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

Rie Seyama, Shintaro Makino, Mitsuko Shinohara, Masaya Takahashi, Jun Takeda, Satoru Takeda, Atsuo Itakura. *Department of Obstetrics and Gynecology, Juntendo Hospital*

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

Aki Hayashi, Mikio Morine, Mikio Yamazaki, Akane Kondo, Kenji Hinokio, Kazuhisa Maeda. *Shikoku Medical Center for Children and Adults, Japan*

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

Naomi Isomura, Takuma Furukawa, Chika Etou, Yoshimasa Horikoshi, Masako Matumoto, Chizuko Yaguchi, Kazunao Suzuki, Hiroaki Itou. *Department of Hamamatu University school of medicine*

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 $\geq$41 years at the time of delivery, and compared the clinical findings, neonatal findings, and pathological findings of the placenta (Amsterdam classification) between spontaneous pregnancy and that after embryo implantation.
Results: The subjects consisted of 85 who became pregnant spontaneously and 57 who became pregnant after embryo implantation. Primiparae accounted for 27 and 4.4%, respectively ($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$). The mean volume of blood loss on delivery was 628±461 and 886±1,072 mL, respectively ($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$). The mean birth weights were 2,823±602 and 2,869±554 g, respectively. The mean Apgar scores at 1 minute were 7.5 and 8.5, respectively, and those at 5 minutes were 8.5 and 7.3, respectively. Small-for-date (SFD) neonates accounted for 4.7 and 1.7%, respectively ($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

Chika Etou, Naomi Isomura, Takuma Furukawa, Yoshimasa Horikoshi, Masako Matumoto, Chizuko Yaguchi, Kazunao Suzuki, Hiroaki Itou. *Department of Hamamatu University of Medicine*

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,

she delivered a boy weighing 2,960 g in Week 39 of pregnancy (normal transvaginal delivery). In the present case, she became pregnant spontaneously. The course of pregnancy was not contributory. On Day 5 of Week 37, natural labor pain occurred, and she was admitted. On the same day, a boy weighing 3,052 g was born (normal transvaginal delivery). For resuscitation, routine care alone was conducted. After birth, there was no abnormal finding including specific face. After the first session of lactation, vomiting was noted several times. On Day 1 of age, petechia of the face was observed. A blood test showed a leukocyte count of 59,700/μL and a percent blast of 28%. For detailed examination, the neonate was referred to our hospital, and bone marrow biopsy was performed on Day 5 of age. The level of a myelocyte surface marker suggested TAM or acute myelocytic leukemia M7. The blast count was approximately 10,000/μL, but both the leukocyte and blast counts decreased from Day 12 of age. Histopathologically, a large number of blasts were detected in the umbilical and stem villus blood vessels. The villus tissue consisted of mature intermediate and terminal villi, and there was no immature villus. PHA-free G-banding of peripheral blood on admission showed nuclear type 47, XY, +21 [20]. On Day 23 of age, the leukocyte count and percent blast were 13,270/μL and 1%, respectively, showing decreases. The neonate was discharged, and follow-up was continued at the outpatient clinic. The FISH method using a buccal mucosa specimen submitted during admission led to a diagnosis of mosaic Down syndrome. We present pathological findings of the placenta, and review the literature.

33.
CORE2 BETA 1, 6-N ACETYLGLCOSAMINYL TRANSFERASE PROMOTES INVASION OF CHORIOCARCINOMA CELLS THROUGH GLYCOSYLATION TO MICA AND MUC1

Kaoru Niimi [1], Eiko Yamamoto [2], Kenichi Nakamura [1], Yukari Taguchi [1], Eri Watanabe [1], Kimihiro Nishino [1], Fumitaka Kikkawa [1]. [1] *Department of Obstetrics and Gynecology, Nagoya University Graduate School of Medicine;* [2] *Department of Healthcare Administration, Nagoya University Graduate School of Medicine*

Hyperglycosylated human chorionic gonadotropin (H-hCG), which contains much larger sugar chains than regular hCG, is secreted from choriocarcinoma patients but not normal pregnancy or hydatidiform mole. O-linked H-hCG is one of important factors in invasion and growth of choriocarcinoma cells, and core2 beta 1, 6-N acetylglcosaminyl transferase (C2GnT) forms core2 O-glycan. The aim of this study is to examine roles of C2GnT in invasion mechanism of choriocarcinoma cells, especially related to the NK cell immunity. We investigated C2GnT expression in gestational trophoblastic diseases and placentas by immunohistochemistry and western blotting. We established C2GnT knockout (KO) cells with Jar and BeWo cells and investigated cytotoxicity of NK cells against those cells. MICA and MUC1 glycosylation were analyzed by immunoprecipitation. We incubated C2GnT-KO and control with TRAIL and cell viability were analyzed. We inoculated the C2GnT-KO and control cells subcutaneously into nude mice. C2GnT was highly expressed in trophoblasts of choriocarcinoma but not in hydatidiform mole and normal placenta. C2GnT-KO cells were more efficiently killed by NK cells than controls. Sugar chains attached by C2GnT on MICA and MUC1 in C2GnT-KO cells were significantly decreased. The cell viability of C2GnT-KO cells were lower than controls depending on TRAIL amount. C2GnT-KO promoted longer survival as compared with the controls. Choriocarcinoma cells may acquire a high malignant potential by expressing C2GnT with glycosylation to MICA and MUC1.

