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CASE SERIES

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Heart failure due to peripartum cardiomyopathy presenting in the first week of puerperium—A case series from Nepal

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Key Clinical Message

Peripartum cardiomyopathy (PPCM) is a rare cause of heart failure associated with pregnancy without any other known cause. With a prognosis that can vary from the complete recovery of left ventricular function to maternal mortality as well as recurrence with subsequent pregnancies, early diagnosis and treatment of PPCM is important in management. Bromocriptine treatment is beneficial effects on LVEF and mortality in women with severe acute PPCM in addition to standard heart failure therapy. However, further study is required to establish its effect in PPCM.

Abstract

Peripartum cardiomyopathy (PPCM) is a rare cause of heart failure associated with pregnancy without any other known cause. Most of the clinical presentation is similar to symptoms of advanced pregnancy making the diagnosis difficult. Reported are three patients who developed dyspnea, orthopnea, and dry cough during the first week of puerperium. On examination, bilateral lower limb edema and bilateral basal lung crepitation were present in all patients. Chest radiograph showed pulmonary edema in cases two and three, and pleural effusion in case one. All patients had reduced left ventricular ejection fraction and raised N-terminal pro-b-type natriuretic peptide (NT-proBNP) levels. Case two developed PPCM in the background of left pyelonephritis. Case three was complicated by acute kidney injury. All patients were managed with bromocriptine, diuretics, beta-blockers, ACE inhibitors, and fluid restriction. Hence, PPCM though rare should be considered as a differential in women presenting with features of heart failure in later months of pregnancy or within 5 months of delivery.

KEYWORDS

bromocriptine, heart failure, peripartum cardiomyopathy, peripartum dilated cardiomyopathy, pregnancy

1 | INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare cause of heart failure affecting women in the later months of pregnancy or within 5 months of delivery. PPCM often presents when peak volume load, reached just before delivery is greatly reduced after delivery.[1,2] PPCM affects women from all ethnicities globally with wide variation in incidence from 1:20,000 live births in Japan to 1:100 in Zaria, Nigeria.[3,4] With a prognosis that can vary from the complete recovery of left ventricular function to maternal mortality as well as recurrence with subsequent pregnancies, the study of PPCM has been done sparsely in Nepal.[2,5] This case series attempts to increase awareness of disease, diagnosis, and treatment in Nepal.

2 | CASE HISTORY/ EXAMINATION

2.1 | Case 1

A 33-years lady, G_2A_1 at 38 + 6 weeks of gestation, with no significant medical history underwent emergency lower segment cesarean section (LSCS) for non-progression of labor secondary to arrest of descent. On the 4th day of puerperium, she developed dyspnea on exertion, orthopnea, bilateral lower limb edema, and dry cough. On examination, she had increased blood pressure (160/110 mmHg) and bilateral lower limb pitting edema with bilateral basal crepitation on chest auscultation.

2.2 | Case 2

A 31 years lady, $G_2\ P_1\ L_1$ at 40 + 6 weeks of gestation gave birth to a male baby via vaginal delivery with first-degree perineal tear following induction of labor for post-dated pregnancy. On the fourth day of puerperium, she was admitted for puerperal pyrexia with left pyelonephritis, moderate anemia, and hypokalemia. She was treated with antibiotics, potassium supplements, and 2 units of packed red blood cell (PRBC) transfusion. However, on the sixth day of puerperium, she developed shortness of breath, chest pain, dry cough, and orthopnea. On examination, she had bilateral lower limb pitting edema with vitals within normal limits.

