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Features of the Course and Principles of Treatment of Pregnant Women with Antiphospholipid Syndrome

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Abstract: The factors influencing the outcome of pregnancy, the development of an undeveloped pregnancy, and miscarriages were analyzed, and the risks of possible complications of rheumatic diseases in this category of patients were assessed. Special attention is paid to the issues of planning and preparation for pregnancy. The tactics of managing pregnant women with AFS and the dosage regimen largely depend on the previous medical history (the presence/ absence of non-placental thrombosis, the number of spontaneous abortions, an undeveloped pregnancy, and previous therapy). In this regard, the article identifies clinical groups with different types of therapy.

Keywords: antiphospholipid syndrome, pregnancy, prevention of exacerbations.

Introduction:

Pregnancy significantly affects the mother's immune system: depression of the cellular component of the immune system, increased secretion of immunoglobulins, decreased lymphocyte function due to the expression of special PSP (pregnancy-specific proteins) proteins. All these transformations are aimed at fetal survival. The processes of changing the cytokine profile of type 2 T helper cells are dominant in maintaining "immunotolerance" during pregnancy and may have consequences for various autoimmune diseases. There are a number of phenomena that can be used to see the effect of rheumatic pathology on pregnancy and vice versa. These processes are multidirectional: on the one hand, both the onset of systemic autoimmune disease (SAA) and an exacerbation of existing pathology (for example, an outbreak of lupus nephritis) may occur, on the other hand, numerous cases of pregnancy-induced remission of rheumatoid arthritis have been described. In addition, autoimmunization processes with the formation of antiphospholipid antibodies can lead to an increased risk of miscarriage, fetal death, and preeclampsia. Pregnancy causes many physiological changes in the mother's body in addition to the dysfunction of the immune system. Thus, there is a significant increase in the volume of circulating blood (up to 40-45%), which can worsen the course of kidney or cardiovascular diseases. The glomerular filtration rate increases by about 50% during normal pregnancy, so a patient with previous proteinuria will almost certainly have a slight increase in the amount of protein in the urine. As a result of changes in the coagulation link of hemostasis, platelet activity, fibrinolysis, venous stasis, vascular compression by the pregnant uterus, and forced bed rest, the likelihood of thrombotic complications increases. There is swelling and bleeding of the gums, gastro-esophageal reflux, significant bone loss due to pregnancy, lactation, as well as the possible use of glucocorticosteroids. Thus, even a normal pregnancy can worsen the course of CVD. Physiological or pathological changes, including pregnancy-induced hypertension, can also mimic the activity of SAZ, which presents certain difficulties in making a differential diagnosis. For example, redness or hyperpigmentation of the face may mimic a centrifugal zygomatic rash of the "butterfly" type. Palmar erythema in pregnant women may look like cutaneous vasculitis. Physiological leukocytosis, anemia, and low platelet count due to hemodilution, common in pregnant women, can be perceived as hematological manifestations of SAZ.

On the other hand, increased fibrinogen levels, anemia, and accelerated erythrocyte sedimentation rate during pregnancy cannot be objective markers of systemic autoimmune disease activity. Many women complain of arthralgia, muscle and bone pain, especially during their first pregnancy. It is important to note that hypertension, proteinuria, renal failure and edema associated with gestosis can mimic various diseases or their exacerbation, including lupus nephritis, acute scleroderma nephropathy, recurrence of vasculitis, primary glomerulonephritis. HELLP syndrome is a variant of preeclampsia characterized by low platelet counts, elevated liver enzymes, hemolysis, and abdominal pain, and is often mistaken for systemic manifestations of SLE or exacerbation of systemic vasculitis. Finally, eclampsia, which includes convulsive syndrome or impaired cerebral circulation, may be the basis for suspicion in pregnant women of neurolupus or neurovasculitis.

Antiphospholipid syndrome In the early 1950s, antiphospholipid syndrome (APS) was described as a variant of systemic lupus erythematosus or lupus-like syndrome. However, it was soon established that the association between hyperproduction of antiphospholipid antibodies and thrombotic disorders is observed in the absence of reliable clinical and serological signs of SLE or any other leading disease. The term "primary antiphospholipid syndrome" was proposed to define this new nosological form.

