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Expectant management of superimposed preeclampsiaon chronic hypertension at the onset of 22 weeks'gestation: A case report

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Conservative management in chronic hypertensive women superimposed with preeclampsia poses a threat of grave maternal complications, but may not improve perinatal survivals particularly in cases with preeclampsia in early gestations. This report presents a case of surviving baby after expectant management although the pregnancy complicated with superimposed preeclampsia at the onset of pre-viable gestational age. A 35-year-old Thai pregnant woman, underlying with pregestational diabetes mellitus class F and chronic hypertension, was diagnosed as superimposed preeclampsia at 22 weeks of gestation. She refused elective termination and continued her pregnancy until 32 weeks of gestation. Cesarean section was performed and delivered a female baby with birth weight of 1,655 grams and Apgar scores of 10 at both 1 and 5 minutes. The mother was discharged against advice on day 6 after delivery. Complications developed in the newborn included respiratory distress syndrome, patent ductus arteriosus, pneumonia, sepsis, hyperbilirubinemia, necrotizing enterocolitis and bronchopulmonary dysplasia. However, the baby could be taken home at the age of 68 days and her development was within normal limit at the age of 16 months.

Keywords: *Chronic hypertension, diabetes mellitus, expectant management, superimposed preeclampsia.*

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วราลักษณ์ ยมะสมิต, สุรสิทธิ์ ชัยทองวงศ์วัฒนา. การดูแลรักษาแบบประคับประคองในภาวะครรภ์เป็นพิษแทรกซ้อนความดันโลหิตสูงเรื้อรังตั้งแต่อายุครรภ์ 22 สัปดาห์: รายงานผู้ป่วย. จุฬาลงกรณ์เวชสาร 2555 พ.ย. – ธ.ค.; 56(6): 731 – 8

การดูแลรักษาแบบประคับประคองในหญิงที่มีความดันโลหิตสูงเรื้อรังแทรกซ้อนด้วยภาวะครรภ์เป็นพิษอาจก่อให้เกิดภาวะแทรกซ้อนที่อันตรายต่อมารดา แต่อาจไม่ช่วยให้ทารกรอดชีวิตได้ โดยเฉพาะอย่างยิ่งรายที่มีภาวะครรภ์เป็นพิษตั้งแต่อายุครรภ์น้อย ๆ รายงานนี้แสดงผู้ป่วยที่ได้ผลลัพธ์ปริกำเนิดที่ดีหลังการดูแลรักษาแบบประคับประคอง แม้การตั้งครรภ์จะมีภาวะครรภ์เป็นพิษแทรกซ้อนเริ่มก่อนอายุครรภ์ที่ทารกจะสามารถเลี้ยงรอดได้ ผู้ป่วยเป็นหญิงตั้งครรภ์อายุ 35 ปี มีโรคประจำตัวคือเบาหวานกลุ่มเอฟ และความดันโลหิตสูงเรื้อรัง ได้รับการวินิจฉัยว่ามีภาวะครรภ์เป็นพิษแทรกซ้อนที่อายุครรภ์ 22 สัปดาห์ ผู้ป่วยปฏิเสธการยุติการตั้งครรภ์และได้ตั้งครรภ์ต่อจนมีอายุครรภ์ 32 สัปดาห์ จึงรับการผ่าตัดคลอด ได้ทารกเพศหญิงน้ำหนักแรกเกิด 1,655 กรัม และคะแนนแอปการ์เท่ากับ 10 ที่ 1 และ 5 นาที มารดาปฏิเสธการรักษาและกลับบ้านในวันที่ 6 หลังคลอด ภาวะแทรกซ้อนของทารกหลังคลอดได้แก่ กลุ่มอาการหายใจลำบาก เส้นเลือด ductus arteriosus ไม่ปิด ปอดบวม การติดเชื้อในเลือด ตัวเหลือง ลำไส้อักเสบ และโรคปอดเรื้อรัง อย่างไรก็ตาม ทารกกลับบ้านได้เมื่ออายุ 68 วัน และมีพัฒนาการอยู่ในเกณฑ์ปกติที่อายุ 16 เดือน

