Peripartum dilated cardiomyopathy complicated by miliary tuberculosis—a maternal near miss (MNM): Case report

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Abstract

The term ‘Maternal Near Miss’ (MNM) refers to women who have survived serious life-threatening complications during pregnancy, labour or within 6 weeks after termination of pregnancy, either by chance or due to good health care. The goal of this report is to emphasise the need for patients’ education, emergency transportation and availability of multidisciplinary tools at all levels of the health care system. Severe acute maternal morbidity (SAMM) is a measure of maternal mortality that may also be used to assess the quality of obstetric treatment in a certain facility. Also, the motive of this report is to give an idea to primary care physicians of all the preliminary risk factors to be taken into consideration while treating the patient on arrival.

Keywords: Echocardiograph, left ventricular dysfunction, maternal near miss (MNM), miliary tuberculosis, peripartum cardiomyopathy

Introduction

According to WHO (World Health Organization), maternal near miss (MNM) refers to a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy.

Our patient was diagnosed with miliary tuberculosis along with peripartum dilated cardiomyopathy post-delivery during COVID-19 pandemic and was maternal near miss.

Peripartum cardiomyopathy (PPCM) diagnostic criteria have been in place for decades. The following are the current diagnostic criteria: heart failure development in the last month of pregnancy or 5 months post-partum; absence of pre-existing heart disease; indeterminate cause; and ECHO criteria including left ventricular ejection fraction <0.45 or M-mode fractional shortening <30% (or both) and end-diastolic dimension >2.7 cm/m².¹

Now, the 2010 Heart Failure Association of the European Society of Cardiology Working Group revised the definition of PPCM to an ‘an idiopathic cardiomyopathy presenting with HF secondary to LV systolic dysfunction toward the end of pregnancy or in the months following delivery, where no other cause of heart failure is found’.

Traditional pharmacologic heart failure treatments, such as diuretics, angiotensin-converting enzyme inhibitors, vasodilators, digoxin, blockers, anticoagulants and peripartum...
cardiomyopathy-targeted medicines, are used to treat peripartum cardiomyopathy. During pregnancy and breastfeeding, drug safety profiles affect therapeutic decisions. Fortunately, many patients with peripartum cardiomyopathy recover within 3 to 6 months after illness gets started, despite a mortality rate of up to 10% and a significant risk of recurrence in subsequent pregnancies.

Tuberculosis (TB) is a leading cause of mortality globally, claiming the lives of an estimated 1.4 million people in 2019. According to WHO ("Tuberculosis (TB)", n.d.), TB is one of the top ten causes of mortality.

Infection with tuberculosis (TB) in pregnant women and newborns is always difficult. To reduce morbidity and mortality, appropriate therapy is critical. A mother's mental anguish might be increased by a TB diagnosis or exposure to active TB. When the mother's TB status is unknown, the situation might become more difficult for the physician. A multidisciplinary strategy involving a pulmonologist, obstetrician, neonatologist, infectious disease expert and TB public health department is required for effective TB care throughout pregnancy and the post-partum period.

We report a case of maternal near miss (MNM) who presented with breathlessness and falling saturation and was diagnosed with PPCM with superadded miliary tuberculosis in times of COVID-19 pandemic, and we discuss the multidisciplinary approach and diagnostic dilemma we had to face.

**Case Description**

A 25-year-old second gravida para 1 with one live issue, with 34 weeks 5 days POG, came to casualty at night with complaints of bleeding per vaginum and fever since 1 day, cough since 4 days and swelling in both the legs since 1 month. Examination on admission revealed blood pressure of 110/70 mmHg, heart rate of 72 beats per minute with normal sinus rhythm, respiratory rate of 18 breaths per minute and oxygen saturation level of 92% on room air. On physical examination, she was not in any acute distress. On per abdomen examination, symphysio-fundal height was corresponding to approximately 34 weeks of gestational age, cephalic presentation of foetus with scar tenderness. Foetal heart was present, regular and 142 beats per minute on auscultation. On per vaginum examination, cervical os was 2 cm dilated, 50% effaced, station was high up, and pelvis seemed inadequate.

Given the present scenario of COVID-19 pandemic, she was advised RT-PCR in view of fever and low oxygen saturation levels.

