

Case Series: Spontaneous Relapse After Recovery From Peripartum Cardiomyopathy

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ABSTRACT:

BACKGROUND: Peripartum cardiomyopathy (PPCM) is a distinct type of heart failure with reduced ejection fraction (EF) with variable outcomes. Rates of recovery range from 29% to 72% and mortality rates range from 0% to 25%. In studies, outcomes are often determined at 6 to 12 months following diagnosis, and many of those who recover stop following with cardiology and are lost to follow-up.

CASE REPORT: Patient 1 was a 25-year-old G2P1 who was diagnosed with PPCM 5 days after childbirth with an EF of 25%. Initially, her EF improved and first normalized at 4.1 years after diagnosis. It subsequently dropped to 30% without clear heart failure symptoms or identifiable trigger and 1 year later normalized again to an EF of 60%. Patient 2 was a 36-year-old G6P3 who was diagnosed with PPCM 6 weeks after the birth of her third child when echocardiogram revealed an EF of 10%. Time to EF normalization was 3.0 years after diagnosis when her EF was measured at 55%. She remained without symptoms of heart failure for the first 8 years after diagnosis when she developed dyspnea on exertion and lower extremity edema; EF at that time declined to a nadir of 42.5% without apparent cause.

CONCLUSIONS: Women with PPCM can have an unpredictable course, and those who appear to have recovered may have unrecognized subclinical dysfunction that places them at risk for future injury or deterioration.

KEYWORDS: cardiomyopathies, echocardiography, peripartum, systolic heart failure

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Background

Peripartum cardiomyopathy (PPCM) is a distinct type of heart failure with reduced ejection fraction (HFrEF) defined as new-onset heart failure within the month prior to or within 6 months of delivery characterized by left ventricular systolic dysfunction and without alternative cause.¹ Incidence varies throughout the world but is estimated to be 1 in 1000 to 4000 live births in the United States and increasing.^{2,3} Reported outcomes are variable, with rates of recovery ranging from 29% to 72% and mortality rates ranging from 0% to 25%.^{4–9} Typically, a patient is said to be “recovered” if the left ventricular ejection fraction (LVEF) has reached 50% or greater. Many women who recover from PPCM stop following with cardiology and are lost to follow-up.

We report 2 cases of PPCM with apparent complete recovery who spontaneously deteriorated several years later.

Case 1

Patient 1 was a 25-year-old G2P1 with history of asthma, obesity, and prior miscarriage who had given birth to her first child 5 days previously when she presented with exertional dyspnea, orthopnea, nonproductive cough, bilateral lower extremity edema, and weight gain. Echocardiogram at presentation

revealed an EF of 25% with a globally hypokinetic left ventricle (LV), left ventricular internal diastolic diameter 62 mm, dilated mitral annulus with moderate mitral regurgitation, and enlarged right ventricle with elevated right ventricular systolic pressure of 56 mm Hg. She underwent diuresis with significant symptomatic improvement and discharged on furosemide 20 mg daily. She was followed closely with cardiology over the following 12 years. Initially, her EF improved and first normalized at 4.1 years after diagnosis. It subsequently dropped to 30% without clear heart failure symptoms or identifiable trigger and 1 year later normalized again to an EF of 60%. Review of her chart revealed several instances of medication noncompliance, and she required refills on scripts only about every other year. It is unclear which, if any, medications she was taking at the time of her acute decline in function. She was subsequently lost to follow-up.

Case 2

Patient 2 was a 36-year-old G6P3 with a history of hypothyroidism, asthma, and obesity who was diagnosed with PPCM after presenting with dyspnea on exertion, weight gain, and orthopnea 6 weeks after the birth of her third child. She had had 2 uncomplicated pregnancies followed by 3 first-trimester



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Table 1. Left ventricular ejection fraction and dimensions over time, patient 1.

