Placenta 69 (2018) e12–e93

Contents lists available at ScienceDirect

Placenta

journal homepage: www.elsevier.com/locate/placenta

P1.1.
INTRAUTERINE GROWTH RETARDATION EXTINGUISHES SEXUAL DIMORPHISM OF HUMAN VILLOUS TROPHOBLAST

Eva Häußner[1], Nirav Barapatre[1], David Grynspan[2], Christoph Schmitz[1], Franz Edler von Koch[3], Hans-Georg Frank[1]. [1] *LMU Munich, Faculty of Medicine, Institute of Anatomy II, Chair of Neuroanatomy, Munich, Germany;* [2] *University of Ottawa, Department of Pathology and Laboratory Medicine, Ottawa, Canada;* [3] *Clinic for Obstetrics and Gynecology Dritter Orden, Munich, Germany*

Objectives: Human placentas are sexually dimorphic. In the average, the weights of male placentas are slightly higher than those of female placentas. Human placental sexual dimorphism is highly relevant as prenatal hallmark of life-long sex-related health patterns. We hypothesized that the weight differences known at the gross placental level translate into microstructural alterations at the level of the crucial tissue for fetomaternal exchange, i.e. villous trophoblast. Therefore, we implemented a 3D-microscopic analysis of the spatial arrangement of proliferative and non-proliferative nuclei of villous trophoblast. The study determined weights as well as sex-related spatial arrangement of PCNA-positive and PCNA-negative villous trophoblast nuclei in clinically normal and IUGR placentas by two different 3D-microscopic measures.
Methods: We analyzed 42 isolated peripheral villous trees of clinically normal and 40 of placentas of pregnancies with IUGR. Each sample was analyzed by 3D-microscopy and the 3D coordinates of each nucleus (separate for PCNA-positive and PCNA-negative nuclei) of villous trophoblast were recorded. Spatial arrangement of nuclei was determined as i) *mean density of villous trophoblast nuclei* of terminal and preterminal branches (MD), and as ii) *mean nearest neighbor distance of villous trophoblast nuclei* (NND).
Results: The spatial arrangement of PCNA-negative nuclei of villous trophoblast of clinically normal (but not of IUGR) placentas was sexually dimorphic. In male placentas, the MD was smaller (and NND larger) than in female placentas. With the case number studied here, placental weights were not significantly different.
Conclusion: 3D-microscopic analysis of the spatial arrangement of nuclei at the villous surface detects sexual dimorphism of human placentas with high statistical power in small case numbers. It is statistically more powerful than weighing and for the first time opens a path to quantitative analysis of placental sexual dimorphism at microscopic scale.

P1.2.
STUDY ON EFFECT OF SEVERITY OF MATERNAL IRON DEFICIENCY ANAEMIA ON MORPHOLOGY AND REGULATORS OF ANGIOGENESIS IN PLACENTA

Mullapudi Venkata Surekha, Putcha Uday Kumar, Sapna Singh, M. Srinivas, K. Sharada, N. Balakrishna, G. Sailaja. *National Institute of Nutrition, Hyderabad, India*

Objectives:
1) To study the effects of mild, moderate and severe grades of maternal iron deficiency anaemia on placental morphology and foetal outcome.
2) To correlate varying grades of iron deficiency anemia with the expression levels of angiogenic factors like Vascular endothelial growth factor(VEGF), Placental growth factor(PLGF), endothelial nitric oxide synthase(e-NOS) and Nitrotyrosine (NT)residues in placenta.
Methods: Blood collected from mothers before delivery and also from cord blood after delivery was analysed for hemoglobin, red cell indices, ferritin , transferrin receptors.Placentas (villous vascular endothelial cells, cytotrophoblasts and syncytiotrophoblasts) from respective mothers were studied by immunohistochemistry for expression of angiogenic factors like VEGF, PLGF, e-NOS and NT residues. Immunoreactivity for antibodies was scored using a semi-quantitative scale for intensity of staining: 0 negative/ no staining; 1+ weak positive; 2+ moderately positive; 3+ strongly positive.
Results: 20 /48 women (41.7%) had normal Hb levels and the remaining 28 (58.3%) had anaemia of varying grades.Both RDW and HDW levels were elevated in 82.5% women.Cord blood from babies born of anaemic mothers had slightly higher mean haemoglobin (Hb) levels when compared with Hb levels of babies born to normal mothers.Placental weight in anaemic women was lower when compared with controls.Number of capillaries/ villus in the placentas as well as syncytical knots / villus were significantly (p <0.05) increased with increasing severity of anaemia.Moreover, placentas from anaemic mothers showed stronger immunohistochemical staining for VEGF , PLGF , eNOS and NT residues.
Conclusion: Our study for the first time threw light on the finding of increased expression of VEGF, PLGF, eNOS and NT residues in placentas of anaemic women thus showing that hypoxia is probably a risk factor for development of premature arterial hypertension and cardiovascular disease later in adulthood of children born of mothers with anaemia, probably secondary to endothelial dysfunction.