Her labs on admission showed a white cell count 11300/cu.mm with neutrophils 74% and lymphocytes 20%, haemoglobin 9.7 g/dl and platelets 2.22 lacs/cu.mm, which were within normal limits with mild anaemia. Sickling was negative. Liver function tests and renal functions tests were within the normal range, ESR 40, C-reactive protein 5.9 mg/L (normal value 0–5 mg/L), D-dimer 1.90 µg/ml, serum ferritin 128 ng/ml (normal value 6.24–137 ng/ml) and BNP 500 pg/ml (normal value <100 pg/ml). Serology for HIV, HBV and HCV was negative.

She was taken for emergency lower segment caesarean section (LSCS) in view of previous LSCS with impending scar dehiscence in labour with mild anaemia, while awaiting for COVID-19 RT-PCR report.

During intraoperative period, there was maternal bradycardia for which she was given intraoperative crystalloids; also, one unit blood transfusion was given intraoperatively; other than that, intraoperative period was uneventful, and a male baby was born weighing 2.2 kg and was shifted to mother's side; immediate post-operative period was uneventful too.

On post-operative day 2, she developed breathlessness and her oxygen saturation levels were 88% on room air and so she was started with high flow oxygen, but her general condition did not improve. She was hypotensive (90 mmHg SBP) with sinus tachycardia 130 bpm. On auscultation, her chest was full of bilateral coarse crepitations and rales. Urgent physician and cardiology opinion was taken.

ECG revealed diffuse T wave inversion. Chest X-ray PA view was performed which showed cardiomegaly and pericardial and pleural effusion along with military nodules which were bilaterally uniformly distributed all over lung field [Figure 1]. Transthoracic echocardiography revealed substantially deteriorated left systolic function, with an ejection fraction (EF) of 25%, fractional shortening of 12%, mitral regurgitation and mild tricuspid regurgitation. The right and left ventricles were both noticeably enlarged and hypokinetic. The left ventricle’s end-diastolic volume was 116 ml/m2 and its end-diastolic dimension was 6.5 cm, with an end-diastolic dimension index of 3.86 cm/m2. The presence of bi-atrial enlargement was also observed.

![Figure 1: Diagnosis of peripartum cardiomyopathy (PPCM) with miliary tuberculosis](image-url)
HRCT thorax revealed multiple military shadows scattered in bilateral lung parenchyma suggestive of miliary tuberculosis along with patchy areas of consolidation, which were noted in left perihilar region. Also, there is a dilated pulmonary artery with mild cardiomegaly with bilateral mild pleural effusion along with pulmonary oedema. Also, there were ground-glass opacities [Figure 1a–d].

Laboratory investigations on post-op day 2 were sent that revealed a white cell count 10400/cu.mm with neutrophils 88%, lymphocytes 10%, haemoglobin 12.8 g/dl and platelets 3 lacs/cu.mm, which were within normal limits, and anaemia was corrected. Sickling was negative. Liver function tests and renal functions tests were within the normal range, ESR 68, C-reactive protein 14.68 mg/L (normal value 0–5 mg/L), D-dimer 5.12 µg/ml, serum ferritin 120 ng/ml (normal value 6.24–137 ng/ml) and BNP 612 pg/ml (normal value <100 pg/ml). The thyroid function test was normal. Serological testing for the common viral agents that cause myocarditis came up negative.

In the meanwhile, her RT PCR results were negative; therefore, she was transferred to the medicine intensive care unit, where she was put on non-invasive bilevel positive airway pressure (BiPAP) ventilatory support owing to low oxygen saturation. She was in cardiogenic shock, with a blood pressure of 70/50 mmHg in the supine position; therefore, inotropes and vasopressors were given to her. To rectify the hypotension and enhance perfusion, saline was gradually given (1.5 l/24 hours) while keeping a careful eye on the patient for any signs of fluid excess. Because the systolic blood pressure was low (70–80 mmHg), ACE inhibitors were started cautiously. The next day, a low-dose beta-blocker was started (bisoprolol 1.25 mg). The patient was also started on enoxaparin for thromboprophylaxis, because of the enlarged LV with significant dysfunction.

The Mantoux test was negative. Three induced sputum samples were collected and stained for acid-fast bacilli (AFB); however, no acid-fast bacilli were found.

