

Peripartum cardiomyopathy and cardiac resynchronization therapy: Case reports and literature review



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Introduction

Peripartum cardiomyopathy (PPCM) is a rare condition diagnosed by the following criteria: (1) heart failure secondary to left ventricular systolic dysfunction with a left ventricular ejection fraction (LVEF) <45%; (2) occurrence toward the end of pregnancy or in the months following delivery (mostly in the month following delivery); and (3) no other identifiable cause of heart failure.¹ Patients with left bundle branch block (LBBB)-associated PPCM may meet criteria for cardiac resynchronization therapy (CRT) established for idiopathic nonischemic cardiomyopathy (NICM).

For the NEw-Onset LBBB-associated Idiopathic Nonischemic Cardiomyopathy II (NEOLITH II) study, medical records of 401 patients with LBBB-associated NICM who were implanted with CRT between January 1998 and April 2016 were reviewed, as previously described.² Three patients had been excluded for PPCM. On subsequent review, 2 patients met criteria for the diagnosis of PPCM while the third did not have complete information and was described as “possible” PPCM. The 2 patients that met diagnostic criteria for PPCM are presented. A literature review of PPCM and CRT was performed.

Case report

Case 1

In late April 2006, a 35-year-old self-identifying African American woman, G4 P2, with a medical history significant only for hypertension, treated with hydrochlorothiazide monotherapy, had a normal vaginal delivery of a healthy infant. Hydrochlorothiazide had been stopped

during her pregnancy and she did not have any issues with hypertension while pregnant. During the last weeks of pregnancy, she experienced dyspnea on exertion and bilateral lower extremity edema that continued and worsened in the postpartum period. Hydrochlorothiazide was restarted.

In early August 2006, she was evaluated by a heart failure specialist. An electrocardiogram (ECG) demonstrated sinus rhythm with LBBB at 156 ms. There were no prior ECGs available and the LBBB diagnosis was new. An echocardiogram estimated an LVEF of 20%–25% with a left ventricular end-diastolic diameter (LVEDD) of 6.5 cm. Hydrochlorothiazide was discontinued. Guideline-directed medical therapy (GDMT) for heart failure with reduced LVEF was started. This included carvedilol 3.125 mg twice daily, lisinopril 2.5 mg daily, and furosemide 20 mg daily.

In January 2010, she presented for implantation of a cardiac resynchronization therapy-defibrillator (CRT-D) owing to failure of GDMT to sufficiently improve her systolic function. The ECG on the morning of CRT-D implantation demonstrated sinus rhythm at 101 beats/min with a PR interval of 180 ms and an LBBB of 164 ms (Figure 1A). Her most recent echocardiogram, in February 2009, had estimated an LVEF of 20%–25% with an LVEDD of 7.0 cm (Figure 2A). She had successful implantation of a CRT-D (Model D224TRK; Medtronic, Minneapolis, MN) with the coronary sinus lead placed in a lateral branch.

In January 2013, she presented with acute onset of right-sided numbness and weakness. She was administered intravenous tissue plasminogen activator. Computed tomography of her head and neck did not reveal any acute findings. A transesophageal echocardiogram demonstrated an LVEF of 15%–20% with no intracardiac thrombus. The neurology service believed her symptoms to be related to a cardioembolic phenomenon owing to her reduced LVEF. She was discharged on warfarin and aspirin.

In April 2014, she was admitted for heart failure exacerbation and treated with intravenous furosemide. She was discharged the following day. In June 2016, she underwent CRT-D generator change (Model DTBA1D1; Medtronic), as she had reached the recommended replacement time.

KEYWORDS Cardiac resynchronization therapy; Left bundle branch block; Peripartum cardiomyopathy; Shocks; Ventricular fibrillation (Heart Rhythm Case Reports 2021;7:767–772)

Funding sources: The article publishing charge for open access was supported by UPMC Heart and Vascular Institute seed account FBS25 14919. Conflicts of interest: Dr Wang declared no conflicts of interest. Dr Jain receives research support from Abbott, Boston Scientific, and Medtronic. **Address reprint requests and correspondence:** Dr Norman C. Wang, UPMC Presbyterian, 200 Lothrop St, South Tower, 3rd Floor, Room E352.9, Pittsburgh, PA 15213. E-mail address: ncw18@pitt.edu.

