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DIAGNOSTIC ALGORITHM FOR NON-IMMUNE HYDROPS FETALIS

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✓ ***Resume***

This article presents the results of a survey of 24 pregnant women with non-immune hydrops fetalis. Pregnancy was conducted according to the diagnostic algorithm developed for hydrops fetalis and pregnancy outcomes were analyzed. The etiological factors that led to this disease, the methods of their detection, the results of etiological and symptomatic treatment and the principles of pregnancy management in non-immune hydrops fetalis are analyzed. The data on intrauterine interventions and their results in the examined patients with non-immune hydrops fetalis are presented.

Key words: non-immune hydrops fetalis, paracentesis, thoracocentesis, cordocentesis, amnioreduction.

АЛГОРИТМ ДИАГНОСТИКИ ПРИ НЕИММУННОЙ ВОДЯНКЕ ПЛОДА

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✓ ***Резюме***

В данной статье представлены результаты обследования 24 беременных женщин с неиммунной водянкой плода. Беременность велась по алгоритму диагностики, разработанному для водянки плода, и анализировались исходы беременности. Проанализированы этиологические факторы, приведшие к данному заболеванию, методы их выявления, результаты этиологического и симптоматического лечения и принципы ведения беременности при неиммунной водянки плода. Приведены данные о проведенных внутриутробных вмешательствах и их результатах у исследованных пациенток с неиммунной водянкой плода.

Ключевые слова: неиммунная водянка плода, лапароцентез, торакоцентез, кордоцентез, амниоредукция.

NOIMMUN HOMILA SHISHIDA TASHXISLASH ALGORITMI

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✓ ***Resume***

Ushbu maqolada 24 nafar noimmun homila shishi kuzatilgan homilador ayollardagi tekshiruv natijalari taqdim etilgan. Homila shishi uchun ishlab chiqilgan tashxislash algoritmi bo'yicha homiladorlik olib borilgandagi homiladorlik oqibatlari muhokama qilindi. Ushbu kasallikka olib kelgan etiologik faktorlar, ularni aniqlash usullari, etiologik va simptomatik davolash natijalari va noimmun homila shishi bilan homiladorlikni olib borish tamoyillari tahlil qilindi. Noimmun homila shishi kuzatilgan tekshiriluvchi bemorlarda o'tkazilgan homila ichi amaliyotlari va ularning samaralari haqida ma'lumotlar taqdim etildi.

Kalit so'zlar: noimmun homila shishi, laparosentez, torakosentez, kordosentez, amnioreduksiya.

Relevance

At present, special attention has been paid to the development and improvement of perinatal care throughout the world. Currently, the fetus is accepted as a real patient due to the possibility of intrauterine treatment of severe pathological diseases of the fetus. One of the antenatal diseases requiring such high-tech treatment is non-immune hydrops fetalis.

Hydrops fetalis is a polyetiological disease characterized by a pathologically excessive accumulation of fluid in the serous cavities and soft tissues of the fetus. Hydrops fetalis is the last stage for a number of intrauterine diseases. The prevalence of hydrops is 1 in 1000-14000 births. Usually, no more than 20-30% of newborns survive with this diagnosis. Only in the case of the use of modern medical technologies in the antenatal period and intensive management of children in the neonatal period, this figure reaches 80% [1-5,8,11]. Hydrops fetalis, according to the ICD X revision, is subdivided into: 1) Hydrops fetalis caused by hemolytic disease (immune hydrops - P56) and 2) Hydrops fetalis not associated with hemolytic disease (non-immune hydrops - P83.2). The distinction between immune and non-immune hydrops was first identified in 1943 by Edith Potter. At that time, non-immune hydrops was rare and accounted for less than a quarter of children born with hydrops [3,5,9]. Nowadays, given that the incidence of immune hydrops fetalis has decreased due to the widespread use of prophylaxis of Rh sensitization, and non-immune hydrops fetalis (NHF) has become the dominant form of hydrops fetalis. Among all cases of hydrops fetalis, non-immune hydrops accounts for up to 90% [1,7-9,11]. Its frequency, according to large-scale studies, ranges between 1: 2000-1: 3000 pregnant women [5].

Diagnosing a non-immune hydrops fetalis is not a challenge today. The only and effective way to diagnose a non-immune hydrops fetalis is an ultrasound examination, and the main diagnosis is based on the results of this examination. However, determining the etiology of the disease requires a comprehensive approach. Determining the etiology of non-immune hydrops fetalis allows to predict the manifestation of the disease and its outcome [7,11].

