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Clinical and Hemostasiologic Features of Early Pregnancy in Women with Different Genesis of Threat of Abortion

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Abstract: The tactics of managing patients with the threat of early termination of pregnancy should be based on an integrated approach, taking into account etiological factors and identified hemostatic disorders. Antiphospholipid syndrome (APS) in pregnant women is a serious autoimmune disease that can lead to severe complications and even the loss of a child.
Keywords: threat of termination of pregnancy, antiphospholipid syndrome, persistent viral infection, hyperandrogenism, obstetric complications, annexin V.

Introduction

A differentiated approach to the management of patients at risk of termination of pregnancy, based on an in-depth study of the parameters of the hemostasis system and the identification of etiological factors, can significantly increase the effectiveness of therapy and improve pregnancy outcomes.With AFS, the body's immune system mistakenly attacks its own cells, which leads to the formation of blood clots and impaired blood circulation in the placenta. The main risks of AFS during pregnancy are:

-Miscarriages: Recurrent miscarriages in early pregnancy are one of the most common symptoms of AFS.

-Premature birth: Thrombosis in the placenta can lead to impaired fetal nutrition and premature birth.

-Placental abruption: Placental abruption is a serious complication that can endanger the life of the mother and child.

- Delayed fetal development.

One of the main types of gynecological pathology is miscarriage. The number of cases of this complication has remained stable for many years and accounts for 15-20% of all desired pregnancies. Regardless of the reason that caused the loss of pregnancy, adequate hemodynamic processes in the unified mother—placenta—fetus system are the leading condition ensuring the normal course of the gestational process, growth and development of the fetus. Hemostatic disorders in patients with habitual miscarriage are detected in 61.1% of cases. They are most often represented by hyperaggregational syndrome (22.2%), thrombinemia (17.8%), hyperhomocysteinemia (12.2%) and antiphospholipid syndrome (APS) - 20%. However, the development of pregnancy complications

(including miscarriage), accompanied by a number of hemostatic disorders, is also observed in women with hyperandrogenism and the presence of persistent viral infections. At the same time, a number of significant changes occur in the hemostasis system, which are detected using laboratory methods for determining markers of hemocoagulation disorders. The clinical and hemostatic features of the course of pregnancy were evaluated, and the level of placental anticoagulant protein annexin V was studied in 63 women with various risk factors for termination of pregnancy (antiphospholipid syndrome, hyperandrogenism, and persistent viral infection). The control group consisted of 17 healthy pregnant women. Characteristic obstetric complications (anemia, hepatosis, fetoplacental insufficiency) have been identified in antiphospholipid syndrome, accompanied by an increase in the titer of antibodies to annexin V.; persistent viral infection and hyperandrogenism also revealed a number of gynecological complications (early toxicosis, preeclampsia, placental insufficiency, isthmic-cervical insufficiency), however, statistically significant changes in the level of annexin V were not detected. The development of gynecological complications in pregnant women with antiphospholipid syndrome and persistent viral infection was accompanied by disorders in the hemostasis system.

The aim of the study was to evaluate the clinical and hemostasiological features of the course of pregnancy, as well as to study the level of placental anticoagulant protein annexin V in women with various risk of termination of pregnancy in the first trimester of pregnancy.

Materials and methods

At the National Medical Center in the Department of Gynecology, we examined 63 pregnant women at risk of termination of pregnancy, who were divided into three groups: group 1 consisted of 31 women with diagnosed APS, group 2 consisted of 19 patients with hyperandrogenemia, and Group 3 consisted of 13 pregnant women with viral infection. The 4th control group consisted of 17 healthy pregnant women. All patients underwent a comprehensive examination, including the collection of medical history data, objective examination, external obstetric examination, ultrasound examination of the uterus, evaluation of the fetoplacental complex (ultrasound fetometry, Dopplerometry, cardiotocography); bacterioscopic, bacteriological and molecular genetic (PCR) examination of the contents of the vagina and mucus of the cervical canal; clinical and biochemical blood tests. The titer of antibodies to cardiolipins, phospholipids, and lupus anticoagulant was studied in group 1 patients. In women of the 2nd group, the level of total testosterone in the blood serum and the content of 17-ketosteroids in a sample of daily urine were studied. In pregnant women of the 3rd group, the concentration of immunoglobulins of classes G, M, and A for herpes simplex virus type 2 and cytomegalovirus was determined. The state of the blood coagulation system was assessed based on the results of studies of vascular-platelet (platelet count) and hemocoagulation (partially activated thromboplastin time — APTT) links of hemostasis, markers of intravascular coagulation — the formation of thrombin (prothrombin time, prothrombin index) and fibrin (fibrinogen). Using enzyme immunoassay, the serum levels of IgG and IgM antibodies to annexin V were determined in all the examined patients. The value of this indicator was assumed to be less than 5 units/ml.

