardiac examination demonstrated a regular rate and rhythm, normal S1 and S2 with an S3 gallop. On auscultation of the lungs, she had rales at the left base and decreased breath sounds at the right base. The abdomen was soft, non-tender, and non-distended. She had 3+ pitting edema of bilateral lower extremities. She had no upper extremity or periorbital edema.

A chest radiograph demonstrated cardiomegaly, bilateral small pleural effusions, and pulmonary edema. The ECG demonstrated a sinus rhythm with no ST or T wave abnormalities (Figure 3). There was no ECG evidence of left ventricular hypertrophy. Pertinent laboratory values
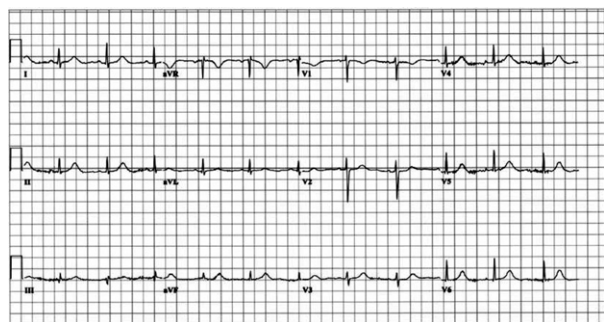

Figure 3. Electrocardiogram from Case 2 demonstrating normal sinus rhythm with no evidence of ischemia.
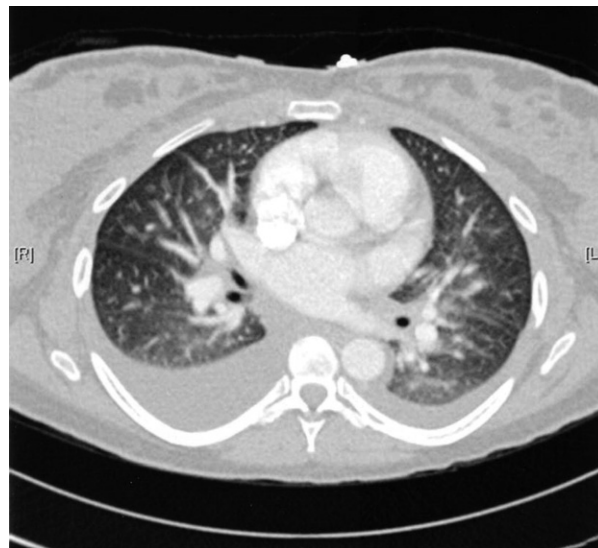

Figure 4. CT scan of the chest from Case 2 demonstrating bilateral pleural effusions and pulmonary edema.

are listed in Table 1, including a positive troponin of 0.16 ng/mL and a B-type natriuretic peptide of 894 pg/mL (negative considered < 100 pg/mL). A computed tomography (CT) scan of the chest revealed no evidence of pulmonary embolism (PE), but did confirm the presence of pulmonary edema and pleural effusions (Figure 4). The patient was given 40 mg of intravenous furosemide with eventual diuresis of 1220 cc and symptomatic improvement. She was started on intravenous heparin, aspirin, and low-dose beta-blocker therapy. The cardiology service was consulted. Echocardiography demonstrated an ejection fraction of 50%, mild global hypokinesis, with areas of focal severe hypokinesis of the left ventricle, and left atrial enlargement.

On hospital day #2, the patient was taken for cardiac catheterization, which demonstrated no evidence of coronary artery disease. During her hospital course, the patient was aggressively diuresed with symptomatic improvement. The troponin reached a peak value of 0.21 ng/mL and subsequently decreased. She was discharged on hospital day #3 on metoprolol, captopril, furosemide, and aspirin. She has not followed-up with the cardiology service, nor has she had a re-admission to our institution.

Case 3

A 32-year-old woman, gravida 1, para 0, presented to our ED status post-cardiac arrest at an outside hospital (OSH) ED during an emergent cesarean section. She presented to the OSH at 37 weeks gestation with dyspnea and a non-productive cough. The dyspnea had been

increasing for 5–7 days before arrival in the ED. She had also noted a marked increase in bilateral lower extremity edema. She denied headache, visual changes, right upper quadrant tenderness, or chest pain. The prenatal course had been uncomplicated without history of proteinuria or hypertension.