P1.3.
INCREASED PLACENTAL VENOUS VESSEL DIAMETERS IN PRE-GESTATIONAL DIABETES

Matina Hakim, John Aplin, Susan Greenwood, Tristan Lowe, Jenny Myers. *The University of Manchester, Manchester, United Kingdom*

Objectives: Pre-gestational diabetes is associated with increased risk of stillbirth, fetal growth restriction or fetal overgrowth. We test the hypothesis that pre-gestational diabetes is associated with abnormal development of the fetoplacental venous system, manifest as an altered venous network at term.
To use 3-D Micro CT scanning of fetoplacental venous casts to provide a three-dimensional replica of the vessels and enable quantitative comparisons of the venous network.
Methods: Batson's Anatomical corrosion kit was used to produce venous casts of placentas from normal pregnancies (n=6) and pregnancies complicated by pre-gestational diabetes (n=6) at term. Casts were scanned in a Nikon metris-XTH225, reconstructed into a three-dimensional virtual object and segmentation software (Avizo 9.40) used to generate the number, diameter and total length of vessel segments.
Results: Median gestational ages (days±IQR) were 257±7d (pregestational diabetes) and 274±2d (controls p=0.005). Mean placental weights (±SD) were 705±86.52g (pre-gestational diabetes) and 556±36.07g (controls; p=0.020). There were no differences in birth weight or centile. The median number of vessel segments with diameter <300μm was 361.7±110.9 and

https://doi.org/10.1016/j.placenta.2018.06.004

408.3±73.5 in placentas from women with and without diabetes (p>0.05). In vessels >300 μm there was a significant non-linear relationship (p<0.0001) between increasing diameter and number of segments (figure 1), which was different between control and diabetes placentas (p=0.08). In control placentas there were no vessel segments of diameter > 8000μm, however 0.9% of vessel segments were >8000μm in casts from women with diabetes.

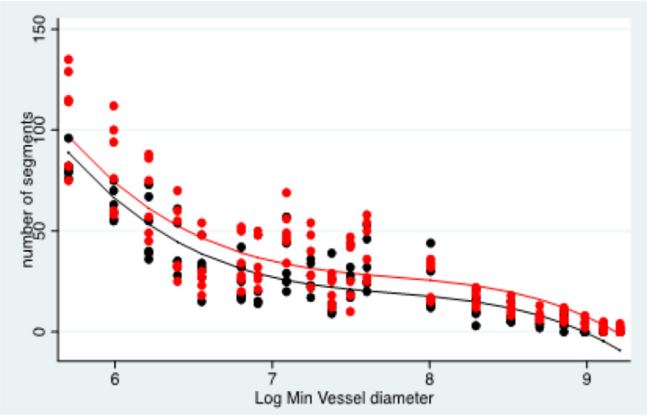

Figure 1. Relationship between number of vessel segments of increasing vessel diameter (300-10000μm) in the chorionic plate of placentas taken from women with (red) and without (black) diabetes

Conclusion: Greater diameters in venous segments of placentas of women with pre-gestational diabetes could impact on umbilical venous blood flow and delivery of nutrients and oxygen to the fetus. Ongoing studies will relate venous and arterial networks to plasma makers of angiogenesis, fetal growth trajectory and maternal glycaemic control earlier in pregnancy.

P1.4.
HISTOLOGICAL ASSESSMENT OF A DEVELOPING PLACENTA *IN UTERO* – WHAT WE CAN LEARN FROM ARCHIVAL FIRST TRIMESTER MATERIAL

Gerit Moser, Monika Sundl, Desiree Forstner, Martin Gauster, Berthold Huppertz. *Medical University of Graz, Graz, Austria*