Results and Discussions

The analysis of the age composition of the patients in the studied groups showed the prevalence of women in the age group from 31 to 40 years (63.8±1.4%). At the same time, the most burdened somatic anamnesis was recorded in patients of the 1st group (77.3±2.3%). The structure of extragenital pathology was dominated by neurological pathology (35.3%), thyroid diseases (17.6%), myopia of varying severity (15.8%), urological pathology — pyelonephritis (14.3%) and diseases of the ENT organs — tonsillitis (14.3%). The study of the frequency of diseases associated with hemostasis pathology also showed the predominance of such diseases among women of the 1st group

(68.2±1.9%). At the same time, hereditary thrombophilia (50%), vascular thrombosis (22.7%), a family history of thrombosis (13.6%), thrombocytopenia and varicose veins (9.1%) were most often detected. Among women in groups 2, 3, and 4, diseases associated with hemocoagulation disorders were recorded 1.5—2 times less frequently (29.4, 42.9, and 22.5%, respectively). The actual pregnancy in the studied women was repeated in 84±2.1% of cases. However, the outcomes of previous pregnancies were different. Thus, spontaneous miscarriages and medical abortions were most often reported in patients of the 1st (40.9%) and 2nd (41.2%) groups. At the same time, habitual miscarriage was more often observed in women with hyperandrogenism (35.3%). In the women of the control group, previous pregnancies more often ended in childbirth (37.5%), spontaneous miscarriages were registered in only 5% of cases. Dynamic monitoring of the course of a real pregnancy in the patients of the studied groups allowed us to identify the most frequent obstetric complications in various trimesters of pregnancy. Thus, in the first trimester of pregnancy, early toxicosis developed in almost 50% of women in group 3 with a viral infection (51.4±1.6%), in contrast to pregnant women in groups 1, 2 and 4 (40.9±2.1, 35.3±1.4 and 25±1.8%, respectively). Anemia prevailed in patients of group 1 (63.6%±2.4%) compared with pregnant women of groups 2, 3 and 4 (17.6±1.5, 28.6±1.7 and 15±0.9%, respectively). The threat of spontaneous miscarriage was also detected in most cases (72.7±2.9%) among women in group 1, in contrast to pregnant women in groups 2, 3 and 4 (64.7±1.2, 34.3±1.6 and 2.5±0.4%, respectively). However, the formation of isthmic-cervical insufficiency was more often noted in pregnant women with hyperandrogenism (29.4±0.8%) compared with patients in groups 1, 3 and 4 (9.1±1.1, 2.9±0.5% and 0, respectively). During the first trimester of pregnancy, the dynamics of changes in hemostasis system parameters was analyzed in the patients of the studied groups. In addition to the hemostasis system, the titer of placental anticoagulant protein annexin V of IgG and IgM classes was evaluated. An increase in the titer of antibodies to IgG class V annexin in patients with APS in the second and third trimesters of pregnancy (6.1±1.4 and 6±0.9 units/ml, respectively), as well as an increased titer of antibodies to IgG class V annexin in the second trimester of pregnancy (6.9±1.2 units/ml). In pregnant women of groups 2, 3, and 4, the titer of antibodies to annexin V of IgG and IdM classes was within the normal range, regardless of the duration of pregnancy.

