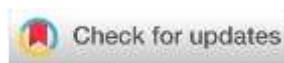


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Research Article

Histopathological Changes in Placenta Previa, Placenta Acreata and Normotensive Plasentas in the 3rd Trimester of Pregnancy

Gamze ERDOĞAN ^{1*}, Engin DEVECİ ¹, Nurullah PEKER ², İbrahim İBİLOĞLU ³, Yavuz TEKELİOĞLU ⁴, Dilek YAVUZ ⁵, Gülb Ebru AKDENİZ ¹, Hasan ERDOĞAN ¹

¹ Dicle University, Medical Faculty, Department of Histology and Embryology, Diyarbakır, Turkey

² Department of Obstetrics and Gynecology, Dicle University School of Medicine, Diyarbakır, Turkey

³ Dicle University, School of Medicine, Department of Pathology, Diyarbakır, Turkey

⁴ Karadeniz Technical University, Medical Faculty, Department of Histology and Embryology, Trabzon, Turkey

⁵ Gazi Yaşargil Training and Research Hospital, Division of Andrology, Diyarbakır, Turkey

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*Address for Correspondence:

Gamze ERDOĞAN, Dicle University, Medical Faculty, Department of Histology and Embryology, Diyarbakır, Turkey

Abstract

Introduction: One of the consequences of improper placentation is placenta previa, a condition in which the placenta is located on or near the internal cervical os. This condition is the major cause of bleeding in the last trimester of pregnancy. It is one of the causes of both maternal and perinatal morbidity and mortality. Placenta accreta is a disorder caused by abnormal invasion of the placental villi into the myometrium. In this study, we aimed to compare the histopathologic changes in placenta previa, placenta acreata and normotensive placentas during the third trimester of pregnancy.

Materials and methods: In our study, placentas of a total of 60 pregnant women including 20 placenta previa, 20 placenta acreata and 20 normotensive pregnant women were used and the placentas were compared histopathologically.

Results: In the control group placentas, the appearance of endothelial cells was normal, with a slight distribution of erythrocytes in the intervillous areas. Fibrinoid structures were observed to be smooth. Dysfunctional development of endothelial cells was observed in the sections of the placenta acreata group. Congestion and edema were observed in the vessels and degeneration was detected in the cells in the syncytial region. In placenta previa sections, muscle cells showed prominent pyknotic nucleus structures. Dilatations and fibrinoid structures were seen in the vessels. Dense erythrocyte accumulation was detected in the intervillous areas.

Conclusion: In our study, we concluded that placenta previa and placenta accreta cause very serious degenerations on the placentas.

Keywords: Placenta, Placenta Previa, Placenta Acreata, histopathology

INTRODUCTION

Placenta formation, which is a complicated mechanism, plays a key role for a successful pregnancy. Problems that occur during the formation and development of the placenta can have negative consequences for maternal and fetal health ¹. The placenta exchanges nutrients such as oxygen, amino acids, amino acids, carbohydrates, minerals and waste products such as carbon dioxide between the maternal and fetal circulatory system. It secretes hormones into both maternal and fetal circulation, affecting uterine function, maternal metabolism, and fetal growth and development. It also metabolizes certain substances and releases metabolic products into both fetal and maternal circulation. The placenta can also help protect the fetus against certain xenobiotic molecules, infections and maternal diseases. Therefore, the adequate function of this organ is crucial for a normal physiologic pregnancy and ultimately for a healthy baby ².

It is thought to result from the absence or deficiency of the Nitabuch layer of the placenta accreta or the spongy layer of

the decidua. It has also been suggested that this is the result of a failure to successfully reconstruct the endometrium/desidua basalis after repair of the caesarean section. Histology usually shows that the trophoblast invades the myometrium without interfering with the decidua. This becomes a problem during labor when the placenta does not detach and there is heavy bleeding³. The hypothesis regarding the etiology of the placenta accreta specimen is that endometrial-myometrial interface defects resulting from uterine scarring lead to a failure of normal decidualization that allows abnormally deep anchorage of the placental villi. Risk factors for placenta accreta include advanced maternal age, multiparity, previous uterine surgeries or abortion, Asherman syndrome and placenta previa. In developed countries, the primary risk factor for placenta accreta is previous cesarean delivery, with an incidence of 0.24% after the first cesarean delivery, increasing to 6.74% in women with six or more cesarean deliveries⁴.

