Peripartum Cardiomyopathy: Two Cases and Discussion

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Abstract

Background: Peripartum cardiomyopathy is a rare myocardial disease of unknown origin diagnosed in young women of childbearing age. Diagnosis is often missed or delayed due to initial symptom similarity to those of late pregnancy or early postpartum period. Treatment is mainly symptomatic and based on guidelines directed at the management of heart failure. The most recent pathophysiological hypothesis of the disease includes oxidative stress-induced prolactin metabolite damage to the myocardium and discourages from breastfeeding. Maternal outcome depends on the timing of diagnosis, initial severity of left ventricular failure as well as subsequent course of the disease, and varies from full recovery to deterioration to cardiogenic shock, use of mechanical cardiac support devices, heart transplantation or death. Cases: Our both patients who had no prior history of cardiac pathology presented with inflammatory response, clinical signs of acute heart failure following delivery and left ventricular ejection fraction (LVEF) \leq 25\% on cardiac echoscopy. The first (Caucasian, aged 38, third pregnancy and labor, 34 week gestation) woman was diagnosed early (11 hours from symptom onset), whereas the second (Caucasian, aged 20, first pregnancy and labor, 39 week gestation) was initially treated in a small hospital and diagnosis was delayed (3 days from symptom onset). Both patients responded to conservative treatment well and did not require mechanical cardiac support. The issue of breastfeeding was managed differently as the first patient expressed strong desire to lactate, whereas the second patient could not tolerate it. Condition of the first patient improved rapidly (LVEF 38\% at discharge and 60\% at 1 month follow-up) whereas the second patient’s course of the disease was worse (LVEF 24\% at discharge and 45\% at 3 month follow-up).

Conclusion: Peripartum cardiomyopathy is associated with substantial morbidity and mortality. The role of prolactin inhibition in the management of peripartum cardiomyopathy remains
debated. Improved awareness of this rare but potentially fatal disease may lead to timely diagnosis, adequate treatment and contribute to a better outcome.

**Keywords**

Peripartum cardiomyopathy, breastfeeding, outcome.

**Background**

Peripartum cardiomyopathy (PPCM) is a pregnancy-related myocardial disease manifesting with left ventricular dysfunction and subsequent heart failure in the weeks antepartum or months postpartum. The incidence of PPCM is relatively low and varies from 0.025% to 0.3% of live births worldwide [1,2]. PPCM risk factors include increased maternal age (> 30 years), multiparity, multi-fetal pregnancy and hypertensive disorders [2–5]. Racial differences have also been reported with higher incidence of PPCM among African American women [6].

Four essential PPCM diagnostic criteria have been proposed as presented in table 1 below [2, 7].

(Table 1)

The exact pathogenesis of PPCM remains poorly understood. Several pathogenetic mechanisms (viral infection; autoimmune response; abnormal hemodynamic response; inflammation; oxidative stress; malnutrition; genetic predisposition; prolonged tocolysis) have been studied and are described in more detail elsewhere [1,2,8]. However, none of them is sufficiently evidence-based.

Unfortunately, the disease is associated with high parturient morbidity and mortality which ranges from 5% to 32% [2,5,6]. Death may occur due to severe heart failure or its
complications, such as thromboembolism and cardiac arrhythmias. Fetal outcome, however, is generally good.

PPCM treatment is mainly symptomatic and based on the guidelines used for the acute and chronic heart failure management. Discontinuation of therapy is recommended only once full recovery of the left ventricular function has occurred [4]. All patients who have survived PPCM are at risk of heart failure during subsequent pregnancy [7].

The aim of our paper is to share experience, address potential issues in diagnosis and management of peripartum cardiomyopathy, and to improve awareness of this rare condition.

Case presentation

Case 1

A 38-year-old multiparous woman, third pregnancy and labor, was admitted to a tertiary perinatology centre due to premature rupture of membranes and imminent preterm labor at 34 weeks of gestation. Her previous two pregnancies and births as well as the present pregnancy have been uneventful. The patient did not take any medications, stated to have no harmful habits such as smoking, alcohol or other substance abuse, and denied any history of heart disease or other health problems. Upon admission she complained of amniotic fluid deflux and irregular painful uterine contractions. Gynecological examination confirmed amniotic membrane rupture and flow of clear amniotic fluid. Tocolytic therapy with calcium channel blockers was started. Laboratory tests showed inflammatory response (leukocytosis–19.37x10⁹/L, C-reactive protein [CRP]–80.14 mg/L). Intrauterine infection was suspected and empirical antibacterial therapy was started. An uncomplicated cesarean section was performed under balanced general anesthesia following fetal lung maturation with corticosteroids. A healthy male neonate was born, Apgar scores 9–9.
After tracheal extubation the parturient suddenly became agitated and complained of shortness of breath; however this was attributed to residual action of general anesthetics. A short episode of desaturation (SpO₂ decreased to 88%) was managed with oxygen therapy and the patient was transferred to the Obstetrics and Gynecology intensive care unit (ICU) for further treatment and monitoring.

