

SEVERE NEONATAL ASPHYXIA IN NEWBORN WITH INTRAUTERINE GROWTH RESTRICTION (IUGR) AND MOTHERS SUFFERING FROM THROMBOPHILIA

MAGDALENA MOGOȘ¹, RALUCA GABRIELA IOAN², LIVIA MANTA³

^{1,2,3}Prof. Dr. "Alfred Rusescu" Institute for Mother and Child Protection, Bucharest

Keywords: asphyxia, growth restriction, preterm
Abstract: Intrauterine growth restriction contributes to neonatal mortality and morbidity of both premature and newborns at term. ECO Doppler fetal flows, respectively the vein duct and umbilical artery are surrogate markers of this entity. However, birth moment remains controversial. Birth up to 30 weeks might be associated with lower rates of cerebral palsy and Griffiths Mental Development Scales (GMDS) under 70.

INTRODUCTION

Intrauterine Growth Retardation contributes to neonatal mortality and to morbidity of pre and full term newborn. Fetal Doppler flows – the ductus venosus and the umbilical vein are the surrogate markers of this entity.(1) Despite these, the birth time remains controversial. Birth before 30 weeks can be associated to lower rates of brain paralysis and Griffiths Mental Development Scales (GMDS) under 70.(2)

Among IURG causes, thrombophilia is one of the major risks for venous thrombosis, being associated to a high risk of intrauterine growth retardation.

Small for Gestational Age (SGA) occurs due to Intrauterine Growth Retardation (IUGR). These infants are below the 10% percentile in the growth graphics, 10% are SGA. There is a multitude of constitutional, maternal, and fetal causes. They can be symmetrical / asymmetrical (weight is smaller only). Symmetrical ones are more suspect of having an initial (genetic) cause.

Perinatal morbidity in such infants is due to asphyxia, acidosis, hypoglycemia, hypocalcemia, hypothermia, and polycythaemia.(1)

According to the Academy of Pediatrics (APP) and the American College of Obstetrics and Gynecology (ACOG) the current definition of asphyxia at birth is given indirectly based on the below parameters:(3)

1. PH in the umbilical blood < 7;
2. APGAR score of 3 at 1 minute remains below 3 after 5 and 10 minutes;
3. signs of hypoxic – ischemic encephalopathy performing as tonus and reflex disorders;
4. changes in other organs (cord, kidneys, liver, intestines).

CASE REPORT

We present the case of a 27-year-old, Caucasian patient, under surveillance since the 8th week of pregnancy. Medical record: second month pregnancy interruption followed by a thrombophilia diagnosis. The patient has no previous births and is a non-smoker. During the current pregnancy the patient has been under Clexane treatment from the beginning, 0.6 ml/day in the evening and folic acid 5mg. BMI = 22.1, normal blood pressure during pregnancy, regular menstrual period. The patient has undergone the double test which revealed a low risk

of chromosomal abnormalities. The Torch test and usual analyses resulted between the normal limits and cervix cultures and urine tests were negative. The echography for fetal determination during the first trimester of pregnancy showed a difference between the chronological fetal age and the clinic fetal age; pregnancy resulted in almost 2 weeks smaller than chronologic age. High resistance on the uterine arteries (left = 0.85 and right = 0.67), with present bilateral diastolic notch. Starting with the 20th week of pregnancy, discrepancy increases progressively between the clinic fetal age and the chronologic one.(1)

Thus, at 26 chronologic weeks and 4 days corresponded to 21 clinic weeks and 6 days. The patient has been under weekly careful surveillance of biometrics, amniotic liquid flow and Doppler flows on the umbilical artery and venous duct. Serial measurements of these were between normal limits, except biometrics indicating a progressive, early and severe IUGR. Active fetal movements were perceived constantly, between normal limits, by the mother. The patient was explained the risks of carrying on this pregnancy and was offered the option to interrupt it, taking into account the early severe IUGR. She chose to carry the pregnancy on. Echographic screening also revealed an amniotic band with no effect on the fetal anatomy (no morphologic abnormalities were determined during the 2nd trimester echography). The patient got hospitalised in Polizu Nursery on the 31st week of pregnancy due to a low perception of MAF. Gynecologic check revealed a shortened permeable cervix, mobile fetal pelvis at the opposite inferior uterine pole, intact membranes, moderate leukorrhea without bleeding. Upon the hospitalisation date a growth retardation of approximately 5 weeks was determined (compared to the corrected fetal age), fetal weight of approximately 600 g, rhythmic BCF of 144 / minute, amniotic liquid of a subjectively reduced quantity (maximum liquid bag = 2.8cm), much reduced MAFs. Resistance on the middle cerebral artery = 0.73, resistance on the umbilical artery = 0.74, resistance on the venous duct = 0.85, absent "a" wave. Anterior bottom placenta, 1st degree of maturity. The amniotic band cannot be visualised anymore, present simple paracervical fascia. The cardiotocographic exam determines non stress test non reactive with variable decelerations on a reduced cardiac variability while uterine contractions are absent. From a biologic