2.3 | Case 3

A 28 years lady, $G_3P_1L_1A_1$ at 37 + 1 weeks of gestation with impaired glucose tolerance, underwent Emergency LSCS for oligohydramnios (amniotic fluid index 4.3 cm). On the 3rd postoperative day, she developed sudden onset shortness of breath. On examination, she was tachypneic (40 breaths/min) with low saturation of oxygen (SaO_2-80% in room air), raised blood pressure (140/100 mmHg), normal heart rate (87 beats per minute) and had bilateral pedal edema. On chest auscultation, bilateral wheezes, and basal crepitations were heard, without any murmurs.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT)

3.1 | Case 1

Chest radiograph showed bilateral minimal pleural effusion. Transthoracic echocardiography (TTE) showed severe left ventricular systolic dysfunction, dilated left atrium (LA), moderate to severe mitral regurgitation (MR), severe tricuspid regurgitation (TR), moderate pulmonary artery hypertension (PAH) and reduced ejection fraction that is <25%. ECG showed T wave inversion in leads V1–V4 and aVL (Figure 1). Serum N-terminal pro-b-type natriuretic peptide (NT-proBNP) was 10,897 pg/mL (Normal <300). With the diagnosis of PPCM, she was managed with fluid restriction, diuretics, beta blockers, angiotensin receptor blockers (ARB), bromocriptine, and antibiotics. Repeat TTE done on the 12th day of puerperium showed EF of 30%. However, she had three episodes of syncopal attack on the 19th puerperal day which was probably due to orthostatic hypotension.

3.2 | Case 2

In the chest radiograph, there were infiltrates in the bilateral lower zone and blunting of bilateral costophrenic angles (Figure 2). Serum NT-proBNP was 1678 pg/mL. TTE showed: dilated left atrium/left ventricle, mild TR, moderate pulmonary artery hypertension, left ventricle systolic dysfunction with an ejection fraction of 40%, and severe mitral regurgitation. She was then managed with the diagnosis of PPCM with left pyelonephritis. She was kept in a propped-up position, daily BP charting and renal function test was done and was managed with fluid restriction, diuretics, beta blocker, angiotensinogen converting enzyme inhibitors (ACEIs), bromocriptine, and antibiotics.

3.3 | Case 3

ECG showed S1Q3T3 (right heart strain) pattern (Figure 3). Serum NT-proBNP was 7269 pg/mL. Renal function test (RFT)was deranged with urea 49 mg/dL, and

