

Original Research

Histological analysis of the placenta in patients with preeclampsia, taking into account the proposed treatment

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Abstract

Background and aims: Preeclampsia is a critical condition syndrome that occurs during pregnancy and may lead to complications and fetal lesions. The aim of this study is to optimize the algorithm for the treatment of patients with high-risk preeclampsia associated with metabolic syndrome by morphologically proven effects on the placental complex. **Material and method:** Material for histological examination was collected from the peripheral, medial, and central parts of the placental disc and placental amnion. Tissue fragments were processed in a LogosOne histoprocessor and embedded in paraffin blocks. **Results:** In the first study group (standard protocol treatment) there were histological changes that should be regarded as morphological markers of functional disorders in the “mother-placenta-fetus” system that accompany late preeclampsia. Metaplasia of the cylindrical epithelium of the fetal surface into a multilayered flat increased proliferative activity of epitheliocytes with the formation of plaque-like structures and growths in the placental amnion was observed. In the second study group (modified treatment) the intensity and prevalence of pathological changes were significantly lower than in the first study group. The citral structure of the amniotic epithelium was preserved and desquamation was not observed. **Conclusions:** Based on the results of histological examination, it can be stated that complex modified therapy of preeclampsia associated with metabolic syndrome allows for normalizing the structure of the placenta, which is objectively confirmed by reducing the frequency of alternative changes in the placental amnion, epithelium, and stroma of chorionic villi.

Keywords: preeclampsia, placenta, histology, metabolic syndrome, treatment.

Background and aims

Preeclampsia is a critical condition of organ dysfunction, which can be both hypo- and hyperdynamic. The dynamic state of preeclampsia is the pathogenesis and clinical manifestations that develop following the structural dynamics of

the ovum. As the structure of the ovum changes, the severity of preeclampsia and the form of its clinical manifestation also changes.

The only correct treatment tactic is resolving issues of childbirth, aimed not only at eliminating the symptomatic manifestations of the disease. Nowadays, biochemical, functional, and morphological changes that characterize the



severity of preeclampsia based on the assessment of hormonal imbalance are not fully identified [1]. Corrective therapy involves reducing the clinical manifestations of the disease, potentiating each other [2–4].

Preeclampsia has always been considered one of the most serious complications of pregnancy and childbirth. Hundreds of years of research into the pathogenesis of the whole disease have formed its poetic name – “Great Disguise” because of its diversity, complexity, and insidiousness [5–7]. Thanks to the research of numerous authors, great importance is attached to the problem of endothelial dysfunction, the combination of inhibition of cytotrophoblast invasion in the spiral arteries of the uterus, oxidative stress, hypercoagulation and microcirculation disorders. The trigger for these processes has not been definitively established. It is known only that the changes formed in the placenta ultimately lead to its hypoxia and contribute to the development of placental insufficiency, forming specific clinical manifestations of preeclampsia. It is proved that at the early beginning of preeclampsia the frequency of various complications is in 1.5–3.4 times higher than at its late manifestation [8, 9].

Recently, many researchers have described a specific histological picture in the morphological examination of the placenta. The border zone between the maternal and fetal parts is disproportionately developed, that incomplete cytotrophoblast penetrates the maternal spiral artery [8]. The increase in the space between the bloodstream and the chorionic villi in the spiral arteries leads to trophoblast ischemia and increased permeability of the placental barrier [10]. The course of angiogenesis is controlled by vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) and soluble endothelial growth factor receptor 1 [5]. A large number of studies have shown that the lack of these factors leads to the development of preeclampsia [10, 11]. For many years, the search for effective pathogenic effects on the manifestations of preeclampsia has not been fully studied.

Therefore, the aim of our study was to optimize the treatment algorithm for patients at high-risk of preeclampsia in the background of

metabolic syndrome by morphologically proven effects on the placental complex.

