CEOG Clinical and Experimental Obstetrics & Gynecology
Case Report

Fetal brain lactate peak measurement by magnetic resonance spectroscopy for prediction of fetal hypoxia in a case of unexplained third trimester recurrent fetal loses

B. Akar[1], R. Aslancan[2], H. Şimşek[3], P. Çakır[4], E. Çalışkan[5]

[1]İstinye University School of Health Sciences, Istanbul; [2]Bahcesehir University School of Medicine, Istanbul
[3]Sakarya Eğitim Araştırma Hastanesi, Adapazarı; [4]Derince Eğitim ve Araştırma Hastanesi, Kocaeli
[5]Department of Obstetrics and Gynecology, Bahcesehir University School of Medicine, Istanbul (Turkey)

Summary

Background: The fetal brain lactate level which is measured by magnetic resonance spectroscopy (MRS) is a compelling indicator for hypoxic/ischemic brain damage. *Aim:* The authors present a case of MRS diagnosed fetal brain lactate peak despite normal fetal development and Doppler indices which lead to a preterm delivered hypoxic fetus. *Case Report:* A 37-year-old woman admitted to this clinic at 30 weeks six days of her gestation because of previous recurrent three unexplained fetal death at third trimester and one neonatal death. At 33 weeks one day of pregnancy, MRS examination showed lactate peak in the fetal brain, despite bi-weekly normal Doppler indices and fetal biophysical profile follow-up. After eight days of daily follow-up since lactate peak measurement, her biophysical profile was 6 despite normal Doppler indices. She developed mild preeclampsia after four days following lactate peak. She had imminent cesarean section at 34th week of gestation and a 1,980-gram neonate with Apgar scores of 5 and 7 at the first and fifth minute was delivered. Fetal hypoxia was diagnosed due to base excess of -14 and a cord blood pH of 7.16. The newborn was discharged in a healthy state after five days of neonatal intensive care. *Conclusion:* The case presents that fetal brain lactate peak can be the only first warning sign in cases of unexplained fetal losses predicting oncoming fetal hypoxia despite normal fetal Doppler and biophysical profile evaluation.

Introduction

Antenatal follow up of fetal well-being has a crucial importance to prevent neonatal hypoxia caused by intrauterine complications. There are different methods used to evaluate fetal well-being, such as biophysical profile and fetal Doppler measurements. In addition to these methods, magnetic resonance spectroscopy (MRS) is a recently proposed method to assess presence of brain lactate peak as an indicator of the manifestation of fetal hypoxia in the brain (Figure 1) [1]. Fetal brain acidosis caused by fetal problems occurs as a consequence of united effects of energy mechanism failure, glutamate leak, nitric oxide toxicity, or lipid peroxidation [2]. Intrauterine cerebral lactate peak is an indicator for fetal hypoxia which may cause intrauterine death so its diagnosis can help planning optimal delivery time or emergency cesarean section for fetal protection [3-5]. Most of the cases suggest that fetal brain lactate peak is present in the fetuses with intrauterine growth restriction (IUGR), and preeclamptic mothers [6, 7]. In this case report, a patient with three intrauterine unexplained fetal losses and one early neonatal loss was diagnosed to have fetal brain lactate peak by MRS as a first sign of fore coming fetal hypoxia and late onset preeclampsia during her present gestation.

Case Report

A 37- year-old woman applied to this clinic at 30 weeks six days of pregnancy because of previous recurrent three unexplained intrauterine fetal death, and one neonatal loss occurred three days after the cesarean section which was performed at 34th week. Her obstetric history revealed gravidity five and parity four without any living child. Oligohydramnios was present in her first pregnancy which was terminated at 32nd gestational week due to sudden intrauterine fetal death. Second and third pregnancies appeared with late onset preeclampsia and intrauterine fetal death at 33 and 34 weeks of gestation despite Doppler measurements or biophysical profile did not show any abnormal findings. The fourth fetus, after elective cesarean section at 33rd week of gestation, which was performed due to her previous losses without any pathological findings in the fetus or the mother, died due to neonatal hypoxia despite three days of neonatal intensive care unit follow-up. The patient has a history of hypothyroidism, and beta fibrinogen 455 on thrombosis panel and homozygous mutation at heterozygote MTHFRA 1298C gene A. In the presented pregnancy she was taking levothyroxine, empirical tinzaparin due to previous unexplained intrauterine fetal deaths, and acetylsalicylic acid to prevent recurrent preeclampsia at the time of admission to our clinic. Obstetric ultrasonographic evaluation was carried out two times weekly with biophysical profile, umbilical artery, ductus venosus, and middle cerebellar artery Doppler measurements. At 33 weeks and one day since conception, MRS examination was performed (Figure 2, 3, and 4) with the patient consent and it showed lactate peak (Figure 1) in the fetal brain

