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Research Article

Investigation of Adhesion Molecules in the Placentas of Patients with Gestational Diabetes Mellitus with Premature Rupture of Membranes

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Abstract

Aim: The aim of this study was to examine the histopathological changes in the placentas of patients with Gestational Diabetes Mellitus (GDM) and premature rupture of membranes (PROM).

Materials and Methods: Placentas of 21 GDM+PROM and 21 healthy pregnant women were sectioned into 4-6 µm sections and stained with Hematoxylin-Eosin.

Results: In GDM+PROM group, fibrinoid deposition in light pink areas, degeneration of chorionic villi and irregularities in villus structure, congestion and dilatation of capillary vessels were observed. Leukocyte infiltration was observed in the intervillous area. Desidua cells showed degeneration and pycnosis. Rupture of the amniotic membrane was observed.

Conclusion: We have demonstrated that GDM+PROM leads to severe pathologic changes in placental structures and is associated with inflammatory and vascular dysfunction.

Keywords: Gestational diabetes mellitus, premature rupture of membranes, placenta

INTRODUCTİON

Gestational diabetes mellitus (GDM) is the name given to the clinical condition that begins during pregnancy in a patient who has not previously been diagnosed with diabetes and progresses with glucose intolerance. The basis of this clinical picture is insulin resistance [1]. This picture, which is usually seen in the 2nd and 3rd trimesters of pregnancy, is one of the most common chronic diseases of pregnancy and affects millions of women every year. In studies, the prevalence of GDM varies between 8% and 13% worldwide, while it is evaluated between 2% and 28% in Turkey [2,3]. Factors such as overweight, obesity, morbid obesity, previous history of GDM, history of macrosomic fetus birth, pregnancy over the age of 35, multiple pregnancy, polycystic ovary syndrome (PCOS), and family history of diabetes are risk factors for GDM [4]. GDM not only causes maternal complications such as preeclampsia, hypertension, and premature rupture of membranes, but also causes many complications in the fetal period, neonatal period, childhood, and advanced adulthood [5, 6] (Table 1). The fact that GDM causes such complications also increases the importance of early diagnosis and treatment. In 1964, O'Sullivan and Mahan defined specific diagnostic criteria for gestational diabetes (GDM) derived from a 100-gram 3-hour oral glucose tolerance test (OGTT) performed on 752 women in the USA during the second and third trimesters of pregnancy [7]. Later, these criteria were revised by various institutions and took their current form with one of two separate methods, the 'single-stage' 75-gram oral glucose tolerance test (OGTT) or the 'two-stage' 50-gram glucose test followed by 100-gram OGTT [8]. The healthy development of the placenta underlies the healthy progression of pregnancy. The placenta is an organ specific to pregnancy that performs many vital functions such as fetal nutrition, thermoregulation, fetal evacuation, and oxygenation through maternal blood during the development of the fetus [9]. Structurally, dense vascular structures contain connective tissue cells and trophoblastic cells. In addition, it is an organ with endocrine properties [10]. The fact that gestational diabetes disrupts the macrovascular and microvascular development of the placenta is one of the reasons for the increase in the incidence of premature membrane

rupture (PROM) in GDM [11]. PROM is the name given to the clinical picture that develops when the fetal membranes rupture at any time before normal labor. It is seen in 5% to 10% of all pregnancies. PROM is one of the most important causes of perinatal mortality and morbidity 12. Despite the developments in obstetric diagnosis and treatment methods, the incidence of PROM has increased [13]. The main purpose in PROM management is to prevent premature birth as much as possible, to postpone the gestational age and to reduce complications related to prematurity [14]. Therefore, in our study, we aim to examine the histopathological changes of GDM+PROM patients and healthy pregnant women and to make a scientific contribution to the literature.

MATERİALS AND METHODS

Study Design and Material Collection

In our study, pregnant women who were diagnosed with gestational diabetes mellitus and premature membrane rupture at the Dicle University Medical Faculty Gynecology and Obstetrics Clinic between 01.06.2023-01.06.2024, aged 18-49, and who met the criteria of not having any other systemic disease or secondary disease were included. All tissues were taken for routine paraffin tissue follow-up. Small pieces were taken from the placentas obtained after delivery from 21 pregnant women with gestational diabetes and premature membrane rupture who gave birth and 21 normal healthy pregnant patients, which were not viable, had no connection with the body, and would not be sent as a pathology sample, for histological follow-up. After the fixation (24 hours), the tissues were washed (1 night), passed through increasing alcohol series (50%, 70%, 80%, 90%, 96% and absolute ethyl alcohol series) and cleared (3x30 minutes in xylene) and then taken to paraffin infiltration at 58°C. Then, the tissues were embedded in paraffin blocks and 4-6 µm thick sections were taken from the blocks with the help of a microtome (catalog no: Leica RM2265, Wetzlar, Germany) for Hematoxylin-Eosin staining.

