

Expression of invasion related MMP-1 was also up-regulated by LC and increased expression of active form of MMP-1 was detected in LC treated cells.

Conclusion: Our results suggest that *Lactobacillus crispatus* promotes trophoblast invasion via up-regulation of MMP-1. Our findings suggest indispensable roles of LC which dominate in healthy human vagina. Our results can explain why BV and other lower female genital tract infections harm successful human pregnancies.

25.

SUPPRESSYN MAY PLAY A CENTRAL ROLE IN TROPHOBLAST CELL FUSION RESPONSE TO OXYGEN ENVIRONMENTS

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Objective: We previously described and analyzed the function of a novel anti-fusogenic protein suppressyn (SUPYN) in cultured trophoblast cells. The physiological state of the placenta is hypoxic varying between 2 and 5% in early pregnancy. Here we performed expression analysis of cell fusion related genes to determine whether SUPYN may play a role in trophoblast syncytialization response to hypoxia and hyperoxia.

Methods: Primary trophoblast cells were isolated from term placenta and cultured under several O₂ conditions. RNA transcripts were collected every 24 hours and subjected to semi-quantitative RT-PCR. A newly-established SUPYN specific ELISA was used to detect alterations in cell associated and secreted forms of SUPYN protein during cell fusion.

Results: Fusion of primary trophoblast cells was predominantly suppressed under the range of "physiologic" hypoxic conditions and both syncytialization and hCG gene expression were lower than in higher O₂ environments. Expression of syncytin-1 was lower but SUPYN transcripts higher in low O₂ environments. This phenomenon was confirmed at the protein for both cell-associated and secreted SUPYN.

Conclusion: Converse syncytin-1 and SUPYN transcriptional and translational responses to surrounding oxygen concentrations suggest both are important in the effects of hypoxia and hyperoxia on placental syncytialization. Further analysis of these fusion-associated transcripts under different O₂ condition will likely improve our understanding of placental physiology and placental diseases like pre-eclampsia and PIH.

26.

A CASE WITH HYDRAMNION AND DIAGNOSED AS PLACENTAL HEMANGIOMA AFTER DELIVERY

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Introduction: Hydramnion is known to be caused by diabetes or fetal congenital malformation, but in rare case, large placental hemangioma can induce hydramnion. We experienced a case of hydramnion caused by placental hemangioma.

Case: A 36-year-old primipara. She had a prenatal care in Australia until 32 weeks, and since then at a midwifery clinic in Japan. On 37 weeks and 1 day, she visited the clinic for amniotic fluid runoff. At that time, hydramnion was recognized (AFI 27.5), so she was transferred to our hospital. Her HbA1c and glycoalbumin were normal, and no apparent malformation was found in fetus. Caesarean section was performed at 37 weeks and 5 days because of induction failure. The baby was born at 3350g, Apgar score 9/9, UA-pH 7.373, and a boy. He had a heart failure and was admitted to NICU for 7 days. No obvious malformation was pointed out, but infantile hemangioma was found throughout the body. A 13.5×10.5×5.5cm well-defined nodular lesion was found in placenta. The pathological diagnosis was placental hemangioma.

Discussion: Placental hemangiomas are found in about 1% of the placenta, and if the tumor diameter is more than 5cm, perinatal complications such as hydramnion may be induced.

In neonates, they may have a heart failure like this case, and there are hemangiomas in the viscera which required treatment in rare case. This case suggests that placental hemangioma should be considered in case of hydramnion. Additionally, neonatal heart failure or hemangiomas may be observed, so advanced facilities is desirable for delivery.

27.

PROGNOSTIC FACTORS FOR THE OUTCOMES OF LOW-LYING PLACENTA BY TRANSVAGINAL ULTRASOUND

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Objectives: Low-lying placenta (LLP) are regarded as high-risk conditions of pregnancy. However, lower uterine segment extension for placental migration related to LLP remain unclear. In this study, we searched placental position and findings on ultrasound on LLP.

Methods: We retrospectively reviewed the cases of LLP for the past 5 years from medical records (2013–2017). Location of placenta, cervical length and spongous (S-) findings suggest venous plexus were defined. Mode of delivery, blood loss and placental weight were also searched.

Results: In our cases, 33 LLP were located on posterior wall attachment and only one was on anterior. This anterior-located LLP with S-finding caused to massive bleeding which massive blood transfusion and 3 times UAE were needed. In contrast, only one case in 33 posterior cases needed transfusion. Average cervical length at diagnosis was significantly longer in the group with S-finding (n=13, 40.2 mm) compared to no S-finding group (n=21, 32.7 mm, p=0.01). Caesarean section was performed in all cases with S-finding. Vaginal delivery was performed in 5 cases in the other group. There was no difference in the amount of blood loss, infant birth weight or placental weight.