Revised manuscript accepted for publication November 15, 2017

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLVI, n. 2, 2019
doi: 10.12891/ceog4464.2019

7847050 Canada Inc.
www.irog.net

Published: 10 April 2019

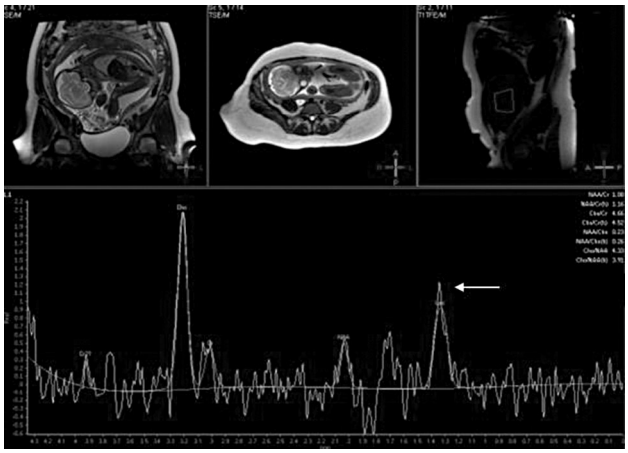

Figure 1. — MRS showing fetal brain lactate peak.

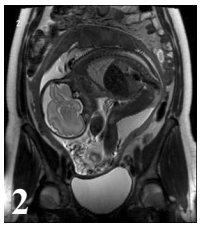

Figure 2. — Fetal MRS coronal view.

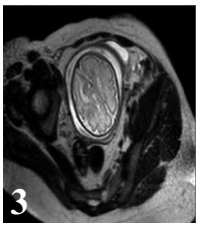

Figure 3. — Fetal MRS sagittal view.

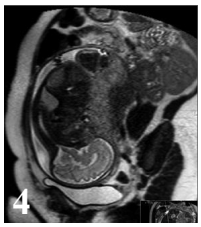

Figure 4. — Fetal MRS axial view.

despite normal Doppler indices and fetal biophysical profile. She had antenatal corticosteroid therapy for possible iatrogenic preterm delivery. After eight days of daily follow-up with biophysical profile and Doppler measurements, her biophysical profile was found to be 6 and she developed mild preeclampsia without proteinuria four days after lactate peak. She had imminent cesarean section at 34th week of gestation and a 1,980 gram neonate with Apgar scores of 5 and 7 at the first and fifth minute was delivered. Fetal hypoxia was diagnosed due to base excess of -14 and a cord blood pH of 7.16. The newborn was discharged in a healthy state after five days of neonatal intensive care. The mother's follow up was uneventful and she was discharged on the second postoperative day.

Discussion

There are a few MRS studies assessing lactate levels of fetal brain. Research by Cetin *et al.* assessed the fetal cerebral lactate peak in a population of five IUGR fetuses [6]. These five fetuses had irregular fetal heart rate, and abnormal umbilical artery Doppler indices. Doger *et al.* performed research on the same topic with IUGR fetuses, and they categorized the patients according to their MRS results and Doppler indices [7]. The study findings show that the number of perinatal deaths due to fetal hypoxia is higher in the presence of lactate peak compared to normal lactate level [7]. Edwards *et al.* and Story *et al.* measured the lactate level of IUGR fetuses by MRS, and higher numbers of subjects showed lactate peak [5, 8]. An MRS study performed by Walsum *et al.* on a hypoxic lamb brain also presented with lactate peak while they were measuring the oxygen saturation of umbilical artery to verify the hypoxic state [9]. Some research promotes an anaerobic metabolism that produces lactic acid occurs because of impaired oxidative phosphorylation [10]. In order to maintain integrity of neurons and protect functions of them, continuous oxygen flow is essential, and since lactate is an end product of anaerobic metabolism, elevated lactate level indicates hypoxia in the fetal brain which could cause ischemic injury if it lasts longer [10].

Unlike the present case, studies showing the fetal lactate peak in the literature predominantly include fetuses with IUGR. Preeclampsia is a common cause of IUGR which results from abnormal trophoblastic invasion to the uterine spiral arteries [11]. The lactate peak has a predictable pathophysiology in the cases of IUGR subjects selected, because both maternal and placental causes of restricted fetal growth have a common fact, inadequate oxygenation of the fetus which is going to lead increase of glycolysis, and as a result, increased lactate level. However, in the present study, there were lactate peak and fetal hypoxia signs in the absence of IUGR and early onset preeclampsia. Since the trigger for lactate peak is unclear in this case, it is not certain if the hypoxia caused by inadequate oxygenation resulted in increased glycolysis and lactate or the lactate peak was aggravating fetal hypoxia and causing late onset preeclampsia.