Placenta previa refers to a placenta located on or near the internal os of the cervix. The placenta is normally located in the upper uterine segment, but in placenta previa, the placenta is completely or partially located in the lower uterine segment [3]. Placenta previa represents one of the most common causes of painless bleeding in the second half of pregnancy, complicating approximately 0.3 to 0.8% of pregnancies. Risk factors for placenta previa include a history of previous cesarean delivery, hysterectomy, termination of pregnancy, smoking, advanced maternal age, multiparity, drug use and multiple pregnancies. Although the risk factors for placenta previa are well characterized, much less is known about its etiology⁵. Approximately 90% of cases of placenta previa diagnosed between 15 and 19 weeks of gestation resolve at term. Repeat ultrasonography is necessary every ≥ 32 weeks to reassess placental placement. Transvaginal sonography has become the most commonly used method for the diagnosis of placenta previa with 88% sensitivity and 99% specificity. Patients with placenta previa alone have better maternal-fetal outcomes than those with placenta accreta⁶.

MATERIAL AND METHOD:

We started our study after the ethical approval of Dicle University Faculty of Medicine Ethics Committee numbered 67 and dated 17.03.2022. This study was supported by Dicle University Scientific Research Coordinatorship with the number TIP.23.003. In the study, placentas were obtained from a total of 60 pregnant patients, including 20 placenta previa, 20 placenta accreta and 20 normotensive patients, with the approval of the informed consent form. At the same time, we received the consent form to use the postpartum placentas of the mothers who applied to the Gynecology and Obstetrics Clinic of Dicle University Faculty of Medicine Hospital in our study. The placentas taken from the operating room were washed with saline and placed in 10% buffered neutral formalin under appropriate conditions for tissue follow-up and brought to the laboratory of the Department of Histology and Embryology, Faculty of Medicine, Dicle University.

Routine Histologic Tissue Following

Sections of 1x1cm³ were taken from the placentas for tissue tracing and the sections were placed in empty vials containing 10% formalin solution. These samples were then kept for 16 hours for fixation procedures, after the fixation stages, they were left under running tap water for 1 night to remove the formalin solution from the tissue pieces. For dehydration, we kept the tissue pieces in 50%, 70%, 80%, 80%, 90% and 96% alcohols for 2 days in total, and finally dehydration was completed by keeping the tissue pieces in absolute alcohol (99.9%) for 2x20 minutes, and the tissues were kept in xylol for 2x15 minutes to remove the alcohol. For infiltration, the tissue pieces were kept in paraffin for 2x1 hour in an oven set at 58°C for infiltration and then embedded in paraffin blocks for blocking. After embedding, 4-6 μ m thick sections were taken from each paraffin block with a fully automatic rotary microtome (Leica RM2265, Germany). Hematoxylin-Eosin (H-E) and Periodic Acid Schiff (PAS) staining methods were applied to the sections obtained and the preparations were examined under light microscope using Zeiss Imager A2 and Zen 3.00 software program⁷.

RUSLTS

Control Group Findings

Control group H-E staining findings

Although the branches of arteries and veins in the umbilical cord were enlarged, the appearance of endothelial cells was normal. Desidua cells were located in the form of a great, which is thought to be normal even though some of them had degenerative changes. There was a mild distribution of erythrocytes in the intervillous areas. There is no excessive increase. Again, in the areas where the chorionic villi were located, freely donated connective tissue cells were commonly observed in solitary form. In addition, fibronoid structures were found to be regularly distributed around (Figure-1).