The etiology of non-immune hydrops fetalis is diverse and develops in the early stages of pregnancy mainly due to chromosomal abnormalities, in addition to cardiovascular, lymphatic system pathologies, syndromic pathologies, infections, FFTS, urinary tract abnormalities and many other causes can lead to the development of non-immune hydrops fetalis[6,10].

Previous foreign studies have shown the influence of etiology on the timing of the manifestation of non-immune hydrops fetalis and their consequences: non-immune hydrops fetalis, manifesting before 22 weeks of pregnancy, are associated with a higher risk of chromosomal abnormalities and adverse outcomes, and the disease after 22 weeks - more favorable outcomes [8-10].

Much attention to the problem of the etiology of non-immune hydrops fetalis is due to the fact that it is a decisive factor in the choice of pregnancy management tactics, intrauterine treatment options and prospects. Thus, according to the Canadian Society of Obstetricians and Gynecologists (SOGC), with a normal fetal karyotype, a gestation period of more than 18 weeks, fetal therapy and/or surgical interventions lead to positive results [1,3,8]. The type of intrauterine intervention is determined depending on the etiology, clinical manifestations and concomitant pathology of non-immune hydrops fetalis.

The aim of this study is to develop an algorithm for the diagnosis and management of pregnancy in non-immune hydrops fetalis.

Materials and methods

24 patients with a diagnosis of non-immune hydrops fetalis who applied to the RSSPMCOG institution were examined. Patients underwent Doppler ultrasound, karyotyping, PCR and IFA studies for infections, diagnostic and therapeutic cordocentesis, amniocentesis, amnioreduction, paracentesis, thoracocentesis, nephroamniotic shunting and conservative treatment.

All patients participating in the study underwent an ultrasound examination and assessed the following parameters: the presence of structural pathology in the fetus, the number of fluid-filled serous cavities, the volume of fluid collected, the presence and degree of pulmonary hypoplasia, cardiac compression, soft tissue edema, thickness, spread and the amount of amniotic fluid and the thickness of the placenta. Dopplerometry assessed the peak systolic blood flow velocity in the middle cerebral artery, which was considered a sign of severe anemia, if the value was above 1.5 MOM. After 20 weeks of

gestation, fetal echocardiography was performed to assess functional and structural pathologies of the heart, valves and magistral vessels, the presence and volume of fluid in the pericardial cavity, and a number of parameters indicating the functional state of the heart.

From the moment of hospitalization of the pregnant woman to the hospital until the moment of delivery, the condition of the fetus was regularly monitored using ultrasound, dopplerometry and cardiotocography.

Result and discussion

Of the 24 examined patients, 22 were singletons. The age of the woman is from 19 to 42 years. The number of primiparous was 8 and the number of multiparous was 16. The median gestational age for which non-immune hydrops fetalis was first detected on ultrasound was 22 weeks, with a lower and upper limit of 10–35 weeks. There were 6 patients diagnosed with non-immune hydrops fetalis before 20 weeks, and 18 patients with a diagnosis of non-immune hydrops fetalis from 20 weeks to 35 weeks. In our studies, in 15 cases, fluid was collected in only one serous cavity.

Of the 24 examined patients with non-immune hydrops fetalis, 5 patients were found to have an infection. Parvovirus B19 was detected in 1 case, CMV + Gordnerella - in 2 patients, HSV - in 1 patient, SARS-CoV-2 - in 1 case. Heart pathology was noted in 4 cases, tachyarrhythmia - in 3 cases, atrial flutter - in 1 case. Congenital cystic adenomatoid malformation (CCAM) was detected in 2 patients. In 2 patients, as a result of FTTS, non-immune hydrops fetalis was developed. Chromosomal abnormalities were observed in 3 patients, syndromic pathologies in 2 patients. Pathology of the lymphatic system was detected in 1 patient, in 5 cases the cause of non-immune hydrops fetalis was not established.

Treatment of non-immune hydrops fetalis includes etiotropic treatment aimed at eliminating the underlying etiology of the disease, and symptomatic treatment aimed at relieving symptoms, reducing complications and prolonging pregnancy.

Etiotropic treatment includes antiarrhythmic drugs used for fetal arrhythmias, cardiac glycosides used for heart failure, intrauterine blood transfusion for fetal anemia, surgical correction of feto-fetal transfusion syndrome.