The importance of fetal MRS in evaluating cerebral ischemic-hemorrhagic lesions and the extension of parenchymal injuries have been discussed in another research. The authors concluded that fetal MRS is significant to provide required information for the parenchymal injury and associated abnormalities of fetal brain [12]. There is a broad relationship between fetal brain lactate measure and later encephalopathy. Some factors such as the depth, duration, and repetition of the insult, maturity and condition of the fetus, pre-existing hypoxia, exposure to pyrexia, and infection/inflammation are modifiers of injury risk. The possibility of more subtle neurological problems can be increased in later childhood in people who do not develop cerebral palsy [13].

Conclusion

The case presents that fetal brain lactate peak measured by MRS can be the only first warning sign in cases of unexplained fetal loss predicting oncoming fetal hypoxia despite normal fetal Doppler and biophysical profile evaluations. Irreversible hypoxic-ischemic injury of fetal brain could be prevented using the non-invasive MRS technique, and birth plans with high-risk fetuses could be considered.

References

[1] Pugash D., Krssak M., Kulemann V., Prayer D.: "Magnetic resonance spectroscopy of the fetal brain". *Prenat. Diagn.*, 2009, *29*, 434.

[2] Perlman, J.: "Intervention strategies for neonatal hypoxic-ischemic cerebral injury". *Clin. Ther.*, 2006, *28*, 1353.

[3] Wolfberg A., Robinson J., Mulkern R., Rybicki F., Du Plessis A.: "Identification of fetal cerebral lactate using magnetic resonance spectroscopy". *Am. J. Obstet. Gynecol.*, 2007, *196*, e9.

[4] Bulterys M., Greenland S., Kraus J.: "Chronic Fetal Hypoxia and Sudden Infant Death Syndrome". *Obstet. Gynecol. Surv.*, 1991, *46*, 270.

[5] Charles-Edwards G.D., Jan W., To M., Maxwell D., Keevil S.F. Robinson R.: "Noninvasive detection and quantification of human foetal brain lactatein uteroby magnetic resonance spectroscopy". *Prenat. Diagn.*, 2010, *30*, 260.

[6] Cetin I., Barberis B., Brusati V., Brighina E., Mandia L., Arighi A., *et al.*: "Lactate detection in the brain of growth-restricted fetuses with magnetic resonance spectroscopy". *Am. J. Obstet. Gynecol.*, 2011, *205*, 350.e1.

[7] Doğer E., Özdamar Ö., Çakıroğlu Y., Ceylan Y., Çakır Ö., Anık Y., Çalışkan E.: "The predictive value of lactate peak detected by the magnetic resonance spectroscopy in the brain of growth-restricted fetuses for adverse perinatal outcomes". *J. Matern. Fetal Neonatal Med.*, 2016, *29*, 3178.

[8] Story L., Damodaram M.S., Allsop J.M., Mcguinness A., Patel A., Wylezinska M., Rutherford M.A.: "Brain metabolism in fetal intrauterine growth restriction: a proton magnetic resonance spectroscopy study". *Am. J. Obstet. Gynecol.*, 2011, *205*, 403.

[9] Walsum A.M.C., Heerschap A., Nijhuis J.G., Oeseburg B., Jongsma H.W.: " Proton magnetic resonance spectroscopy of fetal lamb brain during hypoxia". *Am. J. Obstet. Gynecol.*, 1998, *179*, 756.

[10] Groenendaal F., Roelants-van Rijn A.M., Van Der Grond J., Toet M.C, De Vries L.S.: "Glutamate in cerebral tissue of asphyxiated neonates during the first week of life demonstrated in vivo using proton magnetic resonance spectroscopy". *Biol Neonate*, 2001, *79*, 254.

[11] Meekins J.W., Pijnenborg R., Hanssens M., Mcfadyen I.R., Asshe A.: " A study of placental bed spiral arteries and trophoblast invasion in normal and severe pre-eclamptic pregnancies". *Int. J. Obstet. Gynaecol.*, 1994, *101*, 669.

[12] Manganaro L., Bernardo S., Barbera L.L., Noia G., Masini L., Tomei L., et al.: "Role of foetal MRI in the evaluation of ischaemic-haemorrhagic lesions of the foetal brain". *J. Perinat. Med.*, 2012, *40*, 419.

[13] Robertson N.J., Cox I.J., Cowan F.M., Counsell S.J., Azzopardi D., Edwards A.D.: "Cerebral intracellular lactic alkalosis persisting months after neonatal encephalopathy measured by magnetic resonance spectroscopy". *Pediatr Res.*, 1999, *46*, 287.

Corresponding Author:
R. ASLANCAN, M.D.
Bahcesehir University
Sahrayicedid Mah. Batman Sok No. 66-68
Kadıköy, Istanbul 34732 (Turkey)
e-mail: reyhanaslancan@gmail.com