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The Problem of Antiphospholipid Syndrome in Obstetric Practice

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Abstract Pregnancy and the postpartum period are characterized by a tendency to hypercoagulability. The pathology of the hemostasis system of congenital or acquired genesis against the background of pregnancy can lead to an unfavorable outcome in the form of non-developing pregnancy and miscarriage, and maternal mortality. In the presence of a burdened obstetric history, examination of the hemostasis system, including tests for the diagnosis of thrombophilia, is mandatory. In this article, 4 clinical cases of patients with hemostasis problems during pregnancy, with confirmed APS and received therapy, are considered.

Keywords Antiphospholipid syndrome, Miscarriage during pregnancy, Therapy regimen, Diagnosis of thrombosis

1. Introduction

Hemostasis is a complex balance system aimed at maintaining the liquid state of blood in the vessels, stopping bleeding in case of injury, and dissolving excessively formed clots.

Often, a standard coagulogram includes one or two indicators routinely performed in the laboratory of district polyclinics - clotting time and prothrombin index (PTI), and more than a dozen indicators in the clinical blood coagulation laboratory of a specialized hematology center.

The diagnostic value of tests changes over time, some indicators of the coagulogram become less significant for diagnosis over the years. For example, plasma tolerance to heparin, fibrinogen B, thrombotest, plasma recalcification test, which were previously widely used, are not very informative and are currently not recommended for use in the diagnostic algorithm.

The problem of diagnosing and correcting coagulation disorders is very relevant in the practice of doctors of all directions, including obstetrician-gynecologists and hematologists.

It is known that pregnancy and the postpartum period are characterized by a tendency to develop hypercoagulability. During physiological pregnancy, according to Momot A.P. et al. the level of fibrinogen can vary from 4.5 to 9.1 g / l, the concentration of D-dimer from 135 to 771 ng / ml, depending on the gestational age [1,2,4]. But, the presence of an initial pathology of the hemostasis system of congenital or acquired genesis against the background of pregnancy can be realized in the form of venous thromboembolism, lead to an unfavorable outcome in the form of non-developing pregnancy and miscarriage, and maternal mortality.

Venous thromboembolism (VTE) can occur at any stage of pregnancy with a frequency of 1-3: 1000, but the postpartum period is the time of greatest risk, especially the first 6 weeks, the relative risk of which increases to 12-15: 1000 [6,12].

Clinical manifestations in pregnancy with VTE include leg pain and edema (usually unilateral), and lower abdominal pain, shortness of breath, chest pain, hemoptysis, and collapse [15].

One of the reasons for the failure of pregnancy outcomes is associated with antiphospholipid syndrome (APS), an autoimmune disease that manifests itself in young women with recurrent thrombosis, recurrent miscarriage, thrombocytopenia, and persistent antiphospholipid antibodies. Even positive results of detecting antiphospholipid antibodies require the exclusion of other causes of thrombosis, especially in the presence of risk factors such as smoking, hyperlipidemia, atherosclerosis, varicose veins, and taking oral contraceptives.

APS can be diagnosed if the patient has a history of clinically confirmed venous or arterial thrombosis of various localization, complications of pregnancy in the form of recurrent miscarriage before the 10th week of gestation, or at least one loss of pregnancy after 10 weeks. Also, this can include premature birth before 35 weeks of gestation, due to severe preeclampsia or intrauterine growth retardation, with a laboratory-positive test for lupus anticoagulant (VA), antibodies to cardiolipin (aCL), antibodies to β2

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glycoprotein two or more times with an interval between research for at least 12 weeks [5-8].

The true prevalence of APS in the Uzbek population is still unknown. The frequency of detection of various aCL and VA - in the blood of healthy people varies from 0 to 14% (on average 1–5%; in a high concentration - less than 0.2%) and increases in the elderly, especially with chronic diseases [3,9,11,13].

Like other autoimmune rheumatic diseases, APS is more common in women than in men (5: 1 ratio), usually developing in middle age (about 35 years). With secondary APS, the ratio of women to men is 7.5: 1, and with primary APS, it is 3.5: 1. Primary and secondary APS are detected with almost the same frequency [10,13].

According to numerous studies [6-11], patients with APS and pregnancy are usually recommended heparin preparations and / or low-dose aspirin to prevent miscarriage. Two trials, however, found no significant improvement in pregnancy outcome in patients treated with low molecular weight heparin plus aspirin compared to those treated with aspirin alone. In one third of pregnant women with APS, the protocols mentioned above, as well as additional therapies, including intravenous immunoglobulins, low-dose prednisolone, or apheresis procedures such as plasmapheresis (exchange) and immunoadsorption are ineffective. However, there are currently no recommendations on the ideal strategy of additional treatment in women with APS in women with a high risk of termination of pregnancy [14].