She presented to the OSH ED in moderate respiratory distress. The blood pressure was 122/91 mm Hg, pulse was 126 beats/min, respiratory rate was 20 breaths/min, and oxygen saturation was 97% on 3 L nasal cannula. Fetal heart rate was 150 beats/min. The physical examination was notable for an S4 gallop, bilateral rales in all lung fields, and pitting edema to the knees. A chest X-ray study revealed cardiomegaly and pulmonary edema. The ECG showed a sinus tachycardia with left atrial enlargement, an intraventricular conduction delay (QRS 156 ms), and large Q waves in V1 through V3 (not available).

Repeat fetal heart monitoring demonstrated bradycardia for which an emergent cesarean section was performed by the obstetrical service at the OSH. During the operation, the patient had a cardiac arrest, with wide complex pulseless electrical activity from which she was resuscitated with standard Advanced Cardiac Life Support protocols. In anticipation of the need for tertiary level care, she was transferred to our institution from the community hospital. The ED attending accepted the patient as arrangements were being made for an Intensive Care Unit bed because one was not immediately available in our hospital.

On arrival in our ED, the patient was intubated and unresponsive with a pulse rate of 130 beats/min and blood pressure of 95/67 mm Hg on maximal dopamine and neosynephrine. The blood pressure dropped shortly after arrival, for which norepinephrine was added. Dobutamine was considered, but not administered due to ongoing profound hypotension. Pertinent laboratory values from arrival in our ED are listed in Table 1. Approximately 45 min after arriving in our department, the patient went into pulseless ventricular tachycardia. Cardiopulmonary resuscitation was initiated, and despite standard advanced cardiac life support resuscitation measures, the patient expired. In retrospect, the insertion of a balloon pump may have augmented the cardiac output, although facilitating this intervention with such unstable hemodynamics may have been difficult. An autopsy revealed moderate cardiac hypertrophy with mild dilatation. There was no evidence grossly or histologically of myocardial infarction, vasculitis, myocarditis, or valvular disease. The coronary arteries had minimal atherosclerotic disease and there was no evidence of PE or amniotic fluid embolus. Examination of the lungs noted bilateral pulmonary edema and bilateral serous effusions. Hepatic and splenic passive congestion were also iden-

tified. The final pathologic diagnosis was PPCM and acute pulmonary edema.

DISCUSSION

As these three cases illustrate, the course of PPCM can range from readily treatable to acutely fatal. PPCM can be grouped in the family of dilatated cardiomyopathies. The relationship between pregnancy and dilatated cardiomyopathy was reported as early as 1849 by Ritchie, and subsequently, in 1870, by Virchow and Porak, who described evidence of myocardial degeneration at autopsy of patients who died in the peripartum period (1,11). In 1937, Gouley et al. described a case series of seven women who developed non-ischemic cardiomyopathy late in pregnancy, with persistent cardiac dysfunction postpartum. Four of the seven women died, and autopsy revealed areas of necrosis and fibrosis throughout the heart. All of the women had enlarged hearts (12). In 1971, Demakis formally defined PPCM as otherwise unexplained LV failure in the last month of pregnancy or during the first 5 months postpartum, without prior evidence of heart disease. Additionally, there must be no other identifiable cause of heart failure (13).

PPCM has been associated with multiparity, multigestational pregnancy, advanced maternal age, preeclampsia, pregnancy-induced hypertension, and black race (1,11,13–16). Whether race is an independent risk factor, given the known association between black race and hypertension, is not clear. Additionally, an association has been reported between prolonged tocolytic therapy and development of PPCM (2,17).

Etiology

The etiology of PPCM is unknown. Proposed etiologies include viral infection, pregnancy-related autoimmune response, prolonged tocolysis, and maladaptive responses to the hemodynamic stress of pregnancy. Of the listed etiologies, viral myocarditis is the most substantiated (1,11,18,19). It has been proposed that the relative immunosuppression that occurs during pregnancy may increase the risk of viral myocarditis. At the same time, some women with PPCM have increased titers of autoantibodies to cardiac proteins. Some authors argue that an autoimmune mechanism could also explain the myocarditis found on biopsy in many patients (19). One speculation is that fetal cells enter the maternal circulation and take up residence in the myocardium, triggering an antibody response (1). The mechanism behind the association with beta-agonist tocolytics is not clear from the currently available data, although speculation in-

cludes prolonged tachycardia, excessive adrenergic stimulation, and beta-receptor down-regulation (20).

A recent National Institutes of Health report identifies PPCM as a distinct entity, with an incidence higher than idiopathic cardiomyopathy. The report notes a high incidence of myocarditis found in women with PPCM, a finding that would not be expected if this entity resulted from the unmasking of pre-existing cardiac pathology during pregnancy. Also, the authors note that the definition of the disease, which requires that it occurs no sooner then the last month of pregnancy, effectively excludes underlying cardiac disease as a cause, because the hemodynamic stresses of pregnancy should induce earlier symptoms (1).

