THE FEATURES OF CONVERSION OF SPIRAL ARTERIES IN PREGNANT WOMEN WITH THE GESTATIONAL ENDOTHELIOPATHY

Summary. Transformation of uterine spiral arteries (SAs) is critical for healthy human pregnancy. Endothelial damage and dysfunction are common features of all of the pathological features of pre-eclampsia, stimulating the activation of platelets, neutrophils and the coagulation system, and promoting further vascular damage. 58 specimens of the placental tissues were obtained at 6-9 weeks of physiological pregnancy and pregnancy with gestational endotheliopathy. There were investigated morphological parameters that were reflected the processes of optimal transformation of SAs during the first trimester. It was found that pregnancy with gestational endotheliopathy was accompanied by the significant decrease of the intravascular cytotrophoblast invasion, decrease in the formation of cytotrophoblast plugs, accompanied by a slight expansion of lumen SA.

Key words: gestational endotheliopathy, spiral artery, chorionic villi, trophoblast plugs.

Introduction

Preeclampsia is a severe form of pregnancy-induced hypertension and occurs at frequencies of between 2 % and 8 %. Preeclampsia is a multi-system disorder unique to human pregnancy characterised by hypertension and involvement of one or more other organ systems and/or the fetus. Raised blood pressure is commonly but not always the first manifestation. It can lead to the occurrence of epileptic-like grand mal convulsions (eclampsia) in about 0.1% of pregnancies. Cerebral vascular accident is the most common cause of death. The disease has no known cause and can only be cured by delivery of the fetus and placenta [6].

Preeclampsia remains the major cause of maternal death in the world to-day; it is also a major contributor to maternal and perinatal morbidity and perinatal mortality. Furthermore, recent epidemiological evidence suggests that intrauterine growth retardation (IUGR), the risk of which is increased in preeclampsia, may be linked to the development of cardiovascular disease in adult life. Despite increasing knowledge of its pathophysiological processes, the aetiology of this condition remains obscure. The common pathological feature of the disease, whether in the placental bed, renal microvasculature or cerebral circulation, is vascular endothelial damage and dysfunction [7].

The placenta is a fetal organ that forms a crucial link between the mother and fetus throughout pregnancy, forming both a physical connection to the mother’s uterus and the site of all nutrient and gas exchange. In the first trimester of pregnancy specialized placental cells termed trophoblasts grow out from the chorionic villi and invade into the decidua part of spiral arteries (SAs) as far as the myometrial segments. The trophoblast migrate along the luminal surfaces of the SAs and remodel these vessels by interdigitating between the endothelial cells and replacing the endothelial lining and most of the muscularelastic tissue in the vessel walls such that a high-flow, low-resistance circulation is established to allow a constant and maximal flow of blood to the placenta and fetus as pregnancy progresses [1, 3].

For approximately the first 8-12 weeks of gestation trophoblasts form plugs that occlude the SA, allowing only maternal plasma filtrate to pass through, resulting in a high resistive index and decreased flow rate before 8-12 weeks of gestation. Furthermore, as the process of SAs remodelling during this time involves the dedifferentiation or removal of the smooth muscle layer surrounding the SAs, these arteries also lose the ability to dilate or constrict in order to regulate their shear stress. The trophoblast plugs dissipate between 7 and 12 weeks of gestation, allowing maternal blood to flow freely to the placenta, lowering the resistance and increasing the flow rate in the unpluged arteries [4, 5]. The extent of trophoblast invasion and SA remodelling and the complete occlusion of the SAs by trophoblast plugs are unique to human pregnancy.

Therefore, in this study we aimed to investigate the effect of gestational endotheliopathy on adequate development of trophoblast migration in the first trimester of pregnancy.

Materials and methods

We enrolled pregnant women with gestational endotheliopathy (GE), who were diagnosed when microalbuminuria was more than 5,0 mg/mmol (screening test), and endothelium-dependent vasodilation was less than 10% (approving test) [2].