DAYS AFTER DIAGNOSIS	EF	LVIDD	FRACTIONAL SHORTENING	HEART FAILURE SYMPTOMS PRESENT	MEDICATIONS				
					β-BLOCKER	ACE INHIBITOR	ALDOSTERONE ANTAGONIST	LOOP DIURETIC	THIAZIDE DIURETIC
0	25	62	27	Yes		x		x	
40					x	x		x	
68	20			No					
103	37.5	55	27	No	x	x		x	
Discontinued all cardiac medications for at least 1 year									
587	37.5	55	29	Yes	x	x		x	
849					x	x			
1487	55	55	27		x	x			
2492					x	x			x
2684	40	56	33	No	Not documented				
2993				No					
3048				No					
3308				No	x	x			x
4186	30	55		No	x	x	x		
4553		52		No	x	x	x		

Abbreviations: ACE, angiotensin-converting enzyme; EF, ejection fraction; LVIDD, left ventricular internal diastolic diameter.

spontaneous abortions. All 3 pregnancies that were carried to delivery were complicated by preeclampsia. Symptoms developed 2 weeks after delivery, and she was treated for asthma exacerbation and evaluated for pulmonary embolism prior to establishing a diagnosis.

Echocardiogram at admission revealed an EF of 10%. She underwent diuresis and was discharged on captopril, carvedilol, furosemide, and digoxin. Over the next 11 years, she consistently remained on an angiotensin-converting enzyme inhibitor and a β-blocker with no documented concerns regarding medication adherence. Serial echocardiograms were undertaken for monitoring purposes. Time to EF normalization was 3.0 years after diagnosis when her EF was measured at 55%. She remained without symptoms of heart failure for the first 8 years after diagnosis when she developed dyspnea on exertion and lower extremity edema. However, her clinical picture was complicated by progressive obesity and deconditioning. Ejection fraction (EF) at that time declined to a nadir of 42.5% without apparent trigger; there was no mention of medication noncompliance, viral illness, or concern for ischemia. At the time, she was taking lisinopril 20 mg twice daily and metoprolol succinate 100 mg daily. She subsequently moved out of the area and changed cardiologists.

A time line of the patients' LVEF and other LV dimensions are shown in Tables 1 and 2.

Discussion

The traditional teaching surrounding cardiac function in PPCM is that one-third of women improve, one-third deteriorate, and one-third stay the same. Spontaneous late deterioration in cardiac function, as presented here, is not widely recognized among clinicians. These cases illustrate an atypical clinical course that may influence the management of PPCM patients as well as the time line of future studies. Both patients reported here had EF <30% at diagnosis, enlarged LV dimensions that persisted over many years, and recovery occurred several years later.

Although uncommon, spontaneous late deterioration in cardiac function patients with in PPCM has been reported elsewhere. However, details of these cases are unavailable. Goland et al¹⁰ identified 3 such patients, 2 of whom had previously fully recovered (defined as EF ≥50% in this study), and 1 who had previously achieved a maximum EF of 45%. In a Turkish study of 42 women, 4 patients spontaneously deteriorated at 12, 24, 26, and 34 months after diagnosis.⁸ This phenomenon may be underappreciated, as many patients stop following with cardiology as soon as they achieve a normal EF.

It is unclear at what point in time, if ever, a patient with PPCM may be considered fully "recovered" and heart failure medications safely discontinued. Moreover, normalized systolic function while on a cardiac medication regimen may not

Table 2. Left ventricular ejection fraction and dimensions over time, patient 2.

DAYS AFTER DIAGNOSIS	EF	LVIDD	FRACTIONAL SHORTENING	HEART FAILURE SYMPTOMS PRESENT	MEDICATIONS				
					β-BLOCKER	ACE INHIBITOR	ALDOSTERONE ANTAGONIST	LOOP DIURETIC	DIGOXIN
0	10		0	Yes					
1	12.5	59	5	Yes	x	x		x	x
5	20		0	Yes	x	x		x	x
52	25	55	37	Yes	x	x		x	x
109	35	51	29	No	x	x		x	x
226	35	28	48	No	x	x		x	x
324	52.5	54	40	No	x	x		x	x
554	40	54	18	No	x	x			
1080	55	55	29	No	x	x			
1453				No	x	x			
1941				No	x	x			
2305				No	x	x			
2676				No	x	x			
3046				No	x	x			
3410				No	x	x			
3763	47.5	56		Yes	x	x			
3963				No	x	x			
4278	42.5	56		Yes	x	x			

Abbreviations: ACE, angiotensin-converting enzyme; EF, ejection fraction; LVIDD, left ventricular internal diastolic diameter.

represent true recovery. There are no consensus recommendations about medication duration. Some experts recommend slow weaning of cardiac medications with follow-up imaging to ensure that EF remains stable. Poor compliance to medication may have played a role in the relapse of the first case reported above.