We present our own clinical observations:

S.G., born in 1980 sent by an obstetrician-gynecologist to a hematologist for a consultation against the background of the 3rd pregnancy at a period of 10 weeks. When applying, she complained of pain and swelling of her right leg. Sent for a consultation with a vascular surgeon, diagnosed with deep vein thrombosis (DVT) of the right leg. From the anamnesis: 1 and 2 pregnancies ended in miscarriages up to the 10th week. The 3rd pregnancy also ended in an involuntary miscarriage at the 11th week. Against the background of therapy with low molecular weight heparin (LMWH) drugs for a month, the DVT clinic was resolved, after 3 months of therapy, drug injections were discontinued. Six months later, the patient showed signs of developing retrombosis, already in the left leg. During the examination, a complete blood count without pathology; coagulogram-normocoagulation; identified APS AT.

Considering three pregnancy losses in the period up to 10-11 weeks, twice episodes of thrombosis and the presence of APS AT, a clinical diagnosis of APS was made. The patient started anticoagulant therapy with POAC (oral anticoagulants). The recommended intake of rivaroxoban 10mg, folic acid preparations.

Against the background of taking these drugs for more than 2 years, the fourth pregnancy began, rivaroxoban was discontinued, LMWH was resumed for the entire period of pregnancy, after childbirth, it is planned to take an indirect anticoagulant - warfarin. Currently, the gestation period is 20-21 weeks.

K.M., 1988 year of birth sent to a hematologist for further examination after undeveloped 1st and 2nd pregnancies at a period of 8 weeks. When examining the KLA without pathology, APS antibodies were absent. From the 12th week of the 3rd pregnancy, she took aspirin in small doses, delivery at 38-39 weeks, natural childbirth. The child is a boy, practically healthy. After 2 years, during the 4th pregnancy, she suffered COVID19 for a period of 20-21 weeks. Blood tests without pathology. In the study of the hemostasis system in the patient, a shortening of the activated partial thromboplastin time (APTT) was determined - 22 seconds (with a norm of up to 38 seconds) and the fibrinogen level reached 6 g / L. Since the PCR infection was confirmed, she has been taking small doses of aspirin. The fetus develops without pathology.

A.R., 1996 year of birth sent to a hematologist on the background of the 4th pregnancy at a period of 6-7 weeks. From the anamnesis - three pregnancies were interrupted at a period of 8-10 weeks due to a non-developing fetus. Family history of vascular episodes is negative. BMI = 31. Blood tests were normal. APS antibodies were slightly increased. Phospholipid antibodies of the lupus type (according to screening and confirmatory tests of the analysis for antiphospholipid antibodies (AFA) of the lupus type: test with diluted Russell's viper venom (dRVVT) in the patient - 45/44 (normal values ≤35); Lupus anticoagulant in the subject - 1.1 (normal ratio ≤1.2.) Considering that the examination was carried out during pregnancy, it was recommended to retest for the presence of APS AT outside of pregnancy. After assessing the risk of VTEC, LMWH therapy in a prophylactic dose was started from 28 weeks. In the postpartum period, LMWH continued for 1 week. The child-girl is healthy.

M.M., born in 1993, turned to a hematologist with a referral from an obstetrician-gynecologist against the background of the 2nd pregnancy, IVF 16-17 weeks. 1 pregnancy terminated at 10-11 weeks. From the 12th week she took aspirin preparations 100mg / s. When examining the KLA - without pathology, in the coagulogram - normocoagulation. APS AT were not detected. Delivery at 38 weeks by cesarean section. The child-boy is healthy.

2. Conclusions

According to modern concepts, the diagnosis of APS requires one of the characteristic clinical signs (thrombosis or miscarriage) and one of the laboratory criteria, which are detected during two consecutive visits of the patient with an interval of 12 weeks of pregnancy. In the first clinical case, there are all the components of the APS diagnosis; in the long term, the patient will take anticoagulants for life, and at the onset of pregnancy, she will receive LMWH.

Having identified the risk factors for the development of VTEC and contraindications to the use of anticoagulants

during pregnancy and the postpartum period, it is possible to determine the time of onset and duration of LMWH administration.

According to Momot A.P. (2020), the assessment of blood tests should be carried out in the pregravid period, then at 7-8, 27-28 and 36-37 weeks of pregnancy. The checklist should include platelet count, APTT, prothrombin time and fibrinogen. Moreover, the levels of fibrinogen and D-dimer grow with the growth of pregnancy and cannot be absolute signs for the appointment of anticoagulants [2].

Excessive examination for insignificant and uninformative indicators burdens patients financially, and leads to an incorrect interpretation of blood counts and, as a consequence, to polypharmacy, when they try to prescribe medicinal indicators to correct each slightly changed indicator. Careful collection of anamnesis of the patient and first-line relatives, laboratory examination will help in choosing therapy tactics against the background of pregnancy and the postpartum period.

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