Spontaneous initiation of parturition after two-days-course of lung maturation and controversies in management of pre-eclampsia: A case report

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Abstract. There have been many controversies on how we should treat patients with preeclampsia, how and when we should deliver the baby. This case report is purposed to evaluate one case of spontaneous parturition which ended up with vaginal delivery in one patient with preterm severe preeclampsia. We evaluate the best management which result in the best outcome for the patient and her baby. This is the case of Mrs N, 34 years old in 33-34 weeks gestational age with severe preeclampsia. When she came the blood pressure was 190/120 mmHg, protein urine +3. The blood pressure was controlled with nifedipine. The patient was given magnesium sulphate, N-acetyl cystein, and vitamin C as antioxidants. We were succeeded in completing two days of lung maturation with dexamethasone in order to give the best outcome for the baby. However, at the end, after two days of lung maturation, the patient started to enter the active phase of parturition spontaneously without labor of induction. We hypothesized that the high level of corticosteroid stimulated by the fetus initiated the process of labor. Patient delivered baby boy, 1300 grams, Apgar Score 7/8 that breathed spontaneously in room air. The patient's condition was improving after parturition. Nifedipine, magnesium sulphate was considered the best management in pre-eclampsia. Short course of lung maturation with dexamethasone was also considered to be beneficial for the baby. However, the initiation of parturition and the use of antioxidant as well as n-acetyl cystein in this patients was under debatable discussion.

Key words: pre-eclampsia, lung maturation, parturition, dexamethasone, magnesium sulphate

Introduction

Preeclampsia is a multisystem disorder, characterized by gestational hypertension and proteinuria. It is a common and serious complication in pregnancy. It occurs as much as 10% of pregnancies and poses a significant risk to both the fetus and the mothers. It can be accompanied by maternal symptoms, abnormal maternal laboratory results, or intra-uterine growth restriction. Various hypotheses as to the origin of preeclampsia have been explored but it is difficult to study for several reasons. One limitation is due to the fact that preeclampsia clinically present in the second and third trimester of pregnancy but actually originate early in pregnancy.

The pathophysiology of preeclampsia involved the process of implantation, endothelial dysfunction, systemic inflammatory response, oxidative stress, angiogenetic factors, as well as genetic predisposition. The improper placental implantation contributed to surface molecule expression, systemic inflammatory response, endothelial disfunction, as well as oxidative stress. The clinical course of severe preeclampsia is characterized by progressive deterioration if delivery is not pursued. But in the case of premature patient less than 34 weeks of gestational age with severe preeclampsia, delivery would result in worse prognosis for the fetus due to lung immaturity. Expectant management to induce fetal lung maturity is therefore an option for severe preeclampsia patient less that 34 weeks of gestational age. This paper discuss the essential and benefit of expectant management in patient with severe preeclampsia and preterm fetus in order to improve the outcome for mother and her baby.

Materials and Methods

This is the case report of Mrs N, 34 years old referred by Fauziah Hospital, Bireun, Aceh because of severe preeclampsia and uncontrolled blood pressure. She was in her first pregnancy at 33-34 weeks of gestational age after getting married one year ago. There was no history of using contraceptives and no history of infertility. She went to antenatal care at midwives regularly, once a month and there was no history of hypertension before pregnancy and during her antenatal visit. Her last visit was yesterday when her midwife found her blood pressure was elevated, 170/110 mmHg and referred her to Fauziah General Hospital. Because of there was no intensive care unit and her blood pressure was uncontrolled, she was referred to Zainoel Abidin General Hospital. On admission, there was

no symptoms of severe headache, epigastric pain, nausea, vomiting, and blurred vision. No complaint of vaginal discharge, water broke, vaginal bleeding and contraction. She still felt active movement of her baby. Her menstrual period was unremarkable and regular.

On physical examination, her weight was 50 kg, her height was 160 cm, body mass index was 19,5 kg/m^2. Her systolic blood pressure was 190 mmHg and diastolic blood pressure was 120 mmHg. Her respiratory rate was 20 times per minute and her heart rate was 88 times per minute. General examination was normal, auscultation of lung and heart was within normal limit. There was edema on her lower extremities. On obstetrics examination, the fundal height was 25 cm, head presentation singleton fetus, fetal heart beat was 148 beats per minute and regular, there was no contraction, estimated fetal weight was 1700 grams. On vaginal examination, the cervix was firm, 3 cm thickness, no dilatation, the fetal head was floating from pelvic inlet. Non-stress test cardiotocography was reassuring with baseline 140 beats per minute, variability 5-25 beats per minute, acceleration was positive, no deceleration, and active fetal movement. On ultrasound findings, there was singleton head presentation live fetus, biparietal diameter was 8.13 cm, head circumference was 26.7 cm, abdominal circumference was 21.3 cm, ratio of head circumference to abdominal circumference was 1.25, femur length was 5.5 cm, ratio of systolic to diastolic umbilical artery was 3.00, Amniotic fluid index was 9.5, estimated fetal weight was 1500 gram, placenta was in anterior uterine corpus (Figure 1 and 2)

