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CASE REPORT

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# An unexpected battle with peripartum cardiomyopathy: a case report

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**ABSTRACT**

Peripartum cardiomyopathy (PPCM) is a rare cardiomyopathy marked by systolic dysfunction that presents in late pregnancy or the early postpartum period with an ejection fraction (EF) of less than 45%. Diagnosing PPCM often presents a diagnostic dilemma due to its nonspecific clinical presentation, which usually resembles physiological changes of pregnancy or peripartum pulmonary embolism. Echocardiography is frequently used as a diagnostic modality of choice with management following the GDMT guidelines and delivery. This case presents a 23-year-old patient with a delayed diagnosis of PPCM, followed by a discussion of goal-directed medical therapy (GDMT) and the benefits of early diagnosis and treatment. Common pitfalls in diagnosing PPCM are introduced to encourage clinicians to consider PPCM during late pregnancy. Currently, a new clinical trial is underway investigating the efficacy of dopamine agonists in conjunction with GDMT for treatment of peripartum cardiomyopathy.

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## 1. Background

Peripartum cardiomyopathy (PPCM) is a rare cardiomyopathy marked by systolic dysfunction and presents in late pregnancy or the early postpartum period with an ejection fraction (EF) of less than 45% [1,2]. The incidence of PPCM varies globally, with the highest rates observed in Nigeria (one in 100 live births). In contrast, in the United States, its incidence ranges from one in 900 to one in 4,000 live births, significantly higher among the African American population [3,4]. It is generally associated with advanced maternal age, pre-eclampsia, and multiple gestations, along with the growing prevalence of cardiovascular risk factors such as hypertension, diabetes, and obesity among women of reproductive age [5,6]. PPCM is caused by vascular damage from antivascular or hormonal effects during late pregnancy, and the early postpartum period triggers cardiomyopathy in women with a genetic predisposition [1]. Various sarcomere genes, including the *TTN* gene encoding protein titin and a truncated 16-kDa form of prolactin, have been implicated in the pathogenesis of PPCM [7,8]. The Truncated 16-kDa prolactin has anti-angiogenic and pro-apoptotic effects that damage cardiac and vascular tissue. It also upregulates microRNA-146a (miR-146a), contributing to systolic dysfunction, capillary dropout, and cardiac fibrosis [9,10]. In addition, sFlt-1, an anti-angiogenic protein elevated in pre-eclampsia, may also play a role in the pathogenesis of PPCM [11]. Other potential contributors include increased inflammation, viral infections during pregnancy, autoimmune responses, and genetic susceptibility, though their exact roles in PPCM remain unclear [12] (Figure 1). It is characterized by orthopnea, dyspnea, persistent cough, and pedal edema in the early stages of the disease, with abdominal discomfort, heart palpitations, and postural hypotension during the later stages of the disease [13].

Management of PPCM involves Guideline-Directed Medical Therapy (GDMT) for systolic congestive heart failure (CHF), with multiple studies showing symptomatic improvement in EF after starting GDMT [12,14]. However, if patients remain symptomatic despite six months on GDMT, placement of an Implantable Cardioverter Defibrillator (ICD) or placement of a left ventricular assist device (LVAD) and heart transplant is generally recommended [1].

## 2. Objective

The objectives of this case are to understand the clinical presentation of peripartum cardiomyopathy, discuss differential diagnoses of acute shortness of breath in pregnancy, and describe the treatment options for peripartum cardiomyopathy.

## 3. Case report

A 23-year-old morbidly obese G1P0 female presented to an emergency department at 33 4/7 weeks of gestation with an abrupt onset of shortness of breath, chest pain, and hemoptysis. Her pregnancy was complicated by marginal cord insertion, morbid obesity with a calculated BMI of 48.76 (normal 18.5–24.9), and preeclampsia without severe features. She had previously taken labetalol 200 mg twice daily for preeclampsia but was reportedly nonadherent to the regimen. She had been unable to sleep for several nights due to feeling short of breath while lying down. She had also recently felt increasingly short of breath with ambulation. In addition, she reported new-onset chest pain with breathing. Vital signs on arrival included blood pressures in the 140s/90-110s (normal 100–120/60–80 mmHg), tachycardia in the 110-120s, a respiratory rate of 22–24, and a pulse oximetry of 94% on room