Measures to eliminate ascites and hydrothorax include multiple centesis or shunting procedures to help drain fluid from the serous cavities. The literature describes cases of installing a thoracoamniotic shunt at 22 weeks of gestation, which made it possible to prolong the pregnancy.

In cases where permanent shunting is not possible, thoracocentesis or paracentesis is performed to prevent pulmonary dysplasia. In cases where polyhydramnios is involved, amnioreduction is the method of choice.

The expediency of the practice is decided at a consultation with the participation of an obstetrician-gynecologist, an ultrasound diagnostician, a geneticist, and a pediatric surgeon.

In our study, paracentesis was performed in 6 patients, in 1 patient the operation was repeated 5 times. In all cases, almost complete evacuation of the liquid was achieved. The volume of the extracted liquid ranged from 50 ml to 500 ml. There were no cases of accumulation of fluid in the abdominal cavity after childbirth, repeated paracentesis was not performed. Antenatal fetal death was observed in 2 out of 6 patients due to syndromic pathology and severe fetal heart failure. Preterm delivery occurred in 2 patients (34-35 weeks). In the remaining 2 patients, the pregnancy was prolonged and a live baby was born. The children of 4 patients are now living healthy lives.

Of the 24 patients, thoracocentesis was performed in 2 patients and in both patients the operation was successful, but antenatal fetal death occurred due to multiple fetal malformations. Amnioreduction was performed in 17 patients with polyhydramnios. Four patients received intrauterine infusion therapy, which includes transplacental antiarrhythmic, antibacterial and immunoglobulin treatments. Conservative treatment was carried out in 18 patients, depending on the etiology. Of these, 4 patients received antiarrhythmic therapy, and 10 fetuses with symptoms of heart failure received treatment with cardiac glycosides. Immunoglobulin therapy was carried out in 6 patients who developed non-immune hydrops fetalis against the background of infection, and in 5 cases the treatment was completed successfully, the symptoms of non-immune hydrops fetalis were eliminated, the children were born healthy.

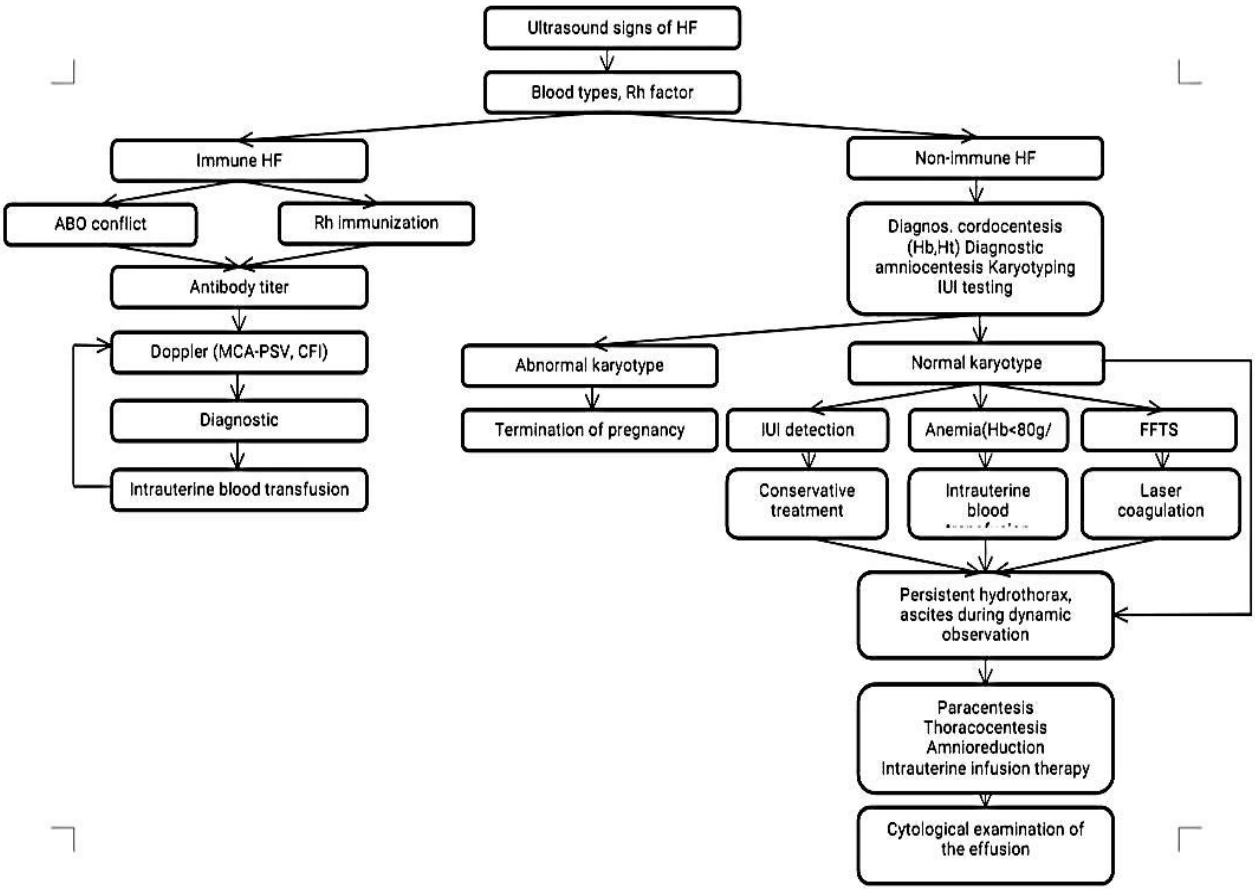
In 5 cases, from 12 to 20 weeks of gestation, women voluntarily terminated the pregnancy. In 3 out of 5 cases, non-immune hydrops fetalis was due to chromosomal abnormalities, in 2 cases - syndromic pathologies.