Hematoxylin-Eosin Staining

Placental tissue sections taken from paraffin blocks were taken to a bain-marie set at 37°C. The sections were kept in a 58-62°C oven for 6 hours to melt excess paraffin on the slide. After the sections were deparaffinized in xylene for 3x15 minutes, they were passed through decreasing alcohol series (100%, 96%, 90%, 70%, 50% ethyl alcohol) for 10 minutes each and brought to distilled water and waited for 5 minutes. Hematoxylin and eosin were applied to the sections. After the staining stage, the sections were quickly dipped into increasing alcohol series (80%, 90%, 96% ethyl alcohol series) and waited for 2 minutes in absolute alcohol. Finally, the sections were kept in xylene for 3x15 minutes and Entellan was dropped onto the tissue and covered with a coverslip.

RESULTS

Hematoxylin Eosin Findings of the Control Group

In the sections of the control group, it was observed that the chorionic villi were composed of syncytiotrophoblast, cytotrophoblast, villous connective tissue and chorionic capillaries in an orderly and structural manner. Minimal fibrin accumulation and syncytial knot were seen. Vascular structures were normal. No pathology was observed in this group. Maternal blood was observed in places in the intervillous area (Figure 1).

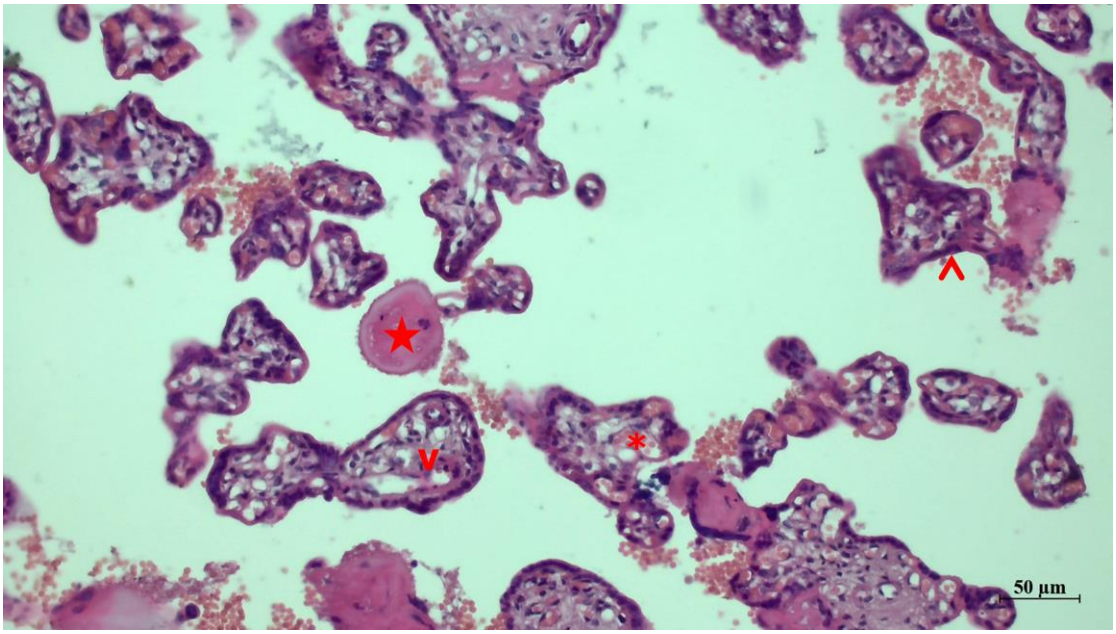

Figure 1: Placental section of the Control Group. V: villus, star: fibrin, *: capillary, arrowhead: syncytial node, Hematoxylin Eosin Staining, Bar: 50 µm, Magnification: 20X

Hematoxylin Eosin Findings of GDM+PROM Group

In GDM+PROM Group, fibrinoid accumulation in light pink areas, degeneration of chorionic villi and irregularities in the villus structure, congestion and dilatation in capillary vessels are observed. Leukocyte infiltration was observed in the intervillous area. Degeneration and pyknosis were observed in decidua cells. Rupture was observed in the amniotic membrane (Figure 2).

