CASE REPORT

Expression of Insulin-like Growth Factor 1 (Igfl) and its Receptor (Igrl) in Two Extremely Pre-Term Placentas

Ilze Kreicberga*, Mara Pilmane**, Dace Rezeberga*

*Department of Obstetrics and Gynecology, Riga, Latvia

**Institute of Anatomy and Anthropology, Riga Stradins University, Riga, Latvia

Summary

Today extremely premature children readily survive; good quality of life can be reached only with research and technology based approaches, therefore understanding of molecular processes taking place in pre-term placentas can be of practical value both for neonatology and pediatric surgery, as complications of prematurity quite often require surgical interventions. The present case report describes the expression of one of the most significant growth factors IGF1 and its receptor IGFR1 in placentas after extremely pre-term deliveries of 22 and 23 gestational weeks and their correlations with clinical findings of corresponding extremely premature children. Significantly more beneficial clinical course is represented by a child with clinically less advantageous situation: smaller gestational age (22w versus 23 w) and birthweight (540g v. 650g), born in the first vaginal delivery (v. repeated delivery) and recently ruptured membranes (v. PPROM > 72 hours). Placental cells of this child contained abundance of IGF1 and IGFR1 positive structures (v. few structures in the other one), possibly revealing better protective features of placenta, improving survival capabilities of the neonate in cases of extreme prematurity.

AIM OF THE DEMONSTRATION

The survival and good quality of life of extremely prematurely born children is one of the most challenging tasks of neonatology; its fulfillment requires research based approaches. Takizawa et al. (1) in 2007 suggested immunohistochemistry (IHC) to be useful for the clinical praxis. We evaluated the expression of 11 markers in the post-delivery placentas of different gestational ages, including the most potent growth factor, described by Peters et al. in 2012 (2) as a diagnostic marker of growth hormone deficiency, IGF1 and its receptor IGFR1. IGF1 and IGFR1 have been found in the placentas of various gestational ages; Kumar et al. (3) in 2012 found down-regulation of IGF1 with an advancing gestational age, alerting its possible role in extreme prematurity. We also found negative correlations of the expressions of IGF1 and IGFR1 with the gestation; just one of the extremely pre-term post-delivery placentas showed unusually weak immunoreactivity, correlating with the clinical findings. Clinically interesting was comparison with another case with a strong immunoreactivity of IGF1 and IGFR1. The other researched molecular markers in those two placentas were not so different.

CASE REPORT

In 2011, an IHC examination of 53 placentas of various gestational ages, acquired in the Riga Maternity hospital, was performed at the Latvian Institute of Anatomy and Anthropology. The study was approved by the Ethics committee of the Riga Stradins university. Samples from identical central and peripheral places of placentas were taken immediately after delivery and placed into preservative; processed by antibodies IGF1 (mouse monoclonal, 1: 50, R&D) and IGFR1 (goat polyclonal, 1: 100, R&D); assessed visually by the same researcher at the same day; amount of cells, containing markers, were evaluated in the range from 0 (none) to ++++ (abundance) (4). IGF1 and IGFR1 mainly were contained by the cells of cytotrophoblast and extravillous trophoblast.

Two placentas: 22w and 23w revealed significantly different expressions of IGF1 and IGFR1 (Figure 1).

Case A: mother 20 years of age, normal 22w pregnancy, first vaginal delivery, a girl of 540g. No antenatal corticosteroids. The girl presented 2nd grade intra-ventricular hemorrhage (IVH) and moderate respiratory distress syndrome (RDS). Unusually benign clinical course for the gestational age.

Case B: mother 36 years of age, normal 23w pregnancy, PPROM > 72 hours, third vaginal delivery of a boy of 650g. No antenatal corticosteroids. The boy presented 3rd grade IVH and severe RDS, died on the third day of life due to extreme prematurity.