Material and method

Study design and patients

Group I – patients received standard protocol treatment. Group II – patients received the proposed modified treatment: L-arginine – 3000 mg, calcium carbonate – 1000 mg, magnesium sulfate – 1000 mg, acetylsalicylic acid – 75 mg, vitamin D – 2000 IU. Group III – physiological course of pregnancy without complications. Material for histological examination was collected from the peripheral, medial, and central parts of the placental disc and placental amnion.

Laboratory, anthropometric and clinical data collection

Tissue fragments were fixated in 10% neutral buffered formalin solution and were processed in a LogosOne histoprocessor and embedded in paraffin blocks. Tissue sections 5 µm thick obtained on a rotary microtome AMR400 were stained with hematoxylin and eosin [12]. The obtained histological specimens were examined using a Nikon Eclipse Ci-E light microscope.

The algorithm of histological examination was regulated by the generally accepted protocol of pathological examination of the placenta. Changes in histological structure in each case were studied in 20 fields of view, so the number of observations for the control group was $n = 40$, for the first study group $n = 80$, and for the second group $n = 80$. The Sigeta M3CMOS14000 digital video camera with Toup View software was used for photo documentation. Morphometric studies were also performed using the tools of this software product.

Results

During the microscopy examination of the placenta in women from the control group, no significant changes from the normal histological

picture were observed which correlates with the anamnestic data and results of clinical examinations of these pregnant women. The level of differentiation of the elements of the chorionic villi was relevant to the mature placenta, there were signs of physiological involution.

In the first study group, there were histological changes, which should be regarded as morphological markers of functional disorders in the “mother-placenta-fetus” system that accompany late preeclampsia. Metaplasia of the cylindrical epithelium of the fetal surface into a multilayered flat was observed in the placental amnion. In some places, increased proliferative activity of epitheliocytes formed plaque-like structures and growths. In addition, dystrophic and degenerative changes of epitheliocytes were detected, sometimes significantly expressed with the transition to necrosis and focal desquamation of cells (Figure 1).

Pathological changes in the first study group were found in the chorionic villi. Hemodynamic disturbances took place, mainly in the form of uneven blood supply, when hyperemic and ischemic areas were fixed in one field of view; such dissociated vascularization was observed in villi of different calibers – the stem, medium caliber, terminal. Occasionally there were more critical disorders of hemocirculation, such as thrombosis of the vessels of the stem villi (Figure 2).

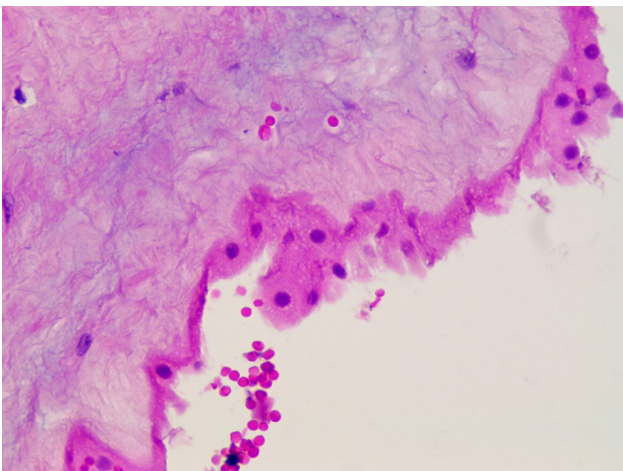


Figure 1: The first study group, placental amnion. Dystrophic and degenerative changes of the epithelium with focal desquamation. Staining with hematoxylin and eosin, $\times 400$.

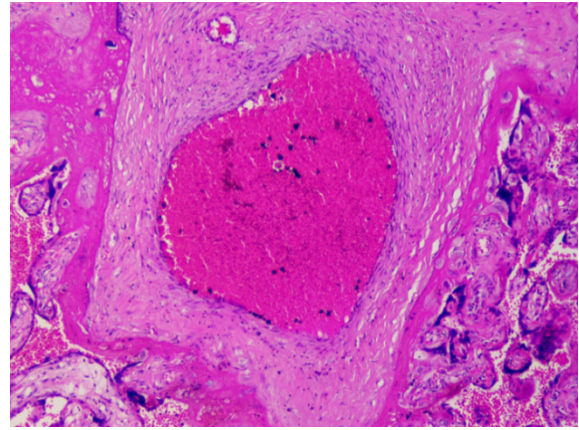


Figure 2: The first study group, villous chorion. Obturating thrombus. Staining with hematoxylin and eosin, $\times 100$.