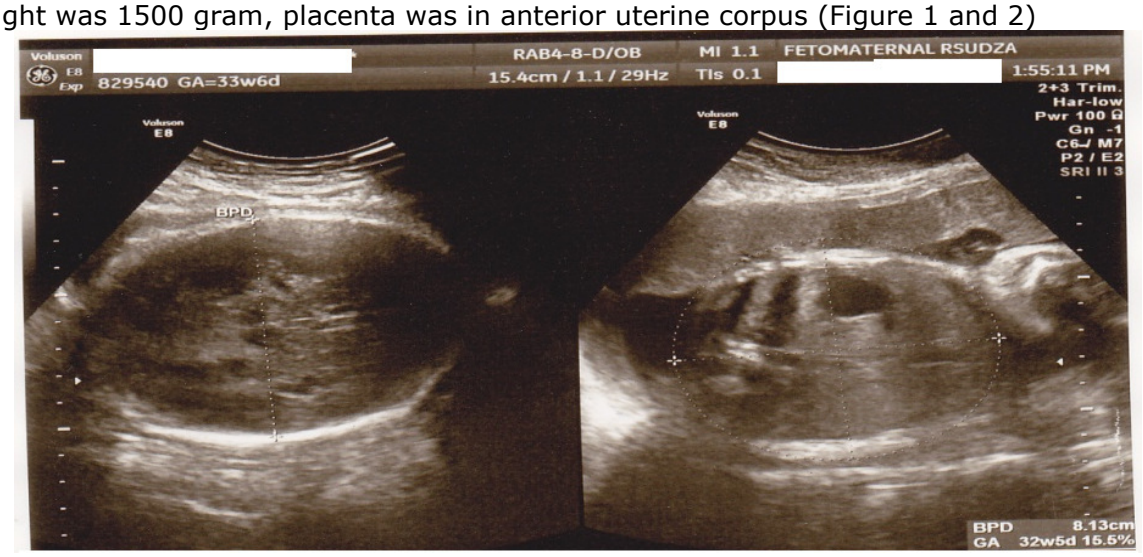

Figure 1. The ultrasound finding showed the elevated ratio of head circumference to abdominal circumference 1.25 (>1) which was typical of suspected growth retarded fetus