Conclusions: Surprisingly, almost all LLP located on posterior wall; anterior-located low-lying placenta showed miserable outcome on delivery. S-finding correlated with cervical length, suggesting that failed uterine lower segment extension contribute to placenta migration can be predicted from this ultrasound finding.

28.

ROLE OF PLACENTAL ATX-LPA SYSTEM AND ITS PATHOLOGIC RELEVANCE TO HYPERTENSIVE DISORDERS OF PREGNANCY

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Objective: Lysophosphatidic acid (LPA), produced by enzymatic action of a secretory protein, autotaxin (ATX), exerts diverse functions through six receptors. Our study aimed to clarify the role of ATX-LPA system in placenta and its association with the pathology of hypertensive disorders of pregnancy (HDP).

Methods: Placental expression of LPA receptors was compared between normal pregnancy and HDP. We assessed the distribution of ATX and LPAR3 in placenta using immunohistochemistry. The impact of LPA stimulation on gene expression profiling was examined in LPAR3-transfected trophoblast cells. Using serum samples, a correlation of ATX levels to oxidative stress markers and fetal growth was evaluated.

Results: ATX expression was ubiquitous, whereas LPAR3 expression was restricted to differentiated trophoblasts. HDP placentas showed increased mRNA expressions of LPARs, whereas the elevation of protein expression was limited to LPAR3. LPA signaling mediated by LPAR3 enhanced the gene expressions involved in immunomodulation and cell differentiation. In normal pregnancy, serum ATX level in the second trimester was negatively correlated with birth weight-to-placental weight ratio. Placental ATX expression in the third trimester decreased in early-onset HDP and increased in late-onset HDP. Serum ATX level was positively correlated to oxidative stress markers.

Conclusion: ATX-LPA system might be involved in a regulatory mechanism of oxidative stress, local immunity and cell differentiation, contributing to a proper control of placental function to support healthy fetal growth.

29. THE ADVANTAGE OF INTRAUTERINE EVACUATION FOR PLACENTAL REMNANT WITH CONTRAST-ENHANCED ULTRASONOGRAPHY AND UTERINE BALLOON TAMPONADE

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Introduction: Placental remnant is one of the cause of the postpartum hemorrhage. Although intrauterine evacuation is performed for placental remnant without adhesion, it may cause a massive hemorrhage because of inability to identify bleeding points during operation. Here, we show the advantage of intrauterine evacuation for placental remnant with contrast-enhanced ultrasonography (CEUS) and uterine balloon tamponade (UBT) with four clinical cases. CEUS has been required to identify the bleeding points and contribute to successful hemostasis.

Method: We experienced four cases of placental remnant and performed intrauterine evacuation combined with CEUS and UBT from 2018 to 2019. Ultrasound contrast agent (Sonazoid®) was infused just before an operation. After the intrauterine evacuation, the uterine balloon (minimetro®) was detained.

Result: Four clinical cases are as follows: a case of placental remnant at the postpartum 10th day, a case of placental remnant 28th days after the cesarean section, the case of suspected pseudoaneurysm at the postpartum 30th days and the case of placental remnant coexist placenta accreta at 27th days after the 19weeks abortion. Intrauterine evacuation combined with CEUS and UBT was performed. In all cases, CEUS could identified bleeding points immediately and hemostasis was confirmed by UBT. In the next day, uterine balloon was taken off and there were no complications in all cases.

Conclusion: CEUS could identified the bleeding points during operation and contribute to successful hemostasis.

30. A CASE OF VAGINAL DELIVERY AFTER INTRAUTERINE FETAL DEATH (IUFD) WITH PLACENTA PREVIA IN SECOND TRIMESTER PREGNANCY BY UTERINE ARTERY EMBOLIZATION

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Introduction: There are few reports on labor management with placenta previa after IUFD in a second-trimester pregnancy. It is very difficult to deal with pregnancy termination of IUFD with placenta previa in second trimester pregnancy. We report a case of successful vaginal delivery after IUFD with placenta previa in second trimester pregnancy.