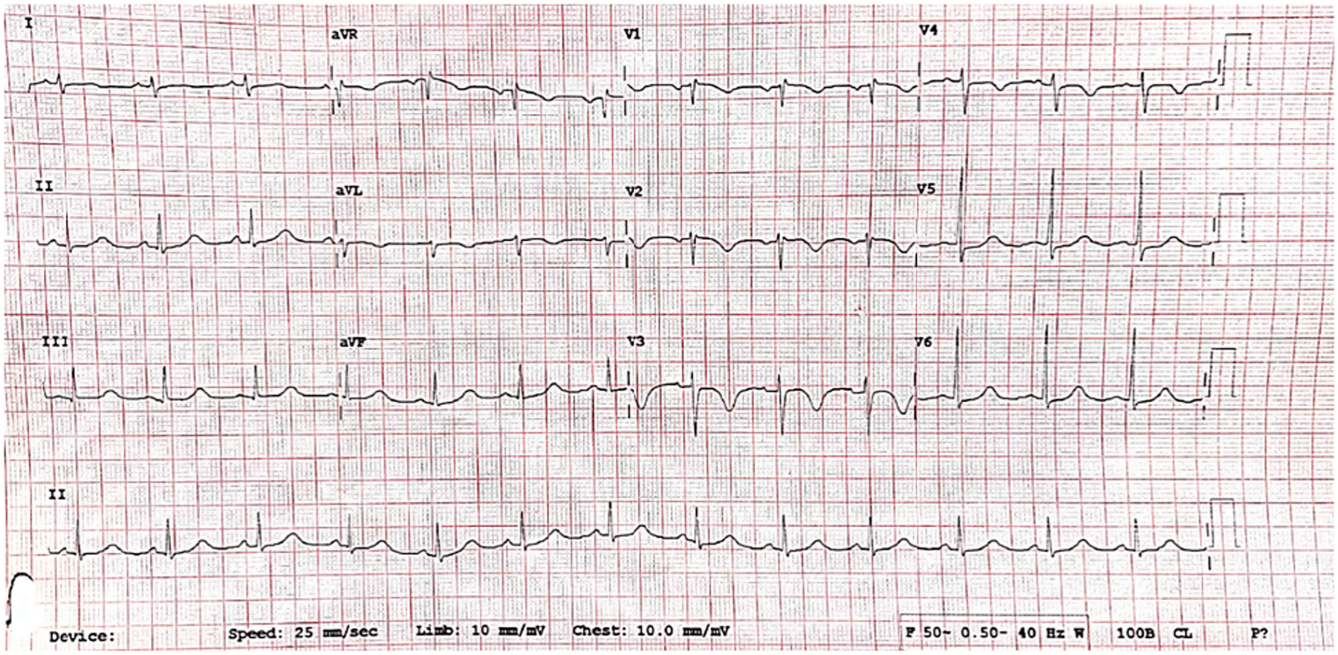

FIGURE 1 ECG of case 1 showing T wave inversion in leads V1-V4 and aVL.

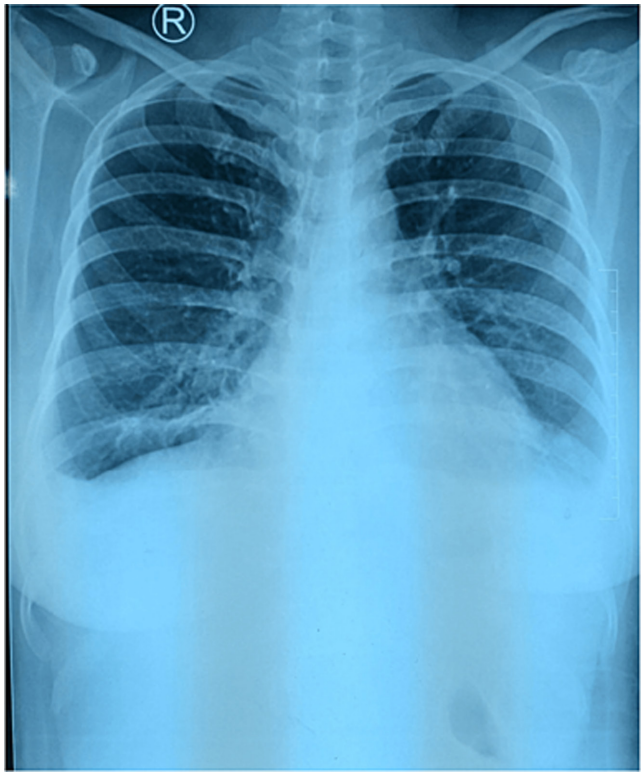

FIGURE 2 Chest X-ray of case 2 showing infiltrates in the bilateral lower zone and blunting of bilateral costophrenic angles.

creatinine 2.2 mg/dL with normal Na+/K+. TTE showed: dilated left atrium and left ventricle, global hypertrophy, left ventricular systolic dysfunction grade II with an ejection fraction of 30%, and mild mitral regurgitation. Pulmonary embolism was unlikely using modified Wells criteria (score 1.5) and negative D-dimer level (0.20 mg/L). She was then managed under the diagnosis of PPCM with acute kidney injury: fluid and salt restriction, input/output charting, daily RFT, BP charting, propped-up position, diuretics, bromocriptine, and ACEIs. TTE repeated 9 days later showed mild hypokinesia of basolateral LV and LVEF of 40%.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

4.1 | Case 1

The patient was symptomatically better and discharged on the 22nd puerperal day with oral ARB and bromocriptine and with close follow-up with cardiology and obstetrics and gynecology clinic. Follow-up examination at 6 months showed stable cardiomyopathy and echocardiography showed improved ejection fraction of 50%–55%.

4.2 | Case 2

The patient was symptomatically better and was discharged on the 14th day of puerperium with empagliflozin, torsemide, carvedilol, and cefixime with advice to follow up in cardiology and obstetrics and gynecology clinic. Her follow-up echocardiogram at 6 months showed normal ejection fraction of 60%.

