Peripartum Cardiomyopathy

87

Hayah Kassis, Maria Patarroyo Aponte, and Srinivas Murali

Case Presentation

A 28 year old African-American woman presented to her primary care physician 3 months postpartum with a chief complaint of progressive shortness of breath. She reported a progressive onset during the last month of gestation which was out of proportion compared to her previous pregnancy. At that time, the symptoms were attributed to normal physiologic changes of gravidity. However, her symptoms did not improve in the first few weeks after delivery and progressed to include orthopnea, nocturnal cough, and lower extremity swelling. A transthoracic echocardiogram revealed four chamber enlargement, severely reduced left ventricular systolic function with an ejection fraction of 5–10 %, right ventricular dysfunction, moderate mitral and tricuspid regurgitation, and an elevated pulmonary artery systolic pressure of 56 mmHg. Additionally, there was a left ventricular thrombus noted on the anteroseptal wall. A right heart catheterization revealed elevated filling pressures and low cardiac output consistent with acute decompensated heart failure with a reduced ejection fraction (HFrEF). She was given intravenous diuretics and intravenous heparin and dobutamine infusions were initiated.

On day 1 of her hospitalization, the patient developed acute mental status changes and right sided hemiplegia. She was emergently intubated for airway protection. CT imaging ruled out intracerebral hemorrhage, but CT angiography revealed a large area of left middle cerebral artery territory ischemia and distal left internal carotid artery occlusion. She underwent catheter embolectomy. Her medical course was further complicated by hemorrhagic conversion of cerebral ischemia and impending central brain herniation prompting emergent craniotomy. On day 4, she was extubated and the right sided paresis improved. Anticoagulation with intravenous heparin was continued throughout her hospitalization.

Inotropic therapy with dobutamine was also continued and she underwent aggressive intravenous diuresis. After her filling pressures and cardiac indices were optimized, the dobutamine infusion was weaned and discontinued. Therapy with an angiotensin converting enzyme inhibitor and a beta blocker was initiated. Given gestational hypertension, preeclampsia history, and an active 10 pack year history of tobacco use, the patient underwent a selective coronary angiogram which ruled out obstructive coronary artery disease. Cardiac MR was obtained for further

H. Kassis • M.P. Aponte
Cardiovascular Institute, Allegheny Health Network, Pittsburgh, PA, USA

S. Murali (✉)
Cardiovascular Institute, Allegheny Health Network, Pittsburgh, PA, USA

Cardiovascular Medicine, Allegheny General Hospital, Pittsburgh, PA, USA
e-mail: srinivas.murali@ahn.org

© Springer International Publishing Switzerland 2017
R.C. Hyzy (ed.), *Evidence-Based Critical Care*, DOI 10.1007/978-3-319-43341-7_87

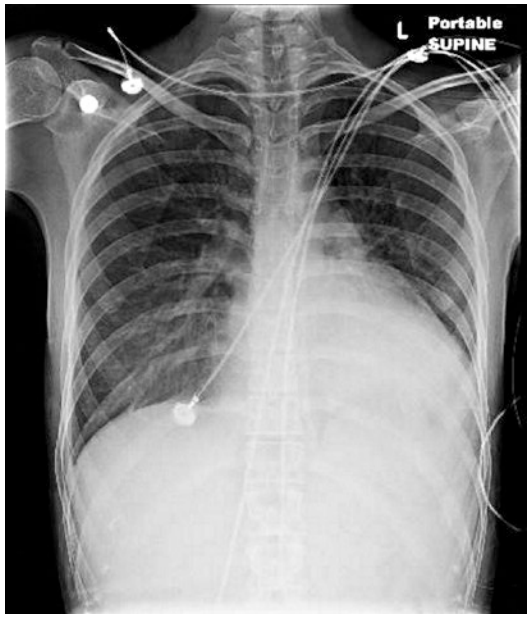

Fig. 87.1 Chest X-ray on admission showing cardiomegaly without significant pulmonary congestion