At approximately 11 hours postoperatively she started complaining of dyspnea at rest, chest discomfort and cough. Re-evaluation of the patient revealed significantly impaired overall condition, forced semi-sitting position, tachypnea 28 breaths per minute, significant bilateral basal crackles on lung auscultation, desaturation to 87% despite the presence of oxygen 8 L/min supplied through a facemask, tachycardia 124 bpm, arterial blood pressure – 114/82mmHg.

Hypoxemia and metabolic acidosis were observed in arterial blood gas analysis: pH–7.30, pO₂–53.8 mmHg, pCO₂–33.1 mmHg, BE– (–9) mmol/l, HCO₃–17.1 mmol/l. D-dimers were increased to 7.8 mg/L. Elevated troponin-I–5.07 mcg/L and N-terminal pro-B-type natriuretic peptide (NTproBNP)–6364 pg/L reflecting myocardial damage were observed. Electrocardiogram (ECG): nonspecific T-wave inversion in thoracic derivations. Chest X-ray: massive interstitial pulmonary edema. Urgent echocardiography: left atrial and ventricular dilation with left ventricular end-diastolic dimension (LVEDD) of 5.5 cm (LVEDD index–3.2 cm/m²), general hypokinesis with poor left ventricular ejection fraction (LVEF–25%) and first-degree mitral leakage, whereas right heart chambers were normal, no pulmonary hypertension. Pulmonary embolism was therefore considered unlikely. Diagnosis of acute coronary syndrome was not supported as the patient had no ischemic heart disease risk factors, did not complain of chest pain and troponin-I decreased to 0.74 mcg/L after 6 hours. Peripartum cardiomyopathy was diagnosed and the patient was transferred to the Cardiology ICU for the treatment of acute HF.
Acute HF management included oxygen therapy, intravenous nitrates and diuretics. After resolution of pulmonary edema, β-blockers and angiotensin converting enzyme (ACE) inhibitors were started. Low molecular weight heparins (LMWH) were given to prevent thromboembolism. Moderate lactation was allowed because the patient expressed a strong desire to breastfeed. During the following 5 days of treatment in the Cardiology ICU significant symptomatic improvement was achieved, pulmonary edema resolved and follow-up echocardiography showed substantial left ventricular function improvement (LVEF–38%). Two weeks later the patient was discharged for further ambulatory treatment (ACE inhibitors, β-blockers and diuretics).

Anticoagulation therapy was discontinued in presence of LVEF > 35%. The risk of heart failure during subsequent pregnancies was explained to the patient and contraception options were presented. Follow-up cardiac echoscopy at 1 month showed normal-sized cardiac chambers, fully recovered left ventricular function (LVEF–60%). All heart failure medications were gradually withdrawn.

**Case 2**

A 20-year-old woman, first pregnancy and labor, was admitted to a county hospital at 39 weeks of gestation in labor. The patient was closely monitored throughout the pregnancy and had no history of any diseases despite sinus tachycardia (110 beats/min) which manifested during the last month of pregnancy.

The patient underwent an uncomplicated emergency caesarean section due to dystocia under spinal anesthesia. A healthy female neonate was born, Apgar scores 9–9.

On the third postoperative day, the patient started complaining of general weakness, fever and dyspnea. Chest X-ray showed infiltrates in the middle and lower lobes of the right lung. Laboratory tests (CRP–102 g/L, leukocytes–13,7x10⁹/L) and clinical symptoms were
consistent with bacterial pneumonia, therefore empirical antibiotic therapy was prescribed.

However, over the next two days patient’s condition continuously worsened. She started complaining of progressive shortness of breath at rest and could only sleep in a semi-sitting position. Transthoracic echocardiography revealed left atrial and ventricular dilation, LVEDD of 6.1 cm (LVEDD index–3.5 cm/m²) and ejection fraction of 25%. The patient was transferred to a Cardiology ICU of a university hospital due to acute HF.

