

- 35 cases of twins and triplets, 32.1%

By histological examination,

- Stem villous edema, intermediate villous vessels occlusions, terminal villous avascular, and decidual vascular and other lesions were observed.

By clinical record:

- 21 cases of GDM, 19.2%
- 20 cases of FGR, 18.3%
- 11 cases of HDP, 10.6%

Conclusions: Twins sharing the same amniotic cavity with just one placenta have many complications with VCI.

VCI is a problem on the fetal side, and it can be easily identified by gross examination, as can the problems in the circulation on the mother's side. VCI shares with HDP the lack of circulation from the mother's side, and clinically, the high rate of complications is due to maternal floor vessels problems.

In regards to GDM, previously the VCI rate was not so high, but recently it has been higher than before. The reason for this is that GDM diagnosis has now become more accurate and can be seen to be more common.

Placental pathology is very effective at explaining clinical states about VCI and my hypotheses regarding the origin of VCI is backed up by both clinical and pathological pictures. These clearly show the link between HDP, GDM, and FGR and lack of circulation on the mother's side and fetal side of the placenta.

69. AVASCULAR VILLI

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Object: Lack or diminishment of capillaries in the villi of the placenta, known as avascular villi, has several causes. Firstly, there is chromosomal abnormality (Hydatidiform mole, Turner syndrome, etc.). Secondly, Villitis of Unknown Etiology (VUE). Thirdly, villus injury from mother's abnormal circulation. And fourthly, occlusive terminal villus capillary from cord occlusion or from occlusion of the vessels on the surface of the placenta.

In this paper I examine the pathological findings and clinical findings from cases of avascular villi over the period of one year, and classified those cases according to these four causes.

Material: I examined 122 singleton avascular villi cases. I classified each pathologically and studied the clinical findings.

Results: Pathologically, there were cases of dysmature villi, avascular villi of VUE, avascular villi from problems with the circulation from mother to placenta, and avascular villi due to bad fetal to placental circulation. I saw all four categories in the 122 cases.

Pathologically, out of 122 cases, I found:

19 cases of dysmature villi

15 cases of VUE

49 cases of avascular villi from bad circulation from mother to placenta

51 cases of coiling or abnormal insertion of cord

Clinically, from the 122 cases, I found:

15 cases of IUFD

16 cases of HDP

18 cases of GDM

24 cases of FGR

18 cases of NRFS (non-reassuring fetal status)

Conclusions: In avascular villi it is usual to expect IUFD, but I also found high rates of complications with HDP, GDM, FGR and NRFS. In this paper I study how widespread avascular villi is commonly associated with more severe perinatal problems.

S-01.

AMINO ACID TRANSPORTATION IN THE PLACENTA AND ITS IMPORTANCE IN FETAL GROWTH

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Objective: Insufficient oxygen supply is closely associated with the pathophysiology of fetal growth restriction (FGR). By using transgenic mice with its oxygen delivering capacity deteriorated, we examined the phenotype of the mice and aimed to elucidate the underlying mechanism by which the phenotype is induced.

Methods: Conditional knockout mice with erythrocyte-specific gene deletion of ENT1 (eEKO), a key adenosine transporter, were utilized in this study. The oxygen delivering capacity was measured by measuring p50 and 2,3-BPG in the erythrocytes. The dams were sacrificed on 17.5 dpc (days post coitus), and blood pressure, proteinuria, and the weight of the pups were measured. Metabolic profiling was used to determine the change of nutrient transports from the dam to the fetus by using maternal plasma and the placenta. We conducted real-time PCR, western blot, and in vivo experiment using human trophoblast cell line (HTR-8/SVneo cells) to access the molecular mechanism underlying the phenotype.

Results: eEKO showed reduction in oxygen delivering capacity in both p50 and 2,3-BPG in the maternal erythrocytes. The dams did not show hypertension or proteinuria, but they showed reduction in fetal weight, suggesting they have FGR phenotype. The immuno-staining in the placenta showed overexpression of HIF-1 α in the placenta of eEKO, suggesting hypoxia in the placenta. Metabolomic profiling showed reduction of broad spectrum of amino acids in the placentas from eEKO, although the amino acids were rather increased in the maternal plasma, which implies the impaired amino acid transport function. Both real-time PCR and the western blot analysis showed reduction of LAT1, amino acid transporter, in the placentas from eEKO. Culturing HTR cells in HIF-1 α stabilized state showed reduction of LAT1 in the placenta.

Conclusion: Our findings suggest that maternal erythrocytes' oxygen delivering capacity mediated by ENT1 is essential for maintaining adequate placental oxygenation to support fetal growth predominantly through LAT1. Strategies to improve erythrocytes' function to deliver oxygen may provide new therapeutic possibilities for FGR.

S-02.

RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN AS AN ANTICOAGULATION THERAPY IMPROVES RECURRENT MISCARRIAGE AND FETAL GROWTH RESTRICTION DUE TO PLACENTAL INSUFFICIENCY

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Objective: Placental insufficiency is one of the major risk factors for growth restriction and preeclampsia. The purpose of this study is to investigate whether recombinant human thrombomodulin (r-TM) as anticoagulant therapy improves fetal conditions and physiological outcomes.

Methods: We used CBA/J \times BALB/C mice as a control and CBA/J \times DBA/2 mice — a well-studied model of recurrent spontaneous miscarriage. Pregnant mice received daily subcutaneous injections of r-TM or saline from day 0-15. The fetal resorption rate, fetal weight, and fetal size were calculated at day 15. Additionally, we analyzed the mRNA expression of angiogenic factors and the concentration of soluble Flt-1 (sFlt-1) using the ELISA kit.

Results: The rate of fetal resorption in CBA/J \times DBA/2 mice treated with r-TM was significantly lower compared with mice without r-TM treatment. Additionally, fetal weight and fetal size were also significantly higher in the r-TM treated mice. Fibrinogen deposition in the labyrinth area of the CBA/J \times DBA/2 mice treated with r-TM was significantly lower compared with deposits in the mice untreated with r-TM. As well, r-TM significantly increased the gene expression level of VEGF and Flt-1 mRNA in the placentas of the CBA/J \times DBA/2 mice. r-TM treatment also significantly