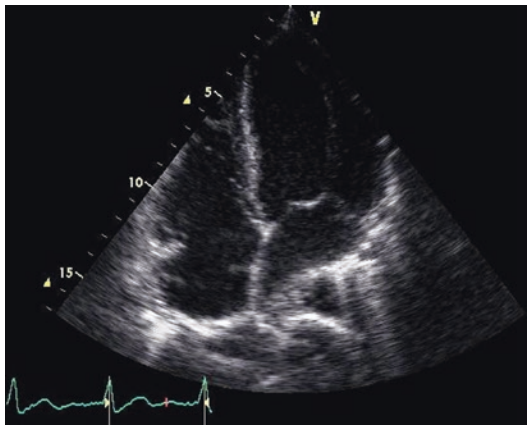

Fig. 87.2 Trans-thoracic echocardiogram 4-chamber view showing enlargement of both left and right ventricles consistent with a dilated cardiomyopathy

assessment of myocardial structure and function. This revealed dissipation of the left ventricular mural thrombus and viable myocardium. There was no late gadolinium enhancement indicative of infarction, inflammation or infiltration. The left ventricular ejection fraction had increased to 35 % (Figs. 87.1 and 87.2).

The patient was discharged to a skilled nursing facility. Guideline directed medical therapy was optimized as an outpatient as tolerated based on heart rate and blood pressure measurements. Transthoracic echocardiogram repeated 3 months post hospitalization revealed normal left ventricular dimensions, only mildly reduced left systolic function (LVEF 50 %), mildly reduced right ventricular systolic function, no significant valvular disease, and borderline elevated pulmonary pressures of 40 mmHg.

Question What is her diagnosis and her treatment regimen?

Answer Peripartum Cardiomyopathy

Peripartum cardiomyopathy (PPCM) is defined as (1) the new development of cardiomyopathy in a previously healthy woman in the final month of gestation or up to 5 months postpartum; (2) demonstration of left ventricular systolic dysfunction (ejection fraction < 45 %, and/or fractional shortening < 30 %, end-diastolic dimension > 2.7 cm/m^2) and; (3) the absence of an identifiable cause or any prior heart disease [1]. The overall incidence is relatively low, less than 0.1 % of pregnancies, and the majority of patients present in the first 4 months postpartum and are in the upper or lower end of the child bearing age. The etiology of PPCM may be multi-factorial and it remains a diagnosis of exclusion. A familial predisposition has been reported. Viral myocarditis has been proposed and supported by findings of myocyte edema, necrosis, fibrosis and lymphocytic infiltration on myocardial biopsy. A pathologic immune response to fetal cells in the maternal myocardium after delivery (micro-chimerism), exaggerated mal-adaptive hemodynamic response during pregnancy characterized by increased cardiac output, decreased afterload, left ventricular hypertrophy and dysfunction, excessive secretion of prolactin, increased pro-inflammatory cytokines, mal-nutrition and selenium deficiency, and prolonged use of tocolytic drugs have all been proposed as mechanisms contributing to the development of PPCM [2].

Symptoms of PPCM include progressive dyspnea, orthopnea, cough, unintentional weight

Table 87.1 Maternal risk factors and adverse events in PPCM

Maternal risk factors	Major adverse events	Long term effects of major adverse events
Advanced maternal age	Cardiopulmonary arrest	Death
African American race	Refractory heart failure	Permanent pacemaker
Non-Caucasian ethnicity	Atrial fibrillation or flutter	Implantable cardioverter defibrillator
Multiparity	Ventricular Arrhythmia	Temporary mechanical circulatory support
Multigravidity	Cerebrovascular accident	Left ventricular assist device
Twin pregnancy	Limb ischemia	Heart transplantation
Poor socioeconomic status		Neurologic deficits
Gestational Hypertension		
Pre-eclampsia		

gain or retention of weight post-partum, and peripheral edema. If mild, these same symptoms may be attributed to physiological changes of pregnancy resulting in a delay in the diagnosis. One series demonstrated a significant correlation between major adverse event rates and several weeks' delay in diagnosis; therefore heightened awareness is crucial [3]. Chest discomfort and palpitations are common and may be due to dysrhythmias. There is a higher incidence of systemic embolization in PPCM. Historical clues indicative of thromboembolic phenomena include transient loss of vision, aphasia, dysphagia, asymmetric lower extremity edema, digital cyanosis, abdominal pain and decreased urine output.

