Histopathologic Changes in the Placenta of Pregnant Women with Preeclampsia

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Abstract

Objective: The placenta plays a key role in the development of pre-eclampsia. Knowledge of the histopathologic changes in the preeclamptic placenta will improve our understanding of the pathophysiology of preeclampsia, which may contribute to the development of timely interventions, prevention strategies or treatment options. Therefore, in this study, we investigated the histopathologic changes in the placentas of pre-eclampsia patients.

Material and Methods: This study was conducted between May 01, 2023, and January 31, 2024, at tertiary hospital. A total of 30 pregnancies were included in the study, 15 with preeclampsia and 15 that were otherwise normal pregnancies. After delivery by cesarean section, the placentas of these patients were taken to the Department of Histology and Embryology examined histologically by staining with hematoxylin-eosin.

Results: Compared to the control group, the placentas of the pre-eclampsia patients showed a more degeneration of the villi, hemorrhage in the intervillous area, the presence of immune cells, vasodilation, and congestion. In addition, there were more fibrinoid accumulations and more syncytial knots in the placentas of the pre-eclampsia patients.

Conclusion: There were histologic differences between the placentas of pre-eclampsia patients and the control group. The studies that search the precursors or markers leading to these histopathologic changes are necessary to improve our understanding of preeclampsia and to develop further strategies such as treatment options and prevention strategies.

Keywords: Preeclampsia, hematoxylin-eosin staining, histopathologic examination

INTRODUCTION

Pre-eclampsia, one of the leading causes of fetal and maternal morbidity and mortality, is a condition characterized by high blood pressure and concomitant proteinuria or organ perfusion abnormalities that typically develops after 20 weeks of gestation.1 2. The placenta plays a key role in the development of pre-eclampsia.3 4 5 6. High resistance and low blood flow in the spiral arteries and the maladaptive immunologic functions of the syncytiotrophoblasts are the main pathophysiological defects in patients with preeclampsia.7 8. During early pregnancy, the outer cells of the placenta, called syncytiotrophoblasts, must invade the decidua basalis and the wall of the spiral arteries to create and maintain a low resistance of the spiral arteries. The smooth muscle cells in the tunica media of the spiral arteries are replaced by invading trophoblasts and fibroblasts, which is also referred to as remodeling of the uteroplacental spiral arteries. As a result, the diameter of these arteries increases by 5-10 times, providing low resistance and high blood flow. Insufficient invasion of extra villous trophoblasts into the myometrium and the spiral arteries leads to impairment of these changes, which ensure a high blood flow to the placenta.

As a result, blood flow is reduced, leading to hypoperfusion of the placenta, hypoxia, ischemia, and tissue damage.5 7. In terms of immunologic functions, the placenta is a unique organ with highly dynamic processes that establish the immunologic balance for harmony between mother and fetus in normal pregnancies. It is assumed that disturbances in the cellular and immunological functions of the placenta play an important role in the development of pre-eclampsia. In addition to activating the immunological cascade that leads to the development of pre-eclampsia, the immunological balance plays a key role in the remodeling of the spiral artery. Studies have shown that disruption of the low flow resistance of the spiral artery affects the histologic structure of the placenta to some extent.11 12.

In this study, we aimed to investigate the histologic features of the preeclamptic placenta by staining the placenta with hematoxylin-eosin.

MATERIAL AND METHODS

This study was conducted between May 01, 2023, and January 31, 2024, at tertiary referred center, which is a third-degree hospital. Informed consent was obtained from all cases.
included in the study. The Dicle University Ethics Committee approved the study (Approval Date: 17.01.2023 and number: 33). The diagnosis of preeclampsia was made according to the ACOG criteria (2), which require two separate blood pressure measurements 4-6 hours apart with a systolic equal or more than 140 mm Hg or more and a diastolic equal or more than 90 mm Hg, and proteinuria more than 300 milligrams/day or organ perfusion abnormalities. The placentas of 15 singleton pregnancies without preeclampsia and other diseases and 15 singleton pregnancies with preeclampsia and without other diseases were analyzed. To reduce changes in the placenta associated with gestational age, only pregnancies delivered between 37- and 39-weeks' gestation were included. In order to reduce the influence of the mode of delivery on the histopathological structure of the placentas, only pregnancies that were delivered by cesarean section were included. The subsequent preparation of the placental tissue and the histological analysis were carried out in the research laboratory for Histology and embryology of the same faculty.

Tissue Tracking

Placenta tissues were first placed in a 10% neutral formalin solution and routine paraffin tissue follow-up begun. After fixation (24 hours) process, the tissues were kept under running tap water for 6 hours. The tissues were passed through 50 %, 70 %, 80 %, 90 %, 96 % and absolute ethyl alcohol series and kept in xylene 3 times for 45 minutes for clearance. Finally, the tissues were placed in paraffin oil at 58°C for infiltration. Then the tissues are embedded in paraffin blocks and 4-6 μm thick sections were taken from the blocks for hematoxylin-eosin staining using a microtome (catalog number: Leica RM2265, Wetzlar, Germany).