The specimens from pregnant women were distributed in three groups. The control group - specimens from women with physiological gestation (n = 22); the second group - pregnant women with gestational endotheliopathy, but without clinical manifestation (n = 17); the third group - pregnant women with clinical manifestation of the gestational endotheliopathy (n = 19).

Samples. Placentae and decidua parietalis (without prior invasion) were obtained, following written informed consent from patients undergoing first trimester elective terminations at the at the maternity hospital №1 (Vinnytsya, Ukraine). Placental bed biopsies were fixed in 10% neutralbuffered formalin for 24 h, processed routinely, embedded in paraffin wax, and sectioned at 3 mm stained with hematoxylin and eosin, Schiff’s reagent by Van Hyzonu onto glass slides. All placental bed biopsies were microscopy selected to confirm...
the presence of decidua, myometrium, and at least 1 spiral artery. The study was approved by Bio-Ethics Committee of the National Pirogov Memorial Medical University in Vinnytsya, and written, informed consent was obtained from all subjects.

Statistical analysis. Descriptive data are expressed as means ± SD or SE. The significance of difference was assessed by two-tailed t-test for groups of nonpaired or paired observations and by one-way analysis of variance when more than two groups were compared.

Results. Discussion
In the present study we found that in physiological pregnancy the expression of vascular invasion internally cytotrophoblast had the maximum rate, but in gestational endotheliopathy, in the majority of cases, we found only a few cells in the inner vascular cytotrophoblast transparent spiral arteries. Reducing the severity of interstitial cytotrophoblast invasion led to the almost complete replacement SAs by fibrinoid in the vessel walls at physiological pregnancy. In pregnant women with preclinical form of gestational endotheliopathy in preparations of SAs was substituted by fibrinoid for less than half of the SA wall, in most cases (65,1 %), which resulted in partial retention of muscle fibers wall spiral arteries. When decidual vasculopathy was diagnosed, in 51,1 % there was a complete lack of fibrinoid. In 48,9 % cases we were noted less than half the replacement of SA wall by fibrinoid.

In normal pregnancy, the transformation of endometrial segments in SAs often were accompanied by the identification cytotrophoblast congestion (70,8%), while the number of preclinical gestational endotheliopathy cytotrophoblast plugs, reached 26,1 %, whereas in the clinical manifestation of the formation of cytotrophoblast plugs was found in only 2 cases (3,9 %). Described structural changes in the spiral arteries utero-placental region have questioned the possibility of optimal inflow in intervillous space arterial blood adequately to the needs of the growing fetus.

During the morphological examination chorionic villi in

Figure 1. The chorionic villi during normal pregnancy (6 - 7 weeks). Villi with a two-layer epithelium, in the lumen of blood vessels typical erythroblasts and red blood cells in approximately equal proportions. H & E stain, x 200.

Figure 2. The decidual segments of the SA with normal pregnancy (6 weeks). Internally-vascular cytotrophoblast partially and completely covers the lumen of arteries. H & E stain, x 200.

Figure 3. The chorionic villi during preclinical gestational endotheliopathy (7 - 8 weeks). Plot with swollen avascular villi. H & E stain, x 200.

Figure 4. The decidual segments of SA (clinical manifestation of gestational endotheliopathy 6-7 weeks). In the lumen of the artery presented inner-vascular cytotrophoblast cells. H & E stain, x 100.
Резюме.
ОСОБЛИВОСТІ КОНВЕРСІЇ СПІРАЛЬНИХ АРТЕРІЙ У ВАГІТНИХ ЖІНОК ПРИ ГЕСТАЦІЙНІ ЕНД ОТ ЕЛІОПАТІЇ

Коньков Д. Г.

Ключевые слова:
резорбция, беременность, гестационная эндотелиопатия.

