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and cervix of Krukenberg tumor

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- Urogynaecology training in South East Asia (SEA) and Asia

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- Problem diagnostic of Krukenberg tumor
- Characteristics of Peripartum Cardiomyopathy (PPCM) pregnancy and preeclampsia in Dr Soetomo Hospital, Surabaya, Indonesia, 2014-2016

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CASE REPORT:**Characteristics of Peripartum Cardiomyopathy (PPCM) pregnancy and preeclampsia in Dr Soetomo Hospital, Surabaya, Indonesia, 2014-2016**Dibya Arfianda¹, Budi Wicaksono¹, Khanisyah Erza Gumilar^{1*}, Andrianto²¹Department of Obstetrics & Gynecology, Faculty of Medicine, Airlangga University, Dr Soetomo Hospital, Surabaya, Indonesia. ²Department of Cardiology and Vascular Medicine, Faculty of Medicine, Airlangga University, Dr Soetomo Hospital, Surabaya, Indonesia.**ABSTRACT**

Objectives: to present data on the characteristics of pregnancy with PPCM and PE. Management of patients with PPCM is almost the same as for patients with acute or chronic heart failure, which uses drug therapy. PPCM and preeclampsia (PE) are two related diseases, although not directly. Both have similar pathophysiological mechanisms.

Case Report: We present 25 pregnancy cases with PPCM at Dr. Soetomo Hospital within 3 years. Data were collected from January 2014 to December 2016, consisting of 5 PPCM cases and the other 20 cases were PPCM with PE cases.

Conclusion: Pregnancy with PPCM-PE has higher morbidity than PPCM only. The diagnosis of PPCM should be established immediately if heart failure symptoms are found in the third trimester and the patient has risk factors, such as age >30 years, multigravida, obesity, and multiple pregnancy.

Keywords: Peripartum cardiomyopathy; preeclampsia

ABSTRAK

Tujuan: Memaparkan data mengenai karakteristik kehamilan dengan PPCM dan PE. Tatalaksana pasien dengan PPCM hampir sama dengan pasien gagal jantung akut atau kronis, yaitu dengan medikamentosa. PPCM dan preeklampsia (PE) merupakan dua penyakit yang terkait meskipun tidak secara langsung. Keduanya mempunyai mekanisme patofisiologi yang serupa.

Laporan Kasus: Dua puluh lima kasus kehamilan dengan PPCM di RSUD Dr. Soetomo dalam kurun waktu 3 tahun (Januari 2014 – Desember 2016). Sebanyak 5 kasus dengan PPCM dan 20 kasus lainnya PPCM disertai PE.

Simpulan: Kehamilan dengan PPCM-PE mempunyai morbiditas yang lebih tinggi dibanding PPCM murni. Penegakan diagnosis PPCM perlu dilakukan segera bila ditemukan simtom gagal jantung yang muncul pada trimester ketiga dan mempunyai faktor resiko, seperti usia >30 tahun, multigravida, obesitas, dan kehamilan ganda.

Kata kunci: kardiomiopati peripartum; preeklampsia

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INTRODUCTION

Based on the definition of Heart Failure Association of the European Society Cardiology Working Group on PPCM in 2010, Peripartum Cardiomyopathy (PPCM) is idiopathic cardiomyopathy with heart failure secondary to left ventricular systolic dysfunction in the final trimester of pregnancy without previous cardiac dysfunction. The incidence of PPCM in the United States varies greatly between 1 in 4,000 live births, while in countries in Africa and Asia it is almost the same, 1 in 1,000 and 1 in 6,000 live births.

PPCM can be diagnosed using echocardiography where there is a decrease in systolic function of the left ventricle below 45%, accompanied by heart decompensation symptoms, such as shortness of breath during daily activities or at rest. Management of PPCM is almost the same in cases of acute and chronic heart failure, which the use of drug therapy.

We found association between PPCM and preeclampsia (PE). This might be related to the same pathophysiology between the two diseases. Data in Dr. Soetomo Hospital from January 2014 to December 2016 showed 25 cases with PPCM, 5 of which comprised PPCM only and 20 other cases of PPCM with PE. This case report presents characteristics of pregnancy data with PPCM and PE.

CASE REPORT

We found that the number of deliveries between January 2014 and December 2016 was 3,405. Cases of pregnancy with PPCM had a percentage of 0.73%. Regarding maternal age, the majority of the patients suffering from PPCM/PPCM-PE was between 30-39 years with a total of 15 (60%) cases. Distribution of parity in PPCM/PPCM-PE cases was 11 (44%) primigravida and 14 (56%) multigravida. The number between primigravida and multigravida was not much different. All cases of PPCM/PPCM-PE were referral cases, with 15 (60%) pregnancy cases and 10 (40%) postpartum cases. Pregnancy with PPCM/PPCM-PE cases all occurred in the third trimester. Pregnancy with gestational age of 28-36 weeks was in 12 cases and above 37 weeks 3 cases.