KEY TEACHING POINTS

- There are few reports in the published literature describing cardiac resynchronization therapy-defibrillator (CRT-D) and cardiac resynchronization therapy-pacemaker (CRT-P) use in patients with peripartum cardiomyopathy (PPCM).
- Appropriate and successful shocks for ventricular fibrillation may occur in patients with left bundle branch block (LBBB)-associated PPCM and CRT-Ds, even years after implantation and when left ventricular ejection fraction (LVEF) has improved.
- CRT-Ds should be strongly considered in patients with LBBB-associated PPCM and LVEF $\leq 35\%$ despite at least 6 months of optimal guideline-directed medical therapy.
- Maintaining a CRT-D generator, as opposed to downgrading to a CRT-P generator, may be preferred at the time of pulse generator change for battery depletion, even in the presence of LVEF improvement and the absence of prior appropriate therapies.
- DF-1/IS-1 leads, as opposed to DF-4 leads, should be considered for downstream flexibility.

On February 12, 2020, she presented to the emergency department for shortness of breath that had been worsening over 2 weeks. A B-type natriuretic peptide level was 1051 pg/mL. Her chest radiograph demonstrated cardiomegaly, pulmonary vascular congestion, and obliteration of her left costophrenic angle. She was admitted for heart failure exacerbation. At 7:18 AM the next day, she received an appropriate shock for ventricular fibrillation (VF) while asleep (Figure 3A, Supplemental Figure S1). It was asymptomatic and it did not awaken her. Later that day, an echocardiogram demonstrated an LVEF of 35%–40% with an LVEDD of 6.1 cm. Carvedilol was maintained at 25 mg twice a day. No antiarrhythmic drugs were started, as it was her first-ever appropriate shock and occurred during decompensated heart failure. She was discharged on February 17. She had a subsequent visit to the emergency department on February 21 for sensations of shocks. These were determined to be phantoms, as CRT-D interrogation did not reveal any shocks.

In May 2021, she underwent her second CRT-D generator change (Model DTPB2D1; Medtronic) for battery depletion. Clinically, she continues to do well.

Case 2

In late March 1997, a 28-year-old woman of white race, G3 P2, presented at 26 weeks' gestational age with contractions.

She also complained of shortness of breath and orthopnea for 2 weeks. Her past medical history included Hodgkin lymphoma, for which she was successfully treated with mediastinal radiation and splenectomy around the age of 16 years. She previously smoked 1 pack per day of cigarettes. She had a spontaneous vaginal delivery of a healthy male infant weighing 748 grams with Apgar scores of 2 and 7. Her ECG was notable for sinus rhythm with an LBBB. An echocardiogram demonstrated an LVEF of 20% and severe mitral regurgitation. She was discharged on warfarin, enalapril, digoxin, and furosemide. She was later started on metoprolol. A cardiac catheterization in April 1997 demonstrated normal coronary arteries with an estimated LVEF of 30%–40% and global hypokinesis.

In April 2001, an ECG revealed sinus rhythm at 64 beats/min with a PR interval of 215 ms and an LBBB of 138 ms (Figure 1B). Four years later, in April 2005, an echocardiogram estimated an LVEF of 20%–25%, an LVEDD of 5.0 cm, and mild-to-moderate mitral regurgitation (Figure 2B).

In October 2007, she had an episode of syncope that lasted several minutes while she was seated and watching television. An echocardiogram demonstrated an LVEF of 25%–30%, an LVEDD of 6.3 cm, and moderate-to-severe mitral regurgitation. In February 2008, she was referred to a heart failure specialist. Metoprolol was changed to carvedilol. An echocardiogram demonstrated an LVEF of 30%–35%, an LVEDD of 5.8 cm, and moderate mitral regurgitation. Later, carvedilol was changed back to metoprolol owing to fatigue. In late July 2008, she was implanted with a CRT-D (Model C154DWK; Medtronic) with the coronary sinus lead placed in a posterolateral branch.

