Heparin successfully improved an early onset intrauterine growth restriction accompanied by severe oligohydramnios

Hong-Nü Chu

The Affiliated Hospital, School of Medicine, Hangzhou Normal University, Hangzhou, China

Abstract: Oligohydramnios is an ominous pregnant complication with high perinatal morbidity and mortality of 80%–90%, if it was observed in second trimester. However, there is no promising modality to cure it at that period. In this case, heparin therapy was successful in an early onset extreme oligohydramnios.

Keywords: fetal growth restriction, oligohydramnios, heparin, therapy

Introduction

Early onset fetal growth restriction accompanied by severe oligohydramnios is an ominous pregnant complication with high perinatal morbidity and mortality of 80%–90% if observed in second trimester (Barss et al 1984; Mercer and Brown 1986). However, there is no promising modality to cure severe oligohydramnios during this period. In this case, heparin therapy was successful in a very early onset (<28 gestational week) fetal growth restriction accompanied severe oligohydramnios (amniotic fluid index <1 cm).

Case report

A 28-year-old woman with 27^{+5} gestational weeks (accordingly to her last regular menstruation and early ultrasound-estimated data at prenatal diagnosis) was referred to my clinic because of severe early onset fetal growth restriction with 5.3 cm of biparietal diameter (BPD) and severe oligohydramnios with amniotic fluid index (AFI) <1.0 cm (less than 1 percentile) by ultrasound (examined 3 times by 3 different persons with 3D color Doppler machine) (GE 730 ATL HDI5000,3.5 Hz; Philips, Solingen, Germany). But she could not be clearly scanned for fetal normality without fluid. She had no heat exposure, vaginal fluid discharge, or fever during this pregnancy. Also there was no identifiable perceived cause such as maternal anemia, smoking status, obesity or diabetes, or hypertensive state. Her body mass index was only 0.21.

Her medical history showed that in the previous year she had a stillbirth because of severe oligohydramnios during the second – third trimester at 24 gestational weeks. There was no special data provided about the stillbirth. She was admitted to hospital. The laboratory data from routine tests showed that she had normal blood, liver, and kidney function. But there were no promising modalities to treat her severe oligohydramnios accompanied by severe fetal growth restriction, based on updated guidelines (USA). In practice, I found that heparin could improve amnion in preeclamptic patients accompanied by hypercoagulable state and reduced amniotic fluid with prophylactic dosage of heparin for prevention from thromboembolism.

Correspondence: Hong-Nü Chu
126 Wenzhou Rd, Hangzhou, China, 310015
Tel +86 138 6742 8407
Fax +86 0571 8802 1730
Email chuhongnu@hotmail.com

The patient was informed above experience. She wanted to be tried for treatment with heparin. After giving written, informed consent, she received 6250 units of unfractured heparin mixed in 5% glucose 500 ml intravenously daily. From 1st Biology and Pharmacy Limited Company, Shanghai. China, NO:070701, 12500U/2 ml, 100 mg in one ample). The patient was monitored by blood routine test, and coagulate state once a day. The fetal surveillance was performed by Doppler waveform analysis, biophysical profile scoring twice a week, and cardiotocographic tracing twice a week. The results showed in the normal range except for the intra-uterine growth retardation.

Surprisingly and fortunately, on the third therapy day, the ultrasonography assessment showed that AFI increased to 6.0 cm with biparietal diameter 5.3 cm without abnormality. The patient received heparin therapy continuously for one week under normal monitoring coagulation parameters. She was discharged with AFI 7.6 cm and BPD 6.0 cm with normal Doppler wave form analysis of umbilical vessel, mid-cerebral artery, ductus venosus, or uteroplacental vessels. She was followed up at clinics twice a month before 36 gestational weeks, once a week after the 36th week, and advised to hospitalize if the AFI decreased again. During follow-up, she was hospitalized twice and received 3125 units unfractured heparin mixed in 5% glucose 500 ml intravenously daily for a week because of oligohydramnios recurrence at 32 gestational weeks and 35 gestational weeks, respectively. At 38^{+} gestational weeks, a normal female infant was born with weight of 1850 g, 10 Apgar score, and clear fluid.