Risk factors associated with the development of PPCM include African American race, advanced maternal age, multiparity, multigravidity, tocolysis, gestational hypertension or preeclampsia [3, 4]. Major adverse events are more common in non-Caucasian women, initial left ventricular ejection fraction ≤25 % and delay in diagnosis, and are attributed to the development of left ventricular thrombus, ventricular arrhythmias, and refractory heart failure [3]. Complications and long term effects include cardiac arrest, thromboembolic events, limb ischemia, neurological deficits, and use of temporary or permanent mechanical circulatory support devices, death, and heart transplantation (Table 87.1). Patients who have suffered a neurological insult have residual long-term morbidity [3–5].

PPCM patients who recover their left ventricular systolic function have a good prognosis. Evidence suggests that 30–50 % of patients can fully recover left ventricular function on optimal medical therapy. There is a risk for recurrence of PPCM among these patients with subsequent pregnancies [6]. The precise risk is difficult to predict, and there are no guidelines on this issue. PPCM patients with persistent left ventricular dysfunction are clearly at risk for recurrence with subsequent pregnancies. They are also at high risk for premature births and spontaneous abortions. These patients should be strongly counseled against future pregnancies. Patients who fully recover their cardiac function have a 20 % risk of relapse with subsequent pregnancies. Patients who have a normal cardiac contractile reserve on an exercise echocardiogram may be at an even lower risk for relapse with subsequent pregnancy. These patients could undergo another pregnancy under careful monitoring with serial echocardiograms, and NT pro-BNP measurements without a relapse of PPCM. It is also not clear if women who fully recover their cardiac function can safely discontinue their heart failure therapy without the risk of decline in their LVEF. In the absence of guidelines, most physicians tend to continue medical therapy in recovered patients. Reported mortality worldwide in PPCM ranges between 5 and 32 % [7, 8]. Patients who present in severe heart failure or shock have a higher mortality. Mortality is also threefold higher in patients who have a fractional shortening of <20 % and a left ventricular end-diastolic dimension of >6 cm at initial presentation. Mortality rates have improved in recent years with early diagnosis and implementation of guideline based medical therapy.

Principles of Management

Diagnosis

Initially, the clinician must to perform a careful bedside clinical assessment looking for signs of hypoperfusion or signs of congestion that will help to identify the hemodynamic profile of the patient [9]. Signs of hypoperfusion include: cool extremities, altered mental status, decreased pulse pressure and renal insufficiency, while signs of congestion include: jugular venous distention, lower extremity edema, rales on auscultation. In most cases, the clinical evaluation will be enough to define the hemodynamic profile of the patient. However, sometimes invasive monitoring with pulmonary artery catheterization may be necessary to make the diagnosis and guide therapy, although there are no studies that compare invasive hemodynamic monitoring plus treatment versus standard of care alone in this population [10]. Once the hemodynamic profile of the patient has been established, the therapy will be guided to relieve congestion and/or improve cardiac output.

Initial assessment in PPCM should include transthoracic echocardiography to evaluate cardiac size and function, and investigate the presence of a left ventricular thrombus which is not uncommon [1]. Cardiac magnetic resonance (CMR) provides a more accurate measurement of both ventricular volumes, ejection fraction, and has a higher sensitivity for the detection of a left ventricular thrombus. Late gadolinium enhancement and T2 weighted imaging can provide important diagnostic information regarding inflammation or myocarditis and fibrosis. Depending on concomitant co-morbidities and maternal age, assessment for ischemia should be made with coronary angiography or stress testing.

Electrocardiogram findings include sinus tachycardia, left ventricular hypertrophy and ST-T wave repolarization abnormalities [11]. Patients may present with supraventricular or ventricular arrhythmias or cardiac arrest, as observed in patients with any form of cardiomyopathy. The electrocardiogram can help differentiate other causes of acute heart failure, including myocardial infarction or ischemia, cardiac tamponade, pulmonary embolus, mitral stenosis, or hemodynamically significant dysrhythmias.

Laboratory investigation includes measurement of NT-pro brain natriuretic peptide (NT-proBNP) or brain natriuretic peptide (BNP). The median serum levels of NT-proBNP observed in the first week postpartum after a normal pregnancy is typically about 100 ng/mL but can reach levels up to 700 ng/mL. This is attributed to increased venous return and preload after decompression of the IVC at childbirth [12–14]. However, in peripartum cardiomyopathy NT-proBNP levels are significantly higher with levels in the range of nearly 1000–3000 ng/mL [14].