Of the 24 patients, 4 had term delivery, 4 had antenatal fetal death, 11 had preterm birth, of which 5 had early neonatal mortality, and 3 had late neonatal mortality. The other 3 are healthy.

As for the algorithm for managing pregnancy in non-immune hydrops fetalis, it is based on the identification of an etiological factor. If non-immune hydrops fetalis are detected in the early stages of pregnancy, the pregnant woman should be informed about the condition of the fetus and its adverse

Figure1. Diagnostic algorithm for Hydrops Fetalis

consequences, especially when chromosomal pathology is detected, the possibility of abortion for medical reasons (Figure1).



Testing for intrauterine infections, including parvovirus, herpes simplex virus, CMV, and Epstein-Barr virus, is one of the necessary tests. When an acute phase of the disease is detected, etiotropic treatment is indicated.

With cordocentesis, the hematocrit and the amount of hemoglobin in the fetal blood are determined. In addition, fetal blood is analyzed for the presence of proinflammatory mediators, procalcitonin, IL-6, C reactive protein, and TORCH infections. Anemia is an indication for intrauterine blood transfusion.

With a normal karyotype, when no signs of an acute infection are detected, and with a normal blood composition, dynamic monitoring is carried out. When persistent or increasing fetal hydrothorax or ascites is observed, as well as in cases where conservative treatment is ineffective, thoracocentesis and / or fetal paracentesis are used to prevent the development of severe pulmonary hypoplasia and other complications. Fluids from the serous cavity are examined for the presence of inflammatory mediators and TORCH infection. Nephroamniotic or vesico-amniotic shunting is performed with stage 3-4 hydronephrosis with hydrops fetalis, that developed against the background of urinary tract pathology. In cases of polyhydramnios, amnioreduction and fluid analysis are performed.

Conclusion

With the development of methods for the prevention and treatment of immune hydrops of the fetus with Rh-sensitization, the prevalence of non-immune hydrops of the fetus is increasing. Although the vital prognosis of the fetus is unfavorable, the algorithm developed by us for managing pregnancy with non-immune fetal hydrops allows us to timely assess the prognosis for the fetus and determine the possibilities and tactics of etiotropic and symptomatic treatment. Early diagnosis of non-immune fetal dropsy is of great importance, as it allows to identify the etiological factor as soon as possible after diagnosis, which expands the possibilities of treatment.

Ultrasound is the most optimal diagnostic tool for antenatal diagnosis of non-immune fetal hydrops with all Doppler studies. Of great importance for the diagnosis of the disease are a detailed anamnestic history and examination of the mother. In addition, serological testing for perinatal infections in the fetus and maternal antibodies may help determine the etiology of non-immune fetal hydrops. For children who have not received antenatal diagnosis and treatment, the outcome is considered very dangerous and unfavorable, with an increase in perinatal morbidity and mortality.

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