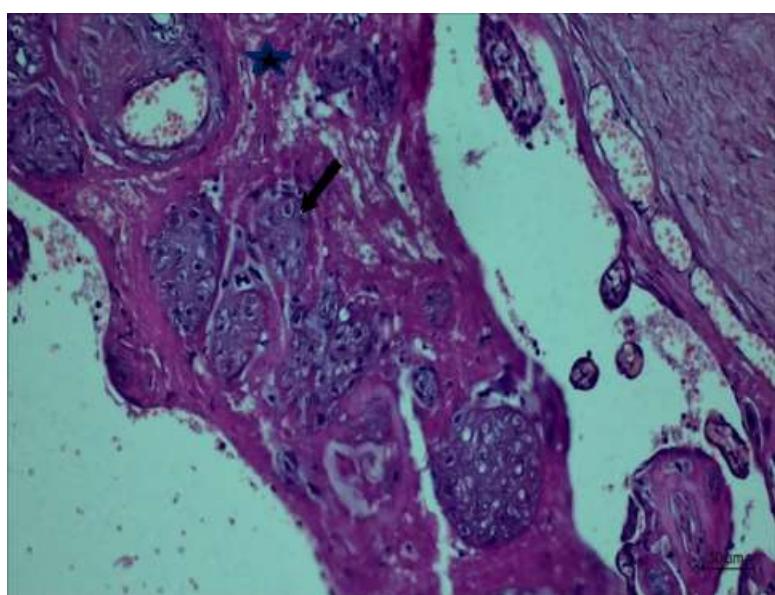


Figure 1: Control group placenta H-E staining, Normal decidua cells (black arrow), fibrinoid structures (asterisk)

Control group PAS staining findings

PAS positive reaction was observed in the transition areas of chorionic villi. Again, PAS positive reaction was detected

especially in the cytotrophoblast region of the floating villi. The vascular endothelial structure and basement membrane structure appeared normal, while syncytial nodes were interconnected but no thickening was detected (Figure-2).

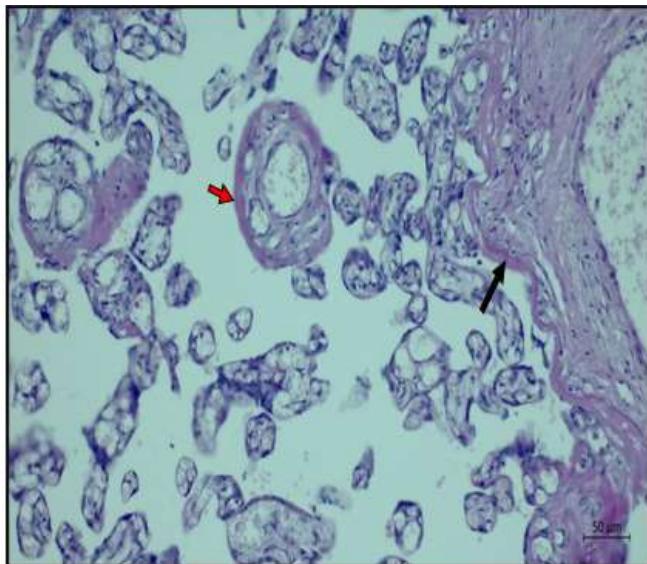


Figure 2: PAS staining of control group placenta; chorionic villi (black arrow) and floating villus cytotrophoblasts (red arrow)

Placenta accreta Group Staining Findings

H-E Staining Findings in Placenta accreta Group

Dysfunctional development was observed in the endothelial cells close to the lumen in the lumen of the blood vessels in the root villi passing through the maternal part of the placenta accreta group. In addition, congestion and edema were observed in the vessels. Degenerative changes were observed especially in the muscle cell in the interplasmic state and in the cells in the syncytial region on the outer side (figure 3).

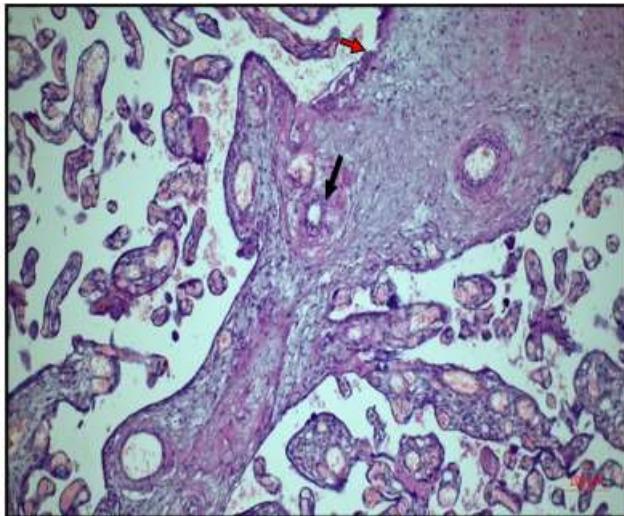


Figure 3: Placenta accreta H-E staining; Dysfunctional endothelial cells (black arrow) and degenerative changes in the syncytial region (red arrow)

