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Research Article

Effect of Urogenital Infections on the Development of Placentary Dysfunction in Women Belonging to Risk Groups

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Abstract
The study involved 36 pregnant women with inflammatory diseases of female genital organs and 40 placentas of women with the physiological course of pregnancy and childbirth. Immunohistochemical and histological methods were used. It has been established that pregnant women with urogenital infections compared to those with physiological pregnancy had a lower concentration of the placental lactogen hormone and more active proapoptic protein of the BAX against the background of the unchanged concentration of the anti-apoptotic protein Bcl-2 in the cytoplasm of the invasive cytotrophoblast of the basal lamina.

Keywords
inflammatory diseases of female genital organs; placenta; invasive cytotrophoblast

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Introduction

Placental dysfunction (PD) is one of the most important problems of modern obstetrics and perinatology, it ranks one of the first among the causes of perinatal morbidity and mortality. According to the results of modern studies, 20-60% of cases of perinatal mortality are directly related to the pathology of the placenta. A high incidence of fetal and newborn pathology in women with PD requires further in-depth study of the mechanisms of its formation and development of methods for its diagnosis.

Primary PD occurs during the period of early embryogenesis and placentation under the influence of various factors (genetic, infectious, chemical ones etc.) which, depending on the biological specificity, can affect the sex cells of the parents, the development of the embryo, the formation of trophoblast and placenta. In the placenta, the inflammatory process against the background of inflammatory diseases of female genital organs (IDFGO) is identified, predominantly, in the basal lamina [1, 2], which is a fragment of the utero-placental area (UPA), which is separated along with the uterine afterbirth in the process of labor. The dopplerometric study found that pregnant women with IDFGO have disorders in utero-placental circulation [3], however, the morphological mechanisms of this phenomenon have not been decoded yet, although their localization is quite understandable - it is UPA. It has already been established that the state of the cells of the macrophage population - deciduocytes is significantly deteriorating against the background of IDFGO [4]. Undoubtedly that this, in a certain way, may affect the state of utero-placental circulation, since decidual cells produce various function regulators for other cells of the UPA [2]. However, the physiologically necessary gestational alterations in the spiral arteries of UPA are known to be predominantly influenced by other cells - invasive cytotrophoblast, since it is they, which, due to their own metalloproteases, immersing into the wall of the spiral arteries, cause their characteristic morphological changes [2]. This process results in a steady dilatation of these vessels, which ensures supply of the maternal blood flow to the interstitial spaces of the placenta which meets adequatelythe fetus's requirements in a given period of gestation. Recently, attention of scientists has been increasingly attracted by apoptosis of the placental cells. Proteins of the Bcl-2 family, especially the pro-apoptotic BAX protein and the anti-apoptotic oncoprotein Bcl-2 itself are the most significant regulators of apoptosis for the placenta as well as for many other organs [2, 4, 5]. The trophoblast function of the UPA is also reflected well by the concentration of the hormone of placental lactogen [2].

Objective. To determine some immunohistochemical parameters of the state of invasive cytotrophoblast of the basal plate of the placenta changed by inflammation in pregnant women against the background of IDFGO.

1. Materials and methods

36 observations in pregnant women with inflammatory diseases of female genital organs and 40 placentas of women with physiological course of pregnancy and childbirth (all placentas with the gestational age 37-41 weeks) have been

studied. The main place of localization of specific and non-specific inflammation of the placenta - basal lamina in women of the main group has been investigated. The peculiarity of the fetal placenta tissue was that they chose places with the largest thickness of the basal lamina. In addition to the general method of staining the histological sections with hematoxylin and eosin and methods for acid-fast bacteria by Ziehl-Neelsen, immunohistochemical methods for determining the proapoptotic protein BAX, the antiapoptotic protein Bcl-2 [5] and the placental lactogen hormone [2] have been used.

Quantitative studies of the intensity and nature of specific staining were carried out as follows. Initially, digital copies of the optical image of fragments of the basal lamina were obtained by means of a digital camera using a microscope lens x70 (water immersion). Then the digital copies of the image were analyzed using a license copy of the computer program "VideoTest - Size 5.0" (Viteotst Ltd., Russia, 2000) - they performed computer micro densitometry. The analysis was carried out on the basis of measurements of the whole area of the cytoplasm section in each cell by two parameters: "Optical density" (in relative units of optical density), "Deviation of brightness" (in units of brightness).