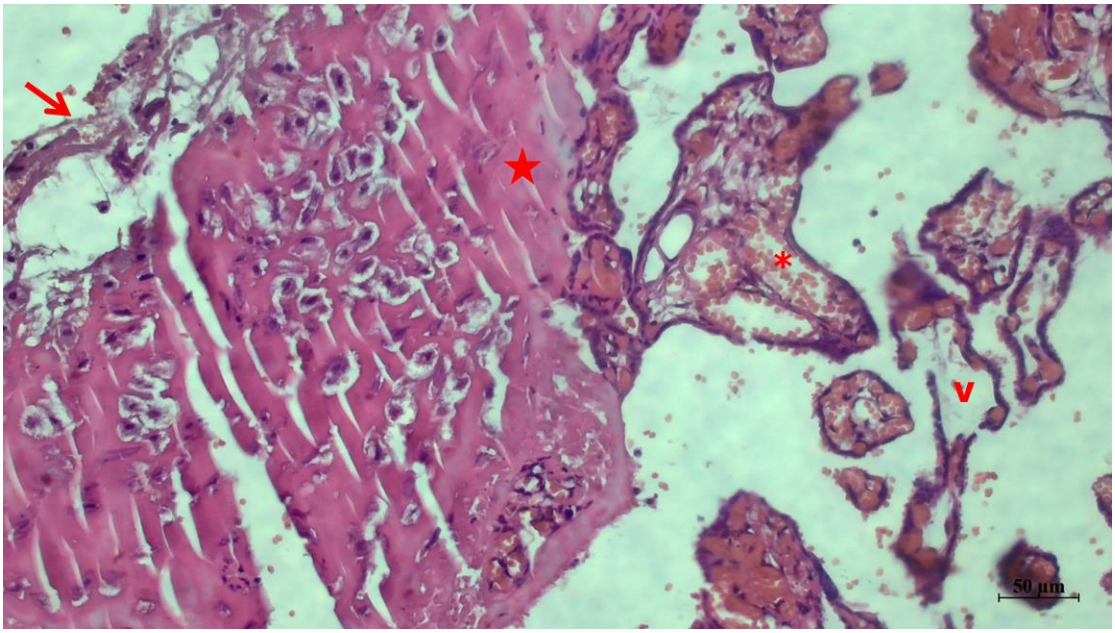

Figure 2: Placental section of GDM+PROM group. V: villus, star: fibrin, *: capillary, arrow: amniotic membrane, Hematoxylin Eosin Staining, Bar: 50 µm, Magnification: 20X

DISCUSSION

Gestational diabetes (GDM) is a glucose metabolism disorder that occurs during pregnancy or is first diagnosed during pregnancy. Histopathologically, significant changes are observed in the placentas of women with GDM. These changes include villous immaturation, basement membrane thickening, capillary proliferation, and stromal fibrosis [15,16]. In addition, hypertrophy and inflammatory cell infiltration in trophoblasts have been reported in pregnant women with GDM. Endothelial dysfunction and increased oxidative stress are considered to be one of the basic mechanisms of these structural changes. Vascular disorders caused by GDM in the placenta can lead to complications such as fetal hypoxia and macrosomia [17,18].

Premature membrane rupture (PROM) is defined as the premature rupture of amniotic membranes before the onset of labor and is associated with factors such as infection, inflammation, and mechanical stress. Histopathologically, chorioamnionitis, decidual degeneration, and inflammatory cell infiltration are frequently observed in placentas with PROM [19,20]. Edema and fibrin accumulation in the villous stroma are indicators of the inflammatory response due to PROM. In addition, increased apoptosis in trophoblastic cells and degenerative changes in the vascular walls were observed. These histopathological findings support the effects of PROM that increase the risk of perinatal complications and intrauterine infection [21,22].

In our study, it was observed in the placental sections in the control group that the chorionic villi preserved their structural integrity, and the syncytiotrophoblast, cytotrophoblast and chorionic capillaries were in normal order. The minimal fibrin accumulation and the observation of syncytial nodes confirmed that there was no pathological process in this group. These findings are indicators of normal placental development, and the localization of maternal blood in the intervillous area was evaluated as a physiological event.

In contrast, significant pathological changes were detected in the GDM+PROM group. In this group, findings such as fibrinoid accumulation, degeneration of chorionic villi, capillary congestion and dilatation indicate placental vascular and structural deterioration. In addition, leukocyte infiltration in the intervillous area and degeneration of decidual cells support the presence of inflammatory processes. This inflammation correlates with pathological changes such as rupture in the amniotic membrane. It is obvious that GDM and PROM disrupt placental structure and functions, thus negatively affecting maternal and fetal health. In our study, we demonstrated that GDM+ PROM causes serious pathological changes in placental structures and that this condition is associated with inflammatory and vascular dysfunction. While normal placental structure was preserved in the control group, findings such as fibrinoid accumulation, villous degeneration and inflammatory infiltration were noted in the GDM+ PROM group.

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Ethical approval: Not applicable

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