DCFC complications varied between DCFC II to IV with 14 (56%) cases of DCFC II, 4 (16%) cases of DCFC III and 7 cases (28%) of DCFC IV. PPCM accompanied by PE showed a higher number compared to PPCM only. LVEF from ECG results ranged from 25% -45%, which was as many as 23 cases and 2 cases below 25%. LVEF was below 25% in one case of PPCM only and one in PPCM-PE. In almost all cases of

PPCM/PPCM-PE the method of delivery was perabdominal in as many as 23 (92%) cases and 2 (8%) vaginal delivery. Among the two vaginal delivery cases, one was vaginal delivery with vacuum extraction.

The most frequent indications of hypertensive labor, both in antepartum and postpartum referral cases, were caused by pulmonary edema, consisting of 17 (68%) cases. Other obstetrics indications were multiple pregnancy, malposition, arrest of descend, fetal distress and Intrauterine Growth Restriction (IUGR). Perinatal output of a total of 28 babies born in PPCM pregnancy cases with or without preeclampsia was birth weight (BBW) of > 2500 g in 7 (25%) cases, BBW 2000 g - 2500 g in 14 (50%) cases, and BBW <2000 g as many as 7 (25%) cases.

The first minute Apgar Score (AS) of infants in PPCM delivery with or without preeclampsia, showed 5 infants with AS <4 (17.9%), 9 infants with AS 4-6 (32.1%), and 6 infants with AS > 6 (21.4%), while data for 8 other infants (28.6%) were not obtained. Data on contraceptive use or sterilization showed that IUD use was 10 (40%) and sterilization was 6 (24%) cases. Patients without contraception were found in 9 cases (36%). Two (8%) cases of antepartum patients and 7 (28%) post-partum cases did not use contraceptives, of which 3 cases were PPCM and 6 cases of were PPCM with preeclampsia.

Maternal mortality in pregnancy with PPCM in Dr. Soetomo Hospital for 3 years (January 2014 - December 2016) occurred in 2 cases. The cause of death in these 2 cases was cardiogenic shock. Both cases occurred at the age above 30 years, multigravida parity and with severe preeclampsia. In both cases the ejection fractions were 43% and 23%. The method of labor in both cases was cesarean section (Table 1).

Table 1. Maternal mortality in the PPCM-PE case

Name/Age	Cause of Death	Complications		EF
		Obstetrics	Non-Obstetrics	
AN/ 34 yrs	Cardiogenic shock	<ul style="list-style-type: none"> • Malposition • Uterine Myoma • Severe eclampsia 	<ul style="list-style-type: none"> • PPCM • DCFC II • AKI 	43%
LI/ 35 yrs	Cardiogenic shock	<ul style="list-style-type: none"> • Severe eclampsia • ALO 	<ul style="list-style-type: none"> • PPCM • DCFC II • Ischemic stroke • Lupus Nephritis • AKI 	23%

Diagnosis

Peripartum Cardiomyopathy (PPCM)

PPCM is not easily detected clinically because the symptoms are similar to normal pregnancies in the last trimester. Symptoms in PPCM are fatigue, palpitations, nocturia, tightness during activity and when lying down, leg edema and orthostatic hypotension. The diagnosis of PPCM can be made by measuring the Left Ventricle Ejection Fraction (LVEF), which is less than 45%, without being based on previous heart disease, and occurs in the third trimester up to 5 months postpartum. Some techniques for measuring LVEF include Echocardiography (ECG), MRI, CT, Gated Myocardial Perfusion Single-Photon Emission Computed Tomography (SPECT), Gated Myocardial Perfusion Positron Emission Tomography (PET). The LVEF measurement which is considered feasible is the ECG.

According to the American Heart Association (2017), DCFC can be classified as follows: Class I: No symptoms, Class II: Mild symptoms during activity or symptoms appear during strenuous activities, Class III: Symptoms appear with minimal activity, and Class IV: Symptoms appear at rest.

Preeclampsia (PE)

Table 2 shows the criteria for PE diagnosis based on ACOG in 2013.