On November 24, 2011, at 6:57 AM, she had a first appropriate shock for VF (Figure 3B, Supplemental Figure S2). On August 16, 2012, she had a second appropriate shock for VF. The patient did not feel either shock. No adjustments were made in her medical regimen, as she did not have rigorous adherence. Improved compliance with GDMT was encouraged. In September 2012, an echocardiogram demonstrated LVEF 50%–55%, an LVEDD of 5.0 cm, and moderate mitral regurgitation. In October 2013, she underwent CRT-D generator change (Model DTBA1D1; Medtronic), as she had reached the recommended replacement time.

Her most recent echocardiogram, in September 2020, demonstrated an LVEF of 49%, an LVEDD of 4.6 cm, and moderate mitral regurgitation. In June 2021, she had a second CRT-D generator change (Model DTPB2D1; Medtronic), given battery depletion. Her device was transferred from the left to the right shoulder to facilitate radiation therapy for left-sided invasive ductal breast cancer.

Literature review

Details regarding the literature review are provided in the Supplemental Material. There were 14 cases of patients with PPCM and CRT reported in 7 articles (Table 1, Supplemental Figure S3).^{3–9} Four articles were case reports with detailed information on 5 patients.^{4,7–9}

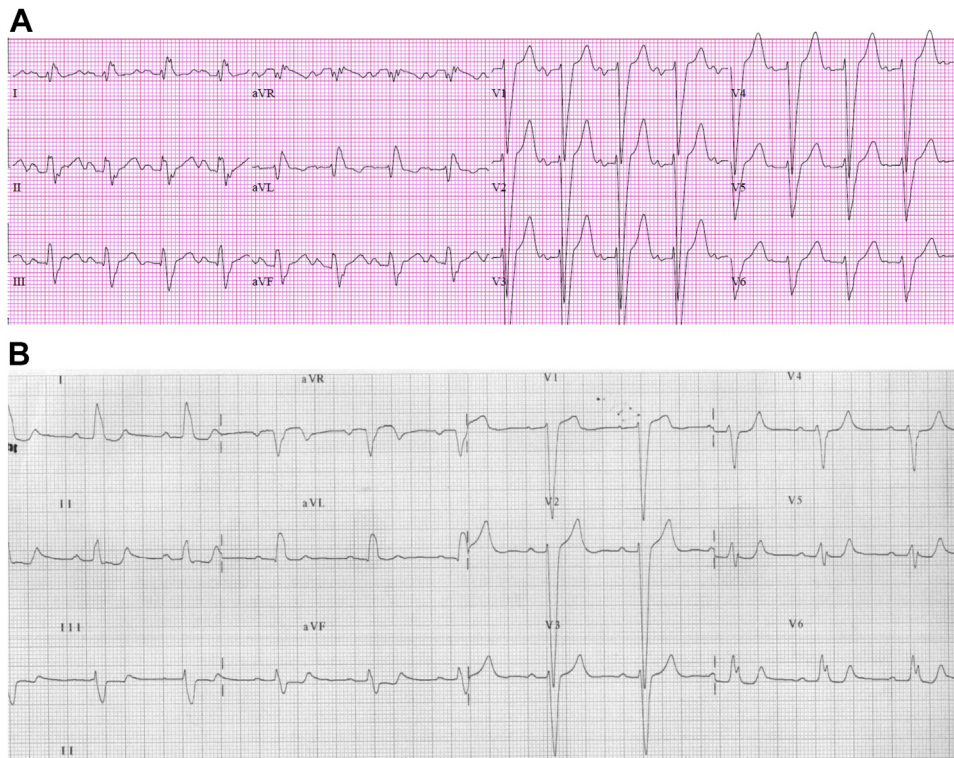


Figure 1 Twelve-lead electrocardiograms. **A:** Patient 1, on the morning of cardiac resynchronization therapy-defibrillator implantation. **B:** Patient 2, approximately 4 years after initial diagnosis with peripartum cardiomyopathy.