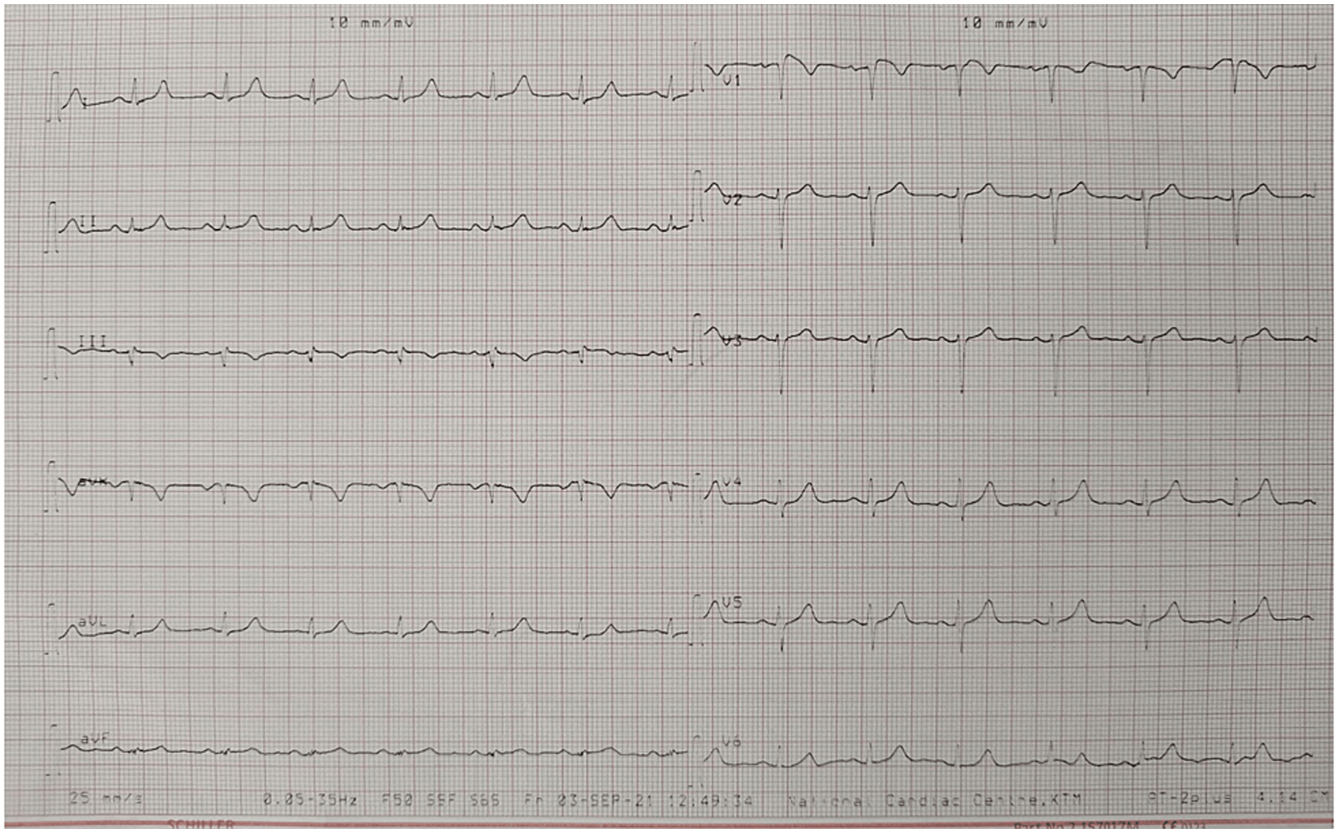

FIGURE 3 ECG of case 3 showing S1Q3T3 (right heart strain) pattern.

4.3 | Case 3

The patient was discharged on ACEIs and bromocriptine which was continued for 2 months. She was followed up for 6 months where she was symptomatically better and her RFTs were normal.