¹Corresponding author: Raluca Gabriela Ioan, B-dul. Lacul Tei, Nr. 120, București, România, E-mail: ioan_raluca@yahoo.com, Phone:+40744 421553

Article received on 27.04.2015 and accepted for publication on 27.08.2015

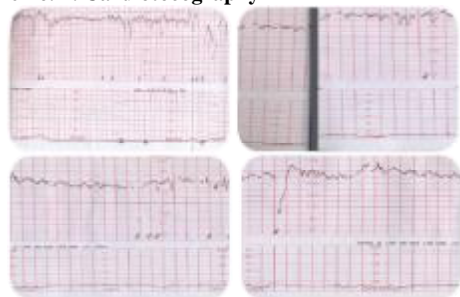
ACTA MEDICA TRANSILVANICA September 2015;20(3):73-75

CLINICAL ASPECTS

point of view the mother is between normal limits. Urine, cervix and lochia cultures are negative.

Taking into account the imminent birth, it was decided to go under corticotherapy. 48 hours later it was decided to terminate the pregnancy by a C-section surgery, given the extreme fragility of this fetus undergoing chronic hypoxia, with very little resources to face a birth labour. A living female fetus was extracted, weighing 500 grams and an IA = 3; intraoperative extraction of placenta revealed its very small weight of only 100 g and a 40 cm umbilical cord, with paracentral insertion.

Figure no. 1. Cardiotocography



After birth, recovery goes between normal parameters, the patient continues anticoagulant treatment during the entire period. The mother breast feeds the newborn.

The 500 g newborn (under the 5th percentile) is in an extremely severe condition, with severe asphyxia, generalised diffuse cyanosis, secondary apnea, absent tonus and archaic reflexes.

Even since the birth room the newborn is placed under radiant heat, mechanically ventilated (CPAP), receiving surfactants and endovenous perfusion for hydro-electrolytic rebalancing and support. Transfontanelar echography determines first degree periventricular haemorrhage. Afterbirth corticotherapy is established, dopamine against hypo blood pressure during the first days, and Humaglobine (human immune globulin).

The newborn is progressively fed by gavage with mother milk, as its weight curve is slightly ascendant, excepting three intercurrent infectious diseases for which it received complex antibiotics. Repeated transfusions, phototherapy against icterus, vitamin D and Haussman Iron were necessary. First degree retinopathy occurred but without requiring ophthalmologic surgery. The newborn was transferred to newborn intensive care section at the age of 72 days, in the premature section, from where it is released in about 3 months after birth, at the weight on 2,250 grams. The central nervous system tests reveal normal parameters, as well as the other apparatuses and systems. Feeding continues with breast milk administered in bottle.

DISCUSSIONS AND CONCLUSIONS

The intrauterine growth retardation is a condition accompanied by chronic fetal hypoxia with deep and long term effects on neonatal morbidity and mortality.(4)

Fetal close monitoring by biometrics and Doppler test on the umbilical, uterine artery and venous duct should be conducted when differences of more than 2 weeks between the clinic fetal age and chronologic age are determined.

The birth moment and checking frequency must be individualised according to the clinic situation of each case. When birth is a must before 34 weeks of pregnancy corticotherapy should take place 48 hours in advance in order to

increase the survival chances of the newborn. Considering the frequent association of preeclampsia and intrauterine growth retardation (5), particularly in women with abnormal Doppler results on uterine arteries during the first trimester of pregnancy, blood pressure monitoring is a must, also urine tests and small doses of aspirin along the pregnancy period. Patients should be advised about the high risk of recurrence in the future pregnancies (22-28%).(6)

Future pregnancies need close monitoring as they are considered risky pregnancies. Infants born with IUGR show a decrease in cognitive scores, often learning difficulties and attention deficiencies.(7,8) IUGR is a condition with high risk of nosocomial infections, newborn showing a low number of granulocytes. Trying to reduce the infection risk by prescribing granulocyte macrophage colony stimulating factor (GM-CSF) was inefficient. These infants are at a high risk to develop ischemia on all vascular territories, so necrotizing enterocolitis. Measures: progressive adding of mother breast milk and probiotics in order to reduce such risks.