Patients who were implanted with CRT-Ds for nonspecific ventricular arrhythmias were considered to have a secondary prevention indication even if these events were not

described as meeting traditional definitions of “sustained” ventricular arrhythmias (ie, >30 seconds, requiring defibrillation for termination).

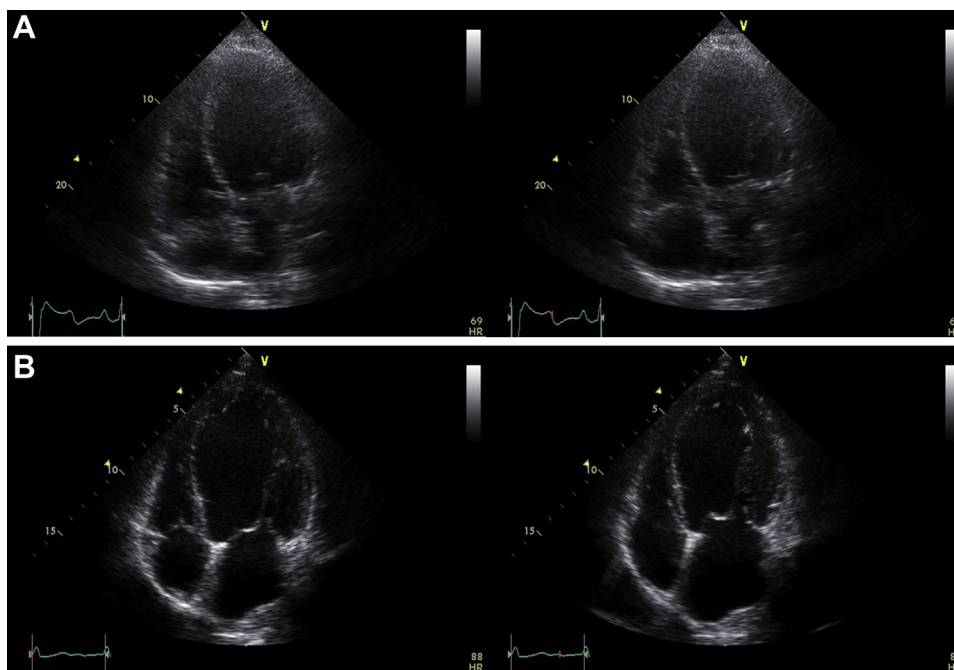
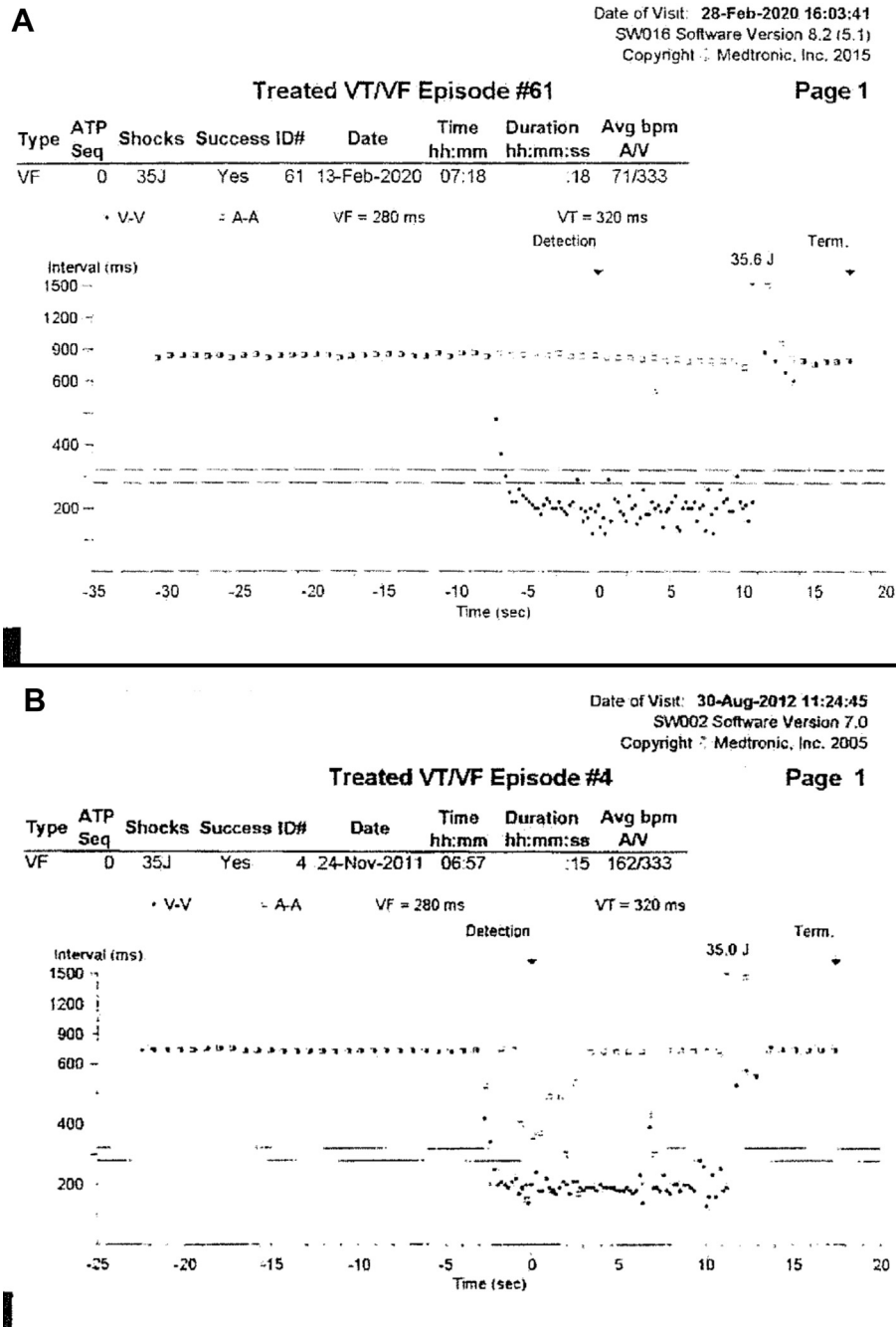