Table 2. Diagnostic criteria for preeclampsia

- Systolic blood pressure = 140 mmHg or diastolic blood pressure = 90 mm Hg at two examinations, at least 4 hours after the first examination in previously normotensive pregnancy over 20 weeks.
- If the systolic blood pressure = 160 mmHg or diastolic blood pressure = 110 mmHg, a repeat examination can be done a few minutes later.
AND
- Proteinuria = 0.3 g in a 24-hour urine specimen or protein/creatinine ratio = 0.3 (mg/mg) (30 mg/mmol).
- Or dipstick = 1+ if quantitative measurements are not available.
OR
- Systolic blood pressure = 140 mmHg or diastolic blood pressure = 90 mm Hg at two examinations at least 4 hours after the first examination in a previously normotensive pregnancy above 20 weeks with new onset as follows (with or without proteinuria):
 - Platelet count <100,000/microL.
 - Serum creatinine >1.1 mg/dL (97.2 micromol/L) or twice as much without previous kidney disease.
 - Liver transaminase increases at least twice the upper limit of normal concentration based on the reference value of the local laboratory.
 - Pulmonary edema
 - Cerebral or visual symptoms (headaches that do not improve with administration of analgesics, blurred vision, scotomata).

Management

Peripartum Cardiomyopathy (PPCM)

Management of pregnant women with PPCM is almost the same as acute or chronic heart failure patients, ie. the provision of oxygen and assisted ventilation if needed, optimization of preload, hemodynamic support with inotropic drugs and vasopressors if needed.

Preeclampsia (PE)

The management of PE patients with gestational age more than or equal to 37 weeks is per vaginal or per-abdominal pregnancy termination according to obstetric indications. If the gestational age is below 37 weeks, conservative treatment can be done by monitoring symptoms, blood pressure, laboratory markers, especially serum creatinine, liver function, and platelets. For the fetus, ultrasound monitoring can be performed to assess fetal well-being.

DISCUSSION

Characteristics of PPCM pregnancy with or without PE in Dr. Soetomo Hospital in 2014-2016

Some factors that cause susceptibility of PPCM in pregnancy are age 30 and more, which is in accordance with the theory put forward by Arany & Elkayam in 2016, that the risk factors are the pregnancy age of more than 28 weeks or in third trimester,¹ which is also in accordance to the theory of Hilfiker-Kleiner et al in 2017, in patients with obesity, and in multiple pregnancies.²

The incidence of preeclampsia in PPCM patients

Of the total 25 cases of PPCM patients who were referred to Dr. Soetomo Hospital in this case report, 20 cases (80%) were PPCM with PE, 18 cases (90%) were cases of severe preeclampsia, 1 case (5%) of eclampsia, and 1 case (5%). Data shows the incidence of PE in PPCM by 80%, which shows a correlation between PE and PPCM. This confirms the theory proposed by Bello that Soluble Vascular Endothelial Growth Factor Receptor-1 (sVEGFR-1) of the placenta triggers PPCM, especially in the third trimester.

Description of ejection fraction in cases of PPCM and PPCM with PE

LVEF in the case of PPCM is one of the prognostic predictors of PPCM. LVEF below 25% indicates higher morbidity and mortality.^{3,4,5} There were two cases with LVEF below 25%. In one case the patient died with LVEF of 23% caused by cardiogenic shock with comorbidities of PEB and Lupus Nephritis. Another

case was PPCM only with multiple pregnancies with LVEF 24%. The mean value of LVEF from all cases was 37.24.

Correlation between albumin value and pulmonary edema in PPCM/PPCM-PE cases

In preeclampsia hypoalbumin often occurs due to the process of systemic vascular spasm. This increases the secretion of angiotensin and damages vascular endothelial cells and increases its permeability, resulting in the leakage of plasma towards the tissue.⁶ Hydrostatic pressure and oncotic pressure also have an important role in intra- and extravascular plasma balance. This is in accordance with the "Starling forces", where high intravascular hydrostatic pressure causes the transfer of plasma from intravascular to the interstitial tissue. Furthermore, oncotic pressure is maintained by proteins, especially albumin. Low oncotic pressure will cause the transfer of plasma from intravascular to interstitial tissue.⁷ This results in acute lung edema (ALO) in preeclampsia. This is different from ALO due to cardiogenic factors, which in this case report occurred in cases with PPCM. ALO in PPCM is caused by cardiac decompensation to pump blood and this has effect on the lungs.

Table 3. Albumin levels in PPCM cases with ALO and PPCM-PE with ALO

Albumin	PPCM + ALO	PPCM + PE + ALO	Total	Correlation coefficient (r)	p
< 3.0	0	10	10	0.286	0.318
≥ 3.0	1	6	7		

Table 3 shows that the correlation between albumin and ALO levels that occurred in PPCM and in PPCM with PE do not have statistical significance. The correlation value of 0.286 shows a positive correlation with weak correlation strength and not clinically significant.