Recommendations for the management of pregnant women with APS The timely establishment of obstetric APS treatment dates back to 1980-1985, when patients with ACLA, HAC, and obstetric failures began receiving glucocorticosteroids (prednisone) and aspirin in small doses. Moreover, the dose of GCS was gradually increased until the HAC or other markers of AFS reached acceptable levels. In the 1990s, studies showed that low-dose heparin combined with low-dose aspirin proved to be as effective as corticosteroids, but with much fewer side effects. Currently, the combination of antiplatelet drugs and direct anticoagulants is standard: the dosage of low-molecular-weight heparin is usually 40 mg of enoxaparin daily, some specialists use 30 mg twice a day, the dose for unfractionated heparin is usually 5000 units twice a day. Studies show that a combination of low-dose heparin and low-dose aspirin is more effective than aspirin monotherapy, with a success rate of about 75% versus 40%. There are no fundamental differences between low and high doses of anticoagulants, as well as between the use of unfractionated and low-molecular-weight heparin. This type of therapy belongs to the first line and is the most effective in terms of preventing pregnancy loss in the early stages. Second-line therapy includes the use of intravenous human immunoglobulin (IVIG). Some experts recommend increasing heparin to general therapeutic doses at this stage. In the only controlled trial using IVIG, there was no significant improvement in pregnancy outcomes. However, there are a significant number of uncontrolled studies, published clinical cases with a brilliant effect when combined with HCV, low-dose aspirin and low molecular weight heparins (NMH). With a further increase in the level of ACLA, plasmapheresis can be successfully used in high blood pressure. The most promising methods of treating APS in the future are complement inhibition, as well as the use of genetically engineered biological therapy. Treatment with medium /high doses of glucocorticosteroids is currently practically not used due to the lack of evidence of their effectiveness and negative effects on the body of both mother and fetus. The use of GCS is justified only if APS develops against the background of some disease (systemic lupus erythematosus, Sjogren's disease, etc.). The use of GCS in these cases is aimed at treating not APS, but the underlying disease. In the postpartum period, anticoagulant therapy should be continued for a period of 6 to 8 weeks, even in patients without a history of thrombosis. The tactics of managing pregnant women with AFS and the dosage regimen largely depend on the previous medical history (the presence/ absence of non-placental thrombosis, the number of spontaneous abortions, and previous therapy).

In this regard, the following subgroups can be distinguished:

1. Patients with only serological markers of AFS (without previous pregnancy, with one episode of unexplained spontaneous abortion before 10 weeks of gestation), without a history of thrombosis. The management tactics of this category of women consists in the use of small doses of acetylsalicylic acid, which is prescribed for the entire period of pregnancy and for 6 months after delivery. If pregnant women have highly positive ACLA (more than 65 UNITS of GPL), it is advisable to prescribe HMG. The risk of developing thrombotic complications is high not only during pregnancy, but also in the

postpartum period (within 6 months. after giving birth). In case of natural delivery, it is advisable to resume treatment of HMG in the postpartum period. In the case of cesarean section, the administration of low-molecular-weight heparins is canceled in 2-3 days and resumed in the postpartum period, followed by a switch to indirect anticoagulants.

2. Patients with APS without a history of non-placental thrombosis and women with serological markers of APS and two or more unexplained spontaneous abortions (up to 10 weeks of gestation) in the anamnesis. The management tactics of this category of pregnant women consists in the combined use of small doses of acetylsalicylic acid (50-150 mg/ day) from conception to delivery and unfractionated heparin (enoxaparin, etc.) or unfractionated heparin (5000-10000 units every 12 hours) from the moment of documented pregnancy until delivery. Treatment with low molecular weight heparins, unfractionated heparin (or warfarin) should be resumed 12 hours after delivery. Long-term heparin therapy in pregnant women can lead to the development of osteoporosis. As a result, all pregnant women receiving heparin therapy must take calcium supplements (1,500 mg/day) and vitamin D3 (at least 1,000 IU/day).

3. Patients with APS and a history of non-placental thrombosis (who received warfarin before pregnancy). It is necessary to cancel warfarin before 6 weeks of pregnancy. Subsequently, the pregnant woman takes acetylsalicylic acid in low doses in combination with unfractionated heparins.

4. If standard therapy is ineffective during the next pregnancy, immunoglobulin i.v. 0.4 g / kg is used for 5 days every month of pregnancy.

Conclusion: All groups and subgroups of pregnant women with AFS should undergo examinations and consult doctors according to the algorithm proposed by us. For proper management and physiological childbirth. During the period of our scientific work, we came to one conclusion: A pregnant woman, if she is at risk, should be constantly monitored for her own benefit. Because APS can behave differently at any time, during the preparation, management and treatment of a pregnant woman, we suggest, along with antiplatelet and anticoagulant therapy, taking an Anti-X factor test at the same time (along with the rest of the proposed tests), in order to avoid bleeding due to the outcome of hypocoaugulation of drugs.

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