Hematoxylin-eosin staining

Placental tissue sections taken from paraffin blocks were placed in a boiler set at 37°C. The sections were kept in an oven at 58-62°C for 6 hours to melt excess paraffin on the slide. The sections were deparaffinized in xylene for 3×15 minutes. Sections were passed through decreasing series of alcohols (100%, 96%, 90%, 70%, 50% ethyl alcohol) for 10 minutes each and then placed in distilled water and kept for 5 minutes. Sections were placed in Harris hematoxylin stain for 8 minutes and then washed under running water for 5 minutes. The sections were rinsed and soaked in alcoholic eosin stain for 6 minutes. Sections were quickly immersed in increasing series of alcohol (above 80%, 90%, 96% ethyl alcohol) and kept in absolute alcohol for 2 minutes. Finally, the sections were placed in xylene for 3×15 minutes, Entellan were dripped onto the tissue and covered with a coverslip.

RESULTS

Large villi were observed in the placental sections of the control group, which were structurally normal. The diameters of the capillaries were normal, and the organization of the trophoblast cells was regular. The floating villi and the stromal area of the villi were normal, and there was minimal fibrinoid accumulation. Compared to the placentas of the pre-eclampsia cases, hemorrhages in the syncytial knots were less frequent in the placentas of the control cases. (Figure 1 and 2)

More villous degeneration, hemorrhage in the intervillous area and the presence of immune cells, vasodilation and congestion were more in the placentas of the pre-eclampsia group than in the control group. Compared to the placenta sections of the control group, the preeclampsia placentas showed increased fibrinoid accumulation and the number of syncytial knots. (Figure 3 and 4)
Figure 2: Close-up of placenta sections from the control group. Trophoblastic layer in normal chorionic villi (arrow), mesenchymal area (asterisk), f: fibrinode, magnification 20x, scale: 50 μm

Figure 3: Hematoxylin and eosin staining of the placenta sections in the preeclampsia group. Degeneration of the chorionic villi (black arrow), heavy hemorrhage in the intervillous area (asterisk), vasodilatation and congestion (asterisk), syncytial nodule (arrowhead), f: fibrinoid accumulation. Magnification 10x, scale bar: 100 μm

Figure 4: Close-up of hematoxylin and eosin staining of placenta sections of the preeclampsia group. Degeneration of chorionic villi (black arrow), stromal degeneration, severe hemorrhage and presence of immune cells in the intervillous area (asterisk), vasodilatation and congestion (asterisk), syncytial knot (arrowhead), fibrinoid accumulation (f). Magnification 20x, scale bar: 50 μm
DISCUSSION

It is well known that there is no cure for pre-eclampsia other than delivery of the placenta. Therefore, most researchers interested in pre-eclampsia have focused on the placenta, including its anatomic, physiologic, biologic, immunologic, and histologic features. It is undeniable that any abnormal finding of these features may lead to finding the etiologic cause, which could contribute to the development of curative or preventive strategies. Histologic examination of the placenta has contributed significantly to the understanding of the role of the placenta in preeclampsia. The underlying pathophysiologic mechanism of these pathologic changes has been shown to be due to inadequate invasion of the cytotrophoblasts into the decidual and the spiral arteries of the uterus, which leads to constriction of the spiral arteries and hypoxia of the placenta and triggers further pathologic processes. When the placenta is exposed to hypoxia, placental tissue undergoes infarcts, necrosis and increased syncytial proliferation, which has been shown to increase in the placenta of preeclamptic patients. 4, 5, 6 Similarly, in our study, there was an increased rate of syncytiotrophoblastic nuclei, fibrinoid accumulation, villous degeneration and hemorrhage in the intervillous area, presumably due to necrosis.

Each placenta has its own unique characteristics, and no one has a similarity to another with 100 percent. In other words, the placenta of cases without preeclampsia has some degree of pathology associated with the characteristics of the placenta of women with preeclampsia. However, the degree of these pathologic findings was less in the cases without preeclampsia than in those with preeclampsia 5,11. Our study showed that the placenta of the control patients had some degree of fibrinoid accumulation, syncytiotrophoblastic nuclei and hemorrhage in the intervillous area, albeit to a lesser extent than the placenta of the patients with preeclampsia. These studies have shown that the clinical course of pregnancy is only affected when the normal functions of the placenta decrease by 60-70%. Similarly, one study showed that there was no placenta-related fetal morbidity or mortality in patients whose intervillous fibrinoid accumulation did not exceed 30-40% 10.

Oxidative stress, hypoxia, ischemia, and tissue necrosis of the placenta are associated with endothelial cell activation and maternal inflammatory responses. Various innate and adaptive immune cells and mediators play a role in this process 12, 13. Regulatory T cells, macrophages, natural killer cells and neutrophils are known to contribute to preeclampsia, but other immune cells such as B cells, inflammatory cytokines and autoantibodies directed against the angiotensin II type 1 receptor have also been recently discovered 13. In our study, an increased number of immune cells was found in the intervillous area. Together with the ischemic process, the activation of these inflammatory processes leads to a vicious circle.

CONCLUSION

Our study has shown that there are significant histologic differences between the control group and the preeclampsia group. In the control group, the components of the placenta were in order; fibrinoid accumulation in the syncytiotrophoblastic nucleus was low and slight hemorrhage was observed in the intervillous area. Findings such as the presence of villous degeneration, intense bleeding in the intervillous area and the presence of immune cells clearly show the effects of pre-eclampsia on the placenta. Increased fibrinoid accumulation and the number of syncytiotrophoblastic nuclei are also associated with pre-eclampsia.

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Conflict of Interests: The authors declare that there are no current or potential conflicts of interest.

REFERENCES