2. Results and discussion

In all 36 observations of infections in pregnant women, there were signs of inflammation in the basal lamina, in particular, in 27 observations there was a focal specific inflammation with the development of caseous necrosis, surrounded by epithelial cells, lymphocytes and rare Langerhans cells, in 9 observations the inflammation was non-specific, with centers of irregular form and sizes in the form of lymphoid-macrophage accumulations. In most of the observations there were acid-fast bacteria in the basal lamina.

The spiral arteries against the background of IDFGO in all pregnant women basically did not have sufficient gestational restructures and therefore were characterized by a narrow lumen, whereas during physiological pregnancy most of the arteries of the named type had the necessary changes in the wall and, accordingly, had wide lumen. In case of infection, compared to the physiological pregnancy, there was a decrease in the number of invasive cytotrophoblast cells in the wall of the spiral arteries on average by 3.8 times ($p < 0.05$), whereas in the surficial parts of the basal lamina, the number of invasive cytotrophoblast cells did not differ in the observation groups ($p > 0.05$).

As a result of immunohistochemical studies, the following has been established.

In all placentas the cytoplasm of the invasive cytotrophoblast of different localization within the basal lamina showed a clear expression of the antigen of the BAX protein, which manifested in a characteristic combination of diffuse and micro-macrogranular coloration. In the process of computer micro densitometry the following parameters were found. In the physiological pregnancy the intensity of the coloration was 0.149 ± 0.011 relative units of optical density, and with IDFGO - 0.289 ± 0.014 relative units of optical density ($p < 0.001$). These data indicate an increase in the concentration of proapoptotic BAX protein in the cytoplasm of the invasive cytotrophoblast of the basal lamina in IDFGO. However, the enhancement of the activity of this protein was also indicated by a change in the nature of its distribution in the cytoplasm, as evidenced by an increase in the degree of granularity of coloration. In particular, the average value of the "deviation of brightness" was 5.6 ± 0.61 brightness units in physiological pregnancy, and 27.2 ± 1.82 brightness units in tuberculosis ($p < 0.001$).

At the same time, there were no differences in the mean concentration of anti-apoptotic protein Bcl-2 in the cytoplasm of the cells of the invasive cytotrophoblast between the physiological pregnancy and IDFGO. For instance, in physiological pregnancy, the intensity of coloration on the protein Bcl-2 was 0.104 ± 0.006 relative units while in IDFGO - 0.106 ± 0.009 relative units ($p > 0.05$). Since the Bcl-2 protein manifests its anti-apoptotic effect mainly due to the neutralization (by chemical binding into the heterodimer) of the proapoptotic BAX protein [6], the above-mentioned situation with the increase in the activity of the BAX protein in the absence of a reaction from the Bcl-2 protein suggests at least two important points.

The first point. Under these conditions there should be an enhanced death of the invasive cytotrophoblast. The aforementioned decrease in the number of cells of the invasive cytotrophoblast in the walls of the vessels of the spiral arteries proves this fact. From the data obtained it can be stated that the processes of apoptosis are already started in the surface layers of the basal lamina, and with the movement (by invasion) of the cytotrophoblast to the wall of the spiral arteries, part of the cells from this population dies.

The second point. As the increase in the activity of the BAX protein causes mitochondrial dysfunction [6], the consequence of which, undoubtedly, should be an energy deficit in the cell that, in turn, can lead to a disturbance in the specific synthetic function of the cytotrophoblast, in particular in relation to its hormones. The results of studying the concentration of the hormone placental lactogen in the cytoplasm of cells of invasive cytotrophoblast have confirmed such an assumption. In particular, it has been established that the intensity of specific immunohistochemical staining on placental lactogen was 0.264 ± 0.012 relative units in the cytoplasm of the invasive cytotrophoblast cells in case of physiological pregnancy, while in IDFGO it was significantly lower - 0.183 ± 0.011 relative units ($p = 0.002$).

3. Conclusions

Pregnant women with inflammatory diseases of female genitalia have lower concentrations of the placental lactogen hormone in the cytoplasm of the invasive cytotrophoblast and more active proapoptotic BAX protein against the background of unchanged concentration of the anti-apoptotic protein Bcl-2 compared to the physiological pregnancy. The indicated facts

of the lesions in the invasive cytotrophoblast population may explain the lack of gestational alterations in the hepatocellular arteries of the utero-placental area in IDFGO.

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