คำสำคัญ: *ความดันโลหิตสูงเรื้อรัง, เบาหวาน, การดูแลรักษาแบบประคับประคอง, ภาวะครรภ์เป็นพิษแทรกซ้อน.*

Preeclampsia is a common pregnancy complication that remains a major cause of maternal and perinatal morbidity.[1] Traditional management of severe preeclampsia or superimposed preeclampsia on chronic hypertension focusing on maternal safety is expeditious delivery.[2] However, delivery at a time remote from term is associated with an increased risk of adverse neonatal outcome and long-term morbidity from prematurity. Several reports[3 - 11] have demonstrated that expectant management in patients at less than 32 - 34 weeks of gestation have resulted in benefit to the neonatal outcome without jeopardizing maternal safety. However, conservative management in cases with a gestational age of lower than 23 weeks could not enhance perinatal survival, but pose a threat of severe maternal complications e.g. eclampsia, HELLP syndrome or even death.[5, 12 – 17] This case report describes a case of optimal perinatal outcomes after prolongation of a pregnancy complicated with superimposed preeclampsia on chronic hypertension at the onset of 22 weeks of gestation.

Case report

A 35-year-old Thai pregnant woman, G_3P_1, was complicated with insulin dependent diabetes mellitus (IDDM) with diabetic nephropathy and chronic hypertension. She had had a miscarriage of her first pregnancy and cesarean delivery at term due to breech presentation of her second pregnancy. She had had IDDM for 20 years with poor glycemic control. Her fasting plasma glucose level had never been less than 200 mg/dL (11.1 mmol/L). Diabetic nephropathy was discovered at 10 weeks of current gestation with 24-hour urine protein of 5.7 g. Her baseline serum creatinine was 0.9 mg/dL (80 μmol/L). Ophthalmic evaluation in the first trimester showed no diabetic retinopathy. Chronic hypertension had been diagnosed 2 months before her current pregnancy. Her blood pressure was well controlled, ranging from 130/90 mmHg to 140/90 mmHg, with methyldopa 750 mg/day and amlodipine 10 mg/day. During the first trimester, an endocrinologist tried to adjust her insulin dosage but her plasma glucose failed to keep within normal limit.

At 22 weeks of gestation, the patient was admitted because she revealed a very high blood pressure of 200/110 mmHg without any symptoms except edema. Laboratory tests showed an elevation of serum creatinine of 1.2 mg/dL (106 μmol/L) but a hematocrit, platelet count, aspatate aminotransferase, alanine aminotransferase, lactate dehydrogenase, uric acid, and coagulogram were normal. The 24-hour urine protein revealed a value of 9.7 g. Multidisciplinary team included maternal-fetal medicine specialists, endocrinologists, nephrologists, cardiologists and neonatologists were consulted to approach the patient. Because her blood pressure abruptly elevated despite good adherence on antihypertensive agents together with increasing proteinuria, superimposed preeclampsia on chronic hypertension was diagnosed. Counseling as well as detailed information regarding severity of the disease, chance for perinatal survival and possible serious maternal complications were fully addressed to the parents. Option to terminate the pregnancy was raised. However, they decided to continue the pregnancy. The methyldopa dosage was twice increased and amlodipine was changed to prazosin 2 mg/day. Her plasma glucose remained within an unaccepted level although the insulin dosage was increased as high as Humalin N 70 units in the

morning and 34 units in the evening plus Humalin R 30 units in the morning and 28 units in the evening. Since the patient complained of decreasing visual acuity, an ophthalmic re-evaluation found nonproliferative diabetic retinopathy (NPDR). The fetal anatomy survey at mid trimester and serial growth were normal. A course of dexamethasone (6 mg intramuscularly administered 12 hour apart for 4 doses) was administered at 24 weeks of gestation to promote fetal lung maturity. Intravenous insulin was infused and adjusted with closely plasma glucose monitoring to prevent acute metabolic complications such as diabetic ketoacidosis which may be aggravated by corticosteroid administration. At 25 weeks of gestation, the patient refused to be monitored in the hospital after her blood pressure returned to an acceptable level; nevertheless, her plasma glucose values were still uncontrolled.