On examination at the ICU she was tachypneic (22 breaths per minute), tachycardic (134 beats/min), had arterial blood pressure of 126/92 mmHg and ankle edema. Auscultation revealed regular heart rate with S3 gallop, bilateral crackles at lung bases. Oxygen saturation was 89%.

Hypoxemia was observed in arterial blood gas analysis: pH 7.40, pO₂–58 mmHg, pCO₂–38 mmHg, BE–2 mmol/L, HCO₃–24 mmol/L. Follow-up chest X-ray confirmed lung infiltrates and showed cardiomegaly. Sinus tachycardia (130 beats/min) with poor R waves in V₂-3, without any ST segment changes was observed on ECG. Echocardiography confirmed previous findings with further progression of left ventricular dysfunction (LVEF−20%). PPCM diagnosis was confirmed.

HF was managed with oxygen therapy, diuretics, β-blockers and ACE inhibitors. LMWH were given for thromboembolism prophylaxis. Antibiotics were continued for intercurrent pneumonia. The patient could not tolerate breastfeeding due to her cardiologic condition.

Significant symptomatic improvement was achieved during a 4 day ICU treatment, and following subsequent two-week treatment in the Cardiology department the parturient was discharged. She was informed about the risk of subsequent pregnancies and was strictly discouraged from conception at least until full recovery. Echocardiographic findings prior to discharge, however, were disappointing: severe left ventricular dysfunction (LVEF−24%) and
dilation of left heart chambers remained. Ambulatory therapy was continued with diuretics, β-blockers and ACE inhibitors. Anticoagulation was continued. At 3 month follow-up her cardiologic status was defined as congestive heart failure, New York Heart Association (NYHA) functional class II. Fortunately, echocardiography showed decreased left ventricular and atrial dilation as well as significant left ventricular function improvement (LVEF–45%). Her heart failure treatment and follow-up are continued.

Summary of patient characteristics is presented in table 2 as follows.

(Table 2)

Discussion


We analyze our experience with two cases of PPCM in the context of contemporary literature, and address the issues associated with definition, diagnosis, management, pathogenetic treatment and prognosis of PPCM.

Definition of peripartum cardiomyopathy

Despite numerous publications dealing with PPCM, there is still lack of consensus regarding PPCM definition. American guidelines tend to follow the classical definition based on the 4 diagnostic criteria as outlined in table 1, whereas European position statement suggests a broader definition excluding strict onset time frame (i.e., from 1 month before delivery up to 5 months postpartum) and echocardiographic cut-offs: "PPCM is an idiopathic cardiomyopathy
[...] presenting towards the end of pregnancy or in the months following delivery. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%\(^\circ\). The rationale for this modification was to prevent underdiagnosis as some patients with PPCM may be slightly out of predefined quantitative ranges [1,2]. According to the literature data, 93% of PPCM cases occur postpartum, of which 75% occur within the first month after delivery, and only 7% during the last trimester of pregnancy [9].

Clinical and echocardiographic signs of our both patients were fully consistent with either of definitions (table 2).

**Diagnosis**

It is well defined that early diagnosis of peripartum cardiomyopathy has favorable influence on patient outcome [2,6]. Unfortunately, diagnosis is often missed or delayed due to initial symptom similarity to those of late pregnancy or early postpartum period (such as general weakness, tachycardia, shortness of breath and ankle swelling) as well as due to inadequate awareness of such a pathology.

We believe that the initial manifestation of heart failure in our first case could have been attributed to residual action of anesthetics and was only noted 11 hours later once patient’s condition significantly deteriorated. Intraoperative fluid overload could have contributed to clinical manifestation of incipient heart failure. However, in presence of high availability of multidisciplinary specialists and diagnostic equipment, the diagnosis of PPCM was established relatively early.

Our second case reflects diagnostic challenges in a setting of poor awareness of this rare disease. Initial signs of respiratory failure were considered as pneumonia due to elevated inflammatory markers and infiltrates on chest X-ray. Heart failure was suspected and cardiac
ultrasound was only performed on the third day following symptom onset in presence of progressive respiratory failure and ineffective antibiotic therapy. The diagnosis of intercurrent pneumonia in our case cannot be rejected as unilateral infiltration was stated by the radiologists of two different institutions. However, the fact that the patient's condition markedly improved with institution of adequate HF treatment makes the diagnosis of pneumonia questionable. Other authors also underline the potential of PPCM to be initially misinterpreted as pneumonia [10]. It is of note that in our second case chest X-ray besides infiltration showed heart enlargement which could also aid in diagnosis.