34.
STERILE INFLAMMATION IN PRETERM BIRTH WITHOUT CHORIOAMNIONITIS

Yasuyuki Negishi [1], Masahiko Kato [2], Yoshio Shima [3], Rimpei Morita [1], Hidemi Takahashi [1], Toshiyuki Takeshita [2]. [1] *Department of Microbiology and Immunology, Nippon Medical School;* [2] *Department of Obstetrics and Gynecology, Nippon Medical School;* [3] *Department of Pediatrics, Nippon Medical School Musashikosugi Hospital*

Introduction: Infectious diseases can induce preterm birth (PB). In particular, chorioamnionitis (CAM) is believed to be a trigger for PB. However, cases of PB without histological CAM and of unknown etiology are often encountered. In this study, the kinetics of immune cells in the decidua of PB without CAM was evaluated.
Methods: The decidua basalis and parietalis were obtained from women with PB without CAM at gestational ages of 24^{+0}–33^{+6} weeks. The participants were classified into two groups: those with labor pain and/or rupture of membrane (nCAM−w-LR) and those without these features (nCAM−w/o-LR). The immune cells in the decidua were analyzed using flow cytometry.
Results: Compared with the nCAM−w/o-LR group, increased population of invariant natural killer T (iNKT) cells and expressions of TLR4, receptor for advanced glycation and products, and CD1d on dendritic cells and macrophages were observed in the decidua parietalis of the nCAM−w-LR group. Moreover, the concentrations of high-mobility group box 1 (HMGB1) proteins in the viable and dead cells were up-regulated in the nCAM−w-LR group than those in the nCAM−w/o-LR group.
Conclusions: The cellular network in the iNKT cells, DCs, and macrophages may contribute to the onset of preterm labor and rupture of membrane without CAM. Endogenous molecules, such as HMGB1, may function as aggravating factors or activation triggers for these innate immune cells, and may subsequently lead to sterile inflammation in the implantation site.

35.
EG-VEGF ENHANCES THE TROPHOBLAST INVASION THROUGH ACTIVATION OF MMP-2 AND MMP-9 VIA PROKR2 IN THE HUMAN TROPHOBLAST CELL LINES

Kazumasa Tani, Sakurako Mishima, Akiko Ohira, Jota Maki, Shoko Tamada, Takashi Mitsui, Eriko Eto, Kei Hayata, Hisashi Masuyama. *Department of Obstetrics & Gynecology, Okayama University*

Objective: Trophoblast invasion is an important event in embryo implantation and placental development. Dysregulation of the finely controlled process of trophoblast invasion can lead to preeclampsia.
This study aimed to unveil the role of EG-VEGF, PROKR1/2, matrix metalloproteinase (MMP)-2 and MMP-9 in trophoblast invasion during spiral artery remodeling in the human trophoblast cell lines (HTR-8/SVneo).
Methods: The expression of HIF1-α, EG-VEGF, MMP-2 and MMP-9 was detected using real-time RT-PCR in HTR-8/SVneo under 5% oxygen condition for 24 h. MMP-2 and MMP-9 expressions were detected using real-time RT-PCR and Western blot in HTR-8/SVneo treated with recombinant EG-VEGF, PROKR1 antagonist, PROKR2 antagonist under 20% oxygen condition for 24 h.
Results: The expression of HIF1-α, EG-VEGF, MMP-2, MMP-9 was increased under 5% oxygen condition. MMP-2 and MMP-9 expressions were decreased with PROKR2 antagonist under 20% oxygen condition.
Conclusion: EG-VEGF enhances the trophoblast invasion through activation of MMP-2 and MMP-9 via PROKR2 in the human trophoblast cell lines.

36.
FREQUENCY OF PERFORMING UTERINE ARTERY EMBOLIZATION FOR TREATMENT OF THE TOTALLY RETAINED PLACENTA

Jun Okayama, Akiko Omoto, Rie Shinno, Yoshiya Suzuki, Akiko Nagasawa, Emiri Nakada, Mariko Inoue, Hirokazu Usui, Makio Shozu. *Department of Maternal and Fetal Medicine, Chiba University Hospital*

Objective: Retained placenta occurs at a frequency of about 2%, often leads to postpartum hemorrhage. Although uterine artery embolization (UAE) is implicated to be useful, there is complication for its use in the management of the postpartum hemorrhage. We reviewed the retained placenta cases managed in our hospital.
Subjects and Methods: During April 2010 and March 2019, there were 50 cases with partially retained placenta and 50 cases with totally retained placenta. The later cases only were the subject of this retrospective study.