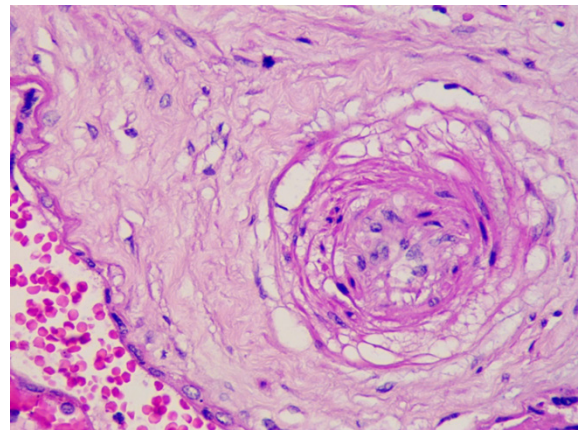


Figure 3: The first study group, chorionic villi. Obliteration of the vessel due to perivascular sclerosis and endothelial proliferation. Staining with hematoxylin and eosin, $\times 400$.

One of the prerequisites for the described circulatory disorders was structural changes in the vascular bed of the chorionic villi: obstruction (and in some places complete obliteration) of arteries and arterioles due to fibrosis, media hypertrophy, and endothelial proliferation (Figure 3).

Swelling and partial desquamation of endothelial cells were noted in some places, which can be interpreted as manifestations of endothelial dysfunction.

The villi epithelium underwent alteration, manifested by its dystrophic changes and, occasionally, partial or complete desquamation. At the same time, the proliferation foci were visualized only in some areas. In the stroma, there were fibrosclerotic processes – focal (mostly

around the vessels) and in some places – total, accompanied by the death of chorionic villi.

Necrotized elements underwent calcification, so there were petrifications of various sizes. The obvious consequence of changes in the chorionic villi was a violation of its differentiation – the presence of full-term areas of immature villi and mature structural elements characterized by a low relative area of the vascular bed (Figure 4).

The intervillous spaces in many cases were narrowed due to the uneven distribution of terminal chorionic villi in the field of view. Blood and thrombi, fibrin masses, various-sized fragments of the exfoliated epithelium of the villi were also found (Figure 5). The consequence of such changes is decreased maternal blood circulation and fetoplacental metabolism.

Areas of degeneration and circulatory disorders were noted in the basal layer of the decidua membrane. A significant number of decidual cells showed signs of alteration (Figure 6).

In the second study group, the tissue structure of the placenta was also characterized by deviations from the histological picture of the control group. However, the intensity and prevalence of pathological changes were significantly lower than in the first study group. In most of the studied histological sections, the citral structure of the amniotic epithelium was preserved, desquamation was not observed (Figure 7).

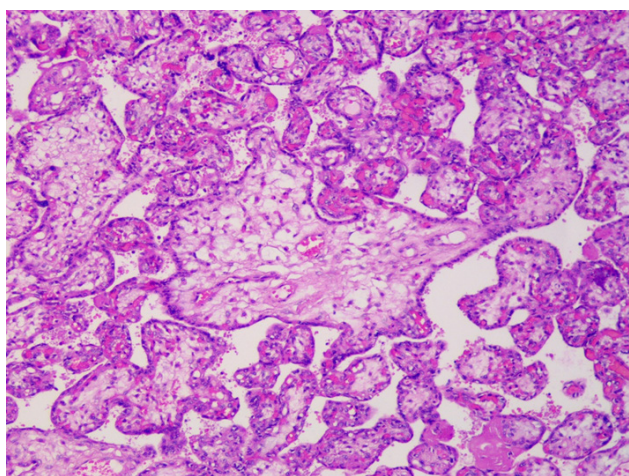


Figure 4: The first study group, chorionic villi. Signs of violation of the differentiation of structural elements – the presence of immature chorionic villi with swollen weakly vascularized stroma and single-layered epithelium. Staining with hematoxylin and eosin, x100.