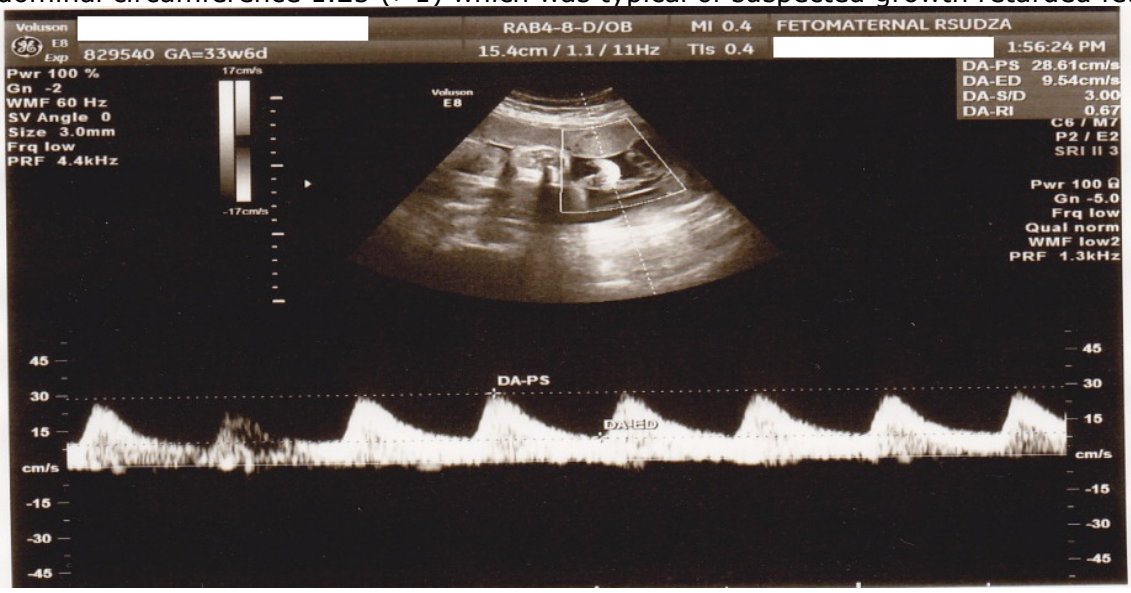

Figure 2. The umbilical artery Doppler showed a slight increase in ratio of systolic to diastolic of 3.00 (≥ 3.00) indicating slight elevated resistance in umbilical artery

Laboratory examination revealed hemoglobin 13.8 g/dl, hematocrite 37%, leucocyte count 9.300/µL, trombocyte count 112.000/µL, random blood glucose 114 mg/dl, ureum/creatinine: 29/0.7, aspartate aminotransferase (AST) 51 U/L, alanine aminotransferase (ALT) 22 U/L, and qualitative protein urine +3.

We diagnosed this patient as gravid 1 33 weeks 6 days of gestational age, suspected growth restricted singleton live head presentation fetus, not in labor with severe preeclampsia. We managed this patient by giving antihypertension with oral nifedipine 10 mg per 6 hours and strictly monitor her blood pressure every 30 minutes to keep the target systolic blood pressure 140-155 mmHg and diastolic blood pressure between 90-105 mmHg. We also gave magnesium sulphae as seizures prophylaxis intravenous loading dose 4 g over 20 minutes, followed by maintenance dose of 1 g/hour. We managed this patient expectantly to give steroid for fetal lung maturity enhancement for 48 hours. The steroid given was dexamethasone 6 mg per 12 hours for 48 hours. We also delivered antioxidant for this patient vitamin C 400 mg every 12 hours intravenous and N-acetylcystein 600 mg every 8 hours per oral.

During the observation the blood pressured was in controlled range, urine output and fluid balance was fine. There was no worsening symptoms of severe preeclampsia, no deterioration of fetal condition. We succeed in completing 48 hours of lung maturation and tried to induce the labor to terminated the pregnancy for this patient. But, after 48 hours, the patient started to feel the contraction and the labor was initiated spontaneously without induction. In 12 hours the patient delivered 1300 g baby boy, 41 cm, with a 1-minute APGAR score of 7 and a 5-minute APGAR score of 8 who breathed spontaneously in room air. Ballard Score was equal to 32-34 weeks of gestational age. The baby was admitted to neonatal intensive care unit for 18 days. After 18 days treated in neonatal intensive care this small for gestational age baby was allowed to go home in fine condition (Figure 3 and 4)

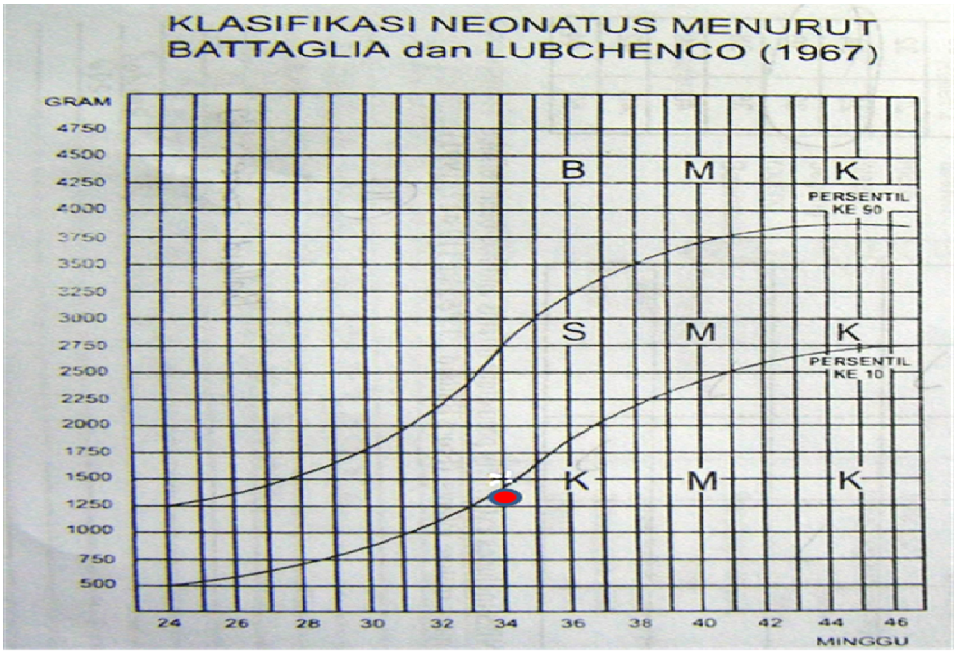

Figure 3. According to Battaglia and Lubchenco curve, the baby was small for gestational age, confirming the condition of growth restricted baby in this patient