The patient was started on 4-drug regimen ATT (isoniazid, rifampicin, ethambutol and pyrazinamide).
In a few days, there was a significant improvement in the general condition of the patient. She was able to maintain saturation in the next 7 days of ICU admission. So BiPAP was gradually weaned off. On day 10 of ICU admission, the general condition of the patient improved significantly. A repeat chest X-ray showed resolution of pulmonary oedema and pleural and pericardial effusions. The patient was discharged from the hospital on day 12 of ICU admission and day 14 of admission, with advice to continue follow-up weekly.

The baby was examined by the neonatology team, and a PPD (purified protein derivative) test was conducted, which came out negative, and the chest X-ray was normal. While waiting for the results of the stomach aspirate TB work-up, the infant was put on INH prophylaxis for a suspected latent TB infection, as per the multidisciplinary team’s strategy. Mom and baby were permitted to be together.

**Follow-up**

Follow-up echocardiogram revealed mild mitral insufficiency by day 30, as well as normalisation of right ventricular size and function, and the elimination of tricuspid insufficiency. While the volumes of the left ventricle decreased, EF remained depressed (30%).

Patients and their children were also extensively monitored in pulmonary, infectious disease, and paediatric clinics. The patient was informed about the importance of medication compliance as well as the potential side effects of the medicine, and she comprehended the instructions completely. The patient and the baby remained compliant with treatment regimen even 2 months after initiation of treatment and did not experience any adverse effects of medications. The baby’s development chart was adequate.

**Discussion**

We will be discussing this case under the following two headings and their implications in peripartum period: what it means for mother and baby; and what understanding should a primary care physician have while coming across such a case.

**Peripartum cardiomyopathy**

The diagnostic and therapeutic difficulty that physicians confront when encountering patients with the rare but intriguing disease of peripartum cardiomyopathy, which necessitates timely diagnosis and treatment, is highlighted in this case report, especially in given COVID-19 pandemic times. Reproductive programs such as maternal care services have been adversely affected by the COVID-19 pandemic lockdown.

The symptoms of PPCM are similar to the normal findings of late pregnancy. Thus, there is a delay in diagnosis usually. The severity and mortality vary from patient to patient. PPCM is usually characterised by classical symptoms and signs of systolic heart failure with ventricular enlargement and dysfunction as seen on echocardiography. Regurgitation of the mitral and tricuspid valves is common. Thromboembolism or hepatic failure related to heart failure is an unusual presentation. In more than 90% of instances, heart failure develops during the post-partum period, with diagnosis occurring at that time. PPCM can strike at any age, although it is more common in women over 30. PPCM is difficult to diagnose since most women suffer dyspnoea, tiredness and pedal oedema in the later months of a normal pregnancy or shortly after birth. The appearance of paroxysmal nocturnal dyspnoea, nocturnal cough, new regurgitant murmurs, pulmonary crackles, jugular venous distention and hepatomegaly should raise the suspicion of heart failure and might aid doctors in the diagnosis.

The aetiology and pathophysiology appear to be complex and poorly understood, with conflicting evidence in the literature. Because PPCM is often related to gestational hypertension, tocolytic treatment and twin pregnancy, these have been postulated as probable risk factors. The possibility of developing PPCM in a surrogate mother whose embryo was received from the commissioning couple and whose mother was diagnosed with PPCM after the birth of her first child, highlights the role of a transmissible agent, either infectious or non-infectious, as well as genetic susceptibility. Familial reports of PPCM imply a hereditary propensity, and family members should be screened since PPCM might be a symptom of a genetic predisposition to cardiomyopathy.

The cause of PPCM is yet unknown. Myocarditis, autoimmunity to foetal antigens, foetal microchimerism and selenium deficiency or high salt intake are among various hypotheses that have been proposed. A recent study, however, shows that PPCM is a vascular illness induced by the placenta and pituitary secreting powerful anti-angiogenic chemicals in late pregnancy, although this idea has been proposed in the past.

A study conducted by Hilfiker-Kleiner et al. in 2008 and Halkein et al. in 2013 showed that endothelium exposed to 16-kDa prolactin dramatically induces the expression of microRNA-146a, which is then packaged and secreted in exosomes, small secreted lipid-encapsulated particles, which are in turn taken up by adjacent cardiomyocytes. The end result is microRNA-mediated regulation of target genes in cardiomyocytes, most notably the neuregulin/ErbB pathway, which was previously identified as a key suppressor of cardiomyocyte death. In vivo, these elegant investigations revealed a new interaction between endothelial cells and cardiomyocytes, as well as a mechanism through which prolactin promotes cardiomyocyte toxicity in PPCM.