Differential diagnoses should guide other diagnostic investigations including left heart catheterization and cardiac biomarkers if there is a suspicion of pregnancy-associated myocardial ischemia or infarction, ventilation-perfusion scanning or CT pulmonary angiogram and D-dimer if pulmonary embolus is suspected, and checking HIV assays as a potential cause for non-dilated cardiomyopathy [5]. Ultimately imaging modalities and laboratory data are complementary to a thorough physical examination and invasive hemodynamic assessment may be needed for directed therapeutic approach (Table 87.2).

Table 87.2 Diagnosis of PPCM

Clinical suspicion	Symptoms and signs	Diagnostic studies
Previously healthy woman with new onset heart failure in the last month of gestation or first 4 months post-partum Risk factors for PPCM Family History	Dyspnea at rest or exertion Fatigue Exercise intolerance Edema Chest pain Palpitations Cough Weight gain Weakness Jugular venous distension Tachycardia S3 or S4 gallop	Complete blood count and differential Complete chemistry BNP or NT-proBNP Cardiac troponin-T (if needed) Chest X-ray (if needed) EKG Transthoracic echocardiogram CMR Endomyocardial biopsy (if indicated)

Standard Medical Therapy for Heart Failure

The medical therapy for acute decompensated heart failure in peripartum cardiomyopathy is the same as to those patients with acute systolic heart failure from other etiologies (Table 87.3). In general, oxygen should be administered to patients with oxygen saturations lower than 90%. If the patient is in distress, they should be promptly intubated and placed on mechanical ventilation to reduce the work of breathing. For patients with pulmonary congestion, especially those who present with pulmonary edema, the use of intravenous diuretics will help with immediate relief of the symptoms. Loop diuretics should be used cautiously in the antepartum period as precipitous decreases in blood pressure from a large diuresis can compromise placental blood flow. Thiazide diuretics may be a useful alternative in these patients. Vasodilators like, nitroglycerine, nitropusside and nesiritide can be used in combination with diuretic therapy and will help to decrease preload and afterload in those patients who present with elevated blood pressures. However, these medications should be avoided in patients with systolic blood pressure less than 100 mmHg. Inotropes like dobutamine and

Table 87.3 Pharmacologic therapy in PPCM

Clinical presentation	Medication	Dose	During pregnancy	During lactation
Acute decompensated heart failure				
Fetal monitoring in antepartum women	Furosemide Bumetanide	20–600 mg daily 0.5–10 mg daily	Compatible Compatible	Compatible Compatible
	If SBP ≥100 mmHg			
	Nitroglycerine	0.1–5.0 mcg/kg/min	Compatible	Compatible
	Nitroprusside	0.2–5 mcg/kg/min	Unknown	Unknown
	Milrinone	0.125–0.75mcg/kg/min	Compatible	Unknown
	Dobutamine	2–10 mcg/kg/min	Compatible	Unknown
	If SBP ≤80 mmHg			
	Norepinephrine	0.01–3 mcg/kg/min	Compatible	Unknown
	Epinephrine	0.01–2 mcg/kg/min	Compatible	Unknown
	Dopamine	2.5–20 mcg/kg/min	Compatible	Unknown
Chronic heart failure				
Angiotensin-converting enzyme inhibitor (ACE-I)	Lisinopril Enalapril Captopril losartan	2.5–40 mg daily 2.5–10 mg BID 6.25–50 mg TID 25–150 mg daily	Discontinue Discontinue Discontinue Discontinue	Discontinue Discontinue Discontinue Discontinue
Angiotensin II receptor blockers (ARBs)	Valsartan	40–160 mg BID	Discontinue	Discontinue
Alternative to ACE-I/ARBs	Hydralazine Isosorbide dinitrite	25–100 mg TID 10–30 mg TID or QID	Compatible Compatible	Compatible Compatible
Beta blockers	Carvedilol Metoprolol succinate	3.125–50 mg BID 12.5–200 mg daily	Discontinue Compatible	Discontinue Compatible
Aldosterone antagonists	Epleronone Spironolactone	25 mg daily 12.5–25 mg daily	Unknown Compatible	Unknown Discontinue
Digoxin		0.125–0.25 mg daily	Compatible	Compatible
Targeted therapies				
	Bromocriptine IV immunoglobulin Pentoxifylline	2.5 mg BID for 2 weeks, then 2.5 mg daily for 4–6 weeks 1 g/kg daily for 2 days 400 mg TID	Compatible Compatible Compatible Unknown	Discontinue Unknown Discontinue Unknown

