

Pathomorphological changes in the placenta during coronavirus infection and its effect on fetuses and babies

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Abstract: In this paper, we performed a structured search for foreign scientific publications on the morphological assessment of the state of placenta in women with coronavirus infection. The publications available in the PubMed, EMBASE, Medline databases from April to September 2020 were analyzed. The purpose of this analysis was to describe and structure the histopathological changes in the placenta of patients with coronavirus infection during pregnancy.

Key Words: Pathomorphologic, pregnant, infection, virus

Introduction

The impact of coronavirus disease on pregnant women and newborns is of particular interest to obstetricians, neonatologists, and pathologists. Histopathological examination of placental tissue can provide important information about the possibility of trans placental transmission of the SARS-Cov-2 virus and the risk of intrauterine infection of the fetus. Opposite opinions are found in the literature: from the complete denial of morphological changes in the placenta during coronavirus infection to the recognition of extremely severe disorders, in which the risk of vertical transmission of the virus to the fetus increases.

The first attempts to identify the morphological features of single placentas in mothers with coronavirus infection were carried out by Chinese scientists. They first reported placental pathology in seven women with SARS-CoV-2 infection in Hong Kong. The placentas of not only women who gave birth in an acute condition, but also those who had recovered from the infection by the time of delivery, showed significant morphological changes. Then, two reports of spontaneous abortion in the second trimester in women with Covid-19 appeared in the English-language literature, where placental findings were also mentioned. In the first case, signs of acute inflammation and deposition of per villous fibrin were revealed in the placenta. In the second, histiocytic intervillitis with viral spike protein was detected in the syncytiotrophoblast, which was demonstrated by immunohistochemistry. The results of a study of the placentas of 50 women with SARS-CoV-2 infection were later presented during pregnancy. This is the first large case series of placental pathology in SARS-CoV-2 and Covid-19 infection reported in the English-language literature.

Materials And Methods

An important task is to detect the virus in placental tissue. Two methods are described: detection of nucleocapsid protein expression by immunohistochemistry and RNA expression by in situ hybridization. In an extremely small number of cases, SARS-CoV-2 RNA was present in the placenta in the form of foci in the cytotrophoblast.

The primary receptor in the SARS-CoV-2 pathway is angiotensin-converting enzyme 2 (ACE2). In the placentas of the first and second trimesters of pregnancy, immunohistochemically analysis of cells revealed the expression of ACE2 and TMPRSS2 receptors. There is an association with branching structure morphogenesis, extracellular matrix interaction, oxygen binding, and antioxidant activity in ACE2+ cells. The presence of ACE2+ cells determines an increased ability for viral invasion, proliferative epithelial cells and cell adhesion. ACE2 expression is localized predominantly in the outer layer of placental villus syncytiotrophoblast, which indicates the potential for trans placental transmission of the SARS-Cov-2 virus. ACE2 regulates the release of angiotensins I-VII, which leads to vasodilation in the mother-fetus system, but at the same time promotes the spread of SARSCoV-2. ACE2 expression was not found in the villus stroma, Hofbauer cells, or endothelial cells.

Immunohistochemically, macrophages and CD4-positive T cells predominate in villous tissue, although an increased number of CD8-positive cells are also present. It can be assumed that they represent maternal antiviral immunity.

The next point is the detection of the main morphological changes in the placenta. Since SARS-CoV-2 is a virus, it can be expected to cause non-specific inflammation, villitis in particular. Chronic villitis is diagnosed by the presence of mixed lymphoid infiltration of the stroma of intermediate and terminal villi. In acute villitis, there is predominantly infiltration with polymorph nuclear leukocytes.

One study described a case of acute histological chorioamnionitis and umbilical arteritis at delivery in the midst of a corona virus infection. Other researchers point to a chronic inflammatory pathology with both low-grade chronic lymphocytic villitis and chronic deciduitis with plasma cell infiltration.

Chronic intervillitis (intervillitis) is a focal lesion of part of the villi with the presence of inflammatory cells in the intervillous space. Chronic histiocytic intervillitis (massive chronic intervillitis) is a rare inflammatory idiopathic disease characterized by monomorphic maternal histiocytic infiltrates in the intervillous space with the presence of CD68+ macrophages, often in combination with intervillous deposition of fetal fibrinoid, in addition, maternal infarcts often occur. It can be assumed that histiocytic intervillitis can be induced by severe systemic inflammation (cytokine storm), since it is extremely rare in asymptomatic patients.

Chronic histiocytic intervillitis can cause pregnancy loss, preterm birth, intrauterine growth retardation, and antenatal fetal death. There is a case report of histiocytic intervillitis in which an unfavorable outcome was noted (pregnancy in the second trimester ended in miscarriage in a Covid-19-positive woman).

Attention is drawn to the frequent occurrence of chorangiomas. Chorangiomas are an increase in the number of capillaries in the terminal villi of the placenta, associated with a decrease in maternal oxygen saturation. Cases of chorangiomas have been described in asymptomatic patients who have recovered by the time of delivery, indicating persistent changes in the placenta.

Results

It was noted that in women with Covid-19, signs of placental pathology were found, indicating a violation of both maternal and fetal blood flow (maternal and fetal malperfusion). Vascular malperfusion is represented by decidual arteriopathy, atherosclerosis and fibrinoid necrosis, and mural hypertrophy of membrane arterioles. The main risk factors for the development of such changes are maternal hypertensive disorders. Peripheral infarcts, agglutination, and accelerated maturation of the villi also occur. Other studies have noted delayed maturation of the villi.

In patients with Covid-19, there is a significant increase in the number of intervillous thrombi. It is assumed that 85% of thrombi are of embryonic origin. Given the tendency to hypercoagulability in coronavirus infection, thrombus deposition is likely to occur in response to viral invasion.

A case of 16-week intrauterine fetal death showed severe changes in the placenta: villous edema and retro placental hematoma. In the placenta, there was a moderate increase in the content of per villous fibrin and acute subchorionitis. No bacterial culture was identified, leading the authors to suggest that the acute inflammatory response is related to SARS-CoV-2. The test result for the fetus was negative. This confirms existing evidence that vertical transmission of the virus is rare and placental changes caused by Covid-19 are associated with maternal infection and inflammation rather than fetal infection.

Pathomorphology of the placenta in Covid-19

Some researchers deny pathomorphological findings in placentas. It is stated that in their sample, decidual vasculopathy was not visualized in any of the placentas of patients diagnosed with coronavirus infection. There were no statistically significant differences in the histopathological characteristics of the placentas in the patients of the study group and the comparison group. The test results for the presence of coronavirus in all newborns were negative. A similar study comparing 20 third-trimester placentas in women with coronavirus infection complicated by pneumonia and 20 placentas in patients with atypical pneumonia and negative Covid-19 test also showed no significant differences. In the SARS-CoV-2+ group, there were no differences between symptomatic

and non-symptomatic patients. Thus, Covid-19, which complicates the course of pregnancy in the third trimester, does not significantly affect the structure and pathology of the placenta.

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