PAS Staining Findings in Placenta accreta Group

Intense PAS positive reaction was observed in the area around the decidua cells in the decidual region in the area where the root villi were located. However, intense PAS positive reaction was detected especially in the fibrinoid tissue within the blood vessels. The vascular endothelium showed marked hyperplasia and thickening especially in the basement membrane region. A marked reaction was detected in the syncytial nodes. An intense inflammatory area was seen in the maternal region. (Figure 4)

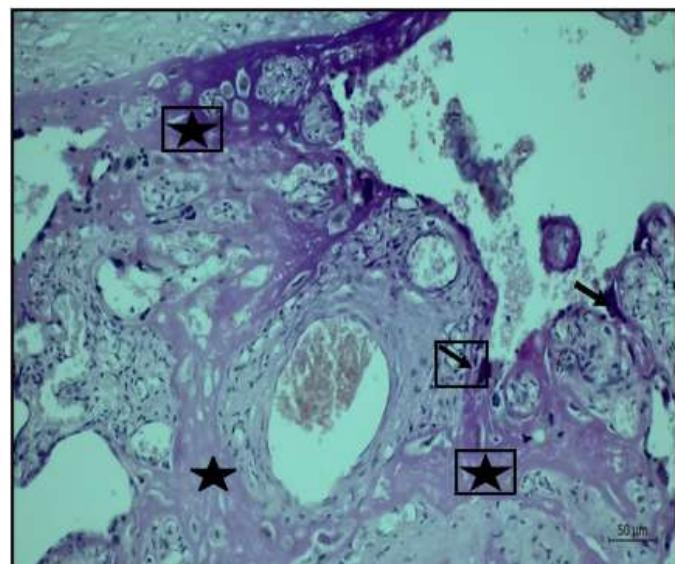


Figure 4: PAS staining of placenta accreta; Fibrinoid areas (stars) and syncytial nodes (black arrows),

Placenta previa Group Staining Findings

Placenta previa Group H-E Staining Findings

Towards the fetal area, especially in the area where the chorionic stem villi were located, one of the striking elements in the placenta previa group was the presence of distinctly pyknotic nucleus structures in the muscle cells. Again, dilatations in the vessels and fibrinoid structures were seen in the syncytial regions. Dysfunctional degenerative changes were observed in some endothelial cells, as well as dense erythrocyte accumulation and thrombotic structures in the intervillous areas (figure 5).

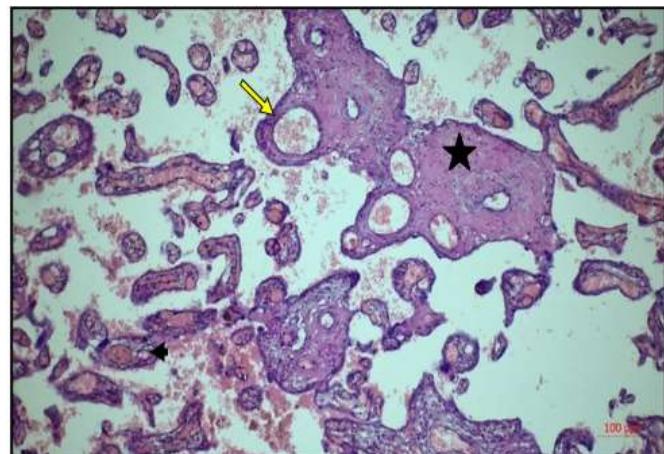


Figure 5: Placenta previa H-E staining; Pyknotic nucleus (asterisk), vascular dilatation (yellow arrow), edema in small villi (black arrow)

PAS Staining Findings in Placenta previa Group

When the maternal area of the root villi was examined, PAS reaction was positive. Pyknotic changes were observed especially in the nuclei of decidua cells and loss of glycogen in the cytoplasm. Fibrinoid areas were enlarged and thickening of the basement membrane of the blood vessels was observed (Figure 6).

