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Discrepancy between Non-stress Test Result and Umbilical Artery Doppler Study in a Pregnancy Complicated by Diabetes; A Case Report

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Pregestational diabetes is a well-known risk factor for perinatal mortality, and regarded as an important cause of stillbirth. Unfortunately, more than half of stillbirths remain unexplained. Nevertheless, there is no consensus regarding the optimal timing and content of antepartum testing in pregnancies complicated by diabetes. A 32-year-old primigravida presented with diabetes diagnosed during pregnancy. Antenatal fetal surveillance tests including nonstress test, biophysical profile, and Doppler waveforms of umbilical arteries were performed twice weekly, beginning at 32 weeks gestation. At 37^{+4} weeks' gestation, a discrepancy in the surveillance test results arose when reversed end-diastolic flow in the umbilical arteries was seen, despite a reactive nonstress test. A male baby was delivered by cesarean section. The umbilical arterial pH at delivery was 7.171. Antenatal fetal surveillance in pregnancies complicated by diabetes should include evaluation of Doppler waveforms in the umbilical vessels, regardless of the presence or absence of maternal vasculopathy.

Key Words : Pregestational diabetes, Unexplained fetal demise, Antenatal fetal surveillance

Pregestational diabetes is a well-known risk factor for perinatal mortality. Although the stillbirth rate of approximately 2-4% in pregnancies complicated by diabetes[1-4] has decreased dramatically over the past three decades because of good glycemic control, it remains several times higher than that in the general population.[3] Unfortunately, more than half of these stillbirths are unexplained. Frequent antenatal fetal surveillance is therefore recommended for all women with pregestational diabetes.[5] However there is no general agreement regarding the optimal timing and content of antepartum testing. The American College of Obstetricians and Gynecologists (ACOG) suggests using fetal movement counting, the biophysical profile (BPP), the nonstress test (NST), and/or the contraction stress test at appropriate intervals.[5] Doppler studies are not recommended as routine tests for fetal surveillance in this population.

We report a case of diabetes diagnosed during pregnancy in which the observation of abnormal Doppler waveforms in the umbilical arteries abruptly progressed to suspected fetal compromise, despite normal findings on other antenatal surveillance tests.

Case report

A 32-year-old primigravida was referred to us at 27^{+4} weeks' gestation because of an abnormal oral glucose tolerance test (OGTT). She had no family history of diabetes mellitus, and her body mass index was 27.6 kg/m^2 and gestational weight gain was 9 kg. The only test the patient had undergone in the first trimester

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was a test for random serum glucose level, which showed normal results. At 24 weeks' gestation, a 50-g OGTT revealed a glucose level of 265 mg/dL. Subsequently, the patient underwent a 3-hour 100-g OGTT, which resulted in elevated glucose levels of 208/349/355/294 mg/dL. She was therefore referred to our clinic for control of blood sugar and antenatal care. At our hospital, her fasting plasma glucose level was 206 mg/dL, and her initial glycosylated hemoglobin level was 9.0%. She had no vasculopathy associated with undiagnosed diabetes. She was treated with insulin to control her blood glucose, and at 35^{+4} weeks' gestation, her postprandial glucose level was an average of 150 mg/dL and glycosylated hemoglobin level had decreased to 6.5%.

We initiated antepartum fetal surveillance testing at 32 weeks' gestation. Testing was performed twice weekly and included NST, BPP, and Doppler studies of umbilical vessels. Until 36 weeks' gestation, NST was reactive, BPP confirmed the fetal well-being status and umbilical Doppler index was within normal limit.

At 37^{+4} weeks' gestation, she was hemodynamically stable (blood pressure, 140/80 mmHg; pulse rate, 78 beats/min), and the NST was reactive. She had an ultrasound scan, which showed an estimated fetal weight of 2.97 kg appropriate to gestational age. The amniotic fluid index was 14.9 and BPP score was 10. But the end-diastolic flow was found to be absent in the umbilical arteries (Fig. 1). Venous Doppler waveforms were normal. A repeat Doppler examination performed six hours later revealed reversed end-diastolic flow (Fig. 2). Her random capillary glucose level at admission was 151 mg/dL. No abnormal findings were observed during continuous cardiotocographic monitoring until delivery. An emergent cesarean section was performed despite the discrepant results of the NST and

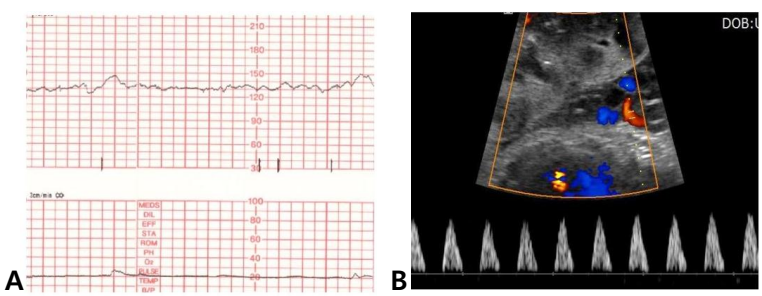

Fig. 1. Results of antepartum fetal surveillance at 37^{+4} weeks' gestation: (A) Normal nonstress test; (B) Doppler waveforms with absent end-diastolic flow velocity in the umbilical artery.