Clinical and Historical Findings

The time of presentation is variable, with some series reporting that the vast majority of patients with PPCM (82%) present within the first 3 postpartum months, whereas 7% are pregnant at the time of presentation (13). Other series, however, report a larger percentage presenting before or concomitant with the onset of labor (4,21). The diagnosis of PPCM can be difficult, because many of the symptoms (e.g., dyspnea, fatigue, and pedal edema) commonly occur during the last month of pregnancy. In our first patient, the diagnosis was facilitated by dyspnea that did not resolve upon delivery. In any case, symptoms of orthopnea, paroxysmal nocturnal dyspnea (PND), or chest pain should raise concern for cardiac disease. Demakis et al. report on a series of 27 patients in which 81% of patients present with PND and 74% with dyspnea on exertion, whereas cough and orthopnea are each present in 70% of patients (22). One patient presented with evidence of an embolic phenomenon (hemiplegia) (22). Finally, Dickfeld presents a case report of PPCM presenting as acute coronary syndrome, presumably secondary to an embolus from a LV thrombus found on echocardiography (23).

Physical examination should focus on signs of heart failure, such as hypoxia, S3 gallop, jugular venous distention, hepatomegaly, and rales. In Demakis' series, all patients presented with an S3 gallop (22). Our three patients also had abnormal heart sounds. The chest X-ray study will show cardiomegaly as well as evidence of pulmonary congestion, and may show pleural effusions (14). This was true of our three patients. The EKG presentation is quite variable. It may show anything from a normal EKG to prolongation of the PR or QRS intervals, evidence of LV hypertrophy and dysrhythmias (11,14).

Echocardiography will reveal a dilatated left atrium and ventricle with a decreased ejection fraction. LV dysfunction is crucial to the diagnosis because dilatation of the left ventricle can occur normally in pregnancy. The first two patients' echocardiograms demonstrated impaired systolic function.

Differential Diagnosis

Aside from common etiologies of dyspnea (asthma, anemia, pneumonia), there are diseases more unique to the peripartum period. Because pregnancy is a hypercoagulable state, immediately life-threatening diseases like PE must be excluded. The risk of venous thromboembolic disease is estimated to be 1 in 1000–1500 deliveries (24,25). An elevated D-dimer is common in pregnancy and into the early postpartum period, limiting its utility as a screening test for PE in this population (26).

Although less common, acute myocardial infarction in pregnancy or the early postpartum period occurs in approximately 1/10,000 pregnancies and is associated with an overall mortality of 21% (27). It is postulated that pregnancy-induced hypertension and preeclampsia, conditions whose pathophysiology is associated with endothelial dysfunction, may contribute to coronary vasoconstriction (28). Women who have received ergot derivatives (e.g., methylergonovine maleate) immediately after labor are also at risk for acute myocardial infarction (27). In acute coronary syndrome, 50% of patients will have normal or non-specific ECGs, making the diagnosis difficult (29). In these patients, cardiac markers are sometimes helpful. Our second patient's laboratory analysis yielded a positive troponin. CK, CK-MB, and myoglobin are released from uterine contractions as well as the placenta and may be elevated in normal labor (30,31). Troponins should not be elevated in normal pregnancy or labor, but may be elevated in preeclampsia and myocarditis (32).

The peripartum patient with severe preeclampsia can also present with dyspnea as a manifestation of this disease. Risk factors for preeclampsia include age < 20 years, advanced maternal age, primigravidity, previous preeclampsia, elevated blood pressure at the onset of pregnancy, multiple pregnancy, and pre-gestational diabetes. Hypertension, edema, and proteinuria are the main clinical findings. As the syndrome progresses and becomes more severe, patients may exhibit pulmonary edema. However, important characteristics of preeclampsia not typically present in PPCM include non-dependent edema, transaminitis, thrombocytopenia, headache, and scotomata.

The other main diagnostic consideration, which was the ultimate diagnosis presented in all three cases, is PPCM. The focus of the evaluation should be to exclude other causes of acute dyspnea, as definitive diagnosis

requires echocardiographic documentation of decreased LV systolic function. This was true in our first two patients, who each had echocardiography demonstrating a dilatated heart with a reduced EF.

ED Management and Subsequent Treatment

All patients should be placed on supplemental oxygen, cardiac monitor, continuous pulse oximetry, and non-invasive blood pressure monitoring. As with all ED patients, first priority must be given to airway and breathing.