milrinone are indicated in patients who present with decreased perfusion or in cardiogenic shock in order to improve the cardiac output and maintain adequate organ perfusion. Other inotropic drugs like levosimendan, although used extensively in other countries, are not approved in the United States [5]. The use of vasopressors like norepinephrine, epinephrine and dopamine is associated with an increase in afterload and a subsequent decrease in the cardiac output and their use should be restricted to patients with marked hypotension despite adequate filling pressures and cardiac output.

Chronic Medical Therapy

Once hemodynamic stabilization is achieved, the patients should be started on chronic therapy for heart failure with reduced ejection fraction in accordance with the AHA/ACC guidelines targeting goal doses, including angiotensin converting enzyme inhibitors (ACE-I) or angiotensin II receptor blockers (ARBs), hydralazine-nitrate for those patients intolerant or with contraindications to the use of ACE-I or ARBs, and aldosterone antagonists. Beta blockers should be started once the patients are euvolemic and no longer requiring intravenous therapies [15]. It is important to remember that during pregnancy the use of ACE-I and ARBs is contraindicated due to fetal toxicity. Eplerenone, an aldosterone antagonist, is generally contraindicated during pregnancy due to lack of studies on fetal toxicity and beta blockers with B2 receptor antagonism should be avoided due to their anti-tocolytic action [5].

Anticoagulation

Acute and/or chronic anticoagulation is needed in patients with paroxysmal or persistent atrial arrhythmias, demonstrable left ventricular thrombus or clinical evidence for embolic event. The use of novel oral anti-coagulants is not recommended in PPCM.

Implantable Cardioverter Defibrillator

Patients with symptomatic, sustained ventricular tachycardia or survivors of cardiac arrest will need an implantable cardioverter defibrillator (ICD) prior to discharge from the hospital. Patients with LVEF <35 % should receive a wearable external defibrillator (Lifevest) at the time of discharge from the hospital. If the LVEF remains under 35 % despite 3 months of optimal guideline based medical therapy at goal doses, they should receive a prophylactic ICD for primary prevention against sudden cardiac death.

Mechanical Support

For those patients who remain unstable and in persistent heart failure despite optimal medical therapy or for those that are inotrope dependent, the use of temporary or durable mechanical circulatory support and heart transplantation evaluation should be considered. Mechanical support with a left ventricular assist device should be considered first in these patients due to the likelihood of full recovery of left ventricular function at 6 months in nearly half of the patients with PPCM [5]. The evidence for use of mechanical circulatory support in these patients is anecdotal and there are no studies comparing the different types of device therapies [10]. For some of these patients, IABP is adequate support as a temporary (up to 5–7 days) bridge to recovery or bridge to LVAD; other temporary support strategies like Centrimag extra-corporeal support system, Impella CP, and Tandemheart pVAD are also helpful for temporary support (2–4 weeks) as a bridge to recovery or LVAD; and finally durable LVADs can be use as a long term bridge to recovery or transplantation [16]. In an analysis from the INTERMACs registry, women with PPCM who received support with LVAD had a better survival than women with other forms of cardiomyopathy [17]. In the same analysis, just 48 % of the women with LVAD and a history of PPCM needed cardiac transplantation after 3 years on mechanical support. It should be noted that cardiac transplantation may carry a higher risk for allograft rejection in these patients.

Delivery

If the cardiomyopathy is diagnosed during gestation, there is no need for early delivery unless the

mother presents with hemodynamic instability [5]. Early delivery can often precipitate and worsen the signs and symptoms of heart failure. In that case, the primary objective is to achieve maternal cardiovascular benefit and vaginal delivery is preferred except in women requiring mechanical support or for obstetrical complications [5].

Postpartum Supportive Care

Women who are malnourished should undergo nutritional counseling and receive appropriate nutritional supplements. Many of the drugs used to treat HFrEF should be avoided if the patient is breast feeding. Perhaps, it is safest to avoid breast feeding in PPCM patients to avoid the risk of getting drugs ingested by the infant through breast milk. Breast feeding does not need to be interrupted for administration of gadolinium to obtain a cardiac MR for diagnostic purposes [5].