Case: A 39-year-old nulliparous pregnant woman was referred at 21 weeks gestation, because of fetal screening. Sonographic findings showed complete placenta previa, fetal growth restriction, velamentous cord insertion and hyper coiled cord and uterine myoma. At 22 weeks, sudden fetal death occurred. To avoid cesarean section, we performed uterine artery embolization (UAE) before vaginal delivery. After the UAE, cervical dilator was inserted for cervical ripening and the fetus was delivered vaginally by using prostaglandin and oxytocin. The total blood loss was only 168g. We have been evaluating and monitoring involution of uterus and postpartum ovarian activity.

Discussion: Several reports suggest as the useful method for pregnant women with placenta previa after IUFD in a second-trimester pregnancy, labor induction after UAE, cesarean section, simple hysterectomy and D&E. At present, however, there is not enough evidence for bleeding and fertility, and we don't have obtained consensus for management in these cases.

31. COMPARISON OF SPONTANEOUS PREGNANCY WITH PREGNANCY AFTER EMBRYO IMPLANTATION IN WOMEN WHO DELIVERED BABIES AT AN ADVANCED AGE AT OUR HOSPITAL

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Objective: Lifestyle changes in females and advances in infertility treatment have elevated the maternal age. In this study, we compared spontaneous pregnancy with pregnancy after embryo implantation in patients who delivered babies at an advanced age.

Methods: Of single-birth patients who delivered babies in our hospital between January 2013 and December 2018, we extracted those aged ≥ 41 years at the time of delivery, and compared the clinical findings, neonatal findings, and pathological findings of the placenta (Amsterdam classification) between spontaneous pregnancy and that after embryo implantation.

Results: The subjects consisted of 85 who became pregnant spontaneously and 57 who became pregnant after embryo implantation. Primiparae accounted for 27 and 4.4%, respectively ($p < 0.01$). As complications, hypertensive disorders of pregnancy (HDP) were observed in 7 and 10.5% of the subjects, respectively ($p = 0.54$), and diabetes mellitus (DM)/gestational diabetes mellitus (GDM) in 15.3 and 10.5%, respectively ($p = 0.46$). Concerning delivery methods, Cesarean section was performed in 42.4 and 61.4% of the subjects, respectively ($p < 0.05$). Of these, emergency Cesarean section was conducted in 15.2 and 10.5%, respectively ($p = 0.46$). The mean volume of blood loss on delivery was 628 ± 461 and $886 \pm 1,072$ mL, respectively ($p = 0.053$). In the spontaneous pregnancy group, there was no placenta accreta in any patient. However, in the post-embryo-implantation pregnancy group, it was observed in 4 patients. Premature birth before Week 36 of pregnancy accounted for 8.2 and 8.7%, respectively ($p = 1.00$). The mean birth weights were $2,823 \pm 602$ and $2,869 \pm 554$ g, respectively. The mean Apgar scores at 1 minute were 7.5 and 8.5, respectively, and those at 5 minutes were 8.5 and 7.3, respectively. Small-for-date (SFD) neonates accounted for 4.7 and 1.7%, respectively ($p = 0.64$). Neonates who were admitted to the neonatal intensive care unit (NICU) with full-term birth respiratory disorder accounted for 4.7 and 15.7%, respectively ($p < 0.05$). The pathological findings of the placenta included abnormalities at the umbilical cord attachment site (velamentous insertion of the cord, furcal adhesion) (5.9 and 17.5%, respectively) ($p < 0.05$). In 1 of the patients with placenta accreta, hemostasis was difficult, and supravaginal amputation of the uterus was performed. Histopathologically, placenta increta was observed. For histopathological examination of the placenta, specimens from 39 patients were submitted. According to the Amsterdam classification, fetal/maternal vascular malperfusion was slightly more frequent in the post-embryo-implantation pregnancy group. The thickness of the decidual nitabuch layer markedly differed among the patients and sites.

Conclusion: At an advanced maternal age, attention should be paid to complications. In particular, the risks of placenta accreta/massive hemorrhage must be considered in patients who became pregnant after embryo implantation.

32. A NEONATE WITH TRANSIENT ABNORMAL MYELOPOIESIS

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Neonatal transient abnormal myelopoiesis (TAM) is primarily associated with GATA-1 gene mutations in the embryonic phase in trisomy 21 neonates. In most cases, this disorder spontaneously subsides, but the concomitant development of organ damage leads to a poor prognosis. In some cases, acute megakaryoblastic leukemia develops after a few years. In this study, we report a neonate TAM who was brought to our hospital by ambulance, and present pathological findings of the placenta. The neonate's mother was a 40-year-old primipara. On the previous pregnancy,