5 | DISCUSSION

PPCM is a rare disease, often dilated cardiomyopathy of late pregnancy or early postpartum period without another known cause of heart failure.[5–7] PPCM has been defined as a heart failure that occurs in the last month of pregnancy or up to 5 months postpartum with left ventricular systolic dysfunction (left ventricular ejection fraction (LVEF) <45% or fractional shortening <30%, or both).[1]

PPCM has been described in less than 0.1 percent of pregnancies with variable outcomes that is, complete recovery or progression to severe cardiac failure and even sudden cardiac death.[8]

The etiology of PPCM is unclear, however, several risk factors have been identified so far. Among them, genetic predisposition, viral myocarditis, stress-activated cytokines, abnormal immune response to pregnancy, maladaptive response to hemodynamic stresses of pregnancy, excessive prolactin excretion, and prolonged tocolysis have been suggested as possible factors.[7,8]

The hormone prolactin, in particular, is cleaved by oxidative stress into the smaller antiangiogenic subfragment, 16-kDa prolactin, which may cause endothelial damage and cause PPCM. Release of endothelial microparticles loaded with active compounds such as microRNAs is also induced by 16-kDa prolactin. This may impair the metabolism of cardiac myocyte and therefore leads to the manifestation of PPCM.[7] Although exact etiology could not be identified in our cases, PPCM in case two might have been precipitated by pyelonephritis.

Since most of the clinical presentations are similar to symptoms of advanced pregnancy, diagnosis can be missed. Majority of patients present with typical features of heart failure such as dyspnea, orthopnea, cough and chest pain, hemoptysis, and paroxysmal nocturnal dyspnea.[5,9] Likewise, two of our three cases presented with symptoms of heart failure like dyspnea, orthopnea, and dry cough during the first week of puerperium. However, case two presented with puerperial pyrexia and acute pyelonephritis which might have precipitated PPCM.

Physical examination usually reveals tachycardia, tachypnea, raised jugular venous pressure, displaced apical impulse, right ventricular heave, S3, and S4 gallop, murmurs

of mitral and TR, rales, hepatomegaly and edema.[8,9] This was consistent with our cases who also had bilateral lower limb edema and bilateral basal lung crepitation.

PPCM is still a diagnosis of exclusion because there isn't a particular test to confirm it.[10] PPCM can be investigated through several diagnostic modalities that include electrocardiography, chest radiography, echocardiography, and lab investigations such as BNP. ECG shows sinus rhythm, often with non-specific ST-segment or T-wave abnormalities which help in identifying cardiac origin of dyspnea. Chest radiography most often reveals indications of heart failure such as cardiomegaly, pulmonary congestion, and pleural effusions.[8] This finding was in keeping up with our cases as the chest radiograph of cases two and three showed pulmonary edema, and that of case one showed pleural effusion. Patients with acute PPCM usually have elevated plasma concentrations of natriuretic peptides which may help during screening of cardiac origin of dyspnea.[10] However, measurement of natriuretic peptides does not differential PPCM from other cardiomyopathies.[10] The diagnosis is confirmed by the echocardiographic findings of left ventricular systolic dysfunction.[1] Likewise, in our study, all cases had elevated natriuretic peptides. In case three, D-dimer test was done which came out to be normal, thus pulmonary embolism was ruled out using modified Weils criteria. In all three cases, echocardiography showed LVEF less than 45%. Thus, PPCM was diagnosed according to the Working Group on PPCM of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) guideline.[2]

The differential diagnosis includes other causes of heart failure such as familial dilated cardiomyopathy, previous myocarditis, drug or toxin-induced cardiomyopathy, adult congenital heart disease, valvular disease, and pulmonary arterial hypertension among others.[6,7]

Acutely presented PPCM is similarly managed as acute heart failure of other etiologies.[10] Women in the peripartum period should be managed by a multidisciplinary approach including cardiologists, intensivists, obstetricians, neonatologists, anesthesiologists, and cardiac surgeons.[7,10] Fluid and salt restriction is the mainstay of volume management, and loop diuretics may be added for symptomatic pulmonary or peripheral edema, taking care to avoid overdiuresis during pregnancy to prevent placental hypoperfusion.[8] Beta-blockers, hydralazine, and nitrates are also indicated for patients with PPCM. However, angiotensin-converting enzyme (ACE) inhibitors, ARB, angiotensin receptor-neprilysin inhibitors (ARNI), ivabradine and mineralocorticoid receptor antagonists (MRAs) are contraindicated because of the possibility of teratogenicity; however after delivery of baby and patient is stable hemodynamically, standard therapy for heart failure can be applied.[7,11]