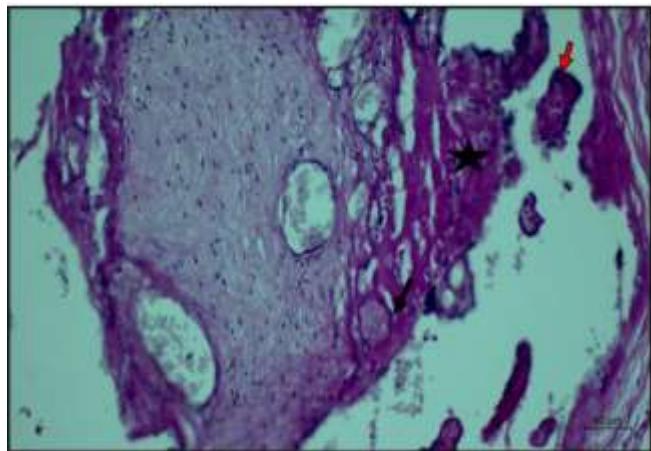


Figure 6: Placenta previa PAS staining; enlargement of fibrinoid areas (black star), thickening of the basement membrane of blood vessels (black arrow), syncytial nodes (red arrow)

DISCUSSION

Placenta previa and accreta are gynecologic problems that can be seen during abnormal gestation and cause severe bleeding and significantly affect fetal development. In some studies, abnormal placenta development has been shown to cause growth angiogenesis and increased trophoblast invasion in which trophoblast insufficiency leads to damaged decidua cell formation (8).

Because of the general absence of decidua in the spectrum of placenta accreta, the chorionic villi are described to be directly associated with myometrial fibers. Here the chorionic villi may implant directly into the myometrium. Patients with placenta accreta speculum pathology often have a complicated delivery and present a significant morbidity for both mother and baby. It has been described that placenta accreta speculum is mostly affected by basal inflammation, maternal vascular malpervision changes, retromembranous and subchorionic interillous hemorrhages (9).

In the histopathologic study, it was determined that there were adherent invasive villi in which the chorionic villi were in direct contact with the myometrium without the intervention of placenta accreta decidua basalis. In these regions, fibril accumulation increased in the basal plaque regions, trophoblast inclusion and fetal artery thrombosis were not observed in any of the 31 cases, placental infarction was observed in 2 cases and intramyometrial vessels were found in 8 cases, and small clusters of villi were found in the lumen. In this study, it was found that especially intervillous thrombosis fibril accumulation was prominent in the basal plaque layer and the distribution of lesions related to the degree of invasive subgroups of structures containing large-scale lacunae was significant (10). Like placenta previa, preeclampsia and covid-19 infection also cause histologic changes in the placenta and umbilical cord (11-13).

In our study, fibrinoid structure was observed in the villi and basal plaque area, while congestion and thrombosis were observed in the blood vessels. Degenerative changes were detected in the syncytial region of the villi. Towards the fetal compartment, fibrinoid structures increased and some villus ruptures were observed. Dysfunction of endothelial cells was observed in a wide range of blood vessels. Generally, the onset of degeneration in the decidua cells in the basal region showed the onset of placental accreta in our sections and a tendency towards the myometrium. Decrease in the number of decidua cells was shown to be one of the important criteria of placental accreta group.

Placenta previa is an abnormal development of the placenta and is one of the important complications that cause mortality and morbidity in pregnancy, especially in villus infarcts and deep implantation of chorionic villi into the myometrium on the uterine wall (3). Since placenta previa is located on the vascularized cervix, changes in the vascularized area caused disruption of the structure of chorionic villi (14). In another study, abnormal placentation in the lower uterine segment with a weak vasculature area, necrosis of the chorionic villi, fibril accumulation in the intervillous space and inhibition of fetal development by negatively inducing the growth of the placenta were observed (15).

