



# Peripartum cardiomyopathy following severe postpartum hemorrhage in a woman with prior lymphoma therapy: A case report

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## Abstract

Peripartum Cardiomyopathy (PPCM) is a rare but potentially life-threatening cause of heart failure occurring toward the end of pregnancy or in the months following delivery. Its diagnosis may be challenging, particularly in patients with complex obstetric and oncologic histories. We report the case of a 38-year-old primiparous woman with a twin pregnancy who developed secondary postpartum hemorrhage requiring hysterectomy. On postoperative day five, she presented with acute heart failure manifested by severe dyspnea, orthopnea, tachycardia, pulmonary edema, and reduced left ventricular ejection fraction (40%). Her history was significant for prior chemotherapy and radiotherapy for Hodgkin and non-Hodgkin lymphoma. Imaging excluded pulmonary embolism and infection. Transthoracic echocardiography revealed dilated cardiomyopathy with systolic dysfunction. She was treated with guideline-directed heart failure therapy, including  $\beta$ -blockers, diuretics, ACE inhibitors (later switched to sacubitril/valsartan), bromocriptine, and anticoagulation. Progressive improvement in cardiac function was observed during follow-up, with left ventricular ejection fraction improving to 61% at 36 months. This case highlights the diagnostic complexity of acute heart failure in the postpartum period, particularly in patients with prior exposure to potentially cardiotoxic oncologic therapies. Early recognition and multidisciplinary management are crucial for favorable outcomes.

**Keywords:** Peripartum cardiomyopathy, Chemotherapy-Induced cardiomyopathy, Twin pregnancy

## Introduction

Peripartum Cardiomyopathy (PPCM) is an uncommon form of Heart Failure (HF) occurring in the last month of pregnancy or in the months following postpartum in women without previously known structural heart disease. The condition remains a diagnosis of exclusion and may be difficult to differentiate from other causes of acute HF in the postpartum period. We present a complex case of acute HF developing after severe postpartum hemorrhage in a woman with a history of treated lymphoma.

## Case report

A 38-year old woman, primiparous, 38 weeks pregnant with twins gave birth to two healthy boys/3550/4200g each by the cesarean section. Secondary postpartum hemorrhage occurred 24 hours after delivery and persisted for up to four days postpartum. Blood cultures were negative. On the first postoperative day, the patient experienced

significant blood loss. She also presented with subfebrile temperature, dry cough, increased heart rate, increased respiratory rate, and dizziness. Postpartum hemorrhage remains a significant challenge in obstetrics, both in terms of diagnosis and management. The patient received uterotonics, packed red blood cells (eight units in saline-adenine-glucose-mannitol solution), additional fresh frozen plasma, and thrombocyte concentrate, and intravenous antibiotics were initiated within the first hour. However, all conservative measures failed to control the bleeding, and the patient's condition remained unstable. On the fourth day following cesarean section, a hysterectomy was performed due to severe bleeding and uterine atony in order to save the patient's life. Despite all efforts, on the fifth day her condition worsened, and she was transferred to the Intensive Care Unit with severe dyspnea, orthopnea, jugular vein distention, peripheral cyanosis, and edema. Oxygen saturation was 85% on room air, respiratory rate was 34 breaths/minute, heart rate was 146 beats/minute, blood pressure was 140/90 mmHg, and temperature was 37.8°C. After

receiving oxygen at 5 L/min via nasal cannula, oxygen saturation improved to 93–95%. On physical examination, a gallop rhythm with a grade II systolic murmur at the apex was noted. Pulmonary auscultation revealed crackles, predominantly on the left side. Peripheral edema was present, mainly in the ankles and legs. The patient reported fatigue and persistent shortness of breath during pregnancy, which worsened in the last month. However, she attributed these symptoms to the twin pregnancy and remained active until term. She reported a history of chemotherapy and radiotherapy for Hodgkin lymphoma (HL) 11 years earlier and non-Hodgkin lymphoma (NHL) 6 years earlier. The treatment was reported to be highly effective, and the patient was considered cured, although no documentation was available. No echocardiographic evaluation had been performed before or during pregnancy. There was no known history of heart disease prior to pregnancy, and only a normal Electrocardiogram (ECG) was recorded during the third trimester. A chest X-ray performed at the obstetrics and gynecology hospital showed pulmonary venous congestion and raised suspicion of left-sided pneumonia. Rapid antigen and Reverse transcription polymerase chain reaction (RT-PCR) tests for COVID-19 did not detect SARS-CoV-2. Chest CT angiography performed to rule out pulmonary embolism demonstrated cardiomegaly, pulmonary edema, and bilateral pleural effusions, predominantly on the left side. ECG showed nonspecific abnormalities, including sinus tachycardia with nonspecific ST-T changes and occasional ventricular premature complexes. Transthoracic echocardiographic revealed left ventricular dilatation and systolic dysfunction with an left ventricular ejection fraction (LVEF) of 0.40%, M-mode Fractional Shortening (FS) of 20%, right ventricular dilatation, biatrial enlargement, moderate mitral and tricuspid regurgitation, and pulmonary hypertension. Laboratory findings showed low plasma albumin levels, no proteinuria, a N-terminal pro-B-type natriuretic peptide (NT-proBNP) level of 743 pg/mL, and negative blood cultures. The patient was treated with digoxin, loop diuretics, spironolactone, bromocriptine, low molecular weight heparin, beta-blockers, and initially ACE inhibitors, which were later replaced with sacubitril/valsartan. She was then transferred to the cardiology department for further management. The patient was discharged in stable condition on the