Objectives: First trimester hysterectomy specimens with placenta *in utero* provide the ideal material for the assessment of fetal-maternal cell interactions occurring in early gestation. Anatomical aspects, such as structure, orientation and degree of uterine vessel and gland remodeling, as well as progression of trophoblast invasion can be analyzed. Moreover, at the end of the first trimester disintegration of trophoblast plugs, giving rise to initiation of utero-placental blood flow, can be localized. The aim was to assess a unique archival specimen of a first trimester placenta *in utero* available at our department and present it to the research community.
Methods: Serial sections of an archival placenta *in utero* from the first trimester were evaluated using immunohistochemical single and double stainings, beside PAS- and Alcianblue-staining. Antibodies against HLA-G, cytokeratin 7 (CK7), von Willebrand Factor (vWF) and CD42b were used.
Results: Staining sections of the placenta in utero with antibodies against HLA-G, CK7 and vWF revealed the pattern of extravillous trophoblast and vessel distribution around placenta and embryo. Extravillous trophoblasts invaded into uterine glands and vessels. Eroded uterine glands can be visualized especially at the margin of the placenta. Staining for the platelet marker CD42b showed platelets accumulating in close proximity of disintegrating endovascular trophoblast plugs, on trophoblast columns of anchoring placental villi and the adjacent lining of the intervillous space.
Conclusion: Although there is neither information of the origin nor the gestational age nor the processing of this archival placenta *in utero*, it is still an invaluable treasure for placental research, especially when re-assessing it with the background of the recent state of knowledge. Placenta *in utero* specimens may enable assessment of the degree of utero-placental perfusion, by detecting glandular secretion products and maternal blood cells in the intervillous space.

P1.5.
A CASE OF COMPLETE HYDATIDIFORM MOLE COEXISTENT WITH A FETUS TREATED BY SIMPLE HYSTERECTOMY

Tomona Matsuoka, Hiroaki Aoki, Ritsuko Kobayashi, Natsuki Matsumoto, Akihiro Ikenaga, Wakiko Shimomai, Kana Hirayama, Keiko Yabuzaki, Taisuke Sato, Michihiro Yamamura, Haruhiko Udagawa, Kazuhiro Kajiwara, Yuki Ito, Taizan Kamide, Osamu Samura, Aikou Okamoto. *The Jikei University School of Medicine, Tokyo, Japan*

Objectives: We report our experience of a case of complete hydatidiform mole coexistent with a fetus treated by simple hysterectomy.
Methods: The patient was a 32-year-old woman, 5 gravida 2 para (including the present pregnancy), with no particular medical history.
Results: Pregnancy was established spontaneously. At 16 weeks of pregnancy, the subject was examined for abnormal vaginal bleeding. On suspicion of placental mesenchymal dysplasia (PMD), at 17 weeks of pregnancy, the subject was referred to our hospital for examination. Human chorionic gonadotropin (hCG) at the time of examination was abnormally high at 976700 mIU/ml. At 18 weeks of pregnancy the subject underwent examination by magnetic resonance imaging (MRI). A normal fetus and multilocular tumor were observed. These Results led to the suspicion of complete hydatidiform mole coexistent with a fetus. Because the part of complete hydatidiform mole covered uterine os completely, there was high risk of bleeding. Furthermore, there was high risk of proceed to invasive mole. The patient gave up to bear the child and wished to treat by operation, and therefore at 19 weeks of pregnancy, simple total hysterectomy was performed as treatment. After operation, the case was diagnosed complete hydatidiform mole coexistent with a fetus by pathological examination. Postoperative hCG levels decreased with satisfactory progress, and at present, 35 weeks after surgery, progress is good.
Conclusion: Hydatidiform mole coexistent with a fetus is an extremely rare condition affecting one per 22,000 – 100,000 pregnancies. We report with slight review of the literature.

P1.6.
PLACENTAL PATHOLOGY PREDICTS INFANTILE PHYSICAL DEVELOPMENT DURING FIRST 18 MONTHS IN JAPANESE POPULATION

Chizuko Yaguchi, Naomi Isomura, Masako Matsumoto, Yoshimasa Horikoshi, Kazuhiro Sugihara, Hiroaki Itoh, Naohiro Kanayama. *Hamamatsu University School of Medicine, Hamamatsu city, Japan*

Objectives: The placenta is the largest fetal organ that links the mother to the fetus and supports most parts of organogenesis through the transport of nutrients, gases, and hormone synthesis. The placenta adapts to the maternal environment by changing its structure as well as function, thereby contributing to the maintenance of fetal development throughout the pregnant period.
The present study aimed to investigate the relationship between placental pathological findings and physiological development during the neonate and infantile periods.
Methods: Study participants were 258 infants from singleton pregnancies enrolled in the Hamamatsu Birth Cohort for Mothers and Children (HBC Study) whose placentas were stored in our pathological division. They were followed up from birth to 18 months of age. Physiological development (body weight and the ponderal index [PI]) was assessed at 0, 1, 4, 6, 10, 14, and 18 months. The pathological findings of placentas were classified into eleven categories in consideration of the current Amsterdam Placental Workshop Group Consensus Statement : i.e. 'Accelerated villous maturation', 'Decidual vasculopathy', 'Thrombosis or Intramural fibrin deposition', 'Avascular villi', 'Delayed villous maturation, 'Maternal inflammatory response', 'Fetal inflammatory response', 'Villitis of unknown etiology (VUE)', 'Deciduitis', 'Maternal vascular malperfusion' and 'Fetal vascular malperfusion'. In order to assess the