In such cases the endothelial layers were preserved at a lower portion of the intima or absent, and the inner-vascular cytotrophoblast to a considerable extent was instead of them (Fig. 2). Intravascular cytotrophoblast were identified in all cases in the lumen of spiral arteries.

Histologically in preparations of chorionic villi among pregnant women with preclinical form of gestational endotheliopathy were found dissociated development of villi. At selected sites were determined supporting villi with the presence of vessels such as arterioles and venules center and which represented a transitional form from the embryonic to intermediate immature villi, whose diameter was less than embryonic villi. Epithelial cover was thinner due to thinning and discontinuity layer villous cytotrophoblast. The villi of mesenchymal type with thinning epithelium and with avascular stroma edema were found (Fig. 3).

According to analyzing the results of our study, chorionic villi in women with clinical manifestation of gestational endotheliopathy, in most cases, they were mesenchymal-type villi, villi size ranged from small to large, with thinning of epithelium. Their stroma was edematous and avascular.

Thus endothelial layer was retained throughout the greater part or intima. Internally-vascular cytotrophoblast in the lumen of the SAs in 29 cases turned out to be in the form of individual scattered cells, and in 23 cases - were undiagnosed (Fig. 4).

Study of the normal physiological process of human decidual spiral artery transformation is critical to identify causative factors of impaired vascular remodeling and reduced utero-placental perfusion associated with gestational endotheliopathy. These results extend our understanding of the temporal sequence of events and mechanisms of remodeling of endometrial part SAs, strongly supporting an integral role of the abnormal decidual vascular transformation in the first trimester in genesis of development of the perinatal pathology.

Conclusions and prospects for future research
1. Gestational transformation of the SAs when was diagnosed endothelial dysfunction is usually weakly expressed or absent, accompanied by a slight expansion of lumen SA.
2. For gestational endotheliopathy determined by the decrease in intravascular cytotrophoblast invasion and the decrease in the formation of cytotrophoblast plugs (3,9 %).

The further research initiatives should be directed in an bid to strengthen the preexisting evidence base for available prevention and to develop novel techniques to aid in the prevention of perinatal pathology due to gestational endotheliopathy. Continued research will further our understanding of the pathophysiology of gestational endotheliopathy and may advance our ability to predict and prevent this potentially serious complication of pregnancy.

References

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Резюме. Трансформація маткових спіральних артерій (СА) має рішенняне значення для розвитку беременності. Повреждення і дисфункції ендотеля є ініціюючими факторами для розвитку гестаційної патології. Була встановлена роль розподілу кровотоку в період першого триместру. Було виявлено, що ендотеля у гестаційній ендотеліопатії змінилася, що впливає на формування і розвиток СА.

Ключові слова: гестаційна ендотеліопатія, спіральні артерії, ворсинки хоріону, трофобластичні затори.

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Резюме. Трансформація маткових спіральних артерій (СА) має рішенняне значення для розвитку беременності. Повреждення і дисфункції ендотеля є ініціюючими факторами для розвитку гестаційної патології. Була встановлена роль розподілу кровотоку в період першого триместру. Було виявлено, що ендотеля у гестаційній ендотеліопатії змінилася, що впливає на формування і розвиток СА.

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ня і дисфункції ендотелію є ініціюючими факторами для розвитку прееклампсії, стимулюючи активацію тромбоцитів, нейтрофілів і факторів згортання, а також сприяючи подальшому пошкодженню судин. 58 зразків плацентарної тканини були отримані при 6-9 тижнях фізіологічної вагітності і гестаційній ендотеліопатії. Були досліджені морфологічні параметри, які відображали процеси оптимального перетворення СА протягом першого триместру. Було встановлено, що вагітність при гестаційній ендотеліопатії супроводжувалася значним зниженням інвазії внутрішньосудинного цитотрофобласту, зниженням утворення цитотрофобластичних заторів, супроводжується незначним розширенням просвіті СА.

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