Figure 2 and 3 the placenta secretes numerous substances into the maternal blood during late gestation in placental animals, most notably a soluble form of the VEGF receptor 1 or soluble fms-like tyrosine kinase 1 (sFlt-1). sFlt-1 binds to and neutralises...
Although the recovery phase does not have to be restricted to the first 6 months following delivery, complete return of systolic function generally occurs during the first 6 months.

**Therapy**

Diuretics, ACE inhibitors, beta-blockers and aldosterone antagonists are all used in the treatment of heart failure. In the case of intolerance to ACE inhibitors, angiotensin-converting enzyme (ACE) inhibitors should be added. Because of the poor left ventricular EF, which predisposes to thrombus formation, anticoagulant treatment should be explored, especially during the peripartum period when a hypercoagulable condition prevails. Haemodynamic support with pressors should be explored in patients who are not improving on conventional therapy or who are in a critical haemodynamic condition with cardiogenic shock. Some reports have surfaced about the usage of extracorporeal membrane oxygenation, intraaortic balloon pump or mechanical assist devices in non-responsive patients, heart transplantation should be explored.

In acute decompensated HF, intravenous vasodilators like nitroglycerin may be needed during pregnancy. Inotrope dobutamine has adverse effects, and levosimendan was not shown to improve outcomes in PPCM. Milrinone and levosimendan showed comparable haemodynamic improvement.

**Labour and delivery**

To reduce maternal and foetal mortality, the cardio-obstetrics team must work together. Experts should be consulted on delivery timing and manner. Stabilisation of the mother is necessary to avoid preterm and related foetal problems. In the event of haemodynamic instability despite medical treatment, an early delivery is recommended. Except for obstetric caesarean section reasons, vaginal delivery is advised in stable individuals. In unstable individuals, invasive haemodynamic adjustment before delivery and careful monitoring are beneficial. Autotransfusion owing to uterine contractions and fluid mobilisation lead to an increase in preload after birth, easing caval compression. Thus, the risk of fluid overload and pulmonary oedema must be taken care of.

**Subsequent pregnancies**

A second pregnancy increases the chance of recurrence, a substantial reduction in left ventricular function and death. The mortality rate during the second pregnancy is estimated to be around 55%, despite the fact that it appears to be linked more with individuals who started the following pregnancy with impaired systolic function, i.e., without achieving a complete recovery.

**Peripartum miliary tuberculosis**

Tuberculosis is a common cause of maternal and foetal morbidity. With the exception of HIV-infected people, who have a greater prevalence of extrapulmonary TB, the vast majority of cases are pulmonary tuberculosis. Our patient presented with pulmonary miliary tuberculosis.

Acute miliary, or progressive haematogenous tuberculosis, has a wide range of clinical symptoms. Two-thirds of individuals develop pleural effusion, peritonitis or meningitis. Because the death rate from miliary TB is significant when treatment is delayed, therapy should be started based on a firm clinical suspicion.

Tuberculosis is an infection that is controlled by a cellular immune response. The T helper 1 (Th1) response is suppressed during pregnancy, which may increase the risk of TB reactivation. Th1 suppression reverses after birth, causing symptoms to worsen.

In our case, we suspect that the process of pregnancy immunoregulation induced the spread of a latent focus of tuberculosis.

**Conclusion**

The diagnosis of PPCM should be considered in all pregnant and post-partum women. Systolic dysfunction is assessed via echocardiography. Treatment should begin as soon as possible to avoid negative consequences. Multidisciplinary team management is rewarding. The optimal duration of medications after recovery is not clearly known. Women who are thinking about having another child should be counselled and supervised. Patients with PPCM require a long-term follow-up.

Severe acute maternal morbidity (SAMM) or a maternal near miss (MNM) is a predictor of better obstetric treatment quality.
Near misses are investigated to quickly define the epidemiologic spectrum at the hospital level and to prioritise maternal health care requirements. Near miss morbidity monitoring in combination with mortality surveillance might aid in the identification of effective preventative measures for potentially life-threatening illness. By promoting evidence-based treatments for life-threatening problems, strengthening referral systems and optimising the use of critical care, severe maternal outcomes might be decreased.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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