At 29 weeks of gestation, her blood pressure rose to 170/100 mmHg. The admission laboratory tests showed a serum creatinine of 1.3 mg/dL (115 μmol/L) otherwise the rest were normal. Her 24-hour urine protein excretion increased to 17.3 g. The ultrasonographic estimated fetal weight was 995 grams that was slightly less than the 10th centile for 29 weeks of gestation (1,089 grams). Umbilical arteries and middle cerebral arteries Doppler studies as well as the fetal biophysical profile were normal. Seventy-five milligrams per day of hydralazine was added as the third antihypertensive agent but her blood pressure could not be well controlled. The patient was managed expectantly with extensive monitoring until 32 weeks of gestation. Because of uncontrolled blood pressure, cesarean section with tubal resection was performed after detailed counseling was given. A female neonate with a birth weight of 1,655 g was delivered with Apgar scores of 10 at 1 and 5 minutes. Her postpartum course was uneventful. Although the glucose level and blood pressure could not be controlled, the patient was discharged against advice on the sixth day postpartum. The newborn's appearance and weight correlated with her gestational age. She developed respiratory distress syndrome complicated with pneumothorax from resuscitation which required assisted ventilation for 29 days. Other morbidities presenting in this neonate included patent ductus arteriosus, pneumonia, sepsis, hyperbilirubinemia, necrotizing enterocolitis and bronchopulmonary dysplasia. She improved with indomethacin, antibiotics, phototherapy, intravenous nutrition, and diuretics and was discharged on the 68th day of age with a body weight of 2,630 g.

After delivery, she failed to follow-up regularly. Her glycemic control remained poor. She developed proliferative diabetic retinopathy (PDR) and diabetic foot resulted in toe amputation at 8 and 15 months after delivery. Her blood pressure was round 140-155/80-90 mmHg and her serum creatinine was 1.6 mg/dL (141 μmol/L). At the age of 16 months, the weight of her baby was 7.2 kilograms. She had feeding problems and occasional lower respiratory infections. However, her development was within normal limit.

Discussion

It is generally accepted that expeditious delivery is justified if severe preeclampsia or superimposed preeclampsia on chronic hypertension develops beyond 34 weeks of gestation. Earlier delivery in gestation, nevertheless, may increase the

risk of perinatal death or adverse neonatal outcomes from prematurity.

Randomized trials[3,4] have reported that expectant management in cases with severe preeclampsia between 28 and 34 weeks of gestation statistically significantly lengthened the gestation. Such management improved neonatal outcomes but there was no increase in maternal complication. Expectant management included prescribing magnesium sulfate for seizure prophylaxis, controlling hypertension by pharmacological agents, administering corticosteroid to enhance fetal lung maturity and extensive maternal and fetal monitoring at a tertiary medical center. To minimize the maternal risks, careful selection of patients who were appropriate for this mode of treatment was crucial. Patients with complications from medical diseases or additional obstetric complications, such as chronic renal disease, IDDM, growth-restricted or non reassuring fetal status, etc. were not good candidates for the treatment approach.

Later several studies[5 - 11] have confirmed benefit of expectant management in women with severe preeclampsia or superimposed preeclampsia. However, the number of reported women with preeclampsia earlier than 25 weeks of gestation treated expectantly remains limited.[5,8,12 - 15] The perinatal death rate ranges from 71% to 100% with few babies surviving without any handicap.[5,14 – 16] Only 27 pregnant women (28 fetuses) who had conservative management before 23 weeks have been reported.[5,15,17] There was no perinatal survivors, but the rates of maternal complications including eclampsia, HELLP syndrome, or death were reported as high as 30 - 67%.[5,15,17]