Pregnancy is a thrombophilic condition in which the activation of intravascular thrombogenesis occurs due to the restructuring of the coagulation, anticoagulation and fibrinolytic blood systems, which reflects the evolutionary adaptation of the female body to reduce blood loss in childbirth after separation of the placenta. Therefore, various etiological factors (APS, hyperandrogenism, persistent viral infection) worsen the state of physiological hypercoagulation, provoking the development of various obstetric complications during pregnancy. Among the patients with various genesis of the threat of termination of pregnancy, obstetric complications were most often developed in pregnant women with AFS (group 1) in all trimesters of pregnancy. At the same time, the threat of termination of pregnancy (68.7±1.4%), anemia (62.1±1.6%), preeclampsia (23.8±0.8%) and fetoplacental insufficiency (21.6±0.9%) prevailed in the structure of obstetric complications. The realization of these pathological mechanisms in the body occurs due to microcirculation disorders, hemostasis and vascular wall pathology. In pregnant women with hyperandrogenism, obstetric complications developed less frequently during pregnancy and were represented by the threat of termination of pregnancy (64.7±1.8%), cervical insufficiency (29.4±0.8%) and arterial hypertension (8.8±0.6%). Pregnant women with persistent viral infection had the lowest number of obstetric complications during pregnancy. At the same time, the structure of the presented complications had its own characteristics: early toxicosis (51.4±1.6%), the threat of termination of pregnancy (50.5±1.9%),

preeclampsia (22.9±0.8%) and placental insufficiency (20±1.7%). In pregnant women with obstetric complications, disorders of the vascular-platelet link of hemostasis of varying severity have been noted. In patients with APS, as pregnancy progressed, a decrease in platelet count (180 · 109 /l), an increase in APTT (54±1.8 s), a shortening of APTT (11±0.9 s) and PTI (127±2.9%), and an increase in the titer of IgG class V antibodies to annexin (6.1±1.4 units/ml) and IdM (6.9±1.2 u/ml), which indicated an increased risk of thrombosis and was an indication for timely anticoagulant therapy. No significant hemocoagulation disorders were observed among patients with hyperandrogenism. An increase in fibrinogen levels (4.2±0.17 g/l) as pregnancy progressed was regarded as a variant of "physiological hypercoagulation". A study of hemostasis system parameters in women with persistent viral infection showed the development of thrombocytopenia (171·109 /l), a shortening of PTB (10±1.2 s) and an increase in fibrinogen levels (5.4±1.3 g/l). The results obtained coincide with the data of the world literature [5], according to which the development of a systemic inflammatory response to the action of an infectious agent contributes to disorders in the hemostasis system and the development of thrombophilic conditions.

Conclusions

1. In patients with various genesis of the threat of termination of pregnancy, the development of obstetric complications has its own characteristics: with AFS, anemia (62.1±1.6%), gestosis (23.8±0.8%), fetoplacental insufficiency (21.6±0.9%) develop; with hyperandrogenism, isthmic—cervical insufficiency (29.4±0.8%), arterial hypertension (8.8±0.6%); with persistent viral infection — early toxicosis (51.4±1.6%), preeclampsia (22.9±0.8%) and placental insufficiency (20±1.7%). The development of obstetric complications is accompanied by disorders in the hemostatic system: with AFS, there is a decrease in the number of platelets (180·109 /l), an increase in APTT (54±1.8 s), a shortening of PTB (11±0.9 s); with persistent viral infection, thrombocytopenia (171·109 /l), a shortening of PTB (10± 1.2 s) and increased fibrinogen levels (5.4±1.3 g/l); no statistically significant hemocoagulation disorders were found in hyperandrogenism.
2. Pregnant women with APS have an increase in the titer of antibodies to IgG class V annexin in the II and III trimesters of pregnancy (6.1±1.4 u/ml) and IdM in the II trimester of pregnancy (6.9±1.2 u/ml). In pregnant women with hyperandrogenism and persistent viral infection, there were no statistically significant changes in the titer of antibodies to annexin V classes IgG and IdM.
3. However, despite all the difficulties, AFS during pregnancy is not a verdict. Modern medicine offers effective treatment methods that can significantly reduce the risk of complications and successfully carry a child. Important: when planning pregnancy, women with AFS should always consult with a hematologist and an obstetrician-gynecologist, rheumatologist, endocrinologist and nephrologist. Timely diagnosis and comprehensive treatment are the key to a successful pregnancy and the birth of a healthy child.

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