12th postpartum day with marked clinical improvement. Subsequent follow-up remained uneventful, with regular monitoring of cardiac function. At 6 months, follow-up, LVEF was 0.43% and M-mode FS was 21.37%. At 18 months, LVEF reached to 0.51% M-mode FS to 26.25%. At the 36 months, LVEF improved to 61%, and M-mode FS to 31%.

## Discussion

There have been a few other case reports published on PPCM associated with chemotherapy therapy [1]. PPCM is defined as an idiopathic form of HF with reduced LVEF that develops toward the end of pregnancy or in the months following delivery, in the absence of another identifiable cause of cardiac dysfunction. [2]. We needed to avoid misdiagnosis and required careful attention to the differential diagnosis between acute pulmonary edema, pulmonary embolism, cardiomyopathy related to sepsis, myocarditis, cardiomyopathy related to SARS-CoV-2, and cardiomyopathy related to chemotherapy. Chest CT angiography ruled out pulmonary embolism, rapid antigen and (RT-PCR) tests for COVID-19 did not detect SARS-CoV-2. Our patient recently had two surgical procedures, cesarean section and hysterectomy, due to severe bleeding and uterine atony. Most cases of secondary postpartum hemorrhage occur due to subinvolution of the uterus secondary to uterine infection. Patients who develop infection are at risk of developing sepsis. A negative blood culture and a maternal temperature of 37.7°C cannot completely rule out sepsis. The right way to prevent sepsis is to treat infections. In our case, we started intravenous antibiotics within the first hour. The most important predictor of culture negativity was the receipt of antibiotics within the preceding 48 hours [3]. Similar to other studies, prior antibiotic use was associated with culture-negative sepsis, as antibiotics may have sterilized the cultures. Sepsis can lead to systemic inflammation and myocardial injury, exacerbating the risk of PPCM development, particularly in susceptible individuals. At the same time, it was difficult for us to rule out cardiomyopathy related to chemotherapy because the patient had a history of chemotherapy and radiotherapy for lymphoma before pregnancy. However, a review of cases shows that overall, peripartum cardiac dysfunction is uncommon in long-term survivors of

malignancy with prior exposure to cardiotoxic therapies, although the relative risk is approximately 55 times greater than in the general population [4]. Complications of cardiomyopathy related to chemotherapy are attributed to the cardiotoxic effects of chemotherapy, particularly doxorubicin and mediastinal radiation exposure, which are related to myocardial injury and left ventricular dysfunction and have similar manifestations, which we kept in mind. Our patient had a history of lymphomas categorized according to their biological characteristics as HL 11 years ago and NHL 6 years ago. The most used regimens for HL are ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine), BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone), and escalated BEACOPP with higher doses of cyclophosphamide, doxorubicin, and etoposide [5]. In NHL, one of the common treatment regimens used is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone), and there are various other regimens depending on molecular and antigenic properties of neoplastic elements [6]. The patient reported that treatment for lymphoma with chemotherapy and local irradiation was highly effective and that she was eventually cured. Anthracyclines have been commonly used since the early 1980s and remain the backbone of HL chemotherapy regimens used today. Cardiac radiation exposure and treatment with anthracyclines are important risk factors for the development of heart failure in HL survivors [7]. According to guidelines, the cardiovascular events related to anti-cancer therapy generally include new cardiovascular symptoms, acute coronary syndromes, cardiac arrhythmias, heart failure, myocarditis, pericardial vascular heart disease, vascular toxicities, and hypertension [8]. Anthracyclines are a significant cause of acute and chronic cardiotoxicity in cancer patients, and long-term cardiotoxicity can lead to death in about one-third of patients. Several molecular pathways have been implicated in the development of anthracycline-induced cardiotoxicity, although the underlying mechanisms are not fully elucidated [9]. According to the study, patients who developed cardiomyopathy had received higher doses of anthracyclines, including doxorubicin and daunorubicin, than those who did not develop cardiomyopathy. Patients in the study who developed cardiomyopathy had a median