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### Article highlights

- There is significant overlap in the presenting symptoms of peripartum cardiomyopathy and those associated with normal physiological changes of pregnancy, including peripheral edema, tachypnea, dyspnea, and orthopnea.
- "Can't-miss" diagnoses like pulmonary embolism require workup when clinical suspicion is high. Still, awareness of cognitive biases in relation to patient characteristics is necessary to prompt an appropriate workup for peripartum cardiomyopathy.
- The diagnosis of peripartum cardiomyopathy is ultimately clinical, but an echocardiogram is necessary to quantify ejection fraction, with EF < 45% required for definitive diagnosis.
- In patients where echocardiography is technically difficult, alternatives to diagnosis include cardiac magnetic resonance imaging (CMR) and endomyocardial biopsy if necessary.
- There is growing evidence that multiple gene mutations may increase the likelihood of the development of peripartum cardiomyopathy, including genes that code for titin and prolactin.
- Management of peripartum cardiomyopathy is with delivery, and treatment during the postpartum period currently follows the same GDMT guidelines seen in patients with systolic dysfunction congestive heart failure.
- The ongoing REBIRTH trial is looking to assess the benefits of bromocriptine and GDMT for management in patients with postpartum cardiomyopathy.

air (normal ≥95%). Fetal heart rate was within normal limits at 150 beats per minute. A physical exam was pertinent for increased work of breathing and bilateral crackles at lung bases. Bilateral lower extremity edema was noted without calf tenderness. There was a regular rhythm with normal S1 and S2 on cardiac auscultation. Initial complete blood count was notable for a white blood count of 16.3/mm3 (normal 3.4–9.6/mm3), hemoglobin 13.6 g/dL (normal 9.5–15 g/dL in 3rd-trimester pregnancy), and platelets 316 thousand/uL (normal 150–450 thousand/uL). Initial comprehensive metabolic panel included sodium of 137 mmol/L (average 135–145 mmol/L), potassium of 4.9 mmol/L (normal 3.5–4.5 mmol/L), creatinine 1.07 mg/dL (normal 0.4–0.9 mg/dL 3rd-trimester pregnancy), BUN 22 mg/dL (average 6–21 mg/dL), albumin 3.0 g/dL (normal 3.4–5.4 g/dL), calcium 8.4 mg/dL (normal 8.5–10.2 mg/dL), and alkaline phosphatase 115 units/L (normal 38–229 units/L 3rd-trimester pregnancy). An NT proBNP of 20,391 pg/mL resulted (normal <300 pg.mL), suggesting heart strain as a result of likely fluid overload. While mild elevation may be anticipated in early pregnancy due to the increased blood volume, this extent of elevation would be more indicative of pathologic changes [15]. She also had a slightly elevated high sensitivity troponin T of 34 ng/L with a repeat of 32 ng/L (normal <14 ng/L) three hours later. This mild elevation, which was delta negative, suggests a degree of myocardial injury without acute myocardial infarction.

Due to high clinical suspicion of pulmonary embolism based on her presenting symptoms and comorbidities, a D-dimer was deferred and an anterior-posterior chest radiograph and CT angiogram were ordered. The radiograph was notable for mild interstitial pulmonary edema, and the cardiothoracic ratio was determined to be approximately 67% (normal <50%), therefore suggesting a degree of cardiomegaly. The CT angiogram showed no evidence of pulmonary embolism, but it did show moderate bilateral pleural effusions and multilevel focal patchy reticulonodular densities. An echocardiogram was ordered to investigate the etiology of pulmonary edema and the atypical clinical picture. The echocardiogram showed severe global hypokinesis, an estimated left ventricular ejection