Our differential diagnosis included pulmonary embolism (PE) bearing in mind acute onset of respiratory symptoms, hypercoagulable state of pregnancy and elevated D-dimer levels. Cardiac echoscopy was very useful in both diagnosis of PPCM and differentiation from PE as it showed poor ejection fraction and left heart dilation without pulmonary hypertension. Other tests such as ECG and troponin-I changes are considered to be non-specific in this disease [4]. Inflammatory markers including CRP are reported to be elevated in PPCM [11].

Different course of the disease in our two cases underlines the importance of time to correct diagnosis and initiation of treatment. Our both parturients had several factors of poor prognosis (left heart dilation, LVEF ≤ 25%, NYHA class IV) but the first woman who had timely diagnosis and adequate treatment fully recovered, whereas the course of our second patient’s disease was significantly worse.

**Heart failure management**

Management of PPCM is generally the same as of any heart failure and usually includes ACE inhibitors or angiotensin-II receptor blockers (ARB), β-blockers, nitrates, inotropes, diuretics and anticoagulants. The therapy is used to stabilize cardiac function, improve blood
flow to vital organs, and to reduce fluid overload and the risk of tromboembolic events. Our treatment was based on the latest acute and chronic heart failure treatment guidelines by the European Society of Cardiologists [12]. It is of note that ACEIs, ARBs and warfarin are contraindicated in pregnancy but can be safely used postpartum. Attention was paid to the safety of medications to breastfeeding mothers [13].

Because of high risk of thromboembolic complications due to persistent hypercoagulable state for 6–8 weeks postpartum and blood congestion caused by severe left ventricular failure, anticoagulation is essential [14]. Warfarin and heparin are not secreted into human milk, therefore they do not limit breastfeeding. Anticoagulation in our patients (LMWH, warfarin) was continued as long as LVEF improved to > 35% [4]. Thromboembolic complications were not observed. However, some authors encourage anticoagulation until full recovery (i.e. LVEF ≥ 50%) [2,15].

There are no evidence-based recommendations on when should pharmacologic treatment be stopped once the cardiac function is fully restored. However, there are suggestions towards continuation of ACE inhibitors and β-blockers for at least 1 year after normalization of EF [3]. Pharmacotherapy should be discontinued gradually under close echocardiographic follow-up.

Despite maximum conservative treatment based on latest guidelines, some patients deteriorate to cardiogenic shock. Successful use of mechanical cardiac support (i.e. intra-aortic balloon pumps, extracorporeal membrane oxygenation, LV assist devices) has been reported in critical cases as a bridge to left ventricular recovery or cardiac transplantation [16,17].

**Breastfeeding, prolactin and its inhibition**

The issue of breastfeeding in our institution has caused a lot of discussions. The debate was unavoidable as the positions stated in American and European PPCM guidelines regarding
whether women diagnosed with peripartum cardiomyopathy should be allowed to breastfeed are quite different. The role of prolactin in oxidative stress to the myocardium and efficiency of its inhibition using bromocriptine is under active research. According to a pathophysiological hypothesis, increased oxidative stress in the heart of a parturient enhances conversion (mediated by cathepsin-D) of prolactin into a 16-kDa subunit which may cause myocardial microvascular damage due to its angiostatic, proapoptotic, vasoconstictive and endothelial cell inhibiting actions. Several reports highlighting LVEF improvement and a better outcome in PPCM patients additionally treated with bromocriptine have been published [18,19].

European position statement on peripartum cardiomyopathy [1] discourages breastfeeding in patients with suspected PPCM based on possible negative effects of prolactin. However, authors acknowledge the fact that this practice is not fully evidence-based. American peripartum cardiomyopathy practice guidelines [2] do not include such recommendation. Moreover, results of a recent study by Safirsten et al. showed that most patients with PPCM could breastfeed without adverse effects and they demonstrated more rapid LV functional recovery [20].

