CASE REPORT

Peripartum cardiomyopathy in a woman with preeclampsia with twin pregnancy

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Accepted 2 November 2014

SUMMARY

A 27-year-old nulliparous Japanese woman with twin pregnancy developed preeclampsia at gestational week (GW) 26. Cardiac function was checked regularly as women carrying twins with preeclampsia are expected to have increased risk of peripartum cardiomyopathy (PPCM). Although conventional parameters including blood pressure, proteinuria, platelet count and liver function did not indicate early delivery, gradual worsening of left ventricular ejection fraction (LVEF) to 44% and plasma brain-type natriuretic peptide level of 254 pg/mL suggested impending PPCM and a need for early delivery at GW 32. A nadir LVEF value of 35% on postpartum day (PPD) 3 followed by a value of 49% on PPD 32 was seen in this patient with PPCM. This case highlights the risk of PPCM among women with preeclampsia carrying twins and the role of pregnancy termination in the clinical course of PPCM.

BACKGROUND

As peripartum cardiomyopathy (PPCM) is a rare complication occurring in 1/3000–4000 women,¹ diagnosis is often delayed, resulting in major adverse events such as death or the necessity for heart transplantation.^{2–3} Multifetal pregnancy and hypertensive disorders in pregnancy are consistent and prominent risk factors for PPCM, accounting for 7–15% and 15–68% of all PPCM cases, respectively,³ although these generally account for less than 1.5% and 5% of all pregnancies, respectively. Therefore, we began this prospective study in April 2014, examining consecutive women treated at our institution. The study protocol was approved by our institutional human research committee (013-0262 dated on 4 April 2014) and conformed to the tenets of the Declaration of Helsinki. Within 3 months after the beginning of this project, we encountered a woman with twin pregnancy who developed preeclampsia and subsequently developed PPCM. This was the 16th twin pregnancy and the 2nd case of preeclamptic twin pregnancy at the time of diagnosis of PPCM in this study period. We present the details of this patient, as this information may be useful to avoid irreversible PPCM. The patient gave informed consent for publication.

CASE PRESENTATION

A 27-year-old nulliparous Japanese woman with monochorionic diamniotic twin pregnancy developed proteinuria (protein to creatinine ratio (P/Cr, mg/mg) in spot urine = 0.74) and hypertension (148/93 mm Hg) at gestational weeks (GW) 25^{–5/7} and 26^{–5/7}, respectively. The patient's blood pressure

remained stable, ranging from 129/83 to 158/101 mm Hg in the absence of antihypertensives, and she did not develop thrombocytopenia ($<130 \times 10^9/L$, liver dysfunction (monitored by aspartate transaminase), renal dysfunction (monitored by serum creatinine), or clinical symptoms, such as dyspnoea. However, her P/Cr increased to 4.8 at GW 32^{–2/7} when emergency caesarean section was performed because left ventricular ejection fraction (LVEF; evaluated in apical two-chamber and four-chamber views using modified Simpson's rule) and plasma brain-type natriuretic peptide (BNP) level worsened gradually to 44% and 254 pg/mL, respectively, suggesting impending PPCM (figure 1). The patient gave birth to two otherwise healthy premature female twins weighing 1672 and 1078 g with 1 and 5 min Apgar scores of 3 and 9, and 4 and 9, respectively, by caesarean section. Although a nadir LVEF value of 35% was seen on postpartum day (PPD) 3, the patient left the hospital on PPD 21 with LVEF of 48% and BNP of 117 pg/mL. The LVEF and BNP recovered to 49% and 56 pg/mL on PPD 32. The patient's height was 160 cm and pre-pregnancy body weight and those on the day of delivery and PPD 32 were 53, 78.5 and 50 kg, respectively. Other treatments given to this patient included intravenous or subcutaneous heparin for the prophylaxis of thrombosis for 21 days (from 3 days prior to delivery until PPD 21), oxygen (2–5 L/min) inhalation with nasal mask for pulmonary hypertension for 14 days (from 4 days prior to delivery until PPD 9), nifedipine (20–80 mg/day) initiated on PPD 2, continuous intravenous nicardipine (1.0–2.8 mg/h) on PPD 3 to PPD 5, continuous intravenous nitroglycerine (1.0 mg/h) on PPD 3 to PPD 9 for the decreased LVEF (35%), and addition of enalapril (2.5–7.5 mg/day) to nifedipine on PPD 9 and thereafter.

DISCUSSION

This case showed gradual worsening and improvement of LVEF and BNP levels ante-partum and post partum, respectively, suggesting that termination of pregnancy functioned as treatment for cardiac dysfunction in this patient. To the best of our knowledge, this is the first case in which cardiac function was serially monitored before and after development of PPCM.