Patients in severe respiratory distress require a more aggressive airway management strategy. It is reasonable to attempt non-invasive ventilation on some of these patients. For those patients requiring intubation, there are no contraindications to the standard rapid sequence intubation medications, even during pregnancy. The pregnant patient has significantly lower functional residual capacity and higher oxygen consumption than non-pregnant patients. Thus, the pregnant patient will more rapidly desaturate once apneic (3 min vs. 8 min in the normal 70-kg patient) (33). Furthermore, when bag-mask ventilation is required, the gravid woman's intra-abdominal pressure will make this process more difficult (33).

If the patient is still gravid, fetal heart monitoring should be obtained. The patient will also require a chest radiograph, 12-lead ECG, and the following laboratory studies: complete blood count, chemistry panel, urine analysis, liver function tests, and cardiac enzymes.

There are no clinical trials to support any particular treatment regimen for PPCM. Recommendations have been based upon the general approach to decompensated heart failure (1). The three primary goals are reduction in preload, reduction in afterload, and increase in inotropy. Whether or not the disease begins before delivery will affect the repertoire of drugs available to the emergency physician.

Preload reduction can be accomplished with all forms of nitrates. In the pregnant patient, the use of nitroprusside may be harmful to the fetus secondary to cyanide toxicity. This risk may be more theoretical than practical because in small case series, no cyanide toxicity has been observed after short-term use (34). Morphine sulfate may also be used for its venodilatatory benefit. Most of these patients will also require diuresis. Diuretics should be used with caution in the pregnant patients, as intravascular volume reduction may compromise placental blood flow. Loop diuretics are classified as class C during pregnancy, but decompensated heart failure will require intravenous therapy with these agents. Although human data are lacking, ethacrynic acid may be safer then other loop diuretics.

With impaired LV function in PPCM, acute afterload reduction is required. In the pregnant patient, this is best achieved with direct vasodilators like hydralazine. Nitrates may be considered in this category, keeping in mind the risk to the fetus of prolonged exposure to nitroprusside. Once the patient is postpartum, angiotensin-converting enzyme inhibitors become the mainstay of treatment (1).

Beta-blockers have been shown to improve survival in patients with dilatated cardiomyopathy (35). Beta-blockers are considered safe during pregnancy, and thus can be used in all patients with PPCM. However, they should not be initiated in the acute decompensated phase of heart failure.

In hypotensive patients, dobutamine, dopamine, digoxin, and phosphodiesterase inhibitors can be used to help stabilize blood pressure. In antepartum patients, all of these medications except dobutamine are listed as class C. Nonetheless, the use of these medications should not be withheld in pregnant patients if medically indicated (11).

Given the variability and rarity of this disease, cardiology can assist in the management of patients with PPCM. Virtually all require admission to the hospital. Obstetric consultants should be involved early. The decision to perform an emergent cesarean section will be based on fetal or maternal well-being, unlike preeclampsia, where delivery is a treatment of the condition. If the mother remains in the ED after the cesarean section, the emergency physician must anticipate rapid shifts in preload and afterload leading to precipitous exacerbation of heart failure. In the case of witnessed maternal death, perimortem cesarean section should be performed in the ED.

Prognosis

The prognosis of women with PPCM varies widely, although generally, women with PPCM have a better prognosis than patients with other forms of dilatated cardiomyopathy (1,21,36). Patients who ultimately survive PPCM, as compared to those who do not, tend to have a higher EF (22.8% vs. 10.6%, respectively) and smaller end-diastolic diameter (5.8 vs. 6.9 cm, respectively) when diagnosed (4,15,21). Also, if there is not significant improvement of cardiac function within the first 6 months after diagnosis and treatment, the prognosis is poor (22). Additional predictors of poor outcome in PPCM are multiparity, black race, and age > 30 years at onset (15).

Some researchers have assessed the outcomes of future pregnancies in patients with PPCM. Women who have return of normal LV function may undertake a

subsequent pregnancy with a low risk for recurrent heart failure (16,22). However, there is not universal agreement on this issue (2,6). Conversely, women whose heart size does not return to normal within 6–12 months of the initial episode tend to be at higher risk for worsening of systolic function during subsequent pregnancies (14,22).

CONCLUSION

We present three cases of women demonstrating the entire spectrum of disease related to PPCM diagnosed in the ED. PPCM is a cause of dilated cardiomyopathy, of which there will be approximately 1000 cases nationwide annually. These patients may present initially to the ED and their evaluation, differential diagnosis, management, and disposition are somewhat different from other patients with congestive heart failure. Even with effective treatment, PPCM may lead to rapid clinical decline and even death.

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