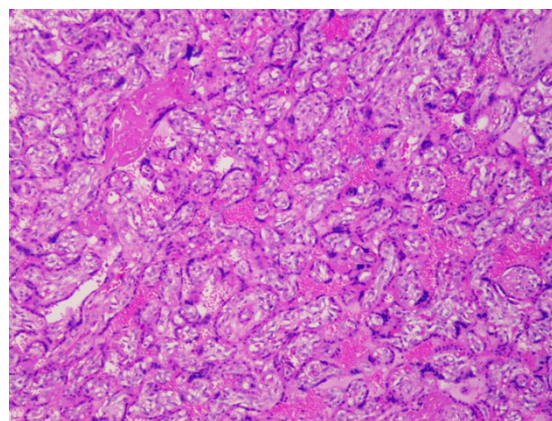


Figure 5: The first study group, chorionic villi. Intervillous spaces are narrowed, contain fibrin, thrombi. Staining with hematoxylin and eosin, ×100.

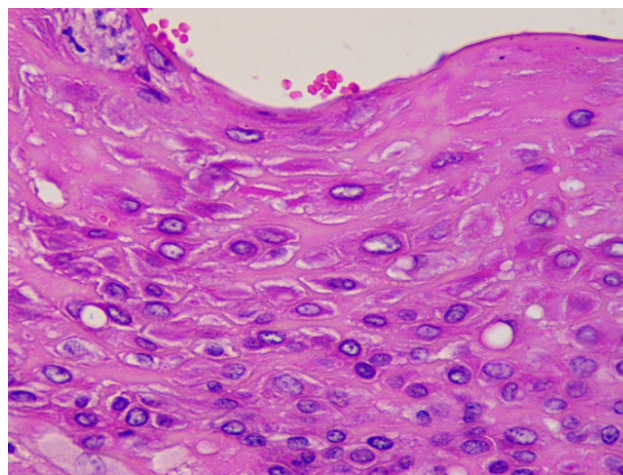


Figure 6: The first study group, decidua shell. Decidual cell dystrophy. Staining with hematoxylin and eosin, ×400.

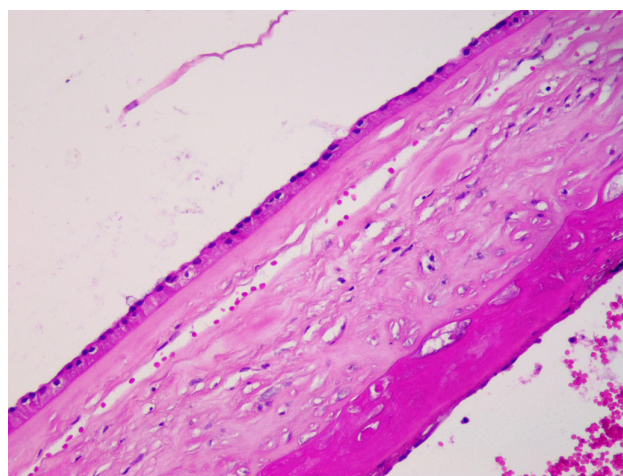


Figure 7: The second study group, placental amnion. Preserved tissue and cell structure. Staining with hematoxylin and eosin, ×200.

Circulatory disorders in the chorionic villi were present but the structure of most vessels remained unchanged. Morphological markers of endothelial dysfunction were also not detected. The structure of the chorionic villi also was the same as in the physiological course of pregnancy. There were changes that indicate the activation of compensatory processes aimed at intensifying blood flow in the chorionic villi with improving metabolic processes in the system “mother-placenta-fetus”. There was angiomatosis of chorionic villi (terminal, small and medium caliber), there was also a shift of capillaries to the basement membrane.