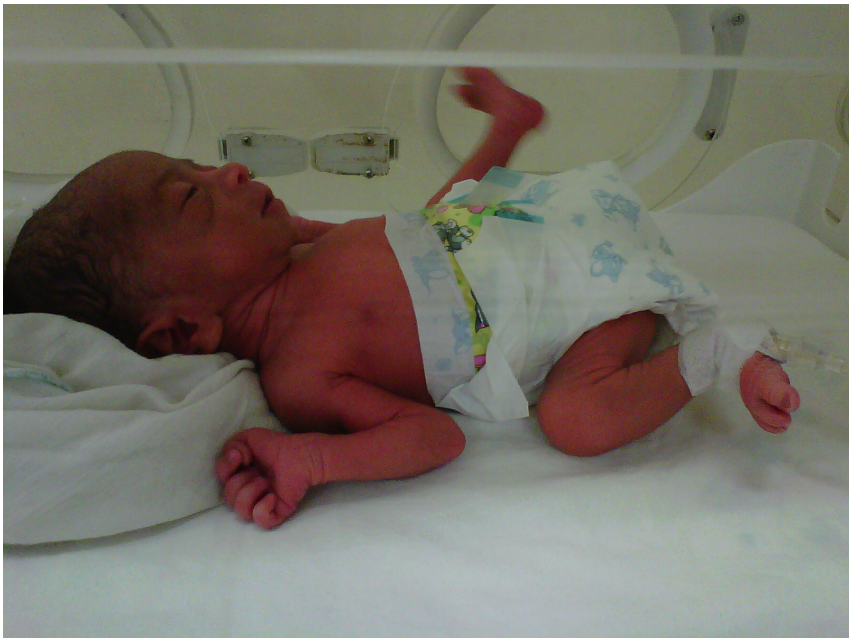

Figure 4. This 1300 gram small for gestational age baby boy moved vigorously and breathed spontaneously in the room air.

Result and Discussion

The risk factors of severe preeclampsia in this patient were advanced maternal age and primigravida. The mechanism was related to inappropriate implantation with a disturbed utero-placental interaction. This was shown by the occurrence of severe preeclampsia in the beginning of third trimester which was characterized by asymmetric intra-uterine growth retarded fetus. Abnormal implantation manifested in disturbance of optimal growth in the last trimester. According to Sibai et al there was a place for expectant management of severe preeclampsia before 34 weeks of gestation in order to give time for lung maturation induction. However, the expectant management was controversial in this patient because of the occurrence of suspected fetal growth restriction. Many studies showed that patients with suspected fetal growth restriction and/or oligohydramnions are not typically considered to be candidates for expectant management beyond completion of antenatal corticosteroid therapy due to increased risk of adverse outcomes of perinatal death and morbidity. This patient was suspected having fetal groth restriction characterized by estimated fetal weight below 10 th percentile in 33 weeks 6 days of gestational age (1500 g; <1600 grams), abdominal circumference below 5th percentile in 33 weeks 6 days of gestational age (21.3; <25.0 cm), elevated ratio of head circumference to abdominal circumference of 1.25 (> 1), slightly increased resistance in Doppler study of umbilical artery (ratio of systolic to diastolic umbilical artery =3), and slightly diminished amniotic fluid index (AFI= 9.5 cm; <10 cm). Because the availability of fetal surveillance in our hospital we were challenging the risk of delaying delivery in this patient in order to give chance for lung maturation induction by corticosteroid.