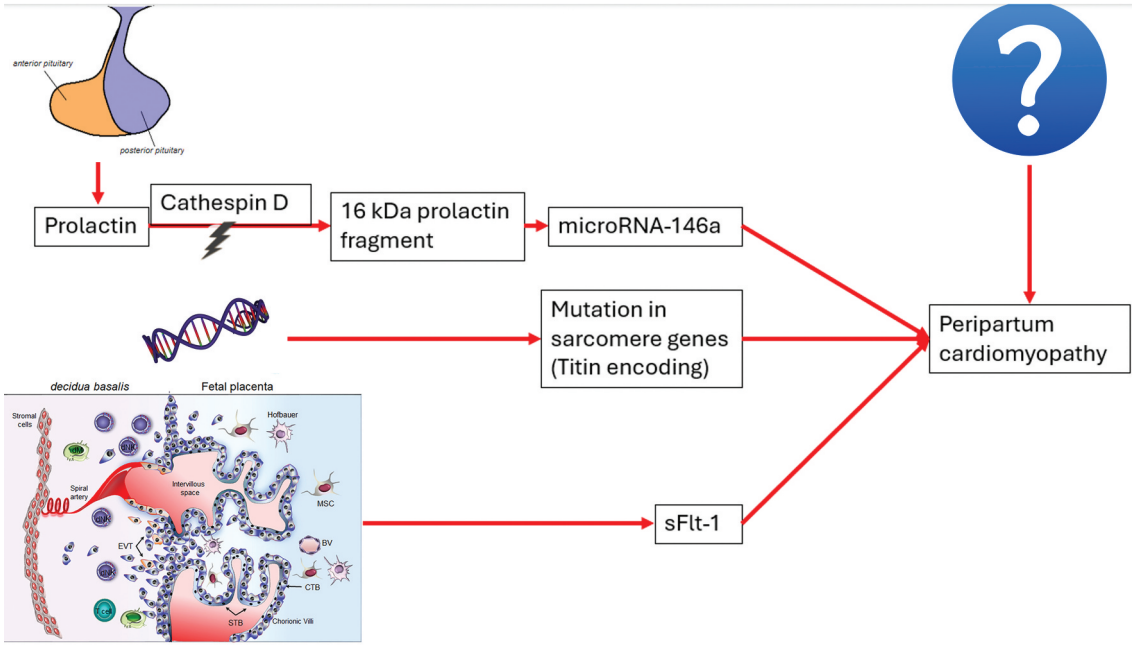


Figure 1. Pathophysiology of PPCM. Prolactin, secreted by the anterior pituitary gets broken to a 16 kDa fragment which results in upregulation of microRNA-146a. Separately, DNA mutations in sarcomere genes, such as *TTN* encoding for titin, contribute to the pathogenesis. The other main contributing factor is from sFlt-1, an anti-angiogenic protein associated with pre-eclampsia. Beyond these three factors, there are still many other unclear factors which are still being investigated. sFlt-1, soluble fms-like tyrosine kinase-1.

fraction of 20–25% (normal 55–75%), a small pericardial effusion, grade III diastolic dysfunction, elevated left ventricular filling pressures, moderately increased left atrial and ventricular size, mild to moderate mitral regurgitation, and mild tricuspid regurgitation (Figures 2, 3). Based on the clinical presentation and echocardiogram findings, she was diagnosed with PPCM. Her condition remained stable while hospitalized. The decision was made to transfer to an alternate center for management due to anticipated cardiac anesthesia, postpartum intensive care unit, and neonatal intensive care unit. A cesarean delivery was performed without complications while hospitalized. The patient's medical management was escalated per the 2022 AHA GDMT recommendations to include empagliflozin, metoprolol, sacubitril-valsartan, and spironolactone. She has been enrolled in the ongoing REBIRTH clinical trial, which investigates the potential benefits of bromocriptine with GDMT compared to receiving GDMT alone. Bromocriptine, a dopamine receptor agonist, decreases prolactin levels through inhibition of the tuberoinfundibular pathway. Given that the pathophysiology of PPCM is theorized to be associated with a truncated 16-kDa form of prolactin, this would inhibit further progression of the disease. Nine months after her initial evaluation, the patient returned for a follow-up echocardiogram. The echocardiogram showed an improvement in her EF to 47% with moderate LV dilation and diffuse hypokinesis. While the patient was happy to have seen this improvement on the echocardiogram, she was still quite disappointed that her cardiac functioning had not fully returned to normal as this indicated she may later need more advanced therapies including a heart transplant.

## 4. Discussion

This case highlights the importance of timely diagnosis and management of peripartum cardiomyopathy as this condition often mimics certain conditions like physiological changes of pregnancy, pulmonary embolism, and heart failure and to avoid cognitive biases, such as premature closure bias, secondary to certain patient characteristics as in this patient who was, initially worked up for suspected pulmonary embolism due to her comorbidities and presenting symptoms. A patient presenting with complaints of shortness of breath, chest pain, and bilateral pedal edema often undergoes echocardiography as it is safe and easy to perform and can help distinguish PPCM from pulmonary embolism as echocardiography usually exhibits right-sided heart dysfunction with associated pulmonary hypertension. Pregnant females are at higher risk of pulmonary embolism during pregnancy and the postpartum period, which often mimics PPCM in terms of signs and symptoms [16]. In addition, echocardiography can also help to distinguish PPCM from physiologic changes in pregnancy, as physiological changes of pregnancy involve increased cardiac output; on the contrary, PPCM involves reduced ejection fraction [17–19]. In addition to echocardiography, CMR (cardiac magnetic resonance imaging) and endomyocardial biopsy are generally reserved for cases in which an alternative diagnosis of heart failure is suspected, like giant cell myocarditis and cardiac sarcoidosis [1].