Evidence Contour

Several studies have suggested a role for inflammation in the pathogenesis of PPCM. There is an increase in inflammatory markers in PPCM patients, including tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), Interleukin-6 and interferon γ [18]. In addition, during pregnancy there is an increase in oxidative stress [19]. In animal models, this increase in oxidative stress leads to an overexpression of the signal transducer and activator of transcription 3 (Stat 3). Stat-3 increases cathepsin D, an enzyme that cleaves prolactin into its active form. This active form of prolactin has pro-apoptotic and anti-angiogenic properties that can lead to a destruction of cardiac myocytes, and cardiac dysfunction [20].

Immunotherapy and Anti-inflammatory Mediators

Based on these findings, some authors have suggested the use of targeted therapies such as intravenous immunoglobulin [21], pentoxifylline (that decreases action of TNF-α, CRP and fas/apoptosis antigen 1) [22] and bromocriptine (a dopamine agonist that decreases prolactin production) [23–26] based on promising results with improvement in mortality, LV function and functional capacity in small studies. Because of the lack of large, randomized clinical studies, these medications are not recommended as part of the routine therapy in PPCM. In addition, bromocriptine use has been associated with several reports of myocardial infarction and anticoagulation should be used routinely with this medication [27].

References

1. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, Ansari A, Baughman KL. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. JAMA. 2000;283:1183–8.
2. Robson SC, Hunter S, Boys RJ, Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol. 1989;256(4 Pt 2):H1060–5.
3. Goland S, Modi K, Bitar F, Janmohamed M, Mirocha JM, Czer LSC, Illum S, Hatamizadeh P, Elkayam U. Clinical profile and predictors of complications in peripartum cardiomyopathy. J Card Fail. 2009;15:645–50.
4. Ntobeko BAN, Bongani MM. Aetiology and risk factors of peripartum cardiomyopathy: a systematic review. Int J Cardiol. 2009;131:168–79.
5. Sliwa K, Hilfiker-Kleiner D, Petri MC, Mebazaa A, Pieske B, Buchmann E, Regitz-Zagrosek V, Schaufelberger M, Tavazzi L, van Veldhuisen DJ, Watkins H, Shah AJ, Seferovic PM, Elkayam U, Pankuweit S, Papp Z, Mouquet F, McMurray JJV. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail. 2010;12:767–78.
6. Elkayam U. Risk of subsequent pregnancies in women with a history of peripartum cardiomyopathy. J Am Coll Cardiol. 2014;64:1629–36.
7. Elkayam U, Akhter MW, Singh H, Khan S, Bitar F, Hameed A, Shotan A. Pregnancy-associated cardiomyopathy: clinical characteristics and comparison between early and late presentation. Circulation. 2005;111:2050–5.
8. Johnson-Coyle L, Jenson L, Sobey A. Peripartum cardiomyopathy. Review and Practice Guidelines. Am J Crit Care. 2012;21:89–98.
9. Stevenson LW. Tailored therapy to hemodynamic goals for advanced heart failure. Eur J Heart Fail. 1999;1:251–7.