The diagnostic criteria for superimposed preeclampsia on chronic hypertension includes a sudden increase of proteinuria or blood pressure or a platelet count of less than 100,000/mm^3 in women with hypertension and proteinuria before 20 weeks of gestation.[18] Although the 24-hour urine protein collection in this case increased from 5.7 to 9.7 g, it might be difficult to distinguish superimposed preeclampsia from the natural progression of diabetic nephropathy during pregnancy. Gordon M *et al*.[19] has described how diabetic nephropathy with a baseline 24-hour urine protein excretion more than 3 g might show an increase of 5.6 $\pm$ 1.7 g during 20 - 28 weeks of gestation. However, the abrupt increase of blood pressure as high as 200/110 mmHg that had been previously well controlled in this patient might differentiate the diagnosis of superimposed preeclampsia on chronic hypertension from hypertension resulting from worsening diabetic nephropathy since the high blood pressure consequence from the latter condition seldom shoot abruptly.[20]

This case was actually not eligible for temporizing management because she manifested very early onset superimposed preeclampsia before 23 weeks of gestation. In addition, IDDM and diabetic nephropathy with baseline 24-hour proteinuria exceeding 3 g as presented in this case was associated with increased risk of poor pregnancy outcomes, e.g., low birth weight, preeclampsia or preterm delivery. The possible serious maternal morbidities from conservative management were thoroughly discussed; nonetheless, the parent decided to continue the pregnancy. After close maternal and fetal surveillance, the pregnancy was

prolonged for 72 days without serious immediate maternal complications. Unfortunately, NPDR developed during expectant management. The rate of development and progression of diabetic retinopathy during pregnancy ranged from 16% to 85%.[21] As for IDDM, 26% of women with no retinopathy have developed mild NPDR as occurred in this case during gestation.[21] Various factors presented in this case influenced her worsening retinopathy, e.g., the pregnantcy itself, the long duration of her diabetes, poor glycemic control before and during pregnancy and the presence of coexisting hypertension. Nevertheless, one-half of patients had complete regression and one-third had partial regression after delivery.[21] Although the rate of regression of diabetic retinopathy in the postpartum period was high, the importance of careful follow-up was thereafter emphasized. However, her compliance was poor. NPDR has rapidly progressed to be PDR 8 months after delivery. Moreover, she developed diabetic vasculopathy and ended up with amputation. Diabetic nephropathy was another concern for this woman since she had 24-hour urinary proteinuria was as high as 17.3 g from the beginning of the 3rd trimester. A fourth of women with diabetic nephropathy will develop end-stage renal failure at a mean of 6 years after pregnancy.[22] The tendency of the progression of diabetic nephropathy in this patient should be rather poor because rapid worsening in other end organs were observed and her high blood pressure, one of the factors which may accelerate renal failure, was suboptimal controlled.

Premature infants face increased risk of mortality and various complications including temperature instability, respiratory distress syndrome, apnea, hypoglycemia, seizures, kernicterus, feeding difficulties and periventricular leucomalacia.[23] Furthermore, the survivors from these infants increase risk of long term sequels, such as neurodevelopmental delay and chronic lung diseases. Although the newborn in this case report born at 32 weeks gestation, she still needed to be treated due to several complications in the neonatal intensive care unit for a month.

To our knowledge, no report has yet detailed the success of expectant management of superimposed preeclampsia on chronic hypertension at an onset earlier than 23 weeks' gestation. The premature neonate without growth restriction could survive with reasonable maternal safety. However, bronchopulmonary dysplasia presented itself and caused occasional lower respiratory infections and delayed growth. Follow-up is needed to determine long term neonatal outcomes.

Although surviving baby after expectant management of superimposed preeclampsia on chronic hypertension at onset of 22 weeks of gestation have been described in this patient, it does not encourage routinely undergoing temporizing management in women with similar clinical profiles because the maternal risks seemingly outweigh the fetal benefits. If the patient chooses to prolong pregnancy, extensive counseling and heightened surveillance with multidisciplinary care at the tertiary center must be provided.

All authors, hereby, report no conflicts of interest.

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