This patient with severe preeclampsia and suspected fetal growth restriction should be hospitalized to confirm the diagnosis, evaluate maternal and fetal condition, and strict monitoring for rapid progression of the disease. Uncontrollable blood pressure, worsening symptoms of severe preeclampsia, occurrence of pulmonary edema, abruptio placentae, disseminated intravascular coagulation, significant and new-onset renal dysfunction (serum creatinine ≥ 1.5 mg/dl), HELLP syndrome, and abnormal fetal surveillance should typically be delivered by vaginal or cesarean delivery as appropriate. There was no such worsening maternal and fetal condition mentioned above in this patient so we believed that two days expectant management to induce lung maturation would give benefit to the fetus. Antenatal corticosteroid treatment resulted in less frequent respiratory distress syndrome, neonatal death, and intraventricular hemorrhage. In this patient, her baby breathed spontaneously in room air and there was no evidence of respiratory distress syndrome. It was still

unknown whether it was caused by the induction of fetal lung maturation by dexamethasone treatment that we gave or because this growth restricted fetus already accelerated his lung maturation by producing adrenal glucocorticoid secretion due to his response to stressful environment. However, prolonging pregnancy to induce fetal lung maturation for 48 hours was recommended as long as the monitoring maternal and fetal condition was available. The decision regarding expectant management for giving induction of fetal lung maturation should be individualized in center where continuous maternal monitoring and daily fetal surveillance are available.

Management policy of severe preeclampsia is to start antihypertension to control blood pressure and magnesium sulfate intravenously to prevent convulsions. Nifedipine was short acting calcium channel blocker proven to be safe in pregnant women without adverse effect. It is simply given initially of 10 mg orally every 6 hours and can be increased as needed up to 20 mg every 4 hours (40-120 mg/day). The aim of antihypertensive therapy is to keep systolic blood pressure between 140-155 mmHg and diastolic blood pressure between 90 and 105 mmHg. If there is recurrent persistent severe hypertension increased from the target range despite adequate or maximum dose of antihypertensive therapy, delivery should be pursued after maternal stabilization. In this patient, nifedipine given 10 mg orally every 6 hours was proven to be effective in controlling the blood pressure in the target range. The Magpie randomized controlled trial collaborative group recommended the use of magnesium sulfate as seizure prophylaxis since it halves the risk of eclampsia and proves to be safe to the mother or baby if it is used in short term. In this patient, magnesium sulphate was delivered intravenously 4 g initially and maintained at the dose of 1 g/hour. The magnesium sulphate was given for 24 hours. No deterioration of maternal and fetal condition observed in this patient supporting the use o magnesium suphate as the safe prophylaxis for eclampsia.

Small scales studies indicated supplementing vitamin C as antioxidant resulted in beneficial effect of biochemical endpoint. Preeclampsia was characterized by oxidative stress and systemic inflammatory reaction suggesting the role of antioxidant such as vitamin C and N-acetylcystein in preeclampsia. According to Cochraine review, the use of antioxidant in preeclampsia remained inconclusive. Some authors suggest the use of antioxidant as the prophylaxis of pregnancy which was delivered earlier before conception in order to give the better result since the indicators of oxidative stress was found before pregnancy. Some other authors suggest that delivery of antioxidant in established third trimester preeclampsia in pregnancy was not associated with adverse maternal and fetal effect and worth to try. In this patient we used vitamin C and N-acetylcystein for antioxidant. There was no compliant for the use of antioxidant in this patient even though several studies reported the complaints of gastrointestinal and abdominal pain from the patients treated with vitamin C as antioxidant therapy.

There were several ways involved in the initiation of parturition. The mechanism involved were corticotrophin-releasing hormone (CRH) from maternal secretion, CRH production by placenta, CRH production stimulated by the fetus, membrane activation, myometrial contraction, progesterone withdrawal, cervical softening, inflammation activation and the onset of labor. This patient was in severe preeclampsia under expectant management using corticosteroid to induce fetal lung maturation. It was in her 34 weeks of gestational age. The initiation of parturition was suspected because of stimulation of the fetal pituitary by CRH increases corticotropin production and, consequently, the synthesis of cortisol by the fetal adrenal gland and maturation of the fetal lungs. In turn, the rising cortisol concentrations in the fetus further stimulate placental CRH production. The maturation of the fetal lungs as a result of increasing cortisol concentrations is associated with increased production of surfactant protein A and phospholipids, both of which have proinflammatory actions and may stimulate myometrial contractility through increased production of prostaglandins by fetal membranes and the myometrium. Feto placental unit aminopeptidase was activated and promoted the initiation of parturition. This patient was given steroid for lung maturation. It was probably that cortisol synthesized by the fetus stimulated feto placental unit which activated CRH production resulting in miometrial contraction, inflammation, cervical softening, membrane activation, and initiation of labor spontaneously.

Conclusion

The management of preeclampsia comprised of maintaining no progression of worsening symptoms for mother and fetus as well as expectant management of severe preeclampsia before 34 weeks of gestation to improve perinatal outcome. This case report suggests that lung maturation, antihypertensive treatment with nifedipine, magnesium sulphate therapy was beneficial in improving the outcome for neonates and mother.

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