Multiple foci of the proliferation of the villi epithelium, which formed multinucleated syncytial nodules and intervillous connections, could be seen in the second group. There were small petrifications in the stroma of the villi and the basal layer of the decidual membrane.

The results of a comprehensive analysis of the prevalence of the above histological

changes are presented in Table 1. The criteria reflected in it were selected on the basis of a standard protocol of pathological placenta examination – medical form No 013-1/o [1].

As can be seen from the presented data, alternative changes in the epithelium of the placental amnion were most common in the first study group. The number of epitheliocyte degeneration foci with their death and exfoliation increased by 33.75% and the number of metaplasia foci increased by 8.75%.

Discussion

At the same time, in the second study group the differences in control values were smaller (Figure 8) degeneration was observed more often by only 5%, necrosis with subsequent desquamation by 10%, and metaplasia by 3.75%.

In the second group, there were signs of the inconsistency of the structure of the

Table 1: Prevalence of histopathological changes in the placenta under conditions of pregnancy complicated by late preeclampsia in different variants of its correction.

Pathological changes	Number of observations / %					
	Control, n=40		The first study group, n=80		The second study group, n=80	
Degeneration of the amniotic epithelium	5	12.5	37	46.25	14	17.5
Necrosis and desquamation of the amniotic epithelium	1	2.5	29	36.25	10	12.5
Metaplasia of the amniotic epithelium	2	5	11	13.75	7	8.75
Angiomatosis of the chorionic villi	17	42.5	21	26.25	39	48.75
Vascular chorionic villi	0	0	6	7.5	2	2.5
Desquamation of the epithelium of the chorionic villi	9	22.5	39	48.75	19	23.75
Monolayer epithelium of chorionic villi	0	0	7	8.75	2	2.5
Proliferation of epithelium of chorionic villi	19	47.5	20	25	54	67.5
Hyperemia of the chorionic villi	8	20	24	30	41	51.25
Fibrosis and sclerosis of the chorionic villi stroma	10	25	44	55	29	36.25
Calcifications in the stroma of the chorionic villi	7	17.5	38	47.5	20	25
Kashchenko-Hoffbauer cells in the stroma of chorionic villi	0	0	6	7.5	1	1.25
Obliterated blood vessels	4	10	28	35	15	18.75
Intervillous fibrin deposition	6	15	22	27.5	14	17.5
Blood and blood clots in the intervillous space	4	10	19	23.75	9	11.25
Decyduocyte dystrophy	7	17.5	39	48.75	21	26.25