10. Carlin AJ, Alfirevic Z, Gyte GM. Interventions for treating peripartum cardiomyopathy to improve outcomes for women and babies. Cochrane Database Syst Rev. 2010;(9):CD008589.
11. Diao M, Diop IB, Kane A, Camara S, Kane A, Sarr M, Ba SA, Diouf SM. Electrocardiographic recording of long duration (Holter) of 24 hours during idiopathic cardiomyopathy of the peripartum. Arch Mal Coeur Vaiss. 2004;97:25–30.
12. Terata M, Nakai K, Fukushima A, Itoh M, Kikuchi A, Sugiyama T. Detection of peripartum myocardial burden by vector-projected 187 channel electrocardiography and serum NT-proBNP. Int Heart J. 2013;54: 140–5.
13. Forester O, Hilfiker-Kleiner D, Ansari A, Sundstrom J, Libhaber E, Tshani W, Becker A, Yip A, Klein G, Sliwa K. Reversal of IFN-γ, oxLDL and prolactin serum levels correlate with clinical improvement in patients with peripartum cardiomyopathy. Eur J Heart Fail. 2008;10:861–8.
14. Yamada T, Koyama T, Furuta I, Takeda M, Nishida R, Yamada T, Morikawa M, Minakami H. Effects of caesarean section on serum levels of NT-proBNP. Clin Endocrinol. 2013;78:460–5.
15. Yancy CW, Jessup M, Bozkurt B, Butler J, Case DE, Drazner MH, Fonarow GC, Geraci S, Horwich T, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240–327.
16. Gevaert S, Van Belleghem Y, Bouchez S, Herck I, De Somer F, De Block Y, Tromp F, Vandecasteele E, Martens F, De Pauw M. Acute and critically ill peripartum cardiomyopathy and 'bridge to' therapeutic options; a single center experience with intra-aortic balloon pump, extra corporeal membrane oxygenation and continuous-flow left ventricular assist devices. Crit Care. 2011;15:R93.
17. Loyaga-Rendon RY, Pamboukian SV, Tallaj TA, Acharya D, Cantor R, Starling RC, Naftel D, Kirklin J. Outcomes of patients with peripartum cardiomyopathy who received mechanical circulatory support. Data from the Interagency Registry for Mechanically Assisted Circulatory Support. Circ Heart Fail. 2014;7:300–9.
18. Sliwa K, Forster O, Libhaber E, Fett JD, Sundstrom JB, Hilfiker-Kleiner D, Ansari AA. Peripartum cardiomyopathy: inflammatory markers as predictors of outcome in 100 prospectively studied patients. Eur Heart J. 2006;27:441–6.
19. Burton GJ. Jauniaux. Oxidative stress. Best Pract Res Clin Obstet Gynaecol. 2011;25:28.
20. Hilfiker-Kleiner D, Kaminski K, Podewski E, Bonda T, Schaefer A, Sliwa K, Forster O, Quint A, Landmesser U, Doerries C, Luchtefeld M, Poli V, Schneider MD, Balligand JL, Desjardins F, Ansari A, Struman I, Nguyen NQ, Zschemisch NH, Klein G, Heusch G, Schulz R, Hilfiker A, Drexler H. A cathepsine D-cleaved 16 kDa form of prolactin mediates postpartum cardiomyopathy. Cell. 2007;128:589–600.
21. Bozkurt B, Villaneuva FS, Holubkov R, Tokarczyk T, Alvarez RJ, MacGowan GA, Murali S, Roenblum WD, Feldman AM, McNamara DM. Intravenous immune globulin in the therapy of peripartum cardiomyopathy. J Am Coll Cardiol. 1999;34:177–80.
22. Sliwa K, Skudicky D, Candy G, Bergemann A, Hopley M, Sareli P. The addition of pentoxifylline to conventional therapy improves outcome in patients with peripartum cardiomyopathy. Eur J Heart Fail. 2002;4:305–9.
23. Sliwa K, Blauwet L, Tibazarwa K, Libhaber E, Smedema JP, Becker A, et al. Evaluation of bromocriptine in the treatment of acute severe peripartum cardiomyopathy: a proof-of-concept pilot study. Circulation. 2010;121(13):1465–73.
24. Forster O, Hilfiker-Kleiner D, Ansari AA, Sundstrom JB, Libhaber E, Tshani W, Becker A, Yip A, Klein G, Sliwa K. Reversal of IFN-gamma, oxLDL and prolactin serum levels correlate with clinical improvement in patients with peripartum cardiomyopathy. Eur J Heart Fail. 2008;10:861–8.
25. Hilfiker-Kleiner D, Meyer GP, Schieffer E, Goldmann B, Podewski E, Struman I, Fischer P, Drexler H. Recovery from postpartum cardiomyopathy in 2 patients by blocking prolactin release with bromocriptine. J Am Coll Cardiol. 2007;50:2354–5.
26. Habedank D, Kuhnle Y, Elgeti T, Dudenhausen JW, Haverkamp W, Dietz R. Recovery from peripartum cardiomyopathy after treatment with bromocriptine. Eur J Heart Fail. 2008;10:1149–51.
27. Hopp L, Haider B, Iffy L. Myocardial infarction postpartum in patients taking bromocriptine for the prevention of breast engorgement. Int J Cardiol. 1996;57:227–32.