In our case, echocardiograms were not pursued early in this patient's care, ultimately delaying diagnosis and exposing the patient to unnecessary radiation. Therefore, it is imperative to educate providers on this disguised condition and the utility

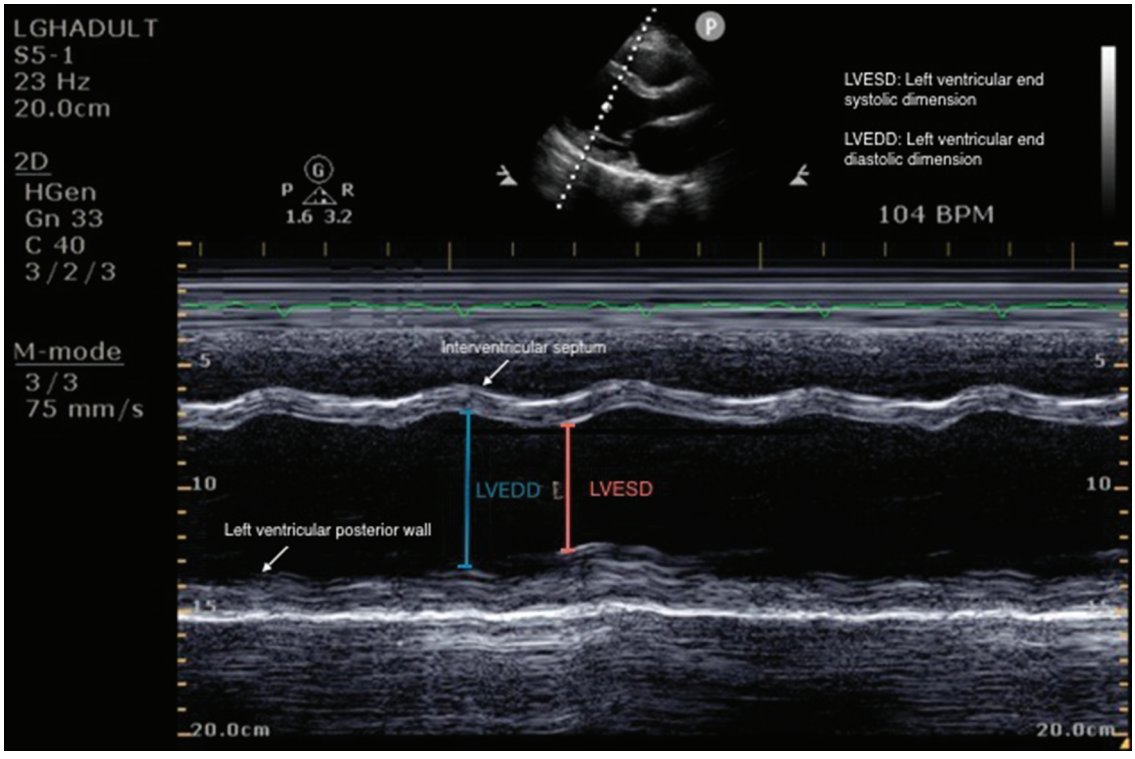


Figure 2. Parasternal long axis view in M mode echocardiogram. M mode displays movement of the heart over multiple cardiac cycles, as shown by the electrocardiogram in the figure. Here we can see a significant reduction in movement along the posterior wall of the left ventricle, which is consistent with the final interpretation of global hypokinesis when taken in context with the wall motion seen from different views. LVESD, left ventricular end systolic dimension; LVEDD left ventricular end diastolic dimension.