Discussion

Oligohydramnios is a common complication of pregnancy, accompanied by fetal growth restriction or other pregnancy-related diseases. It is a major determinant of infant morbidity and mortality both in undeveloped countries and developing countries. It is particularly ominous to observe severe oligohydramnios in the second trimester as perinatal mortality rates then approach 80%–90% (Barss et al 1984; Mercer and Brown 1986). When amniotic fluid is absent, the perinatal loss rate is high at 90% (Moor et al 1989). The lethal nature of the severe forms of oligohydramnios is a result of pulmonary hypoplasia. Currently, obstetricians are looking for some treatment modalities such as maternal hydration, amnioinfusion, transabdominal amniocentesis prior to induction labor, but whether routine antepartum or intrapartum treatment will improve outcome remains to be seen.

In this case, heparin treatment for preterm oligohydramnios was generally successful. The detail mechanisms need to be further studied. As we known, heparin can promote blood circulation and improve placental function by decreasing platelet aggregation, increasing exogenous anticoagulant activity, inhibiting fibrin formation and deposition, and decreasing thrombosis in placentas. According to our current study on the heparinase expression in preeclampsia and eclamptic placentas and several oligohydromnios placentas, we found that the expression of heparinase is stronger in these placentas than in normal placentas (Chu 2004, 2005, 2007a, 2007b; Chu and Huang 2005; Chu and Liang 2007; Chu and Zhou 2007). This is one of the reasons why patients with oligohydromnios need heparin. It may be that overproductions of heparinase in placenta broke endogenous heparin and reduced blood circulation, then reduce the glomerular filtration rate, therefore, fetal urine and lung liquid are reduced and the sources of amniotic fluid decreased. However, the concentration of endogenous heparin has not been tested by now. Therefore, the mechanisms of heparin for oligohydromnios need to be further studied in multiple centers, in randomized control trials.

Otherwise, hydration might exert an increase of AFI in this case. Therefore, a large-sample trials need to be conducted to test whether heparin can improve preterm oligohydramnios successfully subcutaneously not intravenously.

Disclosure

The author reports no conflicts of interest.

References

Barss VA, Benacerraf BR, Frigoletto FD Jr. 1984. Second trimester oligohydramnios, a predictor of poor fetal outcome. *Obstet Gynecol*, 64: 608–12.

Chu HN, Huang HF. 2005. Evaluation of heparin for severe intrahepatic cholestasis of pregnancy at preterm. *Chinese J Med*, 85:420–1.

Chu HN, Liang C. 2007. Heparinase expression in reeclamptic placenta. 3rd Asia Pacific Congress of Maternal-Fetal Medicine, Aug. 2007. Nanjing, China.

Chu HN, Zhou CY. 2007. Severe preeclampsia cured by heparin in a patient with twin-twin transfusion syndrome: case report. *Chin Med J*, 120:263–4.

Chu HN. 2004. Evaluation of heparin for oligohydromnios at preterm pregnancy. *Natl Med J China*, 84:745–6.

Chu HN. 2005. Heparin for high S/D ratio of umbilical artery at preterm pregnancy. *Chin J Obstet Gynecol*, 40:46–9.

Chu HN. 2007a. Heparin for elevated S/D ratio in preterm pregnancy. 3rd Asia Pacific Congress of Maternal-Fetal Medicine, Aug. 2007. Nanjing, China.

Chu HN. 2007b. Should heparin be used for preeclampsia patients routinely? Heparinase expressed in their placentas. 2nd Asia Pacific Congress of OB and GYN, Nov. 2007. Shanghai, China.

Mercer LJ, Brown LG. 1986. Fetal outcome with oligohydramnios in the second trimester. *Obstet Gynecol*, 67:840–3.

Moor TR, Longo J, Leopold G, et al. 1989. The reliability and predictive value of anamniotic fluid scoring system in severe second trimester oligohydramnios. *Obstet Gynecol*, 73:739–742.