Prolactin blocker bromocriptine which blocks the detrimental pathophysiological pathway of 16kD-prolactin mediated PPCM, has beneficial effects on LVEF and mortality in women with severe acute PPCM.[7] The multicentric randomized bromocriptine study by Hilfiker–Kleiner et al. compared short- term (1 week: bromocriptine, 2.5 mg)_and long-term (8 week: 5 mg for 2 weeks followed by 2.5 mg for 6 weeks) bromocriptine treatment in patients with severe PPCM (EF <35%). Both short- and long-term bromocriptine treatment were associated with full recovery of LVEF and low mortality.[12] Bromocriptine treatment should be accompanied by anticoagulation at least in prophylactic dosages due to risk of thromboembolic events (although at higher dosages). Therapy for PPCM has been proposed as BOARD label: Bromocriptine, Oral heart failure therapies, Anticoagulants, vasoRelaxing agents, and Diuretics. [7]In our study, all the three cases developed PPCM during post-partum period, thus treated with ACEIs, ARBs, diuretics and bromocriptine which improved LVEF of all three cases. Prolonged bromocriptine treatment (2.5 mg twice daily for 2 weeks, then 2.5 mg once daily for another 6 weeks) was given to all three cases. Acute pyelonephritis might be the precipitating factor of PPCM due to increased overload to the failing heart as observed in case two. Thus, case two was treated with antibiotics for acute pyelonephritis along with treatment for standard heart failure.

Important complications include severe heart failure, cardiogenic shock, arrhythmias, thromboembolic events, and death.[9] Moreover, there is an increased risk of PPCM in subsequent pregnancies with increased morbidity and mortality, particularly in women with persistent left ventricular systolic dysfunction after the first pregnancy.[13] In our experience, case three developed acute kidney injury during the disease because of hypoperfusion of the kidney.

Recovery typically occurs between 3 and 6 months postpartum, but there may be a delayed recovery as late as 48 months postpartum due to several factors such as delayed diagnosis, higher NYHA functional class, black ethnicity, LV thrombus, multiparity, and coexisting medical illnesses.[5] Mortality rate due to PPCM ranges from 0% to 9% in the white population of the USA to up to 15% in African Americans and in populations in South Africa and Haiti. Recurrence risk of PPCM in subsequent pregnancy is 30%–50%. Thus, even if the LVEF is normalized, because of the risk of recurrence with a new pregnancy, patients should be counseled regarding the subsequent pregnancy while patients with LVEF not normalized should be discouraged of subsequent pregnancy.[11] All three cases of our study recovered symptomatically and had improved LVEF >50% at six-month follow-up echocardiogram. Early recovery in our study could be due to the early diagnosis, All cases were counseled about the recurrence in new pregnancy.

To conclude PPCM despite being rare should be considered in women presenting with features of left ventricular failure in the later months of pregnancy or within 5 months of delivery. Acutely presenting PPCM that is managed as acute heart failure of other etiologies, can have devastating consequences if not diagnosed and treated early.

AUTHOR CONTRIBUTIONS

Sabin Banmala: Conceptualization; data curation; writing – original draft; writing – review and editing. **Shila Awal:** Conceptualization; data curation; writing – original draft; writing – review and editing. **Lokendra Bata:** Conceptualization; data curation; supervision; validation; writing – original draft; writing – review and editing. **Priya Adhikari:** Writing – original draft; writing – review and editing. **Sarita Basnet:** Writing – original draft; writing – review and editing. **Babita Chaudhary:** Writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article and its supplementary information files.

ETHICS STATEMENT

This is a case report; therefore, it did not require ethical approval from ethics committee.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor- in- chief of this journal on request.

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