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Evaluation of the relation between vascular cell adhesion molecule-1 and morbidly adherent placenta

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Objective

Morbidly Adherent Placenta (MAP) is a large clinical condition that includes placenta accreta, increta and percreta. Although The main pathology is accepted as the myometrial invasion of placental villi through the decidual layer, the pathophysiology leading to this is not fully understood. This clinical condition is important because it causes bleeding in life-threatening dimensions at the time of delivery. Vascular Cell Adhesion Molecule-1 is a calcium independent transmembrane glycoprotein. It is involved in Antigen recognition, complement reaction, cell-cell and cell-matrix binding. In various studies VCAM was found to increase invasion in tumor cells. In the current study, we compared morbidly adherent placentas and placentas without any risk factors in terms of VCAM-1 expression.

Methods

Our study was carried out between June 2016 and October 2017 in Bursa Yüksek İhtisas Education and Research Hospital, Obstetrics and Gynecology Clinic. In the study 103 placentas of the patients with the diagnosis of morbidly adherent placenta and 341 placentas of pregnant women without morbidly adherent placenta were included. Patients with history of previous uterine surgery (except previous cesarean section), , placenta previa in previous pregnancies, gestational diabetes, smokers, narcotic users, patients who had IUGR fetuses were excluded from the study. The study was approved by the local ethics committee. Patients who applied to the outpatient clinic were evaluated by transvaginal ultrasonography after physical and vaginal examination. Patients who met all of the criteria defined by Cali et al. Were evaluated as morbidly adherent placenta and included in the patient group Criteria evaluated by the ultrasound: - Completely covering of the placenta originating from uterine anterior surface cervical internal os - loss/irregularity of the echolucent area between the uterus and the placenta ('clearspace'), - thinning ori nterruption of the hyperechoic interface between the uterine serosa and the bladder Wall - irregular intraplacental vascularization - hypervascularity of the uterine serosa - Patients with who have previous cesarean section without MAP appearance on the ultrasound were included in the control group. While all the patients in the control group were delivered by planned cesarean section between 38-39 weeks, all patients in the study group were delivered by planned cesarean with hysterectomy between 36-37 weeks of gestation. All MAP diagnoses verified intraoperatively. Immediately after cesarean section and and post-cesarean hysterectomy, placentas were stored in containers containing 10% formaldehyde (neutral-buffered). Rectangular sections measuring 1. 5 cm x 1 cm in size were taken from the decidual surface of the placentas. Both tissues sampled were buried in paraffin blocks and Samples were taken to a cold compartment Hematoxylin-eosin staining and VCAM-1 as an immune-histochemical staining after antigen retrieval treatment were applied to all sections of 4 micron thickness obtained from the prepared paraffin blocks for all groups (VCAM-1 Antibody MS-1101-P ThermoScientific/LabVision). Prepared slides were examined by Nikon Eclipse Ni Education and Research Microscope that had NIS Elements v4. 30 Nikon Eclipse Ni Imagine Software Programme and pictures were taken. The pathologist evaluating the preparations was blind about the patient group from which the specimen was taken. The placentas were assessed as positive and negative staining for VCAM-1 (Figure-1). SPSS 15. 0 for Windows program was used for statistical analysis of these values determined for each section. Descriptive statistics were given as mean, standard deviation for ordinal variables. Statistical analysis of the ordinal variables was performed by Mann Whitney U test. The ratios in the groups were compared with the Chi square test. A probability value of $p<0, 05$ was considered statistically significant.

Results

When the demographic characteristics (age, gravida, parity, abortion, number of live children, body mass index) of the patients participating in the study were evaluated, no statistically significant difference was found. Statistically significant

difference was found only for gestational weeks at the time of delivery. (Table 1) When the placentas of the patient group was examined, 80 (77. 6%) of 103 placentas were stained with VCAM-1 immuno-histochemical staining. 112 (32. 8%) of 341 placentas were positive for VCAM-1 staining in the control group. The patient group was statistically significantly more stained for VCAM-1 staining (Figure-2). ($p<0.05$).

Conclusion

MAP is a clinical condition of which frequency is increasing day by day. So it is very important to anticipate and prevent that situation. In our study, we observed that the adhesion molecule VCAM-1 was found to be statistically significantly more in MAP cases. Although the etiology of MAP is a multifactorial condition that is not fully understood, we found that the adhesion molecule VCAM-1 may also be involved in placental invasion Common to most placental development, several regulatory circuits are altered during multistage placental progression, which includes control of proliferation, balance between cell survival and programmed cell death (apoptosis), communication with endometrial cells and extra cellular matrix, induction of angiogenesis and trophoblast migration and invasion. Disregulation of each of these steps represents with a placental disorder. In this complex process, more attention has been placed on adhesion molecules, because adhesion molecules are necessary to mediate cell-matrix and cell-cell interactions, also trophoblast invasion. Trophoblast cells invade the superficial layer of the myometrium. Together, groups of the trophoblast cells detach from the columns to invade the lumen of the spiral arteries as endovascular trophoblasts. Both cell-cell and cell-matrix interactions are important for the trophoblast invasion of the Desidual stroma and spiral arteries. Angiogenesis plays a key role in the development of both tumoral and placental tissue. It is known that angiogenesis is controlled by a feedback mechanism in physiological conditions. But this feedback mechanism has been shown to be impaired in tumoral tissues. Abnormal angiogenesis may be considered as an auxiliary factor in increasing invasion for MAP cases. Abnormal expression of VCAM-1 has been shown in a variety of tumors such as epithelial ovarian cancers, gastricarcinoma and glioblastoma. VCAM-1 is important for the invasion of trophoblasts to the decidual stromal and in the development of spiral arteries. Gulubova proposed that VCAM-1 binding to its ligand VLA4 not only results inactivation of vessel endothelial cells, but also leads to shedding of tumor cells and invasion of adjacent tissue. This is the first study on the role of adhesion molecules in MAP cases in the literature. We found that the expression of VCAM-1 was significantly higher in MAP cases. Although this does not elucidate the entire pathogenesis of MAP cases, it appears to be a step in understanding the pathogenesis.