In our study, in the placenta previa group, pyknotic nuclei in some cells in the root villi, dilated blood vessels, fibrinoid structures in the syncytial regions, dysfunctional changes in some endothelial cells, dense erythrocyte accumulation and thrombotic changes in the intervillous areas were observed. In the placenta previa section, apipotic changes in the area where the decidua cells are located and a significant increase in the nodes in the syncytial regions are among the important placenta previa findings.

Placenta previa is one of the important risk factors for placenta implantation (3). Placenta previa has a protective effect against the risk of pregnancy-induced hypertension and preeclampsia. It has been suggested that the placenta implanted in the lower uterine segment has better oxygenation due to the larger diameter and less restricted course of blood vessels. With further implantation of the placenta into the uterine cavity, blood flow may be restricted, leading to hypoxia and release of vasoactive substances into the blood, resulting in an increased risk of pregnancy-induced hypertension and preeclampsia (16). The endometrium of the uterine scar after cesarean section is thin, the decidua basalis is partially or completely absent, and chorionic tissue easily invades the myometrium (17). Due to placenta previa, the lower part of the uterus, or a cervix that does not contain a normal endometrium, the mucosa cannot complete the change of decidualization, causing decidual defects that easily lead to placenta implantation (18).

The pathogenesis of placenta previa and placenta accreta is related to the reduction of normal endothelial blood vessels when the placenta grows (19). In the decidual plaque region, it was observed that the nuclei were degenerated, the vacuolar structures increased, the cytoplasmic structure was degenerated, the nuclei had a pyknotic appearance and the apoptotic process started markedly. It was observed that thrombosomes increased markedly in the villi, syncytial cells showed shrinkage in the nuclei and apoptotic process started, both erythrocytes and leukocyte structures were prominent and increased intensely in the intervillous areas. In another placenta previa group, in the area where the chorionic stem villi were located towards the fetal area in the placenta previa syncytial region, picnotic nucleus structures, dilatations in the vessels, fibrinoid structures in the syncytial regions and dysfunctional degenerative changes in some endothelial cells, as well as intense erythrocyte accumulation and thrombotic structures in the intervillous areas were clearly observed.

Placenta accreta spectrum (PAS) is a complex obstetric complication associated with increased maternal morbidity caused by damage to the endometrium-myometrium interface of the uterine wall. Most ultrasound findings in the uterus and placenta of patients with PAS are secondary findings, except in the case of placenta percreta, where the placenta and uterine myometrium show severe structural deformation. PAS pathologies usually affect the extremely thin tissues between the placenta and the uterine myometrium, and superficial endometrial damage such as placenta creta and increta can only be diagnosed by histologic examination²⁰. During

dissection of the placenta obtained after placental implantation in pregnant women, extravillous trophoblast cells were found to invade and penetrate endothelial blood vessels in the deep muscular layer of the uterus²¹.

They noted that histopathologic specimens from areas of placenta accreta showed thick fibrinoid deposition at the uteroplacental interface on microscopic examination, independent of deeply implanted villous tissue. They concluded that these changes could explain the loss of physiologic separation of the placenta from the uterine wall on PAS, supporting the concept that accreta villous tissue is not truly invasive. The microscopic findings in our second case of diffuse placenta accreta were similar to the microscopic findings in this report. Our study found that the pattern of uteroplacental blood flow may also be reduced in areas containing histologic changes of PAS²².

In our study, while dysfunctional development was observed in the endothelial cells in the blood vessels in the root villi passing through the maternal part of the placenta accreta group, especially in the blood vessels in the maternal part of the placenta accreta group, conjectural and edema were observed in the vessels. Degenerative changes are observed especially in the muscle cells in the interplasmic state and in the syncytial region on the outer side. Fibroid bodies were especially enlarged while syncytial nodes were rarely seen.

In another group of placenta accreta, there were ruptures in the syncytial region in some areas, especially in the area of floating free villi towards the fetal compartment, while one of the most important signs was an increase in fibrinoid structures, as well as the formation of dense congestion structures and platelet structures, ruptures and degenerative changes in the chorionic small villi located close to each other, and small round hypertrophic nuclei in the fibrinoid area.

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