It is possible that all patients have variable courses that have been incompletely captured by infrequent echocardiogram or discharge from cardiology practices. Some experts recommend annual echocardiography in all patients with histories of PPCM.¹¹ As the second case above demonstrates, LV dysfunction can be asymptomatic. When present, symptoms are nonspecific. This is an area that needs more research to help clinicians appropriately counsel women about long-term outcomes. Much of the literature about PPCM emphasizes counseling women about the risk of relapse during a subsequent pregnancy, but our cases highlight the need for counseling women that deterioration in cardiac function can occur, even after recovery, and even in the absence of a subsequent pregnancy.

In addition to uncertainty about timing, there is uncertainty about adequate detection of cardiac function. Although echocardiography provides a gross measurement of function, it has a

limited ability to detect subtle changes and some variability in measurements is expected.¹² Moreover, echocardiography is not sensitive enough to detect recovery on a cellular level, which may lag significantly behind⁶ and leaves a patient vulnerable to future insults. There may be benefit in routine use of cardiac magnetic resonance (CMR) imaging for prognostic value, especially in those who may have been deemed “recovered” or are considering discontinuation of medications or routine cardiac follow-up. The role for CMR has been suggested by small studies in PPCM and in larger studies for other types of nonischemic cardiomyopathy.^{13,14} Alternatively, in patients with apparent recovery, stress echocardiography could be performed to evaluate contractile reserve, which may provide a more accurate assessment of response to therapy and susceptibility to recurrent injury.

Ejection fraction at presentation has been most consistently shown to correlate with outcome,^{4,5,8,15} but no predictors of relapse have yet to be identified. Other echocardiographic parameters that have been studied include LV end diastolic diameter and fractional shortening. For example, Chapa et al⁷ found that patients with both a fractional shortening value less than 20% and left atrial end systolic diameter equal to or greater than 6 cm at the time of diagnosis were associated with

higher risk for persistent LV dysfunction. Neither of the patients presented here met both criteria to fall into a high-risk group. Fett et al¹⁵ likewise found a statistically significant difference in the LV fractional shortening at diagnosis between patients who recovered and those who did not.

Spontaneous deterioration after normalized EF suggests that women who are considered “recovered” may actually have undetected subclinical dysfunction or residual injury that makes them vulnerable to future insults. Even minor decreases in EF that may not be clinically significant still reveal dysfunction. This knowledge is important for long-term counseling of women with a history of PPCM, especially for women contemplating a subsequent pregnancy. Deterioration with subsequent pregnancy has been well documented elsewhere, and relapse in such cases is much higher if there has not been full myocardial recovery.^{7,16} Preconception counseling of patients with PPCM is an important component of care and to do so accurately requires identification of those women with residual subclinical injury.

Conclusions

Women with PPCM can have an unpredictable course, and those who appear to have recovered may have unrecognized subclinical dysfunction that places them at risk for future injury or deterioration. Although there are no data to guide whether or not women with normalized myocardial function would benefit from continuing on HFrEF medications, these patient cases highlight the need for ongoing long-term surveillance and serial monitoring. It is unknown whether women with a diagnosis of PPCM might benefit from life-long medical therapy, even after normalization of EF by echocardiogram. It is possible that the use of other imaging modalities, such as cardiac magnetic resonance imaging, could be informative in gauging complete myocardial recovery and, thus, risk of relapse.

Author Contributions

Conception or design of the work: MKM, MD; data collection: MKM; data analysis and interpretation: MKM, MD;

drafting the article: MKM; critical revision of the article: MD; final approval of the version to be published: MKM, MD.

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