Figure 2 Transthoracic echocardiography apical 4-chamber images prior to cardiac resynchronization therapy-defibrillator implantation. **A:** Images for patient 1 at end-diastole (left) and end-systole (right), 34 months after initial diagnosis of peripartum cardiomyopathy (PPCM), estimated a left ventricular ejection fraction (LVEF) of 20%–25%. **B:** Images for patient 2 at end-diastole (left) and end-systole (right), 8 years after initial diagnosis of PPCM, estimated an LVEF of 20%–25%.



B

Date of Visit: 30-Aug-2012 11:24:45
 SW002 Software Version 7.0
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Treated VT/VF Episode #4 **Page 1**

• V-V - A-A VF = 280 ms
VT = 320 ms

Figure 3 Cardiac resynchronization therapy-defibrillator interrogations demonstrated appropriate and successful shocks for ventricular fibrillation. **A:** Patient 1 had a successful shock delivered at 35.6 joules. **B:** Patient 2 had a successful shock delivered at 35.0 joules.

Of the 14 patients, 13 of the CRT devices were identified as CRT-Ds. In 1 patient, it was not specified whether she received a CRT-D or a cardiac resynchronization therapy-pacemaker (CRT-P).⁷ She did not have a reported history of ventricular arrhythmias and was therefore listed as having a primary prevention indication. There were no appropriate shocks after CRT-D implantation in any of the 14 patients. One series reported 4 patients implanted with CRT-Ds after ventricular arrhythmias were noted on wearable cardioverter-defibrillators.⁶ One case described “salvage”

CRT-D with an epicardial left ventricular lead for end-stage heart failure in the early postpartum period.⁸

Discussion

The cases reported here are the first of appropriate and successful shocks for VF in PPCM patients implanted with CRT-Ds for primary prevention. Shocks occurred years after initial diagnosis and despite LVEF improvement. Notably, these were the only patients who met PPCM diagnostic

Table 1 Published cases of peripartum cardiomyopathy and cardiac resynchronization therapy

Article	First author	Cases	Year	Country	QRS _m	Indication	Final	CRT-D
							LVEF (%)	shocks
1	Goland ³	3	2009	USA	NR	Secondary prevention	NR	0
2	Mouquet ⁴	2	2012	France	LBBB	Primary prevention	45, 50	0
3	Pillariseti ⁵	2	2014	USA	NR	NR	NR	0
4	Duncker ⁶	4	2017	Germany	NR	Secondary prevention	NR	0
5	Farhan ⁷	1	2019	Iraq	LBBB	Primary prevention	60	0
6	Richard ⁸	1	2019	Canada	LBBB	"Salvage" therapy	50	0
7	Dhoon ⁹	1	2020	USA	IVCD	Secondary prevention	NR	0

CRT-D = cardiac resynchronization therapy-defibrillator; IVCD = nonspecific intraventricular conduction delay; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NR = not reported; QRS_m = QRS morphology; USA = United States of America.

criteria from a database of 401 patients with LBBB-associated NICM who received CRT.²

PPCM and LBBB-induced cardiomyopathy are distinct phenotypes. The pathophysiology of PPCM is unclear, although vascular-hormonal models have been proposed.¹ LBBB-induced cardiomyopathy typically presents in the seventh decade.¹⁰ Therefore, LBBB detected in the setting of PPCM is likely secondary to PPCM itself or another underlying condition. In the EURObservational Research Programme, which included 43 countries, LBBB was present in 37 of 398 (9.3%) PPCM subjects.¹¹ Mediastinal radiation for Hodgkin lymphoma is associated with a higher risk for heart failure and may have been a contributing factor in patient 2.¹²

For stable patients, short-term management after initial diagnosis is centered around GDMT for heart failure with reduced LVEF and thromboembolic prophylaxis.¹ Wearable cardioverter-defibrillators may be considered.⁶

There is little data to guide optimal timing to consider CRT implantation. A minimum of 6 months on optimal GDMT has been recommended.¹ Patients with new-onset LBBB-associated idiopathic NICM have poor response to GDMT.¹³ Little is known about LBBB-associated PPCM recovery on GDMT. In fact, LBBB resolution in the postpartum period has been described.¹⁴ The long delay between PPCM diagnosis and CRT-D implantation in our patients raises the question of whether other time point recommendations should be incorporated into future position statements.

Long-term risk for sudden death due to VF must be considered in patients with LBBB-associated PPCM. Prior reports of CRT-D use for primary prevention in PPCM patients have described LVEF improvement and absence of appropriate shocks.^{4,7,8} Heart failure management may be particularly important in preventing VF. Shocks for VF occurred during a hospitalization for heart failure decompensation for patient 1 and in the setting of GDMT noncompliance for patient 2.

Continuation of CRT-D at the time of generator change, as opposed to downgrade to CRT-P, should be given consideration even when substantial LVEF recovery is observed. Use of DF-1/IS-1 leads, rather than DF-4 leads, at the time of initial CRT-D implantation allows for more downstream flexibility

if downgrade to CRT-P is later desired.¹⁵ At present, a DF-4-to-IS-1 lead adaptor is not commercially available.

Conclusion

In LBBB-associated PPCM, VF with associated appropriate and successful shocks may occur years after initial diagnosis and despite LVEF improvement after CRT-D implantation for primary prevention.

Appendix Supplementary data

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.hrcr.2021.08.011>.

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