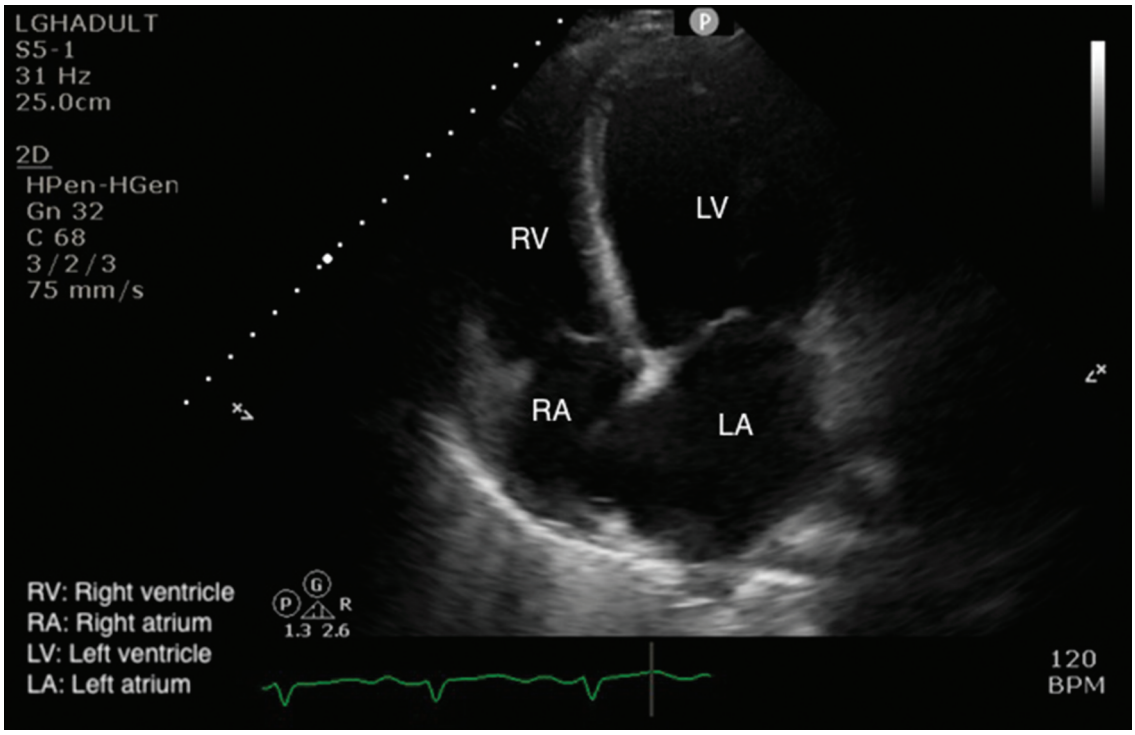


Figure 3. Apical four chamber view echocardiogram. Here we can see global chamber enlargement with accompanying thinning of the myocardium. In addition, the utilization of color Doppler in this view showed both mitral and tricuspid regurgitation. These findings are often seen in dilated cardiomyopathies, which peripartum cardiomyopathy falls within. RV, right ventricle; RA, right atrium; LV, left ventricle; LA, left atrium.

of echocardiograms in diagnostic workups to minimize the burden on patients and health systems.

## 5. Conclusion

This case highlights the significance of the timely diagnosis of PPCM, and clinicians should remain vigilant for a diagnosis of PPCM due to its symptoms being similar to those of physiological changes of pregnancy, which can result in it being overlooked during the initial evaluation. In addition to physiological changes in pregnancy conditions, various pathologic entities like preexisting cardiomyopathy (like familial dilated cardiomyopathy, previous myocarditis, and drug or toxin-induced cardiomyopathy) often pose a diagnostic dilemma as these conditions cause dyspnea and heart failure earlier in pregnancy due to the increase in circulating plasma volume and cardiac output. Echocardiography is often used as a diagnostic modality of choice with management following the GDMT guidelines and delivery.

With continual advancements in genetic testing, the authors suspect that additional genetic variants will be identified that predispose certain patients to development of PPCM. In addition, increased availability of ultrasound machines and healthcare provider training on proper point of care ultrasound technique may contribute to earlier identification and initiation of GDMT where applicable. Both interventions will ideally lead to improved outcomes due to earlier detection of PPCM with initiation of GDMT where appropriate.

While she has had noted improvement with the traditional GDMT regimen, she is also enrolled in the REBIRTH trial. It is currently unknown if she is in the experimental or control group to this trial, although it opens up possible novel future treatments specifically for PPCM. This includes pharmacologic management targeted at its proposed pathophysiology, such as by reducing the systemic prolactin level through dopamine receptor antagonists, such as bromocriptine. Following completion of the clinical trial, recommendations should be revisited to ensure optimal patient outcomes.

## Author contributions

Authors Bryan Tornabene and David Waldron were both members of healthcare teams directly involved in care for the patient discussed in this article. Authors Bryan Tornabene, David Waldron, Hannah Short, and Nicholas Duca were all responsible for drafting and revising the manuscript.

## Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

## Ethical code of research statement

The patient provided verbal informed consent for inclusion before participating in the case report. Although a written consent was not obtained due to geographic limitations, the verbal consent included all components of a written consent. She had no questions following this discussion and was amenable to a case report being published on her experience and the research trial she is currently involved in. Written consent was obtained for release of the echocardiogram images which were initially on a separate electronic medical record system with the express understanding that they would be included in a case report. Treatment during the patient's hospital course adhered to the

standards of care and was performed with appropriate ethical considerations.

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