Characteristics of PPCM patients in intensive care unit (ICU)

Data shows that the shortest treatment in the ICU is 1 day and the longest is 19 days. One case did not need a ventilator aid and was treated in the Cardiology Ward. The case was diagnosed with PPCM without preeclampsia with LVEF of 41%. ICU treatment duration of 1-3 days in PPCM and PPCM+PE was in 4 and 14 cases, respectively. Furthermore, treatment for 4-6 days in PPCM+PE was in 3 cases. The duration of ICU treatment in PPCM+PE was more than seven days in 3 cases, ie. 6 days, 12 days and 19 days. The average length of treatment in the ICU was 3.7 or around 4 days.

Table 4. Duration of treatment at the ICU in cases of PPCM and PPCM with PE

Length of intensive treatment (days)	PPCM	PPCM + PE	TOTAL
1-3	4	14	18
4-6	0	3	3
>7	0	3	3

The use of a ventilator in the ICU patients was found in 14 cases and 10 other cases did not use ventilator. Another case was not treated at the ICU (Table 5).

Table 5. The use of ventilator in ICU patients

Ventilator Use	PPCM	PPCM + PE	TOTAL
Yes	1	13	14
No	4	6	10

Data on the duration of ventilator use for a total of 24 patients treated in the ICU showed there were 8 cases for 1-3 days, 4 cases for 4-6 days, and 2 cases for more than 6 days. Of the two cases, one ventilator was used for 12 days and one for 19 days (Table 6).

Table 6. Duration of ventilator use in ICU patients

Duration	PPCM	PPCM + PE	TOTAL
1-3 days	3	5	8
4-6 days	2	2	4
>6 days	0	2	2

Pharmacological therapy in PPCM patients

Pharmacological therapy used must consider the effects of toxicity on the fetus. The target of therapy is to improve hemodynamics, reduce symptoms of heart failure and optimize long-term outcomes. The PPCM drugs used in Dr. Soetomo Hospital for antepartum patients can be seen in Table 7.

Furosemide is a diuretic that is often used to reduce preload. At the 2012 AHA Guidelines, which we quoted from Johnson-Coyle, it was mentioned that low-molecular-weight heparin should be used if EF <35% is obtained.⁸ In the management of patients at Dr. Soetomo Hospital, the use of LMWH or warfarin is only for intracardiac thrombus detected by echocardiography.

Table 7. Management of pharmacological therapy in PPCM at Dr. Soetomo Hospital

PPCM antepartum management at Dr Soetomo Hospital
Beta-blocker
Bisoprolol
Carvedilol
Vasodilator
Methyldopa (Alpha-2 Adrenergic Receptor Agonist)
Nifedipine (Calcium Channel Antagonist)
Digoxin
Serum level monitoring
Diuretic
Spironolactone
Furosemid
PPCM postpartum management at Dr Soetomo Hospital
ACE Inhibitor
Captopril
Ramipril
Beta-Blocker
Bisoprolol
Vasodilator
Isosorbide dinitrate
Diuretic
Spironolactone
Furosemid

Table 8. Management of pharmacological therapy in PPCM.⁸

PPCM antepartum management
Beta-blocker
Carvedilol
Extended-release metoprolol
Vasodilator
Hydralazine
Digoxin
Serum level monitoring
Thiazide diuretic
Hydrochlorothiazide
Diuretic loop use can be considered
Low-molecular-weight frim heparin if EF < 35%
PPCM postpartum management
ACE Inhibitor
Captopril
Enalapril
Ramipril
Lisinopril
If intolerant to ACE Inhibitor → Angiotensin-receptor blocker
Candesartan
Valsartan
If intolerant to both, consider nitrate/hydralazine
Diuretic loop
Furosemide IV or oral based on creatinine clearance
GFR > 60 mL/min per 1.73 m ² , furosemid 20-40 mg each 12-24 hrs
GFR < 60 mL/min per 1.73 m ² , furosemid 20-80 mg each 12-24 hrs
Vasodilator
Hydralazine
Isosorbide dinitrate
Aldosterone antagonist
Spironolactone
Eplerenone
B-blocker as in antepartum therapy
Warfarin if EF < 35%

CONCLUSION

PPCM and preeclampsia are two pregnancy diseases that are related indirectly because they have the same pathophysiological mechanism. This pathophysiology is related to the antiangiogenic factor sFlt-1 produced by the placenta, which shows an increase in sFlt-1 preeclampsia. Vasculo-hormonal hypothesis states that increased prolactin in the third trimester causes PPCM and can be aggravated by sFlt-1. Data obtained in this study confirmed this hypothesis that higher morbidity is found in pregnancies with PPCM-PE compared to PPCM only. The diagnosis of PPCM should be established immediately if heart failure symptoms are found in the third trimester and the patient has risk factors such as age >30 years, multigravida, obesity, and multiple pregnancies.

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