Research Article

Peculiarities of the Diagnostics of Miscarriage in Early Terms in Women with Recurrent Miscarriage

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Abstract
Missing pregnancy is a consequence of the simultaneous or sequential action of several factors. The main causes of miscarriage and spontaneous interruption of pregnancy include: genetic factors, endocrine disorders, immune and infectious factors, congenital and acquired diseases of female genital organs. In almost 50% of women, it is not impossible to determine the reason of miscarriage, so the question of early diagnosis and prevention of this condition is quite acute.

Materials and methods. In this study, we performed a pathohistological study of the deciduum in order to determine the etiological factor of the pathology of implantation of the embryo and placentation. The study included 88 women with a diagnosis of "recurrent miscarriage" that met the criteria for inclusion and exclusion.

Results of research. In the study group, the age of women was from 19 to 35 years old (mean age was 27.6±4.1 years old). The abortion was observed at different stages of pregnancy, more often during the period of 4-9 weeks of gestation (67 cases - 76.14%). According to the results of the histopathological study of deciduum lymphohistiocytic infiltration was revealed in the stroma of villi in 62 cases (70.45%), other changes were less common.

Conclusions and perspectives of further research. The obtained data indicate that the determination of the etiologic factor of miscarriage of the pregnancy, especially in women with a diagnosis "Reccurent miscarriage of obscure etiology", will allow to predict the development of the pathology of implantation and placentation in subsequent pregnancies. Prospects for further research are to develop adequate preparation before pregnancy and prevention of the pathology of implantation and placentation.

Keywords
recurrent miscarriage; pathology of implantation and placentation; chorionic villi; deciduum

Problem statement and analysis of the recent research
In today’s conditions, spontaneous miscarriage in the early stages is considered as one of the first manifestations of serious pathological changes in reproductive health of women, which in almost 30% are causes of further reproductive loss [1, 4]. The risk of such interruption is 10-20% of all pregnancies, but if we take into account cases of reproductive losses that occur during the first 14 days after conception, which are determined by studying the dynamics of growth of human chorionic gonadotropin, then this number can be significantly increased [1-3]. It is necessary to take into account the frequency of the recurrent miscarriage of pregnancy. Despite numerous studies of etiology and pathogenesis of premature abortion, the frequency of this pathology is still high, but ranges from 10 to 20-15% of their total.

In general, miscarriage is a consequence of the simultaneous or sequential action of several factors. [5] The main causes of miscarriage include: genetic factors, endocrine disorders, immune and infectious factors, congenital and acquired diseases of female genital organs. We can’t identify the cause of miscarriage in almost 50% of such women, so the issue of early diagnosis and prevention of this condition is quite acute. In our study, we conducted a histopathological study of decidium, as the issue of embryoplacental insufficiency, which is now widely discussed. Unfortunately, even with a detailed histological analysis of the sample from the cavity of the uterus and conception products, the etiologic reason for abortion in the early stages is unclear in 50% of cases. For women with a diagnosis of “recurrent miscarriage,” the question of determination of the etiological factor is extremely important as it will enable doctors to form the risk group and provide adequate preparation for the pregnancy, and timely prevention and treatment of pregnancy complications.

Recently, the hypothesis of defects of the implantation, inferiority of trophoblast invasions and placenta, utero-placental ischemia and generalized endothelial dysfunction is dominant. [5, 6] It is known that during the process of gestation a unique, complex functioning system of three endothelial surfaces - fetoplacental endothelium, endothelium of the vessels of the uterus and endothelium of the trophoblast, lining the intervertebral space, is formed.

Fetoplacental complex can be considered from three different, but interconnected sides:
1. As a source of protein and steroid hormones, which come to maternal blood flow.

2. As a participant in the control of the development of the endocrine system of the fetus, its growth and nutrition.

3. As a selective barrier that determines the interaction between maternal and fetal systems.

Implantation of the fetal egg begins within 8 days of conception. The trophoblast is immersed in the endometrium, but it is possible to distinguish 2 layers of the formed placenta. Dipped trophoblast with its villi tightly attached to the endometrium. Differentiated syncytiotrophoblast, which is formed after the fusion of cytotrophoblasts, carries out direct contact with the circulatory system of the mother. Syncytiotrophoblast is the main source of hormonal production and contains all cellular systems required for the synthesis of both steroid and polypeptide hormones. The decidua shell is the so-called endometrium of pregnancy. Decidual cells have the ability to synthesize various polypeptide hormones (prolactin, relaxin, and various paracrine factors). There are several parts in the decidual envelope: a basal that is between the fetal egg and the uterine wall; capsule covering the fetal egg from the side of the uterus; parietal, which lays the entire inner surface of the uterus, except for the area of attachment of the fetal egg [4].