In our two cases the issue of breastfeeding was addressed differently. The first patient despite being informed of possible prolactin-associated risks, expressed a strong desire to breastfeed and moderate lactation was allowed in favor of her baby. She demonstrated rapid recovery without any complications. The second patient could not tolerate breastfeeding due to her cardiologic condition. Bromocriptine was not prescribed. The better outcome of our patient who breastfed could support the more liberal approach to breastfeeding but we cannot overlook the fact that she had more timely diagnosis and treatment of PPCM. Therefore, large and well-organized studies are still necessary to resolve this issue.
Prognosis and subsequent pregnancies

Prognosis depends on left ventricular recovery. Approximately one half of patients diagnosed with PPCM fully recover in 3 to 6 months following diagnosis [4,21]. Delayed recovery, however, occurs in some patients [22]. There are several factors associated with poor prognosis including delayed diagnosis, coexisting medical illnesses, LVEF < 30% and LVEDD > 55 mm [23,24]. Our both patients had poor left ventricular function (EF–25%) and LVEDD ≥ 55 mm at the time of diagnosis. In the second patient this was coupled with delayed diagnosis and intercurrent pneumonia. Influence of these factors is reflected by a significantly worse course of her disease.

All patients are at risk of cardiac functional deterioration during subsequent pregnancy. The risk of PPCM recurrence depends on left ventricular recovery. Women with persistent left ventricular dysfunction have substantially higher risk of heart failure, complications and death. Stress echocardiogram may assist in predicting cardiac behavior in presence of stress caused by a new pregnancy. Nevertheless, careful multidisciplinary follow-up is necessary for every patient who decides to become pregnant [2,4,16]. We informed our patients of the risks, discouraged them from pregnancy at least until full recovery, presented possible contraception options and encouraged on consulting a cardiologist if conception became desirable.

Conclusion

Peripartum cardiomyopathy is a rare disease of women of childbearing age associated with substantial morbidity and mortality. The role of prolactin inhibition in the management of peripartum cardiomyopathy remains debated. Treatment of PPCM is generally directed at heart failure management based on contemporary guidelines. Improved awareness of this rare but
potentially fatal disease may lead to timely diagnosis, adequate treatment and contribute to a better outcome.

Consent

Written informed consent was obtained from our patients for publication of this Case report.

Competing interests

Authors state to have no conflicts of interests.

Authors’ contributions

KR significantly contributed to the idea, design of the paper, was involved in data interpretation as well as writing and revising the manuscript.

GB contributed to data interpretation and critically revised the manuscript.

MR contributed to the design of the paper, data interpretation and writing as well as submission of the manuscript.

LS contributed to data acquisition and writing the manuscript.

AM markedly contributed to the idea of the paper and critically revised the manuscript.

All authors have read and approved the final draft of the manuscript.

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Authors have no financial relations to disclose.
References


### Table 1. Essential PPCM diagnostic criteria

<table>
<thead>
<tr>
<th>Classic</th>
<th>Additional</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Development of cardiac failure in the last month of pregnancy or within 5 months postpartum</td>
<td>4. Strict echocardiographic indication of left ventricular dysfunction:</td>
</tr>
<tr>
<td></td>
<td>a) Ejection fraction &lt; 45%</td>
</tr>
<tr>
<td></td>
<td>and/or</td>
</tr>
<tr>
<td></td>
<td>b) Fractional shortening &lt; 30%</td>
</tr>
<tr>
<td></td>
<td>c) End-diastolic dimension &gt; 2.7 cm/m²</td>
</tr>
<tr>
<td>2. No identifiable cause for the cardiac failure</td>
<td></td>
</tr>
<tr>
<td>3. No recognizable heart disease before the last month of pregnancy</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Summary of patient characteristics

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Pregnancy</th>
<th>History of heart disease</th>
<th>Tocolytic therapy</th>
<th>Delivery</th>
<th>Anesthesia</th>
<th>Initial presentation of PPCM (days postpartum)</th>
<th>Diagnosis of PPCM (days postpartum)</th>
<th>Breastfeeding</th>
<th>LVEF at diagnosis (cm/m²)</th>
<th>LVEDD (cm)</th>
<th>General hypokinesis</th>
<th>LVEF at discharge</th>
<th>LVEF at 1 month follow-up</th>
<th>LVEF at 3 month follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>CS</td>
<td>GA</td>
<td>1</td>
<td>1</td>
<td>Yes</td>
<td>25%</td>
<td>5.5</td>
<td>3.2</td>
<td>Yes</td>
<td>38%</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>CS</td>
<td>SA</td>
<td>3</td>
<td>6</td>
<td>No</td>
<td>20%</td>
<td>6.1</td>
<td>3.5</td>
<td>Yes</td>
<td>24%</td>
<td>32%</td>
</tr>
</tbody>
</table>

SC, cesarean section; GA, general anesthesia; SA, spinal anesthesia; N/A, data not available.