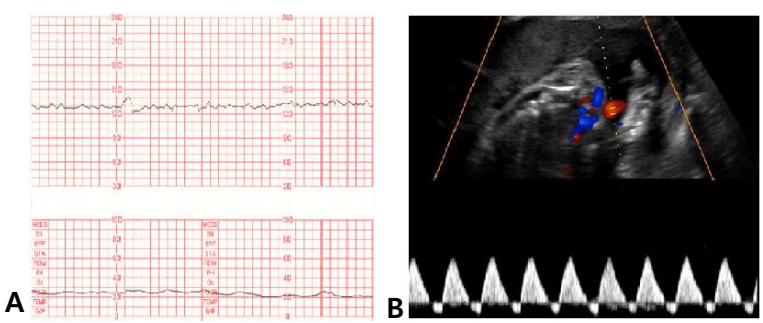

Fig. 2. (A) Nonstress test result and (B) Doppler waveforms with reversed end-diastolic flow velocity in the umbilical artery six hours after the initial Doppler study.

Doppler studies.

A male baby was delivered to weighing 3,000 g, with 1 and 5 minutes Apgar scores of 7 and 8, respectively. The umbilical arterial pH at delivery was 7.171 and its base deficit was 4.0 mmol/L. After birth, glucose level of the infant was 60 mg/dL. The routine baby care was performed. The infant was discharged without complications on the fourth day after birth.

She underwent a 75-g OGTT at 8 weeks after delivery in local clinic and was confirmed as having diabetes. Since then, she had taken the oral hypoglycemic agent.

Discussion

As shown in the present report, the patient was finally diagnosed as having diabetes after delivery by 75g-OGTT. Although she was confirmed to have diabetes after delivery, her fasting glucose level before insulin treatment was above 200 mg/dL and it was considered almost certain that the patient had pregestational diabetes undiagnosed before. Therefore, we performed intensive monitoring for fetal well-being.

Stillbirths without an identifiable cause are a relatively common phenomenon, found primarily in pregnancies complicated by pregestational diabetes. The pathophysiology of late fetal demise in these pregnancies is unclear, although it is generally accepted that the unexplained stillbirths are associated with uncontrolled hyperglycemia.[6] Some authors have made the important observation that fetuses of diabetic mothers have lower cord-blood pH and elevated lactic acid levels.[7,8] In animal studies, the combination of fetal hyperglycemia and hypoxia has resulted in excessive accumulation of lactic acid and an increased risk of stillbirth.[9]

Fetal Doppler assessment is useful in monitoring pregnancies affected by fetal growth restriction. In pregnancies complicated by diabetes, ACOG recommends performing antepartum surveillance with fetal movement counting, the BPP, the NST, and/or the contraction stress test at appropriate intervals.[5] Doppler studies are not recommended as routine tests for fetal surveillance in this population. However, a study by Salvesen et al. revealed that fetal heart rate variability and the biophysical score were of limited value in predicting cord blood acidemia.[10] Two observations provide greater insight into the causes of these fetal deaths. Richey et al. reported that unexplained fetal death occurred in their hospital over a 9-year period in two diabetic pregnancies complicated by macrosomia and hydramnios.[11] In both of these rare cases, they proposed that osmotically induced villous edema and the resultant impaired fetal oxygen transport resulted in the death. In 2008, the observations of Daskalakis et al. provided microscopic evidence of placental dysfunction in women with gestational diabetes[12] when they found that villous immaturity and fetal nucleated red blood cells (indicative of chronic fetal hypoxia) were more frequent in placentas of diabetic women. Both abnormal villi and placental edema may increase placental resistance; because the waveform in the fetal umbilical artery reflects this pathophysiology, it can be a sentinel marker. Changes in flow velocity in the fetal umbilical arteries may thus theoretically alert obstetricians regarding the process of unexplained fetal demise at an early stage.

We report here a case of pregestational diabetes diagnosed during pregnancy in which the finding of abnormal Doppler waveforms in the umbilical artery abruptly progressed to suspected fetal compromise, without corresponding abnormalities in other antenatal surveillance tests. This case suggests that the evaluation of Doppler waveforms should be included antenatal fetal surveillance testing in pregnancies complicated by diabetes, regardless of the presence of maternal vas-

culopathy.

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= 국 문 초 록 =

비수축검사와 제대동맥 도플러 검사의 불일치를 보인 당뇨병이 합병된 산모 1례

인제대학교 일산백병원 산부인과

장지애 · 최예진 · 박정우 · 노지현 · 전경철 · 김영아 · 고재환

임신 전 당뇨는 주산기 사망률의 주요 위험인자로 알려져 있으나 당뇨가 합병된 임신에 대한 최적의 태아 안녕 평가에 대해서 아직 정해진 바가 없는 실정이다. 저자들은 임신 중 당뇨로 진단받고 분만 후 당뇨로 확진된 32세 초산모에서 임신 32주부터 비수축검사, 태아 생물리학적계수, 제대동맥 도플러 검사를 시행하였다. 임신 37주 4일에 비수축검사에서 반응성을 보였으나 제대동맥의 도플러 검사에서 확장기말 혈류의 역전 소견을 보여 응급 제왕절개술로 분만하였고 제대 동맥 pH수치가 7.171의 산혈증을 보였다. 당뇨가 합병된 임신에서 태아감시를 하는데 제대동맥 도플러의 임상적 유용성을 보여주는 증례로 보고하는 바이다.

중심 단어 : 당뇨병 여성의 임신, 원인불명의 태아 사망, 산전 검사