DISCUSSION

Clinically cases A and B were somehow similar: mothers had similar social statuses, body composition (body mass index 24 and 21), no high risks of infections or pre-term deliveries. Both pre-term deliveries were vaginal in the gestation of 22 and 23 weeks, without antenatal prophylaxis of dexamethasone, birthweight of children 540 and 650 grams.

Other studies have shown correlations of IGF1/IGFR1 in the placental tissues with the weight of the neonate: Iniguez et al. (5) found higher expression of IGF1 and IGFR1 in the placentas of small for gestational age (SGA) infants. In our case both of the children were appropriate for their gestational age; placenta A had much stronger expression of IGF1 and IGFR1 (abundant +++) and a child with a lower Ponderal index (PI) of 2.0; placenta B had much weaker (occasional 0/+) expression of IGF1 and IGFR1 and a child with a higher PI (2.96). In this gestational age leanness (lower PI) could be undertaken as disadvantage, in our case it was the beneficial case.

Preterm premature rupture of membranes (PPROM) have been described in 2012 by Blumenfeld et al. (6) as decreasing mortality among children of 24 to 26 weeks of gestation; in our case child A without PPRM showed better survival. Loukovaara et al. (7) in 2002 found no differences of the expression of IGF1 in the cases of PROM; probably PPRM had no impact on the expression of IGF1 in our case. Our findings could be more correlative with studies described by Isgaard et al. (8) in 2007 on the capability of IGF1 to protect and regenerate human brain.

We concluded that the expression of IGF1 and IGFR1 in the placental cells probably indicate the survival capabilities of pre-mature newborns; further studies could suggest application of IGF1 in the management of extremely low birth weight infants.

Conflict of interest: None

REFERENCES

1. Takizawa T, Eguchi H, Namimatsu Sh, Jeschke U, Fuchs R, Robinson JM. Histochemistry for Placenta Research: Theory and Application // J Nippon Med Sch, 2007; 74(4):268-273.
2. Peters CJ, Dattani MT. How to use insulin-like growth factor 1 (IGF1) // Arch Dis Child Educ Pract Ed, 2012; 97(3):114-8. Epub 2012 Jan 20.
3. Kumar N, Leverence J, Bick D, Sampath V. Ontogeny of growth-regulating genes in the placenta // Placenta, 2012; 33(2):94-9.
4. Pilmane M, Rumba I, Sundler F, Luts A. Patterns of distribution and occurrence of neuroendocrine elements in lungs of humans with chronic lung diseases // Proceedings of the Latvian Academy of Sciences, 1998; B,52,144-152.
5. Iniguez G, Gonzalez CA, Arganona F, Kakarieka E, Johnson MC, Cassorla F. Expression and protein content of IGF-I and IGF-I receptor in placentas from small, adequate and large for gestational age newborns // Horm Res Pediatr, 2010; 73(5):320-7.
6. Blumenfeld YL, Lee HC, Gould JB, Langen ES, Jafari A, El-Sayed YY. The effect of preterm premature rupture of membranes on neonatal mortality rates // Obstet Gynecol, 2010 Dec; 116(6):1381-6.
7. Loukovaara M, Koistinen R, Kalme T, Kurki T, Leinonen P, Seppälä M. Serum insulin-like growth factor-I and insulin-like growth factor binding protein-3 in premature rupture of membranes // Acta Obstet Gynecol Scand, 2002 Oct; 81(10):905-8.
8. Isgaard J, Aberg D, Nilsson M. Protective and regenerative effects of the GH/IGF-I axis on the brain // Minerva Endocrinol, 2007 Jun; 32(2):103-13.

Address:

Ilze Kreicberga
Department of Obstetrics and Gynecology,
Riga Stradins University
Dzirčiema street 16, LV - 1007
E-mail: ilze.kreicberga@rdn.lv

Fig. 1. Placenta A. IGF1 IHC, X 250

Fig.2. Placenta B. IGF1 IHC, X 250

Fig. 3. Placenta A. IGFR1 IHC, X 250

Fig. 4. Placenta B. IGFR1 IHC, X 250