dose of anthracyclines of 321 mg/m<sup>2</sup> [10]. A cumulative dose of doxorubicin of 400 mg/m<sup>2</sup> carries a 5% risk of developing HF, which increases to 25–48% at 700 mg/m<sup>2</sup>. As reported by other authors, doxorubicin is classified as type 1 cardiotoxicity with cardiomyocyte death, necrosis, or apoptosis, and as a result is not reversible [11]. We were not sure whether our patient followed this trend or what the total cumulative dose of doxorubicin therapy was. Among HL survivors treated before the age of 25, the risk of cardiovascular events is even higher, and the 40-year cumulative incidence of cardiovascular disease was 50% in this population [12]. Irradiation-induced cardiovascular disease occurs in 10% to 30% of patients within 5–10 years following treatment. Since cardiovascular disease develops slowly, it is normally not seen before more than 15 years of follow-up [13]. A meta-analysis shows that both HL and NHL long-term survivors have an increased risk of death from cardiovascular disease (7.3 and 5.35 times higher, respectively) compared to the general population [14]. According to cardiotoxic side effects, preconception cardiologic evaluation is important for every woman with a history of chemotherapy and radiotherapy who is considering having a family [6]. In contrast, our patient had no regular check-ups at the hospital. Although she reported that after her last treatment for lymphoma the echocardiogram examination was normal, she had no follow-up in the last five years, and there was no echocardiogram performed before or during pregnancy. In our case, there was no known history of heart disease, and she had a normal ECG in the third trimester, but this was not sufficient to exclude cardiotoxic effects of chemotherapy, particularly doxorubicin and mediastinal radiation exposure. Our patient was diagnosed with PPCM in her first postpartum week. Some authors observed that PPCM onset is most frequent in the first month postpartum (44%) and at delivery (23%) [15]. Other authors found that most women present postpartum, mainly during the first month after delivery; a considerable number present in the late antepartum period; and rare cases present as early as the second trimester [16]. The most common clinical presentation consists of acute heart failure occurring in the first weeks after delivery [17]. The symptoms of congestive HF are clinical features of PPCM. However, diagnosis cannot be based only on clinical features. It was necessary to evaluate all symptoms and perform ECG, echocardiography,

serum B-type natriuretic peptide, and other laboratory tests. Frequent delays in diagnosis occur due to under-recognition of this disease and the overlap between normal pregnancy symptoms and those of HF, and these delays are associated with worse outcomes [18]. During pregnancy, cardiac imaging is limited to modalities that do not involve radiation, but echocardiography is safe and should be performed in any suspected case. PPCM may be diagnosed for the first time by ECHO when the following criteria are met: LVEF<0.45 or M-mode FS <30% (or both) and end-diastolic dimension >2.7 cm/m<sup>2</sup> [18]. The echocardiogram of our patient showed left ventricular dilatation and dysfunction, an LVEF< of 0.40, right ventricular dilatation, biatrial enlargement, moderate mitral and tricuspid regurgitation, and pulmonary hypertension. BNP and NT-proBNP are useful supportive biomarkers in suspected PPCM and in our case, levels of NT-proBNP were significantly elevated. Levels of BNP and NT-proBNP, which do not change significantly during normal pregnancy and may be mildly elevated in preeclampsia, are usually markedly elevated in PPCM [19,20]. We also found low levels of plasma albumin. Significantly low levels of plasma albumin, prealbumin, selenium, and zinc have also been reported in PPCM by other authors [21,22]. Our patient was 38 years old, twin pregnancy and older maternal age and multiparity are known as risk factors associated with PPCM. [2,23,24]. Our patient was treated with guideline-directed heart failure therapy with marked improvement. PPCM has been shown to have a good recovery rate, and recovery often occurs within the first 3 to 6 months of treatment or may be delayed for as long as two years after diagnosis [25]. However, 25% of patients develop chronic HF, and others may die during the course of the disease [26]. If the diagnosis is made early and treatment is started immediately, the prognosis is good compared to other forms of cardiomyopathy, as left ventricular function recovers in most cases [27,28]. In our case, full recovery occurred within three years after diagnosis.

## Conclusions

According to cardiotoxic side effects, preconception cardiologic evaluation is important for every woman with a history of chemotherapy and radiotherapy who is considering having a family. Differences and

similarities between PPCM and chemotherapy-related cardiomyopathy must be considered in every cancer survivor of reproductive age. The data from our case suggest that timely diagnosis of PPCM reduces the risk to life and leads to more appropriate treatment as well as postpartum care.

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