By 12-13 days of development of the embryo in the primary villi, which are on the surface of the chorion, which is reversed to the biometry, the connective tissue grows. Thus secondary wings are formed. At the 3rd week of the development of the embryo in the stroma of the secondary villi begin to grow blood vessels (fetal capillaries). Thus, tertiary villi are formed; this process is called placentation. Since the formation of tertiary villi, the transition from the histotrophic nutrition of the embryo (due to the embryotroph) to the hemotrophic begins. This transition ends up at 16-18 weeks of gestation. This completes the vascularization of the tertiary villi and the formation of the placenta.

Therefore, it can be assumed that implantation and placentation processes play an extremely important role in the normal formation of the placenta and the fetal-placental complex, as well as the normal course of pregnancy. Detection of the pathology of implantation and placentation will allow to do some preparations for the pregnancy and, if possible, prevent early reproductive loss.

Objective: reducing the frequency of early reproductive loss by predicting the risk of developing a miscarriage of pregnancy, identifying a possible etiological factor of miscarriage.

1. Materials and methods

The study was performed on the basis of gynecological department VMKPB #2. We examined 88 women with recurrent miscarriage. Criteria for inclusion in the main group: the age of women from 18 to 45 years, the presence of 2 or more abortions in the early stages of pregnancy (missed miscarriage, spontaneous abortion). The exclusion criteria were the following: age of women from 18 to 45 years old, abnormal anamnesis, ovarian-menstrual cycle disorder, uterine and ovarian tumors, pathological conditions of the endometrium and abnormalities of the uterus, presence of inflammatory processes and sexually transmitted infections, thyroid disease, and neuroendocrine syndromes.

In our study, we used the following research methods: clinical, histopathological, mathematical and statistical methods.

2. Results

The clinical examination was carried out according to a specially designed registration card of the patient, which included a detailed collection of anamnestic data. The social status of woman (place of work, occupation, occupational hazards, education, marital status, living conditions) was determined.

In the study group, the age of women varied from 23 to 41 years (the average age was 31.08 ± 5.17 years). Most of the patients were residents of the city. In the analysis of the social status of the examined women, it was determined that among examined women there were predominated women engaged in intellectual work - 61%, 28% of women were housewives, and 11% of women - were engaged in physical labor, indicating an increased proportion of women with intellectual differentiation of labor with psychoemotional and physical activity (Fig. 1).

![Figure 1. Character of occupation of women city residents](image)

In the study group miscarriage was observed at different stages of pregnancy. Most often, termination of pregnancy occurred in the term - 4-9 weeks of pregnancy (67 - 76.14%), in other terms less often (19 - 23.86%) (Fig. 2). Probably this is due to some problems of the processes of implantation of the fetal egg and the processes of placental formation. Some authors call the first trimester of pregnancy a period of lost opportunities, since timely diagnosis and correction of any pathological abnormalities in the early stages of pregnancy are especially important for the further normal development and course of pregnancy. This is especially true for women with the recurrent miscarriage of obscure etiology, the state of which must be monitored at the planning stage of the next pregnancy.
After the histopathological study of decidium in 62 cases (70.45%) lymphostiocyte infiltration was revealed in the stroma of villi, in 23 cases (26.13%) - parts of the fetal egg with centers of necrosis were found, in 8 (9.09%) - parts of the fetal egg with dystrophic changes, in 10 (8.8%) cases there were decidual tissues with inflammation centers, and in 14 cases (15.9%) - chorionic villi with dystrophic changes. Other changes (immature non-vascular villi of chorion, placental tissue with inflammatory foci, partially necrotized placental tissue, etc.) were found to be much less frequent (see Table 1).

### Table 1. Histopathological study of deciduum

<table>
<thead>
<tr>
<th>Patology</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphostiocyte infiltration</td>
<td>62</td>
<td>70.45</td>
</tr>
<tr>
<td>Fetal egg with centers of necrosis</td>
<td>23</td>
<td>26.13</td>
</tr>
<tr>
<td>Fetal egg with dystrophic changes</td>
<td>8</td>
<td>9.09</td>
</tr>
<tr>
<td>Decidual tissue with inflammation centers</td>
<td>10</td>
<td>8.8</td>
</tr>
<tr>
<td>Chorionic villi with dystrophic changes</td>
<td>14</td>
<td>15.9</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>5.68</td>
</tr>
</tbody>
</table>

3. Conclusions and discussion

Violation of one or more parts of the processes of angiogenesis, blood clotting and fibrinolysis leads to a disturbance in the formation of the fetoplacental complex, which in turn leads to inadequate fetus supply with oxygen and nutrients, clinical manifestations of which may be the threat of abortion, pregnancy stall or spontaneous miscarriage. Carrying out a histopathological study will give one more opportunity to determine the etiological factor of non-pregnancy pregnancy, especially in women with a diagnosis of "Recurrent miscarriage of pregnancy unknown etiology", and thus predict the emergence of such pathologies in subsequent pregnancies. Prospects for further research are to develop adequate pre-

References


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