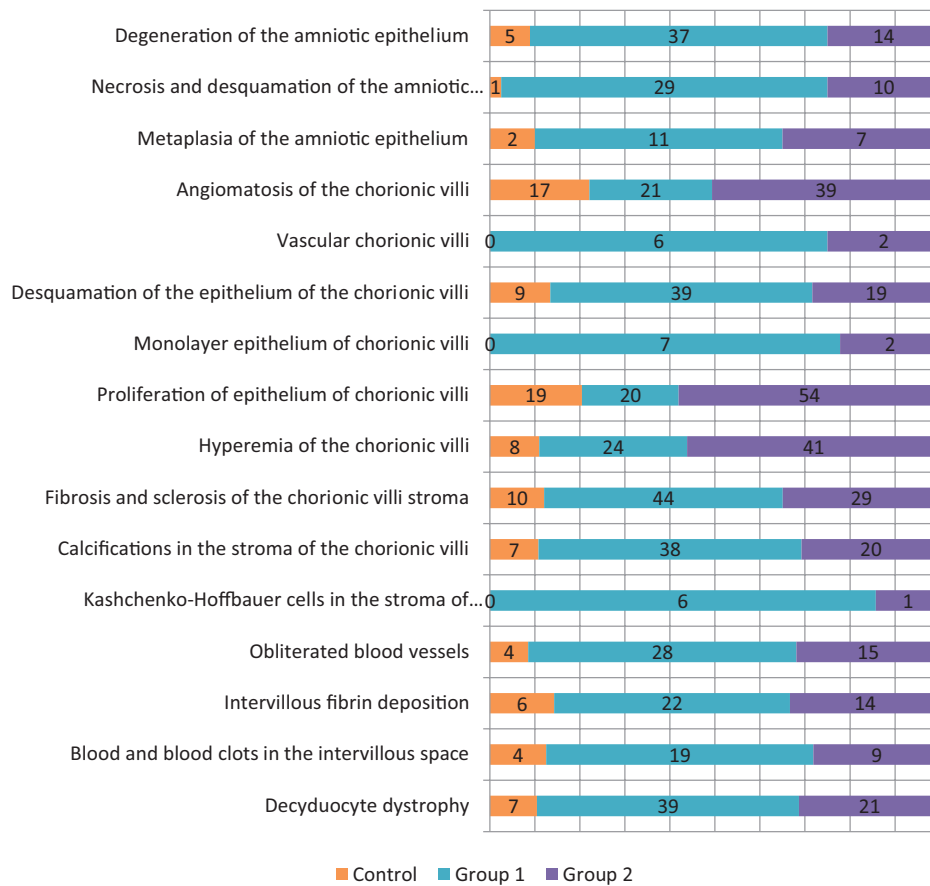


Figure 8: Prevalence of structural changes in control and study groups.

chorionic villi to the histological norm for a full-term pregnancy. Vascular chorionic villi were visualized 7.5% more often than in healthy women, the single-bilayer structure of the chorionic villi epithelium was visualized 8.75% and Kashchenko-Hoffbauer cells were 7.5% more common (Figure 8). Similar changes in the second group were less frequent.

The morphofunctional state of the chorionic villi epithelium was characterized by the following criteria. Exfoliation of epithelial structures in the first group was observed 26.25% more often than in the comparison group. At the same time, in the second group, the difference from the control values was minimal – 1.25%. Different vector dynamics were observed in relation to the proliferative activity of the epithelium: the number of such foci in the first group decreased by 22.5%, and in the second group increased by 20%.

Vortex chorionic vascular remodeling and hemodynamic changes were assessed by the following histological markers. The chorionic villi with signs of increased angiomatosis in the

first group decreased relative to control by 16.25% and increased by 6.25% in the second group. Narrowing of the space due to perivascular sclerosis and endothelial proliferation (the final manifestation of which was complete obliteration) was much more common in the first group – 25% more than in the second group. Increased blood supply to the chorionic villi was more common in the second group (+31.25% relative to control) than in the first group (+10%).

In conditions of impaired blood flow, the stroma of the chorionic villi underwent fibrosclerotic changes, which in the first group were recorded 30% more often than in the control. In the second group, the difference was significantly smaller – 11.25%. The next stage of morphogenesis was the development of dystrophic calcification which were visualized in the first group 30% more often, and in the second group – 7.5% more often.

Pathological changes were registered not only in the chorionic villi but also in the intervillous space, which is a critical part of the

functional system “mother-placenta-fetus”. The accumulation of fibrin was observed in the first group 12.5% more often relative to the control value, in the second group – 2.5% more often, relative to thrombosis of the intervillous space, the difference was 13.75% and 1.25%.

The general trend of structural changes was also preserved in decidual tissue where dystrophic changes of decidualocytes in the first group occurred 31.25% more often than in the control and for the second group the difference was only 8.75%.

Conclusions

Based on the results of histological examination, it can be stated that complex modified therapy of preeclampsia associated with metabolic syndrome allows for normalization of the structure of the placenta, which is objectively confirmed by reducing the frequency of alternative changes in the placental amnion, epithelium, and stroma of chorionic villi. An important role in this process is played by the remodeling of the microcirculatory channel of the chorionic villi and the activation of proliferative processes in the epithelium of the chorionic villi.

Acknowledgements

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Conflict of Interest

The authors declare no conflict of interest.

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