Besides reducing the incidence of neural tube defects, preventive prescription of folic acid before conception also diminishes the negative impacts of smoking on the fetus.(10)

Quitting smoking from the very first trimester of pregnancy should be advised because it improves significantly the obstetrical prognosis and the fetal growth. In cases of IUGR with an early start, genetic testing (amniocentesis) should be taken into consideration, as between 5 and 20% of growth retardations are associated to genetic abnormalities. Other 10 percentages of the total growth retardations also have uterine infections as a cause (CMV, toxoplasmosis, syphilis, rubella, malaria, etc.) so infectious testing is a must. In this case, infectious testing proved to be negative, but genetic testing would have been recommended. Establishing the IUGR cause may often remain difficult as it is in this case, when, despite the correct treatment against thrombophilia, which started early, fetal growth proved to have deficiencies and IUGR could not be prevented.(11)

Sometimes the infant's further evolution can reveal an IUGR cause that remained obscure during pregnancy, such as a type of primary nanism. The favourable evolution of a newborn with severe IUGR is influenced by choosing the best moment to terminate the pregnancy, and the fetal compromise at that moment. Choosing the best moment is essential and the obstetrics doctor must weigh on the one hand the possible complications of prematurity, and the awareness of the risk to extract too late a fetus which may be neurologically compromised by severe chronic hypoxia, with no recovery perspectives, on the other. In the given case, even if the growth retardation was severe and the weight at birth extremely small, close monitoring, prenatal corticotherapy, choosing the best moment to terminate the pregnancy together with the care given to the newborn in a neonatal intensive care section, led to very good and encouraging results for future pregnancies with IUGR.

REFERENCES

1. Prenatal asphyxia, hyperlacticaemia, hypoglycaemia, and erythroblastosis in growth retarded fetuses. Br Med J (Clin Res Ed) 1987; 294 doi: <http://dx.doi.org/10.1136/bmj.294.6579.1051> (Published 25 April 1987) Cite this as: Br Med J (Clin Res Ed) 1987;294:1051.
2. Figueras F, Gardosi J. Intrauterine growth restriction: new concepts in antenatal surveillance, diagnosis, and management, Received: June 2, 2010; Received in revised form: August 10, 2010; Accepted: August 27, 2010;

- Published Online: January 10, 2011. DOI: <http://dx.doi.org/10.1016/j.ajog.2010.08.055>.
3. Sibai BM. Evaluation and management of severe preeclampsia before 34 weeks' gestation Publications Committee, Society for Maternal-Fetal Medicine, Received: July 1, 2011; Accepted: July 7, 2011; Published Online: July 18, 2011 DOI: <http://dx.doi.org/10.1016/j.ajog.2011.07.017> PLoS One. 2015 Jul 9;10(7):e0126020. doi: 10.1371/journal.pone.0126020. eCollection 2015.
 4. Guellec I. Neurologic Outcomes at School Age in Very Preterm Infants Born With Severe or Mild Growth Restriction, the EPIPAGE Study Group. Published online March 7, 2011 Pediatrics. 2011;127(4):e883-e891 (doi: 10.1542/peds.2010-2442).
 5. Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction, Society for Maternal-Fetal Medicine Publications Committee, Division of Maternal-Fetal Medicine at Eastern Virginia Medical School, Norfolk, VA Received: January 11, 2012; Accepted: January 12, 2012.
 6. Perinatal complications and long-term neuro-developmental outcome of infants with intrauterine growth restriction. Presented, in part, as a poster at the 22nd World Congress on Ultrasound in Obstetrics and Gynecology, Copenhagen, Denmark, Sept. 9, 2012.
 7. Sibude J, et al. Placental Growth Factor for the Prediction of Adverse Outcomes in Patients with Suspected Preeclampsia or Intrauterine Growth Restriction, Published: November 28, 2012.
 8. Kimura C, Watanabe K, Iwasakia A, Moria T, Matsushitaa H, Shinoharaa K, Wakatsukia A. The severity of hypoxic changes and oxidative DNA damage in the placenta of early-onset preeclamptic women and fetal growth restriction, Access options. DOI: 10.3109/14767058.2012.733766.
 9. Christian P, Murray-Kolb LE, Tielsch JM, Katz J, LeClerq SC, Khatry SK. Associations between preterm birth, small-for-gestational age, and neonatal morbidity and cognitive function among school-age children in Nepal. 13 BMC Pediatrics 2014;14:58 doi:10.1186/1471-2431-14-58 Obstetrics & Gynecology: October 2013;122(4):869-877 doi: 10.1097/AOG.0b013e3182a265ab Original Research.
 10. McIntyre S, Blair E, Badawi N, Keogh J, Nelson K. Antecedents of Cerebral Palsy and Perinatal Death in Term and Late Preterm Singletons The Journal of Maternal-Fetal & Neonatal . 2013;26(5).
 11. Yao S, Wu H, Yu YH. Early intervention with aspirin for preventing preeclampsia in high-risk women: a meta-analysis. Article in Chinese. Front Physiol. 2015 Jun 8;6:176.