Although preeclampsia developed in this case, its severity did not necessarily indicate early delivery based on current clinical guidelines. However, our study protocol, including prospective echocardiography and determination of plasma BNP level, indicated that she was developing PPCM in the absence of clinical symptoms other than oedema, which is

To cite: Umazume T, Yamada T, Yamada S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-208186

Figure 1 Perinatal changes in maternal body weight, left ventricular ejection fraction (LVEF), left ventricle end-diastolic diameter (LVDd) and blood brain-type natriuretic peptide (BNP) level. Emergency caesarean section was performed at gestational week 32. The LVEF of 44%, LVDd of 59 mm and BNP level of 254 pg/mL soon before caesarean section became 35%, 57 mm and 116 pg/mL on postpartum day (PPD) 3, 48%, 57 mm and 117 pg/mL on PPD 21, and 49%, 53 mm and 56 pg/mL on PPD 32, respectively.

also frequently seen in preeclampsia.⁴ Although evidence was lacking regarding the appropriate time at which medical intervention, such as early delivery, alters the natural clinical course of PPCM, concern regarding irreversible PPCM prompted us to conduct an early caesarean section at GW 32 based on the report by Elkayam,³ and our previous experience in a case of PPCM⁵ that required a long time for cardiac function to recover even with prompt delivery after diagnosis of PPCM.

Our previous PPCM case was a singleton pregnancy and the patient exhibited marked gestational weight gain (from 38.5 kg at GW 12 to 69.1 kg on the day of delivery at GW 34), especially in the late stage of pregnancy, significant proteinuria (P/Cr of 0.36) in the absence of hypertension, oedema, dyspnoea, cardiomegaly on chest X-ray (cardiothoracic ratio of 63%), LVEF of 27% and plasma BNP level of 2024 pg/mL at diagnosis of PPCM and caesarean section.⁵ Although the patient recovered, her LVEF was 39% at postpartum month 9⁵ and it took 18 months for LVEF to reach $\geq 50\%$. As this case suggested that delivery earlier than the actual delivery at GW 34 may have contributed to a more prompt recovery of cardiac dysfunction, the early delivery at GW 32 was performed in the present case with findings of a gradual decrease in LVEF to 44% (LVEF $<45\%$ is the proposed criterion for diagnosis of PPCM⁶) concomitant with elevation of BNP to 254 pg/mL. Indeed, the present case exhibited more prompt recovery of left ventricle (LV) function than that seen in the previous case.

As gestational weight gain and blood volume expansion are greater in twin than singleton pregnancies,^{7,8} cardiac overload may be more likely to occur and the serum precursor protein BNP (NT-proBNP) level in the late stage of pregnancy is significantly higher in twin than singleton pregnancies.⁹ In addition, plasma BNP level is higher for hypertensive than for normotensive pregnant women.¹⁰ We recruited and examined a total of 52 pregnant women consisting of 36 singleton and 16 twin pregnancies in this prospective study begun in April 2014, including five singleton and two twin pregnancies complicated with preeclampsia; the present case was the first to be diagnosed as having PPCM. Although our observations may be incidental at present (prevalence of PPCM in women with singleton vs twin pregnancy complicated by hypertension, 0% (0/5) vs 50%

Figure 2 The first case of twin pregnancy complicated with preeclampsia in our prospective study. This case with a negative test result on dipstick testing for urinary protein at GW 30^{-3/7} developed proteinuria (protein to creatinine ratio (P/Cr, mg/mg), 8.2) and hypertension (141/83 mm Hg) at GW 32^{-3/7} and 32^{-5/7}, respectively. Massive proteinuria (P/Cr, 16.1) and gradual decline in the platelet count to $112 \times 10^9/L$ required an early delivery at GW 33^{-5/7} in this patient. GW, gestational week; BNP, brain-type natriuretic peptide; LVEF, left ventricular ejection fraction; LVDd, left ventricle end-diastolic diameter; PPD, postpartum day.

(1/2)), previous studies suggested that women with preeclampsia with twin pregnancies are at a markedly elevated risk of developing PPCM.³ As shown in figure 2, our first case of preeclamptic twin pregnancy also exhibited a transient cardiac depression peripartum, although changes in parameters were within normal range except for BNP. The present case suggested that there may have been many PPCM women with twin pregnancies in whom procedures for diagnosis of PPCM were not performed, but PPCM resolved spontaneously or remained asymptomatic.

However, delay of diagnostic procedures may lead to delay of delivery causing severe morbidity and mortality in some cases.^{2,3,5} As twin pregnancies account for 1% of all pregnancies, and hypertensive disorders occur in approximately 25% of all twin pregnancies,¹¹ the prevalence of twin pregnancy with hypertensive disorders is approximately 2–3/1000 pregnancies. Women with twin pregnancies exhibiting hypertensive disorders may be candidates for monitoring of LV function. However, insufficient evidence is available at present to confirm whether or not this policy leads to improved outcome in women with preeclampsia with twin pregnancies.

Learning points

- ▶ Peripartum cardiomyopathy (PPCM) is likely to develop in women with preeclampsia with twin pregnancies based on previous reports.
- ▶ Cardiac function was prospectively monitored in a woman with preeclampsia with twin pregnancy.
- ▶ Antenatal gradual worsening of cardiac function, PPCM soon after birth, and improvement of cardiac function post partum were observed.
- ▶ This case may be the first case in which cardiac function was serially monitored before and after development of PPCM.
- ▶ Early delivery may have worked as a preventive treatment for an irreversible PPCM in this patient.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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